Economic Implications of Inflammatory Bowel Disease and Its Management

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Abstract

Crohn's disease and ulcerative colitis, the 2 most common inflammatory bowel diseases (IBDs), are chronic conditions with periods of exacerbation and remission. Patients with IBD experience clinical gastrointestinal (GI) symptoms, as well as the emotional burden that accompanies chronic conditions characterized by reduced quality of life and ability to work. With estimates of direct and indirect costs ranging between $14.6 and $31.6 billion in 2014, there is a significant healthcare burden associated with IBD. Although treatment expenses make up a significant portion of the cost of IBD, studies show that inappropriate treatment, lack of adherence to therapeutic regimens, or suboptimal treatment increase the cost burden. Costs for IBD include hospitalizations, the eventual need for surgery due to disease complications, and physician visits. The staggering economic burden of IBD makes early diagnosis, coupled with effective treatment at onset, imperative. Therefore, management of IBD must evolve beyond symptom control and toward sustained control of GI inflammation as measured by endoscopic, radiologic, and laboratory parameters.

Treatment advances have made deep remission a realistic target for some people with IBD. However, achieving deep remission requires a shift in the management paradigm of IBD, encouraging individualized treatment with biologics that focuses less on treating symptoms and more on preventing potential disease progression. Although expensive at onset, this management strategy may ultimately lead to decreased rates of surgeries and hospitalizations, potentially yielding lower long-term costs for treatment.

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Introduction

Inflammatory bowel disease (IBD) is a term applied to a group of idiopathic, chronic conditions that are characterized by inflammation of the gastrointestinal (GI) tract and a progressive course, which includes periods of exacerbations and remissions.[1,2] The 2 most common IBDs are Crohn's disease (CD) and ulcerative colitis (UC); both are distinguished by a dysregulated immune response. However, CD is typified by inflammation throughout the digestive tract, whereas UC is limited to the large intestine.[3,4] Approximately 1.17 million individuals in the United States currently have IBD, and the total number of patients with IBD increases by approximately 70,000 each year.[1,2]

Impact on Patients

Patients with IBD may experience a range of emotional responses to the unexpected GI exacerbations,[2] which can be painful, inconvenient, and embarrassing. Severe chronic conditions such as IBD can lead patients to feel anger or anxiety and can elevate stress, which, in turn, may cause flare-ups. The chronicity and progressive nature of the disease has been shown to increase disability, as well as reduce quality of life (QOL) and ability to work.[5]

Although the onset of IBD can occur at any age, the peak age for CD onset is 20 to 30 years, coinciding with the beginning of an individual's prime working years.[5,6] The peak age for UC is between 30 and 40 years.[5] The relentlessness of the illnesses, especially during periods of exacerbations, negatively affects various aspects of the patient's QOL, including their daily living, social and sexual lives, ability to work, and self-perception and body image.[5,7] Studies have shown that QOL worsens in association with disease severity, with lower QOL scores in patients with active disease compared with patients in remission.[8,9]

Economic Burden of IBD

The painful flare-ups of CD and UC cause a substantial economic burden on the healthcare system, including both direct and indirect expenditures. IBD ranks as 1 of the 5 most expensive GI disorders despite its being the lowest in prevalence among the list of GI disorders.[10] Based on pharmacoeconomic data from 2004 to 2008, the Crohn's & Colitis Foundation of America (CCFA) extrapolated cost data to the current prevalence estimates of CD and UC, and determined the total annual financial burden of IBD in the United States to be $14.6 to $31.6 billion in 2014.[2,6,11,12] However, recent longitudinal data and reimbursement information for CD indicate that total costs may significantly exceed these earlier estimates.[13]

After 30 years of disease, up to one-third of patients with UC will require surgery. Approximately 70% of patients with CD eventually require surgery, and 30% of these patients will experience recurrence within 3 years.[2] With an estimated 1.9 million physician visits, IBD was the eighth leading diagnosis for GI disorders in outpatient clinic visits in 2009,[14] an increase from a 2004 report that estimated IBD as the primary cause in 1.36 million physician visits.[15,16] Additionally, in 2009, IBD was the first-listed discharge diagnosis in over 100,000 hospitalizations—a 37% increase from discharge diagnoses in 2000. These hospitalizations resulted in 569,918 total hospital days, with a mean cost of $32,965 and aggregate costs of over $1 billion.[14] A year later, in 2010, the National Hospital Discharge Survey showed that the number of hospitalizations due to IBD more than doubled to 208,000.[18] However, hospitalizations make up only a portion of the costs associated with IBD.

Direct Costs

Direct medical costs include expenses for hospitalizations, physician services, prescription drugs, OTC drugs, skilled nursing care, diagnostic procedures, and other healthcare services.[11] In a study estimating the direct costs (based on insurance claims) in the United States, including inpatient, outpatient, and pharmaceutical services, Kappelman and colleagues estimated the overall annual direct costs of IBD treatment to be greater than $6.3 billion in 2004.[11] Based on current prevalence, extrapolated estimated costs in 2014 would be $11 to $28 billion.[2]

In 2004, CD was responsible for more than 800,000 first-listed ambulatory care visits (first-listed refers to the primary diagnosis), and more than 1 million all-listed visits (all-listed refers to any diagnosis other than the first-listed diagnosis).[16] Comparatively, UC was the primary cause of 500,000 ambulatory care visits and about 700,000 all-listed visits in the same year.

For hospital discharges, CD was the first-listed diagnosis for 57,000 stays; it was also mentioned as an additional diagnosis in another 100,000 discharges. Hospitalizations for UC were less common, with 35,000 first-listed discharge diagnoses and 82,000 all-listed diagnoses.[16] (See trends in **Figures 1A**[16] and **1B**[16]) These numbers increased in 2010 when hospital discharges numbered 187,000 for CD and 107,000 for UC.[17] An assessment of healthcare resource utilization and costs from 2003 to 2013 of privately insured US employees with UC showed that, compared with controls, patients with UC had substantially higher baseline hospitalization rates (16.9% vs 6.2%), emergency department visits (31.1% vs 22.0%), and prescription drug use (95.3% vs 72.0%). Overall, adjusted total direct costs were also substantially higher for patients with UC than their counterparts without ($15,548 vs $4812).[18]

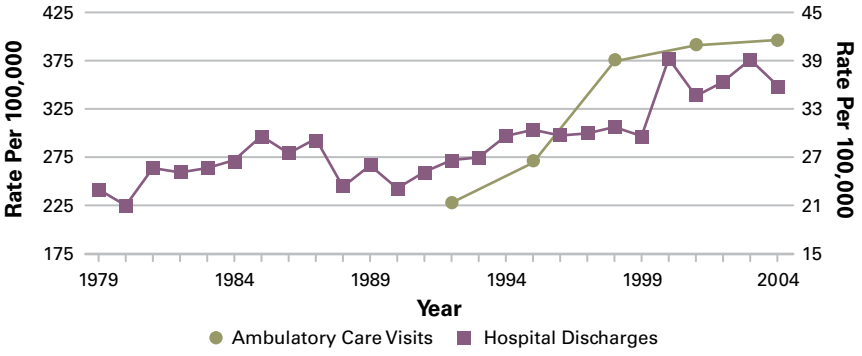
The impact of IBD on overall costs per patient has been evaluated individually and collectively for CD and UC. In patients with CD, an analysis of longitudinal data and health insurance claims data between 2011 and 2013 showed the mean health-plan paid cost per member per year was $18,637.[13] In patients with UC, a retrospective analysis of administrative data from 2004 to 2009 of 100 self-insured US employers revealed that mean annual all-cause total healthcare costs (inpatient, outpatient, and pharmacy claims) for patients with UC were $3821.44 higher than the matched control group (P <.001).[19] In a longitudinal analysis of data from the Medical Expenditure Panel Survey from 1996 to 2011, researchers examined healthcare expenditures of patients with CD or UC[20] and calculated annual mean expenditures per person were $10,364 for CD and $7827 for UC. These were significantly greater than the expenditures for individuals without IBD ($4314; P <.05). IBD-related costs were less for privately insured ($8014) compared with publicly insured patients ($18,067, P <.05). Inpatient care was the leading cost category; however, privately insured patients had higher costs for outpatient care, office-based care, and prescribed medicines.[20] A systematic review showed that treatment of CD cost almost 2 to 4 times as much in the United States as it did in other Western countries.[21,22] An analysis of data from the MarketScan database from 1999 to 2005 showed similar differences in cost for patients with UC in the United States compared with other Western countries.[6,21]

Indirect Costs

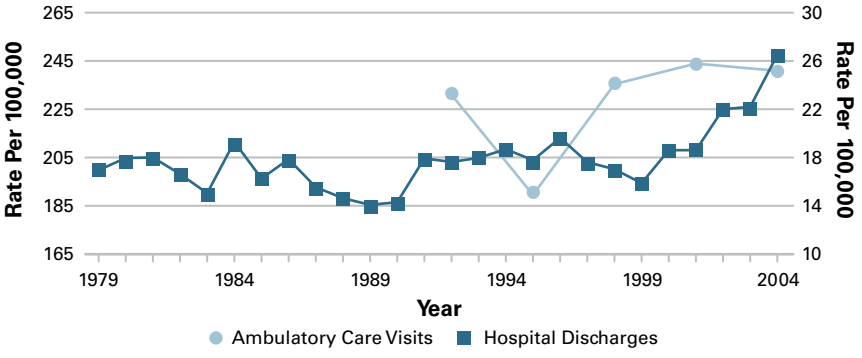
Indirect costs are the value of lost earnings or productivity; they may include the value of leisure time lost.[6] One study focused on the cost of IBD based solely on missed work days: Although the absence burden for employees with CD was not significantly different from matched controls, employees with CD did have a 2.5 times higher probability of receiving short-term disability benefits in the 12 months after diagnosis compared with controls (19.8% vs 7.3%, respectively; P <.01). The burden of short-term disability costs was $972 for people with CD; it was 2.5 times higher for those with the disease ($1627 per patient) compared with controls ($655 per patient) ($P$ <.01).[6] Employees with UC were 2.5 times more likely than controls to receive short-term disability benefits in the 12 months after diagnosis (15.4% vs 6.1%, respectively; P <.01). Based on data from the MarketScan database (1999-2005), the average cost burden for patients with UC was $1386 per year compared with $522 for controls—a difference of $864 per patient with UC per year (P <.01).[6] A later study, which used data from 100 self-insured US employers from 2004 to 2009, detected no differences in all-cause absenteeism costs (P = .834) or mean-annual all-cause short-term disability costs for patients with UC compared with matched controls (P = .283).[19] However, cost data from 2003 to 2013 of privately insured US employees with UC show that, compared with controls, patients with UC had substantially higher adjusted total indirect costs ($4125 vs $1961).[18]

Figure 1. Crohn's Disease and Ulcerative Colitis: Ambulatory Care Visits and Hospital Discharges[16]

A. Crohn's Disease: Age-Adjusted Rates of Ambulatory Care Visits and Hospital Discharges With All-Listed Diagnoses in the United States, 1979-2004



B. Ulcerative Colitis: Age-Adjusted Rates of Ambulatory Care Visits and Hospital Discharges With All-Listed Diagnoses in the United States, 1979-2004



Sources: National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (averages 1992-1993, 1994-1996, 1997-1999, 2000-2002, 2003-2005), and National Hospital Discharge Survey.

Changing Cost-Drivers

The increase in cost in IBD treatment over the past decade may be attributed to the changing cost-drivers in disease management. An economic analysis of data from 2004 shows that nonsurgical hospitalizations resulted in 20% of the total direct costs for either disease.[11] Outpatient services were responsible for 33% and 35% of direct costs, while pharmacy utilization was responsible for 35% and 28% of direct costs for CD and UC, respectively.[11] However, a more recent study of health-plan paid costs paid between 2011 and 2013 for CD suggests that inpatient care costs account for 23% of the total CD-attributable costs and pharmacy utilization constitutes 45.5%, which is almost twice as much as the inpatient costs (Figure 2[13]).

When all medications prescribed for IBD, including those not approved for IBD, were considered, mesalamine was the most costly and most frequently prescribed medication for CD and UC in 2004.[11,15] It was one of several oral aminosalicylates prescribed, accounting for 37% of all prescription costs for CD and almost 50% of all prescription costs for UC.[15] At least 2 claims for oral

aminosalicylates were reported for 39% of patients with CD and 43% of patients with UC.[11]

The evolution of treatment for CD and UC over the past decade, specifically the approval of more effective and more costly tumor necrosis factor (TNF) inhibitors, has changed the landscape of treatment and cost for IBD. Whereas the anti-inflammatory effects of these biologics have decreased acute care costs, including hospitalizations and emergency department visits, they have substantially increased pharmacy utilization costs. TNF inhibitors represented almost 30% of total costs and 65% of pharmacy-related costs for CD between 2011 and 2013. Thirty-two and a half percent of pharmacy costs were attributed to adalimumab and 27% to infliximab (Figure 2[13]). During this timeframe, mesalamine accounted for 10% of total pharmacy costs.[13]

Strategies for Cost Reduction

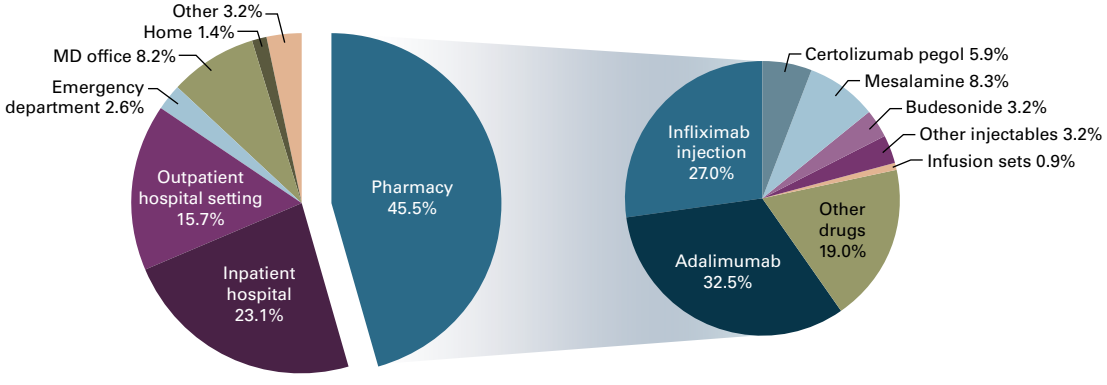
In recent years, pharmacy utilization and acute care costs have been the primary drivers of cost for IBD, but these costs can be curtailed with smarter prescribing and management strategies, especially for CD. Claims data for CD show that 80% of the total costs are attributed to 28% of the patients, with a significant correlation of costs per patient per year and comorbidities ($r = +0.30$; $P < .0001$), regardless of age ($r = 0.01$; $P = .65$).[13] This subgroup of 28% of patients utilized an average of $45,602 per patient per year, and 64% of their claims were associated with TNF inhibitor use. Similar to the overall CD population, TNF inhibitor costs accounted for one-third of total costs for the subgroup.[13] Implementing guidelines that recommend optimizing TNF inhibitor use may help limit these costs, especially in younger patients and those with comorbidities. Fifty-five percent of all patients with CD and 38% of those ≤20 years had at least one comorbidity.[13] Studies have confirmed that younger patients (those ≤20 years) had a disproportionately high use of healthcare resources for both CD and UC.[11,24] Therefore, strategies to streamline the cost of IBD need to focus on:

- Ensuring that all patients have access to treatment that is goal-oriented and effective, utilizing quality measures for overall effective care
- Avoiding high healthcare resource utilization by avoiding complications and comorbidities
- Optimizing treatment regimens based on individual patients, with the goal of long-term remission
- Improving treatment adherence and compliance

Access to Treatment

Guidelines and evidence demonstrating the need for appropriate treatment for cost-effective management explain that effective treatment must be initiated in the right patient at the right time; however, even if the appropriate patient is identified, access still remains an issue. Federal regulations, such as the Affordable Care Act and Medicare Part D regulations imposed by the Centers for Medicare & Medicaid Services, have provided measures to better ensure access for patients with IBD. Although reimbursement decisions are based on therapeutic value, cost-effectiveness, and burden of disease, millions of Americans are in health insurance plans that restrict coverage or reimbursement of specific drugs.[24] The reorientation of the healthcare delivery system around value for patients should require that

Figure 2. Health Plan Paid Costs by Cost-Driver Category and Pharmacy Costs for Crohn's Disease[13]



Adapted from Park KT, Colletti RB, Rubin DT, Sharma BK, Thompson A, Krueger A. *Am J Gastroenterol.* 2016;111(1):15-23.

Table. Physician Quality Reporting System: Effective Clinical Care for Inflammatory Bowel Disease[27]

Measure Title	Measure Description
Preventive Care: Corticosteroid-Sparing Therapy	Percentage of patients 18 years and older with a diagnosis of IBD who have been managed by corticosteroids doses ≥10 mg/day for 60 or more consecutive days to whom corticosteroid-sparing therapy has been prescribed in the last reporting year
Preventive Care: Corticosteroid-Related Iatrogenic Injury—Bone Loss Assessment	Percentage of patients 18 years and older with a diagnosis of IBD who have received corticosteroids doses ≥10 mg/day for 60 or more consecutive days and were assessed for risk of bone loss once per the reporting year
Preventive Care: Influenza Immunization	Percentage of patients 18 years and older with a diagnosis of IBD to whom influenza immunization was recommended, administered, or previously received during the reporting year
Preventive Care: Pneumococcal Immunization	Percentage of patients 18 years and older with a diagnosis of IBD to whom pneumococcal vaccination was administered or who had previously received
Testing for Latent Tuberculosis Before Initiating TNF Inhibitor Therapy	Percentage of patients 18 years and older with a diagnosis of IBD who were screened for tuberculosis and whose results were interpreted within 6 months prior to receiving a first course of TNF inhibitor therapy
Assessment of Hepatitis B Virus Status Before Initiating TNF Inhibitor Therapy	Percentage of patients 18 years and older with a diagnosis of IBD who had hepatitis B virus status assessed and results interpreted within 1 year prior to receiving a first course of TNF inhibitor therapy

IBD indicates inflammatory bowel disease; TNF, tumor necrosis factor.

insurers improve their subscriber's health, focusing on maximizing value over minimizing cost of individual interventions.[25] To make effective reimbursement decisions, managed care directors have to look at the overall picture, taking long-term costs into account along with therapeutic value, cost-effectiveness, and burden of disease. However, evidence suggests that some reimbursement decisions are being made based on immediate budget impact alone[26]; this results in many patients being denied access to coverage or reimbursement of specific drugs or classes of drugs.[26]

To ensure effective care of IBD and its complications and comorbidities, the Institute of Medicine (IOM) developed quality measures as metrics in reimbursement decisions.[27] Physicians and healthcare facilities are rewarded or penalized based on their ability to meet these quality measures; however, these metrics do not address the cost of meeting the high standards of quality care, nor do they provide recommendations to achieve treatment uniformity or remission. To supplement the IOM quality measures, the American Gastroenterological Association developed IBD-specific process measures for the Physician Quality Reporting System (Table[27]). From diagnosis to treatment and referral, these measures are intended to help reflect the processes of medical care, thereby addressing quality improvement efforts with immediate opportunities for quality assessment.[28] However, to be effective, quality measures need to be accompanied by guidance on achieving remission through strategic cost-effective treatment algorithms.

In an attempt to ensure optimal processing of patients, the CCFA developed process indicators for IBD.[28] Unlike academic guidelines that utilize the same set of published studies repeatedly, these indicators use the literature, as well as expert opinion and empirical knowledge.[28,29] They focus on quality improvement during treatment, surveillance, and maintenance. Although treatment with IBD needs to be individualized, optimal and cost-effective care of IBD that leads to long-term remission requires guidance to ensure that effective and appropriate care is administered throughout the continuum of IBD.

The process indicators for treatment of IBD regulate that[28]:

- If a patient with IBD is initiating anti-TNF therapy, then tuberculosis risk assessment should be documented and tuberculin skin testing or interferon-gamma release assay should be performed; and risk assessment for hepatitis B virus should be documented.
- If a patient with IBD requires at least 10 mg of prednisone (or equivalent) for 16 weeks or longer, then an appropriately dosed corticosteroid-sparing agent or operation should be recommended.
- If a hospitalized patient with severe colitis does not improve within 3 days of treatment with intravenous corticosteroids, then sigmoidoscopy with biopsy should be performed to exclude cytomegalovirus and surgical consultation should be obtained.
- If a patient in whom a flare of IBD is suspected with

new or worsening diarrhea, then the patient should undergo testing for *Clostridium difficile* infection at least once.
- If a patient with IBD is initiating azathioprine/6-mercaptopurine, then thiopurine S-methyltransferase (TPMT) testing should be performed before starting therapy.

The process indicators for surveillance of IBD regulate that[28]:
- If a patient with UC is found to have confirmed low-grade dysplasia in flat mucosa, then proctocolectomy or repeat surveillance within 6 months should be offered.
- If a patient with extensive UC or CD involving the colon has had disease for 8 to 10 years, then surveillance colonoscopy should be performed every 1 to 3 years.
- If a patient with UC (of any duration) has coexisting primary sclerosing cholangitis, then surveillance colonoscopy should be performed annually.

The process indicators for maintenance of IBD regulate that[28]:
- If a patient with IBD is on immunosuppressive therapy, then provide education about appropriate vaccinations, including an annual inactivated influenza vaccine and a pneumococcal vaccine with a 5-year booster, and general avoidance of live-virus vaccines.
- If a patient with CD is an active tobacco smoker, then smoking cessation should be recommended and treatment should be offered or suitable referral provided at least annually.

Avoiding Complications and Comorbidities

In a given year, approximately 20% of patients with UC have active moderate or severe disease and 50% are in remission. Seventy percent of those with active disease of any severity and 30% of those in remission will have episodes in the following year.[2] For CD, 55% of patients currently in remission will have a relapse over the next year and 11% will have chronically active disease.[2] Some data show that 10% of patients with CD have prolonged remission.[30] Maintaining remission is the key to reducing total costs; ineffective management of remission is directly associated with increases in hospitalizations and costs.

Flare-ups during active disease can result in complications beyond the signs and symptoms of IBD itself. Complications of CD can result in fistulas, strictures, abscesses, perforated bowel, and/or malabsorption and malnutrition.[2] An analysis of published literature has shown that about half of all patients with CD experience an intestinal complication within 20 years of diagnosis.[30] In particular, the development of fistulas is associated with significantly greater hospital and surgery costs, as well as higher median healthcare costs and overall resource utilization rates.[31]

Complications of UC include heavy, persistent diarrhea that may be accompanied by rectal bleeding and pain, perforated bowel, and toxic megacolon.[2] Compared to patients with mild or moderate UC, total healthcare costs for patients with severe UC were double ($12,154 and $12,731 vs $26,875, respectively). Inpatient costs were more than 4 times higher for those with severe disease ($3235 and $2244 vs $13,516, respectively).[32] A more recent assessment of healthcare resource utilization and costs from 2003 to 2013 showed that, compared with controls, patients with UC had significantly higher baseline comorbidity rates. Those with moderate to severe disease had significantly higher hospitalization rates (26.5% vs 6.2%) and adjusted total direct costs ($23,085 vs $4932) than those with milder disease.[18] In patients with CD, those with fistulas had a higher total median cost per patient compared with those without fistulas: $10,863 versus $6268. These costs were mainly driven by longer hospital stays and higher surgery costs.[31] Optimizing treatment strategies that favor long-term remission is critical in reducing healthcare resource utilization and bringing down the cost of IBD.

Optimizing Treatment Strategies

There are limited real-world data regarding initial treatment selections, therapy changes, and the costs of suboptimal treatment; however, payers, providers, and other healthcare decision makers need that data to properly assess available therapies. Until the data are available, it is incumbent upon healthcare providers to remember that improving patient outcomes is the goal of therapy.

IBD treatment with 5-acetylsalicylic acid (5-ASA) compounds is appropriate for mild to moderate disease and tends to be less expensive than treatment with immunomodulators or biologics.[21] Although mesalamine is the most commonly prescribed agent in this class,[15] early treatment failure can cost an average of $11,500 per patient, and other agents in this class may be equally, or more effective, with lower total long-term costs.[33] This long-term view should be taken into consideration when

prescribing 5-ASA compounds for UC. However, these agents are not as cost-effective in patients with moderate or severe CD and should not be considered for maintenance treatment in these patients.[21]

Although there has not been any analysis evaluating the cost-effectiveness of immunomodulators in recent years, the potential for serious immunosuppressive and/or hepatotoxic adverse effects (AEs) requires routine screening and monitoring, which may become costly. Screening of metabolites, compared with monitoring of red blood cell mean corpuscular volume, is especially expensive.[21] Screening for TPMT before starting immunomodulators is a common practice to prevent potentially life-threatening AEs; this alone may cost from $3861 to $7142.[35]

Approved biologics for IBD, which are the most expensive yet most effective options for IBD, include TNF inhibitors such as infliximab and adalimumab. Depending on the individual dose, in 2006, the cost of infliximab, the most effective agent in this class, ranged from $1900 to $4000 per infusion.[21] The cost of adalimumab was approximately $2000 to $2500 per dose. Priced at $3100 and $5100, respectively, golimumab and certolizumab were the most expensive per dose.[21,35] These costs do not include charges for administration of the infusion, which average $2800 per infusion for commercial insurers.[21,36] Studies from the United Kingdom show that, depending on the patient's weight and length of treatment, infliximab may be cost-effective in the long run.[37,38] Studies in the United States have been inconclusive as to the cost-effectiveness of this class of agents.[21]

In patients with CD, adalimumab may be more cost-effective than infliximab.[39,40] However, the data on individual response and loss of response to treatment is less clear because of varying dosing strategies.[21] Over a 2-year study period, the mean total costs associated with the initiation of natalizumab, infliximab, and adalimumab were $68,372, $62,090, and $61,796, respectively. However, patients taking natalizumab also had the highest mean time spent in remission while on treatment: 4.5 months compared with 2.4 months for infliximab and 2.9 months with adalimumab.[41] When reviewing existing or future therapies for formulary inclusion, it is important for managed care professionals to weigh the cost versus benefit of such treatments, keeping long-term cost-effectiveness in mind.

Because of anti-TNF use, pharmacy utilization costs for CD exceed costs for inpatient care, resulting in higher total healthcare costs. Anti-TNF agents alone accounted for nearly one-third (29.5%) of total costs. According to a study comparing the cost sharing for anti-TNF agents in a commercially insured CD population, patients initiating self-injectables incurred higher out-of-pocket (OOP) costs compared with patients initiating infusions, even though the infusions were still more costly overall. One possible reason could be changes in benefit design, such as increased cost sharing. Of the infusion cohort, 55.7% had cost sharing versus 97.9% of the self-injectables cohort (P <.0001). The average annual OOP costs were $1278 for infusion medication compared with $1609 for self-injectables.[42]

With the increasing use of anti-TNF therapy in IBD, a shift of costs has been observed with medication costs replacing hospitalization and surgery as the greatest source of healthcare expenditure. In a study exploring the impact of the use of anti-TNF therapy on IBD-related costs from a societal perspective, the authors concluded that the proportion of anti-TNF–related healthcare costs increased over 2 years of follow-up, while hospitalization costs decreased. Even though the total costs remain stable, treatment with expensive biologic therapy can substantially increase patient OOP costs.[43] Where the recently introduced integrin receptor antagonists fit into the overall treatment paradigm still remains to be determined. Evaluation of their place in therapy will involve a review of published medical literature regarding efficacy and safety, as well as consideration of drug cost.

Ensuring Treatment Adherence

Optimal therapy in IBD has been shown to benefit not only the patient, but also the managed care organization. The cost of suboptimal therapy among patients with IBD is substantial. Each year, patients with UC and CD cost managed-care payers approximately $5066 and $8265, respectively[44]; these costs are even higher in patients with suboptimal therapy, with estimates at $12,679 for patients with UC and $18,736 for patients with CD based on an evaluation of claims data from January 1, 2011 through December 31, 2013.[42]

The effectiveness of treatments for IBD varies for each individual.[45] Attempts at treatment optimization often entail frequent dose escalation that may result in AEs or preemptive discontinuation of treatment. These initial treatment selections and changes have cost and efficacy implications because of suboptimal treatment. For example, switching from one TNF inhibitor to another has been shown to result in a loss of response due to anti-drug antibody formation.[43] A retrospective analysis of treatment patterns from commercial insurance

claims between 2006 and 2010 examined continuity of treatment, which included discontinuation, switch, dose escalation, augmentation, inadequate loading (for biologics), prolonged corticosteroid use (>3 months), surgery, or hospitalization. Researchers noted that augmentation was a common index therapy change (approximately 20% of 5-ASA initiators, 40% of corticosteroid and immunomodulators initiators, and up to 55% of biologics). Treatment was discontinued or interrupted in almost 50% of 5-ASA initiators. In patients with suboptimal therapy due to interruption in continuity of therapy, the mean all-cause total cost was significantly greater compared with patients without suboptimal care ($18,736 vs $10,878 in CD, P <.001; $12,679 vs $9653 P <.001 in UC).[44]

Ensuring optimal therapy is not always up to healthcare providers, and nonadherence plays an important role in suboptimal management of IBD. An analysis of published literature evaluating adherence to biologics in IBD showed that female gender, smoking, constraints related to treatment, anxiety, and moodiness were associated with nonadherence to biologics. Other predictors for nonadherence included concomitant immunomodulator use and more than 18 weeks since first infusion. Overall, adherence to anti-TNF therapy was 82.6%.[46] Recent studies have demonstrated that 5-ASA nonadherence in patients with UC is associated with more frequent flare-ups and significantly higher healthcare costs. Patients who were adherent to their 5-ASA treatment had 6.9% higher adjusted medication costs but 12.5% lower overall medical costs than nonadherent patients. The relative risk for a flare-up was also higher in nonadherent patients (3.65 to infinity) compared with adherent patients.[47]

In another study, data from the Maryland CareFirst BlueCross BlueShield program showed that nonadherence with 5-ASA was significantly associated with a 2-fold increase in GI-related inpatient costs (22.8% vs 11.7%; P <.01).[48] Nonadherent patients also had increased utilization of outpatient services and office visits. Overall, patients who were adherent to treatment incurred 12.5% lower medical costs (P = .03).[48] Focusing on educating patients to remain adherent to treatment, despite an alleviation of symptoms, is critical in maintaining the lower costs that result from effective therapy.

Conclusion

The significant direct and indirect healthcare costs associated with IBD make it imperative that patients be diagnosed early and treated effectively at onset. Assessing prognosis at an early stage of the disease is essential for the development of an appropriate and effective management plan, meaning one that prevents disease progression and worsening of symptoms. Unfortunately, a recent review of the treat-to-target approach in IBD revealed that setting appropriate therapeutic goals remains a challenge in IBD.[49] Current management programs aim at induction and maintenance of clinical remission, and prevention of disease-related and treatment-induced complications. However, clinical evidence increasingly points toward the persistence of inflammatory activity even in the absence of GI symptoms, resulting in the progressive accumulation of bowel damage, such as fistulae, abscesses, and strictures in CD, and fibrosis, dysmotility, and colorectal neoplasm in UC. As a result, management of IBD has to evolve beyond symptom control toward sustained control of GI inflammation measured objectively by endoscopic, radiologic, and laboratory parameters.

Advances in the treatment paradigm of IBD have made deep remission a realistic target for some patients with CD; however, achieving it may not be simple. A subgroup of patients, primary nonresponders, do not respond to therapy with a TNF inhibitor and show little or no change in symptoms or mucosal healing, but are exposed to the serious potential AEs of these therapies.[50] Another portion of patients, secondary nonresponders, experience a loss of response to TNF inhibitor treatment, necessitating dose intensification, which results in increased healthcare costs.[51,52] In fact, most patients experience a discontinuation or interruption of therapy, upward dose titration, or change of therapy.[44] However, initiating treatment early and adapting it to disease severity may prevent structural bowel damage in the long term. Treating with biologic therapies that go beyond addressing symptoms and prevent potential progression and achieve targeted or optimal patient outcomes will require a personalized approach based on the severity of IBD and the extent of the individual's disease state. Such a strategy may ultimately lead to decreased rates of surgeries and hospitalizations, potentially yielding lower long-term costs of treatment.[49]

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