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Health-related quality of life in pediatric patients with intestinal failure without neurodevelopmental delay: a systematic review and meta-analysis

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Abstract

Background Intestinal failure (IF) is a broad term encompassing various conditions that hinder the body's ability to absorb nutrients for growth and maintenance. These conditions can significantly affect child's well-being, leading to physical limitations, psychological distress, and social isolation. We aimed to evaluate the available data on health-related quality of life (HRQoL) in pediatric patients with IF and without neurodevelopmental delay.

Methods For this systematic review and meta-analysis, we searched CINAHL, EMBASE, PsycINFO, PubMed, and Web of Science. All observational studies of pediatric patients (< 18 years) with IF which measured HRQOL and with evidence of absence of neurodevelopmental delay were included, without language or date restrictions, up to June 2024. We did separate random-effects meta-analyses for overall HRQOL and subgroup domains. Evidence from observational studies was synthesised as differences between standardised mean differences (SMDs) for all subgroup domains. Heterogeneity was assessed using the I^2 statistic and the Cochran Q test. The quality of the evidence was assessed with the Newcastle-Ottawa scale. This study is registered on PROSPERO, number CRD42024561812.

Results Of 491 records identified, 14 were eligible and data were available for 12 studies, all of which had a fair/good quality. The included studies involved a pooled sample of 510 participants (mean age = 7.0 ± 3.6 years). The analysis disclosed that compared to healthy children, pediatric patients with IF had lower overall quality of life in both child- and parent-report (Standardized Mean Difference [SMD]= -0.62; 95% CI [-0.80, -0.43]; $p < 0.001$, and SMD= -0.70; 95% CI [-1.11, -0.28]; $p < 0.001$, respectively), except for emotional and social domains (SMD[child] = -0.23; 95% CI [-0.38, -0.08]; $p = 0.001$ Vs SMD[parent]= -0.23; 95% CI [-0.60, 0.14]; $p = 0.21$, and SMD[child] = -0.40; 95% CI [-0.70, -0.10]; $p = 0.007$ Vs SMD[parent]= -0.24; 95% CI [-0.62, 0.14]; $p = 0.21$, respectively), where parents overestimate emotional and social HRQOL of their children.

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Conclusions This study highlights the significant impact of IF on well-being of pediatric patients. Targeted interventions addressing both physical and psychosocial needs are crucial to improve HRQOL in this population.

Keywords Intestinal failure, Pediatric, Quality of life, Enteral feeding, Enteral nutrition

Introduction

Intestinal failure (IF) is a broad term encompassing various conditions, such as short-bowel syndrome (SBS), intestinal pseudo-obstruction, and congenital enterocyte disorders [1]. These conditions result in insufficient functional gut mass, hindering the body's ability to absorb nutrients for growth and maintenance [1]. Clinical management of IF requires specific approaches tailored to the underlying cause, aiming to address long-term complications like sepsis, dehydration, and malnutrition [2]. Clinical management of this condition often requires the need for home parenteral nutrition (HPN). Pediatric patients with IF often experience psychological problems such as anxiety, fear of medical treatment, depression, and fatigue [3]. In addition, this condition often leads to social detachment of the patient and his/her family from their environmental context and may have neurodevelopmental or cognitive impairment comorbidities [4]. Improved neonatal and surgical care has led to increased survival rates for children with chronic IF on HPN [5, 6]. This shift has led to increased attention to long-term outcomes such as neurodevelopmental status and quality of life. In children and adolescents with IF, both disease-related characteristics (e.g., abdominal pain, increased stool frequency), psychosocial characteristics (e.g., anxiety, shyness), and school-related difficulties (such as missing school because of not feeling well or needing to go to the doctor) can influence overall health-related quality of life (HRQOL) and well-being [3]. HRQOL is a multidimensional assessment of how disease and its treatment affect a patient's overall functioning and well-being. It has been linked to mortality risk and other related outcomes [7]. Given the influence of developmental delay in reducing quality of life [8], it would be useful, in order to evaluate the specific influence of IF on HRQOL, to investigate patients with IF and without neurodevelopmental delay. Existing literature on HRQoL in children with IF presents conflicting findings. For instance, some studies report significantly lower HRQoL in patients with IF compared to healthy controls, suggesting poorer physical health, impaired emotional functioning, and important school related difficulties [3, 6, 9]. On the other hand, other studies report similar HRQOL between pediatric patients in HPN or SBS and healthy controls [10–15].

This systematic review and meta-analysis was aimed to evaluate the available data on HRQOL in pediatric patients with IF without neurodevelopmental delay compared to healthy controls.

Methods

Search strategy

In June 2024 CINAHL, EMBASE, PsycINFO, PubMed, and Web of Science were all searched systematically for observational studies (cohort and cross-sectional studies). We investigated the overall HRQOL in pediatric patients with intestinal failure compared to healthy peers, both as reported by children and by caregivers. Furthermore, we additionally analyzed the domain-specific HRQOL in order to investigate the presence of major impairment in thus domains. We followed the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) statement and recommended guidelines to guide this research [16]. The search blocks that we used were as follows: ["Enteral feeding" OR "Enteral Nutrition" OR "Intestinal Failure" AND ["Quality of Life" OR "QOL" OR "Health Status" OR "Functional Status" OR "Well being"] AND ["Child" OR "Children" OR "Childhood" OR "Pediatric" OR "Adolescent"] (detailed summary of the search terms was summarized in Supplementary File - Table S3). Regarding duplicates, Mendeley software was used to remove them. No publication year or language restrictions were applied. Reference lists of retrieved articles were reviewed for additional eligible studies. Authors were contacted for missing data, if available. We registered the protocol of this study in the international prospective register of systematic reviews (PROSPERO), the registration number is CRD42024561812.

Selection process: eligibility criteria

Screening and selections were performed independently by two blind authors, any conflicts were resolved collaboratively by the authors. The inclusion criteria encompassed the following: observational studies (cohort and cross-sectional studies), written in English, studies conducted in pediatric populations (< 18 years), with evidence of IF in chronic health condition such as short bowel syndrome or intractable diarrhea. Studies should assess HRQOL through validated instruments/tools (both self and proxy-report) presenting the data as continuous variable and with a presence of data of control group or reference population. Exclusion criteria were as follows: non-English studies, systematic reviews, meta-analyses, narrative reviews, case reports/ series, editorials, qualitative, study protocols, commentaries, letters, abstracts and studies without a formal review process were excluded. Studies including IF as secondary impairment of systemic, metabolic or genetic syndrome (such as cystic fibrosis or Crohn's disease) were excluded (due

to the confounding influence of the chronic disease who could reduce the HRQOL beyond the role of IF). Studies reporting a sample of patients with a mention of prior intellectual disabilities or a QI/developmental score < 5 percentiles were also excluded during title/abstract screening process.

The quality of the included studies was independently assessed by two authors using the Newcastle-Ottawa Scale [17], a tool designed to evaluate the quality of non-randomized studies in meta-analyses. This scale assesses bias and methodological quality by assigning a score from 0 to 9 stars across three domains: selection of patients and controls, comparability between groups, and outcome and follow-up. Studies are categorized as poor quality (0–2 stars), fair quality (3–5 stars), or good/high quality (6–9 stars).

Data extraction

Data extraction was performed independently by two authors. Any disagreements that occurred during this process were resolved collaboratively among the authors to ensure high accuracy and maintain consistency. Data was extracted using electronic spreadsheets. Continuous data was recorded as the mean and standard deviation. Data was extracted from all selected studies, including authors, publication year, rater, study design, number of patients in the sample, description of control group, age of the sample, tools used, and country/region. Reference lists of retrieved articles were reviewed for additional eligible studies.

Statistical analysis

For continuous data outcomes, we computed standardized mean differences (SMD), Hedges' G and their associated 95% confidence intervals (CI) utilizing the restricted maximum likelihood (REML) model. If the only available data was reported in median, IQR or ranges we employed the method proposed by Luo and colleagues [18] and Wan and colleagues [19], which incorporate the sample size via a smoothly changing weight in the estimation of the sample mean and standard deviation of the outcome of interest. Cochrane's formula was used to combine groups [20]. In order to evaluate the presence of statistical heterogeneity among the studies, we applied the chi-square test (Cochran's Q test). Furthermore, we computed the I2 value, which indicates the proportion of total variation across studies attributable to heterogeneity rather than random variance. Significant heterogeneity among the studies was determined by either a chi-square test result with a p-value less than 0.1 or an I2 value equal to or exceeding 60%. The random effects model was chosen over the fixed effects model because it accounts for heterogeneity between studies using the inverse variance method [21]. Egger's test and funnel plots were used to investigate evidence of publication bias. All statistical analyses were performed using R [Metafor package (version 4.6-0)] [22].

Results

Summary of studies

From the literature search, 491 studies were identified. After the elimination of duplicates, we screened the titles and abstracts of 406 studies, and only 66 were selected for full-text screening according to our eligibility criteria. The final included studies in this systematic review and meta-analysis were 12: 4 cohorts and 8 cross-sectional studies. The selection process of the study is demonstrated in (Fig. 1). The included studies comprise a total of 510 patients with IF. Majority of the studies used the PedsQL Generic Core questionnaire to evaluate HRQOL [6, 9, 13–15, 23–27], one study used the physical subscale of the PedsQL Generic Core questionnaire as the main outcome [28] and one study used the Auquei questionnaire, Qualin, Ok.ado, and Subjective - Quality of Life Profile questionnaires [12]. Two studies reported results of self-report form [12, 26]; one study reported only the results from parent report module [14] for all other included studies both self and proxy report form results were available. Concerning population included in the study, two studies investigated HRQOL in children in home parenteral nutrition [6, 12], one study the HRQOL in patients with necrotizing entercolitis [23], two studies the HRQOL in patients with short bowel syndrome [13, 26], one study the HRQOL in patients with intestinal failure and short bowel syndrome [27], and six studied reported the HRQOL outcome in patients with pediatric intestinal failure [9, 14, 15, 24, 25, 28]. A summary of characteristics of all the included studies is shown in Table 1. Concerning the number of studies that contributed data to each subsection of the analysis, were as follow: overall HRQOL [any measure] (10 studies [self-report] and 8 studies [proxy-report]); psychosocial domain (8 studies [self-report] and 7 studies [proxy-report]); physical domain (9 studies [self-report] and 8 studies [proxy-report]); emotional domain (8 studies [self-report] and 5 studies [proxy-report]); social domain (8 studies [self-report] and 5 studies [proxy-report]); and school domain (8 studies [self-report] and 5 studies [proxy-report]). Detailed summary of studies that contributed data to each subsection are reported in forest plots (Fig. 2 and supplementary figures S3-S7).

Quality and risk of bias assessment of the studies

The quality assessment focused on risk of bias and quality assessment, with a mean Newcastle-Ottawa scale score of 5.08 (SD = 1.08), which indicates a fair overall quality of the studies included in the review and makes the overall

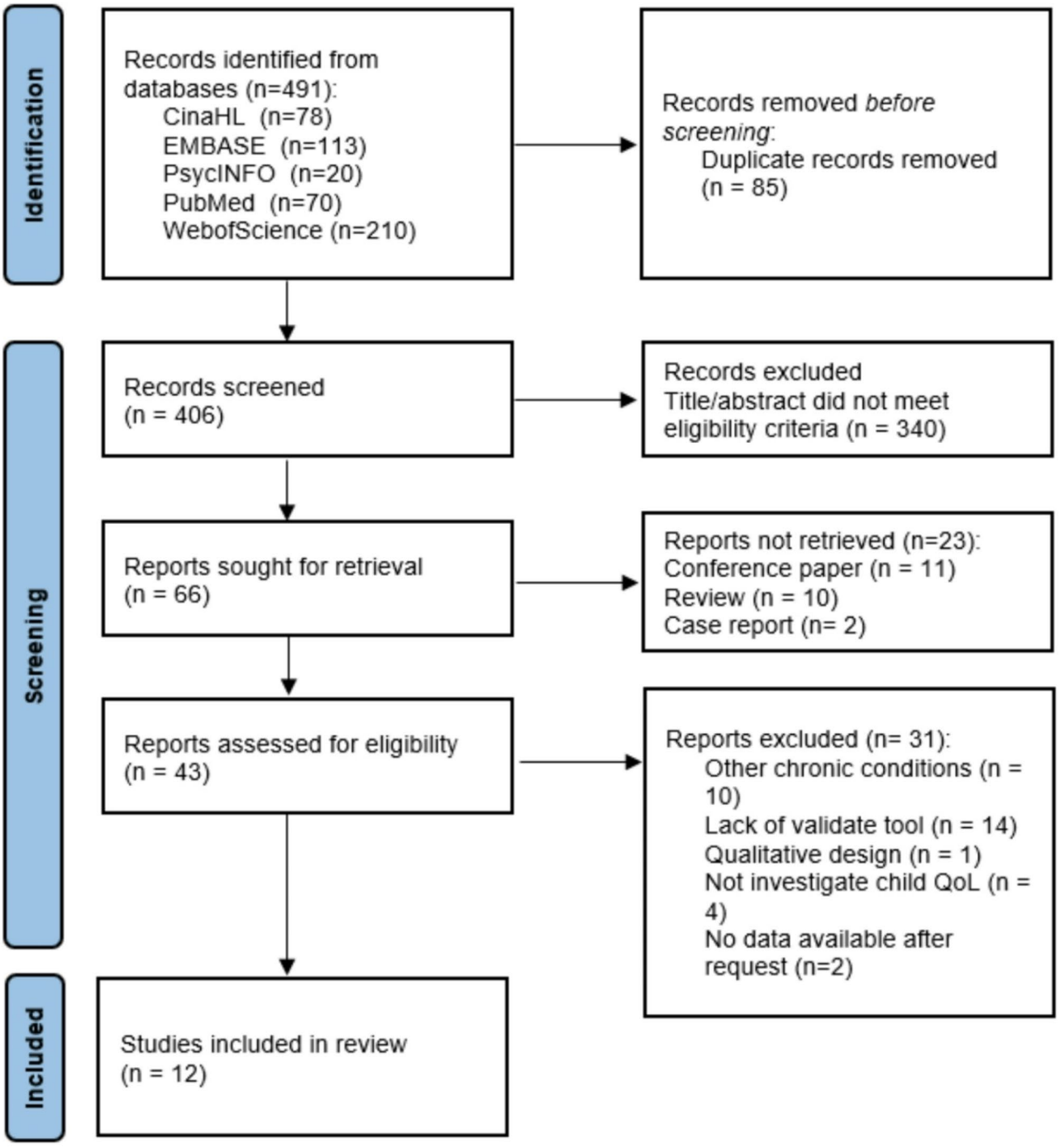

Fig. 1 PRISMA flow diagram

quality acceptable (a detailed summary of risk of bias and quality assessment is reported in Table 2).

Quality of life in pediatric patients with IF

The analysis disclosed that compared to healthy children, pediatric patients with IF had a lower overall quality of life in both child self-rated and parent proxy-report (Standardized Mean Difference (SMD)= -0.62; 95% CI [-0.80, -0.43]; $p < 0.001$, and SMD= -0.70; 95% CI [-1.11, -0.28]; $p < 0.001$, respectively) (Fig. 2). Analysis of the psychosocial domain of HRQOL indicated a significant difference between groups, with children with IF having a worst HRQOL (Supplementary Fig. S5) both in self-rated and parent-report form (SMD: -0.50; 95% CI [-0.66, -0.33]; $p < 0.01$ and SMD: -0.55; 95% CI [-0.91, -0.18]; $p < 0.01$, respectively). Concerning the domain-specific

Table 1 Characteristics of studies included in systematic review and meta-analyses

Authors	Year	Design	Sample size	Rater	Age range		Population	Controls	Outcome measures	Country/ region
					Mean (SD)	*Median (IQR)*				
Gottrand et al.	2005	multicenter study	72	child		4 (NA) years	children receiving HPN	reference pediatric population	Auquei questionnaire, Qualin, Ok.ado, and Subjective Quality of Life Profile questionnaires	France/ Europe
Kum et al.	2024	cross-sectional	29	child/parent		10 (9–13) years	pediatric patients with NEC	age-matched healthy controls	PedsQL™	Hong Kong/ Asia
McCaig et al.	2021	cross-sectional	53	child/parent	6.2 (3.9) years		patients with PIF	reference pediatric population	PedsQL™	US/NA
Mutanen et al.	2015	cross-sectional	36	child/parent		9 (1–27) years	patients with PIF	age-sex-matched healthy controls	PedsQL™	Finland/ Europe
Nagelkerke et al.	2022	observational study	35	child/parent		5.3 (2.9–9.7) years	children receiving HPN	reference pediatric population	PedsQL™	The Netherlands/ Europe
Neam et al.	2020	cross-sectional	91	child/parent	NA (only < 18 years)		patients with PIF	reference pediatric population	PedsQL™	US/NA
Olieman et al.	2012	cross-sectional	31	child/parent	11.8 (4.2) years		children with SBS	age-sex-matched healthy controls	PedsQL™	The Netherlands/ Europe
Pederiva et al.	2018	cross-sectional	30	child	10.9 (NA) years		children with SBS	reference pediatric population	PedsQL™	UK/ Europe
Sanchez et al.	2013	cross-sectional	23	parent	28.54 (16.87) months		patients with PIF	reference pediatric population	PedsQL™	US/NA
Silva et al.	2023	retrospective multicenter study	20	child/parent	7.5 (5.0) years		patients with PIF/SBS	reference pediatric population	PedsQL™	Portugal/ Europe
So et al.	2021	cross-sectional	21	child/parent		8.33 (6.96–11.04) years	patients with PIF	age-sex-matched healthy controls	PedsQL™ Physical Function subscale	Canada/ NA
Wong et al.	2022	prospective study	69	child/parent		8 (6–10) years	patients with PIF	reference pediatric population	PedsQL™	US/NA

Note. HPN = Home parenteral nutrition; SBS = short bowel syndrome; PIF = pediatric intestinal failure; NEC = necrotizing enterocolitis; NA = not available

HRQOL, the analysis showed that children with IF exhibit lower HRQOL in all investigated domains as reported by children, while when investigating the parent report form the HRQOL was lower in children with IF in all domains, except for emotional and social domain (SMD[self] = -0.23; 95% CI [-0.38, -0.08]; $p = 0.001$ Vs SMD[parent]= -0.23; 95% CI [-0.60, 0.14]; $p = 0.21$, and SMD[self] = -0.40; 95% CI [-0.70, -0.10]; $p = 0.007$ Vs SMD= -0.24; 95% CI [-0.62, 0.14]; $p = 0.21$, respectively for emotional and social domains) (detailed summary of random effect model meta-analysis results of SMD between children with intestinal failure vs. healthy children HRQOL was reported in Supplementary file-Table S1 and supplementary figures S1-S5).

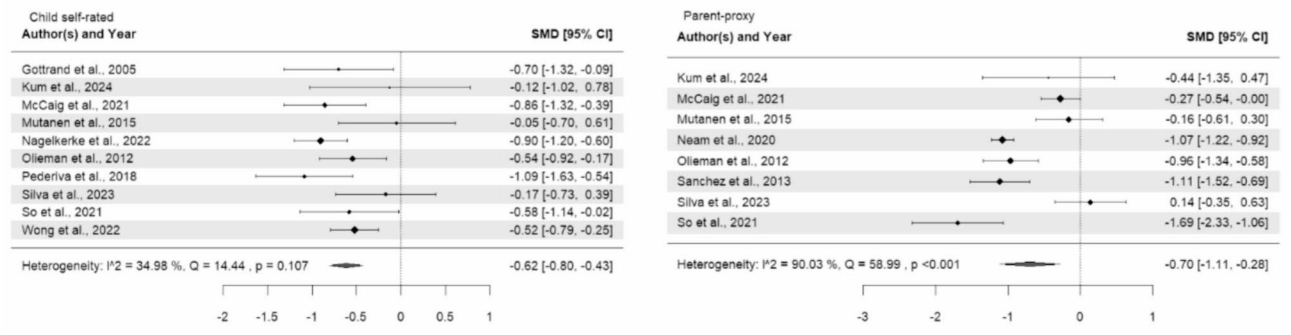

Fig. 2 Forest plot of random effect model meta-analysis standardized mean differences between children with intestinal failure vs. healthy children in overall HRQOL according to raters (self vs. proxy)

Table 2 Summary of the results of risk of bias assessment of the included studies

Authors	Year	Selection			Comparability	Exposure/Outcome	Total score
Gottrand et al.	2005	★	★	★	★	★	5
McCaig et al.	2021	★		★	★	★	4
Kum et al.	2024	★	★	★	★★	★	6
Mutanen et al.	2015	★	★	★	★★	★★	7
Olieman et al.	2012	★	★	★	★★	★	6
Nagelkerke et al.	2022	★		★	★	★	4
Neam et al.	2020	★		★	★	★	4
Pederiva et al.	2018	★		★	★	★	4
Silva et al.	2023	★		★	★	★	6
So et al.	2021	★	★	★	★★	★	6
Wong et al.	2022	★	★	★	★	★	5
Sanchez et al.	2013	★		★	★	★	4

Note. The Newcastle-Ottawa Scale assesses bias and methodological quality by assigning a score from 0 to 9 stars across three domains: selection of patients and controls, comparability between groups, and outcome and follow-up. Studies are categorized as poor quality (0–2 stars), fair quality (3–5 stars), or good/high quality (6–9 stars)

Publication bias for studies assessing HRQOL outcomes

For studies focusing on overall HRQOL, a minor asymmetry was observed in the funnel plot (Supplementary Fig. S11), but the Egger's regression test did not provide significant evidence of publication bias both in self-report and parent report form ($Z = 1.20$; $p = 0.23$ and $Z = 0.09$; $p = 0.92$, respectively). Similarly, when evaluating studies focusing on domains-specific quality of life, the funnel plot revealed a slight asymmetry for physical and social domains as reported by children (Supplementary Fig. S6, S8). However, the Egger's regression test found no significant evidence of asymmetry ($Z = 1.09$; $p = 0.27$ and $Z = 1.33$; $p = 0.18$, respectively). A similar asymmetry was observed in the funnel plot of the studies focusing on HRQOL as reported by parents in emotional and school HRQOL (Supplementary Fig. S6, S11), but the Egger's regression test showed no significant evidence of asymmetry ($Z = 0.68$; $p = 0.49$ and $Z = 0.51$; $p = 0.61$, respectively). A detailed summary of the Egger's regression test of domain-specific HRQOL was described in Supplementary file– Table S2.

Discussion

This systematic review and meta-analysis aimed to investigate the health-related quality of life (HRQOL) of pediatric patients with intestinal failure (IF) without neurodevelopmental delay, in comparison to healthy controls. Our findings consistently demonstrate that pediatric patients with IF experience significantly lower HRQOL across all subgroup domains, and overall psychosocial and total quality of life. These results align with prior narrative reviews reporting inferior HRQOL in pediatric patients with IF/SBS compared to controls [3, 29, 30]. However, our findings contrast with several previous studies that reported comparable HRQOL levels in pediatric patients with IF and healthy controls [10, 12, 15]. Reasons proposed to explain these findings are the higher mean age of participants who had the same health-related quality of life (HRQOL) as controls, higher parental anxiety in studies using parental reports [15], or the fact that children with IF could certainly lead fulfilling lives despite the presence of IF [10]. Moreover, this discrepancy can also be attributed to the heterogeneity of the IF manifestations, as it is an umbrella term

encompassing various clinical conditions with distinct characteristics that differentially affect quality of life [1].

Several factors may contribute to the reduced overall HRQOL in pediatric IF patients. Fear of HPN-associated adverse events, impaired sleep, daytime fatigue, decreased social activities, and disrupted family relationships and friendships can all negatively affect HRQOL. Additionally, family caregivers often assume a significant role in healthcare management, which can disrupt caregiver-patient interaction and their own psychosocial well-being [31]. The poorer physical HRQOL observed in pediatric IF patients can be attributed to the significant impact of multiple hospital admissions, malnutrition, poor growth, and the presence of a stoma, all of which can hinder children's ability to participate in daily and social activities [28, 32]. Moreover, the decreased psychosocial, emotional and social HRQOL in these patients may be influenced by unique challenges that negatively affect their socialization, such as restrictive diets, increased risk of gastrostomy or central line tubes during activities, and frequent school absences [9].

Moreover, age of the child varied across studies reviewed (0–18 years), and it could influence the overall HRQOL results, such as school-aged children [9]. In addition, adolescence, a period marked by biological, psychological, and social changes, including the search for identity, can exacerbate the challenges faced by pediatric IF patients. Adolescents may become more aware of their bodily functioning and the long-term consequences of their disease, leading to feelings of insecurity and vulnerability [13]. Regarding the agreement between parent and child-reports, our findings suggest that both parents and children report lower overall HRQOL in pediatric IF patients compared to healthy controls. Parents tend to overestimate the HRQOL in emotional and social domain of their children. This contrasts with some previous studies reported parents underestimated their children's quality of life [10, 25]. Nevertheless, investigating the domain-specific HRQOL, child self-rated and parent proxy-report seems to show a disagreement in evaluate emotional and social domain, suggesting an underestimation of the emotional and social burden of IF in the child from their caregivers. The underestimate of caregiver-report was consistent with previous studies suggesting that caregiver-perceived HRQOL is higher and more similar to that of healthy children [24]. We speculate, these discrepancies may be attributed to parental anxiety or emotional burden (linked to IF course), and may vary over time and with clinical condition who could lead to hypervigilance to physical health at the expense of psychosocial aspects [33]. A recent study demonstrated a significant burden of care in caregivers of children with IF receiving long-term parenteral nutrition, with elevated parental levels of stress, anxiety, and depression [34]. Finally, we hypothesize that the adoption of inpatient education programs that incorporate recreational and social activities could provide academic instruction and alleviate the stress associated with prolonged medical care. Additionally, initiatives aimed at improving awareness and communication, both with parents and patients, could be highly beneficial for this population.

Strengths and limitations

The random-effect model analysis demonstrates a significant negative association between intestinal failure and HRQOL across all categories. However, the substantial heterogeneity observed in most categories suggests that factors beyond intestinal failure, such as study design, participant characteristics, and measurement methods, may influence the relationship between intestinal failure and HRQOL. Further research with larger samples or a multicenter design is needed to explore these factors and to provide a more complete understanding of the impact of intestinal failure on health-related quality of life (HRQOL). Furthermore, most of the included studies assessed health-related quality of life with the PedsQL generic core, a tool not specifically designed for patients with IF and this fact could lead to an inaccurate assessment of their specific needs.

Conclusion

This systematic review and meta-analysis found that pediatric patients with intestinal failure (IF) who do not exhibit neurodevelopmental delay demonstrate significantly lower overall HRQOL compared to healthy controls. These findings highlight the substantial impact of IF on well-being and emphasize the need for targeted interventions. Future research should explore the long-term impact of IF on HRQOL, particularly in adolescents and young adults. Additionally, investigating the effectiveness of targeted interventions for improving HRQOL in pediatric patients with IF would be valuable.

Abbreviations

IF	Intestinal failure
HRQOL	Health related quality of life
SMD	Standardized mean difference
SD	Standard Deviation
REML	Restricted maximum likelihood
IQR	Interquartile range
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
HPN	Home parenteral nutrition
SBS	Short bowel syndrome

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-03682-9.

Supplementary Material 1

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Not applicable.

Author contributions
FM, DM and AD contributed to the conception, design, developed the literature search, carried out the extraction of data and final approval of the submitted version. FM, DM, TC, LN, SI, FP, GV, GB, CR, SV, and AD, assisted in the critical appraisal of included studies and assisted in writing up. FM carried out the statistical analysis of studies. All authors read and approved the final manuscript.

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Data availability
The datasets of this study are availability from the corresponding author on reasonable request.

Declarations

Human ethics and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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