

Supplement Article

The Impact of Inflammatory Bowel Disease in Canada 2018: Epidemiology

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Abstract

Canada has among the highest incidence and prevalence of inflammatory bowel disease (IBD) in the world. After decades of rising incidence of IBD in Canada during the 20th Century, the prevalence of IBD in 2018 is 0.7% of the Canadian population. Forecasting models predict that prevalence of IBD will continue to rise to 1.0% of the population by 2030. In 2018, the number of Canadians living with IBD is approximately 270,000 and is predicted to rise to 403,000 Canadians in 2030. Inflammatory bowel disease affects all age groups with adolescents and young adults at highest risk of diagnosis. Canadians of all ethnicities are being diagnosed with IBD including known high-risk groups such as Ashkenazi Jews and offspring of South Asian immigrants who were previously thought to be low risk. Moreover, IBD has evolved into a global disease with rising incidence in newly industrialized countries in Asia and South America. The causes of IBD remain unsolved; however, the high rates of disease in Western countries and its emergence in newly industrialized countries suggest that environmental factors associated with urbanization, modernization, or Western diets may be pertinent to understanding the pathogenesis of the disease.

Highlights

1. Canada continues to have among the highest prevalence of IBD in the world.
2. Today, approximately 270,000 Canadians live with IBD. By 2030 it is estimated that nearly 403,000 Canadians will have a diagnosis of IBD.
3. Inflammatory bowel disease has become a worldwide disease with increasing rates in Asia, Africa, and South America—continents where IBD was rarely diagnosed prior to 1990.
4. The causes of IBD are unknown, but the high rates of disease over the past 60 years in Western countries and the emergence of disease in developing countries suggest that factors associated with urbanization, modernization, or Western diets may be pertinent to understanding the pathogenesis of the disease.

5. Many of the leading hypotheses as to the causes of IBD tie in with alteration of the gut microbiome, the suite of organisms that reside in the bowel and maintain bowel health throughout life.

Key Summary Points

1. The incidence (the number of new diagnoses annually) of IBD rose throughout the 20th century in Canada and then stabilized at the turn of the 21st century.
2. The prevalence (the total number of diagnosed persons in the population) of IBD in Canada is among the highest in the world.
3. Today, 270,000 (0.7%, or 7 in 1000) Canadians are estimated to live with IBD. By 2030, that number is expected to rise to 403,000 Canadians (1% or 1 in 100).
4. Inflammatory bowel disease can be diagnosed at any age. However, the age groups that are most likely to be diagnosed are adolescents and young adults from 20 to 30 years of age.
5. Inflammatory bowel disease in Canada affects the lives of Canadians of all ethnicities, including known high-risk groups such as Ashkenazi Jews, and those thought previously to be at low risk, such as first-generation offspring of South Asian immigrants.
6. Canadian health policy makers will need to prepare the Canadian health care system for the rising burden of IBD.
7. As newly industrialized countries in Asia, Africa, and South America are transitioning to a Westernized society, IBD has emerged and its incidence in these countries is rising rapidly.
8. The gut microbiome includes microorganisms that maintain digestive health. Thus, changes in the microbiome, which may change the immune system's response to triggers, may be important in initiating and perpetuating IBD.
9. A number of factors can alter the gut microbiome and early childhood may be a particularly important time such that breastfeeding, early life diet, use of antibiotics, infections, and other environmental exposures may impact the gut microbiome in such a way that facilitates developing IBD.
10. Smoking is associated with an increased risk and worsening disease course of Crohn's disease. Quitting smoking is associated with an increased risk of developing ulcerative colitis. Therefore, never initiating smoking can mitigate the risk for IBD. Educational programs aimed at those at-risk for IBD should emphasize the risk of starting to smoke tobacco.
11. Modifying exposure to environmental risk factors associated with the Westernization of society (e.g., Western diet and lifestyles) may provide an avenue for reducing the risk of IBD in Canada and worldwide.

Gaps in Knowledge and Future Directions

1. While the incidence of IBD appears to be stabilizing in some regions in Canada, IBD may be occurring more frequently in certain populations such as in children, South Asians, Ashkenazi Jews, and immigrants. Future research should focus on the changing demographics of IBD in Canada.
2. The prevalence of IBD will rise steadily over the next decade. To enable better health care system planning and to respond adequately to the increasing burden of IBD, ongoing surveillance of the epidemiology and health services utilization of IBD in Canada is necessary.
3. Most studies have focused on the mortality associated with IBD. Future research is necessary to assess health-adjusted life expectancy and overall life expectancy for those living with IBD.
4. Analyses of resources, infrastructure, and personnel need to be modeled into the future in order to prepare our health care system for the rising burden of IBD.
5. Research on the interaction between genes, microbes, and our environment will inform our understanding of the pathogenesis of IBD, information necessary to prevent IBD in the future.

Keywords: *Epidemiology; Incidence; Inflammatory bowel disease; Outcomes; Prevalence*

Canada has among the highest rates of inflammatory bowel disease (IBD) in the world (1–3). Since the middle of the 20th century, diagnoses of ulcerative colitis and Crohn's disease increased dramatically in Canada (1). In the 21st century, IBD affects nearly 0.7% of Canadians (1, 4). In 2018, over 270,000 Canadians are believed to be afflicted with IBD, which is estimated to cost over \$1.2 billion to the health care system annually (5, 6). Outside the health care system, IBD is estimated to cost Canadian society nearly \$1.5 billion in 2018 from expenses known as indirect costs such as lost work productivity, disability coverage, and premature retirement or death (7–9). Moreover, patients with IBD and their families experience a reduction in quality of life that may affect their school, work, and social interactions (10).

Inflammatory bowel disease is a global disease (1). At the turn of the 21st century, countries in Asia, Africa, and South America reported a rise in IBD locally (11–15). While the occurrence of IBD in Canada greatly exceeds those of newly industrialized countries, IBD is rising at a considerably faster rate in many countries in Asia, Africa, and South America (2). The evolution of IBD following urbanization and Westernization of developing countries highlights the importance of environmental risk factors associated with these societal changes in the pathogenesis of IBD (16). Moreover, immigrants from non-Western countries who arrive in Canada as children and their Canadian-born offspring have an elevated risk of developing IBD compared with immigrants who arrive later in life (17). This observation suggests that early life exposure to the Canadian environment is an important risk factor for IBD (3).

Without discoveries that lead to a cure of IBD or prevention of disease development, the number of people living with IBD is predicted to rise rapidly over the next decade in Canada (18). Consequently, health care systems throughout the nation must prepare for the rising burden of IBD. Over the next decade, gastroenterology clinics will need to optimize the infrastructure, resources, and personnel needed to care for patients with IBD living in Canada (18). This section of the report will characterize the evolution in the rates of IBD in Canada, including the future predicted burden of the disease. Further, we will introduce the genetic, environmental, and microbial associations with IBD. A complete overview of the objectives, working committees, and methodology of creating the report can be found in supplemental file, Technical Document.

INCIDENCE, PREVALENCE, AND MORTALITY OF IBD IN CANADA

Historical Perspective

Ulcerative colitis was first recognized in the late 1800s by Sir Walter Wilks, followed by Crohn's disease in the 1930s by Dr. Burrill Crohn and colleagues (16). Since the 1950s, numbers of

newly diagnosed cases of IBD rose in North America, Europe, and Australia. A comprehensive review that compiled over 200 epidemiological studies on the occurrence of IBD demonstrated that over three-quarters of studies reported rising incidence rates of Crohn's disease and ulcerative colitis throughout the 20th century. However, since 1990, most studies from the Western world have reported that the incidence of Crohn's disease and ulcerative colitis has stabilized and may be decreasing in several regions (1). However, it continues to rise in Canada in certain populations (e.g., children, immigrants) (19).

Incidence of IBD Today

Canada has among the highest incidence rates of IBD in the world (2). Robust disease surveillance systems have tracked the incidence of IBD in provinces across Canada. Table 1 describes the incidence of IBD in provinces with available data. Incidence varies between provinces: The highest incidence of IBD is reported in Nova Scotia at 54.6 per 100,000 people (1996 to 2009). In contrast, the incidence of IBD in Alberta, British Columbia, Manitoba, Ontario, Quebec, and Saskatchewan were similar, ranging from 18.7 to 28.3 per 100,000. The ratio of Crohn's disease to ulcerative colitis was equal in all provinces with the exception of Quebec, which has nearly twice the rate of new diagnoses of Crohn's disease compared with ulcerative colitis. Since 1990, the incidence of IBD was stable in Manitoba, increasing in Ontario, and decreasing in Alberta, Nova Scotia, and Quebec (Table 1) (1, 2, 20).

Age and Sex Distribution of Incidence of IBD

Inflammatory bowel disease can be diagnosed at any age, from infancy to octogenarian. However, the age groups that are most likely to be diagnosed with Crohn's disease and ulcerative colitis are adolescents and those between the ages of 20 to 30 (Figures 1 and 2) (1, 2, 20). Although both ulcerative colitis and Crohn's disease may be diagnosed in seniors (over age 65), ulcerative colitis is more common in this population. In contrast, children are more likely to have Crohn's disease as opposed to ulcerative colitis.

Women may be more likely to be diagnosed with Crohn's disease as compared with men in Canada. The ratio of newly diagnosed females as compared with males ranges from 1.2 to 1.3 in Manitoba, Quebec, Nova Scotia, and Ontario. In contrast the risk of being diagnosed with ulcerative colitis is the same for females and males (1, 21).

Incidence by Ethnicity

During the 20th century, IBD was primarily considered a disease of Caucasians who descended from Western Europe, given the highest incidence rates were found in Western Europe, North America, and Australia with low occurrence in developing countries (22). However, this notion has been modified

Table 1. Incidence of IBD in Canada. Incidence is reported per 100,000 people. Most recent data available is reported in the table

Province	Study Period	Incidence of IBD*	Incidence of Crohn's Disease	Incidence of Ulcerative Colitis	Change in Incidence Over Time
Alberta	2010 to 2015	25.0	10.2	8.4	Incidence is stable
British Columbia	1998 to 2000	18.7	8.8	9.9	Unknown
Manitoba	1990 to 2013	19.8	8.9	10.8	Incidence is decreasing
Nova Scotia	1996 to 2009	51.8	22.6	21.4	Incidence is decreasing
Ontario	1999 to 2011	23.0	10.6	11.1	Incidence is increasing in children and adults aged 30–60, stable in other ages.
Quebec	2001 to 2008	27.3	16.6	10.7	Incidence is decreasing
Saskatchewan	1998 to 2000	23.9	13.5	10.4	Unknown

*Incidence of Crohn's disease plus ulcerative colitis does not necessarily add up to the incidence of IBD because some provinces combine IBD unclassified (IBD-U) with ulcerative colitis and others report IBD-U separately.

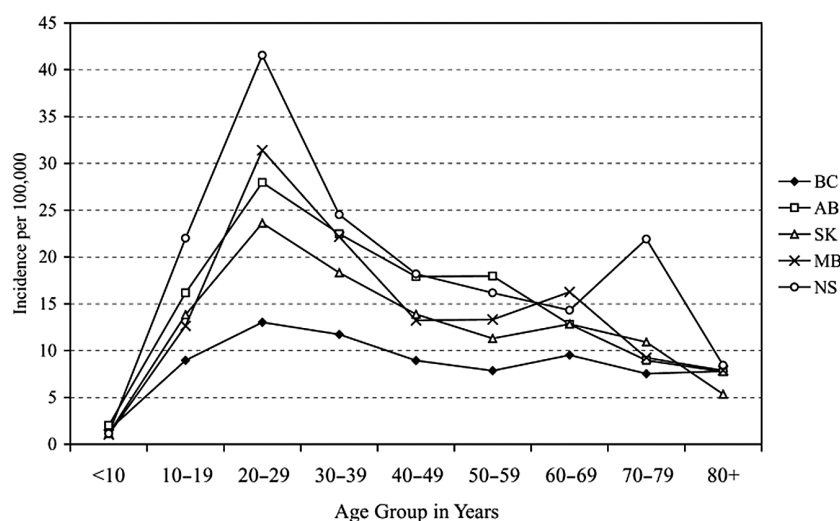


Figure 1. Age distribution of the incidence of Crohn's disease for British Columbia, Alberta, Saskatchewan, Manitoba, and Nova Scotia from 1998 to 2000. Reprinted by permission of the authors (21).

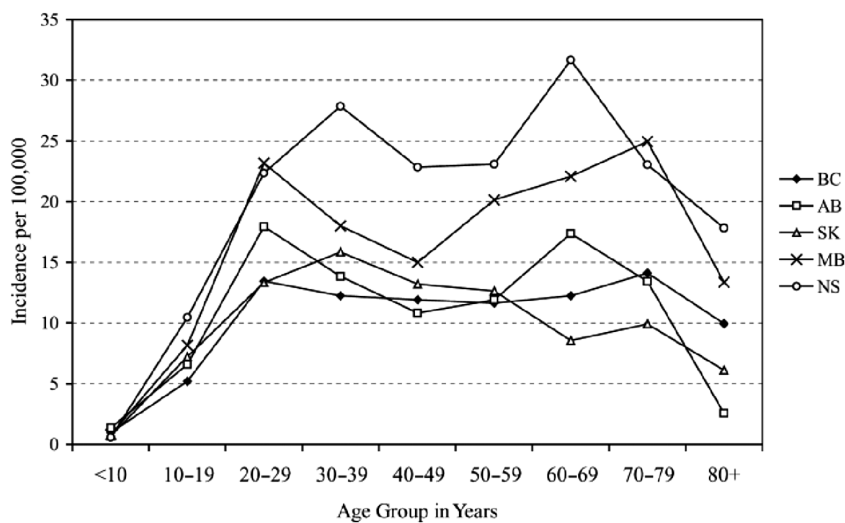


Figure 2. Age distribution of the incidence of ulcerative colitis for British Columbia, Alberta, Saskatchewan, Manitoba, and Nova Scotia from 1998 to 2000. Reprinted by permission of the authors (21).

over the past generation. Individuals who emigrated from South Asia, where IBD was uncommon, to the United Kingdom were found to be more likely to develop IBD. The risk of developing IBD is most striking among the first- and second-generation offspring of these immigrants (23, 24). Immigrants from developing countries are less likely to have IBD than natural-born Canadians. However, these immigrants who arrive to Canada at younger ages are at increased risk: for every decade earlier in life that these immigrants arrive in Canada, the risk of IBD increases by almost 10% (25). There are also differences among the offspring of immigrant groups. First-generation, Canadian-born offspring from parents who emigrated from the Middle East, South Asia, and Africa have a similarly high risk of developing IBD as the children born from nonimmigrant parents (25). In a Vancouver-based study, children of South Asian descent have a much higher incidence of IBD (15.2 per 100,000) compared with non-South Asians (3.7 per 100,000) (26). By contrast, immigrants from East Asia (primarily China and Hong Kong) who now live in Ontario are at very low risk of developing IBD, as are their children (25). These trends suggest that the Canadian environment triggers IBD in certain populations but not others (perhaps due to protective genetics). That being said, IBD in Canada now affects the lives of Canadians of all ethnicities, including those thought previously to be at low risk.

Familial and genetic studies have reported a particularly high occurrence of Crohn's disease among Ashkenazi Jewish people, descendants from those who settled in Eastern/Central Europe. An early study shows that Ashkenazi Jewish people have a two-fold higher likelihood of being diagnosed with Crohn's disease than non-Jewish people (27). A more recent population-based study from Manitoba reports that individuals who are Jewish are over four times more likely to have Crohn's disease as compared with non-Jewish residents (28). Clinicians believe that risk of IBD clustered in Jewish families is inherited, a hypothesis that was subsequently substantiated by genetic studies. Ashkenazi Jews have been found to carry gene mutations that are common

to all patients with Crohn's disease but also have unique mutations that may drive their increased susceptibility (29). The rates of IBD among Jewish Israelis are much lower than rates reported from Canada and Australia, likely due to the more mixed Jewish ethnicities living there. However, recent studies display much higher rates of IBD than previously reported in the Sephardic Jewish and Arab populations in Israel, suggesting that Westernization and environment may have more impact on risk than genetics.

Prevalence of IBD Today

Prevalence is the proportion of the population that suffers from IBD at a particular moment in time. After decades of rising incidence (the number of new cases annually) of IBD in the 20th century and low death rates among young patients affected by these diseases, the prevalence of IBD has ballooned in Canada during the 21st century (2). Based on prevalence data from Alberta, British Columbia, Manitoba, Nova Scotia, and Saskatchewan, the average prevalence of IBD in Canada was estimated to be 0.47% from 1998 to 2000 (21). Table 2 provides historical data on the prevalence of IBD by different provinces, including data from Quebec (0.39% from 2001 to 2008) and Ontario (0.54% in 2008) (2). The number of people with IBD in Canada is estimated to be approximately 270,000 (0.7%) as of 2018 (4). This number breaks down as 135,000 individuals living with Crohn's disease and 120,000 with ulcerative colitis. An additional 15,000 patients have IBD, but their diagnosis is not clearly classified as Crohn's disease or ulcerative colitis (4).

Prevalence of IBD Tomorrow

The prevalence of IBD is expected to climb over the next decade due to the compounding effect of prevalence. Inflammatory bowel disease is a lifelong disease with no cure that is most commonly diagnosed in young individuals. However, the risk of dying from IBD is very low (30, 31). Because the incidence of IBD is much higher than the risk of death from IBD, the prevalence of IBD is estimated to increase by 2.9% per year, such that

Table 2. Prevalence of IBD—historical and predicted. Prevalence reported per 100,000. Most recent data available is reported in the table

Province	Historical Prevalence of IBD in 2008	Predicted Prevalence of IBD in 2018	Predicted Prevalence of IBD in 2030
Alberta	529	729	1048
British Columbia	515	682	912
Manitoba	567	652	819
Nova Scotia	870	1224	1657
Ontario	507	731	1156
Quebec	445	671	940
Saskatchewan	555	636	893
Canada	-	725	981

the estimated prevalence of IBD in 2018 (0.7%) is forecasted to climb to nearly 1% by 2030 (Figure 3) (4). Table 2 presents statistical models of the changing prevalence of IBD over the next decade. By 2030, statistical models predict that approximately 403,000 people will be living with IBD in Canada (4).

Mortality from IBD

The risk of death from IBD is low. Inflammatory bowel disease is unlikely to kill patients directly. However, it is associated with cancers and other complications that result in a slightly higher death rate than the general population. Patients with Crohn's disease have approximately a 25% higher risk of dying than the general population. The risk of death in ulcerative colitis patients is increased in the first year after diagnosis, but beyond that is the same as the general population (31).

Upon examining data from Manitoba, Ontario, and Quebec, we discovered the following findings:

Data from Manitoba:

- Persons with Crohn's disease are more likely than the general population to die of colorectal cancer, non-Hodgkin's lymphoma, pulmonary embolism, or sepsis.
- Persons with ulcerative colitis are more likely to die from colorectal cancer or respiratory diseases.
- The greatest risk for death associated with both Crohn's disease and ulcerative colitis is within the first 30 days following gastrointestinal surgery.

Data from Ontario:

- Persons over age 65 with Crohn's disease have higher rates of mortality directly attributable to IBD compared with middle-age or younger adults.
- IBD-attributed mortality is not different by age in persons with ulcerative colitis.

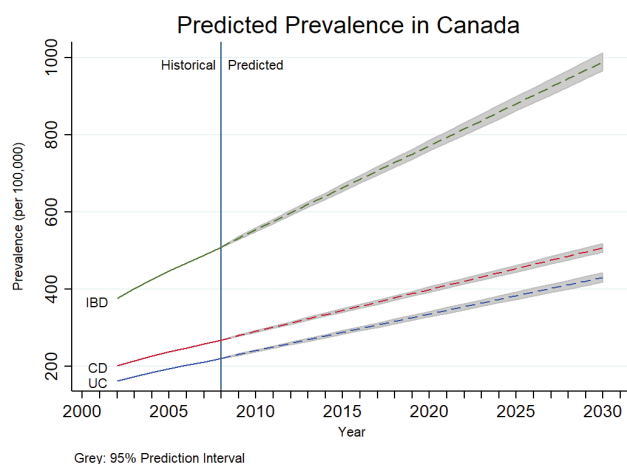


Figure 3. Projected prevalence of IBD in Canada. Reprinted by permission of the authors (4).

- The leading cause of death in senior Crohn's disease and ulcerative colitis patients is solid malignancies—accounting for one-quarter of all IBD-attributed deaths (32).

Data from Quebec (33):

- All-cause mortality was increased in both Crohn's disease and ulcerative colitis when compared with the general population.
- Mortality from digestive conditions and neoplasms (e.g., colorectal, lymphatic, and lung cancer) was significantly higher in Crohn's disease as compared with the general population.
- Mortality from digestive, respiratory, and infectious conditions increased for ulcerative colitis.

Implications

This high prevalence of IBD in Canada will challenge us to provide safe, high-quality, and cost-efficient care to patients with IBD without overwhelming our fiscal, staffing, and infrastructure resources. This challenge can only be met by physicians and health care systems prioritizing innovations in the delivery of care and information technology and finding resources to address the increasing volume of patients in IBD clinics.

COMPARING THE BURDEN OF IBD IN CANADA TO THE REST OF THE WORLD

Global Perspective of IBD in the 20th Century

During the 20th century, IBD was considered a disease of the Western world with the greatest predominance in North America, Europe, and Australia (18). Studies have consistently documented that the incidence and prevalence of IBD in Canada is comparable or greater than most countries in the Western world (1, 2). A nationwide study in the United States reports 0.49% prevalence of IBD from 2008 to 2009 (34). Epidemiologic studies from Europe have shown considerable geographic variability, with the highest incidence of IBD in Western Europe and Scandinavia, lower rates in countries alongside the Mediterranean Sea, and sharp discrepancies throughout Eastern Europe (10). In contrast, the incidence of IBD in the 20th century in developing countries in Asia, Africa, and South America is extremely low (1). At the turn of the 21st century, important epidemiological patterns have shifted and have changed the global perspective of IBD (2).

Global Perspective of IBD in the 21st Century

In the 21st century, the incidence of IBD is plateauing in most Western world countries (2). The incidence of IBD is coalescing around a range of three to fifteen per 100,000 persons for both Crohn's disease and ulcerative colitis. While some countries are

reporting higher incidence rates, it appears that the ceiling for incidence is between twenty and thirty per 100,000 persons for each of Crohn's disease and ulcerative colitis (2). This information is vital to health care systems in Canada and the rest of the Western world to anticipate the rising burden of newly diagnosed patients with IBD (18).

In the 21st century, IBD is considered a global disease that can manifest in any geographic region and within any race or ethnicity (22). Figures 4 and 5 display global maps comparing the incidence of Crohn's disease and ulcerative colitis. Collectively, data from newly industrialized countries in Asia, Africa, and South America highlight the global rise of IBD. The peak in the incidence of IBD has yet to unfold in these continents (18). Only time will tell if the incidence and prevalence of IBD in Asia, Africa, and South America will approximate those of the Western world. If so, the implications are profound for countries like China and India whose populations exceed one billion people.

Implications

In order to manage this relatively new disease, newly industrialized countries in Asia, Africa, and South America need to prime their clinical infrastructure and brace their personnel

for an escalating burden. Moreover, the globalization of IBD demands a collective effort to develop strategies to drive down the incidence of IBD in Canada and throughout the world. Preventing IBD requires a fundamental understanding of the genetic, environmental, and microbial factors underpinning its pathogenesis.

THE BIOLOGY BEHIND IBD: GENES, MICROBES, AND ENVIRONMENT

Crohn's disease and ulcerative colitis are believed to occur in genetically predisposed individuals who have an abnormal immune response to microorganism in the gut (22). Understanding the biology behind IBD is critical in developing novel strategies to improve the quality of life for people living with the disease, including enhancing treatment approaches, exploring possibilities in curing the disease, and identifying avenues for prevention (35).

Genetics

The genetic underpinning of IBD has long been recognized. Early studies on twins show that identical twins are more likely

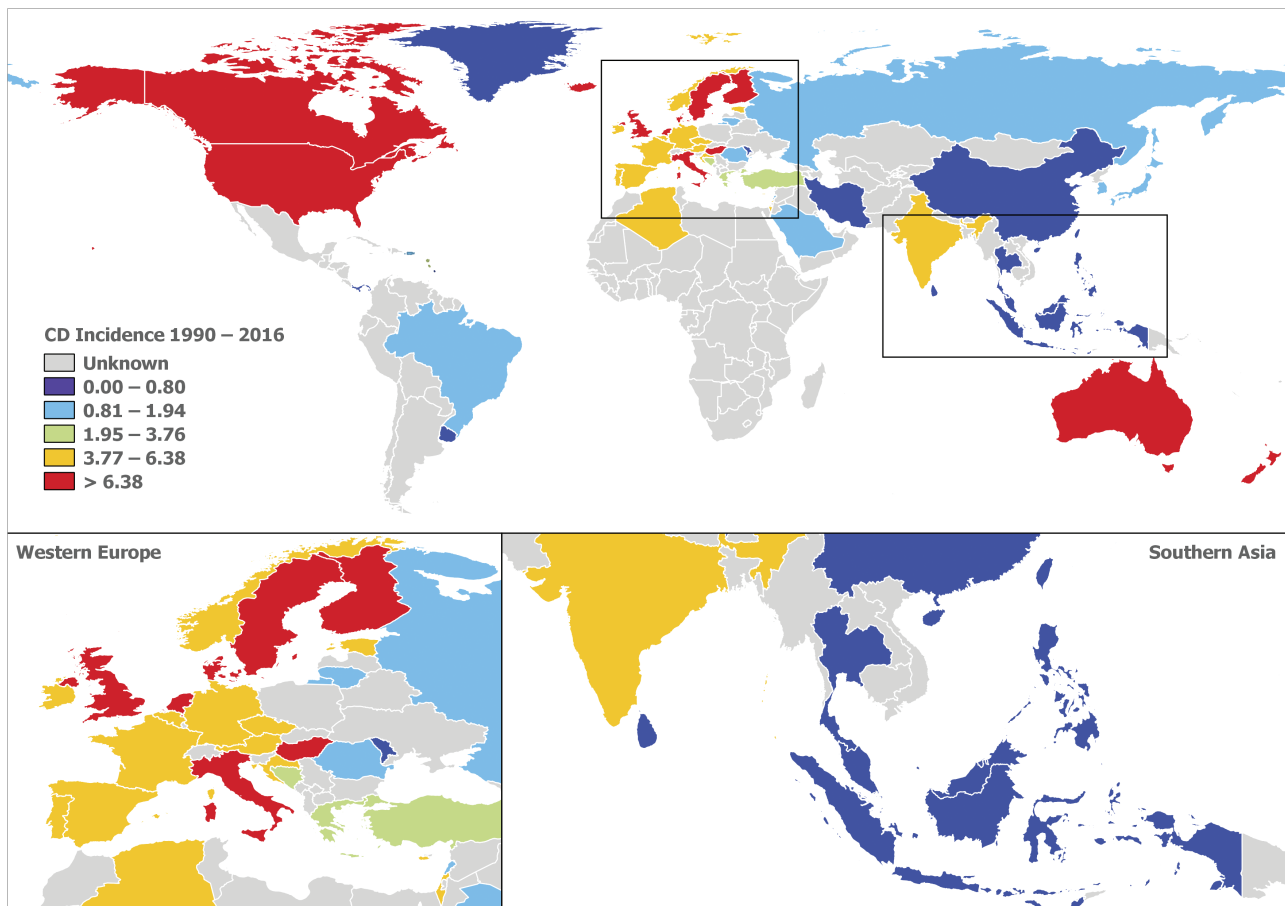


Figure 4. Worldwide incidence of Crohn's disease stratified from low to high incidence (per 100,000). An interactive global map of IBD can be found online: <https://people.ucalgary.ca/~ggkaplan/IBDG2016.html>. Adapted from Ng et al. (2).

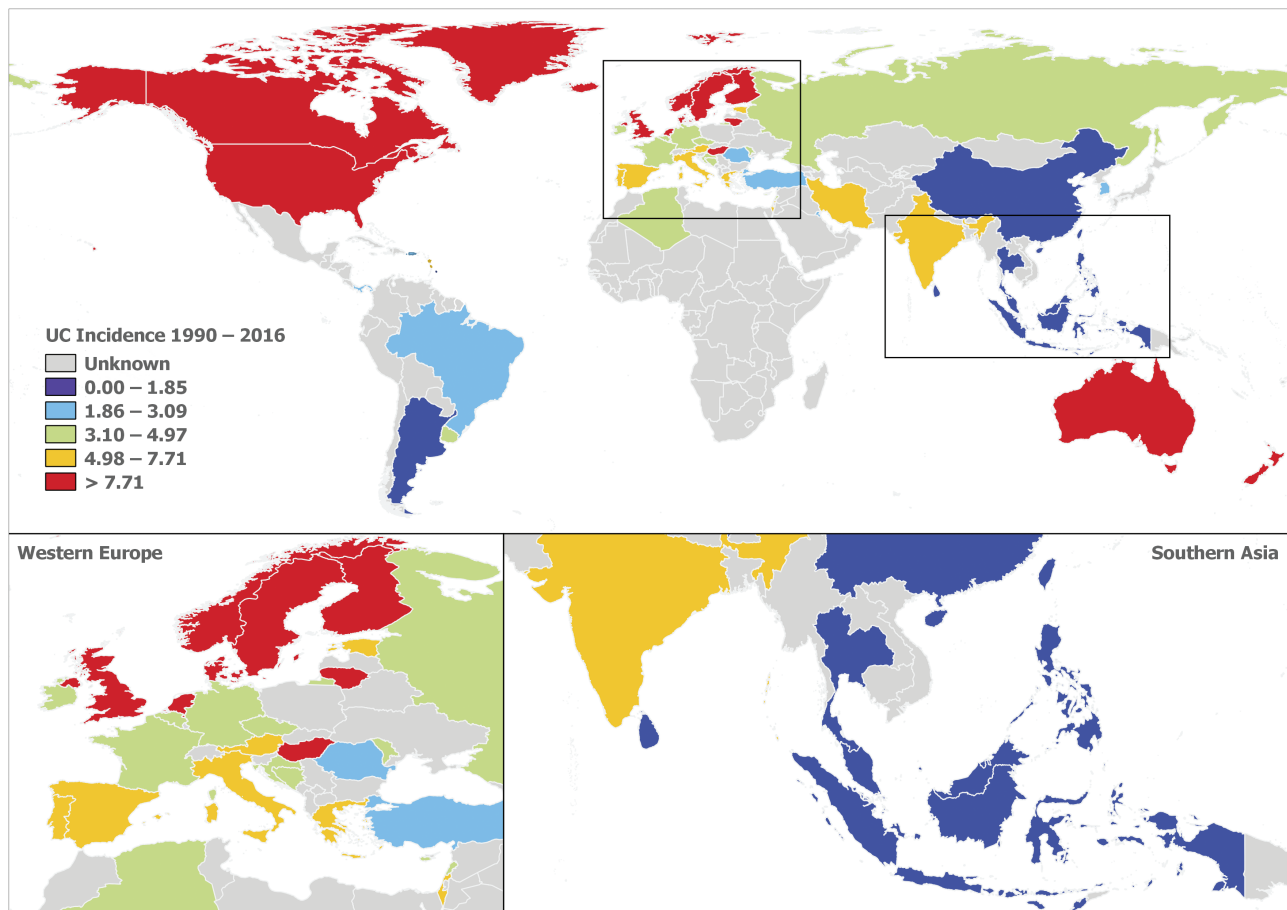


Figure 5. Worldwide incidence of ulcerative colitis stratified from low to high incidence (per 100,000). An interactive global map of IBD can be found online: <https://people.ucalgary.ca/~ggkaplan/IBDG2016.html>. Adapted from Ng et al. (2).

to both have Crohn's disease or ulcerative colitis as compared with fraternal twins (36). In 2001, NOD2, the very first gene linked to Crohn's disease, was discovered. The NOD2 gene provides a clue that Crohn's disease may be driven by the intestinal microbiome because NOD2 is involved in the immune response to gut bacteria (37–39). Subsequently, genetic analyses that sequence vast regions of the human genome (genome-wide association studies) have identified more than 200 genetic mutations associated with the development of Crohn's disease and ulcerative colitis. In many cases, these genetic mutations are shared across both forms of IBD (40). Importantly, around two-thirds of gene mutations linked to IBD are also shared with other immune-mediated disorders including type one diabetes mellitus, celiac disease, rheumatoid arthritis, ankylosing spondylitis, and psoriasis (41). The collective knowledge of the proteins made by these genetic loci paints a clear picture of the critical role between the immune response in the bowel and the 100 trillion microbes living there.

Microbiome

A leading hypothesis on the etiology of IBD is that changes in the gut microbiome trigger immune responses that cause

abnormal inflammation (42). Considering that persons with IBD are studied after the disease has manifested, it is not clear as to whether the changes in the microbiome and immune response are a cause or effect of the disease (43). If changes in the microbiome prove to be germane to the cause of IBD, another key question is how and when do these changes emerge? One working hypothesis suggests that the use of antibiotics, which can alter the gut microbiome even long after the antibiotics are discontinued, may be a sufficient trigger to allow IBD to develop (44). If that hypothesis proves to be viable, then we need to discern the critical period of antibiotic ingestion that impacts on the gut microbiome to facilitate the emergence of IBD. Early childhood is a critical time for microbiome evolution and may be a critical time for antibiotic use. In other words, is there a developmental period in which antibiotic use should be restricted as much as possible in order to prevent, or lower the risk, of a person developing IBD (45)? Much more work is required to understand the exact causes of microbiome changes and the changes that are most relevant to triggering disease so that treatments may be developed to prevent or reverse IBD.

Environmental Exposures

Numerous studies have indicated that environmental exposures are critical in triggering the development of IBD (3, 46).

Hygiene Hypothesis

One prominent explanation for the emergence of IBD is the hygiene hypothesis (47). This hypothesis postulates that children growing up in relatively sterile environments—without adequate exposure to microbes—insufficiently educate their immune system for handling microorganisms. They then develop an abnormal immune response that attacks their organs later in life when exposed to harmful microorganisms. Indirect evidence supporting the hygiene hypothesis includes research showing that Crohn's disease and ulcerative colitis are less likely to occur in individuals who live with pets in childhood, are raised on a farm or rural region, have a larger family, or drink unpasteurized milk (21, 48).

More recent research has shed additional light on the hygiene hypothesis. This research indicates that susceptibility to IBD may be due to early-life exposures that alter the composition of the intestinal microbiome, including the loss of so-called friendly microorganisms that could benefit the host immune response. Inflammatory bowel disease is more likely to develop in those who were exposed to antibiotics within the first year of life and also in those who were not breastfed. Antibiotics and breastfeeding strongly influence the diversity of the microbiome in children, laying down the foundation for either the future development of or protection against IBD. Individuals with a history of infectious gastroenteritis are more likely to be diagnosed with Crohn's disease or ulcerative colitis, particularly among childhood-onset IBD (49–52).

Other Environmental Determinates

Several other environmental determinates have been demonstrated consistently to influence the development of IBD among Canadians:

- Cigarette smoking increases the risk of developing Crohn's disease in adults. However, adults who quit smoking are at increased risk of ulcerative colitis (53).
- Oral contraceptives increase the risk for Crohn's disease particularly among women who smoke (54).
- Nonsteroidal anti-inflammatory drugs may also trigger IBD (55–59).
- Appendicitis diagnosed before the age of ten years protects against ulcerative colitis (60).
- A lack of vitamin D from reduced sun exposure has been hypothesized to increase the risk of developing IBD. This hypothesis stems from the fact that IBD occurs

more commonly in countries in northern latitudes, such as Canada and Scandinavia. Vitamin D is important in regulating the immune system, and its deficiency has been associated with an increased risk of IBD (61).

- Air pollution may increase the risk of developing Crohn's disease in children and young adults (62) as a result of the way it alters the intestinal microbiome (63).

Nutrition

Diet has been studied extensively in IBD with recent evidence supporting the strong influence of dietary factors on the intestinal microbiome. Studies have postulated that a Western diet, one with a higher consumption of fats and refined sugars (64–67) and reduced consumption of dietary fiber (68, 69), profoundly changes the gut's microbiome. Moreover, recent research implicates processed food in a Western diet is a contributor to developing IBD. Work in animal studies, yet to be corroborated in humans, indicates that food additives such as sweeteners and emulsifiers may also incite inflammation in the bowel. In addition to processed foods, pervasive fast food consumption is also associated with IBD. The association between fast food consumption and IBD may be direct via exposure to fatty foods or food additives or indirect via correlated lifestyles such as reduced levels of physical activity (70, 71).

Implications

Identifying environmental risk factors of IBD is important because modifying environmental exposures is a potential avenue to prevent the development of IBD. For example, over the past ten years, we have observed the stabilization of incidence rates in Canada. This may be related to declining in cigarette smoking rates, the most strongly associated environmental risk factor for development of IBD. The frequency of smoking in the general population has dropped by more than one-half—from ~40% of the population in the 1980s to less than 20% today. Canadian public health programs educating adolescents to avoid smoking in the 1980s and 1990s led to a generation of nonsmokers who are unlikely to develop smoking-related complications like cardiovascular disease, lung cancer, and possibly IBD. A recent study from the United Kingdom, which adopted similar antismoking programs as Canada, shows that from 1999 to 2009, the proportion of newly diagnosed people with Crohn's disease who had a prior history of smoking dropped significantly, by some 3% per year (72). The growing knowledge of environmental determinates of IBD serves as a guide for clinicians and policy makers to focus on preventing the onset of IBD. Future research is necessary in order to substantiate the effectiveness of these recommendations and to identify additional environmental determinates of IBD.

CONCLUSION

Inflammatory bowel disease has been predominantly a disease of the Western world, and although incidence rates remain considerably higher in Western nations, newly industrialized nations have seen a marked rise in incidence over the past 25 years. Because population genetics have not changed in such a short period of time, this observation suggests that environmental factors are likely to be of much greater importance in driving the emergence of these diseases. Some potential culprits are environmental changes that alter the gut microbiome, thought to be an important trigger of the disease. Therefore, exposures such as changing breastfeeding patterns, the early childhood use of antibiotics, dietary changes throughout life, and cigarette smoking all may be critical areas of research for the prevention, or reversal, of IBD.

The consistently high incidence rates of IBD in the Western world and the increasing rates in newly industrialized countries of Asia, Africa, and South America lead to a growing worldwide burden of disease that is accompanied by increasing costs in providing care to the growing population of affected individuals. This is especially the case in light of the expensive medications often needed for treatment. Ongoing epidemiologic study of IBD will be critical in determining disease burden and to identify potential etiological clues for management and prevention.

Acknowledgements

The authors would like to thank Shabnaz Siddiq, who acted as a coordinator for this work, and Joseph Windsor and Fox Underwood who edited the articles. This work was funded by Crohn's and Colitis Canada. EB and GN were supported by New Investigator Awards from CIHR, Crohn's and Colitis Canada, and the Canadian Association of Gastroenterology. EB was also supported by the Career Enhancement Program from the Canadian Child Health Clinician Scientist Program. CB was supported in part by the Bingham Chair in Gastroenterology. GN and GK were CIHR Embedded Clinician Research Chairs.

Supplement sponsorship. This article appears as part of the supplement "The Impact of Inflammatory Bowel Disease in Canada 2018," sponsored by AbbVie Corporation and co-sponsored by Crohn's and Colitis Canada.

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