

Dear Professors Hu, Kan, and Pyrsopoulos and the Reviewers,

We greatly appreciated the offer of considering our manuscript entitled “Understanding fatigue in primary biliary cholangitis: from pathophysiology to treatment perspectives” for publication in the World Journal of Hepatology. We thank the Company Editor-in-chief, the Science Editor and the Reviewers for the comments and suggestions, and we hope we have improved our manuscript as we would be very grateful if it could be published on your Journal.

The main corrections in the paper and the responses to the reviewers’ comments are as following:

1. **The Minireview “Understanding fatigue in primary biliary cholangitis: from pathophysiology to treatment perspectives” by Lynch et al. summarizes several aspects of the fatigue associated to primary biliary cholangitis (PBC). It is a well written minireview. However, to claim systematic review of the literature, the authors should follow the PRISMA guidelines (<http://prisma-statement.org/>) provide PRISMA checklist and flow diagram. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021 Mar 29;372:n71. doi: 10.1136/bmj.n71. PMID: 33782057; PMCID: PMC8005924. Readers would ask how the 1172 articles allocated in the 2 databases indicated ended up in a list of only 40 references in the paper. The different sections of the paper should be related to the searches. Pages 8 and 9, “LIFESTYLE ADJUSTMENTS AND DEVELOPING COPING MECHANISMS” section does not provide a single reference. Is this an author opinion statement? Alternatively, the authors may claim a narrative review of the literature rather than a systematic search, and thus remove the methods section.**

Summary tables could be more elaborated/detailed. Adding a reference column is recommended. Placing 2 references on Table 1 does not clarify what is the evidence to link terms in column 1 with those of column 2. Usually a systematic search pursues elaboration of summary tables presenting the experimental evidence available. No room for former reviews is needed.

We thank the Reviewer for the suggestion and have removed the methods section of the manuscript. Although we now have structured the article as a narrative review we appreciate the reviewer's remark and we have added relevant references to Table 2. We have corrected the "LIFESTYLE ADJUSTMENTS AND DEVELOPING COPING MECHANISMS" section by adding references.

- 2. As per the structure of the article it would be interesting to at least mention the assessment of fatigue in the context of peripheral or central.**

We agree that mentioning the different means that could be used to assess peripheral and central fatigue would improve our manuscript and therefore we have modified the specific section.

- 3. Page 5, line 140: "pH recovery time related to fatigue severity" Verb and citation for the observation are missing.**

We have corrected the sentence with verb and reference.

- 4. Line 146, "measured with twitch interpolation" explain what it is and why is important to mention, what is the message?**

We are grateful to the reviewer for the suggestion and have modified the manuscript accordingly.

- 5. Page 6, line 172: "ondansetron, fluvoxamine, or fluoxetine" three treatments and just 1 citation, is this right?**

We have added the specific citations.

Erica Nicola Lynch, a native English speaker, proofread the manuscript and corrected all identified language mistakes.