Review

Role of diet in prevention versus treatment of Crohn's disease and ulcerative colitis

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Received 4 October 2023
Accepted 10 December 2023
Published Online First 9 January 2024

To cite: Halmos EP, Godny L, Vanderstappen J, *et al*. *Frontline Gastroenterology* 2024;**15**:247–257.

ABSTRACT

Diet is a modifiable risk factor for disease course and data over the past decade have emerged to indicate its role in Crohn's disease (CD) and ulcerative colitis (UC). However, literature is riddled with misinterpretation of data, often leading to unexpected or conflicting results. The key understanding is that causative factors in disease development do not always proceed to an opportunity to change disease course, once established. Here, we discuss the data on dietary influences in three distinct disease states for CD and UC—predisease, active disease and quiescent disease. We appraise the literature for how our dietary recommendations should be shaped to prevent disease development and if or how that differs for CD and UC induction therapy and maintenance therapy. In UC, principles of healthy eating are likely to play a role in all states of disease. Conversely, data linking dietary factors to CD prevention and treatment are paradoxical with the highest quality evidence for CD treatment being exclusive enteral nutrition, a lactose, gluten and fibre-free diet comprising solely of ultraprocessed food—all dietary factors that are not associated or inversely associated with CD prevention. High-quality evidence from dietary trials is much awaited to expand our understanding and ultimately lead our dietary recommendations for targeted patient populations.

KEY POINTS

⇒ The role of diet in the management of Crohn's disease and ulcerative colitis is likely different.
⇒ Features of healthy eating are associated with prevention of Crohn's disease, but less certain for ulcerative colitis.
⇒ Exclusive enteral nutrition treats inflammation in Crohn's disease and data are emerging for diets of similar composition exerting similar impact.
⇒ Emerging diets used to treat ulcerative colitis may be different from Crohn's disease.
⇒ The role of diet to maintain remission in Crohn's disease and ulcerative colitis is unknown, so default to healthy eating guidelines is recommended.

INTRODUCTION

Diet has long been hypothesised to impact inflammatory bowel disease (IBD), both Crohn's disease (CD) and ulcerative colitis (UC). The widespread perception is that an unhealthy Western lifestyle alters IBD risk. Westernised diets provide consumers with more choice and longer shelf life at low cost. A consequence of this convenience is that food is comparatively higher in total energy, total and saturated fat, sugar and food additives and lower in fibre.[1] These dietary components that are believed to be key players in IBD development are supported by some epidemiological and preclinical studies, but not necessarily clinical trials.

There is a concept that dietary components causative of IBD development persist in their action and that their modification can be utilised to treat established IBD. However, this concept does not fit all chronic disease. For example, removing gluten, a causative factor for coeliac disease, induces remission in the majority, but the removal of asbestos does not treat mesothelioma. The causative versus therapeutic targets for diet in IBD have been ambiguous and often clouded with dogma.[2] Consideration of diet in different stages of IBD is needed. The aims of this review are to examine the strength of evidence for using diet in pre-disease, active disease and quiescent disease.

Diet for IBD prevention

Identifying modifiable risk factors in the pathogenesis of IBD is appealing to prevent IBD in the general population and specifically in those at high risk, including first-degree relatives of patients with IBD. Establishing the role of diet in IBD prevention is determined via large prospective cohort studies that assess diet through dietary questionnaires in a healthy population that is followed forward. Associations are made between diet and disease development. From these data, there are clear differences between CD and UC, but results are often inconsistent in finding associations.

Specific nutrients and dietary components associated with development of CD or UC are summarised in table 1. For CD, development of disease was associated with protein intake double that of most dietary guidelines[3] and sugar-sweetened beverages.[4] Protective dietary factors included docosahexaenoic acid (DHA),[5] dairy,[6] total fibre, specifically from fruit or grains or both,[7–9] polyphenols in wine, grapes and certain herbs,[10] dietary potassium[11] and zinc.[12 13] For UC, meat intake, particularly red meat, was consistently associated with disease development,[3 14] as was trans-unsaturated fats[15] and n-6 polyunsaturated fatty acids (PUFA).[16–19] Oleic acid[17] and vitamin D[20] were protective.

Another approach is to consider dietary patterns that may consider the complex interactions between foods. This may be assessed through dietary scores based on diet quality indicators, such as a Mediterranean diet (MED) or ultra-processed food (UPF), a marker of a Western diet. Alternatively, indices are developed through associations of inflammatory markers, as with the empirical dietary inflammatory pattern (EDIP). Table 1 summarises dietary patterns associated with CD and UC development and some described below.

MED and healthy lifestyle patterns

A MED, often characterised as plant-based eating, describes a diet rich in wholegrains, fruit, vegetables, legumes, nuts, olive oil, moderate in fish/seafood, dairy, wine and limited in meat, particularly red meat. Features of a MED seem to mimic the data indicating dietary risk of CD, specifically its positive association with protein and negative associations with fibre, DHA found in fish, dairy, and polyphenols in wine and herbs. This relationship has been recognised and developed MED scores assessed through the prospective cohort model in three unrelated studies with inconsistent findings. A study comprising two Swedish cohorts showed reduced risk of CD onset with an MED,[21] but the other two studies found no association.[22 23] One explanation for this inconsistency may be due to the differences in how the MED scores were calculated. Dairy contributed to the MED score of the inversely associated Swedish study but was deducted or not considered in the MED scores for the studies showing no association. MED was not associated with UC development.[21 23 24]

While not specified as a MED, another cohort assessed a healthy lifestyle score (HLS), which considered comparable dietary factors, high in fruit, vegetables, nuts and fish and low in red meat, and also the lifestyle factors body weight, smoking and physical activity. An HLS demonstrated a reduced risk of developing both CD and UC in the Nurses' Health studies and subsequently validated in three other cohorts.[25] These data indicate non-dietary lifestyle modifiers likely play a role in IBD development. Indeed, US Biobank data suggested that adhering to a healthy lifestyle that considers smoking, body weight, sleep, physical activity in addition to a healthy diet mitigates genetic risk. Individuals with a high genetic risk had a 50% reduction in developing CD and UC if following a healthy lifestyle.[26] Conversely, diets considered unhealthy, such as the carnivorous diet, rich in meat and a diet high in discretionary food but low in fruit and vegetables, were associated with UC and CD, respectively.[22]

Empirical dietary inflammatory pattern

The EDIP index is based on 18 inflammatory and anti-inflammatory foods associated with C reactive protein (CRP) and circulating cytokines in a healthy population.[27] The inflammatory foods not only included processed, red and organ meats but also unexpected foods, such as certain fish and vegetables. Beer and pizza were surprisingly 'anti-inflammatory'.[28] However, the predefined foods were curious and often ambiguous. For example, 'pizza' and 'snacks' have variable composition and it was unclear why pizza was selected over, for example, burgers or fried food. Additionally, food categories did not represent usual intake, with 8/39 categories representing beverages but only one for fruit. A subsequent evaluation of the EDIP score across seven countries found no association with CD or UC.[29]

Ultra-processed food

Food defined as UPF via the NOVA classification system typically contains ≥5 ingredients, extracted from food components and often contain food additives[30] and may be considered to be a marker of diet quality beyond considering macronutrient and micronutrient intake. Meta-analysis of five cohort studies showed a consistent increased risk of up to 40% for developing CD from UPF, but not UC.[31] However, there are some difficulties in data interpretation, with misclassifications of UPF likely to exist, even through various modelling scenarios that were applied to the food database.[31] The definition for UPF is of low threshold and the nutritional value and composition of UPF vary hugely. For example, both flavoured tinned tuna and ice cream are considered UPF. Indeed, only when the extremes of UPF intake were compared, there was a risk for CD development identified.[31] This

Table 1 Associations of nutrients, food components or dietary patterns with development of Crohn's disease and ulcerative from prospective cohort studies

Food component	Prospective cohort study	Association with Crohn's disease	Association with ulcerative colitis	Reference
Energy and macronutrients				
Energy and macronutrient profile	EPIC	–	None	85
Protein	E3N/EPIC	↑ Total protein	↑ Animal protein	3
Protein	EPIC	None	↑ Total meat and red meat	14
Fat	EPIC	↓ DHA	–	5
Fat	NHS	None	↑ Trans unsaturated fats	15
Fat	NHS and NHS II	None	↓ High n3:n6 PUFA in certain genotype	16
Fat	EPIC	–	↑ Linoleic acid	19
Fat	EPIC	–	↓ DHA	18
Fat	EPIC	–	↑ Arachidonic acid and ↓ oleic acid	17
Carbohydrate	EPIC	None	None	86
Sweetened beverages	SMC/CoSM	None	None	87
Sugar-sweetened beverages	UK Biobank	↑ Sugar-sweetened beverages	None	4
Micronutrients				
Vitamin D	NHS	None	↓ Diet and supplementary vitamin D	20
Vitamin D	E3N/EPIC	None	None	88
Vitamin D	EPIC	None	None	89
Sodium and potassium	NHS and NHS II	↓ Dietary potassium	None	11
Dietary iron	NHS and NHS II	None	None	90
Zinc	NHS and NHS II	↓ Zinc intake for women	None	12
Zinc	NutriNet-Santé	↓ Dietary zinc	None	13
Specific foods/components				
Dairy	EPIC	↓ Total dairy	None	6
Fibre	NHS	↓ Total fibre and fibre from fruit	None	7
Fibre	EPIC	↓ Fibre from grains in non-smokers	None	8
Fibre	UK Biobank	↓ Total fibre and fibre from fruit and bread	None	9
Fibre & meat	DCH	Not separated into CD and UC—no associations		91
Gluten	NHS and NHS II and HPFS	None	None	92
Alcohol	EPIC	None	None	93
Alcohol	NHS and NHS II and HPFS	None	None	94
Alcohol	UK Biobank	Not separated into CD and UC—variable results		95
Polyphenols	EPIC	↓ Flavones and resveratrol	None	10
Metal elements and disinfectants in drinking water	Yinzhou	Not separated into CD and UC—many associations		96
Food patterns				
Dietary patterns and Mediterranean diet score	EPIC	None	↑ High sugar and soft drinks with low vegetable intake	23
Mediterranean diet	SMC/CoSM	↓ MED score	None	21
Dietary patterns, including MED score	LifeLines	↑ Snacks, prepared meals, non-alcoholic beverages, sauces and low vegetable and fruit ↓ LifeLines Diet Score	↑ Red meat, poultry, processed meat	22
Diet quality	SMC/CoSM	↓ HPDI and modified MED scores	None	24
Healthy lifestyle score	NHS/NHS II/HPFS, EPIC and SMC/CoSM	↓HLS	↓HLS	25
Dietary patterns	NHS II	↓ Prudent diet score	None	97

Continued

Table 1 Continued

Food component	Prospective cohort study	Association with Crohn's disease	Association with ulcerative colitis	Reference
Inflammatory score of diet	EPIC	↑ Two unit increased score	None	98
Cardioprotective diet	UK Biobank	↓ 5–7 score	↓ 5–7 score	99
Special dietary habits	CHEF	None	None	100
EDIP score	NHS and NHS II	↑ Higher 'inflammatory' score	None	28
EDIP score	PURE	None	None	29
UPF	PURE	↑ UPF	↑ UPF	101
Dietary patterns and UPF	NutriNet-Santé	Not separated into Crohn's and UC—no associations		102
UPF	NHS and NHS II and HPFS	↑ UPF	None	103
Unprocessed/minimally processed and UPF	EPIC	↓ Unprocessed/minimally processed food	None	104
UPF	UK Biobank	↑ UPF	None	105

CD, Crohn's disease; CoSM, Cohort of Swedish Men; DCH, Danish Diet, Cancer and Health cohort; DHA, docosahexaenoic acid; EDIP, Empirical Dietary Inflammatory Pattern; E3N, Etude Épidémiologique des femmes de la Mutuelle Générale de l'Education National; EPIC, European Prospective Investigation into Cancer and Nutrition; HLS, Healthy Lifestyle Score; HPDI, Healthful Plant-Based Diet Index; HPFS, Health Professional Follow-up Study; MED, Mediterranean diet; NHS, Nurses' Health Study; PUFA, polyunsaturated fatty acids; PURE, Prospective Urban Rural Epidemiology cohort; SMC, Swedish Mammography Cohort; UC, ulcerative colitis; UPF, ultra-processed food.

should be considered in translating UPF recommendations to the community as complete avoidance is unrealistic for most people.[32] Another limitation with assessing UPF is that it is not known as an accurate marker of poor diet quality. Diets higher in UPF are often also higher in fat, sugar and lower in fibre, but it may be that the ultraprocessing itself rather than the diet composition is associated with health consequences. Notably, IBD guidelines recommend limiting UPF[33] and for offspring of IBD patients.[34]

Interpretation to clinical practice

Prospective epidemiological studies have presented evidence for the role of specific dietary components, diet pattern and lifestyle factors in the development of CD, and, to a lesser extent, UC. The general message that features of a MED that is heavily plant based, moderate in fish and dairy and low in meat and UPF is pleasingly in line with healthy eating guidelines and assurance that these default dietary recommendations are likely to reduce risk of CD development. While dietary associations for UC development are less apparent, with the exception of red meat consumption increasing risk, it is judicious to recommend the same for those at risk of UC.

Diet for IBD treatment

The first dietary intervention to induce remission was exclusive enteral nutrition (EEN) for CD, but it is difficult to maintaining beyond 6–8 weeks. The last decade has seen multiple novel diets emerging as other candidates for induction therapy. As with IBD prevention, the role of diet in CD and UC treatment seems distinct. Induction dietary therapies assessed for IBD and their composition, based on descriptions of the diets rather than food composition analyses, are described in figure 1. For CD, there are no common dietary themes, except that all treatments contain dairy protein and fat. For UC, the two proposed therapeutic diets appear similarly high in fibre, low in meat protein and dairy.

Exclusive enteral nutrition

Efficacy data for EEN, which replaces food with liquid nutritional supplements for 6–8 weeks, are strongest for paediatric patients with CD, with a Cochrane review showing 83% remission rates.[35] This is comparable to clinical remission from corticosteroids[35 36] and superior for mucosal healing (74% EEN vs 33% corticosteroids).[37] Furthermore, EEN in newly diagnosed patients is associated with corticosteroid avoidance over 6 years.[38] The better safety profile of EEN over corticosteroids certainly makes EEN the more appealing option and consensus guidelines recommend EEN as first-line therapy to induce remission in children with active luminal CD.[39] Use of EEN in adults is becoming more popular, although evidence of efficacy is not as strong compared with corticosteroids for clinical remission.[35] However, remission rates vary between 45% and 81% and studies with higher adherence rates show equal efficacy to paediatric patients.[40–42] Consensus guidelines have recently acknowledged EEN usage within an adult IBD service.[33 43 44]

Mechanism of action for EEN is unknown but likely result from complex interactions between mucosal immune response and luminal environment.[45] There are features of EEN composition that seem consistent and provide clues on how diet may be modulated for targeting inflammation. Curiously, most of the compositional features of enteral formula are greatly contrasting to a MED, seemingly protective of CD development (figure 1A). Like the MED, protein

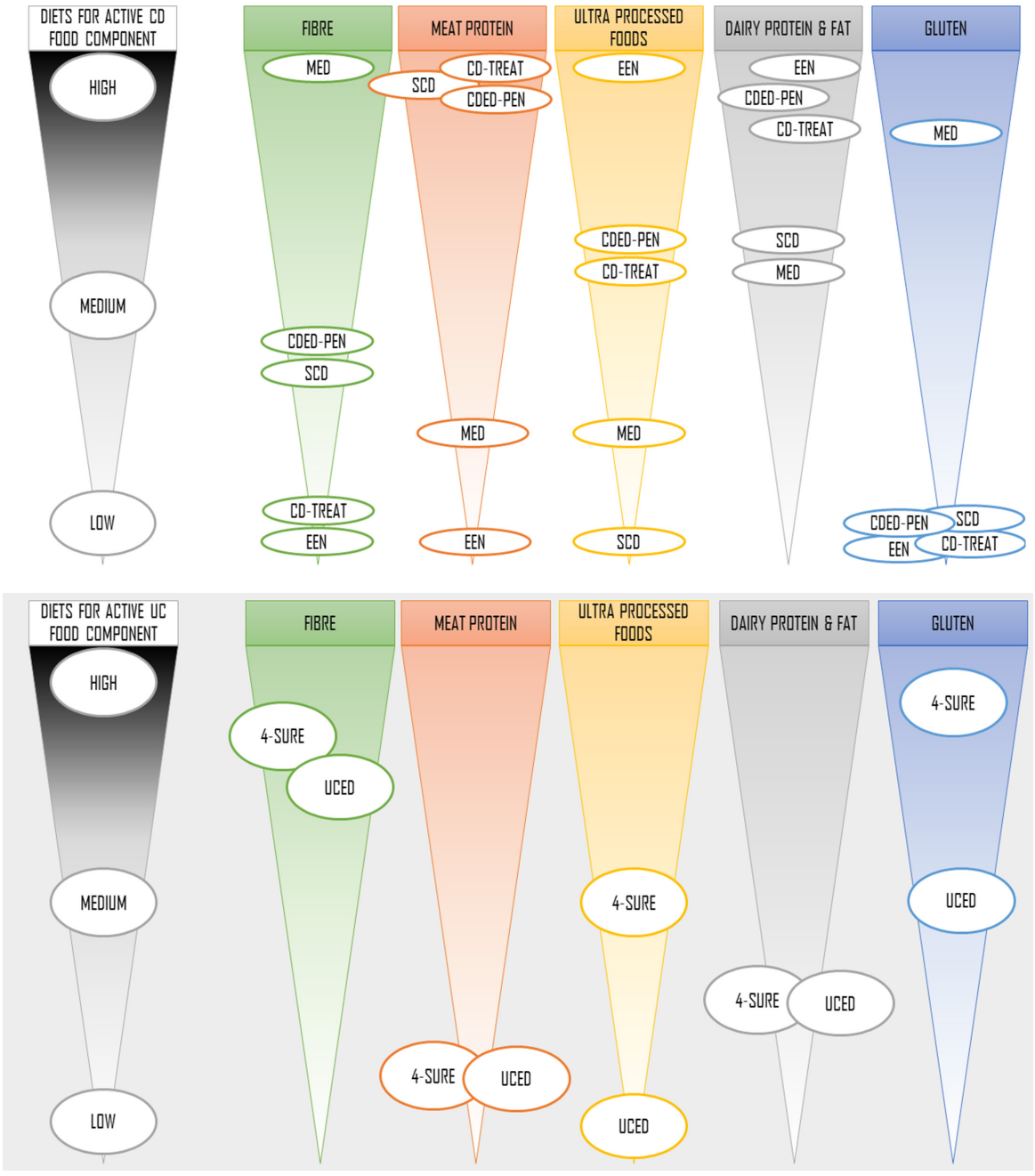

Figure 1 Content of fibre, meat protein, ultra-processed foods, dairy protein and fat and gluten in diets used for treatment of: (a) active Crohn's disease; and (b) active ulcerative colitis. Schematic representations are based on diet descriptions. CDED, Crohn's disease exclusion diet; EEN, exclusive enteral nutrition; MED, Mediterranean diet; PEN, partial enteral nutrition; SCD, specific carbohydrate diet; UCED, ulcerative colitis exclusion diet.

sources are casein, whey and soy protein, but unlike the MED, enteral formulas are free from lactose, gluten and fibre.[46] Maltodextrin, sucrose, glucose syrup and corn starch are the most common carbohydrate sources, found in higher concentrations than diet, the MED, in particular.[46] This is also conflicting with in vitro and animal studies suggesting that food additives such as maltodextrin trigger or deteriorate intestinal inflammation.[47] Furthermore, enteral formula is arguably the most UPF available. This paradox supports the idea that causal factors for CD development may not be targets for treatment.

Partial enteral nutrition

Partial enteral nutrition (PEN) describes a therapy in which only a proportion of food is replaced by enteral nutrition and the remaining diet is unrestricted. There is less evidence for PEN than EEN as a CD induction treatment; however, the percentage of caloric requirements provided by enteral nutrition is likely of

importance on remission rates. Most trials have evaluated 50% of caloric intake from PEN, with remission rates quoted between 15% and 50%.[48 49] Rather than PEN monotherapy, emerging evidence proposes PEN combined not only with biologic agents can enhance efficacy and achieve improved primary disease induction outcomes for active CD[50] but also with dose escalation for biologic loss of response.[51] Given the nature of PEN therapy, it is thought that dietary composition of PEN is similar to that of EEN, particularly as the food proportion of diet is unaltered, with the exception of the Crohn's disease exclusion diet (CDED).

Crohn's disease exclusion diet

The CDED coupled with PEN remains the only diet therapy, containing food, with reproducible evidence of efficacy for managing active CD.[52–54] In paediatric CD patients, CDED with PEN is better tolerated and as effective as EEN in inducing clinical remission and reducing faecal calprotectin.[52] Similar results are seen in adults with and without PEN.[54] The rationale of the diet is that it excludes dietary components implicated in the development of CD from epidemiology and animal studies, including animal fats, red meat, gluten, dairy, maltodextrin and UPF.[47] One would expect that the diet mimics the composition of a CD preventative diet, such as the MED, yet, in reality, the composition of the diet is very different. CDED is mostly studied coupled with PEN in significant volumes (50% of energy intake), which contains food additives, milk fat and milk protein and lacks fibre (figure 1A). However, the food component, comprising approximately a dozen foods and including the mandatory intake of chicken, eggs, potatoes, apple and banana on daily basis, is also high in animal protein (mandatory daily chicken and eggs) and low in fibre (limiting wholegrains, legumes, nuts and most fruit and vegetables). It may be that the similarities between the composition of CDED to EEN explain its efficacy for treating disease. This is further supported by the stable levels of faecal short-chain fatty acids during therapy with CDED and PEN and the similarities in faecal microbial effects of EEN and CDED with PEN previously described, including the reduction in the abundance of fibre-fermenting bacteria such as Bifidobacterium and Prevotella.[52 55]

Other diets targeting treatment of CD

The specific carbohydrate diet (SCD) is a food-based diet that eliminates disaccharides and polysaccharides (lactose, sucrose, starches, grains and most legumes), thus it is relatively low fibre, gluten free and contains lactose-free dairy[56] (figure 1A), similar to EEN. SCD efficacy for active CD has been studied in retrospective studies,[57 58] but recently compared against the MED, two contrasting diets, in patients with symptomatic CD.[59] Symptomatic response was improved with both diets, without difference between them.[59] There were no differences between CRP and faecal calprotectin between the diets, nor did either diet change the inflammatory markers from baseline, although faecal calprotectin was raised in less than a quarter of participants at basal conditions,[59] suggesting that both diets have an impact on symptoms but not necessarily inflammation.

In an attempt to mimic the effects of EEN, the CD-TREAT (Crohn's Disease Treatment-with-EATing) diet was devised. CD-TREAT-induced EEN-alike microbial effects and improved gut inflammatory markers in an animal model of disease.[60] In human trials, CD-TREAT reduced faecal calprotectin and induced clinical remission in a pilot study of five paediatric patients.[60] In a larger cohort of 57 children and adults with relapsing CD, a CD-TREAT course induced 75% remission and reduced faecal calprotectin.[61] Consistent with its rationale, the diet composition is similar to that of EEN, being low fibre, gluten and lactose free, high in milk protein and fat and contains UPF (figure 1A). These pilot open-label data require independent replication and further investigation within controlled trials.

Diets targeting treatment of UC

Therapeutic diets for UC have lagged behind CD, but data from two UC-specific diets are now emerging, with similar themes of dietary modification (figure 1B). Pilot data for the UC exclusion diet (UCED) from an open-label study in children with active UC have shown improved inflammatory activity index in 9/24 patients with diet alone and an additional four with combined antibiotic rescue therapy, six of whom maintained symptom response, although inflammatory markers did not improve.[62] Beyond symptomatic improvement, a subsequent trial in patients receiving UCED alone induced endoscopic remission in 4/15, but no difference when combined with faecal microbiota transplantation (FMT).[63] The UCED is a step-down diet that initially restricts many wholegrains and legumes, with daily limits on animal protein, dairy and wheat and promotes increased fruit, vegetables, including potatoes. Red meat and UPF are avoided.

In a similar fashion, a pilot open-label study of 28 adult patients with UC following the 4-SURE diet (4-strategies-to SUlfide REduction Diet) showed clinical and endoscopic response in 46% and 36%, respectively.[64] The four central strategies adopted by the 4-SURE diet are a limit of total protein to 75–90 g/d, a limit of sulphur-containing amino acids to 1.5–2.0 g/d, avoidance of sulphite/sulphate, nitrite/nitrate and carrageenan food additives and inclusion of 10–15 g/d resistant starch and slowly fermentable non-starch polysaccharide (figure 1B). It is notable that there was no difference in sulphur-containing amino acids between the 4-SURE and habitual diet, thus data may be more reflective of changes in total protein, fibre and resistant starch. A well-powered study with controlled diet comparison is much needed

to substantiate the hypothesised therapeutic components of the diet. Nonetheless, the concepts of both the UCED and 4-SURE diets to avoid red meat align with the evidence to prevent UC development. However, both diets further modify the diet with focus on including resistant starch and other components that modulate distal luminal microenvironment, with basis from pre-clinical models.[65]

Interpretation to clinical practice

To date, EEN and CDED with PEN are the only dietary therapies supported by high-quality trials to treat active CD and are becoming standard-of-care. However, these findings provide a contradiction to those seen of diet-preventing CD. Outwardly, it would seem that a diet low in fibre, gluten and lactose and inclusive of dairy protein and fat, maltodextrin and UPF treats CD. However, a lack of mechanistic studies must preclude specific recommendations of modulating these nutritional components outside of the context of these short-term diets, particularly with the potential risk of harm from diets lacking fibre and high in UPF. While less robust in evidence, diets for treating UC appear to fit with predisease models and generally in agreement with healthy eating guidelines that limit red meat and increase fibre.

Diet preventing IBD relapse

Cumulative data demonstrate the potential for dietary manipulation to maintain remission. This was indicated through the observation that resumption of eating after EEN-induced remission reactivates intestinal inflammation in patients with CD.[66] What is not clearly understood is whether diet as a maintenance agent should follow the principles of treating disease or preventing disease, particularly when there is a discord between the diets, as with CD. A few studies assessing the impact of specific diets on relapse rates in patients with quiescent IBD provide some clues to this question.

Maintaining remission for CD

The role of diet in maintaining remission in patients with CD for at least 6 months has been assessed in a few studies. Three trials evaluating 50% PEN in adults compared with regular diet or thiopurines, reduced relapse rates over the measured 6–24 months.[67–69] Retrospective paediatric studies also indicated benefit at 12 months.[70 71] The studies that have not shown sustained remission from PEN used 20%–30% of caloric requirements[66 72] and as with induction therapy, PEN for maintenance is likely to depend on >35% PEN of total energy.[73]

Considering food, an internet-based trial recommending or limiting red and processed meat in >200 patients with quiescent CD found no associated with symptomatic relapse over 49 weeks.[74] Conversely, a semivegetarian diet, described as reduced animal protein and fat, reduced relapse risk in an observational trial of 16 patients.[75] Perhaps the high fibre component of the diet was protective, which is consistent with a study where >23 g dietary fibre daily reduced flare risk by 40% over 6 months.[76] This presents another discrepancy in CD management as PEN promotes a low fibre intake.

Maintaining remission for UC

Dietary patterns promoted as healthy have been investigated for the prevention of UC relapse, specifically the role of meat with or without the consideration of fibre. Two uncontrolled observational studies showed inconsistent results over 12 months, one demonstrating a fivefold risk of UC relapse with red and processed meat[77] but the other showing no such link.[78] The aforementioned semivegetarian diet, also high in fibre, resulted in reduced relapse rates at 1 and 5 years' in UC patients if incorporated during induction therapy.[79] This study was consistent with an interventional crossover study, in which a diet low in red meat, total fat and high fibre, compared with a standard American diet, increased faecal markers considered protective of IBD relapse, including Faecalibacterium prausnitzii, and a trend for reduced serum amyloid A, a marker of mucosal inflammation.[80] This theme of reduced red meat combined with high fibre, as with a MED, positively altered microbiota, predicting relapse compared with a usual Canadian diet.[81] Finally, in UC patients following total proctocolectomy with ileal pouch-anal anastomosis, adherence to a MED was associated with lower inflammatory markers and lower rates of pouchitis.[82]

More complex diets assessed include an 'anti-inflammatory diet (AID)' that aimed to increase fibre, probiotics, antioxidants and n-3 PUFA and decrease red meat and added sugar. No difference in relapse rates were seen in UC patients when compared with Canada's healthy eating guidelines,[83] but there may be little compositional differences between the diets. Another diet of similar composition, labelled FMT-AID, resulted in sustained deep remission at 12 months compared with standard medical therapy, however, the dietary treatment was administered with FMT, which precluded evaluation of diet alone.[84]

Interpretation to clinical practice

Studies assessing diet to maintain remission for CD have not provided more clarity on whether a diet resembling EEN or MED should be used, with data for fibre, as a surrogate marker differentiating the diets, showing conflicting results, as has associations with red meat. Healthy eating guidelines should be supported in the absence of clear diet pathways. Conversely, the concept of healthy eating is a more promising strategy for retaining UC remission, although whether the effects are due to reduced red meat, high fibre or both are not clear.

CONCLUSIONS

Diet is well established as a modifying player in the prevention and treatment of CD and UC. Multiple epidemiological studies uphold the idea that a healthy diet modelled on the MED, being mostly plant-based with limits on red meat and UPF, is likely beneficial for disease prevention, at least for CD. Less apparent for UC, similar healthy eating principles should be the default messaging, potentially with an emphasis on less red meat. Such advice should remain for active and quiescent UC in the absence of high-quality trials that indicate otherwise. The narrative for CD is more complex with very clear opposing beneficial diets preventing and treating disease. EEN and CDED with PEN are recognised induction therapies but create a paradox that inhibiting putative dietary causative factors, such as protein and UPF, will not necessarily reverse inflammation. Studies of long-term dietary treatments with goals of maintaining remission are needed before healthy eating recommendations for CD can be amended.

Contributors EPH convened the author's group and merged and produced the final draft for submission. EPH and VS are guarantors of the manuscript. All authors contributed to researching data, writing, reviewing, editing and agreed with the final manuscript prior to submission.

Funding EPH is supported through an NHMRC Investigator Grant; APP1195487.

Competing interests EPH has received research grants for investigator-driven studies from Mindset Health Pty Ltd and speaker honoraria from Sandoz Pty Ltd and Mindset Health Pty Ltd; LG received speaker honoraria from Janssen, Takeda, Abbvie, Pfizer, Galapagos, Altman and is involved with studies related to the Mediterranean diet; CSS: Wolfson Medical Center IP for Nestle Health Science, speaking fees from Nestle, Takeda and Ferring, and was involved in the development of the UCED and some studies related to CDED; JV received speaking fees from Janssen, consultancy fees from Ferring; VS was involved in the development of the CD-TREAT diet.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer-reviewed.

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REFERENCES

1 Cordain L, Eaton SB, Sebastian A, *et al*. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr* 2005;81:341–54.
2 Wood JA, Halmos EP, Taylor KM, *et al*. The role of Epidemiological evidence from prospective population studies in shaping dietary approaches to therapy in Crohn's disease. *Mol Nutr Food Res* 2021;65:e2000294.
3 Jantchou P, Morois S, Clavel-Chapelon F, *et al*. Animal protein intake and risk of inflammatory bowel disease: the E3N prospective study. *Am J Gastroenterol* 2010;105:2195–201.
4 Fu T, Chen H, Chen X, *et al*. Sugar-sweetened Beverages, artificially sweetened Beverages and natural juices and risk of inflammatory bowel disease: a cohort study of 121,490 participants. *Aliment Pharmacol Ther* 2022;56:1018–29.
5 Chan SSM, Luben R, Olsen A, *et al*. Association between high dietary intake of the N-3 polyunsaturated fatty acid Docosahexaenoic acid and reduced risk of Crohn's disease. *Aliment Pharmacol Ther* 2014;39:834–42.
6 Opstelten JL, Leenders M, Dik VK, *et al*. Dairy products, dietary calcium, and risk of inflammatory bowel disease: results from a European prospective cohort investigation. *Inflamm Bowel Dis* 2016;22:1403–11.
7 Ananthakrishnan AN, Khalili H, Konijeti GG, *et al*. A prospective study of long-term intake of dietary fiber and risk of Crohn's disease and ulcerative colitis. *Gastroenterology* 2013;145:970–7.
8 Andersen V, Chan S, Luben R, *et al*. Fibre intake and the development of inflammatory bowel disease: A European prospective multi-centre cohort study (EPIC-IBD). *J Crohns Colitis* 2018;12:129–36.
9 Deng M, Dan L, Ye S, *et al*. Higher dietary fibre intake is associated with lower risk of inflammatory bowel disease: prospective cohort study. *Aliment Pharmacol Ther* 2023;58:516–25.
10 Lu Y, Zamora-Ros R, Chan S, *et al*. Dietary Polyphenols in the Aetiology of Crohn's disease and ulcerative colitis-A multicenter European prospective cohort study (EPIC). *Inflamm Bowel Dis* 2017;23:2072–82.
11 Khalili H, Malik S, Ananthakrishnan AN, *et al*. Identification and characterization of a novel association between dietary potassium and risk of Crohn's disease and ulcerative colitis. *Front Immunol* 2016;7:554.
12 Ananthakrishnan AN, Khalili H, Song M, *et al*. Zinc intake and risk of Crohn's disease and ulcerative colitis: a prospective cohort study. *Int J Epidemiol* 2015;44:1995–2005.
13 Vasseur P, Dugelay E, Benamouzig R, *et al*. Dietary zinc intake and inflammatory bowel disease in the French Nutrinet-Santé cohort. *Am J Gastroenterol* 2020;115:1293–7.
14 Dong C, Chan SSM, Jantchou P, *et al*. Meat intake is associated with a higher risk of ulcerative colitis in a large European prospective cohort Studyø. *J Crohns Colitis* 2022;16:1187–96.
15 Ananthakrishnan AN, Khalili H, Konijeti GG, *et al*. Long-term intake of dietary fat and risk of ulcerative colitis and Crohn's disease. *Gut* 2014;63:776–84.
16 Ananthakrishnan AN, Khalili H, Song M, *et al*. Genetic Polymorphisms in fatty acid metabolism modify the association between dietary N3: N6 intake and risk of ulcerative colitis: A prospective cohort study. *Inflamm Bowel Dis* 2017;23:1898–904.
17 de Silva PSA, Luben R, Shrestha SS, *et al*. Dietary Arachidonic and Oleic acid intake in ulcerative colitis etiology: a prospective cohort study using 7-day food diaries. *Eur J Gastroenterol Hepatol* 2014;26:11–8.
18 John S, Luben R, Shrestha SS, *et al*. Dietary N-3 polyunsaturated fatty acids and the Aetiology of ulcerative colitis: a UK prospective cohort study. *Eur J Gastroenterol Hepatol* 2010;22:602–6.
19 IBD in EPIC Study Investigators, Tjonneland A, Overvad K, *et al*. Linoleic acid, a dietary N-6 polyunsaturated fatty acid, and the Aetiology of ulcerative colitis: a nested case-control study within a European prospective cohort study. *Gut* 2009;58:1606–11.
20 Ananthakrishnan AN, Khalili H, Higuchi LM, *et al*. Higher predicted vitamin D status is associated with reduced risk of Crohn's disease. *Gastroenterology* 2012;142:482–9.
21 Khalili H, Håkansson N, Chan SS, *et al*. Adherence to a Mediterranean diet is associated with a lower risk of later-

onset Crohn's disease: results from two large prospective cohort studies. *Gut* 2020;69:1637–44.
22 Peters V, Bolte L, Schuttert EM, *et al*. Western and carnivorous dietary patterns are associated with greater likelihood of IBD development in a large prospective population-based cohort. *J Crohns Colitis* 2022;16:931–9.
23 Racine A, Carbonnel F, Chan SSM, *et al*. Dietary patterns and risk of inflammatory bowel disease in Europe: results from the EPIC study. *Inflamm Bowel Dis* 2016;22:345–54.
24 Khalili H, Hakansson N, Casey K, *et al*. Diet quality and risk of older-onset Crohn's disease and ulcerative colitis. *J Crohns Colitis* 2023;17:746–53.
25 Lopes EW, Chan SSM, Song M, *et al*. Lifestyle factors for the prevention of inflammatory bowel disease. *Gut* 2022:gutjnl-2022-328174.
26 Sun Y, Yuan S, Chen X, *et al*. The contribution of genetic risk and lifestyle factors in the development of adult-onset inflammatory bowel disease: A prospective cohort study. *Am J Gastroenterol* 2023;118:511–22.
27 Tabung FK, Smith-Warner SA, Chavarro JE, *et al*. Development and validation of an empirical dietary inflammatory index. *J Nutr* 2016;146:1560–70.
28 Lo C-H, Lochhead P, Khalili H, *et al*. Dietary inflammatory potential and risk of Crohn's disease and ulcerative colitis. *Gastroenterology* 2020;159:873–83.
29 Narula N, Wong ECL, Dehghan M, *et al*. Does a high-inflammatory diet increase the risk of inflammatory bowel disease? results from the prospective urban rural epidemiology (PURE) study: A prospective cohort study. *Gastroenterology* 2021;161:1333–5.
30 Monteiro CA, Cannon G, Moubarac J-C, *et al*. The UN decade of nutrition, the NOVA food classification and the trouble with ultra-processing. *Public Health Nutr* 2018;21:5–17.
31 Narula N, Chang NH, Mohammad D, *et al*. Food processing and risk of inflammatory bowel disease: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2023;21:2483–95.
32 Koios D, Machado P, Lacy-Nichols J. Representations of Ultra-processed foods: A global analysis of how dietary guidelines refer to levels of food processing. *Int J Health Policy Manag* 2022;11:2588–99.
33 Bischoff SC, Bager P, Escher J, *et al*. ESPEN guideline on clinical nutrition in inflammatory bowel disease. *Clinical Nutrition* 2023;42:352–79.
34 Godny L, Svolos V, Williams A-J, *et al*. Multidisciplinary perinatal care in IBD. *J Crohns Colitis* 2023;17:663–80.
35 Narula N, Dhillon A, Zhang D, *et al*. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst Rev* 2018;4:CD000542.
36 Swaminath A, Feathers A, Ananthakrishnan AN, *et al*. Systematic review with meta-analysis: Enteral nutrition therapy for the induction of remission in Paediatric Crohn's disease. *Aliment Pharmacol Ther* 2017;46:645–56.
37 Borrelli O, Cordischi L, Cirulli M, *et al*. Polymeric diet alone versus corticosteroids in the treatment of active pediatric Crohn's disease: a randomized controlled open-label trial. *Clin Gastroenterol Hepatol* 2006;4:744–53.
38 Connors J, Basseri S, Grant A, *et al*. Exclusive Enteral nutrition therapy in Paediatric Crohn's disease results in long-term avoidance of corticosteroids: results of a propensity-score matched cohort analysis. *J Crohns Colitis* 2017;11:1063–70.
39 Ruemmele FM, Veres G, Kolho KL, *et al*. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J Crohns Colitis* 2014;8:1179–207.
40 Melton SL, Fitzpatrick JA, Taylor KM, *et al*. Lessons from an audit of exclusive Enteral nutrition in adult Inpatients and outpatients with active Crohn's disease: a single-centre experience. *Frontline Gastroenterol* 2023;14:6–12.
41 Verma S, Brown S, Kirkwood B, *et al*. Polymeric versus elemental diet as primary treatment in active Crohn's disease: a randomized, double-blind trial. *Am J Gastroenterol* 2000;95:735–9.
42 Yang Q, Gao X, Chen H, *et al*. Efficacy of exclusive Enteral nutrition in complicated Crohn's disease. *Scand J Gastroenterol* 2017;52:995–1001.
43 Lamb CA, Kennedy NA, Raine T, *et al*. British society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019;68(Suppl 3):s1–106.
44 Lomer MCE, Wilson B, Wall CL. British Dietetic Association consensus guidelines on the nutritional assessment and dietary management of patients with inflammatory bowel disease. *J Hum Nutr Diet* 2023;36:336–77.
45 Melton SL, Taylor KM, Gibson PR, *et al*. Review article: mechanisms underlying the effectiveness of exclusive Enteral nutrition in Crohn's disease. *Aliment Pharmacol Ther* 2023;57:932–47.
46 Logan M, Gkikas K, Svolos V, *et al*. Analysis of 61 exclusive Enteral nutrition formulas used in the management of active Crohn's disease-new insights into dietary disease triggers. *Aliment Pharmacol Ther* 2020;51:935–47.
47 Levine A, Sigall Boneh R, Wine E. Evolving role of diet in the pathogenesis and treatment of inflammatory bowel diseases. *Gut* 2018;67:1726–38.
48 Johnson T, Macdonald S, Hill SM, *et al*. Treatment of active Crohn's disease in children using partial Enteral nutrition with liquid formula: a randomised controlled trial. *Gut* 2006;55:356–61.
49 Lee D, Baldassano RN, Otley AR, *et al*. Comparative effectiveness of nutritional and biological therapy in North American children with active Crohn's disease. *Inflamm Bowel Dis* 2015;21:1786–93.
50 Tanaka T, Takahama K, Kimura T, *et al*. Effect of concurrent elemental diet on Infliximab treatment for Crohn's disease. *J Gastroenterol Hepatol* 2006;21:1143–9.
51 Hisamatsu T, Kunisaki R, Nakamura S, *et al*. Effect of elemental diet combined with Infliximab dose escalation in patients with Crohn's disease with loss of response to Infliximab: CERISIER trial. *Intest Res* 2018;16:494.
52 Levine A, Wine E, Assa A, *et al*. Crohn's disease exclusion diet plus partial Enteral nutrition induces sustained remission in a randomized controlled trial. *Gastroenterology* 2019;157:440–50.
53 Matuszczyk M, Meglicka M, Wiernicka A, *et al*. Effect of the Crohn's disease exclusion diet (CDED) on the fecal Calprotectin level in children with active Crohn's disease. *J Clin Med* 2022;11:14.
54 Yanai H, Levine A, Hirsch A, *et al*. The Crohn's disease exclusion diet for induction and maintenance of remission in adults with mild-to-moderate Crohn's disease (CDED-AD): an open-label, pilot, randomised trial. *Lancet Gastroenterol Hepatol* 2022;7:49–59.
55 Verburgt CM, Dunn KA, Ghiboub M, *et al*. Successful dietary therapy in Paediatric Crohn's disease is associated with shifts in bacterial Dysbiosis and inflammatory Metabotype towards healthy controls. *J Crohns Colitis* 2023;17:61–72.
56 Cohen SA, Gold BD, Oliva S, *et al*. Clinical and Mucosal improvement with specific carbohydrate diet in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr* 2014;59:516–21.
57 Obih C, Wahbeh G, Lee D, *et al*. Specific carbohydrate diet for pediatric inflammatory bowel disease in clinical practice within an academic IBD center. *Nutrition* 2016;32:418–25.
58 Suskind DL, Wahbeh G, Gregory N, *et al*. Nutritional therapy in pediatric Crohn disease: the specific carbohydrate diet. *J Pediatr Gastroenterol Nutr* 2014;58:87–91.

59 Lewis JD, Sandler RS, Brotherton C, *et al*. A randomized trial comparing the specific carbohydrate diet to a Mediterranean diet in adults with Crohn's disease. *Gastroenterology* 2021;161:837–52.
60 Svolos V, Hansen R, Nichols B, *et al*. Treatment of active Crohn's disease with an ordinary food-based diet that Replicates exclusive Enteral nutrition. *Gastroenterology* 2019;156:1354–67.
61 Svolos V, Hansen R, Russell R, *et al*. Dop68 CD-TREAT diet induces remission and improves quality of life in an open label trial in children and adults with active Crohn's disease. *Journal of Crohn's and Colitis* 2022;16(Supplement_1):i112.
62 Sarbagili-Shabat C, Albenberg L, Van Limbergen J, *et al*. A novel UC exclusion diet and antibiotics for treatment of mild to moderate pediatric ulcerative colitis: A prospective open-label pilot study. *Nutrients* 2021;13:3736.
63 Sarbagili Shabat C, Scaldaferri F, Zittan E, *et al*. Use of Faecal transplantation with a novel diet for mild to moderate active ulcerative colitis: the CRAFT UC randomised controlled trial. *J Crohns Colitis* 2022;16:369–78.
64 Day AS, Yao CK, Costello SP, *et al*. Therapeutic potential of the 4 strategies to sulfide-reduction (4-SURE) diet in adults with mild to moderately active ulcerative colitis: an open-label feasibility study. *J Nutr* 2022;152:1690–701.
65 Roediger WEW. Review article: nitric oxide from Dysbiotic bacterial respiration of nitrate in the pathogenesis and as a target for therapy of ulcerative colitis. *Aliment Pharmacol Ther* 2008;27:531–41.
66 Logan M, Clark CM, Ijaz UZ, *et al*. The reduction of Faecal Calprotectin during exclusive Enteral nutrition is lost rapidly after food re-introduction. *Aliment Pharmacol Ther* 2019;50:664–74.
67 Hanai H, Iida T, Takeuchi K, *et al*. Nutritional therapy versus 6-Mercaptopurine as maintenance therapy in patients with Crohn's disease. *Dig Liver Dis* 2012;44:649–54.
68 Takagi S, Utsunomiya K, Kuriyama S, *et al*. "Effectiveness of an 'half elemental diet' as maintenance therapy for Crohn's disease: A randomized-controlled trial". *Aliment Pharmacol Ther* 2006;24:1333–40.
69 Triantafillidis J, Stamataki A, Karagianni V, *et al*. Maintenance treatment of Crohn's disease with a polymeric feed rich in TGF. *Ann Gastroenterol* 2010;23:113–8.
70 Duncan H, Buchanan E, Cardigan T, *et al*. A retrospective study showing maintenance treatment options for Paediatric CD in the first year following diagnosis after induction of remission with EEN: supplemental Enteral nutrition is better than nothing *BMC Gastroenterol* 2014;14:50.
71 Wilschanski M, Sherman P, Pencharz P, *et al*. Supplementary Enteral nutrition maintains remission in Paediatric Crohn's disease. *Gut* 1996;38:543–8.
72 Gavin J, Ashton JJ, Heather N, *et al*. Nutritional support in Paediatric Crohn's disease: outcome at 12 months. *Acta Paediatr* 2018;107:156–62.
73 Gkikas K, Gerasimidis K, Milling S, *et al*. Dietary strategies for maintenance of clinical remission in inflammatory bowel diseases: are we there yet *Nutrients* 2020;12:2018.
74 Albenberg L, Brensinger CM, Wu Q, *et al*. A diet low in red and processed meat does not reduce rate of Crohn's disease flares. *Gastroenterology* 2019;157:128–36.
75 Chiba M, Abe T, Tsuda H, *et al*. Lifestyle-related disease in Crohn's disease: relapse prevention by a semi-vegetarian diet. *World J Gastroenterol* 2010;16:2484–95.
76 Brotherton CS, Martin CA, Long MD, *et al*. Avoidance of fiber is associated with greater risk of Crohn's disease flare in a 6-month period. *Clin Gastroenterol Hepatol* 2016;14:1130–6.
77 Jowett SL, Seal CJ, Pearce MS, *et al*. Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study. *Gut* 2004;53:1479–84.
78 Barnes EL, Nestor M, Onyewadume L, *et al*. High dietary intake of specific fatty acids increases risk of flares in patients with ulcerative colitis in remission during treatment with Aminosalicylates. *Clin Gastroenterol Hepatol* 2017;15:1390–6.
79 Chiba M, Nakane K, Tsuji T, *et al*. Relapse prevention by plant-based diet incorporated into induction therapy for ulcerative colitis: A single-group trial. *Perm J* 2019;23:18-220.
80 Fritsch J, Garces L, Quintero MA, *et al*. High-fiber diet reduces markers of inflammation and Dysbiosis and improves quality of life in patients with ulcerative colitis. *Clin Gastroenterol Hepatol* 2021;19:1189–99.
81 Haskey N, Estaki M, Ye J, *et al*. A Mediterranean diet pattern improves intestinal inflammation concomitant with reshaping of the Bacteriome in ulcerative colitis: A randomized controlled trial. *J Crohns Colitis* 2023;17:1569–78.
82 Godny L, Reshef L, Pfeffer-Gik T, *et al*. Adherence to the Mediterranean diet is associated with decreased fecal Calprotectin in patients with ulcerative colitis after pouch surgery. *Eur J Nutr* 2020;59:3183–90.
83 Keshteli AH, Valcheva R, Nickurak C, *et al*. Anti-inflammatory diet prevents Subclinical Colonic inflammation and alters Metabolomic profile of ulcerative colitis patients in clinical remission. *Nutrients* 2022;14:3294.
84 Kedia S, Virmani S, K Vuyyuru S, *et al*. Faecal Microbiota transplantation with anti-inflammatory diet (FMT-AID) followed by anti-inflammatory diet alone is effective in inducing and maintaining remission over 1 year in mild to moderate ulcerative colitis: a randomised controlled trial. *Gut* 2022;71:2401–13.
85 Hart AR, Luben R, Olsen A, *et al*. Diet in the Aetiology of ulcerative colitis: a European prospective cohort study. *Digestion* 2008;77:57–64.
86 Chan SSM, Luben R, van Schaik F, *et al*. Carbohydrate intake in the etiology of Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis* 2014;20:2013–21.
87 Khalili H, Hakansson N, Chan SS, *et al*. No association between consumption of sweetened Beverages and risk of later-onset Crohn's disease or ulcerative colitis. *Clin Gastroenterol Hepatol* 2019;17:123–9.
88 Jantchou P, Clavel-Chapelon F, Racine A, *et al*. High residential sun exposure is associated with a low risk of incident Crohn's disease in the prospective E3N cohort. *Inflamm Bowel Dis* 2014;20:75–81.
89 Opstelten JL, Chan SSM, Hart AR, *et al*. Prediagnostic serum vitamin D levels and the risk of Crohn's disease and ulcerative colitis in European populations: A nested case-control study. *Inflamm Bowel Dis* 2018;24:633–40.
90 Khalili H, de Silva PS, Ananthakrishnan AN, *et al*. Dietary iron and Heme iron consumption, genetic susceptibility, and risk of Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis* 2017;23:1088–95.
91 Rubin KH, Rasmussen NF, Petersen I, *et al*. "Intake of dietary fibre, red and processed meat and risk of late-onset chronic inflammatory diseases: A prospective Danish study on the "diet, cancer and health" cohort". *Int J Med Sci* 2020;17:2487–95.
92 Lopes EW, Lebwohl B, Burke KE, *et al*. Dietary gluten intake is not associated with risk of inflammatory bowel disease in US adults without celiac disease. *Clinical Gastroenterology and Hepatology* 2022;20:303–313.
93 Bergmann MM, Hernandez V, Bernigau W, *et al*. No Association of alcohol use and the risk of ulcerative colitis or Crohn's disease: data from a European prospective cohort study (EPIC). *Eur J Clin Nutr* 2017;71:512–8.
94 Casey K, Lopes EW, Niccum B, *et al*. Alcohol consumption and risk of inflammatory bowel disease among three

prospective US cohorts. *Aliment Pharmacol Ther* 2022;55:225–33.
95 Liu B-X, Yang J, Zeng C, *et al*. Risk of inflammatory bowel disease appears to vary across different frequency, amount, and subtype of alcoholic Beverages. *Front Nutr* 2022;9:918754.
96 Zhou S, Chai P, Dong X, *et al*. Drinking water quality and inflammatory bowel disease: a prospective cohort study. *Environ Sci Pollut Res* 2023;30:71171–83.
97 Ananthakrishnan AN, Khalili H, Song M, *et al*. High school diet and risk of Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis* 2015;21:2311–9.
98 Guevara M, Salamanca-Fernández E, Miqueleiz E, *et al*. Inflammatory potential of the diet and incidence of Crohn's disease and ulcerative colitis in the EPIC-Spain cohort. *Nutrients* 2021;13:2201.
99 Fu T, Ye S, Sun Y, *et al*. Greater adherence to cardioprotective diet can reduce inflammatory bowel disease risk: A longitudinal cohort study. *Nutrients* 2022;14:4058.
100 Hammer T, Lophaven SN, Nielsen KR, *et al*. Dietary risk factors for inflammatory bowel diseases in a high-risk population: results from the Faroese IBD study. *United European Gastroenterol J* 2019;7:924–32.
101 Narula N, Wong ECL, Dehghan M, *et al*. Association of Ultra-processed food intake with risk of inflammatory bowel disease: prospective cohort study. *BMJ* 2021;374:n1554.
102 Vasseur P, Dugelay E, Benamouzig R, *et al*. Dietary patterns, ultra-processed food, and the risk of inflammatory bowel diseases in the Nutrinet-Santé cohort. *Inflamm Bowel Dis* 2021;27:65–73.
103 Lo C-H, Khandpur N, Rossato SL, *et al*. Ultra-processed foods and risk of Crohn's disease and ulcerative colitis: A prospective cohort study. *Clinical Gastroenterology and Hepatology* 2022;20:e1323–37.
104 Meyer A, Dong C, Casagrande C, *et al*. Food processing and risk of Crohn's disease and ulcerative colitis: A European prospective cohort study. *Clinical Gastroenterology and Hepatology* 2023;21:1607–1616.
105 Chen J, Wellens J, Kalla R, *et al*. Intake of Ultra-processed foods is associated with an increased risk of Crohn's disease: A cross-sectional and prospective analysis of 187 154 participants in the UK Biobank. *J Crohns Colitis* 2023;17:535–52.