Journal of Enterocolitis

Review

Nutritional Challenges and Management in Patients with Inflammatory Bowel Diseases: A Comprehensive Review

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Cite this article as: İstemihan Z, Gallo G, Loy L, Privitera G, Bezzio C, Akyüz F, Armuzzi A. Nutritional Challenges and Management in Patients with Inflammatory Bowel Diseases: A Comprehensive Review. *J Enterocolitis.* 2026;5(1):1-15.

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Received: April 2, 2026 **Accepted:** April 9, 2026

DOI:10.14744/Jenterocolitis.2026.95876

Abstract

Nutritional management in inflammatory bowel diseases (IBD) is transitioning from a calorie-centric approach to a functional paradigm that incorporates body composition, metabolic health, and inflammatory burden. Malnutrition, which may manifest as sarcopenia, myosteatosis, or sarcopenic obesity, affects a significant proportion of patients from the time of diagnosis and has prognostic implications for treatment response, surgical outcomes, and quality of life that go beyond those associated with Body Mass Index (BMI) alone. This narrative review explores the evolving role of nutrition as both a disease modifier and a therapeutic adjunct in IBD, emphasizing mechanistic evidence that links ultra-processed foods and dietary additives to intestinal barrier disruption, dysbiosis, and persistent low-grade inflammation. We propose a phase-specific framework that positions nutritional assessment and dietary intervention as essential components of routine IBD care. During active disease, targeted exclusion diets can function as therapeutic adjuncts or, in selected cases, as primary interventions. During remission, adherence to anti-inflammatory dietary patterns, particularly the Mediterranean diet, promotes microbiota diversity, mucosal integrity, and long-term metabolic resilience. Nutritional interventions should be coordinated with pharmacological therapy to capitalize on the therapeutic window created by inflammatory suppression, thereby overcoming anabolic resistance and optimizing muscle protein synthesis. Standardized screening tools that integrate the Global Leadership Initiative on Malnutrition (GLIM) criteria with body composition analysis facilitate early identification of nutritional phenotypes and guide personalized interventions. By outlining current evidence and identifying remaining knowledge gaps, this review offers a strategic framework for precision nutritional care in IBD, positioning diet as a cornerstone of holistic disease management alongside advanced therapies.
Keywords: Body composition, Crohn's disease, inflammatory bowel disease, nutritional screening, ulcerative colitis.

1. Introduction

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic, relapsing–remitting disorders resulting from a complex interaction between genetic susceptibility, immune dysregulation, and environmental triggers.[1,2] With the global rise in IBD prevalence, modifiable factors, such as diet, have emerged as key drivers of disease onset and progression.[1,2] Modern "Westernized" diets—characterized by a high intake of ultra-processed foods (UPF), emulsifiers, and refined sugars—are thought to disrupt the gut-mucosal interface, promoting dysbiosis, impairing the mucus layer, and increasing intestinal permeability.[3-6] This cascade can trigger immune activation in genetically predisposed individuals.[2]

Beyond disease onset, dietary intake can also modify the clinical course of IBD. A Western diet has been reported to increase the risk of disease flares, particularly with red and processed meat, protein, and alcohol, all of which have been associated with a higher risk of relapse.[7] Nutrition plays a crucial role in regulating immune activity. Specific micronutrients and macronutrients—such as amino acids, vitamins, and minerals—directly modulate both innate and adaptive immune responses. For instance, amino acids like arginine and tryptophan are essential for macrophage function and broader immune metabolic pathways.[8,9] Vitamin A is crucial for the maturation of immune cells (e.g., natural killer cells, lymphocytes) and for maintaining mucosal barrier integrity.[10] Similarly, vitamin D modulates adaptive immunity by reducing pro-inflammatory cytokine secretion.[11] Lastly, minerals like zinc and selenium exert anti-inflammatory effects by inhibiting pro-inflammatory immune actions.

This diet-dependent inflammation extends beyond the gut, influencing body composition and metabolic health. It drives changes in insulin sig-

naling, muscle protein turnover, and adipose tissue distribution, which, in turn, affect disease severity.[12] Malnutrition and alterations in body composition are common complications that contribute significantly to morbidity.[13] These changes are particularly seen in the form of sarcopenia (defined as impaired muscle mass and strength)[14] and myosteatosis (characterized by the pathological accumulation of inter- and intramuscular adipose tissue).[15]

Beyond the classical paradigm of malnutrition as an overt caloric deficiency, which still affects a proportion of patients with IBD, an increasingly recognized phenotype is malnutrition associated with excess body weight, often in the form of sarcopenic obesity. In this condition, excess adiposity masks muscle depletion, leading to poorer outcomes.[16] Crucially, nutritional impairment often exists from diagnosis, regardless of disease activity or Body Mass Index (BMI).[17] This highlights the need to shift from reactive supplementation to proactive, systematic nutritional assessment throughout the disease course.[18]

Such comprehensive evaluation lays the groundwork for targeted dietary strategies, which are increasingly recognized for their potential to modulate inflammation, sustain remission, and optimize long-term outcomes. Integrating objective nutritional metrics with therapeutic decision-making positions diet as an essential component of personalized care in IBD.[18] This review aims to critically examine the evolving nutritional challenges in patients with IBD, moving beyond general dietary advice to explore the pathophysiological synergy between nutritional status, body composition, and targeted dietary interventions. By integrating recent clinical evidence and identifying current knowledge gaps, we aim to provide a strategic framework for individualized nutritional care in the era of precision medicine.

2. Methods

This narrative review was synthesized through a comprehensive literature search aimed at identifying the most relevant evidence regarding nutritional assessment, body composition, and dietary interventions in IBD. A structured search was conducted across major electronic databases, including PubMed/MEDLINE, Embase, and the Cochrane Library, from January 2010 to February 2026. The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords, including but not limited to: "inflammatory bowel disease," "Crohn's disease," "ulcerative colitis," "malnutrition," "nutritional screening," "sarcopenia," "myosteatosis," "myopenia," "body composition," "ultra-processed foods," "inflammatory bowel disease diet," "Exclusive Enteral Nutrition," "Partial Enteral Nutrition," and "Mediterranean diet." Literature was selected based on its clinical relevance to the evolving functional paradigm of IBD management. Selected sources included clinical trials and observational studies investigating the impact of nutrition on disease activity, treatment response, and surgical outcomes, as well as international guidelines and consensus statements. Additionally, pathophysiological evidence from preclinical studies clarifying the role of dietary additives and nutrients in intestinal barrier integrity was incorporated. Priority was given to high-quality, peer-reviewed articles published within the last decade, while landmark studies were also included to provide historical context and a comprehensive understanding of current therapeutic gaps.

3. Nutritional Assessment in the Modern Era: Moving Beyond BMI

Malnutrition in IBD represents a deterioration of physical and mental health due to inadequate intake, often compounded by chronic inflammation.1 Several definitions of malnutrition have been proposed, as outlined in Table 1.

The etiology of malnutrition in IBD is multifactorial. During active disease, oral intake declines due to abdominal pain, nausea, vomiting, and anorexia. Side effects of medications, hospitalization, and long-term dietary restrictions further compound reduced intake. Intestinal mucosal damage from active inflammation leads to malabsorption of iron, folic acid, vitamin B12, vitamin D, and electrolytes.[16] Anemia in IBD is typically multifactorial: iron deficiency anemia (due to chronic blood loss) coexists with anemia of chronic disease, drug-related bone marrow suppression, and anemia secondary to drug-related adverse events.[20] Surgical resection of small bowel segments can precipitate malabsorption by shortening transit time and removing critical absorptive surfaces. Beyond micronutrient deficiency, ileal resection frequently causes bile acid malabsorption, leading to fat malabsorption, steatorrhea, and debilitating diarrhea, further compromising nutritional status.[21]

Notably, a patient can become malnourished even without overt malabsorption, simply due to the catabolic state induced by active inflammation, severe diarrhea leading to fluid and electrolyte depletion, and symptoms that limit eating.[2] Medications play a substantial role: for instance, corticosteroids accelerate muscle catabolism and decrease bone and skin strength, while also causing deficiencies in vitamins D and K, and sulfasalazine inhibits key enzymes for folate absorption.[2]

Over time, this inflammatory-malnutrition axis drives sarcopenia – the loss of muscle mass and strength – which affects 30–55% of patients and is more prevalent in CD than UC.[23] Sarcopenia profoundly impacts clinical outcomes: it reduces quality of life, increases hospital stay length, predicts failure of medical therapies, and raises surgical complication rates.[24]

All patients with IBD are at risk of malnutrition from the time of diagnosis, necessitating routine nutritional evaluation.[25] Studies have demonstrated reductions in both fat-free mass and fat mass in CD patients with longstanding disease, although the influence of factors such as disease location, duration, and phenotype on body composition changes remains incompletely understood and requires further investigation.[23,26] The heterogeneity of existing evidence – with some studies reporting comparable lean mass between CD and UC patients and others showing divergent patterns – underscores the complexity of nutritional assessment in this population.

Crucially, in contemporary IBD management, reliance on BMI is insufficient and potentially misleading. Weight loss and the resulting reduction in BMI are associated with poor prognosis, giving rise to the so-called "obesity paradox," whereby patients with higher BMI appear to experience more favorable outcomes. However, this paradox largely reflects the intrinsic limitations of BMI, which fails to distinguish between lean and fat mass.[27,28] Notably, 15%–40% of adult patients with IBD are classified as obese, and an additional 25%–40% as overweight.[29-33] In this context, excess adiposity often masks concomitant muscle mass depletion, resulting in sarcopenic obesity, a phenotype associated with more severe complications than obesity or sarcopenia alone.[27]

Recognizing this phenotype is essential: skeletal muscle mass plays a critical role in pharmacokinetics by influencing drug distribution and clearance,[34,35] and is a key determinant of postoperative recovery and overall surgical outcomes.[36,37] These observations mandate a paradigm shift: comprehensive nutritional assessment must extend beyond weight-based metrics toward functional characterization that integrates body composition, muscle strength, and physical performance.[38,39]

Table 1. Definitions of Malnutrition According to Different Guidelines

ASPEN*	Requires at least 2 criteria for the diagnosis of malnutrition:
	– Insufficient energy intake
	o Moderate: <75% of estimated energy requirement for ≥1 month
	o Severe: ≤75% of estimated energy requirement for ≥1 month
	– Weight loss
	o Moderate: 5% in 1 month, 7.5% in 3 months, 10% in 6 months, 20% in 1 year
	o Severe: >5% in 1 month, >7.5% in 3 months, >10% in 6 months, >20% in 1 year
	– Loss of muscle mass (e.g., temporalis muscle, pectoralis and deltoids, interosseous muscles, latissimus dorsi, trapezius, quadriceps, and gastrocnemius)
	o Mild or severe
	– Loss of subcutaneous fat (e.g., orbital, triceps, fat overlying the ribs)
	o Mild or severe
	– Localized or generalized fluid accumulation (edema)
	o Mild or severe
	– Reduced hand-grip strength
	o Measurably reduced
ESPEN*	– Body mass index (BMI) <18.5 kg/m²
	Or
	– Weight loss (%)
	o 10% (indefinite period)
	o 5% over the last 3 months
	Combined with either
	– Low BMI (kg/m²)
	o <20 kg/m² if <70 years
	o <22 kg/m² if ≥70 years
	Or
	– Reduced fat-free mass index
	o Men: <17 kg/m²
	o Women: <15 kg/m²
GLIM*	Requires at least 1 phenotypic criterion and 1 etiologic criterion for the diagnosis of malnutrition:
	Phenotypic Criteria:
	– Weight loss (%):
	o 5% within the past 6 months
	o 10% beyond 6 months
	– Low BMI (kg/m²):
	o <20 if <70 years
	o <22 if ≥70 years
	o Asia: <18.5 if <70 years
	o Asia: <20 if ≥70 years
	– Reduced muscle mass
	o Reduced by validated body composition measuring techniques
	Etiologic Criteria:
	• Reduced food intake or assimilation:
	o 50% of energy requirements for >1 week
	o Any reduction for >2 weeks
	o Any chronic gastrointestinal condition that adversely impacts food assimilation or absorption
	• Inflammation:
	o Acute disease/injury
	o Chronic disease-related

ASPEN: American Society for Parenteral and Enteral Nutrition; ESPEN: European Society of Clinical Nutrition and Metabolism; GLIM: Global Leadership Initiative on Malnutrition.

Table 2. Core Differences Among Different Sarcopenia Assessment Frameworks and Their Application in IBD

Framework / Approach	Primary Diagnostic Focus	Key Measures	Strengths	Limitations in IBD
EWGSOP2 *	Muscle strength	Handgrip strength; chair stand test	Clinically intuitive; emphasizes function	Cut-offs derived from geriatric cohorts; may underestimate sarcopenia in younger patients with IBD
SDOC *	Muscle function	Gait speed; physical performance	Strong predictor of disability	Functional testing is often omitted in routine IBD care
GLIM	Malnutrition + Inflammation	Phenotypic (mass loss) + Etiologic (inflammation)	Integrates IBD inflammation as a core criterion	Still requires specific muscle mass cut-offs for IBD
Imaging-based (L3 Morphometry)	Muscle quantity and quality	SMI (CT-derived); Hounsfield Units (HU)	Objective; uses routine scans; linked to drug clearance	Lack of functional data; cut-offs often borrowed from oncology

EWGSOP2: European Working Group on Sarcopenia in Older People; SDOC: Sarcopenia Definition and Outcomes Consortium; IBD: Inflammatory Bowel Disease; SMI: Skeletal Muscle Index; HU: Hounsfield Units.

The clinical implementation of this paradigm, however, faces significant challenges. As detailed in the following sections, the absence of standardized definitions for sarcopenia in IBD (Section 3.1), the emergence of consensus frameworks like GLIM that account for inflammatory burden (Section 3.2), and the availability of opportunistic imaging techniques for precise body composition analysis (Section 3.3) all represent critical pieces of a complex puzzle. Understanding these elements is essential for translating the concept of "nutritional assessment" from theoretical principle into clinical practice – and ultimately for positioning body composition as an integral component of personalized IBD care in the biologic era.

3.1 The Challenge of Diagnostic Heterogeneity

A major hurdle in the clinical management of muscle depletion is the lack of a single, universally accepted definition of sarcopenia, which leads to the use of heterogeneous diagnostic frameworks and considerable variability in the reported prevalence of sarcopenia within the IBD population. Importantly, existing definitions differ substantially in the domains used to characterize sarcopenia. The European Working Group on Sarcopenia in Older People (EWGSOP2) emphasizes low muscle strength, measured as the ability of a muscle to generate force (e.g., handgrip strength), as the primary indicator, whereas the Sarcopenia Definition and Outcomes Consortium (SDOC) prioritizes low muscle function, referring to the capacity to perform physical tasks and movements (e.g., gait speed), as the most clinically relevant predictor of adverse outcomes.[39,40]

In contrast, most IBD-related research focuses on muscle quantity and quality, such as Skeletal Muscle Index and myosteatosis, derived from cross-sectional imaging, often without accompanying functional testing.[13,41] This inconsistency is further compounded by the use of heterogeneous cut-off values, frequently borrowed from oncological or geriatric populations, which may not accurately reflect the metabolic profile of IBD patients.[42] The core differences between these established frameworks are summarized in Table 2, illustrating the importance of an IBD-specific framework that integrates both muscle mass and function in the context of systemic inflammation.

3.2. The GLIM Framework as a Clinical Compass

Inflammatory processes contribute to malnutrition by suppressing appetite and reducing dietary intake, while simultaneously promoting metabolic alterations such as elevated resting energy expenditure and accelerated muscle catabolism. In the context of IBD, intestinal damage further contributes to malnutrition through impaired absorption. The resulting deterioration in body composition, marked by losses in fat-free mass, muscle mass indices, and body cell mass (the metabolically active component of fat-free mass, including muscle and organ cells), is associated with poorer functional capacity and worse clinical outcomes.[43]

Within this context, the implementation of the Global Leadership Initiative on Malnutrition (GLIM) criteria allows for a standardized diagnosis that accounts for the inflammatory burden inherent to IBD.[43,44] The GLIM framework adopts a two-step approach for the diagnosis of malnutrition, beginning with the identification of patients at risk through initial screening using validated tools. The most frequently used tools include general malnutrition screening instruments such as NRS-2002 (Nutritional Risk Screening 2002), MUST (Malnutrition Universal Screening Tool), MST (Malnutrition Screening Tool), as well as IBD-specific tests like the Malnutrition Inflammation Risk Tool (MIRT) and the Saskatchewan IBD–Nutrition Risk (SaskIBD-NR). These tools evaluate factors including recent weight loss, BMI, reduced food intake, and disease impact on nutrition. Patients identified as at risk then undergo a comprehensive diagnostic assessment, including evaluation of phenotypic (weight loss, BMI, muscle mass) and etiologic criteria (inflammation and/or reduced intake or assimilation) as required by the GLIM framework.[45,46]

Unlike earlier tools, GLIM requires the concomitant presence of an etiologic criterion, represented in IBD by the presence of chronic inflammation as well as potentially reduced assimilation, and a phenotypic criterion, identified as non-volitional weight loss or reductions in muscle mass or reduction in BMI. This dual approach allows for a more accurate and clinically meaningful assessment of malnutrition in IBD patients, linking inflammatory burden with functional nutritional status.[47,48]

This diagnostic shift prompts clinicians to transcend simple weight measurements and prioritize tissue quality and composition. Within this framework, traditional markers such as serum albumin need to be reframed: for instance, rather than merely reflecting nutritional deficit, hypoalbuminemia serves as a negative acute-phase reactant, mirroring

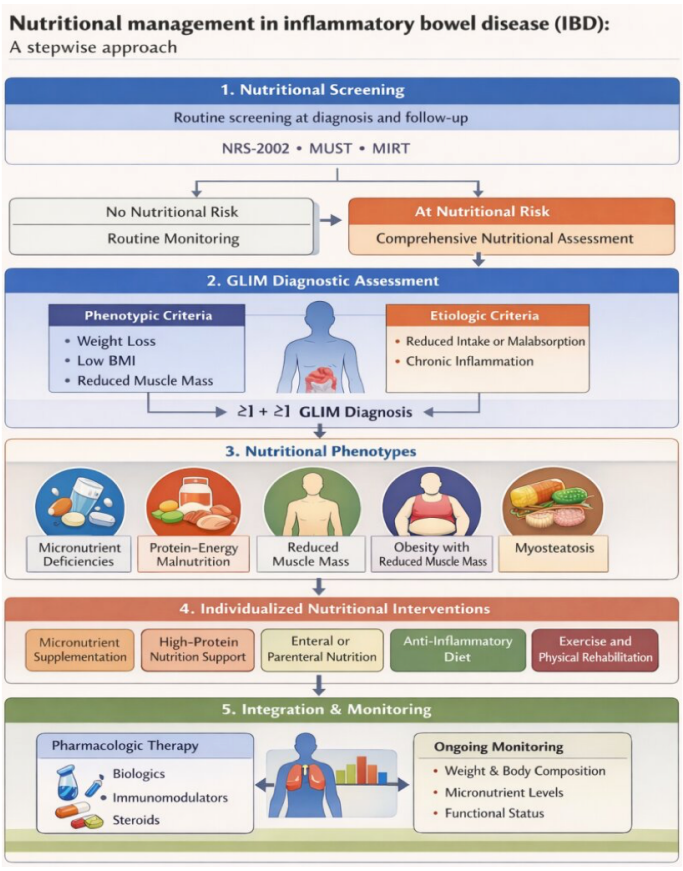

Figure 1. Stepwise Approach to Nutritional Management in Inflammatory Bowel Disease (IBD).
The algorithm begins with routine nutritional screening at diagnosis and follow-up using validated tools (NRS-2002, MUST, MIRT). Patients identified as at nutritional risk undergo a comprehensive assessment according to the Global Leadership Initiative on Malnutrition (GLIM) criteria, which require the simultaneous presence of at least one phenotypic criterion (weight loss, low BMI, or reduced muscle mass) and at least one etiologic criterion (reduced intake/malabsorption or chronic inflammation). The resulting nutritional phenotypes—such as micronutrient deficiencies, protein-energy malnutrition, reduced muscle mass (sarcopenia), obesity with concomitant muscle depletion (sarcopenic obesity), and myosteatosis—guide the selection of individualized interventions. These interventions may include targeted micronutrient supplementation, high-protein nutritional support, enteral or parenteral nutrition, anti-inflammatory dietary strategies (such as the Mediterranean diet, Crohn's Disease Exclusion Diet, or Exclusive Enteral Nutrition), and exercise-based physical rehabilitation. Nutritional care is integrated with pharmacological therapy (biologics, immunomodulators, corticosteroids) and is sustained through ongoing monitoring of weight, body composition, micronutrient levels, and functional status throughout the disease course.

the severity of systemic inflammation and capillary leak rather than protein stores.[18,49] A stepwise algorithm integrating these principles—from initial screening through GLIM-based diagnosis to the identification of distinct nutritional phenotypes and individualized interventions—is proposed in Figure 1.

3.3. Opportunistic Morphometry and the L3 Gold Standard

Computed Tomography (CT) represents an invaluable yet often underutilized resource for body composition analysis in IBD management. Through opportunistic morphometry at the level of the third lumbar vertebra (L3), routine diagnostic scans can be repurposed to objectively quantify the Skeletal Muscle Index (SMI) without additional radiation exposure or cost.[38,42] This approach transcends the inherent limitations of anthropometric measures, providing a high-precision surrogate for total body protein stores.[36,41]

In addition to estimating muscle quantity, L3 morphometry provides radiodensity-based measures (Hounsfield Units) reflecting intramuscular fat infiltration, thereby adding a qualitative dimension to body composition analysis. In IBD, reduced muscle radiodensity has been associated with primary non-response to anti-TNF agents more strongly than BMI, likely reflecting the metabolic consequences of chronic, low-grade systemic inflammation.[35,41]

More recently, ultrasound-based muscle assessment has emerged as a complementary, radiation-free approach for body composition evaluation. Prospective data in IBD cohorts demonstrate that ultrasound-derived measures of the rectus femoris, such as thickness and cross-sectional area, significantly correlate with CT-derived SMI, showing high diagnostic accuracy for sarcopenia detection.[50] This enables bedside assessment of muscle quantity and quality (via echogenicity), providing a dynamic tool for longitudinal monitoring without the constraints of cross-sectional imaging.[50]
These morphometric findings carry profound pharmacokinetic implications. Skeletal muscle constitutes a major determinant of monoclonal antibody distribution; consequently, its depletion is associated with accelerated drug clearance and a shortened biologic half-life.[34] Such pharmacokinetic alterations likely reflect the combined effects of reduced lean distribution volume and persistent inflammatory burden, providing a physiological rationale for sarcopenia-driven variability in drug exposure. Accordingly, patients with significant muscle depletion might benefit from early dose optimization or shortened infusion intervals to maintain therapeutic trough levels and mitigate the risk of secondary loss of response.[51-53] Although prospective validation is required, integrating body composition data into therapeutic drug monitoring (TDM) protocols represents a promising frontier for precision medicine in IBD.

4. Dietary Interventions in IBD

The dietary revolution in IBD has involved a broad recognition of the multifactorial role of diet, not only in managing nutritional needs but also in preventing complications such as sarcopenia and osteoporosis, while simultaneously improving both quality of life and inflammatory disease activity.[54] Consequently, beyond simple nutrient intake, dietary patterns shape intestinal barrier function, microbiota composition, systemic inflammation, and, ultimately, disease activity and remission maintenance.[55] This clinical relevance is supported by robust prospective data: in the PREdiCCt cohort (n=2,629), dietary quality emerged as a primary predictor of disease stability. Specifically, in patients with Ulcerative Colitis, high meat consumption was associated with a significantly increased risk of objective flare (aHR 1.95; 95% CI 1.07–3.56), with relapse rates reaching 26% over two years in the highest intake quartile compared to 12% in the lowest.[56] Mechanistic insights further clarify how specific components drive clinical outcomes. In a randomized, double-blind, placebo-controlled trial involving 60 healthy participants, Wellens et al.[57] first implemented a two-week emulsifier-free diet (EFD), followed by a four-week period of randomized supplementation with either carboxymethylcellulose (CMC), polysorbate-80, carrageenan (CGN), soy lecithin, native rice starch, or placebo delivered through food matrices. The trial revealed that the gut is sensitive to these additives long before inflammation appears; specifically, CMC reduced short-chain fatty acids (SCFAs) levels, and CGN compromised the intestinal barrier, while both triggered subtle shifts in the microbiota. These mechanistic insights into dietary triggers, particularly the det-

rimental role of food additives, have paved the way for the development of targeted exclusion protocols and anti-inflammatory patterns aimed at restoring intestinal homeostasis, the clinical evidence for which is discussed hereafter. Within this framework, distinct dietary strategies can be tailored to specific disease phases and clinical objectives, leading to a nuanced application of the various interventions explored below.[58]

4.1 Diet and Preclinical IBD

Accumulating evidence suggests that dietary patterns preceding disease diagnosis may influence the risk of developing IBD. A comprehensive review evaluating 19 studies with 2,609 IBD patients and 4,000 controls investigated the association between pre-diagnosis dietary intake and subsequent IBD risk. High intake of saturated fats, monounsaturated fatty acids, total polyunsaturated fatty acids (PUFAs), mono- and disaccharides, and meat were associated with increased CD risk; similarly, high intakes of total fats, total PUFAs, and meat increased the risk of UC. On the other hand, dietary fiber and fruits decreased CD risk, and high vegetable intake was protective against UC. Finally, most included studies showed a correlation between high protein intake and IBD risk.[59]

When specific macronutrients are examined separately, the type and quality of fats emerge as particularly relevant. ω-3 PUFAs and long-chain triglycerides exert anti-inflammatory effects, whereas ω-6 PUFAs promote pro-inflammatory responses.6[0] The balance between these fatty acid classes appears critical: animal studies have demonstrated a direct relationship between the arachidonic acid (an ω-6 PUFA) content of inflammatory cell phospholipids and their capacity to produce pro-inflammatory prostaglandin E2 (PGE2). Conversely, feeding with eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA)—both ω-3 PUFAs—reduces PGE2 production and promotes inflammation-resolving mediators.[61,62] These mechanistic insights provide a plausible explanation for the disease-protective effects observed with higher ω-3 PUFA intake.[62]

High consumption of animal protein, particularly red meat, has been consistently associated with increased IBD risk.[63,64] The underlying mechanisms remain incompletely understood but may involve protein-derived metabolites that alter microbiome composition, reduce short-chain fatty acid production, and impact intestinal enterocyte function.[7] Interestingly, while high animal protein intake has been associated with disease exacerbation in UC, this relationship has not been consistently demonstrated in CD, warranting further investigation.[65] Dietary patterns high in refined sugars and low in fiber have also been implicated in IBD pathogenesis.[7] The protective role of dietary fiber, supported by multiple studies, likely reflects its capacity to promote a healthy microbiome, maintain barrier integrity, and modulate immune responses.[66,67]

Collectively, these observations underscore that dietary habits preceding disease onset can meaningfully influence IBD risk. While the precise mechanisms continue to be elucidated, the evidence supports recommendations favoring high fiber intake, adequate fruit and vegetable consumption, limitation of processed meats and refined sugars, and attention to the quality of dietary fats.

4.2. Mediterranean Diet

The Mediterranean diet (MD) is increasingly recognized as a beneficial dietary pattern in IBD,[68] traditionally framed as the anti-inflammatory counterpart to the pro-inflammatory Western lifestyle. However, this conceptual contrast does not automatically translate into definitive evidence supporting the MD as a primary therapy for active disease.[58] Consequently, attention has shifted toward its ability to modulate gut microbial diversity and promote the production of anti-inflammatory metabolites. This is particularly relevant given the limitations of current pharmacological therapies.[69] Nutritional interventions such as the MD emerge as potentially valuable non-pharmacological adjuncts, targeting complementary inflammatory and microbial pathways not fully addressed by current advanced therapies.[70] Recent trials have moved beyond observational studies to evaluate the MD as a structured therapeutic intervention.

The clinical efficacy of MD was robustly assessed in the DINE-CD randomized trial (n=191), a multicenter study comparing the MD against the more restrictive Specific Carbohydrate Diet (SCD), a dietary regimen that eliminates lactose (but not dairy products), sucrose, starchy vegetables (including most legumes), and all grains, in adults with mild-to-moderate CD (defined by a short Crohn's Disease Activity Index [sCDAI] score of 176–399).[71]

The primary outcome of symptomatic remission at week 6 was achieved by comparable proportions in both groups (43.5% in the MD group vs. 46.5% in the SCD group, P = .77), with a similar pattern observed for fecal calprotectin response at week 6 (30.8% for MD vs. 34.8% for SCD, P = .83). Notably, both groups exhibited markedly low rates of C-reactive protein (CRP) normalization. These findings underscore that the MD represents an effective and feasible strategy for symptom management and quality-of-life improvement in CD,[71] even though its impact on biochemical markers appears modest. These biological pathways are consistent with multi-omic analyses, where higher MD adherence associates with the enrichment of beneficial bacteria, favorable shifts in microbial metabolites, and lower inflammatory activity.[72] These microbiota changes correlate inversely with inflammatory markers such as fecal calprotectin, suggesting that diet-driven microbial metabolism contributes to clinical outcomes.[73]

In a 2025 prospective study including 271 patients with newly diagnosed CD, adherence to the MD was correlated with a noncomplicated CD course and lower clinical and biochemical disease activity, as well as reduced dysbiosis. Mechanistically, the MD was linked to an enrichment of SCFA-producing bacteria (Faecalibacterium) and a reduction of species associated with CD (Escherichia coli and Ruminococcus gnavus), alongside a shift towards increased production of anti-inflammatory metabolites and decreased levels of tryptophan metabolites, ceramides, and primary bile acids.[74]

Evidence supporting the MD is emerging also in UC. In a prospective trial enrolling adults with quiescent UC, participants were randomized to either the MD pattern or the Canadian habitual dietary pattern for 12 weeks. During the study period, loss of clinical response was experienced by a significantly higher proportion of patients following the habitual diet group compared to the MD group (31% vs. 13%, P = 0.003), and 75% of patients in the habitual diet exhibited elevated fecal calprotectin (>100 μg/g) compared to 20% in the MD group at week 12. Notably, adherence to the MD was associated with an anti-inflammatory signature in both fecal metabolites (higher total fecal short-chain fatty acids, including acetic and butyric acids) and microbiota composition (increased abundance of Alistipes finegoldii, Flavonifractor plautii, and Ruminococcus bromii).[75] Furthermore, a recent study observed that adherence to the MD was associated with reduced CRP and fecal calprotectin in UC, an effect mediated through reduced dysbiosis.[76]

Overall, the biological rationale for these clinical improvements lies in

the MD's provision of a diverse array of microbiota-accessible carbohydrates, polyphenols, and unsaturated fatty acids that support a healthy gut ecosystem, wherein anti-inflammatory benefits appear to be mediated mainly through selective enrichment of SCFA-producing taxa and associated metabolic pathways, increased microbial richness, and reduced dysbiosis. Specifically, SCFAs, including acetate, butyrate, and propionate, play central roles in modulating immune responses, enhancing epithelial barrier function, and suppressing pro-inflammatory signaling pathways.[77] Collectively, this evidence supports the potential of the MD as a foundational, adjunctive dietary strategy, promoting mucosal homeostasis and complementing pharmacological interventions, particularly for remission maintenance and long-term metabolic health.[68,71,73]

4.3 Exclusive and Partial Enteral Nutrition

Perhaps the largest body of literature on dietary therapy in IBD evaluates exclusive enteral nutrition (EEN), a complete exclusion diet in which patients receive 100% of their caloric intake from formula rather than table foods. EEN can be administered using intact protein, semi-elemental, or elemental formulations, tailored to meet the patient's nutritional requirements.[78] Metagenomic studies have demonstrated that EEN induces rapid and profound changes in the intestinal microbiome, observable as early as one week after initiation.[79] This pattern was reflected in a prospective case–control study of 15 children with CD, in which EEN induced a decline in fecal microbial diversity, including reductions in key commensal taxa, changes that were associated with improvements in clinical disease activity and decreases in inflammatory markers.[80] Notably, these microbiome changes are more pronounced in patients who respond to EEN compared with non-responders, indicating a potential microbial susceptibility.[78]

Clinically, EEN has been shown to improve symptoms, mucosal healing, and nutritional status in pediatric CD, achieving remission rates comparable to corticosteroids. In randomized trials comparing EEN with steroids, both therapies improved clinical symptoms and systemic inflammatory markers, but EEN conferred superior mucosal healing.[81] Similar clinical results have not been reproduced in adults, as EEN resulted in lower rates of clinical response compared with steroids, which may reflect differences in patient adherence rather than intrinsic efficacy.[82]

While EEN is highly effective for the induction of remission, long-term adherence is challenging. A seminal 2006 study in pediatric patients with CD showed that partial enteral nutrition (PEN), providing 50% of daily calories, halved the 2-year relapse rate compared to a free diet (aHR 0.40, 95% CI 0.15-0.98), supporting its role as a maintenance treatment.[83] However, a subsequent study indicated that PEN is inferior to both EEN and anti-TNF for inducing remission in pediatric CD.84 Of note, retrospective evidence suggests that the effectiveness of PEN increases when 80-90% of calories are delivered.[85] Finally, a 2026 open-label randomized trial compared cyclic EEN (administered for 2 weeks every 8 weeks) with PEN in pediatric patients with CD who had achieved clinical remission following EEN induction. Over 12 months of follow-up, cyclic EEN was superior to PEN in reducing relapse risk (aOR 0.29, 95% CI 0.13–0.70), while tolerance to enteral nutrition was excellent, reaching 100% in both groups.[86]

The restrictive nature of EEN has motivated the development of whole-food–based diets, such as CD-TREAT and CDED, which aim to replicate EEN's anti-inflammatory effects while improving long-term acceptability and adherence.

4.4. Solid-Food Alternatives to EEN: From CD-TREAT to Exclusion Diets

Building upon the paradigm of EEN, efforts have increasingly focused on developing solid food-based strategies capable of reproducing its anti-inflammatory effects while improving long-term acceptability. Along this continuum, the Crohn's Disease Treatment-with-EATing (CD-TREAT) diet represents a novel, mechanistically driven approach designed to mimic the nutritional composition of EEN using whole foods—selectively excluding gluten, lactose, and alcohol while matching fiber levels.[87]

CD-TREAT was initially evaluated against EEN in a crossover study focusing on tolerability and microbial shifts: in a randomized controlled trial (RCT) involving 25 healthy adults, CD-TREAT demonstrated higher acceptability, while multi-omic analyses confirmed that both diets induced comparable shifts in the gut microbiome and metabolome.[87] Its anti-inflammatory effect was further validated in HLA-B27 transgenic rats, where a 4-week intervention significantly reduced histopathological ileitis severity ($P = 0.044$) to a degree comparable with EEN. These findings translated into a pediatric pilot trial ($n = 5$): after 8 weeks, 80% of children achieved clinical response and 60% reached remission, with a significant reduction in fecal calprotectin.[87]

While CD-TREAT aims to reproduce the EEN paradigm, other approaches prioritize selective exclusion of modern dietary components implicated in intestinal inflammation. The Crohn's Disease Exclusion Diet (CDED) addresses this by limiting exposure to ultra-processed foods, emulsifiers, and refined sugars—components directly linked to gut barrier disruption and dysbiosis.[88] The efficacy of the CDED is rooted in a profound microbial and metabolic reset, characterized by a significant reduction in Proteobacteria (specifically *E. coli*) and a favorable shift in tryptophan metabolism, marked by decreased fecal kynurenine and increased indole generation, a signature associated with sustained remission.[89] The seminal study by Levine et al.[90] enrolled 78 pediatric patients with mild-to-moderate CD randomized to EEN or CDED with 50% PEN. While efficacy at week 6 was comparable, CDED + PEN demonstrated significantly higher tolerability (OR 13.92, 95% CI 1.68-115.14); notably, following the introduction of a free diet in the EEN group complemented with 25% PEN, week-12 steroid-free clinical remission rates were inferior compared to CDED + 25% PEN, and adherence strongly correlated with clinical outcomes across both regimens. Subsequently, a randomized controlled trial in 44 adults with mild-to-moderate CD showed that CDED + PEN and CDED alone were similarly effective in inducing remission at week 6, with comparable sustained remission rates at week 28 and parallel reductions in CRP and fecal calprotectin.[88]

The Specific Carbohydrate Diet (SCD) represents an alternative, more restrictive nutritional approach. By excluding disaccharides and most polysaccharides, the SCD aims to limit the substrates available for potentially pro-inflammatory gut bacteria, shifting the microbial environment.[71,91] This is achieved through a strict biochemical selection that permits unprocessed meats, fresh fruits, and honey, while categorically restricting all grains, starchy vegetables (e.g., potatoes, yams), and industrial sweeteners.[71] Clinically, while the SCD has demonstrated the potential for deep remission, with small pediatric cohorts showing complete endoscopic healing in up to 40% of cases,[92] data from the DINE-CD trial in adults showed that it was not superior to the Mediterranean Diet in terms of symptomatic remission, fecal calprotectin response, or CRP response.[71]

While both CDED and SCD show therapeutic promise, they share the challenge of a high adherence burden. The risk of nutritional deficiencies and restrictive eating behaviors necessitate structured, multidisciplinary monitoring to ensure that the clinical benefits of "nutritional prehabilitation" and inflammatory control are not compromised by long-term sustainability issues. Addressing this limitation, the Tasty&Healthy (T&H) diet—a whole food diet that excludes processed food, gluten, red meat, and dairy, without requiring formula or mandatory ingredients—has recently been evaluated in children and young adults with CD. Compared to EEN, the T&H diet demonstrated superior tolerability (aOR 7.7, 95% CI 2.4-25.0), with comparable clinical and biochemical efficacy.[93]

Although most solid-food dietary strategies have been developed for Crohn's disease, similar exclusion-based approaches are increasingly being investigated in ulcerative colitis. The CRAFT UC trial (n=62) further underscores the power of targeted nutrition in refractory patients (50% of them had previously failed biologic therapies). This study evaluated the effect of the UC Exclusion Diet (UCED) alone versus standard Fecal Transplantation (FT) with or without diet modification. Remarkably, the UCED alone outperformed standard FT for steroid-free clinical remission (40% vs. 12% and 21% in the FT groups without and with UCED; $P < 0.05$ for both comparisons). Moreover, the UCED was the only intervention to achieve complete mucosal healing (Mayo 0: 20% vs. 0% in both FT groups, $P = 0.022$) and demonstrated superior safety for preventing exacerbations (6.7% vs. 21.1%) and maintaining response at week 12.94 Nevertheless, these findings should be interpreted with caution given the uncertain efficacy of FT in UC.

4.5. Fasting-Mimicking Diets: A Novel Approach

A key barrier to the therapeutic use of diet in IBD is the challenge of sustaining long-term dietary changes, as evidenced by low adherence rates across interventions. Fasting-mimicking diets (FMD) offer an attractive solution, as they do not require patients to modify their baseline diet continuously. FMD consists of short cycles, typically 5 consecutive days per month, of a plant-based, calorie-restricted regimen that is low in calories, sugars, and protein, but relatively high in unsaturated fats, designed to mimic the physiological benefits of fasting. Patients consume their usual diet for the remainder of the month, and cycles can be repeated over several months.[95]

Preclinical studies in mouse models of colitis have demonstrated that FMD promotes intestinal regeneration, modulates the gut microbiota (notably increasing Lactobacillaceae), reduces inflammatory cytokine expression, and supports mucosal healing. In healthy human volunteers, multiple 5-day FMD cycles improved metabolic parameters and reduced mildly elevated C-reactive protein levels, supporting systemic anti-inflammatory effects.[95]

The first randomized controlled trial in patients with mild-to-moderate CD evaluated the safety and efficacy of short-term FMD cycles (n = 97 patients). Compared with controls, a higher proportion of patients in the FMD group achieved the primary endpoint of CDAI-based clinical response (69.2% vs. 43.8%, $P = 0.03$), as well as clinical remission (CDAI ≤150; 64.6% vs. 37.5%, $P = 0.02$). In addition, the FMD group experienced a significant reduction in fecal calprotectin levels (−22.0%), whereas levels increased in the control group (+8.0%; $P = 0.03$).[96]

Periodic fasting-mimicking diets (FMD) may offer a complementary approach to conventional therapy, supporting remission maintenance through improvements in mucosal integrity and metabolic resilience. When paired with the Mediterranean diet during refeeding periods, FMD could further benefit from the diet's anti-inflammatory properties and ability to reinforce gut barrier function.[96] While promising, this approach remains investigational, and further studies are needed to define optimal cycle duration, frequency, and patient selection criteria.

4.6. Nutritional Strategies in the Postoperative Setting: Preoperative Support and Recurrence Prevention

Patients with IBD frequently require surgery during their disease course, and many present with pre-existing nutritional deficits that increase perioperative risk. The identification of sarcopenia and malnutrition through the assessment frameworks discussed in Section 3 carries particular prognostic significance in this setting: patients with weight loss exceeding 10% in the preceding six months, BMI below 18.5 kg/m², hypoalbuminemia, or Nutritional Risk Screening (NRS) score >5 face substantially higher rates of perioperative complications.[97] These observations underscore the importance of preoperative nutritional optimization as a form of "nutritional prehabilitation."

Preoperative nutritional support is strongly recommended, particularly in malnourished CD patients awaiting surgery.[97,98] Systematic reviews have identified preoperative nutritional status as a predictor of postoperative hospital stay length, with serum albumin representing a prognostic factor for complication risk.[99] In patients with severe metabolic risk, preoperative nutritional therapy may be beneficial. Enteral nutrition should be preferred when feasible, with parenteral support reserved for cases where enteral feeding is contraindicated or insufficient. Nutritional status should be reassessed postoperatively to guide ongoing support.

Postoperative recurrence prevention represents a critical extension of these concepts, particularly in CD. Following surgical resection, the intestinal microenvironment remains highly susceptible to inflammatory triggers that can drive early endoscopic recurrence at the anastomotic site.[100] The dietary strategies discussed throughout Section 4 find specific application in this vulnerable period.

In the immediate postoperative period, exclusive enteral nutrition (EEN) has emerged as a potent "bridging therapy" to mitigate this risk. A recent randomized controlled trial including 100 patients demonstrated that postoperative EEN significantly reduces endoscopic recurrence rates of CD (defined as Rutgeerts score ≥ i2) compared to early introduction of a standard solid diet (Relative Risk [RR] 0.474; 95% CI 0.238-0.944; $P = 0.026$).[101] By providing total bowel rest from dietary antigens while ensuring optimal nutrient delivery, EEN facilitates early mucosal stabilization and supports the structural integrity of the anastomosis.[101]

Following this initial stabilization, long-term dietary quality becomes the primary determinant of sustained remission. A landmark multicenter prospective cohort study, evaluating 520 food diaries from 103 patients, highlighted that higher dietary intake of micronutrients typically abundant in the Mediterranean Diet, such as isoflavones, provitamin A, and specific antioxidants, is significantly associated with a reduced risk of long-term endoscopic postoperative recurrence (defined as Rutgeerts score ≥ i2a).[100]

Collectively, these findings support a stratified postoperative nutritional approach, beginning with targeted enteral support via EEN to promote early mucosal recovery, and transitioning to a Mediterranean-style diet enriched with key micronutrients to prevent the progression from subclinical inflammation to clinical recurrence.[68,100-102]

4.7. Synthesis and Practical Considerations

Effective dietary management in IBD requires a personalized, phase-specific approach. During active flares, exclusion diets, most notably the CDED, can mitigate dietary triggers of inflammation, support gut barrier recovery, and enhance anabolic and immune responses in synergy with pharmacological therapy.[88] In the remission phase, adherence to the Mediterranean diet helps maintain a balanced gut microbiome, promotes metabolic homeostasis, and preserves mucosal integrity, while periodic fasting-mimicking interventions may further enhance mucosal regeneration and systemic resilience.[68,95]

Optimal dietary management integrates these strategies within a personalized, phase-specific framework that accounts for disease activity, nutritional status, body composition, and adherence potential. Tailoring interventions to the patient's clinical context allows clinicians to complement pharmacological therapy, improve long-term gut health, and support functional recovery.

Collectively, these dietary approaches provide a foundational layer of nutritional modulation, translating mechanistic insights into real-world care. Aligning nutritional strategies with disease phase and metabolic status, as summarized in Table 3, ensures that diet not only supports therapy but also contributes to sustained patient well-being.

5. Synchronizing Nutrition and Pharmacology: Towards an Integrated Therapeutic Strategy

Nutrition and pharmacological therapy in IBD should not be viewed as alternative interventions, but rather as complementary and interdependent tools. Diet can influence drug responsiveness, while effective pharmacological control of inflammation creates the biological conditions necessary for nutritional interventions to exert their full therapeutic potential. In this framework, nutrition and drugs act synergistically, with the potential to mutually reinforce their clinical effects.

While dietary patterns can directly modulate intestinal inflammation, their therapeutic potential is likely maximized when synchronized with pharmacological therapy. Crucially, nutritional interventions should be considered as complementary to advanced medical therapies both during induction and maintenance phases, with the potential to enhance therapeutic efficacy.

In a prospective open-label study enrolling 56 adult patients with CD, the combination of adalimumab plus partial enteral nutrition (PEN) was superior to adalimumab alone in inducing both clinical and endoscopic improvement.[103] Consistently, a larger retrospective cohort study including 197 patients showed that, compared with biologic therapy alone, the combination of biologics and EEN was associated with higher rates of both clinical and endoscopic response at weeks 16 and 52.104 Another retrospective study evaluating the addition of PEN to treatment escalation in patients with CD who had lost response to biologics reported significantly higher rates of clinical response (64% vs. 25%, P = 0.03) and transmural response (65% vs. 25%, P = 0.03) at week 24 in patients receiving combination therapy.[105]

A pilot RCT (n = 32) evaluated the adjunctive use of a FMD in patients with UC initiating advanced therapies. Although the study terminated earlier due to the COVID-19 pandemic and was underpowered to

Table 3. Dietary Strategies in Inflammatory Bowel Disease: A Comparative Overview

Dietary Intervention	Disease Setting	Main Indication	Key Characteristics	Evidence Level	Feasibility / Adherence
Mediterranean Diet (MD)	CD and UC	Remission maintenance; adjunct in mild disease	Balanced, whole-food diet, rich in fiber polyphenols, and unsaturated fats	RCTs and prospective cohorts	High
Exclusive Enteral Nutrition (EEN)	Primarily pediatric CD; selected adults	Induction of remission; steroid-sparing therapy	100% liquid formula; complete exclusion of table foods for 6–8 weeks	Strong (especially pediatric RCTs)	Low–moderate
Partial Enteral Nutrition (PEN)	CD	Maintenance of remission	~50% calories from formula plus regular diet	Moderate	Moderate
CD-TREAT	CD	Alternative to EEN	Whole-food diet mimicking EEN macro- and micronutrient composition	Pilot clinical studies	Moderate–high
Crohn's Disease of remission Exclusion Diet (CDED)	Mild–moderate CD cohorts)	Induction and maintenance	Exclusion of ultra-processed foods; phased diet combined with PEN	RCTs (pediatric and adult)	Moderate
Specific Carbohydrate Diet (SCD)	CD (mainly pediatric	Induction of remission	Elimination of grains, lactose, refined sugars	Small trials and cohorts	Low
Fasting-Mimicking remission maintenance Diet (FMD)	Mild–moderate CD	Adjunctive therapy; plant-based diet	Short, cyclic, calorie-restricted	Emerging RCT evidence	High (short cycles)
Postoperative EEN + MD	Post-surgical CD	Prevention of recurrence	Short-term EEN followed by MD	RCTs and prospective studies	Moderate
UC Exclusion D iet (UCED)	Mild–moderate ulcerative colitis	Induction of remission	Exclusion of dietary components associated with barrier disruption and dysbiosis	RCT (CRAFT UC trial)	Moderate

demonstrate a statistically significant difference in clinical response at week 8 (57% vs. 35% in favor of the FMD, P = 0.11), exploratory analyses of secondary endpoints suggested greater clinical improvement and higher rates of successful steroid tapering by week 8 in the dietary intervention group.[106]

Collectively, these findings underscore that dietary modulation is not merely a supportive measure but an active modifier of disease pathophysiology. The goal of nutritional therapy in IBD has evolved beyond caloric replacement toward the restoration of gut barrier integrity and skeletal muscle function.18 Integrating nutritional interventions and pharmacological strategies may therefore represent a promising approach to overcome the current therapeutic ceiling, in line with the notion that the patient's metabolic state can substantially influence drug efficacy.[107]

A major barrier to nutritional recovery in IBD is inflammation-induced anabolic resistance, characterized by impaired protein synthesis by the skeletal muscle, despite adequate amino acid availability.[108] During flares, pro-inflammatory cytokines—notably tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6)—impair the Akt–mTORC1–p70S6K signaling pathway, thereby blunting the anabolic response to dietary protein intake. In this context, nutritional strategies based solely on high protein intake may be insufficient to restore muscle protein synthesis.[109]

Indeed, effective nutritional rehabilitation necessitates temporal coordination with pharmacological therapies, generating a "therapeutic window" in which the suppression of inflammatory signaling permits reactivation of mTORC1-dependent anabolic pathways, thereby restoring muscle sensitivity to nutritional stimuli.[108] Targeted biological therapies, particularly anti-TNF agents, appear to play a pivotal role in releasing this "inflammatory brake," enabling protein supplementation to exert its intended anabolic effects.[35,110] The mechanisms underlying this inflammatory blockade and its subsequent therapeutic restoration are summarized in Figure 2.

Finally, this integrated strategy requires systematic elimination of dietary factors capable of sustaining low-grade intestinal inflammation. Specific emulsifiers found in ultra-processed foods, such as carboxymethylcellulose (CMC) and polysorbate-80 (P80), have been shown to impair mucus barrier function and promote metabolic endotoxemia.[111] Their exclusion may help mitigate persistent low-grade inflammation that otherwise compromises mucosal healing and muscle protein synthesis.[90]

5.1 Supplementation

The successful restoration of muscle protein synthesis and functional capacity requires not only inflammatory control but also the correction of specific micronutrient deficits that are nearly ubiquitous in IBD. These deficiencies act as metabolic brakes, limiting the efficacy of both nutritional interventions and pharmacological therapy. Accordingly, supplementation should be viewed not as an isolated intervention but as an integral component of the induction-to-rehabilitation framework outlined above.

Iron deficiency affects approximately 45% of patients and arises from chronic blood loss, mucosal damage, decreased absorption, and inadequate oral intake.[112] Diagnosis requires interpretation in the context of inflammation: ferritin <30 µg/L in the absence of active inflammation, or ferritin <100 µg/L with transferrin saturation <20% in the presence of inflammation, confirms iron deficiency anemia and warrants prompt

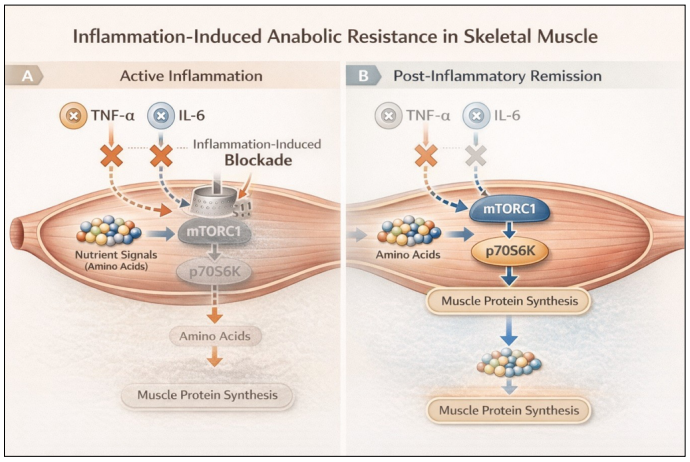

Figure 2. Inflammation-Induced Anabolic Resistance in Skeletal Muscle. During active inflammation, pro-inflammatory cytokines impair Akt–mTORC1 signaling, blunting the anabolic response to amino acid availability. Following inflammatory remission, restoration of mTORC1 activity permits effective stimulation of muscle protein synthesis.

correction.[112] Iron replacement can be administered orally or intravenously. In patients who are clinically, endoscopically, and biochemically in remission with mild anemia (hemoglobin >10 g/dL), oral iron may be sufficient. However, intravenous iron is recommended for severe iron deficiency (hemoglobin <10 g/dL), intolerance or unresponsiveness to oral therapy, and in the presence of active inflammation.[113] Specific considerations on the role of iron in metabolism are discussed in Section 5.2.

Vitamin B12 and folate deficiencies are common in IBD, particularly following uncontrolled inflammation, extensive small bowel resection, or methotrexate and sulfasalazine use.[15] These deficits manifest as macrocytic anemia and should be actively screened. B12 replacement should be administered parenterally when deficiency is confirmed, while weekly folic acid supplementation is recommended for at-risk patients.[15]

Vitamin D deficiency is highly prevalent in IBD and carries particular significance given its immunomodulatory role and impact on bone health. IBD patients have an increased fracture risk compared to healthy individuals, further elevated by glucocorticoid use and vitamin D depletion.[15] Target 25(OH)D levels should exceed 30 ng/mL, achievable through sunlight exposure, dietary intake (oily fish, liver, egg yolks), and supplementation – with some studies suggesting that up to 10,000 IU daily may be required in selected patients.[11]

ω-3 fatty acids merit consideration based on their anti-inflammatory properties, discussed in Section 4.1. IBD patients may exhibit essential fatty acid deficiencies, and supplementation with fish or olive oil-derived ω-3s may improve oxidative stress profiles, support mucosal healing, and potentially reduce the long-term risk of colorectal neoplasia.[115] However, no specific recommendations on their supplementation can be made based on current evidence.

Importantly, these supplementation strategies should not be applied in isolation. Iron deficiency frequently coexists with other deficits, and optimal metabolic recovery requires a multi-nutrient approach that includes B vitamins, zinc, selenium, and vitamin D. Recognizing these interconnected patterns allows supplementation to be integrated into a comprehensive nutritional plan—ensuring that the correction of individ-

ual deficits synergistically supports the restoration of anabolic responsiveness, mitochondrial function, and ultimately, physical resilience.

This integrated view of supplementation naturally leads to a deeper consideration of iron's unique role as a bioenergetic catalyst—a concept explored in the following section, where we examine how iron deficiency and its correction intersect with the pathways of anabolic resistance and metabolic recovery outlined in Figure 1.

5.2 Iron as a Bioenergetic Catalyst: The Energetic Counterpart to Anabolic Resistance

While suppression of the Akt–mTORC1 pathway reflects impaired muscle protein synthesis, inflammation-induced disruptions in iron metabolism constitute a critical limitation in muscle bioenergetics. Effective functional recovery therefore requires not only the restoration of anabolic signaling but also the availability of sufficient metabolic substrate to support tissue repair and contractile activity.[116]

In this context, iron deficiency in IBD should be viewed not merely as a hematological issue but as a critical constraint on mitochondrial energy production.[117] Iron is an essential cofactor for key components of the electron transport chain, including cytochromes and iron-sulfur cluster-containing enzymes; consequently, even subclinical iron deficiency can impair cellular energy production independently of hemoglobin levels.[116]

During systemic inflammation, the upregulation of hepcidin induces a state of functional iron deficiency by sequestering iron within the reticuloendothelial system and limiting its intestinal absorption.[118] Under these conditions, oral iron supplementation is ineffective and sometimes deleterious, as unabsorbed luminal iron can exacerbate dysbiosis, promote oxidative stress, and further amplify mucosal inflammation.[119-121] In contrast, early intravenous (IV) iron administration bypasses inflammation-induced sequestration and is more effective than oral iron in correcting iron deficiency in patients with active IBD. By rapidly replenishing bioavailable iron pools, IV iron supports metabolic recovery in high-turnover tissues.[122] This is particularly relevant for the regenerating intestinal epithelium and metabolically active skeletal muscle, where adequate iron availability supports oxidative metabolism required for tissue repair and functional recovery.[120] IV iron priming may act as a metabolic enabler, enhancing muscular endurance, reducing fatigue, and supporting the restoration of anabolic responsiveness.[123] Speculatively, in selected patients with active inflammation, early IV iron therapy could be considered an integral component of personalized nutritional and metabolic rehabilitation during induction.[117-120]

Importantly, the success of metabolic recovery requires a multi-nutrient approach, as iron deficiency frequently coexists with other deficits. Observational evidence indicates that low serum vitamin D status is common in patients with IBD and is associated with increased odds of clinically active disease, mucosal inflammation, clinical relapse, and lower quality-of-life scores, compared with patients with higher vitamin D levels. This suggests a correlation between hypovitaminosis D and adverse clinical outcomes in this population.[124]

Recognizing these interconnected patterns allows supplementation strategies to be integrated into a comprehensive nutritional plan, ensuring that the correction of iron deficiency is synergistically supported by other targeted micronutrients (e.g., B vitamins, zinc, selenium) to ultimately optimize metabolic recovery and response to therapy.[125,126]

CONCLUSION

Nutritional status is increasingly recognized as a pivotal determinant of therapeutic outcomes in IBD, as chronic inflammation profoundly affects both systemic metabolism and body composition. Moving beyond traditional weight-based metrics, the functional assessment of muscle mass, quality, and overall body composition provides a more accurate risk stratification and a clearer understanding of the metabolic consequences of the disease. This holistic, patient-centered approach has the potential not only to optimize treatment efficacy but also to improve long-term physical function, quality of life, and the likelihood of achieving durable, deep remission.

Diet is emerging as an important—and still underappreciated—modulator of intestinal inflammation and epithelial barrier integrity. Growing evidence implicates ultra-processed foods and dietary additives in the persistence of low-grade inflammation, providing a strong rationale for targeted nutritional interventions to control disease activity.

The integration of standardized nutritional screening tools that account for both inflammatory burden and body composition enables early identification of distinct nutritional phenotypes, allowing clinicians to move beyond reactive supplementation toward proactive, individualized care. When combined with validated diagnostic frameworks such as the GLIM criteria, these tools facilitate a precision medicine approach in which therapeutic decisions are informed by the patient's metabolic reserve, inflammatory status, and functional capacity. Available evidence supports a phase-specific framework for nutritional management in which dietary and metabolic interventions are strategically aligned with disease activity and pharmacological treatment (Table 4). Rather than treating nutrition and drugs as independent domains, this model emphasizes their bidirectional interaction across the disease course. During

Table 4. An Induction-to-Rehabilitation Framework for Nutritional Management in Adult IBD

Clinical Phase	Pathophysiological Target	Representative Interventions
Baseline Assessment	Body composition (sarcopenia) and nutritional risk	Functional evaluations and imaging techniques (e.g., opportunistic L3-CT morphometry to derive skeletal muscle index) allow for a more precise understanding of a patient's metabolic reserve and may predict patient frailty
Induction Phase (inflammatory flares)	Systemic and intestinal inflammation, inflammation-driven anabolic resistance	Nutritional interventions as adjunct or alternative to pharmacological control of inflammation ± early micronutrient repletion (e.g., intravenous iron) in selected patients
Rehabilitation Phase the achievement of symptomatic control)	Nutritional deficits, muscle and functional recovery	Dietary strategies limiting exposure to ultra-processed foods and food (after emulsifiers to reduce relapse risk, targeted protein and caloric supplementation, micronutrient repletion

inflammatory flares, pharmacological suppression of pro-inflammatory cytokines creates a therapeutic window in which nutritional interventions can overcome anabolic resistance and restore metabolic function. Conversely, the elimination of pro-inflammatory dietary factors and the correction of micronutrient deficiencies may reduce the inflammatory burden that drives both disease activity and treatment failure. This synergy positions nutrition not as a supportive measure but as an active modifier of disease pathophysiology. Translating this evidence-based framework into clinical practice requires adherence to several key principles. The following actionable recommendations synthesize the current state of knowledge and provide a roadmap for integrating nutritional assessment and intervention into routine IBD care:

1. Screen early and systematically. All patients with IBD should undergo nutritional screening at diagnosis and at regular intervals thereafter, using validated tools (e.g., NRS-2002, MUST, or IBD-specific instruments such as MIRT or SaskIBD-NR), followed by GLIM-based diagnostic assessment when risk is identified.

2. Look beyond BMI. Body composition analysis (through opportunistic CT morphometry at the L3 level or bedside ultrasound assessment) should be integrated into routine evaluation to identify sarcopenia, myosteatosis, and sarcopenic obesity, which carry prognostic and pharmacokinetic implications that BMI alone cannot capture.

3. Align diet with disease phase. During active disease, exclusion-based strategies (CDED, EEN) can serve as therapeutic adjuncts or, in selected mild-to-moderate cases, as primary interventions. During remission, adherence to a Mediterranean-style dietary pattern should be encouraged to support microbiota diversity, mucosal integrity, and metabolic health.

4. Correct micronutrient deficiencies proactively. Iron, vitamin D, vitamin B12, folate, zinc, and selenium status should be monitored and corrected in a coordinated, multi-nutrient approach. In the presence of active inflammation, intravenous iron should be preferred over oral supplementation.

5. Integrate nutrition with pharmacological strategy. Nutritional interventions should be temporally coordinated with biologic therapy to exploit the therapeutic window created by inflammatory suppression, thereby overcoming anabolic resistance and maximizing the efficacy of both dietary and pharmacological approaches.

6. Minimize pro-inflammatory dietary exposures. Patients should be counseled to reduce intake of ultra-processed foods, dietary emulsifiers, and refined sugars, which have been implicated in barrier disruption, dysbiosis, and persistence of low-grade inflammation.

This review has several limitations that warrant acknowledgment. As a narrative synthesis, the selection of studies was not conducted through a systematic, pre-registered protocol, which introduces the possibility of selection bias. A substantial proportion of the evidence supporting dietary interventions derives from pediatric cohorts, and its transferability to adult patients remains incompletely established. Looking forward, several key questions remain. The optimal timing, duration, and composition of dietary interventions across different disease phenotypes require further clarification through adequately powered randomized controlled trials. The role of body composition as a predictor of drug exposure and therapeutic efficacy warrants prospective validation, as does the potential benefit of early intravenous iron repletion in mitigating inflammation-driven metabolic dysfunction. The development of IBD-specific definitions of sarcopenia and myosteatosis, validated against clinically meaningful outcomes, represents an urgent research priority. Finally, the long-term impact of sustained adherence to anti-inflammatory dietary patterns on mucosal healing, structural bowel damage, and the trajectory of disease progression remains to be established. In conclusion, effective management of IBD extends beyond symptomatic control and immunomodulation to encompass the restoration of metabolic health, preservation of skeletal muscle function, and sustained nutritional resilience. By recognizing nutrition as a cornerstone of personalized care and integrating it systematically with pharmacological therapy throughout the disease course, clinicians can address the pathophysiological synergy between inflammation, body composition, and metabolic homeostasis. This holistic, patient-centered approach has the potential not only to optimize treatment efficacy but also to improve long-term physical function, quality of life, and the likelihood of achieving durable, deep remission.

Conflict of Interest: Giuseppe Privitera received consultancy fees from Alphasigma and Janssen. Cristina Bezzio received lecture fees and served as a consultant for Takeda, MSD, Ferring, Abbvie, Galapagos, Celltrion, Janssen, and Eli-Lilly. Alessandro Armuzzi: consulting and/or advisory board fees from AbbVie, Amgen, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mylan, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Arena, Biogen, Bristol-Myers Squibb, Eli-Lilly, Ferring, Galapagos, Gilead, Janssen, MSD, Mitsubishi-Tanabe, Novartis, Pfizer, Roche, Sandoz, Samsung Bioepis, Takeda; and research grants from MSD, Pfizer, Takeda and Biogen. Filiz Akyüz: consulting fees from Janssen, AbbVie, Pfizer, and Fujifilm. The remaining authors declare no competing interests

Peer-review: Externally peer-reviewed.

Use of AI for Writing Assistance: Figure 1 was designed with the help of artificial intelligence.

Author Contribution: Concept – Z.İ., G.G., C.B., F.A; Design – C.B., F.A.; Supervision – C.B., F.A., A.A; Resource – Z.İ., G.A., A.A.; Materials – Z.İ., G.G., L.L., G.P.; Data Collection and/or Processing – Z.İ., G.G., L.L., G.P., C.B.; Analysis and/or Interpretation – L.L., G.P., A.A.; Literature Review – Z.İ., G.G., L.L., G.P., A.A.; Writing – Z.İ., G.G., L.L., G.P., C.B., F.A., A.A.; Critical Review – F.A., A.A.

Funding: Authors declare that this study have not received any financial support.

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