Reviewer's report

Title: Informant-Reported Cognitive Symptoms That Predict Amnestic Mild Cognitive Impairment

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Reviewer: Eleni Aretouli

Reviewer's report:

The authors of this manuscript report on the utility of the Alzheimer’s Questionnaire (AQ) to distinguish individuals with amnestic mild cognitive impairment (aMCI) from cognitively normal persons. The authors argue that 4 cognitive symptoms as reported by an informant (and in response to 4 questions of the AQ questionnaire) can predict whether an individual would be characterized as cognitively normal or aMCI if undergone a detailed assessment. The idea of identifying persons at risk for dementia (i.e., aMCI) using very brief screening procedures and minimizing cost and resources is definitely appealing. However, the present study, although well-written in general, has some major flaws, described in detail below.

Major compulsory revisions:

My major concerns are basically methodological.

1. First, it is very important to this reviewer that a more detailed description regarding the diagnostic process for aMCI is provided. Since there is no general consensus on how the Petersen criteria should be implemented, the authors are requested to specify in detail how the Petersen criteria were implemented in their study. The authors mention that results of neuropsychological tests were used as part of the diagnostic process. Which tests were included in the neuropsychological battery? Was the AQ questionnaire taken into consideration when the clinician made the diagnosis? If so, then it’s not surprising that items from the AQ questionnaire are predictive of the group membership (whether aMCI or NC).

2. Similarly, what were the exact criteria to characterize a person as CN? “Having no demonstrable cognitively-based limitations of activities of daily living” may exclude the diagnosis of dementia but this does not mean that these persons could not be characterized as MCI. Once again the authors are requested to describe in detail what were the specific procedures used by the neurologist, psychiatrist and neuropsychologist to define someone as CN.

Statistical analysis:

3. The authors found that the responses on certain items of the AQ questionnaire statistically distinguish the two groups of interest and also predict group membership. My major concern is what is the utility of these findings on the individual level.
As can be seen from table 2, 14 out of 47 persons (approximately 30%) would be misclassified as CN based on their informant's response to item no. 3; more than half aMCI would be misclassified as NC according to their informant's responses on the questions regarding knowing the date or ability to manage finances etc. The authors argue that the AQ contributes to the accurate identification of those in need for further assessment. However, based on the individual responses of informants to those 4 items most aMCI persons would not be identified. Also, if the combination of these 4 items is what predicts group membership, is there a mathematical equation (resulting from the regression analysis) that a clinician can use to better identify aMCI based on the responses on the four items of this questionnaire? It is not clear to this reader how clinicians can incorporate these findings into their daily practice, so they can better identify persons with possible MCI.

In summary, I have no doubt that the question this study is addressing is important. However, in addition to the lack of important information concerning the methodology of this study, I am not convinced that the findings in their current form justify why these results are publishable.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests