Author's response to reviews

Title: Epidemiologic heterogeneity of common mood and anxiety disorders over the lifecourse in the general population: a systematic review

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Author's response to reviews: see over
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Dr. Morton Hesse
Associate Editor
BMC Psychiatry

Dear Dr Hesse:

We are resubmitting our manuscript “Epidemiologic heterogeneity of common mood and anxiety disorders over the lifecourse in the general population: a systematic review” for consideration for publication in BMC Psychiatry. Thank you for your continued interest in the manuscript. We are grateful for the reviewers’ comments that we feel have improved the manuscript. We respond to the reviewers’ major and minor comments below.

REVIEWER 1

Major compulsory revisions

1,2,4. “The authors consistently refer to studies as having “identified” sub-types and specific trajectories. However, the statistical approach that each study has used is not even reported. For this reason the authors seem to assume that all strategies for “identifying” sub-types or trajectories are equally valid. However, this may not be the case, and a discussion of appropriate or less appropriate strategies to resolve these questions in individual studies should be included – even if all these studies used state-of-the-art approaches to analyse their data….Also, in terms of the individual study, no information is given regarding the type of data that was collected, the psychometric quality of the data collection procedure, the response rate, or other methodological features that may have a bearing on the validity of the findings….Also, the authors do not distinguish clearly between pre-defined sub-types and empirically derived subtypes”

We agree that it would benefit the reader to provide additional information about the psychometric quality of the data collection procedures employed, as well as the analytic methods. Accordingly, we have made changes to both the tables and text that we hope address the reviewer’s concerns.

In the tables, we have changed the column heading “Timeframe” to “Methods”. The new “Methods” column provides the reader with three types of information. First, similar to our original submission, we provide information on the timeframe used in each study. Second, we identify the scale or...
instrument used by each study to measure each disorder. Third, we provide information on the statistical method used by each study to assess heterogeneity and identify subtypes. By providing this additional information we hope to provide the reader with sufficient information to make relative comparisons of the methodological strengths and weakness of the studies included in this review. We deliberately left out response rates primarily because they are frequently not reported or calculated in different ways, limiting or even biasing comparison across studies. We have made parallel changes to the text.

As Reviewer 1 (and Reviewer 2) pointed out, the studies included in the review utilize many different measures. While we believe that a full review of the psychometric properties or analytic techniques utilized is beyond the scope of our manuscript, we now acknowledge at the end of the Discussion in a new section on Methodological Challenges that “the studies included in this review were population-based and utilized a variety of diagnostic survey instruments that are, to varying degrees, imperfect substitutes for clinician-administered structured interviews. Error in the measurement of the mood and anxiety disorders may influence the validity of individual studies and complicate comparisons between studies. Further information on the validity of common diagnostic instruments can be found elsewhere.” We direct the reader to a recent review by Eaton and colleagues (2007); this is the most comprehensive assessment of the validity of psychiatric diagnostic instruments that we are aware of.

Reviewer 1 also noted that there are many different techniques used to “identify” subtypes and that these methods may not be equally valid. In general, studies that use pre-defined criteria do not identify subtypes, but assess their occurrence. To clarify this, we now report the specific method used by each study in the Tables and ensure that studies based on pre-defined (vs. empirically derived) definitions of subtypes report on their “occurrence” rather than their “identification”. We have also made several revisions to the text. In the Results section we report the prevalence of studies utilizing pre-defined vs. empirical definitions and, for those studies utilizing empirical definitions, comment on the predominant methods used. We also comment on the methods used by individual studies in the Results section. In the Methodological Challenges section of the Discussion we note that methods for defining subtypes often vary according to the outcome of interest and the inferential goal of the analysis. Furthermore, we suggest that the dichotomy between pre-defined and empirically derived subtypes represents a bias-variance trade-off and expound on this point. Finally, we direct the reader to a number of references that provide additional details on the statistical properties of models frequently used by studies in our review.

While not providing a review of the various psychometric instruments or statistical methods utilized by the papers included in the manuscript, we hope that including additional methodological information in the tables and making parallel revisions to the text, including an expanded section on Methodological Challenges, provides a lens through which the reader may adequately appraise the contributions of each paper and weigh the evidence for her/himself.

3. “In terms of being a systematic review, there is little systematic integration of the data…..

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We appreciate the reviewer’s comment and have added additional commentary about the agreement or disagreement between studies in the Discussion and Methodological Challenges sections, as appropriate.

Minor essential revisions

1. “The authors state in the methods section that the studies should use DSM-IV in their assessment. Several studies are reported to have collected their data prior to the publication of the DSM-IV…."

Disorders were selected based on the taxonomy of the DSM-IV. However, studies were not required to use the DSM-IV in their assessment. We have clarified this in the Methods section of the manuscript.

2. “The tables appear more as a separate section that as tables. In order to provide an overview, the tables should be reworked to include less text, and the essential information from the text should be included in the text…."

It was our intention to provide enough information in the tables to allow readers to make their own comparisons. For example, some readers will only be interested in studies of a particular disorder whereas others will only be interested in studies conducted in a certain age group. Because the text cannot be personalized to the preferences of each individual, we hoped to facilitate these comparisons by providing as much information as possible in the tables; we believe that deleting information only make this more difficult. Furthermore, it would be impossible to discuss the main findings from each study in the text. As aforementioned, we have included additional text summarizing the results of studies in the Discussion.

REVIEWER 2

Major compulsory revisions

1. “A discussion of the theoretical arguments that support a componential or heterogeneous view would help the reader understand the context and the rationale underlying this work”

In response to the reviewer’s suggest, we have completely reframed the introduction of the manuscript. We believe the revised Introduction more clearly contrasts the heterogeneous view of mood and anxiety disorders, supported by examples from early clinical studies on diverse disorders, with the homogenous view, represented by the current paradigm for the diagnosis of mental disorders. We hope this provides a stronger rationale for our review. We additionally cite a number of references that provide an overview of heterogeneous vs. homogenous views of mood and anxiety disorders.

2. “The results section needs some re-organization to increase the paper’s clarity. For example, headings should be included to differentiate cross-sectional findings, for example, studies that revealed heterogeneity in terms of the quality of symptoms versus the quantity. In addition, a summary paragraph (and ideally a Table) indicating what is known with respect to the different disorders would help the reader make better sense of the results…..Something similar should be done for longitudinal findings…..”

Determining how to most clearly present a great number of very diverse studies was a challenge we struggled with. In the end, we decided to divide papers first into those assessing heterogeneity of symptom syndromes vs. trajectories, then by disorder, and finally by age category. We appreciate the reviewer’s suggestion to separate cross-sectional from longitudinal studies and subtypes based on clinical features from symptom severity. However, almost all papers on symptom subtypes are cross-sectional and define subtypes based on clinical features. Additionally, all papers on trajectories were, by definition, longitudinal, and most were defined subtypes based on symptom severity. Therefore, we believe that further stratification would likely not increase the paper’s clarity.

3. “The authors mentioned in the method section that they did not include studies that used clinical populations. It is unclear here whether they refer to studies with participants who show clinical levels of mood disorders, whether they refer to studies with participants suffering from health problems (e.g., diabetes), or both.”

Our exclusion refers to studies that recruited participants from clinical settings (e.g., inpatients or outpatients). We have clarified this in the text.

4. “It would be helpful if the authors added to Table 1 the type of scale or instrument used to assess the disorder”

We have added this information to the Tables.

Discretionary revisions

1. “I wonder why the authors decided to include such a diverse array of disorders instead of focusing on depression alone…..”

The reviewer is correct that the majority of studies included in this review were on depression. We chose to include other disorders because many of the arguments for assessing heterogeneity are as valid for other types of mood and anxiety disorders as they are for depression. We have included a few historical examples of this in our revised introduction. We hope that the inclusion of less studied disorders will stimulate further research in these areas.

2. “The authors…..may want to add to their review a study by Contrada et al in Psychosomatic Medicine…..”

We thank the reviewer for this suggestion. However, this study was based on a clinical sample and hence excluded from our review.

We hope that these revisions have adequately addressed the reviewers’ comments. We include with this letter a copy of the revised manuscript with track edits revealed and a copy with all edits.
accepted. If you have any questions, please do not hesitate to contact me. Thank you in advance for your consideration. We look forward to hearing from you.

Sincerely,

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