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

TITLE (PROVISIONAL)	The influence of multisite pain and psychological comorbidity on prognosis of chronic low back pain: Longitudinal data from the Norwegian HUNT Study
AUTHORS	Nordstoga, Anne Lovise; Nilsen, Tom; Vasseljen, Ottar; Unsgaard-Tøndel, Monica; Mork, Paul Jarle

VERSION 1 - REVIEW

REVIEWER	Julie Fritz University of Utah, Salt Lake City, Utah, United States
REVIEW RETURNED	09-Jan-2017

GENERAL COMMENTS	This paper presents data from the Norwegian HUNT cohort study and addresses a relevant question related to the role of widespread pain as a prognostic factor for recovery from chronic LBP. The paper is generally well-written. My recommendations for the manuscript are outlined below. 1. Should the risk ratios reported be for the outcome of non-recovery instead of recovery? It seems odd to discuss the risk of recovering. 2. The methods used to collect data on physical activity levels and physical work demands should be described in the methods. How were these questions posed to participants? 3. In Table 2 - recommend removing the RR values that are adjusted only for age. These do not add anything to the results reporting. 4. Clarify for readers that the number of pain sites includes the participant's LBP complaint. 5. The rationale for excluding participants who were underweight based on BMI is not provided. 6. The paragraph in the discussion section about the Keele screening tool is premature given the limitations of this study. The Keel instrument was designed to predict different outcomes at different time periods. The Keele tool does include questions related to the concept of widespread pain. How different counting pain sites would be would require additional research. I recommend removing this paragraph. 7. Also in the Discussion section, the first paragraph uses terminology that implies causation in a manner not justified by the study design.

REVIEWER	FİLİZ ALTUĞ Pamukkale University, School of Physical Therapy and Rehabilitation, Denizli, TURKEY
REVIEW RETURNED	23-Jan-2017

GENERAL COMMENTS	This is an important article because the study population is very large.

REVIEWER	Antonella Ciaramella Aplysia Onlus, GIFT Institute of Integrative Medicine, Pisa, Italy
REVIEW RETURNED	15-Feb-2017

GENERAL COMMENTS	This paper reports data from the HUNT longitudinal epidemiological study on how multisite pain and psychological comorbidity influence prognosis in lower back pain (LBP). Findings from the HUNT study, conducted on a cohort from the Norwegian general population from 1995 until 2008, on the influence of psychological aspects and/or chronic widespread pain on pain chronicity and other pain-associated complications have already been published (e.g. Munday et al., 2014; Kaasbøll et al., 2014; Heuch et al., 2016 etc), but this is the first time this issue has been addressed. The paper investigates the probability of patients recovering from chronic LBP (recovery is defined as the presence of low back during HUNT2 but not at HUNT 3 (after 11-year follow-up)) as related to the number of pain sites, pain-related disability, psychological symptoms, and self-rated general health. Poisson regression analysis was used to estimate the associations among these variables and risk ratios for recovery. A significant achievement of this manuscript is having shown that the presence of widespread pain comorbidity contributes to poor prognosis in lower back pain, without gender differences (page 14, lines 37–38). However, it is important to note that the HADS questionnaire used, even though considered a valid tool for population-based studies (page 15, lines 50–54), it is not an entirely reliable means of investigating anxiety in chronic low back pain. Indeed it has been found that chronic LBP, more than other forms of chronic pain, is associated with elevated phobic traits, in particular agoraphobia, which HADS is not able to highlight (Ciaramella & Poli, 2015). That being said, I do think this manuscript should be accepted for publication, because it reports new and important knowledge about prognostic factors in chronic low back pain. Furthermore, it concords with the aim and scope of BMJ Open, in particular: a) This study involves epidemiological research into public health b) Despite the publication of several previous articles on the HUNT study, this manuscript provides new and interesting findings c) I have not found published studies ascribed to the first author, so I assume that it has been written by a newcomer researcher d) Statistical analyses are appropriate However, before publication, I believe that the authors should address the following points: 1. The meaning of dose-dependent in this context; please explain. 2. It is not clear if the observed recovery was due to subjects receiving particular treatments; please clarify. 3. Why was 4 taken as a cut-off for pain sites? Please explain. After these minor points have been clarified, I believe that this article will be suitable for publication, and my recommendation is therefore

	as follows: Accept with minor revision

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:
Thank you for your comments and recommendation for the manuscript. We appreciate the comments, and try to accommodate your suggestions below:

1. Should the risk ratio reported be for the outcome non-recovery instead of recovery? It seems odd to discuss the risk of recovering.
Response: We agree that this is a difficult issue and we have discussed this several times during the writing of the manuscript. We think it is important to emphasize improvement and recovery rather than non-recovery, and have chosen to keep this as an outcome in the revised version. Although it may seem odd to discuss risk of recovering, we believe that the appropriate statistical analyses of this prospective study is to estimate differences in risk of recovery between exposure categories. However, risk could also be termed probability and we have rephrased the revised version of our manuscript to reflect that we study “probability of recovery”. We have also clarified this in the “Statistical analysis” section.

2. The methods used to collect data on physical activity levels and physical work demands should be described in the methods. How were these questions posed to participants?
Response: The variables on level of leisure time physical activity and physical work demands were used as confounders along with other variables, and were therefore not explicitly described in the original manuscript. We have now included a brief description of questions and response options for all possible confounders included in the analyses, in the Method under the subsection “Possible confounders”. New subheadings were generated to separate the confounders from the comorbidities.

3. In Table 2 - recommend removing the RR values that are adjusted only for age. These do not add anything to the results reporting.
Response: Our reported age-adjusted estimates have been changed to crude estimates in the revised manuscript. This is in agreement with the STROBE guideline for cohort studies, recommending that unadjusted and confounder-adjusted estimates should be reported to be able to assess the amount of confounding in the data.

4. Clarify for readers that the number of pain sites includes the participant's LBP complaint.
Response: We appreciate this comment. A more thorough description of number of pain sites are now included in the methods subsection “Chronic low back pain” in the revised manuscript.

5. The rationale for excluding participants who were underweight based on BMI is not provided.
Response: We agree that the rationale for excluding participants who were underweight should be described. This has been included in the revised manuscript under the subsection “Study population”.

6. The paragraph in the discussion section about the Keele screening tool is premature given the limitations of this study. The Keel instrument was designed to predict different outcomes at different time periods. The Keele tool does include questions related to the concept of widespread pain. How different counting pain sites would be would require additional research. I recommend removing this paragraph.
Response: We agree that additional research regarding the Keele screening tool is needed and that the studies cannot be directly compared. Thus, we find it appropriate to remove this paragraph in the

revised manuscript.

7. Also in the Discussion section, the first paragraph uses terminology that implies causation in a manner not justified by the study design.
Response: We agree that the terminology we have used could imply causation. This has been changed in the revised manuscript.

Reviewer #2:
We appreciate the recommendation to publish our article.

Reviewer #3:
Thank you for your thorough review and for pointing out the importance of this manuscript. We appreciate your recommendation for publication, and tried to address the points you suggested.

1. The meaning of dose-dependent in this context; please explain.
Response: Thank you for addressing this. We have changed the term to the more appropriate “dose-response” association. Further, we have included a description of the p-trend test in the subsection “Statistical analysis” in the revised manuscript.

2. It is not clear if the observed recovery was due to subjects receiving particular treatments; please clarify.
Response: This is an important point and we appreciate your comment. The current study is based on data from a population study with 11-year follow-up. Unfortunately, information was obtained only at baseline and changes occurring during the follow-up period could not be taken into account. This limitation is addressed in the second last paragraph in the discussion.

3. Why was 4 taken as a cut-off for pain sites? Please explain.
Response: Thank you for addressing this. We have clarified this in the subsection “Statistical analyses” in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Antonella Ciaramella Aplysia onlus, GIFT Institute of Integrative Medicine, Pisa, Italy
REVIEW RETURNED	05-Apr-2017

GENERAL COMMENTS	The authors have responded to all of my comments. However, I find repeated references (ref. 21 and 25) so you need to make corrections