

An ESPGHAN Position Paper on the Use of Low-FODMAP Diet in Pediatric Gastroenterology

*R.A. Thomassen, †V. Luque, ‡A. Assa, §O. Borrelli, ||I. Broekaert, ¶J. Dolinsek, #J. Martin-de-Carpi, **E. Mas, ††E. Miele, ††L. Norsa, §§C. Ribes-Koninckx, ||||M. Deganello Saccomani, ¶¶M. Thomson, ##C. Tzivinikos, ***E. Verduci, †††J. Bronsky, †††N. Haiden, §§§J. Köglmeier, ||||B. de Koning, and ¶¶¶M.A. Benninga

ABSTRACT

Excluding oligo-, di-, monosaccharides and polyols (FODMAPs) from the diet is increasingly being used to treat children with gastrointestinal complaints. The aim of this position paper is to review the available evidence on the safety and efficacy of its use in children and provide *expert guidance regarding practical aspects in case its use is considered*. Members of the Gastroenterology Committee, the Nutrition Committee and the Allied Health Professionals Committee of the European Society for Pediatric Gastroenterology Hepatology and Nutrition contributed to this position paper. Clinical questions regarding initiation, introduction, duration, weaning, monitoring, professional guidance, safety and risks of the diet are addressed. A systematic literature search was performed from 2005 to May 2021 using PubMed, MEDLINE and Cochrane Database of Systematic Reviews. In the absence of evidence, recommendations reflect the expert opinion of the authors. The systematic literature search revealed that the low-FODMAP diet has not been comprehensively studied in children. Indications and contraindications of the use of the diet in different pediatric gastroenterological conditions are discussed and practical recommendations are formulated. There is scarce evidence to support the use of a low-FODMAP diet in children with Irritable Bowel Syndrome and no evidence to recommend its use in other gastrointestinal diseases and complaints in children. Awareness of how and when to use the diet is crucial, as a restrictive diet may impact nutritional adequacy and/or promote distorted eating in vulnerable subjects. The present article provides practical safety tips to be applied when the low-FODMAP diet is considered in children.

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From the *Department of Paediatric Medicine, Division of Paediatric and Adolescent Medicine, Oslo University Hospital, Norway, †Paediatric Nutrition and Development Research Unit, Serra Hunter Fellow, Universitat Rovira i Virgili-IISPV, Spain, ‡The Juliet Keidan institute of Pediatric Gastroenterology and Nutrition, Shaare Zedek Medical Center, The Hebrew University, Jerusalem, Israel, the §Department of Paediatric Gastroenterology, Great Ormond Street Hospital, London, UK, the ||Department of Paediatrics, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany, the ¶Department of Paediatrics, University Medical Centre Maribor, Maribor, Slovenia, the #Department of Paediatric Gastroenterology, Hepatology and Nutrition, Hospital Sant Joan de Déu, Barcelona, Spain, **Service de Gastroentérologie, Hépatologie, Nutrition, Diabétologie et Maladies Hérititaires du Métabolisme, Hôpital des Enfants, CHU de Toulouse, Toulouse, France; IRSD, Ormond Street Hospital, INSERM, INRAE, ENVT, UPS, Toulouse, France, the ††Department of Translational Medical Science, Section of Paediatrics, University of Naples “Federico II”, Naples, Italy, the †††Department of Paediatric Hepatol-

What Is Known

- Excluding Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols.
- (FODMAPs) from the diet is increasingly being used to treat children with various gastrointestinal complaints and disorders.

What Is New

- There is insufficient evidence to routinely recommend the use of the low-FODMAP diet to treat functional gastrointestinal disorders, non-celiac gluten sensitivity, inflammatory bowel diseases or small-intestinal bacterial overgrowth in children.
- Awareness of how and when to use the diet is crucial, as a restrictive diet may impact nutritional adequacy or promote distorted eating in vulnerable subjects.

INTRODUCTION TO THE LOW-FODMAP DIET: DEFINITION AND HISTORY

A low-FODMAP diet is characterized by a limited intake of short-chain carbohydrates that are poorly absorbed and highly fermentable in the small intestine as oligo-, di-, monosaccharides

ogy, Gastroenterology and Transplantation ASST Papa Giovanni XXIII, Bergamo, Italy, §§Paediatric Gastroenterology, Hepatology & Nutrition, La Fe University Hospital & Instituto de Investigacion Sanitaria La FE, Valencia, Spain, the ||||Department of Paediatrics, Woman’s & Child’s University Hospital of Verona, Italy, ¶¶Centre for Paediatric Gastroenterology, Sheffield Children’s Hospital, Sheffield, UK, the ##Department of Paediatric Gastroenterology, Al Jalila Children’s Specialty Hospital, Mohammed Bin Rashid University Of Medicine and Health Sciences, Dubai, UAE, the ***Department of Pediatrics, Ospedale dei Bambini Vittore Buzzi, University of Milan, Italy, the †††Department of Paediatrics, University Hospital Motol, Prague, Czech Republic, the †††Department of Clinical Pharmacology, Medical University of Vienna, Austria, the §§§Department of Paediatric Gastroenterology, Great Ormond Street Hospital, London, UK, the ||||Department of pediatric gastro-enterology, ErasmusMC Sophia Children’s Hospital, Rotterdam, The Netherlands, the ¶¶¶Department of Paediatric Gastroenterology and Nutrition, Emma Children’s Hospital, Amsterdam University Medical Centres, Amsterdam, The Netherlands.

and polyols (FODMAPs). Table 1 summarizes nutrients and compounds included in the FODMAPs definition as well as common foods containing these compounds, associated potential nutrient deficiencies and possible substitutes.

A low-FODMAP diet has, since its introduction by Gibson and Shepherd in 2005 (1), increased in popularity as a possible therapeutic alternative for several gastrointestinal (GI) disorders. The mechanistic hypothesis by which a low-FODMAP diet is used as a *possible* therapeutic alternative is that these poorly absorbed carbohydrates reach the colon undigested, where they are fermented by the colonic flora, leading to higher luminal osmolality and gas generation. In some people, this fermentation might lead to GI symptoms such as abdominal pain, flatulence, bloating and diarrhea, common in functional gastrointestinal disorders (FGID).

When a low-FODMAP diet is indicated as a potential treatment, patients are usually advised to exclude FODMAPs in a top-down approach, i.e. to exclude all FODMAPs and then to re-introduce one carbohydrate group at a time into the diet. The low-FODMAP diet consists of three phases: exclusion, re-introduction and maintenance, as the exclusion phase is not to be maintained indefinitely (2).

As FODMAPs are found in many common foods, especially in foods considered healthy, such as fruits, vegetables and pulses, awareness of how and when to use the diet is crucial, as a restrictive diet may impact nutritional adequacy or promote distorted eating in vulnerable subjects (3). Furthermore, clinical experience suggests there is great variability between subjects in how much and which FODMAPs are tolerated. Moreover, individual tolerance may change over time, thus complicating the establishment of dietary recommendations and implementation of the diet.

In the adult population, there is growing evidence of the effect of the low-FODMAP diet in reducing GI symptoms in patients with irritable bowel syndrome (IBS) (4). Although there is still a need for longer-term high-quality studies, the diet is recommended as a second-line therapeutic approach in adults with IBS by, amongst other groups, the American College of Gastroenterology and the British Dietetic Association (5,6).

Restriction of FODMAPs as a treatment for GI complaints in children has not been extensively studied. Therefore, the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) Gastroenterology Committee, the Nutrition Committee and the Allied Health Professionals Committee sought to answer key questions regarding the use of the low-FODMAP diet in children.

METHODS

A systematic literature search was performed from 2005 to May 2021 using PubMed, the MEDLINE and Cochrane Database of Systematic Reviews was performed by members of the Gastroenterology Committee, the Nutrition Committee and the Allied Health Professionals Committee of the ESPGHAN. The search terms, as well as the flow diagram of publications retrieved and included for analysis, are shown as supplementary online material (<http://links.lww.com/MPG/C855>). Results in Tables were stratified according to the study design. Statements were formed and the authors anonymously voted on each statement. A 9-point scale

was used (1 (strongly disagree) to 9 (fully agree)), and votes are reported in Table 5. It was decided in advance that consensus was reached if $\geq 75\%$ of the authors voted 6, 7, 8, or 9.

OVERVIEW OF THE EVIDENCE OF THE USE OF LOW-FODMAP DIET IN CHILDREN

From 53 publications and registers screened, 7 studies (4 randomized clinical trials (RCT) (8–11) and 3 interventions (12–14) without control group or observational studies) were included – all on functional abdominal pain disorders (Table 2). No pediatric studies were found on non-celiac gluten sensitivity (NCGS), small intestinal bacterial overgrowth (SIBO) or inflammatory bowel disease (IBD). Overall, from all studies, only 111 children received intervention with a low-FODMAP diet and 85 followed a control diet for comparison (healthy, or usual, or typical American for children).

INDICATIONS AND CONTRAINDICATIONS IN PEDIATRIC GI CONDITIONS

Functional Gastrointestinal Disorders (Functional Abdominal Pain, Functional Dyspepsia, Irritable Bowel Syndrome, Constipation, Infant Colic)

The pathophysiology of Functional Abdominal Pain Disorders (FAPDs) in children remains poorly understood. Different mechanisms have been proposed, including visceral hypersensitivity, gut microbiota dysbiosis, impaired mucosal immune function, dysmotility, altered central nervous system processing, psychosocial factors, and diet (15). In this context, a low-FODMAP diet gained interest in the treatment of FAPDs both in adults and children, as FODMAPs may induce gas generation which could potentially be responsible for the symptoms in FAPDs (16). Furthermore, beneficial effects of a low-FODMAP diet *may* also derive from changes in the gut microbiota and metabolism, endocrine cells, immune function, and intestinal barrier, although scientific evidence is, to date, lacking (17–19).

In an open-label study evaluating the effect of a low-FODMAP diet in 8 children with IBS, four children (50%), defined as responders, showed $>50\%$ decrease in abdominal pain frequency while on a low-FODMAPs diet (14). These preliminary results were later confirmed by the same group in a double-blind, crossover trial (11) of 33 children with IBS randomized to either a low-FODMAP diet or a typical American childhood diet (TACD) for 48 h, followed by a 5-day washout period before crossing over to the other diet. Fewer episodes of abdominal pain were reported in children on a low-FODMAP diet compared to children on TACD and baseline. From 33 subjects, 8 (24.2%) were categorized as Responders (significant improvement with low-FODMAP diet only), 15 (45.5%) as non-Responders (not significant improvement), and 10 (30.3%) as Placebo-responders (improved on both diets or only on the TACD diets).

A more recent open-label study evaluated the effect of the low-FODMAPs diet on symptoms in 20 children with FAPDs (FAP,

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Address correspondence and reprint requests to R.A. Thomassen, Department of Paediatric Medicine, Division of Paediatric and Adolescent Medicine, Oslo University Hospital, Norway (email: uxruom@ous-hf.no); and V. Luque, Pediatrics Nutrition and Development Research Unit, Universitat Rovira i Virgili, Spain (email: veronica.luque@urv.cat).

R.A. Thomassen and V.Luque share first authorship.

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TABLE 1. Low-FODMAPs diet definition, nutrients at risk and possible substitutes

Nutrients & compounds	Foods containing these compounds	Nutrients at risk	Possible substitutes (portion control needed)
F	Fermentable		
O	Oligosaccharides: Fructans, fructooligosaccharides (oligo fructose) and Galactooligosaccharides (raffinose, stachyose)	The exclusion of vegetables may lead to a reduction in fiber and natural antioxidants, such as flavonoids, carotenoids, vitamin C, phenolic acid and anthocyanin (7) Reduction in carbohydrate, fiber, and iron intake. Wheat is a major source of phenolic acids (7)	Vegetables: asparagus, bamboo shoot, bok choy, carrot, celery, chives, choko, choy sum, cucumber, eggplant, endive leaves, green bean, lettuce, parsnip, radish, silverbeet, chicory leaves, kale, spinach, Swiss chard, tomato, red and green pepper. Cereals: spelt and wholemeal sourdough fresh bread*, gluten-free couscous, gluten-free flakes, gluten-free pasta, corn tortillas, flour (maize, millet, quinoa, rice, spelt), oats, polenta, potato, rice noodles. Fruits: apple, cherries, clementine, durian, dragon fruit, grapes, kiwi, mandarin, mango, orange, papaya, peach, pineapple, strawberry Nuts and seeds: Brazil nuts, macadamia, peanuts, pecan, seeds (sunflower, pumpkin), walnuts
D	Disaccharides (lactose)	The exclusion of dairy products may favor vitamin D and calcium deficiency (7)	Lactose-free milk, rice beverage, lactose-free yogurts, and hard cheeses
M	Monosaccharides (fructose free or as glucose excess)	The exclusion of fruits may lead to a reduction in natural antioxidants, such as flavonoids or vitamin C (7)	Fruits: apricot, avocado, banana, blackberry, blueberry, clementine, coconut, cumquats, currants, dragon fruit, durian, grapes, kiwi, lemon juice, mandarin, melon, nectarine, orange, papaya, passion fruit, persimmon, pineapple, rhubarb, strawberry. Honey substitutes: golden syrup, maple syrup. Vegetables: asparagus, cauliflower, cucumber, green beans, endive leaves, kale, leek bulb, lettuce, marrow, mushrooms (canned), onion, parsnip, pumpkin, radish, spinach, Swiss chard, tomato, zucchini (marrow). Sweeteners: any sweeteners except polyols
A	And		
P	Polyols (Sorbitol, mannitol, maltitol, xylitol)	The exclusion of vegetables and fruits may lead to a reduction in natural antioxidants, such as flavonoids, carotenoids, vitamin C, phenolic acid and anthocyanin (7)	Fruits: banana, blueberry, carambola, durian, grape, grapefruit, honeydew melon, kiwi, lemon, lime, mango, melon, orange, passion fruit, pineapple, raspberry, strawberry, tangelo, cantaloupe. Vegetables: carrot, radish, lettuce, red pepper, spinach, tomato, zucchini (marrow). Sweeteners: glucose, other artificial sweeteners not ending in “-ol”

The table can be used as a base for diet sheets. *Data obtained from:* <https://www.monashfodmap.com/> accessed on 20 June 2021. Possible substitutes are expected to be tolerated in small amounts (usually ≤75g according to the Monash University FODMAP Diet database). Several possible substitutes are only introduced in the diet when a certain nutrient has been reintroduced for tolerance. Underlined vegetables and fruits are those that would be introduced in the low-FODMAP diet at any time if the portion consumed in a meal is limited (usually ≤75g) as a unique FODMAP source, and therefore, those would be potential substitutes. *Certified low-FODMAP varieties only, check the producer.

TABLE 2. Summary of findings from the systematic review on the effect of low-FODMAP diet in children

Non-RCT references	Participants N, age, characteristic	Intervention & comparison (group size), duration	Outcomes	Tools & statistics used	Results
<i>Dogan G et al 2020</i> (8)	n = 60 Age: 6–18 y IBS (Rome IV)	LFD vs. protective standard diet, 2 months (n = 30 per group)	Patient-reported abdominal pain; Doctor assessed Clinical GI Improvement after 2 months of treatment, and follow-up at 4 months (after 2 months without treatment)	Visualanalogsscale (VAS); Clinical Global Impression Improvement (CGI-I)	Decrease in VAS 3.8 ± 1.1 (LFD) vs. 2.3 ± 1.0 (control) $P < 0.001$. Decrease in CGI-I LFD vs. control ($P < 0.001$). At 4m: a higher increase in VAS for the LFD group (2.97 ± 1.10 vs. 1.63 ± 0.71) & lower CGI-I still persisted ($P < 0.001$). Non-adjusted analyses.
<i>Nogay NH et al 2020</i> (9)	n = 15 Age: 6–17y ASD with constipation and/or abdominal pain (ROME IV)	LFD (n = 7) + control (usual) diet (n = 8), 2 weeks Provided by a dietician	GI and behavioral problems Quality of Life	PedsQL, ABC-C, PedsQL	Statistically significant improvement in GI symptoms (stomach pain, nausea and vomiting, constipation, gas bloating), and worry about stomachache and bowel movements. Non-adjusted analyses.
<i>Boradyn KM et al 2020</i> (10)	n = 27 Age: 5–12 y FAP	LFD (n = 13) vs. NICE (n = 14), 4 weeks	Easiness to follow the diet, symptoms improvement, stools consistency, frequency and intensity of abdominal pain	Wong-Baker FACES pain scale; Bristol scale; changes rated as improvement vs. no improvement.	Easy to follow low-FODMAP 38% of parents vs. NICE 57% of parents ($P = 0.017$); similar efficacy on symptoms reduction with the two diets (reported by parents). % of patients improving in all symptoms were higher for NICE (but not statistically significant). Non-adjusted analyses.
<i>Chumpitazi BP et al 2015</i> (11)	n = 33 Age: 7–17 y IBS (Rome III)	LFD vs. TACD (crossover n = 16 and n = 17), 2 days	Children pain episodes; microbiota analyses. GI symptoms (abdominal discomfort, bloating, flatus, nausea, heartburn) were captured using a 0–10 Likert scale	Pain and Stool Diary 7 days prior to intervention and 2 days at the end of each intervention	Fewer pain episodes per day during the LFD compared to the TACD (1.1 ± 0.2 vs. 1.7 ± 0.4) $P < 0.05$; Eight subjects were categorized as Responders (significant improvement with LFD only), 15 as non-Responders (not significant improvement), and 10 as Placebo-responders (improved on both diets or only on the TACD diets). Non-adjusted analyses.
Non RCT References	Participants N, age characteristics	Study description (diet duration)	Outcomes	Tools used	Results
<i>Cyrkot et al 2021</i> (12)	n = 138 Age: 5–18y n = 46 with CD, n = 46 with mild chronic GI complaints, n = 46 HC	Case controls, observational, cross-sectional, comparing FODMAPs intake (observation of intake for 2 days)	GI symptoms, QoL	GI symptoms (present or absence of GI symptoms & PedsQL, GSS (scores 0–100 for severity), QoL (PedsQL & HRQOL)	No association between FODMAP intake and GI symptoms in CD. High FODMAP intake was positively associated with GSS scores in GIC ($P = 0.02$), FODMAP intake was positively associated with HRQOL in CD and GIC children ($P < 0.05$). In particular, high sorbitol intake was positively associated with child HRQOL. Analyses adjusted by age and gender, or energy intake when appropriate
<i>Baranguán Castro ML et al 2019</i> (13)	n = 22 (20 finished) Age: 8–12 y FAP	Prospective observational, clinical intervention with LFD diet (2 weeks), pre-post assessment without randomization nor control	Abdominal pain (number and intensity), interference with normal life, Stools consistency, accompanying symptoms for 3 days	Visual analog scale for intensity, Likert scale for interference with normal life, Bristol scale.	Fewer daily abdominal pain episodes compared to baseline (1.16 (0.41 – 3.33) vs. 2 (1.33 – 6.33), $P = 0.024$), less pain severity (1.41 (0.32 – 5.23) vs. 4.63 cm (2.51 – 6.39) $P = 0.035$), less interference with daily activities, and less GI symptoms. 15% found it difficult to follow the diet. Non-adjusted analyses.

Continued

TABLE 2. Continued

Non-RCT references	Participants N, age, characteristic	Intervention & comparison (group size), duration	Outcomes	Tools & statistics used	Results
Chumpitazi BP et al 2014 (14)	Children, n = 12 enrolled (n = 8 followed the intervention and fulfilled the forms) Age: 7-16y IBS	Pilot intervention study; LFD (1 week). Provided by a registered dietician	Pain symptoms, stooling characteristics, breath hydrogen and methane, whole intestinal transit time, stool microbiome, and metabolite composition	Pain and stool diary (7 days); pain ratings (validated 0-10 scale). Bristol stool form scale; 14 hourly breath samples. Transit time by carmine red pill ingestion and subsequent discoloration in stools; responders were defined as having a $\geq 50\%$ decrease in pain frequency in response to the LFD.	N = 4 (50%) were classified as responders. Significant decrease in: number & intensity of pain episodes, episodes interfering with activity. No changes in stool form, transit time, hydrogen & methane production. Non-adjusted analyses.

RCT = Randomized Clinical Trial; IBS Irritable bowel syndrome; CD = celiac disease; HC = healthy controls; LFD = low-FODMAP diet; QoL = Quality of Life; PedsQL = Pediatric Quality of Life Inventory; HRQOL = Health-Related Quality of Life; GSS = GI Symptom Scale; ASD = Autism Spectrum Disorder; ABC-C = Aberrant Behavior Checklist-Community; TACD = Traditional American Children diet; FAP = Functional Abdominal Pain; NICE = dietary recommendations from the National Institute for Health and Care Excellence.

IBS, or functional dyspepsia) (13). After two weeks of a low-FODMAPs diet, children showed a significant reduction in the daily number of abdominal pain episodes from 2 to 1.16, as well as a reduction in the intensity of abdominal pain as measured with the 10-cm VAS, from 4.63 to 1.41.

A double-blind, randomized, controlled, single-center trial evaluated the effectiveness of the low-FODMAP diet in reducing gastrointestinal symptoms in 27 children with functional abdominal pain (FAP) (10). Patients were randomized to a low-FODMAP diet or a diet based on the National Institute for Health and Care Excellence (NICE) guidelines for 4 weeks. There was a tendency toward improvement in the abdominal pain intensity and frequency in the low-FODMAP group. Nevertheless, these findings did not reach statistical significance. The NICE group reported a significant reduction of symptoms throughout consecutive weeks of the diet. In contrast to previous studies which did not have a control group on a normal diet (13,14), no significant differences were observed in the abdominal pain intensity and frequency between the 2 groups and no significant change was seen in stool frequency.

A randomized, double-blind, crossover study assessed the effect of a maternal low-FODMAP diet compared to a typical Australian diet on infant crying-fussing durations of infants with colic. Mothers consumed a 10-day low-FODMAP or typical Australian diet, then alternated without washout. Mean crying-fussing durations fell by a median of 32% on the low-FODMAP diet, significantly more compared with 20% on the typical Australian diet. This finding was not related to changes in maternal psychological status, infant feces, or gross changes in breast milk. Indeed, in breast milk, lactose concentrations remained stable and other known dietary FODMAPs were not detected (20). As the intervention did not modify maternal milk content, and infantile colic could be a physiological maturation process, the reported improvement on infant's wellbeing could simply be due to the infants' maturation or a placebo effect on the mother.

Overall, studies were not adjusted for possibly relevant confounders such as gender, age, level of adherence to the diet or the quality of the diet.

In conclusion, the evidence regarding the effectiveness of the low-FODMAPs diet in the treatment of FGID in children is currently insufficient to guide clinical practice.

Non-Celiac Gluten Sensitivity

Celiac disease, wheat allergy, and non-celiac gluten sensitivity (NCGS) are gluten-related disorders. Unlike celiac disease or wheat allergy, allergic or immune phenomena cannot be demonstrated in patients with NCGS. Moreover, not only gluten but also, lipopolysaccharides, amylase/trypsin inhibitors, wheat germ agglutinins and FODMAPs are considered to be potentially responsible for NCGS. Although affected individuals experience symptoms of bloating, abdominal pain, alternating bowel habits and flatus following the ingestion of wheat or gluten, the effect of a wheat or gluten challenge in patients with suspected NCGS is inconsistently reported in the literature (21). Wheat is not only rich in gluten but also FODMAPs. Studies in adults suggest that a low-FODMAP diet may be associated with symptom reduction in NCGS patients (22-24) and that particularly fructans may be a major trigger for clinical symptoms in patients reporting gluten intolerance (24). The true prevalence of NCGS in children is unknown, as data are based on patient-reported symptoms rather than objective biomarkers and few studies focus on children (25). Whilst there is some evidence to suggest the avoidance of FODMAPs in adult patients with NCGS, data supporting a similar recommendation in children are missing.

Inflammatory Bowel Disease

The potential efficacy of a low-FODMAP diet in patients with IBD has been studied in the adult population (26,27). A systematic review from 2018 performed in adults concluded that adherence to a low-FODMAP diet resulted in significant improvement of common symptoms such as diarrhea, abdominal pain, fatigue, and nausea (28) but had no effect on clinical activity indexes or objective inflammatory markers. Currently, no data exist on the use of a low-FODMAP diet in children with IBD.

Small Intestinal Bacterial Overgrowth (SIBO)

The most common manifestations reported in patients with SIBO are abdominal pain, abdominal distension, flatulence and diarrhea (29). These signs and symptoms are nonspecific and may overlap with manifestations of IBS or other FGID. Several studies reported that SIBO might be a frequent underlying diagnosis in children with FGID (30–32). The underlying hypothesis for using a low-FODMAP diet to treat patients with SIBO is that the diet may modify the intestinal flora and hence reduce the fermentation and gas production (33,34). Considering the pathogenesis of SIBO, which involves excessive bacterial growth within the small intestine, there is a biological plausibility that a low-FODMAP diet may play a beneficial role in the treatment of SIBO by reducing the fermentable substrates in the small bowel for the bacterial biomass (35). However, to date, there are no available studies assessing the impact of a low-FODMAP diet on small intestinal bacterial overgrowth (SIBO).

In conclusion, further studies are needed to specifically elucidate the role of the low-FODMAP diet in the treatment of SIBO.

In summary, the available evidence on the efficiency of a low-FODMAP diet in pediatric GI disorders/conditions is scarce. Only a decrease in pain episodes and frequency has been described in small samples of children with IBS. However, when compared to a healthy diet, there were no differences, and when analyzing the proportion of responders to treatment or how much abdominal pain interfered with daily life activities, the results were weak.

MICROBIOTA IMPLICATIONS OF THE LOW-FODMAP DIET IN PEDIATRIC PATIENTS

The microbiota has been related to the use of a low-FODMAP diet at different levels, discussed below: (a) potential etiological factor and possible trigger of symptoms (b) microbiota changes caused by the dietary intervention and (c) determinant of response to the low-FODMAP diet.

Microbiota as a Possible Etiological Factor

Rajilić-Stojanović et al reported an approximately twofold increase in the *Firmicutes/Bacteroidetes* ratio as the major bacterial phyla in 62 adults with IBS compared with 46 healthy subjects (36). This finding has been observed in several other studies, in which the abundance of *Firmicutes* was enriched together with a reduced abundance of *Bacteroidetes* in subjects with IBS compared with healthy subjects (37,38).

Changes in Microbiota Produced by a Low-FODMAP Diet

Naseri et al (38) reported that a dietary intervention with a low-FODMAP diet was associated with changes in the microbial communities among IBS patients. The ratio of *Firmicutes* to *Bacteroidetes* was significantly decreased ($P = 0.001$) after the dietary intervention. Moreover, several RCTs have reported that a Low-FODMAP diet resulted in a short-term reduction of *Bifidobacteria* (39–43).

However, long-term changes in *Bifidobacteria* were not found in a recently published RCT of adults with IBS, adherent to a Low-FODMAP diet (44). Instead, there was a marked reduction in the relative abundance of *Bacteroides spp.* and, at the species level, of *F. prausnitzii*.

Moreover, the authors reported the effects of a low-FODMAP diet on stool microbial metabolite concentrations in the long term, by reductions in short-chain fatty acids (SCFAs). These data are of potential concern given the role of SCFAs in intestinal permeability, immunomodulation, and secretory functions in the gut. This was confirmed in a study by Zhang Y et al (45). They found a reduction of bacteria typical of carbohydrate fermentation (*Bifidobacterium* and *Bacteroidetes*) in patients responding to a low-FODMAP diet. As a consequence, a reduction of SCFAs and gas production was also observed. They also noted a reduction in *Fusobacterium*, a proinflammatory bacterium.

Microbiota as a Factor of Response to a Low-FODMAP Diet

In the aforementioned study conducted by Zhang Y et al (45), patients with IBS who responded to a low-FODMAP diet presented a high fermentation index before the treatment. Fecal samples contained a high percentage of acetic acid and a low percentage of butyric acid, indicative of dysbiosis. As a result, the authors suggested quantifying the fecal SCFAs before starting a Low-FODMAP diet to identify patients with IBS who would be more likely to respond to the intervention.

Some authors have tried to identify microbiota-based biomarkers that could predict response to a low-FODMAP diet (46,47). Data from 5 distinct studies showed that the patients' response to a low-FODMAP diet was predictable from the fecal microbiome before starting the diet. The authors proposed that the diet should be recommended to patients with high colonic methane and SCFAs production.

Literature in children is scanty. In the randomized cross-over clinical trial published in 2015 by Chumpitazi BP et al (11), children with IBS were assigned to the low-FODMAP diet or a Typical American Childhood Diet (TACD) for 48h. Results showed that both baseline gut microbiome composition and microbial metabolic capacity were associated with the low-FODMAP diet efficacy. Indeed, the operational taxonomic units (OTUs; sequences that share $\geq 97\%$ similarity) were enriched at baseline with greater saccharolytic metabolic capacity within the *Bacteroidaceae* family (e.g. *Bacteroides*), *Clostridiales* order (e.g. *Ruminococcaceae*, *Dorea*, and *Faecalibacterium prausnitzii*), and family *Erysipelotrichaceae* in children who responded to the low-FODMAP diet. Non-Responders were uniquely enriched at baseline with the *Turicibacter* genus from the *Turicibacteraceae* family. These findings suggest that the identification of microbiota with greater saccharolytic capacity may serve as a biomarker of responsiveness to a low-FODMAP diet in children with IBS.

Recently, the same authors tried to provide a biomarker of response to a low-FODMAP diet by profiling fecal microbiota in children with IBS through a cross over provocation using fructans (a FODMAP) and maltodextrin (placebo) solutions (48). Those classified as 'fructan-sensitive' differed in their fecal microbiota on alpha diversity, and abundances of *Holdermantia* and 14 Clostridial genera from those deemed 'fructan-tolerant'. Furthermore, fructan-sensitive children with IBS appeared to have different gut microbiome responses (composition and abundances) when given fructans compared to fructan-tolerant children. Authors suggested that future studies may investigate

the potential role of fructan-derived microbial fecal metabolites on both symptoms and IBS-relevant physiologic factors (e.g. colonic motility).

Thus, clinical trials are needed to determine whether these observations can be converted into a tool to perform indications to a low-FODMAP diet to potentially responsive candidates. At the moment, the methodology used to define fructan sensitivity is not standardized (49).

In summary, certain bacteria have a greater FODMAPs fermentation capacity, which may trigger undesirable symptoms. Thus, treatment with a low-FODMAP diet could promote changes in these species, reducing fermentation products, gas production and pain. The identification of microbiota with greater fermentation capacity may serve as a biomarker of responsiveness to a low-FODMAP diet.

SAFETY AND RISKS OF THE LOW-FODMAP DIET IN PEDIATRIC PATIENTS

The main potential risks include nutritional deficiencies and psychosocial implications of following a very restrictive diet.

Nutritional Deficiencies

The low-FODMAP diet requires the exclusion of long lists of plant foods as well as dairy foods, and therefore, could lead to nutrient deficiencies. Data regarding macro- and micro-nutrient intakes during a low-FODMAP diet derived from both pediatric and adult-based studies are limited. In the aforementioned double-blind, crossover pediatric trial comparing a low-FODMAP diet and TACD, no differences in the intake of total energy, carbohydrates, protein and fiber were observed (11).

In a pediatric RCT (9) of patients with autistic spectrum disorder, intake of micronutrients was not different between the low-FODMAP group and control group (habitual diet), except for the intake of vitamin B12, which was marginally lower in the low-FODMAP diet group. Nevertheless, energy, protein, and carbohydrate intake were lower in the low-FODMAP diet group at follow-up compared with baseline as well as lower intake of folate and sodium.

In adult patients with IBS, Staudacher et al found no difference in micronutrient intake compared with controls, except for a lower calcium intake (7), presumably due to a reduced intake of dairy foods. The same mechanism may cause lower vitamin D intake and thus may pose a risk for vitamin D deficiency in specific populations (high-risk geographic regions and dark skin) (50). However, a prospective long-term follow-up study of 103 adult patients with IBS, in which 84 patients adhered to a low-FODMAP diet for 6–18 months, demonstrated that macro- and micro-nutrient intake, including calcium intake, were no different from habitual diet (51). In a comparative study between two different diets in adults with IBS, a statistically significant reduction in mean daily intake was seen in thiamin, riboflavin, calcium, and sodium, after a 4-week low-FODMAP diet. However, when looking at energy-adjusted micronutrient intake for the low-FODMAPs group, the only decrease in intake observed was for riboflavin (52). Another study in adult patients with IBS which compared low-FODMAP diet to habitual diet demonstrated that intake of micronutrients was not different between groups, except for the intake of selenium and vitamin B12, which were both higher in the low-FODMAPs group (7). Several studies, including three RCTs, showed that fiber and protein intake are not different when compared with control patients, including the proportion of patients meeting the recommended intake (39,53,54). These studies also reported an overall adequate energy intake.

It may be concluded that a dietician-supervised low-FODMAP diet does not significantly compromise nutrient intake, despite the restriction of many nutrient-rich foods across several food groups, suggesting that it can be implemented for a limited time period without major nutritional concerns. However, access to dietitians trained in the low-FODMAP diet may be difficult. Training and guidelines are therefore urgently needed if the diet is to be adopted more widely in the pediatric population. In the absence of trained health professionals there is a risk that parents introduce the diet to their children following the guidance of peers and social media.

Psychosocial Implications of low-FODMAP Diet

In a systematic review of adult patients with celiac disease (55), IBS, and IBD, a prevalence between 5 and 44% of eating disorders was found. The authors hypothesized that gastrointestinal symptoms in patients with eating disorders may result in an aversion to foods and alterations in dietary patterns. Vulnerable subjects are anxious about unfamiliar foods or preparation and avoidance of food-related social situations. Such traits are typical of orthorexia nervosa and can be found in patients who are strongly adherent to diet therapy. Unfortunately, there is scanty evidence assessing the psychological conditions and well-being of these patients.

Mari et al (56) recently evaluated eating disorder behavior using the Sick Control One stone Fat Food (SCOFF) questionnaire in adults with IBS who were instructed to commence a low-FODMAP diet. Based on the SCOFF results and measured adherence, the authors suggested that strict adherence to a low-FODMAP diet should raise the suspicion of a possible underlying eating disorder in particularly orthorexia nervosa. Chumpitazi et al (57) in their commentary to this study pinpointed that the SCOFF instrument is a screening questionnaire and not the gold standard for diagnosis of an eating disorder or the presence of eating disorder behavior.

However, whilst being aware of a possible eating disorder in any population is certainly important, particularly when dietary modification is advised, one should be careful. Social implications may also occur as the limited choice in ready-to-eat processed foods may hinder the duration of longer traveling for example (58).

Finally, Scarlata K (59) reported that avoidant restrictive food intake disorder (ARFID) in relation to IBS is emerging among adults. These data underline the importance of assessing nutritional status and risk of maladaptive eating in this population, as well as the need for evidence-based guidelines for practice. A screening tool to detect ARFID is still lacking for patients with IBS. And, as food-related fear and avoidance are found in people with food intolerances, the authors suggested including a psychologist in the personalized nutritional approach.

It is recommended that if the patient already has modified or restricted his or her eating habits, a thorough evaluation to establish the presence of maladaptive eating about weight loss, energy intake, nutrient intake, eating behaviors, psychological distress, patients' beliefs or attitudes should be performed.

In conclusion, in children with ongoing IBS symptoms, a low-FODMAP diet can be considered, under the expert supervision of a specialized dietician, only when the risk of eating disorders is low (using disorder eating screening) and when feeding difficulties, such as food refusal and selective eating, are minimal, and hence appropriate low-FODMAPs substitute foods will be accepted (3).

PRACTICAL ASPECTS

Recommended Assessment before Initiation of the Diet

Based on an accurate and detailed clinical history and physical examination to establish classical ‘red-flag’ symptoms, a practical clinical approach should be straightforward and guide the pediatrician/pediatric gastroenterologist in the decision of whether investigations are necessary or not. When significant pathologies are a potential differential diagnosis (Table 3), children should be referred to a pediatric GI team before the introduction of a low-FODMAP diet. A review by a multidisciplinary GI team should include assessment of nutritional status, objective observation of symptoms, and where appropriate, specific investigations according to the child’s clinical presentation. In suspected FGID, the detailed history and physical examination with focus on the presence of red flags (see Table 4) is the core of the diagnostic process.

Assessment of Symptoms

Once a decision has been made that a child may be a potential candidate for a low-FODMAP diet, the current symptoms, their severity and frequency of occurrence, and how these impact the child’s quality of life should be documented. Ideally, a standardized questionnaire should be used before and following the start

TABLE 3. Pathologies that should be discarded before the initiation of a low-FODMAP diet

- GERD
- Gastritis and peptic ulcer disease (*H pylori* related or not)
- Allergic gastrointestinal inflammation/ dysmotility
- Celiac disease
- Food allergy (e.g. cow’s milk protein allergy)
- Inflammatory bowel disease
- Pancreatic exocrine insufficiency
- Giardia infection
- Disaccharides’ deficiency
- Fructose intolerance
- Abdominal migraine
- Pediatric intestinal pseudo-obstruction

TABLE 4. Red flags as core diagnostic of functional gastrointestinal disorders

Abdominal pain
Nausea and vomiting
Faltering growth
Micronutrient deficiencies
Mouth ulcers
Systemic symptoms such as anemia
Blood/mucous in the stools
Profuse diarrhea
Significant constipation
Dysphagia

Before the initiation of a low-FODMAP diet, relevant GI pathology should be ruled out (Table 3).

of the diet to assess objectively the effect of the low-FODMAP diet. Validated tools such as the Pediatric Quality of Life Inventory (PedsQL) Gastrointestinal Symptoms and Gastrointestinal Worry Scales are available (60). These allow a detailed analysis of multiple GI symptoms in the child and can be used both for the assessment of functional as well as organic GI disorders. Both parents and children of five years of age and above can complete the questionnaire. The PedsQL Family Information Form can be used in addition to obtain useful information about demographics such as the child’s age, gender, ethnic background and parenteral education, which may help decide if a low-FODMAP diet is feasible and realistic to achieve (60). The PedsQL forms can be obtained from the website <https://eprovide.mapi-trust.org>.

Dietetic Interview and Risk Assessment

After an initial screening process by the pediatrician, a dietitian should carry out a thorough assessment of the child’s dietary intake to highlight any potential deficiencies, which could be exacerbated by the restrictions of the low-FODMAP diet. The concept of low-FODMAPs should be discussed and the dietitian should establish what foods high in FODMAPs the child is eating. Foods to be avoided on a low-FODMAP diet should be discussed with the parents along with advice on suitable replacement foods to ensure adequate nutritional intake.

Potential difficulties, such as providing a suitable lunch at school or what to do when the child is staying at a friend’s house need to be addressed to increase diet adherence (55–57,61,62). The quality of the child’s current diet, level or parenteral understanding and psychosocial background should be included in the evaluation of whether the patient is a candidate for trying the low-FODMAP diet or not. Written information about FODMAPs sources and suitable replacement foods and, if required, a meal plan will minimize diet mistakes and the risk of offering a diet insufficient in essential nutrients.

Introduction, Duration and Weaning of the Dietary Restrictions in Children

The duration of the low-FODMAP diet in children should be analyzed in terms of the minimum time required for efficacy, maximum time accepted for feasibility, and nutritional risks.

As outlined in the ‘‘Review of the evidence’’ section of this manuscript, there are only four RCTs on low-FODMAP diet in children with IBS or FAP (8–11). In these RCTs, (frequently after a baseline or wash-out period), children were randomized to a low-FODMAP diet (or a control diet) for 2 days to 2 months. These studies showed that the low-FODMAP diet decreased abdominal pain, compared to baseline and to the TACD, but not compared to a healthy diet.

Evidence on low-FODMAP diet’s duration is also lacking for adult patients with IBS. The American College of Gastroenterology in the latest guidelines on IBS recommended a limited trial of 4–6 weeks of low-FODMAP diet (63). The recommendation, graded as conditional with very low quality of evidence, was based on a meta-analysis of 7 RCTs on FODMAPs in IBS (64). The panel of experts acknowledged that RCTs mainly focused on the FODMAPs restriction phase. From those studies, it could be evincible that responders to the diet could be identified within 2–6 weeks. However, RCTs on low-FODMAPs in IBS have high risks of bias with no standardization of the diet nor study of the re-introduction phase (65). On a low-FODMAP diet, there is an improvement of IBS score in 75% of adult patients (66). Meanwhile, an improvement of about 70%, after 6 weeks of low-FODMAP diet, was similar to that of gut-directed hypnotherapy; this improvement was maintained after 6-months follow-up (67). One recent study

in children (8) used a 2-months intervention with a low-FODMAP diet. Participants reported not being able to continue longer with such a restrictive diet. In summary, when instituting a low-FODMAP diet in children, the effect should be checked after 2–4 weeks. If there is symptom relief, the diet period may be continued for a total of 4–6 weeks before re-introduction.

There is a lack of data on the re-introduction of FODMAPs. Based on clinical expertise, the principles of the low-FODMAP diet and the re-introduction phase are to identify triggers, to decrease the restrictive diet and to increase prebiotic intake (66,68). Patients who report a clinical improvement during the low-FODMAP diet should re-introduce one FODMAP subgroup at a time, e.g. one challenge for 3 days and then a break of 2–3 days. Some suggested foods such as milk for lactose or honey for fructose, in amounts of 1 teaspoon on the first day to 2 teaspoons on the 3rd day. The tolerance of challenged foods could be improved if they are consumed every other day. Such a protocol could help to determine tolerance threshold and to maintain the durability of response (67).

Furthermore, there are several criticisms concerning low-FODMAP diet in children which could affect duration: the lack of specific cutoff levels for FODMAPs content, the paucity of data on safety and long-term efficacy and the possible impact on nutrient intake and on psychosocial outcomes (62).

In order to fill this important research gap on the tolerability of 4 weeks low-FODMAP diet in children, a specific RCT has been designed planning to enroll 77 children with functional abdominal pain disorders (FAPDs). The data collection is still ongoing (69).

Monitoring of Nutrients during the Dietary Treatment

The low-FODMAP diet is restrictive and therefore thoughtful consideration should be given prior to its initiation to ensure that nutritional status is not compromised. The substitution of selected foods across several food groups may result in inadequate intake of nutrients, particularly carbohydrates, fiber, iron, B vitamins, and calcium. Table 1 shows a list of potential nutritional risks and possible food substitutes. It is worth highlighting that, there is scarce evidence on potential nutrient deficiencies when following a low-FODMAP diet and, even when suitable substitutes are used, nutrient deficiencies may still occur. The diet should be commenced and followed under a specialized dietician's advice while dietary intake and body mass index should be monitored routinely, especially if the diet is employed for long periods of time. Vitamin D and Calcium intake and status should be assessed and supplemented if required. A schema of a low-FODMAP diet considering all necessary food groups can be found as Supplementary on-line material (<http://links.lww.com/MPG/C855>).

Description of Professional Guidance during the Dietary Treatment

Implementation of a low-FODMAP diet is ideally a multi-disciplinary holistic approach with many factors taken into consideration including nutritional and growth requirements as well as the psychosocial environment.

A restricted diet such as the low-FODMAP diet in children and adolescents needs to be instituted and supervised mainly by a specialized pediatric dietitian trained in the use of this diet, directed by a detailed history of the patient and tailored to the individual needs (19). After the appropriate assessment, as already recommended in this manuscript, the dietitian should explain the appropriate management of the diet to the patient and the parents (19). Education on the therapeutic intervention should be provided in an empathetic and warm manner, providing ample time for the family

to ask questions and to create a supportive patient-health professional relationship (70). Studies have not only shown the importance of dietary education for patients with FGID but also how more knowledge in general about the disorder, including pharmacological and nutritional therapy and the importance of follow-up, can enhance patient's quality of life (71,72). Ostgaard et al showed that adult patients with IBS who received two sessions of dietary guidance compared to those who did not, continued to have a healthy diet, improved quality of life, and reduced symptoms even after two years (73). Alfaro-Cruz et al showed that in children with FGID only 20% received an educational consult by a registered dietitian (61). This group also showed that physicians caring for children with FGID should be more cognizant to provide dietary education and to refer to a registered dietitian not only for enhancing the education and adherence to the diet but also for the overall nutritional management, which in turn might lead to a better clinical outcome (74).

A low-FODMAP diet needs to be carefully implemented due to the nutritional and also psychological risks of a restrictive diet (3). The diet should be personalized, based on individual tolerance to avoid over-restriction with potential nutritional imbalances and to ensure adherence to a balanced diet (62). Furthermore, considering the complexity of psychosocial implications of restrictive diets in children and adolescents with IBS and or other FGID, appropriate screening for altered eating behaviors should be performed before and during the dietary treatment implementation (75). Therefore, close collaboration in a team including a doctor, a dietitian and a psychologist, and the possibility of a smooth transfer to a psychologist in case of a suspected eating disorder may be very helpful.

Training courses for health professionals caring for adults and the low-FODMAP diet exist. Indeed, health professionals caring for children may need to work with specialized centers to receive the appropriate training in the management of the diet.

There is increasing evidence that internet-based strategies may be of value in the treatment of gastrointestinal diseases. There are several websites and software applications providing information on the low-FODMAP diet, but the information is often of low quality with a wide variety of recommendations (76,77). The advantages of software applications and home monitoring include offering the patient quick and easy access to nutritional advice and providing patients with more individualized treatment (78). Self-management promotes patient engagement and empowerment and may present a unique opportunity for patients with chronic GI diseases requiring life-long follow-up and maintenance treatment (78). However, it may be challenging to differentiate between reputable and non-reputable sources. Social media can when used appropriately, be of great benefit but it cannot replace the input of a qualified and evidence-based dietitian for dietary management with a low-FODMAP diet, particularly given that a trusting patient and health professional relationship is the cornerstone of clinical management (77). Even if the software applications are easy to use, they should only be considered as a helpful tool for following the dietitians' recommendations and care (79,80).

After comprehensive nutrition counseling by a dietitian, studies have shown that adherence to the low-FODMAP diet may be very good (13,61,62,81). Baranguan-Castro et al showed that 12 from 20 patients found the low-FODMAP diet (very) easy to follow, and nearly all families reported a high level of adherence to the diet associated with better symptom control (13). However, compared to other forms of dietary restriction, the low-FODMAP diet may seem more difficult to follow, and this may have an impact on its effectiveness and acceptability (10). Patients' difficulties in following the low-FODMAP diet may stem from limited access to the recommended foods in regular supermarkets, the higher prices of products, insufficient information in the menu, or lower palatability of new products (10).

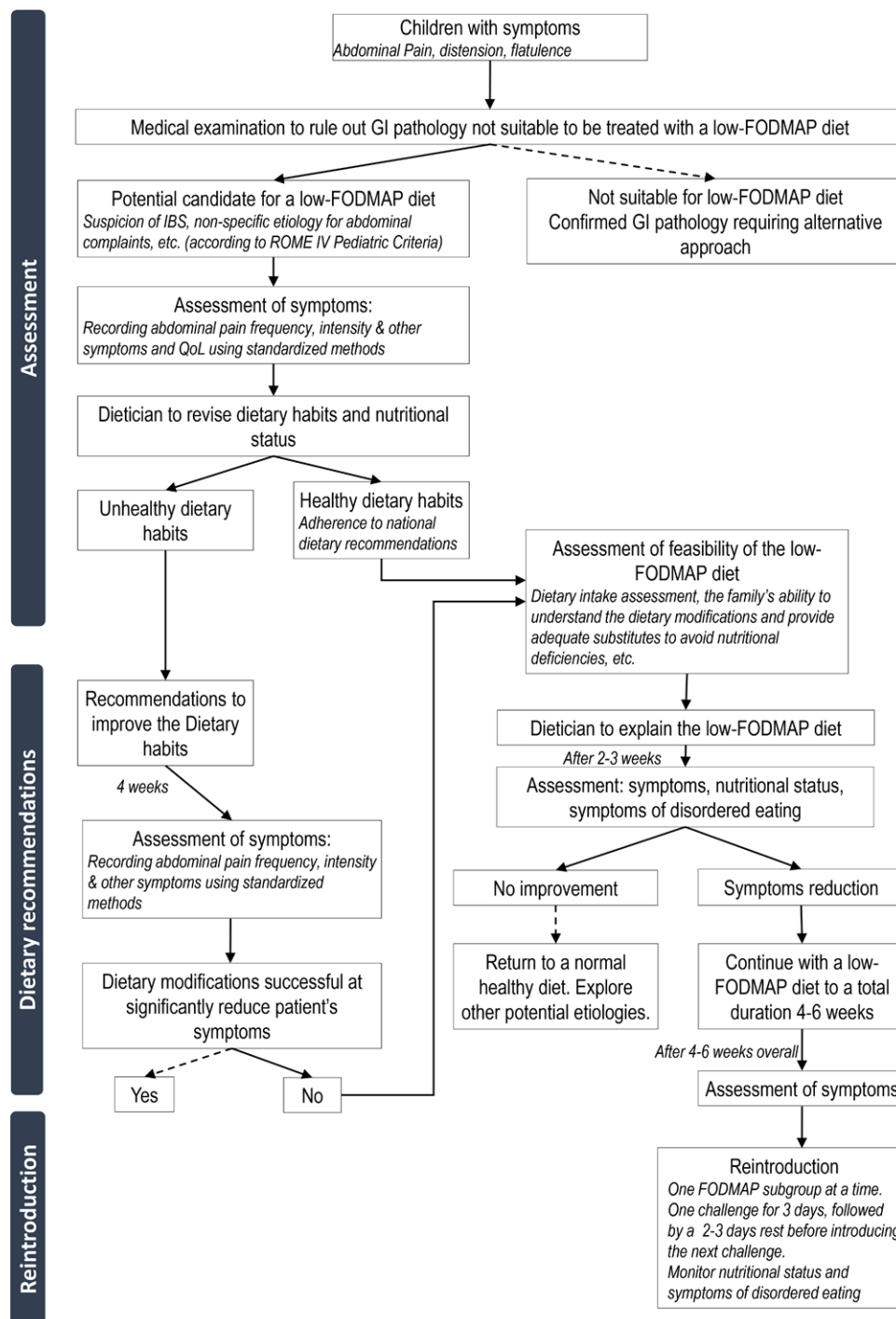


FIGURE 1. Algorithm to assess, consider and implement a low-FODMAP diet in children with suspicion of FGIDs.

A further caveat in instituting a low-FODMAP diet can be caused by unlabeled FODMAPs content in foods. Chumpitazi et al showed that in several processed foods e.g. in gluten-free baked products, an unlabeled high FODMAPs content may be found (82). Based on current nutrition labeling requirements, this content may not be readily apparent. Further research should consider the quality and the adherence to the diet as possibly relevant confounders, considering (for example) the use of processed food products.

The authors concluded that determining FODMAPs content in foods may support educational and dietary interventions (82) and it underlines that guidance of the low-FODMAP diet by an experienced dietitian is paramount. Figure 1 proposes a summarized decision tree when considering the use of low-FODMAP diet in children. Statements regarding the use of low-FODMAP diet in children with GI complaints are summarized in Table 5. Consensus was reached for all statements

TABLE 5. Considerations in the prescription and use of a low-FODMAP diet in pediatric patients

1. The evidence regarding the effectiveness of the low-FODMAP diet in the treatment of Functional Gastrointestinal Disorders in children is currently insufficient to guide clinical practice. Votes: 9,8,9,9,8,9,8,9,9,9,8,8,9,9,9,8,8,8,9
2. Whilst there is some evidence to suggest the avoidance of FODMAP in adult patients with Non-Coeliac gluten sensitivity, data supporting a similar recommendation in children are missing. Votes: 9,8,9,9,8,9,8,9,9,9,8,8,9,9,9,7,8,8,9
3. Currently, no data exist on the use of a low-FODMAP diet in pediatric Inflammatory Bowel Disease or SIBO. Votes: 9,7,9,9,9,8,9,8,9,9,9,9,8,9,9,8,9,8,9
4. The available evidence on the efficiency of a low-FODMAP diet in pediatric gastrointestinal disorders is scarce. Only a decrease in severity and frequency of pain episodes has been described in some patients from small samples of children with Irritable Bowel Syndrome. Votes: 9,7,9,9,9,9,7,9,9,9,8,8,9,9,9,9,8,8,9,8,9
5. The identification of microbiota with greater fermentation capacity may serve as a biomarker of responsiveness to a low-FODMAP diet. Votes: 9,7,9,9,8,8,7,9,9,8,5,8,9,5,9,4,5,6,6,8
6. In children with ongoing Irritable Bowel Syndrome symptoms, a low-FODMAP diet can be considered for a limited period, only when the risk of an eating disorder (using disordered eating screening) and feeding difficulties (such as food refusal and selective eating), are minimal, under the expert supervision of a specialized dietician. Votes: 9,9,7,9,9,9,9,9,9,9,8,8,9,7,9,9,7,8,8,8
7. In this case, a dietician-supervised low-FODMAP diet, for a limited period, does not significantly compromise nutrient intake, despite the restriction of many nutrient-rich foods across several food groups, suggesting that it can be implemented without major nutritional concerns. Votes: 9,9,9,9,9,8,8,9,9,7,8,8,9,7,9,9,8,9,8,8

CONCLUSIONS

Despite some evidence available in adults, there is no evidence to recommend the use of the low-FODMAP diet to treat FGID, NCGS, IBD, FAPDs, or SIBO in children. Limited evidence supports the use of a low-FODMAP diet in children with IBS. Nevertheless, the diet may have a place in the treatment of selected children with IBS. Awareness of how and when to use the diet is crucial, as a restrictive diet may impact nutritional adequacy or promote distorted eating in vulnerable subjects including the pediatric population. The present manuscript provides practical safety tips to be applied when used.

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