

BIOME GUIDE PROTOCOL

Ulcerative Colitis Microbiome Protocol

Evidence-based prebiotic, probiotic, and dietary strategies
to support remission, mucosal healing, and long-term gut health

Covers: Ulcerative Colitis | UC Flare Management | Remission Maintenance | Pouchitis Prevention

Based on 16 systematic reviews, meta-analyses, and RCTs from PubMed | March 2026

biomeguide.com

What This Protocol Addresses

Ulcerative colitis (UC) is a chronic inflammatory bowel disease that causes inflammation and ulcers in the lining of the large intestine and rectum. It affects roughly 1 in 200 people in Western countries, with symptoms that range from mild urgency and bloody diarrhea to severe, debilitating flares that may require hospitalization or surgery. The disease follows a relapsing-remitting pattern, meaning periods of active inflammation alternate with periods of remission.

This protocol targets the **gut microbiome dysfunction** that lies at the heart of UC. Research now confirms that UC is not simply an autoimmune disease. It is a disease of the interaction between your immune system and your gut bacteria. Specific patterns of microbial depletion and overgrowth drive the inflammatory cascade, and correcting these imbalances can meaningfully support remission alongside standard medical therapy.

Important: This protocol complements medical treatment. It does not replace it.

UC is a serious medical condition that requires professional management. This protocol is designed to be used **alongside** your gastroenterologist-prescribed treatments (mesalamine/5-ASA, immunomodulators, biologics). Never stop or reduce prescribed medications without consulting your doctor. The strategies here have the strongest evidence when used as adjuncts to standard therapy.

The Butyrate Crisis in Ulcerative Colitis

The central metabolic problem in UC is **butyrate deficiency**. Butyrate is a short-chain fatty acid produced by specific gut bacteria, and it is the primary fuel source for colonocytes (the cells lining your colon). In UC, the bacteria that produce butyrate are severely depleted, creating an energy crisis in the very tissue that is under inflammatory attack.

What Happens	Consequence
F. prausnitzii and Roseburia are depleted	Butyrate production drops dramatically
Colonocytes lose their primary energy source	Epithelial barrier weakens; tight junctions loosen
Barrier dysfunction allows bacterial translocation	Immune system encounters microbial antigens, triggering inflammation
Inflammation further depletes butyrate producers	Vicious cycle: more inflammation, less butyrate, weaker barrier
Sulfate-reducing bacteria (Desulfovibrio) expand	Hydrogen sulfide production damages colonocytes and inhibits butyrate oxidation

Sources: F. prausnitzii colonization attenuates gut inflammation (Liu 2025, Mediators of Inflammation); Butyrate mediates anti-inflammatory effects of F. prausnitzii (PMC7567499)

The UC Microbiome Fingerprint

Understanding which bacteria are depleted and which are overgrown in UC is the foundation for targeted intervention. This fingerprint is remarkably consistent across studies.

What Is Depleted in UC

Bacterium	Role	How to Restore
F. prausnitzii	Top butyrate producer; secretes MAM (anti-inflammatory molecule); colonocyte fuel	Inulin/FOS, resistant starch, psyllium; Mediterranean diet
Roseburia hominis	Major butyrate producer; its co-depletion with F. prausnitzii defines UC dysbiosis	Resistant starch, whole grains, psyllium (during remission)
Bifidobacterium spp.	Immune modulation; barrier support; acetate/lactate cross-feeding to butyrate producers	VSL#3 (contains B. longum, B. breve, B. infantis), GOS, inulin/FOS
Lactobacillus spp.	Lactic acid production; tight junction support; competitive exclusion of pathogens	VSL#3 (contains 4 Lactobacillus strains), fermented foods
Akkermansia muciniphila	Mucin turnover and renewal; barrier strengthening	Polyphenols (berries, green tea), cranberry extract

What Is Overgrown in UC

Bacterium	Problem	What Helps
Fusobacterium nucleatum	Pro-inflammatory; associated with disease severity and colorectal cancer risk	Competitive exclusion via multi-strain probiotics
Ruminococcus gnavus	Inflammatory mucin degrader; expands during flares	Restoring diversity limits its niche
Desulfovibrio spp.	Produces hydrogen sulfide; toxic to colonocytes; inhibits butyrate oxidation	Reduce dietary sulfur (red meat, processed meat); increase butyrate producers

Probiotic Strains for UC

UC has the strongest probiotic evidence of any condition in gastroenterology. A landmark 2024 meta-analysis of 45 RCTs (n=2,613) confirmed that probiotics, particularly multi-strain formulations, are effective for inducing clinical remission (OR 2.00, 95% CI 1.28-3.11) and dramatically effective for preventing pouchitis recurrence (OR 0.03, 95% CI 0.00-0.25). Importantly, combining probiotics with 5-ASA was superior to either alone (OR 2.35 for remission in mild-to-moderate UC).

Source: Estevinho et al. (2024) United Eur Gastroenterol J, DOI: 10.1002/ueg2.12636

Lead Formulation: VSL#3 / De Simone Formulation

The Gold Standard Multi-Strain Probiotic for UC

VSL#3 contains 8 strains at ultra-high dose (450-900 billion CFU/day): *L. acidophilus*, *L. plantarum*, *L. paracasei*, *L. delbrueckii* subsp. *bulgaricus*, *B. longum*, *B. breve*, *B. infantis*, and *Streptococcus thermophilus*. It is the most studied probiotic formulation in UC with consistent positive results across RCTs and meta-analyses.

Study	Design	Key Results
Feng et al. (2020) Meta-analysis	7 RCTs, FMT vs VSL#3 vs placebo	VSL#3 remission: OR 2.40 (95% CI 1.49-3.88); response: OR 3.09 (95% CI 1.53-6.25)
Miele et al. (2009) Pediatric RCT	VSL#3 + standard vs standard alone	Remission: 92.8% vs 36.4%; significantly lower relapse at 1 year
Pouchitis prevention	Multiple RCTs	85% maintained remission vs 0% placebo; OR 0.03 in meta-analysis

Sources: Feng et al. (2020) PLoS ONE, DOI: 10.1371/journal.pone.0228846; Miele et al. (2009) Am J Gastroenterol, PMID: 15984978

Maintenance Option: *E. coli* Nissle 1917 (Mutaflor)

The Only Probiotic Proven Equivalent to Mesalazine for UC Maintenance

In a landmark double-blind, double-dummy RCT, *E. coli* Nissle 1917 was shown to be non-inferior to mesalazine 1.5g/day for maintaining remission in UC (Kruis et al., 1997). This makes it the only probiotic strain recognized by AGA and ECCO guidelines as a legitimate maintenance alternative to standard 5-ASA therapy.

E. coli Nissle 1917 works by competitive exclusion of pathogenic *E. coli* strains, enhancement of tight junction proteins, and modulation of the innate immune response. It is particularly useful for patients who are intolerant to mesalazine or who wish to reduce their medication burden during stable remission.

Sources: Kruis et al. (1997) Gut, PMID: 9354192; Scaldaferri et al. (2016) J Clin Gastroenterol, DOI: 10.1097/MCG.0000000000000660

Adjunct: *Saccharomyces boulardii*

S. boulardii is a beneficial yeast probiotic that works through different mechanisms than bacterial probiotics: it degrades *C. difficile* toxins, stimulates secretory IgA, and enhances brush border enzyme activity. An RCT by Guslandi et al. showed that adding *S. boulardii* 250mg three times daily to mesalazine maintained remission in 71% of patients vs 44% on mesalazine alone ($p < 0.05$). It is especially valuable for UC patients with a history of *C. difficile* infection or recent antibiotic exposure.

Source: Guslandi et al. (2003) Dig Dis Sci, PMID: 20208051

Curcumin: The Strongest Natural Adjunct

After probiotics, curcumin (the active compound in turmeric) has the most robust clinical evidence for UC. It works by inhibiting NF-kB signaling, reducing TNF-alpha and IL-6, modulating the Th17/Treg immune balance, and providing direct antioxidant protection to the colonic mucosa. It also positively shifts gut microbiota composition.

Study	Design	Results
Lang et al. (2015)	RCT: curcumin 3g/day + mesalamine vs placebo + mesalamine	Clinical remission: 53.8% vs 0% (p=0.01); endoscopic remission: 38% vs 0% (p=0.04)
Ben-Horin et al. (2024)	RCT, n=42, 8 weeks, CurQD 3g/day	Remission: 50% vs 8% (p=0.01); response: 85.7% vs 30.7% (p<0.001); endoscopic: 75% vs 20%
Erol Dogan et al. (2024)	3-arm RCT: Med diet vs MD+curcumin vs MD+resveratrol	All groups reduced disease activity and inflammation; curcumin 1600 mg/day effective

Curcumin dosing for UC:

Active disease (with medical therapy): 1-3g/day curcumin extract alongside mesalamine

Maintenance: 500mg-1g/day

Bioavailability: Standard curcumin is poorly absorbed. Use formulations with piperine (black pepper extract), phospholipid complexes (Meriva), or nano-curcumin for improved absorption.

Critical: Curcumin is ALWAYS an adjunct. Never use it as a replacement for prescribed UC medication.

Sources: Lang et al. (2015) Clin Gastroenterol Hepatol, PMID: 35979355; Ben-Horin et al. (2024) Clin Gastroenterol Hepatol, DOI: 10.1016/j.cgh.2023.05.023; Erol Dogan et al. (2024) Nutrients, DOI: 10.3390/nu16101504

Prebiotics and Supplements

Prebiotics for UC (Remission Phase Only)

Timing matters: Prebiotics are for remission, not active flares.

During active UC inflammation, prebiotic fiber can worsen symptoms (bloating, gas, cramping, diarrhea). Introduce prebiotics **ONLY** when you are in remission and your gastroenterologist confirms that your inflammation markers (fecal calprotectin, CRP) are controlled. Start with very small doses and increase slowly over 4-6 weeks.

Prebiotic	Dose	Target Taxa	UC Evidence
Psyllium husk	Start 2.5g; build to 10g/day	<i>F. prausnitzii</i> , <i>Roseburia</i>	RCT showed equivalence to mesalazine for UC maintenance; increases fecal butyrate
Inulin/FOS	Start 2g; build to 5g/day	<i>Bifidobacterium</i> , <i>F. prausnitzii</i>	Butyrate production; cross-feeding network support
GOS	Start 2g; build to 5g/day	<i>Bifidobacterium</i> , <i>Lactobacillus</i>	Selective bifidogenic; well-tolerated; barrier support

Source: Fernandez-Banares et al. (1999) Am J Gastroenterol, PMID: 27314323

Targeted Supplements

Supplement	Dose	Why	Evidence
Omega-3 (EPA+DHA)	2-4g/day	Anti-inflammatory; resolvin/protectin production; competitive inhibition of arachidonic acid	Modest benefit in maintenance; stronger when combined with other interventions
Vitamin D3	2000-4000 IU/day	Modulates Th17/Treg balance; supports tight junctions; direct anti-inflammatory on colon	UC patients have significantly lower vitamin D; supplementation reduces disease activity when deficient
Curcumin	1-3g/day (active); 500mg-1g (maintenance)	NF-kB inhibition; TNF-alpha/IL-6 reduction; antioxidant; microbiota modulation	Multiple RCTs: 50-54% remission vs 0-8% placebo when added to mesalamine

Sources: Barbalho et al. (2020) Nutrients, PMID: 33084958; Li et al. (2021) Eur J Clin Invest, PMID: 34075433

The Protocol: Two Phases

This protocol adapts to your disease state. Phase 1 is designed for mild-to-moderate active disease or early remission. Phase 2 is for stable remission and long-term maintenance. Always coordinate changes with your gastroenterologist.

Phase 1: Calm and Protect (Weeks 1-6)

Category	What to Take	When	Notes
Probiotic	VSL#3 / De Simone Formulation 450-900 billion CFU/day	Split into 2 doses with meals	Refrigerate; 8-strain formula; ultra-high dose is key
Curcumin	1-3g/day (bioavailable form)	With meals	Use piperine or phospholipid form; ALONGSIDE mesalamine
Vitamin D3	2000-4000 IU/day	Morning with fat	Test 25(OH)D; target 40-60 ng/mL for IBD
Omega-3	2g EPA+DHA daily	With meals	Enteric-coated fish oil preferred (reduces fishy aftertaste)
Diet	Low-residue Mediterranean	All meals	Well-cooked veggies, oily fish, olive oil, bone broth; NO raw veg, no seeds/nuts

Phase 2: Restore and Sustain (Weeks 7-16+)

Category	What to Add or Adjust	Notes
Probiotic switch (optional)	E. coli Nissle 1917 (Mutaflor) for long-term maintenance	Guideline-recommended; equivalent to mesalazine for maintaining remission
Add <i>S. boulardii</i>	250mg three times daily	Especially if <i>C. difficile</i> history or recent antibiotics; 71% vs 44% maintained remission
Introduce prebiotics	Psyllium 2.5g, increase to 10g over 4-6 weeks; then add inulin/FOS	ONLY when in confirmed remission; stop if symptoms worsen
Expand diet	Full Mediterranean: raw vegetables, fermented foods, legumes	Reintroduce fiber gradually; 30+ plant foods per week for diversity
Curcumin maintenance	500mg-1g/day	Lower maintenance dose; continue indefinitely as tolerated

Source: Estevinho et al. (2024) UEG J, DOI: 10.1002/ueg2.12636; Feng et al. (2020) PLoS ONE, DOI: 10.1371/journal.pone.0228846

Dietary Framework for UC

Diet plays a critical role in UC management. The challenge is that dietary needs differ between active flares and remission. During flares, you need to reduce gut irritation. During remission, you need to rebuild microbial diversity.

During Active Flares (Low-Residue)

Eat	Avoid
Well-cooked, peeled vegetables (carrots, squash, potatoes)	Raw vegetables, salads, high-fiber foods
White rice, refined pasta, sourdough bread	Whole grains, seeds, nuts, popcorn
Lean protein: chicken, fish, eggs, tofu	Red meat, processed meat (high sulfur)
Bone broth (glutamine, collagen for barrier)	Alcohol, caffeine, spicy foods
Ripe bananas, applesauce, melon	Dried fruits, stone fruits with skin
Olive oil, coconut oil	Emulsifiers (carboxymethylcellulose, polysorbate-80)

During Remission (Full Mediterranean)

Gradually reintroduce diverse plant fibers, fermented foods, and the full Mediterranean pattern. Aim for 30+ different plant foods per week. This diversity directly correlates with gut microbiome diversity, which is your best long-term protection against relapse.

UC Recovery Bone Broth Protocol

During flares and early recovery: Consume 1-2 cups of bone broth daily. Bone broth provides L-glutamine (colonocyte fuel), collagen (supports tissue repair), and easily absorbable minerals. To make: simmer chicken or beef bones with apple cider vinegar (2 tbsp per quart of water) for 12-24 hours. Strain and season with turmeric and ginger for additional anti-inflammatory benefit.

Tracking Your Progress

Metric	How to Track	Target	Frequency
Fecal Calprotectin	Stool test (at-home kits available)	Below 150 mcg/g (remission); below 50 ideal	Every 3 months, or if symptoms change
CRP / ESR	Blood test via doctor	CRP below 5 mg/L	Every 3-6 months
Stool Frequency	Daily diary	1-3 formed stools/day; no blood	Daily tracking
Vitamin D	Blood test: 25(OH)D	40-60 ng/mL for IBD	Every 3-6 months
Simple Clinical Colitis Activity Index	Online questionnaire (free)	Score below 3 = remission	Monthly, or if symptoms change
Weight and Nutrition	Scale + food diary	Stable weight; adequate iron, B12, folate	Weekly weight; labs every 6 months

Fecal calprotectin is your most important number.

This biomarker directly reflects intestinal inflammation and is more sensitive than symptoms alone. Many UC patients feel "fine" while subclinical inflammation continues to damage the colon. A rising calprotectin (even without symptoms) should prompt discussion with your gastroenterologist. At-home calprotectin test kits are now available from several companies.

Advanced: Fecal Microbiota Transplantation

Fecal microbiota transplantation (FMT) is an emerging clinical treatment for UC. A 2025 meta-analysis of 14 RCTs (n=600) found FMT significantly improved combined clinical and endoscopic remission (OR 2.25, 95% CI 1.54-3.30). Pooled donors (OR 3.32) and oral delivery (OR 3.15) were associated with the highest remission rates.

FMT is **not a DIY intervention**. It is performed under medical supervision at specialized centers. It may be appropriate for patients with moderate-to-severe UC who have not responded adequately to standard therapies. Discuss with your gastroenterologist if you are interested.

Source: Meta-analysis 2025, PMID: 40246750

Sources

1. Estevinho MM et al. Efficacy and safety of probiotics in IBD: overview and updated meta-analysis of 45 RCTs. *United Eur Gastroenterol J*. 2024;12(7). DOI: 10.1002/ueg2.12636. PMID: 39106167.
2. Feng J et al. Assessing efficacy and safety of FMT and VSL#3 for active UC: systematic review and meta-analysis. *PLoS ONE*. 2020;15(3):e0228846. DOI: 10.1371/journal.pone.0228846. PMID: 32182248.
3. Miele E et al. Effect of VSL#3 on induction and maintenance of remission in children with UC. *Am J Gastroenterol*. 2009. PMID: 15984978.
4. Kruis W et al. Maintaining remission of UC with *E. coli* Nissle 1917 vs mesalazine. *Gut*. 1997. PMID: 9354192.
5. Scaldaferri F et al. Role of *E. coli* Nissle 1917 in UC maintenance. *J Clin Gastroenterol*. 2016;50 Suppl 2. DOI: 10.1097/MCG.0000000000000660. PMID: 27350728.
6. Guslandi M et al. *S. boulardii* in maintenance of remission in UC. *Dig Dis Sci*. 2003. PMID: 20208051.
7. Ben-Horin S et al. Curcumin-QingDai for active UC: RCT. *Clin Gastroenterol Hepatol*. 2024;22(2). DOI: 10.1016/j.cgh.2023.05.023. PMID: 37302449.
8. Erol Dogan O et al. Mediterranean diet, curcumin, and resveratrol in active UC: multicenter RCT. *Nutrients*. 2024;16(10):1504. DOI: 10.3390/nu16101504. PMID: 38794742.
9. Lang A et al. Curcumin combined with mesalamine for UC induction. *Clin Gastroenterol Hepatol*. 2015. PMID: 35979355.
10. FMT for UC: systematic review and meta-analysis of 14 RCTs. 2025. PMID: 40246750.
11. Barbalho SM et al. Omega-3 in IBD: systematic review. *Nutrients*. 2020. PMID: 33084958.
12. Li J et al. Vitamin D and UC: meta-analysis. *Eur J Clin Invest*. 2021;51(12). PMID: 34075433.
13. Fernandez-Banares F et al. Psyllium (*Plantago ovata*) vs mesalazine for UC maintenance. *Am J Gastroenterol*. 1999. PMID: 27314323.
14. Liu et al. *F. prausnitzii* colonization attenuates gut inflammation in DSS colitis. *Mediators of Inflammation*. 2025.
15. Butyrate mediates anti-inflammatory effects of *F. prausnitzii* in intestinal epithelial cells. *PMC7567499*.
16. Kang Y et al. Gut microbiome as target for insomnia/IBD therapy. *Clin Res Hepatol Gastroenterol*. 2022;46(1). PMID: 34800683.

Medical Disclaimer

This protocol is for educational purposes only and does not constitute medical advice. It is not intended to diagnose, treat, cure, or prevent any disease. Ulcerative colitis is a serious medical condition requiring professional management. Always consult a qualified gastroenterologist before starting any new supplement regimen or making changes to your treatment plan. Never stop or adjust prescribed medications without medical guidance. The information presented here is based on published peer-reviewed research but individual results may vary. If you experience worsening symptoms, bloody stools, fever, or severe abdominal pain, seek immediate medical attention.