**Reviewer’s report**

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

**Version:** 3  **Date:** 15 Jul 2019

**Reviewer:** Jared Smith

**Reviewer's report:**

There has been an improvement of the manuscript according to changes made in response to the recommendations of the reviewers, most notably, the clarification of study aims/objectives. But the paper has some structural problems and (regression) analyses remain problematic with findings difficult to interpret in places, which would need to be addressed before being considered as suitable for publication.

Major points

1. **Structure:** The paper remain difficult to follow structurally. For example, the aims are stated in list format on page 3 (lines 46-52), then immediately repeated in prose format on page 4 (lines1-7) and again at the beginning of the Methods (p.4, lines 11-16). Unusually, strengths of the study are stated in the Methods (p.4 lines 21-30). Sample size estimation would be better placed in the statistical analysis subsection (with regression analysis text).

2. **Introduction.** The clarity of study aims/objectives has improved largely as a result of removing the focus of urban versus rural clinics, which in the absence of relevant (comparative) data, was difficult to follow.

3. **Methods p.7 Lines 13,40. Results pp.8-10.** As noted in previous review, the adopted alpha value for the study is stated as 0.05 but earlier in the paragraph it is stated that the Bonferroni correction was used. This needs clarifying (the authors' response in reply letter did not help here). Simply put, are the p values subsequently stated in the text and tables of the Results the original p values or the Bonferroni-corrected values? If the former, then the statement about Bonferroni correction needs to be removed. If Bonferroni is too conservative, the authors could use False Discovery Rate or perhaps simply adopt a smaller p value threshold (e.g., p $<$ 0.01)?
4. Results pp.7-10. Although wary of introducing more analyses into an already complicated manuscript, I wonder if there is any merit in comparing patients with and without chronic pain on key variables.

5. Results Table 2. Inclusion of the means and standard deviation values for univariate comparisons yielding significant differences is warranted here.

6. Results pp.9-10 Tables 4,5. The regression analyses remain problematic. Although forced entry methods are preferable to stepwise approaches, the analyses are underpowered due to the large number of predictors (14 in Tables 4 and 5) given the (maximum) sample size of 113 chronic pain patients (to this end the sample size calculations on page for regression analyses based on 200 participants are largely redundant and do not state number of predictors, rendering them difficult to interpret). A better approach might be to include only those variables identified as significant associates in univariate analyses for depression and for quality of life.

Minor comments:

1. Results, Table 3. Were any tests or examinations performed on the EQ-5D and PHQ-9 subgroup scores in Table 3 to establish that the distributions were approximately normal in comparisons? I ask because it is implied that the comparisons of continuous data used parametric approaches. If a Gaussian distribution is rejected in some comparisons, then tests of association should be done using appropriate tests (e.g., Mann-Whitney, Kruskal Wallis).

2. Results Tables 2,3,4,5 Specifying in the table titles that the (sub)sample only included those with chronic pain and providing the overall n value for would help the reader.

3. Results Tables 2,4,5. Providing both unstandardized and standardized betas in regression models may be helpful. These can be difficult to interpret for categorical variables, particularly in this instance where 'educational level' has 3 categories (presumably each numbered 0, 1 and 2?).
4. Results Table 2,3,4,5. The variable 'How long do you have it, specialist consultation for pain relief' appears to be 2 separate variables in some tables but combined in others. Requires clarification.

5. Discussion p.12 Lines 20-50. This paragraph largely repeats the Results of the study with statistical notion - all findings should ideally be discussed with reference to other studies.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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