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Impact of the Rome II Pediatric Criteria on the Appropriateness of the Upper and Lower Gastrointestinal Endoscopy in Children

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**Impact of the Rome II Pediatric Criteria on the
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16 **Upper and Lower Gastrointestinal Endoscopy in Children**
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Abstract

Background: The demand for pediatric GI endoscopy has increased, resulting in a significant rise in overall costs. **Aim:** to assess the clinical impact of the Rome II criteria for FGIDs in selecting pediatric patients who underwent GI endoscopy. **Methods:** Indications and findings of GI endoscopic procedures performed before and after the publication of the Rome II criteria were retrospectively evaluated. **Results:** Upper GI endoscopy was performed in 1124 children, whereas 500 subjects underwent colonoscopy. Six-hundred-seven (54%) EGDs were positive, and 517 (46%) were negative, whereas 306 (61.1%) colonoscopies were positive, and 194 (38.9%) were negative. Of the 1624 procedures, 26% were considered inappropriate according to the Rome II criteria. Inappropriate procedures decreased significantly after publication of the Rome II criteria (OR, 3.7; 95% CI, 1.8-7.5). Of 1202 appropriate GI endoscopies, 502 EGD (62.7%) were significantly contributive, compared with only 105 (32.5%) of the 323 inappropriate procedures (OR, 3.5; 95% CI, 2.6-4.6;), whereas 265 (65.8%) colonoscopies were significantly contributive, compared with only 41 (42.3%) of the 97 inappropriate procedures (OR, 2.6; 95% CI, 1.6-4.1). **Conclusions:** The use of the criteria for FGIDs makes a significant positive impact in reducing unnecessary pediatric GI endoscopy.

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Introduction

Functional gastrointestinal disorders (FGIDs) are defined as a variable combination of chronic or recurrent gastrointestinal symptoms unexplained by structural or biochemical abnormalities. In 1997, a pediatric working team met in Rome to standardize the diagnostic criteria for various FGIDs in children. The first pediatric criteria for FGIDs were published in 1999 as the Rome II criteria (1). These criteria were created as a diagnostic tool and as a way to advance empirical research, providing clinicians with a positive approach to treating pediatric patients. Recently, in light of emerging scientific research and on the basis of clinical experience, the Rome II pediatric criteria have been updated and revised. The Rome III pediatric criteria represent an evolution from Rome II and should prove useful for both clinicians and researchers dealing with childhood FGIDs (2, 3).

The demand for gastrointestinal endoscopy has increased in most developed countries, resulting in a significant rise in overall costs for endoscopic procedures (4). During the past few years, various organizations have tried to develop criteria for selecting patients most likely to benefit from gastrointestinal endoscopy (5). Official recommendations on the appropriate use of endoscopy in adults have been released (6, 7). Although few studies have compared the efficiency of gastrointestinal endoscopy to other diagnostic procedures in pediatric patients, recommendations were issued in 1996 by the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) (8). In addition, a technical report by NASPGHAN concluded that, in the evaluation of chronic abdominal pain “there is little evidence to suggest that use of endoscopy and biopsy in the absence of alarm symptoms has a significant yield of organic disease” (9).

Adult studies suggest, however, that alarm features may not discriminate functional from organic disease (10). There are few studies examining the diagnostic outcomes of

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gastrointestinal endoscopy in children (11). The diagnostic yield of esophagogastroduodenoscopy (EGD) in children with abdominal pain was 3.6% in the existing literature, but this data was based on studies which were compromised by small simple size, variable findings, selection bias and the use of not standardized diagnostic criteria (11). None of the studies used the Rome II pediatric criteria for functional abdominal pain. Few of them examined the predictive value of blood work obtained prior to endoscopy and none of them analysed the association of alarm symptoms or signs to diagnostic yield (11). To our knowledge, there are no studies evaluating appropriateness and diagnostic yield of colonoscopy in the management of children with gastrointestinal disorders.

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The main purpose of this study was to assess the impact of the Rome II pediatric criteria for FGIDs in selecting pediatric patients who underwent upper or lower gastrointestinal endoscopy. The secondary objectives were to evaluate the association of alarm symptoms or signs to diagnostic yield and the predictive value of blood work obtained prior to endoscopy.

Patients and Methods

The study was a retrospective, single-center, cross-sectional study of 1624 consecutive children who underwent upper or lower GI endoscopy at the Department of Pediatrics of the University of Naples "Federico II" from January 1998 to December 2006. To avoid repeated measures from patients with multiple exams during the study period, only the patients' first procedure was eligible for the study. No patient was excluded on the grounds of having a concomitant chronic disease.

A chart review was performed on all patients who met inclusion criteria. Procedure note, pathology report, laboratory reports, and history and physical examination performed

1 up to 1 month prior to the procedure were considered. For those patients who lacked a
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3
4 qualifying history and physical examination, ICD9 codes were reviewed in the electronic
5
6 medical record. Clinical information was collected prior to the procedure information to
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8 mask the reviewer to the outcome of the endoscopy. A review of laboratory tests, which
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10 had been obtained up one month prior to the procedure, included hemoglobin level,
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12 erythrocyte sedimentation rate (ESR), C - reactive protein (CRP), albumin and fecal
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14 calprotectin. Alarm symptoms or signs were evaluated included involuntary weight loss,
15
16 deceleration of linear growth, gastrointestinal blood loss, vomiting, chronic severe
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18 diarrhea, persistent right upper or right lower quadrant pain (12). Chronic diarrhea was
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20 defined as the passage of 3 or more watery stool per day for at least two weeks (13).

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21 The decision to perform endoscopy was made by the hospital-based pediatric
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23 gastroenterologist who evaluated symptoms reported by the parents or family and applied
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25 the Rome II pediatric diagnostic criteria after their publication.

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27 Endoscopic examination was carried out using standard, forward-viewing pediatric
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29 Olympus endoscopes (Europe GMBH, Hamburg, Germany) by experienced pediatric
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31 gastroenterologists (EM, AS). The upper or lower GI endoscopies were performed in
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33 either an endoscopy room or an operating room. Those patients who underwent the
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35 procedure in an endoscopy room were sedated, while those in the operating room were
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37 put under general anesthesia. The decision between these two modalities was based on
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39 patient age, reason for endoscopy, and medical history. Sedation, when used, consisted of
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41 midazolam, administered intravenously (0.1 mg/kg). During the colonoscopy, three
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43 biopsies were taken from the ileum and subsequently a minimum of two biopsies was
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45 taken from every segment of the colon. In the case of an EGD, biopsies were taken from
46
47 the duodenum, antrum, corpus and esophagus.

48 Endoscopic findings were reported according to internationally accepted terms and
49
50 definitions whenever possible. Review of the final pathology report provided the data

1 source for histologic diagnosis. Endoscopic procedures were considered positive if they
2 had direct impact on treatment (ie, gross abnormalities, clinically relevant biopsy findings
3 such as celiac disease and inflammatory bowel disease). They were considered negative if
4 their findings were normal or showed abnormalities that did not affect treatment, such as
5 non-specific endoscopic findings (e.g., erythema, increase or loss vascularity, pallor) and
6 descriptive histological changes (e.g. reactive changes, edema, mild inflammatory
7 changes) (14, 15).
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15 Based on the symptoms, endoscopic procedures were considered inappropriate if
16 the Rome criteria had been met and appropriate if they hadn't been met. Two
17 investigators (EG and AT), who were unaware of the endoscopic findings judged the
18 appropriateness of the indication of the endoscopic findings, according to the Rome II
19 pediatric criteria. To evaluate the effect of the Rome II pediatric criteria on practices,
20 indications and findings of GI endoscopic procedures, performed before the publication of
21 the FGIDs, diagnostic criteria were compared with those procedures performed under
22 them (1). The Rome II diagnostic criteria are summarized in Table 1.
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31 Means and medians were calculated for dimensional variables after controlling for
32 normality of distribution. The Student's t test for normally distributed variables and the
33 Mann-Whitney U test and χ^2 and Fisher exact tests for categorical variables were used
34 where appropriate.
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38 Logistic regression has been used in order to estimate the probability of positive
39 events occurring in upper as well lower GI endoscopy. The probability of the event
40 occurring was obtained by the linear combination of the contribution of the following
41 indicator variables which significantly contributed, positively as well as negatively, to the
42 prediction of the event: deceleration of linear growth, gastrointestinal blood loss, significant
43 vomiting, persistent right upper or right lower quadrant pain involuntary weight loss,
44 chronic severe diarrhea. The sign of the regression coefficient suggests positive or
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negative contribution: the coefficient can be interpreted as the change in the log odds associated with one-unit in the independent variables. A forward stepwise selection was adopted. Odds ratio and accompanying 95% C.I. were calculated using maximum likelihood ratio method.

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Statistical analysis was carried out using SPSS statistical software package for Windows (13.0, SPSS Inc., Chicago, IL). The study was approved by the Institutional Review Board of the University of Naples "Federico II".

Results

During the study period, 1916 GI endoscopic procedures were performed in 1713 patients of which 292 were excluded. Ninety-six were excluded because of repeated endoscopies, 136 because they had undergone incomplete procedures, and 60 were excluded because their data were incomplete. Thus, the present study was based on 1624 procedures, each performed in an individual patient. The patients' mean age was 7.4 years (range: 2 months-18 years; 732 boys and 892 girls). EGD was performed in 1124 children, whereas 500 subjects underwent colonoscopy. Two hundred sixty-nine (23%) upper GI endoscopies and 64 colonoscopies (12.8%) were performed before the September 1999 publication of the Rome II criteria in *Gut* (1). Table 2 details the indications or symptoms for which endoscopy was performed. Six hundred seven (54%) EGDs were positive, and 517 (46%) were negative (155 with normal appearance, and 362 with non-specific endoscopic findings), whereas 306 (61.1%) colonoscopies were positive, and 194 (38.9%) were negative (46 with normal appearance and 152 with non-specific endoscopic findings). Diagnoses of the upper and lower GI endoscopies are reported in the Table 3.

Gender and age were not predictors of diagnostic yield OR=1, 95% CI, 0.8-1.3, $\chi^2=0.2$, p=0.33; OR=1.2, 95% CI, 0.9-1.5, $\chi^2=0.4$, p=0.54 (Table 4).

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Patients with one or more alarm symptoms who underwent EGD did not have significantly better diagnostic yield than those without (53.4% vs 56.6%, $p=0.43$). All patients who underwent colonoscopy had at least one alarm symptom. Among alarm symptoms, deceleration of linear growth was associated with increased diagnostic yield of EGD (OR, 2.5; 95% CI, 1.7-3.7; $\chi^2=21.1$; $p=0.0001$), whereas gastrointestinal blood loss, vomiting, chronic severe diarrhea and persistent right upper or lower quadrant pain were significantly associated with a negative diagnostic yield of EGD (OR, 0.2; 95% CI, 0.1-0.3; $\chi^2=45$, $p=0.0001$; OR, 0.5; 95% CI, 0.4-0.7; $\chi^2=26$, $p=0.0001$; OR, 0.3; 95% CI, 0.2-0.5; $\chi^2=33$, $p=0.001$; OR, 0.7; 95% CI, 0.6-0.9; $\chi^2=6.6$, $p=0.01$, respectively) (Table 5). As regards colonoscopy weight loss, deceleration of linear growth, gastrointestinal blood loss, chronic severe diarrhea and persistent right upper or lower quadrant pain resulted significantly associated with increased diagnostic yield (OR, 8.4; 95% CI, 5.1-14; $\chi^2=82$, $p=0.0001$; OR, 2; 95% CI, 1.1-3.5; $\chi^2=6.7$, $p=0.01$; OR, 2.5; 95% CI, 1.5-4; $\chi^2=16$, $p=0.0001$; OR, 4.6; 95% CI, 3-7; $\chi^2=63$, $p=0.001$; OR, 5.5; 95% CI, 3.6-8.6; $\chi^2=64$, $p=0.01$ respectively).

Laboratory parameters including hematocrit, albumin, ESR, CRP and fecal calprotectin were not predictive of diagnostic yield of EGD ($\chi^2=0.09$, $p=0.4$; $\chi^2=0.04$, $p=0.5$; $\chi^2=0.003$, $p=0.5$; $\chi^2=0.2$, $p=0.3$; $\chi^2=0.3$, $p=0.3$). However, we found a predictive value of the diagnostic yield of colonoscopy for hematocrit, CRP and of fecal calprotectin ($\chi^2=34$, $p=0.02$; $\chi^2=65$, $p=0.001$; $\chi^2=56$, $p=0.007$).

Of the 1624 procedures, 26% were considered inappropriate according to the Rome II pediatric criteria. [Kappa coefficient between the two investigators resulted 0.91 \(95% CI: 0.88-0.93; agreement: 0.97; SE: 0.01\)](#)

A total of 420 children satisfied the Rome II criteria for the various FGIDs (Table 6). The number of inappropriate procedures as a percentage of the total number of

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procedures performed decreased significantly (from 38% to 14%) after publication of the Rome II pediatric criteria (OR, 3.7; 95% CI, 1.8-7.5; $p < 0.001$). The probability of finding a clinically relevant lesion was significantly higher in appropriate endoscopies compared to those that were inappropriate according to the Rome II pediatric criteria. Of 1202 appropriate upper or lower GI endoscopies (801 EGD; 500 colonoscopies), 502 EGD (62.7%) were significantly contributive, compared with only 105 (32.5%) of the 323 inappropriate procedures (OR, 3.5; 95% CI, 2.6-4.6; $p < 0.001$), whereas 265 (65.8%) colonoscopies were significantly contributive, compared with only 41 (42.3%) of the 97 inappropriate procedures (OR, 2.6; 95% CI, 1.6-4.1; $p < 0.001$).

After the publication of the Rome II pediatric criteria, the proportion of upper GI endoscopy performed for celiac disease was significantly higher than before criteria publication (42.9% vs 21.4%; $\chi^2 = 123$; $p = 0.00001$); no significant difference was observed in the proportion of the procedures performed for peptic ulcer disease (21.7% vs 20.6%; $\chi^2 = 0.18$; $p = 0.6$); whereas a significant decrease in the proportion of negative upper GI endoscopy was found (56.8% vs 36.4%; $\chi^2 = 44.9$; $p = 0.00001$). A significant increase in the proportion of lower GI endoscopy for inflammatory bowel disease (IBD) was observed when performed under the Rome II pediatric criteria (22.9% vs 63.9%; $\chi^2 = 38$; $p = 0.00001$). Because of the difference in distribution, we also found a significant decrease in the proportion of lower endoscopy performed for GI polyps (18.5 vs 7.3%; $\chi^2 = 7.68$; $p = 0.051$), as well as a significant decrease in the proportion of negative colonoscopies (58.5% vs 28.7%; $\chi^2 = 20$; $p = 0.00006$).

To determine which alarm symptoms were significant predictors of diagnostic yield exploratory multivariate conditional logistic regression was conducted in SPSS. Data were screened for predictors as involuntary weight loss, deceleration of linear growth, gastrointestinal blood loss, vomiting, chronic severe diarrhea, persistent right upper or right

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Miele et al

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2 lower quadrant pain. Deceleration of the linear growth was independently correlated with
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4 an increased diagnostic yield of EGD, while vomiting, gastrointestinal blood loss
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6 (hematemesis, hematochezia, occult lower GI bleeding) and persistent right upper or right
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8 lower quadrant pain predicted a negative diagnostic yield of EGD. As regards
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10 colonoscopy, involuntary weight loss, chronic diarrhea, persistent right upper or right lower
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12 quadrant pain and gastrointestinal blood loss (hematochezia, occult lower GI bleeding)
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14 remained independently associated with an increased diagnostic yield (Table 7).
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For Peer Review

Discussion

GI endoscopy is an essential tool for the evaluation of gastrointestinal disorders in children. Upper and lower endoscopic procedures may be useful if the physician suspects organic pathology, such as inflammatory bowel disease, allergic/eosinophilic gastrointestinal disease, or peptic ulcer disease. These disorders may also present with additional alarm symptoms or signs such as involuntary weight loss, growth failure, gastrointestinal bleeding, chronic diarrhea, unexplained fever, vomiting, or family history of inflammatory bowel disease (9). A recent systematic review demonstrated that the diagnostic yield of EGD in children with unexplained abdominal pain is low, however existing studies are insufficient. The effect of EGD on change in treatment, quality of life, improvement of abdominal pain, and cost-effectiveness is unknown. The predictors of significant findings are unclear (11).

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A retrospective study suggested that colonoscopy is the investigative method of choice in children with prolonged rectal bleeding. In patients presenting with accompanying complaints such as abdominal pain or diarrhea, it is advisable to perform ileocolonoscopy combined with EGD. This combines a high diagnostic yield with a safe procedure (16).

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Standardized symptom-based criteria were introduced in 1999 with the publication of the Rome II criteria for FGIDs in children (1). Since their publication, the Rome II criteria have been used to assess the prevalence of FGIDs in community settings (17, 18) and have served as selection criteria in laboratory studies of pediatric FGIDs (19). Several empirical studies have used the Rome II criteria to estimate the rates of various FGIDs among children with primary symptoms of abdominal pain (20-22).

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To our knowledge, this is the first study examining the appropriate use of upper and lower gastrointestinal endoscopy in children using the Rome II pediatric criteria (1). A

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2 retrospective design was used since one of our objectives was to compare the periods
3 before and after publication of the Rome II pediatric criteria, and this is why we did not
4 apply the Rome III criteria published in 2006 (2). A potential source of error inherent in the
5 retrospective design of the present study could be that some of the patients included may
6 have had symptoms that were not recorded in the medical charts.
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11 In this study, the overall yield was 54% for EGD and 61.1% for colonoscopy, similar
12 to what others have found in pediatric and adult series, with celiac disease (53.3%), reflux
13 esophagitis (25.9%), *H. Pylori* infection (13.7%) and inflammatory bowel disease (43.4%)
14 being the most frequent findings (23- 25).
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19 After the Rome II pediatric criteria were instituted, the proportion of EGDs
20 performed for celiac disease significantly increased and the presentation has changed.
21 According to previous studies, an increasingly large proportion of children are presenting
22 with non-gastrointestinal symptoms, with almost one in four children being diagnosed by
23 targeted screening (26).
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29 According to a previous pediatric study, IBD was the most common cause in
30 children referred for colonoscopy both before and after the institution of Rome II pediatric
31 criteria (16). This finding confirms the rise in incidence of IBD in childhood (27).
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36 The probability of the endoscopic detection of a clinically relevant finding was higher
37 in those examinations judged as appropriate compared with those deemed inappropriate,
38 according to the Rome II pediatric criteria. However, the low specificity of the Rome II
39 criteria could be indicated by the presence of patients who underwent an appropriate
40 procedure that resulted in a negative finding, as well as by the presence of those patients
41 who underwent an inappropriate endoscopic procedure that resulted in a positive finding
42 (1). By comparing endoscopic procedures performed before the publication of the
43 diagnostic criteria with those procedures performed after its publication, we found that the
44 Rome criteria significantly reduced the proportion of negative endoscopies. Nevertheless,
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2 the value of a negative endoscopy should not be overlooked, as it can influence the
3 subsequent management of the patients, and allows unnecessary therapies to be
4 excluded. In a previous study, 67% of the negative endoscopies in adult patients were
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6 excluded. In a previous study, 67% of the negative endoscopies in adult patients were
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8 judged to have influenced patient management (28).

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10 The mean number of GI endoscopies was 166.5 per year before Rome II criteria
11 publication, while it increased to 236 per year after publication of the diagnostic criteria.
12 This data could be explained by several factors. The higher number of procedures could
13 be due to an increased visibility of our GI endoscopy centre. However, the number of
14 inappropriate endoscopies significantly decreased, according to the hypothesis that
15 primary care physicians may be using Rome II pediatric criteria to filter their referrals.
16 During the study period, no systemic/procedural changes occurred that may have resulted
17 in improved appropriateness of endoscopy over time, except from experience of pediatric
18 gastroenterologists.

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27 The role of alarm symptoms in predicting endoscopic findings is still controversial.
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29 Alarm symptoms are traditionally thought to be associated with organic disease (10). A
30 technical report by the American Academy of Pediatrics and NASPGHAN suggested that
31 alarm symptoms should be used to screen children for endoscopy (Evidence D) (9). In
32 contrast, Ashorn and Maki noted that endoscopic abnormalities in their patients did not
33 correlate with the symptoms associated with chronic abdominal pain (29). In addition, a
34 recent study by Thakkar et al found that several alarm symptoms other than vomiting were
35 not significantly predictive of diagnostic yield (30). In our cohort, alarm symptoms (apart
36 from deceleration of linear growth) were predictive of decreased diagnostic yield. On the
37 basis of these results, alarm symptoms seem to be inaccurate and should not be used for
38 deciding who to select for EGD among pediatric patients with upper GI symptoms.
39 However, our retrospective study has the potential for recall bias that may result in
40 overestimation of the prevalence of "alarm" symptoms prior to endoscopy. The situation
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2 regarding lower gastrointestinal pathology looks more promising, (10, 31). In addition,
3 laboratory parameters including hematocrit, albumin, ESR, C-reactive protein (CRP) and
4 fecal calprotectin were not predictive of EGD diagnostic yield, whereas a predictive value
5 of ESR, CRP and fecal calprotectin has been observed for colonoscopy in previous
6 pediatric studies (32-34).
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12 In conclusion, this is the first pediatric, retrospective, observational study, evaluating
13 the impact of the Rome II pediatric criteria on the appropriateness of GI endoscopy. The
14 study finds that the use of the criteria for FGIDs makes a significant positive impact in
15 reducing unnecessary GI endoscopic procedures, improving the diagnostic yield and the
16 cost-effectiveness of pediatric endoscopy. However, further refinement and clarification of
17 the Rome pediatric criteria may be needed to improve diagnostic agreement. Further
18 steps are required to update and standardize the guidelines for gastrointestinal pediatric
19 endoscopy and to promote educational programs for pediatric gastroenterologists.
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Infant regurgitation¶
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Regurgitation 2 or more times per day for 3 or more weeks¶
No retching, hematemesis, aspiration, apnea, failure to thrive, or abnormal posturing 1–12 mo old and otherwise healthy¶
¶
No evidence of metabolic, GI, or CNS disease to explain the symptom¶
¶
Functional diarrhea¶
¶
For >4 wk, daily painless recurrent passage of 3 or more large, unformed stools, in addition to all of these characteristics:¶
¶
Onset of symptoms begins between 6 and 36 mo of age¶
¶
Passage of stools occurs during waking hours¶
¶
No failure to thrive if adequate caloric intake¶
¶
Irritable Bowel Syndrome ¶
¶
In children mature enough to provide an accurate pain history, at least 12 wk (need not be consecutive) within the preceding 12 months of:¶
¶
Abdominal discomfort or pain that has 2 of 3 features:¶
¶
Relieved with defecation ¶
¶
Onset associated with a change in frequency of stool¶
¶
Onset associated with a change in form (appearance) or stool¶
¶
There are no structural or metabolic abnormalities to explain the symptoms¶
¶
Cyclic vomiting syndrome¶
¶
History of 3 or more periods of intense, acute nausea and unremitting vomiting lasting hours to days, with intervening symptom-free intervals lasting weeks to months¶
¶
No metabolic, GI, or CNS structural or biochemical disease to explain symptoms ¶

... [1]

Table 2. Indications or Symptoms for Upper and Lower Gastrointestinal EndoscopyDeleted: ¶
¶

	Before Rome II Criteria n. 333		After Rome II Criteria n. 1291		All Subjects n. 1624	
	N	(%)	N	(%)	N	(%)
Failure to thrive	36	(10.8)	121	(9.3)	157	(9.6)
Unexplained Weight loss	92	(27.6)	392	(30.3)	484	(29.8)
Dysphagia	74	(22.2)	266	(20.6)	340	(20.9)
Recurrent abdominal pain	236	(70.8)	572	(44.3)	808	(49.7)
Vomiting/Regurgitation	132	(39.6)	189	(14.6)	321	(19.7)
Bleeding from GI tract	99	(29.7)	436	(33.7)	535	(32.9)
Chronic diarrhea	88	(26.4)	323	(25.1)	411	(25.3)
Anemia	32	(9.6)	152	(11.7)	184	(11.3)
Suspected esophageal varices	19	(5.7)	78	(6.0)	97	(5.8)
Celiac disease	30	(9)	376	(29.1)	406	(25)

* More than one indication or symptom was reported in some subjects

Table 3. Diagnoses and appropriateness according to the Rome II criteria of Upper and Lower Gastrointestinal Endoscopy

EsophagoGastroDuodenoscopy				
	<i>Subjects</i> n. 607 (%)		<i>Appropriate</i> n. 504 (83)	<i>Inappropriate</i> n. 103 (17)
Celiac disease	325	(53.5)	301 (92.6)	24 (7.4)
Reflux esophagitis	157	(25.9)	109(69.4)	48 (31.6)
<i>H. Pylori</i> infection	83	(13.7)	61 (73.5)	22 (26.5)
Eosinophilic Esophagitis	25	(4.1)	18 (72)	7 (28)
Focal gastritis or duodenal inflammation	12	(2)	9 (75)	3 (25)
Crohn's disease	5	(0.8)	4 (80)	1 (20)
Colonoscopy				
	<i>Subjects</i> n. 306 (%)		<i>Appropriate</i> n. 265 (86.6)	<i>Inappropriate</i> n. 41 (13.4)
Inflammatory Bowel Disease	133 (43.4)		122 (91.7)	11 (8.3)
Ulcerative Colitis	71	(53.4)		
Crohn's Disease	53	(39.8)		
Indeterminate Colitis	9	(6.8)		
Polyps	40	(13)	34 (85)	6 (15)
Allergic colitis	30	(9.8)	25 (83.3)	5 (16.7)
Infectious	6	(2)	6 (100)	0 (0)
Lymphonodular hyperplasia	39	(13)	32 (82.1)	7 (17.9)
Eosinophilic Colitis	18	(5.8)	15(83.3)	3 (16.7)
Focal colitis	40	(13)	31(77.5)	9 (22.5)

Table 4. Clinical Characteristics of Children undergone Upper and Lower GI Endoscopy**EsophagoGastroDuodenoscopy**

	<i>Appropriate</i>	<i>Inappropriate</i>
<i>Subjects</i>	801	323
<i>Mean Age(Years, range)</i>	6.7 (0 to18)	7.5 (0 to18)
<i>Gender</i>		
Male	318	120
Female	483	203
<i>Positive</i>	501	106
<i>Negative</i>	299	218

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Colonoscopy

	<i>Appropriate</i>	<i>Inappropriate</i>
<i>Subjects</i>	403	97
<i>Mean Age(Years, range)</i>	10.3 (2 to18)	10.2 (2 to 18)
<i>Gender</i>		
Male	206	50
Female	197	47
<i>Positive</i>	265	41
<i>Negative</i>	138	56

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Table 5. Diagnostic Yield of Upper and Lower Gastrointestinal Endoscopy for Alarm Symptoms * (8).

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Subjects	Upper GI Endoscopy			Colonoscopy		
	Positive (%)	Negative (%)	p	Positive (%)	Negative (%)	p
Any Alarm Symptom						
Present	491 (80.9)	428 (83)	0.43	222 (72.7%)	385 (26.3%)	NA
Absent	116 (19.1)	89 (17)				
Weight loss						
Present	164 (27)	143 (27.6)	0.73	153 (50)	21 (10.8)	0.0001
Absent	443 (73)	374(72.4)		153 (50)	173 (89.2)	
Deceleration of linear growth						
Present	96 (15.8)	36 (7)	0.0001	52 (17%)	19 (10)	0.01
Absent	511 (84.2)	481 (93)		254 (83)	175 (90)	
Gastrointestinal blood loss						
Present	29 (4.8)	89 (17.2)	0.0001	267 (87.5)	150 (77.7)	0.0001
Absent	578 (95.2)	428 (82.8)		39 (12.5)	44 (22.3)	
Significant vomiting						
Present	164 (27)	214 (41.4)	0.0001			
Absent	443 (73)	303 (58.6)				
Chronic severe diarrhea,						
Present	38 (6.3)	89 (17.2)	0.0001	216 (70.8)	68 (22.2)	0.001
Absent	569 (93.7)	428 (82.8)		90 (29.2)	238 (77.8)	
Persistent right upper or right lower quadrant pain						
Present	308 (50.8)	302 (58.6)	0.01	267 (87.5)	107 (55.5)	0.0001
Absent	299 (49.2)	215 (41.4)		39 (12.5)	87 (44.5)	

* More than one finding was reported in some subjects

Table 7. Potential Predictors Associated with Diagnostic Yield of EGD and Colonoscopy in a Multivariate Analysis

	<i>Regression coefficient</i>	<i>Odds Ratio</i>	<i>95% CI</i>
EGD			
Deceleration of linear growth	0.17	1.24	1.16-1.32
Gastrointestinal blood loss	- 0.15	0.85	0.78-0.93
Significant vomiting	-0.07	0.93	0.89-0.96
Persistent right upper or right lower quadrant pain	-0.09	0.9	0.82-0.95
Colonoscopy			
Involuntary weight loss	0.27	1.21	1.13-1.3
Gastrointestinal blood loss	0.16	1.2	1.11-1.3
Chronic severe diarrhea	0.22	1.19	1.13-1.27
Persistent right upper or right lower quadrant pain and	0.2	1.28	1.2-1.37

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Deleted: 6. FGIDs in the Studied Population According to the Rome II Criteria¶

Disorder	No. of Studied Children	% Among Population	% of FGIDs
Infant regurgitation	152	9.4	36.4
Functional diarrhea	29	1.8	6.3
Functional dyspepsia	127	7.8	30.4
IBS	78	4.8	18.6
Functional constipation	34	2.1	8.3
Total	420	26	100

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Figure 1. A significant increase of the mean rate of the upper GI endoscopy performed for celiac disease was observed after 1999 when the criteria were published (42.9% vs 21.4%; 95% CI: -30.1 to -12.7; p=0.004); no significant difference was observed in the mean rate of the procedures performed for ulcer peptic disease (21.7% vs 20.6%; 95% CI: -11.5 to 13.6; p=0.84); a significant decrease of the mean rate of negative upper GI endoscopy was found (56.8% vs 36.4%; 95% CI: 1.3 to 4; p=0.006). ¶

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Figure 2. A significant increase of the mean rate of lower GI endoscopy for inflammatory bowel disease was observed when performed under the Rome II criteria (22.9% vs 63.9%; 95% CI: -58.6 to -23.2; p=0.001); a significant decrease of the mean rate of lower endoscopy performed for GI polyps (18.5 vs 7.3%; 95% CI: 0.0 to 22.4; p=0.05), as well as a significant decrease of the mean rate of negative colonoscopies were found (58.5% vs 28.7%; 95% CI: 1.9 to 6; p<0.001).

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Table 1. FGIDs: Rome II Diagnostic Criteria

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Infant regurgitation

Regurgitation 2 or more times per day for 3 or more weeks

No retching, hematemesis, aspiration, apnea, failure to thrive, or abnormal posturing 1–12 mo old and otherwise healthy

No evidence of metabolic, GI, or CNS disease to explain the symptom

Functional diarrhea

For >4 wk, daily painless recurrent passage of 3 or more large, unformed stools, in addition to all of these characteristics:

Onset of symptoms begins between 6 and 36 mo of age

Passage of stools occurs during waking hours

No failure to thrive if adequate caloric intake

Irritable Bowel Syndrome

In children mature enough to provide an accurate pain history, at least 12 wk (need not be consecutive) within the preceding 12 months of:

Abdominal discomfort or pain that has 2 of 3 features:

Relieved with defecation

Onset associated with a change in frequency of stool

Onset associated with a change in form (appearance) or stool

There are no structural or metabolic abnormalities to explain the symptoms

Cyclic vomiting syndrome

History of 3 or more periods of intense, acute nausea and unremitting vomiting lasting hours to days, with intervening symptom-free intervals lasting weeks to months

No metabolic, GI, or CNS structural or biochemical disease to explain symptoms

Functional dyspepsia

In children mature enough to provide an accurate pain history, at least 12 wk (need not be consecutive) within the preceding 12 months of:

Persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus)

No evidence (including at upper endoscopy) that organic disease is likely to explain symptoms

No evidence that dyspepsia is exclusively relieved by defecation or associated with the onset of a change in stool frequency or stool form

Functional constipation

In infants and preschool children, at least 2 wk of:

Scybalous, pebble-like, hard stools for a majority of stools

Firm stools 2 or fewer times per week

There is no evidence of structural, endocrine, or metabolic disease

Functional fecal retention

From infancy to 16 years of age, a history of at least 12 wk of:

Passage of large-diameter stools at intervals <2 times per week

Retentive posturing, avoiding defecation by purposefully contracting the pelvic floor; as pelvic floor muscles fatigue, the child uses the gluteal muscles, squeezing the buttocks together

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