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Ying Dou
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Manuscript NO: 48165

Manuscript Type: Systematic Review

Title: Chronic pain, posttraumatic stress disorder, and opioid intake: A systematic review.

Dear Mrs. Ying Dou,

The comments provided by the reviewer have assisted us in the revision process and were much appreciated.

Below, we indicate the comments by the reviewer and our replies. The changes that have been made in the text are highlighted in yellow.

We appreciate the time and effort taken to provide feedback on our manuscript. We hope that our revisions address the issues raised and that the manuscript is now suitable for publication. If you have any questions please contact us by email. We await your editorial decision.

Best regards,

A.E. López-Martínez, Ph.D.

University of Málaga (Spain)

Reviewer's code: 03604107

Kindly try to focus more consistently on your principal aim and findings; the paper is highly professional, but some aspects render it confusing.

Reply: Thank you for your positive feedback. We appreciate the time and effort taken to provide feedback on our manuscript.

This systematic review has been carried out on a recent field of study. The general purpose of this review has been to analyze the studies that relate the three main aspects that guide this manuscript; namely, chronic non-cancer pain, post-traumatic stress disorder, and opioid intake (i.e. prescription, misuse, and abuse). In fact, only 151 records were identified through database searching (5 databases: PubMed, Medline, PsycInfo, Web of Science, and PILOTS), which shows that this is an area with very little research trajectory. In addition, the review was conducted according to the PRISMA 2009 Checklist and PICOS criteria were formulated a priori in the protocol of the systematic review. Selected studies were also assessed for methodological quality using the Scottish Intercollegiate Guidelines Network checklist for cohort studies. Despite this, the findings of the 10 studies that were finally included offer a heterogeneous picture that makes it difficult to focus results more consistently.

How come all studies under your scrutiny were performed only and exclusively in the United States? This might be an important bias that will render findings poorly reliable. The number of 196516 comorbid CNCP and PTSD makes the overall figure hard to homogenize. The figure is excessively high, which doesn't surprise me: US authors largely over-diagnose PTSD.

Reply: Thank you for your comment. Indeed, as you point out, all the studies that have been included in our review have been carried out in the United States. Even more, half of the studies included in the review were conducted on samples recruited from the health care of U.S. veterans. As you rightly point out, American war veterans are often diagnosed with post-traumatic stress disorder. Probably because many of these people have been exposed to traumatic situations because of their military profession. In light of this, we have added the following comment to the text setting out the limitations of our review: "Finally, half of the studies included in the review were conducted with samples from US veterans,

which limits the generalizability of the results to other populations of people with chronic non-cancer pain and comorbid posttraumatic stress disorder”.

What do you mean with "the authors read the full text of the 17 selected studies"... is this an appraisal? When I write a single case report, I read at least twenty previous studies related to the theme.

Reply: this phrase refers to the eligibility step established by PRISMA guidelines for systematic review study selection. However, the review of articles that we have done to draft our paper is far superior. In fact, the number of references cited in the manuscript is 65.

A lot of statistical findings (data) are mentioned within the lines, making their follow-up from the reader really hard. Please compile a separated table and omit AOR1; CI etc... from the narrative.

Reply: Thank you for your comment. We apologize for this. Nevertheless, the studies included in our review are heterogeneous in many respects, making it difficult to extract a sufficient number of common data to include in a table. For this reason, and since only 10 studies have been included in the review, we have opted for the most precise description of those results that could not be shown in the table already presented in the manuscript.