

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	BOrderliNe symptoms and suicidal-related outcomes: proTOcol for a systematic review/meta-analysis and an individual patient data meta-analysis (BONITO study)
<b>AUTHORS</b>	Calati, Raffaella; Romano, Daniele; Lopez-Castroman, Jorge; Turolla, Federica; Zimmermann, Johannes; Madeddu, Fabio; Courtet, Philippe; Preti, Emanuele

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Berihun Dachew Curtin University
<b>REVIEW RETURNED</b>	15-Sep-2021

<b>GENERAL COMMENTS</b>	<p>Please check the title of your research for capitalizations. "BOrderliNe symptoms and suicidal thoughts and behaviours: proTOcol for a systematic review/meta-analysis and an individual patient data meta-analysis"</p> <p>Introduction Describe the gap in evidence your review is aiming to fill and the rationale for why a review is important.</p> <p>Methods More description of study methods, particularly related to recruitment of participants, participation rates, and representativeness of the samples.</p> <p>I recommend the authors to use the MeSH dictionaries (and its Emtree equivalent) throughout. Some of the terms they indicate are not MeSH terms "borderline"</p> <p>Can you provide more information about the quality assessment; what information is used for rating, what is the scoring for each item, and the method used for grading quality.</p> <p>The description of the study inclusion and exclusion criteria is completely insufficient.</p> <p>The description of what exactly will be extracted from the eligible articles, what information will be used for effect size calculation is superficially described.</p> <p>Add coverage dates for all databases e.g. EMBASE 1947 – present. Different institutions have access to different versions of databases, so adding the dates provides transparent reporting of the actual data source you are using. If there is no beginning date available for the database use inception e.g. PubMed from its inception – present.</p> <p>Add a full search strategy that can be reproduced by a reader. State which database the search strategy is for.</p>
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<b>REVIEWER</b>	Falk Leichsenring University Hospitals Giessen and Marburg Campus Giessen
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<b>REVIEW RETURNED</b>	16-Jan-2022
<b>GENERAL COMMENTS</b>	<p>The authors submitted a study protocol on the relationship between borderline symptoms and suicidal thoughts and behaviors. This is an interesting and clinically important question that may help to identify predictors of suicidal behaviors. The authors are planning to address this question by a systematic review/meta-analysis and additionally by an individual patient data meta-analysis.</p> <p>In sum, the submitted protocol is methodologically sound. However some clarifications will help to further improve it.</p> <p>With regard to the inclusion criteria it is not fully clear whether only studies with patients diagnosed with a borderline personality disorder are planned to be included.</p> <p>Furthermore, are specific methods of diagnosis required for making the diagnosis of borderline personality disorder (e.g. DSM diagnosis, specific diagnostic instruments ?)</p> <p>Will the authors include comparison population, for example patients with other personality disorders or no personality disorders?</p> <p>For some suicidal-related events reliable assessment may be difficult, for example for death wishes.</p> <p>With regard to study quality, do the authors plan to include a risk of bias assessment? If so, will the risk of bias ratings be taken into account with regard to the relationships between borderline symptoms and the suicidal behaviors?</p> <p>The authors cite a review on borderline personality disorder by Lieb et al (2004). There are more recent reviews on BPD in the Lancet, for example by Leichsenring et al (2011) or Bohus et al (2021) that should be taken into account.</p> <p>If the authors take these issues adequately into account, the manuscript can be re-commended can be recommended for publication in the Journal.</p>

**VERSION 1 – AUTHOR RESPONSE**

Reviewer # 1

Please check the title of your research for capitalizations.

“BOrderliNe symptoms and suicidal thoughts and behaviours: proTOcol for a systematic review/meta-analysis and an individual patient data meta-analysis”

Reply:

We checked the title and we found it correct (BOrderliNe symptoms and sulcidal thoughts and behaviours: proTOcol for a systematic review/meta-analysis and an individual patient data meta-analysis (BONITO study)). Thank you anyway.

Introduction

Describe the gap in evidence your review is aiming to fill and the rationale for why a review is important.

Reply:

We have better articulated the rationale of the review in relation to the polythetic consideration of BPD diagnosis.

#### Methods

More description of study methods, particularly related to recruitment of participants, participation rates, and representativeness of the samples.

#### Reply:

We consistently improved the methods' section. Concerning the recruitment, the participation rates and the representativeness of the samples, we do expect to have representative samples because we do not apply any specific restrictions: in fact, we will include studies of subjects regardless of age, sex or ethnicity, psychiatric diagnosis, inpatient or outpatient or mixed or community settings. Moreover, through the quality assessment tools (we improved their description) we will be able to focus on these aspects (recruitment, participation rates, and representativeness) for each single study.

I recommend the authors to use the MeSH dictionaries (and its Emtree equivalent) throughout. Some of the terms they indicate are not MeSH terms "borderline"

#### Reply:

Thank you for the precious suggestion. We corrected the keywords (MeSH), we added Emtree equivalents (pages 12) and we added an Appendix (B) with each string used for each database.

Can you provide more information about the quality assessment; what information is used for rating, what is the scoring for each item, and the method used for grading quality.

#### Reply:

We agree with this point and we added more information about the quality assessment (page 15-16).

The description of the study inclusion and exclusion criteria is completely insufficient.

#### Reply:

We added some details (pages 9-10). However, our inclusion criteria are extremely wide (and this may be the reason why they seem insufficient) because 1) we will include studies with the availability of our data of interest even if their primary outcome was not the association between BPD symptoms and suicidal-related outcomes and even if this association was not calculated in the original study (we better specified this point), and 2) we will include any type of study population (clinical and non-clinical) and any type of study design (cohort, cross-sectional, case-control studies). The reason of the wide inclusion criteria is the fact that we hypothesized a reduced number of includible studies since we already performed a preliminary pilot search and data extraction. We hope that now this point is clearer.

The description of what exactly will be extracted from the eligible articles, what information will be used for effect size calculation is superficially described.

#### Reply:

We improved the extraction paragraph (pages 13-14).

Add coverage dates for all databases e.g. EMBASE 1947 – present. Different institutions have access to different versions of databases, so adding the dates provides transparent reporting of the actual data source you are using. If there is no beginning date available for the database use inception e.g. PubMed from its inception – present.

Reply:

We completely agree with the reviewer. However, since we will search each database from 1974 (some years before the introduction of DSM current personality disorders' criteria) until September 2021, we simply stated this specification (page 11).

Add a full search strategy that can be reproduced by a reader. State which database the search strategy is for.

Reply:

We added the full search strategy in the Appendix B.

Reviewer # 2

The authors submitted a study protocol on the relationship between borderline symptoms and suicidal thoughts and behaviors. This is an interesting and clinically important question that may help to identify predictors of suicidal behaviors. The authors are planning to address this question by a systematic review/meta-analysis and additionally by an individual patient data meta-analysis. In sum, the submitted protocol is methodologically sound. However some clarifications will help to further improve it.

Reply:

We thank the reviewer for his generally positive evaluation.

With regard to the inclusion criteria it is not fully clear whether only studies with patients diagnosed with a borderline personality disorder are planned to be included.

Reply:

We thank the reviewer for this comment because it allows us to better specify this important point that was not clear. See under objectives this paragraph (pages 8): "We plan to perform separate analyses for 1) patients with a full BPD diagnosis, 2) patients without a BPD diagnosis, and 3) individuals without a BPD diagnosis from the general population".

Furthermore, are specific methods of diagnosis required for making the diagnosis of borderline personality disorder (e.g. DSM diagnosis, specific diagnostic instruments ?)

Reply:

Again thank you for this point. See among inclusion and exclusion criteria (pages 9-10). We added this point. We will consider studies focusing on the DSM-III version or subsequent, since only in DSM-III personality disorders diagnoses have been introduced.

Will the authors include comparison population, for example patients with other personality disorders or no personality disorders?

Reply:

We better specified this point under objectives (pages 8): “We plan to perform separate analyses for 1) patients with a full BPD diagnosis, 2) patients without a BPD diagnosis, and 3) individuals without a BPD diagnosis from the general population”.

For some suicidal-related events reliable assessment may be difficult, for example for death wishes.

Reply:

We agree. However, we decided to include all the suicidal-related outcomes to better cover the entire suicidal spectrum. If possible we will consider only suicidal-related events measured with a standardized scale but we are not sure about that because we foresee a paucity of available data.

With regard to study quality, do the authors plan to include a risk of bias assessment? If so, will the risk of bias ratings be taken into account with regard to the relationships between borderline symptoms and the suicidal behaviors?

Reply:

Yes, we will rate the risk of bias according to GRADE and we better specified this point in the relative section (pages 14-15). We will take into account the risk of bias together with other methodological aspects with regard to the relationships between borderline symptoms and the suicidal behaviors in different ways: we will prepare summary of findings tables according to GRADE (<https://training.cochrane.org/introduction-grade>) and we will consider the scores in statistical analyses to evaluate the impact of different aspects of the quality on the results we will obtain.

The authors cite a review on borderline personality disorder by Lieb et al (2004). There are more recent reviews on BPD in the Lancet, for example by Leichsenring et al (2011) or Bohus et al (2021) that should be taken into account.

Reply

We thank the reviewer for the suggestion. We now included references to these more recent reviews.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Falk Leichsenring University Hospitals Giessen and Marburg Campus Giessen
<b>REVIEW RETURNED</b>	24-Mar-2022
<b>GENERAL COMMENTS</b>	<p>Reviwer 2: I asked the the authors whether tthey plan to include comparison populations, for example patients with other personality disorders or no personality disorders.</p> <p>The authors response did not answer this important question. Again, my question refers to the COMPARISON poulations.</p>

## VERSION 2 – AUTHOR RESPONSE

Reviewer # 2

I asked the the authors whether tthey plan to include comparison populations, for example patients with other personality disorders or no personality disorders.

The authors response did not answer this important question. Again, my question refers to the COMPARISON poulations.

Reply:

We are sorry for the confusion.

As stated in the manuscript, we plan to perform separate analyses for 1) subjects with a full BPD diagnosis, and 2) subjects without a BPD diagnosis (we now improved this description).

This will not be a statistical comparison among the groups but 2 different types of analyses (that can be qualitatively compared once done).

In fact, through the meta-analytic technique it may be possible to perform – in the presence of the necessary data - different sets of separate analyses including:

1) subjects with a full BPD diagnosis (comparing N of BPD subjects with the specific BPD symptom/N of BPD subjects with the suicidal-related outcome versus N of BPD subjects with the specific BPD symptom/N of BPD subjects without the suicidal-related outcome);

2) subjects without the full BPD diagnosis (N of subjects with the specific BPD symptom/N of subjects with the suicidal-related outcome versus N of subjects with the specific BPD symptom/N of subjects without the suicidal-related outcome);

To perform the analysis that you suggested (to include comparison populations, for example patients with other personality disorders or no personality disorders) will imply that a number of studies compared BPD patients to for example patients with other personality disorders or no personality disorders and we cannot be sure about that. However, in the case these data will be present, we will perform these analyses. Moreover, we stated in the manuscript (p. 17): “if there is a sufficient number of studies for each suicidal outcome, we will investigate potential sources of heterogeneity using (...) subgroup analyses by (...) clinical characteristics (e.g., primary and secondary psychiatric diagnoses”. Thank you for the suggestion.