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Nutrition and Obesity (O Pickett-Blakely, Section Editor)

Popular Diet Trends for Inflammatory Bowel Diseases: Claims and Evidence

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Abstract

Purpose of review Patients with inflammatory bowel disease (IBD) frequently look to diet to improve symptoms. Although regularly asked for dietary guidance, gastroenterologists are often unprepared to provide evidence-based recommendations. This review will summarize popular diets claiming benefits in IBD, as well as current data evaluating their efficacies.

Recent findings The Specific Carbohydrate Diet has demonstrated symptom improvement and even mucosal healing; however, large trials and prospective data are lacking. The low FODMAP diet has shown benefit for functional symptoms in IBD, yet efficacy regarding inflammation is lacking. Large studies for the gluten-free diet yielded mixed results in IBD outcomes, while suggesting a negative impact on psychological well-being. Data on an "anti-inflammatory" diet were positive but remain severely limited. A currently planned large trial for the Mediterranean diet in IBD may provide much needed clinical data.

Summary We provide an overview of frequently utilized diets in IBD. The body of evidence does not currently support clear dietary recommendations in IBD, as larger, prospective studies are needed.

Introduction

Inflammatory bowel diseases (IBD), composed primarily of Crohn's disease (CD) and ulcerative colitis (UC), are characterized by chronic inflammation of the gastrointestinal tract. The pathogenesis of IBD is complex and



remains incompletely understood, although it most likely involves the interaction between genetic and environmental factors. The rising incidence of IBD in countries with previously low incidences have led some to hypothesize that their increasingly "Westernized" lifestyles and diets may be primary contributors [1–3].

Diet, as a modifiable factor, is particularly appealing to both patients and medical providers, representing an opportunity for patients to exert significant control over their disease and quality of life. In an online questionnaire among Dutch adults with IBD, 59% of patients felt nutrition to be at least equally if not more important than medication for treatment of their disease, and 62% of surveyed patients reported success in controlling their IBD symptoms with dietary modification [4]. However, recent guidelines for the management of CD and UC in adults do not advocate for specific oral diets, citing lack of durable benefits [5, 6].

Nonetheless, there has been an expansion of popular diets for therapy in IBD, including socalled "fad diets" (Table 1). Although each individual diet possesses its own unique characteristics, fad diets share common features. Fad diets typically glorify inclusion of certain foods/nutrients while emphasizing exclusion of others. Fad diets may even exclude entire food groups from the diet. These diets are typically based on claims that they offer therapeutic benefits for overall health or treatment of specific conditions; however, there is often minimal or only partial evidence supporting these claims. Although diets may have more robust evidence with regards to a certain condition or conditions, the potential role for the diet in other medical states is often extrapolated.

Patients with CD and UC are frequently exploring diets, including fad diets, as a potential mode of treatment in IBD. Gastroenterologists are commonly faced with inquiries for dietary recommendations from their patients with IBD, including requests for recommendations with regards to popular fad diets. In this review article, we will review multiple popular diets with claims of therapeutic benefit in IBD, focusing on the existing scientific data regarding each diet's utility.

Specific carbohydrate diet

Dr. Sidney Hass originally developed the Specific Carbohydrate Diet (SCD) in the 1920s for the treatment and management of celiac disease [7]. In the 1950s, the 8-year-old daughter of the Canadian biochemist Elaine Gottschall followed the diet under the supervision of Dr. Haas to aid in treatment of UC. The use of the SCD was reported to be successful as her daughter became symptom-free, which prompted Gottschall to later promote the SCD in her book "Breaking the Vicious *Cycle*" [8]. The premise behind the SCD is that more complex carbohydrates that require enzymatic digestion are difficult for the body to digest, resulting in undigested di- and polysaccharides arriving in the colon and causing fermentation, overgrowth of bacteria and yeast (shifting toward a more pro-inflammatory microbiome profile), and subsequent intestinal injury and inflammation [9, 10]. Monosaccharides, however, do not require enzymatic digestion and thus are emphasized for inclusion, allowing consumption of unprocessed meats, most fresh fruits and vegetables, all fats and oils, aged cheeses, and lactose-free yogurt. Notable prohibited foods include grains, milk, soft cheeses, and non-honey sweeteners. The SCD is intended to be followed for 1 year during active flares and to be followed for another year once symptoms resolve. For the reintroduction phase, one food can be added on a weekly basis while observing for symptoms. If there are symptoms, the diet then should be resumed.

A case series of 50 adults with IBD self-treating with the SCD found a 66% clinical remission after a mean of approximately 10 months following the diet and multiple patients reporting the ability to discontinue corticosteroid therapy

Table 1. Summary of	claims and evidence of	diets promoted in IBD			
Diet	The restricted nutrient of focus	The rationale and claims for its use	Level of evidence	Foods to eat (sample list)	Foods to limit (sample list)
Specific Carbohydrate Diet	Carbohydrates (all except for monosaccharides)	Eliminating all carbohydrates that require enzymatic digestion will reduce bacterial fermentation upon those carbohydrates and thus will reduce inflammation and iniury.	Although some studies have shown improvement on inflammatory markers, mucosal healing, and symptoms, data continues to be limited, especially for the adult population.	Fresh meat, poultry, fish, eggs, lactose-free dairy (e.g., hard cheeses, all fruits and non-starchy vegetables, honey)	Processed meats, high-lactose dairy (e.g., cow's milk), all grains (e.g., breads, pastas), starchy vegetables (e.g., corn, potatoes), table sugar
Low FODMAP diet	Carbohydrates (the fermentable carbohydrates)	Reducing intake of highly fermentable FODMAPs may reduce functional symptoms similar to the functional symptoms experienced by those with IBS.	A few studies have shown reduction in functional symptoms that were similar to IBS in IBD patients. There are minimal data on the impact of the diet on inflammation. The diet can be utilized to manage functional symptoms in IBD patients as long as adequate nutrition is monitored.	Meat, poultry, fish, eggs, lactose-free dairy, gluten-free grains (e.g., bananas), regetables (e.g., spinach), sugar, most nuts, most spice and herbs, garlic-infused oil	High-lactose dairy (e.g., cow's milk), grains (e.g., wheat, barley, rye), fruits (e.g., stone fruits), vegetables (e.g., cauliflower), legumes (e.g., lentils), cashews, honey, garlic, onion
Gluten-free diet	Gluten	Removing all gluten containing foods from the diet may reduce inflammation and symptoms.	The diet's role is well established in celiac disease and, to some extent, has shown to improve IBS-like symptoms in those with non-celiac gluten sensitivity. Some studies have shown improvement in symptoms in IBD patients, but overall, when compared to those who were not	Meat, poultry, fish, eggs, gluten-free grains (e.g., quinoa), plain dairy, all fruits and vegetables, all fresh spices and herbs	Grains with gluten (e.g., wheat, barley, rye, malt), hidden gluten (e.g., soy sauce)

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Table 1. (Continued)					
Diet	The restricted nutrient of focus	The rationale and claims for its use	Level of evidence	Foods to eat (sample list)	Foods to limit (sample list)
			following a gluten free diet, there were no significant differences found in outcomes for disease activity, hospitalizations, surgery, or complications. The role of the diet in IBD remains uncertain.		
Anti-inflammatory diet	Carbohydrates (refined) Saturated fats	Adding plant-based foods high in phytonutrients, especially fruits and vegetables, plant-based protein as primary protein, spices and herbs, and fish rich in omega-3 polyunsaturated fats may reduce inflammation.	Very limited data in IBD. A small study has shown improvements in symptoms and a reduction in the use of medications. Data is limited by small sample size and retrospective design. No data available on the impact of the diet on mucosal healing or inflammation.	Fish, low-fat dairy, whole grains, all fruits and vegetables, nuts, plant based protein (e.g., beans), all spices and herbs	Meat, poultry, eggs, high-fat dairy, refined grains, concentrated sweets
Mediterranean diet	Carbohydrates (refined) Saturated fats	Restricting refined carbohydrates, trans fat, saturated fats, and including plant-based foods rich in phytonutrients, olive oil as the primary oil, nuts and fish rich in polyunsaturated fats (omega-3 fatty acids) may reduce inflammation.	Very limited data in IBD. A small study has shown that with a Mediterranean diet, there were altered expressions of more than 3000 genes and trends progressing toward normalization in intestinal microbiota and inflammatory markers.	Fish, low-fat dairy, whole grains, all fruits and vegetables, nuts, all legumes, olive oil, all spices and herbs	Meat, poultry, eggs, high-fat dairy, trans fats, refined grains, concentrated sweets

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[11]. An anonymous online survey completed by 417 adult patients with IBD following the SCD (47% CD, 43% UC, and 10% indeterminate colitis) revealed 33% and 42% of patients experienced symptomatic remission after 2 and 6–12 months on the diet, respectively [12]. Improvement in self-reported symptoms of abdominal pain, limitations of activities, diarrhea, blood in the stool, and weight loss were all noted with SCD.

A retrospective study of 26 pediatric patients with IBD (20 CD, 6 UC) at a tertiary care center on the SCD demonstrated improvement in disease activity index scores and laboratory markers of inflammation [13]. Another retrospective pediatric study with 11 CD patients showed improvements in erythrocyte sedimentation rate (ESR), hematocrit, and albumin with the SCD [14]. Most improvements in laboratory parameters persisted after mild liberalization of diet. The impact of the SCD on mucosal healing has also been partially assessed in the pediatric CD population. A prospective study published in 2014 including 9 pediatric patients with active CD demonstrated significant improvements in both clinical disease indexes and mucosal healing based on capsule endoscopy after 12 weeks of SCD [15]. Of the seven patients that continued SCD for 52 weeks, two demonstrated sustained mucosal healing and one exhibited continued mucosal improvement.

Robust prospective data for SCD in the adult IBD population is currently lacking. Among the encouraging findings of studies thus far, the SCD is one of the few diets with some (although limited) data suggesting impact on mucosal inflammation/healing in addition to clinical symptoms. Nonetheless, the stringent exclusions of the SCD also call into question the feasibility of adherence.

Low FODMAP diet

Similar to the SCD, the premise behind a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) is the reduction of short-chain, highly fermentable, and poorly absorbed carbohydrates that can lead to downstream bacterial overgrowth (intestinal dysbiosis), intestinal injury/inflammation, excess gas formation and luminal distension through bacterial fermentation, and water secretion [16-18]. The concepts between the two diets are similar, although SCD favors the consumption of monosaccharides, while the low FODMAP diet discourages the consumption of monosaccharides. Foods that are high in FODMAPs include high-lactose dairy (e.g., non-lactose-free cow's milk), excess fructose (e.g., watermelon), fructans/ galactans (e.g., wheat, onions), and polyols (e.g., stone fruits such as peach). Prior studies have shown wheat and onions to contribute the vast majority of fructans to the standard American diet, with additional frequent contributions from ripe bananas and garlic [19]. Foods that have moderate FODMAPs are allowed if specific portions are consumed (e.g., two Brussels sprouts). Foods that are low in FODMAPs are lactose-free dairy, low fructose (e.g., strawberries), and low fructans/galactans (e.g., oats). When patients initiate a low FODMAP diet, it is typically recommended that they follow an initial 4–6 weeks of strict diet adherence with subsequent re-introduction of FODMAPs while monitoring symptoms, with the goal of arriving upon a more relaxed restriction of FODMAPs that optimizes symptoms [20]. The low FODMAP diet is perhaps best studied with regards to its utility in irritable bowel syndrome (IBS), in which the diet is a widely accepted management strategy for IBS patients, although data on the diet's efficacy remains somewhat mixed [21]. It is estimated that greater than 30% of patients with IBD have concomitant IBS [22]. Functional gastrointestinal symptoms are observed approximately three times more frequently in patients with IBD compared to the general population [23].

Pedersen et al. published results of a randomized controlled open-label trial consisting of 89 adult IBD patients (28 CD, 61 UC) in clinical remission or with mild-to-moderate disease with functional gastrointestinal symptoms similar to IBS [24•]. Subjects were randomized to regular diet or low FODMAP for a period of 6 weeks, with study results based on subject questionnaire completion demonstrating improvement in IBS-like symptoms and quality of life. A randomized, double-blinded, placebo-controlled, crossover, re-challenge trial examined individuals with IBD in remission that also possessed functional gastrointestinal symptoms meeting criteria for IBS [25]. Utilizing serial FODMAP challenges, it was found that fructans significantly exacerbated functional gastrointestinal symptoms in patients with IBD compared to placebo, while galacto-oligosaccharides and sorbitol did not. Additionally, a randomized, controlled crossover trial including 8 patients with CD revealed improvement in overall gastrointestinal symptoms but no impact on fecal calprotectin levels [26].

Given the significant overlap of IBS and IBS-like symptoms in patients with IBD, the findings of these studies are encouraging and, at least to a limited extent, expected. Recently released clinical practice updates from the American Gastroenterological Association for management of functional gastrointestinal symptoms in IBD include a recommendation that low FODMAP may be offered to address functional symptoms in IBD patients as long as adequate nutrition is carefully monitored [27]. While a role for the low FODMAP diet for IBS-like symptoms in IBD patients is more widely accepted, there remains little information regarding the diet's impact on underlying inflammation. As mentioned above, the available data with respect to intestinal markers of inflammation are less promising. Finally, the restrictive nature of the low FODMAP diet, especially when not managed with the oversight of a dietitian familiar with the process for both exclusion and re-introduction of FODMAPs, again places patients at high risk for micronutrient deficiencies and malnutrition.

Gluten-free diet

The gluten-free diet, traditionally utilized for individuals with celiac disease, emphasizes elimination of gliadin, a protein found in wheat, barley, and rye. Hidden sources of gluten may also include thickening or flavoring agents used to enhance the taste of food. Foods allowed on the gluten-free diet include gluten-free grains made from rice and corn, fresh meat or poultry, fresh fruits, fresh vegetables, and dairy. This diet has further been expanded to use in individuals with non-celiac gluten sensitivity, a disorder characterized by improvement in IBS-like gastrointestinal symptoms with gluten elimination, despite lacking the genetics and immunologic phenotype that define celiac disease [28, 29]. While the diet's role in celiac disease is well understood, the mechanism behind any utility in IBD is less clear. Potential mechanisms for benefit in IBD may be similar to those proposed for non-celiac gluten sensitivity, such as immune system activation by amylase-trypsin inhibitors and/or wheat germ agglutinin [29–31]. There is also the hypothesis that gliadin interferes with cellular tight junction proteins, thus leading to increased intestinal permeability, bacterial translocation, and activation of the innate immune response [32]. Symptomatic improvement may potentially be related to reduction in FODMAPs associated with gluten-free diet [29, 30].

A large, cross-sectional study of 1647 patients with IBD in the Crohn's and Colitis Foundation Partners cohort examined the prevalence of celiac disease, non-celiac gluten sensitivity, and gluten-free diet adherence [33]. The study found a 0.6% prevalence of celiac disease diagnosis among the cohort, along with 4.9% reporting a diagnosis of non-celiac gluten sensitivity. 19.1% of the study cohort had previously trialed a gluten-free diet and 8.2% were currently adhering to the diet. Nearly 2/3 of patients who had tried a gluten-free diet reported improvement in gastrointestinal symptoms and 38.3% reported less frequent or less severe flares of their IBD. Another large study involved the prospective collection of data from greater than 1300 patients with IBD in the Swiss Inflammatory Bowel Disease Cohort Study regarding adherence to gluten-free diet [34•]. Of the 4.7% of respondents that followed a gluten-free diet, with the vast majority of these patients not having a concomitant diagnosis of celiac disease, no significant differences in disease activity, hospitalization, surgery, or complication were found when compared to those that did not follow gluten-free diet. Interestingly, IBD patients following a gluten-free diet reported worse overall psychological well-being. This finding of worsened psychological well-being in patients with IBD following a gluten-free diet appears to be a novel finding in the IBD population that has otherwise not been explored; however, it seems to conflict with data regarding gluten-free diet in other non-IBD patient cohorts. For example, a large national survey in the USA demonstrated lower rates of depression in individuals who avoided gluten but no significant increase in depression in individuals with celiac disease [35]. Similarly, in pediatric patients with celiac disease, adherence to a gluten-free diet has been associated with improvement in depressive symptoms [36].

As evidenced above, significant proportions of IBD patients appear to be experimenting with the gluten-free diet, proportions that easily exceed subsets of IBD patients with a more clear indication for the diet like concomitant celiac disease or non-celiac gluten sensitivity. The number of studies addressing the gluten-free diet in IBD is small, although relevant studies do have the benefit of relatively large sample sizes from national cohorts. Findings from these studies do not lead to a clear conclusion regarding the utility of this diet in IBD. Although there were some findings of symptomatic improvement, findings from a similar large national cohort seemed to find no major differences in more objective outcomes like hospitalization, surgery, or complication. Additionally, negative impacts of such a diet on psychological well-being may be again secondary to the restrictive nature of this type of exclusion diet. Strict adherence to a gluten-free diet also has potential nutritional consequences, including micronutrient and dietary fiber deficiencies [37].

Anti-inflammatory diet

Published in 1995, *The Zone Diet* by Dr. Barry Sears is often identified as one of the earliest anti-inflammatory diets, focusing on utilization of particular macronutrient ratios to manage diet-mediated inflammation through optimization of cortisol and insulin [38, 39]. The premise of the diet is to reduce inflammation through daily consumption of "anti-inflammatory" nutrients, such as phytonutrients found in various plant based foods (e.g., fruits) and spices (e.g., turmeric) and omega-3 polyunsaturated fatty acids (e.g., fish). The diet promotes the daily inclusion of fruits and vegetables to comprise the majority of the diet due to its rich phytonutrient. Key anti-inflammatory micronutrients include vitamin C, vitamin E, and beta carotene (valued for their antioxidant properties), as well as vitamin B3, vitamin B6, zinc, and magnesium (highlighted for their roles as key enzymatic cofactors in fatty acid metabolism). Although the diet permits consumption of animal protein, plant-based protein (e.g., legumes) is recommended to be the primary protein source.

Olendzki et al. developed the IBD-Anti-Inflammatory Diet (IBD-AID), publishing results of a retrospective case series of the diet's use in a limited number of patients with IBD with disease either refractive to pharmacotherapy or with otherwise inadequately controlled symptoms [40]. The principle features of IBD-AID were carbohydrate restriction (lactose, refined/processed complex carbohydrates), ingestion of pre- and probiotics, modification of fat intake (decreasing saturated fats and increasing polyunsaturated fats through omega-3 fatty acids), detection of nutrient deficiencies and food intolerances, and finally the modification of food texture as needed to improve nutrient absorption and reduce intact fiber (e.g. ground or blenderized forms of foods). All 11 patients that met study criteria (8 CD, 3 UC) noted improvement in symptoms based on clinical assessment scoring systems and were able to reduce their medications.

Vegetarian and vegan diets have gained significant popularity in the general population, in part due to presumed anti-inflammatory properties of diets that avoid meat and animal products, respectively. Data are extremely limited on the role of vegetarian and vegan diets as anti-inflammatory options for patients with IBD. Nonetheless, a recent randomized trial showed that a diet low in red and processed meat does not reduce the rate of clinical relapse with CD [41]. IBD patients following a vegetarian diet in the Swiss IBD Cohort Study demonstrated no differences in key outcomes including disease activity, hospitalization rates, and surgery rates compared with those not following the diet [34•]. Additionally, low fiber diets and high fiber diets have both had proposed roles in IBD [42, 43]. The role of such "anti-inflammatory" vegetarian and vegan diets remains unclear in IBD.

While the principle of "anti-inflammatory" foods for management of chronic inflammatory diseases of the gastrointestinal tract like CD and UC appeals to reason at a more broad level, data regarding such a diet's efficacy are severely limited by small sample size and retrospective design. Additionally, the limited data provides information on symptom improvement but provides no insight on mucosal healing or inflammation. Additionally, potential anti-

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inflammatory consequences of vegetarian or vegan diets in IBD require further investigation.

Mediterranean diet

The Mediterranean diet is one of the most thoroughly studied diets with regards to impact on chronic disease. The Mediterranean diet is modeled after the dietary patterns of populations residing near the Mediterranean Sea, like those of southern Italy, Crete, and Greece. The diet shares similarities with the antiinflammatory diet with its rich use of phytonutrients, omega-3 polyunsaturated fats, unsaturated fats like olive oil in place of saturated and trans-fatty acids, plant-based foods, high-fiber whole grains, nuts, and low intake of red meats [44, 45]. The impact of a Mediterranean-style diet on disease has perhaps best been evaluated with regards to cardiovascular disease, with adherence to such a diet demonstrating a significant impact on primary and secondary prevention of cardiovascular disease [46, 47]. The diet has also been associated with reduced risk of developing type 2 diabetes mellitus and has demonstrated utility in combating the metabolic syndrome [48, 49]. Adherence to a Mediterranean diet has been associated with lower inflammatory markers [50, 51]. This reduction in inflammation from the Mediterranean diet, despite the allowance of fat (traditionally viewed to have pro-inflammatory properties), is often termed the "Mediterranean Paradox" and is yet not clarified. On the other hand, some studies suggest that the anti-inflammatory benefits from the Mediterranean diet may instead stem from the types of fat it incorporates. In particular, olive oil polyphenols possess antioxidant, anti-inflammatory, antisteatotic, and antimicrobial effects (PMID 31137753).

Given the diet's evidence on combatting other chronic diseases and inflammation, the Mediterranean approach has peaked interest among gastroenterologists and researchers as a potential intervention for IBD. A systematic review published by Hou et al. in 2014 examined pre-illness diets and found high fruit and fiber diets protective against CD, while high vegetable intake was protective against developing UC [52]. The same study found high intake of meats, omega-6 fatty acids, polyunsaturated fatty acids, and total fats correlated with increased risk of developing CD and UC. These findings of protective benefits of fruits and vegetables, as well as harmful effects of fats and meats, seem to suggest promise for components found in a Mediterranean-inspired diet.

Transcriptome level analytics of eight adult patients with CD subjected to 6 weeks of a Mediterranean-inspired diet resulted in significantly altered expression of more than 3000 genes, as well as non-statistically significant trends toward "normalization" of the intestinal microbiota and inflammatory markers [53]. A single-center, cross-sectional study evaluated the dietary patterns of 67 adult patients with CD, specifically examining how the macro- and micronutrient intake compared with the Mediterranean diet [54]. With regards to specific components of the Mediterranean diet, the CD patients evaluated used olive oil infrequently as the primary fat source. Few patients met Mediterranean diet criteria for vegetables, legumes, or fruits. Intake of fish and nuts was inadequate in greater than 80% of patients, and 30% of male patients exceeded Mediterranean diet recommendations for red or processed meats. Although there is currently a paucity of clinical research directly evaluating the impact of the Mediterranean diet on IBD, current research underway will have the potential to contribute much needed data to the field. The Trial of Specific Carbohydrates and Mediterranean Diets to Induce Remission of Crohn's Disease (DINE-CD) study, funded by the Crohn's and Colitis Foundation and Patient-Centered Outcomes Research Institute, is a multicenter, openlabel, randomized clinical trial that compares the efficacy of the SCD with the Mediterranean diet on reducing symptoms and inflammation in adults with Crohn's disease (ClinicalTrials.gov identifier NCT03058679). Unlike the typical fad diets, the Mediterranean diet leaves patients less susceptible to nutritional deficiencies.

Conclusion

Despite the recent expansion of fad diets in popular culture, the role for such nutritional interventions in IBD remains uncertain. Review of the current literature involving popular diets in IBD reveals an overall paucity of data, with available research frequently limited by small sample sizes and/or retrospective data collection. Additionally, while the vast majority of research has focused on patient symptoms, very little is known regarding the impact of specific dietary interventions on inflammation at the endoscopic and cellular levels. Gastroenterologists are instructed to manage patients with CD and UC under the treat-to-target model, focusing not only on symptomatic improvement but also on mucosal healing [55]. The current quality of evidence does not allow for clear dietary recommendations for individuals with IBD, a conclusion supported by a recent 2019 systematic review, which included 18 randomized controlled trials [56•]. More robust research methodologies and larger sample sizes will be needed in order to begin to draw more definitive conclusions.

Patient-initiated trials of certain popular diets, including fad diets, will likely continue to be seen regularly in current practice, and physicians should be prepared to counsel on the body of evidence regarding such diets, and perhaps more importantly, where such data are lacking. Additionally, given the nature of food/nutrient exclusion frequently seen in fad diets, physicians will be required to counsel on potential negative consequences, particularly nutritional deficiencies, that initiation of a fad diet for IBD may portend. As knowledge in the field continues to expand exponentially, we are optimistic that future research will continue to clarify the role for diet in the primary or adjunctive management of IBD.

Compliance with Ethical Standards

Conflict of Interest

Andrew T. Weber, Neha D. Shah, Jenny Sauk, and Berkeley N. Limketkai declare no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet. 2018;390(10114):2769–78. https://doi.org/ 10.1016/S0140-6736(17)32448-0.
- Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. Gastroenterology. 2004;126(6):1504–17.
- Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 2012;142(1):46–54 e42; quiz e30. https://doi.org/10. 1053/j.gastro.2011.10.001.
- 4. de Vries JHM, Dijkhuizen M, Tap P, Witteman BJM. Patient's dietary beliefs and behaviours in inflammatory bowel disease. Dig Dis. 2019;37(2):131–9. https://doi.org/10.1159/000494022.
- Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical guideline: management of Crohn's disease in adults. Am J Gastroenterol. 2018;113(4):481–517. https://doi.org/ 10.1038/ajg.2018.27.
- Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019;114(3):384–413. https://doi.org/10.14309/ajg.000000000000152.
- 7. Haas SV, Haas MP. The treatment of celiac disease with the specific carbohydrate diet; report on 191 additional cases. Am J Gastroenterol. 1955;23(4):344–60.
- 8. Gottschall EG. Breaking the vicious cycle: intestinal health through diet. Ontario: Kirkton Press; 1994.
- 9. Knight-Sepulveda K, Kais S, Santaolalla R, Abreu MT. Diet and inflammatory bowel disease. Gastroenterol Hepatol (N Y). 2015;11(8):511–20.
- 10. Limketkai BN, Wolf A, Parian AM. Nutritional interventions in the patient with inflammatory bowel disease. Gastroenterol Clin N Am. 2018;47(1):155–77. https://doi.org/10.1016/j.gtc.2017.09.007.
- Kakodkar S, Farooqui AJ, Mikolaitis SL, Mutlu EA. The specific carbohydrate diet for inflammatory bowel disease: A Case Series. J Acad Nutr Diet. 2015;115(8):1226–32. https://doi.org/10.1016/j.jand. 2015.04.016.
- 12. Suskind DL, Wahbeh G, Cohen SA, Damman CJ, Klein J, Braly K, et al. Patients perceive clinical benefit with the specific carbohydrate diet for inflammatory bowel disease. Dig Dis Sci. 2016;61(11):3255–60. https://doi.org/10.1007/s10620-016-4307-y.

- Obih C, Wahbeh G, Lee D, Braly K, Giefer M, Shaffer ML, et al. Specific carbohydrate diet for pediatric inflammatory bowel disease in clinical practice within an academic IBD center. Nutrition. 2016;32(4):418–25. https://doi.org/10.1016/j.nut.2015.08.025.
- Burgis JC, Nguyen K, Park KT, Cox K. Response to strict and liberalized specific carbohydrate diet in pediatric Crohn's disease. World J Gastroenterol. 2016;22(6):2111–7. https://doi.org/10.3748/wjg.v22. i6.2111.
- Cohen SA, Gold BD, Oliva S, Lewis J, Stallworth A, Koch B, et al. Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn disease. J Pediatr Gastroenterol Nutr. 2014;59(4):516–21. https://doi.org/10.1097/MPG.000000000000449.
- Gibson PR, Shepherd SJ. Personal view: food for thought-western lifestyle and susceptibility to Crohn's disease. FODMAP hypothesis Aliment Pharmacol Ther. 2005;21(12):1399–409. https://doi.org/10. 1111/j.1365-2036.2005.02506.x.
- Barrett JS, Gearry RB, Muir JG, Irving PM, Rose R, Rosella O, et al. Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon. Aliment Pharmacol Ther. 2010;31(8):874–82. https://doi.org/ 10.1111/j.1365-2036.2010.04237.x.
- Ong DK, Mitchell SB, Barrett JS, Shepherd SJ, Irving PM, Biesiekierski JR, et al. Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. J Gastroenterol Hepatol. 2010;25(8):1366– 73. https://doi.org/10.1111/j.1440-1746.2010.06370. x.
- Moshfegh AJ, Friday JE, Goldman JP, Ahuja JK. Presence of inulin and oligofructose in the diets of Americans. J Nutr. 1999;129(7 Suppl):1407S–11S. https:// doi.org/10.1093/jn/129.7.1407S.
- 20. Barrett JS. How to institute the low-FODMAP diet. J Gastroenterol Hepatol. 2017;32(Suppl 1):8–10. https://doi.org/10.1111/jgh.13686.
- 21. Kamal A, Pimentel M. Influence of dietary restriction on irritable bowel syndrome. Am J Gastroenterol. 2019;114(2):212–20. https://doi.org/10.1038/ s41395-018-0241-2.
- 22. Halpin SJ, Ford AC. Prevalence of symptoms meeting criteria for irritable bowel syndrome in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol. 2012;107(10):1474–82. https://doi.org/10.1038/ajg.2012.260.
- 23. Farrokhyar F, Marshall JK, Easterbrook B, Irvine EJ. Functional gastrointestinal disorders and mood disorders in patients with inactive inflammatory bowel

disease: prevalence and impact on health. Inflamm Bowel Dis. 2006;12(1):38–46.

- Pedersen N, Ankersen DV, Felding M, Wachmann H, Vegh Z, Molzen L, et al. Low-FODMAP diet reduces irritable bowel symptoms in patients with inflammatory bowel disease. World J Gastroenterol. 2017;23(18):3356–66. https://doi.org/10.3748/wjg. v23.i18.3356This prospective trial compared low FODMAP diet to regular diet in patients with IBD. The low FODMAP diet resulted in improved functional gastrointestinal symptoms and quality of life.
- Cox SR, Prince AC, Myers CE, Irving PM, Lindsay JO, Lomer MC, et al. Fermentable carbohydrates [FODMAPs] Exacerbate functional gastrointestinal symptoms in patients with inflammatory bowel disease: a randomised, double-blind, placebo-controlled, cross-over, re-challenge trial. J Crohns Colitis. 2017;11(12):1420–9. https://doi.org/10.1093/eccojcc/jjx073.
- Halmos EP, Christophersen CT, Bird AR, Shepherd SJ, Muir JG, Gibson PR. Consistent prebiotic effect on gut microbiota with altered FODMAP intake in patients with Crohn's disease: a randomised, controlled crossover trial of well-defined diets. Clin Transl Gastroenterol. 2016;7:e164. https://doi.org/10.1038/ ctg.2016.22.
- Colombel JF, Shin A, Gibson PR. AGA Clinical Practice update on functional gastrointestinal symptoms in patients with inflammatory bowel disease: expert review. Clin Gastroenterol Hepatol. 2019;17(3):380–90 e1. https://doi.org/10.1016/j.cgh.2018.08.001.
- Elli L, Tomba C, Branchi F, Roncoroni L, Lombardo V, Bardella MT, et al. Evidence for the presence of nonceliac gluten sensitivity in patients with functional gastrointestinal symptoms: results from a multicenter randomized double-blind placebo-controlled gluten challenge. Nutrients. 2016;8(2):84. https://doi.org/10. 3390/nu8020084.
- 29. Niland B, Cash BD. Health benefits and adverse effects of a gluten-free diet in non-celiac disease patients. Gastroenterol Hepatol (N Y). 2018;14(2):82–91.
- Fasano A, Sapone A, Zevallos V, Schuppan D. Nonceliac gluten sensitivity. Gastroenterology. 2015;148(6):1195–204. https://doi.org/10.1053/j. gastro.2014.12.049.
- Dalla Pellegrina C, Perbellini O, Scupoli MT, Tomelleri C, Zanetti C, Zoccatelli G, et al. Effects of wheat germ agglutinin on human gastrointestinal epithelium: insights from an experimental model of immune/ epithelial cell interaction. Toxicol Appl Pharmacol. 2009;237(2):146–53. https://doi.org/10.1016/j.taap. 2009.03.012.
- 32. Drago S, El Asmar R, Di Pierro M, Grazia Clemente M, Tripathi A, Sapone A, et al. Gliadin, zonulin and gut permeability: effects on celiac and non-celiac intestinal mucosa and intestinal cell lines. Scand J Gastroenterol. 2006;41(4):408–19. https://doi.org/10.1080/ 00365520500235334.

- Herfarth HH, Martin CF, Sandler RS, Kappelman MD, Long MD. Prevalence of a gluten-free diet and improvement of clinical symptoms in patients with inflammatory bowel diseases. Inflamm Bowel Dis. 2014;20(7):1194–7. https://doi.org/10.1097/MIB. 000000000000077.
- 34.• Schreiner P, Yilmaz B, Rossel J-B, Franc Y, Misselwitz B, Schari M, et al. Vegetarian or gluten-free diets in patients with inflammatory bowel disease are associated with lower psychological well-being and a different gut microbiota, but no beneficial effects on the course of the disease. United Eur Gastroenterol J. 2019. https:// doi.org/10.1177/2050640619841249

This large national cohort study analyzed the impact of gluten-free diet on patiens with IBD. The gluten-free diet diet not demonstrate significant improvement in activity scores, hospitalization, surgery, or complications. Additionally, patients that followed the gluten-free diet had higher anxiety and depression scores, as well as scores indicating worse psychological well-being.

- Zylberberg HM, Demmer RT, Murray JA, Green PHR, Lebwohl B. Depression and insomnia among individuals with celiac disease or on a gluten-free diet in the USA: results from a national survey. Eur J Gastroenterol Hepatol. 2017;29(9):1091–6. https://doi.org/10. 1097/MEG.00000000000932.
- Simsek S, Baysoy G, Gencoglan S, Uluca U. Effects of gluten-free diet on quality of life and depression in children with celiac disease. J Pediatr Gastroenterol Nutr. 2015;61(3):303–6. https://doi.org/10.1097/ MPG.000000000000799.
- 37. Theethira TG, Dennis M, Leffler DA. Nutritional consequences of celiac disease and the gluten-free diet. Expert Rev Gastroenterol Hepatol. 2014;8(2):123–9. https://doi.org/10.1586/17474124.2014.876360.
- Sears B, Lawren B. The Zone: A dietary road map. 1st ed. Regan Book: New York, NY; 1995.
- Ricker MA, Haas WC. Anti-inflammatory diet in clinical practice: a review. Nutr Clin Pract. 2017;32(3):318– 25. https://doi.org/10.1177/0884533617700353.
- 40. Olendzki BC, Silverstein TD, Persuitte GM, Ma Y, Baldwin KR, Cave D. An anti-inflammatory diet as treatment for inflammatory bowel disease: a case series report. Nutr J. 2014;13:5. https://doi.org/10.1186/ 1475-2891-13-5.
- Albenberg L, Brensinger CM, Wu Q, Gilroy E, Kappelman MD, Sandler RS, et al. A diet low in red and processed meat does not reduce rate of Crohn's disease flares. Gastroenterology. 2019;157(1):128–36 e5. https://doi.org/10.1053/j.gastro.2019.03.015.
- Koga H, Iida M, Aoyagi K, Matsui T, Fujishima M. Long-term efficacy of low residue diet for the maintenance of remission in patients with Crohn's disease. Nihon Shokakibyo Gakkai Zasshi. 1993;90(11):2882– 8.
- 43. Ananthakrishnan AN, Khalili H, Konijeti GG, Higuchi LM, de Silva P, Korzenik JR, et al. A prospective study of long-term intake of dietary fiber and risk of Crohn's disease and ulcerative colitis. Gastroenterology.

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2013;145(5):970-7. https://doi.org/10.1053/j.gastro. 2013.07.050.

- 44. Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, et al. Mediterranean diet pyramid: a cultural model for healthy eating. Am J Clin Nutr. 1995;61(6 Suppl):1402S–6S. https://doi.org/10. 1093/ajcn/61.6.1402S.
- 45. Widmer RJ, Flammer AJ, Lerman LO, Lerman A. The Mediterranean diet, its components, and cardiovascular disease. Am J Med. 2015;128(3):229–38. https:// doi.org/10.1016/j.amjmed.2014.10.014.
- Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med. 2018;378(25):e34. https://doi.org/10.1056/ NEJMoa1800389.
- 47. de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation. 1999;99(6):779–85.
- Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, et al. Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA. 2004;292(12):1440–6. https://doi.org/10.1001/jama.292.12.1440.
- Koloverou E, Esposito K, Giugliano D, Panagiotakos D. The effect of Mediterranean diet on the development of type 2 diabetes mellitus: a meta-analysis of 10 prospective studies and 136,846 participants. Metabolism. 2014;63(7):903–11. https://doi.org/10.1016/j. metabol.2014.04.010.
- Sureda A, Bibiloni MDM, Julibert A, Bouzas C, Argelich E, Llompart I, et al. Adherence to the Mediterranean diet and inflammatory markers. Nutrients. 2018;10(1):E62. https://doi.org/10.3390/ nu10010062.
- 51. Dinu M, Pagliai G, Casini A, Sofi F. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials. Eur J Clin Nutr. 2018;72(1):30–43. https://doi.org/10.1038/ejcn.2017.58.

- 52. Hou JK, Abraham B, El-Serag H. Dietary intake and risk of developing inflammatory bowel disease: a systematic review of the literature. Am J Gastroenterol. 2011;106(4):563–73. https://doi.org/10.1038/ajg. 2011.44.
- Marlow G, Ellett S, Ferguson IR, Zhu S, Karunasinghe N, Jesuthasan AC, et al. Transcriptomics to study the effect of a Mediterranean-inspired diet on inflammation in Crohn's disease patients. Hum Genomics. 2013;7:24. https://doi.org/10.1186/1479-7364-7-24.
- 54. Taylor L, Almutairdi A, Shommu N, Fedorak R, Ghosh S, Reimer RA, et al. Cross-sectional analysis of overall dietary intake and mediterranean dietary pattern in patients with Crohn's disease. Nutrients. 2018;10(11):E1761. https://doi.org/10.3390/ nu10111761.
- 55. Peyrin-Biroulet L, Sandborn W, Sands BE, Reinisch W, Bemelman W, Bryant RV, et al. Selecting therapeutic targets in inflammatory bowel disease (STRIDE): determining therapeutic goals for treat-to-target. Am J Gastroenterol. 2015;110(9):1324–38. https://doi.org/ 10.1038/ajg.2015.233.
- 56.• Limketkai BN, Iheozor-Ejiofor Z, Gjuladin-Hellon T, Parian A, Matarese LE, Bracewell K, et al. Dietary interventions for induction and maintenance of remission in inflammatory bowel disease. Cochrane Database Syst Rev. 2019;2:CD012839. https://doi.org/10.1002/ 14651858.CD012839.pub2

This recent systematic review evaluating the safety and efficacy of dietary intervention in IBD included 18 randomized controlled trials with greater than 1800 participants. The study concluded that the data were lacking for drawing definitive conclusions for dietary recommendations, as benefits and harms remain unclear. This systematic review is the most comprehensive evaluation of dietary intervention in IBD to date.

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