

World Journal of Gastroenterology
Lian-Sheng Ma,
Science Editor, Company Editor-in-Chief, Editorial Office

D. Roorda, MD & J.P.M. Derikx, MD, PhD
Department of Pediatric Surgery
Emma Children's Hospital, Amsterdam UMC
Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands

DATE

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E-MAIL

d.roorda@amsterdamumc.nl

SUBJECT

Revisions manuscript (MS # 68919) "Generic and disease-specific health-related quality of life in patients with Hirschsprung disease: a systematic review and meta-analysis"

Dear Editor-in-chief,

We thank you for your decision to accept our systematic review and meta-analysis (MS # 62689 "*Generic and disease-specific health-related quality of life in patients with Hirschsprung disease: a systematic review and meta-analysis*") after minor revisions for publication in *World Journal of Gastroenterology*.

We have now made further revisions to the manuscript as requested, which are outlined in a point-by-point response in this letter.

We hope the current manuscript meets the standards for publication in *World Journal of Gastroenterology*.

Yours sincerely,

Veerle Huizer, MD

Naveen Wijekoon, MD, PhD

Danielle Roorda, MD

Marc A. Benninga, MD, PhD, Professor

Jaap Oosterlaan PhD, Professor

Shaman Rajindrajith, MD, PhD, Professor

Joep P.M. Derikx, MD, PhD

Reviewer 1:

Well-written manuscript on a relevant topic and directly related to the practice of clinical follow-up of patients treated for Hirschsprung's Disease. The methodology used is quite robust and meets the international guidelines used for systematic reviews and meta-analyses. The conclusions are grounded and do not extrapolate the results found. I have just two observations:

1. in the Results section, I suggest that the funnel plots related to publication bias be presented as supplementary materials (attachments).

We have now added the funnelplots related to publication bias to the supplementary materials. Please see page ...

2. in the Discussion section, on page 14, in the second paragraph, I think it is worth pointing out that the generic HRQoL did not differ significantly between age groups in this study.

We have added to the discussion of our findings that the generic HRQoL did not differ significantly between age groups (please see Discussion, page 14): *“Our findings indicated that generic HRQoL is not influenced by sex and type of respondent (parental proxy or self-report) and that generic HRQoL did not differ significantly between different age groups.”*

Reviewer 2:

The authors present a systematic review and meta-analysis and found no evidence for impaired quality of life outcome in patients with Hirschsprung disease compared to healthy controls, neither for the moderating effect of sex, parental proxy or self-report on outcome.

1. The limitations of the study are not properly detailed.

We have now added a more detailed description of the limitations of our study to the Discussion (please see Discussion section, page 16 and 17):

“Although for a few factors the moderation on HRQoL findings was tested in this study, this was done by meta-regression or group-comparison of meta-analytic findings. This type of analysis does not allow for the calculation of direct relations but calculates relations between studies’ averages or proportions and studies effect sizes.”

“A last limitation of this meta-analysis is that different instruments to measure HRQoL make different estimations, we aimed to correct for this by including the difference of patients with Hirschsprung disease with normative data in the meta-analysis, which is less vulnerable to a bias introduced by variance between instruments than directly including scores.”

Editorial comments:

1. Add more references in recent 5 years

We have now added the most recently published references (# 54, #63, #68) to our Discussion.

2. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

We have now added the decomposable Figures in one single Powerpoint file to our submission.