Reviewer's report

Title: A Population-based study of dementia in the oldest old: the Monzino 80-plus Study Design, methodological challenges, and population characteristics

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Reviewer: Ananya Roy

Reviewer's report:

General comments

This is an important area of investigation and this article has the potential to advance our understanding of cognition among a relatively understudied general population. The study has been well designed with indepth and varied assessment of cognitive and behavioral assessment. However, this article is descriptive and does not address a clearly outlined question.

The methods section is detailed, with pertinent information on validity of assessment tools and quality control. It can be improved for clarity and needs to be made more concise.

The major limitation of this study is the handling of the data. Also the statistical analysis needs further refinement to confirm the correlations presented in the paper and later discuss them.

- Major Compulsory Revisions

Methods

1) Study design, para 6: “since dementia has been associated with shorter survival…… at least six months after the last interview”

The reasoning behind estimation of mental status of the participants who died before the interview is not clear. In fact it seems that this may actually bias any assessment of cognitive function among the living elderly, by skewing the distribution.

Also given that the overall design of the study is prospective such retrospective assessments would muddy the study design as this is retrospective assessment of mental status after the death has happened.

Please reconsider this.

2) Study design, para 6: “modifications which arose…… were not taken into consideration”

This is not clear. If it means that cognitive changes associated with entering the
last stages of life, ailing health etc, were not taken into consideration, then this
has the pit fall of leading to immense recall bias and misclassification of cognitive
and behavioral function, as it would be hard to determine which aspects of
behavior and mental ability were due to aging and those due to illness
preceeding death. This could either bias any association between cognitive
function and risk of death away from the null or over correct and bias it strongly
towards the null, which ever direction, it would be impossible to determine the
true relationship between cognitive ability and risk of death. Instead limiting the
assessment to those who are alive, would give a robust estimate of risk, with less
chance of misclassification.

3)Methods, Measurements, Cognitive performance and competence,

It needs to be clear where proxy measures were taken and where the subjects
themselves were assessed/ or answered questions. These would need o be traeted differently, as the patterns of recall bias would be different among the two
groups. Also information gathered from GP's or from institution documents can
not be lumped with that gathered from family members, as assessment of family
members is purely dependent on their experience wit only their loved one, where
frequency reported by institutions or GP’s is tempered by experience of dealing
with large numbers of patients. This can introduce systematic bias, as those with
higher levels of disability would be institutionalized.

4)Methods, statistical analysis

The data collected in this study has the depth and breadth to illuminate a large
number of questions. Statistical analysis is usually guided by questions and
hypotheses. The fact that there is no clearly defined question/s causes confusion
in understanding the results and discussion.

From the results it seems that emphasis is to provide:
a) a description of the population in terms of demographic information, medical
history and life style and socio economic status.
b) Describe the neurocognitive and neurobehavioral profile of the population
c) explore the relationships between neurocognitive and neurobehavioral status
and age
d) Compare the profile of deceased and alive participants as well as those with
MMSE vs. those with the c-MMSE

It would be best to clearly out line these and then describe the statistical methods
used to address each.

The statistical analysis presented here is appropriate for simple descriptive
purposes ( a and b). It would be important to explore the distribution of the
cognitive and behavioral assessments ( normal/ skewed). It seems from the
comparison of the mean and the medians presented that they are skewed.

This means that later utilization of the Pearson correlation coefficient is not
appropriate, spearman rank correlation coefficient should be used.

The later analyses (c &d) (correlation coefficients and bivariate ANOVA or Chi square tests) are only correlational and susceptible to bias due to confounding, by socio economic status, social activity, gender, education, clinical conditions etc. It would be important to carry out regression analysis, with appropriate selection of confounders and present these in the results.

5) Discussion

a) The discussion of the results need to be contextualized with existing literature. For example, How do the scores of cognitive ability in this population compare to those in other studies/ populations?

b) Limitations of the study need to be elaborated.

c) “Failing to consider the deceased or untested results in bias”

The arguments outlined in this has problems.

It is to be expected that people with and with out MMSE scores would have different levels of disability, as that is why the subjects were unable to carry out the MMSE to begin with. This limits the population that can be studied using the MMSE, but does not bias any association, just limits the generalizability of the study.

This is not the case with the observed behaviors and the informant survey information and thus is an advantage of those tools of assessment as has been pointed out by the authors. These arguments should also be supported with by appropriate references.

“Subjects alive and with out MMSE…..behavioral profile than those with.”

With out correcting for medical conditions any association between institutionalization, age and mental status would be confounded. As people with severe medical disability have a higher probability of dementia and they have a higher probability of being institutionalized. Thus with out correcting for medical conditions no association between institutionalization and mental status can be parsed out.

- Minor Essential Revisions

1) Methods

The study design of this particular article is cross-sectional with collection of covariate information and cognitive assessment being carried out at one time point. It is not clear whether the study is to be carried forward in time with further follow up visits making it prospective. Use of the term “prospective” causes confusion.

2) Results

Given that the title of the article is “A population based study of dementia in the
oldest old” it would be important to report the prevalence to diagnosed dementia in this population. Also, the methods describe the procedure for diagnosis, so the reader does look for this in the article. Also then this would need to be discussed later.

- Discretionary Revisions

Methods, Measurements, Cognitive performance and competence,
Para 3:
“MMSE showed a very high correlation coefficient with both SBI-SI…..[0.87 X SBI-SI]

How much of the variation in MMSE is explained by the substitute measures? A strong correlation may not be sufficient to estimate another measure as different aspects are measured by the different tests. The BIMC does not measure any function dependent on visual or manual ability and thus would differ from the whole MMSE. It would be interesting to see how accurately the formula provided here tracks the assessed MMSE in this sub-population that may have all the measures (the BIMC, SBI-SI and MMSE), providing an empirical assessment of this method.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests