



LETTERS TO THE EDITOR

Some flaws that could change the effect sizes and limit the extrapolation of these results[☆]



Alguns pontos fracos que podem alterar os tamanhos dos efeitos e limitar a extrapolação desses resultados

Dear Editor,

We have carefully read the article published by de Mello et al.,¹ and we have found several important issues to discuss.

Regarding the clinical topic, inclusion of studies was based on Rome III Criteria; however, we found that authors misclassified four out of the nine articles included in this systematic review: Castillejo et al.,² actually used functional constipation (FC) criteria according to Rome II; Mozaffarpur et al.,³ included patients classified using both Rome III criteria and the Paris Consensus on Childhood Constipation Terminology Criteria; Loening-Baucke⁴ defined FC according to the Medical Position Statement of the North American Society for Pediatric Gastroenterology and Nutrition in 1999; finally, Kokke et al.,⁵ included patients according to Loening-Baucke.⁴ This unappropriated inclusion of studies might have led to different effect sizes due to clinical heterogeneity. The authors should have stated that they were going to include different Rome Criteria and afterwards, they should have conducted a sensibility or a subgroup analysis to identify the alteration in effect sizes.

Regarding the methods used to perform this systematic review, we have found some flaws in the following issues⁶:

1. Protocols for systematic reviews and meta-analysis must be published in PROSPERO before performing the entire process and the publication of the final manuscript.

2. The search strategy must be based on patient (population), intervention, and study design according to different manuscripts. This one was based on patient, outcome, and study design, which might lead to selection bias.
3. Using two tools for assessing bias is unnecessary (RoB Cochrane tool and Jadad score). If the authors wanted to perform another analysis, assessing the quality of evidence using the GRADE tool would have been important and interesting.
4. There was no appropriate description of the strategy to identify non-published literature, for example, Google Scholar, Open Grey database, clinical trials registries, and conferences, among others. This might have created publication bias.

Consequently, we suggest caution in the use of the findings when extrapolating results to clinical practice.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Piccoli de Mello P, Eifer DA, Daniel de Mello E. Use of fibers in childhood constipation treatment: systematic review with meta-analysis. *J Pediatr (Rio J)*. 2018;94:460–70.
2. Castillejo G, Bullo M, Anguera A, Escribano J, Salas-Salvado FJ. A controlled, randomized, double-blind trial to evaluate the effect of a supplement of cocoa husk that is rich in dietary fiber on colonic transit in constipated pediatric patients. *Pediatrics*. 2006;118:e641–8.
3. Mozaffarpur S, Naseri M, Esmailidooki M, Kamalinejad M, Bijani FA. The effect of cassia fistula emulsion on pediatric functional constipation in comparison with mineral oil: a randomized, clinical trial. *DARU J Pharm Sci*. 2012;20:83.
4. Loening-Baucke V, Miele E, Staiano FA. Fiber (glucomannan) is beneficial in the treatment of childhood constipation. *Pediatrics*. 2004;113:e259–64.
5. Kokke F, Scholtens P, Alles M, Decates T, Fiselier T, Tolboom FJ. A dietary fiber mixture *versus* lactulose in the treatment of childhood constipation: a double-blind randomized controlled trial. *JPGN*. 2008;47:592–7.
6. Higgins J, Green FS. *Cochrane handbook for systematic reviews of interventions* version 5.1.0. The Cochrane Collaboration; 2011.

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Answer to Letter to the Editor “Some flaws that could change the effect sizes and limit the extrapolation of these results”[☆]



Resposta à Carta ao Editor “Alguns pontos fracos que podem alterar os tamanhos dos efeitos e limitar a extrapolação desses resultados”

Dear Editor,

We appreciate the attention of those who read and analyzed our work; we found the comments and considerations made about the recently published article very interesting. Please find below the answers to the main points raised in the Letter to the Editor:

Constipation is an increasingly present condition found in the pediatric population. It can be classified as organic, when it is associated with intestinal and extra intestinal disorders, and as functional, when there are no warning symptoms or organic causes, which occurs more frequently.¹ The pathophysiology of functional constipation is not well understood, but it is known to be multifactorial. Recently, the diagnostic criteria for functional constipation were updated and redefined in the Rome IV consensus, aiding in the differentiation between functional constipation and constipation with an organic cause.²

Intestinal constipation is a frequent disease in the pediatric population and the initial management often includes advice on increasing the fiber intake. However, there have been few studies that have proven the efficacy of fiber use in the treatment of childhood intestinal constipation. The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), in its Consensus on the management of childhood intestinal constipation in 2014, for the first time emphasized that there was no evidence to justify prescribing an increase in fiber consumption.³ Aiming to gather more current evidence on the use of fiber in the treatment of constipation in pediatric patients, a systematic review with meta-analysis was proposed.

The search strategy is one of the most relevant aspects in a systematic review. We decided to implement a comprehensive strategy, including multiple terms to define the study population and study design. We did not include endpoint criteria in our search terms, in order to increase sensitivity. Moreover, we searched for articles published in five different languages (Portuguese, English, Spanish, French, and German) and in four databases (PubMed, Embase, LILACS, and the Cochrane Library), above what is recommended in the Cochrane Handbook.

Additionally, our search in the gray literature occurred through the evaluation of references in the 42 articles that were fully read. We did not search smaller databases or non-indexed poster publications in the main databases because this would have required resources beyond those available to us, with low probability of finding large studies with good methodological quality.

The lack of publication in PROSPERO (<https://www.crd.york.ac.uk/prospero>) is a real limitation of our study; however, its absence does not prevent the use of the results in clinical practice, since our search was broad.

The assessment of the quality of evidence selected for this systematic review with meta-analysis was performed using the Cochrane Collaboration tool and the Jadad Scale. This evaluation determines the strength of the recommendation, but also represents the degree of confidence on which to base a decision or recommendation.⁴ We understand that the use of these two tools for bias evaluation is not entirely necessary, but there is no loss for the reader in having this information available.

Unfortunately, because this is a field with few studies and low methodological consistency, we chose not to exclude studies based on diagnostic criteria for functional constipation. In fact, the current Rome IV criteria, published in 2016, were not used by any of the studies. Moreover, the type of intervention varied in the studies, which further exacerbates the outcome heterogeneity. Therefore, we decided to include all the studies in the final analysis because they showed a similar patient profile.

The analysis of sensitivity through one-by-one exclusion of the studies, published in the article, found consistency of the main results in the outcomes of bowel movement frequency, fecal consistency, therapeutic success, abdominal pain, and fecal incontinence outcomes. We then performed a sensitivity analysis excluding articles that did not use the Rome diagnostic criteria in their research, as suggested by Kokke et al.⁵ and Loening-Baucke et al.⁶; once again, no significant alteration in the analyzed outcomes was found.

We still think that large studies with clear inclusion criteria, continuous follow-up, and well-defined treatment are

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