

Reviewer #1:

Specific Comments to Authors: I would like to thank the authors for their work. Notes on manuscript: English language: needs extensive revision. (There is no English revision certificate) Title: Comparison of Bowel Cleaning Efficacy and Patient Tolerability of Same-Day Single Does and Large-Volume Split-Does Regimens of Polyethylene Glycol for Bowel Preparation: an Updated Systematic Review and Meta-Analysis Please correct, "Does" to "dose" (and all over the rest of the text)

Answer: The article had been revision, "Does" had been transformed to "dose". and We have abstained english revision certificatie.

Abstract: #Background: The author stated that their aim was " The meta-analysis was aimed to evaluate the efficacy and tolerability of SSDs of PEG for bowel preparation. – The meta-analysis was aimed to compare the Bowel Cleaning Efficacy and Patient Tolerability between Same-Day Single Does and Large-Volume Split-Does Regimens of Polyethylene Glycol for bowel preparation ", but this meta-analysis as the title and methods stated is to "compare" the standard split dose versus the Single dose regimens, please modify.

Modify: This meta-analysis aimed to compare the efficacy and tolerability between SSDs and large-volume SpDs of PEG for bowel preparation.

#Methods: abbreviations mentioned for the first time without full text (RR or MD) please add full text when mentioned for the first time. The authors stated, " Random effects model or fixed effects model were reported for a heterogeneity analysis among studies." Kindly elaborate which one was used first, and which was used when heterogeneity detected, and at what level of heterogeneity?

Answer: relative risk ratio (RR) and Mean Difference (MD) have been added in the modified sentence. In the Statistical analysis part, we have elaborated the content as follows:

Statistical heterogeneity was measured by graphic examination of forest plots and statistically through a homogeneity test based on the chi-square test ($I^2 \geq 50\%$ suggests heterogeneity) in which $P < 0.10$ was considered significant for heterogeneity. A fixed-effects model was used unless there was significant heterogeneity, in which case a random-effects model was applied.

#Results: The authors stated " Eighteen RCTs studies were included." Kindly state the type of studies e.g. RCTs or cohort etc. The authors mentioned " There was no statistically significant difference between (2L/4L)" and " The pooled analysis offered to favor of SSDs for less sleep disturbance " etc., please state in numbers what is the RR or MD for all the outcomes, not just the CI.

Answer: the sentence has been revised by "A total of eighteen studies were included". Yes, the type of studies were RCTs. We have stated numbers of RR or/MD for all the outcomes in the revised content.

Keywords: kindly change " Split-does" to Split-Dose"

Answer: the word " Split-does" has been changed to "Split-Dose" in the revised content.

Introduction: #Authors wrote " but some patients were unsatisfaction">>change to "unsatisfie" # The authors stated " We hypothesize that SSDs of PEG-based bowel preparation solution is not inferior in bowel cleanliness and better patient tolerance to sleep disturbance and side effects." But I think this is not the correct way to write the research question, because they are biased in their hypothesis, they could state a neutral

research question (to compare between the two interventions not predicting the effect from the start), as written later on.

Answer: the sentence of " but some patients were unsatisfaction" has been revised(deleted). We change it (We hypothesize that...) to the sentence "In order to evaluate bowel cleanliness of SSDs of PEG and patient tolerance in terms of sleep disturbances and side effects for bowel preparation" in the revised content.

Methods: 1- The search words is a weak presentation of the search strategy, a better search strategy is using all of the synonymous terms to the keywords and using effective Boleyn search tools according to the database they are searching.

Answer: The search strategy used the Medical Subject Heading along with the keywords "polyethylene glycol AND (bowel preparation OR bowel preparation solution) AND (split dose OR split-does) AND randomized controlled".

2- The authors wrote " References from the reviewed articles were also searched in order to identify relevant articles that may have been missed." did they mean review articles on the topic.

Answer: We reviewed articles by the topic, abstract and full text.

3- The authors mentioned the data extraction without mentioning the results of their research, how many duplicates as they searched different databases (also please add to the flow chart). And how they did the screening, whether one or two authors conducted the screening independently?

Answer: We have complemented the flowchart. (revised, question:how many duplicates). Yes, two authors conducted the screening independently. Revised the sentence" Two authors independently conducted the screening and extracted the data from selected trials" in data extraction part.

4- The authors mentioned that they used " modified Jadad scoring system" could the authors explain why didn't they use the risk of bias tool ROF2 only in RevMan? as they stated without any details " The Cochrane risk tool was also used to assess study bias.". Also the authors stated that most studies had unclear risk of bias in (other types of bias) as shown in figure 2 but they didn't state what are the items of the other risks they found in the individual studies.

Answer: We have added the GRADE. SOF in the revised content.

We have revised the assessment of study quality shown in Figure 2 according to Cochrane risk of bias tool, bias including selection bias, performance bias, detection bias, attrition bias, and reporting bias have been stated specifically, so there was no other types of bias for all included studies.

5- The authors stated they used "Weighted mean differences", do they mean SMD (which is the one present in revman)?

Answer: Weighted mean differences were used for outcomes measured on different scales. It did not mean SMD.

#Results:

1- In FIGURE 1. Flow diagram of trial selection": The flow chart didn't show each stage (duplicates, title and abstract screening, full text screening) it only states the number of studies retrieved, please modify to include this data.

Answer: We have modified to include this data in revised content.

2- sometimes the authors use I² or I-square please unify throughout the text according to the journal guidelines.

Answer: Yes, we have made I² uniform in the revised article.

3- there is no mention of publication bias, although the authors included 18 studies where they could draw funnel plot to assess publication bias

Answer: A funnel plot was added in the revised content.

#Discussion: How the authors explain the discrepancy between their results and the previous meta-analysis done (4-Liter Split-Dose Polyethylene Glycol Is Superior to Other Bowel Preparations, Based on Systematic Review and Meta-analysis. Enestvedt, Brintha K. et al. *Clinical Gastroenterology and Hepatology*, Volume 10, Issue 11, 1225 – 1231

Answer: Enestvedt, Brintha K. et al compared 4-L split-dose PEG with other bowel preparation methods mainly including 4-L PEG single-dose the night before procedure and non-PEG solution of MiraLAX/Gatorade, however, in our meta-analysis, we only compared Same-Day Single Does (not the night before procedure) with Large-Volume Split-Does Regimens of PEG. In short, different drug style and prepare time.

#References: 1- The paper has no references to check at the end?? 2- I found a lot of RCTs not mentioned in the table of included references (only mentioned by first author-year).

Answer: Yes, the references have been left out.

Reviewer #2:

Specific Comments to Authors: Thank you very much for the opportunity to evaluate this article. The manuscript deals with an important topic to evaluate the efficacy and tolerability of SSD PEG-based arm versus large-volume ($\geq 3L$) SpDs of PEG solutions for bowel preparation before colonoscopy, with regardless of adding adjuvant laxative. The manuscript is very well written in English, and this review topic is of great clinical importance. I suggest the authors consider the following comments to improve the quality of the manuscript.

Major comments - This review did not fully follow the PRISMA statements. Please review and complete the PRISMA 2020 checklist. In particular, there is no assessment of publication bias and GRADE approach.

Answer: We review and complete the PRISMA 2020 checklist, and have added the funnel plot and GRADE approach in revised content.

Minor comments Introduction - As mentioned in the second paragraph of the discussion, the author should describe the differences from previous systematic review and the novelty of the current study in the introduction section.

Answer: Previous systematic review by Enestvedt BK revealed that 4L split-dose PEG is better than other bowel preparation comparators including regimen of 4L single-dose PEG the night before procedure and MiraLAX/Gatorade solutions, regardless of adjuvant laxative use. However, in order to evaluate bowel cleanliness of same-day single does regimens

(SSDs) of PEG and patient tolerance in terms of sleep disturbances and side effects for bowel preparation, we conducted a systematic review and meta-analysis to compare the efficacy and tolerability of SSD PEG-based arm versus large-volume ($\geq 3L$) split-dose PEG solutions for bowel preparation before colonoscopy, regardless of adjuvant laxative use.

Methods - Please provide a complete electronic search strategy that can be used repeatedly as well as search terms. - Please indicate whether there are any language restrictions in the literature search. - For any missing data, please specify whether the authors asked the original author or not. - The authors should specify assessment for publication bias (e.g. funnel plots and Egger's tests). - The authors should add an assessment of the quality for each outcome, not each study, using the GRADE approach.

Answer: 1. The search strategy used the Medical Subject Heading term along with the keywords "polyethylene glycol AND (bowel preparation OR bowel preparation solution) AND (split dose OR split-does) AND randomized controlled". 2. Only full texts published in English were included. 3. In this meta-analysis, there is no missing data, we should not ask the original author by email. 4. We have added the funnel plots and GRADE ROF in the revised content.

Results - The authors should evaluate publication bias (e.g. funnel plots and Egger's tests). - The authors should evaluate the certainty of the evidence according to GRADE approach for each outcome.

Answer: Yes, the funnel plots and GRADE ROF have been added in the revised content.

Discussion - The authors should discuss the certainty of the evidence. Appendix - PRISMA statement has been updated to the PRISMA 2020 Statement (BMJ. 2021;372:n71.).

Answer: 1. We have added the content to discuss the certainty of the evidence: There are several advantages to this meta-analysis. we perform the extensive retrieval strategy and include only randomized controlled trials. Also, advantages are essentially related to the quality of the included studies and to the publication bias. The methodological quality assessment of the included studies turns out to be a moderate to high results according to the Cochrane risk of bias tool and modified Jadad score. For the publication bias, in our meta-analysis a better symmetry was present with the use of funnel plots and GRADE approach.

2. The PRISMA 2020 Statement has been updated in the revised content.