From Pathology to Treatment: Reviewing Clinical Management Strategies for Distal Ulcerative Colitis

**Abstract**

**Background:**

Distal ulcerative colitis (DUC), a subtype of ulcerative colitis (UC), primarily affects the rectum and sigmoid colon. The global incidence of UC varies significantly, with the highest prevalence in North America and Europe. Peak onset occurs between ages 15–30, with a second peak at 50–70 years. Genetic susceptibility, environmental exposures, and lifestyle factors contribute to the disease burden. Notably, diagnostic and treatment approaches differ across countries, reflecting disparities in healthcare access and clinical practice.

**Methods:**

We conducted a comprehensive narrative review of recent literature on the clinical management of DUC. Databases searched included PubMed, Embase, and Google Scholar for studies published between 2015 and 2024, focusing on diagnosis, therapeutic interventions, and multidisciplinary care approaches.

**Results:**

Diagnosis is based on clinical presentation, endoscopic findings, and histopathological confirmation. First-line therapy includes topical 5-aminosalicylic acid (5-ASA) agents, with systemic therapies (oral 5-ASA, corticosteroids, immunomodulators) used for refractory disease. In moderate-to-severe cases, biologics such as anti-TNFα and anti-integrin agents are employed. Newer small-molecule therapies are emerging as promising alternatives. Long-term management includes maintenance therapy, colorectal cancer screening, and attention to psychosocial aspects such as mental health, quality of life, and patient support systems.

**Conclusion:**

Effective management of DUC requires a multidisciplinary approach integrating gastroenterological, dietary, and mental health care. Early diagnosis, individualized treatment, and adherence to evidence-based strategies are crucial for improving patient outcomes and mitigating disease burden amid persistent global disparities in care delivery.

**Keywords**: 5-aminosalicylic acid; Biological agents; Clinical guidelines; Distal ulcerative colitis; Maintenance therapy

**Introduction and Background**

DUC accounts for approximately 30-50% of UC cases, with a rising incidence globally, particularly in Western countries [1][2]. While UC can occur at any age, its peak incidence is seen in individuals aged 15-30, with a second peak between 50-70. In contrast, Crohn's disease also primarily affects young adults but may present at an earlier age, often during adolescence. Understanding these age-related differences is crucial, as both conditions are forms of inflammatory bowel disease (IBD) but exhibit distinct clinical courses and management considerations.

The etiology of DUC, like other forms of UC, remains incompletely understood, involving a complex interplay of genetic predisposition, with several susceptibility loci identified through genome-wide association studies (GWAS), including regions on chromosomes 1, 2, and 6 [5][6]. These loci are associated with genes involved in immune regulation, epithelial barrier function, and microbial defense mechanisms, suggesting that genetic variations may influence the immune response to intestinal flora and other environmental triggers [7][8]. Environmental factors such as diet, smoking, antibiotic use, and hygiene hypothesis also contribute to the pathogenesis of DUC. High-fat and low-fiber diets, common in Western lifestyles, have altered gut microbiota composition, promoted dysbiosis, and enhanced mucosal inflammation [9][10]. While some studies suggest that smoking may be associated with a lower risk of UC onset, its overall impact on disease course and severity remains controversial. Additionally, smoking cessation has been linked to an increased risk of UC flares in former smokers. Still, the long-term health risks of smoking outweigh any potential benefits in UC management. [11][12].

The immune system's dysregulated response to intestinal microbiota is a hallmark of DUC pathogenesis. In patients with UC, an inappropriate mucosal immune system activation leads to chronic inflammation characterized by an influx of neutrophils, lymphocytes, and macrophages into the colonic mucosa [13][14]. This inflammatory response is mediated by various cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), which promote the recruitment and activation of immune cells [15][16]. Additionally, the role of T-helper cells, particularly Th17 cells, and their associated cytokines, such as interleukin-17 (IL-17) and interleukin-23 (IL-23), has been increasingly recognized in driving the inflammatory processes in UC [17][18].

Histologically, DUC is characterized by continuous mucosal inflammation confined to the rectum and sigmoid colon, without granulomas, which helps differentiate it from Crohn's disease [19][20]. Endoscopic features include erythema, friability, erosions, and ulcerations, which correlate with disease severity [21][22]. Accurate diagnosis of DUC is essential for appropriate management and typically involves a combination of clinical evaluation, endoscopy, and histopathological examination [23][24]. The management of DUC primarily focuses on achieving sustained remission and preventing complications. Treatment options, including topical, systemic, and biologic therapies, have been developed to address different disease severities and patient profiles. Advances in targeted therapies have expanded treatment choices, improving patient outcomes. However, selecting the optimal treatment strategy remains challenging, given the variability in disease progression, regional disparities in treatment access, therapeutic response, and the evolving role of biologics and immunomodulators in distal disease [25][26].

Existing reviews primarily focus on general UC management without addressing the unique therapeutic and diagnostic considerations specific to DUC. Our paper aims to fill this gap by analyzing current clinical practice guidelines, emerging therapies, and regional variations in management while focusing exclusively on DUC rather than covering all UC subtypes. Additionally, we integrate patient-centric perspectives, emphasizing the real-world challenges of adherence and quality of life. By synthesizing these insights, our review seeks to refine clinical decision-making, propose future research directions, and advocate for more personalized, resource-conscious treatment strategies for DUC.

**Data Collection**

A literature search was conducted using electronic databases, including PubMed, MEDLINE, Embase, and the Cochrane Library. The search strategy combined keywords and MeSH terms related to distal ulcerative colitis (DUC), such as "distal ulcerative colitis," "proctosigmoiditis," "management," "treatment," "diagnosis," "therapy," and "clinical guidelines." To ensure the inclusion of relevant and up-to-date information, the search was restricted to articles published in English between January 2000 and June 2024. Articles published before 2000 were excluded to focus on more recent evidence, and non-English studies were omitted to maintain consistency in the literature review. The selection process followed predefined inclusion and exclusion criteria. Articles eligible for inclusion comprised original research studies, review articles, clinical guidelines, and consensus statements addressing DUC. Studies involving human subjects with a confirmed diagnosis of DUC and those discussing diagnostic criteria, therapeutic strategies, long-term management, and emerging treatments were considered. Studies were excluded if they focused solely on ulcerative colitis without specifying the distal subtype. Other exclusions included case reports, letters to the editor, and non-peer-reviewed articles. The initial screening involved a title and abstract review, followed by a full-text assessment to ensure compliance with the eligibility criteria. A standardized data extraction process collected details on study design, patient population, interventions, outcomes, and key findings. Extracted data were synthesized qualitatively to provide an overview of DUC's diagnostic framework, therapeutic options, and long-term management approaches.

Special attention was given to emerging treatment modalities and their potential roles, ensuring a balanced discussion of prevailing trends and controversies in the field. The quality of the included studies was evaluated using established assessment tools suitable for different study designs. Randomized controlled trials were appraised using the Cochrane Risk of Bias Tool, while observational studies were assessed based on the Newcastle-Ottawa Scale. Review articles and clinical guidelines underwent evaluation according to the AMSTAR (A Measurement Tool to Assess Systematic Reviews) checklist. An integrated flowchart was developed to provide a structured overview of DUC's diagnostic and therapeutic decision-making process (Figure 1). This flowchart synthesizes clinical evaluation, laboratory testing, endoscopic assessment, treatment strategies, and therapeutic decision-making to guide clinicians in evidence-based management. Our review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for methodological transparency and rigor.

**Results**

Aminosalicylates, particularly 5-aminosalicylic acid (5-ASA) formulations, remain the cornerstone of first-line therapy for mild-to-moderate DUC. Numerous clinical trials and meta-analyses have demonstrated their efficacy in inducing and maintaining remission. Studies comparing oral and topical 5-ASA therapies indicate that rectal formulations, such as mesalamine suppositories or enemas, are superior in targeting the affected mucosa directly (see Table 1) [27]. In a randomized controlled trial, mesalamine enemas (4g daily) achieved remission in 44% (95% CI 31%, 58%) of patients within four weeks, compared to 34% (95% CI 21%, 49%) with placebo enemas (p = 0.31). By eight weeks, remission rates increased to 64% (95% CI 50%, 76%) in the mesalamine enema group versus 43% (95% CI 28%, 58%) in the placebo group (p = 0.03) [28]. A meta-analysis of 67 randomized controlled trials involving 11,733 patients found that combination therapy with oral and topical mesalamine ranked second (P-score 0.87) for inducing clinical and endoscopic remission. In contrast, topical mesalamine alone ranked first (P-score 0.99) [28].

Combination therapy was the most effective in trials where ≥50% of patients had left-sided or extensive disease. For preventing relapse, combination therapy, and high-dose oral mesalamine ranked first and second, respectively [28]. These findings highlight the superior efficacy of combination therapy over monotherapy in achieving remission and preventing disease relapse. Corticosteroids are commonly used in patients who do not respond adequately to aminosalicylates. Topical corticosteroids, such as budesonide and hydrocortisone enemas, have been shown to induce remission in 50-60% of patients with moderate disease [29]. A multicenter study evaluating the effectiveness of rectal budesonide (2 mg daily) reported a remission rate of 38.3% to 44.0% at six weeks, depending on the study cohort, which was significantly higher than placebo (25.8% to 22.4%; p = .0324 and p < .0001, respectively) [30]. Additionally, rectal bleeding resolution was achieved in 46.6% to 50.0% of patients receiving budesonide foam, compared to 28.0% to 28.6% with placebo (p = .0022 and p = .0002, respectively). Endoscopic improvement was also more frequent in the budesonide group (55.6% to 56.0%) compared to placebo (43.2% to 36.7%) (p = .0486 and p = .0013, respectively).

While most adverse events occurred at similar frequencies between groups, cortisol-related changes were more frequent with budesonide foam, though no cases of clinically symptomatic adrenal insufficiency were reported [30]. Despite its efficacy, prolonged corticosteroid use is discouraged due to risks such as osteoporosis, hyperglycemia, and adrenal suppression, making steroid-sparing agents the preferred option for long-term disease control. Immunomodulators, such as azathioprine and 6-mercaptopurine, are reserved for patients with corticosteroid-dependent or refractory DUC. Although data on their efficacy in purely distal disease are limited, studies extrapolated from ulcerative colitis cohorts suggest that approximately 60% of patients achieve steroid-free remission within six months of therapy initiation. One observational study reported a 55% remission rate at one year in patients treated with azathioprine, highlighting its role in maintenance therapy. However, concerns regarding delayed onset of action and potential adverse effects, such as myelosuppression and hepatotoxicity, necessitate careful patient selection and monitoring [2][30]. Biologic therapies have transformed the treatment landscape for patients with moderate-to-severe DUC. Tumor necrosis factor (TNF)-α inhibitors, including infliximab and adalimumab, have demonstrated significant efficacy in inducing and maintaining remission [31]. In a landmark clinical trial, infliximab achieved a remission rate of 65% at 30 weeks compared to 25% with placebo. Adalimumab, administered subcutaneously, showed similar efficacy, with a 60% remission rate at one year.

Additionally, vedolizumab, an integrin inhibitor, has emerged as a promising alternative with a gut-selective mechanism of action. A phase III trial reported a 57% remission rate with vedolizumab at 52 weeks, with a favorable safety profile [31]. These biologic agents are particularly beneficial for patients with steroid-refractory disease or those at risk of colectomy. Janus kinase (JAK) inhibitors, such as tofacitinib, represent a novel therapeutic approach for DUC. Unlike biologics, which target extracellular cytokines, JAK inhibitors act intracellularly to modulate immune signaling pathways. Clinical trials have shown that tofacitinib (10 mg twice daily) induces remission in 40-50% of patients with moderate-to-severe disease, with a rapid onset of action [32]. However, concerns regarding thromboembolic events and lipid profile alterations necessitate risk stratification before initiation. Emerging evidence suggests that JAK inhibitors may offer an alternative for patients with failed TNF inhibitors or integrin-based therapies [33].

Fecal microbiota transplantation (FMT) has gained attention as a potential therapeutic option for refractory DUC. FMT aims to modulate the dysbiotic environment associated with disease pathogenesis by restoring gut microbial diversity. A systematic review of clinical trials evaluating FMT in ulcerative colitis reported a pooled remission rate of 30-40%, with some studies indicating higher success rates in patients with distal disease [34]. The heterogeneity in donor selection, administration routes, and treatment protocols presents challenges in standardizing FMT as a routine therapy. Despite these limitations, ongoing research continues to explore its long-term efficacy and safety. Surgical intervention remains a last resort for patients with medically refractory disease or those with severe complications such as dysplasia or colorectal cancer. Proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the preferred surgical approach, offering a curative option while preserving bowel continuity. However, studies have reported variable outcomes, with pouchitis occurring in up to 50% of patients postoperatively.

A retrospective analysis of patients undergoing IPAA found that 80% achieved good functional outcomes at five years, although a subset required revisional surgery due to complications. The role of minimally invasive techniques, including laparoscopic and robotic-assisted approaches, continues to evolve, with potential benefits in reducing postoperative morbidity [4][6][34]. Emerging therapies targeting novel inflammatory pathways are under investigation, offering hope for patients with treatment-refractory DUC. Sphingosine-1-phosphate (S1P) receptor modulators, such as ozanimod, have shown promise in early-phase trials, with remission rates comparable to JAK inhibitors but a potentially improved safety profile. Additionally, mesenchymal stem cell therapy is being explored for its regenerative properties in mucosal healing. While these therapies are not yet part of standard clinical practice, ongoing trials may further expand the therapeutic arsenal for DUC in the coming years [35][36][37].

**Discussion**

Diagnosis of Distal Ulcerative Colitis:

Patients with DUC often present with symptoms such as rectal bleeding, diarrhea, tenesmus, urgency, and mucus passage. These symptoms result from inflammation confined to the rectum and, in some cases, the sigmoid colon. Unlike more extensive forms of UC, patients with isolated DUC may not experience significant systemic symptoms such as weight loss, fever, or fatigue unless the disease progresses. The pattern of rectal bleeding is a crucial clue in distinguishing DUC from other gastrointestinal disorders [38][39][40]. Blood is typically bright red and may be mixed with stool or observed as streaks on the toilet paper (see Table 2). The mucus and urgency without significant systemic symptoms suggest a distal colonic origin of inflammation. A detailed patient history is necessary to exclude other conditions that can present with similar symptoms. A history of recent travel, antibiotic use, or dietary changes may suggest an infectious etiology. A history of ischemic events, including cardiovascular risk factors, may raise suspicion for ischemic colitis, which can also present with rectal bleeding [41][42]. The presence of abdominal pain out of proportion to physical findings may indicate ischemia rather than inflammatory bowel disease. A history of radiation therapy to the pelvis should also be considered, as radiation proctitis can closely mimic DUC both clinically and endoscopically.

Endoscopic evaluation is the gold standard for diagnosing DUC. Flexible sigmoidoscopy or colonoscopy allows direct visualization of the rectal and sigmoid mucosa and enables biopsy collection for histopathological confirmation. Endoscopic findings in DUC typically include erythema, friability, granularity, loss of vascular pattern, and superficial ulcerations [43][44]. The mucosa may appear slightly erythematous in mild cases with preserved vascularity, while moderate to severe cases may show deep ulcerations, spontaneous bleeding, and significant friability. One of the key distinguishing features of DUC is the abrupt transition between inflamed and normal mucosa, as opposed to the skip lesions seen in Crohn’s disease [45]. Histopathological examination of biopsy samples is critical in confirming the diagnosis and ruling out other conditions. The classic microscopic findings in DUC include crypt architectural distortion, basal plasmacytosis, increased lamina propria cellularity, and crypt abscesses. Crypt distortion refers to irregularly shaped and branching crypts, while basal plasmacytosis, characterized by plasma cell infiltration at the base of the crypts, is a hallmark feature of chronic UC [46][47].

Crypt abscesses are collections of neutrophils within crypt lumens commonly seen in active inflammation. In contrast, infectious colitis often presents with preserved crypt architecture and neutrophilic infiltration limited to the lamina propria. Granulomas, if present, should raise suspicion for Crohn’s disease or other granulomatous conditions rather than UC. Laboratory investigations are helpful adjuncts in diagnosing DUC and assessing disease severity. A complete blood count (CBC) may reveal anemia due to chronic blood loss, while an elevated white blood cell count may suggest active inflammation or secondary infection. Inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often elevated in active disease but may be normal in mild or localized inflammation [48][49][50]. Fecal markers, including fecal calprotectin and lactoferrin, serve as noninvasive indicators of intestinal inflammation and can help differentiate inflammatory bowel disease (IBD) from irritable bowel syndrome (IBS). Elevated fecal calprotectin levels correlate with mucosal inflammation and may be useful in monitoring disease activity and response to treatment. Stool studies are essential to exclude infectious causes of colitis, particularly in patients with acute symptoms. Bacterial stool cultures, Clostridioides difficile toxin assays, and tests for ova and parasites should be performed to rule out infectious etiologies [51][52].

Clostridioides difficile infection can mimic or exacerbate DUC, and its identification is crucial for appropriate management. Cytomegalovirus (CMV) colitis should be considered in immunocompromised patients or those with refractory disease. CMV infection can be detected through polymerase chain reaction (PCR) testing of stool samples or histopathological examination of colonic biopsies with immunohistochemical staining. Though not the primary diagnostic tool for DUC, imaging studies may be useful in specific situations [53][54]. Abdominal radiographs are generally not required unless there is suspicion of complications such as toxic megacolon. Computed tomography (CT) and magnetic resonance imaging (MRI) enterography can help assess the extent of colonic inflammation and rule out other abdominal pathology. While cross-sectional imaging is more commonly used in Crohn’s disease, it may be employed in severe UC cases to evaluate disease extent and detect complications such as perforation or abscess formation [55[[56].

Differentiating DUC from other causes of colitis is a critical step in diagnosis. The differential diagnosis must consider inflammatory conditions such as Crohn’s, infectious, ischemic, and microscopic colitis (see Table 2). Crohn’s disease can affect any part of the gastrointestinal tract and is characterized by skip lesions, transmural inflammation, and granuloma formation. Unlike UC, Crohn’s disease often involves perianal disease, fistulae, and strictures [57][58]. Infectious colitis, caused by bacterial, viral, or parasitic pathogens, typically presents with acute onset diarrhea, fever, and systemic symptoms. Fecal leukocytes and stool cultures can help differentiate infectious colitis from DUC. Ischemic colitis primarily affects older adults with cardiovascular risk factors and is characterized by sudden onset abdominal pain and hematochezia. Endoscopic findings in ischemic colitis include segmental inflammation, pale mucosa, and ulcerations in watershed areas such as the splenic flexure [59][60]. Histologically, ischemic colitis demonstrates lamina propria hemorrhage, crypt withering, and submucosal edema rather than the chronic inflammatory changes seen in DUC. Microscopic colitis, including collagenous and lymphocytic colitis, presents with chronic watery diarrhea but lacks the endoscopic findings of UC. Histopathology reveals increased intraepithelial lymphocytes and a thickened subepithelial collagen band in collagenous colitis [61].

The presence of rectal sparing or patchy inflammation in a patient suspected of having DUC should raise the possibility of an alternative diagnosis. Crohn’s disease, infectious colitis, and medication-induced colitis can present with segmental involvement. In some cases, DUC may evolve into more extensive UC over time, necessitating repeat colonoscopy and reassessment of disease extent. In addition to diagnosing DUC, assessing disease severity is crucial for guiding treatment decisions [62][63]. The Truelove and Witts criteria classify UC severity based on clinical and laboratory parameters. Mild disease is characterized by fewer than four daily bowel movements, minimal rectal bleeding, and normal inflammatory markers.

Moderate disease presents with more frequent bowel movements, mild anemia, and slightly elevated inflammatory markers. Severe disease is defined by more than six bloody stools per day, systemic symptoms such as fever and tachycardia, and significant anemia requiring transfusion [64][65]. Endoscopic severity scoring systems, such as the Mayo endoscopic subscore, objectively measure disease activity. A score of 0 indicates normal mucosa, while scores of 1, 2, and 3 correspond to mild, moderate, and severe inflammation, respectively. Mucosal healing, a Mayo score of 0 or 1, is an important treatment goal associated with better long-term outcomes. Noninvasive biomarkers, including fecal calprotectin and lactoferrin, have been increasingly used to assess disease activity and predict relapse [66][67]. Elevated fecal calprotectin levels correlate with active inflammation and can help differentiate between ongoing disease activity and functional symptoms. Regularly monitoring fecal biomarkers allows for early relapse detection and treatment optimization before clinical deterioration occurs.

International Guidelines for Distal Ulcerative Colitis Management:

The American College of Gastroenterology (ACG), the European Crohn's and Colitis Organisation (ECCO), the British Society of Gastroenterology (BSG), and the World Gastroenterology Organisation (WGO) all provide structured recommendations on the diagnosis, treatment, and follow-up of DUC. While these guidelines share common principles, they differ in specific treatment recommendations, approaches to disease severity classification, and the emphasis on patient-centered care [68][69]. The ACG guidelines prioritize a stepwise approach to managing DUC, starting with topical therapies for mild disease and escalating treatment based on severity (see Table 3).

The ECCO guidelines emphasize a stratified approach based on disease extent and severity while integrating emerging evidence on novel therapies. The BSG guidelines incorporate similar principles but emphasize risk stratification and individualized patient care. The WGO guidelines, developed for a global audience, highlight the need for cost-effective and resource-sensitive strategies, particularly in low- and middle-income countries where access to advanced therapies may be limited [70][71]. All four guidelines recommend that the initial assessment of DUC should involve a combination of clinical symptoms, endoscopy, histopathology, and laboratory markers. The ACG emphasizes distinguishing DUC from other causes of colitis, recommending stool studies to rule out infections, particularly Clostridioides difficile, which can mimic or exacerbate disease symptoms. The ECCO guidelines align with this approach but incorporate fecal calprotectin as a biomarker to differentiate inflammatory from functional disorders [1][2].

The BSG guidelines advocate for a thorough diagnostic workup, including endoscopic and histologic confirmation of disease extent. The WGO, recognizing the variability in healthcare access worldwide, advises that in resource-limited settings, a clinical diagnosis based on symptoms and simple laboratory tests may be necessary when endoscopy is unavailable. In terms of treatment initiation, the guidelines universally recommend topical mesalamine (5-aminosalicylic acid, 5-ASA) as the first-line therapy for mild to moderate DUC [4][5]. The ACG specifies that rectal mesalamine suppositories are preferred for proctitis, while mesalamine enemas are more effective for more extensive distal disease. Combination therapy with oral and rectal 5-ASA is encouraged for better symptom control. The ECCO guidelines echo this recommendation, highlighting that rectal 5-ASA is superior to rectal corticosteroids for inducing remission. The BSG guidelines support this approach but also discuss the role of adherence challenges, particularly in younger patients, and suggest alternative strategies for those who struggle with topical therapies. The WGO acknowledges the efficacy of mesalamine but also highlights the potential limitations in access to rectal formulations in lower-income regions, where oral therapy may be the only feasible option [9][10]. For patients with moderate to severe DUC or those who do not respond to 5-ASA therapy, escalation to corticosteroids is recommended by all guidelines. The ACG advises using rectal corticosteroids for patients with persistent symptoms and systemic corticosteroids for those with more extensive disease. The ECCO guidelines emphasize that systemic corticosteroids should only be used for remission induction, not as long-term maintenance therapy.

The BSG guidelines similarly discourage prolonged steroid use, highlighting the risks of steroid dependence and the need for steroid-sparing strategies [11][12]. The WGO recommends budesonide rectal foam as an alternative to conventional corticosteroids, recognizing that systemic corticosteroids may not be viable in all healthcare settings due to cost and side effects. When it comes to maintenance therapy, all guidelines agree that patients with DUC who achieve remission should continue on long-term therapy to prevent relapse. The ACG recommends rectal mesalamine as the preferred maintenance treatment, with oral mesalamine or sulfasalazine as alternative options [13][14]. The ECCO guidelines suggest that patients in remission of rectal mesalamine should continue therapy at the lowest effective dose. The BSG guidelines support these recommendations and discuss patient education's role in improving adherence to maintenance therapy. The WGO acknowledges the challenges of long-term medication adherence, particularly in regions where medication supply may be inconsistent, and advises that patients should be educated about the importance of continued treatment even in the absence of symptoms [15].

The guidelines differ in their approach to advanced therapies for patients with refractory disease who do not respond to standard therapies. The ACG recommends considering immunomodulators such as azathioprine or biologic therapies such as anti-TNF agents (infliximab, adalimumab) for patients with corticosteroid-dependent or refractory disease. The ECCO guidelines similarly advocate for biologics in patients with chronic active disease but also discuss the role of newer agents such as vedolizumab and ustekinumab [16][17]. The BSG guidelines provide additional guidance on selecting biologic agents, recommending that disease severity, patient comorbidities, and prior treatment response guide treatment decisions. The WGO, recognizing the cost limitations of biologics in many parts of the world, suggests that thiopurines and methotrexate may be more feasible alternatives in low-resource settings. Surgical management is addressed in all guidelines as a last resort for patients with medically refractory DUC or those who develop complications such as dysplasia or cancer. The ACG recommends proctocolectomy with ileal pouch-anal anastomosis (IPAA) as the preferred surgical option for patients with severe disease who fail medical therapy [18][19].

The ECCO guidelines provide detailed recommendations on surgical indications, emphasizing the importance of early referral to colorectal surgeons for patients with high-risk diseases. The BSG guidelines highlight the need for shared decision-making between patients and clinicians regarding surgical options, acknowledging that some patients may opt for a permanent ileostomy rather than IPAA. The WGO, recognizing the variability in surgical expertise worldwide, advises that patients in resource-limited settings should be referred to specialized centers whenever possible. All guidelines emphasize the importance of colorectal cancer surveillance in patients with longstanding DUC [20][21]. The ACG recommends that patients with more than eight years of disease undergo regular colonoscopic surveillance with biopsies to detect dysplasia. The ECCO guidelines provide specific recommendations on surveillance intervals based on individual risk factors, such as disease duration, extent, and family history of colorectal cancer. The BSG guidelines support risk-stratified surveillance, advocating for more frequent monitoring of patients with additional risk factors. The WGO advises that where access to regular colonoscopy is limited, noninvasive biomarkers and stool-based screening tests may be considered alternative surveillance strategies [22][23].

Patient-centered care is a common theme across all guidelines, strongly emphasizing shared decision-making, mental health support, and quality-of-life considerations. The ACG guidelines stress the importance of discussing treatment options with patients and addressing concerns about medication side effects. The ECCO guidelines recognize the impact of DUC on mental health and recommend that psychological support be integrated into patient care [24][25[. The BSG guidelines highlight the role of patient advocacy groups in providing education and support. The WGO acknowledges the need for culturally sensitive approaches to patient education and encourages the development of community-based support programs (Table 3). The ACG and ECCO guidelines provide detailed recommendations on biologics, reflecting the increasing availability of these therapies in North America and Europe. The BSG guidelines align closely with these recommendations but place greater emphasis on individualized treatment strategies. The WGO, by contrast, focuses on practical and cost-effective approaches that can be applied globally, recognizing that access to biologics remains limited in many regions [26][27].

Regional Variations in DUC Management:

In many parts of sub-Saharan Africa, Latin America, and South Asia, the diagnosis of DUC is often delayed due to insufficient endoscopic facilities and trained gastroenterologists. In settings where colonoscopy is not readily available, physicians rely on clinical presentation and empirical treatment, leading to misdiagnoses or inadequate management [28][29]. The absence of routine fecal calprotectin testing further complicates disease monitoring, as patients may be treated based on symptom severity rather than objective markers of inflammation (see Table 4). In these regions, the reliance on symptom-based diagnosis increases the risk of undertreatment or overtreatment, which has significant implications for disease progression and quality of life [30][31]. The lack of histopathological confirmation in some areas results in the inappropriate use of antibiotics for presumed infectious colitis, delaying appropriate anti-inflammatory treatment.

Additionally, limited access to routine laboratory monitoring prevents early detection of medication-induced side effects, increasing the likelihood of complications related to long-term corticosteroid use and immunosuppressive therapy. In contrast, healthcare systems in high-income countries have established structured care pathways for DUC, focusing on early diagnosis, personalized treatment strategies, and multidisciplinary management [32][33]. Patients in these regions benefit from access to advanced endoscopic techniques, biomarkers for disease monitoring, and a wide range of treatment options, including newer biologics and small-molecule drugs. Regular follow-ups with gastroenterologists, dietitians, and mental health professionals allow for comprehensive disease management, improving adherence to therapy and overall outcomes. Moreover, patient education programs and support groups enhance disease awareness, empowering individuals to manage their condition actively [34][35].

However, even in well-resourced settings, disparities in healthcare access persist, particularly among low-income populations and minority communities, where insurance coverage, medication affordability, and health literacy influence treatment adherence. Regional variations in the affordability and availability of medications significantly impact treatment decisions. In many low-resource settings, mesalamine—the first-line therapy for DUC—is prohibitively expensive, leading physicians to prescribe sulfasalazine, which is more affordable but associated with a higher risk of adverse effects. Although sulfasalazine remains a viable alternative, its side effects, including nausea, headache, and male infertility, often result in poor adherence [36][37]. The high cost of rectal formulations, such as mesalamine suppositories and enemas, limits their use despite their proven efficacy in treating distal disease. Patients who cannot afford these medications frequently resort to oral therapies alone, which may be less effective in achieving mucosal healing. The unavailability of topical corticosteroids in many regions also forces physicians to prescribe systemic steroids for mild-to-moderate disease, increasing the risk of steroid dependence and associated complications such as osteoporosis, hyperglycemia, and adrenal suppression [38][39].

The use of immunomodulators such as azathioprine and methotrexate is similarly restricted by cost and the need for regular laboratory monitoring. In settings where access to routine blood tests is limited, clinicians may hesitate to prescribe these agents due to concerns about hepatotoxicity, myelosuppression, and increased infection risk. This challenge is particularly evident in rural healthcare facilities, where follow-up care is inconsistent, and patients may be unable to travel long distances for periodic bloodwork [40]. In contrast, biologic therapies such as infliximab and adalimumab remain largely unavailable in low-resource settings due to their exorbitant cost and complex administration requirements. While biosimilars offer a more affordable alternative, their adoption is still limited in many regions due to regulatory hurdles, supply chain issues, and a lack of physician familiarity with these agents. As a result, patients with refractory disease in low-income countries often have no option other than prolonged corticosteroid use or colectomy, both of which significantly impact the quality of life [41][42]. Surgical management of DUC also varies by region, with significant disparities in access to experienced colorectal surgeons and postoperative care. In well-resourced settings, colectomy with ileal pouch-anal anastomosis (IPAA) is the preferred surgical approach for medically refractory disease, offering patients the possibility of disease remission while preserving bowel continuity. However, in many low-income countries, colectomy is often performed as a last resort, with limited availability of specialized surgical teams to perform IPAA.

As a result, patients undergoing colectomy in these settings may receive a permanent ileostomy, which can have profound psychological and social implications [43]. The lack of access to ostomy care nurses and affordable ostomy supplies further exacerbates the challenges faced by patients, leading to poor stoma care and complications such as peristomal skin irritation, dehydration, and nutritional deficiencies. Beyond medical and surgical interventions, dietary management of DUC differs across regions due to cultural dietary practices and economic constraints. In high-income countries, patients can access dietitians who provide personalized nutritional guidance based on evidence-based recommendations. Specialized diets, including low-residue and elimination, are often employed to minimize symptom exacerbation and improve gut health. However, in resource-limited settings, dietary modifications are often dictated by economic factors rather than medical advice [44]. Many patients cannot afford specialized diets and rely on staple foods that may not be optimal for disease management. Additionally, misconceptions about diet and DUC persist in many communities, leading to the adoption of unproven or restrictive diets that may result in malnutrition. The role of traditional and alternative medicine in disease management is also more pronounced in certain regions, with many patients seeking herbal remedies or traditional healers due to skepticism about conventional medicine or distrust in healthcare institutions. The burden of mental health disorders among patients with DUC is another aspect of care that varies widely by region. In high-income countries, integrated care models incorporate mental health support, recognizing the high prevalence of anxiety and depression among individuals with chronic inflammatory bowel disease (Table 4) [45][46].

Access to psychological counseling, psychiatric care, and peer support groups plays a crucial role in addressing the psychosocial impact of DUC. However, in many low-resource settings, mental health services are severely underdeveloped, and the psychological burden of chronic disease is often overlooked. Patients struggling with depression and anxiety may not receive adequate support, leading to decreased adherence to treatment and lower overall quality of life. Cultural perceptions of mental health also influence help-seeking behaviors, with the stigma surrounding psychiatric conditions preventing many patients from seeking professional care [47][48]. Workplace and social challenges faced by DUC patients also differ across regions. In countries with robust labor protections, patients have access to workplace accommodations, medical leave policies, and disability benefits that allow them to manage their disease while remaining employed. In contrast, in low-income settings where labor protections are weak or nonexistent, patients with DUC may face job insecurity, workplace discrimination, or loss of income due to frequent absences. The financial burden of chronic disease management often forces patients to prioritize work over health, leading to delayed treatment and poorer outcomes [49][50][51].

The impact of healthcare policies and government initiatives on DUC management cannot be ignored. Countries with universal healthcare systems provide broader access to diagnostic services and treatments, reducing disparities in disease management. In contrast, many patients cannot afford necessary care in regions with predominantly out-of-pocket healthcare systems. This leads to reliance on suboptimal treatments or unregulated over-the-counter medications [52]. The availability of patient assistance programs and non-governmental organizations supporting inflammatory bowel disease (IBD) care varies widely, influencing the level of support that patients receive.

Patient Perspectives in Ulcerative Colitis Management:

Patient-centric perspectives, including medication adherence challenges and the broader effects of UC management on quality of life, are essential in optimizing care. Adherence to prescribed treatment regimens is often influenced by multiple factors, including medication side effects, dosing complexity, cost, and personal beliefs about illness and treatment [45][46]. Studies have shown that non-adherence in UC can be as high as 40%, leading to increased relapse rates, hospitalizations, and a higher likelihood of colectomy. A common barrier to adherence is the frequency and mode of drug administration. Oral therapies, such as mesalamine, often require multiple daily doses, which can be challenging for patients to integrate into their daily routines. The burden is even greater for those requiring rectal therapies, such as enemas or suppositories, which many patients find inconvenient or socially uncomfortable [47][48].

In addition to the logistical difficulties associated with medication use, side effects also contribute to poor adherence. Immunomodulators like azathioprine and methotrexate can cause nausea, fatigue, hepatotoxicity, or myelosuppression, discouraging consistent use. Biologic therapies, while effective, introduce concerns regarding infections, infusion reactions, and the long-term risks of malignancy. Patients undergoing treatment with Janus kinase (JAK) inhibitors or sphingosine-1-phosphate receptor (S1PR) modulators may experience adverse effects such as headaches, gastrointestinal disturbances, or increased risk of thromboembolic events, further complicating adherence [49][50]. Addressing these concerns requires shared decision-making between patients and healthcare providers, ensuring that patients are adequately informed about the benefits and risks of each therapy. Regular follow-up appointments, medication counseling, and patient education programs can help mitigate adherence challenges and improve disease outcomes. The financial burden of UC management is another significant factor influencing treatment adherence and quality of life. The cost of biologic and small-molecule therapies is particularly high, often making these options inaccessible for patients without comprehensive insurance coverage.

Even in healthcare systems with subsidized medication programs, indirect costs such as transportation to infusion centers, time off work, and additional dietary modifications or supportive care expenses contribute to financial strain [51][52]. Patients who cannot afford their prescribed medications may resort to dose reduction, delayed administration, or complete discontinuation, leading to disease flares and complications. Affordability concerns underscore the need for policies that expand access to cost-effective treatments, including biosimilars and patient assistance programs. Beyond medication adherence, UC significantly affects the quality of life in various domains, including physical well-being, mental health, social interactions, and professional life. The unpredictable nature of UC symptoms, characterized by intermittent flares of diarrhea, rectal bleeding, abdominal pain, and fatigue, disrupts daily activities and creates emotional distress [53]. Many patients report heightened anxiety and depression stemming from the uncertainty of flare-ups and concerns about disease progression. Studies have shown that individuals with UC have a higher prevalence of psychiatric comorbidities than the general population, emphasizing the need for integrated mental health support in UC care.

The psychological impact of UC is further compounded by the stigma associated with bowel disorders. Patients often feel embarrassed discussing their symptoms or seeking medical attention, leading to delays in diagnosis and treatment. Social isolation is a common consequence, as individuals may avoid public outings, long commutes, or social gatherings due to concerns about urgency and incontinence [54]. This isolation severely contributes to diminished self-esteem and reduced overall life satisfaction. Addressing these psychosocial aspects requires a holistic approach, incorporating psychological counseling, peer support groups, and cognitive-behavioral therapy to help patients cope with the emotional burden of UC. Dietary considerations are another critical factor in patient experience and quality of life. While no single diet has been universally proven to control UC, certain food triggers can exacerbate symptoms. Many patients experiment with dietary modifications, such as low-residue diets, gluten-free regimens, or specific carbohydrate diets, to reduce inflammation and manage symptoms. However, restrictive eating patterns can lead to nutritional deficiencies, weight loss, and disordered eating behaviors [55].

The role of dietitians in UC management is vital, as they provide evidence-based guidance on maintaining a balanced diet while minimizing symptom exacerbation. Emerging research on the gut microbiome and its role in UC pathogenesis has fueled interest in probiotics and microbiota-targeted therapies. While some studies suggest that probiotic supplementation can improve symptoms and reduce relapse rates, the evidence remains inconclusive, and more robust clinical trials are needed to determine its efficacy. For patients with refractory UC, the prospect of surgery introduces additional concerns about body image, postoperative complications, and long-term quality of life. Colectomy with ileal pouch-anal anastomosis (IPAA) is the most common surgical intervention for UC, offering the possibility of disease resolution but also introducing new challenges such as pouchitis, altered bowel habits, and fecal urgency. Patients undergoing IPAA often experience a period of adaptation, during which bowel frequency and consistency fluctuate [56][57]. Despite these adjustments, most patients report improved quality of life following surgery, particularly those who have struggled with debilitating symptoms for years. However, the decision to undergo colectomy is complex and requires thorough counseling about the risks, benefits, and potential need for additional surgical procedures.

Reproductive health is another important but often overlooked aspect of UC management. Women with UC may face concerns about fertility, pregnancy complications, and medication safety during gestation. Active disease at the time of conception has been associated with increased risks of miscarriage, preterm birth, and low birth weight. Certain medications, such as methotrexate, are contraindicated in pregnancy due to teratogenic effects, necessitating careful preconception planning [58][59]. Biologic therapies, including anti-tumor necrosis factor (TNF) agents, are generally considered safe during pregnancy, but their long-term effects on fetal development remain an area of ongoing research. Pregnancy counseling should be integrated into routine UC care, providing patients with the information needed to make informed decisions about family planning. Fatigue is another common yet underappreciated symptom in UC, often persisting even in periods of clinical remission. Chronic inflammation, anemia, sleep disturbances, and medication side effects contribute to persistent fatigue, significantly affecting work productivity and daily functioning. Many patients describe fatigue as one of the most debilitating aspects of UC, interfering with personal relationships, career aspirations, and overall well-being [60][61].

Addressing fatigue requires a multifaceted approach, including optimizing disease control, treating anemia when present, and implementing lifestyle interventions such as structured exercise programs and sleep hygiene practices. Employment and career prospects can also be adversely affected by UC. Many patients struggle with maintaining full-time employment due to the need for frequent medical appointments, sick days during flares, or unpredictable symptom onset. Workplace accommodations, such as flexible work schedules or remote work options, can help patients manage their condition while remaining professionally engaged [62]. However, employer awareness and understanding of UC-related challenges vary, and some patients face discrimination or job insecurity due to their health condition.

Legal protections, such as disability rights and workplace accommodations, ensure that individuals with UC can continue to work without undue hardship. The role of patient advocacy organizations in supporting UC patients cannot be overstated. Groups such as the Crohn's & Colitis Foundation provide valuable resources, including educational materials, support networks, and funding for research initiatives to improve treatment options. These organizations also advocate for policy changes that enhance access to care, reduce healthcare disparities, and promote research into novel therapeutics. Involvement in patient advocacy groups empowers individuals with UC, fostering a sense of community and providing platforms to share experiences and insights [63][64][65].

Special Considerations:

Pregnancy presents a special consideration in DUC management, as disease activity can impact both maternal and fetal outcomes. Women with active DUC during conception or pregnancy have a higher risk of complications, including preterm birth, low birth weight, and fetal growth restriction. Maintaining remission is crucial, as uncontrolled inflammation poses more significant risks than most DUC treatments. Mesalamine is considered safe during pregnancy, but corticosteroids should be used cautiously due to potential adverse effects on fetal development. Biologic therapies, such as infliximab and adalimumab, have been used safely during pregnancy, though careful monitoring is necessary [66][67].

Pregnant patients should be closely managed by a team of gastroenterologists and obstetricians specializing in high-risk pregnancies to ensure optimal maternal and fetal health. Pediatric DUC patients require distinct management strategies due to differences in disease behavior, growth considerations, and treatment responses. Children with DUC may present with more extensive disease involvement than adults, and their treatment must account for growth and development. The impact of chronic inflammation on growth velocity, bone health, and puberty requires careful monitoring. Corticosteroid use should be minimized in pediatric patients due to the risk of growth suppression and bone demineralization [68][69]. Exclusive enteral nutrition (EEN) has been explored as a steroid-sparing approach, though its efficacy in ulcerative colitis remains less established than in Crohn's disease. Pediatric patients, including pediatric gastroenterologists, dietitians, and psychologists, benefit from a multidisciplinary care team to address medical and psychosocial challenges. The elderly population with DUC presents another set of challenges, as aging-related factors can influence disease progression, treatment response, and medication tolerance. Older patients are more susceptible to adverse effects of corticosteroids, including osteoporosis, muscle atrophy, and increased infection risk [70][71]. Immunosuppressive and biologic therapies must be used cautiously due to the heightened risk of infections and malignancies.

Additionally, polypharmacy is a concern in elderly patients, as drug interactions with other common medications, such as anticoagulants and antihypertensives, may complicate treatment. Physicians must balance the benefits of aggressive therapy with the risks associated with immunosuppression in older adults. Regular bone density monitoring and fall prevention strategies should be part of the management plan for elderly patients receiving long-term corticosteroids or immunosuppressants. Fertility considerations are another important aspect, particularly for patients undergoing long-term treatment with immunosuppressive agents [72][73]. While mesalamine and biologics do not appear to impact fertility, thiopurines and methotrexate significantly can have teratogenic effects and should be discontinued in patients planning conception. Patients should receive preconception counseling to ensure safe medication use and disease stability before pregnancy. For men receiving thiopurines, concerns about sperm quality have been raised, though the evidence remains inconclusive. Fertility preservation strategies should be discussed with patients considering long-term therapy with potentially gonadotoxic medications [74].

**Limitations, Future Directions, and Multidisciplinary Care**

This patient's history is based on an original case observed and managed by the authors at our clinic. A 38-year-old male with a three-year history of left-sided ulcerative colitis presented with worsening rectal bleeding, tenesmus, and nocturnal urgency despite maintenance therapy with mesalamine. His disease had been relatively well controlled, but he had experienced two previous flares requiring corticosteroids. He was hemodynamically stable on examination, with mild tenderness in the left lower quadrant. Laboratory tests revealed mild anemia (Hb 11.2 g/dL) and elevated fecal calprotectin (550 μg/g). Flexible sigmoidoscopy demonstrated active inflammation in the rectosigmoid region, with moderate ulcerations and loss of vascular pattern.

Biopsy confirmed active colitis without dysplasia. Given his steroid dependence and inadequate response to conventional therapy, a decision was made to initiate combination therapy with rectal mesalamine and azathioprine. His symptoms improved significantly within eight weeks, with endoscopic reassessment showing mucosal healing. This case underscores the importance of an individualized, multidisciplinary approach in managing DUC, particularly in steroid-dependent cases. Despite robust evidence supporting current therapeutic strategies, potential biases in the reviewed literature must be acknowledged. Many randomized controlled trials (RCTs) focus on short-term efficacy, often spanning 6 to 12 weeks, with limited long-term follow-up data on relapse rates and sustained remission [75][76].

However, recent large-scale trials, such as the SELECTION and True North studies, have provided stronger evidence of emerging therapies' long-term efficacy and safety in moderate to severe UC [77][78]. Publication bias may favor studies demonstrating positive outcomes, while smaller, less favorable trials remain unpublished. Another limitation is the heterogeneity of patient populations across studies, with variations in disease severity, treatment history, and concurrent medications influencing outcomes. Observational studies, including real-world registry analyses, are increasingly shaping clinical practice, providing valuable insights into drug durability and patient-reported outcomes beyond RCTs. Emerging therapies, including Janus kinase (JAK) inhibitors, sphingosine-1-phosphate (S1P) receptor modulators, and microbiome-based treatments, represent significant advancements in DUC management. JAK inhibitors, such as tofacitinib, have demonstrated rapid remission induction in steroid-refractory cases, with data from the OCTAVE trials highlighting their efficacy in achieving mucosal healing [79]. Newer agents, such as upadacitinib and filgotinib, offer selective inhibition with potentially improved safety profiles, addressing concerns about thromboembolic events and infections associated with earlier JAK inhibitors.

Similarly, S1P receptor modulators, like ozanimod and etrasimod, modulate lymphocyte trafficking, reducing gut inflammation while preserving systemic immunity [80]. These therapies have gained regulatory approval based on phase III trials but require further long-term safety monitoring to define their role in treatment algorithms. Microbiome-based therapies, including fecal microbiota transplantation (FMT) and next-generation probiotics, are being explored as adjunct treatments, particularly in refractory cases. Clinical trials have shown promising remission rates with repeated FMT in mild to moderate UC, although its role in DUC remains under investigation [81]. Additionally, stem cell therapies, such as mesenchymal stem cell infusions, are being evaluated for their regenerative potential in chronic inflammation and mucosal healing. Early-phase trials suggest potential benefits, but larger studies are needed to establish efficacy and safety. Precision medicine approaches, including genomic and biomarker-driven treatment selection, hold promise for optimizing therapy by predicting individual responses to biologics and small-molecule drugs [82]. Another critical area requiring further research is the long-term monitoring of patients, particularly those at risk for complications such as colorectal cancer (CRC).

Chronic inflammation in DUC predisposes patients to dysplasia and malignancy, necessitating regular surveillance colonoscopies. Current guidelines recommend risk-stratified screening, with annual or biennial surveillance, based on disease duration, severity, and family history of CRC [83]. However, adherence to these guidelines remains suboptimal, often due to patient reluctance, resource limitations, or variations in physician recommendations. Advances in noninvasive monitoring, including stool DNA tests, gut microbiome signatures, and artificial intelligence-assisted endoscopic assessment, are being integrated into clinical workflows to enhance early dysplasia detection [84]. Future studies should explore strategies to improve surveillance adherence through patient education initiatives and risk-adapted screening algorithms. Multidisciplinary care is pivotal in optimizing outcomes for DUC patients, yet its implementation remains inconsistent across clinical settings. Effective management extends beyond pharmacologic interventions, encompassing dietary modifications, psychological support, and surgical considerations when necessary.

Gastroenterologists, colorectal surgeons, dietitians, and mental health professionals must collaborate to develop individualized treatment plans tailored to patient needs. For instance, patients with persistent symptoms despite optimal medical therapy may benefit from a dietary review, identifying potential triggers such as high-residue foods or poorly tolerated fiber sources [85]. Similarly, psychological interventions, including cognitive-behavioral therapy, have demonstrated efficacy in improving coping mechanisms and reducing disease-related anxiety [86]. Early surgical consultation is essential to discuss colectomy options and potential complications in severe or refractory cases. While proctocolectomy with ileal pouch-anal anastomosis (IPAA) remains the preferred surgical approach, it is not without risks, including pouchitis and altered bowel habits [87]. Recent advances in surgical techniques, including minimally invasive and robotic-assisted colectomy, have improved postoperative outcomes and reduced recovery times [88]. Additionally, research into optimizing pre- and postoperative microbiome modulation may help prevent complications such as pouchitis and dysbiosis-related relapse. Shared decision-making between the patient and a multidisciplinary team ensures that surgical timing aligns with quality-of-life considerations and disease trajectory.

**Conclusion**

The cornerstone of DUC management remains mesalamine-based therapy, with rectal formulations proving highly effective for inducing and maintaining remission. However, adherence to rectal therapy remains a significant barrier, requiring patient education, shared decision-making, and alternative strategies such as combined oral and topical regimens. For patients with moderate to severe disease or those refractory to standard therapy, corticosteroids, immunomodulators, and biologics offer additional therapeutic options. Despite these advancements, treatment selection should be guided by a balance between efficacy, safety, and long-term tolerability, particularly in vulnerable populations such as pregnant women, pediatric patients, and the elderly.

**Suggestion**

Healthcare disparities remain a significant barrier to optimal DUC management, particularly in low-resource settings where access to specialized care, advanced diagnostics, and biologic therapies is often limited. Many patients rely on symptomatic treatment rather than disease-modifying therapies due to cost constraints, leading to higher relapse rates and disease progression. The inconsistent availability of rectal mesalamine preparations further compounds these challenges, resulting in suboptimal treatment adherence. Addressing these gaps requires urgent action from healthcare policymakers, providers, and researchers. Governments and healthcare systems must prioritize cost-effective strategies, such as expanding access to generic formulations, implementing subsidy programs, and integrating telemedicine solutions to bridge the care gap. Digital health interventions can enhance patient education, improve adherence, and facilitate remote consultations, particularly in underserved areas. A concerted effort among stakeholders is essential to ensure equitable access to evidence-based treatments and improve outcomes for all patients with DUC.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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Figure 1: Diagnostic and Management Pathway for Distal Ulcerative Colitis

Patient presents with symptoms (rectal bleeding, urgency, tenesmus, diarrhea)

Clinical Evaluation (history, symptom assessment)

Physical Examination (abdominal tenderness, rectal exam)

Initial Laboratory Tests

CBC (anemia, leukocytosis)

CRP/ESR (inflammatory markers)

Fecal Calprotectin (intestinal inflammation)

Stool Tests (rule out infections)

Endoscopic Assessment (sigmoidoscopy/colonoscopy)

Characteristic Findings???

Yes → Proceed to Histology

No → Consider other diagnoses (e.g., infectious colitis, Crohn’s disease)

Histopathological Confirmation (crypt abscesses, mucosal inflammation)

Confirmed DUC Diagnosis

Assess Disease Severity

Mild to Moderate

First-line: Rectal Mesalamine ± Oral 5-ASA

Alternative: Rectal Steroids if refractory

Maintenance: Continued 5-ASA therapy

Moderate to Severe

Induction: Oral corticosteroids ± 5-ASA

Consider Biologics (TNF inhibitors, integrin inhibitors)

Maintenance: Biologics ± Immunomodulators

Refractory Disease

Advanced Therapies (JAK inhibitors, S1P modulators)

Surgery (proctocolectomy) in severe cases

Treatment Response???

Good → Continue Maintenance Therapy

Poor → Escalate Therapy (Biologics, Immunomodulators)

Refractory → Consider Advanced Therapies or Surgery

*Diagnostic and management pathway for distal ulcerative colitis, integrating clinical evaluation, laboratory testing, endoscopic assessment, treatment strategies, and therapeutic decision-making—source: Authors' Creations.*

**Table 1:** Our Key Findings and Treatment Algorithms for DUC

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Therapeutic Approach | Mechanism of Action | Indication | Efficacy Rates | Advantages | Limitations | Adverse Effects | Notable Studies | Future Directions |
| Aminosalicylates (5-ASA) | Anti-inflammatory (inhibits prostaglandins, leukotrienes) | Mild-to-moderate DUC | Remission: 64% (mesalamine enema at 8 weeks) | Topical formulations (suppositories, enemas) directly target mucosa | Less effective for extensive disease | Headache, nausea, nephrotoxicity (rare) | Meta-analysis of 67 RCTs [28] | Exploring novel formulations for enhanced delivery |
| Corticosteroids | Suppresses immune activation, reduces inflammation | Moderate disease, 5-ASA failure | Budesonide: 38-44% remission at 6 weeks | Rapid symptom relief | Not suitable for long-term use | Osteoporosis, adrenal suppression, hyperglycemia | Multicenter trial on rectal budesonide [30] | Investigating non-steroidal alternatives |
| Immunomodulators (Azathioprine, 6-MP) | Inhibits purine synthesis, reduces T-cell activity | Corticosteroid-dependent/refractory DUC | 55-60% steroid-free remission at 1 year | Long-term maintenance therapy | Delayed onset (3-6 months) | Myelosuppression, hepatotoxicity, infection risk | Observational study on azathioprine [2][30] | Personalized therapy using genetic testing |
| TNF-α Inhibitors (Infliximab, Adalimumab) | Blocks TNF-α, reducing inflammation | Moderate-to-severe DUC, steroid-refractory | Infliximab: 65% remission at 30 weeks | Effective in severe/refractory cases | High cost, loss of response over time | Infection risk, malignancy concerns | Landmark clinical trials [31] | Biomarker-driven therapy selection |
| Integrin Inhibitors (Vedolizumab) | Blocks α4β7 integrin, gut-specific immune modulation | Moderate-to-severe DUC, TNF failure | 57% remission at 52 weeks | Gut-selective, fewer systemic effects | Slower onset of action | Headache, nasopharyngitis, infusion reactions | Phase III trial [31] | Evaluating combination regimens |
| JAK Inhibitors (Tofacitinib) | Inhibits intracellular cytokine signaling | Moderate-to-severe DUC, biologic failure | 40-50% remission, rapid onset | Oral formulation, works after biologic failure | Risk of thromboembolism, lipid alterations | Thrombotic events, infections | Clinical trials on JAK inhibitors [32][33] | Assessing long-term safety |
| Fecal Microbiota Transplantation (FMT) | Restores gut microbiota balance | Refractory DUC | 30-40% remission | Non-drug, modulates microbiome | Standardization issues | Infection risk, variability in donor response | Systematic review of FMT trials [34] | Optimizing donor selection, administration routes |
| Surgical Intervention (IPAA) | Removal of diseased colon, anastomosis | Medically refractory cases, dysplasia | 80% good functional outcomes at 5 years | Curative for colonic disease | Risk of pouchitis, long-term complications | Pouch failure, bowel obstruction | Retrospective IPAA studies [4][6][34] | Advancements in minimally invasive techniques |
| Emerging Therapies (S1P Modulators, Stem Cells) | Modulates immune cell trafficking, promotes tissue repair | Treatment-refractory DUC | Preliminary efficacy similar to JAK inhibitors | Potentially safer than JAK inhibitors | Limited long-term data | Infection risk, unknown long-term effects | Early-phase clinical trials [35][36][37] | Expanding therapeutic options for refractory cases |

*DUC = Distal Ulcerative Colitis; 5-ASA = 5-Aminosalicylic Acid; TNF = Tumor Necrosis Factor; JAK = Janus Kinase; IPAA = Ileal Pouch-Anal Anastomosis; FMT = Fecal Microbiota Transplantation. Data sourced from referenced clinical trials and meta-analyses.*

**Table 2:** Diagnosis of Distal Ulcerative Colitis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Clinical Features | Endoscopic Findings | Histopathology | Laboratory Tests | Fecal Markers | Stool Studies | Imaging Studies | Differential Diagnosis | Severity Assessment |
| Rectal bleeding, diarrhea, tenesmus, urgency, mucus passage | Erythema, friability, loss of vascular pattern, ulcerations | Crypt distortion, basal plasmacytosis, crypt abscesses | CBC (anemia, WBC elevation), CRP, ESR | Fecal calprotectin, lactoferrin (elevated in active inflammation) | Stool cultures, C. difficile toxin, ova and parasites, CMV testing | CT/MRI enterography (for complications), abdominal radiograph (if toxic megacolon is suspected) | Crohn’s disease, infectious colitis, ischemic colitis, microscopic colitis | Truelove and Witts criteria, Mayo endoscopic subscore, fecal biomarkers |

*DUC diagnosis is based on clinical presentation, endoscopic findings, histopathology, laboratory tests, fecal markers, stool studies, imaging, differential diagnosis, and severity assessment—source: Authors' Creations.*

**Table 3:** International guidelines for distal ulcerative colitis (DUC) management across different organizations

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Aspect | ACG | ECCO | BSG | WGO |
| Approach to Disease Severity | Stepwise escalation from topical to systemic therapy | Stratified approach integrating novel therapies | Risk stratification and individualized care | Cost-effective, resource-sensitive strategies |
| Initial Assessment | Clinical symptoms, endoscopy, histopathology, stool studies to rule out infections | Similar approach with additional emphasis on fecal calprotectin | Comprehensive diagnostic workup including endoscopic confirmation | Symptom-based diagnosis in resource-limited settings |
| First-Line Therapy (Mild-Moderate) | Rectal mesalamine preferred; combination of oral and rectal 5-ASA encouraged | Rectal 5-ASA superior to corticosteroids for remission induction | Similar approach with emphasis on adherence challenges | Oral therapy may be the only feasible option in some regions |
| Escalation to Corticosteroids | Rectal corticosteroids for persistent symptoms, systemic steroids for extensive disease | Systemic corticosteroids for induction only, not for maintenance | Avoid prolonged steroid use, encourage steroid-sparing strategies | Budesonide rectal foam recommended as an alternative |
| Maintenance Therapy | Rectal mesalamine preferred, with oral mesalamine or sulfasalazine as alternatives | Continue rectal mesalamine at the lowest effective dose | Supportive of long-term adherence education | Educate on medication adherence despite supply inconsistencies |
| Advanced Therapies | Consider immunomodulators (azathioprine) and biologics (anti-TNF agents) | Use biologics for chronic active disease; newer agents like vedolizumab, ustekinumab discussed | Guidance on biologic selection based on severity, comorbidities | Thiopurines and methotrexate as cost-effective alternatives |
| Surgical Management | Proctocolectomy with IPAA for refractory disease | Early referral for high-risk patients emphasized | Shared decision-making on surgical options | Referral to specialized centers in resource-limited areas |
| Colorectal Cancer Surveillance | Colonoscopy with biopsy after 8 years of disease | Surveillance intervals based on risk factors | Risk-stratified approach with more frequent monitoring for high-risk patients | Stool-based tests as alternatives in areas with limited colonoscopy access |
| Patient-Centered Care | Shared decision-making, addressing medication concerns | Psychological support integrated into care | Role of patient advocacy groups in education and support | Culturally sensitive approaches and community-based programs |

*Adapted from the American College of Gastroenterology (ACG), European Crohn's and Colitis Organisation (ECCO), British Society of Gastroenterology (BSG), and World Gastroenterology Organisation (WGO) guidelines on distal ulcerative colitis management—source: Authors' Creations.*

**Table 4:** The regional variations in Distal Ulcerative Colitis (DUC) management

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Aspect | Sub-Saharan Africa, Latin America, South Asia | High-Income Countries | Impact | Common Challenges in Low-Resource Settings | Diagnostic Limitations | Medication Accessibility | Surgical Management | Dietary Considerations | Mental Health & Social Impact |
| Diagnosis | Delayed, symptom-based, limited endoscopy | Early diagnosis with endoscopy, biomarkers | Misdiagnosis & undertreatment | Limited endoscopic facilities, lack of trained gastroenterologists | No routine fecal calprotectin testing | Reliance on symptom severity rather than markers | N/A | N/A | N/A |
| Treatment Approaches | Empirical treatment, limited medication options | Personalized treatment, advanced drugs | Risk of overtreatment or undertreatment | No structured care pathways | Absence of histopathological confirmation | Misuse of antibiotics for suspected infectious colitis | N/A | N/A | N/A |
| Medication Access | Expensive mesalamine, reliance on sulfasalazine | Biologics, immunosuppressants available | Poor adherence due to side effects | Cost limits availability | Systemic steroids overused due to lack of rectal formulations | Limited access to lab monitoring for immunomodulators | N/A | N/A | N/A |
| Surgical Options | Colectomy as last resort, permanent ileostomy | Colectomy with IPAA for remission | Psychological burden of ileostomy | Limited colorectal surgeons | N/A | N/A | IPAA often unavailable | N/A | N/A |
| Dietary Management | Based on economic constraints, not medical advice | Dietitian-guided personalized plans | Poor disease control due to diet | Limited access to specialized diets | N/A | N/A | N/A | Reliance on staple foods, misinformation about diet | N/A |
| Mental Health Support | Limited, stigma surrounding psychiatric care | Integrated mental health services | High psychological burden | Lack of mental health services | N/A | N/A | N/A | N/A | Anxiety, depression affect adherence |
| Workplace & Social Impact | Weak labor protections, job insecurity | Accommodations, disability benefits | Treatment delays due to financial constraints | Workplace discrimination | N/A | N/A | N/A | N/A | Patients forced to prioritize work over health |
| Healthcare Policy Impact | Predominantly out-of-pocket healthcare | Universal healthcare access | Disparities in treatment affordability | Limited government support, few NGOs | N/A | N/A | N/A | N/A | Limited access to patient assistance programs |

*Regional disparities in DUC management stem from differences in diagnostic access, treatment availability, healthcare policies, and socioeconomic factors, which impact patient outcomes and quality of life—source: Authors' Creations.*