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Bridging the Gap: Reporting Baseline Characteristics, Process and Outcome Parameters in Hirschsprung's Disease. A Systematic Review.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:

Introduction

The variation in standardized, well-defined parameters in Hirschsprung's disease (HSCR) research hinders overarching comparisons and complicates evaluations of care quality across healthcare settings. This review addresses the significant variability observed in these parameters as reported in recent publications. The goal is to compile a list of commonly described baseline characteristics, process and outcome measures, and to investigate disparities in their utilization and definitions.

Materials and methods

A systematic review of literature on the primary care process for HSCR was performed according to PRISMA guidelines. Relevant literature published between 2015 and 2021 was obtained by combining the search term "Hirschsprung's disease" with "treatment outcome", "complications", "mortality", "morbidity", "survival" in Medline, Embase and the Cochrane Library. We extracted study characteristics, reported process and outcome parameters, and patient and disease characteristics.

Results

We extracted 1026 parameters from 200 publications and categorized these into patient characteristics (n=226), treatment and care process characteristics (n=199), and outcomes (n=601). 116 parameters were reported in more than 5% of publications. The most frequently reported characteristics were sex (88%), age at surgery (66%), postoperative Hirschsprung-associated enterocolitis (64%), type of repair (57%), fecal incontinence (54%), and extent of aganglionosis (51%).

Conclusion

This review underscores the pronounced variation in reported parameters within HSCR studies, highlighting the necessity for consistent, well-defined measures and reporting systems in order to foster improved data interpretability. Moreover, it advocates for the use of these findings in the development of a Core Indicator Set, complementing the recently developed Core Outcome Set. This will facilitate quality assessments across pediatric surgical centers throughout Europe.

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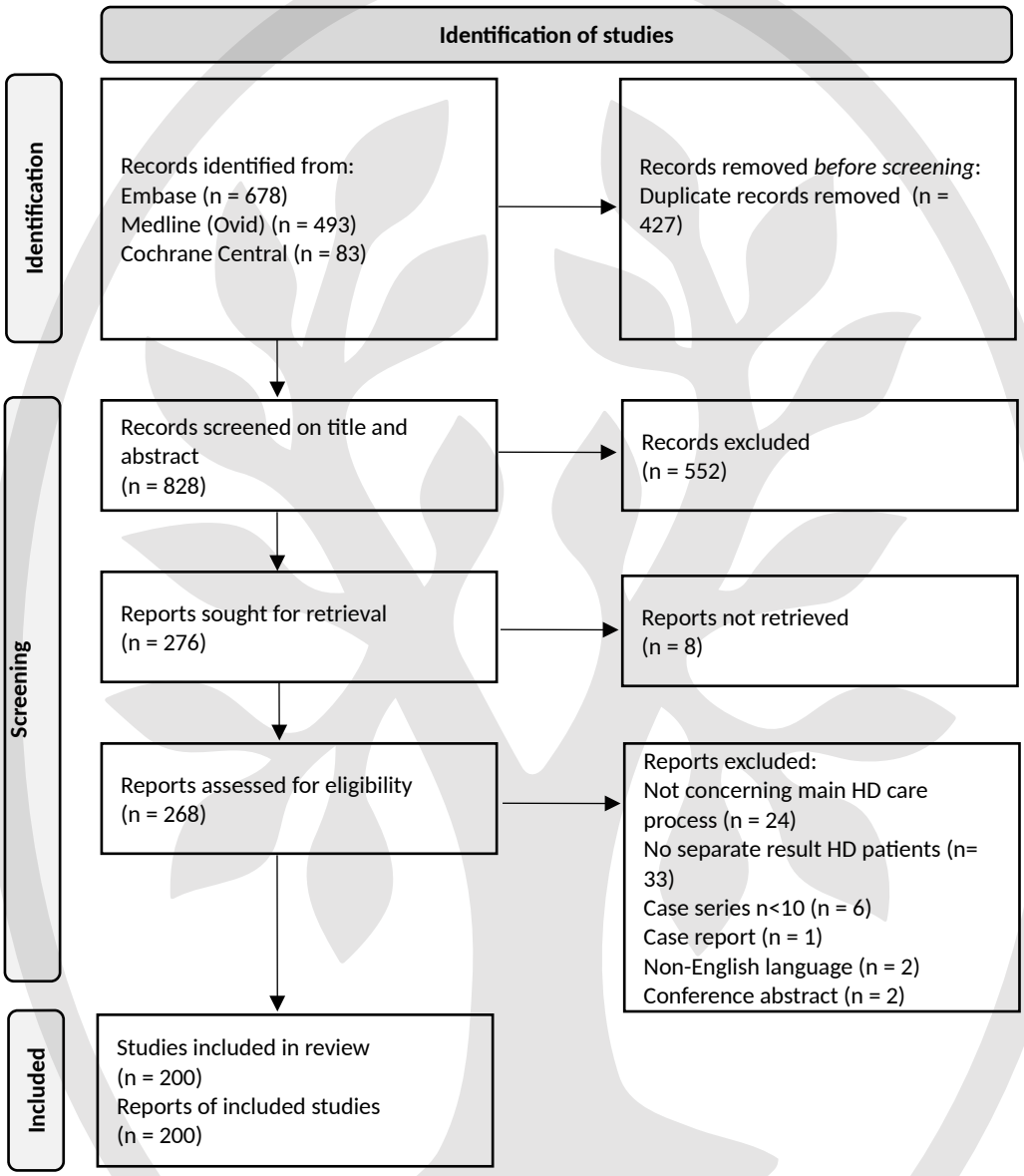

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INTRODUCTION

Hirschsprung's disease (HSCR) is a rare congenital condition that affects 1 in 5000 newborn children. It is characterized by the absence of ganglion cells in the enteric nervous system of the rectum, with variable involvement of the colon and small bowel. Current understanding suggests that this abnormality arises from disruptions in embryonic development stages, particularly the migration and survival of enteric nervous system precursor cells[1,2].

Infants with HSCR present with symptoms of functional intestinal obstruction, such as delayed passage of meconium, abdominal distention, vomiting, and chronic constipation. Currently, establishing the diagnosis predominantly relies on rectal suction biopsies revealing an absence of ganglion cells. Aimed at re-establishing regular bowel functionality, the treatment generally involves resection of the aganglionic colon segment and reconnecting the ganglionic intestine segment to the anus. Surgical strategies include the Swenson[3], Duhamel[4], and Soave-Boley[5,6] resection techniques, fashioned as single- or multi-stage, open, laparoscopic, or total transanal procedures[1,7].

Due to the rarity of HSCR, prospective, controlled, multi-center trials with adequate patient numbers are notably scarce. Furthermore, despite the increase in HSCR-related publications in recent decades, which could potentially contribute to more evidence-based practice, the usability of these research findings is limited. This limitation stems from the substantial variability in the reported research parameters and their respective definitions, preventing the possibility of comprehensive comparisons. Although a HSCR core outcome set has been

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formulated, this has not yet attained widespread recognition or utilization within the scholarly community[7,8]. These circumstances further prevent the resolution of existing evidence gaps, particularly in understanding short-term complications and long-term interactions between functional outcomes and quality of life[9]. Presently, guidelines for the management of HSCR often rely on expert opinion or consensus rather than comprehensive research, which implies that there is substantial room for improvement in the evidence-based practice.

The lack of standardized, well-defined parameters not only hinders overarching comparisons in research, but also adds complexity to the evaluation and comparison of (quality of) HSCR care across hospitals, regions, or even countries. A pivotal step in advancing HSCR care has been the initiation of the European Pediatric Surgical Audit (EPSA) for several congenital malformations, including HSCR. This quality-of-care measurement tool for clinicians makes use of quality indicators to reliably identify, monitor, and evaluate variation in clinical practices and outcomes[10-12]. Improvement efforts could then be aligned with the findings from this evaluation. Indicators can be classified into three categories–structure indicators, process indicators, and outcome indicators–each evaluating different aspects of the care pathway. Examples of structure indicators are patient volumes and the availability of certain imaging techniques. Process indicators can involve factors such as the elapsed time between diagnosis and surgery, and the proportion of patients undergoing a particular diagnostic test. Outcome indicators might encompass elements such as survival rates or complication rates[13]. To develop a universally acknowledged set of quality indicators for evaluating and identifying variations in the quality of care for HSCR patients, it is essential to ascertain which parameters are

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considered most important by HSCR researchers and clinicians treating this disease. These identified outcomes can then serve as the basis for a consensus-driven process to delineate the new set of quality indicators. This initiative requires comprehensive understanding of all possible outcomes highlighted in HSCR research, as well as patient characteristics and treatment and care process characteristics, in order to adjust for case variability when comparing care quality. Such endeavors could provide an even deeper understanding of inter-hospital variability, further supporting future advancements in the care of this patient population.

The primary objective of this study was to compile a list of outcome measures described in recent peer-reviewed publications on HSCR and to explore the discrepancies in their utilization, definition, and reporting. The secondary objective was to identify patient characteristics and treatment and care process characteristics that would facilitate a more informed interpretation of future comparative analysis results.

MATERIALS AND METHODS

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement and guidelines[14]. We developed a comprehensive search strategy in collaboration with a medical librarian of the Erasmus University Medical Center. The search was based on the search term 'Hirschsprung's disease', combined with the terms 'morbidity' or 'mortality' or 'survival' or 'outcome' or 'complication'. The search criteria were applied to the databases Medline, Embase, and the Cochrane Library. Duplicate publications

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were removed and subsequently all studies published from 2015 up to and September 2021 were selected. Complete search strategies are provided in Supplementary Material 1. The search was performed in October 2021.

Inclusion and exclusion criteria

All publications related to any aspect of the main HSCR care process, including surgical and non-surgical management, were included. To ensure contemporaneousness, papers published before the year 2015 were excluded. Other criteria for exclusion were the following: non-English-language publications, animal research, in vitro studies, case series with fewer than ten patients, editorials, letters, meeting abstracts, reviews, guidelines, and consensus statements.

Selection process

Four reviewers participated in the selection process of the publications. NT and AG separately screened the titles and abstracts of all publications resulting from the search to determine their suitability in terms of reporting on the care for and management of patients with HSCR. NT, DR and AG then independently reviewed the full texts of the selected publications to ascertain their relevance to the study. Any disagreements were resolved by TW, who served as a third reviewer. The reviewing authors were not blinded to the title, authors, or journal names during the screening process.

Data collection, analysis and reporting

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DR and NT performed the data extraction, which included recording the origin and year of publications, study design, the number of included patients per study (as shown in Table 1) and all relevant parameters in a primary Excel-based framework. Parameters were categorized and, when feasible, merged based on consensus among the reviewers. For each parameter, the number of publications in which it was mentioned and the proportion relative to the total number of included publications were calculated. The parameters mentioned in more than 5% of the included publications were then recorded in a separate Excel file. Additionally, all definitions of studied parameters were extracted, as well as the types of instruments or tools, either standardized or not, with which the parameters were assessed, such as medical scores, scales and questionnaires. This review did not include the extraction or interpretation of parameter estimates, nor did it involve the evaluation and assessment of methodological quality of the included publications. Statistical analyses were conducted utilizing a customized data computational approach implemented within the Excel environment.

RESULTS

Included publications

The search strategy resulted in 1254 publications. After removal of duplicates and limiting the results to articles published between 2015 and 2021, 828 articles remained, of which 200 met the inclusion criteria (Figure 1). The study characteristics of all included publications are summarized in Table 1. An individualized overview of included studies and corresponding study characteristics can be found in Supplementary Material 2.

Data extraction

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Full-text analysis of the 200 included publications identified 1026 studied parameters described in at least one of the included publications. The parameters were categorized into patient characteristics (n=226), treatment and care process characteristics (n=199), and outcomes (n=601). As several parameters could arguably be included in more than one category, categorization followed agreement between the first two authors. To facilitate the comparison of variation in studied parameters within similar subjects, we further arranged the parameters by topic, such as comorbidities, primary treatment, specific complications and long-term outcome. A list of all identified, categorized items is attached in Supplementary Material 3-5.

Measured parameters

Of the 1026 identified studied parameters, 116 were described in at least 5% of included publications (Table 2). Predominantly described patient characteristics were sex (88%), age at surgery (66%), and the extent of aganglionosis (histological level of transitional zone, 50.5%). Frequently studied treatment and care process characteristics included the type of repair (56.5%), duration of follow-up (39%) and preoperative stoma (35.5%). The most frequently mentioned outcome measures were postoperative Hirschsprung-associated enterocolitis (HAEC) (63.5%), incontinence (53.5%) and constipation (48%). The primarily described complications after surgical treatment were anastomotic stricture and anastomotic leakage, cited in 38% and 28% of the publications, respectively. Other significant areas of focus encompassed length of primary hospital stay (highlighted in 35.5% of the studies), mortality (26.5%), reoperation rate (42.5%) and readmission rate (12.5%). Because the definitions of analyzed parameters and the used (standardized) measurement tools diverged significantly

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across different publications, it was challenging to derive clear-cut definitions or compare these results. Consequently these results specifically concerning the definitions of the extracted parameters are not delineated in this report. An overview of the standardized clinical tools, scores and scales applied in the studies is presented in Table 3.

DISCUSSION

This study aimed to create a comprehensive overview of patient characteristics, treatment and care process characteristics, and outcome measures. To our knowledge, it represents the first attempt to compile such an extensive summary of parameters investigated in HSCR research. From the 200 publications on HSCR spanning from 2015 to 2021 that were included, we identified a total of 1026 unique studied parameters, which could be categorized into 226 patient characteristics, 199 treatment and care process characteristics, and 601 outcomes. Among these, 116 parameters were described in at least 5% of the included publications, of which only six mentioned in more than 50% of the included publications. These six parameters were postoperative HAEC, incontinence, type of repair, sex, age at surgery, and extent of aganglionosis.

The current body of research of interest for this review primarily consists of retrospective, single-center studies with low patient volumes[15]. A substantial portion of the surveyed literature (69%) is based on data derived from cohorts comprising fewer than 100 patients, and more than three-quarters of the studies are single-center studies. This underscores the need for more multi-center and prospective studies involving larger patient cohorts to yield more robust

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results. Such approaches may include randomized controlled trials or the implementation of standardized data collection within patient registries, such as clinical audits. This study also confirms that contemporary research on HSCR tends to focus more on outcomes (59% of extracted variables) rather than on characteristics used to evaluate care processes (19%), and more on short-term than on long-term outcomes. Furthermore, considering the 1026 distinct parameters mentioned in the included publications, we substantiated that data collection and reporting lacks uniformity across studies, making it harder to consolidate and analyze findings cohesively. We also demonstrated substantial variation in parameter definitions and the tools used across studies to measure important parameters such as quality of life or other patient-reported outcome measures (PROMs)[16], as illustrated in Table 3. This lack of uniformity hinders comparing and contrasting of results across different studies, and once more indicates an urgent need for creating and implementing standardized, reliable and well-defined parameters and tools that are both patient-centric and disease-specific. Concurrently, it is essential to acknowledge that the NETS1HD study introduced a novel HSCR core outcome set through rigorous methods[7]. In contrast to this study, our approach not only centered on outcome measures but also encompassed a comprehensive analysis of treatment and diagnostic characteristics, as well as patients' baseline characteristics. We focused on identifying the most extensively studied parameters and did not consult a panel of experts for their ratings and definitions. Promoting the adoption of this core outcome set and similar initiatives and implementing these standardized data sets in both large and small pediatric surgical studies is crucial, as it will enhance relevance, minimizes bias, and facilitate future meta-analyses.

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Standardization of research parameters is especially important in rare disease research, as the rare nature of the studied conditions often inherently complicates generating high-quality evidence, as we have confirmed with this review. Because of the demonstrated lack of high-quality evidence, current guidelines and clinical practices still predominantly hinge on expert opinions and consensus statements. Moreover, as opposed to the previously mentioned HSCR core outcome set, which was developed to standardize research, it is vital to acknowledge the current deficit in standardized measures for evaluating the quality of HSCR care and the absence of a common benchmarking system. In the modern healthcare landscape there is a growing emphasis on the quality of provided care, and standardized measures are essential for precise benchmarking and the accurate interpretation of outcomes. Consequently, the development and implementation of standardized benchmarking through measuring predefined quality indicators could significantly enhance the overall quality of HSCR care. Current clinical guidelines and consensus statements and the list of treatment and care process characteristics and outcomes resulting from this systematic review may function as a starting point for a consensus method to develop quality indicator sets for such tools, involving both the international HSCR expert community as well as patient representatives. The European Reference Network for Inherited Congenital Anomalies and its registry (EPSA) have the potential to play a critical role in the more effective collection and analysis of comparative quality data, ultimately leading to the establishment of best practices and bridging the gap between short-term and long-term outcomes[10].

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By adhering to the PRISMA guidelines, we ensured a structured and transparent methodology. The extensive data extraction and categorization allowed for interpretation of the current most important parameters for clinical researchers in the field. This approach has markedly reduced the likelihood of overlooking crucial parameters, as we have included all parameters mentioned in at least 5% of the selected studies. Our findings emphasize the necessity for standardization of data collection, definitions and use of clinical tools and instruments. By addressing a significant gap in HSCR research–namely the lack of uniformity in parameter measurement and reporting methods–we not only bring to light the existing discrepancies but underscore the urgency for a cohesive approach in future studies. Additionally, the resulting list could lay the groundwork for determining which parameters are important for assessing the quality of HSCR care. Our research also has some limitations. Firstly, as we pooled data from children and adults without providing a distinct analysis for each group, the findings are not age-specific. It is recommendable to study the functional changes HSCR patients undergo throughout their lifespans. Secondly, our research is limited by a specific time frame, focusing solely on studies published between 2015 and 2021. While this provides insight into recent clinical practices, it may overlook critical insights from publications after 2021. Thirdly, although we identified significant variations in definitions, the abundance of these definitions prevented us from exhaustively detailing each one.

As we are transitioning into prioritizing evidence-based practice and patient-centered outcomes, embracing a unified approach and adopting quality indicators are crucial. This approach will not only refine our understanding and management of HSCR but also fortify the

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foundations of pediatric surgical research, driving meaningful advancements in pediatric patient care.

CONCLUSION

This review highlights the substantial variation in the reporting of patient characteristics and outcomes in Hirschsprung's disease research, with 1026 parameters identified in recent literature. It suggests an urgent need for adopting the newly developed core outcome set, and establishing a standardized core indicator set. The comprehensive list of studied parameters identified in our review can facilitate this process. Implementing standardized measurement and reporting systems is vital, promising enhanced interpretability of results and the potential for effective quality-of-care benchmarking across pediatric surgical centers in Europe. Looking ahead, the European Pediatric Surgery Audit (EPSA) emerges as a crucial entity to realize this vision, heralding a new era in pediatric surgical research and care.

CONTRIBUTIONS

The study was designed by DR, AG, NT, TW and RW. Inclusion and exclusion criteria, assessment strategy, and the utilized Excel-based data extraction framework were developed by all authors. NT developed the search strategy, and NT, DR and AG were responsible for screening, as well as data extraction and analyses. DR drafted the manuscript; all authors read, provided feedback, and approved the final manuscript.

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CONFLICT OF INTEREST

None declared.

REFERENCES

1. Kyrklund K, Sloots CEJ, de Blaauw I, et al. ERNICA guidelines for the management of rectosigmoid Hirschsprung's disease. *Orphanet J Rare Dis*. Jun 25 2020;15(1):164. doi:10.1186/s13023-020-01362-3
2. Chhabra S, Harwood R, Kenny SE. Hirschsprung's disease. *Surgery (Oxford)*. 2019;37(11):640-645. doi:10.1016/j.mpsur.2019.09.005
3. Swenson O, Bill AH, Jr. Resection of rectum and rectosigmoid with preservation of the sphincter for benign spastic lesions producing megacolon; an experimental study. *Surgery*. Aug 1948;24(2):212-20.
4. Duhamel B. A new operation for the treatment of Hirschsprung's disease. *Arch Dis Child*. Feb 1960;35(179):38-9. doi:10.1136/adc.35.179.38
5. Soave F. A NEW SURGICAL TECHNIQUE FOR TREATMENT OF HIRSCHSPRUNG'S DISEASE. *Surgery*. Nov 1964;56:1007-14.
6. Boley SJ. NEW MODIFICATION OF THE SURGICAL TREATMENT OF HIRSCHSPRUNG'S DISEASE. *Surgery*. Nov 1964;56:1015-7.
7. Allin BSR, Bradnock T, Kenny S, et al. NETS(1HD) study: development of a Hirschsprung's disease core outcome set. *Arch Dis Child*. Dec 2017;102(12):1143-1151. doi:10.1136/archdischild-2017-312901
8. Owens E. *The qualitative and quantitative outcomes of children with Hirschsprung's Disease and Anorectal Malformations*. University of Liverpool; 2023.
9. Davidson JR, Kyrklund K, Eaton S, et al. Long-term surgical and patient-reported outcomes of Hirschsprung Disease. *J Pediatr Surg*. Sep 2021;56(9):1502-1511. doi:10.1016/j.jpedsurg.2021.01.043
10. Teunissen NR, D; Wouters, M.W.; Eaton, S; van Heurn, E.; Wijnen, R; on behalf of the EPSA| ERNICA Registry Group. The European Paediatric Surgical Audit: improving the quality of care in rare congenital malformations.
11. van Heurn E, de Blaauw I, Heij H, et al. Quality Measurement in Neonatal Surgical Disorders: Development of Clinical Indicators. *Eur J Pediatr Surg*. Dec 2015;25(6):526-31. doi:10.1055/s-0034-1396416
12. Beck N, van Bommel AC, Eddes EH, et al. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg*. Apr 2020;271(4):627-631. doi:10.1097/SLA.0000000000003665
13. Donabedian A. Evaluating the quality of medical care. 1966. *Milbank Q*. 2005;83(4):691-729. doi:10.1111/j.1468-0009.2005.00397.x

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14. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *Bmj*. 2021;doi:10.1136/bmj.n160
15. 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*. Nov 2 2020;106(5):484-90. doi:10.1136/archdischild-2020-320310
16. Besner AS, Ferreira JL, Ow N, et al. Patient-reported outcome measures in pediatric surgery - A systematic review. *J Pediatr Surg*. May 2022;57(5):798-812. doi:10.1016/j.jpedsurg.2021.12.036

Figure 1. PRISMA Flowchart: systematic review of studied parameters in Hirschsprung's disease research

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SUPPLEMENTARY 1: search strategy

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('Hirschsprung disease'/de OR (Hirschsprung* OR Hirschprung* OR ((aganglion*) NEAR/3 (colon* OR intestin* OR megacolon* OR rectosigmoid*)) OR ((congenit* OR idiopathic*) NEAR/3 (megacolon*)) OR megasigmoid*):ab,ti,kw) AND ('morbidity'/exp OR 'mortality'/exp OR 'survival'/exp OR 'health care quality'/de OR 'benchmarking'/de OR 'clinical indicator'/de OR 'performance measurement system'/de OR 'practice guideline'/de OR 'clinical pathway'/de OR 'clinical protocol'/de OR 'consensus development'/de OR 'professional standard'/exp OR 'treatment outcome'/exp OR 'complication'/exp OR (morbidit* OR mortalit* OR surviv* OR benchmark* OR bench-mark* OR clinical-indicat* OR performance-measurement-system* OR guideline* OR clinical-pathway* OR (clinical* NEAR/3 protocol*) OR consensus* OR professional-standard* OR audit OR audits OR outcome* OR complication*):ab,ti,kw) NOT ([conference abstract]/lim OR [editorial]/lim OR [letter]/lim) AND [English]/lim NOT ('review'/exp OR (review):ti) NOT ((animal/exp OR animal*:de OR nonhuman/de) NOT ('human'/exp)) AND [2015-2021]/py

Medline (Ovid)

(Hirschsprung Disease/ OR (Hirschsprung* OR Hirschprung* OR ((aganglion*) ADJ3 (colon* OR intestin* OR megacolon* OR rectosigmoid*)) OR ((congenit* OR idiopathic*) ADJ3 (megacolon*)) OR megasigmoid*).ab,ti,kf.) AND (Morbidity/ OR exp Mortality/ OR mortality.fx. OR Survival/ OR Quality of Health Care/ OR Benchmarking/ OR Practice Guideline/ OR Critical Pathways/ OR Clinical Protocols/ OR Consensus/ OR Standard of Care/ OR exp Treatment Outcome/ OR (morbidit* OR mortalit* OR surviv* OR benchmark* OR bench-mark* OR clinical-indicat* OR performance-measurement-system* OR guideline* OR clinical-pathway* OR (clinical* ADJ3 protocol*) OR consensus* OR professional-standard* OR audit OR audits OR outcome* OR complication*).ab,ti,kf.) NOT (letter* OR news OR comment* OR editorial* OR congres* OR abstract* OR book* OR chapter* OR dissertation abstract*).pt. AND english.lg. NOT (exp Review/ OR (review).ti.) NOT (exp animals/ NOT humans/)

Cochrane Central

((Hirschsprung* OR Hirschprung* OR ((aganglion*) NEAR/3 (colon* OR intestin* OR megacolon* OR rectosigmoid*)) OR ((congenit* OR idiopathic*) NEAR/3 (megacolon*)) OR megasigmoid*):ab,ti,kw) AND ((morbidit* OR mortalit* OR surviv* OR benchmark* OR bench NEXT mark* OR clinical NEXT indicat* OR performance NEXT measurement NEXT system* OR guideline* OR clinical NEXT pathway* OR (clinical* NEAR/3 protocol*) OR consensus* OR professional NEXT standard* OR audit OR audits OR outcome* OR complication*):ab,ti,kw)

SUPPLEMENTARY 2: included publications

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Author	Title	Year	Continent	n =	Study design		
Aubdoollah T, et al.	Clinical outcomes and ergonomics analysis of three laparoscopic techniques for Hirschsprung's disease	2015	Asia	90	Compa rative	Retros pective	Cohort
Aubdoollah T, et al.	Hybrid Single-Incision Laparoscopic Approaches for Endorectal Pull-Through in Hirschsprung's Disease	2015	Asia	36	Obser vation al	Retros pective	Cohort
Chung P, et al.	Clinical and manometric evaluations of anorectal function in patients after transanal endorectal pull-through operation for Hirschsprung's disease: A multicentre study	2015	Asia	37	Compa rative	Retros pective	Cohort
Deng X, et al.	Comparative Analysis of Modified Laparoscopic Swenson and Laparoscopic Soave Procedure for Short-Segment Hirschsprung Disease in Children	2015	Asia	42	Compa rative	Retros pective	Cohort
Graneli C, et al.	Development of Frequency of Stools over Time in Children with Hirschsprung Disease Posttransanal Endorectal One-Stage Pull-through	2015	Europe	31	Obser vation al	Prospe ctive	Case-control
Granström A, et al.	Adult outcomes after surgery for Hirschsprung's disease: Evaluation of bowel function and quality of life	2015	Europe	39	Compa rative	Retros pective	Case-control
Hukkinen M, et al.	Postoperative outcome and survival in relation to small intestinal involvement of total colonic aganglionosis	2015	Europe	21	Compa rative	Prospe ctive	Cohort
Khalil M	Long-term health-related quality of life for patients with Hirschsprung's disease at 5 years after transanal endorectal pull-through operation	2015	Africa	53	Obser vation al	Prospe ctive	Cohort
Khazdouz M, et al.	Clinical outcome and bowel function after surgical treatment in Hirschsprung's disease	2015	Asia	161	Obser vation al	Prospe ctive	Cohort
Martínez-Criado Y, et al.	Results of transanal endorrectal descent in Hirschsprung's disease	2015	Europe	73	Obser vation al	Retros pective	Cohort
Miyano G, et al.	Rectal mucosal dissection commencing directly on the anorectal line versus commencing above the dentate line in laparoscopy-assisted transanal pull-through for Hirschsprung's disease: Prospective medium-term follow-up	2015	Asia	74	Compa rative	Retros pective	Cohort
Stensrud K, et al.	Anal endosonography and bowel function in patients undergoing different types of endorectal pull-through procedures for Hirschsprung disease	2015	Europe	52	Obser vation al	Prospe ctive	Cohort
van den Hondel D, et al.	Psychosexual Well-Being after Childhood Surgery for Anorectal Malformation or Hirschsprung's Disease	2015	Europe	36	Obser vation al	Retros pective	Cohort
Wang H, et al.	Nursing Intervention for Outpatient Rehabilitation in Pediatric Patients with Hirschsprung Disease after Colectomy	2015	Asia	85	Compa rative	Retros pective	Trial
Wester T, et al.	Botulinum toxin is efficient to treat obstructive symptoms in children with Hirschsprung disease	2015	Europe	18	Obser vation al	Retros pective	Cohort
Xiong X, et al.	Long term quality of life in patients with Hirschsprung's disease who underwent heart-shaped anastomosis during childhood: A twenty-year follow-up in China	201	Asia	92	Compa rativ	Retros pec	Case-con

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Ladi-Seyedian S, et al.	A comparative study of transcutaneous interferential electrical stimulation plus behavioral therapy and behavioral therapy alone on constipation in postoperative Hirschsprung disease children	2016	Asia	30	Compa rative	Retros pective	Trial
Aworanti O, et al.	Does Functional Outcome Improve with Time Postsurgery for Hirschsprung Disease?	2016	Europe	51	Obs ervational	Pro spective	Cohort
Banasiuk M, et al.	3D high-definition manometry in evaluation of children after surgery for Hirschsprung's disease: A pilot study	2016	Europe	14	Compa rative	Retros pective	Cohort
Chen X, et al.	Pathological changes of interstitial cells of Cajal and ganglion cells in the segment of resected bowel in Hirschsprung's disease	2016	Asia	58	Compa rative	Retros pective	Cohort
Chia S, et al.	Epidemiology of Hirschsprung's Disease in Taiwanese Children: A 13-year Nationwide Population-based Study	2016	Asia	629	Obs ervational	Retros pective	Cohort
Feng C, et al.	Rates and burden of surgical site infections associated with pediatric colorectal surgery: Insight from the National Surgery Quality Improvement Program	2016	North-America	457	Obs ervational	Retros pective	Cohort
Granström A, et al.	Population-based study shows that Hirschsprung disease does not have a negative impact on education and income	2016	Europe	389	Compa rative	Retros pective	Cohort
Imvised T, et al.	Multicenter experience of primary transanal endorectal pull-through operation in childhood Hirschsprung's disease	2016	Asia	76	Obs ervational	Retros pective	Cohort
Li Q, et al.	The mid-term outcomes of TRM–PIAS, proctocolectomy and ileoanal anastomosis for total colonic aganglionosis	2016	Asia	19	Compa rative	Retros pective	Cohort
Lukač M, et al.	Effectiveness of various surgical methods in treatment of Hirschsprung's disease in children	2016	Europe	84	Compa rative	Pro spective	Cohort
Muller C, et al.	Long-Term Outcome of Laparoscopic Duhamel Procedure for Extended Hirschsprung's Disease	2016	Europe	30	Obs ervational	Retros pective	Cohort
O'Hare T, et al.	A Retrospective Cohort Study of Total Colonic Aganglionosis: Is the Appendix a Reliable Diagnostic Tool?	2016	Europe	91	Obs ervational	Pro spective	Cohort
Onishi S, et al.	Long-term outcome of bowel function for 110 consecutive cases of Hirschsprung's disease: Comparison of the abdominal approach with transanal approach more than 30 years in a single institution – is the transanal approach truly beneficial for bowel function?	2016	Asia	110	Obs ervational	Pro spective	Cohort
Oulads aiad M	How to manage a late diagnosed Hirschsprung's disease	2016	Africa	15	Obs ervational	Pro spective	Cohort
Singh V, et al.	Congenital Neonatal Intestinal Obstruction: Retrospective Analysis at Tertiary Care Hospital	2016	Asia	17	Obs ervational	Retros pective	Cohort
Sosnowska P, et al.	Are there any factors influencing the course of multistage treatment in Hirschsprung's disease?	2016	Europe	29	Compa rative	Retros pective	Cohort
van den Hondel D, et al.	Children with congenital colorectal malformations often require special education or remedial teaching, despite normal intelligence	2016	Europe	20	Obs ervational	Pro spective	Cohort

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Xia X, et al.	Single-incision laparoscopic versus conventional laparoscopic surgery for Hirschsprung's disease: A comparison of medium-term outcomes	2016	Asia	75	Comparative	Retrospective	Cohort
Yang S, et al.	Prognostic factors in children with total colonic aganglionosis treated with the soave procedure: The experience of 43 patients from a single institution	2016	Asia	43	Observational	Retrospective	Cohort
Zarei T, et al.	Evaluation of Hirschsprung's disease in a pediatric hospital in southern Iran during 2005-2013	2016	Asia	425	Observational	Retrospective	Cohort
Adıgüzel Ü, et al.	Transanal endorectal pull-through for Hirschsprung's disease: experience with 50 patients	2017	Eurasia	50	Observational	Retrospective	Cohort
Bing X, et al.	Transanal pullthrough Soave and Swenson techniques for pediatric patients with Hirschsprung disease	2017	Asia	148	Observational	Retrospective	Cohort
Bjørnland K, et al.	A Nordic multicenter survey of long-term bowel function after transanal endorectal pull-through in 200 patients with rectosigmoid Hirschsprung disease	2017	Europe	200	Comparative	Prospective	Cohort
Bradnock T, et al.	Hirschsprung's disease in the UK and Ireland: Incidence and anomalies	2017	Europe	305	Observational	Retrospective	Cohort
Cheng S, et al.	Pathologically assessed grade of Hirschsprung-associated enterocolitis in resected colon in children with Hirschsprung's disease predicts postoperative bowel function	2017	Asia	80	Comparative	Retrospective	Cohort
Collins L, et al.	Quality of life outcomes in children with Hirschsprung disease	2017	Oceania	60	Observational	Retrospective	Cohort
Ghosh D, et al.	Transition zone pull-through in Hirschsprung's disease: a tertiary hospital experience	2017	Oceania	50	Observational	Retrospective	Cohort
Granéli C, et al.	Diagnosis, Symptoms, and Outcomes of Hirschsprung's Disease from the Perspective of Gender	2017	Europe	51	Comparative	Retrospective	Cohort
Hasserius J, et al.	Treatment and Patient Reported Outcome in Children with Hirschsprung Disease and Concomitant Congenital Heart Disease	2017	Europe	53	Observational	Retrospective	Cohort
Kyrklund K, et al.	Social Morbidity in Relation to Bowel Functional Outcomes and Quality of Life in Anorectal Malformations and Hirschsprung's Disease	2017	Europe	61	Observational	Retrospective	Cohort
Li S, et al.	Clinical effects of ascending colon patching ileorectal heart-shaped anastomosis on total colonic aganglionosis	2017	Asia	15	Observational	Prospective	Cohort
Li X, et al.	Laparoscopic-assisted endorectal pull-through for Hirschsprung's disease. A retrospective study	2017	Asia	22	Observational	Retrospective	Cohort
Löf Granström A, et al.	Mortality in Swedish patients with Hirschsprung disease	2017	Europe	739	Observational	Prospective	Cohort
Lu C, et al.	Single-stage transanal endorectal pull-through procedure for correction of Hirschsprung disease in neonates and nonneonates: A multicenter study	2017	Asia	415	Comparative	Prospective	Cohort
Miyano	Laparoscopy-Assisted Duhamel-Z Anastomosis for Total Colonic	2	Asia	1	Obs	Pro	Co

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G, et al.	Aganglionosis: Outcome Assessed by Fecal Continence Evaluation	2017		1	Observational	Prospective	Cohort
Neuvonen N, et al.	Lower urinary tract symptoms and sexual functions after endorectal pull-through for Hirschsprung disease: controlled long-term outcomes	2017	Europe	59	Comparative	Retrospective	Cohort
Neuvonen M, et al.	Bowel function and quality of life after transanal endorectal pull-through for Hirschsprung's disease	2017	Europe	79	Observational	Retrospective	Cohort
Onishi S, et al.	The bowel function and quality of life of Hirschsprung disease patients who have reached 18 years of age or older – the long-term outcomes after undergoing the transabdominal soave procedure	2017	Asia	16	Observational	Prospective	Cohort
Sosnowska P, et al.	Definitive surgery for Hirschsprung's disease under 4 months of age is associated with long-term complications: A cohort study	2017	Europe	31	Observational	Retrospective	Cohort
Stenström P, et al.	Patient-reported Swedish nationwide outcomes of children and adolescents with total colonic aganglionosis	2017	Europe	27	Observational	Retrospective	Cohort
T. Taguchi T, et al.	Current status of Hirschsprung's disease: based on a nationwide survey of Japan	2017	Asia	1087	Observational	Retrospective	Cohort
Tannuri A, et al.	Long-term results of the Duhamel technique are superior to those of the transanal pullthrough: A study of fecal continence and quality of life	2017	South-America	41	Observational	Retrospective	Cohort
Thakkar H, et al.	Functional outcomes in Hirschsprung disease: A single institution's 12-year experience	2017	Europe	72	Observational	Retrospective	Cohort
Tian Y, et al.	Difference of efficacy between Laparoscopic Modified Soave operation and Open Radical Resection in the treatment of Hirschsprung's disease	2017	Asia	216	Comparative	Prospective	Trial
Yan J, et al.	Comparison of transcolostomy single-incision laparoscopic and open procedures in secondary operations for Hirschsprung's disease	2017	Asia	37	Comparative	Retrospective	Cohort
Zhang J, et al.	A 5-year follow-up study of neonates with Hirschsprung's disease undergoing transanal Soave or Swenson surgery	2017	Asia	29	Comparative	Retrospective	Cohort
Zhang X, et al.	Laparoscopic Duhamel Procedure with Ex-Anal Rectal Transection for Right-Sided Hirschsprung's Disease	2017	Asia	18	Comparative	Retrospective	Cohort
Hao Y, et al.	Application of a modified reflux enema method with indwelled anal canal in infants with long-segment Hirschsprung's disease	2018	Asia	104	Comparative	Retrospective	Trial
Amin R, et al.	Long-term Quality of Life in Neonatal Surgical Disease	2018	North-America	46	Observational	Retrospective	Cohort
Anderson J, et al.	Epidemiology of Hirschsprung disease in California from 1995 to 2013	2018	North-America	2464	Observational	Retrospective	Cohort
Chung P, et al.	Are all patients with short segment Hirschsprung's disease equal? A retrospective multicenter study	2018	Asia	45	Observational	Retrospective	Cohort
Frykman P, et	Critical evaluation of the Hirschsprung-associated enterocolitis (HAEC) score: A multicenter study of 116 children with Hirschsprung disease	20	Intercont	11	Observa	Prospe	Cohort

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Granström A, et al.	Increased Risk of Inflammatory Bowel Disease in a Population-based Cohort Study of Patients with Hirschsprung Disease	2018	Europe	739	Observational	Retrospective	Cohort
Gunadi, et al.	Outcomes in patients with Hirschsprung disease following definitive surgery	2018	Asia	67	Observational	Prospective	Cohort
Hashim I, et al.	Modified Duhamel pull through procedure in patients with Hirschsprung's disease	2018	Asia	75	Observational	Prospective	Cohort
Huang W, et al.	Prevalence, Risk Factors, and Prognosis of Postoperative Complications after Surgery for Hirschsprung Disease	2018	Asia	181	Observational	Prospective	Cohort
Jiao C, et al.	A Long-Term Follow-Up of a New Surgery Method: Laparoscope-Assisted Heart-Shaped Anastomosis for Hirschsprung's Disease	2018	Asia	110	Comparative	Retrospective	Cohort
Li T, et al.	Long term outcomes for neonates of Hirschsprung's disease undergoing transanal Swenson or Duhamel pull-through by a 5 year follow-up study	2018	Asia	79	Comparative	Retrospective	Cohort
Miyano G, et al.	Hirschsprung's disease in the laparoscopic transanal pull-through era: implications of age at surgery and technical aspects	2018	Asia	106	Observational	Prospective	Cohort
Nah S, et al.	Anorectal malformation & Hirschsprung's disease: A cross-sectional comparison of quality of life and bowel function to healthy controls	2018	Asia	44	Comparative	Retrospective	Cohort
Palazón P, et al.	Bilateral hydrosalpinx in patients with Hirschsprung's disease	2018	Europe	17	Comparative	Retrospective	Cohort
Parahita I, et al.	Comparison of Hirschsprung-associated enterocolitis following Soave and Duhamel procedures	2018	Asia	100	Comparative	Retrospective	Cohort
Pathak M, et al.	Hirschsprung's disease and neonatal intestinal obstruction: Where does it lie in the spectrum?	2018	Asia	17	Comparative	Retrospective	Cohort
Roorda D, et al.	Long-term outcome and quality of life in patients with total colonic aganglionosis in the netherlands	2018	Europe	51	Observational	Retrospective	Cohort
Sood S, et al.	The long-term quality of life outcomes in adolescents with Hirschsprung disease	2018	Oceania	83	Observational	Prospective	Cohort
Tran V, et al.	Interest of anorectal manometry during long-term follow-up of patients operated on for Hirschsprung's disease	2018	Europe	53	Comparative	Retrospective	Cohort
Tran V, et al.	Long-Term Outcomes and Quality of Life in Patients after Soave Pull-Through Operation for Hirschsprung's Disease: An Observational Retrospective Study	2018	Europe	53	Comparative	Retrospective	Cohort
Urla C, et al.	Surgical treatment of children with total colonic aganglionosis: functional and metabolic long-term outcome	2018	Europe	11	Observational	Retrospective	Cohort
Veras L, et al.	Impaired growth outcomes in children with congenital colorectal diseases	201	North-Ame	71	Observation	Retrospec	Cohort

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Widyasari A, et al.	Functional outcomes in Hirschsprung disease patients after transabdominal Soave and Duhamel procedures	2018	Asia	53	Compa rative	Retros pective	Cohort
Xi Z, et al.	Long-term complications of modified soave radical correction in the treatment of Hirschsprung's disease and its influences on life quality	2018	Asia	50	Compa rative	Retros pective	Cohort
Yokota K, et al.	Single-stage laparoscopic transanal pull-through modified Swenson procedure without leaving a muscular cuff for short- and long-type Hirschsprung disease: a comparative study	2018	Asia	43	Compa rative	Retros pective	Cohort
Zhang X, et al.	Laparoscopic-assisted Duhamel procedure with ex-anal rectal transection for total colonic aganglionosis	2018	Asia	23	Compa rative	Pros pectiv e	Cohort
Zheng Z, et al.	Transanal endorectal stepwise gradient muscular cuff cutting pull-through method: Technique refinements and comparison with laparoscopy-assisted procedures	2018	Asia	172	Compa rative	Retros pective	Cohort
Amin L, et al.	Swedish national population-based study shows an increased risk of depression among patients with Hirschsprung disease	2019	Europe	739	Compa rative	Pros pectiv e	Cohort
Ashjaei B, et al.	Early oral feeding versus traditional feeding after transanal endorectal pull-through procedure in Hirschsprung's disease	2019	Asia	33	Compa rative	Pros pectiv e	Trial
Askarpour S, et al.	Complications after transabdominal Soave's procedure in children with Hirschsprung's disease	2019	Asia	160	Obs erva tion al	Pros pectiv e	Cohort
Chung P, et al.	Risk factors for the development of post-operative enterocolitis in short segment Hirschsprung's disease	2019	Asia	96	Obs erva tion al	Retros pective	Cohort
Dingemans A, et al.	Urinary Outcomes in Patients with Down's Syndrome and Hirschsprung's Disease	2019	Europe	104	Compa rative	Retros pective	Cohort
Drissi F, et al.	Long-term Outcome of Hirschsprung Disease: Impact on Quality of Life and Social Condition at Adult Age	2019	Europe	34	Obs erva tion al	Pros pectiv e	Cohort
El Ç, et al.	A significant cause of constipation and growth retardation: Hirschsprung's disease	2019	Eurasia	19	Obs erva tion al	Retros pective	Cohort
Freedman-Weiss M, et al.	Delay in operation for Hirschsprung Disease is associated with decreased length of stay: a 5-Year NSQIP-Peds analysis	2019	North-America	282	Compa rative	Retros pective	Cohort
Fusaro F, et al.	Autologous intestinal reconstructive surgery in the management of total intestinal aganglionosis	2019	Europe	14	Obs erva tion al	Retros pective	Cohort
Ghorbanpour M, et al.	Early and long-term complications following transanal pull through Soave technique in infants with Hirschsprung's disease	2019	Asia	55	Obs erva tion al	Retros pective	Case series
Granström A, et al.	No increased risk of attention deficit hyperactivity disorders in patients with Hirschsprung disease	2019	Europe	739	Compa rative	Retros pective	Cohort
Gupta D, et al.	Experience with the Redo Pull-Through for Hirschsprung's Disease	201	Asia	32	Obs erva tion	Pros pectiv	Case seri

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Gustafson E, et al.	Controlled outcome of Hirschsprung's disease beyond adolescence: a single center experience	2019	Europe	123	Compa rative	Retros pective	Cohort
Han J, et al.	Why Do the Patients with Hirschsprung Disease Get Redo Pull-Through Operation?	2019	Asia	657	Obs erva tion al	Retros pective	Cohort
Hedbys J, et al.	Children with Hirschsprung's Disease and Syndromes with Cognitive Dysfunction: Manifestations, Treatment, and Outcomes	2019	Europe	63	Obs erva tion al	Retros pective	Cohort
Hoff N, et al.	Classification of short-term complications after transanal endorectal pullthrough for Hirschsprung's disease using the Clavien–Dindo-grading system	2019	Europe	69	Obs erva tion al	Retros pective	Cohort
Iacusso C, et al.	Minimally invasive techniques for Hirschsprung's disease	2019	Europe	145	Compa rative	Retros pective	Cohort
Jiang M, et al.	Laparoscopic Redo Pull-Through for Hirschsprung Disease Due to Innervation Disorders	2019	Asia	836	Obs erva tion al	Retros pective	Cohort
Jiao C, et al.	Results of rectoanal manometry after a novel laparoscopic technique: laparoscope-assisted heart-shaped anastomosis for Hirschsprung's disease	2019	Asia	80	Obs erva tion al?	Retros pective	Cohort
Le-Nguyen A, et al.	Factors influencing the incidence of Hirschsprung associated enterocolitis (HAEC)	2019	North-America	171	Compa rative	Pros pectiv e	Cohort
Louis-Borrione C, et al.	Neurostimulation-guided Anal Intrasphincteric Botulinum Toxin Injection in Children With Hirschsprung Disease	2019	Europe	15	Obs erva tion al	Retros pective	Cohort
Meinds R, et al.	Long-term functional outcomes and quality of life in patients with Hirschsprung's disease	2019	Europe	830	Compa rative	Pros pectiv e	Case-control
Nakamura M, et al.	Treatment of classic-type Hirschsprung's disease: rectoplasty with posterior triangular colonic flap versus transanal endorectal pull-through with rectoanal myotomy	2019	Asia	64	Compa rative	Pros pectiv e	Cohort
Nataraja R, et al.	Management of Hirschsprung disease in Australia and New Zealand: a survey of the Australian and New Zealand Association of Paediatric Surgeons (ANZAPS)	2019	Oceania	-	Obs erva tion al	Pros pectiv e	Cohort
Obata S, et al.	The outcomes of transanal endorectal pull-through for Hirschsprung's disease according to the mucosectomy-commencing points: A study based on the results of a nationwide survey in Japan	2019	Asia	1087	Compa rative	Retros pective	Cohort
Obata S, et al.	Nationwide survey of outcome in patients with extensive aganglionosis in Japan	2019	Asia	1088	Obs erva tion al	Retros pective	Cohort
Pini Prato A, et al.	Hirschsprung disease and Down syndrome: From the reappraisal of risk factors to the impact of surgery	2019	Europe	385	Obs erva tion al	Pros pectiv e	Cohort
Purcell L, et al.	Characteristics and outcomes in paediatric patients presenting with congenital colorectal diseases in sub-Saharan Africa	2019	Africa	82	Obs erva tion al	Retros pective	Cohort
Sola R, et al.	The relationship of eosinophilia with outcomes of Hirschsprung disease in children	2019	North-America	100	Compa rative	Retros pective	Cohort

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Wang Y, et al.	Three-Dimensional Versus Two-Dimensional Laparoscopic-Assisted Transanal Pull-Through for Hirschsprung's Disease in Children: Preliminary Results of a Prospective Cohort Study in a Tertiary Hospital	2019	Asia	80	Compa rative	Retros pective	Cohort
Xu P, et al.	Transumbilical enterostomy for Hirschsprung's disease with a twostage laparoscopy-assisted pull-through procedure	2019	Asia	53	Compa rative	Retros pective	Cohort
Youn J, et al.	Botulinum toxin injection for internal anal sphincter achalasia after pull-through surgery in Hirschsprung disease	2019	Asia	15	Obser vation al	Retros pective	Cohort
Zhu T, et al.	Optimal time for single-stage pull-through colectomy in infants with short-segment Hirschsprung disease	2019	Asia	198	Compa rative	Prospe ctive	Cohort
Aliev M, et al.	A comparative study of the surgical procedures to treat Hirschsprung's disease in children	2020	Asia	138	Compa rative	Retros pective	Cohort
Bawazir O	Laparoscopic-assisted transanal pull-through in Hirschsprung's disease: Does laparoscopic dissection minimize anal overstretching?	2020	Asia	74	Compa rative	Retros pective	Cohort
Brooks L, et al.	Resection margin histology may predict intermediate-term outcomes in children with rectosigmoid Hirschsprung disease	2020	North-America	45	Compa rative	Retros pective	Cohort
Dai Y, et al.	Parental Self-efficacy and Health-related Outcomes Among Children with Hirschsprung Disease: A Cross-sectional Study	2020	Asia	84	Obser vation al	Retros pective	Cohort
Dariel A, et al.	Analysis of enteric nervous system and intestinal epithelial barrier to predict complications in Hirschsprung's disease	2020	Europe	18	Obser vation al	Retros pective	Cohort
Fang Y, et al.	Laparoscopic Soave procedure for long-segment Hirschsprung's disease - single-center experience	2020	Asia	31	Obser vation al	Retros pective	Cohort
Fosby M, et al.	Bowel function after transanal endorectal pull-through for Hirschsprung disease – does outcome improve over time?	2020	Europe	50	Obser vation al	Retros pective	Cohort
Gabriela G, et al.	Long-term growth outcomes in children with Hirschsprung disease after definitive surgery: A cross-sectional study	2020	Asia	21	Compa rative	Prospe ctive	Cohort
Giuliani S, et al.	Outcomes of Primary versus Multiple-Staged Repair in Hirschsprung's Disease in England	2020	Europe	1333	Compa rative	Retros pective	Cohort
Gunadi, et al.	Growth outcomes in Hirschsprung's disease patients following pull-through	2020	Asia	64	Compa rative	Prospe ctive	Cohort
Gunadi, et al.	Postoperative enterocolitis assessment using two different cut-off values in the HAEC score in Hirschsprung patients undergoing Duhamel and Soave pull-through	2020	Asia	83	Compa rative	Prospe ctive	Cohort
Halleran D, et al.	Does Hirschsprung-Associated Enterocolitis Differ in Children With and Without Down Syndrome?	2020	North-America	86	Compa rative	Prospe ctive	Cohort
Hosseinpour M, et al.	Mechanical Bowel Preparation versus No Preparation in Duhamel Procedure in Children with Hirschsprung's Disease	2020	Asia	80	Compa rative	Retros pective	Trial
Iozsa	Postoperative fecal incontinence in Hirschsprung's disease – technical surgical	2	Eur	2	Obs	Ret	Co

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D, et al.	error or an inevitable complication?	2020	ope	4	ervational	rospective	hort
Kastenberg Z, et al.	The effect of multidisciplinary colorectal center development on short-term hospital readmissions for patients with anorectal malformations or Hirschsprung disease	2020	North-America	131	Observational	Prospective	Cohort
Meng X, et al.	Long-term outcomes of single-incision laparoscopic technique in Soave procedure compared with heart-shaped anastomosis for Hirschsprung disease	2020	Asia	204	Observational	Retrospective	Cohort
Mille E, et al.	Quality of life and neuropsychological development at school age in Hirschsprung's disease	2020	Europe	15	Comparative	Retrospective	Case-control
Napar N, et al.	Classical Swenson abdomino-perineal pull through technique in the treatment of Hirschsprung's disease-4 years experience	2020	Asia	50	Observational	Retrospective	Cohort
Neuvonen M, et al.	A population-based, complete follow-up of 146 consecutive patients after transanal mucosectomy for Hirschsprung disease	2020	Europe	146	Observational	Retrospective	Cohort
Oh C, et al.	The Patients with Hirschsprung's Disease Who Underwent Pull-Through at Age Less than 1 Year: Longitudinal Bowel Function	2020	Asia	396	Observational	Retrospective	Cohort
Peters N, et al.	Modified Duhamel's Two-Staged Procedure for Hirschsprung's Disease: Further Modifications for Improved Outcomes	2020	Asia	69	Observational	Prospective	Cohort
Pini Prato A, et al.	Totally robotic soave pull-through procedure for Hirschsprung's disease: lessons learned from 11 consecutive pediatric patients	2020	Europe	11	Observational	Retrospective	Case series
Pini Prato A, et al.	Minimally Invasive Redo Pull-Throughs in Hirschsprung Disease	2020	Europe	16	Observational	Retrospective	Case series
Pruitt L, et al.	Impact of consolidation of cases on post-operative outcomes for index pediatric surgery cases	2020	North-America	2030	Observational	Retrospective	Cohort
Pruitt L, et al.	Hirschsprung-associated enterocolitis in children treated at US children's hospitals	2020	North-America	2030	Observational	Retrospective	Cohort
Quiroz H, et al.	Pull-through procedure in children with Hirschsprung disease: A nationwide analysis on postoperative outcomes	2020	North-America	36355	Observational	Retrospective	Cohort
Saad S, et al.	Histopathological perspective of the pulled-through colon in Hirschsprung disease: Impact on clinical outcome	2020	Africa	35	Observational	Retrospective	Cohort
Saysoo M, et al.	Quality of life of patients with Hirschsprung disease after Duhamel and Soave pull-through procedures: A mixed-methods sequential explanatory cohort study	2020	Asia	11	Comparative	Retrospective	Cohort
Schlund D, et al.	A national analysis of operative treatment of adult patients with Hirschsprung's disease	2020	North-America	32	Comparative	Prospective	Cohort
Stenström P, et al.	Total colonic aganglionosis: multicentre study of surgical treatment and patient-reported outcomes up to adulthood	2020	Europe	116	Comparative	Retrospective	Cohort
Svetanoff W,	Inpatient management of Hirschsprung's associated enterocolitis treatment: the benefits of standardized care	20	North-	27	Compa	Prospe	Cohort

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Taghavi K, et al.	Contemporary management of Hirschsprung disease in New Zealand	2020	Oceania	246	Observational	Prospective	Cohort
Tang J, et al.	Application of enhanced recovery after surgery during the perioperative period in infants with Hirschsprung's disease – A multi-center randomized clinical trial	2020	Asia	148	Comparative	Prospective	Trial
Thakkar H, et al.	Variability of the transition zone length in Hirschsprung disease	2020	Europe	48	Observational	Retrospective	Cohort
Vriesman M, et al.	Outcomes after enterostomies in children with and without motility disorders: A description and comparison of postoperative complications	2020	Europe	18	Observational	Retrospective	Cohort
Wall N, et al.	Use of an enterocolitis triage and treatment protocol in children with Hirschsprung disease reduces hospital admissions	2020	North-America	87	Observational	Prospective	Cohort
Yan J, et al.	Clinical Outcomes After Staged and Primary Laparotomy Soave Procedure for Total Colonic Aganglionosis: a Single-Center Experience from 2007 to 2017	2020	Asia	35	Comparative	Retrospective	Cohort
Zhang X, et al.	Primary laparoscopic endorectal pull-through procedure with or without a postoperative rectal tube for Hirschsprung's disease: a multicenter perspective study	2020	Asia	383	Comparative	Retrospective	Trial
Ali A, et al.	The Prevalence and Clinical Profile of Hirschsprung's Disease at a Tertiary Hospital in Bahrain	2021	Asia	18	Observational	Retrospective	Cohort
Allin B, et al.	Outcomes at five to eight years of age for children with Hirschsprung's disease	2021	Europe	239	Observational	Retrospective	Cohort
Apfeld J, et al.	Benchmarking utilization, length of stay, and complications following minimally invasive repair of major congenital anomalies	2021	North-America	450	Observational	Retrospective	Cohort
Apfeld J, et al.	Relationships Between Hospital and Surgeon Operative Volumes and Surgical Outcomes in Hirschsprung's Disease	2021	North-America	1268	Observational	Prospective	Cohort
Arafa A, et al.	Laparoscopic-assisted transanal pull-through for Hirschsprung's children older than 3 years: A case series	2021	Africa	15	Observational	Retrospective	Case series
Ashjaei B, et al.	What is the appropriate aganglionic bowel length on contrast enema for attempting single stage transanal endorectal pull-through in Hirschsprung disease?	2021	Asia	48	Observational	Retrospective	Cohort
Askarpour S, et al.	Oblique vs. Circular anastomosis in the children underwent Soave's pull-through surgery for the treatment of Hirschsprung's disease: which is best?	2021	Asia	70	Observational	Retrospective	Cohort
Beltman L, et al.	Risk factors for short-term complications graded by Clavien-Dindo after transanal endorectal pull-through in patients with Hirschsprung disease	2021	Europe	106	Observational	Retrospective	Cohort
Boguszb B, et al.	Laparoscopic histological mapping for the determination of the length of aganglionic segment in children with Hirschsprung disease	2021	Europe	14	Observational	Retrospective	Cohort
Byström C, et al.	Evaluation of Bowel Function, Urinary Tract Function, and Quality of Life after Transanal Endorectal Pull-Through Surgery for Hirschsprung's Disease	202	Europe	30	Comparativ	Retrospec	Case-con

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Chan K, et al.	Long-Term Results of One-Stage Laparoscopic-Assisted Endorectal Pull-Through for Rectosigmoid Hirschsprung's Disease in Patients Aged above 5 Years	2021	Asia	41	Observational	Retrospective	Cohort
Chen F, et al.	Laparoscopic vs. Transabdominal Treatment for Overflow Fecal Incontinence Due to Residual Aganglionosis or Transition Zone Pathology in Hirschsprung's Disease Reoperation	2021	Asia	30	Observational	Prospective	Cohort
Davidson J, et al.	Outcomes in Hirschsprung's disease with coexisting learning disability	2021	Europe	32	Comparative	Retrospective	Cohort
Davidson J, et al.	Long-term surgical and patient-reported outcomes of Hirschsprung's Disease	2021	Europe	186	Comparative	Prospective	Cohort
Delgado-Miguel C, et al.	Robotic Soave pull-through procedure for Hirschsprung's disease in children under 12-months: long-term outcomes	2021	North-America	15	Observational	Prospective	Cohort
Gunadi, et al.	Functional outcomes of patients with short-segment Hirschsprung disease after transanal endorectal pull-through	2021	Asia	50	Observational	Prospective	Cohort
Gunadi, et al.	Comparison of Two Different Cut-Off Values of Scoring System for Diagnosis of Hirschsprung-Associated Enterocolitis After Transanal Endorectal Pull-Through	2021	Asia	70	Observational	Retrospective	Cohort
Kastenberg Z, et al.	Perioperative and long-term functional outcomes of neonatal versus delayed primary endorectal pull-through for children with Hirschsprung disease: A pediatric colorectal and pelvic learning consortium study	2021	North-America	82	Observational	Retrospective	Cohort
Li Q, et al.	Surgical approach and functional outcome of redo pull-through for postoperative complications in Hirschsprung's disease	2021	Asia	36	Observational	Prospective	Cohort
Liang Y, et al.	Role of mechanical and oral antibiotic bowel preparation in children with Hirschsprung's disease undergoing colostomy closure and pull-through	2021	Asia	64	Observational	Retrospective	Cohort
Lin Z, et al.	Outcomes of preoperative anal dilatation for Hirschsprung disease	2021	Asia	95	Comparative	Retrospective	Cohort
Liu Q, et al.	Application of trinity new model home nursing in postoperative management of children with Hirschsprung's disease	2021	Asia	80	Comparative	Retrospective	Cohort
Loganathan A, et al.	Assessment of Quality of Life and Functional Outcomes of Operated Cases of Hirschsprung Disease in a Developing Country	2021	Asia	86	Observational	Retrospective	Cohort
Min J, et al.	Clinical predictors of readmission after surgery for Hirschsprung disease	2021	Asia	162	Observational	Retrospective	Cohort
Mohamed W, et al.	Optimism for the Single-stage Transanal Swenson in Neonates	2021	Africa	23	Observational	Prospective	Cohort
Nguyen L, et al.	Suspension sutures facilitate single-incision laparoscopic-assisted rectal pull-through for Hirschsprung disease	2021	Asia	40	Observational	Retrospective	Case series
Olivos M, et al.	Current practice of rectal biopsies for the diagnosis of Hirschsprung's disease in Latin America: an international online survey	2021	South-America	0	Observational	Retrospective	Cohort

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Pecoraro A, et al.	Factors Affecting Higher Readmission Rates and Costs in Pediatric Patients With Hirschsprung Disease	2021	North-America	3345	Observational	Retrospective	Cohort
Peng C, et al.	Redo transanal soave pull through with or without assistance in Hirschsprung's disease: An experience in 46 patients	2021	Asia	46	Observational	Retrospective	Cohort
Pini Prato A, et al.	Congenital anomalies of the kidney and urinary tract in a cohort of 280 consecutive patients with Hirschsprung disease	2021	Europe	280	Observational	Retrospective	Cohort
Rentea R, et al.	Impact of Botulinum Toxin on Hirschsprung-associated Enterocolitis After Primary Pull-Through	2021	North-America	1439	Comparative	Retrospective	Cohort
Roorda D, et al.	Intrasphincteric botulinum toxin injections for post-operative obstructive defecation problems in Hirschsprung disease: A retrospective observational study	2021	Europe	131	Observational	Retrospective	Cohort
Roorda D, et al.	Risk factors for enterocolitis in patients with Hirschsprung disease: A retrospective observational study	2021	Europe	146	Observational	Prospective	Cohort
Sakurai T, et al.	Predictive factors for the development of postoperative Hirschsprung-associated enterocolitis in children operated during infancy	2021	Asia	35	Comparative	Retrospective	Cohort
Shankar G, et al.	Long-term outcomes in children with Hirschsprung's disease and transition zone bowel pull-through: impact of surgical techniques and role for conservative approach	2021	Asia	11	Observational	Prospective	Cohort
Shojaeian R, et al.	Bioavailability of rectal acetaminophen in children following anorectal surgery	2021	Asia	20	Comparative	Prospective	Cohort
Taylor M, et al.	Comparison of Hirschsprung Disease Characteristics between Those with a History of Postoperative Enterocolitis and Those without: Results from the Pediatric Colorectal and Pelvic Learning Consortium	2021	North-America	299	Comparative	Prospective	Case-control
Yang J, et al.	Colonoscopic Diagnosis of Postoperative Gastrointestinal Bleeding in Patients With Hirschsprung's Disease	2021	Asia	24	Observational	Retrospective	Cohort
Yuan Y, et al.	The Efficacy of Biofeedback Therapy for the Treatment of Fecal Incontinence After Soave Procedure in Children for Hirschsprung's Disease	2021	Asia	46	Observational	Retrospective	Cohort

SUPPLEMENTARY 3: Extracted baseline characteristics

*As several parameters could arguably be included into more than one category, categorization was determined through agreement between the first two authors. Furthermore, we arranged the parameters by topic, such as patient characteristics, comorbidities, primary treatment, to facilitate the comparison of variation in studied parameters among similar subjects. Underlined items were studied in more than 5% of included publications. The items indicated as 5% but not underlined were identified in 4.5% of the included publications.

[a] Classic triad refers to the presence of delayed passage of meconium, bilious vomiting and abdominal distension.

[b] Extent of aganglionosis refers to the histological level of transitional zone, namely rectal, sigmoid, rectosigmoid, distal descending colon.

Patient characteristics

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	n=	%
Sex	176	88%
Birth weight	42	21%
Small for gestational age	1	<1%
Birth height	2	1%
Ethnicity	18	9%
Gestational age	36	18%
Premature	21	11%
Mode of delivery	1	<1%
Normal vaginal delivery	1	<1%
Family history of HSCR	28	14%
Age at first symptom	2	1%
Age at presenting symptom	15	8%
Duration of symptoms	2	1%
Age at biopsy	4	2%
Age at diagnosis	34	17%
Weight at diagnosis	1	<1%
Diagnosis during neonatal period	8	4%
Age at first contact with pediatric surgeon	1	<1%
Age at surgery	132	66%
Surgery during neonatal period	8	4%
Age at follow-up/study	71	36%
Age at redo surgery	4	2%
Weight at surgery	40	20%
Height at surgery	1	<1%
Previous surgery	6	3%
Age at admission	2	1%
Marriage/Relationship status	4	2%
Place of residence	1	<1%
Salary / Income	2	1%
Mother language	1	<1%
Socio-economic status	2	1%
Maternal education level	1	<1%
Education	5	3%
Special education services	1	<1%
School for special education	1	<1%
Remedial teaching	1	<1%
Occupation	3	2%
Length at time of surgery	2	1%
BMI at time of surgery	1	<1%

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Disease characteristics

	n=	%
Initial clinical symptoms (cumulative)	55	28%
Abdominal distention (preoperative)	19	10%
Fever (preoperative)	3	1%
Delay passage of meconium	25	13%
Absent meconium release	2	1%
Time until first excretion of meconium	3	2%
Vomiting (preoperative)	17	9%
Lower intestinal obstruction (preoperative)	3	2%
Signs of intestinal obstruction (preoperative)	6	3%
Enterocolitis (preoperative)	45	23%
Causing pathogenic organisms enterocolitis	1	<1%
Constipation (preoperative)	19	10%
Diarrhea (preoperative)	2	1%
Intestinal perforation (preoperative)	10	5%
Neonatal jaundice (preoperative)	1	<1%
Poor feeding/ failure to thrive (preoperative)	14	7%
Anemia requiring blood transfusion	2	1%
Fatigue (preoperative)	2	1%
Melena (preoperative)	2	1%
HSCR diet and probiotics (preoperative)	2	1%
Other presenting symptoms	1	<1%
Not opening bowels (preoperative)	1	<1%
Distended bowel (preoperative)	1	<1%
Classic triad [a]	4	2%
Neonatal bowel obstruction (preoperative)	1	<1%
Need for glycerin enema's (preoperative)	2	1%
Toxic megacolon (preoperative)	1	<1%
Paleness (preoperative)	1	<1%
Urinary tract infection (preoperative)	1	<1%
Fecaloid mass (preoperative)	4	2%
Weakness (preoperative)	1	<1%
Explosive discharge of gas and stools after rectal examination	2	1%
Age at reflux enema method	1	<1%
History of central nervous system infection (preoperative)	1	<1%
Weight loss (preoperative)	1	<1%
Incidence of HSCR	7	3%
Prevalence of HSCR	2	1%
Serum total protein at time of surgery	1	<1%

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Serum albumin at time of surgery	4	2%
Serum prealbumin at time of surgery	1	<1%
Hemoglobin at time of surgery	4	2%
White blood cells at time of surgery	1	<1%
Blood urea nitrogen at time of surgery	1	<1%
Extent of aganglionosis [b]	101	51%
Length of ileum involvement	1	<1%
Aganglionic segments extending to descending colon	3	2%
Aganglionic segments extending to transverse colon	2	1%
>30cm of aganglionotic length	1	<1%
Muscular sleeve >4cm	1	<1%
Dilated segments extending to ascending colon	1	<1%
Length of transition zone	3	2
Distance of transition zone to the terminal ileum	1	<1%
Distance of transition zone to the dentate line	1	<1%
Dependence of parenteral nutrition at surgery	2	1%
Intestinal dysplasia	1	1%

Comorbidities

	n=	**%**
Associated anomalies	38	19%
Other major anomalies	2	1%
Incidence associated anomalies	1	<1%
Other diseases	3	2%
Major comorbidity	2	1%
Isolated associated anomaly	1	<1%
Co-existent developmental condition	1	<1%
Number of malformations	2	1%
Unspecified congenital malformations	2	1%
Congenital anomalies of eye, ears, face and neck	7	4%
Hemangioma of the scalp	1	<1%
Skin	2	1%
Trigonocephalia	1	<1%
Club feet	1	<1%
Cleft lip/palate	6	3%
Cardiovascular anomalies	40	20%

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Congenital heart disease/anomaly	40	20%
Congenital circulatory system anomaly	1	<1%
Fallot's triad	2	1%
CHD with or without underlying syndrome	2	1%
Cardiac myopathy	1	<1%
Atrial septal defect	4	2%
Ventricular septal defect	6	3%
Bicuspid aortic valve	1	<1%
Aortic stenosis	1	<1%
Vena Galeni malformation	1	<1%
Hypoplastic left heart syndrome	2	1%
Congenital pulmonary anomaly	12	6%
Congenital central hypoventilation syndrome	4	2%
Congenital diaphragmatic hernia	2	1%
Bronchopulmonary dysplasia	1	<1%
Neurologic anomalies	19	10%
Congenital anomaly of nervous system	10	5%
Neurologic alterations	2	1%
Mental retardation	1	<1%
Hydrocephalus	1	<1%
Epilepsy	3	2%
Ganglioneuroblastoma	1	<1%
Ganglioneuroma	1	<1%
Congenital anomaly of digestive system	19	10%
Intestinal malrotation	3	2%
Anorectal malformation	4	2%
Gastroesophageal reflux	1	<1%
Duodenal atresia	3	2%
Small bowel atresia	2	1%
Esophageal atresia	1	<1%
Pyloric stenosis	1	<1%
Meckel's diverticulum	1	<1%
Congenital anomaly of musculoskeletal system	9	5%
Vertebral	2	1%
Osteogenesis imperfecta	1	<1%
Congenital anomalies of the urogenital system	23	12%
Renal/genitourinary anomalies	23	12%
Hypospadia	6	3%
UTI (really mentioned as associated anomaly)	3	2%
Neurogenic bladder requiring intermittent catheterization	1	<1%
Urological anomaly with or without underlying syndrome	1	<1%

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Genital anomaly	3	2%
Vesicoureteral reflux	3	2%
Atrophic kidney	1	<1%
Hydrocele	1	<1%
Single kidney	1	<1%
Kidney dysplasia	2	1%
Congenital hydronephrosis	2	1%
Micropenis	1	<1%
Ureteral duplication	1	<1%
Kidney agenesis	1	<1%
Horseshoe kidney	1	<1%
Multicystic kidney disease	1	<1%
Unilateral kidney cyst	1	<1%
Posterior urethral valves	1	<1%
Bartter syndrome	1	<1%
Hinman syndrome	1	<1%
Cryoglobulinemic kidney failure	1	<1%
Thyroid disorders	6	3%
Diabetes	1	<1%
Celiac disease	2	1%
Polydactyly	1	<1%
Visual impairment	3	2%
Hearing impairment	2	1%
Hematologic problem	2	1%
Endocrinologic problem	2	1%
Umbilical hernia	1	<1%
Primary immunodeficiency disease	1	<1%
Adenoid hypertrophy	1	<1%
Hip dysplasia	1	<1%
Syndromal, genetic and chromosomal disorders	80	40%
Trisomy 21 (Down)	65	33%
Bardet-Biedl Syndrome	5	3%
Mowat-Wilson	9	5%
Hair-cartilage hypoplasia	4	2%
DiGeorge syndrome	1	<1%
Ondine	4	2%
Pallister Hall	1	<1%
Gilbert's syndrome	1	<1%
Currarino syndrome	2	1%
Noonan syndrome	1	<1%
IgA deficit and celiac disease	1	<1%
G6PD Deficiency	1	<1%
EDNRB mutation	1	<1%
RET mutation	4	2%
Syndromal (unspecified)	3	2%

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Chromosomal anomaly	5	3%
Genetic anomalies	2	1%
Haddad	7	4%
Shah-Waardenburg	8	4%
Bresheck syndrome	3	2%
Marker-chromosome syndrome	2	1%
Marcus Gunn syndrome	2	1%
Kabuki syndrome	2	1%
Asperger syndrome	1	<1%
MEN 2A syndrome	2	1%
Klinefelter	1	<1%
Translocation 20-21	1	<1%
13q deletion syndrome	2	1%
Deletion chromosome 1	1	<1%
phox2b mutation	1	<1%
Goldberg-Sphrintzen syndrome	1	<1%
McKusick-Kaufman syndrome	1	<1%
1q partial trisomy, 3p partial monosomy	1	<1%
Trisomy 20q	1	<1%
Coffin-Lowry syndrome	1	<1%
Smith-Lemli-Opitz syndrome	1	<1%
Beckwith-Wiedeman syndrome	1	<1%
Chromosome 22 abnormalities	2	1%
Turner	1	<1%
Cat-eye syndrome	1	<1%

Parental characteristics

		n=	**%**
Age mother		5	3%
Age father		1	<1%
Occupation parents		1	<1%
Single parity (first and only child)		1	<1%
Insurance		9	5%

SUPPLEMENTARY 4: Extracted treatment and care process characteristics

*As several parameters could arguably be included into more than one category, categorization was determined through agreement between the first two authors. Furthermore, we arranged the parameters by topic, such as diagnostics, perioperative workup, primary treatment, treatment of complications, to facilitate the comparison of variation in studied parameters among similar subjects. Underlined items were studied in more than 5% of included publications. The items indicated as 5% but not underlined were identified in 4.5% of the included publications.

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Hospital structure

	n=	%
Medical costs	8	4%
Hospital volume (number of patients)	3	2%
Specific surgeon performing surgery	3	2%
Received sufficient information about HSCR	1	<1%
Follow-up rate	21	11%
Total number of follow-ups	1	<1%
Number of counseling sessions during first 6 months	1	<1%
Number of planned visits	4	2%
Time since surgery until follow-up	6	3%
Misdiagnosis rate	5	3%

Diagnostics

	n=	%
Prenatal ultrasound	1	<1%
Prenatal ultrasound: bowel dilation	1	<1%
Prenatal ultrasound: polyhydramnios	1	<1%
Prenatal ultrasound: oligohydramnios	1	<1%
Anorectal manometry (preoperative)	13	7%
Age at anorectal manometry	1	<1%
Findings preoperative anorectal manometry: lack of the rectoanal inhibitory reflex	1	<1%
Findings preoperative anorectal manometry: rectal rest pressure	3	2%
Findings preoperative anorectal manometry: anal canal rest pressure	1	<1%
Findings preoperative anorectal manometry: anal canal length (in cm)	1	<1%
Findings preoperative anorectal manometry: amplitude anal contraction (in mmHg)	1	<1%
Findings preoperative anorectal manometry: frequency anal contraction (per minute)	1	<1%
Preoperative contrast enema	27	14%
Preoperative contrast enema: wrong or correct determination of transitional zone	6	3%
Contrast enema examinations with delayed X-ray	1	<1%
Contrast study: location of barium residue	1	<1%
Contrast study: clear transition zone	3	2%
Contrast study: barium retention for >24h	1	<1%
Contrast study: microcolon	1	<1%
Contrast study: relationship caliber change and proximal ends of barium residue	1	<1%

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Rectal biopsies	26	13%
Age at rectal suction biopsies	2	1%
Number of rectal suction biopsies	3	2%
Rectal mucosal biopsy	5	3%
Rectal full-thickness biopsy	6	3%
Distance from biopsy taken and dentate line	1	<1%
Histochemical studies for acetylcholinesterase	4	2%
Histochemical studies for hematoxylin and eosin	2	1%
Histochemical studies for calretinin	2	1%
Abdominal X-ray (preoperative)	9	5%
Findings preoperative abdominal X-ray: swelling of intestinal loops	1	<1%
Findings preoperative abdominal X-ray: lack of distal air	2	1%
Findings preoperative abdominal X-ray: fecaloma/faecal stasis	2	1%
Findings preoperative abdominal X-ray: air fluid levels	6	3%
Findings preoperative abdominal X-ray: cut-off sign	5	3%
Findings preoperative abdominal X-ray: distended bowel loops	5	3%
Findings preoperative abdominal X-ray: Sawtooth appearance with irregular mucosal lining	4	2%
Findings preoperative abdominal X-ray: Pneumatosis intestinalis	4	2%
Findings preoperative abdominal X-ray: features of intestinal obstruction	1	<1%
Leukocytosis	6	3%
Left shift on blood count	4	2%
Radiological and intraoperative transition zone match	2	1%
Intraoperative biopsies	18	9%
Intraoperative gross transition zone	2	1%
Intraoperative frozen section with ganglion cells	6	3%
Histopathological analysis of the appendix	1	<1%
Sensitivity and specificity of appendix as diagnostic tool	1	<1%
Histopathological analysis: development (maturity) of ganglion cells in proximal intestine	2	1%
Genetic testing	1	<1%
Full thickness colon biopsies during enterostomy	1	<1%

Perioperative work-up

Colon irrigations (mechanical bowel preparation) (preoperative)	18	9%

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Effective preoperative bowel preparation by rectal washout	2	1%
Preoperative management with repeated bowel washes	1	<1%
Duration of bowel preparation	3	2%
Rectal wash-outs	4	2%
Rectal wash-outs at home	3	2%
Duration of indwelling anal catheter for coloclysis	1	<1%
Time used for each coloclysis	1	<1%
Amount of liquid used for each coloclysis	1	<1%
Intestinal tract cleanliness after coloclysis	1	<1%
Degree of comfort of coloclysis	1	<1%
Perianal skin redness after coloclysis	1	<1%
Complications after coloclysis	1	<1%
Discharge time after coloclysis	1	<1%
Enterocolitis during coloclysis	1	<1%
Subjective feeling of infant after coloclysis	1	<1%
Duration of restoration of child's faeces color and smell to normal (in days)	1	<1%
Duration of relief of abdominal distension and vomiting disappearance (in days)	1	<1%
Duration of restoration of appetite to normal (in days)	1	<1%
Intravenous antibiotics 1-2 days preoperative to 3 days postoperative	5	3%
Duration intravenous antibiotics	4	2%
Duration intravenous fluid suppletion/administration	1	<1%
Feeding gastrostomy/jejunostomy	3	2%
Preoperative stoma / Primary stoma	71	36%
Preoperative ileostomy	16	8%
Preoperative jejunostomy	2	1%
Preoperative colostomy	20	10%
Preoperative transverse colostomy	2	1%
Preoperative sigmoidostomy	2	1%
Blowhole transverse colostomy	1	<1%
Stoma without initial trial rectal washouts	1	<1%
Colectomy before reconstruction	1	<1%
Age at preoperative stoma	9	5%
Rate histopathologically proven/diagnosis before surgery	3	2%
Home before definitive surgery	1	<1%
Preoperative complications	1	<1%
Irrigations performed during admission	2	1%
Time (in days) from histopathological diagnosis to surgery	8	4%
Time (in days) from histopathological diagnosis to reconstruction	1	<1%
Time (in days) from symptoms onset to contact with pediatric surgeon	1	<1%

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Time (in days) from symptoms onset to surgery	1	<1%
Time from first contact with pediatric surgeon to surgery	5	3%

Primary treatment

	n=	%
Type of repair	113	57%
Single- or multiple staged	19	20%
Causes of staged repair	2	1%
Intraoperative complications	18	9%
Rate primary surgery without enterostomy	2	1%
Number of stoma's	1	<1%
Time (in months) from surgery until closure of stoma	4	2%
Age at closure of ileostomy	1	<1%
Time between stoma and radical surgery	4	2%
Stoma closure at time of definitive repair	5	3%
Stoma at time of surgery	3	2%
Duration oral antibiotics	1	<1%
Coloanal anastomosis: interrupted sutures	1	<1%
Coloanal anastomosis	1	<1%
Anastomotic incongruence	1	<1%
Plication procedure	1	<1%
Number of stitches	1	<1%
Ileoanal anastomosis	2	1%
Peroperative ileostomy	1	<1%
Operation duration	46	23%
Laparoscopic phase duration	1	<1%
Conversion laparoscopy to laparotomy	14	7%
Laparoscopy or laparotomy or trans-anal	40	20%
Abdominal approach using laparotomy	3	2%
Insertion of additional trocar during laparoscopy	2	1%
Number of ports used during laparoscopic surgery	2	1%
Peroperative impression of colon	1	<1%
Anal dissection time	1	<1%
Length of resected aganglionic and dilated segments	40	20%
Length of remaining intestines	3	2%
Length of remaining small intestine	1	<1%
Level of pull-through	1	<1%
Level of anastomosis	1	<1%

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Antegrade Colonic Enema (ACE)	14	7%
Indications for ACE	2	1%
Time (in days) to start feeding	11	6%
Time (in days) to full enteral feeding	5	3%
Need for parenteral nutrition postoperatively	8	4%
Duration parenteral nutrition	4	2%
Need for a gastrostomy	4	2%
Anal tube	1	<1%

Treatment of complications

	n=	%
Anal dilatations	33	17%
Anal dilatation under general anesthesia	12	6%
Anal dilatation, 2 weeks postoperatively	2	1%
Anal dilatation, 2 weeks postoperatively up to 6 months	1	<1%
Anal dilatations, 1 year postoperatively	1	<1%
Anal calibrations, 1 year postoperatively	1	<1%
Median number of anal dilatations	3	2%
Gentle calibrating and dilating weekly	1	<1%
Dilatation for stricture	8	4%
Number of calibrations	2	1%
Examination under anesthesia	3	2%
Postoperative dilatations duration (in days)	1	<1%
HAEC pathological grade system: stenosed segment (Elhalaby et al.)	2	1%
HAEC pathological grade system: transitional segment (Elhalaby et al.)	1	<1%
HAEC pathological grade system: dilated segment (Elhalaby et al.)	1	<1%
HAEC pathological grade system: overall resected (Elhalaby et al.)	1	<1%

Treatment of long-term morbidity

	n=	%
Current contact with medical care (at time of study)	3	2%
Duration follow-up	78	39%
HSCR consultations 1 year postoperatively	1	<1%
Time between leaving the hospital and the first counseling postoperatively (in days)	2	1%

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Toilet training	1	<1%

Follow-up

	n=	%
Anorectal manometry: follow-up	12	6%
Complete manometry	1	<1%
Age at manometry	1	<1%
Anorectal manometry (follow-up): enhanced pressure curve	1	<1%
Anorectal manometry (follow-up): pressure response to maintained voluntary contraction	1	<1%
Anorectal manometry (follow-up): pressure response to perianal stimulation	1	<1%
Anorectal manometry (follow-up): pressure response to voluntary contracting	1	<1%
Anorectal manometry (follow-up): ano-anal reflex	1	<1%
Anorectal manometry (follow-up): cough reflex	2	1%
Anorectal manometry (follow-up): rectosphincteric reflex	1	<1%
Anorectal manometry (follow-up): resting pressure	7	4%
Anorectal manometry (follow-up): squeeze pressure	4	2%
Anorectal manometry (follow-up): simple pressure curve	1	<1%
Anorectal manometry (follow-up): RAIR (relaxation pressure during rectal balloon distention)	3	2%
Anorectal manometry (follow-up): mean sphincter pressure	2	1%
Anorectal manometry (follow-up): sphincter pressure response to coughing	1	<1%
Anorectal manometry (follow-up): length of high pressure zone	1	<1%
Anorectal manometry (follow-up): length verge to centre	1	<1%
Anorectal manometry (follow-up): rectal compliance	1	<1%
Anorectal manometry (follow-up): anal canal resting pressure	2	1%
Anorectal manometry (follow-up): inhibitory reflex	1	<1%
Anorectal manometry (follow-up): Anal canal length (cm)	1	<1%
Anorectal manometry (follow-up): Amplitude anal contraction	1	<1%
Anorectal manometry (follow-up): frequency anal contraction	1	<1%
Anorectal manometry (follow-up): endurance squeeze	1	<1%
Anorectal manometry (follow-up): defecation patterns	1	<1%
Profilometry: rectal volume	1	<1%
Anoendoscopy: follow up	1	<1%
Anoendoscopy (follow-up): recognition of the IAS	1	<1%
Anoendoscopy (follow-up): IAS defects yes or no	1	<1%

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Anoendoscopy (follow-up): number of IAS defects in individual patients	1	<1%
Anoendoscopy (follow-up): total angular distribution of IAS defects	1	<1%
Anoendoscopy (follow-up): EAS defects yes or no	1	<1%
Anoendoscopy (follow-up): size of IAS defects	1	<1%
Anoendoscopy (follow-up): IAS thickness	1	<1%

SUPPLEMENTARY 5: Extracted outcomes

*As several parameters could arguably be included into more than one category, categorization was determined through agreement between the first two authors. Furthermore, we arranged the parameters by topic, such as complications, readmission and reoperation, morbidity, to facilitate the comparison of variation in studied parameters among similar subjects. Underlined items were studied in more than 5% of included publications. The items indicated as 5% but not underlined were identified in 4.5% of the included publications.

Complications

	n=	**%**
Blood loss	41	21%
Intraoperative blood transfusion	6	3%
Postoperative blood transfusion	6	3%
Chronic low gastrointestinal bleeding needing blood transfusion	1	<1%
Bleeding anemia requiring transfusion	2	1%
Bleeding from anastomosis	1	<1%
Intraoperative blood loss	4	2%
Intraoperative blood loss during laparoscopic phase	1	<1%
Time until onset of gastrointestinal bleeding	1	<1%
Wound issues	32	16%
Wound dehiscence	11	6%
Wound infection	27	14%
Time (in weeks) until healing wounds	1	<1%
Incisional hernia	3	2%
Perianal issues	38	19%
Perianal dermatitis	9	5%
Diaper rash	1	<1%
Anal pain score	1	<1%
Perianal erosion	5	3%
Anal excoriations	24	12%
Injection site complications after botox	2	1%
Perianal fistula	2	1%

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Organ/space surgical site infection (abdominal infection)	4	2%
Abcess	10	5%
Cuff abcess	3	2%
Perineal abcess	2	1%
Itches	1	<1%
Persistent internal sphincter achalasia	4	2%
Pelvic infection	3	2%
Infection	10	5%
Residual aganglionosis	24	12%
Incomplete/Transitional zone pull-through	10	5%
Retained aganglionotic segment	1	<1%
Residual aganglionosis because of error in histologic interpretation	2	1%
Residual aganglionosis because of sampling error	1	<1%
Residual aganglionosis because of error in surgical technique	1	<1%
Ganglion cell loss	1	<1%
Hypoganglionosis	2	1%
Immature ganglion cells	2	1%
Intestinal neuronal dysplasia type B	1	<1%
Repeat biopsy normal	1	<1%
Repeat biopsy postoperative	2	1%
Anastomotic leakage	56	28%
Anastomotic dehiscence/retraction	8	4%
Anastomotic abces	1	<1%
Anastomotic stricture/stenosis	76	38%
Recurrent stricture	2	1%
Anastomotic volvulus	1	<1%
Outlet obstruction	4	2%
Stenosis of muscular cuff	5	3%
Obstructed pouch	1	<1%
Anastomotic fistula	7	4%
Rectovestibular fistula/urinary	5	3%
Fistula to the seminal vesicle	2	1%
Rectovaginal fistula	2	1%
Enterocutaneous fistula	2	1%
Urinary-rectal fistula	3	2%
Intestinal obstruction	49	25%
Anorectal obstruction	1	<1%
Sub-obstruction due to adhesions	1	<1%
Ileus/bowel obstruction due to adhesions	20	10%
Paralytic obstruction	1	<1%
Intussusception	2	1%
Hospitalization for obstruction	1	<1%
Twisted bowel	7	4%

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Peritonitis	2	1%
Pelvic floor fibrosis	1	<1%
Osteomyelitis	1	<1%
Pouchitis	3	2%
Short bowel syndrome	3	2%
Sepsis	13	7%
Bloodstream infection	2	1%
Rectal prolapse	15	8%
Total colon prolapse	3	2%
Pneumonia	3	2%
Perforation colon	1	<1%
Intestinal perforation	8	4%
Iatrogenic dehiscence when inserting rectal catheter	1	<1%
Iatrogenic/incidental injury	2	1%
Bowel injury	3	2%
Urethral injury	5	3%
Ureter injury	2	1%
Vaginal injury	3	2%
Retraction	2	1%
Recurrence	1	<1%
Toxic hepatitis	1	<1%
Hepatic failure	1	<1%
Botulinum toxin	31	16%
Botulinum toxin injection for outlet obstruction	9	5%
Number of botulinum toxin injection treatments	6	3%
Multiple botulinum toxin injection	1	<1%
Delay between first and second injection	1	<1%
Age at first botulinum toxin injection treatment	4	2%
Weight at first botulinum toxin injection treatment	1	<1%
Time (in days) pull-through to botulinum injection	1	<1%
Time from botulinum injection to follow-up	1	<1%
Effect of (first) botulinum injection	4	2%
Myectomy because of bowel outlet obstruction	4	2%
Postoperative Hirschsprung's Associated Enterocolitis (HAEC)	127	64%
Hospitalized for enterocolitis at least once	8	4%
At least one episode of enterocolitis	8	4%
Single episode of enterocolitis	5	3%
Multiple episodes of enterocolitis	14	7%
More than 3 episodes of HAEC	1	<1%
Rate of HAEC in first postoperative year	1	<1%
Incidence of HAEC	13	7%

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Hirschsprung Associated Enterocolitis Recurrence	14	7%
HAEC treated by conservative management (non-operative)	16	8%
Number of episodes of enterocolitis	7	4%
Age at time of HAEC	1	<1%
Time between surgery and ulceration diagnosis (in days)	1	<1%
Time between enterocolitis and surgery (in days)	5	3%
Time from pull-through to initial episode of HAEC	3	2%
Time from pull-through to second episode of HAEC	1	<1%
Endoscopy performed in HAEC	1	<1%
HAEC endoscopy: Longitudinal peri anastomosis Crohn like ulcerations	1	<1%
Type of medication for ulceration HAEC	1	<1%
Type of medication for enterocolitis	1	<1%
Broad-spectrum antibiotic therapy for enterocolitis	2	1%
Duration of antibiotics	1	<1%
Microorganisms in stool during enterocolitis	1	<1%
Severity of HAEC (according to grading system by Elhalaby et al)	3	2%
Severity of HAEC (according to 'standardized' grading system)	1	<1%
Severity of HAEC (clinical, according to Murphy et al.)	1	<1%
HAEC score (by Pastor et al.)	5	3%
HAEC score at diagnosis	2	1%
Consistent HAEC score (Pastor et al.) in every episode	1	<1%
Intestinal failure	4	2%
Intestinal failure: need for Itx/transplantation	3	2%
End-stage liver disease	2	1%
Intestinal failure-associated liver disease	1	<1%
Misplacement of an epidural catheter	1	<1%
Respiratory complication	6	3%
Hemothorax	1	<1%
Upper respiratory tract infection	2	1%
Neurologic complication	3	2%
Seizures	2	1%
Stoma complications	15	8%
Stoma stenosis	3	2%
Stoma prolapse	7	4%
High-output stoma	3	2%
Stoma needing revision	1	<1%
Ostomy prolapse requiring surgical revision	2	1%
Number of surgeries on stoma	1	<1%
Stoma leakage	1	<1%

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Stoma excoriation	1	<1%
Redness of skin around stoma	2	1%
Stoma retraction	2	1%
Parastomal hernia	1	<1%
Contrast enema in follow-up	1	<1%
Reintubation	1	<1%
Early postoperative complications	26	13%
Postoperative complications within 1 month after pull-through	3	2%
Adverse reaction rate	1	<1%
Late/long term complications	6	3%
Complications	30	15%
Postoperative complications unrelated to surgery	1	<1%
Number of times hospitalized for complications of disease	3	2%
Complication rate	2	1%
Presentation from home	1	<1%
Number of emergency visits	5	3%
Acute HSCR consultations 1 year postoperatively	1	<1%
Postoperative pain	3	2%
Epidural catheter complication	1	<1%
Received opiates not in compliance with normal postoperative course	1	<1%
Postoperative nasogastric decompression for 12-24 hours	1	<1%
Stoma at time of follow-up	21	11%

Readmission and reoperation

	n=	%
Readmission	25	13%
Reoperation	85	43%
Reoperation type	10	5%
Time between first surgery and reoperation	3	2%
Reoperation due to complications (no timeframe)	10	5%
Reoperation due to anastomotic leakage	8	4%
Reoperation due to twisted bowel / volvulus	7	4%
Reoperation due to perforation after biopsy	1	<1%
Reoperation due to perforation after postoperative calibration	1	<1%
Reoperation due to postoperative fistualization between bowel and urinary tract	4	2%
Reoperation due to wound dehiscence	1	<1%
Reoperation due to bleeding	2	1%
Reoperation due to stricture	9	5%

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Reoperation due to obstruction/occlusion	10	5%
Laparotomy with adhesiolysis and ileostomy because of adhesions	2	1%
Reversal ileostomy that was closed earlier	2	1%
Reoperation due to transition-zone pull-through	7	4%
Reoperation due to residual aganglionosis	10	5%
Reoperation due to wall abcess	3	2%
Secondary colostomy due to fistula	2	1%
Reoperation: ileostomy	5	3%
Reoperation for bowel resection	2	1%
Number of reoperations	5	3%
Reoperation due to residual rectal spur (post Duhamel)	5	3%
Reoperation: intestinal transplantation	2	1%
Reoperation: false negative biopsy	1	<1%
Reoperation due to adhesive intestinal obstruction	5	3%
Reoperation due to post myectomy persistence of symptoms	1	<1%
Reoperation due to fecal fistula	1	<1%
Reoperation due to anal sphincter tear secondary to dilated colon in long segment disease	1	<1%
Number of unplanned/emergency surgeries	5	3%
At least one unplanned/emergency surgery	1	<1%
Reoperation within 30 days	1	<1%
Reoperation within 1 year	1	<1%
Abnormal histological findings on full-thickness biopsies during reoperation	1	<1%
Number of surgeries	3	2%
Number of laparotomies	1	<1%
Number of episodes of general anaesthesia (before 2 years of age)	1	<1%
Need for transfer to a pediatric surgical center	1	<1%
Number of hospitalizations	4	2%

Growth

	n=	**%**
Growth/Weight/Failure to thrive	32	16%
BMI at time of follow-up	7	4%
Height (in cm) at time of follow-up	8	4%
Weight (in kg) at time of follow-up	13	7%
Failure to thrive according to growth charts that correlate height, weight and age	3	2%
Growth	3	2%
Weight-for-age	4	2%

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Height-for-age	1	<1%
Nutritional status during follow-up	7	4%
Stunting	2	1%
Underweight	1	<1%
Head circumference at time of follow-up	1	<1%

Morbidity

	n=	%
Gastrointestinal symptoms during follow-up	40	20%
Pain during defecation	3	2%
Fecal impaction	6	3%
Fecal loading	1	<1%
Abdominal pain	7	4%
Intensified flatulence / bad smelling gas	3	2%
Halitosis	1	<1%
Intestinal rumbling	1	<1%
Diarrhea	12	6%
Diarrhea with explosive stool	4	2%
Diarrhea with foul smelling stool	5	3%
Diarrhea with bloody stool	5	3%
Stool retention with explosive stools at night	1	<1%
Enterospasm	1	<1%
Heartburn	1	<1%
Eructation	1	<1%
Simple gastroenteristis requiring hospitalization	2	1%
Fever	10	5%
Abdominal distension	18	9%
Vomiting	4	2%
Lethargy	3	2%
Explosive discharge of gas and stool on rectal exam	3	2%
Decreased peripheral perfusion	4	2%
Previous history of suspected enterocolitis	5	3%
Enterocolitis before aganglionosis diagnosis	1	<1%
Enterocolitis between aganglionosis diagnosis and corrective surgery	1	<1%
Inflammatory bowel disease (IBD)	1	<1%
Age at IBD diagnosis	1	<1%
Prevalence of IBD	1	<1%
IBD for which surgery/medication	1	<1%
Crohn's disease	2	1%
Ulcerative colitis	2	1%
Ulcerative ileitis	1	<1%

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Intestinal continuity	2	1%
Constipation	96	48%
Constipation: bloating	3	2%
Constipation: flatulence	2	1%
Constipation: need for repeated defecations to empty the rectum	1	<1%
Constipation: need to strain at defecation / difficult defecation	4	2%
Constipation: supporting around anus at defecation	1	<1%
Constipation: manageable with diet	12	6%
Constipation: manageable with laxatives	15	8%
Constipation: manageable with enema	14	7%
Recurrent constipation	12	6%
Duration of constipation symptoms after surgery	1	<1%
Fecaloma formation	1	<1%
Cleveland Clinic Constipation Scoring System	3	2%
Hospitalization for constipation	2	1%
Lumpy or hard stools	1	<1%
Incomplete evacuation	1	<1%
Manual maneuvers	1	<1%
Form of stool/consistency	15	8%
Defecation frequency	52	26%
Defecation frequency, 1 month postoperatively	4	2%
Defecation frequency, 1 week postoperatively	2	1%
Defecation frequency, 3 months postoperatively	4	2%
Defecation frequency, last day of hospital stay	2	1%
Time (in months) until normal defecation frequency	3	2%
Defecation frequency, early postoperative	1	<1%
Defecation frequency after two years	3	2%
Defecation frequency after six months	5	3%
Defecation frequency before six months	1	<1%
Defecation frequency after one year	1	<1%
Defecation frequency after one month	1	<1%
Defecation frequency after nine months	1	<1%
Normal defecation function	37	19%
Normal anal defecation function	6	3%
Regular defecation at night time	1	<1%
Normal sense of defecation control	3	2%
Feeling need for defecation	13	7%
Voluntary bowel movement	6	3%
Time until normal bowel movement	3	2%
Satisfying bowel control	3	2%

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Ability to hold back defecation	13	7%
Rectal sensation	5	3%
Sense of stool condition	1	<1%
Time required for bowel movement	2	1%
Bowel function deteriorating during viral infections	1	<1%
Sensation for flatulence	2	1%
Control of bowel movement	2	1%
Number of bowel movements per week	1	<1%
Number of bowel movements per day	2	1%
Regular bowel movement	1	<1%
Defecation urgency	6	3%
Urgency: deferring time loose stool (in minutes)	1	<1%
Urgency: deferring time solid stool (in minutes)	1	<1%
Urgency: need to rush to the toilet	1	<1%
Urgency: use of pad daytime	4	2%
Urgency period	2	1%
Incontinence	107	54%
Soiling	72	36%
Urge incontinence	2	1%
Fecal contamination/fecal accidents	17	9%
Incontinence: Miller incontinence score	2	1%
Incontinence: Postoperative Fecal Incontinence Score	1	<1%
Incontinence: Jorge-Wexner score	1	<1%
Baylor Continence Scale	2	1%
Wingspread criteria	4	2%
Visick score	1	<1%
Continence evaluation score	1	<1%
Incontinence in children >5 years	1	<1%
Occasional incontinence	1	<1%
Overflow incontinence	1	<1%
Incidents of fecal incontinence at least once a week	1	<1%
Daily incontinence	1	<1%
Required (night) diapers	4	2%
Number of fecal accidents	3	2%
Social continence	1	<1%
Involuntary loss of stools	1	<1%
Involuntary loss of stools (only at night)	2	1%
Involuntary loss of stools when provoked (physical activities, emotions, coughing, sneezing)	1	<1%
Impaired continence	1	<1%
Duration of fecal incontinence	1	<1%

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Use of bowel regulating medication	32	16%
Use of bowel regulating medication: daily laxative or enemas	5	3%
Use of bowel regulating medication: daily enemas	1	<1%
Use of bowel regulating medication: daily oral medication	3	2%
Use of bowel regulating medication: daily rectal medication	1	<1%
Use of bowel regulating medication: occasional laxative or enemas	1	<1%
Use of bowel regulating medication: enemas if necessary	1	<1%
Use of bowel regulation medication: use of enemas	13	7%
Use of bowel regulation medication: use of laxatives	13	7%
Use of bowel regulation medication: use of loperamide or equivalent	7	4%
Bowel management for constipation	1	<1%
Bowel management for incontinence	1	<1%
Postoperative enema duration	1	<1%
Appendicostomy/Received terminal ileum fistulization	8	4%
Regular rectal wash-outs/irrigations	7	4%
Sacral stimulating device implementation	1	<1%
Laxative diet	3	2%
Diet to make stools more solid	2	1%
Sensitivity to foods	1	<1%
Significant bowel changes with diet	1	<1%
Bowel changes by milk products	2	1%
Milk protein allergy	1	<1%
Diet control	1	<1%
Food restriction	2	1%
Dietary disorder	2	1%
Dependence on parenteral nutrition during follow-up	6	3%
Additional peroral nutrition	2	1%
Regular supplementation with vitamins	2	1%
Regular follow-up dietician at time of follow-up	1	<1%
Regular use of ORS	2	1%
Hospitalization for rehydration / salt imbalance (at least once)	1	<1%
Iron supplement	1	<1%
Sodium chloride supplement	1	<1%
Bowel function (any standardized scoring)	54	27%
Pediatric Incontinence and Constipation Scoring System	3	2%
Bowel Function Score according to Holschneider	7	4%
Bowel Function Score according to Holschneider, adapted by Lindahl et al	1	<1%

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Fecal continence index based on the clinical evaluation of fecal continence (Holschneider criteria)	1	<1%
Bowel Habit Diary	1	<1%
Evacuation score of the Japan Society of ARM Study group	2	1%
Stooling Survey (El Sawaf et al.)	3	2%
Bowel function Score (Rintala et al.)	20	10%
Vancouver Dysfunctional Elimination Syndrome Survey (VDESS)	2	1%
Kelly Scale Score for recovery of bowel function	1	<1%
Postoperative bowel function score	1	<1%
HSCR anal function criteria (proposed by Reding)	1	<1%
Wingspread score	1	<1%
Krickenberg classification system	6	3%
Rome IV criteria	1	<1%
Permanent stoma	31	16%
End-jejunostomy/Santulli jejunostomy	3	2%
Loop-jejunostomy	1	<1%
Colostomy at time of follow-up	6	3%
Ileostomy at time of follow-up	8	4%
Urinary function	27	14%
Urinary complaints	4	2%
Difficulties emptying the urinary bladder	1	<1%
Micturition functional recovery	1	<1%
Problems with urinary incontinence	10	5%
Removal urinary catheter after 72h	1	<1%
Retention of urine/uroschesis	8	4%
Time (in days) indwelling catheter in place	1	<1%
Temporary dysuria	2	1%
Bladder dysfunction	1	<1%
Urinary voiding	1	<1%
Straining to void	2	1%
Symptoms of urinary urgency	2	1%
At least one type of Lower Urinary Tract Symptom (LUTS)	3	2%
Prevalence of any LUTS >1/week	1	<1%
Urination frequency	2	1%
Social problems due to LUTS	2	1%
Urinary tract infection (UTIs)	5	3%
Stricture of bladder neck	2	1%
Urochesis	1	<1%
Vesicoureteric reflux	1	<1%
Urinary leakage	2	1%
Urinary accidents	1	<1%
Stress incontinence	1	<1%

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Nocturnal enuresis	1	<1%
Child pees in underwear during the day	1	<1%
Volume of pee in underwear	1	<1%
Rate that child pees in the bathroom	1	<1%
Rate that child rushes to the bathroom	1	<1%
Rate that child holds pee by crossing legs/sitting down	1	<1%
Rate that pee hurts	1	<1%
Rate that child wets the bed	1	<1%
Rate that child wakes up to pee at night	1	<1%
Rate that peeing starts and stops	1	<1%
Rate that child has to push or wait for the pee	1	<1%
Dysfunctional elimination	1	<1%
Shape of flowmetry curve	1	<1%
Voided volume	1	<1%
Time of flow	1	<1%
Max. flow rate	1	<1%
Time to max. flow	1	<1%
Flow rate	1	<1%
Post-void residual	1	<1%
Discontinuous flow	1	<1%
Residual urine volume	1	<1%
Renal tract ultrasound	1	<1%
Level of urinary care necessary	1	<1%
Time until disappearance dilated colonic segments	1	<1%
Bowel function problems that affected choice of occupation	1	<1%
Bowel care preventing the child to leave the house	2	1%
Bowel care making child afraid to go outside	1	<1%
Afraid to go out due to fecal incontinence	1	<1%
School absenteeism	2	1%
Patients worrying about smell of their fecal incontinence	1	<1%
Bowel function had negative impact on daily life	1	<1%
Bowel care preventing the parent to leave the house	1	<1%
Bowel problems affecting relations parents	2	1%
Bowel problems causing anxiety in parents	2	1%
Parents worrying about smell of their child's fecal incontinence	1	<1%
Bowel problems affecting employment/job of parents	1	<1%
Bowel problems affecting household tasks of parents	2	1%
Regular visits psychologist as parent	1	<1%
Current contact with psychologist as parent	1	<1%

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Difficulties with socializing/social adaptation/relationships	18	9%
Anorectal problems that affected social relations	1	<1%
Children's social adaptation ability	1	<1%
Social problems related to bowel function	4	2%
Bowel problems affecting the relationship with siblings	2	1%
Bowel problems affecting child's ability to socialize and make friends	2	1%
Bowel problems affecting the relationship other children	1	<1%
Peer rejection	2	1%
Soiling with social impact	2	1%
Bowel function impacting mood	4	2%
Unhappiness or anxiety	2	1%
Age at diagnosis depressive disorder	1	<1%
Prescription of anti-depressants/medication	1	<1%
Bowel problems causing depressed feelings	2	1%
Regular visits psychologist as child	1	<1%
Current contact with psychologist as child	1	<1%
Motor/neuro development and behavior	7	4%
ADHD	2	1%
Oppositional defiant disorder	1	<1%
Pervasive developmental disorder	1	<1%
Reactive attachment disorder of infancy or early childhood	1	<1%
Psychological counselling at home	1	<1%
Delayed neuromuscular development	1	<1%
Depressive disorder	1	<1%
Intelligence (Rakit | WISC-III-NL)	1	<1%
Memory (WISC-III)	1	<1%
Attention (Dot cancellation test)	1	<1%
Self-esteem (SPPC)	1	<1%
Cognitive disability	2	1%
Neurologically impaired	2	1%
WISC IV	1	<1%
NEPSY	1	<1%
Kidscreen 10	1	<1%
Sexual (dys)function	6	3%
Sexual dysfunction: erectile problems	2	1%
Sexual dysfunction: problems with ejaculation	1	<1%
Sexually active	1	<1%
International index of Erectile Functioning	1	<1%
Female sexual functioning index	1	<1%
Female sexual distress scale	1	<1%
Sexual education questionnaire	1	<1%

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Sexual functional outcomes	1	<1%
Normal erectile functioning (Erectile Hardness Score)	1	<1%
Age at first ejaculation	1	<1%
Age of coital debut	1	<1%
Age at menarche	1	<1%
Conception desire	1	<1%
Fertility issues or treatment	2	1%
Having children	2	1%
Presenting symptoms hydrosalpinx	1	<1%
Unilateral hydrosalpinx	1	<1%
Bilateral hydrosalpinx	1	<1%
Sexually active at time of diagnosis hydrosalpinx	1	<1%
Unilateral salpingectomy	1	<1%
Bilateral salpingectomy	1	<1%
Ultrasound guided drainage of hydrosalpinx	1	<1%
Length of primary hospital stay	71	36%
Length of cumulative hospital stay	4	2%
Length of primary hospital stay after one-stage repair	3	2%
Length of primary hospital stay after two-stage repair	2	1%
Time from discharge until first counseling	1	<1%
Number of inpatient days in first year of life	1	<1%
Parent-reported learning problems	1	<1%

Quality of life

	n=	**%**
Quality of Life	28	14%
HSCR and ARM QoL scale (HAQL)	4	2%
SF-36	5	3%
GIQLI	4	2%
Peds QL	8	4%
Peds QL (Psychosocial score)	3	2%
Peds QL (Physical score)	3	2%
Peds QoL Generic Core scale	1	<1%
Peds QoL General wellbeing score	1	<1%
Peds QoL Family Impact Module	2	1%
PedsQLTM4.0	2	1%

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Number of PedsQL surveys completed	1	<1%
Fecal Incontinence and Constipation Quality of Life	2	1%
WHO QOL-BREF	1	<1%
AQLCAFI - Assessment of QoL in Children and Adolexcents with fecal incontinence	1	<1%
Relationship of caregiver respondent	1	<1%
CHQ-PF50	1	<1%
CHQ-CF87	2	1%
WHOQOL-100	2	1%
Scoring system by Bai et al. In patients with HD	1	<1%
Barrena score	1	<1%
TCCQOL - total score	1	<1%
TCCQOL - physical function	1	<1%
TCCQOL - motor function	1	<1%
TCCQOL - self-care ability	1	<1%
TCCQOL - cognitive ability	1	<1%
TCCQOL - communicative ability	1	<1%
TCCQOL - positive emotion	1	<1%
TCCQOL - negative emotion	1	<1%
HAQL - Sexual functionign	1	<1%
KIDSCREEN 52	1	<1%
Need for adressing sexuality with special interest to the congenital anomaly during medical care	1	<1%
Parent satisfaction	4	2%
Compliance of parents	1	<1%
Rate of satisfaction for discharge without treatment	1	<1%
PSE-HDAM (Patient self-efficacy in the management of home care of children with HD and ARM)	1	<1%

Mortality

	n=	**%**
Mortality	51	26%
Survival	7	4%
Cause of death	17	9%
Age at death	3	2%
Mortality rate preoperative enterocolitis	2	1%

Other

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	n=	%
Cosmetic result	4	2%
Keloid / hypertrophied scars	1	<1%
Manchester scar scale: visible scar on abdomen	3	2%
(Number of) visible scars on the abdomen	2	1%
Postoperative appearance of umbilicus	1	<1%
Scar appearance on the abdomen	1	<1%
Scar appearance on the abdomen after 1 week	1	<1%
Scar appearance on the abdomen after 4 months	1	<1%
Scar appearance on the abdomen after 8 months	1	<1%
Liver biochemistry: normal or abnormal	2	1%
Fecal calprotectin levels	1	<1%
Plasma alanine transferase levels (ALT/ALAT)	2	1%
Albumin	1	<1%
Bilirubin	2	1%
Liver histology	2	1%
C-kit positive cells	1	<1%
NeuN expression	1	<1%
Number of CD4positive T-lymphocytes	0	0%
Number of CD4positive T-lymphocytes	1	<1%
Ratio of CD4/CD8 T lymphocytes	1	<1%
Level of pro-inflammatory cytokines TNF-a, IFN-y and IL-6	1	<1%
Level of anti-inflammatory cytokine IL-10	1	<1%
Time (in hours) until first passage of flatus	3	2%
Time (in hours) until first defecation	4	2%
Time to recovery of peristalsis	1	<1%
Normal urine cultures	1	<1%
Normal urine creatinine	1	<1%
Normal serum creatinine	1	<1%
Level of K+	1	<1%
Level of Na+	1	<1%
Level of Cl-	1	<1%
Level of HCO3-	1	<1%
Level of Hb	2	1%
Level of albumin	4	2%
Level of prealbumin	2	1%
Level of retinol binding protein	1	<1%
Level of globulin in serum	1	<1%
IgA level	1	<1%
Transferrin level	1	<1%
Vitamin b12	1	<1%
Folic acid in serum	1	<1%

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pH in stool	1	<1%
Glucose in stool	1	<1%
Hemoccult test in stool	1	<1%
Calprotectin in stool	1	<1%
Mean arterial pressure (MAP)	1	<1%
Heart rate	1	<1%
Saturation (SpO2)	1	<1%

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Table 1: Study characteristics of included publications			
		n =	**%**
Originated in	Africa	6	(3%)
	Asia	99	(49%)
	Europe	62	(31%)
	Eurasia	2	(1%)
	North America	23	(12%)
	Oceania	5	(3%)
	South America	2	(1%)
	Intercontinental	1	(1%)
Study timing	Retrospective	130	(65%)
	Prospective	30	(15%)
	Cross-sectional	39	(19%)
	Mixed design	1	(1%)
Type of study	Observational	120	(60%)
	Comparative	80	(40%)
Study design	Cohort	179	(90%)
	Case series	6	(3%)
	Case-control	7	(3%)
	Trial	8	(4%)

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Study scale	Single-center	150	(75%)
	Multi-center	33	(17%)
	National	17	(8%)
Year of publication	2015	16	(8%)
	2016	20	(10%)
	2017	27	(13%)
	2018	27	(13%)
	2019	33	(17%)
	2020	38	(19%)
	2021	39	(20%)
Number of included patients	<25	36	(18%)
	25-100	102	(51%)
	101-300	34	(17%)
	301-1000	17	(9%)
	>1000	11	(5%)

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Table 2: Identified studied parameters in HSCR research appearing in >5% of the included articles

		n =	%
Baseline characteristics	Sex	176	(88%)
	Age at surgery	132	(66%)
	Extent of aganglionosis [a]	101	(51%)
	Syndromal, genetic and chromosomal disorders	80	(40%)
	(of which) Trisomy 21	65	(33%)
	Age at follow-up	71	(36%)
	Associated anomaly (cumulative)	58	(29%)
	Initial clinical symptoms (cumulative)	55	(28%)
	Gestational age or prematurity	45	(23%)
	Enterocolitis (preoperative)	45	(23%)
	Birth weight	42	(21%)
	Cardiovascular anomalies	40	(20%)
	Weight at surgery	37	(19%)
	Age at diagnosis	34	(17%)
	Family history of HSCR [b]	28	(14%)
	Delay in evacuation/passage of meconium		

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	Congenital heart disease	25	(13%)
	Renal/genitourinary anomalies	25	(13%)
	Abdominal distention (preoperative)	23	(12%)
	Constipation (preoperative)	19	(10%)
	Neurologic anomalies	19	(10%)
	Gastrointestinal anomaly [c]	19	(10%)
	Ethnicity	19	(10%)
	Vomiting (preoperative)	18	(9%)
	Age at presenting symptoms	17	(9%)
	Poor feeding/malnutrition/failure to thrive (preoperative)	15	(8%)
	Congenital anomalies of the urogenital system	14	(7%)
	Pulmonary/respiratory anomalies	13	(7%)
	Intestinal perforation (preoperative)	12	(6%)
	Congenital anomalies of the nervous system	10	(5%)
		10	(5%)
Diagnostics, treatment and care process	Type of repair	113	(57%)
	Duration follow-up	78	(39%)
	Preoperative / primary stoma	71	(36%)

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	Operative time (pull-through)	46	(23%)
	Blood loss (pull-through)	41	(21%)
	Laparoscopy or laparotomy or transanal approach	40	(20%)
	Length of resected aganglionic and dilated segments	40	(20%)
	Anal dilatations (preoperative)	33	(17%)
	Contrast enema (preoperative)	27	(14%)
	Rectal biopsies (preoperative)	26	(13%)
	Follow-up rate	21	(11%)
	Preoperative / primary colostomy	20	(10%)
	Single- or multiple staged procedure	19	(10%)
	Daily preoperative colon irrigations (mechanical bowel preparation)	18	(9%)
	Intraoperative biopsies at time of pull-through	18	(9%)
		18	(9%)
	Intraoperative complications (pull-through)	16	(8%)
	Preoperative / primary ileostomy	14	(7%)
	Conversion laparoscopy to laparotomy (pull-through)	14	(7%)

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	ACE [d]	13	(7%)
	Anorectal manometry (preoperative)	12	(6%)
	Postoperative anal dilatation under general anesthesia	12	(6%)
	Anorectal manometry: follow-up	11	(6%)
	Time to start oral feeding		
Outcome	Postoperative Hirschsprung Associated Enterocolitis (HAEC [e])	127	(64%)
	Fecal incontinence	107	(54%)
	Constipation	96	(48%)
	(Any) reoperation	85	(43%)
	Anastomotic stricture/stenosis	76	(38%)
	Soiling	72	(36%)
	Length of primary hospital stay	71	(36%)
	Anastomotic leakage	56	(28%)
	Bowel function (standardized scoring)	54	(27%)
	Mortality	53	(27%)
	Defecation frequency	52	(26%)
	Intestinal obstruction	49	(25%)
	Gastrointestinal symptoms during follow-up	40	(20%)

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	Perianal issues (cumulative)	38	(19%)
	Normal defecation function	37	(19%)
	Use of bowel regulating medication	32	(16%)
	Growth/weight/failure to thrive during follow-up	32	(16%)
	Wound issues (cumulative)	32	(16%)
	Permanent stoma	31	(16%)
	Botulinum toxin	31	(16%)
	Quality of life	28	(14%)
	Complications (mentioned as such)	28	(14%)
	Urinary function	27	(14%)
	Wound infection	27	(14%)
	Early postoperative complications (mentioned as such)	26	(13%)
	Readmission	25	(13%)
	Anal excoriations	24	(12%)
	Residual aganglionosis	24	(12%)
	Stoma at time of follow-up	21	(11%)
	Bowel function score, Rintala et al. [17]	20	(10%)
	Ileus/bowel obstruction due to adhesions	20	(10%)

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	Abdominal distension	18	(9%)
	Difficulties with socializing/social adaptation/relationships	18	(9%)
	Cause of death	17	(9%)
	Fecal contamination/fecal accidents	17	(9%)
	HAEC treated by conservative management	16	(8%)
	Constipation manageable with laxatives	15	(8%)
	Form/consistency of stool	15	(8%)
	Rectal prolapse	15	(8%)
	Stoma complications (cumulative)	15	(8%)
	Constipation manageable with enema(s)	14	(7%)
	Multiple episodes of enterocolitis	14	(7%)
	HAEC recurrence	14	(7%)
	Weight at time of follow-up	13	(7%)
	Feeling the need for defecation	13	(7%)
	Ability to hold back defecation	13	(7%)
	Use of enemas	13	(7%)
	Use of laxatives	13	(7%)
	Sepsis	13	(7%)

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	Incidence of HAEC	13	(7%)
	Diarrhea	12	(6%)
	Constipation manageable with diet	12	(6%)
	Recurrent constipation	12	(6%)
	Wound dehiscence	11	(6%)
	Fever	10	(5%)
	Problems with urinary incontinence	10	(5%)
	Reoperation type	10	(5%)
	Reoperation due to complications (cumulative, no timeframe)	10	(5%)
	Reoperation due to obstruction/occlusion	10	(5%)
	(Any) reoperation due to residual aganglionosis	10	(5%)
	Abscess	10	(5%)
	Infection (cumulative)	10	(5%)
	Incomplete/transitional zone pull-through	10	(5%)

[a] Extent of aganglionosis refers to the histological level of transitional zone, namely rectal, sigmoid, rectosigmoid, distal descending colon.

[b] HSCR: Hirschsprung's disease

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[c] Gastrointestinal anomalies: excluding Hirschsprung's disease

[d] ACE: Antegrade Colonic Enema

[e] HAEC: Hirschsprung-associated enterocolitis

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Table 3. Identified tools/instruments utilized and reported in one or more included publications.

		N=	%
Incontinence scores	Wingspread criteria	4	(2%)
	Miller incontinence score	2	(1%)
	Baylor Continence Scale	2	(1%)
	Postoperative Fecal Incontinence Score	1	(<1%)
	Jorge-Wexner score	1	(<1%)
	Visick score	1	(<1%)
	Continence evaluation score	1	(<1%)
Scores for bowel function	Bowel function Score (Rintala et al.)[17]	20	(10%)
	Bowel Function Score according to Holschneider	7	(4%)
	Krickenberg classification system	6	(3%)
	Pediatric Incontinence and Constipation Scoring System	3	(2%)
	Stooling Survey (El Sawaf et al.)	3	(2%)
	Evacuation score of the Japan Society of ARM Study group	2	(1%)
		2	(1%)

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	Vancouver Dysfunctional Elimination Syndrome Survey (VDESS)	1	(1%)
	Bowel Function Score according to Holschneider, adapted by Lindahl et al	1	(<1%)
	Bowel Habit Diary	1	(<1%)
	Kelly Scale Score for recovery of bowel function	1	(<1%)
	Postoperative bowel function score	1	(<1%)
	HSCR anal function criteria (proposed by Reding)	1	(<1%)
	Wingspread score	1	(<1%)
	Rome IV criteria		
Motor- and neurologic development and behavior	Intelligence (Rakit | WISC-III-NL)	1	(<1%)
	Memory (WISC-III)	1	(<1%)
	Attention (Dot cancellation test)	1	(<1%)
	Self-esteem (SPPC)	1	(<1%)
	WISC IV	1	(<1%)
	NEPSY	1	(<1%)
	Kidscreen 10	1	(<1%)

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Sexual function	International index of Erectile Function	1	(<1%)
	Female sexual functioning index	1	(<1%)
	Female sexual distress scale	1	(<1%)
	Sexual education questionnaire	1	(<1%)
	Normal erectile functioning (Erectile Hardness Score)	1	(<1%)
Hirschsprung's associated enterocolitis scores	HAEC score (by Pastor et al.)	5	(3%)
	Grading system by Elhalaby et al.	3	(2%)
	Grading system by Murphy et al.	1	(<1%)
Quality of life	Pediatric Quality of Life Inventory (PedsQL)	8	(4%)
	Short Form 36 (SF-36)	5	(3%)
	HSCR and ARM QoL scale (HAQL)	4	(2%)
	Gastrointestinal Quality of Life Index (GIQLI)	4	(2%)
	Peds QoL Family Impact Module	2	(1%)
	Fecal Incontinence and Constipation Quality of Life	2	(1%)
	Child Health Questionnaire-Child Form 87 items (CHQ-CF87)	2	(<1%)

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	World Health Organization Quality of Life 100 (WHOQOL-100)	1	(<1%)
	Peds QoL Generic Core Scale	1	(<1%)
	Peds QoL General Wellbeing Score	1	(<1%)
	WHO QOL-BREF	1	(<1%)
	Assessment of QoL in Children and Adolescents with fecal incontinence (AQLCAFI)	1	(<1%)
	Child Health Questionnaire - Parent Form 50 (CHQ-PF50)	1	(<1%)
	Scoring system by Bai et al. in patients with HD	1	(<1%)
	Barrena score	1	(<1%)
	Taiwanese Child and Caregiver Quality of Life (TCCQOL)	1 1	(<1%)
	Hirschsprung's Disease/Anorectal Malformation Quality of life Questionnaire (HAQL)	1	(<1%)
	KIDSCREEN 52		

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Skin and subcutaneous	Manchester scar scale	3	(2%)
[a] Multiple instruments or tools may have been used in one publication.			

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