Author's response to reviews

Title: Cognitive behaviour therapy response and dropout rate across purging and nonpurging Bulimia Nervosa and Binge Eating disorders: DSM-5 implications

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Author's response to reviews: see over
Dear Prof. Fassino,

Please find attached the electronic file of the manuscript entitled “Cognitive behaviour therapy response and dropout rate across purging and nonpurging Bulimia Nervosa and Binge Eating disorders: DSM-5 implications” to be resubmitted to BMC Psychiatry.

The present version of the manuscript includes modifications in response to the concerns raised by the reviewers and some further additional changes, which we thought could improve the paper significantly. For the sake of clarity and conciseness, we refer to each topic in the same order as listed by the reviewers. Please read below:

Reviewer(s)’ Comments to Author:

Reviewer's 1 report:

This is an interesting paper reporting about treatment outcome in a large sample of ED patients. I have only some minor concerns to suggest.

Major revisions
1. I would suggest to authors to avoid a so large number of comparisons (to avoid type 1 errors) without statistical correction. I would suggest to choose some more relevant variable before the statistical analyses.

Reply: We thank the reviewer for the positive feedback. In this study, Bonferroni-Holm’s correction (Holm, 1979) was used to prevent increase in Type I error (the total alpha level for the set of comparisons was established at 0.05). This method is
considered an example of a closed-test-procedure and operates controlling the family-wise error rate for all the hypotheses at the $\alpha$ level (this value is established by the researcher). It is more powerful than the regular Bonferroni’s-adjustment and statistical studies have demonstrated that it can always be used as a reliable and useful substitute. This has been indicated under each table and in the last paragraph of the statistical analysis section: "Due to the multiple comparisons, Bonferroni-Holm’s correction was used to prevent increase in Type I error (the total alpha level was established at 0.05). This method for adjusting global $\alpha$-level is included into the closed-test-procedures and it controls the family-wise error rate, operating in a more powerful way than the usual Bonferroni’s-adjustment".

2. Remission rates should be reported as row rates (as now) and as intent-to-treat analysis (including patients who dropped out).

Reply: Remission rates for completers (patients who completed the treatment) and total sample (including the patients who dropped out) are shown in the Table 2 of the reviewed paper. These new results have also been described in the results section: “The remission rates for the total sample (including the participants who drop-out, as an intent-to-treat analysis) showed similar results: the probability of full remissions were 47.1% for BED (95% CI: 36.6% to 57.6%), 30.0% for BN-NP (95% CI: 15.8% to 44.2%) and 27.2% for BN-P (95% CI: 22.4% to 32.0%).”

Minor revisions
3. It would be interesting to know how many patients would maintain their diagnosis with DSM-5

Reviewer's 2 report:

This paper addresses an understudied aspect related with the bulimic-spectrum syndromes (differences in the treatment responses and in the treatment dropout), aspects that can be useful to the study of the boundaries across these syndromes, what is a current and useful debate.

I have only minor essential revisions to suggest:

Overall, this was a well-designed and conducted investigation.

The methods appear appropriate and the data sound; the clinical assessment and the experimental approach seemed very professional. The title and abstract convey the point of the study.

Reply: We deeply appreciate the reviewer’s comments.
It would be important to specify what kind of treatments the patients did before and if they were medicated with psychotropic drugs during the study.

**Reply:** We agree with the reviewer, therefore we have added the following in limitations: "...although patients were asked whether they received previous treatment for their eating disorder (and we found no significant differences in the number of previous treatments for ED), the type of treatment was not recorded".

We fully agree with the reviewer that information regarding the number of patients treated with psychotropic medication during the study would have strengthened the paper. Unfortunately this information was not systematically collected. This limitation has been added in the discussion section “Furthermore, future studies should control for pharmacotherapy during CBT, as the lack of this data is a limiting factor of the present study”.

Where is written “Socio-demographic characteristics” it would be more correct to write “Socio-demographic characteristics and information regarding eating disorders”, since the authors also write characteristics related with eating disorders: body mass index, age of onset…

**Reply:** We agree with the reviewer, therefore this aspect has been rewritten.

In the discussion section, I think the authors should discuss other hypotheses to explain the “higher dropout rates in BED group”. Why would it be expected that “the rapid response of symptom reduction (binges reduction in the first treatment sessions)” could be related with a higher dropout rate? If their “own motivation” to the treatment was similar to the BN-P group why they showed a higher dropout rate? The authors also hypothesize that the higher dropout rates in the BED group could be related with the “lack of weight lost while on treatment” – where is the weight loss quantified? Should it be expected that the BED group showed a lack of weight loss if they had the better response to the treatment?

**Reply:** We agree with the reviewer, therefore the following information has been added in the results: "Regarding BMI, no statistical differences emerged in the pre-post changes in each diagnostic subtype (p=.259)". The text has also been clarified and rewritten to read: "Our results showed no significant differences in the clinical or psychopathological variables between BED patients who dropout vs. non-dropout, except on Body Dissatisfaction. Therefore, based on a clinical perspective, we hypothesized that the higher dropout rates in BED group could be related to the lack of weight lost while on treatment as many BED were found to be overweight or obese [22] and dieting while in treatment was not allowed. On the basis of these findings, a recent study found that CBT improves eating disorder psychopathology and psychosocial functioning in BED patients, but the lack of weight loss negatively influences the improvement profile [42]. Moreover, the higher scores on Body Dissatisfaction in BED patients who dropped out suggest that the dissatisfaction with shape and weight in these patients and the urge to lose weight may have influenced the high dropout rates".
The authors discuss in a relevant way the limitations of the study, since the psychiatric co-morbidity could explain some results.

The authors should complete the list of abbreviations, since it does not include all the abbreviations present in the paper (SCID-I, BN, DSMIV-TR, BMI, EDNOS…).

**Reply:** As suggested by the reviewer this aspect has been corrected and all the abbreviations have been included in the appropriate section.

**Reviewer's 3 report:**

Reviewer's report:

**A. DISCRETIONARY REVISIONS**

- Could you indicate the coefficient alpha of your data for EDI-2 and SCL-90-R?

**Reply:** We fully agree with the fact that the manuscript would benefit from specifying coefficient alpha for EDI-2 and SCL-90-R. However, we have not introduced in the database each item one by one (only the total score of the subscales), which is a requisite in order to calculate coefficient alpha.

**B. MINOR ESSENTIAL REVITIONS**

- Page 3 second paragraph: "...studies comparing BED vs. BN have shown difference..": should type "differences"

**Reply:** As suggested by the reviewer this aspect has been corrected.

- Table 1: Could you specify what is the level of significance of "*"?

**Reply:** As required, p-values have been included in Table 1 for the post-hoc comparisons that achieved significance.

- In order to more easily interpret your results by a reader it would be better to indicate the t value instead of the Mean difference of means in Tables 1 and 3.

**Reply:** As suggested by the reviewer, Tables 1-3 includes now both, the statistical parameters of comparisons (F or T values) and the contrasts (mean difference or OR). These last values are required as a descriptive measure of the effect-size of the differences.

**C. MAYOR COMPULSORY REVISIONS**

- Even if there is not a clear agreement on the criteria to define what response/remission/recovery is in the field of EDs, considering that the diagnostic
criteria that allow a DSM-IV-TR diagnosis of BN and BED call for a minimum of 3 months of symptoms for BN and 6 months for BED, a period of only 4 consecutive weeks free of eating symptoms is quite low to define a "full remission". Please, could the authors explain why did they choose this threshold?

**Reply:** As the reviewer suggests, to use the term "recovery" requires a long period of abstinence from bulimic behavior. However, we have used the term "remission" based on the previous literature which suggests that "recovery" could be differentiated from "remission" on the basis of time (Field et al, 1997), and also the criteria of remission requires at least 1 month without bulimic symptoms (Mitchell et al, 1989).

- Not only, the authors have only considered the behavioral (eating behavior) but not the psychological symptoms (Criterion D: Self-evaluation is unduly influenced by body shape and weight) to define the remission of patients after CBT. Daily-food and purging diary is a very poor tool to define remission.

**Reply:** We agree with the reviewer. We also considered improvement in psychological symptoms measured by clinical questionnaires (mainly Drive for Thinness, Body Dissatisfaction and Bulimia EDI-2 subscales). This aspect has been clarified and more detailed in the manuscript has been added: "Primary outcome was based on the food and purge diary and the response of some clinical questionnaires in the field of ED. The working definition of a "full remission" outcome required the absence of binging and purging (laxatives and/or vomiting) behaviors for at least 4 (consecutive) weeks and psychological improvement measured by clinical questionnaires".

- The “commonly applied questionnaires in the field of EDs” could have given further information about the improvement of the psychological symptoms after CBT. Why did you not re-test your samples with them (or others as EDE) to evaluate the improvement?

**Reply:** We agree with the reviewer, therefore a new table has been added with the pre-post comparison in each diagnostic condition (BN-P, BN-NP and BED) for the EDI-2 and the SCL-90-R mean scores. We have also included this information in the results and discussion sections.

- In the statistical analysis section the authors do not clearly describe the use of logistic regressions, whose results are not shown in the results section. Further, they do not describe the univariate analysis (t-Student, Chi-Squared) that seems to be later used in the results section.

**Reply:** The statistical analysis section has been reviewed. Logistic regression and ANOVA procedures (used to compare clinical outcomes between diagnostic conditions) have been more detailed.
- If you have considered three groups along your research, it is not clear the reason why you put together both BN groups in Table 3; it should be better to follow the same scheme.

**Reply:** We agree with the reviewer, therefore we have included a new Table (Table 3) with the results of the comparisons stratified by the three diagnostic conditions: BN-P, BN-NP and BED.

We are really grateful for the reviewer’s comments.

Yours sincerely on behalf of the authors,

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