

PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Interventions to treat pain in paediatric CFS/ME: A systematic review
AUTHORS	Ascough, Caitlin; King, Hayley; Serafimova, Teona; Beasant, Lucy; Jackson, Sophie; Baldock, Luke; Pickering, Anthony; Brooks, Jonathan; Crawley, Esther

VERSION 1 – REVIEW

REVIEWER	Reviewer name: dr david vickers Institution and Country: cambridgeshire community services nhs trust Competing interests: none
REVIEW RETURNED	04-Dec-2019

GENERAL COMMENTS	I think this is a useful review, showing the paucity of trials in pain management in cfs. My revision is that they should put more emphasis on this finding, as the trials really either managed pain as part of cfs overall management, or used treatments not used in UK. Otherwise I would recommend acceptance.
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REVIEWER	Reviewer name: Jo Nijs Institution and Country: Vrije Universiteit Brussel, Belgium Competing interests: none
REVIEW RETURNED	19-Dec-2019

GENERAL COMMENTS	<p>This is an important contribution to the scientific literature.</p> <p>The review is of high level, in line with what one can expect from one of the leading groups in the field of pediatric CFS.</p> <p>The paper reads very well and addresses an important issue. The study findings highlight the lack of studies using pain as an outcome measure in pediatric CFS trials. Also the lack of studies exploring pain-targeted treatment options for pediatric CFS is highlighted. Hence, the review identified 2 major knowledge gaps = research priorities.</p> <p>Who conducted the search strategy, and was this performed by more than one researcher? Preferentially, the search strategy is done by 2 independent researchers.</p> <p>Page 6, lines 15-17: 'objective or subjective measure of pain': I understand what you are trying to say, but per definition pain is a subjective experience. Consequently, objective measures of pain are a contradictio in terminis.</p> <p>The results of the risk of bias assessment are presented in the results section after the description of the study findings of the identified papers. It seems as if the 2 are presented separately, while both should be integrated.</p>
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	Typically a systematic review implies that the weight given to certain study results depends on the risk of bias. Also the risk of bias is typically presented first, as often studies are excluded for further consideration due to high risk of bias. Please revise the results and discussion section accordingly.
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VERSION 1 – AUTHOR RESPONSE

Response to comments from Dr David Vickers

R1.1 Comment: I think this is a useful review, showing the paucity of trials in pain management in cfs. My revision is that they should put more emphasis on this finding, as the trials really either managed pain as part of cfs overall management, or used treatments not used in UK. Otherwise I would recommend acceptance.

R1.1 Response: Thank you for your feedback. We agree that this is a particularly important finding that should be highlighted in this paper. To put additional emphasis on this we have added the following words:

Section: Abstract (conclusion)

‘Despite the prevalence and impact of pain in children with CFS/ME surprisingly few treatment studies measured pain. In those that did measure pain, the treatments used focused on overall management of CFS/ME and we identified no treatments that were targeted specifically at managing pain.’

Section: What this study adds

We have adjusted the first point to state ‘Despite the prevalence and impact of pain in children with CFS/ME few treatment studies have measured pain as an outcome and no interventions targeted pain.’

Response to comments from Dr Jo Nijs

R2.1 Comment: This is an important contribution to the scientific literature. The review is of high level, in line with what one can expect from one of the leading groups in the field of pediatric CFS. The paper reads very well and addresses an important issue. The study findings highlight the lack of studies using pain as an outcome measure in pediatric CFS trials. Also the lack of studies exploring pain-targeted treatment options for pediatric CFS is highlighted. Hence, the review identified 2 major knowledge gaps = research priorities.

R2.1 Response: Thank you for this positive feedback.

R2.2 Comment: Who conducted the search strategy, and was this performed by more than one researcher? Preferentially, the search strategy is done by 2 independent researchers.

R2.2 Response: Thank you, we agree that this is how the search strategy should be performed. Therefore, the search strategy was developed and conducted by the lead author in conjunction with a data specialist from the University of Bristol. We have added the following text to the methods section to clarify this ‘The search strategy was developed in conjunction with a data specialist at the University of Bristol’

R2.3 Comment: Page 6, lines 15-17: ‘objective or subjective measure of pain’: I understand what you are trying to say, but per definition pain is a subjective experience. Consequently, objective measures of pain are a contradictio in terminis.

R2.3 Response: Thank you for this comment. We have removed the phrasing 'objective or subjective'. We have also removed the phrasing 'in addition to subjective measures' in the following paragraph.

R2.4 Comment: The results of the risk of bias assessment are presented in the results section after the description of the study findings of the identified papers. It seems as if the 2 are presented separately, while both should be integrated. Typically a systematic review implies that the weight given to certain study results depends on the risk of bias. Also the risk of bias is typically presented first, as often studies are excluded for further consideration due to high risk of bias. Please revise the results and discussion section accordingly.

R2.4 Response: Thank you for raising this. We have moved the paragraph that discussed the findings of the risk of bias assessment so that it comes before the description of the study findings. It is now integrated into the paragraph entitled 'Summary of Included Studies', rather than being a separate paragraph.

Some of the studies included were felt to have a high risk of bias. We felt that, particularly in light of the paucity of trials reporting pain outcomes, it was important still to present the findings of these studies. We have made this clear in the results by stating that 'Due to the paucity of studies that measured pain outcomes in paediatric CFS/ME all studies were included in the review and the risk of bias was taken into account when evaluating study findings'.

However, we have made several changes to incorporate the findings of the risk of bias assessment to a greater extent into the discussion. This has helped to clarify the weight that can be given to each of the study findings. In the results section titled 'Change in pain scores following treatment' for each study we have added wording to reiterate what the risk of bias is. In the discussion we have also changed the wording from 'However, in those that do recover, pain is less compared to those that do not recover.' to 'However, in those that do recover, pain appears to be less compared to those that do not recover.' to account for the fact that the studies that showed this finding had a moderate or high risk of bias.