



Crohn's and Colitis
Foundation of Canada

Fondation canadienne des
maladies inflammatoires
de l'intestin



THE IMPACT OF INFLAMMATORY BOWEL DISEASE IN CANADA 2012 Final Report and Recommendations

mission

Find the cure.

vision

The Crohn's and Colitis Foundation of Canada (CCFC) believes that a cure will be found for Crohn's disease and ulcerative colitis. To realize this, the CCFC is committed, first and foremost, to raise increasing funds for medical research.

The CCFC also believes it is important to make all individuals with inflammatory bowel disease (IBD) aware of the Foundation, and educate these individuals, their families, health professionals and the general public about these diseases.

This report was commissioned by the CCFC and developed under the guidance and input of an expert Steering Committee.

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ABOUT THE CROHN'S AND COLITIS FOUNDATION OF CANADA

The Crohn's and Colitis Foundation of Canada (CCFC) is a volunteer-based registered charity dedicated to finding cures for Crohn's disease and ulcerative colitis, collectively referred to as inflammatory bowel disease (IBD). To achieve our mission, the Foundation is committed to raising funds for medical research. Medical research is the best hope for finding a cure for, and improving the lives of, persons affected with Crohn's disease or ulcerative colitis.

The CCFC invests in IBD research, education and awareness and is Canada's top funder of cure-directed research. As of July 2012, the CCFC has invested more than \$76 million in IBD research and is the world leader in non-governmental funding per capita of such research. The CCFC has more than 65,000 supporters, including volunteers in approximately 80 local groups across Canada.

Due to the research investments made by the CCFC and others, significant progress has been made in understanding the fundamental biology of the intestine and the genetic and environmental contributors to inflammatory bowel disease. Much work, however, remains in order to find cures and to continue to improve the quality of life for all those living with IBD.

In 2011, the Board of Directors of the CCFC committed to advancing three specific public policy priorities: increase government funding for IBD research and awareness; ensure timely and equitable access for IBD medications and treatments; and improve public bathroom access for those living with IBD. The CCFC has taken a leadership role in advancing these priorities, and is committed to working with key stakeholders to address the recommendations highlighted in this report.

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EXECUTIVE SUMMARY

Inflammatory bowel disease (IBD) is a group of disorders that causes sections of the gastrointestinal tract to become severely inflamed and ulcerated. An abnormal response of the body's immune system plays a role in each of the two main forms of IBD; namely Crohn's disease (CD) and ulcerative colitis (UC). In the absence of a cure, current therapies are directed at achieving and maintaining freedom from symptoms. Most people require ongoing medication; when this fails, surgery is often required. These are lifelong diseases, usually starting in early adulthood in otherwise healthy, active individuals. CD and UC also occur in children and IBD is increasingly being diagnosed in young children. IBD severely impacts quality of life through ongoing debilitating symptoms, reduction in ability to work, social stigma, management of bathroom access issues, difficulty with physical intimacy, and restriction in career choices.

People with IBD in Canada

There are approximately **233,000 Canadians living with IBD**: 129,000 with CD and 104,000 with UC. Over 10,200 new cases are diagnosed every year – 5,700 with CD and 4,500 with UC. Canada has among the highest reported prevalence (number of people with CD or UC) and incidence rates (number of new cases per year) of IBD in the world. The prevalence of IBD currently in Canada is nearly 0.7%, equating to more than **1 in every 150 Canadians**. IBD can be diagnosed at any age, but has a typical age of onset in the twenties. Incidence of IBD has been rising, particularly since 2001, and significantly so in children under the age of 10 years. An estimated 5,900 Canadian children have IBD. People with IBD have an elevated risk of developing colorectal cancer. People with CD face a significantly elevated risk of premature death (47% higher) than the general public. IBD is more than twice as common as multiple sclerosis or Parkinson's disease; about as common as Type I diabetes or epilepsy; and somewhat less common than other chronic diseases such as schizophrenia or rheumatoid arthritis. Compared to the general population, quality of life in IBD is low across all dimensions of health.

Economic Costs of IBD

Economic costs for IBD are conservatively estimated at **\$2.8 billion in Canada in 2012 (over \$11,900 per person with IBD every year)**. Direct medical costs totalled over \$1.2 billion and are dominated by medications (\$521 million), followed by hospitalizations (\$395 million), and physician visits (\$132 million). Costs are higher for CD than for UC, due to more frequent hospitalizations and greater use of newer, expensive drugs. Indirect costs (to society and to the patient, including loss of productivity) are greater than direct medical costs: over \$1.6 billion in 2012. Indirect costs are dominated by lower labour participation rates (long-term work losses of \$979 million), followed by patient out-of-pocket expenses (\$300 million) and then short-term work absences (\$181 million). Indirect costs are similar between CD and UC.

Areas of Greatest Challenge

In addition to the tremendous impact that IBD has on quality of life, people living with IBD often face many other challenges in the current environment. These include lack of awareness of IBD as a chronic disease, late or inappropriate diagnosis, inequitable access to health care services and expensive medications, diminished employment prospects and limited community-based supports.

Recommendations

The Crohn's and Colitis Foundation of Canada recommends:

- Increased funding for cure-related and epidemiological IBD research, and research addressing the physical, psychological and social issues surrounding IBD.
- Greater investment in IBD research and commercialization strategies that will expedite translation of academic-based research discoveries into clinical application in humans.
- Recognition of IBD as a national health priority and increased resource allocation for chronic care models that reflect the episodic nature of IBD and optimize healthcare delivery.
- Education programs and a national public health campaign be developed and implemented to raise awareness and knowledge among health care professionals to facilitate earlier diagnosis, increase awareness and reduce social stigma associated with IBD.
- Public and private sector programs that will foster open access to bathroom facilities for people with IBD.
- Timely and appropriate access to gastro-intestinal (GI) specialists, allied healthcare professionals, endoscopy and radiology for those Canadians waiting for diagnosis or treatment of IBD.
- Enhanced and harmonized public and private drug plans so that patients with IBD - no matter where they live in Canada, their age or their socio-economic status - have better access to medically-prescribed pharmaceuticals that improve the health and quality of life.
- Improved drug review processes so therapies of benefit to people with IBD are approved and available more quickly.
- Fair insurance access and policies for people with IBD, reflecting the episodic nature and partial genetic basis of IBD; further research is needed in this area.
- Appropriate income security measures and employer programs for people whose IBD may otherwise prevent them from being fully or partially employed or presents them with unreasonable financial burdens.

Adults and children with living with IBD face a number of critical challenges. Moreover, the burden that IBD places on individuals, the healthcare system and society is significant and will continue to grow as the number of patients with IBD increases. To improve the current landscape of IBD in Canada, the CCFC calls upon government, media, the general public, and other key stakeholders to move these recommendations forward.



INTRODUCTION

KAYLYN HEINE

"I want you to know that you can still do stuff even though you are sick. You can still live a normal life when there is something you really like a lot."

**THIS IMPACT OF IBD REPORT
IS INTENDED TO COLLECT AND
COMMUNICATE INFORMATION
ON IBD WHICH IS RELEVANT
TO CANADA AND WHICH CAN
BE APPRECIATED BY THE LAY
PUBLIC.**

This work aims to raise awareness and understanding of IBD in Canada, resulting in new research opportunities and improved quality of life for people with IBD. This report builds on, updates, and extends the CCFC-commissioned report from 2008: *The Burden of Inflammatory Bowel Disease in Canada*.

BACKGROUND

Inflammatory bowel disease (IBD) is the name of a group of disorders that cause the intestines to become inflamed (red and swollen). The main forms of IBD are Crohn's disease (CD) and ulcerative colitis (UC). IBD has a tremendous impact on quality of life due to a host of devastating symptoms, as well as a substantial personal burden. In the broader community and among the families and coworkers of people with IBD, there is sometimes a lack of understanding of the disease and the intimate nature of symptoms. IBD usually starts in early adulthood (but may occur at any age) and is a lifetime disease. Although most people with IBD can lead full, productive lives with the use of medications and surgery, there is currently no cure for IBD.

In Canada, there is a lack of public awareness of the impact of Crohn's disease and ulcerative colitis. Raising awareness is important to reduce the social stigma that is common with these diseases, and to help individuals maximize their overall quality of life. A better public understanding of IBD can also help to raise and direct funds for research, which could lead to improved treatments, and ultimately, a cure.

The Crohn's and Colitis Foundation of Canada (CCFC) was established with a two-fold purpose. First, the CCFC believes cures will be found for IBD, and is committed to raising funds for research. Second, the CCFC believes it is important to make all individuals with IBD aware of the Foundation, and to educate all individuals affected by IBD, their families, and the general public about these diseases.

To fulfill this vision, it is essential to gather and share high quality, current and relevant information on IBD. In Canada, we are fortunate to have many top-level researchers, who have conducted some of the landmark research on IBD in the world – much of which has been funded by the CCFC and its partners. The work that they have completed and published in the scientific literature will increase our knowledge about these diseases, and ultimately lead to better treatments that will improve lives for all people living with IBD.

OBJECTIVE

This impact of IBD report is intended to collect and communicate information on IBD which is relevant to Canada and which can be appreciated by the lay public. This work aims to raise awareness and understanding of IBD in Canada, resulting in new research opportunities and improved quality of life for people with IBD. This report builds on, updates, and extends the CCFC-commissioned report from 2008: *The Burden of Inflammatory Bowel Disease in Canada*.

The different areas of information to be addressed in this report include:

- Background information on IBD;
- Occurrence of IBD (how many Canadians have IBD);
- Costs of IBD to the health care system, individuals and society;
- Non-financial costs of IBD (quality of life impact);
- Directions for future strategies.

METHODS

General Overview

This work builds on the existing high-quality scientific research on IBD in Canada – much of which has been funded by the CCFC to generate a single, publicly-accessible document exploring the comprehensive impact of IBD in Canada.

To undertake this review, a Steering Committee was formed, composed of academic experts in gastroenterology and health economics. The Steering Committee selected and defined the topics and provided overall research guidance. The report was researched and written by a third-party organization.

Steering Committee

A Steering Committee was formed, composed of the following members:

- Gastroenterologists:
 - o Eric Benchimol, MD, PhD, FRCPC, University of Ottawa
 - o Charles Bernstein, MD, FRCPC, University of Manitoba
 - o Alain Bitton, MD, FRCPC, McGill University
 - o Brian Feagan, MD, FRCPC, University of Western Ontario
 - o Subrata Ghosh, MD, FRCPC, FRCP(E), University of Calgary (Chair)
 - o Remo Panaccione, MD, FRCPC, University of Calgary

- CCFC Staff:
 - o Kevin Glasgow, MD, FRCPC, Chief Executive Officer
 - o Aida Fernandes, MBA, Chief Science and Education Officer
 - o Fiona Knight, MPPA, Manager, Public Policy & Stakeholder Relations
 - o Tina Smith, BA, Research & Education Assistant

The Steering Committee guided the activities of the project consultant, Angela Rocchi, MSc, Axia Research, and was responsible for determining the methodology and content of the report. The Steering Committee was also responsible for identifying appropriate research and data sources, reviewing and approving the report.

Overview

Disease background

General information about both CD and UC are presented to provide a background for the average reader about these diseases. Symptoms are described, followed by currently recommended treatment options (including medications and surgeries).

Epidemiology

Epidemiology is the science that examines the patterns and occurrence of disease. This section estimates the current number of individuals in Canada with CD and UC. Other aspects of epidemiology reported include: factors associated with getting the disease; the rate at which individuals are newly diagnosed with disease; the age of people with IBD; mortality associated with IBD and a comparison of results within Canada with other geographic areas.

Direct costs

Direct costs are incurred by the public health care system in Canada and include: medications, hospitalizations, surgeries, physician visits, emergency room visits, allied health care professional visits, laboratory tests and procedures, etc. The total Canadian cost was calculated by multiplying the amount that was used per person by the total number of individuals who have disease.

Indirect costs

Indirect costs are incurred by individuals and society outside of the health care system. Individuals incur costs such as: non-prescription medications; travel to medical appointments; care giving and household support. Society incurs costs for worker absences and loss of productivity associated with: short and long-term disability; reduced participation in the work force and death. Workforce absences are due to the individual with disease or a caregiver of the individual with disease (such as a parent). The total Canadian cost was determined by multiplying the costs per person by the total number of individuals who have disease.

Non-financial costs

IBD has substantial impact on quality of life, and causes considerable personal, emotional and social burden. It is not well accepted to place a 'price' or attach a cost to this impact of IBD. Instead, information on quality of life is discussed for individuals with IBD, without determining a specific cost for the severe impact of IBD.

Conclusions and recommendations

A final section was developed with two objectives: to place the Canadian experience of IBD in context with other diseases in Canada, by comparing costs for IBD from other countries and to develop a set of recommendations for the future of IBD in Canada.

Literature Review

For each section of this report, an extensive literature review was conducted to obtain the most recent and relevant research. Wherever possible, Canadian-based data and research were used. Scientific publications were the most important source for data. The scientific literature was searched using key words such as IBD, CD or UC plus costing, quality of life, or epidemiology. There was a focus on retrieving work that was set in Canada. Published literature was supplemented, where appropriate, by the expertise and unpublished research of the Steering Committee members.

Additional data sources were also used where appropriate. For example, information on the costs of prescriptions was obtained from electronic databases of prescription drug claims from insurance plans. Websites were also used, such as the Statistics Canada website to track the census population of Canada.

Strong and robust research has been conducted in Canada with respect to epidemiology, utilization of health care resources, productivity, patient costs, and quality life. On occasion, it was necessary to use non-Canadian research to supplement locally-derived data.

Analysis

Information from the various data sources was combined and converted into a burden of illness summary. First, it was necessary to determine best estimates for important factors, such as: the current number of individuals with IBD in Canada, the average per-person cost for medications and hospitalizations, and the average per-person costs in lost productivity. Where there was one particularly strong information source, it was used to generate the best estimate. For example, a landmark study has been published reporting on the number of people with IBD in Canada; this study was used as the primary data source for this factor. Where there were a number of different information sources, with differing results, the data were combined using statistical techniques to determine a best estimate. For example, there were ten different studies reporting international experiences of premature mortality with CD; these data were combined statistically to calculate a single best estimate of mortality risk.

Second, it was necessary to attach prices or costs to the amount of resources that are used for IBD. For example, studies would estimate the average number of hospitalizations or the average amount of lost productivity per person. This was multiplied by the total number of people with CD or UC to determine the total amount of resource utilization. Then, prices were determined for each element such as the cost of a hospitalization or physician visit, or the average wage rate. These prices were determined from public sources. Costs for health care resources were determined primarily from the Ontario health care system. Productivity losses were priced using the Canadian average wage rate as reported by Statistics Canada.

Costs were summed for a national total, but were also broken down by disease (CD versus UC) and by province.



BACKGROUND

KADE CLAYTON

"I was diagnosed with ulcerative colitis when I was just over 2 ½ years old. I spent the next 5 months in the hospital trying different medications and therapies to help stop the bleeding. We were set up to have surgery to remove my entire colon, but things improved for me at the very last moment."

INFLAMMATORY BOWEL DISEASE (IBD) IS THE NAME OF A GROUP OF DISORDERS THAT CAUSE THE INTESTINES TO BECOME INFLAMED AND ULCERATED. THE MAIN FORMS OF IBD ARE CROHN'S DISEASE (CD) AND ULCERATIVE COLITIS (UC).

Because the symptoms of CD and UC are similar, it is sometimes difficult to establish the diagnosis definitively. In fact, approximately 10% of colitis cases are unable to be defined as either UC or CD and are called IBD-type unclassified.

INFLAMMATORY BOWEL DISEASE

Both CD and UC are marked by an abnormal response by the body's immune system. Normally, the immune system protects the body from infection. In people with IBD, however, it reacts inappropriately. For unknown reasons, the immune system mistakes microbes, such as bacteria that are normally found in the intestines, as foreign or invading substances, and launches an attack. In the process, the body sends white blood cells into the lining of the intestines, where they produce chronic inflammation. These cells then generate harmful products that ultimately lead to ulcerations and bowel injury. When this happens, the patient experiences the symptoms of IBD.

Currently, there is no cure for CD; therapies focus on maintaining remission (freedom from symptoms) and achieving a normal quality of life. The approach is similar with UC, although UC technically can be 'cured' by surgical removal of the large intestine (although this option is reserved until medical therapy fails).

Although CD most commonly affects the lower end of the small intestine (the ileum) and the beginning of the large intestine (the colon), it may involve any part of the gastrointestinal (GI) tract. In UC, the GI involvement is limited to the colon (or, to a lesser extent, the stomach). In CD, all layers of the intestine may be affected; this can result in deep ulcers that go through the wall of the bowel completely. These ulcers can cause complications such as abscesses in the abdomen or can lead to the development of connections between the bowel and other organs (fistulas) -- for example, there can be connections between the small bowel and bladder (leading to recurrent urinary tract infections). CD is often discontinuous, with normal healthy bowel in between patches of diseased bowel. In contrast, UC affects only the superficial layers (the mucosa) of the colon in a more even and continuous distribution, which starts at the level of the anus. Differences between UC and CD are summarized in Table 1.¹

Patients experience symptoms such as abdominal pain, rectal bleeding, fatigue, vomiting, diarrhea, itchiness or irritation around the anus, flatulence, and bloating. Weight loss and anemia also pose significant problems. Additionally, the complications associated with IBD can affect a patient's bones (leading to osteoporosis), liver, skin, eyes, height and weight, and mental health (leading to depression or anxiety).

IBD is a lifelong disease, usually starting in early adulthood and increasingly diagnosed in childhood in otherwise healthy, active individuals. IBD can significantly impact the quality of life of the patient, their caregiver/s and family, workplace, and community. It can impact career choices, lead to reduced work hours, impact family planning decisions, and lead to income disparity and depression. There are also concerns involving ongoing drug treatment, recurrent hospitalizations and surgeries. IBD can also complicate travel, life and working arrangements due to the need for bathroom access.

People with IBD can lead generally normal lives most of the time, but with ongoing medication needs and occasional flares that may require hospitalization with surgery. The unpredictability of symptoms and the prospect of eventual surgery burden daily life. Finally, due to the intimate nature of the symptoms, there may be a stigma attached to the disease from family, friends and workplace colleagues.

Table 1: Comparisons of Characteristics of CD and UC

	CD	UC
Occurrence	More females than males All ages, peak onset 15-35 years	Similar for males and females All ages, usual onset 15-45 years
Symptoms	Diarrhea, fever, sores in the mouth and around the anus, abdominal pain and cramps, anemia, fatigue, loss of appetite, weight loss, pain and swelling in the joints	Bloody diarrhea, mild fever, abdominal pain and cramps, anemia, fatigue, loss of appetite, weight loss, pain and swelling in joints
Terminal ileum involvement	Common	Not
Colon involvement	Often	Always
Rectum involvement	Often	Always
Peri-anal disease	Common	Never
Distribution of Disease	Patchy areas of inflammation	Continuous area of inflammation but can be patchy once treated
Endoscopic Findings	Deep and snake-like ulcers	Diffuse ulceration endoscopic changes can be mild
Depth of inflammation	May be transmural, extending through or affecting the entire thickness of the wall of an organ or cavity deep into tissues	Shallow, mucosal
Fistulas between organs	Common	Never
Stenosis	Common	Rarely
Granulomas on biopsy	Common	Rarely
Surgical 'cure'	Often returns following removal of affected parts, decreased likelihood of pregnancy	Usually 'cured' by removal of colon (colectomy), decreased likelihood of pregnancy after ileoanal pouch
Treatment	Drug treatment (antibiotics sulfasalazine, corticosteroids, immune modifiers, biologic therapies) Diet and nutrition Surgery (repair fistulas, remove obstruction, resection and anastomosis)	Drug treatment (5-aminosalicylates, antibiotics sulfasalazine, corticosteroids, immune modifiers, biologic therapies) Surgery (rectum/colon removal) with creation of an internal pouch (ileoanal pouch)
Cure	No existing cures. Maintenance therapy is used to reduce the chance of relapse	Through colectomy only. Maintenance therapy is used to reduce the chance of relapse
Complications	Blockage of intestine due to swelling or formation of scar tissue, abscesses, sores or ulcers (fistulas), malnutrition	Bleeding from ulcerations, perforation (rupture) of the bowel, malnutrition
Smoking	Higher risk for smokers	Lower risk for smokers
Mortality risk	Increased risk of colorectal cancer and overall mortality	Increased risk of colorectal cancer. No change in mortality risk

CROHN'S DISEASE

As noted above, CD is a chronic (ongoing) disorder that causes inflammation of any area of the GI tract from the mouth to the anus, although it most commonly affects the small intestine and/or colon. The symptoms and complications of CD differ, depending on what part of the intestinal tract is inflamed. CD is classified as mild, moderate or severe based on the age at diagnosis, the location of the disease, and the disease behaviour (penetrating and/or stricturing [scarring] or neither).²

Symptoms

Persistent diarrhea (loose, watery, or frequent bowel movements), crampy abdominal pain, fever, and, at times, rectal bleeding are the hallmark symptoms of CD, but they vary from person to person and may change over time. Loss of appetite and subsequent weight loss may also occur. However, the disease is not always limited to the GI tract; individuals may experience symptoms outside of the intestine, which may affect the joints, bones, eyes, skin and liver. Fatigue is another common complaint. Children who have CD may suffer osteoporosis, and may fail to develop or grow properly.

Some patients may develop tears (fissures) in the lining of the anus, which may cause pain and bleeding, especially during bowel movements. Inflammation may also cause a fistula to develop. A fistula is a tunnel that leads from one loop of intestine to another, or that connects the intestine to the bladder, vagina or skin. Fistulas occur most commonly around the anal area. If this complication arises, the patient may drain mucus, pus, or stool from this opening.

Symptoms may range from mild to severe. Because Crohn's disease is a chronic but fluctuating disease, patients will go through periods in which the disease flares up, is active, and causes symptoms. These episodes are followed by times of remission – periods in which symptoms disappear or decrease and good health returns. In general, people with CD lead mostly full, active and productive lives.

Treatment Options

People with CD in Canada are treated in step-wise approaches – the traditional “step-up” or the newer “top-down” approaches. The “step-up” approach treats patients with corticosteroids during periods of disease flare, to reduce symptoms and induce remission. These drugs are not generally taken on a long-term basis. For long-term control, immune modifiers are typically initiated.

If patients have tried one or two different immune modifiers and doses have been maximized yet they still have problems or cannot tolerate these agents, then biological therapies are tried.³ In the “step-up” sequence, biologicals are reserved for later use because they are the most expensive of the drugs available. Patients with fistulizing disease may start a biological therapy early, because other drugs are not effective. Best practices for the use of biologicals are still being defined, and there may be a variety of current practice patterns. For example, some researchers and clinicians now think that it may be worthwhile in selected patients to try these drugs early in a “top-down” approach since they can be very effective and they could change the course of the disease, by reducing bowel damage and eventual surgery.

Since there is no cure for CD as of yet, the short-term goal of medical treatment is to reduce or bring symptoms under control, (or remission), by suppressing the inflammatory response to induce a remission. Remission leads to normalization of quality of life, and is hopefully associated with healing of the damaged bowel. The long-term goal is to maintain this remission, that is, to use medical therapy to decrease the frequency of disease flares and to prevent complications.

Several groups of drugs are used to treat CD today, including:

- **Corticosteroids:** Prednisone and budesonide, among other steroids, are available orally and rectally. Corticosteroids can also be given intravenously (methylprednisolone). They non-specifically suppress the immune system and are used to treat moderately to severely active CD. They are very effective agents but may be associated with significant short- and long-term side effects. They should not be used as a maintenance medication.
- **Immune modifiers:** Azathioprine, 6-Mercaptopurine (6-MP), methotrexate and cyclosporine, sometimes called immunomodulators, are used to help decrease corticosteroid dependency. In addition, immune modifiers may help maintain disease remission.
- **Antibiotics:** Metronidazole and ciprofloxacin are used to treat anal fistulas and Crohn's colitis.
- **5-Aminosalicylates (5-ASA):** This class of anti-inflammatory drugs includes sulfasalazine and oral formulations of mesalamine and 5-ASA drugs; also may be administered rectally. These medications typically are used to treat mild symptoms of proctocolitis.
- **Biological therapies:** Infliximab and adalimumab are currently approved in Canada for moderately to severely active CD in patients who have not responded adequately to conventional therapy, infliximab is currently approved for UC as well. Given by infusion or injection, these drugs are produced by live cells (hence the name 'biologicals'). They work by blocking the immune system's production of tumour necrosis factor-alpha (TNF-alpha), a cytokine (chemical) that intensifies inflammation. Other biologic agents for both CD and UC have been shown, in some cases, to be effective in clinical trials (for example, certolizumab or natalizumab). These therapies have been approved for use in other countries and may be approved by Canadian regulatory authorities over the next few years.

Surgery

Historically, two thirds to three quarters of patients with CD have required surgery at some point during their lives,⁴ although surgery has become less frequent with modern medical management (Nguyen 2011, Benchimol 2011, Bernstein 2012). Surgery becomes necessary when medications are not working (medically refractory disease) and if complications arise such as fistulas, abscesses or scarring and narrowing of the bowel, or if dysplasia (precancerous cells) or cancer of the colon is detected. In most cases, the diseased segment of bowel and any associated abscess is removed (resection). The two ends of healthy bowel are then joined together in a procedure called an anastomosis. While resection and anastomosis may allow many symptom-free years, the disease frequently recurs at or near the site where the bowel is joined together.

An ostomy may be required when surgery is performed for CD when there is no healthy bowel

to connect. This may happen in patients with disease of both the rectum and the colon. After the surgeon removes the colon, the small bowel is brought to the skin, so that waste products may be emptied into a pouch attached to the abdomen. The result is an ileostomy or a colostomy. The overall goal of surgery in CD is to conserve bowel, where possible, and return the individual to the best possible quality of life.

Complications

The most common complication of CD is blockage of the intestine due to swelling and the formation of scar tissue. This usually results from repeated bouts of inflammation and ulceration. The result is the thickening of the bowel wall and a significantly narrowed intestinal passage. Symptoms include “crampy” pain around the mid-abdomen frequently associated with vomiting. The abdomen may also become bloated and distended. Medications may relieve the obstruction by reducing the local area of inflammation, but surgery may be required if the obstruction is severe and does not respond to medical treatment. Surgery may also be required if the blockage recurs frequently.

Another complication is ulcers within the intestinal tract that sometimes turn into fistulas. These affect about 30% of people with CD and often become infected. If the fistula is small, medical treatment may heal it. Large or multiple fistulas, on the other hand, may require surgery, particularly if they are accompanied by fever or abdominal pain or severe diarrhea. Occasionally a fistula forms an abscess, or collection of pus, near the intestine. This is a pocket of infection that requires drainage either through a catheter inserted by a radiologist or a special drain that is surgically inserted. The areas around the anus and rectum are often involved. In addition to fistulas, cracks or fissures may also develop in the lining of the mucus membrane of the anus.

Another complication commonly encountered in people with CD is related to malnutrition or the presence of nutritional deficiencies. These are deficiencies of proteins, calories, and vitamins. They generally do not develop unless the disease is extensive and of long duration, resulting in inadequate dietary intake and poor absorption of nutrients. Medical treatment and/or nutritional supplements are usually effective in the replacement of nutrients.

Low risk of cancer of the colon and small bowel is also a potential complication of longstanding CD.

ULCERATIVE COLITIS

UC is a chronic (ongoing) disease of the colon. The disease is marked by inflammation and ulceration of the colon mucosa, or innermost lining. Tiny open sores, or ulcers, form on the surface of the lining, where they bleed and produce pus and mucus. Because the inflammation makes the colon empty frequently, symptoms typically include diarrhea (most often bloody) and often “crampy” abdominal pain. There is also a sense of “dry heaves of the rectum” after bowel movements along with urgency. Some patients will have false urges and pass only tiny amounts of blood and mucus.

The symptoms of UC, as well as possible complications vary depending on the extent of inflammation in the rectum and the colon. The rectum is mostly involved, but can extend up to and including the entire colon.

Symptoms

The first symptom of UC is a progressive loosening of the stool. The stool is generally bloody and may be associated with “crampy” abdominal pain and severe urgency to have a bowel movement. The diarrhea may begin slowly or quite suddenly. Loss of appetite and subsequent weight loss and fatigue are common. In cases of severe bleeding, anemia may also occur. In addition, there may be skin lesions, joint pain, eye inflammation, and liver disorders. Children with UC may fail to develop or grow properly.

Approximately half of all patients with UC have relatively mild symptoms: multiple stools a day, with or without blood, some pain and cramping, a constant feeling of the need to empty the bowel, and no fever or a low-grade fever. Severely ill people experience more than six bloody stools a day, with fever and/or anemia. In general, the severity of symptoms correlate with the extent of colon involved with the disease. The symptoms of UC tend to come and go, with fairly long periods in between flare-ups in which patients may experience no distress at all. Periods of remission can span months or even years, although symptoms do eventually return. The unpredictable course of UC may make it difficult for physicians to evaluate whether a particular course of treatment has been effective or not.

Treatment Options

The treatment of UC involves medications that decrease the abnormal inflammation in the colon lining and thereby control the symptoms, with the goal of maintaining this induced remission. Medical options are centered around 5-ASAs and topical (rectal) therapy for people with mild to moderate symptoms. ASAs are more effective in UC than CD. Probiotics in combination with 5-ASA are also used in mild to moderate UC. However, due to long-term side effects they should not be used for maintenance therapy. Immune modifiers can be used to replace corticosteroids once symptoms of a flare come under control. Biological therapy (infliximab) is indicated in patients who have failed conventional therapy or who are hospitalized with severe UC not improving with corticosteroids. Cyclosporine, a potent immunosuppressant used to prevent rejection in transplant medicine may be used for a hospitalized patient with severe UC.

Surgery

In one-quarter to one-third of patients with UC, medical therapy is not completely successful or complications arise. Under these circumstances, surgery may be considered. This operation involves the removal of the colon (colectomy). Unlike CD, which can recur after surgery, UC is “cured” once the colon is removed.

Depending on a number of factors, including the extent of the disease and the patient’s age and overall health, one of two surgical approaches may be recommended. The first involves the removal of the entire colon and rectum, with the creation of an ileostomy or external stoma (an opening on the abdomen through which wastes are emptied into a pouch, which is attached to the skin with adhesive). A more recently developed procedure also calls for removal of the colon, but it avoids an ileostomy. By creating an internal pouch from the small bowel and attaching it to the anal sphincter muscle, the surgeon can preserve bowel integrity and eliminate the need for the patient to wear an external ostomy appliance.

Complications

Complications of UC include profuse bleeding from deep ulcerations, perforation (rupture) of the bowel, or simply failure to respond appropriately to the usual medical treatments.

Another complication is severe abdominal distension. A mild degree of distention is common in individuals without any intestinal disease and is somewhat more common in people with UC. However, if the distention is severe or of sudden onset, and if it is associated with active UC, fever, and constipation, a physician may suspect toxic megacolon. This is a rare development that is produced by severe inflammation of the entire thickness of the colon, with weakening and ballooning of its wall. The dilated colon is then at risk of rupturing. Treatment is aimed at controlling the inflammatory reaction and restoring losses of fluid, salts, and blood. If there is no rapid improvement, surgery may become necessary to avoid rupture of the bowel.

As with CD, risk of colorectal cancer is a potential complication of longstanding UC.



EPIDEMIOLOGY

HEATHER FEGAN

Heather was diagnosed with Crohn's disease at 14 years of age. Since that time she has worked tirelessly conducting radio and TV interviews, sitting on panels organized by the CCFC and speaking on behalf of young people with Crohn's disease.

key findings:

- IBD is largely a disease of the developed world, with initially the emergence of UC in developing countries, and then the eventual predominance of CD as a country becomes industrialized.
- Genetics is involved in IBD, shown by clustering within families and the identification of several genes which are more common in people with CD.
- Environmental factors are presumably involved in IBD, but it is not well understood how they influence the development of IBD.
- There is a higher frequency of CD in female adults in Canada, while boys are more commonly affected by IBD than girls in childhood.
- In 2012, the best estimate of the prevalence of IBD is 233,000 Canadians with IBD: 129,000 with CD and 104,000 with UC (0.67% of the Canadian population).
- Using the self-report CCHS data, upper bound for the prevalence of IBD: 306,000 individuals (0.88% of the Canadian population).
- The pattern of incidence mirrored the pattern of prevalence: lowest in BC, and highest in NS and QC.
- The average Canadian incidence is 16.3 new cases of CD and 12.9 new cases of UC for every 100,000 people. This means that the number of people newly diagnosed with CD is greater than the number of people newly diagnosed with UC.
- Every year, there are 10,200 new cases of IBD: 5,700 people with CD and 4,500 people with UC.
- The prevalence of CD and UC increases with increasing age; it climbs to its peak level by age 30, and remains at this level, only decreasing after age 80.
- IBD had a prevalence of 56.3/100,000 in Ontario in 2005, using a strict case definition and limited to children below the age of 18. There are more boys with IBD than girls. This is one of the highest rates of childhood-onset IBD in the world.
- Incidence has been rising, particularly since 2001, and significantly so in children under the age of 10.
- In 2005, there were 1,621 children living with IBD in Ontario, of whom 327 had new diagnoses of IBD that year.
- Updating these results to 2012 and extrapolating to the rest of the country, it is estimated that there may be 5,900 children under 18 years old with IBD in Canada.
- There is an excess risk of premature mortality for people with CD. There is a 47% increased risk of death, and an increased risk of colorectal cancer.
- There is no excess risk of premature mortality for people with UC, although there is an increased risk of colon cancer.

SUMMARY:

- IBD is more common in developed countries, and is influenced by genetics, environment, ethnicity and gender.
- Canada has among the highest frequency of people with CD and UC in the world.
- An estimated 129,000 people live with CD and 104,000 people live with UC in Canada in 2012, for a total of 233,000 individuals with IBD (0.67% of the population).
- Over 10,200 people every year are newly diagnosed with IBD: 5,700 people with CD and 4,500 with UC.
- The age of onset is typically in the twenties for CD, and throughout adulthood for UC. The number of people with disease peaks around age 30 for both diseases, and does not decline until age 80.
- Children in Canada are increasingly being diagnosed with IBD, particularly those under the age of 10. An estimated 5,900 Canadian children have IBD.
- Compared to people without disease, there is 47% increased risk of premature death with CD, which includes an increased risk of colorectal cancer. There does not seem to be an increased risk of premature death with UC.

INTRODUCTION

This section of the report covers the following epidemiological aspects:

- Risk factors (also known as etiology): the causes of IBD and/or the factors that are linked to the occurrence of IBD;
- Prevalence: the number of people who have IBD at a given point in time;
- Incidence: the number of new cases of IBD that can be expected each year;
- Mortality: the occurrence of death in people with IBD.

ETIOLOGY

The causes of CD and UC have not been determined. There is growing evidence suggesting that there is a combination of genetic and environmental factors that inappropriately activate the gastrointestinal immune system. Research looking into internal and external factors contributing to IBD includes the search for specific bacterial triggers, as well as other environmental triggers such as diet, antibiotic use and lifestyle. The possibility of more than one environmental or infectious trigger that leads to a similar set of symptoms confounds the research agenda to find both a cause and a cure for IBD.

While the specific causes of IBD are not known, there are some patterns of disease occurrence that have been observed. The strongest of these is the geographical pattern. IBD is emerging as a global disease, but with distinctly different patterns among nations. For reasons that are not clearly understood, IBD is largely a disease of the developed world, particularly Europe and North America. IBD seems low in developing countries, but as these societies become more industrialized, UC emerges. Subsequently, CD rates begin to climb, ultimately predominating in developed nations.⁵ When people migrate, they take on the frequency of disease of the new country.⁶ In support of the role of environmental factors, children of migrants from developing countries are much more likely to develop IBD than their parents. In Canada, for example, South Asian children in Vancouver are three times more likely to develop IBD than non-South Asian children.⁷

IBD clusters in families, although on most occasions there are no affected relatives. Siblings are most likely to be affected; the risk of IBD in a sibling is 10 to 20 times higher than the general population.^{8,9} The strongest evidence is from twin studies. Up to 50% of identical twins will both have CD, while 10% will both have UC.^{10,11} However, the reverse is also true: for at least 50% of identical twins, only one of the two will have IBD, and the other twin will not have CD.

Researchers have found links to the development of IBD with more than 160 genes and loci. The growing number of identified mutations associated with CD and also UC may help to understand the pathways that lead to disease and identify new targets for treatment. The most important mutation identified thus far is in a gene known as NOD2/CARD 15; it occurs up to three times as frequently in people with CD than in the general population.^{12,13,14} This single mutation cannot predict who will get the disease, since it also occurs in people without CD (in other words, many people who will never get CD also carry this mutation). Mutations like this one may eventually serve as a marker for type and/or severity of disease.^{15,16} The growing number of identified mutations associated with CD and also UC may help to understand the

pathways that lead to disease and identify new targets for treatments.¹⁷

Some factors in the environment have been linked to IBD. The ‘hygiene hypothesis’ has been suggested to explain why chronic diseases, with inappropriate immune system reactions (like IBD), occur in modern ‘cleaner’ environments. High levels of hygiene may reduce childhood exposure to bacteria and viruses and/or change the type of bacteria found in the gut. There are conflicting reports on childhood infections and whether they are a risk factor for IBD.¹⁸ Canadian researchers have found that children who had one or more prescriptions for an antibiotic in the first year of life are more likely to develop IBD.¹⁹ Smokers and ex-smokers have a higher risk of CD, but not UC.^{20,30,14} Because IBD is more common in developed nations, air pollution has been investigated for a link to IBD. Certain pollutants were associated with an increased risk of development of IBD, but only in younger patients.²¹ Diet may also be associated with IBD development, with high intake of total fat, polyunsaturated fatty acids, omega-6 fatty acids and red meat reported as increasing the risk.²² People who have had an appendectomy also have a lower occurrence of UC.²³ It is important to note that an association with IBD does not necessarily imply causality. In other words, just because something occurs more or less frequently in people with IBD, it does not mean that this causes (or prevents) IBD.

IBD is more common in some ethnic groups, such as Jews of European descent,^{24,14} while others appear to have a lower occurrence, such as aboriginal Canadians and New Zealand’s Maori.^{25,26,27} In the United States, Caucasians more often have IBD, but rates have been increasing in African Americans.²⁸ Rates remain comparatively low in Americans of Hispanic or Asian origin.^{28,29}

In Canadian adults, there is a higher frequency of CD in women (1.3 females are affected for every 1 male).^{30,33} There is no gender difference in UC. Slightly more cases of UC are found in urban settings than rural settings; there is no such association for CD.³⁰ By contrast, in Canadian children, CD is more common than UC and boys are more commonly affected than girls 1.25 males affected for every 1 female.³⁵

key findings:

- **IBD is largely a disease of the developed world, with initially the emergence of UC in developing countries, and then the eventual predominance of CD, as a country becomes industrialized.**
- **Genetics is involved in IBD, shown by clustering within families and the identification of several genes which are more common in people with CD.**
- **Environmental factors are presumably involved in IBD, but it is not well understood how they influence the development of IBD.**
- **There is a higher frequency of CD in female adults in Canada, while boys are more commonly affected by IBD than girls in childhood.**

PREVALENCE

Prevalence is the **number** of people with CD or UC in a population at a given point in time or over a period of time (usually per year). The **percentage** of people in a population who have a disease is also usually determined; this is called the prevalence proportion.

There are different methods to measure the prevalence of a disease in a population. One method is to conduct a survey in a representative sample of the entire population. This will capture everyone with a diagnosed disease, including people who are not currently engaged in the health care system (for example, people in remission). This is particularly important for CD and UC, which have fluctuating courses of disease. In a population-based survey, a random sample of a population is asked if they have a given disease. The assumption is that people can accurately report if they have been diagnosed with a disease. This assumption has limitations because people can be confused with imprecise wording or may use different words to describe their disease.

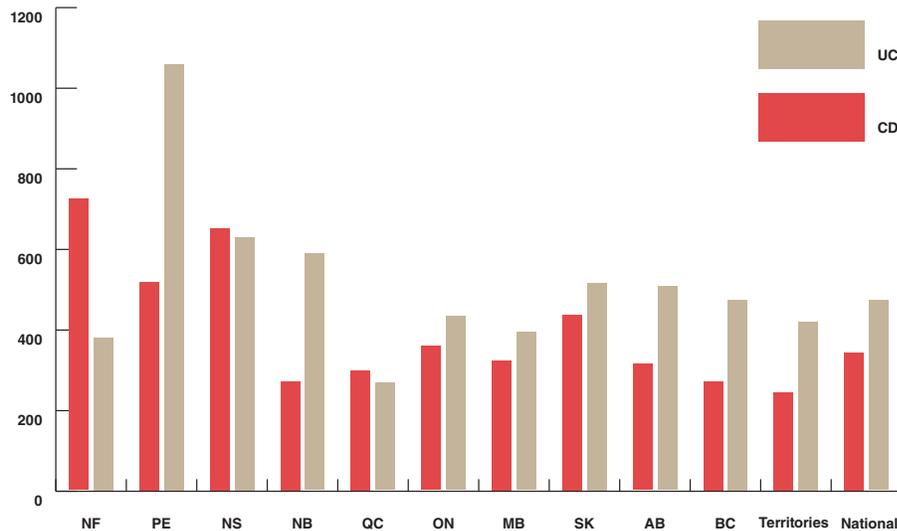
Another method is to examine a database of health records. Every time a person visits a physician or is admitted to a hospital in Canada, the visit and the reason are recorded in electronic databases. These databases are made anonymous by removing all identifying patient information to ensure patient privacy and then made available to qualified researchers. In a database study, records are searched for people who match a set of criteria (such as, a physician visit due to IBD). This will capture people who have a disease as diagnosed by a physician and who seek health care. Because decades of medical history are contained within the databases, they should also capture people with fluctuating disease (who may go several years without any health care contacts for their disease). In Canada, with universal access to health care, electronic health database studies include the entire population of a province.

Canada is fortunate to have both survey and database studies of the prevalence of UC and CD. This report will focus on the Canadian-specific research, especially since we know that prevalence varies considerably by country. There will also be an international comparison to place the Canadian findings in context.

Canadian Community Health Survey

The Canadian Community Health Survey (CCHS) was conducted by Statistics Canada to provide cross-sectional estimates of health issues across Canada. Approximately 130,000 Canadians were surveyed in 2005 and asked a variety of health-related questions, including: “Do you suffer from a bowel disorder such as Crohn’s disease, ulcerative colitis, irritable bowel syndrome or bowel incontinence diagnosed by a health professional?” Based on the responses, the number of people and percentage of people in the population was estimated for each province. Results are presented in Figure 1 for CD and UC.

Figure 1: CCHS Survey – Prevalence per 100,000 Population, CD and UC³¹



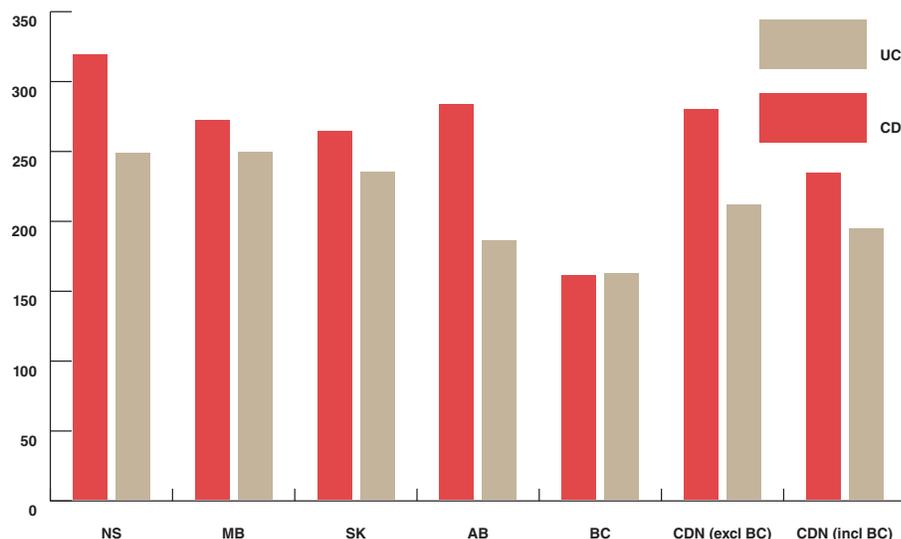
CCHS Survey 2005

key findings from 2005 Canadian Community Health Survey:

- Approximately 206,000 Canadians reported having CD or UC out of the 27 million sampled for the survey; that is, 758 cases per 100,000, or 0.76% of the population. Based on these self-reported data, UC was more common than CD. However, self-report data are typically an overestimate.
- UC was more common than CD, both nationally and in most regions (except QC, NS and NF). There were estimated to be 113,000 cases of UC and 92,000 cases of CD.
- There were large differences between provinces, particularly in less populous provinces where a random sample could generate a less precise estimate.

Canadian IBD Epidemiology Database Study

A landmark study was conducted by Canadian researchers to estimate the prevalence and incidence of CD and UC in Canada.³⁰ Funded by the Crohn's and Colitis Foundation of Canada, this study was led by researchers in Manitoba, who had first developed and tested a case definition which was capable of selecting almost all of the people with the disease of interest (sensitivity) but almost none of the people without the disease (specificity).³² The definition of a case was someone who had at least five health system contacts (outpatient visit or hospitalization) recorded for IBD. For people who were registered in the health system for less than two years, this was reduced to three contacts. There were five provinces that participated; all provinces had at least thirteen years of records available. Results are estimated as of July 1, 2000 and are presented in Figure 2.

Figure 2: Prevalence per 100,000 Population, by Province³⁰

key findings from 2000 Canadian IBD Epidemiology Database Study:

- Canadian prevalence was estimated at 468.1 per 100,000 for UC and CD combined, or 0.47% of the population.
- Prevalence was found to be lower than in the survey; typically, population surveys are over-estimates, as they rely on patient recall.
- Results were relatively consistent across provinces. The only exception in this study was BC, which had substantially lower prevalence. Therefore, a Canadian average was calculated by excluding BC.
- CD was more common than UC in all provinces except BC, where they were similar.
- Females were substantially more likely than males to have CD (1.31 females for every 1 male). There was no gender difference for UC.
- Overall there was no difference in prevalence for urban versus rural settings for CD; for UC, there were 1.13 urban dwellers for every 1 rural dweller.

Quebec Study

Using the same case definition as the Canadian IBD Epidemiology Database Study, researchers in Quebec have conducted a similar study to determine the prevalence of CD in that province over the years 1993 to 2002. Over that period of time, the prevalence of CD rose steadily, from 82.6 in 1993 to 270.4 in 2002 (with an average prevalence of 189.7/100,000). For the year 2000 – the same year as the database study in the other provinces – the prevalence of CD in Quebec was 243/100,000.³³ These results are in line with most other provinces in the database study, and support that BC was an exception to the general pattern seen in the rest of Canada.

The gender distribution also mirrored the results from the other provinces, with a female: male ratio of 1.30 for the 15 to 64 age group for IBD.

The Ontario Crohn's and Colitis Cohort

In 2009, a case definition was validated in Ontario to identify children diagnosed with IBD within Ontario's health databases. This resulted in the Ontario Crohn's and Colitis Cohort (OCCC) - housed and updated annually by the Institute for Clinical Evaluative Sciences. The OCCC tracks childhood-onset IBD in Ontario from 1991 onward. This resulted in the landmark pediatric study showing rising incidence of IBD in children.³⁵ At present, the OCCC is being expanded to include patients with adult-onset IBD, creating one of the largest surveillance programs for IBD in the world. This research is ongoing, and will contribute to future iterations of this Impact of IBD report. It is important to continue research using population-based health administrative and clinical databases across all provinces, in order to have a more robust estimate of IBD epidemiology and impact.

Estimated Current Prevalence

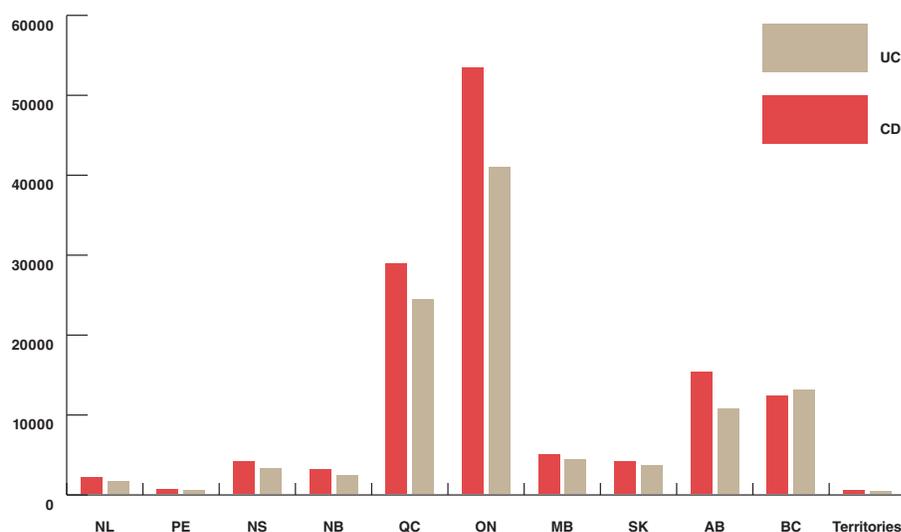
The current prevalence of IBD in Canada can be estimated using either or both sets of prevalence results. The survey was more likely to over-estimate the total number of people with IBD because of imprecise understanding of medical questions in the general public, but it included all regions of Canada. The database study was more likely to be accurate for the provinces that contributed data, but it was missing some provinces.

To estimate the current number of Canadians with IBD, the database studies were extended to all remaining provinces and territories using the Canadian average (excluding BC). Over time, there was an increase in the population of Canada, which would increase the number of people with IBD. More importantly, every year there are new cases diagnosed (see Section 3.3). The new cases have to be added to the existing group of people with IBD to calculate a current estimate. On the other hand, there are also losses due to migration and death, and these cases need to be subtracted.*

In 2012, there are predicted to be 129,000 Canadians with CD and 104,000 Canadians with UC, for a total of 233,000 people (0.67% of the population). The results are depicted for each province in Figure 3.

* (Note: total incidence for IBD was 29 new cases per year per 100,000 but 'net' incidence – new cases minus deaths and migration – was 17).

Figure 3: Estimated 2012 Prevalence, CD and UC



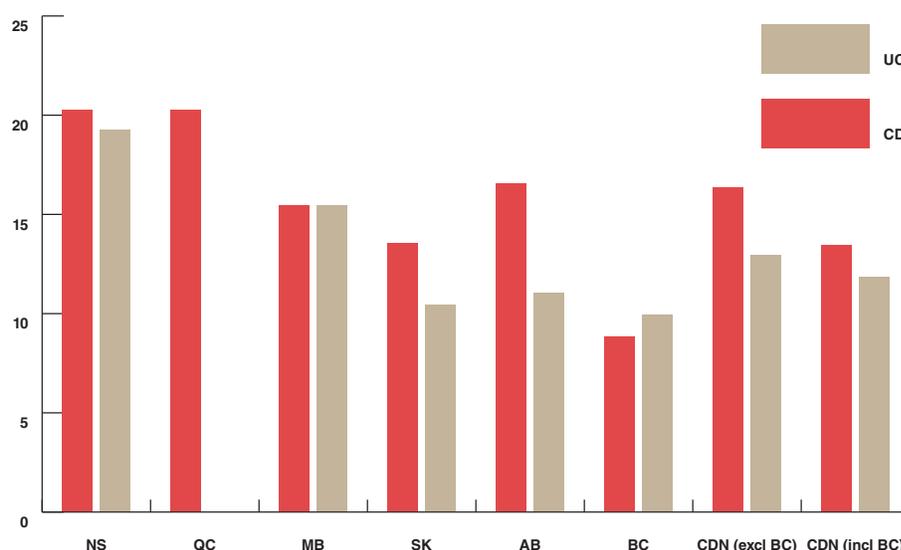
key findings:

- In 2012, the best estimate of the prevalence of IBD is 233,000 Canadians with IBD: 129,000 with CD and 104,000 with UC (0.67% of the Canadian population).
- Using the self-report CCHS data, upper bound for the prevalence of IBD: 306,000 individuals (0.88% of the Canadian population).

INCIDENCE

The number of new cases per year (incidence) was calculated in the Canadian IBD Epidemiology Database Study plus the Quebec study, as the average annual rate for 1998-2000. The findings are presented in Figure 4.

Figure 4: Incidence per 100,000 by Province^{30,33}



key findings:

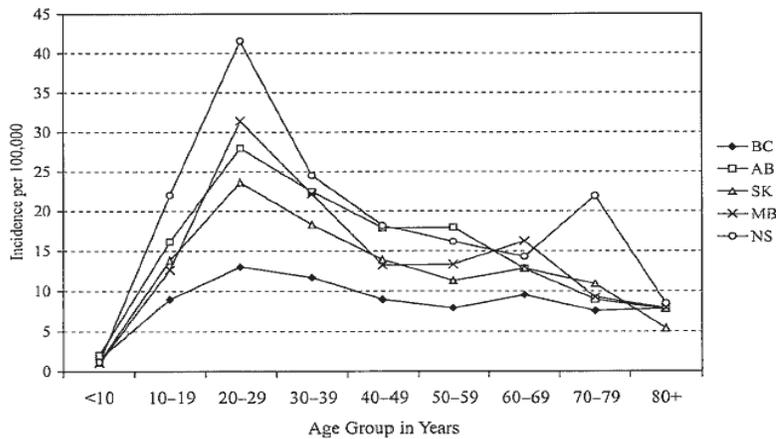
- The pattern of incidence mirrored the pattern of prevalence: lowest in BC, and highest in NS and QC.
- The average Canadian incidence is 16.3 new cases of CD and 12.9 new cases of UC for every 100,000 people. This means that the number of people newly diagnosed with CD is greater than the number of people newly diagnosed with UC.
- Every year, there are 10,200 new cases of IBD: 5,700 people with CD and 4,500 people with UC.

Age Distribution

The Canadian IBD Epidemiology Database Study investigated the ages of people with CD and UC; the Quebec study looked at the ages of people with CD only.

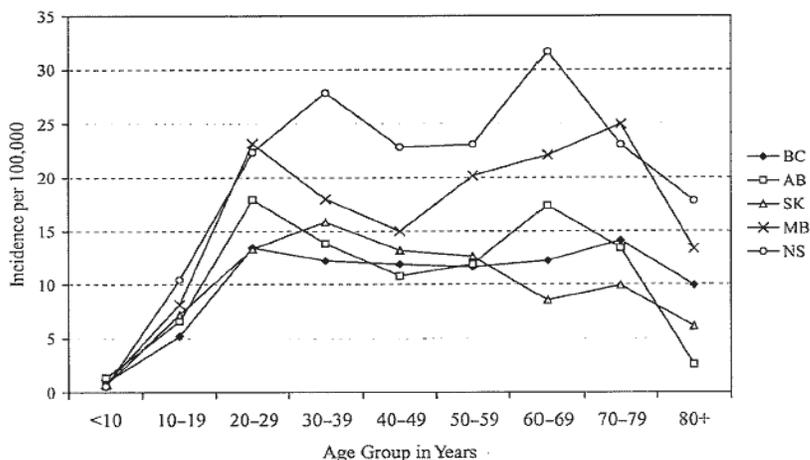
The age-specific incidence is shown in Figures 5 and 6. This reflects the age of onset for the disease, that is, the age at which the disease was diagnosed.

Figure 5: Incidence by Age, CD³⁰



Bernstein et al 2006

Figure 6: Incidence by Age, UC³⁰



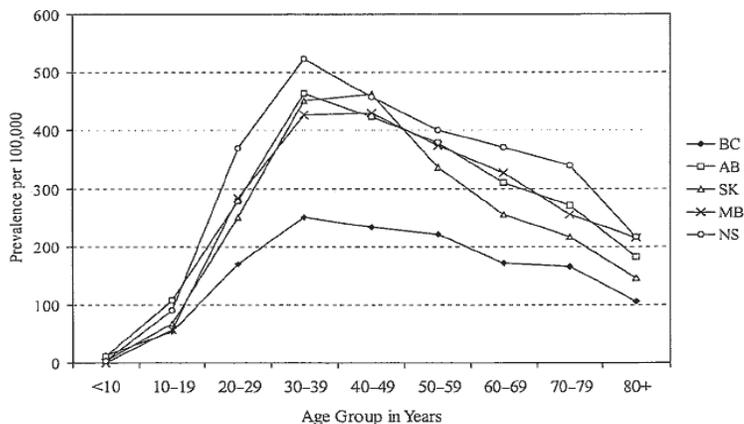
Bernstein et al 2006

key findings:

- The age of onset is most commonly in the twenties for CD, across all provinces (including Quebec).
- There was no single peak age of onset for UC; there was an initial peak in the twenties, followed by a plateau, and possibly a second peak in later years.

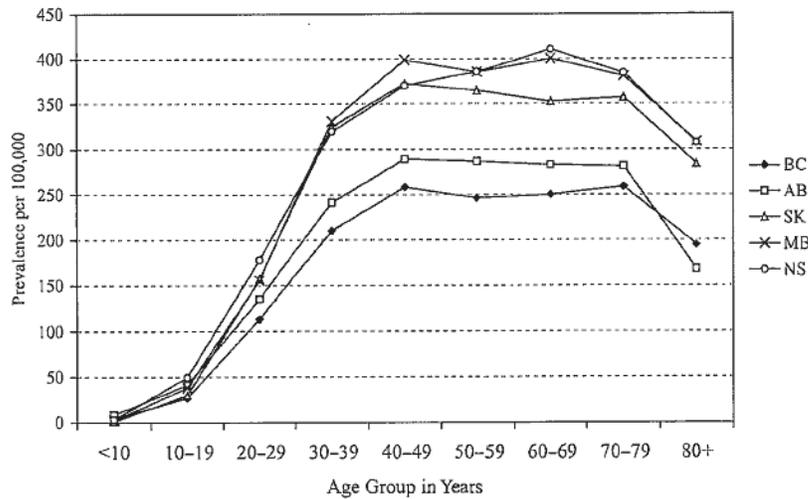
CD and UC can be diagnosed at a young age, but new cases continue to appear in older ages. As a result, as people age, there are more and more cases in the population. In other words, the prevalence stays high in older age groups – see Figures 7 and 8.

Figure 7: Prevalence by Age, CD³⁰



Bernstein et al 2006

Figure 8: Prevalence by Age, UC³⁰



Bernstein et al 2006

key findings:

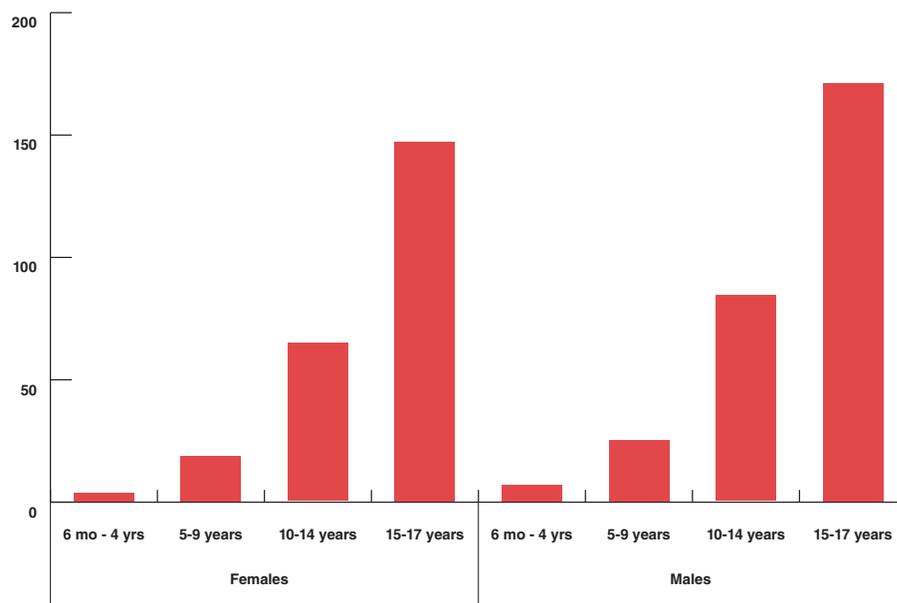
- The prevalence of CD and UC increases with increasing age; it climbs to its peak level by age 30, and remains at this level, only decreasing after age 80.

PEDIATRIC EPIDEMIOLOGY

CD and UC also occur in children. In fact, 20-30% of IBD patients present with the illness before they are 20 years old. Given that the most common age of IBD onset is when a person is in their twenties, many 18 and 19 year olds will be diagnosed with IBD. However, pediatric IBD occurs not only in older teens, and is even diagnosed in children under the age of four. Canadian researchers have used health records in the province of Ontario to investigate pediatric IBD, among children exclusively under 18 years of age. These health records provided data on the largest population sample of pediatrics with IBD in the world, and defined IBD cases with a high level of accuracy.

The results showed that the prevalence of pediatric IBD in Ontario was higher than expected, and has been rising rapidly over the past decade. Prevalence increased from 42.1/100,000 in 1994 to 56.3/100,000 in 2005. Data by age group for the year 2005 are presented in Figure 9. Amongst IBD cases, CD was more common than UC (32.8 versus 20.3 cases per 100,000). IBD is more common in male children.

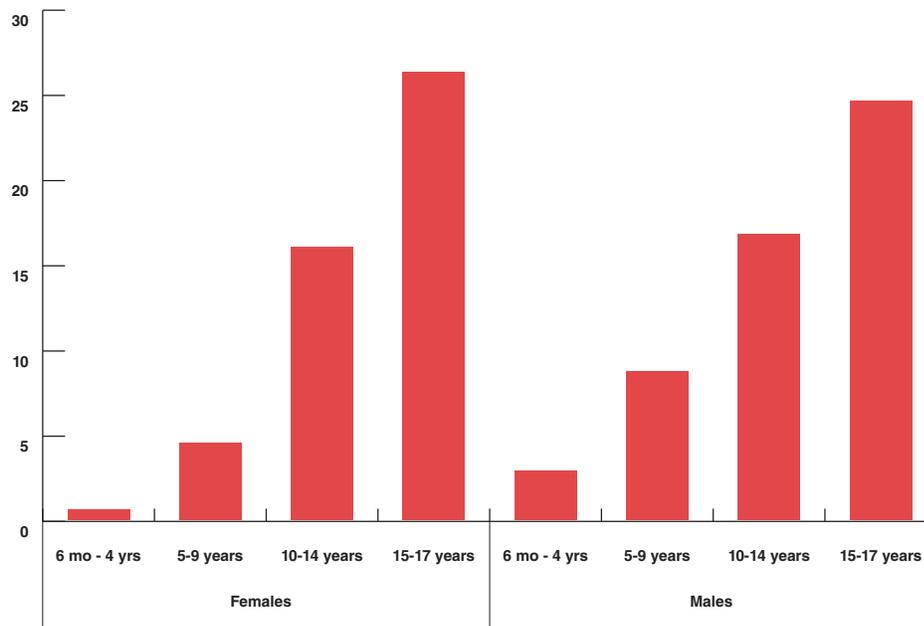
Figure 9: Pediatric IBD – Prevalence per 100,000 in Ontario, 2005



Benchimol 2009

Incidence has increased from 9.5/100,000 in 1994 to 11.4/100,000 in 2005 (Figure 10). Interestingly, most of this increase has occurred since 2001. This may be related to an undetermined environmental factor or due to patterns of migration. Incidence is increasing significantly in children aged 0-4 years and 5-9 years, but rates are stable in 10-14 and 15-17 year-olds. This means that IBD is increasing most rapidly in young children, those below 10 years of age – a troubling finding. The higher incidence in older female children shows that the adult pattern emerges after puberty -- when more females will be diagnosed with IBD and eventually outnumber males.

Figure 10: Pediatric IBD – Incidence per 100,000 in Ontario, 2005



Benchimol 2009

key findings:

- IBD had a prevalence of 56.3/100,000 in Ontario in 2005, using a strict case definition and limited to children below the age of 18. There are more boys with IBD than girls. This is one of the highest rates of childhood-onset IBD in the world.
- Incidence has been rising, particularly since 2001, and significantly so in children under the age of 10.
- In 2005, there were 1,621 children living with IBD in Ontario, of whom 327 had new diagnoses of IBD that year.
- Updating these results to 2012 and extrapolating to the rest of the country, it is estimated that there may be 5,900 children under 18 years old with IBD in Canada.

International Comparison

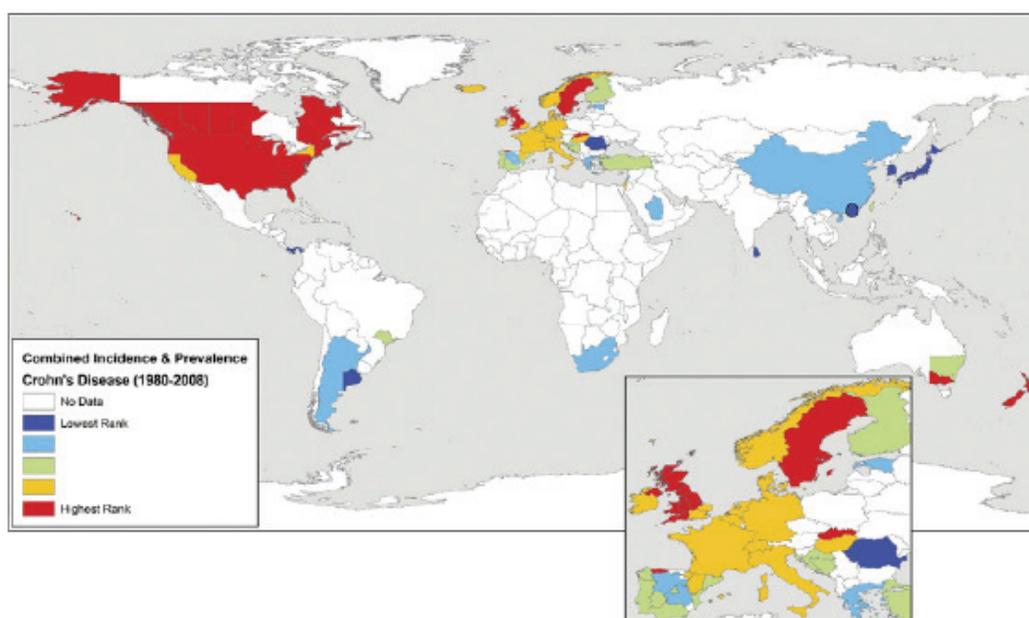
Overall, Canada has among the highest reported prevalence and incidence of IBD in the world.

Historically, countries in more northerly latitudes have a higher occurrence of both CD and UC.⁶ There is more disease in the developed countries of northern Europe and North America than in southern Europe, Asia, Africa and Latin America. This may explain why BC has a substantially lower rate of CD than the rest of Canada – it has given more residents of recent Asian immigration. As noted earlier, children of South Asian immigrants may have a high occurrence of IBD, as the effect of the environment serves to “catch up” this population to the much-higher Canadian average.³⁶

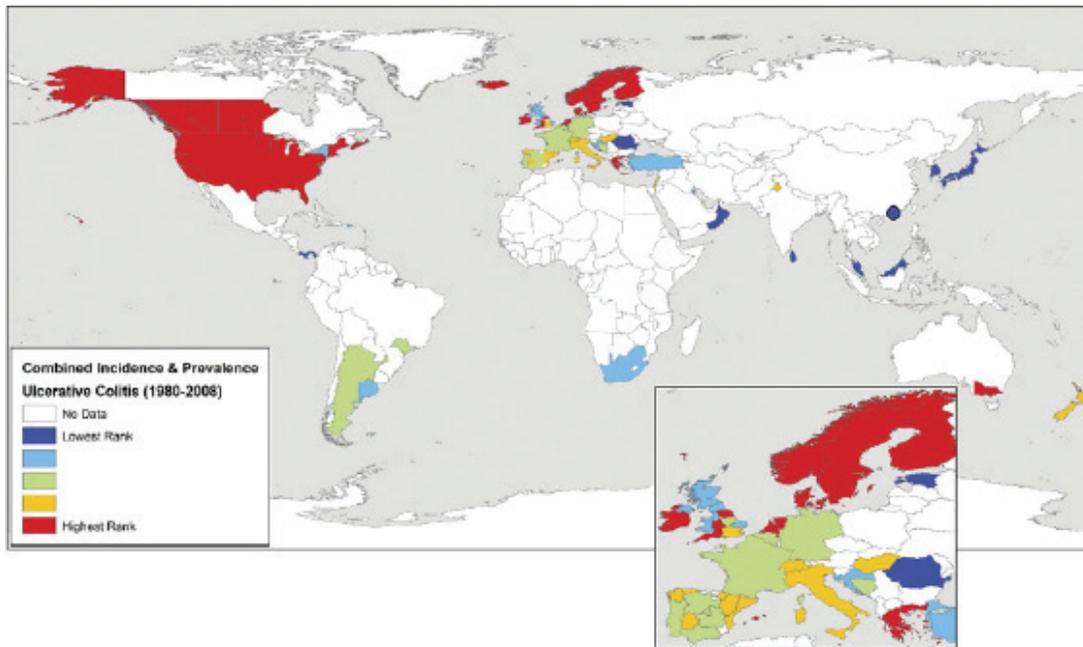
In the past, international studies of IBD used a mixture of methods, different definitions of IBD and different definitions of the study population, etc. The quality of research was not always high and the underlying variation resulted in a broad range of results. This made it difficult to do precise international comparisons. The Canadian IBD Epidemiology Database Study set a new standard in the measurement and reporting of IBD epidemiology. It is encouraging to see that recent studies have adopted this rigorous methodology.

Canadian researchers have recently conducted a landmark comprehensive review of the literature, to determine changes in worldwide incidence and prevalence of IBD in different regions and over time.³⁷ They identified 260 research papers that contributed data to this question. Figures 11 and 12 show the results across the globe, focusing on data reported after 1980. Research in developing countries is comparatively scarce, but the work that has been done has been reported since 1980. Research methodology in the developing world remains inconsistent in quality, and generally underestimates results.

Figure 11: International Comparison, Crohn's Disease (CD)



Molodecky 2012

Figure 12: International Comparison, Ulcerative Colitis (UC)

Molodecky 2012

Canadian results consistently fall into the highest quintile (the top 20%) for both incidence and prevalence of CD and UC. Others in this quintile are largely northern European countries, Australia and the United States. The lowest quintile includes Asian and other developing countries that have contributed data to the analysis.

Several studies have found that incidence is rising internationally, particularly for CD.^{38,39,40,41} The comprehensive international overview found that 75% of CD studies, and 60% of UC studies, documented an increasing incidence of disease at a level that was statistically significant. This means that UC and especially CD are being diagnosed more frequently, and that the number of people with these diseases will increase over time. Furthermore, it also appears that populations with historically low incidence (Asia, south Europe) may be experiencing accelerated growth in these diseases.^{6,42} Since IBD is most often diagnosed in the young, this means that the population burden of IBD is an increasing and a global concern.

The distribution of IBD across the globe, with a current concentration in developed countries but increasing growth in developing countries, highlights the influence of environmental factors. There is an opportunity to understand IBD better by conducting further research on these factors.

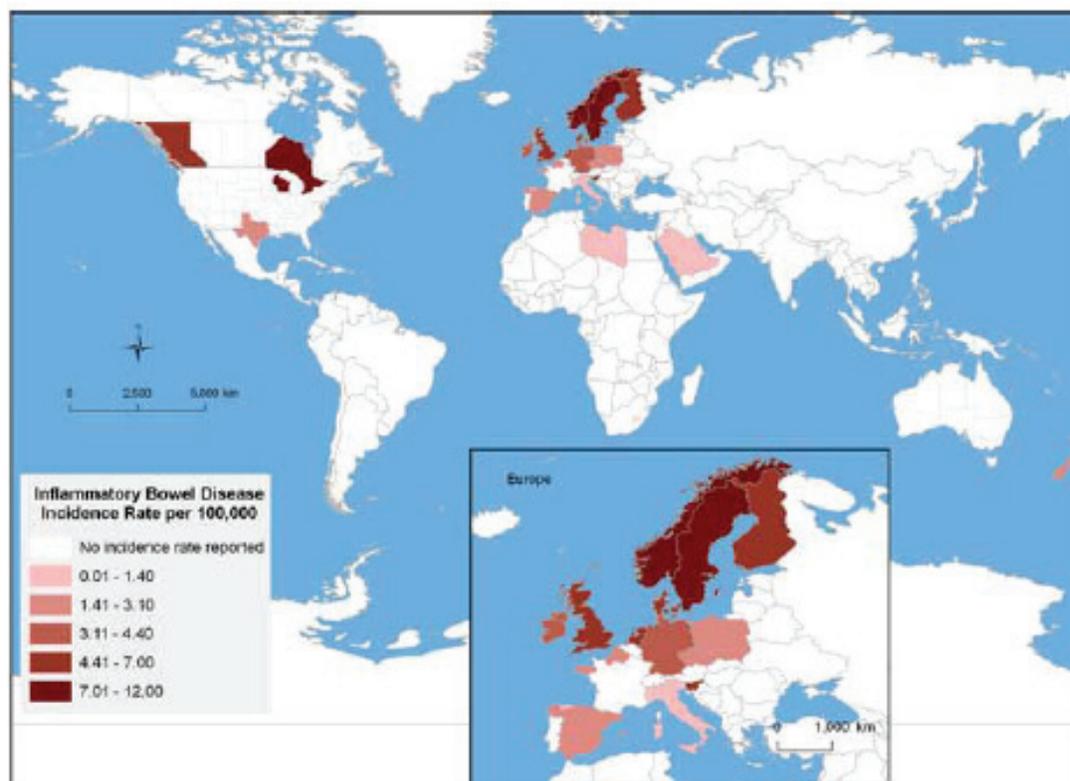
International studies are very similar to Canadian findings with respect to other aspects of epidemiology, specifically age of onset and prevalence by age. Findings from the recent broad American database study found reasonably similar results for incidence and prevalence in the pediatric population.⁴³ It confirmed that the gender bias was reversed in children: although CD was more common in adult females (as in Canada), CD was more

common in pediatric males.⁴³ That is, males were more likely to get CD as children, while females were more likely to get CD as adults.

Pediatric International Comparison

Canadian researchers have also conducted a comprehensive review of the literature on pediatric IBD, yielding 139 studies from 32 countries.⁴⁴ Most countries did not report incidence or prevalence data. Figure 13 shows the pattern with respect to incidence, and once again, Canadian rates are in the top quintile (top 20%). Of the studies that looked at trends over time, the majority (78%) reported statistically significantly increased incidence of pediatric IBD. This means that there are globally rising rates of pediatric IBD (primarily CD) in both developing and developed nations.

Figure 13: International Pediatric IBD



Benchimol 2010

MORTALITY

There have been many international studies of mortality in IBD, although none has been conducted specifically with a Canadian population. It is reasonable to assume that the risk of death is similar in European and North American countries, given a uniformly high standard of medical care and life expectancy. Therefore, the international studies were reviewed to determine estimated Canadian mortality from IBD.

It is difficult to study mortality in IBD, for two reasons. First, the majority of people with IBD

are relatively young. There are very low rates of death in younger people, even for those with severe disease. This means that it is necessary to study a very large group of people, and/or study them for a very long period of time, in order to identify any trends of increased death. Second, it can be difficult to decide if a death was due to the underlying presence of IBD, even for people who die from a gastrointestinal disease.

Crohn's Disease

There have been at least ten population-based studies of mortality in CD patients. Seven of these studies have found an increased risk of death, while three studies have reported a slightly lower risk of death. When faced with conflicting results from multiple studies, researchers can conduct a meta-analysis. This is a statistical technique which combines data from multiple independent studies to generate a more precise estimate. Studies which are similar in methods and in quality can be combined, with more weight given to studies which include more patients (and less weight given to smaller studies).

A meta-analysis was conducted for the Crohn's and Colitis Australia, previously known as Australian Crohn's and Colitis Association (ACCA), in 2006. It combined ten studies and found that CD was associated with a statistically significant 47% increase in the mortality risk (range, 30-67%).⁴⁵

The results of this meta-analysis were very close to the result of a recently published meta-analysis of thirteen studies, which found 52% increase in the risk of mortality (range, 32%-74%).⁴⁶ Since the conduct of these meta-analyses, two other important studies have been published, from California and Denmark; they reported similar results (a 40% increase in mortality risk in California and 31% in Denmark).^{47,48}

There were increased death rates from cancer, cardiovascular disease, respiratory disease, GI diseases, infections, and complications following medical and surgical interventions.⁴⁵ Meta-analyses of colorectal and small bowel cancer studies have found that people with CD had an elevated risk of colorectal cancer, estimated at 2.9% over the ten years following diagnosis of CD.^{49,50}

Ulcerative Colitis

Similarly, there have been several studies of ulcerative colitis mortality, with conflicting results. Crohn's and Colitis Australia conducted another meta-analysis, using these studies: three studies reporting an increased risk, and five studies reporting a decreased risk. However, with UC, there was no significant difference in mortality risk. That is, people with UC experienced the same mortality risk as the general population. These results were duplicated in two studies published since the meta-analysis: the large California study⁴⁷, as well as a large European study (limited to the first ten years since diagnosis of UC).⁵¹

It appeared that people with UC had increased deaths from some diseases (gastrointestinal diseases, infections, colon cancer) but these were offset by low rates of other diseases (cardiovascular disease, lung cancer).⁴⁵ This could be due to the fact that people with UC are

more likely to be non-smokers, and thus are less likely to suffer from cardiovascular disease and lung cancer. Recent Canadian research has contradicted this, however, with evidence for increased cardiovascular disease in UC as well as in CD.^{52,53}

key findings:

- **There is an excess risk of premature mortality for people with CD. There is a 47% increased risk of death, and an increased risk of colorectal cancer.**
- **There is no excess risk of premature mortality for people with UC, although there is an increased risk of colon cancer.**



DIRECT COSTS

JASON, JULIE AND HUDSON ZANATTA

"We didn't want other couples and young adults to suffer and feel alone. The disease is usually diagnosed in young adults...it's heartbreaking as this is the age you are starting your life. Many young adults are starting careers, seriously dating/engaged and travelling the world. These activities carry a lot of stress without the addition of a chronic auto-immune disease."

key findings:

- Prescription drug costs have changed dramatically in the past ten years, due to increasing use of high-cost biologicals.
- Currently, prescription drugs for IBD cost about \$521 million in Canada in 2012 (approximately \$2,200 per person per year).
- There are dramatic differences between provinces in per-capita drug costs and in the percentage of drug costs that are borne by public versus private drug plans.
- Excess hospitalizations related to IBD cost \$395 million per year for people with IBD.
- The annual per-person cost is \$2,521 for IBD related inpatient and out-patient hospitalizations and physician visits.
- Most patients experience their first hospitalization within two years of diagnosis.

SUMMARY:

- Direct medical costs for IBD are estimated at \$1.2 billion in Canada in 2012. These costs are in addition to any non-IBD medical needs.
- Prescription drug therapy, including biologicals, will cost \$521 million in Canada in 2012 – the single largest component of direct medical cost. Drug therapy has changed dramatically in the past ten years. Current drugs are more expensive but can prevent hospitalizations and improve health outcomes. Access to these drugs may vary by province and by socioeconomic status.
- Hospitalization and surgery are the second largest component of direct medical cost at \$395 million in Canada in 2012. Hospitalization and surgery rates have decreased over time for adults with CD. Surgical rates have decreased in children with CD. This may be related to increased specialist care and more aggressive use of medication to control disease.
- Physician visits are estimated at \$132 million in Canada in 2012. Outpatient hospitalization events will total \$61 million.
- Other aspects of direct medical costs have not been directly estimated in Canada, such as: laboratory tests, other health professionals (nutritionist, occupational therapist, etc.), and social services (home making, meal delivery, etc.). A conservative estimate based on international measurements is \$101 million in Canada in 2012.
- Costs depend on many factors such as age, severity, and decade of diagnosis. An average cost per patient is estimated to be at least \$5,200 per year.

INTRODUCTION

Direct costs are costs for resources that are offered by the Canadian public health care system. Typically, these include: hospitalizations, surgeries, emergency department visits, physician services, medications, laboratory tests and procedures, allied health care professional visits (for example, physiotherapist, occupational therapist, dietitian, chiropractor, massage therapist), social services (home health care, meal delivery, transit for handicapped, etc.), and long-term care (nursing homes, institutional care, etc.).

Currently, there is no cure for either CD or UC. People with IBD live with symptoms – usually at a milder level while in remission and at a more severe level during disease flares. Between 75-90% of patients are in remission at any given point in time.⁵⁴ A Canadian survey of people with IBD reported severe disease activity among 9% of people with UC and 11% of people with CD.⁵⁵ Disease severity is important, because medical costs vary dramatically by severity; studies have shown that a minority of patients with severe disease incur the majority of costs.^{56,57,58,59}

To manage their disease, people with IBD need ongoing medical care – they use physician visits, medications, and laboratory tests on a regular basis. Other health care professionals, especially dietitians, are also helpful. With increasing disease activity and flares, medications are increased and hospitalizations for surgery become common. People who have severe disease may require high levels of care, including home health care and (very rarely) institutional care.

There has been considerable research into the costs of disease, especially for CD. One limitation with this research is that prices and patterns of use for health care services reflect local health care systems and practices. While there can be considerable similarity across countries, the most reliable way to measure direct medical costs in Canada is to use research conducted in Canada.

PRESCRIPTION DRUGS

Many people with IBD require regular medications to control their disease. These medications must be taken all the time (even while in remission) to prevent IBD from flaring, and to keep their symptoms at a manageable level. During times of increasing symptoms and higher disease activity, most patients will require increased doses or additional medications to reduce symptoms, prevent complications, and return to remission.

For disease flares, corticosteroids are powerful drugs to control the immune system and induce remission. However, these drugs have long-term safety concerns, so it is not desirable to stay on these drugs for prolonged periods of time. For long-term control, people are treated with medications such as immune modifiers and 5-aminosalicylates to control their disease on an ongoing basis. More recently, new drugs called ‘biologicals’ became available for IBD. These drugs are made by live cells (hence the name ‘biologicals’) and are classified as anti-TNF drugs because they are directed against a molecule which promotes inflammation – tumour necrosis factor (TNF). They are used by people with moderately active to severe disease. They are much more expensive than conventional, older drugs, given the complicated way that they are produced, but they are also quite effective, especially for people who have responded well to other drugs. They have reduced the need for surgeries and hospitalizations; patients

can achieve remission using drugs instead of surgery, for both CD and UC.^{60,61,62,63} This has changed the type of costs that are incurred for CD and UC over previous years. This creates a problem when measuring medical costs.

To get a current estimate of prescription drug use, a national drug claims database was used to identify prescriptions for the typical drugs used to treat IBD.⁶⁴ Many of these drugs can be used for non-IBD diseases, so total cost was factored by the percentage of use that was specific to IBD indications. Drug claims data across public and private payers showed that costs for the most recent year (2011) totaled \$460 million. About 84% of these costs were for the biological drugs infliximab and adalimumab. There has been steady and significant growth in drug costs over the past several years, as biologicals have become the standard of care for people with more severe disease. For example, an analysis of IBD drug claims in Manitoba for 2005/6 showed that biologicals comprised about half of the total cost of prescription drugs at that time.⁶⁵ Using conservative growth estimates, prescription drug claims could cost at least \$521 million in 2012. This figure excludes costs for patients who pay out of pocket for drugs – those who have neither a public nor a private drug plan to pay for their drugs. However, at least for the biologicals, most people cannot afford to pay out of pocket, so these products are almost all paid within drug plans. It was conservative to exclude drug costs that are borne by the individual, although they may be significant and a burden to the person and family.

The biological drugs are quite expensive, for example, infliximab, a prescription intravenous (IV) infusion medication used to treat patients with Crohn's disease and ulcerative colitis are given based on an individual's weight. An average-sized adult can expect to be billed approximately \$4,333 for each infusion⁶⁶, and infusions are given every 6 to 8 weeks which can lead to individual patient costs approximately \$20,000 to \$50,000 per year depending upon the dose and frequency of treatment. Many health insurance policies have out-of-pocket maximums that limit a patient's expenses. But those maximums vary greatly, leaving many insured individuals to face thousands of dollars in annual expenses. In Canada, ten provincial and two territorial drug plans pay 46% of that total, private insurance and workplace health plans 36%, and uninsured patients 18%, according to the Canadian Institute for Health Information⁶⁷ people who receive them incur high levels of health care costs. However, Canadian research shows that biological-users required substantial health care resources before they receive biologicals.^{65,68} In other words, people who were prescribed biologicals were those who required frequent physician visits and/or expensive hospitalizations and surgeries due to difficulties with their IBD in the year before being prescribed a biological. After about two years, rates of hospitalization and physician visits fell back to the levels that were seen in other people with IBD. This suggests that biological drugs can improve IBD-related health outcomes.

There were important differences in costs across the country, with per-capita drug costs twice as large in some provinces as in others. This could reflect differences in treatment practices or differences in access (funding) available for the biological drugs. There was also a three-fold difference in the percentage of drug costs that was paid for by public plans versus private plans. This is due to the differences between the provincially-administered public drug plans, in both the type of drug that is funded and the extent of the population that is covered.

It is concerning that drug access can be an issue in treatment decisions. Although Canada has universal health care, drugs are outside of the system in most provinces. Everyone may access physicians, specialists, emergency rooms and hospitals, but not everyone has the same opportunity for drug coverage. A study among children with IBD found that socioeconomic status played an important role: children from lower income households were more likely to be hospitalized, visit the emergency room, see their physician, and receive surgery.⁶⁹ It is speculated that the difference could be related to access to the most effective but also expensive medications, which may be easier to obtain via private drug plans of working parents versus public drug plans for families on social assistance.

key findings:

- **Prescription drug costs have changed dramatically in the past ten years, due to increasing use of high-cost biologicals.**
- **Currently, prescription drugs for IBD cost about \$521 million in Canada in 2012 (approximately \$2,200 per person per year).**
- **There are dramatic differences between provinces in per-capita drug costs and in the percentage of drug costs that are borne by public versus private drug plans.**

HOSPITALIZATIONS, SURGERIES AND PHYSICIAN VISITS

Canadian studies on inpatient costs include database studies in Manitoba and a national survey of members of the Crohn's and Colitis Foundation of Canada.

Researchers in Manitoba checked health records for people who had been identified as having IBD over several time points, with the most recent data from 2005/6.^{70,71} Health records were examined to determine the annual costs of hospitalizations, surgeries, physician visits and drugs. For these four items, people with IBD had an average of \$3,896 in direct medical costs in 2005/6. This amount was twice that of people without IBD (matched for age and gender). CD was more expensive than UC (\$4,232 versus \$3,522). Although average costs were higher for people with CD, it seemed due to the fact that there were higher costs for the more 'extreme' CD cases.

The most expensive cases fell into four categories: people in their first year post-diagnosis (\$6,611), those who were hospitalized overnight (\$13,494), those who had surgery (\$18,749), and those using infliximab (\$31,440). As is typical in costing studies, a small minority of costly patients accumulated a disproportionate amount of cost – in the case of this study, 11% of IBD cases contributed to 56% of total costs.

As mentioned above, more recent data were used to estimate drug costs. Therefore, the costs due to drug therapy were removed from the total. The Manitoba study was essential for the estimation of inpatient hospitalization, outpatient hospitalization (same-day stays and procedures), and physician visits. After subtracting drug costs, the average cost for these three items was \$2,260 in 2005/6, or \$2,521 per person in 2012 dollars. Of this amount, 67% was due to hospitalization, 22% to doctor visits, and 10% to outpatient visits. Extrapolated to the 233,000 Canadians with IBD, the total cost for these items would be \$587 million (\$395 million for hospital inpatient, \$132 million for physician visits, and \$61 million for hospital outpatient).

Previous research showed that individuals with IBD were twice as likely to have a hospitalization (15% per year), compared to people without IBD (7% per year).⁷⁰ People with CD were more likely to have a hospitalization than people with UC. A considerable amount of hospitalization occurs within the first years of diagnosis of disease.⁷² For those people who will have an IBD hospitalization, 58% of these hospitalizations occur within the first two years of diagnosis, and 36% of surgeries also occur within the first two years. Similar patterns are found in the United States.⁷³

Historically, hospitalizations and surgeries were inevitable for most people with IBD. A Canadian survey was conducted in people with IBD who had a mean duration of disease of 18 years for CD and 15 years for UC. Amongst those with CD, 84% had been hospitalized and 65% had received surgery. For people with UC, 51% had been hospitalized, and 16% had ever received surgery.⁵⁵

The inevitability of surgery may be changing. There have been interesting trends in the patterns of hospitalization and surgery over time for people with CD, which have been observed and reported around the world. Surgical rates have been falling, and since half of all CD hospitalizations involve surgery, the rate of hospitalization has fallen as well.⁷⁴ People diagnosed with CD since 2001 were much more likely to see a gastroenterologist within the first year of diagnosis, and have a reduced use of surgery and associated hospitalizations.⁷⁵ They also had higher use of immunomodulators and biologics. Specialist care from the outset of the disease is associated with these trends to reduced surgery and more aggressive use of medication to manage disease. These changes affect not only the type and total cost of care for people with IBD, but also change lives and health outcomes. (Note that the Manitoba study that was used to estimate direct medical costs, relied on health care records from the most recent time period, and therefore the estimated direct medical costs reflect current trends).

Children with IBD have been observed to have greater use of pediatric gastroenterologists (versus adult gastroenterologists) in recent years, which may contribute to improvements in overall care and better outcomes in this age group. Since the 1990s, there has been a stable rate of age-adjusted hospitalization amongst children with IBD, but there has been a 30% decrease in the need for surgery in children with CD (no change in the surgical rate for children with UC). Finally, children are more likely to receive immunomodulatory and biological therapy than previously.⁷⁶

key findings:

- **Excess hospitalizations related to IBD cost \$395 million per year for people with IBD.**
- **The annual per-person cost is \$2,521 for IBD related inpatient and out-patient hospitalizations and physician visits.**
- **Most patients experience their first hospitalization within two years of diagnosis.**

OTHER COSTS

Other health care system costs have not been studied in Canada (such as, laboratory tests and procedures, non-physician professional services, home care, long-term care). They have not been well studied, if at all, in other countries. Often, they are reported without enough detail in order to accurately convert data to a current Canadian cost. As mentioned earlier, patterns of care in other countries are not necessarily the same as in Canada. However, international studies are needed to get an estimate of these other costs, because there are no Canadian sources. In this situation, it is important to be as conservative as possible – that is, to underestimate the costs wherever there is uncertainty in the results. We can piece together estimates from other countries where they do not overlap with any other resources. This procedure may end up missing some costs, but it is conservative estimate.

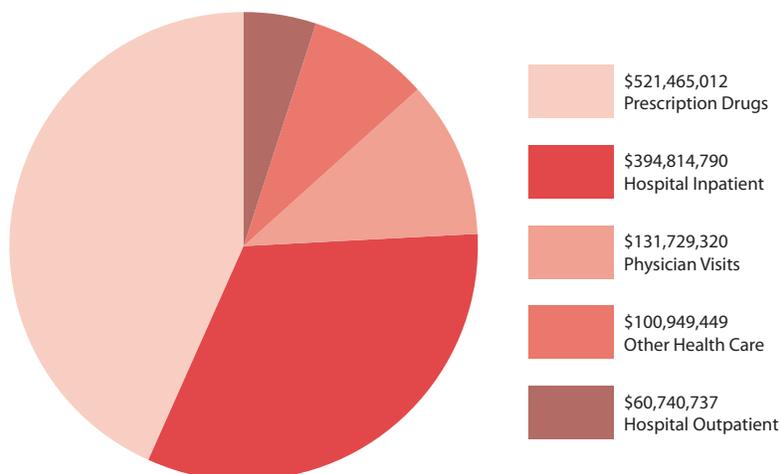
Diagnostic and investigative laboratory tests and procedures have been measured in an IBD clinic in the UK from 2000.⁵⁹ They reported the frequency of use for such resources as X-rays, blood work and ultrasounds separately for people with CD and UC. This type of test needed to be added to the direct costs for IBD. Canadian prices⁷⁷ were applied to the UK estimates of resource use (for example, number of blood tests, number of X-rays).

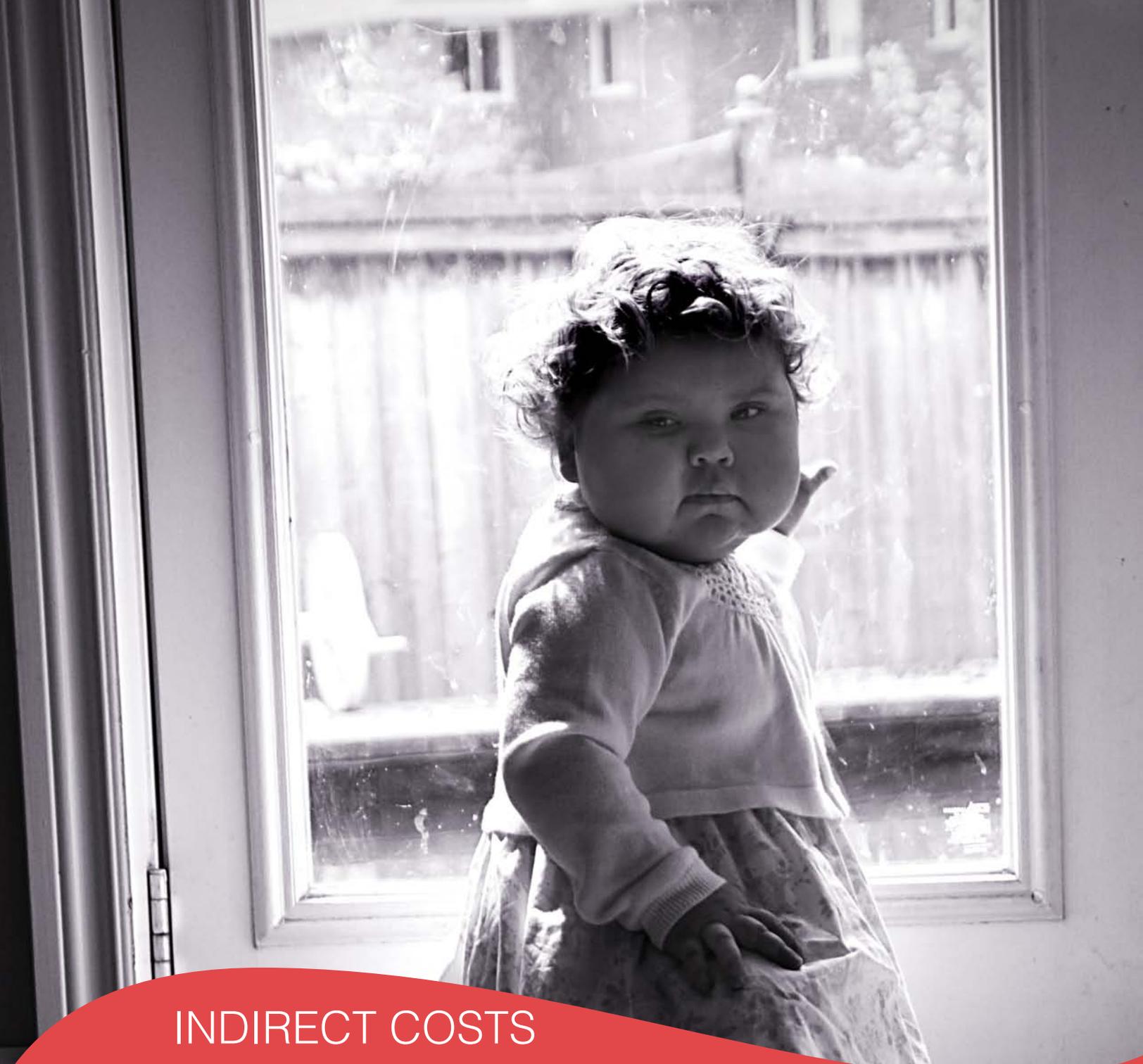
An Australian study of IBD patients reported on the use of institutional care and other health care professionals.⁷⁸ Emergency room visits were measured in an American study of people with CD, using records from a health maintenance organization.⁵⁷ In each case, the cost in Canada was estimated based on the cost in the US or in Australia, to reflect the size of the Canadian IBD population. A total of \$101 million in additional health care system costs is estimated for IBD in Canada, corresponding to \$433 per person per year.

TOTAL DIRECT COSTS

Total direct costs top \$1.2 billion, and are shown in Figure 1. They are not broken down into CD versus UC because the prescription drug costs could not be reliably and accurately separated by disease. Drug costs were the single largest component of cost, followed by inpatient hospitalization. Together these two items constituted 76% of the direct medical costs of IBD.

Figure 1: Direct Medical Costs





INDIRECT COSTS

BRYGETTE PARK

"My little girl is living a normal life because of IBD research. Brygette rides a bike, swims and runs on the beach singing 'I'm free.' I never thought we would be this happy again," says Penny Park, mother

key findings:

- 43% of employed persons with IBD required time off due to IBD.
- Short-term work losses were estimated at 7.2 days per employed person with IBD per year, strictly due to IBD.
- This costs \$181 million per year in short-term work losses in Canada for the 140,000 actively-employed individuals with IBD in 2012.
- People with IBD have a lower labour participation rate (3-13%) than the general population.
- The costs of reduced labour participation could range from \$326 million (with 3% non-participation) to \$1.4 billion (with 13% non-participation due to IBD). The best estimate is a minimum of \$979 million (9% non-participation – 21,000 individuals).
- There are 18 deaths per year in employed people with CD, at an average age of 49 years. The productivity loss associated with these deaths is \$9.4 million.
- No costs were assigned to premature deaths in people with UC.
- There are very limited data with which to estimate caregiver costs.
- At a minimum, parental care giving for pediatric cases of IBD could cost \$7 million a year. Potentially, care giving for severely ill people with IBD costs \$86 million per year.
- Use of complementary and alternative medicines related to IBD costs approximately \$32 million per year.
- Other out-of-pocket expenses (travel, household support, patient activities) related to IBD cost \$268 million per year.

SUMMARY:

- Indirect costs are higher than direct medical costs and are estimated at \$1.6 billion in Canada in 2012 (\$868 million for CD, and \$693 million for UC).
- Short-term work absence strictly due to IBD averages 7.2 days per employed person with IBD, or \$181 million in Canada in 2012.
- People with IBD are more likely to have lower labour participation rates than the general population, ranging from 3% to 13% less employment. The most likely minimum estimate is that this loss of productivity costs \$979 million per year since at least 21,000 individuals would not be able to be in paid employment.
- Productivity losses from premature deaths are estimated at \$9 million per year.
- Caregiver work absences are estimated to be \$7 million per year for parents of pediatric IBD cases, plus \$86 million per year for severely ill people with IBD.
- The individual's out-of-pocket expenses are estimated at \$300 million (non-prescription medicines, household support, travel for medical care, etc.).

INTRODUCTION

Indirect costs are costs that are borne by people and by society, rather than the health care system. Typically, the largest contribution to indirect cost is productivity losses, or work absences – both short-term (sick leave) and long-term (disability leave and/or early retirement). For some diseases, premature death is an important cause of productivity loss. In addition, some people may never enter the work force, or may work part-time hours, for reasons related to health. Also, caregivers (including parents) may have to take time off from work. Economists classify productivity losses as costs that are borne by society in general. Other costs are borne by the individual personally – out-of-pocket expenses such as, home aids and modifications, formal care (housekeeping, daycare), travel for medical appointments, nutritional products, and complementary and alternative medicines.

Most people living with IBD have had the disease for most of their adult lives. People with milder disease may experience some periods of poorer health and long periods of relatively normal health. This may allow them to be in regular employment, but with some absences for sick leave and/or medical appointments. People with more severe disease may have to reduce their hours, change their type of employment, or withdraw from work altogether.

Living with IBD can influence employment choices. Easy access to a bathroom may restrict the types of jobs an individual can perform, such as production line work, outdoor work or jobs with frequent travel, with a trend to select sedentary occupations.^{78,80}

People with IBD worry that their disease may affect their job and career, including having limited choice to remain in a particular job because of the health benefit coverage of expensive drugs. A German study found that 47% of people with CD thought their careers were affected by IBD, as did 39% of people with UC.⁸¹ Similarly, a UK study found that 24% of people with CD felt that their disease had limited their employment prospects and had either prevented them from seeking promotion or had actually prevented promotion.⁸² Finally, IBD can have a broad impact, with 11% of spouses reporting that IBD had compromised their professional careers.⁸³

EDUCATION IMPACT

IBD is often diagnosed in childhood, adolescence or early adulthood. This can impact educational attainment as well as the selection of a career. Education can be affected by temporary absences from school and difficulty with studying or sitting for exams, as well as lack of understanding and discrimination from teachers.^{82,84} Overall, however, while the individual may face difficulties and challenges, the levels of educational attainment do not differ statistically for those with IBD from the general population or a healthy comparison group. No costs or deficits were assessed for impact on education.

SHORT-TERM WORK LOSSES

Employed people with IBD may miss work due to medical appointments, illness, or hospitalization.

At a minimum, days spent in hospital must be days missed from work, for those who are employed. In reality, the true number of days missed from work is much higher. In order to find

out how many days are missed due to IBD, the most realistic method is to survey people with IBD. Since it is not feasible to survey workplaces to collect data on how many days of sick leave are taken per employee with IBD, and the reasons for sick leave.

There are few Canadian-specific data on short-term work losses due to IBD. It is widely thought that productivity losses are ‘transferable across borders’; that is, people in different countries are just as likely to respond to illness by taking time off work. This implies that productivity data collected in one country can be transferred to another country, since the number of days off work per person is unlikely to vary much between countries with similar labour practices and sick leave policies. Among the countries with reported data (Canada, Australia, and Western Europe), we assumed that labour practices are likely to be relatively similar.

There have been nine studies that report data on short-term work losses. The diversity in the collection and reporting of results required a meta-analysis to determine an average estimate of the expected sick leave per employed person with IBD.⁸⁵

Few studies separated costs for CD versus UC. Overall, it was reasonable to assume that there were similar costs for time off work for both CD and UC.

On average, 43% of employed people with IBD took time off work per year, and each employed person with IBD took 7.2 days off per year due to IBD. These papers reported an average rate of employment of 60%; this is almost identical to the rate of labour participation reported by people with IBD in Manitoba.⁸⁰

To convert this to a Canadian cost, the total number of days lost per person can be multiplied by the number of people with disease, the percentage who are employed, and the mean daily wage rate (\$179.54 per day, according to Statistics Canada).⁸⁶ The total cost of short-term work loss was \$181 million for the 140,000 actively employed individuals with IBD.

key findings:

- **43% of employed persons with IBD required time off due to IBD.**
- **Short-term work losses were estimated at 7.2 days per employed person with IBD per year, strictly due to IBD.**
- **This costs \$181 million per year in short-term work losses in Canada for the 140,000 actively-employed individuals with IBD in 2012.**

LONG-TERM WORK LOSSES

Long-term work losses can result from long-term absences from employment (disability), long-term reduction in hours of work, premature retirement, and premature mortality.

It can be difficult to isolate the specific factors why an individual has withdrawn from the workforce (or has never entered the workforce). Often there are multiple factors involved. This makes it difficult for people with IBD to single out a reason why they are employed or not.

Instead, it is more reliable to compare overall rates of employment in people with IBD to rates in the general population. The assumption is that any difference in employment rates can be due to IBD. There are likely additional costs from people who reduce their work hours, but this has not been measured in any survey.

Impact on Employment

There were two studies in Canada, two in Australia, two in Europe, and one in the United States which looked at employment rates in people with IBD. A meta-analysis of these seven studies found that IBD was associated with a 13% reduction in the probability that a person will be employed. In other words, since the Canadian general population has a labour participation rate of 80%, then an IBD population would have a labour participation rate of (80% - 13% = 67%). Each year, this would correspond to \$1.4 billion for 30,000 Canadians with IBD not able to work.

Two Canadian studies had inconsistent findings. The first was conducted in the province of Manitoba, using people who were definitely identified as having IBD based on repeated health care system contacts due to IBD.⁸⁰ Their employment status was compared to that of the general Manitoba population. They found that after diagnosis, people with IBD gradually withdrew from work and were more likely to be unemployed, disabled or retired. Compared to the general population, people with IBD had a statistically significant reduction of about 9.3% in employment rate.

In a different approach, researchers asked Canadians who participated in the National Population Health Survey whether they had IBD. The labour participation rates were compared between people who reported IBD and those who did not. This approach can be limited by recall and the wording of the question, that is, whether people accurately report whether they have IBD. In fact, 1.7% of the population reported having IBD in the survey. This is much higher than expected (0.6%) suggesting that some people reported having IBD when in fact they did not. The results of this study were that non-participation in the workforce due to IBD was found to be only 2.9%.⁸⁷ By contrast, an American general population health survey was done by the same researchers who did the Canadian survey. In this survey, the percentage of people who reported IBD was 0.4% of the population – pretty much what would be expected, given the prevalence of IBD. In this survey, the excess rate of non-participation was 12.3% - very close to the meta-analysis finding.⁸⁸ The main difference between the surveys was that too many people in the Canadian survey described themselves as having IBD when they likely did not and these individuals had a rate of labour participation similar to the national average.

New research on disability rates in Norway found that ten years after diagnosis, 19% of people with IBD received a disability pension.⁸⁹ The disability rate was similar for both CD and UC. People under 40 were at highest risk for workplace disability compared to the general population. This research supports that society incurs ongoing costs of IBD; as people withdraw from the work force and are replaced by other workers, employers continue to bear the burden of IBD disability.

key findings:

- People with IBD have a lower labour participation rate (3-13%) than the general population.
- The costs of reduced labour participation could range from \$326 million (with 3% non-participation) to \$1.4 billion (with 13% non-participation due to IBD). The best estimate is a minimum of \$979 million (9% non-participation – 21,000 individuals).

Premature Retirement

Premature retirement was investigated in one Swedish study. This study looked at people with CD only. The investigators reviewed national registers of social services and determined that each year, approximately 1% of the CD population was granted early retirement pensions, with an average duration of 14 years of early retirement.⁹⁰ In Canada, with 129,000 people living with CD, there could be 1,290 persons taking premature retirement due to CD each year. However, it is difficult to separate these cases from the preceding analysis on long-term employment impact. Long-term absence could be from people who did not enter the workforce, but also from premature retirement (people who entered the work force, but left early). To avoid the potential for double-counting, there was no separate calculation for premature retirement in the analysis.

- Costs from premature retirement were assumed to be included in the estimate of costs from long-term work absences.

Premature Mortality

From a purely economic standpoint, premature mortality from IBD can cause productivity losses to society. In Canada, there were an average of 85 deaths due to CD and 43 deaths due to UC per year from 2004-2008 (most recent data available).⁹¹ Of these, there are an average of 30 deaths from CD and 14 deaths from UC in people under the age of 65 (the typical cut-off for the working population). Based on the mortality analysis, UC does not cause excess mortality. It can be conservatively assumed that none of the UC deaths contributed to productivity losses. That is, these deaths would have occurred even in the absence of UC. Therefore, the focus was on CD only.

Of the 30 deaths per year in CD, assuming that 60% of people with IBD are employed, then there would be 18 deaths in potentially employable people with CD. The average age at death was 49 for those who died before age 65; this corresponds to 16 years of lost employment. There would be a productivity loss of \$523,000 per person, or \$9.4 million for the 18 premature deaths each year.

key findings:

- There are 18 deaths per year in employed people with CD, at an average age of 49 years. The productivity loss associated with these deaths is \$9.4 million.
- No costs were assigned to premature deaths in people with UC.

CAREGIVERS

Caregivers are people who provide informal (unpaid) care to others who need assistance for health reasons. Caregivers may take time off work to accompany people to medical appointments, stay with or visit hospitalized people, or care for them at home. Caregivers may also take time off work to do the unpaid work of the person with IBD such as housekeeping and grocery shopping, when the individual is unable to do so. Caregivers are needed for the most severely affected people with IBD, and also for children with IBD (whose parents would need to be involved in their care). However, there are very few data available on the economic impact of IBD on caregivers.

For pediatric cases of IBD, at least one parent would be involved in care of the affected child. If the typical employed person with IBD required 7.2 days per year of sick leave for their own disease management,⁸⁵ it could be reasonably assumed that the same amount might be required to manage a child's illness. Parents of children with IBD could be assumed to have a labour participation rate equal to the general public (81.5% according to the large national surveys in Canada and the US).^{87,88} An average work wage should be assigned to employed parents,⁸⁶ while a minimum wage is typically assigned to non-employed individuals (homemakers, etc.).⁹² Minimum expected caregiver costs for parents of children with IBD total \$7 million for parents of the estimated 5,900 children with IBD in Canada in 2012.

For severely affected people with IBD, there are survey data from an Australian study on caregivers. This survey found that there were 2,600 primary caregivers for people whose main condition was disease of the digestive system.⁹³ However, there was a very small sample size for this estimate, and the results should be treated with caution. Applying prevalence estimates, approximately 23% of these caregivers would be for people with IBD. This translates into one caregiver per 100 persons with IBD (presumably, those with the most severe disease, who would be unable to function normally). Overall, primary caregivers in the survey averaged 30 hours a week caring for people with disabilities. Assuming that 1% of people with IBD required 30 hours a week for care giving, with a Canadian prevalence of 233,000 people with IBD (2,330 severely ill people), care giving would cost approximately \$86 million (at minimum wage).

key findings:

- **There are very limited data with which to estimate caregiver costs.**
- **At a minimum, parental care giving for pediatric cases of IBD could cost \$7 million a year. Potentially, care giving for severely ill people with IBD costs \$86 million per year.**

OUT-OF-POCKET EXPENSES

Only a few studies have examined out of pocket expenses for people with IBD. These expenses include ostomy supplies, home aids and modifications, formal care (housekeeping, daycare, etc.), travel for medical appointments, nutritional products, and complementary and alternative medicines.

A survey of members of the Crohn's and Colitis Foundation of Canada found that use of complementary and alternative medicines was quite common.⁹⁴ Half of the respondents had

used (24%) or were currently using (another 24%) complementary or alternative medicines. Herbal or plant-based therapies were the most commonly reported. Special diets were also used by 28% of respondents. The average person with IBD who uses these medicines spends \$568 (CDN\$2012) per year; given that 24% of people with IBD are current users, this converts to \$136 per person with IBD, or \$32 million per year.

A German population study surveyed people with IBD over a broad range of costs, including out-of-pocket expenses: for example, travel, household support, and patient activities. The mean cost per four weeks was 50 Euros per person with CD and 46 Euros per person with UC (2004 Euros).⁹⁵ This converts to \$1,152 (2012\$CDN per year) – and a total cost of \$268 million per year for the 233,000 people with IBD in Canada.

Canadians with IBD who have had portions of their bowel surgically removed require specific care to maintain their ostomy (the surgically-created opening in the body for the discharge of wastes). Products used for ostomy care are variably reimbursed across the country, and can represent a significant individual burden. The province of Ontario, for example, reimburses up to \$600 per year per ostomy, yet the estimated annual expenses are approximately \$3,000. To be conservative, it was assumed that patient-related expenses for ostomy care were included in general out-of-pocket expenses.

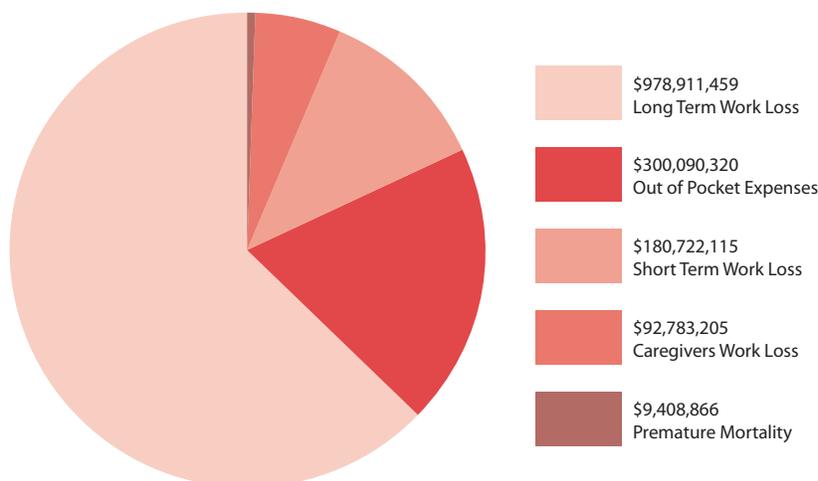
key findings:

- Use of complementary and alternative medicines related to IBD costs approximately \$32 million per year.
- Other out-of-pocket expenses (travel, household support, patient activities) related to IBD cost \$268 million per year.

SUMMARY

Total indirect costs are presented in Figure 1, and top \$1.5 billion. These costs are split between CD and UC based on their prevalence: \$869 million for CD (56%), and \$693 million for UC (44%) – plus the adjustment that premature mortality occurs only in CD.

Figure 1: Indirect Costs by Type of Cost



INDIRECT COSTS (TECHNICAL SUPPLEMENT)

SHORT-TERM WORK LOSSES

Table 1 lists the nine studies that report data on short-term work losses.⁸⁵ Most studies used different reporting time periods (for example, work loss over 4 weeks or over 6 months). This required some adjustment for the results to be in a standard format: the number of days missed per person per year. The diversity in the collection and reporting of results required a meta-analysis to determine an average estimate of the expected sick leave per employed person with IBD.

On average, 43% of employed people with IBD took time off work per year, and each employed person with IBD took 7.2 days off per year due to IBD. These papers reported an average rate of employment of 60%; this is almost identical to the labour participation reported by people with IBD in Manitoba.⁹⁷

To convert this to a Canadian cost, the total number of days lost per person were multiplied by the number of people with disease, the percentage in active employment, and the mean daily wage rate.

The average wage rate was determined from Statistics Canada while the number of people with disease was obtained from this report (Section 3). In 2012, the national average weekly wage rate was \$897.72 (or \$179.54 per day).⁹⁸ See Figure 2 for an analysis of the short-term work losses due to IBD in 2012.

Table 2: Short-Term Work Losses Due to IBD, Canada 2012

Number of days of sick leave per employed person with IBD	7.2 days
Average daily wage rate in 2012	\$179.54
Cost of short-term work losses per employed person with IBD	\$1,292.86
Employment rate in people with IBD	60%
Number of persons with IBD in Canada in 2012	233,000
Estimated number of employed persons with IBD	140,000
Total annual cost of short-term work losses (140,000 employed persons at \$1,292.86 per person per year)	\$181 million

Table 1 : Summary of Short-Term Work-Loss Studies⁸⁵

	ABS (2004-5) ⁹⁹	Bassi (2004) ¹⁰⁰	Blomqvist (1997) ¹⁰¹	Boonen (2002) ¹⁰²	Pinchbeck (1988) ¹⁰³	Sorensen (1987) ¹⁰⁴	Stark (2006) ¹⁰⁵	Wyke (1988) ¹⁰⁶				
Country	Australia	UK	Sweden	Netherlands	Canada	Denmark	Germany	UK				
Year of study	2004-5	2000	1994	2000		1984	2004	1979 1985				
Disease	IBD	CD UC	IBD	CD UC	CD	CD	CD UC	IBD				
Data source	Community based	University hospital based	National registers & surveys	Hospital register	Hospital & physician recruited	Hospital recruited	Organization recruited	Hospital recruited				
# with IBD	-	172	284	N/A	282	359	2430	106	241	242	170	144
Mean age	43	46	N/A	37	44	44	41	43	43	43	43	48
% Male	44%	41%	N/A	38%	52%	40%	35%	45%	52%	52%	52%	51%
% Employed	65%	39%	39%	62%	69%	65%	63%	67%	68%	68%	68%	65%
% using sick leave	8.1% over 2 weeks	50% over 6 mo.	32% over 6 mo.	12% of cases	29% over 1 yr	41% over 1 yr	50% over 1 yr	72% used < 11 days	14% over 4 weeks	15% over 4 weeks	42% over 1 yr	46% over 1 yr
Forecasted % sick leave per year	43%	57%	39%	-	29%	41%	50%	-	41%	42%	42%	46%
Days leave per sick person	1.61 over 2 weeks	-	-	-	16.7 over 1 yr	10.1 over 1 yr	19.8 over 1 yr	-	1.4 over 4 wks	1.7 over 4 wks	-	-
Days leave per employed person per yr	9.0	-	-	5.4	4.9	4.2	9.9	-	7.8	9.3		

CROHN'S AND COLITIS AUSTRALIA 2007

LONG-TERM WORK LOSSES

Table 3 lists the seven studies that report data on long-term work losses.⁸⁵

Table 4 presents a range of values for long-term work losses, using the most important of these different studies: the meta-analysis, the two Canadian studies, and the American survey.

Table 4: Long-Term Work Losses Due to IBD, Canada 2012

Average weekly wage rate in 2012	\$897.72
Average yearly wage rate in 2012	\$46,681.52
Number of persons with IBD in Canada in 2012	233,000
Meta-analysis⁸⁵	
Percent reduction in labour participation due to IBD	13%
Total annual cost of long-term work losses (30,000 employed persons)	\$1.4 million
Manitoba Survey⁹⁷	
Percent reduction in labour participation due to IBD	9%
Total annual cost of long-term work losses (21,000 employed persons)	\$979 million
Canadian Survey⁸⁷	
Percent reduction in labour participation due to IBD	3%
Total annual cost of long-term work losses (7,000 employed persons)	\$326 million
American Survey⁸⁸	
Percent reduction in labour participation due to IBD	12%
Total annual cost of long-term work losses (28,000 employed persons)	\$1.3 million

Table 3: Summary of Long-Term Work Loss Studies⁸⁵

	ABS (2003) ¹⁰⁹	ABS (2004-5) ⁹⁹	Bernstein (2001) ⁹⁷	Longobardi (2003a) ¹⁰⁷	Longobardi (2003b) ¹⁰⁸	Sorensen (1987) ¹⁰⁴	Boonen (2002) ¹⁰²		
Country	Australia	Australia	Canada	Canada	US	Denmark	Netherlands		
Year of study	2003	2004-5	1995-96	1999	1999	1984	2000		
Diseases	IBD	IBD	IBD	IBD	IBD	CD	CD UC		
Data sources	SDAC	NHS	IBD-Register	Health Administration data linked with census	Canadian National Population Health Survey (NPHS)	National Health Interview Survey (NHIS)	Hospital recruited	Hospital Register	
# with IBD	101	65	2,476	80	187	187	106	282	359
Number of Controls	36,140	25,841	14,177	26,082	10,704	23,462	75	1,504	1,504
Average Age	-	43	42	35.9	42.7	42.2	44	37.3	43.6
Proportion Male	-	44%	45%	48%	37%	34%	65%	38%	52%
Proportion Employed (IBD)	62.7%	65%	59%	67%	71%	68%	65%	62%	69%
Proportion Employed (Controls)	74%	74%	68%	77%	82%	85%	64%	70%	73%
Estimated Relative Risk	0.84	0.87	0.86	0.87	0.87	0.8	1.02	0.89	0.95
Confounders Controlled	No	No	Age	Age	Various	Various	None	Age	Age

Premature Mortality

Of the 30 deaths per year in CD, assuming that 60% of people with IBD are employed, then there would be 18 deaths per year in employed people with CD. The average age at death was 49 for those who died before age 65; this corresponds to 16 years of lost employment. Taking the average weekly wage in Canada, and applying a 5% discount rate to convert future costs into present-day dollars, there would be a productivity loss of \$523,000 per person, or \$9.4 million for the 18 premature deaths each year (Table 5).

Table 5: Costs from Premature Mortality

Annual deaths from CD in people under 65	30
Employment rate in people with CD	60%
Annual wage rate	\$46,681.52
Number of years of lost employment	18
Cost per premature death (discounted at 5%)	\$522,715
Total cost due to premature mortality	\$9.4 million

CAREGIVERS

Table 6: Parental Caregiver Work Losses

Number of People < 20 with IBD in Canada, 2012	5,900
Days of Work Loss per Parent	7.2 days
Labour participation rate	81.5%
Daily wage rate, employed	\$179.54
Daily wage rate, non-employed* (minimum wage, ON)	\$76.88
Total cost of work loss in parents	\$7 million

*Minimum wage (\$10.25/hour) in Ontario, 7.5 hours/day¹¹⁰



NON-FINANCIAL COSTS

THE FREY FAMILY

"I am really looking forward to seeing the research we fund being translated from bench to bedside, especially thinking about what may lie ahead for my kids." - Lori Anne Frey, mother

There are many difficulties associated with IBD. There are ongoing medical issues to contend with, from the experience of symptoms (pain, diarrhea, fatigue) to the worry about how the course of the disease will affect overall quality of life.

SUMMARY:

- IBD causes non-financial costs to individuals who bear the burden of disease and their families, including reduced quality of life, loss of leisure time, and limited choices of career, travel and other personal options.
- Quality of life is most affected by disease activity: individuals with moderate to severe symptoms have the most reduced quality of life. However, even people without symptoms suffer from distress, anxiety, and fear leading to a loss of quality of life.
- CD and UC have a comparable effect in the reduction of quality of life.
- Individuals with IBD have a lower quality of life, compared to the general population, across almost all different dimensions of health. People with moderate to severely active disease have very significantly impaired quality of life, but even those in remission have a quality of life below the population average.
- Adolescents with IBD may be particularly troubled by psychological and behavioural issues related to their IBD and its impact on their quality of life.
- Quality of life can be significantly improved with effective treatment, including both surgery and drug therapy. Treatment-improved quality of life often leads to restored productivity.
- It is difficult to quantify the cost of loss of quality of life but, based on Australian research, the cost of IBD in Canada for loss of quality of life may be more than \$4 billion (CAD).

INTRODUCTION

This report has explored the financial costs associated with IBD, from the viewpoint of the individual with IBD, the health care system, and society. However, beyond out-of-pocket expenses, individuals with IBD also experience tremendous additional personal cost, that is, the burden of having a disease. There are many difficulties associated with IBD. There are ongoing medical issues to contend with, from the experience of symptoms (pain, diarrhea, fatigue) to the worry about how the course of the disease will affect overall quality of life. The fluctuating nature of IBD can make it very difficult to plan for the future. In particular, there is reduced quality of life from living with the disease, as well as reduced choices with respect to career, travel and other personal options. Another aspect that is not traditionally “costed” is the value of non-work time which is spent being ill or dealing with illness. This includes leisure time for working-age people, but also all of the time for non-working people (such as students, retirees, and homemakers).

It is possible to calculate a dollar cost for the individual's burden of suffering from a disease, and it has been done when estimating the burden of an illness (both for IBD and for other diseases).^{111,112} However, in order to convert a decrease in quality of life into a dollar cost, it is necessary to place a price on the value of life, health and suffering. This is a controversial topic, and it can be difficult to come up with an acceptable solution. Also, when costs are assigned for a decrease in quality of life, these costs are generally very high, and in fact can dwarf the actual financial costs of a disease. For example, researchers in Australia estimated the financial cost of IBD to be almost \$500 million, but the additional cost of the quality of life decrease was \$2.7 billion (Australian dollars).¹¹¹ Given that Australia is a medium prevalence IBD country with 20 million people compared to the high prevalence reported in Canada with a population of 32 million, a conservative estimate for the quality of life cost in Canada (based on the report from Crohn's and Colitis Australia) is \$4 billion (CAD). Rather than debate the price of health, this section of the Impact of IBD Report describes the impact of IBD to the individual's health, and will not attempt to further quantify the burden with a dollar amount.

QUALITY OF LIFE

Quality of life can be measured using questionnaires, which people complete with respect to their current state of health. Sometimes the questions might be symptom-related, such as: Do you often have diarrhea? How often are you tired? Quality of life questions that relate to health might be: How do you feel about your state of health? Does your health prevent you from physical activities? From social activities? More general questions about quality of life might be: How often do you feel sad? Are you often worried about the future?

There are three types of quality of life questionnaires that will be discussed: disease-specific, generic, and utility questionnaires. Table 1 briefly states these three types of questionnaires, with more detail in each subsequent section.

Table 1: Quality of Life Questionnaires

Type	Audience	Primary Advantage
Disease-specific	Can only be given to people with the specific disease	Very informative within the disease
Generic	Can be given to anyone	Allows for comparison between diseases
Utility	Can be given to anyone	Allows for numerical comparison between diseases

IBD-Specific Quality of Life

Quality of life instruments that focus on a specific disease help us to understand what aspects of a disease are most troubling and what factors impact quality of life for people with the disease of interest. The Inflammatory Bowel Disease Questionnaire (IBDQ) has been the most commonly used quality of life instrument. It can be given to people with either CD or UC. It has been used in many different countries. Researchers around the world have found that quality of life is decreased in people with IBD. Using the IBDQ, it has become clear that quality of life is most strongly impacted by severity of disease.^{113,114,115} That is, people with more severe disease have the greatest reduction in quality of life, and people with milder disease have less reduction in quality of life. They have also found that women are more likely to have lower quality of life than men with IBD.^{114,115} Both CD and UC have a similarly negative impact on quality of life, and there are no significant differences in quality of life between people with CD and UC.

It is important to note that all people with IBD can have reduced quality of life, even those who do not have symptoms (due to a fluctuating disease, or because their medications have caused a remission). Canadian researchers, using the Manitoba database of individuals with IBD, have done some interesting work comparing people with consistently active versus fluctuating disease. A comparison of lifetime prevalence suggest higher rates of panic, generalized anxiety and OCD and major depression and lower rates of social anxiety and bipolar disorders in the IBD sample than in national samples.¹¹⁶ However, even those without symptoms have psychological distress (stress, anxiety, fear about pain, and worry about the consequences of their disease).^{117,118} They have confirmed the results of other international studies that found a higher rate of depression and anxiety disorders in people with IBD.¹¹⁹ Poor sleep quality is very common in people with IBD, whether or not their disease is active.¹²⁰ Other researchers have found similar results, that quality of life is driven most by disease activity, but is followed by psychological distress – common to those with symptoms and those without. On the other hand, factors such as personality or sociodemographic characteristics (age, income, education, ethnicity, etc.) are not important to quality of life in IBD, although they are often relevant for other diseases.¹²¹

Health care professionals may not fully appreciate the impact that the disease and its symptoms may have on patient quality of life. A Canadian/European survey in UC found that physicians significantly underestimated whether UC disrupted their patients' quality of life, compared to what their patients reported. Physicians did not fully appreciate which symptoms

were important to patients' lives, or the severity of the disease experience.¹²²

Pediatric Issues

Quality of life affects everyone who has IBD, adults and children. It is important to distinguish that children may experience a disease differently, and thus have different impacts of their disease. An IBD-specific measure to assess quality of life impact for children has also been developed.¹²³ Children with IBD have a reduced quality of life, as do children with other diseases; however, teenagers are most strongly affected by their IBD.^{124,125} Adolescents are significantly affected in multiple ways; they have reduced functioning and autonomy, at an age when separation and independence are extremely important. Their social functioning is compromised, when this is a critical factor in their lives. Attendance with school can be difficult, at a time when important lifetime choices need to be made (such as, post-secondary education). Adolescents easily fall prey to negative emotions and poor self-esteem, resulting in troubled behaviour or depressive issues.

Quality of Life and Treatment

Since quality of life is most affected by disease activity, it makes sense that effective treatment can improve quality of life by reducing symptoms, inducing remission, and helping people feel that they are in control of their disease.

Surgical treatments are associated with a normalization in quality of life, both for CD and for UC.^{126,127} As well, conventional drugs such as steroids and azathioprine have been proven effective at improving quality of life.¹²⁸ More recently, the new biological agents have shown significant increases in quality of life for all types of disease: UC, CD and fistulizing CD.^{129,130,131} The improvement in quality of life seen with treatment can effectively place a person suffering from active disease into a state of remission, without significant symptoms. It can also be important to the individual with IBD that effective treatment provides them with some feeling of control or predictability to their disease, reducing the fear and anxiety that are problematic even when people are not suffering from active disease.

Quality of Life and Productivity

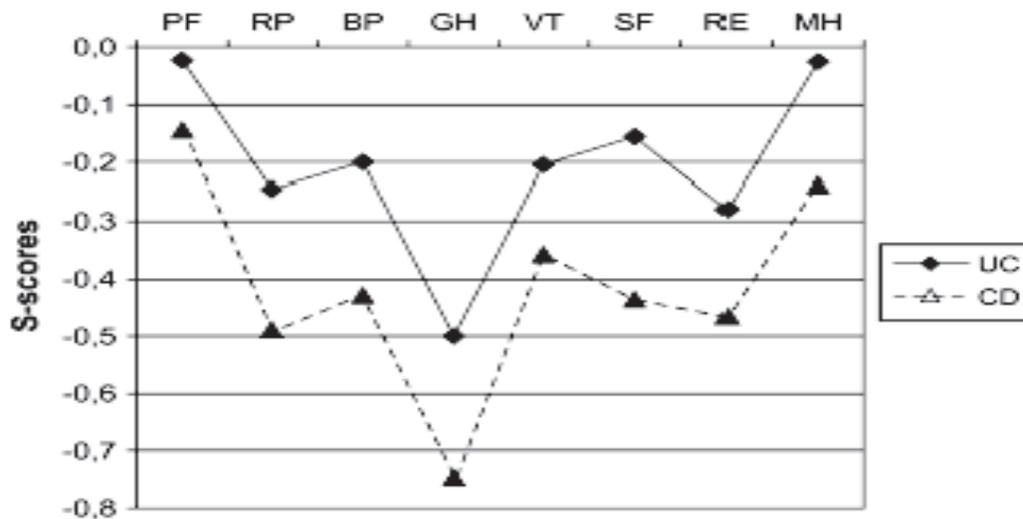
Quality of life has a direct relationship with productivity. Unemployment, disability and sick leave are related to low quality of life.¹³² Conversely, quality of life is higher in people with IBD who are employed.¹³³ People who achieve remission with effective drug therapy often report not only an improvement in quality of life but also a return to employment – either returning to work (for those who were not employed) or returning to full-time work (for those who were employed part-time). A study in CD found that people who responded to treatment had twice the employment rate than for people who did not respond to treatment after a year of therapy.¹³⁴ A study in UC found similar dramatic results, with responders 2.5 times more likely to be employed and three times more likely to not receive disability compensation.¹³⁵

COMPARISON BETWEEN IBD AND THE GENERAL POPULATION

The second way to measure quality of life is to use a “generic” questionnaire, meaning a questionnaire that can be given to anyone and everyone, regardless of their health or whether they have a specific disease. This type of survey is very good for comparing quality of life across different diseases. It allows us to see what the normal level is for the general population, and then compare to individuals with a specific disease. It is important to note that the general population norm is made up of people with all kinds of levels of health and all kinds of diseases. This is not the same as “good health”, it is instead “average health” for a mixture of people in the community – some will be very fit and healthy, and others will have various chronic diseases.

The most common generic quality of life tool is called the Short Form 36 (SF-36, so called because it has 36 questions, and is a shorter – but just as accurate – version of a longer questionnaire). Compared to the population norm, people with both CD and UC scored lower on the SF-36.¹³⁶ Scores were lowest for those with the most symptoms. Scores were significantly different for almost all of the eight different aspects of quality of life measured by the SF-36 (such as, physical functioning, social functioning, mental health). Figure 1 compares the people with UC and CD to the standard population. The “general health” dimension was the worst compared to the standard population, followed by role-physical and role-emotional.

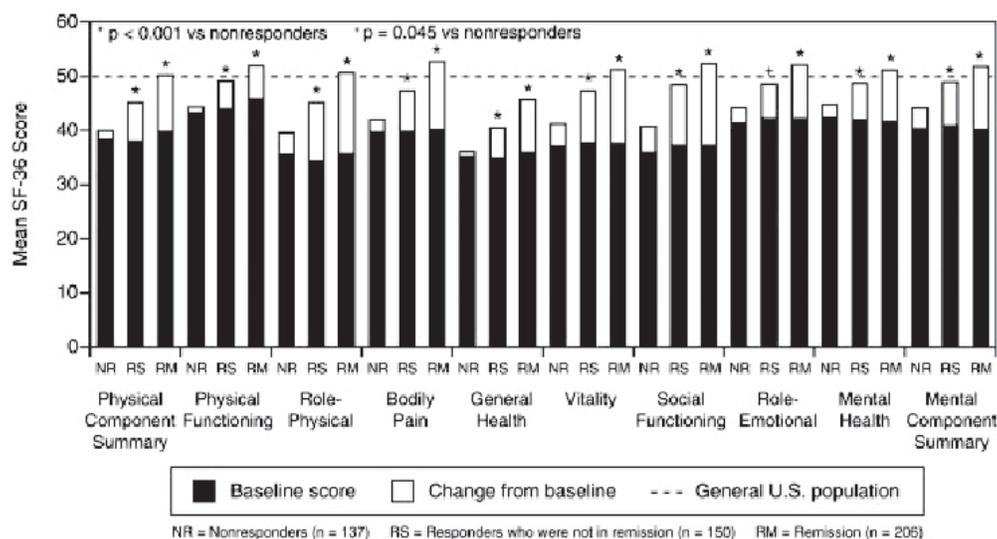
Figure 1: Standardized scores for patients with UC and patients with CD, adjusted for age, sex, and educational level (0 = reference population)



PF = physical functioning, RP = role physical, BP = bodily pain, GH = general health, VT = vitality, SF = social functioning, RE = role emotional, MH = mental health

When people with IBD receive effective treatment, their quality of life can approach that of the general population. A study in UC patients measured the change in quality of life using the SF-36.¹³⁵ Study subjects who experienced remission with treatment had quality of life improvements that restored them to typical levels of quality of life, while those who did not respond had minimal improvement. In between these groups, the patients who had some response (but not a remission) had an intermediate improvement in quality of life (see Figure 2).

Figure 2: Mean Change in SF-36 Summary and Individual Scale Scores from Baseline to Week 30 by Response Status



UTILITY

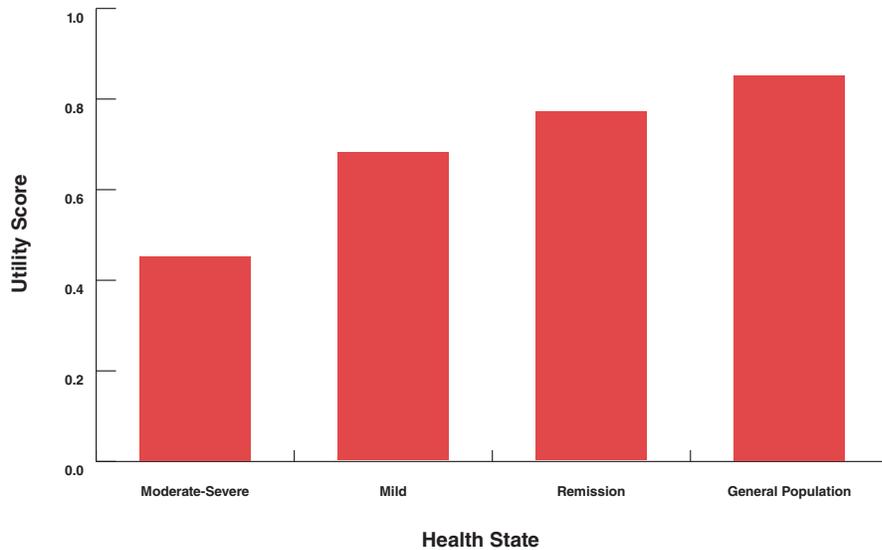
Utility Scores

A third type of quality of life questionnaire is known as a utility instrument. This is a generic quality of life questionnaire, because it can be given to anyone. It has two extra features: first, the resulting score is a single number making comparisons easy (in contrast, the SF-36 gives a set of scores for each of the eight different aspects of quality of life that it measures); and second, the score has a specific meaning. The utility score is assigned with reference to a top and a bottom score. A top score of 1 is a state of perfect health. A bottom score of 0 is a state of death. Different diseases have scores in between 0 and 1, depending on how strongly people feel they would prefer one disease compared to another. For example, the average utility score for the US population is 0.85 – reflecting a mix of people and states of health, some good and some bad.¹³⁷

People with IBD score below the US average, even when they are in a state of remission. Only a few studies have used utility instruments in IBD, but they have found consistent results.^{138,139} People with moderate to severe disease scored very low at 0.45, which indicates a very significant impairment in quality of life. People with mild disease scored at 0.68, typical of

many chronic diseases; while people in remission scored 0.77 – still well below the population average (see Figure 3). Both of these studies were conducted in CD, but research has shown that quality of life impairment is similar for CD and UC.

Figure 3: Utility Scores for CD versus General Population



It is encouraging that effective treatment can restore utility values to higher levels. For example, a new biological for CD increased the utility score by 34% to achieve remission, and a further 7% to maintain remission.¹⁴⁰ These are very substantial gains in utility score and hence, quality of life.



Summary, Challenges and Recommendations

Marilyn Finkelstein, CCFC Co-Founder

“The haystack’ is getting smaller. There is a light at the end of this tunnel. I would like to be present at the closing of this foundation.”

233,000

**CANADIAN ADULTS AND
CHILDREN LIVING WITH IBD**

1 in 150

CANADIANS HAVE IBD

10,200

NEW CASES DIAGNOSED EVERY YEAR

SUMMARY:

- There are almost 233,000 Canadian adults and children living with IBD (up from 200,000 in 2008): 129,000 with CD and 104,000 with UC.
- Canada has among the highest reported prevalence (number of people with CD or UC) and incidence (number of new cases per year) of IBD in the world.
- The prevalence of IBD currently in Canada is nearly 0.7%, equating to more than 1 in every 150 Canadians.
- IBD is more than twice as common as multiple sclerosis or Parkinson's disease; about as common as Type I diabetes or epilepsy; and somewhat less common than other chronic diseases such as schizophrenia or rheumatoid arthritis.
- Over 10,200 new cases are diagnosed every year – 5,700 with CD and 4,500 with UC.
- Incidence of IBD in Canada has been rising, and significantly so in young children under the age of 10 – a troubling finding.
- Compared to the general population, quality of life in IBD is low across all dimensions of health.
- Costs for people with IBD average \$11,900 per person annually – with indirect patient and societal costs at 56% of the total, and direct medical costs at 44%.
- The total cost of IBD in Canada for 2012 is \$2.8 billion.

common challenges

A number of critical challenges face the IBD community, including:

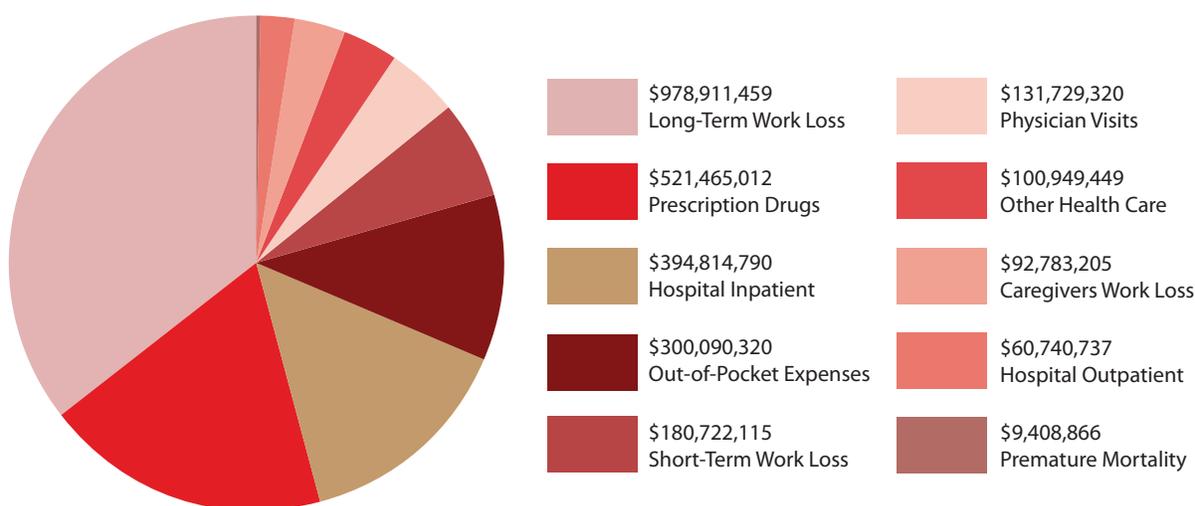
- Awareness of IBD – low recognition of IBD as a chronic disease, resulting in unnecessary social stigma
- Diagnosis of IBD – late diagnosis or inappropriate diagnosis
- Access to IBD specialists and procedures – regional disparities and untimely access to care
- Access to IBD medications – expensive and often cost-prohibitive medications; variable access and coverage across public provincial drug plans
- Employment issues – lower labour participation and vulnerable IBD employees due to their youth and lack of seniority for employment protection
- Support for people with IBD and their caregivers – absence of community-based support mechanisms, particularly for parents of children with IBD
- Research – limited resources to study the “cause, care and cure” of IBD, and for monitoring and evaluation research to improve estimates of prevalence and costs of IBD

COSTS SUMMARY

Total annual costs in IBD are \$2.8 billion – approximately \$11,900 per person with IBD. Figure 1 reflects the distribution of the different types of costs. Indirect costs (from societal losses and personal expenses) are higher than direct medical costs (56% versus 44%, that is, \$6,700 per person for indirect costs, and \$5,200 per person for direct costs). Unfortunately, costs cannot be further disaggregated into CD versus UC, because the pharmaceutical costs could not be split by disease.

Both are conservatively estimated and may be at the low end of potential costs.

Figure 1: Total IBD Costs

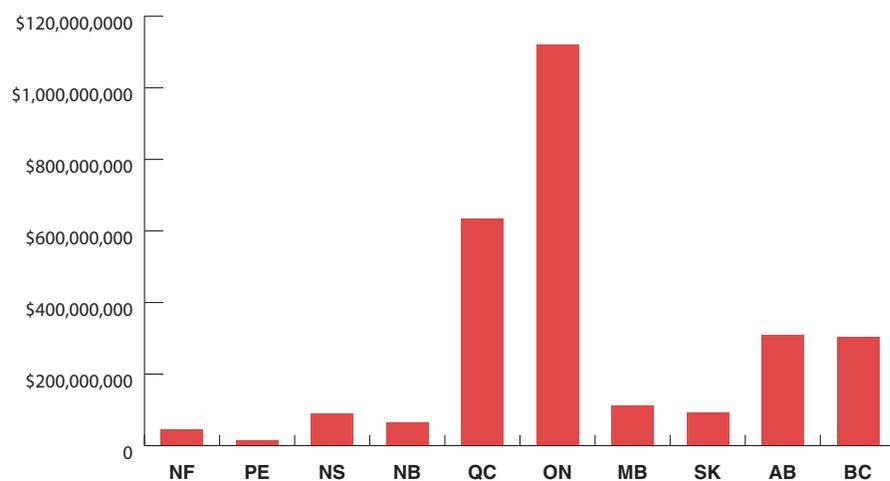


These costs are also presented in Table 1, showing the percentage of total cost which is allocated to each type of cost:

Table 1: Distribution of Total Costs

Short-Term Work Loss	\$180,722,115	6.5%
Long-Term Work Loss	\$978,911,459	35.3%
Premature Mortality	\$9,408,866	0.3%
Caregivers Work Loss	\$92,783,205	3.3%
Out-of-Pocket Expenses	\$300,090,320	10.8%
Hospital Outpatient	\$60,740,737	2.2%
Hospital Inpatient	\$394,814,790	14.2%
Physician Visits	\$131,729,320	4.8%
Prescription Drugs	\$521,465,012	18.8%
Other Health Care	\$100,949,449	3.6%
Total Indirect	\$1,561,915,965	56.4%
Total Direct	\$1,209,699,308	43.6%
Total Costs	\$2,771,615,273	100%

The cost of IBD broken down by province reflects the size of the population in each province, plus differences in the geographic distribution of the disease (particularly a relatively low rate in British Columbia).

Figure 2: IBD Annual Costs by Province

INTERNATIONAL COMPARISON OF IBD COSTS

It can be useful to compare Canadian costs of IBD to the costs in other countries. However, there can be large differences in the costs that are reported, for many different reasons. First, total costs depend on the total number of individuals with IBD. Greater numbers of individuals with IBD mean greater costs. Canada has one of the highest prevalence of IBD in the world, so Canadian costs might be expected to be high. Second, different researchers will use different methods and data to determine costs. Depending on the accuracy of the data, and the types of costs that are included, results may not be directly comparable across countries. Third, prices of items can differ between countries. For expensive items like hospitalization, this would have an impact. Finally, the timing of the research is important, as we know that there have been dramatic shifts over time – with increasing drug costs and declining surgery/hospitalization costs. Recall that Canadian direct costs for this report were estimated at \$5,200 per person with IBD, using data from 2005/6 for most medical costs, with 2011 data for drug costs.

American researchers used large administrative databases to examine the direct medical costs incurred by people with IBD versus those without IBD.¹⁴¹ There were about 20,000 people with IBD in the study – a large sample. The difference in annual cost between these two groups was assumed to be the amount attributable to IBD. Using data from 2003/4, they determined that per-person mean annual costs were US\$8,265 for CD and US\$5,066 for UC (2004 US\$). CD costs were equally split between pharmaceutical claims (35%), outpatient care (33%) and hospitalization (31%). UC costs were weighted more to hospitalization (38%) and outpatient care (37%) than pharmaceuticals (27%, perhaps because biologicals were less used for UC at that time). Compared to earlier research, hospitalization costs have decreased from 55% to 31% for CD, with a corresponding increase in drug costs from 4% to 35%.^{142,143} A striking finding was that IBD costs were significantly higher for children under 20 compared to adults. Drug costs were not so different between children and adults, but hospitalizations and outpatient services were higher for children. Given that there were just under 1 million Americans with IBD at the time of the research, IBD-attributable annual direct costs were estimated at \$6.3 billion.

A recent German study looked at the database records in 2006/7 for about 1,000 people with IBD at gastroenterologist practices.¹⁴⁴ Average annual direct medical costs were €3,767 for CD (CDN\$4,859) and €2,478 for UC (CDN\$3,197). Use of biologicals, inpatient stays, gender and severity status all had a significant influence on costs. The vast majority of costs were for pharmaceuticals (68% for CD and 74% for UC).

Crohn's and Colitis Australia conducted a comprehensive report on the costs of IBD in Australia in 2007.¹⁴⁵ Unlike the situation in Canada, they did not have reliable Australian data on prevalence of IBD, which was an important limitation. They determined that there were approximately 61,000 individuals with IBD in Australia (with a population of about 20 million, this is a prevalence of 0.3%). For these individuals, the total cost (direct plus indirect) was \$406 million – or approximately \$6,600 per individual with IBD.

COMPARISON OF CANADIAN PREVALENCE WITH OTHER DISEASES

It is important to provide a context of the prevalence of IBD compared to other chronic diseases in Canada. One should look to other chronic diseases which occur in working age adults for a point of comparison. Many chronic diseases are uncommon in younger individuals, but dramatically more common in older people; these are less appropriate as comparisons.

With a prevalence of 233,000 people, IBD is:

- more common than multiple sclerosis (68,000)¹⁴⁶ or Parkinson's disease (100,000)¹⁴⁷;
- about as common as epilepsy (204,000)¹⁴⁸ or Type 1 diabetes (233,000)¹⁴⁹;
- not as common as rheumatoid arthritis (340,000)¹⁵⁰ or schizophrenia (340,000)¹⁵¹.

CHALLENGES

The challenges facing persons with IBD, their family members, and caregivers are significant and vary from province to province. The common challenges facing the IBD community include but are not limited to dimensions of awareness; diagnosis; timely and equitable access to treatment and medications; health services delivery; employment; support systems; and research.

Awareness

The following problems in relation to awareness provide a starting point for communications efforts across Canada:

- The prevalence of IBD estimates, outlined in this document, make it clear that CD and UC are not “orphan diseases” in the technical sense¹⁵². Low awareness and lack of understanding, however, make IBD feel orphaned from the family of diseases typically considered to be chronic diseases (for example, diabetes, arthritis, asthma).
- Due to the nature of IBD, these conditions are not preventable and therefore, do not fall under existing chronic disease prevention policies and programs funded by governments across Canada. Therefore IBD is not part of public health awareness campaigns that target prevention and management of chronic diseases.
- While there is consensus in the medical community that CD and UC are chronic diseases, the variability of symptoms and time course also tend to “orphan” IBD from other chronic diseases. A chronic care model modified to suit the episodic nature of IBD would be beneficial to help better coordinate care and engage public and private funders.
- General community awareness levels are low, with frequent misunderstanding about IBD and between IBD and irritable bowel syndrome (IBS).
- Stigma is often associated with the conditions because of the nature of the symptoms.
- Lack of bathroom access in public settings (e.g., bathrooms are kept locked, inaccessible to non-patrons), can significantly limit freedom and mobility for persons living with IBD.
- Currently, there are no local or national campaigns to raise awareness of the urgency related to IBD to facilitate near-immediate access to public bathroom facilities.

Diagnosis

The evidence suggests that late diagnosis and inappropriate investigation and management are substantial problems with IBD. Spray et al.¹⁵³ found, based on referrals to specialists, a median delay of 47 weeks for CD and 66 weeks for those without diarrhea; in UC the median was 20 weeks but was three years in the worst cases. A similar study for children only had similar findings (7.1 months for CD and 6.7 months for UC).¹⁵³ In terms of symptoms, a study conducted by Rath et al.¹⁵⁴ found that 38% of CD patients had an interval of more than a year between onset of symptoms and diagnosis. Pimentel et al.¹⁵⁵ found people could be symptomatic for years before diagnosis (a prodromal period of 7.7 ± 10.7 years for CD and 1.2 ± 1.8 years for UC), due to insidious onset as well as delays after presentation.

- Patients may be slow to present in part due to lack of information/awareness and stigma (Grandbastien et al.¹⁵⁶).
- Symptoms may mimic functional disease (IBS) leading to misdiagnosis and delays.
- There can be a lack of awareness within the primary care community and emergency departments, which can impede diagnosis. At least some of the delay in diagnosis is due to the patient and the primary care physician not recognizing the symptoms, which further emphasizes the importance of education.
- Differential diagnosis may be difficult for CD and UC.
- Not only do CD and UC elevate the risk of colorectal cancer but their symptoms can delay a diagnosis of colorectal cancer.
- IBD is increasing in incidence, so health professionals may not have seen much of it previously.
- Access to endoscopy, gastroenterologists and radiology shows significant regional variation making it difficult for some Canadians to be assessed in a timely fashion.
- Access to gastroenterologists (i.e. medical specialists in gastrointestinal disease) is likely to get worse in Canada for the foreseeable future. Demographics indicate that greater numbers of these specialists are approaching retirement and limited training and residency opportunities drive this trend.¹⁵⁸

Timely and Equitable Access to Treatment

- Equal and timely access to clinically appropriate medications is vital to persons living with IBD. In Canada, drug plan formulary decisions are based on the pharmoeconomic evaluations conducted by the Common Drug Review and provincial drug plans. However, the current system leads to untimely and inequitable access to medications across the country that is not based on patients' needs but a reflection where people live and their financial means.
- Recent treatment options can help prevent hospitalizations and improve health outcomes and quality of life for people with IBD. Unfortunately, many of these therapies are expensive and may not be available, or have restricted access, through provincial drug plans.
- The cost of pharmaceuticals can be prohibitive, and there is significant variability in access to and coverage for vital medications between provincial formularies, forcing some patients into surgeries (with their associated impacts) that might otherwise be avoidable.
- Biological therapies, in particular, pose significant access issues due to their high cost. Access and coverage may depend on the insurance status of the patient – those with private health insurance may be able to obtain a limited supply – while those without, depend on variable provincial drug plans.

Health Services

- There are significant regional disparities in diagnosis and treatment across and within provinces and territories. It would be worthwhile identifying the areas most in need of attention.
- With declining numbers of gastroenterologists, poor referral practices to IBD specialists will likely be exacerbated.
- Wait times¹⁵⁹ for and access to endoscopy are issues which have an impact on the delay preceding confirmed diagnosis. The recent Survey to Access to GastroEnterology (SAGE) data show that a patient with a high likelihood of severe IBD can expect a total wait time of 126 days. Of these 126 days, patients wait on average 72 days for a consultation and 44 days for a diagnostic endoscopy. Given the target total wait time of 14 days for this disease category, these patients are waiting 16 weeks longer than the recommended wait time target.

Employment Issues

- Crohn's disease and ulcerative colitis can have long-term impacts on employment prospects, particularly due to the age of onset early in life. These demographic factors also mean that the person may not have built up adequate leave entitlements and pension contributions, in comparison to diseases with later onset where more leave is able to be taken, which can then act to impede dismissal.
- There is poor employment protection against redundancy and demotions due to time required away from work, and reports of job loss due to illness are common.
- The effect of symptoms – fatigue, diarrhea, pain and the secondary effects of medications – are not well understood or accommodated in the workplace.
- There can be poor information and support for employers and employees in relation to IBD.

Support for People with IBD and their Caregivers

- There is a need for support for families dealing with a child with IBD, in particular in relation to sibling issues and strain on the parents' relationship with each other.
- Currently there is no public funding of community-based delivery of support services for people with CD or UC. Foundations raising funds for these efforts are limited and are not active in many parts of Canada.

Research, Ongoing Monitoring and Evaluation

- Currently available treatments for IBD can have substantial side effects contributing to or exacerbating other chronic illnesses such as osteoporosis and arthritis. More research is needed into the 'cause, care and cure' of IBD.
- Given the current research funding environment, there are limited resources available to study the underlying causes of disease, build capacity in the IBD research community, and commercialize academic-based discoveries. This will further impede progress towards new and improved treatments for IBD patients and ultimately, towards finding a cure.
- Environmental trigger research is a promising area for research efforts – especially when

the factors may be modifiable.

- Additional epidemiological research is needed to investigate the observation that the incidence of IBD is increasing, especially in children, (for currently unknown reasons) fairly rapidly, that is, within generations rather than over generations.
- Prevalence estimate updates and new estimates for remaining provinces using the administrative database methodology would provide improved national estimates.
- National estimates will further be improved by establishing modified and tested pediatric prevalence estimation approaches.
- More studies are needed to measure the direct and indirect costs by severity of illness, to update the costs/practice patterns associated with biologicals, and to provide more current hospitalization rates (post-impact of biologicals). In addition, new methods to measure other direct costs (such as, non-health care professionals, labs) will help to improve economic impact estimates for IBD.

RECOMMENDATIONS

The CCFC has undertaken a public policy priority-setting exercise to identify its key initiatives. The options were derived from a number of sources including: the 2008 Burden of IBD Report; a strengths, weaknesses, opportunities and threats (SWOT) analysis undertaken in 2009 by the CCFC senior staff and Board of Directors; discussions in CCFC-related social media channels and direct requests for support from CCFC members and people with IBD. A framework was developed to filter and assess these public policy priorities. Given the results of this assessment and the organization's mandate and resources, in 2011, the Board of Directors of the CCFC committed to advancing three specific public policy priorities: increase government funding for IBD research and awareness; ensure timely and equitable access for IBD medications and treatments; and improve public bathroom access for those living with IBD. The CCFC has taken a leadership role in advancing these priorities, and is committed to working with key stakeholders to address the recommendations highlighted in this report.

RECOMMENDATIONS

The Crohn's and Colitis Foundation of Canada recommends:

- Increased funding for cure-related and epidemiological IBD research, and research addressing the physical, psychological and social issues surrounding IBD.
- Greater investment in IBD research and commercialization strategies that will expedite translation of academic-based research discoveries into clinical application in humans.
- Recognition of IBD as a national health priority and increased resource allocation for chronic care models that reflect the episodic nature of IBD and optimize healthcare delivery.
- A national public health campaign and patient education programs be developed and implemented to raise awareness and knowledge among the general public and health care professionals to facilitate earlier diagnosis, increase awareness and reduce social stigma associated with IBD.
- Public and private sector programs that will foster open access to bathroom facilities for people with IBD.
- Timely and appropriate access to gastro-intestinal (GI) specialists, allied healthcare professionals, endoscopy and radiology for those Canadians waiting for diagnosis or treatment of IBD.
- Enhanced and harmonized public and private drug plans so that patients with IBD - no matter where they live in Canada, their age or their socio-economic status - have better access to medically-prescribed pharmaceuticals that improve the health and quality of life.
- Improved drug review processes so therapies of benefit to people with IBD are approved and available more quickly.
- Fair insurance access and policies for people with IBD, reflecting the

episodic nature and partial genetic basis of IBD; further research is needed in this area.

- Appropriate income security measures and employer programs for people whose IBD may otherwise prevent them from being fully or partially employed or presents them with unreasonable financial burdens.

Adults and children with living with IBD face a number of critical challenges. Moreover, the burden that IBD places on individuals, the healthcare system and society is significant and will continue to grow as the number of patients with IBD increases. To improve the current landscape of IBD in Canada, the CCFC calls upon government, media, the general public, and other key stakeholders to move these recommendations forward.

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1 in 150 Canadians

At least one person you know lives with Crohn's disease or ulcerative colitis.



Crohn's and Colitis
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