Author’s response to reviews

Title: Type D personality is a predictor of prolonged acute brain dysfunction (delirium/coma) after cardiovascular surgery

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Version: 3 Date: 27 Jan 2019

Author’s response to reviews:

January 28, 2019

Dear Dr. Lynn Williams,

We wish to express our strong appreciation to the Reviewers for their insightful comments on our manuscript. Their comments have helped us significantly improve the manuscript. Here, we submit the revised version of the manuscript entitled “T Type D personality is a predictor of prolonged acute brain dysfunction (delirium/coma) after cardiovascular surgery” I hope that
these changes are satisfactory and that the manuscript will now be accepted for publication in BMC Psychology.

Please contact me freely with any further questions, comments, revisions or concerns you may have.

Sincerely Yours,

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Responses to reviewers

REVIEWERS' COMMENTS and RESPONSES:

To Reviewer #1

Dear Dr. Michael Smith

I appreciate your kind response, and my response to each comment is below.

Reviewer reports:

Michael Smith (Reviewer 1): Thank you for giving me the opportunity to once again review this manuscript. Below, please find some comments on the Results and Discussion sections, for consideration.

Figure 2 could be revised to make it more informative. Please re-label the x-axes, to make clear that these represent 'Days' (assuming I've understood the figure correctly). Should the data presented in Figure 2 be accompanied by inferential statistics? From eyeballing the data presented in the figure, it appears that the Type D effects are driven by an exacerbation of coma...
and delirium during the days immediately following surgery, but this effect seems to normalise within a week. So there could be a moderating effect of time?

Response: Thank you for pointing this out. I revised the x-axis for this figure. I believe this figure helps to understand the overall variance of the postoperative week 1 for readers. As you mentioned, time might affect the presence of type-D personality as it is much stronger just after the operation. To this end, I have added the inferential statistics analyzed by liner mix model statistics, including interaction for time variance, and type D personality.

Please kindly check figure 2 and the updated method.

Given that SI and NA independently predict DCFDs, could the authors comment on whether it is Type D that is driving the observed effects, or whether it is the independent effects of NA and/or SI? There is much contention around this issue in the Type D literature (see, for example, Horwood & Anglim, 2017).

Response: Thank you for your comment! I have addressed this issue in the updated Discussion.

Page 20, lines 5-6 should be reworded, as they imply that mediation was observed, when no such analysis was performed.

Throughout the Discussion, including in the Conclusions paragraph the authors refer to 'Type D personality-associated depressive symptoms'. I'm not sure that this accurately captures what the data are telling us. The interaction between Type D and depression is indicating that the effect of Type D personality on DCFDs is being moderated by depressive symptoms, whereby, depressive symptoms in the presence of Type D personality inflates the Type D effect on DCFDs. In my view this effect is also misinterpreted on page 18 lines 11-15. The authors should consider throughout the Discussion their interpretation of the interaction effect.

Response: Thank you for pointing this out and we apologize for this part. I added the mediation analysis. Please kindly check the new result and discussion parts.

Title. I would like to suggest the authors to adapt a little bit as follows:

"Type D personality is a predictor of prolonged acute brain dysfunction (delirium/coma) after cardiovascular surgery."

It is more straightforward to refer directly to the main outcome under investigation, which is brain dysfunction. Reduced delirium/coma-free days is an operational definition of this outcome
measure; therefore, I would place it between brackets after brain dysfunction. Since the operational procedures in this study also include vascular surgery, it is better to refer to cardiovascular surgery (instead of cardiac surgery).

Response: Thank you for your recommendation. We have updated our title to reflect this important point.

Dependent variable in analyses.

In the analyses, Tables and text, please use acute brain dysfunction as the dependent variable. Since the authors would like to investigate the association between Type D personality and brain dysfunction, it would seem more logical to me to use "Prolonged delirium/coma days" as a measure, and not the reverse, "Delirium/coma free days" (as now is the case). This would not change anything in terms of findings, but sure would make the interpretation of findings much more simple and straightforward.

For example, in Table 2 it is now reported that Type D personality is associated with an OR=0.3, meaning that Type D is associated with a 70% decreased odds of days without brain dysfunction. In other word, you need to read this as a decreased odds of an (desirable) event that is not occurring. If the authors would reverse the dependent variable from "delirium/coma free days" into "delirium/coma days", the OR and 95% CI of Type D personality will become greater than 1, indicating that Type D personality is associated with an increased odds of brain dysfunction as an undesirable event.

Response: Thank you for your recommendation. I agree that setting dependent values as delirium/coma days is easy to understand for readers, so I revised table 2 and the result part.

Sum score of negative affectivity and social inhibition is not valid.

The authors refer to Horwood and Anglim (2017, Ref #38) and Stevenson & Williams (2013, Ref #37) to indicate that they also used the sum of negative affectivity and social inhibition (NA+SA) as a continuous measure of Type D personality. As pointed out correctly by the authors, Horwood and Anglim (2017, Ref #38) did indeed use the sum of the negative affectivity and social inhibition subscales as a continuous measure of Type D personality, but they should not have done so. Negative affectivity and social inhibition refer to two different personality traits, and should not be added together as a total score. Therefore, the findings on the total Type D score reported in Table 3 are not valid, and Table 3 should be deleted in the manuscript. Moreover, Table 3 does not add anything above and beyond the findings reported in Table 2.
Hence, the sentence in the Results section on p.14 stating that: "Assuming type D personality is a continuous value, increasing total scores of Type D personality (Total score of NA + SI) were also associated with significantly decreased DCFDs (OR = 0.9, 95% CI = 0.9-0.9) (Table 3)" should also be deleted. However, the sub-analyses using the continuous scores of negative affectivity and social inhibition as separate, independent components of Type D personality are certainly meaningful, and may be included in the manuscript (instead of being reported in a Supplemental File, as now is the case).

Finally, please notice that Stevenson and Williams (2013, Ref #37) did not calculate the sum score of NA and SI but rather used the interaction term of NA and SI (NA X SI) as a continuous measure of Type D personality.

Response: Thank you for your comment for this issue. For my opinion, I totally agree with your opinion that Negative affection and Social inhabitation would not sum up so I deleted Table 3. Moreover, I added the comments for each affect (NA, SI) for the DCD (delirium coma days) as suggested by Reviewer 1. Please kindly check the discussion part.

Use of the terms "Non-Type D patients" and "Non-Type D personality".

In the Type D dichotomy, a distinction is made between "Type D patients" (presence of Type D personality) and "non-Type D patients" (absence of Type D personality).

Please avoid using the term "normal patients" in comparisons with Type D patients (because this seems to imply that Type D patients are "abnormal") but rather use the term "non-Type D patients".

By analogy, the Type D literature refers to Type D personality and Non-Type D personality (as the authors also have correctly noted in Table 1).

Please notice that Type D is always written with a capital "T", also in the text.

Response: Thank you for pointing this out. I rephrased “normal patients” as “Non- Type D personality” and rechecked to ensure that Type D was always capitalized.

Abstract.

In the abstract, "type D (distress)" should be changed to "Type D (distressed)" personality.

"A total of 142 patients … and the total prevalence of delirium was found to be 33%, of which 26% of the patients were Type D”. I find this sentence a bit confusing; I suppose you want to
indicate that 26% of all patients had a Type D personality, but now it looks as if 26% of the patients with delirium also had Type D.

I would also make clear in the Abstract that Type D personality remained associated with prolonged brain dysfunction, even after adjustment for depressive symptoms.

Response: Thank you for pointing this out. I rewrote the abstract to address this point.

Figure 2. I would like to suggest to change the title of figure 2 as follows:
"Distribution of normal, delirium, and coma days, stratified by Type D personality.

Please consider the upper panel (Total population) from this figure, because it distracts from the main findings of your study on personality differences.

Please use the labels "Non-Type D patients" and "Type D patients" (instead of "Normal patients" and "Type D personality patients").

Response: Thank you for your advice. I corrected figure 2. Please kindly check it.

Figure 3. Label above the red arrow pointing to the left: please use "Prolonged brain dysfunction" as a label (and not "Prolong delirium/coma days"; in any case, prolong should be prolonged).

In Figure 3, please use the term "Non-Type D personality" (instead of "Not Type D personality).

It is not clear to me what the label "Depressive symptom" refers to in this figure. Is this the OR of brain dysfunction associated with depressive symptoms in the study? (because in that case, "Depressive symptoms" should be noted below Non-Type D personality, instead of "Total population")

Response: Thank you for pointing this issue out. This figure showed depressive symptoms’ interaction effect between DCDs and Type D personality. In this figure, we see basically the same result of figure 2 (regression model including interaction between Type D personality and depressive symptoms). However, to make it easy to understand the interaction, we divided the pool into two groups (Type D personality present or not) and showed the differences of the effect of depressive symptoms for DCDs.
Discussion.

I agree with the authors that inflammation and endothelial dysfunction is a potential biological pathway that may help to explain the link between Type D and acute brain dysfunction following surgery (p. 19). There is a recent publication that reports on a clear association of Type D personality with endothelial dysfunction - the authors may wish to refer to this publication (Denollet J, van Felius RA, Lodder P, et al., Predictive value of Type D personality for impaired endothelial function in patients with coronary artery disease. Int J Cardiol. 2018;259:205-210).

Response: Thank you for your advice. I read the paper and added the reference.

References.

Please double-check the accuracy of the references in the reference list.

For example, Ref. # 15 does not report the correct title of the article, does not include journal title, volume number or pages, and was not published in 1997. The correct title and reference is: "Usefulness of Type D personality in predicting five-year cardiac events above and beyond concurrent symptoms of stress in patients with coronary heart disease. Am J Cardiol. 2006; 97(7):970-973."

As another example, References #17, #33, #45, and #46 do not include Journal name, volume number or pages. Please correct, and make sure that all references are accurate.

Response: Thank you for your advice. I double checked and corrected the references.