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**Epidemiology of functional gastrointestinal disorders in children and adolescents: a systematic review**

Boronat AC *et al* Functional gastrointestinal disorders in children and adolescents

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**Abstract**

***AIM***

To assess the prevalence of functional gastrointestinal disorders (FGID) prevalence in children and adolescents.

***METHODS***

PubMed, EMBASE, and Scopus databases were searched for original articles from inception to September 2016. The literature search was made in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations. For inclusion, each study had to report epidemiological data on FGID in children between 4 and 18 years old and contain standardized outcome Rome II, III or IV criteria. The overall quality of included epidemiological studies was evaluated in accordance with Loney’s proposal for prevalence studies of health literature. Two reviewers assessed each study for data inclusion and extraction. Discrepancies were reconciled through discussion with seniors.

***RESULTS***

A total of 659 articles were identified from the databases and 16 through manual search. A total of 43 articles fulfilled the eligibility criteria to a full-text reading with 26 remaining to be included in the final analysis. All studies were written in English, and published between 2005 and 2016. Eight articles (30.8%) were performed in North America, five (19.2%) in Latin America, five (19.2%) in Europe, seven (27%) in Asia, and one (3.8%) in Africa. Sample size varied between 114 and 99,416 subjects, totaling 132,600 individuals. Fourteen studies (53.9%) recruited their target samples from schools, 11 (42.3%) from healthcare settings and the remaining one (3.8%) from online panel community. The overall FGID prevalence rates for student samples ranged from 9.9% to 29% to as high as 87% in clinical samples. Cyclic vomiting, irritable bowel syndrome and functional constipation were the most researched conditions, with a prevalence ranging from 0.2% to 6.2%, 0% to 45.1% and 0.5% to 86.9%, respectively. The qualitative appraisal revealed that most of the studies showed average or below average generalizability.

***CONCLUSION***

The heterogeneity of the studies on FGID must be improved in order to allow comparison. Improvements should include appropriate sampling of representative population, comparable study setting, and consistent data collection.

**Key words**: Functional gastrointestinal disorders; Epidemiology; Prevalence; Children; Adolescents

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**Core tip**: Epidemiological studies on functional gastrointestinal disorders in children and adolescents provide variable prevalence rates in both non-clinical and clinical settings. The scarcity of good quality prevalence data for functional gastrointestinal disorders in light of recent Rome IV criteria reveals an urgent need for more trustworthy information to construct evidence-based health policy. The current literature review suggested higher impact of cyclic vomiting, irritable bowel syndrome and functional constipation that affect children and adolescents.

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**INTRODUCTION**

Functional gastrointestinal disorders (FGID) are considered common, even in children and adolescents. During the last years, the burden of FGID is rising[1-4] but, to date, no biomarkers[5] or gold standard tests are available for diagnosing gastrointestinal (GI) disorders without an established etiology[6].

Pediatric guidelines are dynamic over time and must be driven by evidence-based medicine[7]. The Rome criteria have been used for FGID diagnosis, currently in its new 4th edition (Rome IV, May 2016), its the result of investigators effort in accurate the definition and identification across lifetime. This guideline is based on a detailed clinical evaluation that must contain complete clinical history, physical examination and growth curves to help clinicians in daily practice[5,8-10] .

In the child/adolescent Rome IV chapter, there are two main changes: (1) the term “no evidence for organic disease” was removed from all definitions and replaced by “after appropriate medical evaluation the symptoms cannot be attributed to another medical condition”; and (2) the FGIDs can co-occur with other medical conditions that themselves result in GI symptoms[11].

Table 1 summarizes main Rome IV categories concerning frequency, duration and synonym, subtypes or approximate terms in three broad sections: (H1) nausea and vomiting disorders; (H2) abdominal pain-related disorders; and (H3) defecation disorders.

Agreed-upon description of GI syndromes and accurate estimates of FGID prevalence are required for defining the need for treatment in overloaded healthcare settings. Projected proportion of pediatric FGID cases in the community and different levels of healthcare setting obtained through epidemiological studies might help to proper allocation of financial support and organize health service delivery.

The aim of this literature review is to critically examine current evidence of knowledge on FGID in children and adolescents, through systematic search of frequency or prevalence data on common functional GI problems. Furthermore, we have assessed the quality of existing studies on the target topic.

**MATERIAL AND METHODS**

***Search strategies***

A literature search was conducted in the following databases: PubMed, EMBASE, and Scopus in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[12]. The search terms were “functional gastrointestinal disorder” OR “functional gastrointestinal symptoms” AND “epidemiology” OR “prevalence” OR “incidence”. In addition, for each eleven specific category of FGID in children and adolescents, new search was performed with the disorder’s nomenclature and equivalent and/or approximate terms. For example, “cyclic vomiting” AND “periodic vomiting” were combined with epidemiological terms (Appendix in the Supplementary Online Content).

 There was no language restriction and the period covered was from inception to September 30, 2016. For inclusion, each study had fulfilled all of the following criteria: (1) contain children and adolescents between 4 and 18 years old (y.o.); (2) report functional gastrointestinal symptoms and/or disorders according to Rome II, III or IV criteria[13,14] (<http://www.romecriteria.org/>); (3) design sample from birth-cohort, population-based, school-based or clinical setting; and (4) report epidemiological outcomes - prevalence, incidence or frequencies for general FGID and subtypes. “Similar articles” option and manual search of reference list of review articles, book chapter, and gray literature completed the investigation. Experts in pediatric gastroenterology were contacted to request full text or unpublished data. Independently, two reviewers (ACB and APFM) assessed each study for inclusion and extracted data. Discrepancies were reconciled through panel discussion with senior authors (AM and YPW).

***Critical appraisal of literature***

The overall quality of the studies included was evaluated in accordance with Loney’s proposal for prevalence studies in health literature[15]. All studies were scored on eight criteria: (1) sample size; (2) sampling adequacy; (3) unbiased sampling frame; (4) measures of outcomes; (5) unbiased assessors; (6) response rate with refusals described; (7) prevalence with confidence intervals and by relevant subgroups; and (8) appropriate description of study subjects for the research question. The study receives one point for each criterion met, which possible score ranging from zero to eight. Higher score indicate better study quality.

The sample size criterion was not used to exclude studies. However, we considered the sample size to be adequate if it was projected for the study on the basis of local population estimates or if it was higher than 370. This minimum sample size was calculated to allow outcome assessment using simple random sampling, with a conservative estimate of distinct FGID of 13.9% in the age bracket of children and adolescents[16], confidence level of 95%, and precision of 1.8%, resulting in a minimum sample size of 370 subjects.

Two reviewers (ACB and APFM) performed the evaluation and final results were discussed one by one with senior author (YPW).

***Methodological issues***

For accurate evaluation of the methodological issues on pediatric epidemiological studies, two questions need be highlighted: (1) how representative of the target population are the recruited participants? (2) are the outcome measures reliable and valid?

**how representative of the target population are the recruited participants?** The most appropriate study design to determine the prevalence of a goal condition (prevalence of FGID) is the population-based observational study covering the whole target population, *e.g.*, by census of all subjects between 4-18 y.o. within a certain area. This is not always possible or feasible as it is a high cost or time-consuming method. Probability sampling, in turn, is essential in prevalence studies to ensure that each potential respondent has an equal chance of selection (non-zero probability), warranting the representativeness of the intended population[15,17].

 Convenience sampling provides lower quality epidemiological data than population-based studies. Participants recruited from particular communities (*e.g.*, social network or online panel), schools, primary care and specialty care would result in some type of selection bias. In order to obtain unbiased frequency estimates, all eligible persons susceptible to develop a clinical condition should be included in sampling design, regardless of refusal or reasons of exclusion (*i.e.*, loss to follow up, incomplete data, and organic exclusion). Otherwise, the rate of disease frequency would be either inflated or reduced.

Assuming that most of children and adolescents are enrolled in school (except those homeless, correctional institutionalized and hospitalized), conducting a survey in randomly selected schools might be an acceptable alternative. In healthcare treatment settings, the Berkson’s bias may skew the sample characteristics by selecting more symptomatic treatment-seeking individuals.

Sample size is important to ensure measurement precision using confidence limits. Either the confidence intervals (CI) or the information needed to calculate CI must be reported to allow quantifying the degree of uncertainty associated with the frequency estimates. Non-representative sampling cannot always be fixed through very large samples. Typically, in case of high rate of non-response (more than 20%), the socio-demographic characteristics of non-respondent group must be compared with those of respondent group, to evaluate potential selection bias and impact in frequency estimates of target condition[17].

Non-representativeness of recruited participants is a serious threat to external validity by curbing generalization of the results. Hence, effort to fix unequal selection chance is recommended. Weighting procedure orpost-stratification adjustment are alternatives to fit the data to target-population structure.

**are the outcome measures reliable and valid?** The type of informant and the method of data assessment represent potential sources of error for estimating the prevalence rate of clinical conditions. Standardized data collection methods provide reliable and valid measurement of target outcome.

 Expert opinions may diverge on the constellation of signs and symptoms of a functional disorder, as well as the frequency and duration of GI ailments. One of the Rome IV’s goals is to operationalize the construct of FGID through reproducible criteria, since to date there is no gold standard assessment for it. The validity of categories of FGID is still a matter of intense research.

In pediatrics, mainly in younger children samples, it is usual to obtain GI information only through parental report. Studies in older children and adolescents have demonstrated that parent-child/adolescent concordance was largely poor[18]. The administration of validated questionnaires like the Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS/QPGS-RIII, parental and/or self-report form)[17,19] is a feasible strategy for ascertaining the symptoms of FGID, but the establishment of a case based barely on questionnaire responding may mislead to under or over-estimation of problems in children and adolescents. When objective laboratory measure is lacking, as in the case of FGID, multisource informants (parent, children or adolescent), validated questionnaires plus clinical evaluation may constitute the best strategy for the best diagnose possible, mitigating information bias.

It is recommended that interviewers are impartial to children’s health status and trained for identification of cases based on external criteria and decision rules for disease diagnosis (FGID)[15,17]. Further investigation or therapeutics may confirm or rule out the suspected illness.

Ultimately, the validity and reliability of outcome measures for GI symptoms are intrinsically linked to sensitivity and specificity of the standardized operational procedures, either by independent assessors or assessment tools.

**RESULTS**

***Literature search and general description of included studies***

The search flow diagram is displayed in Figure 1. A total of 659 articles were identified through the databases and 16 through the manual search. After removing duplicate records, 149 articles remained for title and abstract reading. Of these, 43 articles fulfilled the eligibility criteria for full-text reading, remaining 26 to be included in the present review. The 17 studies excluded were listed in the Supplementary Online Content.

All of the articles included (*k* = 26), were written in English and published between 2005 and 2016. Eight studies were performed in North America[8,18,20–25], five in Latin America[26–30], five in Europe[31–35], seven in Asia[6,16,36–40], and one in Africa[41]. Five studies were performed by the same Latin American consortium, the Functional International Digestive Epidemiology Research Survey (FINDERS), which adopted a similar methodology thus allowing comparing the data.

Five articles detailed the distribution of demographic characteristics of the study population. Among the participants, no significant variation for gender[6,20,26,36], age or race[26] was observed.

Concerning FGID outcome criterion, the majority of studies (*k* = 18) used Rome III criteria to define each specific GI category[6,16,23–30,32–35,38–41]. Five studies used the Rome II criteria to define FGID[19,20-22,37], while three others provided comparable data for the version II and III of Rome criteria[8,31,36]. Until the time of review, no study had reported epidemiological data of FGID using of Rome IV criteria.

In the great majority of eligible articles, the sample was recruited by convenience (*k* = 19, 73.1%). Six additional studies described some type of random selection and one study conducted the survey by means of quota sampling. Sample size varied between 114 and 99416 subjects, totaling 132600 individuals. Although most studies (*k* = 19) recruited participants achieving sufficient sample size, the representativeness of FGID epidemiological data from children and adolescent populations constitutes a threat to its external validity.

Regardless recruitment methods, the sampling setting diverges. Fourteen studies recruited target sample from schools, 11 studies from healthcare settings and the remaining study recruited participants from an online panel community. As such, the overall FGID prevalence rates for student samples ranged from 9.9% to 29%[26,41] to as high as 87% in a specialty gastroenterological care service after organic exclusion[35]. This great prevalence variation was reliant on the type of sampling setting.

Seven school-based studies included multiple schools without randomization[6,26–30,34]. Among healthcare settings, most of studies (*k* = 8) recruited participants in single tertiary care center[8,19-24,31,33], two from secondary care[32,35], and the remaining one from primary care[22]. As such, the proportion of FGID in treatment patient samples was much higher than school-based student samples.

Specific categories of FGID in half of the articles (*k* = 13) were exclusively informed by questionnaire, either parental report and/or self-report by children and adolescents[23,25–30,34,36,38–41], while the other half (*k* = 13) also included clinical evaluation and/or medical records[6,8,16,19,20-22,24,31–33,35,37].

Of interest, the agreement rate between dyads of informants (parents and children) and informant-physician varied greatly in magnitude[19,21,24], within the groups of FGID. This non-agreement rate, as expressed through the kappa coefficient, is a serious issue to the prevalence data, as follows.

**H1:** Functional nausea and vomiting disorders: the parent-children agreement for cyclic vomit was moderate (*k* = 0.42) [19] and aerophagia ranged from no to substantial agreement[19,24].

**H2:** Functional abdominal pain disorders: the parent-children agreement for dyspepsia was fair to substantial[19,21,24], but this concordance could not replicate for informant-physician dyads (kappa range: 0.02 to -0.06)[24]. Considerable disagreements across all dyads were reported for the irritable bowel syndrome (kappa range: 0.03 to 0.44) and functional abdominal pain (kappa range: -0.10 to -0.02)[24]. Likewise, the agreement for abdominal migraine ranged from poor to moderate in the parent-children dyad[18,24].

**H3:** Functional defecation disorders: while the agreement rate for constipation was fair across all dyads[24], no evidence of agreement was reported for fecal retention and nonretentive fecal soiling[19].

Because there is no reliable concordance between dyads, the quality and the magnitude of prevalence data of FGID in children and adolescent can be distorted by the type of informant. The observed rate of 7.7% for any FGID among German children cannot be trusted, since the data were solely based on parent report[34].

 In terms of outcome criteria, the agreement between Rome II and Rome III to diagnose FIGDs was poor (*k* = 0.114)[31]. Under more sensitive Rome III criteria, the reported prevalence of FGID might at least double in relation to Rome II[8,36]. Since there are no published data based on Rome IV criteria, the effect of this new version on FGID prevalence could not compared.

The appraisal of the 26 included studies indicated that good quality researches reporting the epidemiology of main categories of FGID in children and adolescents were scarce, likewise recent reviews of FGID in infants and toddlers[42,43].

According to Loney’s proposal[15], the higher score of six was achieved by three school-based studies conducted in Japan[16,40] and China[37]. In general, the studies presented poor quality in half of the retained articles (*k* = 13), scoring 2 or maximum of 3 points. By far, the most common problem was prevalence rates without confidence interval and/or no detailed information on subgroup (*k* = 21), inappropriate sampling frame (*k* = 21), inadequate sampling method (*k* = 19), refusers not described (*k* = 14) and/or insufficient sample size (*k* = 7) (Table **S1**).

Regarding the main epidemiological results on FGID, we describe sequentially in Table 2the group H1 for vomiting and aerophagia, Table 3H2 abdominal pain-related functional GI disorders, andTable 4H3 constipation and incontinence. Among the single categories of FGID, cyclic vomiting, IBS and constipation were the most researched conditions.

***Vomiting & aerophagia***

There were 12 studies reporting frequency data on vomiting and aerophagia in children and adolescent (Table 2). The choice of the QPGS or parental report to assess the FGID symptoms was the rule. Seven studies were school-based surveys[6,16,26–28,30,36]. Six studies also included external clinic assessment and/or medical records[6,16,19,22,24,35]. For the remaining ones, nine studies used information self-reported by the children or adolescent, while nine used parent report, and six studies used both types of forms.

Cyclic vomiting and aerophagia were uncommon FGID in this age group, although they were the most frequent data collected on the group H1, there were dissimilar rates reported across studies, ranging from 0.2% to 6.2%[6,19] and 0% to 15%[24,35], respectively, for cyclic vomiting and aerophagia. The investigation setting, namely school-based or healthcare centers, can be considered as influencing factors

Information on rumination was less reported; the rates ranged from 0.3% to 5.3% in nine studies. There is no available data for functional nausea and functional vomiting since these are new categories proposed in the Rome IV criteria.

***Abdominal pain-related functional GI disorders***

Twenty-three studies addressed this FGID group H2 (Table 3), being irritable bowel syndrome (IBS) the most reported category across eligible studies. Two large sample studies in China (*n* = 3671 and 5403) dedicated to explore the prevalence of IBS in school-based settings[37,38]. Data on dyspepsia, abdominal migraine and abdominal pain-NOS were reported in 21 studies. Similarly to the H1 group, QPGS was also the standard assessment tool for reporting the symptoms of abdominal pain-related disorders. School and healthcare setting were the major source of participant recruitment.

Given its disabling feature, there was a major interest to understand the occurrence and clinical characteristic of the IBS. Across all studies with children and adolescent, the rates of IBS ranged from 0% to 45.1%[8,22] according to the setting of recruitment. Possibly, the prevalence rate of IBS would be lower in schools and inflated in healthcare settings due to its disabling condition.

Similarly, the wide prevalence variations of other categories of abdominal pain were liability of the representative sample selection. For instance, the prevalence rate for dyspepsia ranged from 0.2% to 25.7%[25,33,34], abdominal migraine 0% to 23.1%[8,33], and abdominal pain-NOS 0.3% to 39.8%[26,28,33]. Noteworthy, the prevalence rates of H2 group were much higher than the seen in H1 group, suggesting frequent help-seeking behavior and greater burden.

***Defecation problems***

Table 4 shows14 epidemiological studies on defecation problems in children and adolescents (H3 group). Twelve studies used self-report form for children and adolescent or parent report with QPGS form, and six studies also included some type of clinical evaluation (physical examination, laboratory exams, or medical records). Most investigations (*k* = 9) conducted the study in schools.

Constipation was investigated in all 14 studies and discrepant rates of prevalence ranged from 0.5% to 86.9%[6,31]. School-based studies reported the lowest prevalence and the tertiary care the highest rate. In comparison with the Rome II criteria, the use of broader Rome III also expanded the prevalence rate[31].

Nonretentive fecal incontinence seemed to be a rare disorder, with prevalence ranging from 0% to 1.8%[25,28] in all retained studies (*k* = 10). Even in non-health settings, low prevalence of GI disorder was observed, requiring further careful assessment in more representative samples.

**DISCUSSION**

This study is a systematic review on the epidemiology of functional gastrointestinal disorders in children and adolescents. From a total number of 675 identified articles addressing the issue, 26 were included in the final analysis (around 132600 subjects). Search strategies, methodological issues and critical appraisal of literature were systematically presented to summarize prevalence data on FGID in pediatric population. Cyclic vomiting, irritable bowel syndrome and constipation were the most researched conditions, with prevalence ranging from 0.2% to 6.2%, 0% to 45.1% and 0.5% to 86.9%, respectively. This wide variation in prevalence rate hampers the comparability of epidemiological data, which reliability needs improvements. The qualitative appraisal revealed that most of the studies showed average or below average generalizability. Several limitations of eligible studies have been acknowledged concerning, *e.g.*, correct sampling of representative population, study setting, and data collection. Future directions in the field of epidemiological studies concerning pediatric FGID must follow a more correct methodology, such as appropriate sampling of representative population, comparable study setting, and consistent collection of functional GI symptoms. The scarcity of good quality prevalence data for FGID in light of recent Rome IV criteria reveals an urgent need for a more trustworthy information to construct evidence-based health policy.

 To the best of our knowledge, comprehensive review of prevalence of FGID in the age bracket of children and adolescents as a group is lacking. Since the prevalence of a disease can cater for decisions and investments on health policies, good quality epidemiological data are required to understand the brain-gut axis neurobiology of the FGID, in view of pursuing applicable treatments in pediatrics.

After reviewing eligible papers on FGIDs, the problem of sample selection must be regarded as the foremost concern. The large variation on the prevalence rates can be attributable to lack of representative children and adolescent sample population. The fact that most of studies in present review recruited their participants by convenience increases the chance to assess a biased sample with some specific characteristics, mostly in particular schools, chosen by suitability[28,30] or specialized treatment centers[33,35]. Ideally, some type of randomization should be included before the sample recruitment. Clustered or stratified samplings are alternative approaches when a complete list of population is not available[16,37,40,41]. The more the sample resembles the general population, the better is the quality data.

The type of setting also contributes to skew the sample selection. In the case of children and adolescent aged between 4 and 18 y.o., school-based sample is a reasonable approach in epidemiological surveys, provided that most of population in that age bracket is enrolled in a school. Conversely, hospitalized, institutionalized, and homeless populations are not included. On the other hand, only a minor part of the population can be represented in samples drawn from treatment centers, which may exhibit high tendency to help-seeking behavior. Patient samples incur in a double problem, as far as parents interfere on the decision of medical encounter and more symptomatic individuals are recruited into the study. The very large variation reported in the prevalence rates across all retained studies suggest imprecise estimates: while school-based studies may exemplify the closer magnitude of FGID rate[16,40], healthcare centers used to provide inflated rates[8,33,35].

Rome criteria are based on detailed clinical evaluation[5,8–10]. To date, no biomarkers[5] or standard tests are available to diagnose functional disorders[6]. Still, some studies in this review approached the sample only by questionnaires, without clinical assessment[22,27,28,30,36]. The lack of medical evaluation can misdiagnose the complaint of FGID symptoms, leading to non-agreement between informants[19,21,24]. Some evidence of concordance between parent-children was described for cyclic vomit, abdominal migraine and constipation. When high level of disagreement occurs, *e.g.*, irritable bowel syndrome and dyspepsia, the type of informant is critical to the quality of the data. Therefore, wider dissemination of clear operationalized criteria, as in the Rome IV criteria, should be recommended for researchers and practicing pediatricians[44].

***Limitation***

Taking all appraisals into account, conclusive recommendation on the results of the epidemiology of FGID should be avoided. There are enormous rate differences and unequivocal methodological limitations across studies. Bearing this in mind, some limitations of current review need to be discussed. Reporting bias in cross-sectional data is commonly due to publication delay (file drawer bias) and language bias. After trying to contact experts to request non-published data (*e.g.*, non-accessible journals, poster presentation, conference paper) and surveys in other language, we were not able to get access to four studies identified in initial search. Therefore, it is reasonable to assert that the prevalence heterogeneity of present review is more attributable to the quality caveats of accessible investigations than to publication bias.

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**COMMENTS**

***Background***

Functional gastrointestinal disorders (FGID) in children and adolescents are mainly a clinical condition and the most common diagnose in gastroenterology, with a risen burden and, until now, without biomarkers or gold standards diagnosing test available. Furthermore, etiology remains non-established and valid epidemiological data are scarce. The aim of this review is to examine current evidence of knowledge on FGID in children and adolescents, through systematic search of frequency or prevalence data on common functional GI problems. The authors also assessed the quality of existing studies on the target topic.

***Research frontiers***

The validity of explicit diagnostic criteria and the reliability of psychometric tools for FGID is still limited. Pediatricians must rely on patient’s symptoms to diagnose and be aware that there are differences between patient and parents reports. Adequate adoption of structured guidelines is useful when replicability is necessary. Reliable data from prospective studies based on structured criteria is necessary to achieve more accurate prevalence data on GI symptoms. Hence, public health decisions can only be established after well-conducted surveys.

***Innovations and breakthroughs***

FGID in children and adolescents seem to be common in clinical and non-clinical settings, mainly cyclic vomiting, irritable bowel syndrome and functional constipation. Conversely, few good quality population-based studies on epidemiology concerns were conducted so far and good quality epidemiological data to support diagnostic criteria are lacking. As an effort to optimize FGID identification, the use of Rome criteria proved to be a helpful tool. A Rome criteria update, recently launched as Rome IV, merges scientific features and clinical practice, improving the diagnostic classification system. Therefore, its incorporation into epidemiological surveys and clinical practice may increase the pathophysiological comprehension of GI conditions, leading to diagnostic improvement of an important group of functional diseases with a growing burden in pediatric and adolescent population.

***Applications***

This review highlights future directions for research: (1) epidemiological, well-designed (sample recruitment, representativeness and clinical assessment) and structured (reproducible) studies shall be conducted along all pediatrics levels; (2) classification system on FGID must be simple and easy to comprehend, looking for a wider use among pediatricians; and (3) multidimensional approach may bring advances for the Rome criteria symptom-based classification.

***Terminology***

FGID comprise chronic or recurrent symptoms that arise in the absence of anatomic abnormality, inflammation, or tissue damage. The symptoms are variable among children and adolescents.

***Peer- review***

This systematic review has been presenting a well-designed study on the epidemiology of FGID in children and adolescents. Based on the whole data the authors indicate the need for methodology improvement in future epidemiological studies concerning FGID.

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Table 1 Classification of functional gastrointestinal disorders in children and adolescents

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Rome IV nomenclature1** | **Frequency** | **Duration** | **Synonym, subtypes or approximate terms** |
| **H1. Functional nausea and vomiting disorders** |
| H1a. | Cyclic vomiting syndrome | ≥ 2 periods of intense, unremitting nausea and paroxysmal vomiting | h-d/6 mo | Periodic vomiting  |
| H1b1. | Functional nausea  | ≥ 2 nausea episodes/wk  | ≥ 2 mo | Bothersome nausea |
| H1b2. | Functional vomiting | ≥ 1 vomiting episode/wk | ≥ 2 mo | - |
| H1c. | Rumination syndrome | Repetitive regurgitation and rechewing or expulsion of food | ≥ 2 mo | Adolescent rumination syndrome2; regurgitation, reswallowing, spitting |
| H1d.  | Aerophagia | Repetitive belching and/or increased flatus | ≥ 2 mo | **-** |
| **H2. Functional abdominal pain disorders** |
| H2a. | Functional dyspepsia | ≥ 1 symptom for ≥ 4 d/ mo | ≥ 2 mo | Postprandial distress syndrome; Epigastric pain syndrome |
| H2b.  | Irritable bowel syndrome | Abdominal pain for ≥ 4 d/ mo | ≥ 2 mo | Abdominal discomfort2;Manning criteria |
| H2c. | Abdominal migraine |  ≥ 2 intense abdominal pain episodes  | ≥ 1 h/ 6 mo | Periumbilical pain2 |
| H2d. | Functional abdominal pain – not otherwise specified | ≥ 4 episodic or continuous abdominal pain/ mo | ≥ 2 mo | Functional abdominal pain2; Functional abdominal pain syndrome2 |
| **H3. Functional defecations disorders** |
| H3a. | Functional constipation | ≤ 2 defecations/ wk≥ 1 fecal incontinence/ wk | ≥ 1 mo | - |
| H3b. | Nonretentive fecal incontinence | Episodes of fecal loss | ≥ 1 mo | - |

1After appropriate evaluation, the symptoms cannot be fully explained by another medical condition; 2Rome III nomenclature.

Studies included in qualitative synthesis
(*k* = 26)

Hand search
(*k* = 16)

Records excluded (*k* = 106)

Records screened
(*k* = 149)

Records after duplicates removed
(*k* = 149)

Records identified through database searching
(*k* = 659)

Reasons of study exclusion (*k* = 17):

- No specific data for age bracket (*k* = 6) ⌘

- No data for subtypes of FGID (*k* = 4) §

- Case-control study (*k* = 1)

- No full text available (*k* = 5)

- Overlapping of sample (*k* = 1)

## Identification

## Eligibility

## Included

## Screening

Reasons of study exclusion (*k* = 17):

 No specific data for age bracket (*k* = 6)2

 No full text available (*k* = 5)

 No data for subtypes of FGID (*k* = 4)3

Case-control study (*k* = 1)

 Overlapping of sample (*k* = 1)

Full-text articles assessed for eligibility
(*k* = 43)

**Figure 1 Flow diagram for identifying eligible articles1.** 1Flow diagram according to PRISMA ([www.prisma-statement.org](http://www.prisma-statement.org)); 2age bracket 4-18 years old; 3Prevalence only for general FGID. FGID: functional gastrointestinal disorders.

**Table 2 Prevalence or frequency of functional gastrointestinal disorders: nausea and vomiting problems in children and adolescents**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  | **FGID subtypes prevalence %(CI 95%)** |
| **Author, year, country** | **Study design, setting** | **Sample size (participation %)** | **Age bracket yo** | **Case definition** | **Case ascertainment** | **Score1** | **Cyclic vomiting** | **Aerophagia** | **Rumination** |
| Bhatia *et al*[6], 2016, India | Cross-sectional, school-based | 1200 (93.3) | 10-17 | Rome III | Self-reported QPGS-RIII Medical recordsPhysical examination | 5 | 0.2 | 1.5 | 0.3 |
| Caplan *et al*[18], 2005, Canada | Cross-sectional, tertiary care | 315 (NR) | 4-18 | Rome II | Self-reported QPGSParental QPGSCinical evaluation | 3 | p 4-9yo= 6.2p 10-18yo= 2.2a 10-18yo= 4.3 | p 4-9yo= 1.1p 10-18yo= 2.2a 10-18yo= 1.4 |  |
| Devanarayana *et al*[36], 2010, Sri Lanka | Cross-sectional, school-based | 464 (92) | 12-16 | Rome IIRome III | Self-reported QPGS  | 4 | 0.20.5 | 6.16.3 | 4.0 |
| Helgeland *et al*[35], 2009, Norway | Cross-sectional, secondary care | 192 (79.1) | 4-15 | Rome III | Parental QPGS-III Clinical evaluation Medical recordsPhysical examinationLaboratory exams | 3 | 6.0 | 15.0 | 2.0 |
| Játiva *et al*[30], 2016, Ecuador | Cross-sectional, school-based | 420 (99.3) | 8-15 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 | 1.0 | 2.6 | 0.7 |
| Lewis *et al*[25], 2016, United States | Cross-sectional, online painel community | 1447 (NR) | 4-18 | Rome III | Parental QPGS-RIII PedsQL4.0 | 2 | 1.1 | 4.3 | 0 |
| Lu *et al*[28], 2016, Panama | Cross-sectional, school-based | 436 (82.8) | 8-14 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 4 | 0.3 (0.0-0.9) | 0.3 (0.0-0.9) | 0.0 |
| Sagawa *et al*[19], 2012, Japan | Cross-sectional, school-based | 3976 (NR) | 10-17 | Rome III | Self-reported QPGS-RIII Self-reported PedsQL4.0Clinical evaluation | 6 | 0.2 | 2.0 | 0.1 |
| Saps *et al*[26], 2014, Colombia | Cross-sectional, school-based | 488 (83.2) | 10.0 (mean age) | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 4 | 0.3 (0.0-1.7) |  |  |
| Uc *et al*[22], 2006, United States | Cross-sectional, primary care | 243 (100) | 4-17 | Rome II | Parental QPGSClinical evaluation | 4 | 0.8 | 2.5 |  |
| van Tilburg *et al*[13], 2013, United States | Cross-sectional, tertiary care | 135 (NR) | 4-18 | Rome III | Self-reported QPGS-IIIParental QPGS-III Clinical evaluation Medical records | 3 | p= 0.8c/a= 5.3ph= 0 | p= 0.8c/a= 3.5ph= 0 | p= 0.8c/a= 5.3ph= 0 |
| Zablah *et al*[27], 2015, El Salvador | Cross-sectional, school-based | 434 (NR) | 8-15 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 |  | 0.5 | 0.2 |

1Score Methodological strength of study (maximum 8) by Loney’s criteria. yo: year-old; NR: not reported; w: with; p: parents; c: children; a: adolescents; ph: physician; QPGS-RIII: Questionnaire on Pediatric Gastrointestinal Symptoms – Rome III; QPGS: Questionnaire on Pediatric Gastrointestinal Symptoms – Rome II; PedsQL4.0 Pediatric Quality of Life version Inventory 4.0.

**Table 3 Prevalence or frequency of functional gastrointestinal disorders: abdominal pain problems in children and adolescents**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  | **FGID subtypes prevalence %( 95%CI)** |
| **Author, year, country** | **Study design, setting** | **Sample size (participation %)** | **Age bracket yo** | **Case definition** | **Case ascertainment** | **Score1** | **Dyspepsia** | **Irritable bowel** | **Abdominal migraine** | **Abdominal pain - NOS** |
| Baber *et al*[8], 2008, United States | Cross-sectional, tertiary care  | 548 (80.1) | 8-17  | Rome IIRome III | Parental QPGS Clinical evaluationMedical recordsLaboratory exams | 5 | 19.615.2 | 44.0 45.1 | 5.723.1 | 2.717.4 |
| Bhatia *et al*[6], 2016, India | Cross-sectional, school-based | 1200 (93.3) | 10-17 | Rome III | Self-reported QPGS-RIII Medical recordsPhysical examination | 5 | 2.7 | 1.3 | 1.4 | 0.8 |
| Caplan *et al*[18], 2005, Canada | Cross-sectional, tertiary care | 315 (NR) | 4-18 | Rome II | Self-reported QPGSParental QPGSCinical evaluation | 3 | p 4-9yo = 13.5p 10-18yo= 14.4a 10-18yo= 10.2 | p 4-9yo= 22.0p 10-18yo= 23.9a 10-18yo= 35.5 | p 4-9yo= 0p 10-18yo= 0.7a 10-18yo = 2.2 | p 4-9yo= 0p 10-18yo= 2.9a 10-18yo = 2.9 |
| Cristofori *et al*[33], 2014, Italy | Cross-sectional, tertiary care | 992 (NR) | 4-16  | Rome III | Clinical evaluationMedical recordsLaboratory exams | 4 | 25.7 | 34.5 | 0 | 39.8 |
| Devanarayana *et al*[36], 2010, Sri Lanka | Cross-sectional, school-based | 464 (92) | 12-16 | Rome IIRome III | Self-reported QPGS  | 4 | 1.23.5 | 2.87.0 | 0.20.2 | 1.43.0 |
| Dong *et al*[37], 2005, China | Cross-sectional, school-based | 5403 (NR) | 6-18 | Rome II | Self-reported standard questionnaire Parental standard questionnaireMedical records | 6 |  | 13.2 |  |  |
| Gijsbers *et al*[32], 2014, the Netherlands | Cross-sectional, secondary care | 220 (NR) | 4-16 | Rome III | Clinical evaluation Medical recordsLaboratory exams | 3 | 3.6 | 5.0 | 0 | 15.0 |
| Gulewitsch *et al*[34], 2013, Germany | Cross-sectional, school-based | 3658 (43.1) | 5-12 | Rome III | Parental QPGS-RIII Parental CSI Parental SDQ  | 2 | 0.2 | 4.9 | 1.0 | 3.6 |
| Helgeland *et al*[35], 2009, Norway | Cross-sectional, secondary care | 192 (NR) | 4-15 | Rome III | Parental QPGS-III Clinical evaluation Medical recordsPhysical examinationLaboratory exams | 3 | 10 | 43 | 23 | 15 |
| Játiva *et al*[30], 2016, Ecuador | Cross-sectional, school-based | 420 (99.3) | 8-15 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 | 0.5 | 4.8 | 2.4 | 3.1 |
| Lewis *et al*[25], 2016, United States | Cross-sectional, online painel community | 1447(NR) | 4-18 | Rome III | Parental QPGS-RIII PedsQL4.0 | 2 | 0.2 | 2.8 | 9.2 | 11.6 |
| Lu *et al*[29], 2016, Colombia | Cross-sectional, school-based | 4751 (89.8) | 8-18 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 |  | 4.8 |  |  |
| Lu *et al*[28], 2016, Panama | Cross-sectional, school-based | 436 (82.8) | 8-14 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 4 | 0.9 (0.0-2.0) | 5.6 (3.1-8.1) | 1.7 (0.2-2.9) | 3.7 (1.7-5.8)0.3 (0.0-0.9) |
| Sagawa *et al*[19], 2012, Japan | Cross-sectional, school-based | 3976 (NR) | 10-17 | Rome III | Self-reported QPGS-RIII Self-reported PedsQL4.0Clinical evaluation | 6 | 0.9 | 5.9 | 1.8 | 4.2 |
| Saps *et al*[23], 2012, United States | Cross-sectional, Community  | 984 (25) | 4-18 | Rome III | Parental QPGS-III  | 2 |   |  |  | 8.1 |
| Saps *et al*[26], 2014, Colombia | Cross-sectional, school-based | 488 (83.2) | 10.0 (mean age) | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 4 | 1.7 (0.8-3.9) | 5.4 (3.9-8.8) | 1.0 (0.3-2.8) | 2.7 (1.6-5.2)0.3 (0.0-1.7) |
| Schurman *et al*[21], 2005, United States | Cross-sectional, tertiary care | 205 (75) | 8-18 | Rome II | Self-reported QPGSParental QPGSClinical evaluation  | 3 | p= 47c/a= 35ph= 57 | p= 20;c/a= 30;ph= 12 | p<10c/a<10;ph<10 | p<10c/a<10ph<10 |
| Uc *et al*[22], 2006, United States | Cross-sectional, primary care | 243 (100) | 4-17 | Rome II | Parental QPGSClinical evaluation | 4 | 0.8 | 0 | 0.4 | 0.4 |
| Udoh *et al*[41], 2016, Nigeria | Cross-sectional, school-based | 856 (NR) | 10-18 | Rome III | Self-reported QPGS-RIII Standard questionnaires | 4 | 0.4 | 5.6 | 1.8 | 2.6 |
| Walker *et al*[20], 2004, United States | Cross-sectional, tertiary care | 114 (NR) | 4 – 17  | Rome II | Parental QPGS Clinical evaluation Parental standard interviewMedical recordsPhysical examinationLaboratory exams | 3 | 15.9 | 44.9 | 4.7 | 7.5 |
| Yamamoto *et al*[40], 2015, Japan | Cross-sectional, school-based | 99416 (92.2) | 12-18 | Rome III | Self-reported standard questionnaire | 6 |  | 18.6 (17.9-19.2) |  |  |
| Zablah *et al*[27], 2015, El Salvador | Cross-sectional, school-based | 434 (NR) | 8-15 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 | 1.7 | 3.7 | 0.7 | 3.0 |
| Zhou *et al*[38], 2011, China | Cross-sectional, school-based | 3671 (NR) | 12-18 | Rome III | Self-reported standard questionnaire | 5 |  | 19.8 (18.6-21.1) |  |  |

1Score Methodological strength of study (maximum 8) by Loney’s criteria; yo: year-old; NR: not reported; w: With; p: Parents; c: Children; a: Adolescents; ph: Physician; QPGS-RIII: Questionnaire on Pediatric Gastrointestinal Symptoms – Rome III; QPGS: Questionnaire on Pediatric Gastrointestinal Symptoms – Rome II; PedsQL4.0 Pediatric Quality of Life version Inventory 4.0

CSI: Children’s Somatization Inventory; SDQ: Strengths and Difficulties Questionnaire.

**Table 4 Prevalence or frequency of functional gastrointestinal disorders: defecations problems in children and adolescents**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  | **FGID subtypes prevalence % (CI 95%)** |
| **Author, year, country** | **Study design, setting** | **Sample size (participation %)** | **Age bracket yo** | **Case definition** | **Case ascertainment** | **Score1** | **Constipation** | **Nonretentive fecal incontinence** |
| Bhatia *et al*[6], 2016, India | Cross-sectional, school-based | 1200 (93.3) | 10-17 | Rome III | Self-reported QPGS-RIII Medical recordsPhysical examination | 5 | 0.5 | 0.4 |
| Burgers *et al*[31], 2012, Netherlands | Cross-sectional (retrospective), tertiary care | 176 (NR) | 6-18  | Rome IIRome III | Clinical evaluationMedical recordsPhysical examination | 3 | 5.786.9 |  |
| Caplan *et al*[18], 2005, Canada | Cross-sectional, tertiary care | 315 (NR) | 4-18 | Rome II | Self-reported QPGSParental QPGSCinical evaluation | 3 | p 4-9yo= 19.2p 10-18yo= 13.8c/a 10-18yo= 15.2 | p 4-9yo= 0.6p 10-18yo= 0.7c/a 10-18yo= 0.7 |
| Devanarayana *et al*[36], 2010, Sri Lanka | Cross-sectional, school-based | 464 (92) | 12-16 | Rome IIRome III | Self-reported QPGS  | 4 | 1.44.2 | 0.20.2 |
| Helgeland *et al*[35], 2009, Norway | Cross-sectional, tertiary care | 192 (NR) | 4-15 | Rome III | Parental QPGS-III Clinical evaluation Medical recordsPhysical examinationLaboratory exams | 3 | 6.0 |  |
| Játiva *et al*[30], 2016, Ecuador | Cross-sectional, school-based | 420 (99.3) | 8-15 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 | 11.8 | 0.2 |
| Lewis *et al*[25], 2016, United States | Cross-sectional, online painel community  | 1447 (NR) | 4-18 | Rome III | Parental QPGS-RIII PedsQL4.0 | 2 | 12.9 | 1.8 |
| Lu *et al*[29], 2016, Colombia | Cross-sectional, school-based | 4751(89.8) | 8-18 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 | 12.7 |  |
| Lu *et al*[28], 2016, Panama | Cross-sectional, school-based | 436 (82.8) | 8-14 | Rome III | Rome III Self-reported QPGS-RIII Parental standard questionnaire | 4 | 15.9 (11.9-19.9) | 0 (0.0-0.0) |
| Rajindrajith *et al*[39], 2013, Sri Lanka | Cross-sectional, school-based | 1855 (96.7) | 13-18 | Rome III | Self-reported QPGS-RIII Self-reported PedsQL4.0 | 5 | 7.7 |  |
| Sagawa *et al*[19], 2012, Japan | Cross-sectional, school-based | 3976 (NR) | 10-17 | Rome III | Rome III Self-reported QPGS-RIII Self-reported PedsQL4.0Clinical evaluation | 6 | 0.3 | 0.2 |
| Saps *et al*[26], 2014, Colombia | Cross-sectional, school-based | 488 (83.2) | 10.0 (mean age) | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 4 | 14.0(12.0-19.3) | 1.5(0.7-3.6) |
| Uc *et al*[22], 2006, United States | Cross-sectional, primary care | 243 (100) | 4-17 | Rome II | Parental QPGSClinical evaluation | 4 | 16.1 | 0.4 |
| Zablah *et al*[27], 2015, El Salvador | Cross-sectional, school-based | 434 (NR) | 8-15 | Rome III | Self-reported QPGS-RIII Parental standard questionnaire | 3 | 10 | 0 |
| Zhou *et al*[38], 2011, China | Cross-sectional, school-based | 3671 (NR) | 12-18 | Rome III | Self-reported standard questionnaire | 5 | 24.9 (23.5-26.3) |  |

1Score Methodological strength of study (maximum 8) by Loney’s criteria. yo: year-old; NR: not reported; w: With; p: Parents; c: Children; a: Adolescents; ph: Physician; QPGS-RIII: Questionnaire on Pediatric Gastrointestinal Symptoms – Rome III; QPGS: Questionnaire on Pediatric Gastrointestinal Symptoms –Rome II; PedsQL4.0 Pediatric Quality of Life version Inventory 4.0.