



Quality of life outcomes in children after surgery for Hirschsprung disease and anorectal malformations: a systematic review and meta-analysis

Irina Oltean,¹ Lamia Hayawi,² Victoria Larocca ¹, Vid Bijelić,² Emily Beveridge,¹ Manvinder Kaur,¹ Viviane Grandpierre,¹ Jane Kanyinda,¹ Ahmed Nasr ¹

To cite: Oltean I, Hayawi L, Larocca V, et al. Quality of life outcomes in children after surgery for Hirschsprung disease and anorectal malformations: a systematic review and meta-analysis. *World Jnl Ped Surgery* 2022;5:e000447. doi:10.1136/wjps-2022-000447

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/wjps-2022-000447>).

Received 10 May 2022

Accepted 12 October 2022

ABSTRACT

Background No systematic review and meta-analysis to date has examined multiple child and parent-reported social and physical quality of life (QoL) in pediatric populations affected by Hirschsprung's disease (HD) and anorectal malformations (ARM). The objective of this systematic review is to quantitatively summarize the parent-reported and child-reported psychosocial and physical functioning scores of such children.

Methods Records were sourced from the CENTRAL, EMBASE, and MEDLINE databases. Studies that reported child and parent reported QoL in children with HD and ARM, regardless of surgery intervention, versus children without HD and ARM, were included. The primary outcome was the psychosocial functioning scores, and the secondary outcomes were the presence of postoperative constipation, postoperative obstruction symptoms, fecal incontinence, and enterocolitis. A random effects meta-analysis was used.

Results Twenty-three studies were included in the systematic review, with 11 studies included in the meta-analysis. Totally, 1678 total pediatric patients with HD and ARM underwent surgery vs 392 healthy controls. Pooled parent-reported standardized mean (SM) scores showed better social functioning after surgery (SM 91.79, 95% CI (80.3 to 103.3), $I^2=0$). The pooled standardized mean difference (SMD) showed evidence for parent-reported incontinence but not for constipation in children with HD and ARM after surgery that had a lower mean QoL score compared with the normal population (SMD -1.24 (-1.79 to -0.69), $I^2=76\%$ and SMD -0.45 , 95% CI (-1.12 to 0.21), $I^2=75\%$). The pooled prevalence of child-reported constipation was 22% (95% CI (16% to 28%), $I^2=0\%$). The pooled prevalence of parent-reported postoperative obstruction symptoms was 61% (95% CI (41% to 81%), $I^2=41\%$).

Conclusion The results demonstrate better social functioning after surgery, lower QoL scores for incontinence versus controls, and remaining constipation and postoperative obstruction symptoms after surgery in children with HD and ARM.

INTRODUCTION

Hirschsprung's disease (HD) and anorectal malformations (ARM) are congenital

intestinal anomalies, typically manifesting during early infancy, and contribute to symptoms of severe constipation and intestinal obstruction.¹⁻³ HD and ARM affect 1 in 5000 live births with a slight male preponderance (ie, male-to-female sex ratio of 4:1).⁴⁻⁶ Surgical techniques have improved the results of children with HD by decreasing operation time, blood loss, length of hospital stay, and frequency of postoperative complications at 3 years after surgery.⁷⁻⁹ Despite these short-term advantages, bowel dysfunction and enterocolitis persist long-term and can adversely affect the psychosocial health of children with HD and ARM into adulthood.¹⁰⁻¹³ Quality of life (QoL) is a construct aimed at measuring the physical and psychosocial sequelae of parents and their children afflicted by gastrointestinal diseases.^{14 15} When applied to medicine, QoL refers to the 'subjective health status' of a patient and measures the effect of illness or disease, moving past physician assessment to consider the patient's well-being and progress.^{16 17} The results pertaining to the social adjustment of children with ARM are mixed with certain studies reporting difficulties forming relationships,¹⁸ elevated behavior problems,¹⁹ absence of psychological maladjustment,²⁰ or the presence of emotional disturbance in children experiencing frequent soiling accidents.²¹ Into older age, the major determinant of QoL continues to be fecal incontinence.²² Multiple meta-analyses have already investigated the short-term and mid-term postoperative outcomes in patients with HD who underwent different surgical approaches, yet the rates of postoperative complications are still variable.²³⁻²⁷

There has been no systematic review and meta-analysis to date, which encompasses multiple social and physical dimensions in a pediatric population with consideration of



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Surgery, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada

²Clinical Research Unit, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada

Correspondence to

Dr Ahmed Nasr; anasr@cheo.on.ca

parent perspectives. Our aim is to conduct a systematic review of existing literature to quantitatively summarize the parent and child-reported psychosocial and physical functioning scores and frequencies of children affected by HD and ARM and in comparison to children without these diseases if data permit.⁵

METHODS

This review followed the Cochrane Methodology to identify and select the studies²⁸ and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.²⁹

Search strategy and selection criteria

A systematic search for relevant studies was performed on November 5, 2019 and again on December 17, 2020, identifying six additional studies.^{6 30–34} MEDLINE, including Epub Ahead of Print, In-Process and Other Non-Indexed Citations, were searched between 1946 to October 25, 2020, Embase from 1947 to 2019 October 25, and the CENTRAL Trials Registry of the Cochrane Collaboration (September 2019 Issue) using the Ovid interface. Searches were designed and conducted by librarian experienced in systematic reviews, using a method designed to optimize term selection.³⁵ Search strategies can be found in the online supplemental file 1). The study protocol has been registered in Open Science Framework (10.31219/osf.io/zqbgx). All duplicate records were removed online, and records retrieved by the electronic search were downloaded and imported into a Reference Manager database, and then uploaded to Covidence (www.covidence.org) for title and abstract screening and full text review. Five reviewers (EB, IO, MK, VG, VL) screened independently at title/abstract level and full text review stages, and citations were excluded if at least two reviewers agreed to exclude; disagreements were reviewed and resolved by the study leads, where necessary (AN). The study colead (IO) reviewed all eligible citations to confirm eligibility.

Inclusion criteria

Case-control, cohort studies, and randomized-control trials examining child and parent reported QoL in children aged less than 18 years with HD and ARM, regardless of surgery intervention (ie, Duhamel, Swenson, endorectal pullthrough, laparoscopy-assisted pullthrough and open pull through), were included.

Exclusion criteria

Case studies, literature reviews, systematic reviews, editorials, letters to the editor, conference abstracts, and commentaries were excluded. Primary studies published before 2007 that were not written in English were also excluded. A previous systematic review captured studies before 2007; hence, why we excluded studies published before 2007.

Data extraction

Three authors (IO, EB, MK) performed data abstraction using a predesigned, piloted, and modified sheet in Excel V.14.7.7, which was validated by our statisticians (LH, VB). The extracted information included the following: study details including study design; type of QoL report (parent proxy or child), length of follow-up, age of children when QoL was assessed, QoL instrument facilitated, threshold for interpreting QoL scales, and parent-reported versus child-reported QoL scores, in addition to the sample sizes of children who presented with physical complications postoperatively.

Outcome definitions

The primary outcome was the mean scores on the psychosocial functioning domains. The secondary outcomes included the followings: reported frequencies and mean scores on QoL instruments of physical symptoms for constipation, intestinal obstruction, fecal incontinence, and enterocolitis. Definitions for each outcome depended on the QoL instrument used (online supplemental file 2, table S1). We defined short-term follow-up as: results from QoL interviews or questionnaires obtained before 2 years from study onset, while long-term follow-up referred to measurements after 2 years. Parents may have reported on study outcomes if children were too young to report themselves.

Assessment of risk of bias (ROB) within studies

Two reviewers (MK and IO) independently reviewed each study. The validated Methodological Index for Non-Randomized Studies (MINORS) criteria was used to assess the quality of the studies.³⁶ Based on the Cochrane handbook for considering bias, reasons for disagreement were explored and resolved.³⁷ Items assessed included: clearly stated aims, inclusion and representativeness of patients, reliable prospective data collection, appropriate and unbiased endpoints, sufficient follow-up period, follow-up loss, adequate study size calculation, contemporary groups (to address historical bias), baseline equivalence, and adequate statistical analysis.³⁶ Items 1–7 apply to non-comparative studies, while items 8–12 for comparative ones. Records were given scores of zero through two. The maximum (ideal) global score is 24 for comparative studies and 16 for non-comparative studies. One study was a randomized control trial (RCT).³⁸ Therefore, the Cochrane Risk of Bias tool was used. The ROB tool covers six domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Within each domain, assessments are made for one or more items and support for judgment is made by providing a free text description and assigning judgment into high, low, or unclear risk of material bias for each item.³⁹

Statistical analysis

All statistical analyses were performed using the R statistical programming language (V.4.0.).⁴⁰ Data were

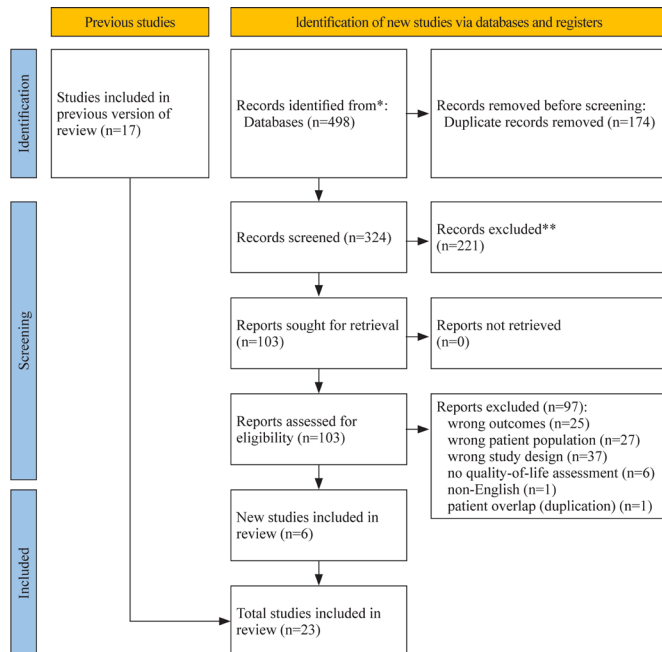


Figure 1 PRISMA flow diagram. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). **If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.²⁹ PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

meta-analyzed using a random effects model with R package ‘meta’.⁴¹ Scores of all QoL instruments were scaled to 0–100 scale using the ‘min-max scaling’ method (Hogg, p. 69).⁴² All scores were standardized—scores closer to 100 indicated higher or better QoL. Pooled proportions and pooled QoL standardized mean scores with 95% CI were reported in cases of low heterogeneity ($I^2=75\%$). In cases of high heterogeneity, the mean scores of individual studies without pooled estimate were presented by subgroups of potential sources of variability: duration of outcome (short 0–2 vs long 2+ years), instrument type, and scale (0–100 vs other). The results were reported separately for the child and parents.

RESULTS

Our initial search yielded 498 studies. After an update was performed, there were 6 additional studies that met our inclusion criteria and 23 (22 observational and 1 RCT) included in the systematic review, with two studies included in the meta-analysis for child-reports and nine for parent-reports (figure 1). One study was excluded, due to patient overlap.²²

Study characteristics and individual results

In total, 1678 pediatric patients with HD and ARM who underwent surgery vs 392 healthy controls without HD and ARM were included (online supplemental file 3). Children were typically between the ages of 2 and 18

years. A mean age was not reported because the timing of symptom presentation may have differed for each outcome. There were three prospective case control studies,^{43–45} two prospective case and retrospective control data studies (ie, established controls from literature),^{5 46} one retrospective case control study,³³ nine retrospective cohort studies,^{32 34 47–53} six prospective cohort studies,^{6 15 30 54–56} one RCT,³⁸ and one mixed-method sequential explanatory cohort study.³¹ These studies were implemented in various pediatric centers around the world, including Japan,⁴³ Australia,^{5 44} the Netherlands,^{46 48} United Kingdom,^{30 32} China,^{33 34 38 52} Sweden,⁵⁵ Egypt,¹⁵ Ireland,⁴⁷ Finland,⁵³ and the USA.^{49 51} Prevalent surgical approaches, included the trans anal endorectal pull-through, and the Duhamel methods. No study recruited patients with congenital diseases, neurological defects and other syndromes (eg, Down syndrome). The minimum follow-up was 6 months and maximum was 28 years, for QoL assessment.

Risk of bias across studies

Two reviewers (MK, IO) independently assessed RoB of the included studies. Common reasons for disagreement, included discrepancies on unbiased endpoints (ie, blinded interviewers for QoL assessments), follow-up period (2 years minimum), and loss to follow-up (<95% loss). The discrepancies were resolved by consensus (online supplemental file, table S3). Online supplemental file, tables S3 and S4 (online supplemental file 4) displays the quality appraisal results. MINORS scores for comparative studies (n=7) ranged from 14 to 20, with mean 16.4 ± 2.1 . MINORS scores for non-comparative studies (n=15) ranged from 10 to 14, with a mean of 11.7 ± 1.0 . Based on these mean scores, the MINORS criteria suggests fair study quality. Weaknesses in the comparative studies included a follow-up period of less than 2 years, greater than 5% loss to follow-up, insufficient double blinding, and no exploration of confounders or evidence of a statistical test when demographic characteristics differed between cases and controls (age and sex). Weaknesses of the non-comparative studies were: high attrition bias (>5%), no indication for Research Ethics Board (REB) approval, and potential for experimenter bias when administering QoL questionnaires (online supplemental file, table S3). The RCT published by Wang *et al*^{38 38} demonstrated fair quality due to absence of reporting bias. A lack of reporting in compliance and social adjustment did not bias additional outcomes such as incontinence (online supplemental file, table S4).

Primary outcomes

Psychosocial QoL outcomes

Pooled parent-reported mean scores showed better social functioning after surgery (91.79, 95% CI (80.3 to 103.3), $I^2=0$) (figure 2). Due to high heterogeneity for parent-reported emotional and psychosocial domains, only a narrative synthesis is presented, suggesting high emotional and psychosocial scores after surgery (online

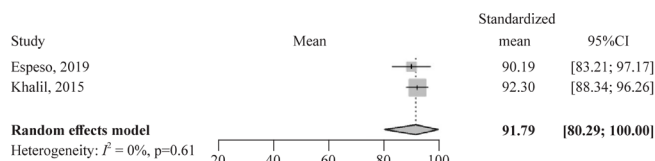


Figure 2 Pooled quality of life score mean estimate and 95% CI for parent-reported social functioning domain for Hirschsprung's disease only.

supplemental file 5). Please refer to the supplementary files that describe the altering of original scores using min-max scaling.

Secondary outcomes

Physical QoL outcomes in cases versus controls

The pooled effect for parent-reported shows evidence for incontinence but not for constipation. Children with HD and ARM after surgery have a lower mean QoL score compared with the normal population (standardized mean difference (SMD) -1.24 (-1.79 to -0.69), $I^2=76\%$ and SMD -0.45 , 95% CI (-1.12 to 0.21), $I^2=75\%$) (figure 3), respectively. For parent-reported incontinence scores, a subgroup analysis based on instrument type was performed (scale from 0 to 100 vs transformed to 0 to 100). Regardless of instrument type, incontinence scores are high or better after surgery (online supplemental file 5).

Physical complications

Pooled prevalence of child-reported constipation was 22% (95% CI (16% to 28%), $I^2=0\%$) (figure 4). Subgroup mean score for short-term versus long-term parent-reported constipation were showed, with short-term proportions ranging from 4% to 41% and long-term from 8% to 76% (online supplemental file 5). Pooled prevalence of parent-reported obstruction symptoms was 61% (95% CI (41% to 81%), $I^2=41\%$) (figure 5).

DISCUSSION

The objective of this systematic review was to capture the parent and child-reported psychosocial and physical functioning scores and physical complications of

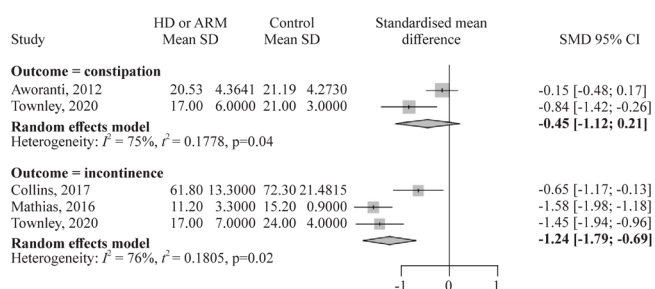


Figure 3 Pooled estimates and 95% CI for parent-reported constipation and incontinence scores. ARM, anorectal malformations; HD, Hirschsprung's disease; SMD, standardized mean difference.

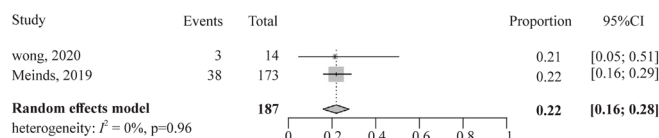


Figure 4 Pooled prevalence plot for child-reported constipation.

children affected by HD and ARM. Our main, low heterogeneity results demonstrate: (1) better social functioning after surgery; (2) lower QoL scores for incontinence versus controls; and (3) remaining constipation and obstruction symptoms after surgery in children with HD and ARM. In accordance with our findings, previous literature suggests that parents typically report better social functioning, such as good social relationships with friends in their children with HD and ARM.^{5 57 58} One potential explanation for this finding is that older pediatric patients with chronic disease experience a 'response shift', in that they respond to their new reality living with the disease and adjust to functional norms. In other words, they are able to emotionally and mentally shift to living with their chronic disease, giving them feelings of greater control.

This theory might help explain why parents observed better social functioning in their children, based on the internal coping strategies the children may have employed.⁵⁸⁻⁶⁰ However, relying on purely parent responses alone is not the only reliable method for assessing social functioning QoL in children with chronic disease. This is because discrepancies in QoL reporting persist with their children, and a combination of both is recommended.⁶¹ In fact, children with HD may report poor psychosocial and social functioning after surgery^{62 63} in comparison to their parents. Moreover, one systematic review found that children with HD and ARM experience difficulties with anxiety, peer rejection, and behavioral problems, while adolescents report low self-esteem, poor body image, and depression.⁶⁴

Our review found that children with HD and ARM have lower QoL scores for incontinence versus published controls but no evidence were found for constipation, which is in agreement with another 2021 systematic review⁶⁵ that did not determine the significant difference of constipation rates (42%) between HD children and the general population, when strict clinical definitions for constipation were used to monitor these patients.^{1 66} Therefore, when thresholds to qualify as constipation are set high, children may not meet all the

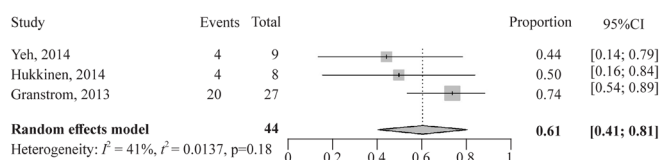


Figure 5 Pooled prevalence plot for parent-reported obstruction symptoms.

criteria at the time of assessment. Hence, constipation rates in our review may be underreported. Additionally, numerous studies have echoed that children with HD have increased or worse incontinence scores and lower physical functioning, compared with age and gender matched controls,^{5 44 48 67 68} regardless of the QoL instrument used. Interestingly, incontinence scores correlate with lower QoL scores for behavior and self-esteem, unlike in normal controls.⁴⁶ Plausible reasons why children with HD and ARM suffer from fecal incontinence might be due to increasing severity of fecal incontinence over time, as children age, which consequently negatively affects their QoL.

Conversely, children without these conditions may not experience the same complications.⁵ In our review, we included children between the ages of 0 and 18 years. Younger patients who have not lived long enough with HD may not cope positively to effectively manage their ongoing functional symptoms, thus reporting poorer physical QoL relative to controls.⁴⁴ Last, children with only a few functional problems are frequently discharged from follow-up and not transitioned to adolescent or adult care. As such, it is possible that this review underreported the functional problems of constipation and incontinence among cases.⁴⁸ Twenty-two per cent of children reported having constipation after surgery, while long-term parent-reported constipation was as high as 76% in our review. Parent-reported postoperative obstruction symptoms was 61%, and incontinence ranged from 13% to 68%. Comparing these findings to prior literature is difficult, given that clinical definitions for constipation, postoperative obstruction symptoms, and incontinence vary greatly across studies and may be captured differently based on the data collection method used.⁶⁵ In fact, certain studies report no HD patients experiencing constipation^{69 70} vs 30%–76% after surgery.^{48 66} Similarly, cohort studies document ranges of incontinence from 19% to 82%.^{44 62 71–76} Long-term follow-up after surgery may increase the ability for researchers to detect the incidence of constipation and incontinence. Moreover, the pediatric population is heterogeneous in that they may present with neurological impairments and syndrome-associated diseases, which are correlated with increased constipation and incontinence scores.^{1 65 77} No children in studies included in our review possessed such impairments.

Limitations

Limitations of the evidence included in this review mainly stem from the wide variability in child and parent documented psychosocial and physical QoL outcomes, which we attempted to examine via subgroups for instrument type, scale, and duration of outcome. Heterogeneity was likely due to underlying clinical differences in the pediatric population and/or discrepancies between parent and child reports. Furthermore, sample sizes in cohort studies were small, and certain case control studies captured

control data from previously established literature, rather than controls recruited during their study. We also surmise that physical complications were more likely to be detected during long-term postoperative follow-up.

Future directions

Given the variability in psychosocial and physical functioning QoL instruments, there is a need to standardize child and parent-reported QoL measurements to improve the robustness and generalizability of the current evidence. Moreover, creating validated, age-specific child QoL measurements would also be beneficial to explore differences in QoL by age. In terms of the complications of constipation and incontinence, standardizing clinical definitions and treatment plans are encouraged. Prospective, multicentered, and longitudinal studies with consistent monitoring of QoL and complications of children with HD and ARM into adulthood, is an area of future research.

Clinical implications

For clinical benefits, postsurgical treatment interventions should target reducing constipation, postoperative obstruction symptoms, and incontinence scores based on consultation with patients and their health risk profile. In order to obtain an accurate perception of child social functioning, more informants (children, parents, teachers) in clinical research are recommended, to support patients and their families after surgery.^{64 78 79}

Acknowledgements We thank Margaret Sampson, MLIS, PhD, AHIP (Children's Hospital of Eastern Ontario) for developing the electronic search strategies and Lindsey Sikora, MSc, MEd (University of Ottawa) for peer review of the MEDLINE search strategy.

Contributors Five reviewers (EB, IO, MK, VG, VL) screened independently at title/abstract level and full text review stages, and citations were excluded if at least two reviewers agreed to exclude; disagreements were reviewed and resolved by the study leads, where necessary (AN). The study colead (IO) reviewed all eligible citations to confirm eligibility. Two analysts (LH, VB) were responsible for assisting with the analysis. IO was responsible for writing the final manuscript with assistance from VL.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Victoria Larocca <http://orcid.org/0000-0002-1907-4494>

Ahmed Nasr <http://orcid.org/0000-0001-8410-6352>

REFERENCES

- Catto-Smith AG, Trajanovska M, Taylor RG. Long-term continence after surgery for Hirschsprung's disease. *J Gastroenterol Hepatol* 2007;22:2273–82.
- Singh SJ, Croaker GDH, Manglick P, et al. Hirschsprung's disease: the Australian paediatric surveillance unit's experience. *Pediatr Surg Int* 2003;19:247–50.
- Kenny SE, Tam PKH, Garcia-Barcelo M. Hirschsprung's disease. *Semin Pediatr Surg* 2010;19:194–200.
- Bergeron K-F, Silversides DW, Pilon N. The developmental genetics of Hirschsprung's disease. *Clin Genet* 2013;83:15–22.
- Collins L, Collis B, Trajanovska M, et al. Quality of life outcomes in children with Hirschsprung disease. *J Pediatr Surg* 2017;52:2006–10.
- Espeso L, Coutable A, Flaum V, et al. Persistent soiling affects quality of life in children with Hirschsprung's disease. *J Pediatr Gastroenterol Nutr* 2020;70:238–42.
- Deng X, Wu Y, Zeng L, et al. Comparative analysis of modified laparoscopic Swenson and laparoscopic Soave procedure for short-segment Hirschsprung disease in children. *Eur J Pediatr Surg* 2015;25:430–4.
- Gunnarsdóttir A, Larsson L-T, Arnbjörnsson E. Transanal endorectal vs. Duhamel pull-through for Hirschsprung's disease. *Eur J Pediatr Surg* 2010;20:242–6.
- Lukač M, Antunović SS, Vujović D, et al. Efikasnost različitih hirurških procedura U lečenju Hiršprungove bolesti kod dece. *Vojnosanit Pregl* 2016;73:246–50.
- Chung PH-Y, Wong KK-Y, Leung JL, et al. Clinical and manometric evaluations of anorectal function in patients after transanal endorectal pull-through operation for Hirschsprung's disease: A multicentre study. *Surg Pract* 2015;19:113–9.
- Bischoff A, Levitt MA, Bauer C, et al. Treatment of fecal incontinence with a comprehensive bowel management program. *J Pediatr Surg* 2009;44:1278–84.
- Levitt MA, Peña A. Pediatric fecal incontinence: a surgeon's perspective. *Pediatr Rev* 2010;31:91–101.
- Engum SA, Grosfeld JL. Long-Term results of treatment of Hirschsprung's disease. *Semin Pediatr Surg* 2004;13:273–85.
- Frazier TW, Hyland AC, Markowitz LA, et al. Psychometric evaluation of the revised child and family quality of life questionnaire (CFQL-2). *Res Autism Spectr Disord* 2020;70:101474.
- Khalil M. Long-Term health-related quality of life for patients with Hirschsprung's disease at 5 years after transanal endorectal pull-through operation. *Qual Life Res* 2015;24:2733–8.
- Gotay CC, Korn EL, McCabe MS, et al. Quality-Of-Life assessment in cancer treatment protocols: research issues in protocol development. *J Natl Cancer Inst* 1992;84:575–9.
- Cohen C. On the quality of life: some philosophical reflections. *Circulation* 1982;66:29–33.
- Hassink EA, Rieu PN, Brugman AT, et al. Quality of life after operatively corrected high anorectal malformation: a long-term follow-up study of patients aged 18 years and older. *J Pediatr Surg* 1994;29:773–6.
- Bai Y, Yuan Z, Wang W, et al. Quality of life for children with fecal incontinence after surgically corrected anorectal malformation. *J Pediatr Surg* 2000;35:462–4.
- Ludman L, Spitz L. Psychosocial adjustment of children treated for anorectal anomalies. *J Pediatr Surg* 1995;30:495–9.
- Ditesheim JA, Templeton JM. Short-Term V long-term quality of life in children following repair of high imperforate anus. *J Pediatr Surg* 1987;22:581–7.
- Grano C, Aminoff D, Lucidi F, et al. Long-Term disease-specific quality of life in children and adolescent patients with arm. *J Pediatr Surg* 2012;47:1317–22.
- Zimmer J, Tomuschat C, Puri P. Long-Term results of transanal pull-through for Hirschsprung's disease: a meta-analysis. *Pediatr Surg Int* 2016;32:743–9.
- Zhang S, Li J, Wu Y, et al. Comparison of laparoscopic-Assisted operations and laparotomy operations for the treatment of Hirschsprung disease: evidence from a meta-analysis. *Medicine* 2015;94:e1632.
- Thomson D, Allin B, Long A-M, et al. Laparoscopic assistance for primary transanal pull-through in Hirschsprung's disease: a systematic review and meta-analysis. *BMJ Open* 2015;5:e006063.
- Guerra J, Wayne C, Musambe T, et al. Laparoscopic-assisted transanal pull-through (LAP) versus complete transanal pull-through (CTP) in the surgical management of Hirschsprung's disease. *J Pediatr Surg* 2016;51:770–4.
- Dai Y, Deng Y, Lin Y, et al. Long-Term outcomes and quality of life of patients with Hirschsprung disease: a systematic review and meta-analysis. *BMC Gastroenterol* 2020;20:1–13.
- Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for systematic reviews of interventions version 6.2*, 2019.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
- Allin BSR, Opondo C, Bradnock TJ, et al. Outcomes at five to eight years of age for children with Hirschsprung's disease. *Arch Dis Child* 2021;106:484–90.
- Saysoo MR, Dewi FST, Gunadi. Quality of life of patients with Hirschsprung disease after Duhamel and Soave pull-through procedures: a mixed-methods sequential explanatory cohort study. *Ann Med Surg* 2020;56:34–7.
- Townley OG, Lindley RM, Cohen MC, et al. Functional outcome, quality of life, and 'failures' following pull-through surgery for Hirschsprung's disease: A review of practice at a single-center. *J Pediatr Surg* 2020;55:273–7.
- Wong CWY, Chung PHY, Tam PKH, et al. Quality of life and defecative function 10 years or longer after posterior sagittal anorectoplasty and laparoscopic-assisted anorectal pull-through for anorectal malformation. *Pediatr Surg Int* 2020;36:289–93.
- Zhuansun D, Jiao C, Meng X, et al. Long-Term outcomes of laparoscope-assisted Heart-shaped anastomosis for children with Hirschsprung disease: a 10-year review study. *J Pediatr Surg* 2020;55:1824–8.
- Bramer WM, de Jonge GB, Rethlefsen ML, et al. A systematic approach to searching: an efficient and complete method to develop literature searches. *J Med Libr Assoc* 2018;106:531–41.
- Slim K, Nini E, Forestier D, et al. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003;73:712–6.
- Boutron I, Page MJ, Higgins JPT, et al. Chapter 7: Considering bias and conflicts of interest among the included studies. In: Higgins JPT, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for systematic reviews of interventions version 6.3 (updated February 2022)*. Cochrane, 2022. <https://training.cochrane.org/handbook/current/chapter-07>
- Wang H, Guo X-N, Zhu D, et al. Nursing intervention for outpatient rehabilitation in pediatric patients with Hirschsprung disease after colectomy. *Eur J Pediatr Surg* 2015;25:435–40.
- Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
- R Core Team. A language and environment for statistical computing, 2018. Available: <https://www.r-project.org/> [Accessed 17 Sep 2020].
- Balduzzi S, Rucker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health* 2019;22:153–60.
- Hogg R, McKean J, Craig A. *Introduction to mathematical statistics*. 8th ed. Boston: Pearson education, 2005. <https://minerva.it.manchester.ac.uk/~saralees/statbook2.pdf>
- Yamataka A, Kaneyama K, Fujiwara N, et al. Rectal mucosal dissection during transanal pull-through for Hirschsprung disease: the anorectal or the dentate line? *J Pediatr Surg* 2009;44:266–70.
- Sood S, Lim R, Collins L, et al. The long-term quality of life outcomes in adolescents with Hirschsprung disease. *J Pediatr Surg* 2018;53:2430–4.
- Mathias AL, Tannuri ACA, Ferreira MAE, et al. [Validation of questionnaires to assess quality of life related to fecal incontinence in children with anorectal malformations and Hirschsprung's disease]. *Rev Paul Pediatr* 2016;34:99–105.
- Meinds RJ, van der Steeg AFW, Sloots CEJ, et al. Long-Term functional outcomes and quality of life in patients with Hirschsprung's disease. *Br J Surg* 2019;106:499–507.
- Aworanti OM, McDowell DT, Martin IM, et al. Comparative review of functional outcomes post surgery for Hirschsprung's disease utilizing the paediatric incontinence and constipation scoring system. *Pediatr Surg Int* 2012;28:1071–8.

- 48 Roorda D, Witvliet MJ, Wellens LM, *et al.* Long-Term outcome and quality of life in patients with total colonic aganglionosis in the Netherlands. *Colorectal Dis* 2018;20:719–26.
- 49 Levitt MA, Hamrick MC, Eradi B, *et al.* Transanal, full-thickness, Swenson-like approach for Hirschsprung disease. *J Pediatr Surg* 2013;48:2289–95.
- 50 Yeh Y-T, Tsai H-L, Chen C-Y, *et al.* Surgical outcomes of total colonic aganglionosis in children: a 26-year experience in a single Institute. *J Chinese Med Assoc* 2014;77:519–23.
- 51 Lane VA, Nacion KM, Cooper JN, *et al.* Determinants of quality of life in children with colorectal diseases. *J Pediatr Surg* 2016;51:1843–50.
- 52 Yang S, Zheng S, Huang Y, *et al.* Prognostic factors in children with total colonic aganglionosis treated with the Soave procedure: the experience of 43 patients from a single institution. *Int J Clin Exp Med* 2016;9:8770–4.
- 53 Hukkinen M, Koivusalo A, Rintala RJ, *et al.* Restorative proctocolectomy with J-pouch ileoanal anastomosis for total colonic aganglionosis among neonates and infants. *J Pediatr Surg* 2014;49:570–4.
- 54 Grano C, Aminoff D, Lucidi F, *et al.* Disease-Specific quality of life in children and adults with anorectal malformations. *Pediatr Surg Int* 2010;26:151–5.
- 55 Granström AL, Husberg B, Nordenskjöld A, *et al.* Laparoscopic-assisted pull-through for Hirschsprung's disease, a prospective repeated evaluation of functional outcome. *J Pediatr Surg* 2013;48:2536–9.
- 56 John V, Chacko J, Mathai J, *et al.* Psychosocial aspects of follow-up of children operated for intermediate anorectal malformations. *Pediatr Surg Int* 2010;26:989–94.
- 57 Hartman EE, Oort FJ, Aronson DC, *et al.* Quality of life and disease-specific functioning of patients with anorectal malformations or Hirschsprung's disease: a review. *Arch Dis Child* 2011;96:398–406.
- 58 Nah SA, Ong CCP, Saffari SE, *et al.* Anorectal malformation & Hirschsprung's disease: A cross-sectional comparison of quality of life and bowel function to healthy controls. *J Pediatr Surg* 2018;53:1550–4.
- 59 Athanasakos EP, Kemal KI, Malliwal RS, *et al.* Clinical and psychosocial functioning in adolescents and young adults with anorectal malformations and chronic idiopathic constipation. *Br J Surg* 2013;100:832–9.
- 60 van Tilburg MAL, Murphy TB. Quality of life paradox in gastrointestinal disorders. *J Pediatr* 2015;166:11–14.
- 61 Loganathan AK, Mathew AS, Kurian JJ. Assessment of quality of life and functional outcomes of operated cases of Hirschsprung disease in a developing country. *Pediatr Gastroenterol Hepatol Nutr* 2021;24:145–53.
- 62 Diseth TH, Bjørnland K, Nøvik TS, *et al.* Bowel function, mental health, and psychosocial function in adolescents with Hirschsprung's disease. *Arch Dis Child* 1997;76:100–6.
- 63 Menezes M, Corbally M, Puri P. Long-Term results of bowel function after treatment for Hirschsprung's disease: a 29-year review. *Pediatr Surg Int* 2006;22:987–90.
- 64 Svetanoff WJ, Kapalu CL, Lopez JJ, *et al.* Psychosocial factors affecting quality of life in patients with anorectal malformation and Hirschsprung disease—a qualitative systematic review. *J Pediatr Surg* 2022;57:387–93.
- 65 Kawaguchi AL, Guner YS, Sømme S, *et al.* Management and outcomes for long-segment Hirschsprung disease: a systematic review from the apsA outcomes and evidence based practice Committee. *J Pediatr Surg* 2021;56:1513–23.
- 66 Teitelbaum DH, Drongowski RA, Chamberlain JN, *et al.* Long-Term stooling patterns in infants undergoing primary endorectal pull-through for Hirschsprung's disease. *J Pediatr Surg* 1997;32:1049–53.
- 67 Tran VQ, Mahler T, Dassonville M. Long-Term outcomes and quality of life in patients after Soave pull-through operation for Hirschsprung's disease: an observational retrospective study. *Eur J Pediatr Surg* 2018;2815:445–54.
- 68 Byström C, Östlund S, Hoff N, *et al.* Evaluation of bowel function, urinary tract function, and quality of life after transanal endorectal pull-through surgery for Hirschsprung's disease. *Eur J Pediatr Surg* 2021;31:40–8.
- 69 Choe EK, Moon SB, Kim HY, *et al.* Outcomes of surgical management of total colonic aganglionosis. *World J Surg* 2008;32:62–8.
- 70 Stenström P, Brautigam M, Borg H, *et al.* Patient-Reported Swedish nationwide outcomes of children and adolescents with total colonic aganglionosis. *J Pediatr Surg* 2017;52:1302–7.
- 71 Neuvonen MI, Kyrklund K, Rintala RJ, *et al.* Bowel function and quality of life after transanal endorectal pull-through for Hirschsprung disease: controlled outcomes up to adulthood. *Ann Surg* 2017;265:622–9.
- 72 Stensrud KJ. Transanal endorectal pull-through for Hirschsprung disease – outcome in relation to surgical approach, age and anal canal morphology. Oslo, 2016. Available: <https://www.duo.uio.no/bitstream/handle/10852/52541/PhD-Stensrud-DUO.pdf?sequence=1>
- 73 Ieiri S, Nakatsuji T, Akiyoshi J, *et al.* Long-term outcomes and the quality of life of Hirschsprung disease in adolescents who have reached 18 years or older—a 47-year single-institute experience. *J Pediatr Surg* 2010;45:2398–402.
- 74 Bai Y, Chen H, Hao J, *et al.* Long-Term outcome and quality of life after the Swenson procedure for Hirschsprung's disease. *J Pediatr Surg* 2002;37:639–42.
- 75 Mills JLA, Konkin DE, Milner R, *et al.* Long-Term bowel function and quality of life in children with Hirschsprung's disease. *J Pediatr Surg* 2008;43:899–905.
- 76 Diseth TH, Egeland T, Emblem R. Effects of anal invasive treatment and incontinence on mental health and psychosocial functioning of adolescents with Hirschsprung's disease and low anorectal anomalies. *J Pediatr Surg* 1998;33:468–75.
- 77 Bjørnland K, Pakarinen MP, Stenström P, *et al.* A Nordic multicenter survey of long-term bowel function after transanal endorectal pull-through in 200 patients with rectosigmoid Hirschsprung disease. *J Pediatr Surg* 2017;52:1458–64.
- 78 Goodrich N, Naslund R, Bossert W, *et al.* Learner perceptions of family-centred rounds. *Clin Teach* 2020;17:1–5.
- 79 Till JE, Osoba D, Pater JL, *et al.* Research on health-related quality of life: dissemination into practical applications. *Qual Life Res* 1994;3:279–83.