



ICDS2022SORRENTO

19th INTERNATIONAL CELIAC DISEASE SYMPOSIUM

IBS and Celiac disease

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IBS and Celiac disease

Outline

➤ **The impact of celiac disease in patients with chronic abdominal pain (AP)**

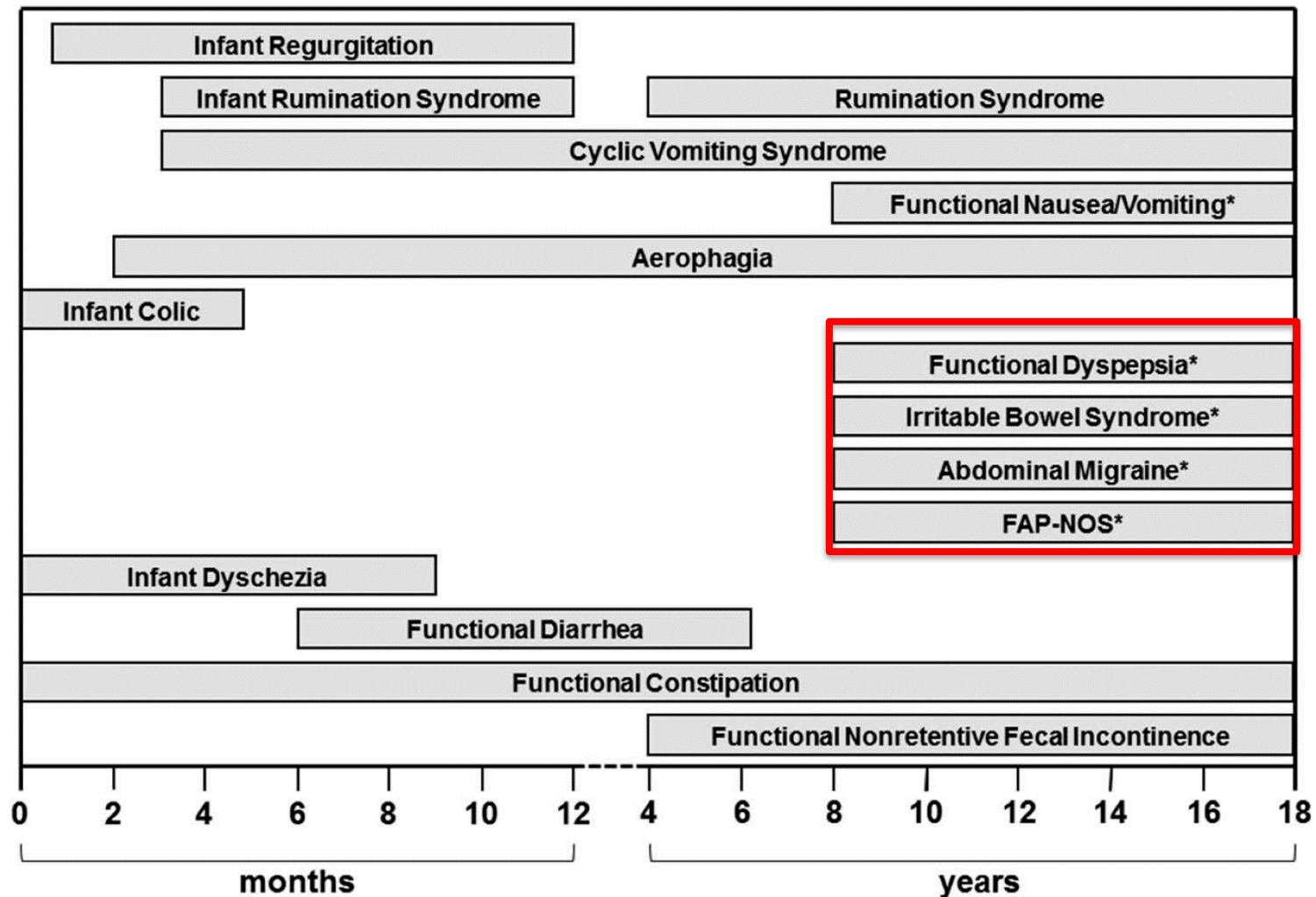
1. *How frequently children with celiac disease show AP as the main symptom?*
2. *How frequent is celiac disease in children with AP?*

➤ **The risk of celiac children of developing Functional GI Disorders (FGIDs)**



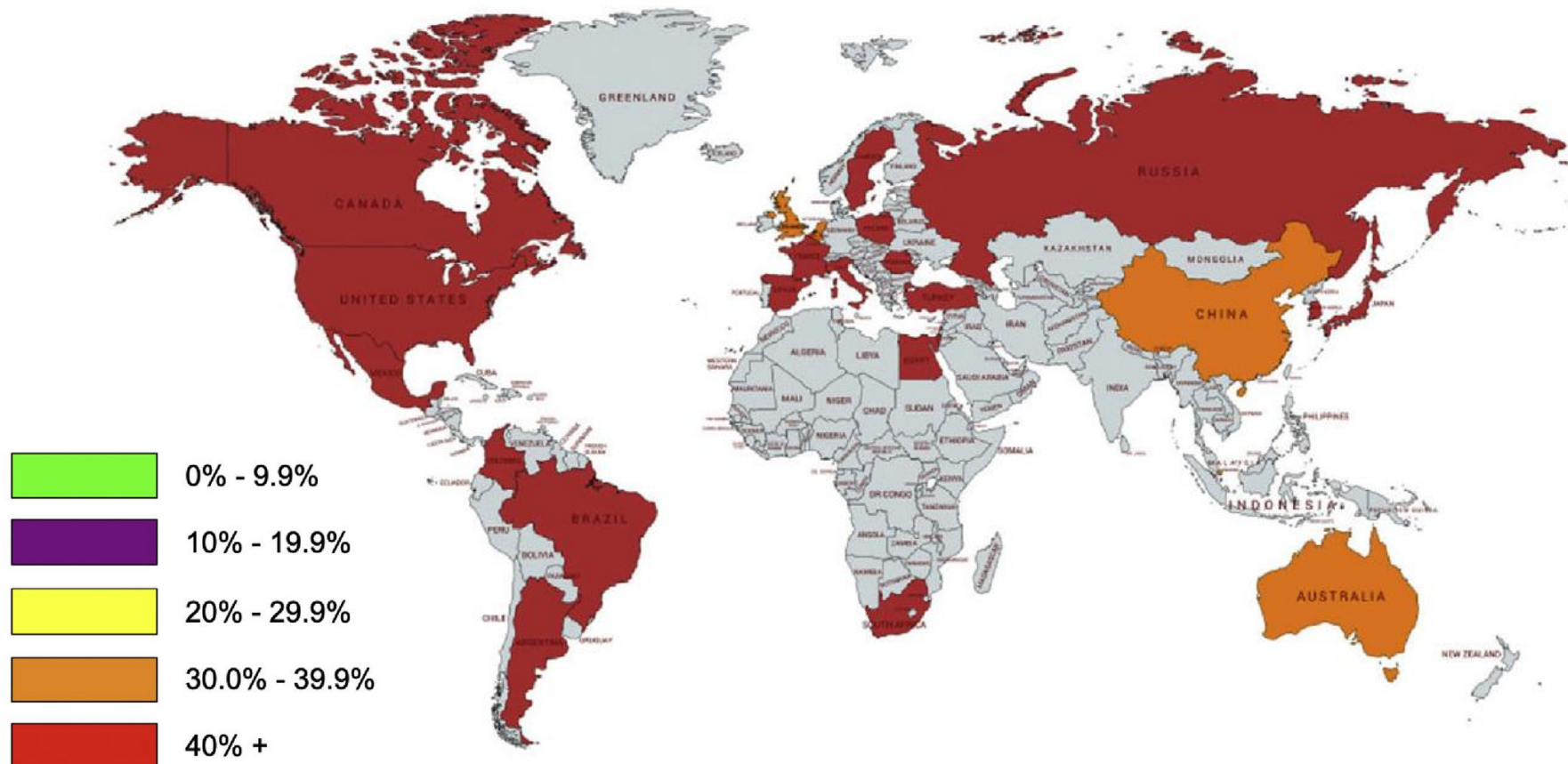
IBS and Celiac disease

Age related Functional GI Disorders





Global maps showing study countries color-coded for prevalence of having any FGIDs





Irritable Bowel Syndrome

H2b. Diagnostic Criteria^a for Irritable Bowel Syndrome

Must include all of the following:

1. Abdominal pain at least 4 days per month associated with one or more of the following:

➤ Pediatric IBS can be divided into subtypes analogous to adults reflecting the predominant stool pattern:

a. Related to defecation

b. A change in frequency of stool

c. A change in form (appearance) of stool

☐ **IBS with constipation**

☐ **IBS with diarrhea**

☐ **IBS with constipation and diarrhea**

☐ **Unspecified IBS**

Infection, celiac disease, carbohydrate malabsorption, less commonly, inflammatory bowel disease, warrant particular consideration

in children with constipation, the pain does not

resolve with resolution of the constipation (children in whom the pain resolves have functional constipation, not irritable bowel syndrome)

3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

^aCriteria fulfilled for at least 2 months before diagnosis.



IBS and Celiac disease

1. **How frequently celiac children show abdominal pain as the main symptom at diagnosis?**
2. ***How frequent is celiac disease in children with abdominal pain?***



European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020

TABLE 2. Symptoms and signs suggesting coeliac disease

Gastrointestinal	Chronic or intermittent diarrhea*
	Chronic constipation not responding to usual treatment
	Chronic abdominal pain
Extraintestinal symptoms	Distended abdomen
	Recurrent nausea, recurrent vomiting
	Weight loss, failure-to-thrive*, stunted growth/ short stature*
	Delayed puberty, amenorrhea
	Irritability, chronic fatigue
	Neuropathy
	Arthritis/arthralgia
	Chronic iron-deficiency anaemia
	Decreased bone mineralization (osteopenia/osteoporosis), repetitive fractures
	Recurrent aphthous stomatitis, Dermatitis herpetiformis–type rash
Specific conditions	Dental enamel defects
	Abnormal liver biochemistry
	First-degree relatives with CD
	Autoimmune conditions: T1DM, thyroid disease, liver disease
	Down syndrome, Turner syndrome
	Williams-Beuren syndrome
	IgA deficiency

CD = coeliac disease; T1DM = type-1 diabetes mellitus.

*Common symptoms.



Incidence and distribution of coeliac disease in Campania (Italy): 2011–2013

Table 4. Modes of CD clinical presentation

Clinical presentation	Classical presentation (malabsorption symptoms ^a) (%)	Non-classical presentation (other symptoms ^b) (%)	Non-classical presentation (only anaemia) (%)	Asymptomatic (%)	Missing (%)
All age	813 (39.7)	433 (21.1)	154 (7.5)	266 (13)	383 (18.7)
<4	207 (44.3)	68 (14.7)	25 (5.3)	44 (9.4)	123 (26.3)
5–19	174 (29.4)	123 (20.8)	43 (7.3)	114 (19.2)	138 (23.3)
All children	381 (36)	191 (18)	68 (6.4)	158 (15)	261 (24.6)
20–29	148 (45.5)	82 (25.2)	22 (6.8)	37 (11.4)	36 (11.1)
30–49	217 (40.7)	138 (25.9)	52 (10)	63 (11.8)	62 (11.6)
50–69	55 (49.6)	20 (18)	9 (8.1)	6 (5.4)	21 (18.9)
70+	12 (54.6)	2 (9.1)	3 (13.6)	2 (9.1)	3 (13.6)
All adults	432 (43.6)	242 (24.5)	86 (8.7)	108 (10.9)	122 (12.3)

^aAt least one among: diarrhoea, weight loss, failure to thrive.

^bAt least one among: lack of appetite, vomit, meteorism, abdominal pain, constipation, asthenia, dyspepsia.



IBS and Celiac disease

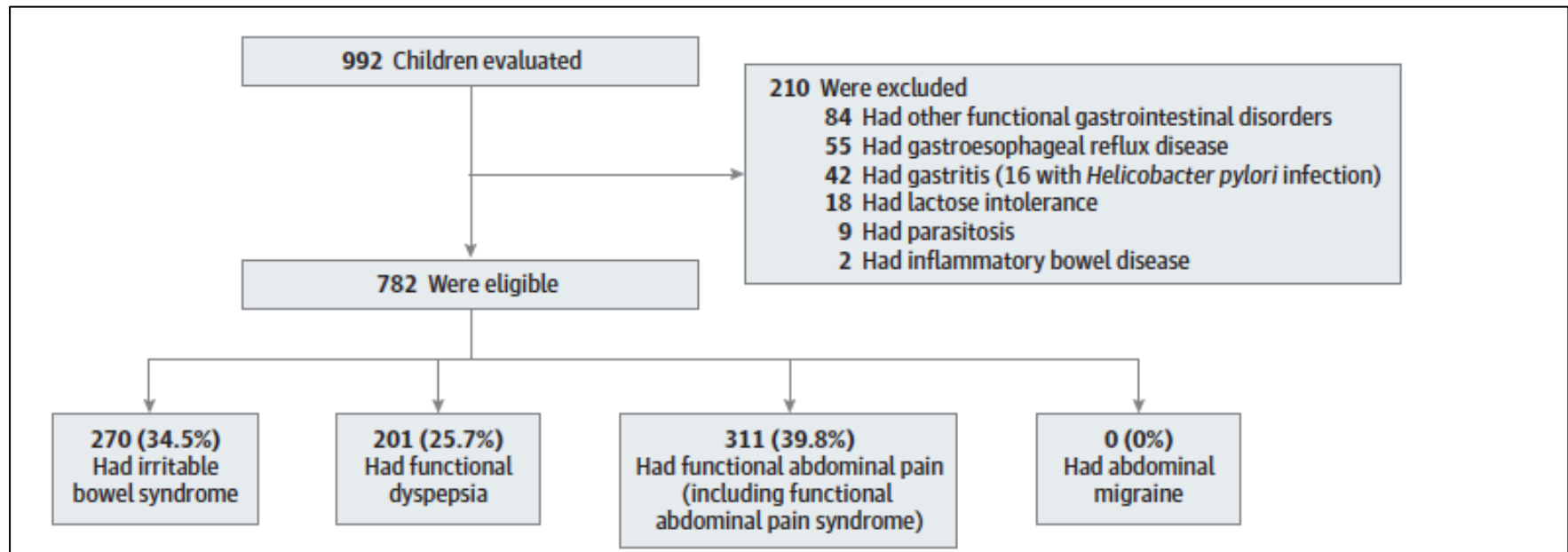
1. *How frequently celiac children show abdominal pain as the main symptom at diagnosis?*
2. *How frequent is celiac disease in children with abdominal pain?*



Original Investigation

Increased Prevalence of Celiac Disease Among Pediatric Patients With Irritable Bowel Syndrome A 6-Year Prospective Cohort Study

- Prospective observational cohort study conducted between 2006 and 2012
- The study population included all children consecutively referred for recurrent abdominal pain





Original Investigation

Increased Prevalence of Celiac Disease Among Pediatric Patients With Irritable Bowel Syndrome A 6-Year Prospective Cohort Study

Table 1. Prevalence of Celiac Disease in the Different Diagnostic Subgroups

Functional Gastrointestinal Disorder	Patients, No.	Patients With Celiac Disease, No.	Prevalence of Celiac Disease, % (95% CI)
Irritable bowel syndrome	270	12	4.4 (2.5-7.6)
Functional dyspepsia	201	2	1.0 (0.2-3.5)
Functional abdominal pain	311	1	0.3 (0.1-1.7)
Abdominal migraine	0	0	0.0 (0.0-0.0)



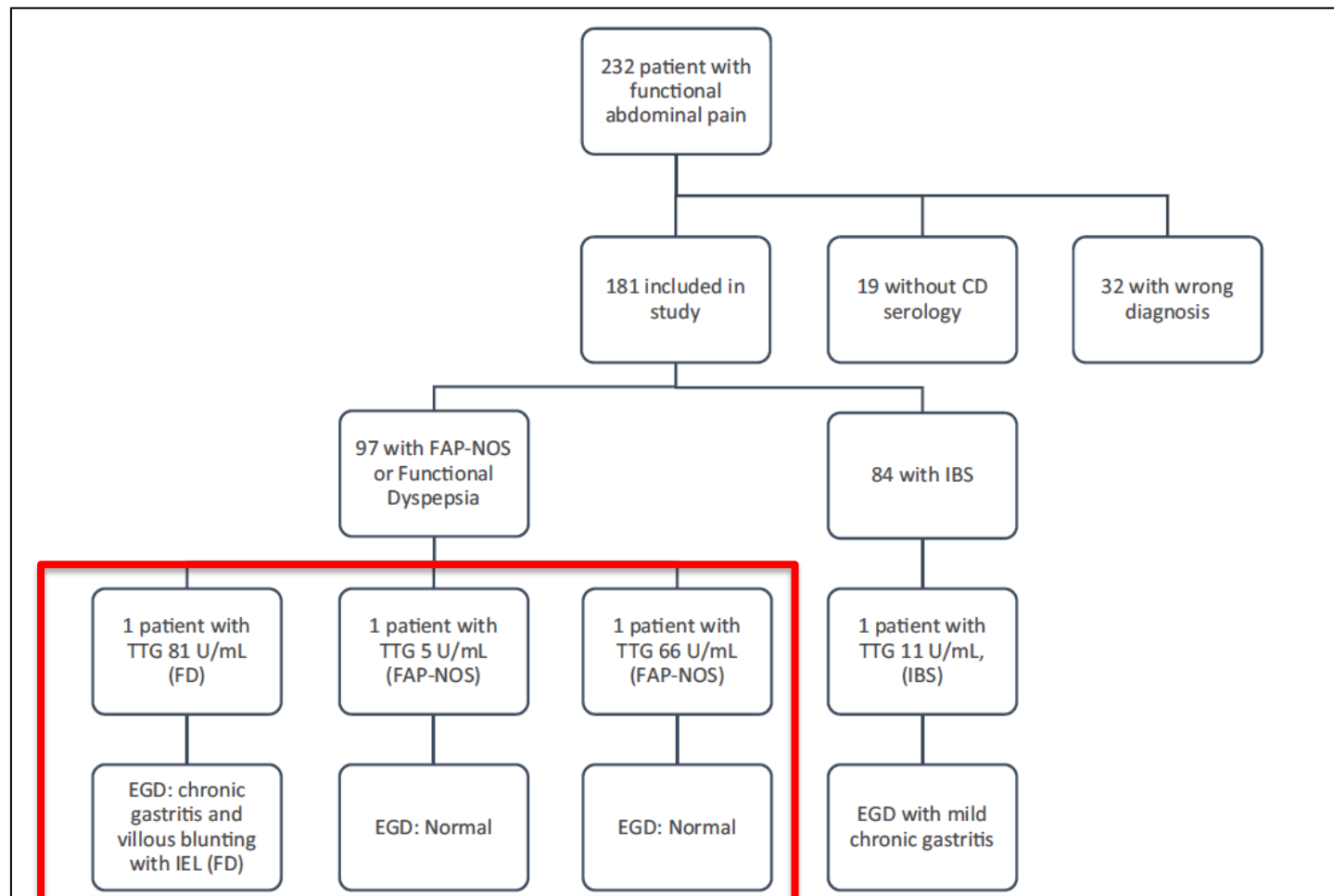
A Million-dollar Work-up for Abdominal Pain: Is It Worth It?



- Retrospective chart review on 122 children diagnosed with a PP-FGID
- All of the children included in the study had undergone at least 1 diagnostic investigation to rule out inflammatory bowel disease, celiac disease, and other inflammatory or infectious conditions
- Of 64 children undergoing celiac serology **only 1 (1.5%) showed positive TTG** with negative endoscopy
- **Total costs** incurred by the patients in the study were **\$744,726**. **Average cost per patient** with PP-FGID was **\$6104.30** (range \$1052–\$20,994)

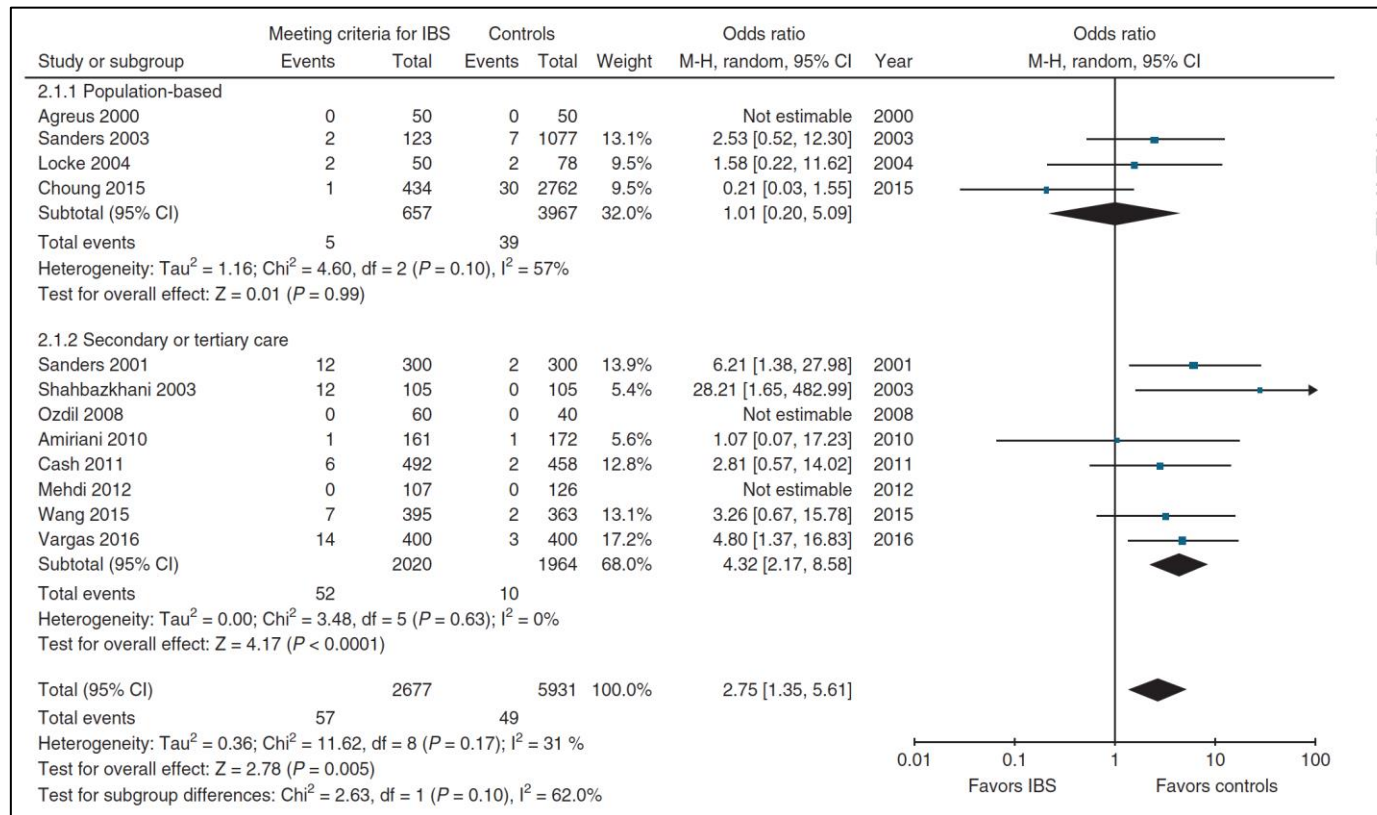


Is Celiac Disease Testing Necessary in Functional Abdominal Disorders? A Study in Predominantly Latino Children





Screening for Celiac Disease in Irritable Bowel Syndrome: An Updated Systematic Review and Meta-analysis



Pooled odds ratio for a positive EMA and/or tTG in cases with IBS-type symptoms compared with controls without IBS-type symptoms.



Management of Irritable Bowel Syndrome: Guidelines of Joint Italian Societies of Gastroenterology and Endoscopy (SIGE), Neurogastroenterology and Motility (SINGEM), Hospital Gastroenterologists and Endoscopists (AIGO), Digestive Endoscopy (SIED), General Medicine (SIMG), Gastroenterology, Hepatology and Pediatric Nutrition (SIGENP) and Pediatrics (SIP).

Statement 1.5: We recommend serologic testing for celiac disease if the prevalence in the population is >1% (as in Italy).

- Given the increased odds of CD among patients with IBS symptoms, independent from the predominant pattern, the significant potential consequences of missing the diagnosis of CD, the availability of highly effective treatment, and the apparent cost effectiveness of an early diagnosis, we recommend serologic testing with quantitative IgA levels and IgA anti-tTG to rule out CD in patients with any IBS subtype.
- This is mandatory, if CD prevalence in the population is >1% (as in Italy), since it has an acceptable cost and is worthwhile.



IBS and Celiac disease

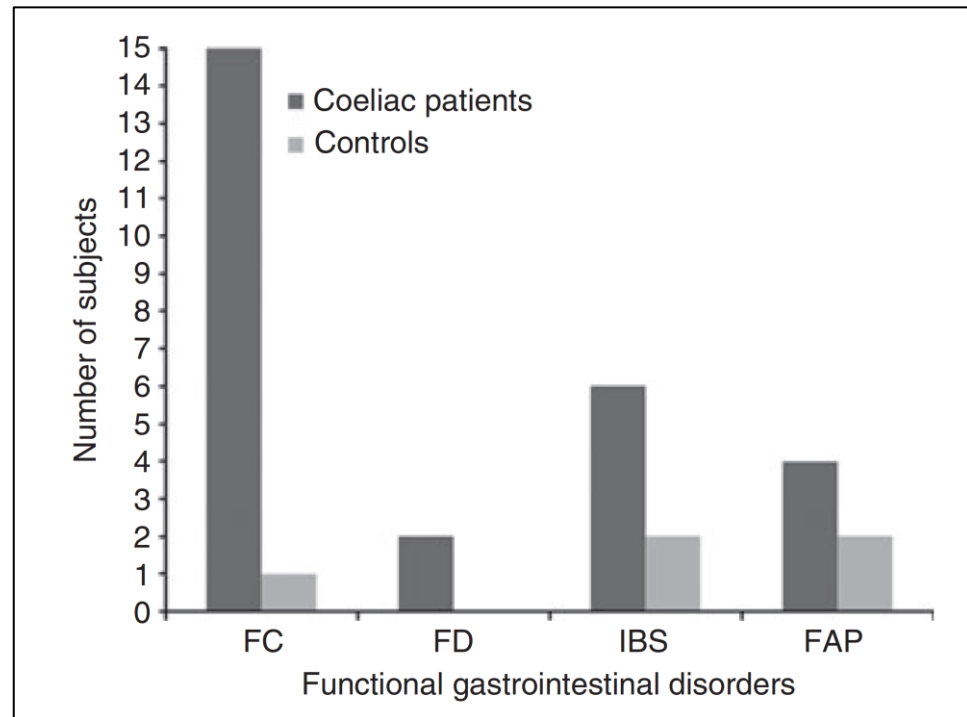
Outline

- **The impact of celiac disease in patients with chronic abdominal pain (AP)**
 1. *How frequently children with celiac disease show AP as the main symptom?*
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- **The risk of celiac children of developing Functional GI Disorders (FGIDs)**



The association of coeliac disease in childhood with functional gastrointestinal disorders: a prospective study in patients fulfilling Rome III criteria

- Prospective cohort study: 100 children with a diagnosis of celiac disease were followed-up at 1 year from diagnosis
- 82 showed with negative serology and were matched with healthy controls
- FGIDs prevalence was assessed through Rome III questionnaires
- Enrolled patients fulfilled also Children's Depression Inventory (CDI) and the State-Trait Anxiety Inventory for Children (STAIC).





Journal Pre-proof

Functional Abdominal Pain Disorders and Constipation in Children on Gluten-Free Diet

- A cohort of 417 children with CD after one year of gluten free diet and negative serology
- ***Irritable bowel syndrome (IBS)*** and ***functional constipation (FC)*** defined by the Rome IV criteria, ***were more prevalent in patients with coeliac disease (7.2% for IBS and 19.9% for FC)*** than controls (3.2% for IBS and 10.5% for FC) ($P<.05$ and $P<.001$);

Conclusion:

- The demonstration of a higher prevalence of IBS and FC in CD children should prompt an early detection of these conditions in order to anticipate its diagnoses and to program possible therapeutic interventions and educational programming.



Abdominal Pain-Associated Functional Gastrointestinal Disorder Prevalence in Children and Adolescents with Celiac Disease on Gluten-Free Diet: A Multinational Study

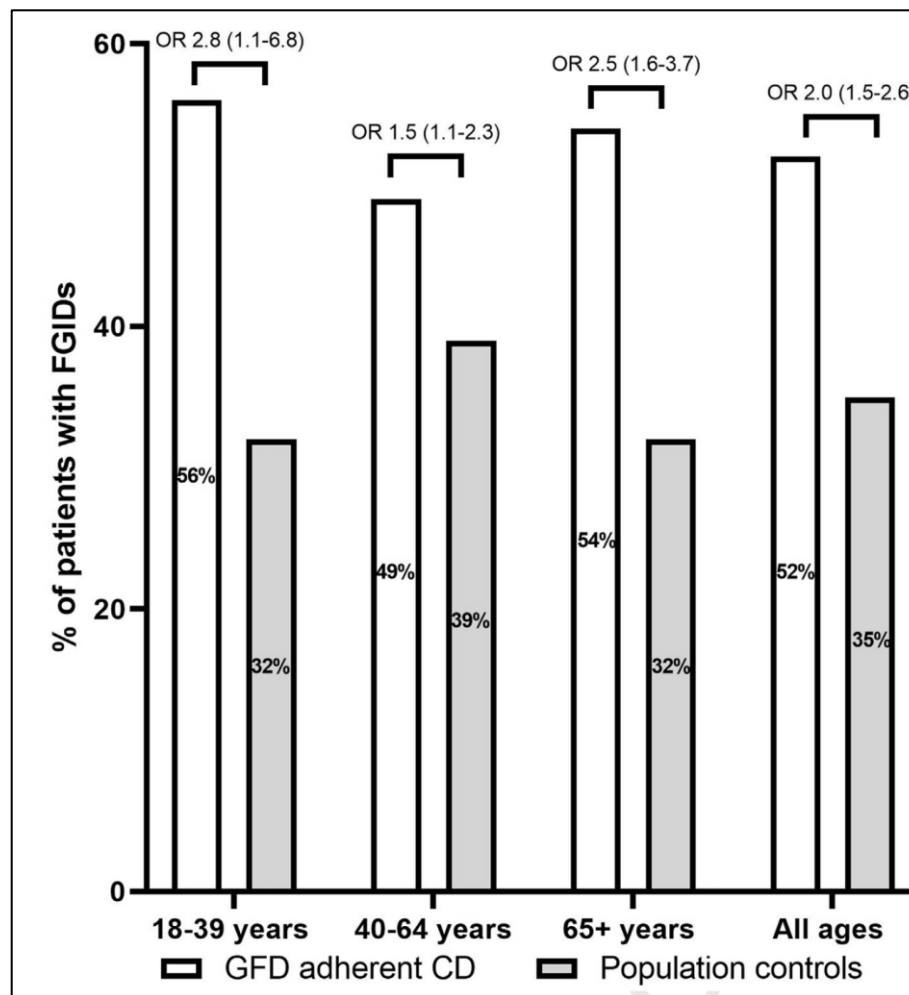
- Multinational cross-sectional study performed from 2014 to 2015
- Patients 4-18 years of age with CD on gluten-free diet for longer than 6 months were recruited from pediatric CD clinics in US and Italy
- Control groups included siblings of children with CD and unrelated controls. Subjects or parents completed the Rome III Questionnaire

Table I. Chronic AP and AP-FGID in children with CD, siblings, and unrelated children

	CD	Sibling	Unrelated	<i>P</i> value*	<i>P</i> value [†]	<i>P</i> value [‡]
Italy	43	43	44			
Chronic AP	20 (46%)	13 (30%)	15 (34%)	.18	.34	.88
AP-FGID	6 (14%)	4 (9%)	2 (4%)	.74	.16	.43
US	53	53	53			
Chronic AP	10 (19%)	9 (17%)	6 (11%)	.80	.42	.58
AP-FGID	2 (4%)	4 (8%)	0 (0%)	.68	.50	.12
Total	96	96	97			
Chronic AP	30 (31%)	22 (23%)	21 (22%)	.26	.18	.96
AP-FGID	8 (8%)	8 (8%)	2 (2%)	1.00	.06	.06



Functional Gastrointestinal Disorders and Associated Health Impairment in Individuals with Celiac Disease





Gluten and Functional Abdominal Pain Disorders in Children

Which factors concur to the development of FGIDs in celiac children?

- RESIDUAL INFLAMMATION
- VISCERAL HYPERALGESIA
- MICROBIOME ALTERATIONS
- PSYCHOLOGICAL FACTORS
- DIETARY FACTORS



Which factors concur to the development of FGIDs in celiac children?

Sensitizing medical events:

Distension

Inflammation
(infection,
allergies)

Motility
disorder



Sensitizing psychosocial events:

Depression
Anxiety

Family
stress

Coping
style

Secondary
gains

Abuse
history

Stress



The association of coeliac disease in childhood with functional gastrointestinal disorders: a prospective study in patients fulfilling Rome III criteria

- Children with celiac disease and FGIDs showed higher scores of the State-Trait Anxiety Inventory for Children (STAIC) demonstrating increased levels of anxiety when compared to those without FGIDs and to healthy controls

Table 2 | Psychological scores in coeliac disease (CD) patients and controls

Psychological scores	CD pts >6 years			Controls >6 years n = 31(%)	P
	Total n = 46 (%)	With FGIDs n = 17 (%)	Without FGIDs n = 29 (%)		
STAIC >35	10 (21.7)	7 (41.1)	3 (10.3)	1 (3.2)	0.022



Functional Gastrointestinal Disorders and Associated Health Impairment in Individuals with Celiac Disease

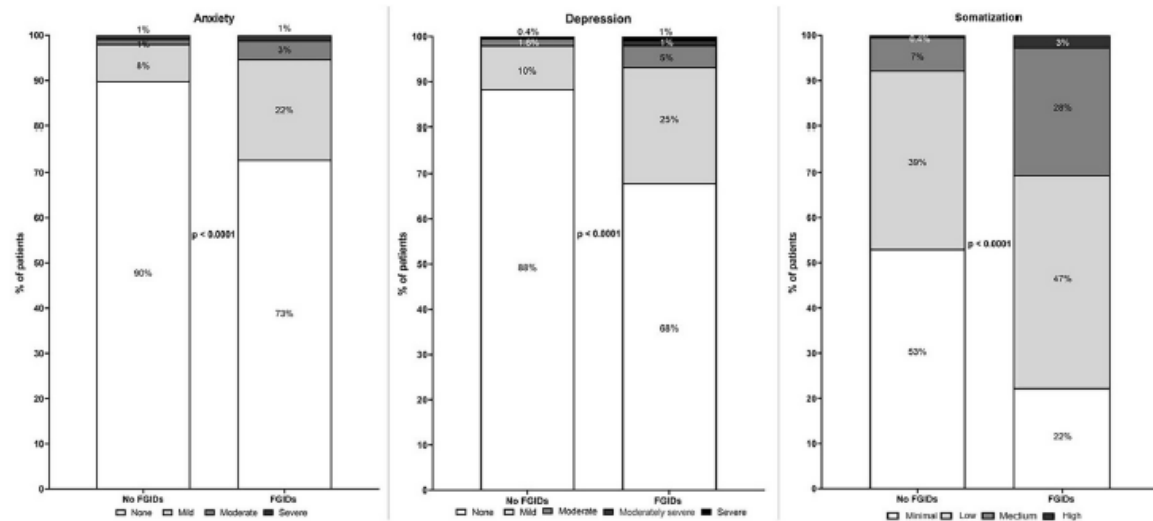
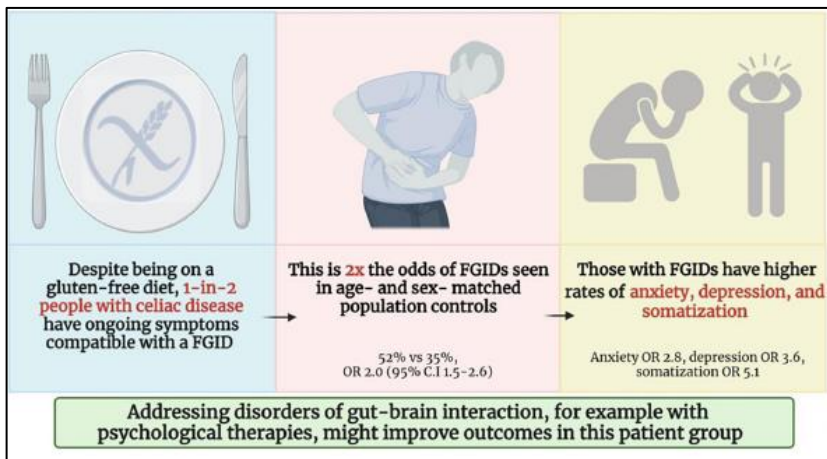


Figure 3. Levels of psychological distress and somatization in GFD-adherent subjects with CD, with and without associated FGIDs.



IBS and Celiac disease

TAKE HOME MESSAGES

- Screening for celiac disease may be worthwhile in children with chronic abdominal pain fulfilling Rome Criteria for FGIDs, mostly in those countries with high celiac prevalence;
- Children with celiac disease seems to be at risk of developing FGIDs after remission of disease induced by gluten free diet;
- Several factors may work concurring to persistent abdominal pain despite negative serology;
- Further studies are however needed in order to improve the care of these patients.