

Value of Medicines for Inflammatory Bowel Disease

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) describes conditions with chronic or recurring immune response and inflammation of the gastrointestinal (GI) tract. The two main types of inflammatory bowel disease are ulcerative colitis (UC) and Crohn's disease (CD). UC specifically affects the large intestine whereas CD can affect any part of the GI tract.^{1,2}

Patients with IBD are often diagnosed in their teens and early 20s and may have manifestations of their illness beyond intestinal symptoms and gut dysfunction such as joint, skin, and eye conditions.³ These patients will face a lifetime of challenges related to the disease and its complications, including the effect of the disease on their psychological well-being and the ability to meet their individual needs for function and productivity.⁴ IBD is also a concern for older individuals. Approximately 10 to 30 percent of IBD cases are found in those over the age of 60.⁵

Symptoms of UC frequently include bloody diarrhea, weight loss, fatigue, cramp-like abdominal pain, severe urgency to have a bowel movement, and tenesmus (the feeling of incomplete evacuation).⁶ Symptoms of CD are similar and include recurring diarrhea, weight loss, abdominal pain and cramping, and a feeling of low energy.⁷

Chronic illnesses such as IBD can be emotionally burdensome. Symptoms of IBD can flare up unexpectedly and be painful, uncomfortable, inconvenient, and at times embarrassing. Patients with IBD have an increased risk of developing anxiety or depression, which in turn can contribute to IBD symptoms.⁸ IBD patients may also have elevated stress levels. Stressful situations, even those unrelated to the disease itself, may lead to flare-ups of symptoms creating a cycle of stress-flare up-stress.⁹ Patients also mention the invisibility of the illness can contribute to stress; accusations of faking or imagining symptoms can be demoralizing. In a recent study, patients identified four key IBD-related impacts on lifestyle: taking medication, restricting diet, modifying behaviors that triggered symptoms, and maintaining close proximity to toilets.¹⁰ These patients also noted significant negative impacts on work and relationships.

Ulcerative Colitis

Ulcerative colitis (UC) is a chronic disease that causes inflammation on the inner lining of the large intestine (or colon). Multiple other organ systems beyond the gastrointestinal tract in UC can be affected, including the bones and joints, skin, eyes, and lungs. The exact cause of UC is unknown. Researchers believe that factors such as an overactive intestinal immune system, genetics, and the environment may play a role. UC may start at any age; however, it is rare in children under the age of five. UC is more likely to develop between the ages of 15 and 30 years but can also develop in older individuals.¹¹ UC is most common in those of European descent, especially those descended from Ashkenazi Jews.¹² It is seen more commonly among people who have lived for generations in Eastern Europe and Russia. The condition is rarest among those of Asian descent but rates are increasing.¹³

Crohn's Disease

Crohn's Disease (CD) is a chronic IBD characterized by inflammation of the digestive or gastrointestinal (GI) tract. The exact cause of CD is also unknown. CD can affect any part of the GI tract, from the mouth to the anus, but it is more commonly found at the end of the small intestine where it joins the beginning of the large intestine (or colon). It can also affect the eyes, skin, and joints. CD is caused by a combination of factors involving genetics, the environment, and an overactive immune system. Like UC, CD may start at any age, but is most commonly seen in persons aged 20 to 29 years.¹⁴

KEY TAKEAWAYS

Approximately 1.2 million Americans and 2.5 to 3 million Europeans have inflammatory bowel disease.^{17,18}

Recent population-based studies indicate that incidence rates are accelerating in newly industrialized countries. Research suggests that the incidence of ulcerative colitis and Crohn's disease is rapidly rising in South America, Eastern Europe, Asia, and Africa.^{16,41}

The total annual direct cost for all patients with inflammatory bowel disease in the United States is estimated to be between \$11 billion and \$28 billion.²⁴

Advanced treatments for inflammatory bowel disease improve work productivity by 40 percent through decreases in both absenteeism and on-the-job impairments.³⁹

Prevalence

IBD has emerged as a global disease with estimated worldwide prevalence and incidence rates growing past 5 million people.¹⁵ New population-based studies indicate that incidence rates are accelerating in newly industrialized countries. Research suggests that the incidence of UC and CD is rapidly rising in South America, Eastern Europe, Asia, and Africa.¹⁶



Approximately
1.2 million
Americans have IBD.

Around
25% of patients
are diagnosed with IBD
before the age of 20.



There may be as many
70,000
children in the United States with
Inflammatory Bowel Disease.

See: www.cdfa.org/assets/pdfs/updatedibdfactbook.pdf

Rosen, M.I., Dhanraj, A., Saeed, S.A. (2016). "Inflammatory bowel disease in children and adolescents." *JAMA Pediatr.* 169(11):1053-60.

In 2009, approximately 1.2 million Americans had IBD, with as many as 70,000 of these being children (<20 years of age).^{17,18} An estimated 2.5 to 3 million people in Europe are affected by IBD.¹⁹

In Asia, the incidence of IBD is increasing. Between 1997 and 2006, the number of UC cases in Hong Kong nearly tripled to approximately six cases per 100,000 persons.²⁰ In Taiwan, the number of new UC and CD cases has increased by 4 percent each year between 1988 and 2008.¹⁶ The role of industrialization could play a role in the increasing trends; Seoul, the capital of South Korea, saw an yearly increase of approximately 10 percent for UC and 14 percent for CD between 1991 and 2005.¹⁶

In an analysis of trends over time, it was found that the burden of IBD is globally increasing over time but varies by region.^{21,16} The

Financial Costs

There are both direct and indirect costs associated with IBD.^{23,24} Direct medical costs include expenses for hospitalizations, physician services, prescription drugs, over-the-counter drugs, skilled nursing care, diagnostic procedures, and other healthcare services. Indirect costs include the value of lost earnings or productivity and the value of leisure time lost.



IBD has emerged as a global disease with estimated worldwide incidence rates surpassing

5 MILLION PEOPLE

The highest annual increase in new cases of UC include:

6 in Asia and the Middle East



per 100,000 persons annually.

19 in North America



24 in Europe



The highest number of IBD cases was also found in Europe with:



505 per 100,000
IN NORWAY

322 per 100,000
IN GERMANY

www.efcc.org/en/science.

Molodtsova, N.A., et al. (2012). Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterol.* 142(1):46-54.e42.

Hg, S.C., et al. (2017). Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *The Lancet.* 390:27 69-78.

highest annual increase in new cases of UC is in Europe with over 24 cases per 100,000 persons followed by over 19 per 100,000 in North America, and then roughly six per 100,000 persons in Asia and the Middle East. The highest number of cases was also found in Europe with 505 cases of UC per 100,000 persons (Norway) and 322 cases of CD per 100,000 persons (Germany).¹⁶ The number of existing cases in North America were approximately half that of Europe but CD prevalence rates were similar between Europe and North America. Specifically:

- In the U.S., 34 children per 100,000 persons have UC, while for adults the prevalence is 263 per 100,000 persons. It is estimated that 593,000 Americans have UC.²²
- The overall prevalence of CD in the U.S. pediatric population was 58 per 100,000. In the adult population, 241 persons per 100,000 have CD. It is estimated that 565,000 Americans have CD.²²

Direct Costs²⁴

- Studies have estimated the annual direct cost of UC in the U.S. is \$15,548 per patient per year.
- Studies have estimated the annual direct cost of CD in the U.S. is \$18,637 per patient per year.
- The total annual direct costs for all patients with IBD (both UC and CD) in the U.S. is estimated to be between \$11 billion to \$28 billion.



Annual Direct cost of UC in the U.S.

\$15,548 per patient

Annual Direct cost of CD in the U.S.

\$18,637 per patient

TOTAL ANNUAL DIRECT COSTS

for all patients with IBD
(including CD and UC) in the U.S.

\$11-\$28 Billion

Mehta, F. (2016). Economic implications of inflammatory bowel disease and its management. *Am J Manag Care*. 22:S51-60.

Indirect Costs

Based on a 2016 analysis of national health survey data, nearly 32 percent of symptomatic IBD patients reported being out of the workforce in a one-year period.²³ Indirect costs for UC and CD were 2.7 and 2.5 times higher than matched controls, respectively. Indirect costs for UC patients were \$1,386 per year and \$1,627 per year for CD patients.²⁴

Non-Adherence Costs

The effect of taking medications as properly prescribed can also influence the amount of healthcare resources used and their associated costs. For example, a claims study found that the costs for inpatient admissions among patients with ulcerative colitis were approximately twice as high for non-adherent patients (\$29,000) compared with adherent patients (\$14,500).²⁵

Treatment

There are two primary goals of medical treatment for UC and CD: achieving remission and maintaining remission. There are several approaches including medicine and surgery. Conventional therapies include anti-inflammatory drugs (e.g., 5-aminosalicylates) and corticosteroids, which are considered first-line therapies for most patients.²⁶ For mild to moderate UC, anti-inflammatory drugs are the primary therapy due to their established efficacy and safety. However, there are side effects associated with both of these therapies, especially in the elderly, and patient monitoring is essential to avoid long-term associated issues.²⁷

Benefits of Treatment

Newer advanced therapies (e.g., biologics, etc.) are considered a breakthrough in the management of IBD.²⁸ These therapies represent a major technological improvement over alternative therapies among moderate-to-severely active UC patients with 6 or 8-week response rates ranging from 50-70 percent.^{29,30,31,32} For moderate to severe disease when anti-inflammatory drugs are considered, many patients do not respond (19 to 58 percent of cases). In addition, some initial responders will discontinue therapy due to secondary loss of response (17 to 22 percent of cases), or develop intolerance (up to 48 percent).^{33,34} This loss of response underscores the need for new therapies. Research continues to develop more effective maintenance therapies for UC, and better treatments for severe, refractory, acute UC. Novel drugs are under development that will promote greater mucosal healing as well as control of the acute symptoms of the disease.³⁵

Real-world studies have shown that advanced therapy can improve specific symptoms as well as overall patient quality of life.³⁶ A recent review found that the risk of intestinal surgery following diagnosis has decreased significantly over the past six decades for both UC and CD. This change has been attributed to, among other factors, the availability of more efficacious treatments such as immunomodulators.³⁷

A review of eight advanced treatment intervention studies found that rates of absenteeism and presenteeism (on-the-job impairment) improved by 40 percent or more over the course of the study, with an absolute improvement of 7 to 15 percent in absenteeism and an absolute improvement of 15 to 20 percent in presenteeism.³⁸ Employed patients with controlled UC reported that approximately 10 percent of their work time was missed or rendered ineffective due to their UC. For employed patients with uncontrolled disease, this level of impairment varied between 20 (mild uncontrolled) to 50 (severe uncontrolled) percent.³⁹

Rates of Absenteeism and Presenteeism (on-the-job impairment)



Absenteeism

7-15% absolute improvement

Presenteeism

15-20% absolute improvement

Employed patients with controlled UC

10% work time missed or rendered ineffective

Employed patients with uncontrolled UC

20-50% work time missed or rendered ineffective

Blisch, K., et al. (2014). Sick leave and disability pension in inflammatory bowel disease: a systematic review. *J Crohns Colitis*. 8(11):1362-77.

Van Assche, G., et al. (2014). Different therapeutic approaches on quality of life in patients with inflammatory bowel disease. *BMC Gastroenterol*. 14:199.

Summary

Inflammatory bowel disease can be physically and emotionally devastating with patients reporting painful, inconvenient, and sometimes embarrassing symptoms. As the incidence of UC and CD has increased globally in the past few decades, so too have advances in the understanding of the immune system and in treatment options. The treatment of inflammatory bowel disease has evolved over the past decade due to the advent of therapies designed to target specific components of the immune system. Newer agents are more effective, increase productivity, and improve the quality of life for millions of people who suffer from IBD.⁴⁰

Endnotes

1. See: www.crohnscolitisfoundation.org/assets/pdfs/updatedibdifactbook.pdf.
2. Abdalla, M.I., et al. (2017). Prevalence and impact of inflammatory bowel disease: Irritable bowel syndrome on patient-reported outcomes in CCFA partners. *Inflamm Bowel Dis.* 23(2):325-31.
3. Vavricka, S.R., et al. (2015). Extraintestinal manifestations of inflammatory bowel disease. *Inflamm Bowel Dis.* 21(8):1982-92.
4. Marin-Jimenes, I., et al. (2017). Management of the psychological impact of inflammatory bowel disease: Perspective of doctors and patients - The ENMENTE Project. *Inflamm Bowel Dis.* 23(9):1492-8.
5. Taleban, S., et al. (2015). Inflammatory bowel disease and the elderly: A review. *J Crohns Colitis.* 9(6):507-15.
6. See: www.pamf.org/gastroenterology/conditions/inflammatory-bowel.html.
7. See: www.crohnsandcolitis.com/crohns/disease-symptoms.
8. Goodhand, J., et al. (2012). Mood disorders in inflammatory bowel disease: Relation to diagnosis, disease activity, perceived stress, and other factors. *Inflamm Bowel Dis.* 18:2301-09.
9. Mawdsley, J.E., and Rampton, D.S. (2005). Psychological stress in IBD: New insights into pathogenic and therapeutic implications. *Gut.* 54:1481-91.
10. Devle, J., et al. (2014). The burden of inflammatory bowel disease: A patient-reported qualitative analysis and development of a conceptual model. *Inflamm Bowel Dis.* 20(3):52.
11. See: www.niddk.nih.gov/health-information/digestive-diseases/ulcerative-colitis.
12. Kenny, E.E., et al. (2012). A genome-wide scan of Ashkenazi Jewish Crohn's disease suggests a novel susceptibility loci. *PLoS Genet.* 8(3):e1002559.
13. Ko, Y., Butcher, R., and Leong, R.W. (2014). Epidemiological studies of migration and environmental risk factors in the inflammatory bowel diseases. *World J Gastroenterol.* 20(5):1238-47.
14. See: www.niddk.nih.gov/health-information/digestive-diseases/crohns-disease/definition-facts.
15. See: www.efcca.org/en/science.
16. Ng, S.C., et al. (2017). Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *The Lancet.* 390:2769-78.
17. Koppelman, M.D., et al. (2013). Recent trends in the prevalence of Crohn's disease and ulcerative colitis in a commercially insured US population. *Dig Dis Sci.* 58:519-25.
18. Rosen, M.J., Dhawan, A., Saeed, S.A. (2016). Inflammatory bowel disease in children and adolescents. *JAMA Pediatr.* 169(11):1053-60.
19. Burisch, J., Jess, T., Martinato, M., and Lakatos, P.L. (2013). The burden of inflammatory bowel disease in Europe. *J Crohns Colitis.* 7(4):322-37.
20. Konkel, L. (2016). Inflammatory bowel disease in Asia. *Environ Health Persp.* 124(3):A49-54.
21. Molodecky, N.A., et al. (2012). Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterol.* 142(1):46-54.e42. See: www.ccfa.org/assets/pdfs/updatedibdifactbook.pdf.
22. See: www.crohnscolitisfoundation.org/assets/pdfs/updatedibdifactbook.pdf.
23. Petryszyn, P.W., et al. (2016). Costs in inflammatory bowel disease. *Prz Gastroenterol.* 11(1):6-13.
24. Mehta, F. (2016). Economic implications of inflammatory bowel disease and its management. *Am J Manag Care.* 22:551-60.
25. Mitro, D., Hodgkins, P., Yen, L., Davis, K.L., Cohen, R.D. (2012). Association between oral 5-ASA adherence and health care utilization and costs among patients with active ulcerative colitis. *BMC Gastroenterol.* 12:132.
26. Kornbluth, A., and Sachar, D.B. Practice Parameters Committee of the American College of Gastroenterology. (2010). Ulcerative colitis practice guidelines in adults: American Colleges of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol.* 105:501-23.
27. Nanne, K.H., et al. (2007). Dose-dependent influence of 5-aminosalicylates on thiopurine metabolism. *Am J Gastroenterol.* 102:2747-53.
28. Moss, A.C. (2015). Optimizing the use of biological therapy in patients with inflammatory bowel disease. *Gastroenterol Rep (Oxf).* 3(1):63-8.
29. Rutgeerts, P., et al. (2005). Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 353:2462-76.
30. Reinisch, W., et al. (2011). Adalimumab for induction of clinical remission in moderately to severely active ulcerative colitis: results of a randomised controlled trial. *Gut.* 60:780-7.
31. Sandborn, W.J., et al. (2014). Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis. *Gastroenterol.* 146:85-95.
32. Sandborn, W.J., et al. (2012). Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. *Gastroenterol.* 142:257-65.e1-3.
33. Gisbert, J.P., et al. (2015). Systematic review with meta-analysis: the efficacy of a second anti-TNF in patients with inflammatory bowel disease whose previous anti-TNF treatment has failed. *Aliment Pharmacol Ther.* 41(7):613-23.
34. Gordon, J.P., et al. (2015). Characterizing unmet medical need and the potential role of new biologic treatment options in patients with ulcerative colitis and Crohn's disease: a systematic review and clinician surveys. *Eur J Gastroenterol Hepatol.* 27(7):804-12.
35. Ulcerative Colitis; Decision Resources Pharmacor Study. November 2014.
36. Panés, J., et al. (2015). Randomized trial of tofacitinib in active ulcerative colitis: analysis of efficacy based on patient-reported outcomes. *BMC Gastroenterol.* 15:14.
37. Xu, J., et al. (2014). Different therapeutic approaches on quality of life in patients with inflammatory bowel disease. *BMC Gastroenterol.* 14:199.
38. Büsch, K., et al. (2014). Sick leave and disability pension in inflammatory bowel disease: A systematic review. *J Crohns Colitis.* 8(11):1362-77.
39. Van Assche, G., et al. (2016). Burden of disease and patient-reported outcomes in patients with moderate to severe ulcerative colitis in the last 12 months - Multicenter European cohort study. *Dig Liver Dis.* 48(6):592-600.
40. Seo, G.S., and Chae, S.C. (2014). Biological therapy for ulcerative colitis: An update. *World J Gastroenterol.* 20(37):13234-8.
41. Komm, M.A. (2017). Rapid changes in epidemiology of inflammatory bowel disease. *The Lancet.* 390:2741-2.