Author’s response to reviews

Title: Patients with chronic Pain: Evaluating Depression and their Quality of Life in a single center study in Greece

Authors:

Ekaterini Rapti (ksprapti2@gmail.com)
Dimitrios Damigos (ddamigos@gmail.com)
Paraskevi Apostolara (v.apostolara@gmail.com)
Vasiliki Roka (vassoroka2003@yahoo.gr)
Christos Lionis (lionis@galinos.med.uoc.gr)

Version: 3 Date: 24 Jun 2019

Author's response to reviews

Title: Patients with chronic Pain: Evaluating Depression and their Quality of Life in a single center study in Greece

Authors:

Ekaterini Rapti (ksprapti2@gmail.com)
Dimitrios Damigos (ddamigos@gmail.com)
Paraskevi Apostolara (v.apostolara@gmail.com)
Vasiliki Roka (vassoroka2003@yahoo.gr)
Chara Tzavara (htzavara@med.uoa.gr)

Christos Lionis (lionis@galinos.med.uoc.gr)

Version: 3 Date: May 31, 2019
We would like to thank both reviewers for their comments. We have revised the manuscript. We hope that this revision will meet the high quality standards of BMC Psychology, and we are hoping for a positive decision concerning publication of the manuscript.

For convenience of reviewers, we are sending the manuscript and in track change form.

Reviewer reports:

Jared Smith (Reviewer 3)

Major points

1. Abstract. p.1 Lines 27-44. The Results section of the Abstract is unclear - are results stated from univariate or regression analyses - if the associations reflect findings from the regression analyses, then best to make that clear and note in an appropriate manner (e.g., Regression analyses revealed that female gender, having a chronic mental disorder… were independently related to decreased quality of life).

Answer

Thank you. It was corrected.p1, paragraph 3.

2. Introduction. The strength of this study is the population under study and the large number of variables examined. While the Introduction does provide some rationale for the study, this could be developed further.

Answer

Thank you for your comment, we have included a paragraph in the introduction about the variables that we examined, according to your suggestion.p., lines 8-12

3. Results pp.7-10. It is unclear why the analyses pertaining to impact of chronic pain, which appears to be the focus of the paper, included all patients presenting to the (primary care) clinic. This especially makes interpretation of the regression analyses complicated (for example, in Table 5, do the significant independent variables suggest these patient characteristics are important in depression for patients attending primary care, or are they important in patients with chronic pain attending primary care?). Would be more informative to analyze (at least in associative analyses) only patients with chronic pain.
Answer

All analyses were conducted again in the group of patients with chronic pain and the new results are now presented and discussed. p. 8-10.

4. Results Tables 2,3. Why are only continuous variable correlates of PHQ-9 scores considered in Table 2 and all univariate analyses for EQ-5D scores presented in Table 3? Would be preferable to have both PHQ-9 and EQ-5D considered in the same manner (preferably in a single table).

Answer

All univariate analysis for both PHQ-9 and EQ-5D is now presented in the same table. p.20, table 3.

5. Results pp.9-10 Tables 4,5. The regression analyses are problematic. The use of pain severity and pain interference as dependent measures in one set of analyses (Table 4) and then independent variables in subsequent analyses (Table 5) is unhelpful and renders focus unclear. Further, stepwise regression methods are most appropriate for use in exploratory research. The relationship between pain intensity/interference and depression/quality of life in patients with chronic pain is already well established - a forced entry or hierarchical approach (according to type of variable; e.g., demographic, pain-related, other clinical) including those variables identified as significant correlates in univariate analyses for depression and for quality of life would be a preferred method.

Answer

A forced analyses are now presented for all dependent variables and all independent variables are shown.

6. Results pp. 9-10 Tables 4,5. What was the overlap between depression as determined by PHQ-9 cut-off and the chronic mental disorder - if significant, then including both indices of mood in regression models is largely unwarranted.

Answer

Thank you for the comment. Chronic mental disorder was removed from the regression analysis that included the PHQ-9.
7. Discussion p.10 Lines 36-49. Literature pertaining to studies of chronic pain, depression and quality of life in patients presenting to primary care services would be especially helpful here (e.g., Arnow et al., 2006).

Answer

Thank you. We have already used the study Arnow et al., 2006 in the discussion section.p. 11, lines 8.

8. Discussion p.11 Lines 6-23. The findings of chronic pain in more than half the attending patients is important. Would be helpful to compare with other pain prevalence studies, especially those concerning patients in primary care settings.

Answer

We added some more sentences about the prevalence of chronic pain in primary care.p. 11 lines 6-7.

9. Discussion p.14 Lines 4-22. A primary limitation of the study is the cross-sectional design, which limits firm statements about the direction of causality between pain and psychological dysfunction (e.g., depression). This should be noted.

Answer

Thank you. We did so accordingly. p. 14 lines 18-19.

10. Discussion p.14 Lines 4-22. Another important limitation of the study is the absence of measurement of pain-specific constructs (other than pain interference) such as pain catastrophizing, acceptance and self-efficacy, all of which have been associated with psychological dysfunction and quality of life in individuals with chronic pain (e.g., Mason et al., 2008; Sullivan et al. 2005; Turner et al., 2005). This should be acknowledged.

Answer

We thank the reviewer for these suggestions and have updated the references accordingly.p14, lines 20-26.
Minor comments:

1. **Introduction p.3 Lines 9-20.** The sentence beginning 'However, this subject has not received much attention in…' needs rephrasing.

   **Answer**

   Thank you for your comment. We added some more sentences to make it clear. p.3, lines 7-9.

2. **Introduction p.3 Line 41.** '…main types of pain..' could perhaps be more clearly described as '…pain characteristics (e.g., location)...'.

   **Answer**

   Thank you. We have replaced it. p. 4, lines 1-2.

3. **Methods p.4 Lines 41-43.** The statement 'For the purpose of this study, chronic pain is defined as constant pain or pain that flares up frequently, and has been experienced for at least 3 months' needs a reference.

   **Answer**

   We have added the reference accordingly. p. 4, line 14.

4. **Methods p.5 Line 50.** What qualified as a 'chronic disease'? Some examples would be helpful.

   **Answer**

   With the phrase ‘chronic disease’ we meant disease like cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease etc. The information was added in the text. P. 6, lines 8-9.
5. Methods p.6 Lines 37-43. Best to refer to the questionnaire as EQ-5D-3L (and state the three severity levels), considering that the more recent EQ-5D-5L is commonly adopted in pain research. Also, a statement detailing the EQ-VAS is warranted here.

Answer

Thank you. We noted it in the text. p.7.

6. Results p.8 Lines 41-52. Providing means (SD) or medians (IQR) for these variables where significant differences were observed would be helpful here.

Answer

Mean and medians for the associations not presented in the tables are shown in the text.

7. Results p.9 Lines 24-28. t and r values for these analyses are clearly displayed in Table 3. As such, no need to repeat values in text.

Answer

We removed them from the text.

8. Results p.9 Lines 24-28. How do the EQ-Health and EQ-VAS scores compare with the general Greek population (from normed studies)?

Answer

According to the study "Validity of the EuroQoL (EQ-5D) Instrument in a Greek General Population from Nick Kontodimopoulos et al" the mean EQ-5D score was 0.80 (SD=0.27) and the mean VAS score was 75.06 (SD=20.49). Subjects that reported chronic pain in our study had significantly lower scores on both EQ-5D (p<0.001) and VAS (p<0.001).

9. Methods p.7 Lines 13,40. Results pp.8-10. The adopted alpha value for the study is stated as 0.05 but earlier in the paragraph it is noted the Bonferroni correction was used. This needs clarifying. Also, are the p values subsequently stated in the text and tables of the Results the original p values or the Bonferroni-corrected values?
The Bonferroni correction in the analysis was applied for the comparisons made in the same group of the same independent variable as a post-hoc procedure after ANOVA. Due to the large number of comparisons presented in the table the Bonferroni correction was not set for all of them, since this could lead to a very high rate of false negatives.

10. Results Table 1. Would be easier to read if each variable/construct was classified under appropriate headings (sociodemographic, clinical, pain etc.).

Answer

Thank you for your comment. We have added some headings in the table 1.

11. Results pp.9-10 Tables 4,5. The power analyses (p.5) used to estimate sample size for regression analyses assumed an effect size of 0.13. What were the observed effect sizes in regression analyses? Also, a summary value for total variance explained by models, such as adjusted R-squared, would be helpful.

Answer

Cohen computed effect sizes ranged from 0.14 to 1.38. R-squared were added in the regression tables, thank you for the reminder.

12. Discussion p.14 Lines 5-7. I'm not sure a chronic pain sample size of 200 is small as suggested by the authors.

Answer

Thank you. We have corrected it.

13. General. There remains several places where decimal points and commas are missing or interchanged.

Answer

We have made appropriate corrections. Thank you!
Sarah Harrisson (Reviewer 4):

Title:
The study reports on patients with and without non-cancer pain. Please re-write the title to reflect the patients in the study.

Answer
We have corrected it.

Introduction:
The readers that may be interested in this manuscript are likely to be those working with patients with pain in Greece. We already know about chronic pain populations in primary care settings in for example the UK (for example see John McBeth's work on pubmed). The research in this manuscript gives an account of patients with chronic pain in Greece and a more succinct account of this would be useful to the reader.

Note: the abbreviation CP is used inconsistently.

Answer
The abbreviation CP for chronic pain is widely used in literature.

Rationale, aims and objectives for the study:
I do not think the rationale for the study, the aims or the objective are not terribly clear and a similar point was raised by reviewers of this manuscript in the past. My suggestion is to clarify why this study is important. For example, is it thought that chronic pain +/- depressive symptoms/ poor quality of life (QOL)) is less prevalent in costal areas than in urban areas and explain what would be the implication of this (for example on resource allocation). Or is it thought that patients visiting primary care in Greece with chronic pain may be different (in terms of depression/ QOL) than those patients in primary care settings outside of Greece?
Thank you for the observation. You are right about the vagueness which is created relating to the geographical correlation and the chronic pain and depression. Given the fact that some studies refer high frequency in depression in urban areas in comparison to the suburban and rural ones, we tried to verify that. Unfortunately, it did not come as a fact in our study. Because of the vagueness that this paragraph creates, we decided to omit it.

Page 3, lines 37 to 43:

Objective 1. What is meant by burden, do the authors mean prevalence? What is meant by a visit to a primary health care unit, is this a consultation with a family doctor, practice nurse? Please clarify.

Answer

By burden we meant the magnitude of the pain. By primary health care unit we meant primary care center in which two family doctors and two practice nurses work.

Objective 2. Please clarify and expand on what is meant by "to analyze the main types of pain". The methods suggest that this is a descriptive analysis of the patients with and without chronic pain.

Answer

Thank you for your comment. We have replaced the phrase with ‘’ to identify pain characteristics like duration, frequency, location…”

Objective 3. Please clarify what is meant by "to refer to the recognition and discussion of the impact of chronic pain on depression and the quality of life"

Answer

We meant ‘’to examine and discuss the impact of chronic pain on depression and the quality of life”
Methods

This appears to be an observational study design. Please provide more details of the study design and the participants. A useful reference for reporting on this type of study design is "The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies" (http://dx.doi.org/10.1016/S0140-6736(07)61602-X).

Answer

We have done so at the best of our abilities following the guidelines STROBE statement.

Exclusion criteria: I am interested to see that patients who had MSK injuries in the previous 3-months were excluded and wonder if the authors meant MSK trauma? I suspect many patients would consult with an episode of increased pain severity +/- new injury and this may have excluded many appropriate patients. Similar comment re excluding those unable to walk- it's likely that those unable to walk had poorer quality of life and more often are depressed. The previous reviewer raised a question about how representative the sample was and I am not sure that this has been addressed sufficiently.

Answer

With MSK injuries we meant trauma. We didn’t include the MSK trauma the previous 3 months because we have perceived like acute pain. With the phrase "unable to walk" we meant conditions that reduce the ability to walk like common injuries caused by falling included fractures (spine, legs, feet), multiple sclerosis, Parkinson disease, ataxia, other conditions that can impair walking. These patients have more often pain and that’s the reason that we excluded them from the study.

Statistical analysis: page 7, lines 3 to 7 (sentence 1). Please clarify what is meant by this sentence. My impression is that this analysis uses quantitative data only, do the authors mean to differentiate between categorical and continuous data?

Answer

We have changed the terms of quantitative and qualitative, with continuous and categorical, respectively.

General comment: I am unsure why quasi-randomisation was used as there was no intervention. Please provide a brief account on the likely effect of this on the results and why it was thought to be important in the discussion.
Answer

Thank you for your comment. We wrote quasi-randomization after suggestion of Mr Haruo Fujino, Ph.D. (Reviewer 1). We have deleted it now.

Results

Descriptive data: This looks like a description of the study sample (please refer to STROBE for a checklist on how to report observational studies).

Main results: Would it be useful to report on prevalence of chronic pain, then report the characteristics (depression/ QOL) of those with and without pain? Overall, this looks like a comparison between patients with and without chronic pain this needs to be clearer throughout.

Answer

Thank you for the comment. Comparisons for all study scales between those with and without chronic pain are now reported.

Linear regression analysis results: Please refer to STROBE for a checklist on how to report outcomes from observational studies.

Answer

Linear regression analysis results were changed and additional information for the models was added.

Discussion

It would be nice to see the key findings in the first couple of sentences of the discussion. I am unclear what the key findings are and how patients who visit Greek primary care settings are the same or different to those in more urban Greek settings or to those in other countries. Please provide more explicit key findings, then make a comparison to the previously published literature of this patient population in and out of Greece.

Answer

We have done so at the best of our abilities in the discussion section.