Author’s response to reviews

Title: A systematic review of the role of inflammatory biomarkers in acute, subacute and chronic non-specific low back pain

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Author’s response to reviews:

Dear Dr. Alessandro Chiarotto,

On behalf of my co-authors I would like to thank you again for the fast turn around of the manuscript. Please see below a point by point response to the comments.

Editor

Please add information in the abstract regarding (the use of) the GRADE approach, both in the methods and results of the abstract.

I have now added information about the GRADE approach both in the methods and the results section of the abstract.

Additionally, I still find the information you report in the methods section of the manuscript on the GRADE approach too succinct. Please add a paragraph at the end of the section describing on what the GRADE approach consists, and the possible reasons for downgrading the quality of the body of evidence. The GRADE adaptation for prognostic studies is not widely used, therefore readers may find it informative to know more about it.

A paragraph has been added to the methods section as suggestions and reads: “The level of evidence was rated using the modified GRADE approach for prognostic factors research. This modified GRADE approach allows for the evaluation of features specific to prognostic research and can be expanded to other epidemiological evaluations as well as narrative synthesis. Grading...
starts with the identification of the phase of investigation. Phase 2 and 3 studies conducted to confirm independent associations between outcomes and prognostic factors, and to understand the underlying process for the prognosis respectively, should be judged as high-quality evidence. Phase 1 studies conducted to generate hypothesis provide weaker evidence. Similar factors used for grading interventions studies are then taken into consideration and quality of evidence is downgraded for: study limitations (high risk of bias), inconsistency (unexplained heterogeneity of results assessed either using statistical heterogeneity statistics for meta-analysis or evaluating point estimates and confidence intervals for narrative reviews), indirectness (study characteristics do not reflect review question), imprecision (small sample and imprecise estimates for meta-analysis and no sample size calculation, less than 10 outcome events for each prognostic variable and imprecision of estimates) and finally, publication bias (downgraded unless predictor has been evaluated on a number of phase 2 and 3 studies). In addition, identification of moderate or large effect sizes and the identification of a exposure-response gradient (large amount of predictor is linked to larger or lower effect sizes) should be considered for upgrading the quality of evidence.”

Sincerely,

Luciana Macedo, PT, PhD

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