

To Prof. Lian-Sheng Ma,  
Editor-in-chief of World Journal of Gastroenterology

Ref.: ESPS Manuscript NO: 33206: "Epidemiology of Functional Gastrointestinal Disorders in Children and Adolescents: a systematic review", Revised manuscript and answers to reviewers

Dear Prof. Lian-Sheng Ma,

On behalf of the co-authors, I wish to thank you for managing this submission and allowing the opportunity to revise the manuscript. All comments from the reviewers were extremely pertinent and helpful to improve the article. Please, find below our point-by-point answers. All changes made in the text were highlighted in yellow.

Hoping that all recommendations from reviewers have been adequately addressed, we feel the manuscript has improved greatly to merit a publication in your prestigious World Journal of Gastroenterology. I look forward to hearing from you in due course.

Kind regards,

Yuan-Pang Wang,  
On behalf of co-authors

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Reviewer # 1

The systematic review titled "Epidemiology of Functional Gastrointestinal Disorders in Children and Adolescents" has been presenting an excellent sample of systematic review study. We can realize once again that the standardized/improved questionnaires and clinical findings should be evaluated together for diagnosis making decision in diseases which have not any objective, gold standard diagnostic test. As known, it is a big dilemma for clinicians. This review could not give an exact data about the prevalence rate of diseases, however it takes a different look for future studies.

R. Dear reviewer #1, thank you for accepting this article and the acknowledgment of value of this review for future studies.

Reviewer # 2

It is a very well written article on a systematic review of epidemiological literature to assess the prevalence of functional gastrointestinal disorders. Few systematic research is regarding this research.

R. Dear reviewer #2, we thank you for approving this manuscript. Professional English teacher and sworn translator mad the proofreading of the manuscript.

Reviewer # 3

This is an interesting paper that concerns a rather tricky issue, in agreement with the wide variability of data about functional gastrointestinal disorders in children and adolescents.

R. Dear reviewer #3, we are grateful for your assessment and suggestions on our manuscript.

The manuscript itself is a little confounding at the first reading. Instead of having the classic structure of Introduction, Methods, Results and Discussion, here we have INTRODUCTION.

MATERIAL AND METHODS: which include: *Search strategies, Methodological Issues (How representative of the target population are the recruited participants? Are the outcome measures reliable and valid?) Critical appraisal of literature.* The "methodological issues" would be better

included in the discussion in my opinion.

RESULTS: whose first paragraph (*Literature search*) should be better inserted in METHODS, as well as several comments about *measurement of FGID* which could be better have place in the DISCUSSION.

DISCUSSION.

LIMITATIONS.

COMMENTS: which should be inserted in the DISCUSSION

FUTURE DIRECTIONS: which could be better defined as the Core Tip of the paper.

The research is accurate and indeed limitations are well defined. It is difficult to disagree from the somehow pessimistic but realistic conclusions of the authors, looking at the results presented. Better definition and understanding of FGID in children, a rather equivocal and indeterminate issue, is mandatory before collecting trustable data.

Therefore, the message is clear but the little confusing way it is presented is worth of a better arrangement of the manuscript.

R. We agree that the classical IMRD structure is the model for most of scientific articles. However, the *World Journal of Gastroenterology* recommends a specific guideline for **Systematic Review**, as following:

The main text contains Introduction, Materials and methods, Results, Discussion, Acknowledgments, Conclusion, Comments (Background, Research frontiers, Innovations and breakthroughs, Applications, and Terminology), and References.
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**MATERIAL AND METHODS:** We believe that the “*Methodological Issues*” would assist the reader to understand the theoretical issues underlying the Methods we have chosen to perform in this systematic review. In addition, theoretical acquaintance of these methods would be helpful for the interpretation of the Results. Therefore, we believe that this section must appear before the Results. Now we have moved the “*Methodological Issues*” to the end of MATERIAL AND METHODS section.

**RESULTS:** Since we choose the PRISMA statement as reference, in its checklist #17, the part concerning “Study selection” (the first paragraph of our manuscript in Results section) is recommended to allocate in the RESULTS.

Initially subtitles arrangement could bring some fragmentation, confounding readers. We

revised the Results format and changed the Results presentation structure, taking out the subtitles and moving the critical appraisal subtopic to the end of the result part.

The option to include some comments in “Measurement of FGID” was to keep the scope of the Discussion section more wide and comprehensive, since there were many topics to cover and don’t divert readers’ attention. Also, those we understood that those comments were important enough to be left aside.

**LIMITATION:** It is now inserted as lowercase in DISCUSSION section.

**COMMENTS:** It was rearranged in accordance to WJG guideline for Systematic Review.

**FUTURE DIRECTIONS:** It was incorporated in subtitle Applications of COMMENTS section. Similarly, the WJG recommends as Core Tip, as following:

a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments. The purpose of the Core Tip is to attract readers’ interest for reading the full version of your article and increasing the impact of your article in your field of study.

The search was conducted from “inception” to 2016. Could the authors better explain and define “inception”?

R. The word “inception” in the text, is a reference that no initial date restriction was made for article insertion. What it means is that, we accept any database since the beginning of PUBMED, SCOPUS and EMBASE records.

Inception means “*beginning of something*” and can be read as a synonym of “*beginning, commencement, start, start point, onset, establishment, origin, launch, source, foundation, constitution, formation*” [1,2,3].

Example of the use of “inception” in scientific literature:

*“The structure of this manual follows the methods for development of NICE public health guidance from inception to publication”*[4].

Citations:

1. Oxford Advanced Learner’s Dictionary Fourth Edition (1989), page 629.

2. Roget's International Treasurus, Fifth Edition, Harper Collins Publishers (1992), pages: 569,610, 613.
3. The American Heritage Dictionary", Houghton Mifflin Publishers, Rev ed. (1976); page: 650.
4. In "The Guide to Clinical Preventive Services 2014: Recommendation of the U.S. Preventive Services Task Force"; by The National Institute for Health and Care Excellence, September 2014.  
[www.ncbi.nlm.nih.gov/pubmedhealth/PMH0089896/pdf/PubMedHealth\\_PMH0089896.pdf](http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0089896/pdf/PubMedHealth_PMH0089896.pdf), last access in 15/03/17.

The definition of such clear-cut limit of 370 for sample size, although well explained, seems a little bit restrictive and harsh.

R. Sometimes it may seams a bit hard and hampers the methodological plan, but it characterizes the quality of an epidemiologic study. "Large sample size produces a narrow confidence limits"<sup>[1]</sup>. Then, adequate sample size is one of the points that turn the study valid in terms of representativeness.

Our critical appraisal reference was the PRISMA study<sup>[1]</sup>, and in accordance: "the best sampling technique is random (probability) sampling of persons from a defined subset of the population. Stratification sampling purposely from subgroups may be required to appropriately represent subgroups"<sup>[1]</sup>. Considering this aspect, the best representativeness study, from those selected to our Systematic Review, was the Sagawa et al. 2013<sup>[2]</sup>, with 3976 students of 40 schools registered at Gunmar Prefecture, both randomly selected.

Though we used it to determinate the adequate sample size.

Still, sample size was not exclusion criterion, but a measure for quality score and just 30,8% did not met this criterion.

We use the Australian National Statistical Service website<sup>[3]</sup>, where an on-line Sample Size Calculator is provided, to easily reassure the valid Sample Size calculation.

Citations:

1. **Loney PL**, Chambers LW, Bennett KJ, Roberts JG, Stratford PW. Critical appraisal of the health research literature: prevalence or incidence of a health problem. *Chronic Dis Can.* 1998; **19**(4):170-176. [PMID: 10029513]
2. **Sagawa T**, Okamura S, Kakizaki S, Zhang Y, Morita K, Mori M. Functional gastrointestinal disorders in adolescents and quality of school life. *J Gastroenterol Hepatol.* 2013; **28**(2):285-290. [PMID: 27605889 DOI: 10.1111/j.1440-1746.2012.07257.x]
3. [www.nss.gov.au/nss/home.nsf/pages/Sample+size+calculator](http://www.nss.gov.au/nss/home.nsf/pages/Sample+size+calculator), last access in 19/03/17.

There could be a little improvement of English language (now grade B)

R. We understand and are grateful that we could count with a collaboration of a Professional English teacher and Sworn Translator for a proofreading of the revised

version of the manuscript.