

Dear Editor of World Journal of Meta-Analysis

Thank you for your time in reviewing our manuscript and for your helpful comments. We have made changes to our manuscript according to all of your comments and details are below.

1 Details of your submission

Journal title: World Journal of Gastroenterology

Manuscript NO: 48518

Title: Efficacy of treatment options for rumination syndrome – A Systematic Review

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2 Peer-review report

Reviewer #1: The authors conducted a systematic review of the treatment options for adult patients with rumination syndrome (RS) characterized by recurrent postprandial regurgitation of recently ingested food from the stomach to the oral cavity. They selected 12 articles evaluating the efficacy of various treatment modalities for RS, ranked them in order of level of evidence, identified diaphragmatic breathing (DB) and baclofen treatment as the most effective and concluded that both should be considered. Since the RS is a relatively rare condition with a general lack of consensus on the most appropriate treatment options the authors paper fills this gap. Comments: 1) The study is overall well performed and well designed. 2) Title: "Efficacy of treatment options for rumination syndrome – A Systematic Review". I suggest to change it to: Treatment options for rumination

syndrome – A Systematic Review 3) The authors should add the following papers to the references list: a) Halland M, Pandolfino J, Barba E. Diagnosis and Treatment of Rumination Syndrome. Clin Gastroenterol Hepatol. 2018 Oct;16(10):1549-1555. doi: 10.1016/j.cgh.2018.05.049 and b) Absah I et al. Rumination Syndrome: pathophysiology, diagnosis, and treatment. Neurogastroenterol Motil. 2017 Apr;29(4). doi: 10.1111/nmo.12954 4) Similarity analysis showed that 36% of the text matches 36 fragments from 15 sources on the web or academic database. This is understandable since the authors reviewed and cite other publications, but preferably should be reduced to less than 20%.

Answer: Thank you for your comment. Title has been changed as per request by reviewer. Halland et al is already included in the references. We have read Absah et al as well, but could not find anywhere to reference it as much of the information was also mentioned in Halland et al.

Reviewer #2: Congratulations on your review. I think you obtained a maximum of information from the articles available. However, more research needs to be performed regarding this condition, as it is essentially a psychological disorder and medical interventions should be supported by specific therapies.

Answer: Thank you for your comment. We agree that more research has to be done in this field.

Reviewer #3: Major Comment: This manuscript claims to deal with the efficacy of treatment options for rumination syndrome. Its major drawback is that it is not rewarding for the reader - the expectations are not fulfilled. The literature on this subject is scarce and very heterogeneous. This is, of course, not the fault of the authors; however, it makes it impossible to provide a valid evaluation on efficacy and relevance of the therapeutic options. Minor Comment: A linguistic/stylistic review is required (e.g., "All relevant articles were access in full text. We extracted data on study design, location, patient profile, duration of symptoms, follow up periods, date, diagnostic criteria, intervention, outcome, and follow-up were extracted", etc.) - and this also pertains to the introductory statements (e.g., "The manuscript has not been and will not be published elsewhere and have not been considered or submitted elsewhere for publication").

Answer: Thank you for your comment. We presented the available data as it is, and unfortunately as the reviewer says, there is limited literature on this subject. We have made the grammatical changes as rightfully pointed out by the reviewer in the manuscript.

Reviewer #4: 48518 Efficacy of treatment options for rumination syndrome – A Systematic Review, by Ong et al., 2019. This is a "systematic review" on treatment options for rumination syndrome. The authors searched 4 databases and identified 12 eligible articles, encompassing 254 patients (most of them women). Behavioral therapies (diaphragmatic breathing), baclofen, fundoplication, and lifestyle changes were proposed treatments for rumination syndrome. Also, 3 studies investigated the combination of pharmacological, behavioral and psychotherapies. The risk of bias was assessed independently via Cochrane Risk of Bias tool and Newcastle-Ottawa Scale. The authors pointed out that evidence for treatment options is limited. I appreciate the opportunity to review this interesting review on rumination syndrome. The authors have endeavored to retrieve relevant articles. However, there are many essential issues for improvement. Major points: 1. Inclusion criteria: There is a fundamental problem in the study selection, as the efficacy of treatment of rumination syndrome only can be assessed through experimental designs. For example, there were 2 randomized controlled trials and 10 observational studies (possibly, the design is better qualified as quasi-experimental type). This need to be better described in Methods. 2. Exclusion criteria: Not all studies were rigorously assessed before entering in the studies. Small sample size of all studies reduces the effect size. The selection of participants was highly biased, with patients recruited from healthcare settings, allowing the Berkson's bias to emerge. Please clarify the rationale of retaining observational studies. 3. I would like to read the rating of the quality of each individual studies in Results, as a separate Table. Probably, most of "observational studies" were of dubious or low quality, with high risk of bias. For those 10 "observational studies", a careful assessment of the validity should be provided in Discussion. Given their design, serious threats of external and internal validity should be circled throughout the Discussion. 4. The Discussion on the data displayed in Table 1 should be scaled up, with a careful narrative synthesis of the 12 eligible articles. It is unusual to summarize the quality of studies (Table

2) in Discussion. Table 2 should be moved to Results, along with a descriptive synthesis of the data. 5. In view of troublesome methodological problem of most studies, it is early to propose a stepped treatment option for rumination syndrome (Table 3). It is unacceptable to rely clinical practice in untrustworthy evidence. Before disseminating Table 3 column of "Treatment Outcome", more logical reasoning and examination is required. 6. In view of scarcity of the existing evidence of treatment option, I would suggest changing the methodological framework to that of scoping review, where the quality of retrieved studies is a secondary issue. The main conclusion refers to the huge research gap in the treatment of rumination syndrome. Accordingly, the Title also may be changed to a suitable one to account for the results of your review.

Answer: Thank you for your comment. The limitations of the literature mentioned by the reviewer is true and we have therefore written a paragraph to elaborate on these limitations. We have also clarified that our suggested treatment options are not based on strong evidence but rather what is available in the literature.

The paragraph now reads

"It was difficult to make strong conclusions based on the strength of the data as only 3 studies were controlled and only 2 were randomized interventions. In view of the limited literature available in this field, we retained observational studies despite knowing that they were prone to bias, and thus our recommendations are not based on strong evidence, but rather a summary of what is available in the literature (Table 2 and 3). "

Reviewer #5: n/a

Reviewer #6: This is a review article of rumination syndrome. 1) Discussion is too long and some descriptions are duplicates of the results. That should be shortened. 2) Some abbreviations are not defined such as EMG, LES, EGJ, and TLESR.

Answer: Thank you for your comment. We have trimmed the discussion and also elaborated on the abbreviations