Reviewer's report

Title: A new approach for exploring comorbidity in dementia: A cross-sectional study of primary care patients

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Reviewer: Jesus de Pedro-Cuesta

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The study consists of a cross sectional combined approach using (1) logistic models of the associations of dementia diagnosis with a number of other diagnoses in primary care and (2) factor analysis applied within the pool of diagnoses collected in patients diagnosed with dementia. The background is a primary care population served by a number of primary care centres where diagnoses are systematically computer-stored and patients identified by personal cards. The public nature of the health care system and high access of citizens, as well as the one-year observation period guaranteed selection bias is reduced. The study with logistic models currently constituted a frequent approach. The study using factor analysis is based an important preceding study of the same group (Prados-Torres et al PLOS One 2012) which replicates preceding approaches with similar methodology and application field (Schäffer et al PLOS One 2010).

The study unveils a dozen of statistically significant, moderate or low in magnitude, associations, present in men and women and identified three factors in men and women (1 Cascular, 2 Neurodegenerative and cerebrovascular, 3 frequently musculoskeletal), and one more (depression and behavioural) in women, already described for the whole population in the above mentioned Prados-Torres et al paper.

Given the current discussion about shared nature of Type 2 diabetes, and neurodegenerative and arteriosclerotic disorders associated with misfolded protein deposits, the study purpose (latest paragraph introduction section) appears to be quite opportune despite authors appear to neglect such key etiologic and patho-physiologic crossroad.

Methods are clear and straightforward.

MAJOR COMPULSORY REVISION

I find that there two interrelated aspects described below, which require a clear positioning from the authors.

First, the authors indicate at introduction end that epidemiological knowledge on comorbidities associated with dementia and the presence of patterns is scarce if non existent. However at discussion they mention studies by Zuliani et al, Newcorner et al, Sanderson et al, Marengoni et al, Schäfer et al, approaching the
simultaneous presence of chronic ailments and dementia. I find such assertions contradictory and not compatible with the title where a NEW APPROACH is announced. I suggest authors recognize such prior work at the introduction and discuss the present study results instead of merely listing results of prior work.

Second. The epidemiologic study of comorbidities of an index diagnosis (dementia in this case) is complex since, as Ording and Sørensen recently indicated, concepts such as morbidity, comorbidity, and complications have been confusing, and some of them are used interchangeably. Furthermore, the different potential approaches (cross-sectional, lifecourse) and reasons for methodologic choices have to be made explicit not only in methods but also in discussing results. For instance, Benito-Leon et al Neurology 2006, observed an association of essential tremors with dementia in a prevalence study and Bermejo-Pareja F et al Mov Dis 2007 show a high incidence of dementia in a cohort of patients with essential tremor. I suggest authors focus at the introduction their main interest and state-of-art in studying comorbidity in dementia and define alternative potential approaches. I guess the cross-sectional one is one of them; perhaps the most immediate to provide a perspective to built a longitudinal and more specific approaches.

Third. The DISCUSSION section requires structure and elimination of speculative recommendations.

MINOR ESSENTIAL REVISIONS

INTRODUCTION first paragraph. “its prevalence has increased continuously over the past decades” constitutes a misleading statement. In recent door-to-door studies prevalence of dementia among a Swedish population (Qiu C, von Strauss E, Bäckman L, Winblad B, Fratiglioni L. Neurology. 2013) remained stable (with longer duration of disease an likely decreasing incidence – as shown at the Rotterdam cohort). Changes in crude prevalence due to aging populations is a different issue or should be specified. The World Alzheimer Report is quoted using a reference (Phelan et al JAMA 2012) on high increase of hospital use and not the original one.

INTRODUCTION frist paragraph. Phelan at el JAMA 2012 a paper on a high OR 1.45 hospital admission is used to quote a statement of the fraction of health care costs attributed to the elderly population. A different data source should be provided.

RESULTS first paragraph. Dementia is referred to “12.34% had dementia as the only disease”. Since at introduction authors properly state that dementia “is a syndrome”, perhaps the use of a different term “coded diagnosis” or “diagnosis” at RESULTS may be preferred “.

Negative associations are not reported. Were they found in logistic regression?. Those with neoplasms would perhaps be expected. A more complete report of results in table 3 including negative associations would be needed. Competing risks and the role of survival bias may have to be discussed.
DISCUSSION

First paragraph. The discussion of the association of dementia (assuming it mainly refers to Alzheimer’s Disease) with Type II Diabetes requires inclusion of recent knowledge on shared molecular mechanisms (see as an example Götz J et al Frontiers in AGING NEUROSCIENCE, 2013).

First and second paragraphs. First page is devoted to discuss associations with hypertension, diabetes, and entities denoted as “new chronic diseases” (first line second paragraph). The term “new” is not motivated. Should be erased.

Reference 22 is incomplete, lacks editors, authors, chapter and pages and likely peer review.

Second page. Largely devoted to methodology, I do not see a clear message. The term “spontaneous “ in the expressions “visualization of spontaneous associations between…” is unclear.

The two last paragraphs constitute unmotivated proposals, suggestions and recommendations which should be preceded by a rationale or suppressed.

Section Comparison to other studies

Findings in other studies should be structured, compared to own study results and perhaps not a list of each study results deprived from criticisms. I suggest they are mentioned when single associations are first discussed.

Section Limitations

Should be early described in DISCUSSION and useful for interpreting results. Those due to the cross-sectional design are crucial and authors are well aware of them.

CONCLUSION

The paper lacks conclusions a part from the 12 reported associations. An explicit text, free from speculative considerations or recommendations, should be provided after interpretation of study results.

OTHER REVISIONS

Part of the CONCLUSION might be elaborated and moved to discussion after suggesting how a longitudinal study of the dementia cohort may be approached using causal or predictive models.

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

Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests' below