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Dietary Guidance From the International Organization for the Study of Inflammatory Bowel Diseases

Arie Levine,[*,a] Jonathan M. Rhodes,[‡,a] James O. Lindsay,[§,a] Maria T. Abreu,[||,a] Michael A. Kamm,[¶,a] Peter R. Gibson,[#,a] Christoph Gasche,[**,a] Mark S. Silverberg,[‡‡,a] Uma Mahadevan,[§§,a] Rotem Sigall Boneh,[*] Eyton Wine,[||||,¶¶] Oriana M. Damas,[||] Graeme Syme,[##] Gina L. Trakman,[¶] Chu Kion Yao,[#] Stefanie Stockhamer,[‡‡] Muhammad B. Hammami,[§§] Luis C. Garces,[||] Gerhard Rogler,[***,a] Ioannis E. Koutroubakis,[‡‡‡,a] Ashwin N. Ananthakrishnan,[§§§] Liam McKeever,[||||||] and James D. Lewis[||||||,a]

*Pediatric IBD Center, Wolfson Medical Center Holon, Tel Aviv University, Tel Aviv, Israel; ‡Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom; §Centre for Immunobiology, Blizard Institute, Barts and the London School of Medicine, Queen Mary University of London, London, United Kingdom; ||Division of Gastroenterology, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida; ¶St Vincent's Hospital and University of Melbourne, Melbourne, Australia; #Monash University and Alfred Health, Melbourne, Australia; **Medical University Vienna, Vienna, Austria; ‡‡Zane Cohen Centre for Digestive Diseases, Mount Sinai Hospital, University of Toronto, Toronto, Canada; §§University of California, San Francisco, San Francisco, California; ||||Department of Pediatrics, University of Alberta, Alberta, Canada; ¶¶Department of Physiology, University of Alberta, Alberta, Canada; ##The Royal London Hospital, Barts Health NHS Trust, London, United Kingdom; ***University Hospital, Zurich, Switzerland; ‡‡‡University Hospital of Heraklion, Heraklion, Greece; §§§Massachusetts General Hospital, Boston, Massachusetts; and ||||||Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania

Recent evidence points to a plausible role of diet and the microbiome in the pathogenesis of both Crohn's disease (CD) and Ulcerative Colitis (UC). Dietary therapies based on exclusion of table foods and replacement with nutritional formulas and/or a combination of nutritional formulas and specific table foods may induce remission in CD. In UC, specific dietary components have also been associated with flare of disease. While evidence of varying quality has identified potential harmful or beneficial dietary components, physicians and patients at the present time do not have guidance as to which foods are safe, may be protective or deleterious for these diseases. The current document has been compiled by the nutrition cluster of the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) based on the best current evidence to provide expert opinion regarding specific dietary components, food groups and food additives that may be prudent to increase or decrease in the diet of patients with inflammatory bowel diseases to control and prevent relapse of inflammatory bowel diseases.

Keywords: Crohn's Disease; Ulcerative Colitis; Meat; Fruit; Vegetables; Food Additives.

The inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC), have long been thought to arise from inappropriate and maladaptive stimulation of the immune system. Emerging evidence demonstrates that environmental factors, including diet, may play an important role in the pathogenesis and inflammation. This highlights the need to provide guidance to physicians and patients regarding which foods may be harmful, beneficial, or safe to consume.

To address this gap in patient care and education, the International Organization for the Study of Inflammatory Bowel Disease (IOIBD) formed a working group to formulate recommendations for physicians, dietitians, and patients based on best available evidence. These recommendations focus on dietary patterns to control and prevent relapse of IBD.

Methods

The IOIBD Nutrition Cluster is composed of 12 members from 3 continents (https://www.ioibd.org/clusters/). Following an organizational meeting in March 2018, 7 food groups, dietary components, and 5 food additives were selected as the most important to

[a]IOIBD Nutrition Cluster members contributed equally to this manuscript.

Abbreviations used in this paper: CD, Crohn's disease; CI, confidence interval; EL, evidence level; IBD, inflammatory bowel disease; IOIBD, International Organization for the Study of Inflammatory Bowel Disease; OR, odds ratio; P80, polysorbate-80; PUFA, polyunsaturated fatty acid; RCT, randomized controlled trial; SCFA, short-chain fatty acids; UC, ulcerative colitis.

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address for patient dietary guidance. These included dairy, red meat, processed meat, poultry, eggs, fruits and vegetables, fat, refined sugar, wheat and gluten, alcohol, emulsifiers, maltodextrins and artificial sweeteners, gums and thickening agents, and nanoparticles. The group assigned members to review the published literature for each of the chosen foods or additives. The reviewer was to summarize the published data separately for studies involving humans and animal models. Animal data received more attention when human data were absent or the animal models were considered reproducible and of clinical importance. Given the broad scope of the topic and the quality of the existing data, no attempt was made to produce summary risk estimates.

The members prepared a concise document that included overall recommendations and a narrative summary. Where there were fewer data from studies in humans, more data were presented from animal models. Although it would be ideal to know the exact amount of each food that patients with IBD should consume, this could vary by age, sex, weight, and so forth. Additionally, there generally were insufficient published data for such specific recommendations. Therefore, recommendations were provided separately for CD and UC, and were chosen from 4 categories (prudent to increase consumption, to decrease or avoid consumption, safe to consume, or insufficient evidence to make a claim). During group discussion, some items were modified to state that it "may be prudent to increase or decrease consumption."

The cluster chairs (AL and JDL), in collaboration with the workgroup co-leads (JOL and JMR) edited the first drafts to create a common format. The IOIBD cluster members reviewed the data and the recommendations at a face-to-face meeting in March 2019 and voted on the recommendations and wording, with consensus defined as >75% agreement. Following the meeting, the chairs slightly revised the wording of a few of the recommendations during the manuscript drafting in response to comments by the authors. Subsequently, a final vote was taken via a REDCap survey in July 2019, using the same definition of consensus. The evidence level (EL) supporting the recommendation was categorized loosely based on the following scale: randomized controlled trials (RCTs) provide high-level evidence, observational studies in humans provide low-level evidence, and everything else is very-low-level evidence. Level of evidence could be increased or decreased based on the strength of association and reproducibility of findings, or quality of studies. Because the objective of the guidance document is to help patients with established diagnosis of IBD, studies examining the role of diet in the etiology of IBD were categorized as EL very low. When possible, the review focused on the effect of diet on inflammation and symptoms, although in some cases, data were only available for symptom control. Exclusive enteral nutrition, a known effective therapy for CD, was not addressed. All recommendations were made without consideration of other comorbid conditions that may influence choice of dietary patterns.

Recommendations

Consensus was achieved for all food types except pasteurized dairy consumption (Table 1).

Fruit and Vegetables

In CD, it is prudent to recommend moderate to high consumption of fruits and vegetables (EL low). In patients with symptomatic or significant fibrostricturing disease, insoluble fiber intake should be restricted (EL very low).

In UC, there is insufficient evidence to recommend any specific change or restriction in intake of fruit and vegetables. (EL very low).

Fruits and vegetables are a diverse group of foods that generally have in common high-fiber content. Fibers are undigested in the human small intestine, but most are fermented by bacterial enzymes within the colon, soluble fiber usually more rapidly than insoluble. Fermentation produces short-chain fatty acids (SCFA), such as butyrate, that act as carbon and energy sources for the colonic epithelium. Decreased production of SCFA may occur in patients with active IBD.[1]

Significant dietary restriction of fiber leads to greater bacterial consumption of colonic mucus, which might contribute to inflammation.[2] Specific soluble fibers, including plantain (banana) and broccoli pectins, reduce bacterial adherence and translocation by the epithelium[3]; fiber may also serve as growth substrates for important SCFA-producing commensal bacteria.

Epidemiologic studies suggested that patients with IBD consume less fruit and vegetables before disease onset, particularly for CD.[4–6] In the prospective Nurses' Health Study, women in the highest quintile for fruit fiber had approximately half the risk for subsequent CD development.[6] However, in the European Prospective Investigation into Cancer and Nutrition (EPIC) study, no association between fiber intake and subsequent risk for CD or UC was found.[7] Higher intake of fruits and vegetables has been associated with lower endoscopic activity of UC.[8] An Internet-based prospective study found that, among people with CD in remission, those in the highest quartile for fiber consumption were nearly half as likely to flare during 6-months follow-up, but there was no such association in UC.[9] Patients with stricturing CD tend to avoid high-fiber foods.

An RCT of 2-years high-fiber/low-sugar diet showed no significant benefit or harm in adults with inactive or mildly active CD.[10] In another trial among patients with CD, symptoms were worse with supplementation of inulin than placebo.[11]

Data from additional studies are presented in Supplementary Table 1.

Table 1. IOIBD Dietary Recommendations for Patients With IBDs

Dietary component	Recommendation UC (evidence level, % agreement)	Recommendation CD (evidence level, % agreement)	Source of evidence	Clarifications
Fruits	Insufficient evidence to recommend specific dietary changes (very low, 100%)	Prudent to increase exposure (low, 84.6%)	Epidemiology Clinical studies	Reduce insoluble fiber if stricture present (evidence level very low)
Vegetables	Insufficient evidence to recommend any specific changes (very low, 100%)	Prudent to increase exposure (low, 84.6%)	Epidemiology Clinical studies	Reduce insoluble fiber if stricture present (evidence level very low)
Refined sugars and carbohydrates	Insufficient evidence to recommend any specific changes in refined sugar or complex carbohydrate intake (low, 92.3%)	Insufficient evidence to recommend specific changes in refined sugar or complex carbohydrates (low, 100%)	Epidemiology	
Wheat/gluten	Insufficient evidence to recommend restriction of wheat and gluten (low, 100%)	Insufficient evidence to recommend restriction of wheat and gluten (low, 100%)	Epidemiology Animal models	Gluten has been associated with ileitis in a mouse model of CD
Red/processed meat	Prudent to reduce intake of red and processed meat (low, 100%)	Insufficient evidence to recommend restriction of intake (high, 100%)	Epidemiology Animal Models	
Poultry	Insufficient evidence to recommend dietary changes (low, 100%)	Insufficient evidence to recommend restriction of intake (high, 100%)	Epidemiology	Lean chicken breast is a low animal fat and low taurine source of protein and is allowed in the CD exclusion diet
Pasteurized dairy products	Unable to reach consensus (92.3%)	Unable to reach consensus (92.3%)	Epidemiology Animal models	Dairy products encompass a wide range of products Lactase deficiency and lactose intolerance is common among patients with IBD Prudent to reduce dairy fat and processed dairy rich in maltodextrins and emulsifiers
Unpasteurized dairy products	Prudent to avoid in all patients (100%)	Prudent to avoid in all patients (100%)	Expert opinion Case reports	Avoid infections that can result from consumption of unpasteurized dairy products
Dietary fats	Prudent to reduce consumption of myristic acid (palm oil, coconut oil, dairy fats) (low, 100%) Prudent to avoid trans fat (very low, 100%) Prudent to increase dietary consumption of omega-3 fatty acids (DHA and EPA) from marine fish (low) but not from dietary supplements (high, 100%)	Prudent to reduce exposure to saturated fats (GRADE low, 100%) and avoid trans fat (very low, 100%)	Prospective, observational studies	Myristic acid linked to UC is found in palm and coconut oil, dairy fat, and meat from grain-fed as opposed to grass-fed animals Natural omega-3 fatty acids are found mainly in wild marine fish
Alcoholic beverages	Insufficient evidence to recommend changes in low-level alcohol consumption (low, 100%)	Insufficient evidence to recommend changes in low-level alcohol consumption (low, 100%)	Epidemiology	A trial of avoidance of alcohols containing high levels of sulfites (ie, beer and wine) is reasonable (evidence level 3b)
Food additives				
Maltodextrins/ artificial sweeteners	It may be prudent to limit intake of maltodextrin-containing foods and artificial sweeteners (very low, 92.3%)	It may be prudent to limit intake of maltodextrin-containing foods and artificial sweeteners (very low, 92.3%)	Epidemiology Animal models	

Table 1. Continued

Dietary component	Recommendation UC (evidence level, % agreement)	Recommendation CD (evidence level, % agreement)	Source of evidence	Clarifications
Emulsifiers and thickeners	It may be prudent to limit intake of carboxymethylcellulose and polysorbate-80 (very low, 92.3%)	It may be prudent to limit intake of carboxymethylcellulos and polysorbate-80 (very low, 92.3%)	Animal models Epidemiology	E433, polysorbate-80 E466, carboxymethylcellulose
Carrageenans	It may prudent to reduce intake of processed foods containing carrageenan (very low, 92.3%)	It may prudent to reduce intake of processed foods containing carrageenan (very low, 92.3%)	Epidemiology Animal models One very small RCT	Found in dairy-based desserts, frozen meals, and processed meats
Titanium dioxide and other nanoparticles	It may prudent to reduce intake of processed foods containing titanium dioxide and sulfites (very low, 92.3%)	It may prudent to reduce intake of processed foods containing titanium dioxide and sulfites (low, 92.3%)	Clinical trial in CD Animal models and translational studies in UC	The inconsistent results of the 2 clinical trials of low-nanoparticle diets led to a downgrading of the evidence

NOTE. Bold text refers to a recommendation to increase consumption. Italic text refers to a recommendation to reduce consumption.
CD, Crohn's disease; IBD, inflammatory bowel disease; IOIBD, International Organization for the Study of Inflammatory Bowel Disease; RCT, randomized controlled trial; UC, ulcerative colitis.

Refined Sugar and Carbohydrates

In CD, there is insufficient evidence to recommend any specific change of intake of complex carbohydrates or refined sugars and fructose (EL low). It may be prudent to use a low FODMAP diet for patients with persistent symptoms despite resolution of inflammation and absence of strictures (EL low).

In UC, there is insufficient evidence to recommend any specific change of intake of complex carbohydrates or refined sugars and fructose (EL very low). It may be prudent to use a low FODMAP diet for patients with persistent symptoms despite resolution of inflammation (EL low).

Several cross-sectional and case-control studies have observed increased sugar consumption in patients with CD,[6,12–20] although others suggest that this reflects a "modern lifestyle" and is not necessarily causal. Evidence is lacking for UC. A randomized, controlled, multicenter study, including 352 patients with CD compared diets rich either in carbohydrate in its refined form or carbohydrate in its natural unrefined form without finding a significant difference in worsening clinical disease activity.[10] Another randomized, controlled, multicenter dietary study, including 134 patients with CD in remission[21] who were instructed either to adhere to a low-carbohydrate diet (of $<$84 g per day), mainly in a fiber-rich form, or diet as usual. The intention-to-treat analysis showed no significant difference relative to the control group for prevention of relapse after 1 year, although patients seemed to have a symptomatic benefit during time that they adhered to the diet. A small uncontrolled study of the specific carbohydrate diet that excludes sucrose and other refined sugars, fructose, and other refined sugars demonstrated reductions in symptoms and mucosal inflammation as assessed by capsule endoscopy among children with CD.[22]

There is no evidence of a role for altering the intake of slowly absorbed and nondigestible short-chain carbohydrates (collectively known as FODMAPs) in modulating inflammatory activity of IBD.[23] Placebo-controlled trials involving 15 g/day fructo-oligosaccharides in patients with CD[11] and challenge for 3 days with specific FODMAPs in patients with quiescent IBD did not significantly change inflammatory activity,[24] although fructans in both induced symptoms. Lowering of FODMAP intake in patients with symptomatic but quiescent IBD was associated with amelioration of functional gastrointestinal symptoms in an uncontrolled study[25] in comparison with those on a placebo diet without change in inflammatory status,[24–26] suggesting that these patients suffered from concomitant irritable bowel syndrome. Similar findings were noted in a feeding crossover study.[27]

Wheat and Gluten

In CD, there is insufficient evidence to recommend restriction of wheat and gluten (EL Low).

In UC, there is insufficient evidence to recommend restriction of wheat and gluten (EL Low).

Current evidence for restriction is based largely on 3 cross-sectional surveys where the prevalence of presumed gluten-associated symptoms was 5%–28% in patients with IBD (Supplementary Table 2).[28–30] Presumed gluten-associated symptoms were more common among those with stricturing or more severe CD and active disease.[28,30] In one study of gluten restriction, a high prevalence (65%) of patients observed improvements in 1 or more IBD symptoms, 38% described reduced frequency and severity of disease flares, and strict dietary adherence was associated with marked improvement in fatigue.[29] There are no data to indicate whether mucosal healing can be achieved via this dietary approach. Because gluten coexists in cereals with FODMAPs, improved symptoms might be related to reduced FODMAP intake.

Gluten is hypothesized to modulate immune pathways in the small intestine,[31] but the only supportive evidence comes from tumor necrosis factor knockout mice.[32] Other wheat-protein components, such as amylase trypsin inhibitors, may drive intestinal inflammation.[33]

Red Meat, Processed Meat, Poultry, and Eggs

In CD, there is evidence that it is unnecessary to restrict moderate consumption of unprocessed red meat, lean chicken meat (breast of chicken), and eggs (EL high).

In UC, it is prudent to reduce intake of red and processed meat (EL low).

In a systematic review, 6 of 8 studies demonstrated an association between red meat intake and incidence or worsening of UC, 2 of which were statistically significant. In a prospective French inception cohort of 67,581 people,[34] high animal protein intake was associated with a significantly increased risk of IBD, CD, and UC for the highest versus the lowest tertile of consumption (IBD overall hazard ratio, 3.03; 95% confidence interval [CI], 1.45–6.34; $P_{trend} = .005$ corrected for energy intake). Red meat intake was also associated with a greater than 5-fold increase in the odds of a UC relapse in 1 prospective study,[35] but not in a recent smaller study that combined patients with CD and UC.[36] A cross-sectional study in 103 adults in remission[37] also demonstrated a higher risk of relapse with an odds ratio (OR) of 3.6 for the highest quartile of red meat consumption. However, a more recent study[38] in 412 adults with UC in remission and followed until relapse demonstrated that the intake of fats and specifically myristic acid was associated with flares, whereas processed meats were not. Myristic acid is a saturated fatty acid enriched in coconut oils and dairy fats, but also in beef from grain-fed cattle.[39] Red meat was not assessed independently in this study.

One prospective clinical trial comparing high versus low levels of consumption of red meat or processed meat has been conducted in adults with CD.[40] Relapse rates did not differ between the 2 treatment groups. Recently published clinical trials involving a diet that required daily consumption of chicken breast and 2 eggs per day for 12 weeks was associated with high rates of remission in active CD[41–43] suggesting that these products are safe to consume in moderation as a source of protein in CD. A summary of studies of meat consumption is included in Supplementary Table 3.

Dairy

Consensus was not obtained for CD or UC for pasteurized dairy products. Consensus was obtained that unpasteurized dairy products should not be consumed.

Dairy products include a wide variety of natural and processed foods that may vary greatly from one product to another because of differences in processing, fat content, and food additives. Most contain lactose, but some do not. In the developed world, dairy products often contain significant amounts of emulsifiers, carrageenans, and other thickening agents, which are subsequently reviewed. This complicated the discussion and led to lack of consensus.

Exposure to casein in a dextran sodium sulfate mouse model of UC led to increased severity of colitis. However, human data are lacking to confirm this experiment.[44] In the prospective EPIC study, there were no statistically significant trends between the intake of dairy products and the development of CD or UC (Supplementary Table 4).[45]

Prospective cohort studies report a prevalence of lactase deficiency of 40%–50% in CD and 27%–40% in UC, both higher than in healthy control subjects.[46,47] A recent systematic review and meta-analysis of 17 studies reported an OR compared with control subjects for lactose malabsorption in patients with CD of 2.29 (1.09–4.80; $P = .03$) and in UC of 1.14 (0.69–1.86; $P = .62$).[48] Therefore, it seems that lactose malabsorption is more common in patients with CD than healthy control subjects.

Baseline dairy intake was not associated with risk of disease flare in adults with quiescent UC and eliminating dairy in a small randomized trial had no apparent benefit on pediatric patients with UC.[35,49]

Unpasteurized milk should be avoided by all patients with IBD given the potential risk of infections.

Fat

In CD, it is prudent to reduce exposure to saturated fats (EL low) and avoid trans fat (EL very low).

In UC, it is prudent to reduce consumption of myristic acid (palm oil, coconut oil, dairy fats) (EL low). It is prudent to increase dietary consumption of omega-3 fatty acids (DHA and EPA) from marine fish (EL low), but not from supplements (EL high). It is prudent to avoid trans fat (EL very low).

Total fat. In a prospective cohort of adult patients with UC, increased meat consumption, especially processed meats, and sulfur were associated with a higher risk of relapse.[35] The highest tertile of consumption of fat also had a higher risk for flare than the medium tertile of fat consumption (OR, 2.52; 95% CI, 1.06–5.97). Total fat intake is associated with active CD in some, but not all studies.[50,51] Studies of enteral nutrition formulas show no consistent variation in efficacy for CD based on total fat content.[52]

Saturated fats. Among 412 patients with UC in clinical remission on mesalamine, only higher intake of myristic acid, a saturated fatty acid found in coconut oil, palm oil, and dairy products, was independently associated with an increased odds of flare within 1 year (OR, 3.01; 95% CI, 1.17–7.74), with a dose-response effect.[38]

Unsaturated fats. Monounsaturated fat, including palmitoleic acid and oleic acid, is found in plant-based oils including olive oil, and in macadamia nuts, beef tallow, and lard. Enteral nutrition supplemented with either oleic acid (a monounsaturated fatty acid) or linoleic acid (an n-6 polyunsaturated fatty acid [PUFA]) found that linoleic acid had higher remission rates in CD, although neither was as efficacious as steroids for clinical remission.[53] However this was only 1 study. Studies with the Crohn's Disease Exclusion Diet allow unlimited olive oil rich in monounsaturated fatty acids and this diet was associated with clinical remission and reduction in inflammation.[39] Patients with UC treated with olive oil derivatives had reduction in peripheral and intestinal T-cell activation and interferon-γ production.[54]

Foods rich in n-3 PUFA include marine fish, such as salmon, mackerel, and herring, and certain nuts and seeds (eg, walnuts, flax, hemp, and chia seeds). A small study found a nonsignificant decrease in disease activity in patients with UC who consumed 600 mg of Atlantic salmon weekly for 8 weeks.[55] In 1 study, patients whose diet approximated a ratio of n-3/n-6 closer to 1, were more likely to be in remission than those with a higher ratio of n-6 foods.[56] Higher dietary intake of α-linolenic acid (a precursor of long-chain n-3 PUFA) was associated with increased risk of UC relapse, whereas total n-3 PUFA without supplementation was protective.

In a meta-analysis of 3 trials looking at maintenance of remission in UC with n-3 PUFA supplementation, there was no added benefit to supplementation (relative risk for relapse, 1.02; 95% CI, 0.51–2.03).[57] Similarly, a systematic review looking at n-3 PUFA supplementation for treatment of any IBD found no consistent benefit for prevention of UC relapse among 4 available studies.[58]

In CD, 2 large placebo-controlled multicenter RCTs using 4 g/day of supplemental n-3 PUFA found no efficacy for the prevention of relapse.[59] However, a meta-analysis of 6 heterogeneous trials with 1039 patients showed a small benefit of supplementation for reduction of relapse (relative risk of relapse, 0.77; 95% CI, 0.61–0.98; $I^2 = 58.4\%$; $P = .03$).[57] Therefore, current evidence is inconclusive for n-3 PUFAs (eg, fish oil) in IBD. By contrast, foods naturally high in n-3 PUFAs and low in n-6 PUFAs may be beneficial, although evidence is weak.

Trans fats (unsaturated fat). A case-control study comparing 62 newly diagnosed patients with UC with 124 healthy control subjects found higher consumption of total fats and *trans* fats to be significantly associated with increased risk of UC.[60] In a prospective cohort, higher long-term intake of *trans* fats demonstrated a trend toward increased incidence of UC.[61] Moreover, *trans* fats are believed to have other deleterious health effects. Although data in humans regarding the effect of *trans* fat on inflammation are lacking, because of the deleterious nature we recommend avoiding *trans* fat.

Alcohol

In CD, there is insufficient evidence to recommend changes in low-level alcohol consumption (EL low).

In UC, there is insufficient evidence to recommend changes in low-level alcohol consumption (EL low).

Alcohol use before a diagnosis of inflammatory bowel disease. A meta-analysis of 9 UC studies did not find a significant association (relative risk, 0.95; 95% CI, 0.65–1.39) with risk for UC comparing the highest with the lowest alcohol intake.[62] In CD, 1 study reported that alcohol (≥1 drink/week) was not associated with new-onset disease,[63] whereas another reported increased alcohol consumption ($P = .009$) in recently diagnosed patients with CD compared with healthy control subjects.[64] The EPIC study found no association between alcohol consumption before recruitment and subsequent UC or CD development.[65]

Triggering flares. In a small prospective cohort study, patients with UC in the top tertile for alcohol consumption had a 2.7-fold higher odds of flare compared with the bottom tertile (Supplementary Table 5).[35] In contrast, a daily glass of red wine was associated with a reduction in fecal calprotectin in patients with inactive IBD.[66]

In an Internet-based survey of 2329 patients with IBD, alcohol consumption was identified as a potential trigger of worsening gastrointestinal symptoms.[67] However, patients with inactive IBD consume alcohol at rates similar to that of the general US population, although 75% reported its impact on gastrointestinal symptoms.[68] Of patients with CD who consumed alcohol, 40% reported symptom worsening, whereas 41% did not; there was no association with a particular type of alcoholic beverage.

Maltodextrin and Artificial Sweeteners

In CD, it may be prudent to limit intake of maltodextrin-containing foods and artificial sweeteners (EL very low).

In UC, it may be prudent to limit intake of maltodextrin-containing foods and artificial sweeteners (EL very low).

In vitro and in vivo studies have linked food additives, artificial sweeteners, and their components to IBD.[69–71] Maltodextrin is a hydrolyzed starch and a common dietary polysaccharide used as a thickener for foods and confections.[72] Splenda, an artificial sweetener, is comprised of 1% sucralose and ∼99% maltodextrin as a filler.

Increased consumption of artificial sweeteners over the past few decades parallels the increased incidence of IBD cases.[73] This trend is similar for rising maltodextrin availability within the American diet.[74] Several epidemiologic studies correlated consumption of added sweeteners and sugar in soft drinks with an increased IBD risk (Supplementary Table 6).[75–77]

In animal models, consumption of artificial sweeteners has been shown to increase inflammatory markers in the gastrointestinal system (Supplementary Table 7). In vitro studies of gastrointestinal tissue exposed to maltodextrin observed enhanced cellular biofilm formation of CD-associated *Escherichia coli* strains, which adhered to intestinal epithelial cells and mimicked dense biofilm formations found in the gut of patients with CD.[70] MalX (maltose/maltodextrin binding protein gene) is a gene central to maltodextrin metabolism. Studies of Splenda supplementation in SAMP mice and in vitro culturing of gastrointestinal tissue with maltodextrin observed an increase in bacterial malX gene expression in the ileal mucosa obtained from patients with CD and murine model of CD relative to healthy control subjects ($P < .0175$; $P < .03$).[69,70] This association links maltodextrin to CD pathogenesis by suggesting that its metabolism promotes the colonization and translocation of these CD-associated bacteria. Finally, common artificial sweeteners and maltodextrin induced alterations in the mouse gut microbiota that are similar to those observed in IBD.[69,78–81]

It is notable that maltodextrin is found in many nutritional supplements, including some used for exclusive enteral nutrition, which has been demonstrated to be an effective therapy. Thus, although there is theoretical and animal model data to support avoidance of maltodextrin among patients consuming a whole-food diet, these data or recommendations should not dissuade the use of exclusive enteral nutrition in appropriate situations.

Emulsifiers and Thickeners

In CD, it may be prudent to reduce intake of processed foods that contain carrageenan, carboxymethylcellulose, and polysorbate-80 (EL very low).

In UC, it may be prudent to reduce intake of processed foods that contain carrageenan, carboxymethylcellulose, and polysorbate-80 (EL very low).

Manufacturers add emulsifiers to processed foods to improve food texture and quality.[82,83] The most extensively used emulsifier, lecithin, is derived from egg or soya, and consists of varying proportions of phosphatidylcholine, ethanolamine, or inositol.[84] Other emulsifiers and thickeners include carboxymethylcellulose, carrageenan, and polysorbate-80 (P80). Epidemiologic data support an association between some emulsifier exposures and IBD incidence.[84–86]

A carrageenan-free diet supplemented with food-grade carrageenan ($n = 5$) or placebo capsules ($n = 7$) was administered to subjects with quiescent UC.[87] Three carrageenan-exposed but no control subjects relapsed.

Tobacman[88] reviewed 45 studies on the health effects of degraded and undegraded carrageenan in rats, mice, guinea pigs, rhesus monkeys, and rabbits. Study durations and carrageenan doses ranged from 1 day to 1 year and 0.1% to 10%, respectively. Carrageenan exposure led to intestinal lesions, neoplasia, ulceration, carrageenan accumulation in intestinal lymph nodes, stricture, and UC-like inflammatory changes. Ulceration correlated with dose and duration of carrageenan exposure. Whether the doses used are relevant in humans is questionable.

Effects of carrageenan exposure also include increased occult blood in stool,[89] mucosal ulcerations,[90,91] serum inflammatory makers,[91,92] small bowel and colonic lesions,[93] reduction in crypts number and length,[91,94] inflammatory cell infiltrate,[90,91] and epithelial damage (Supplementary Table 8).[91,92]

Two emulsifiers or thickeners (P80 and carboxymethylcellulose) have been evaluated in animal models. P80 was been shown to increase intestinal permeability in mice.[95] Chassaing et al[96] demonstrated that addition of carboxymethylcellulose and P80 to drinking water can reduce mucus thickness, elevate levels of fecal lipocalin-2, and induce colitis in interleukin-10 knockout mice.

Hydrolyzed carrageenan induced IBD in piglets, with associated increases in Proteobacteria and decreases in Firmicutes, Actinobacteria, and Bacteroidetes.[97] In wild-type and colitis-susceptible mice exposed to carboxymethylcellulose and P80, microbial diversity decreased and *Akkermansia muciniphila* and Proteobacteria increased.[98] Transplanting cecal content from emulsifier-treated to germ-free mice caused microbial epithelium encroachment and low-grade inflammation, mediated by altered bacterial composition and elevated fecal lipopolysaccharide and flagellin.

Recent studies in animal models of IBD also indicated that various EDTA compounds (Ca-EDTA, Na-EDTA, Fe-EDTA) as used for food preservation or iron fortification have proinflammatory and proneoplastic effects.[99]

Nanoparticles and Sulfites

In CD, it may be prudent to reduce exposure to processed foods containing titanium dioxide and sulfites (EL low).

In UC, it may be prudent to reduce exposure to processed foods containing titanium dioxide and sulfites (EL very low).

Sulfites are used to preserve wine and beer, commercial lemon juice and vinegars, dried or canned fruits, and processed meats. When used as preservatives, they generally are not nanoparticles, but can be when used in other formulations, such as iron sulfite. In interleukin-10 knockout mice, dairy fat induced dysbiosis and colitis via a bloom of sulfite-reducing bacteria *Bilophila wadsworthia*.[24] Bacteria, such as *Bilophila*, are potential intestinal pathobionts that may grow with a high-fat diet or high-dairy-fat diet. An exogenous source of sulfites from food could theoretically have the same effect; whether exogenous sulfites would exert the same effect was not tested.

Nanoparticles, such as titanium dioxide (TiO_2) and aluminum silicates (AlSi), are used as food additives to color, coat, or preserve food. Nanoparticles are highly stable and resistant to degradation. TiO_2 is a white, crystalline powder, used as a pigment in confectionery, white sauces, dressings, nondairy creamers, and toothpaste.[100] AlSi is added to salt and other powdered foods to prevent clumping.

In mice, oral administration results in TiO_2 accumulation in intestinal epithelial and immune cells with activation of the NLRP3 inflammasome.[101] Oral administration of TiO_2 nanoparticles also enhances intestinal inflammation in a murine model of colitis.[101] Similar findings have been reported for dietary aluminum intake, which also impairs intestinal barrier function.[102]

TiO_2 is normally trapped in the intestinal mucus layer,[103] although systemic absorption has been reported after supraphysiological intake in volunteers with normal intestinal permeability.[104] Nanoparticles (mostly TiO_2 and AlSi) have been identified within phagocytes located in intestinal lymphoid aggregates in patients with IBD. In addition, patients with active UC have higher serum titanium levels than patients with UC in remission and control subjects.[101]

Two dietary intervention studies have assessed the impact of TiO_2 on CD (Supplementary Table 9). A pilot study randomized 20 patients with active ileal or ileocolonic disease (Crohn's Disease Activity Index >150) off immunosuppressive therapy to a TiO_2/AlSi-restricted diet or a control diet for 4 months.[105] A significant reduction in mean Crohn's Disease Activity Index was seen in the intervention group only, with 7 patients on the intervention diet (70%) compared with 0 on the control diet (0%) achieving clinical remission (Crohn's Disease Activity Index <150).[105] A subsequent 16-week multicenter study that randomized 83 patents with active CD to a low or normal nanoparticle diet indicated no differences in remission or clinical response between groups.[106] Of note, patients in the pilot study followed a more restrictive diet, avoiding all processed foods. Given the first positive study combined with the animal models, the level of evidence for CD was rated as low.

Discussion

This dietary guidance consensus document from the IOIBD is based on the best available evidence to date. For patients with CD, we recommend regular intake of fruits and vegetables (in the absence of symptomatic strictures) and reduced intake of saturated, *trans*, and dairy fat; additives, such as P80 and carboxymethylcellulose; processed dairy or foods rich in maltodextrins; artificial sweeteners containing sucralose or saccharine; and processed food containing nanoparticles. For patients with UC, we recommend increased consumption of natural sources of omega-3 fatty acids (eg, from wild salmon and other natural sources, not from supplements). The foods that patients with UC should avoid are similar to CD with the possible addition of red and processed meat (Figure 1). There was insufficient evidence to recommend changes in the consumption of fruits or vegetables for patients with UC. For patients with either CD or UC, there was insufficient evidence to recommend changes in consumption of wheat or gluten, poultry, alcoholic beverages other than binge drinking (in the absence of other liver disease), and refined sugars. The committee was unable to come to a consensus on pasteurized dairy products. None of these recommendations are meant to

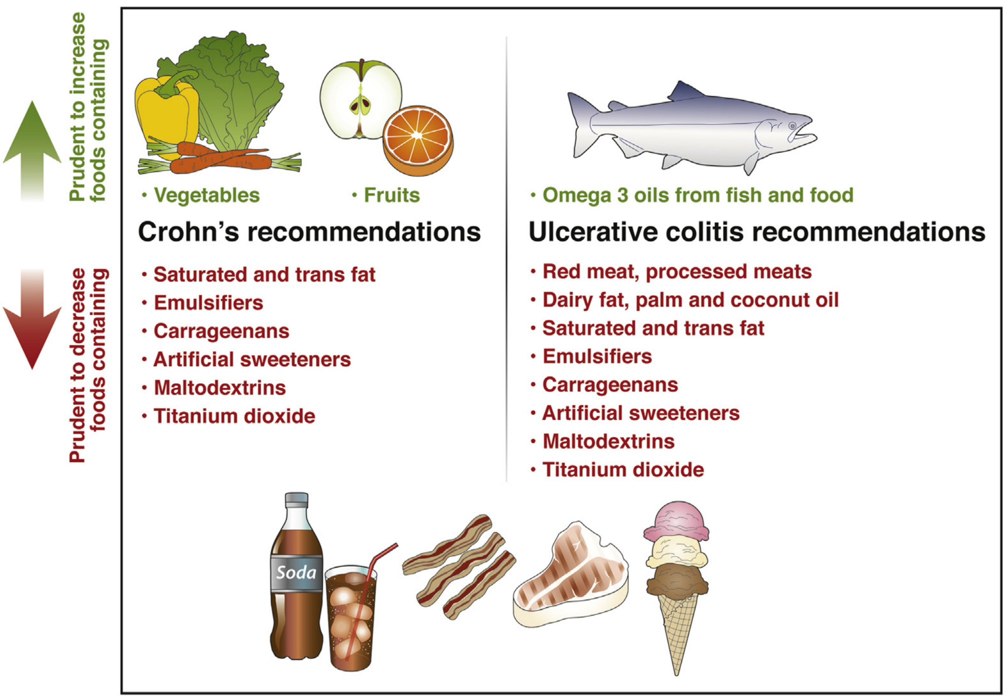

Figure 1. Dietary guidance for patients with inflammatory bowel diseases.

exclude the role of nutritional assessment for malnutrition and correction of deficiencies when needed. Our main recommendations are aimed at reducing symptoms and inflammation. For patients with persistent symptoms despite resolution of inflammation and absence of strictures, a low FODMAP or lactose-free diet may improve symptoms.

We acknowledge several limitations of this consensus document from the nutrition cluster of IOIBD. The recommendations were the consensus opinion of a relatively small group of IBD clinicians and scientists with expertise in the field. Dietary studies are particularly challenging to implement and therefore may be subject to various forms of bias.[107] For example, blinding study participants to treatment arm is difficult. When a food is eliminated, it is necessary to replace the calories usually obtained from this food with a different food. Sample sizes have historically been small, and therefore the studies were often underpowered. Additionally, several of the recommendations are based largely on the results of experiments in animals, such as the effect of thickeners, emulsifiers, and maltodextrin. Moreover, some of these are in contrast to the known efficacy of exclusive enteral nutrition. For some of the members, the vote to reduce intake may be in part because these food additives are not believed to have nutritional value. However, we did not quantify this in the process of voting. Finally, these recommendations may require change as new information becomes available.

There are several dietary patterns that are commonly recommended for patients with IBD (eg, Mediterranean diet, Specific Carbohydrate Diet, Crohn's Disease Exclusion Diet). At the outset, we hoped to make recommendations regarding specific dietary patterns. However, the lack of RCTs testing these dietary patterns precluded coming to strong recommendations. As such, we limited our recommendations to components of the diet. Nonetheless, several trials have just completed or are ongoing and may allow for stronger recommendations in the near future.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.01.046.

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Reprint requests

Address requests for reprints to: James D. Lewis, MD, MSCE, University of Pennsylvania, Center for Clinical Epidemiology and Biostatistics, 7th Floor, Blockley Hall, 423 Guardian Drive, Philadelphia, Pennsylvania 19104-6021. e-mail: lewisjd@pennmedicine.upenn.edu; fax: (215) 573-2265.

Conflicts of interest

These authors disclose the following: Arie Levine received honorarium, IP, consulting, or grants from Nestle Health Science, Janssen, AbbVie, Takeda, and Megapharm. Jonathon M. Rhodes with the University of Liverpool and Provexis UK, holds a patent for use of a soluble fiber preparation as maintenance therapy for Crohn's disease plus a patent for its use in antibiotic-associated diarrhea. Maria T. Abreu has served as a consultant to Prometheus Laboratories, Takeda, UCB Inc, Pfizer, Janssen, Focus Medical Communications, and Eli Lilly Pharmaceuticals; is a trainer or lecturer for CME Outfitters and Imedex, Inc; serves on the scientific advisory board of AbbVie Laboratories, Celgene Corporation, Shire Pharmaceuticals, Roche Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals, AMGEN, Allergan, SERES, Nestle Health Science, and GILEAD; and serves on the board of directors for the GI Health Foundation. Peter R. Gibson has served as consultant or advisory board member for Allergan, Janssen, MSD, Pfizer, Anatara, Atmo Biosciences, Immunic Therapeutics, and Takeda; his institution has received speaking honoraria from Janssen, Shire, Bristol-Meyers Squibb, and Pfizer; he has received research grants for investigator-driven studies from MSD and A2 Milk Company; his department financially benefits from the sales of a digital application and booklets on the low FODMAP diet; and he has published an educational/recipe book on diet. Boneh R. Sigall has received Speaker Honorariums from Nestle Health Science, Takeda, and Megapharm. Eyton Wine has received honoraria from AbbVie (advisory board; speaker fee), Janssen (speaker fee), and Nestle (speaker fee). Chu Kion Yao has received research support for investigator-driven studies for Ferring Pharmaceuticals Pty Ltd, Danone, and Yakult Australia. Ioannis E. Koutroubakis has served as advisory board member for AbbVie, Astelas, Genesis, Janssen, MSD, Pharmacosmos, Pfizer, Shire, and Takeda; as a Speaker for AbbVie, Astelas, Genesis, Janssen, MSD, and Takeda; and received research support from AbbVie and Ferring. James D. Lewis has received honorarium from Nestle Health Sciences, Pfizer, Gilead, UCB, Arena Pharmaceuticals, Samsung Bioepis, Bridge Biotherapeutics, and Bristol-Myers Squib; grant funding from Nestle Health Science, Takeda, and Janssen; and honorarium for participation in CME programs from Nestle Health Science. The remaining authors disclose no conflicts.