Author’s response to reviews

Title: Memory of pain in adults. A protocol for systematic review and meta-analysis

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Responses to reviewers’ comments

Response to Reviewer #1

Reviewer #1: Thank you for the opportunity to review this revised manuscript that I believe to be suitable for publication (subject to minor changes), and I thank the authors for their responses to my and the other reviewers' previous comments. I think there are still a few concerns to be addressed, but I would be happy to allow the editor to approve these - at the editor's discretion, of course.

Response: Thank you for a very detailed review of our protocol. This time we paid particular attention to the risk of bias assessment since this part has been reviewed for the first time. Please find our responses below.

Reviewer #1: I see that the other reviewer pointed out that 'type of pain' had not been clearly operationalised, and you have addressed this by operationalizing it by duration and origin - i.e.
acute clinical pain, chronic clinical pain and experimental pain. However, the sentence starting in line 39 of page 3 now no longer makes sense, because practitioners would typically classify pain as acute or chronic based on its duration - i.e. the 'type of pain' would depend on the time since onset.

Response: Thank you for this comment. We are going to elucidate the effect on memory of pain of 1) ‘type of pain’, which refers to the origin of pain and its duration (acute experimental pain, acute clinical pain, chronic pain), and 2) ‘recall delay’, which refers to the time that has passed since the experience of pain to its reporting. To remove possible ambiguities, these terms have been clarified in the manuscript

Reviewer #1: Incidentally, the phrasing also doesn't quite make sense - 'time that has passed since the painful experience' suggests the painful experience has ended, which is rarely the case when a patient presents for clinical help.

Response: We do not think that situations in which a patient provides past pain reports is rare in clinical practice. Patients are not always able to contact the doctor at the exact moment they feel pain or perceive a significant change in the severity of pain. Moreover, pain is not always the main reason for seeking medical help. Pain often occurs as a symptom accompanying another disease which is the reason for seeking medical help. Nevertheless, we corrected the sentence which refers to the moment of interest.

Reviewer #1: Unfortunately, in the process of revision, several writing errors have emerged, so I would suggest that this manuscript is carefully read and corrected by a first-language English speaker with good grammatical knowledge. Examples of this include: [abstract] 'medical decisions taken both by patients and health-care professionals' (incorrect placement of 'both'), 'recollection of pain can either be accurate, overestimated or underestimated' (inappropriate use of 'either' for three - rather than two - terms); [page 3-4] 'the results of the studies differing in terms of recall delay and type of pain could be compared systematically in order to elucidate their effect on the memory of pain'(implies that the studies have the effect on the memory of pain); [page 4] 'Previous studies showed that chronic pain can be overestimated [16, 25], while acute pain can be either overestimated [19, 26-28] or underestimated [22-24, 29].' (presumably this should be 'is' rather than 'can be', because of course chronic pain can also be underestimated).

Response: The current version of the protocol has been checked and corrected by a native speaker of English.
Reviewer #1: The authors have explained that they plan to review the contents of selected journals not manually but using an electronic search strategy. However, they also specified, in the response to Reviewer #3, that this would naturally be limited to the online listings of these journals. I would anticipate the online listings of the journals' own websites to reflect the online listings within the major databases, such as Medline or PubMed. If this is not the case, then this step is worth including; if it merely produces duplicates then it could be omitted. Also, the text should clearly explain that the search will be electronic, not manual.

Response: Thank you, the protocol has been corrected accordingly.

Reviewer #1: Page 9, lines 41-45: This explanation of the second and third types of pain implies that only pain attributed to these causes will be considered relevant to the review. I suggest rephrasing this. In some cases of clinical pain, no clear cause can be identified.

Response: Indeed, many pain states are non-specific in nature. This section has been modified accordingly.

Reviewer #1: Page 9, line 43 - Caesarian section is a type of surgery.

Response: The sentence has been corrected according to Reviewer’s suggestion.

Reviewer #1: Page 14, line 30 - why would you include studies in which the 'quantitative dimension' differed for the comparison and outcomes? Surely using these data would skew the findings? I would suggest excluding such studies altogether, as they share problems with studies in which a different qualitative dimension (intensity vs unpleasantness) was assessed.

Response: Indeed, we did a literature search and we found that in most of the studies pain severity depends on the type of the scale being used. For example, it has been shown that pain assessed using the Numeric Rating Scale has a higher or slightly higher level compared to assessment done on the Visual Analogue Scale (e.g. Price et al., 1994; Leigheb et al., 2017; Holdgate et al., 2003). We have therefore decided to exclude studies that assessed pain at two time points using different scales.

Reviewer #1: Page 15 - relevance to clinical practice. I would recommend exercising caution when linking the findings of this review to recommendations for clinical practice. Presumably the idea would be to provide guidance to clinicians on how to interpret their patients' pain reports, but such guidance could be severely misguided because this review will handle only
group data, not individual data, and individuals may vary considerably in how they recall pain. An individual patient data meta-analysis would be a more suitable basis for such recommendations. This comment may be more relevant for the discussion of your actual review manuscript than for the protocol.

Response: Thank you, the discussion section has been modified.

Reviewer #1: Modified Downs and Black checklist (Table 2):

Question 5 - please consider specifying what characteristics will be relevant to this decision. Presumably you would not give 'points' for characteristics that are irrelevant to your review question.

Response: Thank you for the comment to our protocol. We decided to score articles this way for general methodological reasons, and for the purpose of our systematic review. In our opinion, a sample should be described as extensively as possible because this makes studies more comparable. There are many characteristics that can influence the way participants recall pain intensity and if an extensive list of their characteristics is provided, we could at least make certain assumptions as to what might have influenced the results and whether potential (new) confounders could be identified. In the case of experimental studies, an extensive list of participants’ characteristics would enable us to estimate whether the sample was representative or not. However, following careful consideration of your comment, we decided to modify the question. Articles reporting certain characteristics that may influence the memory of pain, such as the type of pain, intensity of pain experienced during recall, etc. will receive more points than articles that do not include them, no matter how long the list of other reported characteristics is.

Reviewer #1: Question 4 or 8 - I would suggest substituting some consideration of context for one of these questions. For example, if the comparator (actual pain rating) is obtained in a very different setting to the outcome (recalled pain rating) (e.g. post-operative recovery room vs home visit), one might expect a difference.

Response: Thank you for the suggestion and for bringing our attention to this important issue. Indeed, testing memory of pain in a setting different from the one where the initial self-report pain assessment was performed may be a source of bias. We fear that if we included this criterion in the risk of bias assessment, it would automatically give experimental research an unfair advantage (similarly to question no 13, which you pointed out as giving an advantage to experimental research). Experimental studies are routinely performed in the same contextual setting and the kind and level of affect is often controlled as well. Clinical research is usually performed in hospital during the initial assessment, but the recall phase is often done remotely.
However, after careful consideration of your comment we decided to add this item to the risk of bias checklist in order to emphasize how important we believe this issue to be methodologically.

Reviewer #1: Question 13 - I suggest omitting question 13 for experimental studies - or the experimental studies will have a better score than the clinical studies, by default. However, perhaps this question ought to be omitted altogether, considering you are not considering an intervention.

Response: Thank you for the suggestion. We agree that this question would give an advantage to experimental studies. We will exclude this question from our risk of bias assessment.

Reviewer #1: Question 14 - again, this question refers to an intervention, so the relevance to your question needs to be explained.

Response: Thank you for the comment on our protocol. This question was left without modification in order to assess whether at the time of self-report pain assessment the participants were informed that they would at some later time be asked to remember how intense their pain had been. However, leaving the question unaltered does not make it clear. We will therefore modify this question as such: ‘Was an attempt made to blind study subjects to the fact that they would be asked to recall the intensity of their pain later?’.

Reviewer #1: Question 16 - if results were due to 'data dredging' and the authors declared that, surely that would still not reduce the risk of bias associated with such dredging? Yet, the planned score allocation is 1.

Response: Thank you for the comment on our protocol. You have touched on the very important subject of the transparency of the data analysis. We have considered this question very carefully. Since our search encompasses articles published since the 1970s, and the demand for transparency and the open science movement in general are new phenomena, this question would give an advantage to the latest studies that have been published since this new standard was brought into operation. However, we agree that reporting ‘data dredging’ does not make the bias smaller. Therefore, in accordance with your suggestion, we decided not to give any points if ‘data dredging’ is reported.

Reviewer #1: Other - You provided a rationale for omitting a score for the consistency of instructions given to participants from this checklist, but I am unable to agree with your reasoning. That most authors have failed to report the instructions given does not render the
instructions irrelevant to risk of bias. In fact, the results of your review could be influenced by different instructions, but you would be unable to identify the risk of that bias in your findings if you choose not to make provision for this possibility in your risk of bias assessment. In addition, systematic reviews can be a driver for improved study methodology and reporting, and if you were to point out that authors should be reporting the instructions in detail, some may start to do so and thus improve the quality of research in the field. I think the same applies to your reasoning for not planning to account for other factors that are known to influence memory of pain - e.g. pain at the time of recall: these factors are expected to skew results, but you are effectively planning to ignore them. I understand that you anticipate not having enough information to conduct a sensitivity analysis, but I think your risk of bias assessment should explicitly account for them.

Response: Thank you for this comment on our protocol. Certainly, instructions are relevant to the risk of bias whether they are reported or not. Unfortunately, very few studies actually report what instructions were given to the patients, especially as checking memory of pain was often not the main subject of the study. However, we do think it is worthwhile to point out that instructions should be reported verbatim in order to improve the quality of research. We will make a point of discussing this problem thoroughly in our final systematic review.

Response to Reviewer #2

Reviewer #1: The authors provided clear responses to all my questions and improved the manuscript. Although I agree with another reviewer that it would be very interesting and relevant to include other factors that could predict memories of pain (such as distress during experience or pain at the moment of recall), I understand author's rationale to keep the review manageable. Clearly, more review papers on memories of pain are needed.

Response: Thank you very much for your valuable comments. Considering the very wide spectrum of studies on memory of pain, for pragmatic reasons we decided to not focus on factors such as distress. This variable might be a subject of another meta-analysis on memory of pain, e.g. in children.

Reviewer #2: My only concern for the meta-analytic part relates to the questions concerning the type of pain. By removing diary studies, many studies which explored memory of pain among chronic pain patients will be excluded. This might lead to a situation, in which the investigated type of pain will be predominantly acute - either experimentally induced or naturally occurring (e.g. labor, surgery).
Response: We partly share the concerns raised by the Reviewer, yet there are some reports that at first glance could be included in the review. These reports consider chronic pain without diary-like assessments, e.g. Bryant et al. (2008), Porzelius et al (1995), Williams et al. (2007).

Reviewer #2: The authors should also add diary studies as an exclusion to Table 1.
Response: The table with inclusion and exclusion criteria has been updated.

Reviewer #2: I wish to congratulate the authors on this endeavor, and I am looking forward to the results of this study.
Response: Thank you for your kind comment.

Response to Reviewer #3
Reviewer #3: The authors have addressed my comments sufficiently and I can recommend this manuscript for publication.
Response: Thank you very much for your recommendation.