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# Polyethylene glycol-based bowel preparation and gut dysbiosis: Clinical implications beyond colon cleansing

Melgaço ACC *et al.* PEG bowel preparation and gut dysbiosis

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**Abstract**

Owing to their efficacy and safety profile, polyethylene glycol (PEG)-based formulations are the gold standard for bowel preparation before colonoscopy and colorectal surgery. However, PEG lavage may transiently disrupt gut microbial diversity, reduce short-chain fatty acid-producing bacteria, alter mucus barrier integrity, and promote the expansion of opportunistic taxa. These ecological alterations may influence mucosal recovery, immune homeostasis, and susceptibility to inflammatory or infectious complications, particularly in vulnerable individuals. Nevertheless, current evidence remains heterogeneous, and direct causal relationships between PEG-induced dysbiosis and adverse clinical outcomes remain indefinite. Accordingly, this opinion review critically discusses the mechanisms underlying PEG-associated microbiota disruption, including mechanical washout, osmotic stress, mucus layer alterations, and metabolic depletion. The review also examines the potential implications for infection risk, immune modulation, and postoperative outcomes while highlighting the limitations and controversies surrounding the interpretation of microbiome studies. Finally, the review discusses emerging strategies aimed at minimizing ecological disruption while preserving bowel cleansing efficacy.

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**Key Words:** Polyethylene glycol; Dysbiosis; Bowel preparation; Microbiota; Mucosal recovery; Infection risk

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**Core Tip:** Polyethylene glycol (PEG)-based bowel preparation may transiently alter gut microbial diversity, mucus barrier integrity, and short-chain fatty acid production. Although these ecological changes are increasingly associated with immune

modulation and postoperative outcomes, current evidence remains heterogeneous and largely observational. Suitably, this opinion review critically examines the mechanisms and potential clinical implications of PEG-induced dysbiosis. The review also emphasizes the need for microbiota-preserving bowel preparation strategies and personalized approaches based on host resilience and baseline microbiota composition.

## INTRODUCTION

Owing to their efficacy, safety profile, and minimal systemic absorption, polyethylene glycol (PEG)-based formulations are the gold standard for bowel preparation before colonoscopy[1,2]. However, the gut microbiota is increasingly recognized as a major regulator of metabolic homeostasis, mucosal barrier integrity, and colonization resistance. Hence, interest in the ecological consequences of bowel cleansing has intensified. In particular, PEG administration may transiently reduce microbial diversity, alter the relative abundance of key bacterial taxa, and disrupt intestinal metabolic pathways, including short-chain fatty acid (SCFA) and bile acid metabolism[3,4].

The most commonly reported alterations include reductions in butyrate-producing Firmicutes and relative expansion of Proteobacteria and Verrucomicrobiota, and these microbial patterns are frequently associated with dysbiosis states[5,6]. Furthermore, PEG-induced osmotic lavage may affect mucus barrier integrity, luminal osmolality, and host–microbiota interactions[7]. Although many of these alterations appear transient, their magnitude and duration may vary according to PEG formulation, exposure frequency, and host-related factors[4,8].

Accordingly, this opinion review critically discusses the mechanisms and potential clinical implications of PEG-associated ecological disruption while emphasizing current limitations in microbiome interpretation. The review argues that bowel preparation should be viewed as both a procedural requirement and a transient ecological intervention that may benefit from microbiota-conscious and personalized strategies.

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## EFFECTS OF PEG-BASED BOWEL PREPARATION ON GUT MICROBIOTA

PEG exerts a cleansing effect through osmotic water retention, which accelerates luminal transit and mechanically flushes the colon. However, this process also removes microbial biomass and disrupts ecological niches. In multiple studies, PEG preparation has been associated with the following patterns (Table 1).

### *Reduced alpha-diversity*

PEG-based bowel preparation induces a transient but pronounced reduction in gut microbial alpha-diversity, particularly within Firmicutes and Bacteroidetes. This is characterized by decreased richness and evenness of intestinal bacterial communities immediately after lavage. Although the microbiota may partially recover within days or weeks, bowel cleansing promotes an acute dysbiotic state associated with disruption of microbial homeostasis[8-10].

### *Expansion of Proteobacteria*

PEG bowel preparation promotes the expansion of facultative anaerobic Proteobacteria, particularly *Enterobacteriaceae*, such as *Escherichia* and *Shigella*. An increased abundance of opportunistic taxa, including *Veillonella*, has also been reported. These alterations are likely related to transient oxygenation of the intestinal lumen and disruption of the anaerobic colonic niche following osmotic lavage[10,11].

### *Loss of butyrate-producing species*

Bowel preparation with PEG is associated with depletion of beneficial butyrate-producing bacteria, particularly *Faecalibacterium prausnitzii* (*F. prausnitzii*). This species plays a major role in maintaining intestinal anti-inflammatory activity and epithelial barrier integrity through butyrate production. Hence, a reduction in *F. prausnitzii* is considered a hallmark of intestinal dysbiosis and impaired mucosal homeostasis[9,12,13].

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### *Depletion of SCFAs*

PEG-induced depletion of SCFA-producing bacteria reduces the concentration of SCFAs, mainly butyrate and propionate. These metabolites are essential for colonocyte energy metabolism, regulation of epithelial barrier function, immune modulation, and mucus production. Therefore, reduced SCFA availability after bowel preparation may compromise intestinal resilience and promote transient inflammatory responses[4,12,14].

### *Altered metabolic pathways*

PEG bowel preparation disrupts microbial metabolic activity, including carbohydrate fermentation and bile acid metabolism. Specifically, depletion of obligate anaerobic fermenters impairs saccharolytic metabolism and SCFA biosynthesis, whereas alterations in bile acid transformation may further contribute to intestinal dysbiosis and altered host–microbiota interactions[4,12,14].

### *Disruption of mucus layer and enrichment of Akkermansia*

PEG-induced osmotic lavage may disrupt the intestinal mucus layer by reducing mucus thickness and altering mucin availability. These changes reshape the mucosa-associated microbiota and favor the enrichment of mucin-degrading bacteria, such as *Akkermansia muciniphila* (*A. muciniphila*). Given that butyrate is essential for goblet cell activity and mucus secretion, alterations in mucus integrity are also linked to reduced SCFA production[5,15,16].

Although the microbiota typically begins to recover within days, full restoration may only occur after weeks. Moreover, recovery may remain incomplete in older adults, patients with inflammatory bowel disease (IBD), and individuals with baseline dysbiosis[17-19].

## MECHANISMS OF PEG-INDUCED DYSBIOSIS

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The dysbiotic effects of PEG arise from a combination of mechanical, osmotic, and biochemical perturbations.

***Mechanical washout***

A central mechanism for PEG-induced dysbiosis is extensive mechanical washout caused by rapid bowel evacuation. The large-volume cathartic effect physically removes luminal microorganisms, mucus-associated bacterial communities, and biofilm structures attached to the intestinal surface[20]. Many commensal anaerobes depend on stable adhesion niches within the mucus layer. Therefore, bowel cleansing disproportionately affects beneficial resident taxa while reducing overall microbial biomass. This abrupt microbial depletion disrupts ecological interactions, such as cross-feeding and colonization resistance, which temporarily destabilizes the intestinal ecosystem[5,9,21]. In addition, biofilm disorganization alters the spatial distribution of microbes along the epithelial surface. This impairs normal host–microbiota communication and favors recolonization by fast-growing opportunistic organisms during the recovery phase[5,11,22].

***Osmotic stress***

PEG acts as a non-absorbable osmotic compound that induces substantial water influx into the intestinal lumen, thereby generating profound osmotic stress within the gut environment. These abrupt osmolarity changes negatively affect the viability of many obligate anaerobic bacteria that are highly sensitive to environmental fluctuations[5,23]. Simultaneously, osmotic perturbation creates selective pressure that favors osmotolerant and facultative aerobic taxa, particularly members of the Proteobacteria phylum. Notably, transient osmotic disturbances can also induce long-lasting alterations in microbial ecology by destabilizing anaerobic microbial networks and modifying nutrient gradients within the colon. Increased luminal oxygen diffusion associated with fluid displacement may further contribute to the expansion of

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facultative pathogens, such *Escherichia* and *Shigella*, thereby reinforcing the dysbiotic profile observed after bowel preparation[5,12].

***Disruption of mucin layer***

PEG-induced lavage may transiently disrupt the intestinal mucus barrier by reducing mucus thickness and altering the composition and availability of mucins. The mucus layer constitutes a critical ecological niche that spatially separates intestinal microorganisms from epithelial cells and simultaneously serves as a nutrient source for specialized commensals[24]. Therefore, its disruption profoundly alters the habitat of mucosa-associated bacteria and reshapes microbial colonization patterns. In particular, thinning of the mucus layer may expose epithelial surfaces to microbial products and inflammatory stimuli, thereby increasing susceptibility to epithelial stress and transient inflammation. Furthermore, depletion of the mucus barrier may selectively favor mucin-degrading microorganisms, such as *A. muciniphila*, which expand under conditions of increased mucin turnover. Considering that butyrate is essential for goblet cell differentiation and mucus secretion, alterations in mucus integrity are also closely associated with reductions in butyrate-producing bacteria[15,16,25]

***Metabolite depletion***

A major metabolic consequence of PEG-induced dysbiosis is depletion of SCFAs, particularly butyrate and propionate. This results from the loss of obligate anaerobic fermentative bacteria, such as *F. prausnitzii*[4,26]. SCFAs play fundamental roles in intestinal physiology by serving as the principal energy source for colonocytes and regulating epithelial barrier integrity, immune homeostasis, and mucus production[27]. Reduced butyrate availability impairs the expression of tight-junction proteins, including claudins and occludins, thereby weakening epithelial barrier function and increasing intestinal permeability[28]. In parallel, diminished SCFA concentrations compromise colonization resistance against opportunistic pathogens by altering luminal pH and reducing antimicrobial peptide production. Given that SCFAs also

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modulate regulatory T-cell differentiation and anti-inflammatory signaling pathways, their depletion may contribute to transient mucosal inflammation and delayed microbial recovery following bowel preparation[12,29].

*Nutrient and pH shifts*

PEG-based bowel preparation induces substantial biochemical alterations within the intestinal lumen. These include changes in pH, substrate availability, and nutrient gradients. Rapid evacuation removes fermentable dietary residues and endogenous microbial metabolites, thereby disrupting trophic interactions that normally sustain anaerobic microbial communities[18]. Reduced availability of complex carbohydrates impairs saccharolytic fermentation pathways and limits SCFA biosynthesis, particularly among butyrate-producing Firmicutes[4,11]. Concurrently, alterations in luminal pH may create conditions that are unfavorable for strict anaerobes while supporting the growth of facultative and stress-adapted microorganisms. These environmental shifts destabilize microbial community structure and promote transient expansion of opportunistic taxa commonly observed after PEG administration. Disturbances in nutrient availability may additionally affect bile acid metabolism and microbial enzymatic activity, which further amplifies functional dysbiosis during the post-cleansing period[14,22].

These mechanisms collectively create an environment conducive to opportunistic expansion and reduced microbial resilience.

## MUCOSAL AND ECOLOGICAL CONSEQUENCES OF PEG BOWEL PREPARATION

Although PEG-based bowel preparation is generally considered clinically safe and non-inflammatory, osmotic lavage may induce subtle but biologically relevant alterations in both mucosal integrity and gut microbial ecology. In particular, under conditions of repeated PEG exposure or preexisting intestinal vulnerability, transient increases in

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epithelial permeability, mucus layer thinning, mild inflammatory infiltration, and alterations in intestinal metabolic homeostasis are observed[7].

Pronounced reductions in *MUC2* expression and alterations in goblet cell activity have been observed following PEG-induced lavage. These changes may contribute to transient disruption of the mucus barrier and reshaping of the mucosa-associated microbiota. These structural changes are frequently associated with fluctuations in the abundance of mucin-degrading organisms, such as *A. muciniphila*. However, microbial responses appear heterogeneous and may vary according to bowel preparation formulation, osmotic conditions, and timing of post-lavage assessment[5]. In parallel, ecological alterations, including depletion of commensal anaerobes and reduced SCFA production, may further impair microbial resilience and mucosal homeostasis.

In healthy individuals, microbiota recovery appears to begin within 48-72 hours and may progress over subsequent weeks. However, the magnitude and duration of post-preparation alterations are highly variable and may be influenced by baseline microbiota composition, dietary habits, antibiotic exposure, age, comorbidities, and underlying intestinal diseases. Therefore, patients with IBD, metabolic dysfunction, or compromised microbial resilience may exhibit delayed mucosal restoration and prolonged dysbiosis.

Despite growing interest in PEG-associated ecological disruption, the interpretation of current evidence remains challenging. Most available studies are observational, involve relatively small cohorts, and employ heterogeneous bowel preparation protocols, sequencing methodologies, and sampling intervals. Furthermore, many investigations rely predominantly on taxonomic profiling rather than functional microbial assessment. This limits accurate translation of observed compositional changes into clinically meaningful biological dysfunction. Importantly, a substantial proportion of the mechanistic evidence linking PEG-induced microbiota alterations to mucosal inflammation, barrier dysfunction, immune modulation, or postoperative complications derives from experimental and preclinical models. Consequently, although bowel preparation-associated dysbiosis represents an increasingly relevant

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translational concept, direct causal relationships with adverse clinical outcomes in humans remain insufficiently established and should be interpreted cautiously.

Collectively, these findings support the concept of bowel preparation being viewed as a mechanical cleansing intervention as well as a transient ecological and mucosal stressor. Moreover, these biological consequences may vary substantially according to host resilience and baseline microbiota stability.

## CLINICAL IMPLICATIONS: INFECTION RISK, IMMUNE MODULATION, AND POSTOPERATIVE OUTCOMES

### *Infection risk*

Colonization resistance is a fundamental protective function of the gut microbiota that limits the expansion of opportunistic pathogens. However, PEG-induced dysbiosis may transiently impair this mechanism. The reduction of commensal anaerobic bacteria and depletion of SCFAs, particularly butyrate, weaken epithelial barrier integrity and reduce antimicrobial defense mechanisms within the colon[30]. This altered microbial environment may facilitate the overgrowth of pathogenic organisms, including *Clostridioides difficile* (*C. difficile*), especially in hospitalized or antibiotic-treated patients. Notably, disruption of microbial diversity and loss of colonization resistance are major predisposing factors for *C. difficile* infection[31,32].

In addition, bowel preparation and colonoscopic manipulation may promote transient bacteremia. This is particularly evident after mucosal interventions, such as polypectomy or endoscopic mucosal resection. Although post-polypectomy bacteremia is generally uncommon and self-limited in healthy individuals, the risk may increase in older adult patients, immunocompromised individuals, and those with impaired mucosal barrier function[33,34]. Considering that microbial imbalance may facilitate pathogen translocation and impair mucosal healing, PEG-associated microbiota alterations have been hypothesized to influence susceptibility to postoperative infectious complications. However, direct causal evidence remains limited[35]. Despite these concerns, the absolute incidence of severe infectious complications remains

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relatively low, and current evidence regarding the magnitude of risk directly attributable to bowel preparation remains heterogeneous.

***Immune modulation***

Disruption of the intestinal microbiota after PEG bowel preparation may greatly affect mucosal immune homeostasis[11]. Commensal anaerobic bacteria and their metabolites, particularly SCFAs, are essential regulators of immune tolerance and epithelial integrity[36]. A reduction in SCFA-producing taxa decreases regulatory T cell (Treg) differentiation and anti-inflammatory signaling pathways, which creates a transient pro-inflammatory intestinal environment[37]. Moreover, butyrate deficiency impairs Treg activity and compromises the maintenance of mucosal immune equilibrium[7].

Microbiota depletion may also increase epithelial expression of inflammatory cytokines, such as interleukin (IL)-6 and IL-8, which are involved in neutrophil recruitment and amplification of inflammatory responses[38,39]. In parallel, altered microbial antigen exposure modifies dendritic cell activation and antigen presentation dynamics within the intestinal mucosa. These immunological disturbances may influence postoperative inflammatory responses, delay epithelial repair, and impair wound healing after colorectal procedures[40]. Although most immune alterations appear transient, they may become clinically relevant in patients with advanced age, malignancy, inflammatory disorders, or immunosuppression[41,42].

***Postoperative outcomes***

Bowel preparation-associated dysbiosis may influence postoperative outcomes following colorectal surgery; however, the clinical relevance of this observation remains controversial[43]. In particular, alterations in microbial composition and intestinal motility have been associated with an increased risk of postoperative ileus in susceptible patients[44]. Moreover, depletion of commensal anaerobes and changes in microbial metabolite production may impair enteric nervous system signaling and intestinal recovery after surgery, thereby delaying gastrointestinal transit[41,45].

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Microbiota-mediated mechanisms have also been proposed to play a role in the pathogenesis of anastomotic leakage[46]. Certain collagenase-producing bacteria, including opportunistic *Enterococcus* species, may proliferate under dysbiotic conditions and disrupt anastomotic tissue integrity[47]. Furthermore, microbial imbalance modulates local inflammation, collagen remodeling, and epithelial repair processes involved in anastomotic healing[48,49].

Microbial composition may influence several aspects of colorectal carcinogenesis and postoperative recovery. However, whether transient bowel preparation-associated ecological alterations exert meaningful long-term effects on neoplasia biology or recurrence risk remains unknown. Overall, current evidence is limited, heterogeneous, and largely indirect, and this hypothesis is biologically intriguing. However, definitive clinical conclusions cannot yet be established[50-53].

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## STRATEGIES TO MITIGATE DYSBIOSIS WHILE PRESERVING CLEANSING EFFICACY

Several clinical strategies have been proposed to mitigate PEG-induced bowel preparation dysbiosis without compromising colonic cleansing efficacy (Table 2). Dietary modulation and the use of supplements are among the most promising approaches. Specifically, low-residue diets enriched with fermentable substrates, such as prebiotics and fibers, partially preserve the basal metabolic activity of the microbiota and accelerate post-colonoscopy ecological recovery. Similarly, the combined administration of insoluble fiber (wheat bran) with the probiotic *Bifidobacterium animalis* subsp. *lactis* resulted in high cleansing efficacy and superior tolerability, thereby indicating a tangible benefit in maintaining intestinal homeostasis[11,54].

Peri- and post-colonoscopy probiotic administration as an adjuvant therapy has also revealed favorable outcomes. Supplementation with strains from the genera *Lactobacillus* and *Bifidobacterium* is strongly associated with swift restoration of the microbiome following lavage-induced stress and mitigation of adverse gastrointestinal symptoms, such as abdominal pain and distension[55]. A recent systematic review

reiterated the clinical benefits of introducing probiotics before and after the examination; however, it also highlighted heterogeneity in quantitative outcomes across current literature[52]. Additionally, the use of multi-strain formulations has proven particularly effective in reducing intestinal discomfort and aiding mucosal functional recovery[56,57].

The development of low-volume PEG formulations represents a pivotal advancement in the optimization of lavage protocols. Preparations containing 1 L of PEG associated with an ascorbate complex ensure efficacy comparable with that of conventional high-volume regimens, yet with lower exposure of the lumen to osmotic stress and better tolerability than that of conventional regimens. Although the exact impact of these low-volume solutions on microbial ecology warrants further elucidation, the reduction in osmotic load may attenuate the magnitude of the induced alterations[55]. Complementarily, the adoption of split-dose administration regimens induces considerably fewer disruptions to the bacterial community than that of single-dose regimens. This strategy effectively preserves microbial diversity and accelerates microbiota recovery by reducing mucosal exposure to physical and osmotic trauma of the fluid[11,58].

Finally, emerging strategies focused on the direct protection and regeneration of the mucosal barrier have gained prominence. Notably, supplementation with bioactive compounds, such as glutamine and butyrate, demonstrates promising potential in restoring epithelial integrity. The mechanism of action of these metabolites relies primarily on modulating the expression of tight-junction proteins and consequently reducing procedure-induced intestinal permeability. Although specific clinical data focused on the post-PEG bowel preparation period remain limited, experimental models robustly indicate that replenishment of these compounds accelerates barrier repair and mitigates inflammatory cascades secondary to acute dysbiosis[59,60].

## FUTURE DIRECTIONS

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Key research priorities regarding PEG-based bowel preparation include the following: (1) Identifying microbiota resilience biomarkers to personalize bowel preparation; (2) Developing microbiota-sparing cleansing agents; (3) Evaluating long-term ecological effects in patients undergoing repeated colonoscopies; (4) Integrating metabolomic and immunologic endpoints into bowel preparation trials; (5) Testing microbiota-directed foods to accelerate recovery; and (6) Elucidating the effects of PEG in populations with metabolic syndrome, IBD, and cancer.

The field is advancing toward a holistic understanding of bowel preparation as both a procedural and ecological intervention.

## CONCLUSION

Although PEG-based bowel preparation remains essential for modern colonoscopy and colorectal surgery, increasing evidence suggests that osmotic lavage may transiently disrupt gut microbial composition, metabolic homeostasis, and mucosal integrity. These ecological alterations may influence immune responses, barrier function, and postoperative recovery, particularly in vulnerable individuals with reduced microbiota resilience. However, current evidence remains heterogeneous and largely observational. Moreover, direct causal relationships with adverse clinical outcomes have not been sufficiently established. Collectively, these findings support the notion that bowel preparation should be viewed as both a mechanical cleansing procedure and transient ecological intervention (Figure 1). Therefore, future microbiota-conscious strategies should balance cleansing efficacy with the preservation of microbial and mucosal resilience.

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## Figures and Tables

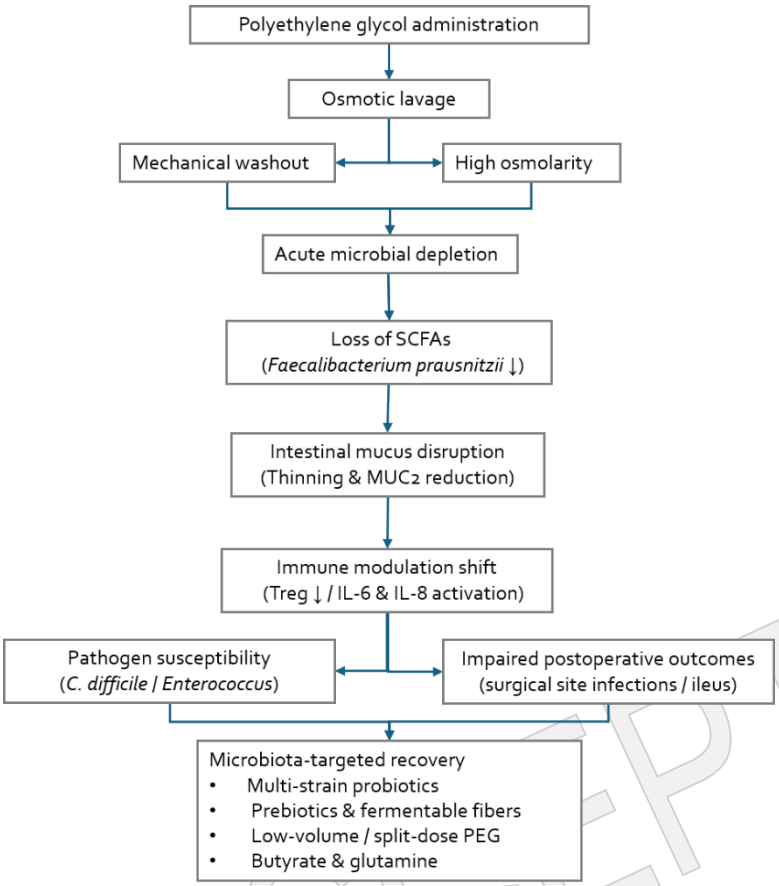



**Figure 1 Mechanistic cascade of polyethylene glycol-induced dysbiosis, mucosal impairment, and targeted recovery strategies.** SCFA: Short-chain fatty acid; Treg: Regulatory T cells; IL: Interleukin; PEG: Polyethylene glycol; *C. difficile*: *Clostridioides difficile*.

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**Table 1 Major microbiota and mucosal alterations associated with polyethylene glycol bowel preparation**

| Alteration | Main findings | Proposed biological consequence | Evidence level |
|---|---|---|---|
| Reduced microbial diversity[8,9] | Transient decrease in alpha-diversity after lavage | Ecological instability and reduced resilience | Human observational |
| Depletion of butyrate-producing Firmicutes[9,13] | Reduction in SCFA-producing taxa | Impaired epithelial energy supply and barrier maintenance | Human + mechanistic |
| Expansion of Proteobacteria[10,11] | Relative increase in opportunistic taxa | Potential loss of colonization resistance | Human observational |
| Altered bile acid metabolism[4,12] | Shifts in microbial metabolic pathways | Immune and metabolic dysregulation | Metabolomic |
| Mucus layer thinning[5,15,16] | Reduced *MUC2* expression and goblet cell alterations | Increased epithelial permeability | Experimental |
| Altered immune signaling[40,42] | Increased IL-6/IL-8 and reduced Treg activity | Transient pro-inflammatory state | Experimental |
| Delayed microbiota recovery in vulnerable hosts[53,54] | Prolonged dysbiosis in elderly/IBD/metabolic disease | Reduced mucosal resilience | Clinical observational |

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SCF: Short-chain fatty acid; IL: Interleukin; Treg: Regulatory T cells; IBD: Inflammatory bowel disease.

**Table 2 Strategies to mitigate polyethylene glycol-associated dysbiosis while preserving bowel cleansing efficacy**

| Strategy | Proposed mechanism | Potential benefit | Current evidence |
|---|---|---|---|
| Split-dose PEG[59] | Reduced continuous osmotic stress | Faster microbiota recovery | Clinical |
| Low-volume PEG formulations[59] | Lower luminal osmotic burden | Reduced ecological disruption | Emerging clinical |
| Probiotics[55-58] | Restoration of microbial balance | Reduced GI symptoms and faster recovery | Clinical + meta-analysis |
| Prebiotic/fiber-enriched diets[54] | Support of SCFA-producing bacteria | Enhanced microbial resilience | Clinical observational |
| Butyrate/glutamine supplementation[60,61] | Barrier protection and epithelial repair | Reduced permeability and inflammation | Experimental |

PEG: Polyethylene glycol; GI: Gastrointestinal; SCFA: Short-chain fatty acid.

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