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Dietary content and eating behavior in ulcerative colitis: a narrative review and future perspective

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Abstract

Ulcerative colitis (UC) has experienced a steady increase in global incidence and prevalence recently. Current research into UC pathogenesis focuses on the complex interplay of genetic and environmental factors with the immune system and gut microbiome, leading to disruption of the intestinal barrier. Normally, the microbiome, intestinal epithelium, and immune system interact to maintain intestinal homeostasis. However, when this equilibrium is disturbed, a harmful cycle of dysbiosis, immune dysregulation, and inflammation emerges, resulting in intestinal barrier dysfunction and UC progression. Among various risk factors, diet significantly influences epithelial barrier integrity and architectural stability through both direct and indirect mechanisms, shaping the entire UC continuum from pre-clinical prevention to active phase treatment and remission maintenance. This review provides insights into the impact of dietary content and eating behaviors on UC, focusing on specific food, food groups, nutrients, and intermittent fasting, while providing a detailed explanation of why the gut microbiota may mediate the sustained effects of diet across all stages of UC. Additionally, it addresses the limitations of current studies, explores underexamined areas in UC dietary research and proposes potential directions for future research and expansion.

Clinical trial number

Not applicable.

Keywords Ulcerative colitis, Inflammatory bowel disease, Diet, Macronutrients, Intermittent fasting

Introduction

Ulcerative colitis (UC) is a form of inflammatory bowel disease (IBD) that has witnessed a significant surge in global incidence and prevalence, with rates exceeding 400 cases per 100,000 individuals in North America [1–3]. The focal point of ongoing studies on UC's pathogenesis is the complex interaction among genetic susceptibility, environmental factors, and the nuanced dynamics between the immune system and the gut microbiome. This multifaceted interplay disrupts intestinal barrier function [4]. In particular, immune dysregulation creates an oxidative environment [5], leading to dysbiosis. This state of prolonged microbial imbalance further exacerbates immune dysregulation and ensuing inflammation [6–8]. Under normal circumstances, a harmonious relationship among the gut microbiota, the intestinal epithelium, and the immune system is essential for maintaining intestinal homeostasis [9]. However, disturbances in this equilibrium initiate a harmful cycle of dysbiosis, immune dysfunction, and inflammation. Such

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disturbances ultimately impair the intestinal barrier's functionality, driving the progression of UC.

In the realm of UC etiology, both genetic predispositions and environmental influences play critical roles. These factors are instrumental in causing structural damage to the intestinal epithelial tissue and modifications in the thickness of the mucous layer [10], thereby directly undermining the integrity of the intestinal barrier. Additionally, these factors are capable of provoking chronic inflammation through mechanisms such as dysbiosis and immune dysregulation [11, 12]. This inflammation leads to epithelial cell apoptosis, alterations in the expression and localization of tight junctions (TJs) [10, 13], and disturbances in the expression, synthesis, and secretion of mucins [14–16]. Collectively, these effects contribute to the compromise of epithelial barrier integrity and its architectural stability, underscoring the multifactorial nature of UC pathogenesis.

Concerning the subsequent indirect pathway mentioned in the previous paragraph, diet [17, 18] play a significant role in reshaping the microbial communities within the gut, thus promoting the onset of dysbiosis [19, 20]. This state of dysbiosis is characterized by reduced microbial diversity, an increase in pathogenic bacteria, a decrease in beneficial commensals [21], and heightened bacteriophage activity [8]. Such shifts in the gut flora and phage population can influence mucosal immune responses, either directly or indirectly [22–25], leading to immune dysregulation. This process results in the increased production of pro-inflammatory cytokines, including IL-1β, IL-6, TNF-α, and the cytokines associated with Th1, Th2, and Th17 cells [26–30]. The nutritional status of individuals significantly influences the functionality of various bodily systems, including the immune system, colonic mucosa, gut microbiome, as well as innate and adaptive immune responses [31]. Imbalances in nutrient levels, whether due to deficiencies or excess intake, can lead to significant immunodeficiency [32] (Fig. 1). Apart from individuals' dietary choices, the maternal diet during pregnancy may play a role in shaping susceptibility to inflammation over one's lifespan, although this remains a possibility primarily supported by findings from animal research [33, 34].

The role of diet in managing UC spans the entirety of the disease's spectrum, from pre-clinical prevention through to the maintenance of remission and treatment

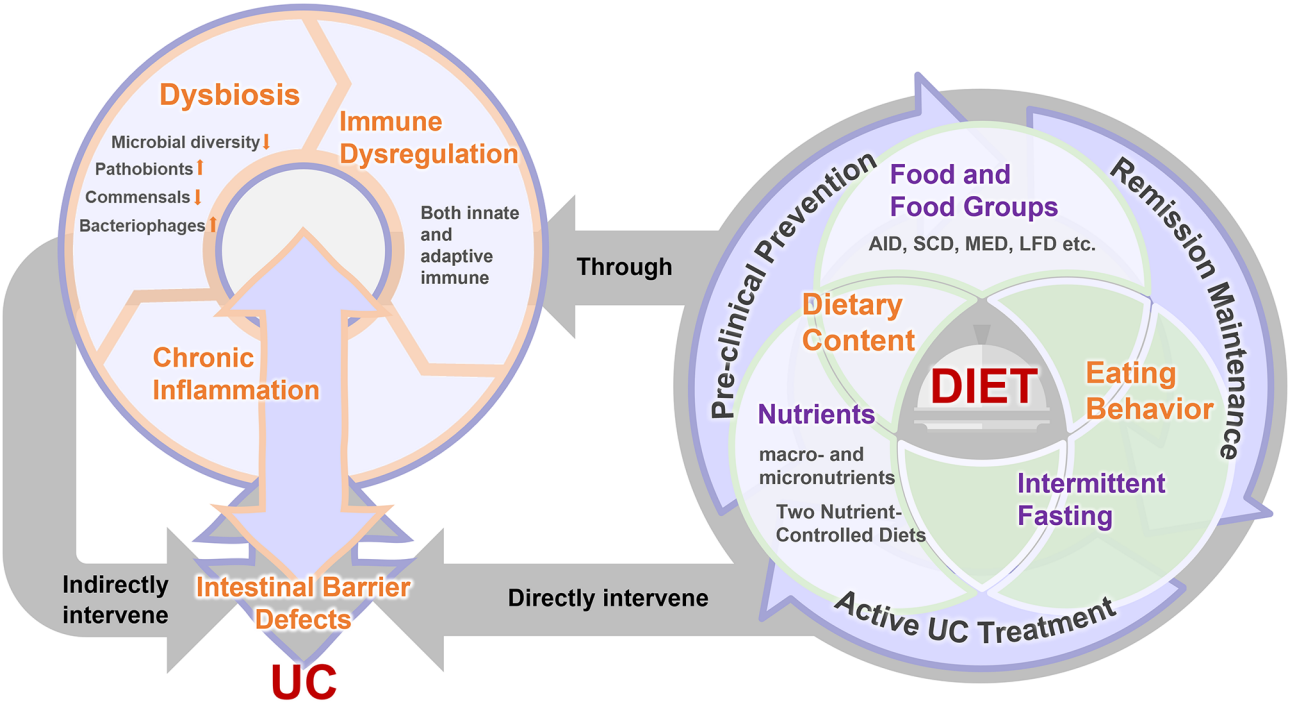

Fig. 1 Pathogenesis of ulcerative colitis (UC) and the impact of diet. Under normal conditions, symbiotic interactions between the microbiome, intestinal epithelium, and immune system are crucial for maintaining intestinal homeostasis. However, any disturbance in this balance can lead to dysbiosis, immune dysregulation, and inflammation, all of which contribute to impairments in the intestinal barrier. The ensuing barrier dysfunction further amplifies the cycle of pathogenic mechanisms at the heart of UC. As the disease progresses, these pathogenic factors intensify, leading to an escalation in symptoms (left). Diet emerges as a critical factor among various risk elements, impacting epithelial barrier integrity and stability through both direct and indirect pathways. It influences the entire trajectory of UC management, from pre-clinical prevention through to remission maintenance and treatment during active phases. This review provides current insights into the role of dietary content and eating behaviors in UC, detailing the effects of specific foods and food groups, nutrients, and the practice of intermittent fasting (right). AID = the Anti-Inflammatory Diet; SCD = the Specific Carbohydrate Diet; MED = the Mediterranean diet; LFD = the low-FODMAP diet

during active phases. Despite certain inherent challenges, the influence of various foods and nutrients on UC has been the focus of extensive research over the years. Beyond specific conditions related to food allergies or intolerances, dietary impacts on UC can generally be categorized as either detrimental or beneficial. This classification is based on their primary effects, although there are instances of conflicting evidence regarding specific foods and nutrients [35]. Recent research efforts have been organized into two main categories by the authors: dietary content and eating behavior. The former includes a detailed analysis of food groups, nutrients, and dietary components, while the latter focuses on the practices surrounding intermittent fasting (IF) (Fig. 1).

Food and food groups

In 2020, the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) formulated dietary guidelines for the control and prevention of IBD, grounded in existing research [36]. By 2024, the American Gastroenterological Association (AGA) had published tailored dietary recommendations for patients with IBD, addressing different phases such as remission, active disease, and instances of intestinal failure [37]. Although research into dietary influences on UC has expanded significantly, limitations in the existing evidence have constrained the ability to update established consensus guidelines. Current findings largely align with prior recommendations, with only a few emerging perspectives offering potentially novel insights. However, these new findings remain preliminary and require further validation before they can be integrated into clinical practice.

Food

Foods impacting UC onset

Dietary guidelines are in a state of continual refinement as research advances. Drawing from a body of relatively high-quality, population-based studies, several key findings have been consistently observed regarding the link between diet and the risk of developing UC: consumption of red and processed meats [38–43], margarine [40, 43–45], processed food [43, 46, 47], and certain food additives like maltodextrins and artificial sweeteners [48, 49] is associated with an increased risk of UC. On the other hand, diets rich in vegetables [50–52], fruit [51–54], legumes [53, 55] and tea [56–58] have been shown to offer protective benefits against the disease.

Table 1 below summarizes the impacts of various food types on the risk of UC development, based on research into the effects of dietary habits prior to the clinical onset of UC on its incidence and severity. Foods for which there is insufficient research or that demonstrate no significant correlation with UC are excluded from this summary. It is important to note that the relatively small number of animal studies is due to the common practice of combining dietary interventions with colitis models in research aimed at preventing UC. This analysis is limited to studies where dietary modifications were implemented before the induction of colitis models.

Foods influencing UC relapse

In the realm of diet's impact on UC relapse, a substantial body of research indicates that many individuals with IBD consider dietary factors to play a pivotal role in both the onset and recurrence of the condition [95–97]. One previous study investigating the subjective experiences of IBD patients during relapse periods found that 36% reported specific dietary choices as alleviating their symptoms. Notably, white and plain foods (56%) and low-fiber options (19%) were most commonly identified as beneficial [97]. Another investigation highlighted a negative correlation between the consumption of pulses and potatoes over a year and the occurrence of disease flares, whereas a higher intake of meat was positively associated with relapse risk. The study did not find a statistically significant link between the consumption of vegetables, grains, dairy, or fish and the frequency of disease flares [98]. Furthermore, a recent study conducted in the Netherlands with 724 IBD participants pinpointed a dietary pattern linked to relapse. This pattern, comprising cereal products, cooking oils and fats, potatoes, processed meats, red meats, condiments and sauces, as well as sugars, cakes, and sweets, was significantly associated with relapse in 24.8% of the patients during the follow-up [99]. Additionally, carrageenan consumption was associated with an earlier relapse in patients in remission [100]. It's important to note that these studies did not differentiate between Crohn's disease (CD) and UC, focusing instead on the broader category of IBD.

Research into the dietary factors linked with flare-ups in UC remains scarce. A notable prospective study identified a significant association between the consumption of red and processed meats (OR 5.19, 95%CI 2.1–12.9), protein (OR 3.00, 95% CI 1.25–7.19), and alcohol (OR 2.71, 95% CI 1.1–6.67) with an increased risk of UC relapse [101]. Furthermore, evidence suggests that a shift towards a plant-based diet and a reduction in animal protein consumption may mitigate the risk of disease flare-ups [102, 103]. Conversely, a different prospective multicenter study focusing on UC patients undergoing maintenance treatment with mesalamine did not find any significant correlation between the intake of processed meats, proteins, alcohol, and high-sulfur foods with a heightened flare-up risk. However, higher consumption of myristic acid (OR 3.01, 95% CI 1.17–7.74) and alpha-linolenic acid (OR 5.50, 95% CI 1.56–19.34), calculated based on portion size and intake frequency,

Table 1 The role of specific foods in UC development

Food	Protective	Harmful	No Association
Meat and Alternatives			
Red and processed meats		Population-based study[38, 39, 41–43]; Systematic review and meta-analysis[40, 52]; Animal experiment[59]	Population-based study[47, 60]; Systematic review and meta-analysis[61]
Fish and seafood	Population-based study[60]	Population-based study[62, 63]; Systematic review and meta-analysis[64]; Mendelian randomization[65]	Population-based study[39, 42, 54, 66]
Dairy	Population-based study[63]; Systematic review and meta-analysis[61]; Animal experiment[67, 68]		Population-based study[39, 44, 47, 60, 62]
Eggs	Population-based study[44]	Systematic review and meta-analysis[50, 64]	Population-based study[39]
Legumes	Population-based study[53, 55, 63]		Population-based study[47]
Nuts	Population-based study[43]	Population-based study[63]	
Vegetables and Fruits			
Vegetables	Population-based study[60]; Systematic review and meta-analysis[50–52]; Mendelian randomization[69]		Population-based study[47]
- Green vegetables		Population-based study[63]	Population-based study[70]
- Cruciferous vegetables	Population-based study[63, 71]; Systematic review[72]; Animal experiment[73, 74]		
Fruit	Population-based study[53, 54]; Systematic review and meta-analysis[51, 64]; Mendelian randomization[69]	Population-based study[63]	Population-based study[47, 60, 70]; Systematic review[50]
Sweets and Desserts			
Honey	Animal experiment[75]	Population-based study[63]	
Cocoa and Chocolate		Population-based study[76, 77]	
Beverages			
Sweetened beverages	Population-based study[60, 77]	Population-based study[76, 78]; Systematic review and meta-analysis[52, 57, 58]	Population-based study[79–82]
Alcohol		Animal experiment[83]	Systematic review and meta-analysis[57]
- Red wine	Population-based study[84]		
- Other alcoholic beverages		Population-based study[84]	
Coffee	Population-based study[56, 77]; Systematic review and meta-analysis[52, 57, 64]		Mendelian randomization[85]
Tea	Population-based study[56]; Systematic review and meta-analysis[57, 58]; Animal experiment[86]	Population-based study[87]	Population-based study[77]
Processed Foods			
Margarine		Population-based study[43–45], Systematic review and meta-analysis[40]	
Processed foods		Population-based study[43, 46, 47]	Meta-analysis[88]
Miscellaneous			
Salt		Population-based study[43, 63]; Animal experiment[89–91]	
Food additives		Population-based study[48, 49]; Animal experiment[92–95]	

was associated with an increased risk of relapse, with a dose-response relationship observed for myristic acid intake and UC recurrence [104]. In summary, the paucity of research on the impact of diet on UC relapse has hindered the formation of a clear consensus. Additionally, the evidence remains inconclusive regarding whether factors implicated in the initial development of UC, such as processed meat consumption, continue to affect the course of the disease after its onset.

Foods in UC active phase treatment

Can specific dietary components offer therapeutic benefits for UC? Numerous investigations have delved into the potential of specific dietary components as therapeutic agents in experimental colitis models, suggesting their viability as drug candidates for UC management. However, the complex composition of foods, including a vast array of macro- and micronutrients, non-nutrient compounds, and chemicals generated during cooking [6], complicates the direct translation of a single ingredient's efficacy to a therapeutic effect on UC.

Current research has only begun to scratch the surface in identifying specific bioactive components in foods, often approaching the subject tentatively. For instance, studies using animal models have shown promising outcomes with eggs. Hen egg lysozyme has exhibited anti-inflammatory and immunomodulatory effects in a porcine colitis model [105]. In addition, egg yolk lipids have been found to mitigate colitis induced by dextran sodium sulfate (DSS) through inhibition of NLRP3 inflammasomes and modulation of the gut microbiota [106]. The activation of the NLRP3 inflammasome, a crucial innate immune complex, has been linked to decreased intestinal inflammation. Whether it is activated [107] or knocked out [108], it can influence the gut microbiota composition. Egg yolk phosphatidylcholine also exhibits beneficial effects in BALB/c mice with colitis by suppressing colonic inflammatory markers, enhancing intestinal epithelial barrier function, and altering the gut microbiome composition [109]. Furthermore, peptides extracted from preserved egg whites have been shown to improve clinical symptoms and decrease the gene expression of pro-inflammatory cytokines in mice with colitis [110].

In the domain of functional food research, various teams have probed the therapeutic potential of food components in animal models, aspiring to convert these findings into practical applications through the development of functional ingredients. However, such efforts remain limited in their scope, as they often focus on isolated components without fully addressing the intricate and multifaceted role of diet in disease management. While components like lysozyme, lipids, and phosphatidylcholine in eggs have been examined for their beneficial effects [39, 44, 50, 64], population-based studies on egg consumption and UC yield inconsistent results, with no specific investigation into the efficacy of eggs in UC management. This gap highlights the necessity of understanding the interactions among various food components, which may collectively influence their therapeutic potential. It also emphasizes the inherent challenges in extrapolating findings from animal studies to human clinical scenarios, where factors such as individual variability, dietary patterns, and the complexity of UC pathophysiology further complicate the translation of experimental evidence into actionable dietary recommendations.

Food groups

Several well-structured food groups interventions have shown benefits for patients with UC. These include the Anti-Inflammatory Diet (AID) [35, 111–114], exclusion diets (such as gluten-free plus milk-free diets, elimination diets, and diets excluding specific foods and components) [115–119], the 4 Strategies to SUlfide-REduction (4-SURE) diet [120], the Specific Carbohydrate Diet (SCD) and its modified version (MSCD) [121], plant-based diet [103, 122], the Mediterranean diet (MED) [123–125], and the low-FODMAP diet (LFD) [126–129]. Among these, the evidence supporting the benefits of AID and MED is relatively strong, while other dietary interventions require further research to substantiate their efficacy.

The AID, for example, was developed based on previous research findings regarding the efficacy of specific foods for UC, as detailed in the previous section of this article. This diet reduces the intake of gluten-containing grains, dairy products (except curds), margarine, red and processed meats, food additives, and refined sugars, while promoting fresh fruits, vegetables, and fermented foods [35, 111–114]. A clinical randomized controlled trial evaluated the effectiveness of AID during the remission phase of UC. Participants followed either the AID or the dietary recommendations from Canada's Food Guide for six months. The results indicated that the AID group had a lower rate of UC relapse and effectively avoided subclinical inflammation [114].

In addressing active UC, another randomized controlled trial investigated the efficacy of combining AID with Faecal Microbiota Transplantation (FMT) in patients with mild to moderate disease severity. This study demonstrated that the FMT-AID combination successfully induced both clinical and endoscopic remission. Furthermore, maintaining AID exclusively for one year was shown to preserve these therapeutic benefits [112]. Another study explored the efficacy of combining AID with fecal transplantation (FT) in active UC. This randomized controlled trial showed that FT did not achieve the anticipated therapeutic effect. However, patients who

Table 2 The role of specific food groups in UC

Food Groups	Restricted Items	Allowed Items	Conclusion and Evidence
AID	gluten grains, dairy products, margarine (except curds), red and processed meats, food additives, and refined sugars[35, 112–115)	fruits, vegetables, and fermented foods[35, 112–115]	AID lowers UC relapse in remission and prevents subclinical inflammation [115]. In active UC, AID, with or without FMT, offers therapeutic potential for achieving remission [112–114]
Exclusion diet			
- Milk-free, low-roughage diet	Milk and dairy products (except butter)[116, 117]	All foods except excluded foods[116, 117]	The gluten-free plus milk-free diet outperformed the dummy diet in inducing endoscopic and histologic remission and preventing relapses in UC patients [116, 117].
- Gluten-free plus milk-free diet	Gluten, all milk and dairy products [116, 117]		
- "Dummy" diet	Fried foods, condiments, ice cream[116, 117]	All foods except excluded foods; encourage milk and dairy products[116, 117]	
- Elimination diet	Dairy products (week 1), refined sugars, preservatives, additives, flavors, condiments, beverages, fried foods, and food triggered symptoms in participants[118]	Grains, fruits, vegetables, meat and fish[118]	An elimination diet can induce remission in patients with mild to moderate UC [118].
- anti-inflammatory exclusion diet	Red meat, ultra processed food, fried foods, high-lactose foods, fast food, beverages, safflower oil, corn oil[119].	Fruits, vegetables, dairy products, cereals, lean meat, olive oil[119]	UC and CD patients following an exclusion diet exhibited a higher frequency of maintaining clinical remission, although the difference was not statistically significant [119].
- UC exclusion diet	Foods abundant in sulfated amino acids, total protein, heme, animal fat, saturated and polyunsaturated fat, food additives, tryptophan, as well as natural sources of pectin and resistant starch[120]	Fruits, vegetables, rice, potatoes, chicken, eggs, yoghurt, pasta and other foods except excluded foods [120]	Clinical remission was achieved solely with a UC exclusion diet in 9 out of 24 children (37.5%) with mild to moderate UC, along with reductions in the Pediatric UC Activity Index and fecal calprotectin (FC) [120].
4-SURE diet	Sulfite, sulfate, nitrite, nitrate, and carrageenan food additives[121]	10–15 g/d of resistant starch; 5 g/d of slowly fermentable non-starch polysaccharides; 75–90 g/d total protein intake from animal and plant sources; ≤1.5–2.0 g/d sulfur-containing amino acids intake; total FODMAP intake not increased[121]	In mild to moderate UC, the 4-SURE diet showed high adherence, resulting in clinical and endoscopic improvements in 46% and 36% of participants, respectively, along with increased fecal SCFA levels and improved quality of life[121].
SCD	Potatoes and yams, certain legumes like chickpeas and soybeans, grains, canned fruits and vegetables, processed, canned, and most smoked meats, milk[134]	Fresh fruits and vegetables (except potatoes and yams), certain legumes like lentils and split peas, unprocessed meats, saccharin and honey as sweeteners, certain cheeses with minimal lactose content, fully fermented yogurt [134]	In patients aged 7–18 years with active UC and CD, SCD and MSCD demonstrate partial improvements in clinical symptoms and inflammatory markers, yet their efficacy in consistently alleviating symptoms or inflammation remains inconclusive[122].
MSCD		Rice, oats, potatoes, maple syrup, and cocoa[122]	
Plant-based diet	Meat, minced or processed meat, fish, cheese, butter, margarine, sweets, soft drinks, alcohol, and bread[104, 123]	Vegetables, fruits, pulses, potatoes, rice, miso soup, green tea, and plain yogurt[104, 123]	The relapse rates in UC with plant-based diet were notably lower compared to those observed with conventional therapy [104].

Table 2 (continued)

Food Groups	Restricted Items	Allowed Items	Conclusion and Evidence
MED	red meat and processed foods[135]	fruits, vegetables, whole grains, legumes, nuts, olive oil, dairy products, poultry and red wine[135]	.Low adherence to the MED exhibited a positive correlation with UC diagnosis (OR: 2.3; 1.2–4.5)[136]. Pediatric patients with mild to moderate UC and CD receiving stable medications experienced greater reductions in clinical scores, FC, and inflammatory cytokines following MED compared to maintaining their regular diet[125]. MED also induces gut microbiome changes associated with protective effects in colitis, resulting in short-chain fatty acids (SCFAs) production and reduced FC in UC remission [126].
LFD	Fruits (apples, pears, peaches, plums, mangoes, watermelon); vegetables (broccoli, cauliflower, garlic, onions, peas); honey; cow's, goat's, and sheep's milk; wheat and rye in any form (bread, pasta, biscuits)[137]	Fruits (bananas, blueberries, grapes, lemons, limes, oranges, raspberries, strawberries); vegetables (tomatoes, carrots, corn, eggplants, lettuce); sweetener (maple syrup or any other sweetener except polyols); lactose-free milk substitutes[137]	In patients with mild to moderate IBD or in remission with coexisting IBS-like symptoms, LFD improves functional gastrointestinal symptoms but does not impact stool consistency, pain and bloating scores, or mucosal inflammation in UC [127–130].

UC = Ulcerative Colitis; IBD = Inflammatory Bowel Disease; AID = the Anti-Inflammatory Diet; 4-SURE = 4 Strategies to The SUlfide-Reduction Diet; SCD = the Specific Carbohydrate Diet; MSCD = the Modified Specific Carbohydrate Diet; MED = the Mediterranean diet; LFD = the low-FODMAP diet

followed the AID intervention alone reached a clinical remission rate of 40%. Particularly, in patients with a mild disease state, characterized by a Simple Clinical Colitis Activity Index (SCCAI) less than 9, the remission rates were 50% for those receiving only AID, compared to 27.3% for those undergoing FT. However, due to the small sample size, these differences were not statistically significant. Despite the termination of the trial due to the poor performance of the two FT-involved groups, AID still demonstrated potential therapeutic effects in patients with active UC [113]. Overall, these findings highlight the potential of AID as an effective dietary intervention for managing active UC, both alone and in combination with other treatments.

Table 2 outlines the specific composition and relevant research evidence regarding their primary effects of various food groups. Notably, a recent meta-analysis highlighted that dietary interventions targeting different food groups have shown beneficial effects in maintaining clinical remission [RR 0.75 (95% CI 0.57–0.97), I^2 = 24%] and have had positive impacts on endoscopic and histologic remission. However, the correlation between these positive effects and clinical remission was inconsistent [RR 1.49 (95% CI 0.96–2.31), I^2 = 46%]. This variability may stem from differences in efficacy evaluation criteria across studies [130]. Furthermore, an updated meta-analysis compiling data from prospective studies on food group interventions for IBD concluded that no specific diet had been conclusively shown to induce or maintain remission in UC [131, 132].

Overall, current research on dietary interventions primarily targets CD, with a relatively scant focus on UC and generally low quality of evidence for the studies conducted. The limited evidence available lacks sufficient rigor and consistency to establish strong conclusions regarding the efficacy of specific dietary patterns or food groups in UC management. The heterogeneity in study designs, sample sizes, and intervention protocols further complicates the ability to draw reliable inferences. Therefore, any proposed benefits of particular food groups for managing UC or reducing its incidence in genetically predisposed populations should be interpreted cautiously. High-quality, large-scale randomized controlled trials are urgently needed to elucidate the effects of specific food groups on UC development and management, providing a stronger foundation for evidence-based dietary recommendations tailored to this patient population.

Additionally, there is a lack of comparative studies on the efficacy differences between various dietary groups in UC. To date, only one study has focused on the differences in therapeutic efficacy between the MED and the SCD in mild to moderate CD [137], with no equivalent research for UC. Such comparisons are valuable but should ideally be conducted once high-quality evidence

on the efficacy of individual food groups in UC management is established. High-quality trials are thus essential to establish this foundational evidence, followed by comparative studies to evaluate relative benefits and identify optimal dietary choices for UC patients.

Nutrients

At the nutrient level, an elevated risk of UC development is associated with excessive consumption of animal protein [62, 63], fat [138, 139] and sugar [54, 71, 80, 140], alongside insufficient intake of dietary fiber [141, 142], n-6 polyunsaturated fatty acids (PUFAs) [64, 69, 143]. In contrast, n-3 PUFAs [69, 144–147], vitamin D [58, 64, 69, 148, 149], and adequate dietary fiber consumption [150, 151] are linked with protective effects against UC.

Protein

Population-based studies have identified a correlation between high-protein diets and increased risk of UC [50, 62, 152]. However, findings are mixed, as the effects of high-protein diets appear to vary depending on the protein source.

For instance, a prospective study found no link between protein intake from processed meats, fish, shellfish, eggs, poultry, and dairy products and the incidence of UC, with the notable exception of proteins from red meat [39]. Similarly, a recent meta-analysis including this study concluded that animal protein intake generally showed no significant association with IBD risk. Specifically, proteins from fish, eggs, poultry, and processed meats had no associations or dose-response relationships with IBD, CD, or UC risk, while dairy protein intake appeared potentially protective against IBD [61]. Conversely, a study on children with UC found that eliminating milk proteins had no significant effect on UC treatment outcomes in children without milk protein sensitivities [153].

In animal models, the adverse effects of high protein intake on UC pathogenesis are well-documented. Intriguingly, maternal high-protein diets have been shown to reduce gut microbiome diversity in offspring mice, increasing their susceptibility to IBD [154]. In light of the lack of consensus on the benefits and risks associated with specific dietary protein sources, researchers have investigated these effects further in animal studies.

For example, one study demonstrated that administering a high-protein diet sourced from soy protein prior to modeling significantly diminished MUC-1 and TFF-3 expression in the mouse colon. This intervention mitigated the effects of DSS on inflammation scores, TNF-α gene expression, and colon shortening, in contrast to diets based on casein or whey protein [155]. Conversely, diets high in casein protein displayed an opposite trend in these parameters. Another recent study found that animal protein-rich diets (casein) increased susceptibility to both acute and chronic DSS-induced colitis compared to plant protein (wheat gluten) diets, with this effect dependent on both a high animal protein intake and the presence of gut microbiota [156]. Further evidence suggests that substituting animal proteins in a Western diet with plant-based proteins like soy or pea can mitigate IBD severity [157]. However, one study found that high-protein diets, irrespective of protein source—casein, whey, or soy—aggravated DSS-induced acute colitis [158].

A study comparing the dietary habits of Dutch IBD patients with the general population between 2011 and 2013 found that IBD patients had a higher consumption of total and animal protein, with plant protein intake remaining similar across both groups [159]. Conversely, data from 2013 to 2016 indicated a shift, with both UC and CD patients reporting lower total and animal protein intake compared to the general population [160]. These contrasting findings suggest an evolving dietary pattern among IBD patients, potentially influenced by increased patient education over time.

It is important to consider the nutritional implications of reduced meat and dairy consumption in IBD patients, including potential deficits in essential micronutrients like calcium and iron [161]. Iron deficiency anemia, a prevalent extraintestinal complication of IBD [162, 163], notably diminishes the quality of life [164]. Furthermore, a systematic review revealed that over a third of adult IBD patients are affected by sarcopenia or pre-sarcopenia, with nearly one-fifth being diagnosed with sarcopenia [165], a condition associated with adverse clinical outcomes [166]. Low dietary protein intake contributes to the onset of sarcopenia [166], whereas increased protein consumption has been shown to enhance muscle mass in IBD patients [167]. Consequently, recommendations to reduce protein intake in UC patients require careful consideration, underscoring the need for a nuanced approach in advising on optimal protein intake levels.

Fat and fatty acid

Human studies have shown that high consumption of fats [50], especially those derived from animal sources, and cholesterol is significantly associated with an increased risk of UC [54, 63]. A meta-analysis encompassing both Eastern and Western populations found that in the Eastern cohort, a higher intake of cholesterol (OR = 1.66, 95%CI 1.26–2.20) and fatty acids (OR = 1.43, 95% CI 1.19–1.72), including saturated and monounsaturated fats, was linked to a greater risk of UC, an association not observed in Western populations [64]. Another study over six months involving healthy adults aged 18–35 compared the effects of diets with varying fat levels: low-fat (20% of energy), moderate-fat (30% of energy), and

high-fat (40% of energy). This study indicated that a diet richer in fat increased the fecal levels of arachidonic acid and the activation of the lipopolysaccharide biosynthesis pathway, alongside a rise in proinflammatory factors in plasma post-intervention [168].

Animal studies have further investigated the mechanisms by which fat intake influences UC. While some evidence suggests a high-fat diet may reduce DSS-induced colitis and mucosal damage [169], the bulk of evidence points towards the negative impact of high-fat intake on the development of UC. Excessive dietary fat disrupts intestinal permeability through altered tight junction dynamics, shifts bile acid composition towards more hydrophobic forms, promotes oxidative stress, activates inflammatory pathways, modifies mucus composition, and destabilizes gut microbiota—collectively heightening the risk of intestinal disease [170]. Additionally, high-fat diets lead to atrophy in critical gastrointestinal regions such as the small intestine, colon, and gut-associated lymphoid tissues. This condition is marked by a reduction in intraepithelial and lamina propria lymphocytes, with these effects lingering for up to two weeks, even after reverting to a standard diet [171]. Recent research also shows that mice on a prolonged high-fat regimen exhibit compromised macrophage activity in clearing apoptotic neutrophils and reduced IL-10 production, a key factor in intestinal barrier repair and the activation of anti-inflammatory mechanisms. This underscores the direct impact of dietary lipids on the homeostatic functions vital for the resolution of tissue damage [172].

Fat is composed of glycerol and fatty acid molecules. Glycerol possesses a relatively simple molecular structure, whereas fatty acids vary significantly in type and chain length, largely defining the properties and characteristics of fats through their fatty acid composition. Fatty acids are categorized into three main types based on their molecular structure: saturated fatty acids, monounsaturated fatty acids, and PUFAs, distinguished by the presence, absence, or number of double bonds. Further, fatty acids are classified by carbon chain length into SCFAs, medium-chain fatty acids (MCFAs), long-chain fatty acids (LCFAs), and very long-chain fatty acids (VLCFAs) [173].

SCFAs, generated via bacterial fermentation in the gut, play a pivotal role in UC therapy and will be discussed more in the section on dietary fiber. Among LCFAs, saturated, trans, and n-6 PUFAs are known to promote inflammation, while oleic acid and n-3 PUFAs exert anti-inflammatory effects. Polyunsaturated fatty acid-derived lipid mediators serve as biologically active molecules that can influence immune cell function, exhibiting both pro-inflammatory and anti-inflammatory actions. Furthermore, MCFAs and VLCFAs show promise in modulating inflammation in IBD, enhancing mucosal barriers, and influencing the gut microbiota composition [174].

Investigating the precise effects of dietary fats on colonic inflammation, a comprehensive prospective cohort study involving 170,805 women found no statistically significant correlation between the overall consumption of fats, including saturated fatty acids, monounsaturated fatty acids, and PUFAs, and the risk of UC. Nonetheless, there was a noticeable trend indicating a potential reduction in UC risk with higher intake of n-3 PUFAs (HR 0.72, 95%CI 0.51 to 1.01). Conversely, trans PUFAs appeared to slightly elevate the risk of UC (HR 1.34, 95% CI 0.94 to 1.92) [175]. In another study focusing on fatty acids and UC relapse, an initial prospective analysis identified significant correlations between intake of various fatty acids (including saturated, monounsaturated, and n-3 PUFAs) and disease exacerbation in both univariate analyses and trend assessments ($p < 0.05$). However, after adjusting for multiple comparisons using a stringent statistical threshold (FDR < 0.05), these associations were no longer significant, hinting at the possibility of confounding factors or chance. In contrast, multivariate analyses identified a significant association between higher consumption of myristic acid (OR 3.01, 95% CI 1.17–7.74) and alpha-linolenic acid (OR 5.50, 95% CI 1.56–19.34) with an increased risk of relapse, demonstrating a dose-response relationship for myristic acid intake and UC flare-ups [104].

Additionally, animal experiments compared the effects of a fat mixture simulating the MED (high in monounsaturated fatty acids, a 2:1 ratio of n-6 to n-3 PUFAs, and moderate in saturated fatty acids), corn oil rich in n-6 PUFAs, olive oil rich in monounsaturated fatty acids, and milk fat rich in saturated fatty acids on the progression of spontaneous colitis in *Muc2-/-* mice. The findings indicated that the fat composition mirroring the MED led to a reduction in disease activity, decreased levels of inflammation-related biomarkers, and improved metabolic indices in the *Muc2-/-* mouse model [176]. These results highlight the potential benefits of the MED's fat profile in managing disease conditions. Nonetheless, it underscores the necessity for further research to elucidate the varied impacts of different dietary fat compositions on UC.

Carbohydrates

Carbohydrates are broadly classified into simple and complex categories. Simple carbohydrates, also known as sugars [177], include monosaccharides (such as glucose, fructose, and galactose) and disaccharides (such as sucrose, lactose, and maltose). In contrast, complex carbohydrates are comprised of fiber, starch, and glycogen. Studies have shown that individuals with IBD tend to consume higher quantities of carbonated beverages,

sweets, and refined sugars [159, 160, 178], which are predominant sources of simple carbohydrates.

Although there are some studies that offer conflicting views [79, 81, 179], a comprehensive portion of the literature consistently supports a significant association between sugar consumption, particularly through soft drinks, and an increased risk of UC [80, 140, 180, 181]. Additionally, the consumption of beverages high in sugar and those artificially sweetened is linked with a heightened risk of adverse cardiovascular outcomes and all-cause mortality among individuals with IBD [182].

In studies involving mice on a high-sugar diet, primarily consisting of sucrose, several adverse effects were observed: increased intestinal permeability, higher serum levels of lipopolysaccharides, reduced microbial diversity, and lower levels of fecal SCFAs. These changes made the mice more prone to colitis [183]. Another investigation focused on the effects of a diet high in fructose. The results revealed that elevated fructose intake compromised the integrity of the intestinal mucosal barrier by thinning and altering the quality of the colonic mucus. Moreover, it prompted shifts in the gut microbiome and its metabolic functions, marked by a decline in beneficial commensal and bile salt hydrolase-producing microbes and an increase in conjugated bile acids within the gut lumen [184]. A further study systematically assessed the impact of glucose, fructose, and sucrose on DSS-induced colitis. It found that a high-sugar diet led to significant alterations in the gut microbiome, notably increasing the prevalence of mucus-degrading bacteria such as *Akkermansia muciniphila* and *Bacteroides fragilis*. This shift resulted in an enhanced presence of bacterial mucolytic enzymes, contributing to the erosion of the colonic mucus layer [185].

In summary, sugar's detrimental effect on intestinal barrier integrity is mediated through modifications in the gut microbiome, echoing the mechanisms through which other dietary components influence health [185, 186].

Dietary fiber

Dietary fiber, a complex carbohydrate, is differentiated into less fermented insoluble fibers and highly fermentable soluble fibers based on their solubility in water [187]. Key types such as β-glucan, pectin, starch, inulin, fructooligosaccharides, and hemicellulose have been identified as beneficial in the prevention and management of IBD by diminishing pro-inflammatory cytokines, modulating the gut microbiome, and mitigating gastrointestinal side effects [142]. As a non-digestible polysaccharide, dietary fiber remains intact in the distal gut throughout digestion, acting as an essential substrate for microbial fermentation by the gut microbiota [188]. This process yields SCFAs [189], notably acetate, propionate, and butyrate [190], which are pivotal for reinforcing the epithelial barrier, driving anti-inflammatory actions, and modulating immune responses via several mechanisms [191], such as the induction of colonic regulatory T (T_{reg}) cells [192–194]. Furthermore, in conditions of chronic or intermittent dietary fiber deficiency, the gut microbiota may degrade host-secreted mucus glycoproteins for sustenance. This can lead to the thinning of the colonic mucus layer, thus exacerbating the risk and severity of colitis [195].

Numerous clinical and experimental studies have highlighted the preventive and therapeutic potentials of incorporating various dietary fibers, sourced from different foods, in both the preventative and treatment phases of IBD [196–203]. Nevertheless, a prospective cohort study found no association between dietary fiber intake and disease flares in patients with UC [204]. An exploratory study utilizing ex vivo fermentation of fecal samples from CD and UC patients in remission, with dietary fiber as the fermentation substrate, demonstrated that existing gut microbiome imbalances, characterized by reduced bacterial diversity, were not ameliorated. This suggests that fiber supplementation alone may not be sufficient to revert the IBD microbiome's altered composition back to a healthy state [205].

Moreover, evidence suggests that a high dietary fiber intake during UC can provoke a toxic response to immunotherapy [206]. Another investigation highlighted the significant impact of dietary fiber on intestinal pH, revealing that increased consumption of fermentable fibers in patients with quiescent UC significantly lowers colonic pH and maintains it below 6 for extended periods. Such alterations could adversely affect the luminal release patterns of pH-dependent medications [207]. These findings underscore the importance of closely examining how increased dietary fiber intake may influence medication efficacy in UC treatment.

Two nutrient-controlled diets

To explore the impact of diets akin to those consumed in real-world scenarios on the prevention and management of UC, researchers have utilized nutrient-controlled diets in animal studies, despite acknowledging the challenges in replicating the full complexity of human diets. Among these, some experiments have mimicked the dietary habits characteristic of a Western diet [208], specifically high in fats and simple carbohydrates, by using animal feed enriched with high-fat and high-sucrose content. Findings from these studies indicate that diets rich in fat and sucrose foster a specific inflammatory milieu by promoting intestinal dysbiosis, thereby increasing the risk of intestinal inflammation [7, 209–211]. A study recently published revealed that while the intake of a sucrose solution alone did not provoke intestinal inflammation in mice, its combination with a high-fat diet significantly

exacerbated inflammation, evidenced by higher inflammation scores, submucosal edema, and infiltration by $CD45^+$ cells [212]. Similarly, another research explored the combined effects of a high-fat diet and sucrose solution on inducing intestinal inflammation, with the key mechanism involving overexpression of TAS1R3 in the intestine. Specifically, TAS1R3-deficient mice did not exhibit inflammatory responses to this diet, as its action impacts the mTOR-PPARγ pathway, leading to increased expression of PPARγ, significantly elevating levels of tight junction proteins and various antimicrobial peptides, while reducing the expression of inflammatory cytokines such as TNF-α, IL-1β, IL-6, and IL-8 [213].

A study investigating the influence of a diet high in fat and protein on UC highlighted its pro-inflammatory role in both the development of UC and its interaction with Bin1 immunotherapy [206]. Additionally, a clinical trial employing a crossover design demonstrated that a diet low in fat and high in fiber not only reduced inflammatory markers in fecal samples but also mitigated gut microbiome dysbiosis, leading to an enhanced quality of life for patients with UC in remission [214].

In conclusion, research into dietary effects on UC has largely concentrated on Western diets, known for their high fat and sugar content. However, diets from other regions, featuring distinct nutritional profiles, have been less explored. For example, in China, there has been a notable shift away from traditional diets rich in whole grains and legumes towards increased consumption of edible oils, meat, and sugary beverages [215–219]. This transition towards a diet excessively rich in refined grains and meat [220, 221] calls for further research, encouraging investigators to conduct comprehensive simulations incorporating high simple carbohydrates and high protein levels to understand their impacts fully.

Intermittent fasting

The concept of dietary behavior encompasses a range of variables, including food intake, choice, preference, and hedonic response. Research indicates that patients with IBD exhibit a higher propensity for disordered eating behaviors like emotional eating and binge eating compared to healthy individuals [222, 223]. This behavior is associated with cognitive and psychological factors, such as exaggerated concerns and anxiety regarding adverse outcomes from consuming unfamiliar foods, as well as heightened levels of anxiety and depression [224, 225]. Physiological factors also play a role, with elevated pro-inflammatory cytokines leading to reduced appetite [226, 227] and gastrointestinal motility [228], along with influences from the gut microbiota [229–232], metabolites, and neurotransmitters [233] that regulate appetite and eating behavior through the microbiota-gut-brain axis.

However, studies focusing on eating behaviors (both pathological and therapeutic) in UC patients remain limited, with significant emphasis on intermittent fasting (IF). IF is thought to replicate ancestral periods of extended food scarcity, thereby potentially helping the immune system revert to a more favorable physiological state [22, 234]. Recognized as a method of dietary restriction [235], IF has been utilized since 1915 as an efficacious approach for weight loss in individuals with obesity [236]. Moreover, it has shown promise in alleviating autoimmune diseases by diminishing inflammation and oxidative stress, modulating immune responses, altering the composition of the gut microbiome, and promoting autophagy, among other effects [237–239]. Given these potential benefits, researchers have expressed a keen interest in exploring the therapeutic implications of IF for UC, along with its underlying mechanisms of action.

Research reveals that IF has emerged as a relatively prevalent dietary practice among patients with IBD, alongside their regular diet. In a survey of 434 IBD patients, 30.8% reported engaging in IF or avoiding specific foods; within this subset of patients, 56.7% practiced fasting with the aim of controlling gastrointestinal symptoms such as abdominal pain and diarrhea [240]. Another survey identified that 20% of IBD patients followed an IF regimen [241]. Common IF approaches vary by the fasting period's duration and caloric intake, including 0% alternate day fasting (0% ADF), where no calories are consumed on alternate days; 25% alternate day fasting (25% ADF), which permits roughly 25% of daily caloric needs on fasting days; and the 5:2 method, where two days per week are designated for low to zero calorie intake, with unrestricted eating allowed on the remaining five days [242]. Nevertheless, existing studies on IF in IBD patients do not distinguish between these specific fasting regimes, which limits a more nuanced understanding of IF's effects and patterns among individuals with IBD.

Research into the specific impact of IF on UC remains limited but shows promising therapeutic potential in animal models. One study examined the effects of a 4-day fasting-mimicking diet (FMD) cycle on mice with DSS-induced colitis, finding that FMD reduced intestinal inflammation, increased stem cell numbers, fostered a protective gut microbiome, and mitigated DSS-induced intestinal damage. Conversely, fasting with water alone enhanced regeneration and decreased inflammatory markers without reversing the pathological changes [243]. Another investigation reported similar therapeutic outcomes with a 3-day FMD cycle, which ameliorated intestinal inflammation and pathology, extended colon length, and boosted colonic crypt and stem cell numbers [244]. Additionally, a comparative study on three IF methods—alternate-day fasting, time-restricted feeding, and intermittent-energy restriction—demonstrated

that both time-restricted feeding and intermittent-energy restriction were beneficial in protecting against colitis and related behavioral disorders. These protective effects were linked to improvements in gut microbiome composition and maintenance of intestinal barrier and mucosal layer integrity, effectively reducing inflammation and oxidative damage in the colon and brain [245].

Clinical research into the effects of IF on UC patients has yielded mixed results. A cohort study conducted during Ramadan in 2006 observed a significant decrease in the clinical activity index for colitis among UC patients following a fasting period [246]. In contrast, a more recent prospective study, also during Ramadan, found a notable increase in Mayo scores for UC patients post-fasting, particularly among older individuals and those with elevated baseline calprotectin levels [247]. Furthermore, a retrospective analysis revealed no statistically significant differences in disease activity reduction between fasting and non-fasting IBD patients, indicating no apparent therapeutic benefit of fasting on disease improvement [248]. Adding to this body of research, Stanford University is currently conducting a clinical trial to evaluate whether three cycles of a five-day fasting-mimicking diet over three months can provide therapeutic benefits for UC patients, with completion expected by December 2025 [249].

The inconsistency in these findings can be attributed to various factors, including differences in study design, specific IF protocols employed, selection of assessment markers, potential confounders, and overall study quality. There is a clear need for more comprehensive and well-structured prospective studies to better understand the role and underlying mechanisms of IF in UC.

Long-term dietary influence on UC via gut microbiome

Ongoing research into the pathogenesis of UC emphasizes the complex interaction among genetic predispositions, environmental triggers, the immune system, and the microbiome, which together compromise the integrity of the intestinal barrier. In UC, dietary factors not only cause direct structural harm to the intestinal epithelium and modify the mucous layer's thickness but also indirectly undermine the epithelial barrier's integrity and stability through mechanisms both dependent on and independent of the microbiota, as extensively discussed in the literature [17, 18, 22–24].

Although conclusive evidence is yet to be established, data from certain studies indicate that the consumption of red and processed meats, as well as high protein intake, adversely affects the onset and recurrence of UC. In contrast, AIDs have shown potential benefits in both the prevention and management of UC. This highlights the ongoing influence of diet across various clinical stages of UC, primarily due to the continuous effects of dietary intake, composition, and patterns on the modulation of the gut microbiome [17, 18, 250].

Gut microbiome in UC development

The development of UC is dependent on the presence of the intestinal microbiota. In animal models with specific genetic mutations, particularly those affecting immune system functions, there's an increased risk of immune dysregulation. However, mutations that cause spontaneous chronic colitis in typical environments—such as in HLA-B27 transgenic rats [251, 252], *TCR-alpha*-/- mice [253, 254], *IL-2*-/- mice [255], *IL-10*-/- mice [256], and other models with targeted gene deletions—do not lead to immune activation or the development of subclinical colitis under germ-free conditions. This underscores the pivotal role of the resident gut bacteria in the pathogenesis of UC.

Furthermore, the changes in the microbiome's composition and diversity are not only consistent between individuals predisposed to UC and those with the condition [20, 257] but also persisted throughout the entire trajectory of UC, from the stages before onset to those after its development [59, 88, 91, 94, 156]. These changes include a reduction in α-diversity and shifts in specific microbial populations, marked by a decrease in anti-inflammatory bacteria and an increase in pro-inflammatory bacteria [258–263].

Microbial communities associated with UC can enhance susceptibility to the disease. Transferring disease-associated microbiota through FMT from donors has been observed to increase the risk of UC in recipients. Several studies have demonstrated that dysbiosis can precipitate the onset of colitis even in individuals with low genetic predisposition by transplanting a dysbiotic gut microbiome from UC patients or colitis-afflicted mice into germ-free mice [156, 264–269]. However, findings from two specific studies [270, 271] challenge this perspective. The occurrence and severity of colitis following FMT are influenced by the genetic background of the recipient mice [265] and the selection of donors, constrained by variables such as a limited pool of donor patients [271], their disease progression, and the unique characteristics of their microbiome, which could impact the efficacy of the isolated microbiota in inducing colitis. These factors underline the complexity of isolating disease-associated microbiota and its potential role in the development of colitis post-FMT.

Conversely, beneficial microbial communities may lower UC risk and alleviate symptoms. Probiotics, such as *Lactobacillus*, are widely used as adjunctive treatments and preventative measures in IBD management. For instance, *Bifidobacterium longum* has been shown to reduce experimental colitis, suggesting its potential

as an alternative or adjunct therapy for IBD [272–275]. Another notable bacterium is *Akkermansia muciniphila*, a symbiotic bacterium within the gut mucus layer. Research indicates that *A. muciniphila* can reduce DSS-induced experimental colitis by activating the NLRP3 inflammasome [276], regulating tryptophan metabolism, and triggering the aryl hydrocarbon receptor signaling pathway [277], underscoring its potential therapeutic role in UC management [278–280].

Long-term dietary shaping of microbial composition

Long-term dietary patterns distinctly shape gut microbial profiles, influencing UC onset and treatment through the effects of both beneficial and harmful bacteria. An individual's dietary history fosters a specific enterotype that can impact UC progression.

Population studies indicate that diets high in animal proteins, specific amino acids, and saturated fats foster an enterotype rich in *Bacteroides*, with elevated levels of *Alistipes* and *Parabacteroides*. In contrast, diets lower in these nutrients but higher in carbohydrates and monosaccharides support an enterotype dominated by *Prevotella*, with increased *Paraprevotella* and *Catenibacterium*. These profiles closely mirror Western and traditional agrarian diets, respectively [250].

However, these findings are primarily at the genus level, potentially overlooking the distinct roles of individual species. Within the same genus, specific bacterial species may exert opposite effects in UC. For instance, high protease levels from *Bacteroides vulgatus* are observed in certain subgroups of active UC patients, and transplanting feces from these individuals into germ-free mice induces colitis in a protease-dependent manner [237]. Conversely, *Bacteroides uniformis*, another species within the same genus, has demonstrated therapeutic potential in treating colitis and other gut barrier-related disorders [238, 239].

A large-sample meta-analysis found that high intake of animal protein and fat was associated with an increased abundance of Firmicutes and a reduced presence of Bifidobacterium, a protective factor for IBD as mentioned. Conversely, diets rich in nuts, oily fish, fruits, vegetables, grains, and red wine were associated with higher levels of commensal bacteria, including *Roseburia*, *Faecalibacterium*, and *Eubacterium* spp., known for their anti-inflammatory effects through fiber fermentation into SCFAs [17]. These findings align with the conclusions of this paper, suggesting that red and processed meats, along with high protein intake, negatively influence UC by altering gut microbiota, while AID offers protective effects in both the prevention and management of UC.

In conclusion, understanding the function and metabolism of individual bacterial species under varying dietary conditions, as well as how dietary composition shapes their activity and metabolites, will be essential areas for future research.

Microbiome-mediated dietary effects on UC

In UC, the impact of specific foods and nutrients significantly depends on the presence of the gut microbiome. For example, the development of colitis in mice due to dietary monosaccharides necessitates the existence of gut microbiota. Remarkably, the use of antibiotics or the maintenance of germ-free conditions in mice halted the progression of sugar-induced colitis. In contrast, germ-free mice that were later colonized with microbiota from sugar-fed mice exhibited a heightened vulnerability to colitis [185]. Another study demonstrated that a high-protein diet from animal sources aggravated DSS-induced experimental colitis, a condition reliant on both the consumption of high amounts of animal protein and the presence of gut microbiome. To delve deeper into this phenomenon, researchers induced colitis in germ-free mice and then colonized them with gut microbiota from two different dietary regimes based on animal products: a group on a standard protein diet and another on a high-protein diet. It was crucially observed that this aggravating effect occurred independently of the adaptive immune system [156].

The influence of dietary components on health extends beyond the presence of the gut microbiome to include modulation by individual variations in microbiota composition. For example, consumption of inulin was shown to affect intestinal stem cell activity and promote homeostatic remodeling of the colonic epithelium. This regulatory mechanism was not present in germ-free mice, demonstrating that the effects of inulin on epithelial remodeling depend on the gut microbiome [281]. Further research emphasizes the critical role of the gut microbiome in determining dietary fiber's efficacy. One study with genetically identical gnotobiotic mice, each hosting distinct complex gut microbiomes, exposed the mice to four isocaloric diets varying in fiber types. The outcomes revealed significant differences between the groups colonized with different microbial communities, establishing a direct link between individual variations in the gut microbiome and the differential impacts of dietary fiber on host metabolic phenotypes [282].

Similarly, A study has shown that the beneficial effects of fructans on the intestinal barrier are mediated by the gut microbiome. In this research, dietary fructans resulted in increased villi height and deeper crypts in rats colonized with *Bacteroides vulgatus* and *Bifidobacterium longum*, compared to those harboring a human fecal flora, an effect not observed in germ-free rats. Rats with bacterial colonization also displayed a thicker mucus layer on the colonic epithelium, alongside elevated levels of goblet cells, acidic mucins, and mucosa-associated

bifidobacteria, unlike their germ-free counterparts [283]. Further, recent studies indicate that the genetic and functional diversity among Bacteroidetes species may predict their competitive edge in metabolizing dietary fructans. One investigation identified a hybrid two-component signaling sensor that binds fructose, which in turn regulates the fructan utilization locus within Bacteroidetes. The variation in the composition of this locus among Anabaena species affects the range and specificity of fructans they can utilize [284], highlighting the complex interaction between dietary components, the gut microbiome, and the host's intestinal health.

These studies suggest that while general conclusions are valuable, individual differences are common. Therefore, alongside universally applicable guidelines, personalized dietary recommendations based on an individual's unique gut microbiota profile may become essential in the future.

Individualized dietary interventions

In 2021, a panel of experts introduced a clinical staging system for IBD that underscores the progressive nature of the condition. Stage 1 is characterized by exposure of genetic predispositions and environmental risk factors, including dietary influences. At Stage 2, high-risk individuals begin to exhibit signs of altered gut microbiota, immune dysregulation, and compromised intestinal barrier function. Stage 3 is defined by the initiation of a harmful cycle that involves dysbiosis, further immune system dysregulation, and the escalation of chronic inflammation and mucosal damage. This series of events eventually leads to Stage 4, where clinical symptoms become apparent, and a diagnosis is formally made [285].

According to this framework, interventions that are implemented at the earlier stages of the disease process are more effective than those initiated after a diagnosis has been made, potentially leading to the attenuation, delay, or even prevention of the disease [285, 286]. The scarcity of clues in the preclinical phase of UC and the sudden onset of symptoms often observed clinically [285–287] suggest two possibilities: the preclinical phase of UC may either be highly concealed or relatively brief. significance of dietary interventions as a gradual and seamlessly integrated preventive or therapeutic strategy in daily life. By stabilizing and modulating gut microbiota composition, supporting immune function, and reinforcing the intestinal barrier, appropriate dietary measures can exert beneficial effects across all stages of disease progression (Stage 1–4). Furthermore, dietary adjustments can serve as a complementary approach to pharmacological treatments in more advanced disease stages, offering a synergistic therapeutic effect. In addition, Dietary modifications hold several advantages over pharmacological treatments in terms of sustainability, feasibility, economic cost, and safety. They not only positively impact the management of UC but also offer broader health benefits.

The link between diet and the microbiome is consistently observed in both individuals with UC and the general population [17]. Previous dietary patterns, through their association with the gut microbiota, influence the host's response to current dietary interventions [288]. Additionally, the gut microbiota can in turn affect the host's dietary choices and behaviors, potentially through mechanisms such as the regulation of essential amino acid availability [289]. The above further elucidates the cumulative effect of dietary influences, as well as the bidirectional interaction between the gut microbiota and dietary impacts. Furthermore, it highlights the necessity of personalized strategies in applying the outcomes of dietary intervention studies to clinical individuals.

New horizons

Deciding what and how to eat is a daily challenge, a decision that becomes critically important for individuals with UC due to the significant impact of diet on the condition.

Despite existing dietary guidelines offered by organizations such as the IOIBD [36] and the AGA [37], the majority of UC patients do not adhere to these recommendations after their diagnosis [241]. This divergence stems from the complexities surrounding patients' access to dietary information, as well as the often broad or conflicting nature of the dietary advice available, leading to confusion and skepticism [290–293]. Research indicates that faced with uncertain dietary choices, many individuals with IBD resort to avoidance or restrictive diets [95, 290, 294]. Considering that patients with IBD frequently experience compromised nutritional status and are at risk of malnutrition, even during remission or in the early stages of the disease [295, 296], such restrictive dietary practices could further endanger their nutritional health, substantially affecting both their survival and quality of life.

Recent reviews on UC and diet have summarized the roles of different food groups in UC management [130, 297, 298]. One review concluded that the principles of a healthy diet could be broadly beneficial across various disease states [298], aligning with our findings. Unlike prior reviews, this article begins with a succinct overview of UC pathogenesis, emphasizing how the vicious cycle of dysbiosis, immune dysregulation, and inflammation that leads to intestinal barrier impairments and UC progression. We provide a comprehensive summary of the beneficial and detrimental effects of foods, food groups, nutrients, and IF across different stages of UC.

The effects of specific dietary components and eating behaviors are mediated through both

microbiota-dependent and independent pathways. These pathways can directly interact with the gut's mucosal defenses and inflammatory cells or significantly influence the balance between beneficial and pathogenic gut bacteria. This review dedicates a full section to exploring these microbiota-mediated mechanisms, which may explain the sustained dietary effects observed throughout UC's progression.

This review explores several underexplored aspects. First, it highlights the discrepancy between the efficacy of specific food components observed in animal studies and the inconsistent benefits reported in human clinical trials, emphasizing the need to understand food component interactions and the challenges of translating preclinical findings to clinical practice. Second, it stresses the need for comparative studies on the efficacy of dietary groups in UC management, grounded in robust evidence of individual food group effects. Lastly, it examines research on two nutrient-controlled diets, underscores the importance of investigating region-specific dietary patterns alongside Western diet models.

While the earlier sections emphasize the unique contributions of this review, it is equally important to expand on specific aspects discussed in the main text to provide a more comprehensive perspective. The following discussion addresses key challenges and unresolved questions, while also exploring future directions for research and clinical application.

For food and nutrient studies yielding contradictory outcomes, more rigorously structured experimental designs are essential to generate high-quality evidence. Additionally, for nutrients and foods where consensus is broadly reached, detailed investigations into the effects of varying intake levels and different food preparation and processing techniques are critical. This is necessary to offer precise dietary recommendations for managing the initiation and progression of UC.

Particularly for foods or components with protective properties, it is crucial to assess the timing and dynamics of dietary protection by implementing interventions at various stages of disease modeling. This approach will enhance their development as therapeutic options and their precise application in clinical practice.

Furthermore, in examining studies that cover diverse food groups, it becomes apparent that there are both commonalities and unique differences in their composition. These specific compositional variances lead to differences in nutrients, bioactive compounds, and other elements, highlighting the necessity for comparative efficacy studies among various food groups. Such studies should control for factors like total energy intake and cooking methods.

Additionally, unlike more established dietary frameworks like the low FODMAP diet, the AID is in a continuous process of refinement. It is therefore vital for research teams to apply consistent compositional principles in future studies to enhance the applicability and generalizability of AID research findings.

In the realm of dietary research, while studies on single foods in highly controlled environments are valuable, it's crucial to acknowledge the importance of examining the cumulative or counteracting effects of various dietary components within food group studies. The practical application and research into food groups necessitate a careful balance of different foods and nutrients, emphasizing the interplay and potential synergies between them.

Regarding eating behaviors, the current body of research has mainly concentrated on IF as a distinct pattern, yet there's a notable lack of comprehensive, prospective studies to elucidate its specific role, underlying mechanisms, and viable implementation strategies for UC. Intermittent, controlled fasting has the potential to affect both innate and adaptive immunity, leading to alterations in T cell metabolic pathways, bolstered immune responses, and diminished inflammatory activity in monocytes. Hence, further investigation is imperative to grasp the impact of IF on T cell function and phenotype, the regulation of monocyte inflammatory activity (including macrophages and dendritic cells), and the modulation of pertinent innate and adaptive immune pathways within the context of UC. Beyond eating behaviors outlined in Sect. 4, investigating the influence of other eating behaviors on UC is paramount. This includes patterns of eating times, meal frequency, the speed of eating, the context of shared meals, and the association with disorders such as anorexia nervosa and eating disorders, areas that are significantly understudied. Addressing these gaps in research could offer new insights and potentially beneficial strategies for managing UC through modifications in eating behaviors.

Additionally, research on the interplay between diet and pharmacotherapy remains limited, with most studies focusing on CD and few addressing UC [299–304]. Food-drug interactions encompass pharmacokinetic and pharmacodynamic effects, as food intake can affect drug absorption, distribution, metabolism, and excretion, with specific food components directly interacting with drugs [305–307]. Furthermore, both short-term [308] and long-term [17, 250] diets significantly influence gut microbiome composition, with detectable microbiome alterations within 24 h of dietary changes [250]. These microbial shifts can modulate drug response by enzymatically modifying drug structures, affecting bioavailability, bioactivity, or toxicity—an area known as Pharmacological Microbiomics [309, 310].

Notably, certain foods traditionally used in diets, such as yam (*Rhizoma dioscoreae*), white lentil *(Lablab semen*

album), lotus seed (*Nelumbinis plumula*), and coix seed (*Coicis semen*), also serve as botanicals in ethnomedicine. Beyond their dietary roles, these foods can be decocted with medicinal herbs like *Panax ginseng*, *Poria cocos*, *Atractylodes macrocephala*, and *Glycyrrhiza glabra* (as in the "Shenlingbaizhu" formula) for UC treatment [311]. This dual functionality suggests that some foods can act as both nutrition and medicine, potentially creating synergies when used alongside pharmacotherapy. Therefore, personalized treatment strategies that consider individual dietary habits and medication regimens are essential to enhance therapeutic outcomes and reduce adverse effects, promoting comprehensive clinical management.

Finally, as we advance research into the diet for UC, recognizing the challenges of applying research findings to clinical practice is critical. The vast diversity of foods, cooking methods, and dietary preferences across different cultures, regions, and individuals poses significant challenges to the practical application of research insights. Moreover, without ongoing guidance from nutrition experts, the process of acquiring dietary knowledge, procuring appropriate ingredients, and meal preparation demands considerable time, energy, and financial investment from patients. It is crucial for researchers to weigh these investments against the potential therapeutic benefits, aiming to find a balance that supports patient well-being and disease management effectively.

This review has several limitations. It is not a systematic review or meta-analysis, so the conclusions presented are not derived from standardized statistical methods and may involve some subjective interpretation. Furthermore, constraints in length and scope limited our ability to address the effects of various nutritional supplements on UC or to provide detailed discussions on the specific mechanisms by which individual foods or nutrients influence UC.

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