PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between severity of depressive symptoms and chronic knee pain in Korean adults aged over 50 years: a cross-sectional study using nationally representative data
AUTHORS	HAN, SUBIN; Lee, Sook-Hyun; Ha, In-Hyuk; Kim, Eun-jung

VERSION 1 – REVIEW

REVIEWER	Alan Rathbun Assistant Professor of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA
REVIEW RETURNED	07-Aug-2019

GENERAL COMMENTS	This manuscript highlights a cross-sectional analysis of secondary data from a national survey study conducted in Korea that assessed the relationship between depressive symptoms and knee pain. There are several conceptual and methodological issues with this manuscript that compromise what little clinical utility this study has to offer. All of these problems aside, the primary issue with this study is the lack of novelty. The purported innovation in the current report, i.e., research gap it intends to fill, is assessing the relationship between depressive symptoms and pain using a numerical rating scale (NRS) for knee pain severity. A plethora of prior studies have examined the relationship between depressive symptoms and pain severity in osteoarthritis patients using a wide variety of patient-reported pain scales, of which, the NRS represents. Even if true, which is questionable given the paucity of appropriate references, using a specific type of patient-reported outcome measure for pain does represent an advance beyond existing research in terms of this etiological relationship. Other major issues include: 1) the discussion that is almost entirely a re-iteration of the results and fails to evaluate the findings in the context of current research; poor literature review that misses the majority of new studies that have been conducted in this area; and poor writing, particularly in terms of organization and English language.

REVIEWER	Michelle Yau Hebrew SeniorLife, USA
REVIEW RETURNED	23-Sep-2019

GENERAL COMMENTS	This study aims to establish the relationship between depressive symptoms and knee pain in a nationally representative cohort of individuals in Korea using the KNHANES. Limitations are that the

study is cross-sectional and the longitudinal or even bi-directional relationship between depressive symptoms and knee pain cannot be determined.

While I appreciate that the authors identified a relationship between depressive symptom severity and knee pain severity in the Korean population, my major criticism is that these findings do not add much to what is already known. An association between depressive symptoms and knee pain inherently assumes greater depressive symptoms should be associated with greater knee pain since the underlying distribution is continuous. The key finding that depression severity is associated with intensity of knee pain seems incremental. The manuscript does not go beyond this to explore whether the relationship may linear (or U, J-shaped, etc.) or to identify factors that may mediate the relationship.

Minor concerns:

1) It was unclear why analyses were restricted to individuals 50 years of age and above. The sample size would have been much larger if those ages less than 50 years of age were included.
2) The terms depression and depressive symptoms are used interchangeably – the questionnaire does not diagnose depression so depressive symptoms should be used consistently throughout the manuscript.
3) Authors attribute the relationship between knee pain and lower prevalence of smoking and alcohol use to the higher proportion of women with knee pain. The basis of this claim is unclear. Would the same relationship be observed if analyses were stratified by gender? What else could explain this unexpected finding?
4) The authors erroneously claim that that they found a linear correlation/relationship based on increasing magnitudes for odds ratios. Logistic regression based on categorical variables may identify a relationship, but this may not necessarily be linear. Further, methods for the trend analysis were not provided.
5) There is inconsistent use of 95% CIs and p-values with an excessive number of decimal places. ORs and 95% CIs do not need to be repeated in discussion as these values were already provided in the results. Further, 95% CIs provide more info than p-values so my preference would be to only include 95% CIs rather than p-values or both 95% CIs and p-values.
6) Line 195 should be 'Clinical Characteristics of Participants with chronic knee pain…' rather than 'Clinical Characteristics of Participants with chronic depression…'. Line 417 should state '…differences between groups with/without depression' not '…differences between groups with/without knee pain'

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Comment 1: Reviewer: 1
Reviewer Name: Alan Rathbun
Institution and Country: Assistant Professor of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA
Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

This manuscript highlights a cross-sectional analysis of secondary data from a national survey study conducted in Korea that assessed the relationship between depressive symptoms and knee pain. There are several conceptual and methodological issues with this manuscript that compromise what little clinical utility this study has to offer. All of these problems aside, the primary issue with this study is the lack of novelty.

The purported innovation in the current report, i.e., research gap it intends to fill, is assessing the relationship between depressive symptoms and pain using a numerical rating scale (NRS) for knee pain severity. A plethora of prior studies have examined the relationship between depressive symptoms and pain severity in osteoarthritis patients using a wide variety of patient-reported pain scales, of which, the NRS represents. Even if true, which is questionable given the paucity of appropriate references, using a specific type of patient-reported outcome measure for pain does represent an advance beyond existing research in terms of this etiological relationship.

Our response: Thank you for the suggestion. Previous longitudinal study (reference 16) demonstrated that pain severity was a strong predictor of subsequent depression severity. However, our study is a cross-sectional study which analyzed both aspects of severity of chronic knee pain and severity of depressive symptoms, using NRS and PHQ-9. We found chronic knee pain is a risk factor of severe depressive symptoms, and depressive symptom is also related with severe chronic knee pain.

Comment 2: Other major issues include: 1) the discussion that is almost entirely a re-iteration of the results and fails to evaluate the findings in the context of current research; poor literature review that misses the majority of new studies that have been conducted in this area; and poor writing, particularly in terms of organization and English language.
Our response: We agree that there was a re-iteration of the results in the discussion part. We deleted the re-iteration part from the discussion, and described the signification of our study. Regarding English language, we requested English correction, and attach certificate.

Reviewer: 2
Reviewer Name: Michelle Yau
Institution and Country: Hebrew SeniorLife, USA
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
This study aims to establish the relationship between depressive symptoms and knee pain in a nationally representative cohort of individuals in Korea using the KNHANES. Limitations are that the study is cross-sectional and the longitudinal or even bi-directional relationship between depressive symptoms and knee pain cannot be determined.

While I appreciate that the authors identified a relationship between depressive symptom severity and knee pain severity in the Korean population, my major criticism is that these findings do not add much to what is already known. An association between depressive symptoms and knee pain inherently assumes greater depressive symptoms should be associated with greater knee pain since the underlying distribution is continuous.
Our response: As a retrospective cross-sectional study, we described that the results of this study cannot reveal cause-effect relationship between chronic knee pain and depressive symptoms. However, we found a strong relationship between severity of chronic knee pain and severity of depressive symptom, and to our knowledge, our study is first to analyze both aspects of severity of depressive symptoms and intensity of chronic knee pain.
Comment 1: The key finding that depression severity is associated with intensity of knee pain seems incremental. The manuscript does not go beyond this to explore whether the relationship may linear (or U, J-shaped, etc.) or to identify factors that may mediate the relationship.

Our response: Thank you for valuable comment. According to a previous longitudinal study, pain severity was a strong predictor of subsequent depression severity. The results of Table 4 demonstrate that in mild knee pain (NRS 0-4), 1.7% of the study population showed moderately sever depressive symptom. In moderate knee pain (NRS 5-7), 3.4% of the study population showed moderately severe depressive symptom, and in intense knee pain (NRS 8-10) 10.8% of the study population showed moderately severe depressive symptoms. These results demonstrate that severe knee pain and severe depressive symptoms are related, and this is a cross-sectional proof of previous longitudinal study. Figure 2 has been replaced by a linear graph rather than a bar graph.
Minor concerns:

Comment 2: It was unclear why analyses were restricted to individuals 50 years of age and above. The sample size would have been much larger if those ages less than 50 years of age were included.
Our response: Thank you for your valuable comment. Since the questionnaire regarding chronic knee pain was only asked to respondents aged 50+ in KHANES VI-2, analyzed data was limited to population aged over 50. (Page 6, lines 157-159).

Comment 3: The terms depression and depressive symptoms are used interchangeably – the questionnaire does not diagnose depression so depressive symptoms should be used consistently throughout the manuscript.
Our response: We unified the interchangeably used term of 'depression' and 'depressive symptom' to 'depressive symptom'. However, when a reference related to 'Depression' was quoted, the term 'Depression' was still used.

Comment 4: Authors attribute the relationship between knee pain and lower prevalence of smoking and alcohol use to the higher proportion of women with knee pain. The basis of this claim is unclear. Would the same relationship be observed if analyses were stratified by gender? What else could explain this unexpected finding?
Our response: Thank you for your valuable comment. We did not intended to attribute the relationship between knee pain and lower prevalence of smoking and alcohol use to the higher proportion of women with knee pain. Because of the cultural differences in Korea, it seems that differences in smoking and alcohol use between men and women have occurred, and we have tried to adjust them. Therefore, we deleted repeated description of results of Table 1 and Table 2 and a vague expression (This result is attributable to a high percentage (77.8%) of women in the study population with knee pain) in the discussion part.

Comment 5: The authors erroneously claim that that they found a linear correlation/relationship based on increasing magnitudes for odds ratios. Logistic regression based on categorical variables may identify a relationship, but this may not necessarily be linear. Further, methods for the trend analysis were not provided.
Our response: Thank you for your valuable comment. We agree that logistic regression based on categorical variables may not necessarily be linear. Therefore, we were able to obtain a linear graph between pain and depression through re-verification. To verify linear relationship between intensity of chronic knee pain and depressive symptoms, we used Cochran-Armitage trend test and complex samples logistic regression. Moreover, 'p for trend' of pain and depressive symptom was derived from Chi-Square test. We added this in the 'Statistical Analysis' part of Methods, and table of Cochran-Armitage trend test and figure of complex samples logistic regression are attached as a supplementary Table 1, Supplementary Figure 1 and Supplementary Figure 2. (Page 7, lines 190-195)

Comment 6: There is inconsistent use of 95% CIs and p-values with an excessive number of decimal places. ORs and 95% CIs do not need to be repeated in discussion as these values were already provided in the results. Further, 95% CIs provide more info than p-values so my preference would be to only include 95% CIs rather than p-values or both 95% CIs and p-values.

Our response: Thank you for your valuable comment. Based on your comment, we deleted repeated results, ORs and 95% CIs in the discussion. In addition, we revised as present both 95% CI and p-values in the description of the results.

Comment 8: Line 417 should state '…differences between groups with/without depression' not '…differences between groups with/without knee pain'
Our response: Thank you for your valuable comment. Based on your comment, we revised the manuscript. (page 14, lines 364-365)

VERSION 2 – REVIEW

REVIEWER	Michelle Yau Hebrew SeniorLife, USA
REVIEW RETURNED	04-Nov-2019

GENERAL COMMENTS	The study is a relatively simplistic and straightforward examination of the cross-sectional relationship between severity of depressive symptoms and severity of knee pain. Despite the improvements made in the manuscript, I still think that the main findings are incremental given the number of publications that have already examined this question. However, most studies have been conducted in European ancestry populations and this study provides a glimpse into the relationship between depression and knee pain in a Korean population using a large nationally representative survey (Korean National Health and Nutrition Examination Survey, KNHANES). Note that KNHANES and KHANES is used interchangeably throughout the manuscript – the correct acronym should be used. The manuscript should be edited for English grammar.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: Michelle Yau
Institution and Country: Hebrew SeniorLife, USA
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
The study is a relatively simplistic and straightforward examination of the cross-sectional relationship between severity of depressive symptoms and severity of knee pain. Despite the improvements made in the manuscript, I still think that the main findings are incremental given the number of publications that have already examined this question. However, most studies have been conducted in European ancestry populations and this study provides a glimpse into the relationship between depression and knee pain in a Korean population using a large nationally representative survey (Korean National Health and Nutrition Examination Survey, KNHANES).
Note that KNHANES and KHANES is used interchangeably throughout the manuscript – the correct acronym should be used. The manuscript should be edited for English grammar.
Our response: Thank you for valuable comment. We revised the wrong term 'KHANES' to 'KNHANES'. (page 5 line 131, page 5 line 136, page 7 line 183, page 9 line 278. In addition, we revised some a typing errors(relationsh210ip), and deleted some repeated descriptions (confirming a

clear association between depressive symptoms and chronic knee pain, PHQ 9 is a reliable measure of depressive symptoms, and has been used by previous studies to measure severity of depressive symptoms.). Moreover, we added a sentence (page 5, line 122) and a reference (page 4 line 92-93) in introduction to clarify our intentions. We also deleted a reference, because it did not match with our intention (Guilak F. Biomechanical factors in osteoarthritis. Best Practice & Research. Clinical Rhematology. 2011;25(6):815-23.) Regarding English grammar, our manuscript is edited and reviewed by an English editing company.