Reviewer's report

Title: Prognostic-factors for neurodegeneration in chronic moderate-to-severe traumatic brain injury: A systematic review protocol

Version: 0 Date: 05 Nov 2019

Reviewer: Sue Harnan

Reviewer's report:

I have enjoyed reading your protocol, which is clearly written. I have a few points for you to consider, though I understand that as a funded project the scope for amendments to your protocol may be limited. I hope they will be useful.

Abstract:

Typo: "such as low levels of cognitive of physical activity."

What is meant by "serial neuroimaging" - a consecutive series of patients, or a series of neuroimages in an individual?

Main text:

Please provide answer to Prisma-P item 5c

Search strategy is quite limited as you have not included MeSH or Thesaurus terms. Please consider improving this. You may want to consider PRESSing your search strategy: https://www.cadth.ca/resources/finding-evidence/press

Minor point: "This systematic review protocol was registered and conducted in accordance with the…" - I think a protocol cannot be conducted, but a review can be. Unclear if you mean the protocol was written or designed, or that the review was conducted.

Typo in: "This is because when is imaging is undertaken earlier post injury"

As this is a review of prognostic factors, PICOS is not the best question formulation. Did you consider using PICOTS (see Riley et al 2019, BMJ: https://www.bmj.com/content/364/bmj.k4597), or PFO (population, prognostic factor, outcome)? I would be happier to see what you have defined as "secondary outcomes" defined as prognostic factors, and moved under an appropriate heading according to a PICOTS or PFO formulation.

Which study designs are eligible for inclusion in the review? E.g. cohort studies, case-control, case-cohort etc.
Will your data extraction form be piloted and amended before applying to all studies? Seems odd that the people using the form are not designing and adapting it, but that is a minor point.

If you are including case-control designs (see point above) how will these be quality assessed? Did you consider using the QUIPS tool, which is specifically designed for prognostic factor studies? See https://www.bmj.com/content/364/bmj.k4597 and Hayden et al 2013, Annals Internal Medicine: https://annals.org/aim/article-abstract/1650776/assessing-bias-studies-prognostic-factors

The definition of neurodegeneration is a little loose. What constitutes a change in brain volume, or white matter integrity? Is there a quantification of this?

Do you perhaps mean the DerSimonian and Laird method of meta-analysis? Mantel-Haenszel is a fixed effect method according to the Cochrane handbook. The BMJ article already mentioned above has some good advice on tackling heterogeneity in prognostic studies, and recommend that a number of smaller analyses may need to be performed according to various characteristics.

You have not addressed the issue of whether estimates will be adjusted or unadjusted. Again, the BMJ article has some good advice on this. You may need to define what factors estimates should be adjusted for as a minimum.

Please provide a reference for the Centre for Reviews and Dissemination guidelines.

Level of interest
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

Quality of written English
Please indicate the quality of language in the manuscript:

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