Reviewer’s report

Title: Pharmacotherapies for fatigue in chronic liver disease (CLD): a systematic review and meta-analysis (protocol)

Version: 0 Date: 13 Oct 2017

Reviewer: Chaturaka Rodrigo

Reviewer’s report:

This protocol addresses an interesting research question. I have several comments for improvement.

Defining chronic liver disease as duration of a liver pathology greater than 6 months is a very simplistic view. There can be asymptomatic patients with ongoing liver damage at microscopic level (chronic persistent hepatitis). There needs to be a better definition of what you include as chronic liver disease. For example does it have to be confirmed by biopsy or persistent elevation of liver enzymes is enough?

There are many aetiologies for chronic hepatitis. Giving an ad hoc list of selected aetiologies is grossly insufficient. Since you cannot list all possible causes, it may be wise to mention the broad categories and give a few examples for each.

I cannot understand why the authors are excluding non-pharmacological therapies. The evidence base will be more complete if these are also included in the review.

There can be many confounders for fatigue such as thyroid status, anaemia, post viral infection and mental health. How do authors propose to adjust for these complexities?

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