

Supplement Article

The Impact of Inflammatory Bowel Disease in Canada 2018: Children and Adolescents with IBD

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Abstract

Canada has among the highest rates of childhood-onset IBD in the world. Over 7000 children and youth under 18 years old are living with IBD in Canada, and 600 to 650 children under 16 years old are diagnosed annually. While the peak age of onset of IBD is highest in the second and third decades of life, over the past two decades incidence has risen most rapidly in children under 5 years old. The treatment of children with IBD presents important challenges including therapeutic choices, risk of adverse events to medications, psychosocial impact on the child and family, increased cost of health care and the implications of the transition from pediatric to adult care. Despite the unique circumstances faced by children and their families, there is a lack of research to help understand the causes of the rising incidence and the best therapies for children with IBD. Scientific evidence—and specifically clinical trials of pharmaceuticals—are too often extrapolated from adult research. Health care providers must strive to understand the unique impact of childhood-onset IBD on patients and families, while researchers must expand work to address the important needs of this growing patient population.

Highlights

1. In 2018, there are over 7000 children and youth under 18 years old living with IBD in Canada, and 600 to 650 young children (under 16 years) diagnosed every year.
2. The number of children in Canada living with IBD is growing rapidly, increasing 50% in the first decade of the 21st century.
3. Inflammatory bowel disease is still rare in children younger than 5 years of age, but it is occurring in such young children more often than in the past.

Received: July 24, 2018; Accepted: October 30, 2018

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4. Children with IBD are different from adults. For example, delayed growth, extent of disease and difficulties encountered during adolescence are all unique to the pediatric experience.
5. We must consider the psychosocial well-being of both children and their families, given that caring for a child with IBD can affect the global functioning of families.
6. Treatment approaches in children sometimes differ from those in adults. However, to date, all effective therapies in adults have also been effective in children. There is great need for clinical trials of new therapies in children so that they have equal access to emerging treatments and optimal pediatric dosing can be established.

Key Summary Points

1. Rates of new diagnoses in children under 16 years old were increasing most rapidly in Ontario (increased 5.8% per year) and Quebec (increased 2.8% per year).
2. Nova Scotia has the highest rate of pediatric IBD, with lower rates in Quebec and Ontario. However, even Ontario and Quebec have higher rates of pediatric IBD than most countries in the world.
3. Inflammatory bowel disease is caused by the interaction between genes, environmental risk factors, the microbiome and the immune system. Since children experience shorter exposures and possibly fewer environmental risk factors, the interaction between these risk factors and genes may be stronger with childhood-onset IBD.
4. The microbiome is mostly established in early childhood and is affected by a number of factors such as environment, diet, pregnancy/delivery factors and antibiotic use. Changing the microbiome to a healthier state may prevent the disease and may also be a novel therapeutic target to treat active inflammation in children with IBD.
5. Children with IBD are different from adults. They are more likely to have extensive involvement of their intestines, especially in ulcerative colitis, and are at risk for growth impairment, osteoporosis, and psychosocial difficulties affecting their families.
6. Children with IBD may incur more direct health costs for treatment of their IBD compared with adults. However, this is not universally true for all children because those who are very young at diagnosis (2 to 6 years old) may have milder disease or respond better to medications. This may result in decreased use of the health system, fewer hospitalizations and less risk of surgery than older children and adolescents.
7. The choice of treatments for children with IBD may be different from that of adults. It is important to consider pediatric-specific disease considerations. Delayed growth, deficient bone development, psychosocial well-being of the child and family, disease extent, disease severity and risk of poor outcomes during transition from pediatric to adult health care are all important considerations when choosing the best treatment for children and adolescents.
8. While the medications used are similar in children and adults with IBD, research to assess the effectiveness and safety of these medications in children (especially very young children) is sparse.
9. Children with IBD may be more responsive to treatment than adults because they are more likely to have inflammatory (rather than stricturing) disease. Therefore, treating the inflammation earlier in the course of disease may prevent long-term complications such as strictures, obstruction, need for surgery and need for hospitalization.
10. Some medications used in IBD have unique or more pronounced risks in children compared with adults. For example, chronic prednisone use is associated with growth impairment and stunting in children. Anti-TNF biologics are the only medications proven to improve growth in children with Crohn's disease and should be considered early in the course of disease in patients with severe IBD or those with marked growth impairment at the time of diagnosis.
11. Some medications are used differently, depending on the sex of the patient. For example, azathioprine (with or without biologics) is associated with hepatosplenic T cell lymphoma (and other forms of lymphoma) in adolescent and young adult males more often than females. Methotrexate is associated with birth defects in the growing fetus and therefore should be avoided in adolescent

and adult women of child-bearing age who are not using two or more forms of birth control.

12. A small group of children, typically presenting in the first two years of life, have single-gene mutations that cause an IBD-like bowel disease and also immune system dysfunction. These patients may not respond to traditional IBD medications and may require therapies such as bone marrow transplant. Canada is leading research efforts to investigate, diagnose and treat this small group of very vulnerable children.
13. Inflammatory bowel disease (especially when it is active) can affect school attendance, social interactions, concentration and learning. Schools should be aware of the implications of IBD and make allowances for these factors in children with active inflammation and symptoms to optimize their chances of academic and social success.

Gaps in Knowledge and Future Research Directions

1. We have limited knowledge on what causes IBD in children and why rates are rising most rapidly in young children. We must better understand the interaction between genes, the environment, the immune system and the microbiome in order to better prevent and treat the disease.
2. Treatment for infants with IBD-like illnesses and single-gene mutations is limited. Future research should work towards identifying these children and learning how best to treat them.
3. There are few clinical trials for biologics in children, and most exclude very young children. Support for such trials is important to understand whether the treatments work, how they should optimally be given and whether they are safe for young children with IBD.
4. Considering the effectiveness of dietary therapies for children with Crohn's disease (exclusive enteral nutrition), we should work to understand how diet affects intestinal inflammation and the microbiome in order to better use dietary therapies to treat IBD.
5. Health services researchers, health care providers and policy-makers should work together to understand why variation in the access to treatment and medical care of children with IBD exists. We must work together to improve the quality of care provided to these children and ensure they have the highest quality of care.
6. Psychosocial implications of IBD in children and their families are of importance to long-term and overall well-being. Children with a chronic, incurable disease are at risk for mental illness associated with their disease. We should design interventions to improve the psychosocial status, mental health and quality of life of children with IBD and their families.
7. While nonlive immunizations are safe for children with IBD, we must understand how to improve their effectiveness in children who are immunosuppressed. While the peak onset of IBD occurs in the second or third decades of life, the frequency of new diagnoses in younger children is rising rapidly. In Canada, the fastest growing group of newly diagnosed people with IBD are children aged under 5 years (termed 'very early onset [VEO] IBD'). These young children have not been included in clinical trials of new medications, resulting in a lack of scientific evidence of safety and effectiveness of treatments in this group, and clinical experience has shown that they do not respond to usual medications used for the majority of children with IBD. Providing children with IBD with high-quality care and social support also poses other challenges to care providers, families and the health system. This section will focus on the unique challenges facing Canadian children with IBD. A complete overview of the objectives, working committees and methodology of creating the report can be found in the supplemental file, Technical Document.

Keywords: *Costs; Crohn's disease; Epidemiology; Health services research; Incidence; Inflammatory bowel disease, Pediatrics; Prevalence; Ulcerative colitis*

EPIDEMIOLOGY

Approximately 10% to 20% of newly diagnosed IBD will occur in children under 18 years old (1). As with adult-onset IBD, Canada has among the highest rates of pediatric-onset IBD in the world (2). Recent population-based studies using provincial health administrative data demonstrated some alarming trends in Canadian children.

Data from the Ontario Crohn's and Colitis Cohort reported a striking rise in rates of IBD in children under 18 years old. Between 1994 and 2009, the number of new diagnoses (incidence) of IBD in children under 18 rose from 9.4 per 100,000 children to 13.2 per 100,000 children (3). The rate rose most rapidly in children under 10 years, in whom the number of new diagnoses increased 7.4% per year. By contrast, the rate in children 10 to 18 years old rose by 2.2% per year. A more recent study from the Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC) examined rates of IBD in children under 16 years old from five Canadian provinces (Alberta, Manitoba, Nova Scotia, Ontario and Quebec) between 1999 and 2010 (4). This study found the following:

- There were nearly 3000 children under 16 years old living with IBD in Canada, and 600 to 650 children are diagnosed every year.
- The number of young children in Canada living with IBD is growing rapidly, increasing 50% in the first decade of the 21st century (in children under 16 years old, rising from 33.2 per 100,000 in 2000 to 46.2 per 100,000 in 2008) (see Figure 1).
- Rates of new diagnoses in children under 16 years were growing most rapidly in Ontario (increased 5.8% per year) and Quebec (increased 2.8% per year).
- More children under five years of age are now being diagnosed with IBD (increased 7.2% per year nationwide).
- Nova Scotia has the highest rate of pediatric IBD, with lower rates in Quebec and Ontario. However, even Ontario and Quebec have higher rates of pediatric IBD than most countries in the world.

Another study from CanGIEC estimated the number of children and youth under 18 years living with IBD in Canada and projected future prevalence based on past trends. This study found the following:

- In 2008, the prevalence of IBD in children and youth under 18 years was 68 per 100,000 (in six Canadian provinces). This equates to 4730 children and youth living with IBD in Canada.
- A projection model estimated that in 2018, prevalence had increased to 101 per 100,000, equating to almost 7254 children and youth living with IBD in Canada. This represents a 53% increase in children with IBD over the last 10 years.

- In 2030, we project 13,685 children and youth with IBD living in Canada (172 per 100,000 children). This means almost double the number of children will live with IBD in 2030 compared with 2018 and almost triple the number of those living with IBD in 2008.

The variation in rates of IBD across the country in children is demonstrated in Figure 2.

THE PATHOGENESIS OF CHILDHOOD-ONSET IBD: GENETICS AND THE MICROBIOME

Twin studies in Crohn's disease, which demonstrated greater concordance in monozygotic twins (sharing all genes) versus dizygotic twins, provided the best initial evidence that genes were involved in causing IBD. However, just as IBD is a diverse group of disorders with complex pathogenesis, the genetic basis is similarly complex. In most patients, IBD is not monogenic (i.e., Mendelian) but driven by multiple genes. Evaluation of the complete set of genetic variants (i.e., genome-wide association studies [GWAS]) have defined over 230 locations of genes (disease loci) linked to IBD (5). Interestingly, 80% to 90% of GWAS-identified loci exert their effect through altering how a gene is expressed rather than as an altered product of the gene (6). However, studies using GWAS could not determine distinct differences in the genetic profiles of adolescent-onset IBD compared with adult-onset disease (7).

Using different genetic technologies, more than 50 rare monogenic (single-gene) disorders have been identified that can present with intestinal inflammation and, therefore, mimic Crohn's disease or ulcerative colitis (5). These monogenic disorders are so rare that they would not be identified in GWAS studies. Onset in infancy and extremely severe disease are features which warrant a search for a single gene defect. Nevertheless, monogenic disorders still account for a minority of children with IBD, even those who develop IBD before the age of 6. While some monogenic disorders always present in infancy, specific disorders (e.g., XIAP deficiency) may have variable onset between neonatal period to adult-onset disease, and only 30% to 40% of those with this gene alteration even develop IBD-like disease (5). Many of these monogenic disorders with IBD-like disease have predominant immune-based defects that do not respond to usual therapies for IBD but have been cured with allogeneic bone marrow transplantation. However, in some of the monogenic disorders resulting in epithelial defects, stem-cell transplants will not be helpful (5).

Although genetic testing of common variants as a screening or diagnostic tool has little clinical value in the general population (6), known genetic risk variants for Crohn's disease are associated with specific localization of disease but do not influence the disease course or predict response to therapy (6, 7). In a large

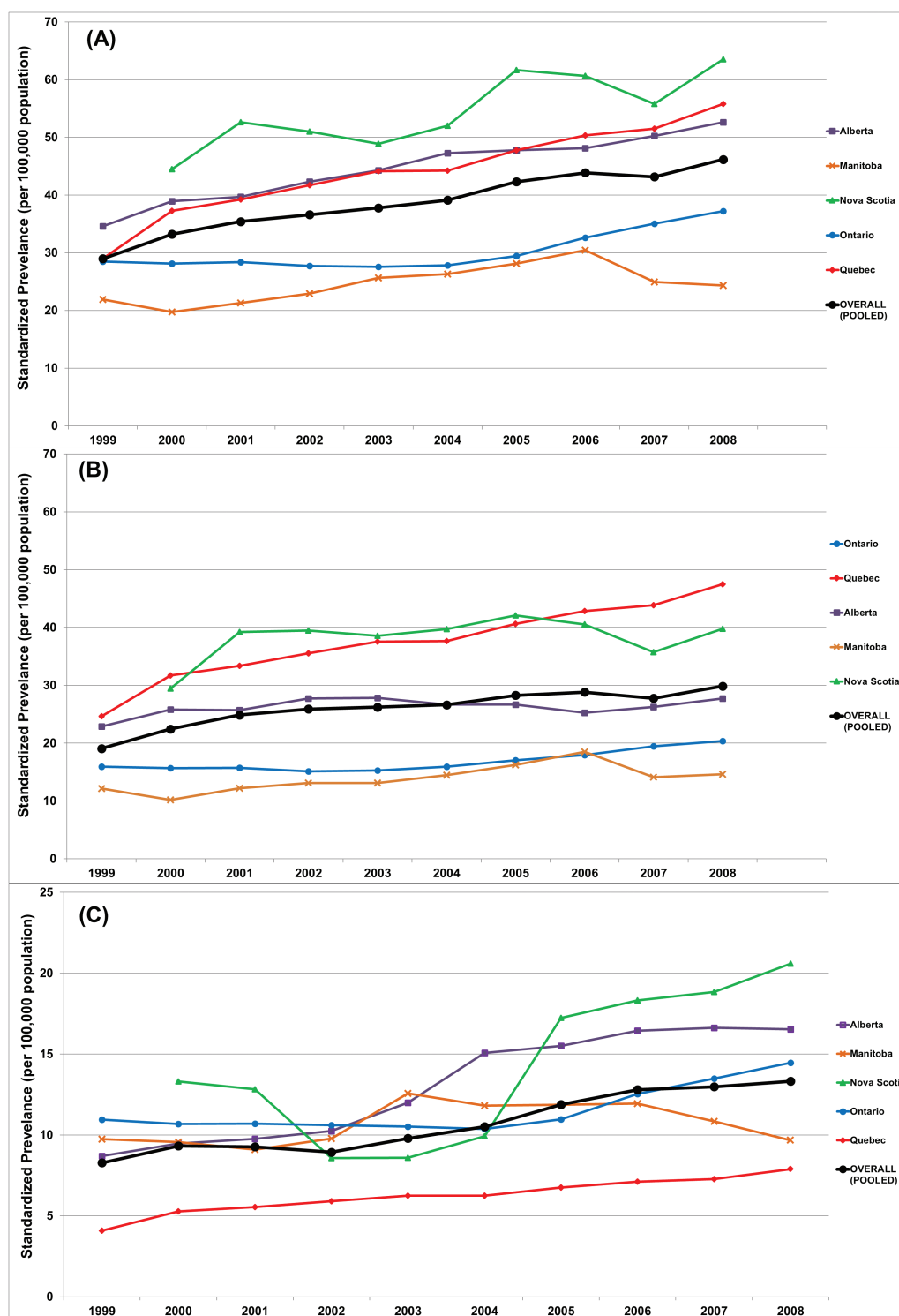


Figure 1. Annual standardized prevalence (per 100,000 population) of (A) IBD, (B) Crohn's disease and (C) ulcerative colitis in Canada. Reprinted by permission from Benchimol et al. 4).

study of children with Crohn's disease, early anti-TNF biologic therapy was associated with reduced rates of internal penetrating, but not stricturing, disease complications. A novel ileal extracellular matrix gene signature, which if present at diagnosis, was discovered to be associated with future stricturing complication, regardless of exposure to early anti-TNF (8). Genetic

factors, along with environmental factors, have been shown to affect intestinal bacterial profile and function, and individual gene variants can have specific effects (6, 9, 10).

A fundamental question in determining the cause of IBD is whether the observed changes in the bacteria (i.e., microbial dysbiosis of the microbiome) present in the intestinal tracts of

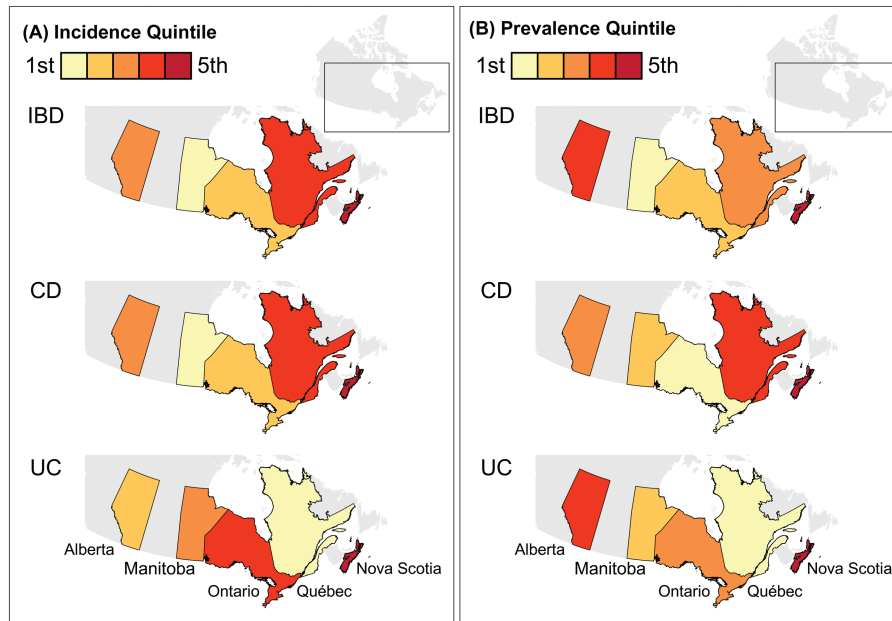


Figure 2. (A) Incidence of IBD (1999–2010) and (B) prevalence of IBD in Canada. Reprinted by permission from Benchimol et al. (4).

those with IBD are a cause or a consequence of inflammation. Most work has been done on bacterial changes in the intestinal tract of IBD patients, but there is also emerging evidence that fungi, viruses and archaea (single-cell microorganisms) may be playing a role as well (10). Converging lines of evidence from mice studies (10) and human research, such as studies in which antibiotics have been linked to Crohn's disease (11), have helped elucidate causation. The effect of antibiotics in triggering Crohn's disease is greater in children than in adults (12). One report of children with new-onset Crohn's disease demonstrated worse clinical disease and microbial profiles of fewer anti-inflammatory bacteria when on antibiotics at the time of their diagnosis as compared with children not on antibiotics (12). Such findings point to the complexity of microbial communities that are involved in cause and chronicity of IBD. The products produced or suppressed by the dysbiotic environment (13) and their function on immune responses are involved in health versus disease of the lining of the intestinal tract (10). New technologies and systems-level approaches to study the role of the intestinal microbiome are now being applied to determine interactions between the intestinal microbiota and host right at the site of disease, at the mucosa-luminal interface (13). These technologies will allow us to move beyond description of different bacteria that can be present in IBD. We must also understand how they function and are involved in the development and chronicity of the mucosal inflammation and how they affect intestinal cell function (8, 13). It is becoming clear that changes in bacteria are not random changes but relate to community-level interactions among the microbes and their effects on the host functioning, leading to permissive dysbiotic environments (13). Targeting the dysbiotic environment

and its effect on disease will open up new treatment paradigms beyond current strategies that, to a large extent, currently target human inflammatory pathways. Therefore, not only does the microbiome play a role in the risk and development of IBD, but it may represent a novel therapeutic target to help treat patients with active disease.

ENVIRONMENTAL RISK FACTORS OF CHILDHOOD-ONSET IBD

With the exception of children with infantile-onset disease (under 2 years of age) and a small number of children and adults with single-gene mutations, the genetic contribution to the risk of IBD is not enough to predict which children will get IBD or when they will get it. With the new understanding of the gut microbiome as a potential source of disease, the search for environmental risk factors that alter the microbiome and increase the risk of IBD has taken on new urgency. A number of environmental risk factors have been associated with childhood-onset IBD (14). In fact, it appears that certain environmental risk factors identified by various studies have a greater effect at increasing the risk of IBD in children compared with older people (14). In addition, because children are exposed to fewer environmental toxins in their short lives, scientists believe that we may be more successful in identifying risk factors and therefore preventing the disease in children. However, we are still very early in our ability to prevent IBD.

While the smoking of cigarettes is strongly associated with Crohn's disease in adults (15), smoking rates are very low in children. However, passive (second-hand) smoke exposure has been associated with childhood-onset IBD (16). A small study

found that exposure to passive smoke around the time of birth greatly increased the risk of later development of IBD (17), reinforcing the recommendation that smoking near children should be avoided. When the interaction between smoking and NOD2, the first discovered Crohn's disease susceptibility gene, was studied, a negative interaction was found between smoking and the 1007fs variant of NOD2 (17). This implies that this variant protects smokers from developing IBD. However, the 1007fs variant was less prevalent in people with adult-onset Crohn's disease compared with children, while smoking prevalence increased with age (17). This emphasizes the potential importance of interactions between age and genetics when assessing the role of environmental risk factors on the risk of IBD.

One example of the age-related effect of environmental risk factors is air pollution. A study of United Kingdom residents found that increased levels of certain air pollutants (nitrous dioxide and particulate matter) increased the risk of IBD, but only in younger people (18). A Canadian study found that feeding mouse pups particulate matter resulted in harmful changes to the gut microbiome (19) and an increased risk of developing IBD earlier in the mouse's life (20). If this is true in humans, exposure to air pollutants in early life may permanently alter the gut microbiome in a way that predisposes to IBD in childhood.

Some believe that living in a more hygienic environment increases risk of IBD in children. Markers of cleaner environments such as smaller family size, availability of flush toilets and lack of household pets have been associated with increased risk of Crohn's disease. In Canada, IBD patients tend to have a smaller number of people living in their houses when they were under 5 years old, and being higher in the birth order (i.e., having fewer siblings early in life) resulted in increased risk of Crohn's disease (21). In addition, living in an urban household has been associated with increased risk of IBD in many international studies (22). A CanGIEC study published in 2017 demonstrated that this effect was strongest in childhood-onset IBD and that living in a rural household within the first five years of life was highly protective against later development of IBD (4). In a German study, early-life exposure to farm animals reduced the risk of both Crohn's disease and ulcerative colitis (23). One hypothesis is that early life exposure to certain bacteria, viruses or other organisms helps to establish the gut microbiome in a way that is protective against IBD. Therefore, the cleaner environment present in the Western world and in cities may increase the risk of IBD, while reducing the risk of life-threatening infections or other diseases.

Western diet has also been associated with risk of IBD. Westernized diets are higher in animal fats and some carbohydrates but lower in fruits, vegetables and their attendant resistant starches and omega-3 fatty acids derived from fish (24, 25). However, it is possible that breastfeeding in infancy may reduce

the risk of subsequent IBD development (26), particularly during childhood (27).

The highest rates of IBD have been reported in Canada and Northern European countries. In addition, a north-south gradient in IBD prevalence has been noted in France and the UK, with northern latitudes being associated with higher rates of IBD. This has raised interest in a possible role of vitamin D deficiency, very common among Canadians, and the risk of IBD (28). There may be an association between vitamin D and the functioning of the NOD2/CARD15 gene (29). Vitamin D may also drive inflammation through the TNF- α pathway (30). In addition, being deficient in vitamin D during pregnancy was associated with increased risk of IBD and lupus in the offspring (31). These associations are not yet proven, but clinical trials are underway in children to examine whether supplementation with vitamin D results in fewer flare-ups or complications of IBD.

Infections have long been suspected to trigger new IBD in children and adults. This may be through changes in the microbiome or an altered immune response as the body tries to fight the infection. Alteration in intestinal mucosa barrier function as a consequence of dysregulated immune activation may favour the development of IBD in susceptible individuals. However, multiple Canadian studies have demonstrated that early-life antibiotic usage increases the risk of later development of IBD, particularly when they are given within the first years of life (32–34). These findings suggest that intestinal dysbiosis may affect development of gut immune tolerance or function of the intestinal microbiome and facilitate chronic intestinal mucosal inflammation. The movement toward judicious use of antibiotics and restricting their use only to children who have bacterial infections (and not viruses) may help reduce IBD risk.

HOW IS CHILDHOOD-ONSET IBD DIFFERENT?

While the underlying disease process and appearance of the bowel is similar between childhood- and adult-onset IBD, there are some significant differences between the two age groups, resulting in unique challenges to children with IBD. Firstly, males are more likely affected with Crohn's disease than females. This is unexplained and changes around the time of puberty, when rates in males and females are approximately equal. Younger females are slightly more likely to be diagnosed with ulcerative colitis than males, but around puberty, the ratio of males to females again becomes about equal. When children are afflicted with IBD, there are also differences in the way the IBD looks and in the complications of the disease.

Disease Extent and Severity

Compared with adults, children with IBD are likely to present with more extensive disease (35, 36). In Crohn's disease, this

means that children are more likely to have both their small and large bowels affected, whereas adults are more likely to have disease isolated to the ileum (last part of the small bowel). In addition, children may be more likely to have upper gastrointestinal tract disease (i.e., disease that affects the esophagus, stomach and duodenum) and longer segments of small bowel affected. This may also result in children with IBD being treated more aggressively early in their disease course. Children may also present with more subtle signs and symptoms early in their disease course, which have been associated with delayed diagnosis. Unexplained fevers, iron deficiency anemia, poor growth or nonspecific abdominal pain may be the only presenting complaints, requiring pediatricians and pediatric gastroenterologists to remain vigilant.

While more of the bowel may be affected in children, they may have better overall rates of response to medications used to treat Crohn's disease because IBD drugs are designed to halt inflammation. With time, inflammation left untreated in the bowel results in scarring of the bowel (stricturing disease). There are no treatments designed to reverse fibrosis and scarring of the intestinal mucosa, which may lead to many symptoms that mimic mucosal inflammation. Thus, scarred portions of the bowel are treated with surgery to remove that portion of intestine. In addition, inflammation burrows deep into the bowel wall, resulting in fistulas and abscesses in the abdomen (i.e., penetrating disease), which can be potentially life-threatening. Because fibrostenosis and penetrating disease take time to develop as a result of chronic, inadequately controlled inflammation, children have lower surgical rates than adults. The risk of surgery to remove bowel in children from Ontario and Manitoba with Crohn's disease is 8% to 9% in the first year after diagnosis, 21% to 23% at five years, and 27% to 29% at 10 years (37, 38); these are significantly lower rates than in adults (35). In addition, children with Crohn's disease are less likely to have complications of their disease such as fistulas and abscesses (35). This suggests that medications are more effective at preventing severe and life-threatening complications in children. This is likely because the disease is more 'inflammatory' and less 'stricturing' (36). This means that children—especially children under the age of 6—are less likely to need surgery to remove pieces of their bowel. This may also explain why children in clinical trials of anti-TNF biological medications and immunosuppressive treatments had higher rates of successful remission than those reported in adult studies. This is good news; Crohn's disease caught early enough (i.e., during the time when the intestinal mucosa is inflamed rather than scarred) is responsive to treatment and severe complications may be prevented.

Among those with ulcerative colitis, more than 80% of children have extensive colitis (affecting more than three-quarters of their large bowel) (36). By contrast, in a Scottish study, less than 50% of adults have extensive colitis (36). In addition,

ulcerative colitis restricted to the rectum (the last part of the colon, termed isolated proctitis) is extremely rare in children, comprising 1.4% of children, compared with 17% of adults (36). Unfortunately, pancolitis (i.e., disease affecting most or all of the colon) is more severe and harder to treat successfully with medications. This means that children are more likely to be hospitalized for ulcerative colitis, especially around the time of diagnosis, and may be more likely to undergo colectomy (i.e., permanent surgical removal of their colon). Approximately 6% of children need a colectomy within one year of diagnosis, 12% to 16% at five years, and 15% to 21% at 10 years (37, 38). By comparison, in adults with ulcerative colitis, colectomy rates are 7.5%, 10.4% and 14.8% at five, 10 and 20 years, respectively (39). Population-based studies of children with ulcerative colitis in Canada (38) and the United States (40) have demonstrated stable colectomy rates in recent years before the widespread use of biologics in children. However, large Canadian-run studies of the treatment of children with ulcerative colitis (41) and the availability of newer medications have helped advance our understanding of how best to treat children with ulcerative colitis. It remains to be seen whether our improved knowledge will result in fewer colectomies.

Growth Failure

Impaired growth and short stature were historically a manifestation of Crohn's disease in children. Growth impairment in Crohn's disease results primarily from the direct effects of pro-inflammatory cytokines released from the intestine on the growth plates of bones. Since growth is only possible until puberty is complete, pediatric gastroenterologists are aware of the need to treat Crohn's disease aggressively in order to avoid stunting. Corticosteroid medications (a previous mainstay of treatment for Crohn's disease) are known to slow growth and so are no longer used repetitively or for long periods of time. Their judicious use has allowed growth potential to be attained in most adolescents with IBD. The anti-TNF biologic medications are the only proven treatment to avoid growth failure in teenagers. Therefore, anti-TNF biologics should be considered as first-line treatment in growth delayed children and especially adolescents who have a more limited time to attain their growth potential. This presents challenges in health systems that currently require children to fail traditional therapies (i.e., steroids and immunosuppressives) before approving funding for the expensive biologic agents. In pediatric IBD, time and expertise are essential to avoid permanent life-long short stature.

Bone and Muscle Deficits

As with growth failure, Crohn's disease affects bone cells in children, resulting in reduced bone mineral density (42). This bone deficit is, in part, due to loss of muscle strength in children, resulting in less healthy strain on the bone and therefore

decreased bone strength (42). It is also due to direct effects of pro-inflammatory cytokines on bone cell function. The growth period is an important time to lay down strong and healthy bones; treatment of the underlying inflammation is therefore time-sensitive. As with growth failure, steroids are known to cause decreases in bone cell mass in both children and adults. Therefore, physicians may need to avoid corticosteroids and choose to use anti-TNF biologic medications or exclusive enteral nutrition at diagnosis to treat children with very poor bone health.

HEALTH SERVICES UTILIZATION AND COST OF CARE

Childhood-onset IBD has been recognized to have distinct challenges in diagnosis and treatment requiring the care of teams of health care providers who are experts of the condition. Therefore, children with IBD have been cared for increasingly by pediatric gastroenterologists and pediatric allied health care providers, with reduced care by adult gastroenterologists and surgeons (43). In Ontario, this was associated with fewer surgeries in children with Crohn's disease and more use of biologic medications (43). In addition, Manitoba children with IBD had far more physician visits in the five years before their IBD diagnosis, likely due to the difficulties making the diagnosis. This increased health services utilization spiked in the year around the diagnosis date and then decreased. However, even five years after diagnosis, children with IBD visited physicians more than twice as often as children without IBD (Figure 3) (38).

Unfortunately, this comes at a price. An American study demonstrated that direct health care costs of providing care to

children with IBD were 20% to 30% higher than adults with Crohn's disease (\$9000 to \$10,000 in children versus \$8000 in adults per patient per year) and more than double the cost of adults with ulcerative colitis (almost \$10,000 in children versus \$4000 to \$5000 in adults per patient per year) (44). This difference was not as great in a 2018 study from Manitoba in patients treated with anti-TNF biologics. In the year before anti-TNF initiation, direct costs in children <18 years were \$10,054 (compared with \$9177 in adults aged 18 to 40 years and \$8643 in adults aged 40 years and older). In the year following infliximab initiation, costs were actually lower in children (\$34,593) compared with adults 18 to 40 (\$39,318) and over 40 (\$44,050). Direct health care costs in children who failed the initial anti-TNF therapy were greater than in those who responded (\$44,391 versus \$33,793).

A large Ontario study found that children with IBD were less likely to require surgery or die during a hospitalization for IBD (45). This difference was more pronounced in patients with Crohn's disease than ulcerative colitis, with adult Crohn's disease patients more than twice as likely to undergo major bowel resection surgery compared with children. However, children with IBD were more likely to be re-admitted to hospital after an initial hospitalization compared with adults (3, 45). Another Ontario study examined health services utilization and surgical risk in children with VEO IBD (diagnosed before age 6) compared with those diagnosed aged 6 to 10 years and 10 to 18 years (3). Those with VEO IBD had fewer outpatient visits, hospitalizations and emergency department visits and required surgery less for Crohn's disease than children with disease onset at older ages (Figure 4) (3). This may be because their disease is different but may also be because their disease was diagnosed earlier

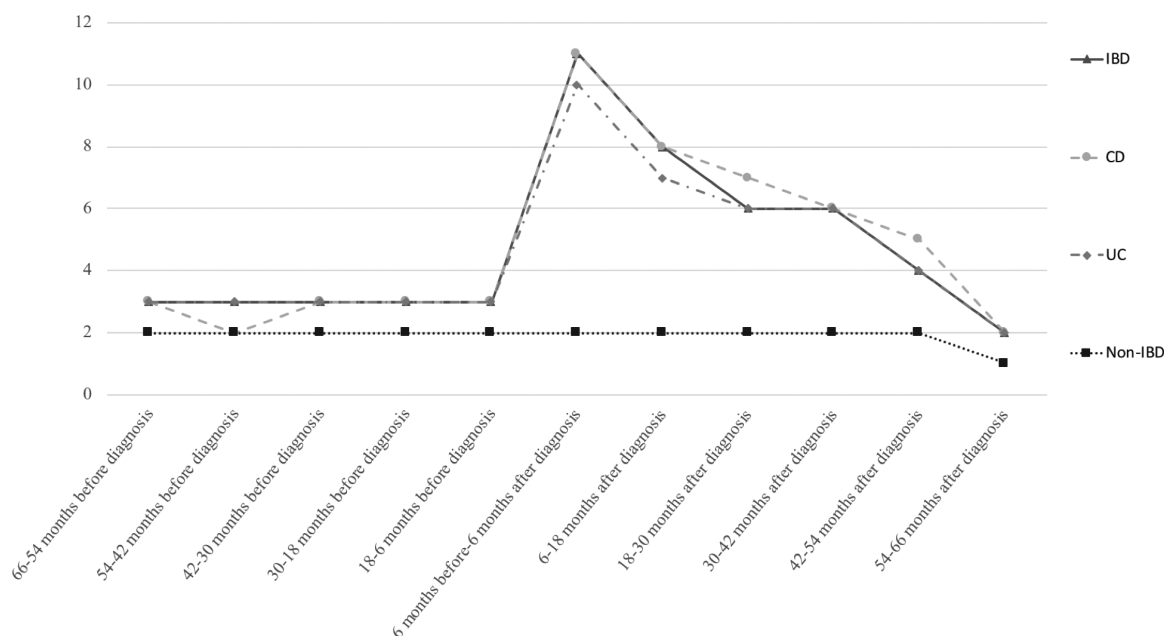


Figure 3. Outpatient physician visits in children with IBD in Manitoba, compared with non-IBD controls. Adapted from Singh et al. (38).

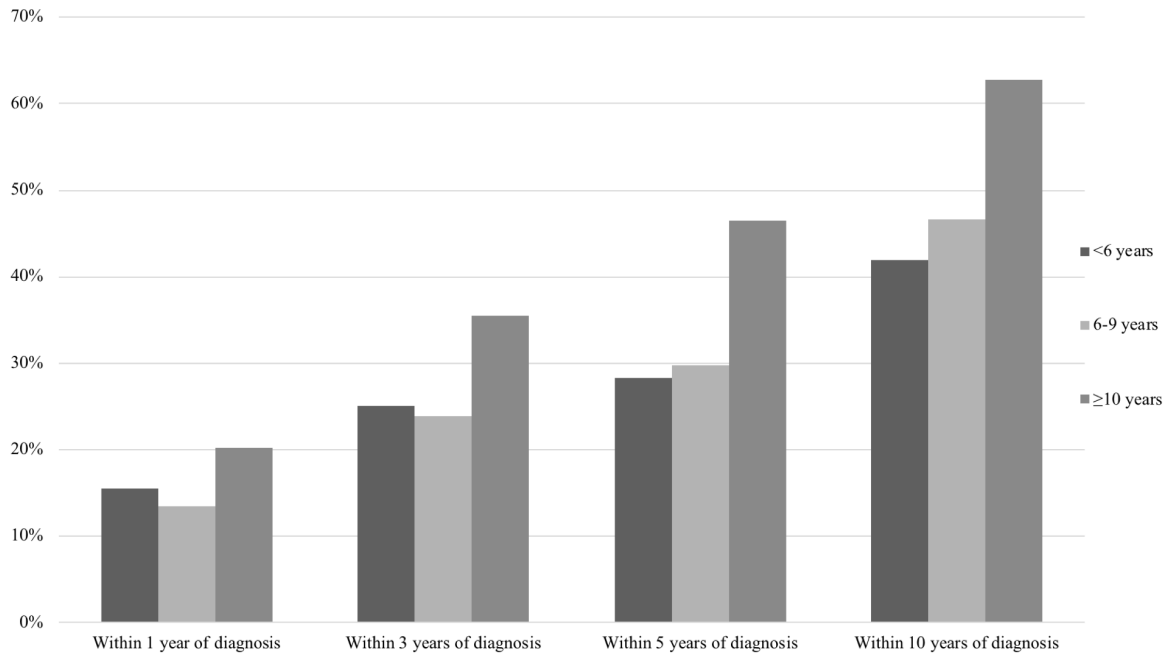


Figure 4. Risk of emergency department use in Ontario children with IBD. Adapted from Benchimol et al. (3).

in life, before the inflammation had the opportunity to damage and scar the bowel and, therefore, was more responsive to medications. While increasing rates of IBD in very young children is not good news, our ability to diagnose them earlier in life and therefore treat the inflammation before complications arise is positive news.

In Ontario, children of lower income families had greater health services utilization for IBD and were more likely to undergo surgery for Crohn's disease (37). This was particularly true after the year 2000 when biologics began to be used. The authors hypothesized that lower income families on social assistance had worse access to the expensive biologic medications than higher income families with private insurance, which was also demonstrated in Canadian adults (46). Therefore, access to newer treatments remains a significant barrier for many children.

Another significant influence on the care provided to children is the availability of multidisciplinary teams of allied health care professionals. While more care is being provided by pediatric gastroenterologists in specialized centres, a 2015 summit of patients and health care providers, convened by Crohn's and Colitis Canada, recommended that children with IBD be treated by multidisciplinary teams consisting of specialist physicians, nurses, dietitians, social workers and mental health care providers (47). Such a multidisciplinary team has also been endorsed by the European Crohn's and Colitis Organization as the standard of care for children with IBD (48). Unfortunately, the degree to which allied health care providers and specialists are available to care for children with IBD in Canada varies greatly by centre (49). In particular, the availability of social

workers and mental health care professionals to help with the care of children with IBD is highly variable, with some Canadian centres having no social workers or psychologists dedicated to IBD care.

MEDICATIONS AND TREATMENTS

Goals of Treatment

The goal of management of pediatric IBD is multifaceted (Table 1). The natural course of IBD over time is one of relapsing, remitting cycles of inflammation. Thus, treatment is geared towards control of this inflammatory activity and the prevention of disease and treatment complications. Some differences exist in treatment options between Crohn's disease and ulcerative colitis because of the differences in location of disease and the nature of the inflammatory behaviour. In general, the goals are the same:

- control intestinal inflammation to prevent long-term tissue injury and complications
- optimize physical, pubertal and psychological growth, nutrition and quality of life
- minimize treatment-related toxicity

To achieve these goals, strategies to maximize treatment adherence must also be carefully considered.

Treatment is generally broken into two phases: induction of remission (switching off the active inflammation) and maintenance of remission (keeping the inflammation switched off). Some therapies have generalized anti-inflammatory actions while others are targeted therapies focused on specific elements

Table 1. Treatment Goals for Pediatric IBD. Adapted from Pediatric Gastrointestinal and Liver Disease, Elsevier Health Sciences, 2015, p. 520 (50).

Controlling intestinal inflammation (achieve mucosal healing, prevent intestinal damage)
Promote physical growth and nutrition
Promote psychological growth
Improve quality of life
Minimize toxicity
Prevent disease complication
Maximize adherence

of the body's immune response and inflammatory pathways. The choice of therapy needs to be individualized for each patient and clinical scenario, and there may be more than one acceptable treatment strategy (51).

Several important considerations set pediatric IBD treatment apart from adult IBD management.

- First, there has been less research conducted in pediatric patient populations, so data regarding dosing, efficacy and safety need to be carefully interpreted in the pediatric setting. This has implications for drug availability in pediatric populations. In many cases, newer drug therapies do not have regulatory approval for use in pediatric patients or may have certain age restrictions applied. As a result, pediatric patients requiring such treatments may need special access approval which can delay therapy and may have specific health care resource ramifications.
- The use of placebo in the clinical trials of children with IBD was deemed unethical by an international consortium of experts, except when it is used as "add-on" therapy to standard care (52). Drug regulatory agencies should be aware of this when considering the scientific evidence for approval of drugs for use in children with IBD.
- Children are not just little adults. The pediatric patient may metabolize drugs differently, may need different dosing and interval schedules, and may have disease that behaves quite distinctly from that of adult patients. This can create problems for drug approval and reimbursement funding bodies that may enforce strict criteria around drug access and funding.
- Growth impairment and puberty delay are interrelated but unique problems in pediatric IBD that are not relevant to adults. Special cognizance is needed to ensure normalization of growth potential and appropriate pubertal development (53). Some therapies have been associated with a failure to return patients to normal growth patterns despite their successful use in adult populations to control inflammation.
- Children and young adults, by virtue of their age at diagnosis, are typically exposed to both inflammation and treatments for a longer amount of time. Therefore, issues such

as cumulative dosing, monitoring, cost and long-term risks may be unique to pediatric-onset IBD. In particular, the potential additive toxicities of combination therapies may be of concern. As many of these events are extremely rare, safety surveillance requires large patient numbers with long-term follow-up, necessitating multicentre collaboration both nationally and internationally.

Ultimately, this highlights the important need for pediatric-focused research and post-marketing safety surveillance. However, it simultaneously raises special research ethics challenges as well as 'duration of treatment' risk versus benefit uncertainties.

Medication safety in children

All medications have the potential for side effects but so too does untreated or poorly treated IBD. Disease complications can be far more common and severe than many treatment-related side effects or adverse outcomes. Hence, one of our primary goals in determining treatment is to maximize disease control while minimizing the potential for medication toxicity or treatment burden.

Many are used in both children and adults with equal or similar efficacy and potential safety. However, there are some important considerations with several of these therapies that warrant specific mention. Specific to children with IBD is the ability to use exclusive enteral nutrition (EEN) as an alternative to corticosteroids in Crohn's disease to induce remission (54). Exclusive enteral nutrition can be an effective, nonpharmacologic approach to induce remission that also allows physicians to correct possible nutritional needs of the child compromised by inflammatory disease. While the exact mechanism by which EEN works remains unclear, it is believed to alter the microbiome and induce an anti-inflammatory environment in the bowel while simultaneously promoting mucosal healing. This nutritional intervention has no side effects or immunosuppression as seen in many other therapies and thus is an option in the care of children and young adults. The main concern relates to the potential impact on the patient's quality of life. Exclusive enteral nutrition is usually administered for 6 to 12 weeks and is

the sole source of nutrition provided as a polymeric or elemental formula. Taken orally in most cases, some children develop taste fatigue and will require the placement of a nasogastric tube to facilitate adequate intake. Costs, health care system utilization and complexity of care can be greater than with medications. A supportive family and medical care team can minimize these challenges and thereby maximize the likelihood of successful utilization of this treatment option.

Thiopurines (azathioprine and 6-mercaptopurine) have been used in the treatment of IBD for decades as immunomodulators designed to manipulate the abnormal immune response that underpins the chronic inflammatory activity in IBD.

- The main short-term concerns relate to myelosuppression (low blood counts), hepatotoxicity (elevated liver enzymes) and cancers. Routine monitoring of blood labs is warranted during both initiation of treatment and in established drug therapy.
- Pancreatitis is also a concern in approximately 5% of patients and is an idiosyncratic drug reaction (dose independent event), making it more difficult to predict or prevent (55).
- The major concern with thiopurine use is the risk of developing malignancy, in particular lymphomas and non-melanoma skin cancers. These concerns resulted in a 'black box warning' for these medications and understandably can engender significant anxiety for patients and parents.
- Lymphoma is about four times more likely in IBD patients treated with thiopurines compared with those not treated with thiopurines. Longer duration of therapy is associated with increased risk (56). While most cases of lymphomas associated with thiopurine use are classified as non-Hodgkin's lymphoma, there is also a rare and often fatal form that has been reported in younger patients.
- Hepatosplenic T cell lymphoma (HSTCL) has primarily been reported in young adult males treated with thiopurines alone or in combination with anti-TNF therapy such as infliximab. This resulted in a 'black box warning' and a tendency for pediatric patients to be prescribed anti-TNF monotherapy or to substitute methotrexate in favour of thiopurines (57, 58).

Methotrexate, another immunomodulator agent, works in a different manner from the thiopurines and is used more in Crohn's disease than ulcerative colitis. It too can be used alone or in combination with other therapies. Toxicity is still possible with myelosuppression and hepatotoxicity, still warranting routine monitoring of blood tests. However, in patients with IBD, there has been no reliable evidence that the risk of malignancy is increased with methotrexate use (59). Methotrexate is contra-indicated in pregnancy and breastfeeding due to the risk of major fetal defects, spontaneous miscarriages and toxicity in infants. This may influence the decision to use such a

medication in adolescent females and young women who have the potential to become pregnant.

Although a 'black box warning' regarding HSTCL and anti-TNF therapies such as infliximab exists, data do not support the concept that there is an increased risk of malignancy associated with anti-TNF monotherapy in children (60). Overall, the safety profile of such therapies appears to be more favourable than that of the thiopurines (61). There is an increased risk of infections including tuberculosis, serious bacterial infection and invasive fungal infections such that all patients, including children, should undergo screening for previous exposure to tuberculosis and hepatitis B before starting anti-TNF therapies. There is the potential for patients to develop antibodies against anti-TNF therapies, which may increase the risk of infusion reactions but may also neutralize the drug, leading to loss of treatment efficacy over time. Combination therapy (anti-TNF therapies used in conjunction with thiopurines or methotrexate) has been shown to reduce this risk and to improve remission rates over time. The safety of such combinations must be carefully considered. Emerging therapies targeting pathways outside that of TNF are being utilized increasingly in pediatric populations, but data in children are still relatively limited, and pediatric-specific controlled clinical trials are needed to assess which agents best balance safety and efficacy.

IMMUNIZATIONS

Immunizations Do Not Cause IBD

Much has been discovered about the complex origins of IBD and the important roles of genetics, the environment, the microbiome and early life exposures. This has led researchers to focus on childhood infections and immunizations as potential triggers for IBD development. Despite early concerns around measles as a cause of IBD, specific studies examining this relationship have not produced any evidence to support this hypothesis. Furthermore, there is no known association between perinatal infection or measles vaccination and the development of IBD (62–66).

Despite this, unfounded concerns about the safety of the measles-mumps-rubella (MMR) vaccine causing neurological problems in children such as autism have, at times, been prominent. This has led directly to decreased use of the vaccine internationally and in some regions in Canada. Consequent measles outbreaks in children in North America and Europe have resulted in associated deaths or permanent disability in those developing the measles infections (62, 67–69). Recent studies have further reinforced the absence of any data to support a link between IBD, measles infection or any disease, the MMR vaccine, or indeed any routine childhood vaccine administration. Similarly, there is no evidence that H1N1 (swine flu), influenza or human papilloma virus (HPV) cause IBD (65, 67, 70, 71).

Immunizations in Children with IBD Are Safe and Important

In general, IBD does not confer any greater risk from vaccinations compared with healthy children, except in the case of live vaccines in children who are immunosuppressed. Malnutrition, active inflammatory disease and the use of immunosuppressive medications may place children with IBD at higher risk of naturally acquired infections and infection-related complications. However, research indicates that children with IBD who were vaccinated against influenza did not experience any increased IBD-related or unrelated adverse events compared with the general population (70). There are no data to suggest an increased risk of adverse events or disease severity following vaccination (70, 72–74).

Patients with IBD are at increased risk of bacterial, fungal and viral infections, as well as more severe infection-related complications (75–77). For the most part, this is related to the frequent use of immune-suppressing medications such as corticosteroids, azathioprine, methotrexate and anti-TNF therapies (e.g., infliximab and adalimumab). However, some infections have been shown to be a trigger for IBD flare-ups or to be associated with rarer disease related complications such as HPV infection, cervical dysplasia/cancer and anal cancer in patients with perianal disease (77–79). Thus, protection of patients against vaccine-preventable infections is an important aspect of high-quality, long-term care.

Canadian children with IBD should complete the usual immunizations schedule where possible (80). Nonlive (attenuated or killed) vaccines can be given at any time, although their effectiveness may be reduced in immunosuppressed patients (75, 76, 80–82). However, once a child is using immune-suppressing medications, live vaccines should not be administered due to the risk of developing the infection against which the child is being immunized. If treatment can be delayed safely, live vaccines should be administered before starting immunosuppressive medications. Exclusive enteral nutrition used as induction therapy (initial therapy to switch off inflammation) provides a window of time to allow catch up immunization in children before starting drug therapy. Once immunosuppressive therapy has been initiated, live vaccines are contra-indicated until the child's immune system is back to normal.

Most guidelines recommend patients with IBD who are immunosuppressed receive both the 13-valent pneumococcal conjugate vaccine (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23) every five years, in addition to the yearly trivalent inactive intramuscular influenza vaccine (83). A large Ontario study demonstrated that children with IBD were less likely to visit their doctors for IBD-related care in the years that they received their flu shot (70), potentially because prevention of flu infection may result in less risk of IBD flare. The intra-nasal influenza preparation is a live vaccine and so should be avoided if the child is immune-suppressed.

Human papilloma virus vaccination is recommended for both girls and boys with IBD (75, 76, 80, 81) because adults with IBD on immunosuppression may be at increased risk for the cancer-related effects of HPV (78, 84).

Travel may create special circumstances in regard to vaccination. Live vaccines, such as yellow fever, are still contra-indicated for patients on immunosuppressive therapy. Appropriate immunization information should be sought regarding the area of intended travel and discussed with a travel medicine physician and the IBD treatment team.

SCHOOL ATTENDANCE AND EDUCATIONAL ACHIEVEMENT

Children with IBD require frequent and regular attendance at specialized medical clinics, often in pediatric health care centres that are far from their homes. These visits may include physician outpatient visits, consultations with dietitians, hospitalizations, procedures, surgeries, radiology tests or medication administration at infusion centres. In addition, children with IBD can experience fatigue and difficulty concentrating due to active inflammation, anemia or medication side effects. In Israel, children with IBD were demonstrated to miss more school days than other children. This was more prominent in children with Crohn's disease (24 missed school days) than ulcerative colitis (21 days) or healthy children (5.1 days) (85). They were also less likely to participate in fitness classes, after-school sports or other after-school activities (85). In addition, when their disease is active, children with IBD require frequent bathroom visits while at school. For these reasons, the Canadian Digestive Health Foundation (cdhf.ca) developed an educational module titled 'Blackboards and Bathrooms' (http://www.cdhf.ca/bank/document_en/95blackboards-and-bathrooms.pdf) with the goal of informing teachers and educational administrators as to the unique challenges faced by children and teens with IBD. Policy-makers and school boards should consider these challenges when establishing educational policy. In particular, school absences for medical reasons should be excused, unlimited bathroom privileges should be provided and examination exemption may be required; no child with a chronic disease should be subject to discrimination in the school system.

Despite these challenges, children with IBD can still achieve success in the educational system. A population-based study from Manitoba demonstrated that children with IBD achieved equal to or better grade 12 educational outcomes than other children (86). However, predictors of worse outcomes included lower socioeconomic status and the diagnosis of mental health problems in the year surrounding the diagnosis of IBD (86). Therefore, those at risk should receive the proper educational and social support in order to achieve the expected success in school.

TRANSITION FROM CHILDHOOD TO ADULTHOOD

Coping with life's transitions is difficult for all adolescents and young adults, and the challenge is amplified when facing a chronic disease. As adolescents with IBD age, they will demand increased autonomy and more control over health care treatment decisions while simultaneously being at increased potential for risky behaviours which could negatively impact their health. They require support to educate, inform and guide them to take control of their disease. Multiple studies have demonstrated that the knowledge of adolescent patients is insufficient. They frequently had problems navigating the health system, such as accessing insurance programs, knowing where their pharmacy was located and obtaining information from pharmacists, and making their own appointments (87). This lack of knowledge has been identified by adult gastroenterologists as a major factor inhibiting the smooth transition to adult care (86). A 2016 Ontario study has demonstrated that adolescents with IBD visit the emergency department and outpatient clinics more frequently after their transfer to adult care but are not hospitalized more frequently (88). This may be due to the adjustment from a pediatric health care model where nurses are readily available to support the patients by phone or a lack of understanding of how to use the outpatient health system.

A 2015 summit of patients with IBD and health care providers organized by Crohn's and Colitis Canada recommended that structured transition programs should be provided to adolescents transitioning to adult care to help educate the maturing adolescent, support adherence to medical therapy and ensure a smooth transfer to adult care (47). This may be facilitated by specialized, multidisciplinary IBD clinics in pediatric health care centres. There should be a dedicated staff person to help provide an anchor at the time of transition as and specialist IBD nurses in the clinic. With dedicated support and a structured program, adolescents with IBD will navigate the move from pediatric to adult health care more easily.

QUALITY OF LIFE

Unique Issues to Consider for Pediatric IBD Quality of Life

Assessing quality of life (QOL) in pediatric patients with IBD requires consideration of key methodological issues: whether to ask children directly (89, 90) and how to allow for varying developmental levels and ages (91, 92). Pantell et al. showed that parents and teachers agreed fairly well in reporting on child functioning but markedly less well for recent functional status, certain types of subjective feelings in regard to illness, information needs, emotional states and family functioning (93).

Pediatric IBD Quality of Life

In the pediatric population, pain was associated independently with impaired quality of life regardless of disease activity. Among children with Crohn's disease experiencing a flare, those without pain experienced significantly decreased disability and depressive symptoms and improved quality of life compared with children in a flare with pain. Although levels of depression did not differ by disease state, depressive symptoms were more severe among children experiencing a disease flare (94).

Ryan et al. reported on the incorporation of health-related quality of life (HRQOL) screening into clinical practice and its clinical utility in predicting disease outcome and health care utilization (95). One hundred twelve IBD youth aged 7 to 18 years of age completed the Pediatric Quality of Life Inventory, Version 4.0 (PedsQL 4.0), with retrospective chart reviews being conducted to examine disease outcomes and health care utilization for 12 months following a baseline QOL assessment. Results of this study demonstrated that youth who reported lower HRQOL at baseline, on average, had increased health care utilization as measured by IBD-related hospital admissions, emergency department visits, use of psychological services, telephone calls to clinicians, GI clinic visits and referral to pain management.

Another important area to consider is how children with IBD fare when compared with children with other chronic illnesses and with healthy peers. To make these comparisons generic, HRQOL tools need to be employed. Preliminary work looking at QOL issues between patients with IBD and those with other chronic illnesses was carried out by Ingerski et al. (96). They compared HRQOL across eight pediatric chronic conditions: obesity, eosinophilic gastrointestinal disorder, IBD, epilepsy, type one diabetes, sickle cell disease, postrenal transplantation and cystic fibrosis (96). Using the PedsQL generic HRQOL tool, these authors showed that it was youth with obesity and eosinophilic gastrointestinal disorders who had lower HRQOL compared with the youth with other chronic illnesses. However, limitations of this work were the small number of patients in some of the chronic illness groups (for example, 34 of 589 patients had IBD) and the considerable variation present across disease groups in terms of demographic and disease-specific sample characteristics (96). Further work needs to be done in this area, but with a priori matching of participants across important demographic and disease-specific factors.

Early work has also been done comparing HRQOL of pediatric IBD with healthy peers (97). When 55 children, ages 7 to 19 years were studied, older children with IBD had significantly lower HRQOL scores compared with age-standardized peers. Kunz et al. have carried out the largest study to date comparing HRQOL assessments of youth with IBD to published group data of chronically ill, acutely ill and healthy comparison groups (98). The 136 youth with IBD who were studied reported lower psychosocial functioning than the healthy comparison group,

higher physical and social functioning than the chronically ill group, and lower school functioning than all published comparison groups. More work needs to be done to better characterize the degree and nature of any differences in HRQOL among pediatric IBD patients and those with other chronic illnesses and with healthy peers. If consistent differences are noted and, in particular, if impairments in HRQOL are demonstrated, then health care providers will have evidence to better advocate for research to identify interventions that will target these HRQOL impairments.

CAREGIVERS

Parenting a child with a chronic illness can be very challenging and can have a negative impact on many areas of a parent's life (98). Parents often balance a number of ongoing demands related to their child's medical plan such as managing the daily treatment responsibilities (administration of medication, special diets), attending clinic visits and mitigating the functional limitations their child experiences as a result of having IBD (99). In a focus group study, Akobeng et al. showed that 65% of parents worry about the effects of their child's IBD on the child's future, and greater than 50% expressed concerns of the bowel condition on their child's education (100). A minority of parents worried about the consequences of their child's illness on the parent's career (15%) or the family's lifestyle (5%) (100). In a small study, Rabbet et al. showed that parents reported that their child's health condition was a factor in the parent's work-related difficulties (44%), impacted family plans (38%), created an increased financial burden (13%) and led to a strain on their marital relationship (6%) (101). These responsibilities and stressors imposed by the chronic illness can contribute negatively to parent and family functioning.

When family life is dysfunctional, there can be decreased emotional and behavioural functioning (102), while adaptive family relationships have been associated with positive psychological functioning (103). Building on data among youth with end-stage renal disease and diabetes that show there is a significant relationship between family functioning and HRQOL, researchers explored these issues in a cohort of adolescents with IBD, seeking to identify which domains of family functioning may be particularly problematic (104). After statistically controlling for known impacts of disease severity and diagnosis, their data showed that teens from families with clinically elevated difficulties in problem solving, communication and general family functioning reported a lower HRQOL. This area needs to be studied further to ascertain whether a causal link exists between family functioning and HRQOL and, additionally in the context of a prospective study, how this may vary over time. Research has also highlighted the importance of examining maternal and paternal functioning separately because there can be a differential impact on HRQOL outcomes (105).

Careful consideration of the potential interplay between the child and parent psychological status and the child's HRQOL is important (106). Hommel et al. studied these issues, and their data suggested that adolescent depressive symptoms worsen parental distress, resulting in worse HRQOL in the adolescent (106). In a study of 99 adolescents with Crohn's disease and their parents, Gray et al. further explored family-level predictors of HRQOL by studying parenting stress as a potential mechanism through which disease activity affects HRQOL (103). This study demonstrated that parenting stress, because of the occurrence of medical stressors, partially mediated the disease severity–HRQOL relation, with a reduction in the relation between these variables. These results would indicate that as disease severity increases, parenting stress also increases and patient HRQOL decreases. Knez et al. reported that parents of children with IBD report a significantly lower psychological health compared with parents of other children and report a significantly lower physical health compared with parents of healthy children (107). Better understanding of the relationship between family functioning and HRQOL may allow practitioners to identify adolescents who are at higher risk for impaired HRQOL and to focus on families in need of support services or psychological intervention (104).

Conclusions

Childhood-onset IBD is becoming increasingly common in Canada and is being diagnosed more frequently in very young age groups. This is particularly noteworthy due to the chronic, noncurable nature of the condition. This changing age demographic may be due to changing environmental risk factors or earlier recognition and diagnosis. Children with IBD face unique challenges due to differences in their disease characteristics, the psychosocial strain on the child and family, and the transition process from child to adult. There is increasing recognition that children with IBD should be treated in specialized, multidisciplinary health care centres by physicians, nurses, dietitians, social workers and mental health professionals with training and expertise in pediatric IBD. However, there is still variation in access to such specialists across the country, and care is provided differently depending on where the child lives and regional availability of health care services (49). There must be more effort to help children and their families access the best quality care and treatments for this lifelong condition.

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. MEK was supported by a post-doctoral fellowship award from CIHR, Crohn's and Colitis Canada, and the Canadian Association of Gastroenterology. 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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