Reviewer's report

Title: The course of Depression in Late Life as measured by the Montgomery and Aasberg Depression Rating Scale in an observational study of hospitalized patients.

Version: 2 Date: 24 April 2015

Reviewer: Sebastian Köhler

Reviewer's report:

GENERAL COMMENTS

In this manuscript, Borza et al. present the results of a clinical cohort study into the natural course of depression in later life. 145 inpatients from nine geriatric psychiatry departments in Norway were assessed at baseline (on average 5.7 days after admission), and followed until discharge (range 16-301 days). Change in MADRS, response to treatment and remission were tested in linear and logistic regression models taking into account center/clustering effects by specifying random intercepts. Largely consistent, though statistically inconclusive, associations were found with different baseline predictors. The manuscript is well written and the topic seems relevant to this journal. Major strengths include the good design and methods, including use of the MADRS to assess change in depressive symptoms. I hope that the following comments help strengthening the manuscript further.

MAJOR ESSENTIAL REVISIONS

1. The study is not particularly new and the reported associations with cognitive impairment, somatic (multi)morbidity and recurrent episodes/chronicity are well known. It is hence not clear what the current study adds to the existing literature, and this could be worked out more. For instance, why is it relevant to study change in specific symptoms?

2. The methods are generally clear and sound, but I wonder
   a. Why were predictor variables dichotomized? This results in loss of information, including non-linear effects.
   b. Why were missing IADL scores imputed using random numbers? This only seems to add noise, resulting in a dilution of potential effects.
   c. Using linear/logistic mixed models is a good way of dealing with cluster effects. Although the authors did not study cross-level effects, and while there is no good rule-of-thumb for required sample size for such analyses, this study is not too large. So I would check if clustering is really so high as to take into account here, instead of simply using center as a covariate. Other less demanding approaches for such type of analyses are robust regression using a sandwich estimator or generalized estimating equations.
   d. Change scores are often used, but suffer from the fact that they do not take
into account differences in baseline values. Yet for most medical outcomes, change from a low baseline value to even lower is different than the same nominal change from a high baseline value. A simple and very efficient way of studying change between 2 time-points is to use the follow-up up score as the outcome and adjust for the baseline score in a multiple linear regression.

MINOR ESSENTIAL REVISIONS
3. Introduction: Please specify what is meant by “short term course of DLL”
4. Methods: Effect size (ES) refers to a lot of different measure; I think you used Cohen’s d.
5. Methods and results: “Multivariate” (multiple outcome/dependent variables) should be change to “multivariable” (multiple predictor/independent variables).

DISCRETIONARY REVISIONS
6. Treatment response is poor in patients with cognitive deficits and such deficits are likely to persist in DLL patients even after remission of depressive symptoms. About 50% of DLL patients with a diagnosis of major depressive disorder have MCI. It has been shown that treatment response also relates to brain white matter lesion and measure of change to the brains microstructure in DTI (e.g. Lui et al Am J Psychiatry 2011; Kohler et al Psychol Med 2010; Sneed et al J Aff Dis 2011). The authors may wish to discuss whether such patients might be part of the refractory group in the present study.
7. Thirteen patients had dementia, and overall they had a poorer prognosis. As the authors acknowledge, the symptoms of dementia might overlap with the clinical presentation of depression such as concentration difficulties, making it more difficult to reach remission since dementia symptoms are primary. Indeed, there is much debate regarding the diagnosis of depression in dementia. Did the authors consider a sensitivity analysis excluding the thirteen dementia cases?

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

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests,