Author's response to reviews

Title: Prevalence of cognitive impairment in individuals aged over 65 in an urban area. The importance of certain personal factors. The DERIVA study.

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Author's response to reviews: see over
Dear Editor:

Following the reviewers suggestions, we enclose a new version of our manuscript entitled: “Prevalence of cognitive impairment in individuals aged over 65 in an urban area. The importance of certain personal factors. The DERIVA study”, Re: 9557193555848233, together with our replies to all the issues raised.

Authors’ replies:

GENERAL COMMENT:

Following the comments and suggestions of the reviewer, we have made some changes to the document. Below we present these corrections, in response to each of the questions put to us. All the changes made in the manuscript (text, tables and figures) are underlined. It has been totally reviewed and some minor changes have been done on the main text, the bibliography (references 4 and 5 were completed; reference; 35 was added) and on the title.

1. Is the question posed by the authors well defined?

Yes, the study seeks to determine the prevalence of cognitive impairment and dementia in an urban population in Spain. In addition it represents a case-control study of potential risk factors for cognitive impairment.

The definition of the question as stated by the reviewer clearly coincides with the main objective of this study. Therefore, wedid not consider it necessary to modify the first part of the manuscript.

2. Are the methods appropriate and well described? Not quite.

2.1. The selection of participants should be described in more detail, including an explanation what “healthcare areas” are and how stratification by these areas was done.

Following the reviewer’s recommendation we have added the following underlined paragraphs, changing the order of the “participants” and “methods” sections on pages 3 and 4 (Study design, Setting, Participants and Data sources and Study size), with the aim of setting out more clearly how we selected the sample. The new text reads as follows:

Study design: An observational, descriptive, cross-sectional population study.
Setting: The reference population was that of the city of Salamanca, with 172,375 inhabitants, of which 19.74% (34,020) were aged over 65. It includes 10 healthcare areas, each with a population of between 9,000 and 26,000 inhabitants.

Participants: We selected all those aged over 65 on 1 January 2009 and living in the city of Salamanca (urban setting). A door-to-door population-based survey was carried out during the months of May to November 2009. Two weeks before the interviews, letters were sent to the selected individuals, explaining the purpose of the study and requesting their cooperation. Confidentiality of data was guaranteed. Ten days after sending the letters, a telephone call was made to arrange a home interview.

The following exclusion criteria were applied: no changes

Ethical aspects: no changes

Training of the evaluators: The principal researcher coordinated the entire process. The evaluators were four psychologists trained by one of the researchers (SMS) to carry out the interview with the programmed questionnaires. A manual was drafted, describing the appointment procedure and application of the interviews, and was reviewed with the interviewers over two sessions. We also used two recorded home interviews in the training sessions. During the study, communication was permanently maintained for resolving any doubts or dealing with incidents in relation to the questionnaires.

Data sources: The sample was taken from the Castilla y León Regional Health Service lists, which cover 99.5% of the population. The lists included both community dwellers and institutionalized elders.

Study size: Accepting an alpha risk of 0.05 and a beta risk of 0.20, estimating a CI prevalence of about 16% [12], with an error of 4%, and considering the current population aged over 65, a total of 320 patients was required. Assuming a loss rate of up to 50% due to non-responses, as observed in similar studies, the calculated sample size was 480 individuals. In the secondary analysis of cases and controls, with a 327 participants sample, the statistical power was of 79.4% to detect an Odds Ratio of 2.5 with a confidence level of 95% (Epidat 4.0).

We carried out a stratified random sampling by health districts. In order to reach the required sample size, we made a replacement for lost participants. The sample size of each health district was proportional to its population over 65 years. In a first stage, 260 interviews were carried out, accounting for 80% of the required sample. Two months later, in a second stage, we replaced the losses within each health district and 67 more people were interviewed.

2.2. The operationalisation of CIND should be provided: how were "low scores" defined, and was a low score on one of the tests sufficient? Was there a prioritisation among tests, given the differences in sensitivity? Similarly, the definition of dementia should be justified. Why did the authors assume that impairment on two areas of activities of daily living is worse than impairment on two, assuming that these areas are highly intercorrelated?

In order to identify how many cognitive areas were affected, we took into account not only the total scores, but also the whole set of explored areas using the alltests
applied. To reflect this more clearly, we have added in the document all the areas we explored by each test. Decisive scores for the classification of “normal” —in range—or “cognitive impairment” were obtained with the MMSE and total score on the 7 Minute Screen. For this reason, we added the values of cut-off scores for every test. Consequently, paragraph 2 on page 5 now reads:

The Katz Index of Independence in Activities of Daily Living (Katz ADL) was applied to assess functional status as a measure of patient ability to perform activities of daily living (ADLs) independently [14]. This test provides information on dependence or independence, not only in terms of the number of areas, but also identifying the specific areas. The information obtained is of a qualitative and descriptive nature, and does not provide a total score on the person’s functional state.

At the beginning of the interview, neuropsychological assessment of patient cognitive status was carried out using a brief neuropsychological test battery including the following: Mini-Mental State Examination (MMSE) [15] in its validated Spanish version [16] to evaluate general cognitive state, with the possibility of assessing cognitive functions separately; the 7 Minute Screen [17] in its validated Spanish version [18] also to evaluate general cognitive state, as well as temporal orientation, memory, constructive praxies and language, separately; the Benton temporal orientation test [19] to evaluate temporal orientation; the Enhanced cued recall test [20] to evaluate episodic memory; the Clock drawing test [21] to evaluate constructive praxies; and the Categorical fluency task [22] to evaluate language. The cut-off points for cognitive impairment established for each test are as follows: MMSE<24; 7MS≤percentile 20; Benton temporal orientation test ≤102; Enhanced cued recall test ≤12; Clock drawing test <3; Verbal fluency ≤10.

Moreover, in the Discussion (Paragraph 3; p.8) we have added:

In our study we took into account the most up-to-date diagnostic criteria [4,5], according to which it is considered that CIND can involve alteration in various higher cognitive functions, and not only in memory. Therefore, we should have obtained higher figures than if we had considered the criteria of Petersen et al. (Petersen et al., 1999). On the other hand, however, the Katz ADL Index is less sensitive for assessing ADLs than for assessing more complex activities.

2.3. How were activities of daily living assessed - by informant interviews? Who were the informants (some of the patients had spouses, some did not - could this be a source of bias)?

To make the text easier to understand, we have made a series of changes in the “Measurements” section (pag. 6) adding the following:

We considered as reliable informants, in order of preference, a family member living in the same house as the individual (spouse, son/daughter, sibling); a person responsible for the care of the individual; someone living in the same house but not a family member; or a relative of the person not living in the same house. At the end of the interview the interviewers drafted a report on the quality of the
information collected and on the social and health conditions of the person interviewed.

Furthermore, in the Discussion we have added, on p. 9 (para. 1) the following reference found in the review of the ADAMS study results (Robert S. Wilson, 2011):

It should also be borne in mind that when a report is requested from an informant about the person’s functional limitations, the prevalence is substantially lower (Robert S. Wilson, 2011).

Regarding the sections about the definition of Cognitive Impairment-No Dementia (CIND) and Dementia, the text now reads as follows:

Classified as cognitive impairment - no dementia (CIND): CIND was defined as (1) mild cognitive or functional impairment reported by the participant or informant that did not meet criteria for dementia; or (2) performance on neuropsychological or functional measures that was both below expectations and ≥0.5 standard deviations below published norms on any test (32).

Classified as dementia: A diagnosis of dementia was made based on the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) criteria: the participant must present the development of multiple cognitive deficits including memory impairment and impairment in at least one other cognitive domain representing a decline from the previous level of functioning and of sufficient severity to cause impairment in function [4, 5]. At a functional level, the person must present dependence in at least two functional areas, leading to interference in basic activities of daily living. Alterations at both the cognitive and functional levels were indicated by low performance and scores below the cut-off points in the neuropsychological and functional tests. As regards functional state, the person must present a minimum level of alteration in at least two functional areas [43]. All of this must be accompanied by concern on the part of the participants about a change at a cognitive level compared to his or her previous state [4].

2.4 Was the sample size large enough for a case-control study and how was it justified?

In response to this question we have added, in the section “Study size”, the following paragraph (page 4):

With the sample of 327 participants, in the secondary analysis of cases and controls, the statistical power is of 79.4% to detect an Odds Ratio of 2.5 with a confidence level of 95% (Epidat 4.0)

3. Are the data sound?
The authors should provide an explanation why the prevalence of CIND was three times higher than the prevalence of dementia, which appears to be out of proportion.
3.1-Following the comments and suggestions by the reviewer, and in order to aid understanding of the data and discussion, we have modified the Discussion, adding the following text on page 9:

**Recent publications suggest that the number of individuals with CIND in the United States is about 70% higher than the number with dementia. In the 71- to 79-year-old age group, 16% had CIND, whereas an additional 5% had dementia. A similar proportion was found in the recent Mexican Health and Aging Study (Mejia-Arango & Gutiérrez, 2011), though the prevalence figures are slightly higher: 6.1% for CIND as against 28.7% for dementia.**

3.2.- And on p. 12 (limitations):

A further limitation of the study is that since the evaluations were carried out by four different psychologists, inter-observer reliability may be affected. However, each evaluation was followed by an appraisal of the interview with a view to test correction and the reduction of possible bias.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes

Despite the favorable opinion of the reviewer, and taking into account all the recommendations, we have adapted the Methods section and the STROBE Statement, modifying some of the subtitles as seen above (in 2.1).

5. Are the discussion and conclusions well balanced and adequately supported by the data? See above comments

6. Are limitations of the work clearly stated? Some additional sources of bias should be mentioned.

We have made some changes in the “limitations” paragraph, in accordance with the suggestions made by the reviewer, as referred to in point 3.2

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes

8. Do the title and abstract accurately convey what has been found? Yes

9. Is the writing acceptable? Yes
Level of interest: An article of limited interest

Following the suggestions and comments from the reviewer Mr. Kurz, we have made a series of changes to the text. The publication of results from the Mexican Health and Aging Study (Mejia-Arango & Gutiérrez, 2011) add interest to our data, given the fact that they also contribute information simultaneously on CIND and Dementia, and stress the important role of specifying the assessment of ADLs. With its new structure, we believe the manuscript to be clearer and easier to understand, thus considerably increasing the interest of the data and of the article as a whole.