PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Clinical Features of Overweight in Acute-Phase Hospitalized Major Depressive Disorder with Co-morbid Anxiety: a cross-sectional study

Authors

Zhang, Hong; Ma, Jun; Wang, Jing; Zhu, Wenting; Liu, Xuebing

VERSION 1 - REVIEW

Reviewer	**1**
Name	**Gomez-de-Regil, Lizzette**
Affiliation	**Hospital Regional de Alta Especialidad de la Peninsula de Yucatan**
Date	**10-Jul-2024**
COI	**None**

This was an interesting paper to read. I found it very clear and concise in its objectives. Although the design and statistics may seem simple; yet, the findings can be very useful for multidisciplinary work in clinical settings.

Recommendations:

- given that it is a cross-sectional study I would not feel accurate to call "risk factors" to those variables that resulted significantly associated with the outcome. We cannot infer from data the direction of the association, neither if there are any mediators for those associations.

- given that it was a finite population i missed the sample size estimation

- no report of cheking the parameters for a normal distribution to support the uso of parametric tests

- no report of power, which may inflate the significance of small differences in big samples.

- although cause-effect cannot be concluded in any direction, it would be worth it to provide possible explanations from the available literature

- authors do not emphasize enough the relevance of their results for the daily clinical practice

BMJ Open: first published as 10.1136/bmjopen-2024-087640 on 22 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 9, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Reviewer 2

Name Huang, Wenbo

Affiliation Juntendo University Graduate School of Medicine, Department of Clinical Translational Science

Date 03-Sep-2024

COI No

Comment：

This cross-sectional study recruited 737 patients among Han Chinese population, aimed to investigate the association between overweight and MDD comorbid anxiety.

Major revison:

1.Study design：The purpose of the study was to examine the prevalence of obesity in the MDD comorbid anxiety group.

1.1

Given that comorbid anxiety is very common among individuals with major depressive disorder (MDD), why is the topic of comorbid anxiety worthy of a separate article, considering the existence of extensive prior research on the association between MDD and obesity? To explore the uniqueness of comorbid condition, why not include an MDD-only (without anxiety) group and an anxiety-only (without MDD) group as a control?

1.2

Since the authors are investigating period prevalence, why do the inclusion and exclusion criteria (lines 90-101) seem more aligned with incidence rather than prevalence? To study the risk factors for a disease, should incidence or prevalence be selected? Additionally, could you explain why patients with a history of previous hospitalizations (lines 93-94) were excluded? How might this history serve as a confounding factor between overweight and MDD comorbid anxiety? Furthermore, why would a history of outpatient treatment introduce a confounding factor (lines 232-234)? If these questions cannot be adequately answered, please consider whether the sample selected by these inclusion and exclusion criteria is sufficiently representative.

2.Outcome：

In Table 1 (lines 20-23), the data provided for the obese group (unmarried: 114, married: 296) and the normal group (unmarried: 114, married: 213) was used to perform a chi-square test. Upon re-calculating the chi-square test for these groups, I found a discrepancy: the chi-square statistic was 3.92 with a p-value of 0.048, which differs from the values reported in

BMJ Open: first published as 10.1136/bmjopen-2024-087640 on 22 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 9, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

the manuscript (chi-square statistic 4.24, p-value 0.039). Please explain and re-check other outcomes.

VERSION 1 - AUTHOR RESPONSE

Comments from Reviewer 1:

 # Comment 1: This was an interesting paper to read. I found it very clear and concise in its objectives. Although the design and statistics may seem simple; yet, the findings can be very useful for multidisciplinary work in clinical settings.

Response: Thank you for recognizing the work we do.

 # Comment 2: given that it is a cross-sectional study I would not feel accurate to call "risk factors" to those variables that resulted significantly associated with the outcome. We cannot infer from data the direction of the association, neither if there are any mediators for those associations.

Response: Thank you for your comments. The inability to obtain “causality” is one of the shortcomings of cross-sectional studies. In the revised version of the manuscript, both in the abstract and in the main text, we have uniformly amended “risk factors” to “positive predictors” and other similar expressions (lines 27,33,35,37,82,174,182,191,209, 221, 250).

 # Comment 3: given that it was a finite population i missed the sample size estimation.

Response: Thank you for pointing this out, and your comments have further motivated us to improve the rigor and integrity of the manuscript. On lines 87-93 of the revised manuscript, we have added a statement about the method of predicting sample size.

 # Comment 4: no report of cheking the parameters for a normal distribution to support the uso of parametric tests.

Response: Thank you for pointing this out. We revised this statistical deficiency in the revised version of the manuscript. We have redescribed the corrected statistics in lines 140-146. More importantly, we performed full normality tests for the continuous variables in **Table 1** and Mann-Whitney U-tests for parameters with non-normal distributions.

 # Comment 5: no report of power, which may inflate the significance of small differences

BMJ Open: first published as 10.1136/bmjopen-2024-087640 on 22 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 9, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

in big samples.

Response: Thank you for pointing this out. In lines 92-93 of the revised version of the manuscript, we account for the value of statistical power.

 # Comment 6: although cause-effect cannot be concluded in any direction, it would be worth it to provide possible explanations from the available literature.

Response: Thank you for your comment. We cite in the discussion section the appropriate literature for describing the relationship between the identified clinical variables and overweight. For example, on lines 213-218, we discuss the effect of married status on being overweight. In lines 226-232, we discuss the potential mechanisms of thyroid function on metabolic disorders.

 # Comment 7: authors do not emphasize enough the relevance of their results for the daily clinical practice

Response: Thank you for the comments, they are very helpful in improving our writing and the quality of our manuscripts. We have separately highlighted the clinical significance of the variables identified as having an impact on overweight (lines 218-220, 232-235).

Comments from Reviewer 2:

This cross-sectional study recruited 737 patients among Han Chinese population, aimed to investigate the association between overweight and MDD comorbid anxiety. Major revison:

 # Comment 1: Study design： The purpose of the study was to examine the prevalence of obesity in the MDD comorbid anxiety group.

Response: Yes, that is the purpose of this study is to explore the incidence of being overweight in patients with acute-phase depression with co-morbid anxiety.

 # Comment 1.1.1: Given that comorbid anxiety is very common among individuals with major depressive disorder (MDD), why is the topic of comorbid anxiety worthy of a separate article, considering the existence of extensive prior research on the association between MDD and obesity?

Response: Thanks for your comment. Under the premise of the prevalence of co-morbid anxiety symptoms MDD, understanding the clinical characteristics of obesity or overweight in the target population is an important prerequisite for implementing effective clinical management. Anxiety symptoms and obesity are all important factors that negatively empower MDD patients, and all three are intertwined and causal, increasing the difficulty of treatment

BMJ Open: first published as 10.1136/bmjopen-2024-087640 on 22 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 9, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

and long-term prognosis of MDD. Based on this, we believe that the MDD population with co-morbid anxiety cannot be overemphasized.

 # Comment 1.1.2: To explore the uniqueness of comorbid condition, why not include an MDD-only (without anxiety) group and an anxiety-only (without MDD) group as a control?

Response: Thanks for your comment. Needless to say, yours raises a very interesting and important question that is worth the extra time and effort of further exploration and research. However, this study was set up as a cross-sectional study used to discover the clinical characteristics of overweight in patients with co-morbid anxiety MDD, rather than a case-control study. Therefore, it is beyond the scope of our study, but it will certainly open up ideas for our next research.

 # Comment 1.2.1: Since the authors are investigating period prevalence, why do the inclusion and exclusion criteria (lines 90-101) seem more aligned with incidence rather than prevalence? To study the risk factors for a disease, should incidence or prevalence be selected?

Response: Thank you for pointing this out. Your comments have enabled us to clarify the difference between prevalence and incidence and to improve the quality and standard of our writing. In the revised version of the manuscript, we have corrected the inaccurate use of "prevalence" (lines 14,27, 81,117,185,192).

 # Comment 1.2.2: Additionally, could you explain why patients with a history of previous hospitalizations (lines 93-94) were excluded? How might this history serve as a confounding factor between overweight and MDD comorbid anxiety?

Response: Thank you for pointing this out. The original intent of the study was to study patients with MDD in the acute phase and to minimize confounding factors of relapse after prolonged illness and prolonged exposure to medications, hence the "first hospitalization" approach. Your comment made us realize that the "first hospitalization" restriction did not seem to completely avoid the above confounders, which was a stimulus to our study design skills. To avoid ambiguity, we have rewritten the study design section to highlight "acute phase" and avoid "first hospitalization" (lines 15-16, 21, 88-89, 104).

 # Comment 1.2.3: Furthermore, why would a history of outpatient treatment introduce a confounding factor (lines 232-234)? If these questions cannot be adequately answered, please consider whether the sample selected by these inclusion and exclusion criteria is sufficiently representative.

Response: Thank you for pointing this out. Your review is an encouragement to our efforts to improve our ability to upgrade our research and is meaningful to our academic abilities. We also realize it's a confounding factor now. Therefore, in the revised version of the manuscript, we emphasized the "acute and hospitalized" disease state of the study population, although this ignored previous antidepressant exposure as a potential confounder. We believe that this will help clinicians and caregivers to inform and warn about weight management in the target population at the time of admission (lines 83-84).

BMJ Open: first published as 10.1136/bmjopen-2024-087640 on 22 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 9, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Comment 2: In Table 1 (lines 20-23), the data provided for the obese group (unmarried: 114, married: 296) and the normal group (unmarried: 114, married: 213) was used to perform a chi-square test. Upon re-calculating the chi-square test for these groups, I found a discrepancy: the chi-square statistic was 3.92 with a p-value of 0.048, which differs from the values reported in the manuscript (chi-square statistic 4.24, p-value 0.039). Please explain and re-check other outcomes.

Response: Thank you for pointing this out. We re-run the original data and the chi-square value of 4.24 and p = 0.039 were the exact arithmetic results. The revised version of the manuscript ensured that all descriptions of the results were consistent with those presented in the Tables.

VERSION 2 - REVIEW

Reviewer	**1**
Name	**Gomez-de-Regil, Lizzette**
Affiliation	**Hospital Regional de Alta Especialidad de la Peninsula de Yucatan**
Date	**30-Jan-2025**
COI	

---

all comments were properly addressed

Reviewer	**2**
Name	**Huang, Wenbo**
Affiliation	**Juntendo University Graduate School of Medicine, Department of Clinical Translational Science**
Date	**02-Jan-2025**
COI	

Thank you for your response. I have no further concerns and wish you a happy and prosperous New Year in 2025.

BMJ Open: first published as 10.1136/bmjopen-2024-087640 on 22 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 9, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.