Author’s response to reviews

Title: Predictors of the effectiveness of an early medication change strategy in patients with Major Depressive Disorder

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Version: 4 Date: 20 Dec 2018

Author’s response to reviews:

Christian Brettschneider PhD
Editor
BMC Psychiatry

December, 20th 2018

Manuscript ID: BPSY-D-18-00571R3

Dear Dr. Brettschneider,
please find attached our revised Ms. “Predictors of the effectiveness of an early medication change strategy in patients with Major Depressive Disorder” by Dreimüller et al. We are grateful to all reviewers for their helpful comments and recommendations. According to your suggestions and the reviewers’ comments we have improved and revised our manuscript. In detail, we have dealt as follows with the comments:

KELTIE MCDONALD (REVIEWER 1):

Comment #1: Light editing for grammatical errors throughout the text.

Reply/Action taken: Document was edited by an English native speaker in order to correct grammar (lines not shown).

Comment #2 Tables: Tables: the use of n rather than no°, age (mean +/- SD), consistency of capitalisation and italics, Bonferroni holm corrected p-value rather just Bonferroni holm corrected

Reply/action taken: We changed the use of no° into n and the presentation of age into mean +/- SD, we checked for the consistency of capitalization and italics and used Bonferroni holm corrected p-value instead of just Bonferroni holm corrected. (Table 1 and 2, pages 10-11; lines 230-231 and pages 12-13; lines 267-268).

Comment #3 (Results section): Reporting results in text: Odds ratio rather than Odd's ratio. Some p-value were reported contrary to convention (e.g. page 14, line 292: p<0.028. Should this be p=0.028?). In some cases 'Bonferroni-Holm corrected significance level' is used and in others 'corrected significance level'.

Reply/action taken: We changed Odd’s ratio into Odds ratio and the presentation of p-values into p=0.028. We checked for the consistency of the wording concerning 'Bonferroni-Holm corrected significance level' is used and in others 'corrected significance level' and changed all into 'Bonferroni-Holm corrected significance level in order to maintain a consistent format. (Results section; page 11 line 244; page 12; lines 249-250, 253, 256-257; page 14; 274, page 25; 636-639, 645-647).
NICHOLAS ARA MISCHEL, M.D., PH.D. (REVIEWER 2):

Comment #1 (General): Some minor concerns still include discussion of the results of the statistical analysis and clinical relevance.

Maintain a consistent format for reporting results of comparisons, if significantly different, something like "patients with ___ showed significantly higher/lower/more favorable/less favorable remission than patients with _____, (regression coefficient β = __; Odd’s ratio = __; 95% confidence interval: _____; p = __; corrected p = ____) If comparisons were not significant different, simply say they were "not significantly different" or "not different" and report the values with "(regression coefficient β = __; Odd’s ratio = __; 95% confidence interval: _____; p = __; corrected p = ____)" or refer to the appropriate table.

Reply/action taken: According to the reviewer’s suggestion we changed the reporting of the results in order to maintain a consistent format as suggested above (Results section; page 12, line 252; page 14; 275-279, 281), but we decided against reporting both the regression coefficient and OR as they provide equivalent information. In revision 2, we deleted the regression coefficient for simplicity, due to a suggestion of reviewer 1 (see Comment 6 in revision 1/last reply letter).

Comment #2 (Results and Discussion): If comparisons were not significantly different after correction, they can't be said to be more or less favorable, higher or lower. There are cases here where comparisons may be underpowered to detect clinically relevant differences that have been shown in other publications, please discuss this in the discussion and limitations.

Reply/action taken: Due to the reviewers suggestion we deleted the passages in the results section defining the not significantly different results as higher or lower. We discussed in the limitations section that there may be cases where comparisons may be underpowered in order to detect clinically relevant differences that have been shown in other publications (results section; page 11 line 243, page 12 line 249, page 14 line 273; discussion section page 18 lines 381-382 and 384-386).

Comment #3 (Discussion): Discuss the results of any power calculations that have been done. It is likely the case that there are more than several subtypes of depression that are themselves. Nevertheless, it is important to report on adequately powered results of well-run, negative or positive. I appreciate the work that has gone into refining this manuscript.
Reply/action taken: As this was a secondary analysis on an exploratory basis, we did not perform any power calculations. This was already stated in the methods section, lines 200-202. Nevertheless, we further added this information to the limitation section in the discussion (page 18 discussion section; lines 381-386).

Waldemar Greil, MD (Reviewer 3):

Comment #1 (General): My criticisms (Reviewer No. 3) are considered and well implemented. The figures are now clearly presented and the results are described in detail in the legends. The revised version has also taken into account the objections of the other reviewers regarding the statistics. Despite many negative results, it is an important study that examines a clinically very important issue and will stimulate further research.

Reply: We thank the reviewer for this positive response.

We again wish to thank the editor and the reviewers for their efforts and very helpful comments and we hope that you will find our revised manuscript now fully suitable for publication.

Nadine Dreimüller, MD

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