

2021
**IMPACT OF
COVID-19 &
INFLAMMATORY
BOWEL DISEASE**
IN CANADA

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COVID-19 Vaccines

Biology, Current Evidence, & Recommendations

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Foreword

The past year has been remarkably difficult for many people due to the challenges of the COVID-19 pandemic. With a promise to find the cures for Crohn's disease and ulcerative colitis and to improve the lives of everyone affected by these chronic diseases, Crohn's and Colitis Canada quickly focused on how we could help our community through this crisis.

Added to the rich research legacy of advancing treatments, improving lives, and ultimately seeking cures was understanding the impact of COVID-19 on people with IBD. The IBD community had questions like, if people with IBD had greater risk of contracting COVID-19 and whether certain medications made people with IBD more susceptible to the virus. Along with this, communication and education programs were essential to helping people navigate through the situation and making informed decisions.

Crohn's and Colitis Canada thanks the COVID-19 and IBD Task Force and the many people behind developing critical research, programs, and this report. The results of this work were tremendous in helping people in Canada and around the world.

This report is a summation of the efforts to date and findings.



Lori Radke
President and CEO
Crohn's and Colitis Canada

Roughly 300,000 Canadians live with inflammatory bowel diseases (IBD), a number expected to rise to 400,000 (1% of the population) by 2030. IBD consists of Crohn's disease and ulcerative colitis. These immune mediated inflammatory diseases are chronic and lifelong conditions for which people frequently require medications that suppress the immune system.

Table of Contents

Foreword	pg 4
Glossary	pg 7

About This Report

Purpose	pg 12
Using this Report	pg 12
Further Information	pg 13

Executive Summary

Summary	pg 15
Key Points	pg 15
Introduction	pg 16
Methods	pg 17
The Impact of COVID-19 on IBD: Report Summary	pg 19
<i>Epidemiology</i>	pg 19
<i>Children and Expectant Mothers with IBD</i>	pg 20
<i>Seniors with IBD</i>	pg 20
<i>Risk Factors and Medications</i>	pg 21
<i>Mental Health and Quality of Life</i>	pg 21
<i>COVID-19 Vaccines and IBD</i>	pg 22
<i>Healthcare Delivery during the Pandemic and the Future Model of IBD Care</i>	pg 23
Conclusion	pg 23
References	pg 24

A Knowledge Translation Strategy

Summary	pg 28
Key Points	pg 29
Introduction	pg 29
Crohn's and Colitis Canada's COVID-19 and IBD Task Force	pg 31
Task Force Recommendations	pg 32
Webinar Series	pg 34
Impact	pg 35
Conclusion	pg 36
References	pg 39

Epidemiology: The Trends of Disease over Time

Summary	pg 42
Key Points	pg 42
Introduction	pg 43
Epidemiologic Determinates of a Pandemic: R_0	pg 43
Epidemiology of COVID-19 in Canada	pg 46
Epidemiology of COVID-19 in People with IBD	pg 50
Conclusion	pg 51
References	pg 52

Children and Expectant Mothers with IBD

Summary	pg 56
Key Points	pg 56
Overview of COVID-19 in Children	pg 57
Outcomes of COVID-19 in Children with IBD	pg 58
Health System Impact of COVID-19 in Children with IBD	pg 59
Mental Health Impacts of COVID-19 in Children and Youth with IBD	pg 60
COVID-19 and Pregnant People with IBD	pg 62
Crohn's and Colitis Canada's COVID-19 and IBD Task Force Recommendations	pg 63
References	pg 64

Seniors with IBD

Summary	pg 68
Key Points	pg 68
Introduction	pg 69
COVID-19 and the Elderly	pg 69
COVID-19 and the Elderly with IBD	pg 71
Conclusions	pg 72
References	pg 73

Clinical Risk Factors and IBD Medications

Summary	pg 78
Key Points	pg 78
Introduction	pg 79
Gathering Information	pg 80
Medications, Disease Activity, and Other Risk Factors	pg 82
<i>Steroids</i>	pg 82
<i>Anti-TNF Therapy</i>	pg 82
5-ASA	pg 82
<i>Immunomodulators</i>	pg 82
<i>New Biologics:</i>	
<i>Vedolizumab and Ustekinumab</i>	pg 82
<i>Small Molecules: Tofacitinib</i>	pg 82
<i>Disease Activity</i>	pg 82
<i>Other Risk Factors</i>	pg 83
Task Force Recommendations	pg 83
References	pg 86

Mental Health and Quality of Life

Summary	pg 89
Key Points	pg 89
Mental Health in the General Population during the Pandemic	pg 90
Mental Health in Persons with IBD during the Pandemic	pg 92
Quality of Life for Persons Living with IBD	pg 94
<i>Health Related Quality of Life for Persons living with IBD Pre-pandemic</i>	pg 94
<i>Health Related Quality of Life for Persons living with IBD during the Pandemic</i>	pg 96
Conclusions	pg 97
References	pg 98

COVID-19 Vaccines: Biology, Current Evidence, & Recommendations

Summary	pg 105
Key Points	pg 105
Introduction	pg 106

Immunity and COVID-19: Natural and Vaccine Immunity	pg 106
Currently Approved SARS-CoV-2 Vaccines:	
Mechanisms, Efficacy, and Safety	pg 108
<i>Messenger RNA (mRNA) Vaccines</i>	pg 109
<i>Adenovirus Vector Vaccines</i>	pg 109
<i>Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT)</i>	pg 110
Vaccine Production and Distribution in Canada	pg 111
SARS-CoV-2 Vaccine Recommendations for People with IBD	pg 111
Vaccines in Special Populations:	
Children and Adolescents	pg 113
Vaccines in Special Populations:	
Pregnant People	pg 113
Vaccines in Special Populations: Seniors	pg 114
Conclusion	pg 115
References	pg 116

Healthcare Delivery during the Pandemic and the Future Model of IBD Care

Summary	pg 123
Key Points	pg 123
Introduction	pg 124
Changes in Healthcare Delivery	pg 125
<i>Outpatient Visits Replaced by Virtual Care</i>	pg 125
<i>Endoscopy and Disease Monitoring</i>	pg 126
<i>Hospital and Surgical Care</i>	pg 126
<i>Multidisciplinary Care</i>	pg 127
Medical Therapy during the Pandemic	pg 128
<i>Immunomodulatory Therapy and Risk of Severe COVID-19</i>	pg 128
<i>Provider Prescribing and Treatment Adherence</i>	pg 128
<i>Access to Biologic Therapies</i>	pg 128
IBD Care Delivery: Lessons for the Future	pg 129
References	pg 132

Glossary

- **ANGIOTENSIN-CONVERTING ENZYME 2 (ACE2):** A protein on the surface of many cell types that provides the entry point for the coronavirus to hook into and infect a wide range of human cells.
- **ANTIBODIES:** Proteins made by white blood cells in response to an **antigen**. Antibodies neutralize **antigens**.
- **ANTIGEN:** A foreign/toxic substance that causes the body to mount an immune response.
- **ANTI-TNF:** (Anti-tumor necrosis factor alpha) Drugs that help stop inflammation; used for inflammatory diseases like ulcerative colitis and Crohn's disease (e.g. Adalimumab or **Infliximab**).
- **ATHEROSCLEROTIC DISEASE:** A type of cardiovascular (heart and blood) disease in which plaque builds up inside the arteries.
- **ATROPHY:** Decrease in size or wasting away of a body part or tissue.
- **BIOLOGICS:** Drugs made from living cells that have large, complex molecular structures. Some biologic medications are engineered to target specific activity in the immune system to treat inflammation.
- **C-REACTIVE PROTEIN (CRP):** A protein made by the liver that is sent into the bloodstream in response to inflammation.
- **CASE-FATALITY RATE:** The percentage of people in a given group who die as a result of acquiring a disease (e.g. COVID-19).
- **COMORBIDITIES:** Two or more disorders or illnesses occurring in the same person.
- **CONCOMITANT IMMUNOMODULATORS:** Medications that suppress the immune system (e.g. azathioprine, 6-mercaptopurine, methotrexate) used together with **biologics** to improve the effectiveness of the **biologics**, reduce the rate of elimination of the **biologics** from a person's body, or decrease the formation of **anti-TNF antibodies**.
- **CORTICOSTEROIDS:** A class of drug that suppresses the immune system and lowers inflammation in the body. Examples include prednisone, prednisolone, methylprednisolone, and hydrocortisone.
- **COVIDENCE:** A proprietary web application and technology platform used for systematic reviews.
- **CVD:** Cardiovascular disease, disease of the heart and blood vessels.
- **CYTOKINES:** Small proteins important in cell signaling. Cytokines are part of the body's immune response to infection.
- **CYTOKINE STORM:** A reaction in which the immune system causes an uncontrolled and excessive release of **cytokines** that can cause multisystem organ failure and death.
- **ENDOSCOPY:** A procedure in which an instrument is introduced into the body to give a view of its internal parts.
- **EPIDEMIOLOGY:** The study and analysis of the distribution, patterns, and determinants of health and disease conditions in defined populations.

- **FECAL CALPROTECTIN:** A biochemical measurement of the protein calprotectin in the stool. Elevated fecal calprotectin occurs during intestinal inflammation, including inflammation caused by inflammatory bowel disease.
- **FRAILITY:** The condition of being weak and delicate typically indicated by unintentional weight loss (10 or more pounds within the past year), muscle loss and weakness, a feeling of fatigue, slow walking speed and low levels of physical activity.
- **HERD IMMUNITY:** When a large enough percentage of the population becomes immune to a disease through vaccination or immunity developed through previous infection to protect those who cannot be vaccinated by limiting the ability of a virus to spread.
- **HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS):** A score commonly used by doctors to determine an individual's level of anxiety and depression.
- **HUMORAL (ANTIBODY-MEDIATED) RESPONSE:** The activation of B cells (a type of cell in the immune system) and secretion of **antibodies** when **antigens** are detected in the body's fluids.
- **INTERFERONS:** A group of signaling proteins made and released by host cells in response to the presence of several viruses causing nearby cells to heighten their anti-viral defenses.
- **INTERLEUKIN-6 (IL-6):** A protein produced by various cells that helps regulate immune responses elevated by inflammation, infection, autoimmune disorders, cardiovascular diseases, and some cancers.
- **IMMUNOGENICITY:** A measure of the type of immune responses a vaccine generates and magnitude over time.
- **IMMUNOMODULATORS:** Medications (e.g. azathioprine, 6-mercaptopurine, methotrexate) that modify the activity of the immune system and decreases inflammatory response.
- **INFLIXIMAB:** A type **anti-TNF biologic** medication marketed in Canada under brand names Remicade®, Renflexis®, Inflectra® and Remsima®.
- **KNOWLEDGE TRANSLATION:** A term increasingly used in science that describes the process of transitioning generated knowledge from research to various stakeholders to inform decision-making and application to real-world problems.
- **LIPID NANOPARTICLE DELIVERY SYSTEM:** A drug delivery system used in **mRNA** COVID-19 vaccines. Lipid nanoparticles, or fatty acid solution, houses the **mRNA** strands for delivery into the body.
- **MORBIDITY:** The proportion of a population who contracts a specific disease or state (e.g. COVID-19).
- **MESSENGER RIBONUCLEIC ACID (mRNA):** A single-stranded molecule that carries genetic code from DNA in a cell's nucleus to ribosomes, the cell's protein-making machinery.

- **MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C):** A rare complication of COVID-19 in children where different body parts can become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs.
- **NATURAL KILLER (NK) CELLS AND TH1-LYMPHOCYTES:** A type of white blood cell in the immune system that limits the spread of infection and subsequent tissue damage.
- **NEUTRALIZING ANTIBODIES:** An antibody that defends a cell from a pathogen or infectious particle by neutralizing any effect it has biologically.
- **NON-REPLICATING VIRAL VECTOR:** A viral vector vaccine uses a harmless version of a different virus, called a vector, to deliver information into the cells to tell the cells to produce a protein that is encoded by that information. The vaccine teaches the body to make copies of the **spike proteins** so the body can recognize it, create **antibodies**, and fight off the real virus later.
- **ODDS RATIO, RISK RATIOS, AND CONFIDENCE INTERVALS:** An odds ratio is comparison of the odds of developing a given outcome for those exposed to a particular factor as compared to the odds of developing the outcome if unexposed to the factor being investigated. The risk ratio is the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group. The confidence interval (typically 95%) estimates the likelihood of a true value falling in that range if an experiment is repeated over and over—the more narrow the interval, the more accurate the statistic is likely to be.
- **PATIENT HEALTH ENGAGEMENT (PHE) SCALE:** A structured framework designed to explain how patient engagement in research and healthcare works and develops.
- **R_0 : BASIC REPRODUCTIVE NUMBER:** The average number of secondary infections produced by a typical infection case in the absence of public health intervention where everyone in the population is susceptible. Used to measure disease transmission potential. If R_0 is 1, it means each individual with the infection is transmitting it to one other person. If R_0 is greater than 1, it means the infection is being transmitted to that number of other people (e.g. if R_0 is 1.5, each person transmits the virus to 1.5 other people on average, or 10 infected people will result in 15 additional people being infected). Similarly, if R_0 is less than 1, it means that each person with the infection is transmitting it to fewer than one other person (e.g. if R_0 is 0.5, each person transmits the virus to 0.5 other people on average, or two people are required to transmit the infection to one additional person).
- **R_t : EFFECTIVE REPRODUCTIVE NUMBER:** An estimate of the average number of infections caused by a single case of infection at a specific point in time—similar to R_0 but takes into account immunity and public health interventions.
- **REAL-WORLD EVIDENCE (RWE):** Data on healthcare observed and documented during routine clinical practice.

- **RANDOMIZED CONTROL TRIAL (RCT):** A scientific experiment that aims to reduce bias by randomly allocating subjects to two or more groups, treating them differently, and then comparing them with respect to a measured response (e.g. vaccinated versus placebo study groups against COVID-19).
- **SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS-2 (SARS-CoV-2) AND CORONAVIRUS DISEASE, DISCOVERED 2019 (COVID-19):** SARS-CoV-2 is the virus that causes COVID-19 in people who are infected; COVID-19 is the disease that results from infection with the SARS-CoV-2 virus.
- **SEROCONVERSION:** Becoming antibody positive based on blood test.
- **SEROCONVERSION RATE:** The rate of people who mount an immune response to an infection or foreign substance (e.g. the COVID-19 spike protein after infection or vaccination), detectable as antibodies in the bloodstream.
- **SPIKE PROTEIN:** A protein which protrudes from the envelope of a coronavirus, enabling the complete virus particle to enter a host cell by binding to a receptor on its surface. This protein is the portion of the virus used in currently approved vaccines against COVID-19.
- **SURVEILLANCE EPIDEMIOLOGY OF CORONAVIRUS UNDER RESEARCH EXCLUSION (SECURE-IBD):** An international database to monitor and report on outcomes of COVID-19 occurring in people with IBD.
- **T-CELL AND B-CELL MEMORY RESPONSES:** During an immune response, T and B cells create memory cells—clones that remain in the body, holding information about each threat the body has been exposed to.
- **T FOLLICULAR HELPER CELL DIFFERENTIATION:** A necessary process in the development of high binding antibodies.
- **TELEMEDICINE:** The remote diagnosis and treatment of individuals by means of telecommunications technology (including telephone, video, email, smartphone apps, and wearable devices).
- **THIOPURINES:** A class of immunosuppressive medication used for the treatment of IBD (e.g. azathioprine, 6-mercaptopurine).
- **TOFACITINIB:** A type of medication marketed under the brand name Xeljanz® that acts to inhibit certain enzymes (called JAK 1 and JAK 3) and maintain remission.
- **TUMOR NECROSIS FACTOR ALPHA (TNF- α):** A protein in your body produced during acute inflammation, responsible for a range of cell signalling events and important for the body's ability to resist infection. Anti-TNF biologics are antibodies that destroy this protein.
- **TRANSMISSIBILITY:** The probability of an infection, given contact between an infected individual and non-infected individual.

- **USTEKINUMAB:** A type of **biologic** drug marketed under the brand name Stelara® that acts to suppress certain cytokines (IL-12 and IL-23) from triggering an inflammatory response.
- **VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA (VITT):** The formation of blood clots throughout the body occurring in rare cases after receiving the COVID-19 adenoviral vector vaccine.
- **VEDOLIZUMAB:** A type of **biologic** drug marketed under brand name Entyvio® that acts to reduce the ability of white blood cells in the gut from entering the tissue to cause inflammation.
- **VIRUS REACTIVATION:** When a dormant virus that has infected a host cell begins to replicate allowing the virus to spread.

About This Report

Purpose

Over 300,000 Canadians are afflicted with the inflammatory bowel diseases (IBD), a number expected to rise to 400,000 (1% of the population) by 2030. IBD consist of Crohn's disease and ulcerative colitis.¹⁻³ These immune mediated inflammatory diseases are chronic and lifelong conditions for which people frequently require medications that suppress the immune system. While clinicians and researchers continue to work on therapies to manage IBD and improve the lives of people living with these diseases, a cornerstone of IBD research over the past year has been to understand the impact of the COVID-19 pandemic on people living with IBD: Determining if certain medications make a person more susceptible to the virus or severe COVID-19; if people with IBD are generally at greater risk; and to make specific recommendations to the IBD community to allow those living with these diseases to make informed, personal risk assessments during the pandemic.

The Scientific and Medical Advisory Council of Crohn's and Colitis Canada has reached out to leading gastroenterologists and IBD researchers in Canada to create this document explaining our current understanding of the impact of the COVID-19 pandemic on the IBD population. The intent of this report is to provide expert scientific and medical information to the IBD community in Canada. With that in mind, this report is specifically written for a non-expert audience; however, in order to present the scientific and medical information, it is sometimes necessary to use industry jargon. Therefore, a [glossary](#) is provided to help the reader understand medical or scientific terms.

Using this Report

The primary purpose of this report is to convey concise information relevant to the IBD community (including clinicians, policy makers, and persons with IBD and their caregivers) regarding the impact of the COVID-19 pandemic. Each section is written by a team of experts in the area to provide the most accurate and up-to-date information possible, as of the date of writing (June, 2021). Specific information is often found in more than one chapter (for example, information on COVID-19 vaccines and children is available in the [Children and Expectant Mothers with IBD](#) chapter or the [COVID-19 Vaccines: Biology, Current Evidence, & Recommendations](#) chapter); when this occurs, we have included hyperlinks to other places in the document, simply click the link, and you will be taken to the other relevant chapter/section to find the information you are looking for. To navigate back to where you were prior to clicking the link (depending on your viewer), simply hold Alt and hit the left arrow (←). Other links in this document will take you to websites where further information is available, such as to Crohn's and Colitis Canada's webpage on [Recommendations on Vaccines for People with IBD](#). For information that evolves at a rapid pace as we learn more about the disease, interaction with various aspects of IBD, or variants of concern, the interested reader should refer back to [Crohn's and Colitis Canada's website](#), as it will be frequently updated with the latest information and guidance.

Further Information

There is a wealth of information in this document, but you may want to know more about a particular topic. Where an external source was used for the information, it is referenced by a number following the sentence so you can find the original article. Perhaps the best source of information for many in the IBD community will be Crohn's and Colitis Canada's Frequently Asked Questions; Recommendations Website; and Past Webinars, which all provide more detailed information, direct answers to questions, and short videos to provide the information through a different medium. Links to answers on a number of different topics are provided on Crohn's and Colitis Canada's [COVID-19 and IBD landing page](#), answers to a variety of specific questions are available on the [COVID-19 and IBD Get Answers page](#), and both future and past webinars can be found on the [COVID-19 and IBD Webinars page](#). For more information on who comprises the Task Force that is providing all this information, you can check out the [COVID-19 and IBD Task Force page](#) or the [section on the Task Force](#) in our Knowledge Translation chapter.

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2. Kaplan GG, Windsor JW. The four epidemiological stages in the global evolution of inflammatory bowel disease. *Nat Rev Gastroenterol Hepatol*. 2021;18(1):56-66.
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EXECUTIVE SUMMARY

Executive Summary

Summary

Persons with Crohn's disease or ulcerative colitis (together, inflammatory bowel disease [IBD]) make up more than 0.75% of the Canadian population in 2021. Early in the COVID-19 pandemic, individuals with IBD, particularly those on immunosuppressive therapies, were concerned that their health status may place them at higher risk of contracting COVID-19 or experiencing more severe disease course if infected with SARS-CoV-2. In response, Crohn's and Colitis Canada developed the COVID-19 and IBD Task Force in March 2020 to rapidly synthesize the evolving knowledge of COVID-19 as relevant to Canadians with IBD. The Task Force communicated expert information directly to the Canadian IBD community through online tools and a webinar series.

In order to understand the full impact of COVID-19 on the IBD community, Crohn's and Colitis Canada commissioned a policy report that was informed through a systematic literature review and synthesized across working groups along the following domains: [Epidemiology](#), [Children and Expectant Mothers with IBD](#), [Seniors with IBD](#), [Mental Health](#), [Risk Factors and IBD Therapy](#), [Vaccines](#), and [Healthcare Delivery during the Pandemic and the Future Model of IBD Care](#). This report from Canadian physicians, researchers, and IBD community representatives highlights the physical, mental, and health systems impact of COVID-19 on the entire spectrum of the IBD community, including children, adolescents, adults, seniors, and pregnant people with IBD. This executive summary provides an overview of the crucial information from each of the chapters of the policy report, supplemented with additional information made available through Crohn's and Colitis Canada's webinar-based [knowledge translation](#) platform.

Key Points

1. In response to the COVID-19 pandemic, Crohn's and Colitis Canada's COVID-19 and IBD Task Force synthesized relevant knowledge on a regular basis and communicated with the IBD community in real-time through expert-generated online tools and frequent webinars for a public audience.
2. The **transmissibility** of severe acute respiratory syndrome coronavirus-2 (**SARS-CoV-2**), the virus that causes COVID-19, for those with IBD follows epidemiologic trends within the general population; most people with IBD are not at increased risk of contracting COVID-19 or having severe COVID-19 compared to the general population.
3. Children with IBD have milder COVID-19 disease course and are less likely to require hospitalization compared to adults with IBD, which is consistent with the observations on the natural history of COVID-19 across the age spectrum in the general population.
4. In the general population, pregnancy is associated with more severe COVID-19 or birth complications; however, the impact of COVID-19 in pregnant people with IBD is not known.
5. Seniors have the highest risk of severe COVID-19 in the general population and among those with IBD.
6. Persons with IBD who have active disease and require a high dose of **corticosteroids** (more than 20 mg per day or, in children, 0.5 mg per kg of body weight per day) are at higher risk of severe complications from COVID-19.

7. **Biologic** maintenance therapies for IBD are not associated with a higher risk of acquiring COVID-19 or having a more serious course following infection from **SARS-CoV-2**.
8. As a result of the COVID-19 pandemic, an increase in distress and worsening mental health has been demonstrated in children, adolescents, adults, seniors, and pregnant people with and without IBD.
9. Real-world evidence suggests that vaccines for COVID-19 are safe and elicit robust immune responses to **SARS-CoV-2** infection following two doses of vaccine in individuals with IBD, although immunity may be less robust following a single dose of vaccine among those receiving **anti-TNF** therapy or conventional immunosuppressants.
10. COVID-19 has necessitated alternate models of delivering care to those with IBD, including virtual care and remote monitoring of disease activity, which will influence healthcare delivery models beyond the SARS-CoV-2 pandemic.

Introduction

Inflammatory bowel disease (IBD) affects more than 0.75% of the Canadian population in 2021.¹⁻³ At the onset of the pandemic, individuals with chronic immune-mediated inflammatory diseases, such as IBD, and those on immunocompromising therapies were identified as potential vulnerable populations with an unknown risk of **SARS-CoV-2** infection. In parallel, Canadian healthcare providers initially lacked evidence-based guidance, leading to a potential risk of heterogeneous communication and management of IBD during the pandemic.

In response, Crohn's and Colitis Canada developed a national representative Task Force made up of physicians (adult and pediatric gastroenterologists, infectious disease specialists), scientists, nurses, and IBD community representatives. In March 2020, Crohn's and Colitis Canada formed the [COVID-19 and IBD Task Force](#) to review the scientific literature on COVID-19 and make recommendations relevant to the IBD community in Canada. Knowledge from the Task Force was communicated to the IBD community through Crohn's and Colitis Canada's website and a regular webinar series, featuring invited panelists who addressed specific topics on COVID-19 and IBD. As of May 2021, Crohn's and Colitis Canada's webpage on COVID-19 has been viewed nearly half a million times, and twenty-five webinars have been produced on COVID-19 and IBD that have been viewed nearly 130,000 times.

Crohn's and Colitis Canada commissioned a policy report on COVID-19's impact on the IBD community at the one-year anniversary of the World Health Organization's declaration of a global pandemic. This executive summary explains the sections of the policy report: [Epidemiology](#), [Children and Expectant](#)

[Mothers with IBD](#), [Seniors with IBD](#), [Mental Health, Risk Factors and IBD Therapy](#), [Vaccines](#), and [Healthcare Delivery during the Pandemic and the Future Model of IBD Care](#). It further provides an overview of the crucial information from each of the chapters of the policy report, supplemented with additional information made available through Crohn's and Colitis Canada's webinar-based [knowledge translation](#) platform.

Methods

A systematic review of the literature established the evidence used by the working groups to create the sections in this report. We searched MEDLINE, EMBASE, PsycINFO, CINAHL, Cochrane Library, the Cochrane COVID-19 Study Register, the World Health Organization's (WHO) [COVID-19 database](#) from 2019 to February 4, 2021 to identify studies describing the impact of the COVID-19 pandemic on people living with IBD. The WHO database includes preprints of all COVID-19 publications from medRxiv and bioRxiv. The search strategy included search terms for IBD (including Crohn's disease and ulcerative colitis) and COVID-19. Our search was left intentionally broad to ensure all relevant articles were identified.

The literature search was updated March 24, 2021. The search of each database was limited according to the available filters in each database. CINAHL and the Cochrane COVID-19 Study Register were searched from February 2021. This updated search included all articles indexed in MEDLINE, EMBASE, and PsycINFO from January 1, 2021. All articles were identified from the Cochrane Library and WHO database. For database searches with overlapping search dates, duplicate references were removed manually. Any articles included in the literature search published prior to 2019 were also excluded.

Any study reporting on the impact of the COVID-19 pandemic on persons with IBD, including: The [epidemiology](#) of COVID-19 in persons with IBD; specific impacts of the pandemic on children or seniors, including their families/caregivers; pregnant people with IBD and/or their newborns; changes in healthcare delivery, including limited

access to **endoscopy** and elective surgery, mental health, vaccines, and quality of life. We included both primary studies and review articles, as well as any clinical practice guidelines, recommendations, or opinion pieces about the care of individuals with IBD during the pandemic. We excluded study protocols, case series of <10 participants, basic or translational science studies, and studies describing the impact of COVID-19 on the gastrointestinal system. No restrictions were placed on the language of publication, and we included studies published in abstract form.

Abstracts of studies identified by the literature search were independently screened by two individuals (JGH, PT, or MSM). The full-text of relevant abstracts was then reviewed independently by two individuals (JGH, PT, or MSM). Conflicts at both stages were reviewed by a third reviewer (MEK). **Covidence** was used to facilitate the review of abstracts and full-texts.⁴

A total of 1,981 references were identified in the initial search (February 4, 2021) and 1,329 additional references were identified in the update (March 24, 2021); 1,105 records remained after removing duplicates. The full texts of 529 studies were assessed for eligibility and 463 were included. Studies pertinent to each chapter of the report were tagged based on the topic or theme of the paper, then distributed to authors of that chapter.

The Impact of COVID-19 on IBD: Report Summary

Epidemiology

SARS-CoV-2 became a global pandemic because of the high **transmissibility** of the virus, the severe **morbidity** and mortality of COVID-19 that overwhelmed healthcare systems, and the novelty of the virus leaving the global population susceptible to infection.⁵ Without public health interventions to control the spread of SARS-CoV-2, the effective reproductive number (R_t) of the virus led to exponential spread across the globe. Public health measures from lockdowns to mask mandates reined in the periodic waves of infections across Canada, serving as a barrier against the virus until vaccines were available and distributed.

Reassuringly, evidence that emerged over the last year consistently demonstrated that the risk of contracting SARS-CoV-2 or experiencing severe COVID-19 if acquired was similar in those with Crohn's disease and ulcerative colitis as compared to the general population; for example, seniors with IBD were at highest risk for hospitalization and death following infection with SARS-CoV-2 regardless of whether they had IBD or not.⁶⁻⁸ However, most studies do not account for potential differences in adherence to public health guidelines among people with IBD and the general population.

Specific to the IBD community, those with actively flaring disease, particularly those requiring high dose **corticosteroids** (>20mg per day), were at risk of the worst outcomes from COVID-19.⁹⁻¹¹

The **epidemiology** of COVID-19 in those with IBD was regularly communicated to the IBD community through the Crohn's and Colitis Canada's COVID-19 and IBD webinar series, whereby the co-moderator (GK) presented on the current global, Canadian, and IBD-specific **epidemiology** of COVID-19. On March 19, 2020 (the first webinar), 782 Canadians were diagnosed with COVID-19; globally, 21 people with IBD who had contracted COVID-19 were reported in the Surveillance Epidemiology of Coronavirus Under Research Exclusion (**SECURE-IBD**) registry.¹² One year later (March 18, 2021, after 23 **webinars**) nearly 1 million Canadians and 6,000 individuals with IBD, worldwide, had contracted COVID-19.

Children and Expectant Mothers with IBD

The Task Force emphasized several special topics, including the impact of COVID-19 on children and pregnant people with IBD. From inception, the recommendations were age-based, with an emphasis on the mild course experienced by most children with COVID-19, even when immunocompromised due to their IBD medications.¹³ Despite the typically mild disease course, the Task Force deemed it important to address the concerns of parents with respect to reducing transmission, especially when in-person schooling resumed. Back-to-school recommendations were incorporated into the recommendations, and a [unique webpage](#) was created to address the concerns of parents and teachers. In addition to recommendations for at-risk individuals, the Task Force made recommendations for family members of at-risk children (such as the siblings of people on systemic **corticosteroids**) to emphasize the importance of shielding the individual from COVID-19 while enabling siblings to attend in-person school and parents to return to work.¹⁴ Pregnant individuals are at greater risk of a more severe COVID-19 disease course or birth complications; however, evidence on the additional impact of IBD on the likelihood of experiencing more severe COVID-19 in pregnancy is lacking.

All the webinars included pediatric healthcare provider representation. Additionally, multiple webinars were focused on educating parents of children with IBD (e.g. Families and Children with IBD: [May 7, 2020](#)) and people who were pregnant (e.g. Pregnancy and Newborns: [March 26, 2020](#)). Subsequent webinars also focused on back-to-school recommendations (Returning to School: [September 10, 2020](#)).

Seniors with IBD

Seniors with IBD represent a highly prevalent population that must contend with managing IBD in the context of age-related **comorbidities**.² The COVID-19 pandemic imposed tremendous stress on the elderly IBD population, as seniors had the highest risk of acquiring COVID-19 or experiencing severe COVID-19 if contracted (defined as hospitalization, ICU admission, or death). However, emerging evidence suggests that seniors with IBD are not at increased risk of acquiring COVID-19 or experiencing worse outcomes from COVID-19 as compared to seniors in the general population.^{8, 15} Nonetheless, due to the higher risk status of the senior population, a number of healthcare adaptations were instituted to reduce the risk of exposure of seniors with IBD to **SARS-CoV-2**, such as increased emphasis on **telemedicine**. While the elderly may have less robust immune responses to vaccines, experiences from other vaccination programs, especially for influenza, have shown that vaccinating the elderly reduces the risk of death in vulnerable people, and also frees resources for our health care system.¹⁶ Thus, messaging from Crohn's and Colitis Canada through the webinar series has consistently supported recommendations to protect seniors with IBD from exposure to **SARS-CoV-2** and to advocate for high rates of vaccine uptake.

Risk Factors and Medications

In March 2020, as Canada entered the first societal lockdown, individuals with IBD and their healthcare providers were making decisions on healthcare management without evidence regarding the impact of COVID-19 on IBD. Initially, guidance was based on expert consensus opinion.¹⁷ However, by July 2020, the first 500 cases from the **SECURE-IBD** registry indicated that the primary risk factor for a poor outcome of COVID-19 was age. Maintenance therapies, such as **anti-TNFs**, were not associated with worse outcomes; though flaring individuals who required high dose **corticosteroids** were more likely to be hospitalized or die from COVID-19.⁹ These data were substantiated in later studies from the **SECURE-IBD** registry as well as from different study populations.^{8, 10, 15}

Consequently, the COVID-19 and IBD Task Force consistently communicated a message to the IBD community not to discontinue effective therapy because cessation of treatment in fear of COVID-19 may lead to a flare, which is associated with an increased risk of worse outcomes from COVID-19.¹¹ Several webinars (e.g. IBD Medications and COVID-19 Risk: [June 18, 2020](#)) were dedicated to communicate efficacy and safety of IBD medications throughout the pandemic.

Mental Health and Quality of Life

Early in the COVID-19 pandemic, community anxiety levels, distress, and depressive symptoms were elevated, which was recognized as a normal response to a highly stressful situation. Individuals with IBD and healthcare providers were concerned that the heightened stress as a result of the pandemic would lead to not just mental health disorders but potentially exacerbating symptoms of IBD. During the webinar series (e.g. Mental Health and Wellness: [May 28, 2020](#)), information was provided on common psychologic reactions to the pandemic, including heightened anxiety, fear, and/or depression, noting reported increases in alcohol and cannabis use. Several factors have contributed to mental health difficulties during the pandemic, including uncertainty regarding risks of contracting COVID-19 and challenges of public health restrictions, social isolation, and financial stressors. Webinars and online communication provided guidance on managing the stress of the pandemic, including: Relaxation and breathing exercises, mindfulness meditation, exercising at home, keeping a regular sleep routine, maintaining connection with friends and family, limiting COVID-19 information overload, and ensuring that IBD care and follow-up is maintained.

COVID-19 Vaccines and IBD

Vaccines to SARS-CoV-2 hold the promise of protecting individuals who may be at higher risk, such as those who are immunocompromised.¹⁸ However, the mRNA vaccines (produced by Pfizer and BioNTech, and Moderna) and non-replicating viral vector (produced by AstraZeneca and Janssen) currently approved by Health Canada, were not originally studied in patients with immune-mediated diseases or those on immunosuppressant medications, including those with IBD.¹⁹⁻²¹ The CLARITY-IBD study assessed vaccine antibody response in those with IBD on biologics. The seroconversion rate after the first dose of vaccine was lower among individuals on infliximab as compared to individuals on vedolizumab, particularly in people on concomitant immunomodulators.²² However, seroconversion was robust following the second dose of the vaccine and after the first dose among those who had recovered from a prior infection to COVID-19.²² Furthermore, a national U.S. cohort study of nearly 15,000 IBD patients reported 80.4% vaccine effectiveness among those who were at least seven days from their second dose of mRNA vaccine.²⁸ Early studies have further shown positive benefits and negligible risk of COVID-19 vaccination among adolescents aged 12 to 15 and among pregnant persons.²⁹ Canadian,³⁰ European,³¹ and international³² organizations recommend that all individuals with IBD be vaccinated against SARS-CoV-2 at the earliest opportunity, irrespective of vaccine type, disease status or treatment, and without interruption of scheduled therapy.

Crohn's and Colitis Canada has strongly advocated for persons with IBD to receive a scheduled second dose of vaccine three to four weeks following the first dose to boost immunity—in line with the schedule followed in the trials—rather than extending the interval for the second dose. Education of vaccine safety and efficacy in the IBD population occurred regularly on our webinar series and evolved monthly as real-world experiences became known regarding safety and efficacy the IBD population. The webinars (e.g. Vaccine Updates and Recommendations: [April 24, 2021](#)) focused on providing the most up-to-date information with the goal of optimizing vaccine uptake by the IBD community.

Healthcare Delivery during the Pandemic and the Future Model of IBD Care

The COVID-19 pandemic dramatically shifted access to and delivery of care for Canadians living with IBD. During the first wave of the pandemic, in the spring of 2020, healthcare systems entirely redesigned ambulatory, diagnostic, and hospital care. The vast majority of healthcare delivery shifted to virtual **telemedicine** (phone or videoconference), whereas in-person healthcare delivery was transformed to adopt strict physical distancing, hygiene, and wearing face masks / personal protective equipment. These measures conserved health system capacity and reduced potential transmission of **SARS-CoV-2**. The rapid and widespread innovation of healthcare delivery from the pre-pandemic era was not without precedent;³³ Crohn's and Colitis Canada had already developed the Promoting Access and Care through Centres of Excellence (PACE) Telemedicine Program in Ontario.³⁴ Moreover, during the pandemic, studies of people with IBD and healthcare providers identified increased satisfaction, improved outcomes, and greater efficiency with the healthcare innovations (e.g. **Telemedicine**) such that the future of IBD care will most likely comprise hybrid models of in-person and virtual healthcare delivery.³⁵

The COVID-19 and IBD webinar series highlighted the adoption of healthcare innovation (**Telemedicine** in the Time of The Pandemic: [April 30, 2020](#)) and the future delivery of care (IBD Clinic of the Future: [June 11, 2020](#)). The key message from these webinars and emerging studies was that the lessons learned during the pandemic will influence models of delivering IBD care well beyond the **SARS-CoV-2** pandemic.

Conclusion

Crohn's and Colitis Canada's COVID-19 and IBD Task Force produced online tools and a series of webinars that served to rapidly synthesize and communicate scientific knowledge on COVID-19's impact on the IBD community. During the first year of the pandemic, clinical evidence indicated that most individuals with IBD followed similar epidemiologic and clinical patterns of the general population following infection with **SARS-CoV-2**. Across the spectrum of children, adolescents, adults, seniors, and pregnant people with IBD who maintained remission with their medical therapies, the risk of transmission and disease severity paralleled the general population. In contrast, individuals with IBD with moderate to severely active inflammation and who required a high dose of **corticosteroids** (>20 mg per day) were at higher risk of severe complications from COVID-19. Increases in distress and mental health disorders, including anxiety and depression, were prevalent across the age span, creating a significant burden on persons with IBD. The rapidly evolving data on vaccines to **SARS-CoV-2** revealed that administering two doses of vaccine was safe and elicited a robust immune response against **SARS-CoV-2** infection in those with IBD. Finally, the paradigm shifting changes to the delivery of care in order to prevent transmission of **SARS-CoV-2**, such as widespread virtual care and remote monitoring of disease activity, led to innovations in healthcare delivery models that will persist beyond the **SARS-CoV-2** pandemic.

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A KNOWLEDGE TRANSLATION STRATEGY

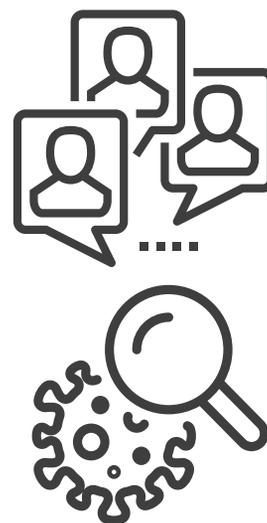
A Knowledge Translation Strategy

Summary

The total number of people living with inflammatory bowel disease (IBD), Crohn's disease or ulcerative colitis, is over 0.75% of the Canadian population in 2021. Many individuals with IBD are immunocompromised. Consequently, the World Health Organization's declaration of a global pandemic uniquely impacted those with IBD.

Crohn's and Colitis Canada formed the COVID-19 and IBD Task Force to provide evidence-based guidance during the pandemic to persons with IBD and their families. The Task Force met regularly through the course of the pandemic, synthesizing available information on the impact of COVID-19 on IBD. At first, the information was extrapolated from expert consensus guidelines, but eventually, recommendations were adapted for an [international registry](#) of worldwide cases of COVID-19 in people with IBD. The Task Force launched a **knowledge translation** initiative consisting of a webinar series and online resources to communicate information directly to the IBD community. Task Force recommendations were posted to [Crohn's and Colitis Canada's website](#) and included guidance such as risk stratification, management of immunosuppressant medications, physical distancing, and mental health. A weekly [webinar series](#) communicated critical information directly to the IBD community.

During the pandemic, traffic to Crohn's and Colitis Canada's website increased with 484,755 unique views of the COVID-19 webpages and 126,187 views of the 23 webinars, including their video clips. Crohn's and Colitis Canada's COVID-19 and IBD Task Force provided critical guidance to the IBD community as the pandemic emerged, the nation underwent a lockdown, the economy reopened, and subsequent waves ensued. By integrating public health guidance through the unique prism of a vulnerable population, Crohn's and Colitis Canada's **knowledge translation** platform informed and protected the IBD community.



Key Points

1. During the COVID-19 pandemic, one of the most essential health services has been the communication of expert health information and population-level advice; for the IBD population, this was achieved through expert-created online materials and frequent webinars geared towards a public audience.
2. Because the **epidemiology** of the COVID-19 pandemic differed by region, emphasis is placed on providing the best information possible so that people with IBD can assess their personal risk based on personal health risk factors, ability to stay home, and the state of local outbreaks.
3. In addition to increased web content and topical webinars, one of the most effective tools at communicating expert information to the IBD population were short topical videos spliced from the full webinar series that allowed individuals to search and find answers to specific questions related to their personal risk and/or the COVID-19 pandemic.

Introduction

Roughly 300,000 people are living with inflammatory bowel disease (IBD) in Canada in 2021, and this number is expected to exceed 400,000 by 2030.¹⁻³ The prevalence (total number of active cases) of IBD in Canadians is estimated to have risen roughly 50% in the last 10 years (from 0.55% of the Canadian population in 2010 to 0.76% in 2020), and is expected to increase to 1% of the Canadian population by 2030 ([Figure 1](#)).^{2, 4} Seniors (those aged 65+) with Crohn's disease or ulcerative colitis represent the fastest growing group of Canadians with IBD and face complications associated with longer disease duration alongside other age-related **comorbidities**.^{5, 6} On the opposite end of the age spectrum, children with IBD are at risk of unique disease complications, such as impairment of linear growth, and may respond differently to treatments or be at greater risk of related side effects as compared to adults.⁷

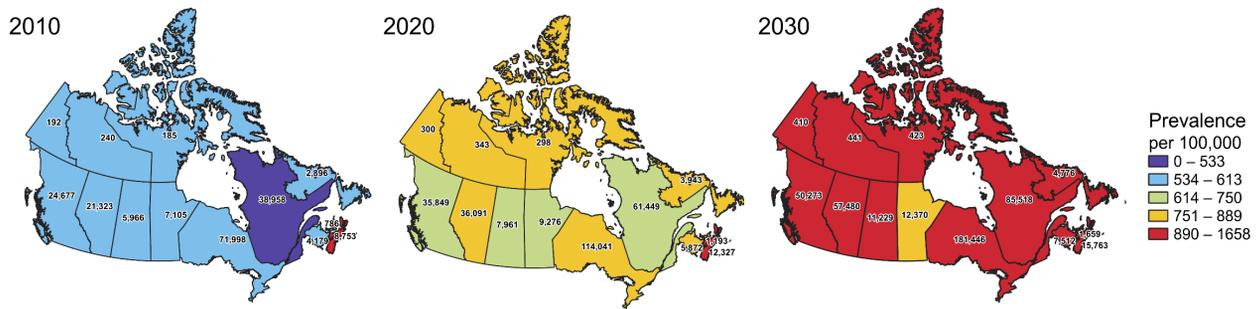


Figure 1: The change in the total number of people with IBD per 100,000 total population (colour gradient) and by estimated case numbers (text in provinces) in Canadian provinces and territories in three time periods: 2010, 2020, and 2030. Data were estimated from administrative healthcare databases from seven provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, and Nova Scotia) and modeled to estimate provinces/territories without direct data and then forecasted out to 2030.²

The World Health Organization (WHO) declared the novel SARS-CoV-2 outbreak a global pandemic on March 11, 2020;⁸ this immediately raised concerns among persons suffering from immune-mediated diseases and their healthcare providers due to their potential immunocompromised status—as a result of their disease or the medications they take for it. Given how little was known about COVID-19 early in the pandemic, the rapid dissemination of information, and the potential susceptibility of immunocompromised people living with IBD, the Scientific and Medical Advisory

Council (SMAC) of [Crohn's and Colitis Canada](#) instituted a Task Force to make evidence-based recommendations to people with IBD. In order to deliver expert recommendations and answers to the IBD community, Crohn's and Colitis Canada launched a **knowledge translation** initiative consisting of a webinar series and online resources.

In this chapter, we detail the dynamic and iterative process of the **knowledge translation** initiatives developed to inform and protect the IBD community during the first year of the pandemic.

Crohn's and Colitis Canada's COVID-19 and IBD Task Force

On March 12, 2020, the SMAC of Crohn's and Colitis Canada met to discuss the COVID-19 pandemic and its potential impact on the IBD community. Together with Crohn's and Colitis Canada leadership, the Council agreed that a broader group of experts was necessary to determine recommendations for the IBD community considering the general lack of knowledge on risk factors and scarcity of supporting scientific evidence.

On March 17, 2020, the [COVID-19 and IBD Task Force](#) convened via videoconference with representatives from across Canada, including: adult and pediatric gastroenterologists, IBD nurses, infectious diseases experts, scientists, public health officials, communications and government relations experts, and patient advisors ([Figure 2](#)).

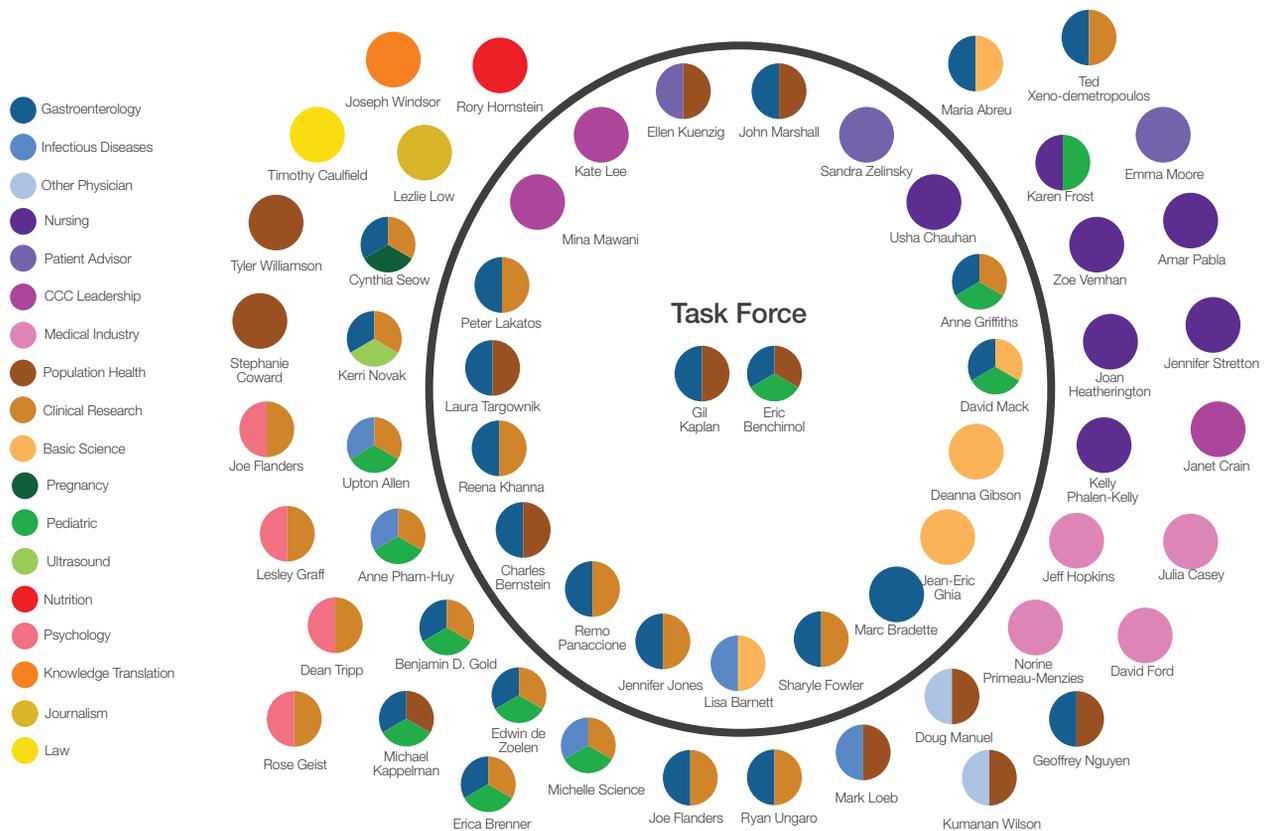


Figure 2: Expertise of Crohn's and Colitis Canada's COVID-19 and IBD Task Force (in the circle) and guest panel speakers/contributors for webinars (outside of the circle).

The Task Force met weekly from March 17, 2020 through June 16, 2020 during the first wave of the pandemic in Canada and reconvened with monthly meetings in September to address the second wave. The main deliverable of this group was guidance for the IBD community with the caveat that COVID-19 knowledge was evolving rapidly, and recommendations would be reviewed and revised regularly. Topics covered during these online videoconferences largely reflected questions and concerns posed directly by persons with IBD and informed the [knowledge translation](#) campaign championed by Crohn's and Colitis Canada.

Over the course of the pandemic, it became clear that Canada's COVID-19 [epidemiology](#) differed by region. The central prairie region (Manitoba and Saskatchewan) and most of the Atlantic region (New Brunswick, Prince Edward Island, Nova Scotia, and Newfoundland & Labrador) initially had low to medium case counts, were able to limit the spread of the virus early on, and experienced fewer total cases.⁹ In order to respect the local [epidemiology](#) of the pandemic in different jurisdictions within Canada, and emphasis was placed on providing the most up-to-date information available and encouraging the IBD community to assess their personal risk. However, individuals were urged to contact their own healthcare providers for individual health advice. The general guidance provided considered factors such as age, medications, and other pre-existing health conditions (referred to as [comorbidities](#) in the health literature).

Task Force Recommendations

Recommendations were based on available evidence that included guidelines from gastroenterology societies (e.g. the International Organization for the Study of IBD [IOIBD]), experience from prior viral outbreaks, and current public health guidance modified for the needs of the IBD community.⁹⁻¹¹ Recommendations were dynamic as knowledge and global outbreaks continued to increase. Thus, recommendations were frequently updated to reflect new data and were communicated to the IBD community in almost real-time. The Task Force determined that recommendations should be presented within the context of various risk factors, such as: age, [comorbidities](#) (i.e. other concurrent diseases or health conditions), status of disease (i.e. new diagnosis, current or recent flare, or remission), and medications (e.g. [corticosteroids](#), [biologics](#)/biosimilars). The goal was to offer guidance to the IBD community so that individuals could assess their own IBD profile and minimize their own personal risk.

Recommendations were posted to [Crohn's and Colitis Canada's website](#) ([Table 1](#)). An explicit statement that the recommendations should supplement, but not replace, the recommendations made by an individual's doctor or local public health authority was included in all communication. Detailed information made available included frequently asked questions (FAQ) sheets and video clips from a weekly webinar series ([Table 1](#)). Over the first six months of the pandemic, recommendations evolved. New evidence emerged regarding risk factors, [transmissibility](#), and medications that may exacerbate negative outcomes from agencies like the Public Health Agency of Canada, the WHO, and the Centers for Disease Control in the U.S..^{9, 12, 13} The breadth of knowledge regarding COVID-19 and IBD-specific risk factors also grew.^{14, 15}

Our understanding of COVID-19 outcomes (i.e. infection, recovery, or severe COVID-19—defined as hospitalization, ICU admission, or death) specific to the IBD community came through multiple data sources^{16, 17} including the Surveillance Epidemiology of Coronavirus Under Research Exclusion ([SECURE-IBD](#)) registry.^{14, 15} SECURE-IBD is a physician self-report database that collects information on global cases of COVID-19 occurring in people with IBD.^{14,15} The registry includes: disease type (Crohn's disease or ulcerative colitis), disease activity (remission, mild, moderate/severe, unknown), age, sex, medications for IBD, country, and outcomes of COVID-19 (recovery, hospitalization, death). [An online interactive map](#) displays the data captured in SECURE-IBD.¹⁸ The first case was reported to the registry on March 13, 2020, and as of June 8, 2021, 6,242 cases have been reported to the

registry. Based on the SECURE-IBD data, the most significant risk factors for negative outcomes of COVID-19 were identified as age, active disease (defined by the physician's assessment), and prednisone use.^{14, 15} Moreover, people with IBD on biologics/biosimilars did not have an increased risk of complications from COVID-19 (i.e. need for hospitalization, intensive care, or death).

The evidence from the registry supported a central message of the Crohn's and Colitis Canada COVID-19 and IBD Task Force: People with IBD in clinical remission on medications and without infectious symptoms should not stop their treatments. This message was consistently delivered through the various waves of the pandemic that saw daily cases of COVID-19 diagnosis in Canada peak at nearly 9,000 cases per day in April 2021 ([Figure 3](#)).

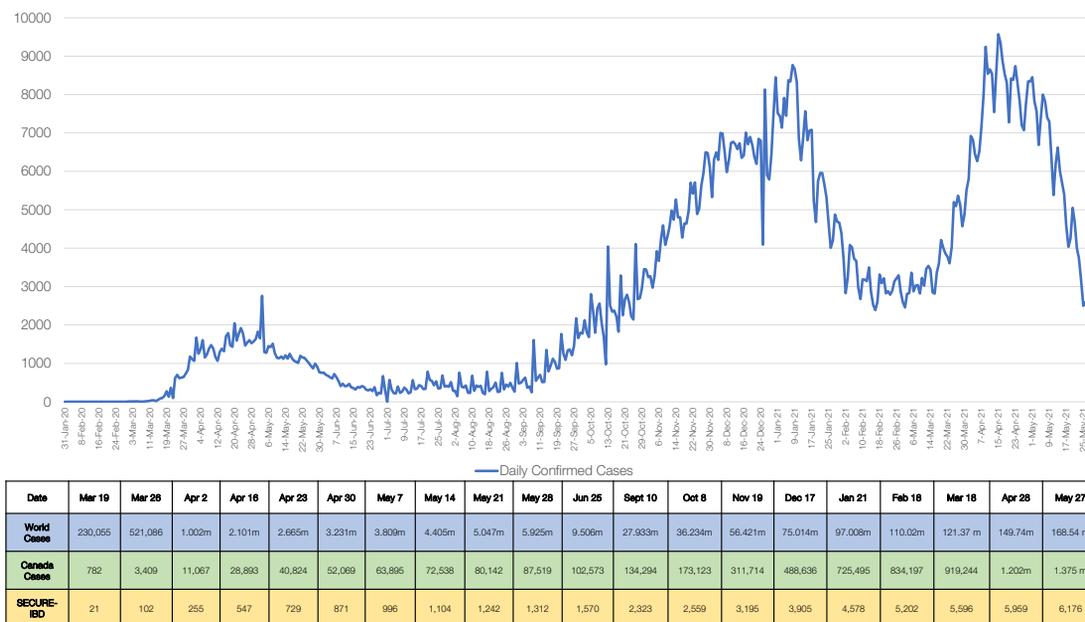


Figure 3: Daily cases of COVID-19 diagnosed in Canada from January 2020 to May 2021 alongside a table showing the cumulative number of diagnosed COVID-19 cases in the world, across Canada, and in the Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE) IBD registry. Source: Gov. of Canada, Coronavirus disease (COVID-19): Outbreak update - Canada.ca: <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html>, updated May 27, 2021.

Webinar Series

The core strategy of the **knowledge translation** initiative was a weekly webinar series moderated by the co-chairs of the Crohn's and Colitis Canada COVID-19 and IBD Task Force (Drs. Kaplan and Benchimol). These webinars were developed as the primary mechanism to communicate critical information directly to the IBD community in a manner that was accessible to a broad audience. The webinars were promoted through email membership and volunteer lists compiled by Crohn's and Colitis Canada, as well as Crohn's and Colitis Canada's social media network (@getgutsycanada Facebook, Twitter, and Instagram). As with the topics for Task Force discussion, content was developed based on questions received directly from the IBD community in a questionnaire filled out during registration for the webinars, from the live chat during the webinar broadcast, or from the post-webinar surveys deployed to all webinar registrants. The direct connection with people with IBD and their families addressed the critical requirement for effective **knowledge translation** with information directly relevant to the audience.¹⁹

Questions and concerns from the IBD community were discussed by Task Force members who collectively determined suitable experts to participate in upcoming webinars as panelists ([Figure 2](#)). An illustrative example comes from the concerns expressed by many individuals regarding infusion clinics very early on in the pandemic: Were they safe, and should those scheduled for infusions keep their appointments? The Task Force gathered a panel of representatives from infusion clinics across the country to share how they were working together to ensure everyone's safety through measures that include: Physical distancing (the removal of some infusion chairs to allow for physical distancing during treatment), sanitation, and pre-screening.

The resulting [webinars](#) were well-received and encouraged the IBD community to express further concerns and topics of importance, including: Mental health; children, pregnancy; risk factors of specific medications; and what to do as businesses, the economy, and schools reopened.

The format of every webinar included an introduction by Crohn's and Colitis Canada; an update on the **epidemiology** of COVID-19 by SMAC Chair, Dr. Gilaad Kaplan; an update of the Task Force recommendations and review of any changes to the website by SMAC Chair-Elect, Dr. Eric Benchimol; followed by the topic segment, usually a guest presentation on the topic and a panel discussion with experts. After each webinar, pertinent discussion was selected to be spliced from the recording and produce two-to-five-minute segments and posted online.

The epidemiologic update included weekly presentations using data from [Johns Hopkins University](#) to illustrate the global **epidemiology** of COVID-19,²⁰ data from the [Public Health Agency of Canada](#) that illustrated the details (including health outcomes) of confirmed Canadian cases of COVID-19,⁹ and an update from the [SECURE-IBD registry](#) that illustrated IBD-specific cases of COVID-19.^{14, 15, 18} The **epidemiology** update was usually followed with one or two case studies prepared for a non-specialist audience to illustrate a key piece of evidence, such as projected possible risk of virus transmission. After the **epidemiology** and Task Force recommendations updates, webinars focused on a particular topic in an episodic nature where a panel of experts was invited to give presentations to the audience or have a virtual round-table discussion. The topics covered in each of the webinars, as well as the confirmed COVID-19 cases globally, in Canada, and in **SECURE-IBD** at the time of each webinar are presented in [Table 2](#).

A detailed [FAQ document](#) was developed from the webinar presentations that was curated into a web-based information source on the Crohn's and Colitis Canada website. The answers to the questions contained links to pertinent clips from the webinars in order to provide more detailed information and an alternate form of information delivery. The webinars were archived on Crohn's and Colitis Canada's [YouTube channel](#) and [webpage](#). View counts of the archived videos were typically four to five times those of live webinars ([Table 2](#)). For specific topics related to recommendations made on the guidance webpages, webinar videos were spliced into segments of five minutes or less and embedded next to the recommendations on the webpage; this allowed readers of the webpage to watch the related webinar segment with experts discussing the reasoning and scientific evidence behind the recommendations.

Impact

The webinars and digital Crohn's and Colitis Canada resources were promoted through social media and email notifications to the IBD community across Canada. The 15 weekly, seven monthly, and one French language webinar saw a total of 24,778 registrations with one third (33%) registering for more than one COVID-19 webinar. Links to the recorded webinars were provided on the Crohn's and Colitis Canada website 24 hours after the live event and added to the organization's [YouTube page](#). Archived webinars were also captioned in French and recent webinars offered live French translations. A further 35,814 views of the full recordings of the webinars have been tallied as of April 1, 2021. The ability to select pieces of each video to augment COVID-19 information on the [Crohn's and Colitis Canada website](#) has proven to be exceptionally impactful with a further 78,862 views of individual clips ([Table 1](#)). As of April 1, 2021, there have been 54,136 views of the webinars (live or recorded full webinars) and 78,862 views of individual webinar segments for a total of 126,187 views. Traffic on Crohn's and Colitis Canada's website increased dramatically since COVID-19 with 484,755 unique views to the COVID-19 webpages. The visitors spent between 0.10 and 28.29 minutes on the pages with a mean duration of 40.29 seconds.

	COVID-19 and IBD: What You Need to Know	Released: March 19, 2020	Hours Watched: 1,600	Registrants: 2,679	Total Views: 10,333
	New Recommendations: COVID-19 Vaccine for IBD	Released: January 21, 2021	Hours Watched: 823.3	Registrants: 3,112	Total Views: 4,114
	COVID-19 Risk Factors: Live Q&A	Released: April 2, 2020	Hours Watched: 443.8	Registrants: 2,169	Total Views: 3,470
	Infusion Clinics, Pregnancy & Newborns	Released: March 26, 2021	Hours Watched: 333.0	Registrants: 1,269	Total Views: 3,364
	Vaccines and “Home” for the Holidays	Released: December 17, 2020	Hours Watched: 423.2	Registrants: 2,672	Total Views: 2,669

Conclusion

Crohn’s and Colitis Canada was able to quickly assemble the COVID-19 and IBD Task Force at the outset of the global pandemic. The Task Force members have met and continue to meet regularly in an effort to ensure that the IBD community has the best available information to support them as they navigate a new reality with COVID-19. Direct communication from the Task Force and the expert community in Canada to people with IBD and their caregivers through a webinar series was an effective and efficient **knowledge translation** vehicle. The spring webinars ably guided the vulnerable IBD community from a population-wide lockdown in March 2020 through to an understanding of risk and appropriate measures to ensure physical and mental health during the re-opening of the country over the summer and through subsequent waves of the pandemic.

On March 18, 2021, the one-year anniversary of the webinar series, Crohn’s and Colitis Canada completed the twenty-third webinar that addressed questions by the IBD community on vaccination. As future waves of the pandemic unfold in Canada, the Task Force is prepared to guide the IBD community.



Table 1:

Recommendations developed by Crohn's and Colitis Canada COVID-19 and IBD Task Force and associated links to website page. <https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD>.

Title	Description	Web-link
General Information on COVID-19	Explanation of COVID-19, epidemiology , symptoms, and outcomes.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/What-is-COVID-19
Visiting Clinics and Testing	Discusses visiting physicians, diagnostic investigation (e.g. blood work), and infusion clinics.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Clinic-Visits-and-Testing
Diet and Nutrition	Reviews diets and nutritional needs for persons with IBD, as well as grocery shopping and restaurants during the pandemic.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Diet-and-Nutrition
Your Wellbeing	Overviews mental health and wellness, including mechanism for coping with stress and anxiety.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Mental-Health-and-Wellness
Information for Health Professionals	Section for healthcare professionals including an overview of the SECURE-IBD Registry and resources for their persons with IBD.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/For-Professionals
Guidance/Recommendations		
Travel and Physical Distancing	Discusses restrictions on travel and appropriate physical distancing during the pandemic.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Travel-and-Physical-Distancing
Risk Profile	Provides self-assessment risk profile with corresponding recommendations.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Are-you-at-Risk
Medications for IBD	Explains the risk associated with medications for IBD.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Medications
Children and Teens	Reviews the risk associated with COVID-19 for children and adolescents with IBD. Discussion of risks associated with returning to in-person school.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Children-with-IBD
Reopening of the Economy	Provides guidance for adults and seniors with IBD as the lockdown ended and the economy re-opened.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Reopening-of-the-Economy
Essential Work and Services	Discusses special considerations for persons with IBD who are involved with essential work (e.g. healthcare providers).	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Essential-Work
Tested Positive for COVID-19	Information for individuals with IBD who test positive for COVID-19.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/If-you-have-COVID-19
Pregnancy and Newborns	Overviews recommendations for persons with IBD who are pregnant or have a newborn.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Pregnancy-and-Newborns
Family Members of Persons with IBD	Explains actions that family members can take to support their household member with IBD.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Guidance/Family-Members-of-People-with-IBD
COVID-19 Vaccines	Describes Crohn's and Colitis Canada recommendation regarding vaccination for persons with IBD for Health Canada approved COVID-19 vaccines.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Vaccines
Frequently Asked Questions	Summary of frequently asked questions based on surveys and feedback from the IBD community during the pandemic.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Get-Answers
Webinars	Information on the next webinar and option for registration. Webpage houses all previously recorded webinars on COVID-19 and IBD.	https://crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/COVID-19-Webinars

Table 2:

Date-specific webinar topics with live registrants and archived video views.

Date	Topic	Registrants*	Live Views	Archived Video Views*
3/19/20	COVID-19 and IBD: What You Need to Know	2,679	1,558	8,775
3/26/20	Infusion Clinics, Pregnancy and Newborns	1,269	667	2,697
4/2/20	COVID-19 Risk Factors, Live Q&A	2,169	987	2,483
4/9/20	COVID-19 Updates, Mental Health, Diet and Nutrition	992	480	1,364
4/16/20	Modeling COVID-19 to Prepare for the Future	762	342	795
4/23/20	Monitoring COVID-19 in persons with IBD (SECURE IBD registry)	843	409	1,210
4/30/20	Telemedicine in the Pandemic	710	346	515
5/7/20	Families and Children with IBD	751	369	764
5/14/20	COVID-19 Risk Factors, Reopening of School and the Economy	557	293	678
5/21/20	COVID-19 Updates, Q&A with IBD Nurses	551	275	540
5/28/20	Mental Health and Wellness	439	204	429
6/4/20	Washroom Access and Reopening of Businesses	382	174	433
6/11/20	IBD Clinic of the Future	420	174	367
6/18/20	IBD Medications and COVID-19 Risk	500	220	2,347
6/25/20	Separating COVID-19 Myths from the Facts	524	195	1,690
9/10/20	Returning to school for families with IBD	598	251	802
10/8/20	Vaccinations and IBD	1542	541	1,867
11/19/20	SECURE-IBD Registry	710	253	641
12/07/2020	Les MII et la COVID-19 : Ce que l'on a appris et les questions qui restent	573	315	606
12/17/20	Vaccines and "Home" for the Holidays	2672	1,058	1,611
01/21/21	New Recommendations: COVID-19 Vaccine for IBD	3,112	1,360	3,054
02/18/21	COVID-19 Updates and Hitting the Pandemic Wall	968	471	926
03/18/21	A Year in Review and Vaccine Updates	1,209	604	1,220

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EPIDEMIOLOGY:
THE TRENDS OF
DISEASE OVER TIME

Epidemiology: The Trends of Disease over Time

Summary

At the beginning of the COVID-19 pandemic, there were many unknowns: How is the virus transmitted, what are appropriate intervention strategies, and does being immunocompromised due to inflammatory bowel disease (IBD) or medications put a person at increased risk for severe COVID-19. Imposing and relaxing of public health restrictions at different times and in different regions in Canada led to different epidemiologies of the virus in different provinces and territories. In order to understand the waxing and waning of waves of the COVID-19 pandemic, it is necessary to understand the effective reproductive number (R_t) and the countervailing forces that exert upward or downward pressure on the spread of the virus at a given point in time. As many regions in Canada deal with subsequent waves, the primary forces affecting the R_t of SARS-CoV-2 are variants of concern and the increasing vaccinations of Canadians leading to increased population-level immunity. Fortunately for the IBD population, current research suggests that those with IBD are not at increased risk of contracting COVID-19, nor of having a more severe disease course when compared to the general population.

Key Points

1. The **transmissibility** (R_t) of **SARS-CoV-2** is affected by the basic properties of the virus, modified by public health measures and uptake of vaccination, which can be measured over time.
2. There is no significant increase in risk for contracting COVID-19 or having severe COVID-19 for people with IBD compared to the general population.
3. The major risk factors for severe COVID-19 among people with IBD continue to be advanced age or high dose (>20 mg/day) **corticosteroid** usage.

Introduction

In December of 2019, China's Hubei province diagnosed dozens of pneumonias from an unknown cause; these cases of Severe Acute Respiratory Syndrome (SARS) were identified as a novel coronavirus (CoV) named **SARS-CoV-2**.¹ By January 20, 2020, **SARS-CoV-2** was found outside of China, in Thailand, Japan, and South Korea.² As of January 23, 2020, a large-scale public health lockdown of Wuhan City (a city of over 11 million people) was instituted to quarantine the epidemic. On February 11, 2020, the World Health Organization (WHO) named the illness caused by **SARS-CoV-2** infection, COVID-19: COrona Virus Disease-2019.¹ Then, on March 11, 2020, the WHO declared COVID-19 a global pandemic.³ A week later, China reported no new domestic cases for the first time since the outbreak began—the end of China's first wave marked the beginning of the first wave in countries throughout the world.¹ Since March 2020, you have repeatedly heard the phrase “bend the curve.” But what does bending the curve actually mean, what factors influence that curve, and why has doing this mattered so much? In this chapter, we explain a fundamental concept of disease **epidemiology**, R_0 (pronounced R-naught), and provide examples with real-world COVID-19 data over the last year to show the effectiveness of the public health guidance.

Epidemiologic Determinates of a Pandemic: R_0

R_0 stands for the basic Reproductive Number; essentially, how fast a virus can spread through a susceptible population. The R_0 of a virus is the average number of people who are infected by a primary source: For example, if a virus has an R_0 of 2, that means that each person who is infected will infect two other people (on average) when no measures are taken to curb the spread of disease. While this may seem unproblematic, think about what happens over time: Person 1 infects two people; each of those two people infect two people (now four active cases); each of those four people infect two people (now eight active cases); each of those eight people infect two people (now 16 active cases); each of those 16 people infect two people... Any R_0 greater than 1, the disease will exponentially spread, at $R_0=1$, the disease is stable in a population (each person only infecting one other person on average), and any R_0 less than 1, the disease will decline.⁴ Without any measures to control the spread of **SARS-CoV-2**, its R_0 is 5.7, more than four times as infectious as seasonal influenza (which is roughly 1.3).⁵ Some of the viral features that cause **SARS-CoV-2** to be so infectious include: The mode of transmission (droplets and airborne); incubation period prior to symptom onset (~5 days); asymptomatic or mild symptoms in the majority of those infected; and the novelty of the virus, meaning that no one had any **antibodies** to fight off infection at the beginning of the pandemic—in other words, the entire population was susceptible.

Additionally, the recent emergence of more infectious variants of concern have further increased the **transmissibility** of SARS-CoV-2.²

SARS-CoV-2 causes severe disease in a subset of individuals, particularly in those of advanced age or with multiple pre-existing health conditions (e.g. hypertension or a chronic inflammatory disease such as diabetes or inflammatory bowel disease [IBD]). At the beginning of the pandemic, prior to advances in treatments (e.g. use of dexamethasone and remdesivir), the **case-fatality** (the number of individuals who died relative to the number diagnosed with COVID-19) was 2–3%, which was more than 20-fold higher than that of seasonal influenza (0.1%).⁶ During the first wave of the pandemic, in the spring of 2020, the net effect of severe COVID-19 (hospitalization, ICU admission or death) led to overwhelmed healthcare systems in the U.S. (e.g. New York City) and Italy (e.g. Milan).⁷ By April 2020, daily deaths from COVID-19 in the U.S. surpassed any other cause, including cancer, cardiovascular disease, and motor vehicle accidents. Moreover, statistical models predicted catastrophic numbers of cases, hospitalizations, ICU admissions, and deaths from **SARS-CoV-2** if the virus were allowed to run rampant throughout society without any intervention.⁸

As mentioned above, R_0 is the basic reproductive number when no measures are taken to prevent the spread of disease. Over time, the effective reproductive number (R_t) can change according to the actual spread of disease at a given time, affected by public health measures and **antibodies** due to previous infections or vaccines (limiting the amount of the population that is susceptible to infection). Due to the high rate of severe disease (i.e. ICU admission or death), governments across the world instituted public health measures to drive R_t down. In order to bring R_t below 1, at which point

infections in the population decrease, public health agencies recommended drastic interventions, including: Stopping travel between countries; increased hygiene (such as handwashing protocols); physical distancing beyond two metres; personal protective equipment for healthcare professionals; wearing masks by the general population; working from home for non-essential occupations; closure of schools and transition to online learning; limits to in-person gatherings; and the closure of non-essential businesses such as entertainment, fitness, and restaurants. At the peak of the first wave of the pandemic, the majority of the population lived under these conditions, and adherence to public health recommendations on limiting interpersonal contact and non-essential travel was high. The result of these early efforts was an initial rapid decline in R_t by preventing transmission between people and leading to the end of the first wave by the summer of 2020 ([Figure 4](#)).

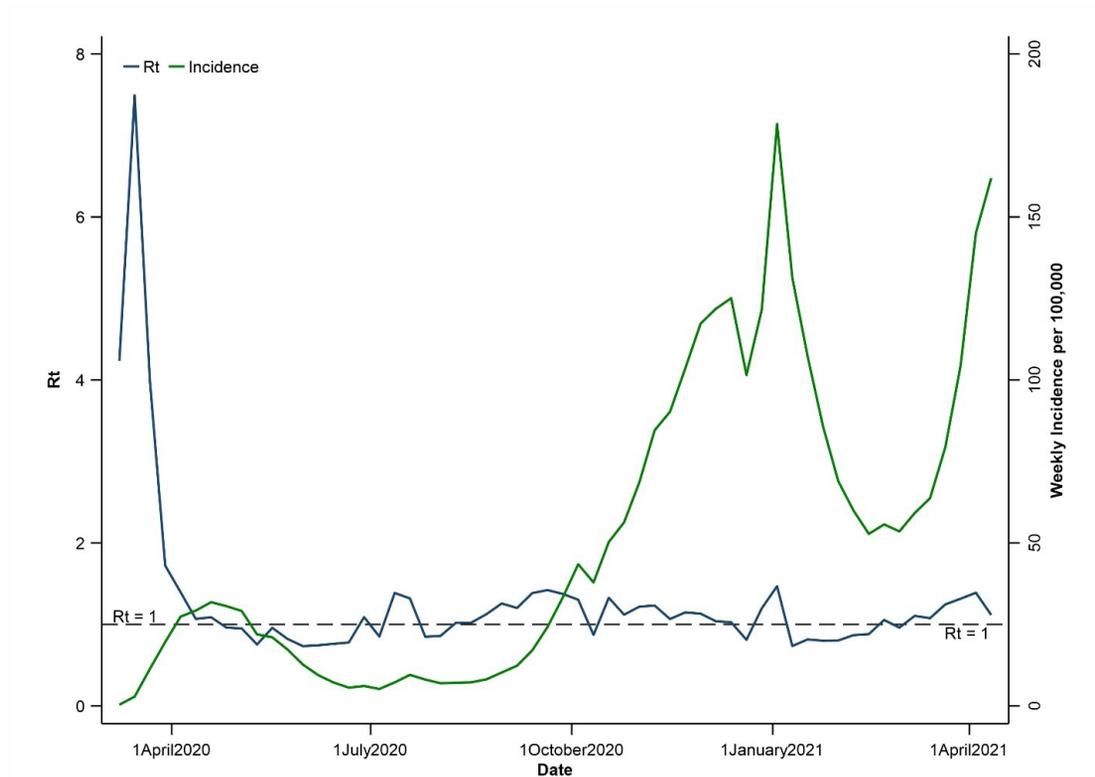


Figure 4: R_t of COVID-19 in Canada (blue) and weekly incidence of new cases per 100,000 total population (green). R_t is the effective reproduction number and represents the rate of transmission of the virus at a given point in time.⁴ R_t was calculated based on a weekly time interval, considering the doubling time and exponential growth of COVID-19 in Canada. This figure demonstrates how minor fluctuations in R_t can lead to exponential growth (or decline) in weekly incidence of cases and gives credence to the need to drive R_t below 1 to manage the pandemic. As seen in the most recent data, with R_t decreasing but still above 1, the rate of new cases can be slowed, but R_t must fall below 1 before the number of weekly cases begins to decline. Weekly case counts for both incidence and R_t calculated from Government of Canada, April 20, 2021 (<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html>).

As governments relaxed restrictions at low points of infection rates, increased contact between individuals allowed SARS-CoV-2 to re-emerge within society, leading to an upswing in R_t . Rising infections in parallel to easing restrictions is a product of low antibody rates in the general population as statistical models projected that over two thirds of Canadians required natural immunity (i.e. herd immunity) to keep the R_t below 1 without public health interventions. By the end of 2020, two opposing factors would pull against the R_t of SARS-CoV-2: vaccines and variants of concern.⁹

The spring of 2021 saw the beginning of a third wave of the pandemic throughout much of Canada. Driving new cases in the third wave are variants of

concern—mutations of SARS-CoV-2 that increase the transmissibility of the virus. These variants are easier to acquire and, in turn, raise the R_t . Counterbalancing the pressure of new cases is: i. the escalating vaccination of Canadians from those on the frontlines to those who are most vulnerable (i.e. seniors and people with certain comorbidities like IBD) and ii. ongoing public health measures that continue to try to prevent the number of cases from overwhelming our healthcare systems. The tug-of-war between variants and vaccines, as well as the actions of the public to prevent transmission, will define the height of the subsequent waves of the COVID-19 pandemic in Canada and, ultimately, the waning of SARS-CoV-2 from the world.

Viral Factors

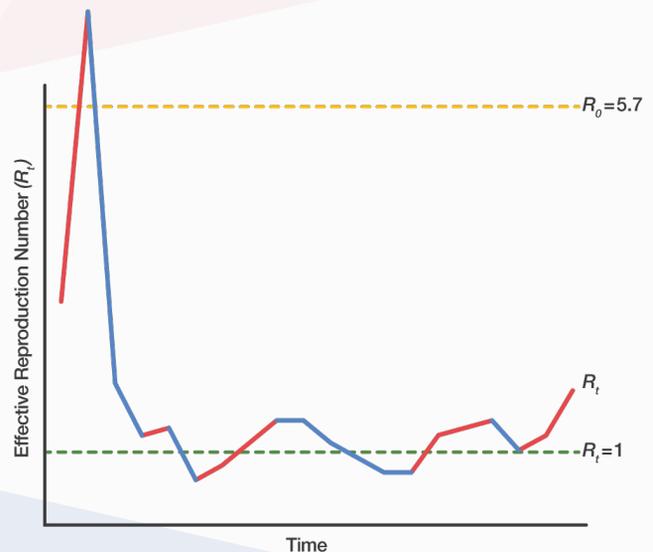
(Upward force on R_t)

- Incubation Period: The length of time between infection and symptoms
- Asymptomatic spread: Individuals who are asymptomatic can still spread the virus
- Novel Virus: No one previously had antibodies to this virus; the entire population is at risk of infection
- Doubling time: The time it takes for the number of infections to double/re-double
- Variants: Novel mutations of the virus that can change the above factors

Public Health Measures

(Downward force on R_t)

- Reducing the risk of transmission
 - Masking
 - Hand Hygiene
 - Physical Distancing
 - Work from Home
 - Contact Tracing/Isolation
 - Vaccines



Epidemiology of COVID-19 in Canada

The global **epidemiology** of COVID-19 is comprehensively maintained by the Center for Systems and Engineering at Johns Hopkins University's [interactive online dashboard](#).¹⁰ On March 19, 2020, over 230,000 individuals were diagnosed with COVID-19 with 9,300 deaths reported. In just over one year, as of April 29, 2021, these numbers have ballooned past 130 million global cases and over 2.8 million deaths. While **SARS-CoV-2** reached virtually every populated region on Earth, the impact of COVID-19 varied by geography.

On January 25, 2020, the first case of COVID-19 was confirmed in Canada, an individual who traveled in Wuhan, China. During the first two months of 2020, COVID-19 cases in Canada were driven largely by those returning from travel outside

the country. However, by March 2020, community spread was recorded in most provinces. The [COVID-19 Canadian Outbreak Tracker](#) provided by Esri Canada is an online interactive dashboard that reports the number of diagnosed Canadians with COVID-19 throughout the pandemic. On March 19, 2020, the database reported 846 Canadians diagnosed with COVID-19, which escalated to over 1 million cases and 23,000 deaths in the span of one year—by April 3, 2021. The per capita rates of COVID-19 in the first wave of the pandemic were highest in Quebec and Ontario, followed by the West and Nova Scotia; the rest of the Atlantic provinces, the prairie provinces, and the territories showed the lowest infection rates per capita during the first wave of the pandemic ([Figure 5](#)).

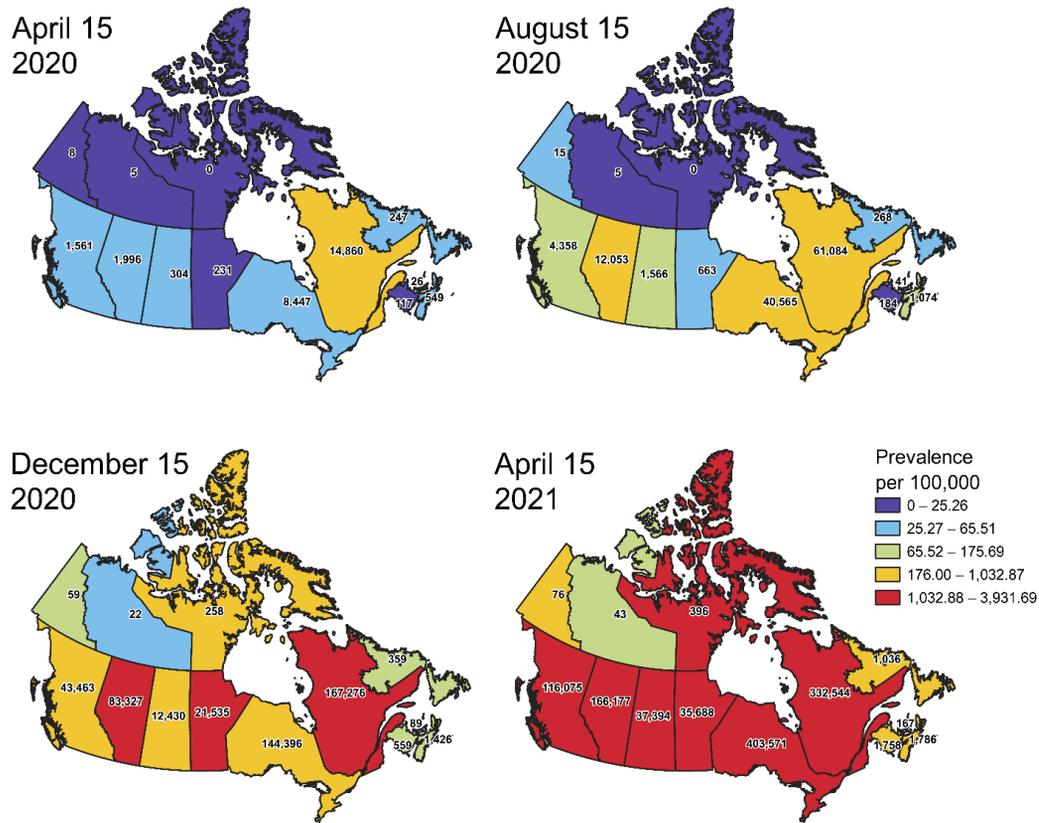


Figure 5: Prevalence (total number) of COVID-19 Cases in Canada per 100,000 population over time. Total cumulative COVID-19 cases (numbers on each province/territory) and prevalence per 100,000 population (2019 population) colour-coded by quintiles from April 15, 2020–April 15, 2021. The prevalence of COVID-19 in Canada changed in different regions throughout the pandemic due to adherence to public health measures; for example, while Nova Scotia was originally one of the hardest-hit provinces by the virus, the R_t of the virus was dramatically reduced after the first wave of the pandemic such that the Atlantic Bubble (Nova Scotia, New Brunswick, PEI, and Newfoundland & Labrador) did not experience a dramatic second wave, worse than the first. Daily cumulative totals retrieved from Government of Canada, April 19, 2021 (<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html>).

In response to the threat of SARS-CoV-2 overwhelming the ability of the Canadian healthcare systems to provide life-preserving care for the infected, every provincial government instituted policies under the guidance of their medical officers of health to reduce the opportunities for viral transmission; this included the closing of non-

essential business, closing in-person instruction at schools and universities and shifting to remote learning, and imposing restrictions on mobility and social contact between households. The sacrifices made by Canadians to lockdown during the first wave of the pandemic flattened the epidemiologic curve of COVID-19, preventing overwhelmed

healthcare systems whereby admissions to hospital and to intensive care units would have otherwise surged past capacity. The combined effect of these restrictions, as well as the high adherence of the population to these restrictions, reduced **transmissibility** of **SARS-CoV-2**, allowing time for healthcare systems to increase capacity, procure additional personal protective equipment, implement testing and contact tracing protocols, and refine our understanding of how **SARS-CoV-2** is spread and the impact of mask wearing on reducing transmission. During this time, we also continued to gather knowledge on how to best improve outcomes for persons with COVID-19, and to begin the trials that would eventually lead to the development of highly effective vaccines.

Throughout Canada, the second wave became apparent in October 2020. To our worst fears, the number of cases in the fall was considerably higher than the first wave in the spring: During the first wave of the pandemic (March to May 2020), daily cases peaked at ~1,500 diagnoses a day, whereas over 8,000 cases a day were reported across Canada in early January 2021. The second wave led to reimplementing of lockdowns that ultimately reduced the number of cases of COVID-19 in February 2021. As restrictions following the second wave were lifted, a third wave followed, with case counts up to 9,000 people diagnosed daily in April 2021, exceeding those at the peak of the second wave.

Relative to many other nations, Canada has been somewhat middle-of-the-pack in mitigating the spread of **SARS-CoV-2**: We have not enjoyed the success of countries that swiftly implemented

strict lockdown laws like New Zealand, Singapore, or South Korea; but neither have we experienced the overwhelming spikes witnessed in countries that prematurely eased restrictions like Brazil, the U.K., or the U.S. The efforts of Canadians to isolate and reduce the spread allowed us to avoid overwhelming our healthcare systems during the first wave of the pandemic (March–June 2020). However, at the time of writing (May 18, 2021), we are passing our third wave, which had higher daily case counts than the peak of our second wave in January 2021. If anything can be learned from the global **epidemiology** of this virus, it is that as vaccine roll-out continues, we will be able to drive weekly case counts down sharply as we get nearer to **herd immunity**. [Figure 6](#) provides a comparison of selected countries with Canada, including some key milestones that have influenced R_t in those regions.

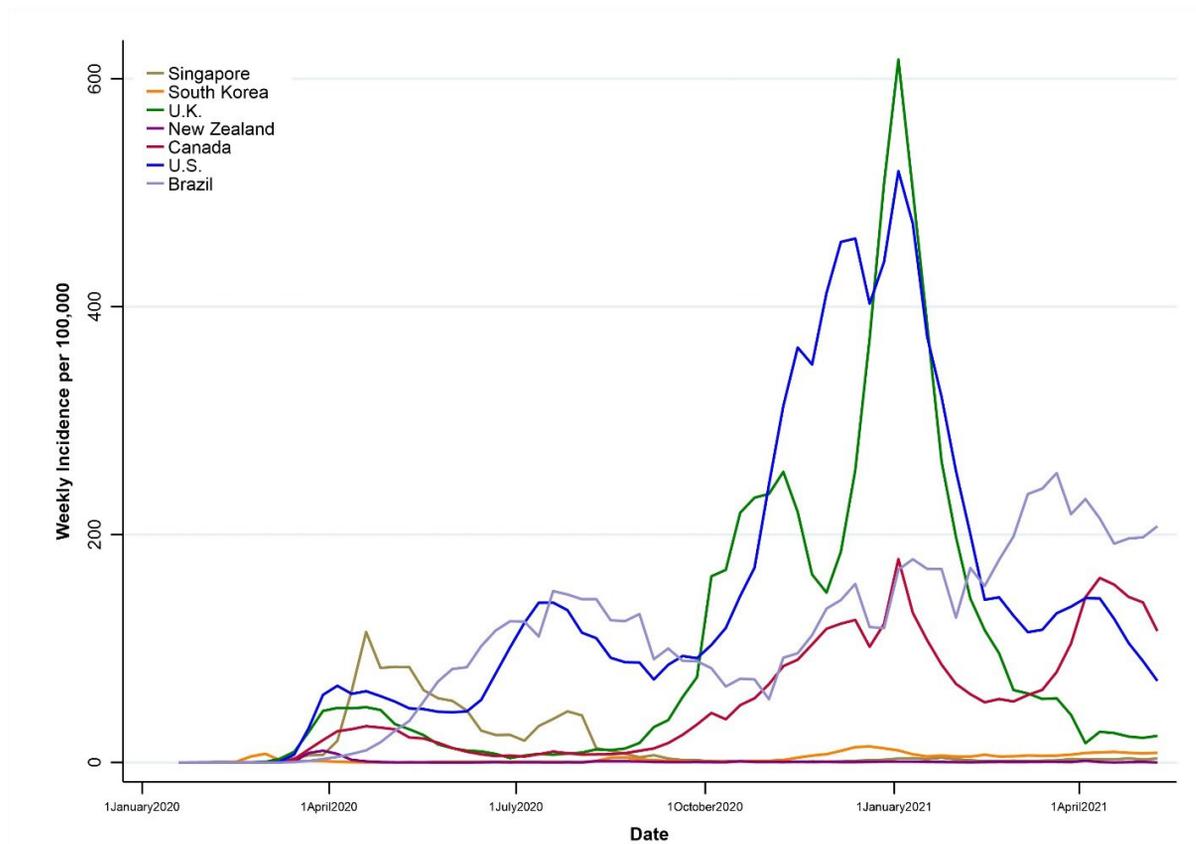


Figure 6: Weekly incident cases in select countries representative of various regions around the world. Weekly incidence per country calculated using data from Johns Hopkins University’s COVID-19 Dashboard by the Center for Systems Science and Engineering (May 18, 2021) and estimated 2020 regional populations from worldometers.info/world-population/population-by-country/ (April 9, 2021). Many nations around the world quickly reacted to the SARS-CoV-2 outbreak by instituting public-health measures in the face of paucity of information about the virus; while so-called lockdown countries like New Zealand, Singapore, and South Korea fared quite well with the virus after the first wave, other countries like Brazil, the U.K., and the Americas saw exponential growth in viral incidence. Other important correlates that can be seen in this graphs are: The rise in cases following premature easing of restrictions, such as the April 2020 easing of restrictions in Brazil; the effectiveness of strict lockdowns in response to outbreaks such as in the case of Singapore’s swift response to incidence peaks in Spring 2020; dramatic increase in weekly cases following community transmission of variants of concern, such the September 2020 identification of the B.1.1.7 variant in the U.K.; and the effectiveness of vaccines (first vaccination in the U.K.: December 8, 2020; first vaccinations in Canada and the U.S.: December 14, 2020) and national masking initiatives (April 14, 2020 in Singapore, July 10–14, 2020 in various regions of the U.K., and January 20, 2021 in the U.S.).

Epidemiology of COVID-19 in People with IBD

When the first wave of the pandemic hit Canada in the spring of 2020, individuals with IBD were alarmed by the unknown risk of COVID-19 among the immunocompromised. Important questions were raised: Are persons with IBD more susceptible to transmission of **SARS-CoV-2**? Would the severity of COVID-19 be worse in those with IBD? In the absence of any data on the risk of COVID-19 in people with IBD, many gastrointestinal societies provided recommendations to persons with IBD that aligned with public health recommendations to reduce transmission.¹¹⁻¹⁴ Early analyses in Asia and Europe suggested that these public health measures may have reduced transmission of **SARS-CoV-2** in the IBD population.^{15, 16}

The proportion of COVID-19 cases in those with IBD reported into the **SECURE-IBD** registry is highest in North America, Europe, and Oceania, consistent with the countries with the highest prevalence of IBD (total number of people living with IBD) in the world. Temporal trend analyses have shown that, across the globe, reporting IBD cases with COVID-19 into the **SECURE-IBD** registry decreased by 4.5% per week from March to September 2020, but then climbed by 10% per week to 2021. However, the rising cases of IBD with COVID-19 were largely driven by reporting from Europe and North America, which was aligned with the second wave of COVID-19 in the general population. These data suggest those with IBD were caught among the waves of cases in the general population despite public health interventions to avoid transmission in this vulnerable population.¹⁰

Most studies suggest that the risk of acquiring COVID-19 is the same across the IBD and general populations. A systematic review of 24 studies

showed proportionally fewer cases of COVID-19 infection in those with IBD (4.02 per 1,000) as compared to the general population (6.59 per 1,000); however, the relative risk difference was not statistically significant.¹⁷ A nationwide study in Denmark during the first wave of the pandemic showed those with IBD were less susceptible to being diagnosed with COVID-19 as compared to the general population,¹⁸ whereas a population-based study from Sweden showed that persons with IBD were more likely to be hospitalized for COVID-19, but the risk of more severe disease (ICU admission or death) was similar to the general population.¹⁹ Similarly, the risk of hospitalization or death after COVID-19 in those with IBD was similar to the general population in a U.S.-based study.²⁰ An Italian study reported that people with IBD were more likely to become infected with COVID-19 and more likely to require hospitalization than the general population.²¹ A key limitation of these studies is their failure to account for potential differences in adherence to public health guidelines (e.g. working from home) among the IBD population relative to the general population and if reassuring data on risk from the first wave of the pandemic influenced these behaviours during the second wave.

A systematic review of the literature on the prevalence (total cases) of COVID-19 in those with autoimmune diseases demonstrated that those with IBD had the lowest prevalence among people with immune mediated diseases.²² Serosurveillance studies (studies that examine the percentage of people who already have **antibodies** against COVID-19) in IBD populations without a known diagnosis of COVID-19 have shown a rate of 1% in Canada,²³ which was lower than in the U.S. (3%)²⁴

and the U.K. (4.3%).²⁵ Overall, the prevalence of COVID-19 in those with IBD likely corresponds to the frequency of SARS-CoV-2 in the general population; for example, in Milan (an epicenter for COVID-19) 5.4% of persons with IBD had antibodies to SARS-CoV-2 as compared to only 0.4% in regions in Italy with lower rates of infection in their general populations.²⁶ Serosurveillance studies in those with IBD should be interpreted cautiously as the CLARITY study in the U.K. demonstrated that the presence of antibodies was influenced by therapy whereby those on anti-TNF (3.4%) had a lower positivity as compared to those on vedolizumab (6.0%).²⁵ Additionally, a study from Canada showed antibodies wane over time in persons with IBD who recovered from an infection from SARS-CoV-2.²³

Conclusion

The epidemiology of SARS-CoV-2 and the disease caused by a resulting infection, COVID-19, is complicated by the waxing and waning of public health measures instituted in different regions at different times, and local compliance with those measures. Different regions around the world serve as case studies for the effectiveness of various public health measures such as masking, hand hygiene, and lockdowns. With the exception of localized outbreaks that overwhelmed some health systems early in the pandemic, general adherence to public health guidelines have bought health researchers the necessary time to discover treatments and vaccines to SARS-CoV-2 and to understand the definition of vulnerable populations to this viral threat: In the early stages of the pandemic, it was not clear if those with IBD would be at greater risk of infection or severe disease; over the course of the past year, we have learned that those with IBD at the greatest risk of severe COVID-19 are those of advanced age and those on high-dose steroids for their IBD. In the second year of this pandemic, the most pressing questions for the IBD community concern vaccines, the amount of immune response mounted by people on immunomodulating therapies for their IBD, and how long immunity can be conferred by prior infection or vaccination in this population.

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CHILDREN AND
EXPECTANT MOTHERS
WITH IBD

Children and Expectant Mothers with IBD

Summary

COVID-19 infection in children with inflammatory bowel disease (IBD) typically results in a mild infection, similar to those without IBD. Children and adolescents have less severe COVID-19 compared to older people, whether or not they have IBD. However, some IBD medications (in particular, **corticosteroids**) are associated with more severe COVID-19. During the first year of the global pandemic, more IBD care was provided with online technology, necessitated by efforts to reduce hospital and clinic visits. Additionally, non-endoscopic monitoring of inflammation has been required due to the cancellation of non-urgent procedures, resulting in longer **endoscopy** wait-times. In contrast, pregnant people (with and without IBD) who contract COVID-19 are at increased risk of complications, death, and preterm delivery, making them a priority for **SARS-CoV-2** protective measures and vaccination. Few studies have examined the effect of COVID-19 on IBD-related disease activity in pregnant people with IBD.

The pandemic has significantly affected the mental health and sense of wellbeing of children and their families, as well as pregnant people with IBD. These groups were much more likely to experience anxiety and depression compared with the same groups prior to the pandemic, even while concern has mostly abated regarding the effect of IBD medications and COVID-19 severity. Unfortunately, the availability of mental healthcare providers who specialize in people with IBD has not kept pace with the increasing demand.

Key Points

1. Similar to most children and adolescents, children with IBD have a more mild COVID-19 disease course compared to older adults and fewer children with IBD require hospitalization for COVID-19 according to the **SECURE-IBD** registry; however, those on systemic **corticosteroids** or 5-aminosalicylates are at risk of more severe COVID-19.
2. Pregnant people are at greater risk of a more severe COVID-19 disease course or birth complications. Data on the impact of COVID-19 in pregnant people with IBD are lacking.
3. Since the onset of the pandemic, worsening mental health, including anxiety and depression, have been demonstrated in children, adolescents, and pregnant people with IBD.
4. Necessitated by protective measures and health system closures, the way in which children, adolescents and pregnant people with IBD are treated within the health system has changed. More care is provided virtually, with online telehealth clinic visits and non-**endoscopy** monitoring of IBD disease activity and inflammation.
5. The Crohn's and Colitis Canada COVID-19 and IBD Task Force provided [detailed guidance](#) for children and adolescents with IBD, including instruction on protective measures, [back-to-school instructions](#), and [vaccination recommendations](#). [Guidance for pregnant people with IBD](#) followed that of the general population.

Overview of COVID-19 in Children

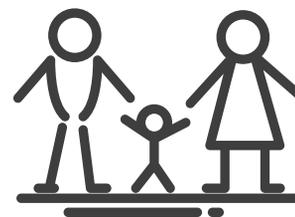
As of June 12, 2021, there have been over 1.4 million cases of COVID-19 in Canada, of which almost 20% occurred in people under 20 years old. Fewer children are severely ill with COVID-19,¹ but there are some unique characteristics of the disease in children.

Most children and adolescents with COVID-19 experience only mild symptoms such as cough, runny nose, fatigue, or intermittent fevers, with approximately 35% being asymptomatic.² This age group makes up only 1.8% of the nearly 75,000 individuals hospitalized with COVID-19 in Canada, and only 1.2% of the total nearly 14,000 intensive care unit (ICU) admissions. That said, some younger people have suffered complications from COVID-19. To date, there have only been 13 deaths in children and adolescents from COVID-19 in Canada. In the U.S., children diagnosed with a chronic condition—like IBD—were three-fold more likely to be hospitalized or admitted to an ICU compared to those without a chronic condition.³ Compared to teenagers, younger children were more likely to experience a severe COVID-19 disease course (such as ICU admission or death), as were males.³

A rare and severe complication associated with COVID-19 called **Multisystem Inflammatory Syndrome in Children (MIS-C)** was recently described;^{4, 5} it can occur up to six weeks after infection with the **SARS-CoV-2** virus, and more frequently affects younger children, and those of Black or Hispanic ethnicity.⁴ This syndrome can affect multiple organs, including the heart, kidneys, lungs, blood, skin, digestive tract, and even the brain and nervous system.⁶ A recent study reported

the rate of **MIS-C** cases to be 2.1 per 100,000 persons under 21 years of age in the U.S., with a wide geographic variation.⁷ The cause of **MIS-C** is unknown, but there are similarities with other multisystem inflammatory vasculitis syndromes triggered in children by other viral infections.⁸

While COVID-19 is typically mild in children, there are some concerns disproportionately facing children and adolescents with the disease. School closures due to public health protective measures may affect socialization, learning, and development. In addition, there is evidence that children are disproportionately affected by mental health concerns as a result of social isolation, pandemic-related anxiety, and lack of physical activity.⁹ Furthermore, children may also be affected by Long COVID Syndrome where symptoms of COVID-19 last for weeks or months, despite an initially mild disease course.^{10, 11}



Outcomes of COVID-19 in Children with IBD

The first reports of COVID-19 in children with IBD were described in a publication from the Pediatric IBD Porto Group of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition.¹² In this case series of seven children who were confirmed or highly suspected of SARS-CoV-2 infection before March 26, 2020, all had mild COVID-19 and none required hospital admission despite their use of immunosuppressive medications for their IBD. A larger study later combined pediatric cases reported before October 1, 2020 to the **SECURE-IBD** registry with cases reported to the Paediatric IBD Porto group registry.¹³ These two registries included a total of 209 children with IBD from 23 countries, 14 of whom were hospitalized, and two required mechanical ventilation. Similar to adults with IBD, predictors of hospitalization in children included use of steroids and 5-ASA medications. While steroids are known to inhibit the immune system in a significant way, 5-ASA medications are not immunosuppressive. It is more likely that use of 5-ASA medications is a marker for poor access to more effective medications and specialist care, which may also be associated with worse COVID-19 outcomes. Children who were using **anti-TNF** monotherapy (without other immune suppressing medications) were less likely to require hospitalization compared to those who were not using **anti-TNFs** (7% vs. 51%, $p < 0.001$). Children with another chronic medical condition, moderate-to-severe active IBD, or gastrointestinal symptoms were also more likely to be hospitalized. The association between 5-ASA medications and hospitalization remained after accounting for disease activity (**Odds Ratio [OR]**: 4.2; 95% **CI**: 1.3, 14.1). However, the small number of hospitalizations in these registries did

not allow for more detailed adjustment of other factors. A case series of 13 children in Texas who tested positive for SARS-CoV-2 was similarly reassuring. Six (46.2%) participants in that study were asymptomatic, and none of the remaining seven (53.8%) who developed symptoms required hospitalization.¹⁴ Finally, a report of COVID-19 cases in people with IBD from Italy compared rates in the first and second waves of the pandemic: The authors found an increased infection rate of in adults during the second wave, but not in children. In that study, no children were reported as being affected with COVID-19 in either wave.¹⁵

At the time of writing (June 12, 2021), there were 41 children less than 10 years old and 650 adolescents 10–19 years old reported to the **SECURE-IBD** registry. Only 30 (4.3%) persons less than 20 years old were hospitalized, three (0.4%) required mechanical ventilation, and none died. The existing literature is reassuring in that children with IBD generally do not have more severe COVID-19 as compared to their non-IBD peers and are likely to experience a mild disease course. Additional research is required to confirm these initial findings, identify who might be at-risk for severe COVID-19, better understand the associations between steroids and 5-ASA and severe COVID-19, clarify why **biologics** are protective, determine the risk of **MIS-C**, and better define Long COVID in the pediatric IBD population.

Health System Impact of COVID-19 in Children with IBD

While available information on COVID-19 outcomes in children with IBD is sparse, there are multiple studies that have evaluated the impact of the COVID-19 pandemic on the healthcare provided to children with IBD. Early in the pandemic, Italian centres described decreases in hospital admissions (including for newly diagnosed IBD), endoscopic re-evaluations, and transfer to adult care, but few Italians with IBD stopped **immunomodulators** or postponed **biologic** infusions due to fear or uncertainty of COVID-19 outcomes.¹⁶ Another multicentre study from the United Kingdom demonstrated similarly reduced access to **endoscopy** and routine investigations in April 2020. In fact, over half of those newly diagnosed with IBD in that month were presumed diagnoses due to lack of access to **endoscopy**.¹⁷ Conversely, a cross-sectional study from Israel surveyed families of children with IBD and found the majority did not perceive any major changes to their healthcare in the first wave of the pandemic.¹⁸ For people with IBD in Canada, non-urgent endoscopic services were severely affected by the first wave of the pandemic, with follow-up procedures to assess therapeutic response cancelled until May–June 2020. Since then, however, these semi-elective procedures have resumed and have not been subject to cancellation, even during the second and third waves when elective surgeries for adults were cancelled for specific hospitals in certain regions, often dictated by the burden of COVID-19 on intensive care units.

One significant change to health services observed during the pandemic was the shift to virtual clinics (i.e. those conducted with telehealth, video conference or by telephone). Both Italy

and the United Kingdom described more than 90% of outpatient visits during the pandemic as virtual.^{16, 17} Similar changes were made in Canada to accommodate outpatient IBD management in pediatric IBD practices. In most centres, more than 80% of outpatient visits to pediatric health centres took place virtually in 2020; but in 2021, this has begun a return to pre-pandemic normal. Families of children with chronic diseases have expressed high rates of satisfaction with virtual clinic visits,¹⁹ particularly for children who are clinically stable. Those who live in remote and rural regions have previously been used to this model of healthcare delivery (e.g. telehealth); however, these platforms often required the individual to travel to a local clinic or health centre to be seen. Newer models allow people with IBD to be seen from home. The families of children with Type 1 diabetes, for example, have indicated they would prefer virtual care be integrated in outpatient visits even when pandemic restrictions are removed.¹⁹ Importantly, though, the clinical practice of IBD is decidedly different with physical examination (e.g. overall appearance, growth parameters, abdominal exam, perianal examination), which is still an important feature of decision-making beyond bloodwork and other laboratory analysis.

There is concern that a shift to a virtual model of care may place some children with IBD at risk for negative outcomes. One drawback may be the inability to accurately assess measurements (e.g. height and weight) in children with IBD at risk for poor weight gain or stunted height. A British study demonstrated that children with IBD had a significantly decreased body mass index (BMI) in the time period after the national

lockdown (July–November 2020). This decrease was present in children with lower BMI prior to the lockdown, and was not present in normally nourished or obese children.²⁰ Another important consideration regarding virtual versus in-person care is that individual patient-physician interactions in the absence of parents usually commences in a clinic setting during the pediatric to adult transition process, and the process, including issues surrounding patient confidentiality, may be impaired by virtual visits. Adherence to follow-up laboratory investigations also may deteriorate when they are not performed on the day of an in-person clinic visit. Finally, some specialized tests (e.g. fecal calprotectin) may require the family to pay out-of-pocket at outside laboratories while many pediatric health centres cover the cost of this test for patients. However, these drawbacks are offset by patient satisfaction, reduced travel costs, and avoidance of work and school absences for medical appointments. While a hybrid model can offer benefits for individuals with IBD and their families, clearly defining parameters for clinic versus virtual visits that carefully considers both personalized disease-related factors and psychosocial factors will be needed.

Mental Health Impacts of COVID-19 in Children and Youth with IBD

There is a growing awareness that measures to control the pandemic may have an impact on mental health, especially for youths.^{21, 22} Concern is even greater for youths with chronic medical conditions, as well as their parents and families, who already face ongoing stress and challenges associated with coping with a medical condition and its treatment. Since early in the pandemic, the unintended consequence of social avoidance has been social disruption. Adolescent development depends on the creation of growing social comfort beyond the family. These connections are central to the ongoing development of a strong personal identity and sense of self on the road to autonomy, which is key to promoting mental health.²³ Moreover, there is a growing literature on the relationship between social development and brain maturation in adolescence.²⁴ It is generally accepted that, for young people, optimal learning occurs in a social, school environment, and that school is a major source of social growth. In this setting, students experience friendship, natural competition, and stimulation from one another; all of this promotes the process of learning and enriches outcomes. However, COVID-19 safety precautions have required young people to stay at home and avoid person to person socialization. Online, at-home learning is being encouraged as an important measure of safety. But, without the social contact that comes with an in-school learning environment, what can we expect when it comes to the impact on learning and other outcomes, especially when this social disruption occurs during adolescence?

In a cross-sectional survey of German youth with IBD (mainly adolescents) and their parents, Reinsh *et al.* found that parents experienced increased

fear of their children contracting COVID-19 in general, but especially in the school environment.²⁵ In fact, school was the environment most feared with respect to contracting the SARS-CoV-2 virus. At the same time, that study found that youth generally coped well with their IBD and adhered to their IBD medications as well as to suggested hygiene protocols.²⁵ These findings suggest that the increased levels of fear were more related to the pandemic than to ongoing health concerns. Further, in a cross-sectional telephone survey in Israel, Dorfman *et al.* found that youth with IBD (mainly adolescents) were very worried about COVID-19 because of their belief that they had an increased susceptibility to contracting the virus.¹⁸ This fear resulted in these people voluntarily increasing their avoidance of attending school beyond the ministry requirements of their country. Unfortunately, despite the need, mental health support may be more difficult to access during the pandemic. Major mental illness frequently first presents in adolescence, which is a particularly vulnerable time. Additionally, pediatric-onset IBD is associated with the later development of psychiatric disorders.^{26, 27} Therefore, it is especially important for young people and their families to be aware that pediatric IBD clinicians can be important sources of mental health support. These team members are not only sources of the most reliable medical information, but they are also trusted authority figures. Pediatric IBD teams should encourage both individuals with IBD and their parents to discuss their beliefs and fears associated with the pandemic. Communication of accurate information regarding IBD and COVID-19 will help to reduce pandemic-related fears; further, promoting an atmosphere in which individuals with IBD and their

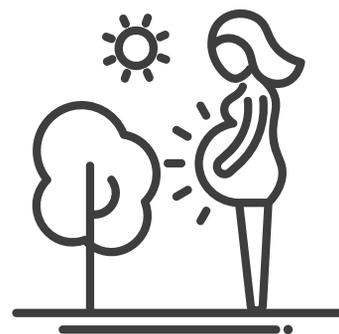
families can discuss their fears will also help to facilitate the identification of a possible psychiatric disorder, where referral to a mental health provider is critical.

For all youth, and especially for youth with IBD, socialization should be encouraged as much as possible, while being mindful of the necessary [safety guidelines](#). Individuals with IBD and parents may not realize they can turn to their IBD care providers for mental health support, and so opportunities should be provided as needed. Providing the correct information about COVID-19 as well as an overall atmosphere in which fears may be openly discussed will go a long way to supporting the mental health of youth with IBD, especially during these trying times.

COVID-19 and Pregnant People with IBD

The association of SARS-CoV-2 infection and negative outcomes of pregnancy is well-described. Early in the pandemic, an association between SARS-CoV-2 infection and preterm births by Caesarean section was described.²⁸ In addition, studies from the U.S.^{29, 30} and Sweden³¹ have demonstrated pregnant people with COVID-19 were more than four-fold more likely to be admitted to the ICU and require mechanical ventilation. A recent review of the scientific literature determined that COVID-19 in pregnancy was associated with an increased risk of preeclampsia (OR: 1.33; 95% CI: 1.03, 1.73), preterm birth (OR: 1.83; 95% CI: 1.38, 2.39), and stillbirth (OR: 2.11; 95% CI: 1.14, 3.90).³² Having severe COVID-19 (compared to mild COVID-19) was associated with increased odds of complications: preeclampsia (OR: 4.16; 95% CI: 1.55, 11.15), gestational diabetes (OR: 1.99; 95% CI: 1.09, 3.64), preterm birth (OR: 4.29; 95% CI: 2.41, 7.63) and low birth weight (OR: 1.89; 95% CI: 1.14, 3.12).³² Another systematic review examined the care provided to pregnant people and their infants internationally during the COVID-19 pandemic compared to pre-pandemic; it found that the pandemic was associated with a significantly increased risk of maternal death (OR: 1.37; 95% CI: 1.22, 1.53) and stillbirth (OR: 1.28; 95% CI: 1.07, 1.54).³³ However, in the pandemic era, there was no increased risk of preterm birth (OR: 0.81; 95% CI: 0.67, 0.97), preterm birth before 28 weeks gestation (OR: 0.84; 95% CI: 0.45, 1.53), serious bleeding after delivery (OR: 1.02; 95% CI: 0.87, 1.19), intensive care unit admission for the infant (OR: 0.90; 95% CI: 0.80, 1.01), or low birthweight (OR: 0.99; 95% CI: 0.90, 1.08). However, the pandemic era was associated with increased postnatal depression.³³

Very few studies have assessed the impact of COVID-19 on pregnant people with IBD. A registry of IBD prenatal care provided in 13 British hospitals found no confirmed cases of COVID-19 among 244 pregnant people with IBD, and a very low rate of negative pregnancy outcomes.³⁴ In that study, the majority of healthcare encounters occurred by telephone (68.2%, compared to 3% prior to the pandemic). Finally, there was no increase in the number of IBD-related questions to their advice-line, compared to before the pandemic.³⁴ Preliminary results from a Canadian survey of pregnant people with IBD also found no confirmed cases of COVID-19, although eight of 29 participants had symptoms of possible COVID-19.³⁵ Respondents with Crohn's disease (not ulcerative colitis) experienced increased symptoms of anxiety, depression and stress compared to before the pandemic.³⁵



Crohn's and Colitis Canada's COVID-19 and IBD Task Force Recommendations

In general, [our recommendations](#) for children with IBD are similar to the recommendations for adults with IBD: In addition to strict adherence to regional public health measures, caution should be exhibited by children with IBD to avoid direct indoor contact with non-family members, adhere to physical distancing and masking guidelines, and awareness of [patient risk profile recommendations](#) described [earlier](#). We recognize the importance of in-person school attendance to the developmental and psychosocial well-being of children and adolescents. We therefore recommend in-person school attendance for children with IBD unless indicated otherwise by regional public health authorities. However, children and adolescents with severe active inflammation—those using systemic **corticosteroids** and/or with moderate-severe malnutrition—should not attend school in-person due to the association of these factors with severe COVID-19. School attendance may be resumed when the youth's IBD is in remission, steroid doses are tapered below 0.5 mg/kg/day (and 20 mg/day), and malnutrition has been treated.³⁶

The COVID-19 and IBD Task Force did not make specific recommendations for pregnant people with IBD. They should follow the guidance provided to all individuals with IBD, as well as regional public health guidelines.

Recommendations regarding [vaccination against COVID-19 for all children and adolescents](#) as well as [pregnant people](#) can be found in their respective sections of the vaccine chapter.

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SENIORS WITH IBD

Seniors with IBD

Summary

The risk of hospitalization and death from COVID-19 increases with age. Those over age 80 are particularly vulnerable, with a **case-fatality rate** (the percentage of people in this group who die as a result of acquiring COVID-19) as high as 15%. Aging of the immune system can lead to impaired inflammatory responses resulting in inadequate clearing of viruses such as SARS-CoV-2. An exaggerated immune response can lead to pneumonia and acute respiratory distress syndrome. **Frailty** and **comorbidity** are both more common in the elderly and these can enhance the **morbidity** and mortality from COVID-19. Studies from Northern California and Italy suggest that seniors with IBD were more likely to acquire SARS-CoV-2 infection than youths with IBD. While the specific impact of age-related **comorbidity** is less well established among people with IBD who acquire COVID-19, data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion (**SECURE-IBD**) database reported that having multiple chronic illnesses was independently associated with developing severe COVID-19 among people with IBD. Despite having exaggerated auto-inflammatory responses, people with IBD do not appear to have an overall increased risk of developing severe COVID-19 than the general population. However, whether seniors with IBD do worse once they acquire COVID-19 compared to seniors without IBD is not known. The advent of telehealth care has posed an information technology challenge for many seniors with and without IBD. Most persons with IBD have expressed satisfaction with virtual IBD healthcare (phone or video-based visits). While the elderly may have less robust immune responses to vaccinations, learning from experiences with other vaccination programs, especially influenza, have shown that vaccinating seniors decreases both **morbidity** and mortality and in turn healthcare resources.

Key Points

1. Seniors have the highest risk of severe COVID-19 in the general population and among those with IBD.
2. Aging of the immune system and various age-related **comorbidities** both enhance the risk of contracting or dying from COVID-19.
3. Seniors with IBD do not have an increased risk of acquiring **SARS-CoV-2** and share a similar risk of complications from COVID-19 as compared to seniors without IBD.
4. Telehealth care has been an important mechanism for seniors with and without IBD to maintain contact with their healthcare providers and ensure their care unrelated to COVID-19 is minimally compromised by the pandemic.
5. While seniors may have less robust immune responses to vaccinations; experiences with other vaccination programs (especially influenza) indicate that vaccinating the elderly decreases both **morbidity** and mortality and, in turn, demand on healthcare resources.

Introduction

Seniors represent the fastest growing demographic with IBD in Canada with nearly 1 in 160 Canadians over the age of 65 affected.^{1, 2} Every day, new diagnoses of IBD are being made in seniors, and the prevalent (i.e. total) IBD population is aging. Consequently, gastroenterology clinics today are contending with an older population and having to balance care of IBD with age related **comorbidities** such as diabetes, cardiovascular disease, and dementia.³ Understandably, the COVID-19 pandemic created significant anxiety among seniors with IBD as the **morbidity** and mortality of COVID-19 disproportionately impacted those of advanced age. This section reviews the impact of COVID-19 in people with IBD living in Canada.



COVID-19 and the Elderly

The risk of hospitalization and death from COVID-19 increases with age.⁴⁻⁶ In the first half of the COVID-19 pandemic in the U.S., people over 65 years of age comprised 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths associated with COVID-19, despite comprising just 17% of the population.⁷ The extreme elderly have been particularly vulnerable, with those over age 80 having a **case-fatality rate** as high as 15%.⁸ Immune aging, **frailty**, and comorbid illnesses may all contribute towards an increased risk of adverse COVID-19-related outcomes among the elderly.

Immune aging refers to age-related changes that tip the balance of immunity in favour of pro-inflammatory pathways. The expression of angiotensin converting enzyme 2 (**ACE2**), which converts angiotensin II to angiotensin, decreases with age and with cardiovascular disease (**CVD**).⁹⁻¹¹ Angiotensin II has pro-inflammatory properties that may mediate acute lung injury through vasoconstriction and increased vascular permeability. **ACE2** is expressed in the lung, heart, kidney, blood vessels, brain, intestine, and in fat tissue. As **ACE2** is also the receptor for the **SARS-CoV-2 spike protein**,¹² reduced **ACE2** expression in these organs could lead to exaggerated inflammatory responses in the elderly in response to **SARS-CoV-2** infection, especially in those with **CVD**.

Aging is also characterized by chronic, low-grade inflammation with a relative increase in the production of pro-inflammatory **cytokines**, such as **IL-6** and **TNF- α** .^{13, 14} Severe cases of COVID-19, including people requiring intensive care admission, showed higher levels of **TNF- α** , among

other proinflammatory **cytokines** like interleukin-6 (**IL-6**).^{15, 16} Aging may further be associated with reduced levels of type I **interferons** (i.e. interferon α and β); these are important for lowering the susceptibility of cells neighboring virus-infected cells from viral entry and replication as well as for activating **natural killer cells and Th1 - lymphocytes**, which amplify the anti-viral response.¹⁷⁻¹⁹ Together, these pro-inflammatory changes might contribute to the development of acute respiratory distress syndrome and multi-organ failure in the elderly.²⁰

Frailty, as reflected by reduced physiologic reserve due to **comorbidities**, bone and muscle **atrophy**, decreased physical activity, and reduced cognition, is more prominent in seniors. Greater **frailty** is associated with increased mortality and **morbidity**, particularly in the setting of systemic infection.²¹⁻²⁴ **Frailty** has also been correlated with higher levels of **IL-6**, **TNF- α** and **CRP**, suggesting an association with a pro-inflammatory state.^{25, 26} These **frailty** factors may place elderly persons at further risk of severe outcomes with COVID-19 infection.

Pre-existing **CVD**, chronic lung disease, hypertension, diabetes, and obesity, which are observed more often in seniors, have all been associated with more severe COVID-19.^{8, 27-29} While the relationships between these conditions and severe COVID-19 are not well understood, it stands to reason that they may predispose to impaired adaptive immunity, increase in pro-inflammatory **cytokines**, and poorer vascular and respiratory reserve to combat infection; leading to greater viral replication, maladaptive immune responses, overwhelming inflammation, and multi-organ failure. Furthermore, in the context of

greater **atherosclerotic disease**, severe COVID-19 infection may increase the risk of cardiac and neurologic complications, such as stroke and myocardial infarction.³⁰⁻³⁴ Additionally, COVID-19 is associated with an increase in arterial and venous thrombotic complications, which may be even more pronounced in the elderly due to underlying **atherosclerotic disease**.³⁵⁻³⁷

COVID-19 and Seniors with IBD

A growing proportion of people with IBD are elderly, and this already vulnerable group may shoulder the brunt of the risk from COVID-19. Despite physical isolation, seniors with IBD seemed to have managed relatively well with respect to mental health compared to younger persons with IBD. The brave new realm of virtual medicine that evolved during the COVID-19 pandemic has also introduced new challenges for the elderly as well as opportunities.

As in the general population, the risk of severe COVID-19 and disease-related mortality is increased in seniors with IBD.³⁸ Certain chronic diseases also increase the risk of COVID-19 severity. Reassuringly, a Swedish population-based study showed that IBD diagnosis among those age ≥ 60 years neither increased the risk of hospitalization with COVID-19 nor COVID-19 severity compared with the general population.³⁹ While the specific impact of age-related **comorbidity** is less well established among people with IBD who acquire COVID-19, data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion (**SECURE-IBD**) registry suggests that having two or more chronic illnesses was independently associated with developing severe COVID-19 among people with IBD (e.g. **CVD**, diabetes, lung disease, hypertension, cancer, history of stroke, chronic kidney disease, chronic liver disease, other).³⁸ Studies from Italy and the Netherlands have similarly shown that **comorbidity** burden is an independent predictor of adverse COVID-19 outcomes among people with IBD.^{40, 41} Notably, despite having exaggerated auto-inflammatory responses, persons with IBD do not appear to have an overall increased risk of developing severe COVID-19 than the general

population.^{38, 42-44} However, a study from Northern California did suggest that persons with IBD older than 66 years were more likely to acquire **SARS-CoV-2** infection than younger persons with IBD.⁴⁵ Another Italian study also showed that elderly persons with IBD (≥ 65 years) had a nearly six-fold higher risk of acquiring COVID-19 related pneumonia compared to non-elderly persons with IBD.⁴⁰ Seniors with IBD, in general, are less likely to be on immunosuppressants, though **corticosteroid** use is similar.⁴⁶ Data from the SECURE-IBD registry suggest that while use of **corticosteroids** and thiopurines did increase the risk of severe COVID-19, use of **biologics**, especially **anti-TNF** agents, may be protective.⁴⁷ Overall, IBD diagnosis does not appear to increase the risk of **SARS-CoV-2** infection or severe COVID-19 in the elderly population by itself.

The COVID-19 pandemic has also had a substantial impact on the mental health of people with IBD in general, with the majority citing negative impact on mood, anxiety, and sleep. Interestingly, in a survey from the U.K., individuals with IBD aged over 55 years were more likely to experience a positive psychosocial impact.⁴⁸ In another Australian survey of people with IBD, younger age was actually associated with greater prevalence of depression and anxiety.⁴⁹ Thus, despite social isolation, elderly persons with IBD seemed to have coped better relative to their younger counterparts.

Beyond the immediate risk posed by COVID-19 to seniors with IBD, another challenge has been accessing continued medical care during lockdowns and business occupancy limits. Throughout the course of the COVID-19

pandemic, IBD health services have transitioned to virtual care throughout most of Canada. Most persons with IBD have expressed satisfaction with virtual IBD healthcare (phone or video-based visits).^{50, 51} For older persons with IBD, adapting to new technology may have posed a substantial challenge. However, flexibility to utilize phone visits and a variety of public, video-based platforms (e.g. Facetime, Skype, Zoom) has made this transition easier. Many individuals with IBD and physicians have expressed a desire to continue **telemedicine** beyond the pandemic, and this may benefit the elderly with IBD who may already have difficulty getting around.

A discussion of COVID-19 vaccines for senior persons with IBD is provided in the [special populations section](#) of the Vaccine chapter.

Conclusions

The COVID-19 pandemic has disproportionately impacted the senior population. Those with IBD who are elderly may be at increased risk of acquiring **SARS-CoV-2** infection and, like the general population, have similarly higher risk of more severe disease and mortality. Despite these risks, seniors with IBD seemed to have fared no worse—if not better—than their younger IBD counterparts from a mental health perspective. Most have adapted reasonably well to virtual care, and there is an opportunity to continue some aspects of these transformative models of healthcare delivery to address the specific needs of this population post pandemic.

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CLINICAL RISK FACTORS AND IBD MEDICATIONS

Clinical Risk Factors and IBD Medications

Summary

IBD is a disease that results from dysregulation of the immune system and frequently requires medications that can affect the immune response to infections; therefore, it was imperative to quickly understand the risk of COVID-19 infection on persons living with IBD and how that risk may be impacted by commonly used IBD medications. The IBD research community in Canada and beyond quickly established collaborative efforts to better understand the specific risk posed by COVID-19 on persons with IBD. We learned that IBD itself is not a risk factor for death or serious complications of COVID-19, and that most commonly used drug classes (with the notable exception of **corticosteroids**) do not increase the risk of COVID-19 related adverse outcomes. The risk factors for serious complications and death from COVID-19 appear to be similar to those in the wider population; those being advanced age, having pre-existing heart or lung disease, obesity, and smoking.

We recommend that persons with IBD do not alter their course of therapy to avoid complications of COVID-19, though the use of **corticosteroids** should be avoided if possible. Persons with IBD should follow the same public health recommendations as the general population to reduce their personal risk of acquiring COVID-19.

Key Points

1. Most people with IBD are not at increased risk of severe complications or death from COVID-19.
2. No **biologic** medication has been shown to increase the risk of severe complications or death from COVID-19.
3. High dose **corticosteroid** use may increase the risk of severe COVID-19 and should be avoided unless absolutely necessary.
4. Persons with IBD should stay on therapy to maintain remission as discontinuation of treatment due to fear of COVID-19 may lead to a flare, which may lead to a flare requiring **corticosteroids**, which elevates the risk of worse outcomes from COVID-19.

Introduction

At the outset of the pandemic, it was paramount to identify factors associated with an increased risk of contracting SARS-CoV-2 and, more importantly, which factors were associated with poor outcomes such as the need for hospitalization, intensive care unit (ICU) admission, mechanical ventilation, or death. This concern was felt strongly by people living with chronic immune-mediated diseases, like inflammatory bowel disease (IBD), who not only suffer from immune dysfunction but are often on therapies that may suppress their immune system.¹ It was unknown if persons with IBD would be more susceptible to infection and, if infected, at increased risk of poor outcomes.

Persons with IBD are more likely to suffer from infectious diseases than the general population.² Prior to the emergence of COVID-19, several factors had already been identified that were associated with an increased risk of infections in people with IBD, including underlying disease activity (active inflammation present when IBD is not in remission), malnutrition, older age, and certain therapies used to treat IBD. Many of these medications, in particular corticosteroids, thiopurines, and anti-TNF biologics have been associated with an increased risk of serious and opportunistic infections.³⁻⁷ Hence, there was concern that these may also be risk factors for contracting SARS-CoV-2 and developing severe complications of COVID-19.

Thus, the most important questions to answer for people living with IBD were:

- o Which individuals with IBD are at increased risk of poor outcomes from COVID-19?
- o Which medications commonly used by people with IBD increase the risk of poor outcomes from COVID-19?
- o What are the steps that individuals living with IBD who are at higher risk for poor outcomes from COVID-19 can take to reduce their personal risk?

Over the past year, there has been a significant expansion in our knowledge and many key learnings, including in the field of IBD. During this time, recommendations were updated in response to updated knowledge, especially about the behaviour of the virus and strategies that were most effective in limiting its spread and its impact. In this chapter, we summarize our understanding about the risk of serious COVID-19 faced by persons with IBD, recommendations made by the Crohn's and Colitis Canada's COVID-19 and IBD Task Force to Canadians living with IBD and their healthcare providers regarding COVID-19 risk management, and what questions still remain unanswered.

Gathering Information

The first article to specifically address how the novel coronavirus infection might impact persons with IBD reported that, among the 20,000 persons with IBD followed at China's seven largest IBD centres, none had yet been diagnosed with COVID-19;⁸ this was the same as the early reports emerging out of Italy.⁹ By this time, advanced age, chronic cardiorespiratory disease, malignancy, and obesity were being recognized as major contributors to COVID-19 related morbidity (i.e. occurrence of disease) and mortality (i.e. COVID-19 related death).¹⁰ Moreover, there did not appear to be an obvious signal of more severe outcomes in persons who either have diseases that suppress the immune system, or who are treated with immunosuppressive medications. However, as the risk of serious infection with SARS-CoV-2 had not yet been well characterized in persons with IBD, it was unclear whether persons with IBD should practice greater physical distancing and other preventative measures than persons who were otherwise healthy.

To understand the true impact of COVID-19 on the IBD community would require a large and comprehensive database of individuals with IBD who were diagnosed with COVID-19. The IBD research community was quick to mobilize to gather data on the IBD-specific risk of COVID-19 and established the Surveillance Epidemiology of Coronavirus Under Research Exclusion ([SECURE-IBD](#)) registry.¹¹ This initiative sought physicians to register confirmed cases of COVID-19 among persons with IBD from all over the world. Within one month, there were sufficient data to draw some preliminary impressions about which individual and disease-related characteristics were associated with an increased risk of severe COVID-19,

defined as infections requiring hospitalization, ICU admission and/or mechanical ventilation, or those resulting in death. As more cases were reported to this registry, our understanding of the risk of severe COVID-19 became more apparent. Despite, the uncertainty of the representativeness of the cases included in the [SECURE-IBD registry](#), these data provide further reassurance as to the mild course of COVID-19 in the vast majority of people with IBD without additional non-IBD related risk factors.¹² Studies on risk factors for severe COVID-19 in those with IBD have also been corroborated in other study populations outside of the [SECURE-IBD registry](#).¹³

As of the end of June 2021, the [SECURE-IBD database](#) has over 6,000 cases of IBD, of whom 15% were hospitalized for severe COVID-19.¹⁴ The overall rate of requiring ICU admission or dying from COVID-19 was 4%. The strongest predictors of severe COVID-19 were advanced age (12% if aged 60–69 years, 18% if aged 70–79 years, and 25% if aged over 80 years), and having multiple other chronic medical conditions (33% risk of ICU admission or death in those with three or more chronic medical conditions, including IBD). For people under the age of 50, the risk of ICU admission or dying was around 1%.¹⁵ Aside from corticosteroid use (13% risk of ICU admission or death) the risk of these more serious outcomes was low, ranging from 1% for persons using anti-TNF monotherapy, to 6% for users of azathioprine or methotrexate. These results were not adjusted for age, so, once again, it could be that the higher rates of serious disease in persons using these drugs may be related to other factors, like the age and overall non-IBD health of those persons.

A research team at the University of Calgary developed an [interactive online dashboard](#) to visualize data from the **SECURE-IBD registry** such as depicting the IBD cases with COVID-19 by time, country, age, sex, disease type, disease activity, and medication usage ([Figure 7](#)), which serves as a useful resource to the IBD community for accessing up-to-the-moment knowledge on COVID-19 risk factors for IBD.¹⁶ Additionally, the

SECURE-IBD consortium has also developed an interactive tool to allow users to [calculate their risk](#) of developing severe COVID-19, based on the demographic and disease related risk factors, which can be used to guide decisions about risk avoidance. The association between severe COVID-19 and the medications used to treat IBD are outlined below with specific recommendations in a [subsequent section](#).

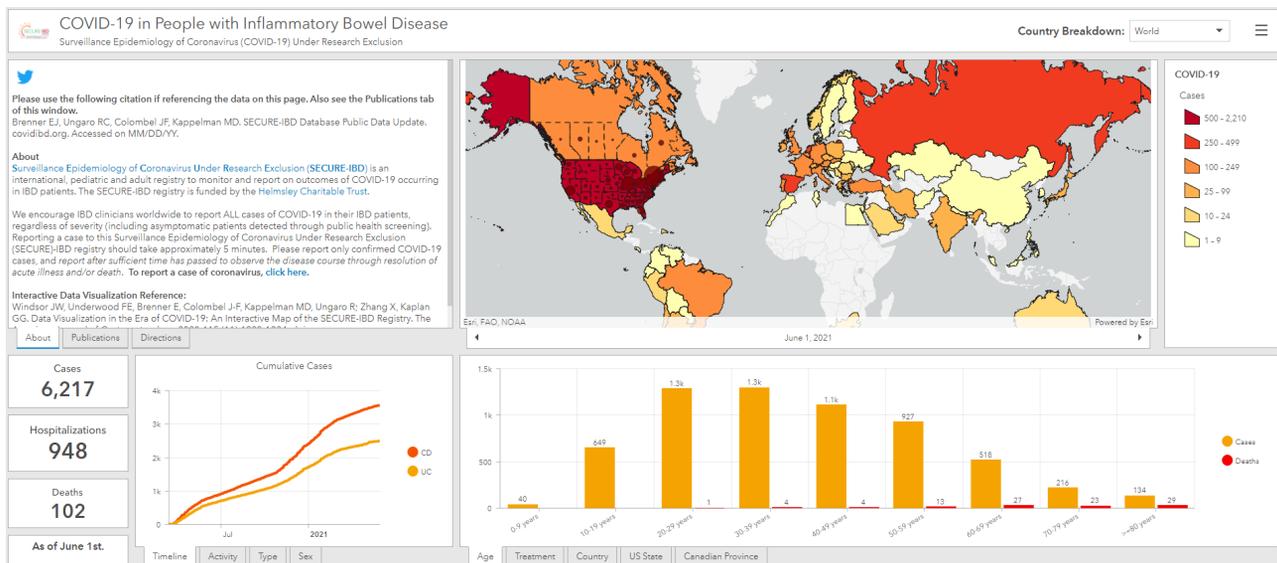


Figure 7: Interactive online dashboard and map of COVID-19 cases in those with Inflammatory Bowel Disease derived from the **SECURE-IBD** database on June 1, 2021: Link to online interactive map: <https://kaplan-secure-ibd-ucalgary.hub.arcgis.com/> Persons at the highest risk were those who were of 65 years of age or older, those with serious non-IBD related medical **comorbidities** like advanced cardiovascular and pulmonary disease, those using over 20mg of prednisone daily, those with moderate to severe inflammation or malnutrition, and those on total parenteral nutrition (TPN). Persons at moderate risk were those under the age of 65 who were using **immunomodulatory** or **biologic**. All other persons with IBD were classified as being at average risk (i.e. the same as the general population).

Medications, Disease Activity, and Other Risk Factors

Steroids

The use of **corticosteroids**, particularly at doses above 20 mg daily (or 0.5 mg per kg of body weight in children)—which may reflect the severity of active IBD—were more frequently seen among persons who developed severe COVID-19.

Anti-TNF Therapy

In the initial release of data, there was no definite signal that **Anti-TNF** use was associated with a higher risk of severe COVID-19.

5-ASA

Although the initial analysis found an association between 5-ASA use and a higher rate of adverse outcomes, this was not believed by most to be plausible given that 5-ASAs are not known to have a systemic immunosuppressive effect. In subsequent analyses on a larger number of individuals, the association between 5-ASAs and adverse events was no longer detected.

Immunomodulators

A more recent publication from **SECURE-IBD** took place in October 2020, and detailed COVID-19 infections in 1,439 persons with IBD in 47 countries. The main finding regarding medications was that the use of thiopurines, with or without **anti-TNF** therapy, was associated with a fourfold higher risk of developing severe COVID-19 outcome (hospitalization and/or death) than using **anti-TNF** therapy alone.¹⁴

New Biologics: Vedolizumab and Ustekinumab

Persons who were using **vedolizumab** were not found to be at higher risk of severe COVID-19 outcomes when compared to people using **anti-TNFs**.¹⁷ There are no definitive data on the risk associated with **ustekinumab** though this agent, like **vedolizumab**, has not been associated with an increased risk of infection in general.¹⁸ Furthermore, **ustekinumab** use has not been shown to increase the risk of COVID-19 in persons with psoriasis, another autoimmune condition where **ustekinumab** is commonly used.¹⁹

Small Molecules: Tofacitinib

By December 2020, the **SECURE-IBD** group also reported that users of **tofacitinib** were not at increased risk of severe COVID-19 when compared to users of **biologic** medications.²⁰

Disease Activity

Early publications from the **SECURE-IBD** registry described a higher risk of severe COVID-19 among individuals with severely active IBD. Further analyses of this association indicated that moderately and severely active IBD (as defined by the Physician's Global Assessment) is associated with hospitalization; severely active IBD was associated with ICU admission, mechanical ventilation, or death only in people ≤50 years of age, even after accounting for the use of steroids.¹⁵

Other Risk Factors

Throughout the publications from the **SECURE-IBD** registry, rates of severe COVID-19 were highest in older people, and those with other health conditions. This is similar to the general population.

Importantly, data from population-based, European healthcare registries has also suggested that having IBD likely did not increase the risk of COVID-19.²¹⁻²³ Therefore, independent of medication use, the risk of more serious COVID-19 in persons with IBD were due mostly from the same types of risk factors that are seen in the general population, including advanced age, chronic lung and heart disease, obesity, and smoking. At this time, there is no definite evidence that having previously undergone intestinal surgery increases the risk of developing more serious COVID-19. However, inflammation and a history of intestinal resections can increase the risk of malnutrition, and malnutrition may be a risk factor for more severe COVID-19. Therefore, the risk of more severe outcomes for people with more active IBD must still be considered.

Task Force Recommendations

Based on the initial data from **SECURE-IBD**, as well as applying what is known generally about the risk factors for infection in IBD, the Crohn's and Colitis Canada COVID-19 and IBD Task Force developed its first set of [risk-based recommendations](#) on how to limit the acquisition of **SARS-CoV-2** and the development of COVID-19. These recommendations were updated regularly as new information became available about the impact of IBD therapies on the risk of severe COVID-19. Persons with IBD were separated into three risk categories, with different levels of physical distancing and shielding recommended based on the degree of risk. These recommendations were based both on data from **SECURE-IBD** and extrapolated from factors known to increase the risk of infection-related **morbidity** (i.e. occurrence of disease) in the general population.

The Task Force also stressed the importance of individuals discussing the risks and benefits of IBD medications during the pandemic with their IBD specialists or primary care providers, particularly considering the risk of a disease flare if medications are stopped. Although newer **biologic** agents such as **vedolizumab** and **ustekinumab** are thought to have a lower risk of other infections, the risk of COVID-19 seems to be similar in those using those **biologics**, compared to **anti-TNF biologics**. Additionally, there are some data that even suggested that persons using **anti-TNF** agents may be at lower risk than non-users for developing severe COVID-19. However, it is premature to consider **anti-TNF** users to be at lower risk than other persons with IBD. The Task Force also advised physicians to avoid prescribing **corticosteroids** unless there were no other reasonable alternatives, given the higher rate of severe COVID-19 and complications seen in the **SECURE-IBD** registry, and other studies, along with the known risks posed by **corticosteroid** use for infection.

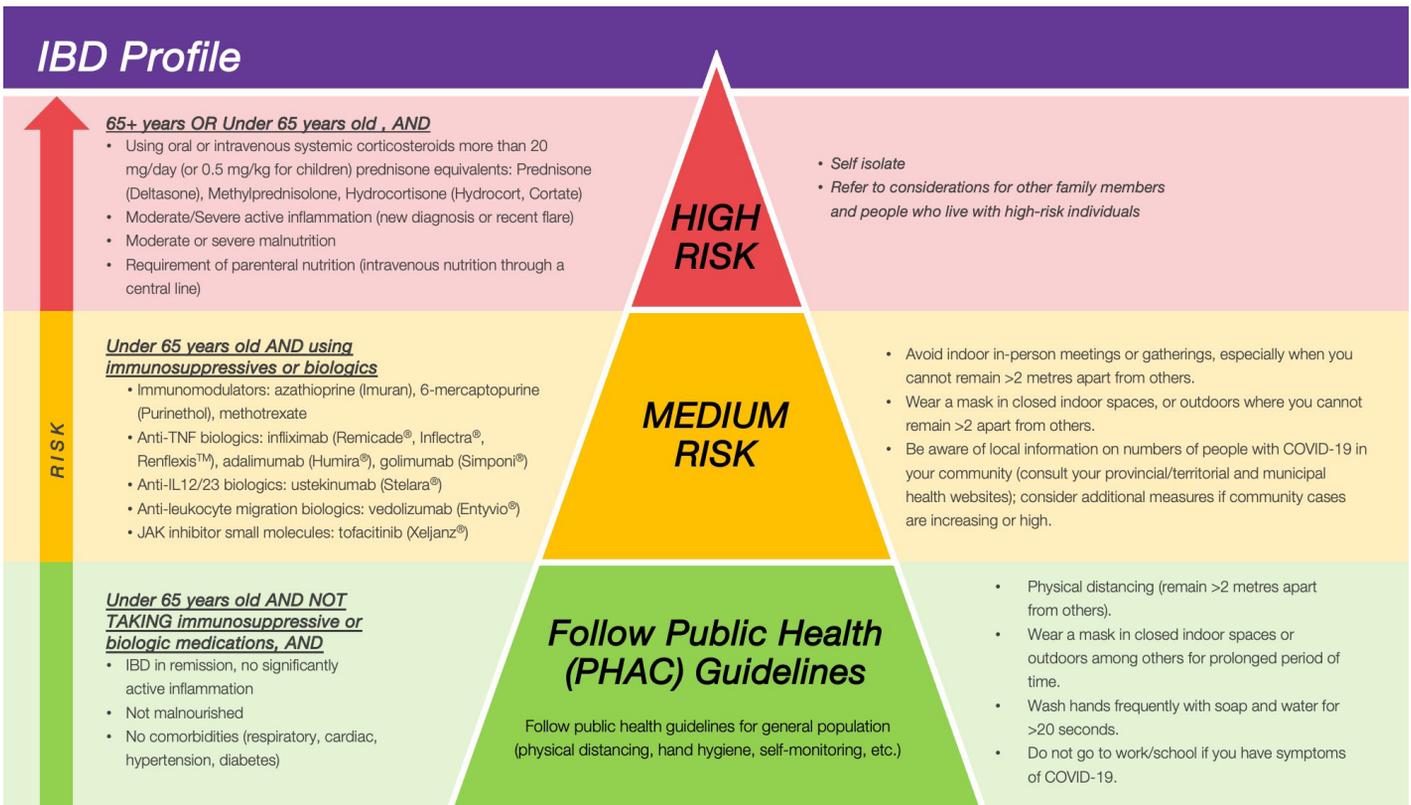
Table 3:

Risk factors for worsened COVID-19 outcomes. 0: no increased risk or no evidence of increased risk; ?: uncertain risk; +: possible increased risk or probable small increased risk (use with caution in settings where risk of COVID-19 acquisition is appreciable); ++: definite increased risk (avoid unless no alternatives in settings where risk of COVID-19 acquisition is appreciable).

Drug Class	Direction of Increased Risk
5-ASAs	0
Corticosteroids	
Over 20mg/d in Prednisone Equivalents	++
Less than 20mg/d in Prednisone Equivalents	?
Immunomodulators	
Thiopurines (Azathioprine/6-MP)	+
Methotrexate	+
Anti-TNFs	
As Monotherapy	0
In Combination with Thiopurines/Methotrexate	+
Vedolizumab	
Ustekinumab	0
Tofacitinib	0

The infographic consists of five vertical blue panels, each with a white circular icon at the top and text below. From left to right:

- Panel 1:** Icon of a boy and girl. Text: "Low risk of severe COVID-19". "At very low risk of Multisystem Inflammatory Syndrome in Children or Long-COVID". "Vaccines against COVID-19 recommended for ages 12+".
- Panel 2:** Icon of a man and woman. Text: "Low risk of severe COVID-19". "Increased risk among people with multiple chronic health conditions". "Vaccines against COVID-19 recommended for all adults".
- Panel 3:** Icon of a pregnant woman. Text: "Low risk of severe COVID-19". "Increased risk of complications (e.g., preeclampsia, preterm birth, maternal death)". "Vaccines against COVID-19 recommended for all adults". "Vaccination while pregnant may confer protection to newborns".
- Panel 4:** Icon of a doctor and patient. Text: "Risk of severe COVID-19 (hospitalisation or death) increased with each decade of life". "Greatest risk incurred by those aged 80+". "Vaccines against COVID-19 recommended for all seniors".
- Panel 5:** Icon of a person with lightning bolts. Text: "IBD at any age does not increase the risk of severe COVID-19". "Severely flaring IBD or high dose corticosteroids can increase the risk of severe COVID-19".



Overall, while the emergence of COVID-19 has increased the level of concern among persons with IBD and the people involved in their care, the overall impact of IBD on COVID-19 related adverse outcomes would appear to be fairly small. The risk of severe COVID-19 outcomes is primarily driven by non-IBD related factors, like heart and lung health, age, and being excessively over or underweight. **Corticosteroid** use appears to significantly increase the risk of severe COVID-19, and the indiscriminate use of **corticosteroids** should be discouraged. As for other medications, their impact on COVID-19 risk is likely small. The Task Force recommends that any decisions made about medications in persons with COVID-19 should be made under the close monitoring of a gastroenterologist.

It is recommended that persons with IBD continue to follow public health advice on physical distancing, mask wearing, being promptly tested for symptoms suggestive of COVID-19 or if exposed to a known case of COVID-19, and be vaccinated at the first available opportunity. It is hoped that over the coming year, with greater rates of vaccination, that the risk of acquiring COVID-19 will be significantly reduced, and with it, the concern about the impact it has on IBD.

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MENTAL HEALTH AND QUALITY OF LIFE

Mental Health and Quality of Life

Summary

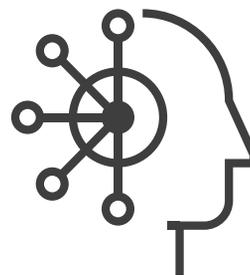
There has been a dramatic rise in mental health difficulties during the COVID-19 pandemic. While young adults have the lowest risk of hospitalization and mortality due to COVID-19, they have been identified as being at highest risk of detrimental mental health outcomes during the pandemic, along with women, those with lower socioeconomic status, and those with pre-existing mental health conditions. A crisis in mental health has emerged across the general population through the evolution of the pandemic. A national Canadian survey identified a quadrupling of those experiencing pervasive symptoms of anxiety early in the pandemic compared to pre-pandemic levels, and a doubling of those with pervasive elevated depressive symptoms.

Independent of the pandemic, persons with IBD can face multiple challenges related to their disease, which can result in a significant psychosocial burden and psychological distress. Anxiety and depression have been found to be more common in persons with IBD. Many potential factors contribute to the increased psychological distress and negative impacts on mental health of the COVID-19 pandemic on persons with IBD; these include the fears of contracting COVID-19 or infecting other people. Many believe that IBD or its treatments predispose them to an increased risk of contracting COVID-19 or a worse outcome if acquired. Concerns about access to healthcare add to mental distress.

People with IBD generally report lower quality of life (QOL). Psychologic interventions, in addition to adequate disease control, have been shown to improve health-related quality of life (HRQOL). Uncertainty is another factor associated with reduced HRQOL. Most studies suggest QOL impairment in persons with IBD during the pandemic in comparison to the pre-pandemic period. Uncertainties brought on by the pandemic are important contributors for some of the reduction in QOL.

Key Points

1. Persons with IBD are at increased risk of having mental health disorders, and the presence of mental health disorders can adversely impact the course of IBD.
2. During the COVID-19 pandemic, the general population has experienced an increase in distress and mental health disorders.
3. Several factors contribute to mental health disorders during the pandemic, including uncertainty of risks for contracting COVID-19 or experiencing severe COVID-19, uncertainty around the optimal prevention strategies, social isolation, and financial stressors from workplace changes.
4. The stresses and uncertainties are exacerbated in persons with a chronic disease, such as IBD, since there are added concerns regarding physical health issues, use of immunomodulating therapies, and access to healthcare.
5. The COVID-19 pandemic has had a significant negative impact on the quality of life of persons with IBD.



Mental Health in the General Population during the Pandemic

The **SARS-CoV-2** outbreak, has had widespread health, economic, and social impacts. Healthcare systems have been challenged to manage an onslaught of severely ill individuals; deaths due to the coronavirus disease (COVID-19) are now in the millions worldwide; and governments have imposed restrictive measures, including lockdowns and business closures to slow transmission. With uncertainty, fear, social isolation, loss, and financial insecurity also being major risk factors for deteriorating mental health,¹ it is anticipated that the mental health effects of the pandemic will last well beyond the acute medical consequences.^{2,3}

Evaluations of population-level mental health early in the pandemic signaled high levels of distress across multiple countries.⁴⁻⁷ Substance use rates, and particularly alcohol consumption, also increased.^{8,9} While many early studies used convenience samples to take a rapid mental health pulse, potentially biasing outcomes,¹⁰ subsequent studies using representative probability samples confirmed initial assessments. A national Canadian survey identified a quadrupling of those experiencing pervasive symptoms of anxiety early in the pandemic compared to pre-pandemic levels (5% compared to 20% as of April, 2020) and a doubling of those with pervasive symptoms of depression (from 4% to 10%).¹¹

Assessing population distress over time, the Canadian survey found these high levels of anxiety and depression symptoms had not subsided by December 2020,¹² and in the most recent national poll in February 2021, were at their highest levels (anxiety: 25%; depression: 17%).¹³ Population prevalence (i.e. total cases) of clinically significant distress in the U.K., measured through their national

longitudinal household survey, identified a significant escalation from 2018–19 levels of 19.4% to 30.6% in April 2020—well above any upward trends predicted from prior years' trajectories,⁸ which persisted over the next months.¹⁴ This study, which sampled the same households, found some indication of population adaptation, with levels of clinically significant distress settling back to pre-pandemic levels in the fall, 2020 measurement.¹⁵ The national longitudinal household survey for the U.S. showed a similar trend with early pandemic distress rates significantly higher than pre-pandemic, and some settling of these rates a few months into the pandemic.¹⁶ These positive adjustments were associated with changes in perception of risk of getting COVID-19 or being financially impacted.¹⁶ While evidence of population adaptation to the pandemic challenges is encouraging, with the pandemic not yet contained (as of spring 2021), the trajectory for mental health impact is unclear, and pronounced distress levels may continue to fluctuate.

In addition to general distress levels, serious outcomes escalated from pre-pandemic levels. A large U.S. epidemiologic study, based on 6 million emergency department visits that involved mental health presentations, compared visits during pandemic months in 2020 to the same period in 2019 and found visit counts were significantly higher in 2020 for suicide attempts and overdoses.¹⁷ Further, the mental health impact of the COVID-19 pandemic has not been uniform. While young adults have the lowest risk of hospitalization and death due to COVID-19, they have been identified as being at highest risk of detrimental mental health outcomes during the pandemic, along with women, those with lower socioeconomic status, and those with pre-existing

mental health conditions.^{6, 9, 14, 18-20} Even outside the context of the pandemic, these groups have elevated risk for mental health concerns; however during the pandemic, there has also been a disproportionate economic impact on these demographic groups, who tend to be overrepresented in lower wage jobs and retail and hospitality sectors, which were hard hit by pandemic restrictions.

Experience from prior severe respiratory disease outbreaks has suggested mental health concerns may be particularly prominent for persons who contracted the disease. A meta-analysis of studies that included data related to SARS (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome), and COVID-19 found high rates post-illness for post-traumatic stress disorder

(32%) as well as depression and anxiety (14%), with mental illness post-SARS persisting up to four years.²¹ An epidemiologic study in the U.S. reviewing over 62 million health records matched 62,000 COVID-19 positive cases with cases of other types of illnesses; the study found that individuals with COVID-19 had more than double the risk of being newly diagnosed with a mental health disorder (i.e. no prior history) in the weeks following the COVID-19 positive diagnosis, compared to the non-COVID illness cohorts.²² Reviewing mental health outcomes over a six month period for more than 236,000 persons with a COVID-19 positive diagnosis, they found that one in three COVID-19 positive persons had neurological or psychiatric diagnoses, with anxiety disorder (17%) being most common.²³

Other associations with increased odds of elevated Anxiety/Depression include: lower socio-economic status, being female, and pre-existing mental health conditions



Seniors' mental health has fared relatively well



General Canadian population is experiencing greater anxiety and depression

Increases in both encounters for mental distress and substance use rates (alcohol and cannabis)



Youths in Canada have experienced the highest impact to mental health



Having IBD puts an individual at increased odds of also experiencing mental health concerns

Mental Health in Persons with IBD during the Pandemic

Persons with IBD can face multiple challenges related to their disease, including the chronic nature of the disease, its incurability, unpredictability, and severity of symptoms, as well as concerns regarding disease and treatment complications; this can result in a significant psychosocial burden and psychologic distress.²⁴ Anxiety and depression have been found to be more common in persons with IBD compared to healthy controls, with rates of anxiety and depression ranging from 19–28% during remission and 34–66% during active flares.²⁵ Untreated mental health disorders have been associated with poor IBD outcomes including more severe IBD symptoms and more frequent flares,^{26, 27} poor medication adherence,²⁸ higher hospitalization rates,²⁹ and increased healthcare costs.³⁰

Many potential factors could contribute to the increased psychologic distress and negative impacts on mental health of persons with IBD related to the COVID-19 pandemic. D'Amico *et al.* sought to elicit the patients' points of view to investigate the concerns, fears, and behaviors of people with IBD during the early phase of the pandemic.³¹ An anonymous web survey was conducted and included 3,815 participants from 51 countries around the world. Most respondents feared contracting COVID-19 (3,242, 85%) or infecting other people (3,330, 87%). Just under a third of respondents believed that IBD predisposed them to an increased risk of COVID-19 (1,150, 30%) and nearly two-thirds believed that immunosuppressive drugs were associated with a higher risk of infection (2,427, 64%). Similar concerns were identified in a study from China, in which 2,277 people with IBD were surveyed.³² Respondents were worried about the risk for SARS-Cov-2 infection for themselves

and their family (58%) and more than half were concerned about the difficulty in seeing physicians (52%). This study also assessed psychosocial impacts of the pandemic and found that more than 50% of participants reported some degree of mood changes, most commonly reporting moderate-to-severe psychologic change in the middle of the outbreak in China (i.e. mid-February 2020). Most respondents (77%) did not change IBD medications during the outbreak. However, of those with a change, the main reasons were recommendations from their treating physician (30%), being unable to receive intravenous infusions (28%), and the availability of physicians or facilities (28%). Despite this, the majority of respondents reported their disease was stable (74% during the initial outbreak from January to March 2020, and 81% in the later phase in mid-April 2020).

Harris *et al.* demonstrated similar findings in a survey of 685 people with IBD in the U.K.³³ In this study, 37% of respondents reported a flare in their IBD symptoms and 87% reported their medications had remained unchanged throughout the lockdown. Over 50% of participants reported a negative or very negative impact of the pandemic on their quality of life. Anxiety or depression were the most common mental health problems seen, self-reported by 14.9% of participants, and were correlated with a greater stress score at all phases in the pandemic. A multi-nation survey of 243 individuals with Crohn's disease also found that an increase in active disease symptoms was associated with increased perceived stress.³⁴ This study used an anonymous survey to retrospectively assess symptoms of Crohn's disease in the months prior to COVID-19 (January and early February 2020) and again during the early

stages of the pandemic (March and April 2020). The Manitoba Inflammatory Bowel Disease Index was used as a measure of disease activity.³⁵ A total of 17% (40/243) of respondents reported a change from inactive to active Crohn's disease symptoms with a 25% relative increase in active symptoms between the pre-COVID-19 period compared to the COVID-19 period ($p < 0.001$). The most frequently reported reason for a change in symptoms was increased stress/and or feeling overwhelmed (50%). The relative percent increase in active symptoms was more pronounced (42%) among those reporting current stress ($p < 0.001$).

Mosli *et al.* further assessed the psychologic impact of COVID-19 on people with IBD in Saudi Arabia through a validated Arabic version of the Hospital Anxiety and Depression Scale (HADS).³⁶ Of the 1,156 persons with IBD assessed, normal, borderline, and HADS-A scores consistent with a diagnosis of anxiety were reported by 36.6%, 15.1%, and 48.4% of participants, respectively. With respect to depression, 69% of participants had normal scores, 30.1% had borderline scores, and no participants reported scores consistent with depression, which would be atypical for most other IBD cohorts. For instance, Trindade *et al.* surveyed 124 persons with IBD from Portugal.³⁷ Most participants (51.6%) presented normal (non-clinically significant) levels of depressive symptoms; 27.4% presented with mild severity, 16.10% moderate, and 4.8% severe. However, with respect to anxiety, 29.8% and 18.5% presented normal and mild anxiety levels, respectively; about half presented with moderate (37.1%) and severe (14.5%) anxiety.

Finally, Castellini *et al.* conducted a survey aimed to explore the role of participants' psychologic predispositions in dealing with the COVID-19 pandemic using the Patient Health Engagement (PHE) Scale.³⁸ This study showed that people with higher levels of PHE had significantly lower levels of the perceived risk of COVID-19 emergency and experienced lower levels of stress and higher levels of coping self-efficacy. Increased health engagement seemed to mitigate negative reactions to the COVID-19 pandemic.

The impact of the pandemic on mental health of children in general and of children with IBD is provided in the [earlier chapter](#) specific to that special population, and additional discussion on the mental health of senior persons with IBD during the pandemic can be found in the [earlier chapter](#) dedicated to that special population.

Quality of Life in Persons with IBD

Quality of life (QOL) is a broad, multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life.^{39, 40} The Centres for Disease Control has defined QOL as “an individual’s or group’s perceived physical and mental health over time.”³⁹ The concept of health related quality of life (HRQOL) and its determinants has evolved since the 1980s to encompass aspects of overall QOL that have been shown to affect either physical or mental health.^{39, 41, 42} HRQOL questions have become an important component of public health surveillance and are considered valid future indicators of unmet needs and intervention outcomes. Self-assessed health status is a more powerful indicator of mortality (i.e. death) and **morbidity** (i.e. occurrence of illness or disease) than many objective measures of health.^{43, 44}

HRQOL in Persons Living with IBD Pre-Pandemic

HRQOL is impaired at some point in every person with IBD, and many live with chronically impaired HRQOL. IBD affects young individuals at a time in their lives when they are most likely to be pursuing major employment, family building, and personal milestones of critical importance. The pursuit of such critical milestones is often impeded by the unrelenting and debilitating symptoms and the psychological distress associated with IBD.⁴⁵⁻⁴⁸ Measuring and evaluating the disability associated with IBD, and the impact of IBD on a person’s QOL, is paramount to understanding the often hidden burden of this disease for persons living with IBD and for society as a whole. On balance, data from most population-based studies suggest that persons living with IBD have significantly lower HRQOL when compared to that of the general population; this is particularly true for those with more severe disease activity,⁴⁹⁻⁵⁵ which remains the most significant predictor of physical and mental HRQOL.⁵⁶ QOL domains most impacted in adult and pediatric persons with IBD are general health, mental health, and social functioning. Youth with IBD have lower HRQOL compared with their healthy peers and higher levels of impaired school-related HRQOL than healthy or chronically ill youth.⁵⁷⁻⁶⁰ Youth-reported reductions in HRQOL have been associated with greater healthcare resource use, including IBD-related hospital admissions, emergency department visits, use of psychologic services, telephone calls to clinicians, GI clinic visits, and referral to pain management.⁶¹ Lower HRQOL has been associated with lower psychosocial functioning and school functioning among youth with IBD in comparison to both healthy comparator groups chronic illness comparator groups.⁶⁰ Several factors reduce QOL for persons living with IBD.^{24, 49-58, 62} Psychologic interventions, in addition

to adequate disease control have been shown to improve HRQOL (See [Table 4](#) for a summary of factors that influence HRQOL).⁶³⁻⁷⁴ Uncertainty is another factor associated with reduced HRQOL.⁷⁵ Health information gathering through the internet by

persons with Crohn’s disease has been associated with reduced certainty.⁷⁵ Therefore, people living with IBD require access to providers with the ability to screen for, and manage, psychological distress as part of a transdisciplinary care approach.

Table 4:
Factors that influence QOL in people living with IBD.

	Impact on QOL		Mechanism of influence on QOL
	Children	Adults	
IBD disease activity	Negative	Negative	<ul style="list-style-type: none"> • Self-esteem • Relationships • Hygiene • Security • Depressive symptoms • Social isolation • Psychologic distress
Psychologic distress	Negative	Negative	<ul style="list-style-type: none"> • Reduced energy • Impaired body image • Maladaptive coping mechanisms • Social isolation
Psychologic interventions	Positive	Positive	<ul style="list-style-type: none"> • Reduction of exacerbating factors related to increased disease-related psychologic distress
Surgery	Negative	Negative	<ul style="list-style-type: none"> • Fear of complications • Need for an ostomy • Body image • More severe form of disease
Pain	Negative	Unknown	<ul style="list-style-type: none"> • Disability • Depressive symptoms • Disease-related psychologic distress
Parental stress	Negative	Unknown	<ul style="list-style-type: none"> • Perceived difficulty of medical stressors
Effective medical therapy	Positive	Positive	<ul style="list-style-type: none"> • Induction of long-term remission
Health information gathering from internet	Negative	Negative	<ul style="list-style-type: none"> • Reduced certainty
Poor sleep quality	Negative	Negative	<ul style="list-style-type: none"> • Fatigue • Daytime dysfunction

Health Related Quality of Life for Persons Living with IBD during the Pandemic

The global community was launched into an extended and ongoing period of uncertainty with the onset of the COVID-19 pandemic. Those living with chronic, immune-mediated diseases were suspected of having the largest reductions in QOL given significant uncertainty relating to **SARS-CoV-2** infection, as well as the relative impact of various immunosuppressive therapies on COVID-19 disease course, and the social isolation and financial hardships of public health restrictions imposed to control population transmission of **SARS-CoV-2**. Exposure to rapidly changing health information from both reliable and unreliable sources, reductions in access to healthcare providers and healthcare resources, as well as changes in how IBD care was being delivered were also potential sources of uncertainty and psychologic distress.

Given the known negative effects of uncertainty and increased psychologic distress on QOL, there has been interest in better understanding how the global COVID-19 pandemic has impacted QOL in persons living with IBD. Most studies suggest impairment of QOL during the pandemic in comparison to the pre-pandemic period.^{33, 76-79} Grunert *et al.* conducted a cross-sectional survey of IBD practices in Germany in order to better understand the impact of the pandemic on daily life for adults living with IBD.⁷⁷ They observed increased fears of infection, hospitalization, and going to public spaces—including hospitals and clinics for **biologic** infusions; these concerns were heightened if they were taking immunosuppressive therapies. As a result, participants responded that they were less likely to leave home compared to their peers. Another U.K. survey was performed

with moderate and high risk IBD populations (IBD populations deemed to be at high risk from COVID-19).³³ Out of 685 respondents, the majority reported a negative impact of the pandemic on QOL as well as significant increases perceived stress. Many respondents identified remote healthcare delivery as a mechanism through which to alleviate this stress. Prospectively conducted interviews of 67 people with IBD in which patient reported outcomes were measured suggested that persons with active disease experienced significant reductions in QOL domains ($p=0.01$) and emotional domains ($p=0.04$).⁷⁹

Conclusions

IBD negatively influences HRQOL and introduces disability that can impair daily activities, thus affecting interpersonal relationships, life activities, social participation, and mental well-being. HRQOL is uniquely impacted in children and adolescents with IBD. Moreover, the entire family can suffer collectively from reduced HRQOL as parental stress is commonly experienced. The SARS-CoV-2 pandemic has been observed to further impair QOL making access to supports and health system interventions to alleviate those factors that are the key drivers of reduction in QOL critically important; however, this proved to be a challenge, even in the pre-pandemic era. These facts highlight the importance of accurate, timely, and reliable information; access to mental health supports; limitations in disruption to care and medical therapies; as well as ongoing, rapid research and patient-centered **knowledge translation** as we make advances in our understanding of COVID-19 disease course in those with IBD as well as the effectiveness and safety of COVID-19 vaccines in persons living with IBD.

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COVID-19 VACCINES:
BIOLOGY, CURRENT
EVIDENCE, &
RECOMMENDATIONS

COVID-19 Vaccines: Biology, Current Evidence, & Recommendations

Summary

The COVID-19 pandemic has ushered a globally focused vaccine development program that produced multiple successful vaccines within a year. As of the time of writing this (May 25, 2021), four **SARS-CoV-2** vaccines have now been approved for use in Canada, using two different technologies, all of which have shown excellent efficacy in reducing the rate of symptomatic infection and 100% efficacy in preventing death from COVID-19.

People with inflammatory bowel disease (IBD), like many others with immune-mediated chronic diseases, were excluded from the pivotal trials of these vaccines resulting in early hesitancy by regulatory bodies to endorse administering the vaccines to these groups. However, recent data has shown that the proportion of adverse events from the **SARS-CoV-2** vaccines among people with IBD is similar to the general population. Early data has further shown that people with IBD are capable of mounting a robust immune response to **SARS-CoV-2** vaccines, particularly following a second dose, although the response to the first dose is limited in those receiving **anti-TNF** therapy or conventional immunosuppressants (e.g. prednisone, azathioprine, 6-mercaptopurine, methotrexate).

Based on these data and evidence from previous vaccine programs among people with IBD, multiple national and international expert panels have recommended that individuals with IBD receive complete vaccination against **SARS-CoV-2** as soon as possible.

Key Points

1. Although people with IBD were excluded from the **SARS-CoV-2** vaccine trials, real-world evidence suggests that these vaccines are safe for people with IBD and elicit robust immune responses and protect against **SARS-CoV-2** infection following two doses of **mRNA** vaccine.
2. The effectiveness of the first dose of vaccine (for a two-dose vaccine) is limited (reduced **immunogenicity**) for people with IBD receiving **anti-TNF** therapy or conventional immunosuppressants (e.g. prednisone, azathioprine, 6-mercaptopurine, methotrexate).
3. National and international expert panels recommend that all people with IBD receive a **SARS-CoV-2** vaccine at the earliest opportunity, regardless of vaccine type, disease status, or medications.

Introduction

In response to the COVID-19 pandemic, international pharmaceutical companies have rapidly developed, tested, and produced highly effective vaccines against the **Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) virus**. More than 200 COVID-19 vaccine candidates are under development or in clinical trials, using both traditional (inactivated or live attenuated vaccines) and newer (recombinant protein vaccines, vectored vaccines, and RNA and DNA vaccines) technologies.^{1,2} Four vaccines have now been approved for use in Canada ([COVID-19 Vaccines: Authorized vaccines: Canada.ca](#)).

Many individuals with immune-mediated chronic diseases, including all persons with inflammatory bowel disease (IBD), were excluded from the clinical trials that ultimately led to the approval of these vaccines; thus, there was initially some uncertainty regarding efficacy and safety of these vaccines in people with IBD. This chapter reviews the immunology, mechanisms, and evidence currently available (as of writing: May 25, 2021) vaccines for COVID-19 and discusses the potential risks and benefits of people with IBD being vaccinated. It also outlines recommendations for COVID-19 vaccination in persons with IBD, and those with IBD in special populations (children and adolescents, seniors, and pregnant people).



Immunity and COVID-19:

Natural and Vaccine Immunity

Natural COVID-19 infection often results in exaggerated and dysfunctional innate and adaptive immune responses.^{3, 4} A severe complication of COVID-19 is something called a **cytokine storm**, caused by increased inflammatory response (inflammasome activation) leading to the overproduction of certain proteins (IL-1 β , IL-6, and TNF- α); this **cytokine storm** results in severe complications of the host's vascular and respiratory systems (often termed vascular and respiratory insults in medical literature).⁵ Indeed, the late-stage disease course in COVID-19 is driven primarily by host immune responses to the **SARS-CoV-2** virus.⁴ Furthermore, evidence suggests that lethal courses of COVID-19 may be due in part to faulty **T follicular helper cell differentiation** (a necessary process in the development of high affinity **antibodies**), this evidence comes from the lack of mature germinal centres and a resultant impairment in the somatic hypermutation process required for class switching to IgG;⁶ in other words, a change in the immunoglobulin necessary for producing virus-specific **antibodies** to fight off current or future infections. Conversely, some studies have found that people who recover from COVID-19 do have circulating T follicular helper memory cells, which are positively correlated with **spike protein-specific neutralizing IgG, IgM, and IgA antibodies**.⁷ While **neutralizing antibodies** will afford protection against **SARS-CoV-2**, a misguided **humoral (antibody-mediated) response** contributes to some of the immunopathology of COVID-19, including autoantibody production.⁸ These autoantibodies not only impair immune function and exacerbate COVID-19 severity but also have long-lasting potential for systemic autoimmune diseases post-infection. Improved understanding of the natural immune response is essential in developing an effective vaccine and other therapeutic strategies.

Controlling COVID-19 requires effective and safe vaccines that provide disease-attenuating immunity, including robust **T-cell and B-cell memory responses** with the development of germinal centres and high-affinity **neutralizing antibodies** against COVID-19 and any variants. As variants of concern circulate through the population, several types of vaccines may become important in achieving **herd immunity** (i.e. when 70–95% of the population is immune).⁹ Vaccine-induced protective immunity is safer and likely to be more effective than natural immunity. There is no evidence to suggest that T follicular helper cells or memory B cells responses would be blunted relative to natural infection or that vaccination would produce the plethora of maladaptive immune and autoimmune reactions seen with natural COVID-19 infection (e.g. **cytokine storm** or **Multisystem Inflammatory Syndrome in Children**). While some early research suggested immunity might be short lived after **SARS-CoV-2** infection, recent studies have shown that **humoral response** is long-lived and **antigen-specific**, including to the **spike protein**,¹⁰ providing good rationale for using the **spike protein** as a vaccine candidate—as is the case with all currently approved **SARS-CoV-2** vaccines in Canada.



Currently Approved SARS-CoV-2 Vaccines: Mechanisms, Efficacy, and Safety

As of the time of writing this (May 25, 2021), four SARS-CoV-2 vaccines have been authorized by Health Canada for use in persons aged 18 years or older; one of these (Pfizer-BioNTech) has recently received approval for use in persons aged 12 years and older ([COVID-19 Vaccines: Authorized vaccines: Canada.ca](#)): 1. Pfizer-BioNTech's mRNA vaccine (Pfizer, Inc., NY, USA; BioNTech SE, Mainz, Germany); 2. NIH-Moderna's mRNA vaccine (Moderna, Inc., Cambridge, USA); 3. AstraZeneca's adenovirus vector vaccine (AstraZeneca plc, Cambridge, England); and 4. Janssen's adenovirus

vector vaccine (Janssen Pharmaceuticals, Beerse, Belgium). Large clinical trials have demonstrated these vaccines to be highly effective and safe.¹¹⁻¹⁴ Mild side effects, such as injection site reactions (muscle pain, redness, and swelling), fatigue, malaise, headaches, joint pains, low-grade fevers, and chills were common in all trials. Serious adverse events were rare, and no deaths attributable to the vaccine were encountered in any trials. Importantly, the approved vaccines do not demonstrate the potential for virus activation or integration into the human genome.

mRNA

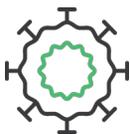
(messenger ribonucleic acid)



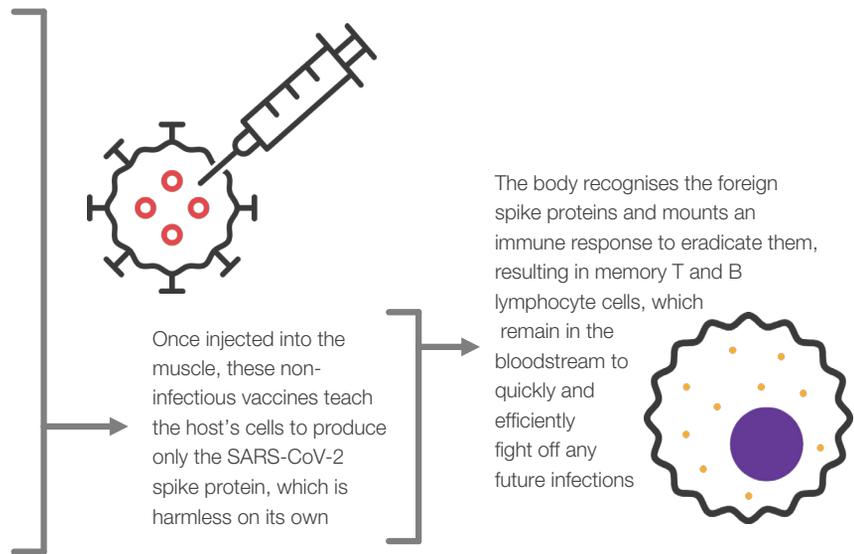
RNA containing the blueprint for the spike protein from the SARS-CoV-2 virus are contained in a lipid nanoparticle (a water-soluble fatty acid)

Adenovirus Vector

(non-replicating viral delivery)



A non-infectious virus is engineered to be harmless to humans, but to carry genetic material for the spike protein from the SARS-CoV-2 virus to host cells



mRNA vaccines (Moderna, BioNTech/Pfizer) are more than 90% effective at preventing COVID-19, and nearly 100% effective at preventing severe outcomes (hospitalization, ICU admission, or death) after two doses.

Adenovirus vector vaccines (Janssen/Johnson & Johnson, Oxford/AstraZeneca) are more than 65% effective at preventing symptomatic COVID-19, and nearly 100% effective at preventing death from COVID-19.

Messenger RNA (mRNA) Vaccines

The Pfizer-BioNTech vaccine (approved by Health Canada December 9, 2020) and the NIH-Moderna vaccine (approved by Health Canada December 23, 2020) use a **lipid nanoparticle delivery system** to transport modified **SARS-CoV-2** genetic material (**messenger ribonucleic acid (mRNA)**) encoding the virus' **spike protein** to host cells.^{11, 12} The viral **mRNA** enters host cells and uses its translational machinery to produce copies of the **spike protein**, which then embed into the host's cell membranes, prompting an adaptive immune response resulting in memory T and B lymphocytes producing **neutralizing antibodies** to the **spike protein**. These lymphocytes recognize and fight future **SARS-CoV-2** infection faster and more effectively than their precursors. Both vaccines are administered as two intramuscular injections, 21 days (Pfizer) or 28 days (Moderna) apart. To vaccinate a maximum number of individuals amid a vaccine shortage, the National Advisory Council on Immunization (NACI) has recommended that the doses may be administered up to 16 weeks apart, based on evidence suggesting high-level protection against COVID-19 beyond 14 days following the first dose of either of these vaccines.^{11, 12, 15}

A large, multinational **randomized control trial (RCT)** in 43,548 persons, 16 years of age or older who were healthy or had stable chronic disease (excluding immune-mediated inflammatory diseases like IBD) demonstrated 95.3% efficacy of the Pfizer-BioNTech vaccine in reducing symptomatic COVID-19 infections at least seven days after the second dose and 90% efficacy in reducing severe disease leading to hospitalization

or death (one versus nine severe COVID-19 cases in vaccinated versus unvaccinated individuals).¹¹ A similarly designed **RCT** conducted in the U.S. in 30,420 persons aged 18 years or older who were healthy or had stable chronic disease demonstrated 94.1% efficacy of the NIH-Moderna vaccine at least 14 days after the second dose and 100% efficacy in reducing severe disease leading to hospitalization or death.¹² Recent data have shown these vaccines to be more than 90% effective out to six months without any serious safety concerns.¹⁶

Adenovirus Vector Vaccines

The AstraZeneca vaccine (approved by Health Canada February 26, 2021) and the Janssen vaccine (approved by Health Canada on March 5, 2021) use a **non-replicating adenovirus vector** to deliver **SARS-CoV-2** DNA encoding the **spike protein** to human cells, which uses the host machinery to produce viral **spike proteins**.¹³ The AstraZeneca vaccine is administered as two intramuscular injections between four and 12 weeks apart, while the Janssen vaccine is administered as a single intramuscular injection.

A pooled interim analysis of 11,636 healthy adults randomized to either vaccine or control (placebo) across four **RCTs** held in the United Kingdom, Brazil, and South Africa showed 66.7% efficacy of the AstraZeneca vaccine in preventing symptomatic COVID-19 infection at least 14 days after the second dose and 100% efficacy in preventing hospitalization and/or death from **SARS-CoV-2**.¹³ Further exploratory analyses have shown that vaccine efficacy between day 22 and day 90 following a single

standard dose was 76.0%; effectiveness ≥ 14 days after the second dose among those who received a second dose of vaccine 12 or more weeks after the first dose was 81.3%. In an RCT of 44,325 healthy adults, the Janssen vaccine was 66.3% effective at preventing laboratory-confirmed symptomatic COVID-19 infection 14 days post-vaccination, 93.1% effective at preventing hospitalization for severe COVID-19, and 100% effective at preventing death due to COVID-19.¹⁷

Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT)

Recent reports of rare cerebral and systemic venous thromboembolic events (VTEs)—reported as blood clots in the media—associated with low counts of a clotting factor called platelets and severe bleeding with both the AstraZeneca and Janssen vaccines have raised concerns regarding the risk-benefit ratio of these vaccines, particularly among younger individuals who are at very low risk of dying from COVID-19.¹⁸⁻²⁰ Termed **vaccine-induced immune thrombotic thrombocytopenia (MITT)**, the VTEs that develop with VITT have often been life-threatening clotting in the brain.^{21, 22} While the rate of VITT with the AstraZeneca vaccine was initially suggested to be about 1 in 250,000 persons,¹⁸ more recent data has suggested that the rate may be much higher (as of May 12, 2021: 1 in 83,000 persons, 0.0012%).²⁰ The risk is expected to be similar for people with IBD.²²

In light of the risk of VITT, NACI has issued [a statement](#) that mRNA vaccines are preferred over non-mRNA vaccines. These facts have also prompted several provincial health authorities to suspend administration of the AstraZeneca vaccine as the first dose until more data are available and to consider

administering an mRNA vaccine for the second dose among those who received the AstraZeneca vaccine for the first dose.^{20, 23} These policy changes have also come in the face of increasing supply of mRNA vaccines, diminishing supply of AstraZeneca vaccine, and decreasing rates of COVID-19 in society.

Importantly, the background risk of VTE in the Canadian population is roughly 0.1%,²⁴ and the risk of VTE among individuals hospitalized with COVID-19 is as high as 15%.²⁵ Considering the adverse impacts of COVID-19, the benefits of these vaccines in preventing symptomatic and severe COVID-19 still outweigh the potential risks, especially in people living in areas of high COVID-19 rates or who have risk factors for severe COVID-19, such as those who are elderly or have pre-existing conditions.¹⁸

Vaccine Production and Distribution in Canada

For many years, Canada was a leader in vaccine production.²⁶ While plants in Toronto and Montreal have continued producing vaccines, they are not equipped to manufacture the COVID-19 vaccines, resulting in the Canadian government seeking vaccines from the U.S., Europe, and India (*Canadian Health Policy*, December 2020. ISSN 2562-492). However, this led to a lag in Canadian vaccine procurement and vaccination efforts when Moderna and Pfizer reduced vaccine production to build capacity for larger-scale production. Further, transport and storage logistics of existing vaccines coming from Europe and the U.S. to a central repository in Canada (and later to regional distribution centres and provincial/territorial points of care) has been challenging for some of the COVID-19 vaccines, particularly those requiring storage at -20° to -80°C .

The Canadian government plans to increase the domestic production capability of COVID-19 vaccines.²⁷ A new facility will be created for the National Research Council in Montreal, where ten million Novavax vaccines will be made, pending Health Canada approval. Additionally, companies that have demonstrated past success in manufacturing capabilities have received massive government investment. For example, Vaccine and Infectious Disease Organization (VIDO) in Saskatoon has been allocated upwards of \$45 million to build a manufacturing plant, and Medicago has been allocated upwards of \$170 million to expand its manufacturing capacity, in addition to a specific order of 76 million doses of its vaccine, pending Health Canada approval.

SARS-CoV-2 Vaccine Recommendations for People with IBD

People with chronic immune-mediated diseases such as IBD were excluded from the trials that evaluated the currently-approved **SARS-CoV-2** vaccines; therefore, concerns have been raised by the IBD community and healthcare providers regarding the safety and efficacy of these vaccines for people with IBD as well as the influence of IBD drug therapies on vaccine **immunogenicity** (i.e. the ability of the vaccine to elicit an immune response) and safety. Importantly, as none of the approved vaccines are live attenuated vaccines, there is no reason to suspect that individuals with IBD receiving immunosuppressive therapy would be at increased risk of **virus reactivation** (i.e. **SARS-CoV-2** infection resulting from the vaccine). Moreover, multiple studies have now been published on outcomes of **SARS-CoV-2** vaccination in people with IBD with no cause for concern indicated.

In a study of 246 people with IBD who received a **SARS-CoV-2** vaccine, the overall rate of adverse events was similar to the general population, while **biologic** therapy was associated with fewer adverse events, possibly due to blunting of an aggressive immune response.²⁸ A study of 1,500 individuals with IBD in the U.K. (CLARITY-IBD) reported people on **infliximab** had less robust immune response to the first dose of the Pfizer or AstraZeneca vaccines as compared to people using **vedolizumab**. Moreover, individuals using azathioprine or methotrexate with their **biologics** had reduced **seroconversion** (i.e. becoming antibody positive based on blood test) with both **infliximab** and **vedolizumab**.²⁹ Similarly, an earlier U.K. study of 7,000 people with IBD reported that serological responses to **SARS-CoV-2** infection were weakened in individuals receiving **infliximab** relative to those receiving **vedolizumab**, and further

blunted by the use of azathioprine or methotrexate.³⁰ Overall, these findings are consistent with studies which founds reduced **immunogenicity** in IBD patients receiving other vaccines while using **anti-TNF biologics**, immunosuppressive medications, or steroids, including vaccines for pneumococcus,³¹⁻³⁴ influenza,³⁵⁻³⁹ hepatitis B,⁴⁰ hepatitis A⁴¹ and herpes zoster.⁴² Immune responses to conventional vaccines do not appear to be impacted by **vedolizumab** (influenza and hepatitis B)⁴³ or **ustekinumab** (influenza, pneumococcal, tetanus).^{44, 45}

Importantly, in the CLARITY-IBD study, there was excellent antibody response following the second dose of vaccine and in individuals who received a vaccine dose following recovery from COVID-19. Furthermore, a national U.S. cohort study of nearly 15,000 (predominantly white males with IBD) receiving a wide spectrum of medications in the Veterans Health Administration System reported that the risk of infection with **SARS-CoV-2** was 1.34% in those who were unvaccinated and 0.11% among those who were at least seven days after their second dose of **mRNA** vaccine (80.4% vaccine effectiveness).⁴⁶

Canadian,⁴⁷ European,⁴⁸ and international⁴⁹ organizations all recommend that people with IBD be vaccinated against **SARS-CoV-2** at the earliest opportunity, irrespective of vaccine type, disease status or treatment, and without interruption of scheduled therapy. Crohn's and Colitis Canada further recommends that persons with IBD receive a scheduled second dose of vaccine three-to-four weeks following the first dose, rather than extending the interval for the second dose by up to 16 weeks as for the general population. This is because patients with IBD who are on **biologics** or immunosuppressive medications

may not mount an adequate immune response to the first dose of vaccine, and therefore may remain at risk for severe COVID-19.^{50, 51} NACI now “preferentially recommends that a complete two-dose vaccine series with an **mRNA** COVID-19 vaccine (Pfizer-BioNTech, Moderna) should be offered to individuals in the authorized age group, including those who are immunosuppressed, have an autoimmune condition, are pregnant or are breastfeeding.” Furthermore, it recommends that “with the increase of COVID-19 vaccine supply in Canada, second doses should be offered as soon as possible, with priority given to those at highest risk of severe illness and death from COVID-19 disease” ([Updated NACI statement](#), May 28, 2021).

Regardless of vaccination status, individuals with IBD should remain vigilant and continue practicing recommended public health measures to prevent **SARS-CoV-2** infection and transmission. Given the impaired serological responses to **SARS-CoV-2** among people on immunosuppressive treatment after one vaccine dose, serological testing and virus surveillance should be considered to detect suboptimal vaccine responses, infection persistence, and viral evolution to inform public health policy.

Vaccines in Special Populations: Children and Adolescents

As vaccines roll out in the adult population, plans for vaccinating children and young teenagers in Canada are still waiting for clinical trial data. All individuals included in the clinical trials leading to approval of the COVID-19 vaccines were aged 16 years or older. Pfizer recently reported 100% vaccine efficacy in a clinical trial of 2,260 adolescents aged 12–15 years,⁵² leading to Health Canada approving the Pfizer vaccine for this age group. Side effects were generally mild and included injection-site pain, headaches, fever, and fatigue. Teenagers were found to have comparable levels of virus-neutralizing antibodies as participants aged 15–25 years one month after the second dose. Results from a similar trial of the Moderna mRNA vaccine in adolescents aged 12–17 years in the U.S. also demonstrated excellent safety and effectiveness, and Health Canada is currently considering whether to approve this vaccine for Canadian adolescents. AstraZeneca recently began a study of its vaccine among participants aged 6–17 years in the U.K., and Pfizer has now started a trial in infants as young as 6 months old. Children and adolescents with IBD should follow general recommendations as their peer groups in the general population.

Vaccines in Special Populations: Pregnant People

[SARS-CoV-2 infection during pregnancy](#) is associated with increased risks of preterm birth, preeclampsia, stillbirth, ICU admission, need for mechanical ventilation, and maternal death.⁵³⁻⁵⁶ While pregnant people were excluded from the COVID-19 vaccine trials, a recent analysis of 35,691 pregnant people from multiple large registries of mRNA vaccinated individuals reported rates of adverse pregnancy and neonatal outcomes that are similar to vaccination studies conducted before the COVID-19 pandemic, including a 13.9% rate of pregnancy loss, 9.4% rate of preterm birth, and 3.2% rate of small size for gestational age, with no neonatal deaths.⁵⁷ A recent cohort study further demonstrated that vaccine-induced antibody titers (i.e. quantity/concentration) in pregnant and lactating people following COVID-19 mRNA vaccination are comparable to those in non-pregnant individuals and are significantly higher than titers induced by SARS-CoV-2 infection itself.⁵⁸ Studies have also found that anti-SARS-CoV-2 IgG antibodies following mRNA vaccination are present in umbilical cord blood and breastmilk, with efficient transplacental antibody transfer, thus conferring passive immunization in utero.⁵⁸⁻⁶⁰ Vaccination earlier in pregnancy further resulted in higher antibody concentrations in the infants.^{59, 60} While early data demonstrated hesitancy among pregnant people to receive the COVID-19 vaccine,⁶¹ more recent data shows better acceptance in this group, particularly among people with better education and employment;⁶² this highlights the need for ongoing vaccine education and strategies to manage vaccine hesitancy. Similar to children and adolescents with IBD, Crohn's and Colitis Canada recommends that pregnant people with IBD follow general guidance as their peer groups in the general population.

Vaccines in Special Populations: Seniors

Similar to COVID-19, the vast majority of seasonal influenza infections and related deaths from the disease occur among the elderly. A Dutch study between 1967 and 1989 reported that 95% of influenza-related deaths occurred among people over 60 years of age.⁶³ Hence, the elderly are a critical group to vaccinate against COVID-19. However, with the aging of the immune system, especially after the age of 60, there is the potential for reduced response to vaccines.⁶⁴ What to expect in the elderly population from COVID-19 vaccines can be drawn from previous studies on influenza vaccine experiences.

Some studies have suggested that influenza vaccination may be less effective among subgroups of elderly populations. For example, a multicentre study suggested that influenza vaccine effectiveness is lessened among frail older adults.⁶⁵ Influenza outbreaks have been reported in retirement homes with excellent vaccine coverage.⁶⁶ However, even with a lower vaccine efficacy, influenza vaccines prevent a large number of hospitalizations, ICU admissions, and deaths in the older adult population. For example, in a modeling study, during the 2012–2013 influenza season a vaccine with 10% effectiveness and 66% coverage was estimated to avert 13,000 hospitalizations among individuals ≥ 65 years of age in the U.S.; a vaccine with 40% effectiveness and the same coverage was estimated to avert 60,000 hospitalizations.⁶⁷ A systematic review reported older adults receiving the influenza vaccine experience less influenza over a single season (2.4% compared to 6%).⁶⁸

Similar results of lower efficacy among individuals greater than 80 years have been reported for pneumococcal vaccination.⁶⁹ On the other hand, the herpes zoster vaccine efficacy is minimally affected by age.⁷⁰ Additionally, individuals with IBD—particularly those treated with combination thiopurines and anti-TNFs—have impaired immunologic response to vaccines, including against influenza.⁷¹ There are, however, no differences in adverse effects among vaccinated individuals with or without IBD.⁷² The CLARITY-IBD study evaluated a subpopulation of individuals with IBD who were over the age of 60 and vaccinated with mRNA or non-viral vector vaccine. Age over 60 years was an independent predictor of lower antibody response to vaccination.²⁹

Extrapolating from all these findings, effectiveness from COVID-19 vaccination among the elderly with IBD may be lower than among younger individuals, particularly compared to those without IBD. However, substantial benefits are likely to occur. A necessary strategy to improve benefits among elderly individuals with IBD is going to be avoiding delays in receiving the second dosage.

Conclusion

The collective efforts of scientists, physicians, politicians, and industry have led to the fastest ever vaccine development program against any infectious disease known to humanity. Moreover, efficacy and safety of the approved vaccines are extremely high. While **SARS-CoV-2** variants of concern are on the rise across the globe, indications as of this writing are that the vaccines are effective against the known variants of concern. Despite people with IBD being excluded from the pivotal COVID-19 vaccine trials, emerging evidence and evidence from other vaccination programs suggest that these vaccines should be similarly safe and effective for people with IBD. As such, the overwhelming recommendation by all societies is that people with IBD should receive any of the available vaccines at their earliest opportunity, without delay or interruption of their IBD treatment. Future research is needed to determine if vaccine efficacy wanes among those receiving **anti-TNF** therapy or conventional immunosuppressive agents and if a timely booster dose is warranted to increase protection. It is important that people with IBD are not excluded from existing vaccination programs and that they do their part to procure timely vaccination and contribute to the ultimate goal of achieving **herd immunity**.



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HEALTHCARE DELIVERY DURING THE PANDEMIC AND THE FUTURE MODEL OF IBD CARE

Healthcare Delivery during the Pandemic and the Future Model of IBD Care

Summary

The SARS-CoV-2 pandemic has had a profound impact on IBD healthcare delivery. The implementation of necessary public health restrictions has restricted access to medications, procedures, and surgeries throughout the pandemic, catalyzing widespread change in how IBD care is delivered. Rapid large-scale implementation of virtual care modalities has been shown to be feasible and acceptable for the majority of individuals with IBD and providers. The SARS-CoV-2 pandemic has exacerbated pre-existing barriers to accessing high quality, multidisciplinary IBD care that addresses healthcare needs holistically. Continued implementation and evaluation of both synchronous and asynchronous eHealthcare modalities are required now and in the future in order to determine how best to incorporate these modalities into patient-centred, collaborative care models. Resources must be dedicated to studies that evaluate the feasibility, acceptability, and effectiveness of eHealth-enhanced models of IBD care to improve efficiency and cost-effectiveness, while increasing quality of life for persons living with IBD. Crohn's and Colitis Canada will continue to play a major leadership role in advocating for the healthcare delivery models that improve the quality of life for persons living with IBD.

Key Points

1. The SARS-CoV-2 pandemic has negatively impacted access to IBD care globally.
2. The global IBD community has successfully pivoted to alternate models of care, inclusive of virtual care and remote monitoring of disease activity, which will influence healthcare delivery models beyond the SARS-CoV-2 pandemic.
3. Ongoing support for rigorous, patient-oriented research that seeks to understand how best to implement and sustain new models of healthcare delivery is needed now and in the future.

Introduction

The SARS-CoV-2 pandemic has led to a dramatic shift in access to and delivery of care for Canadians living with inflammatory bowel disease (IBD).¹ The implementation of substantial public health restrictions globally resulted in the need to physically distance, adopt proper hand hygiene, and wear face masks and, in certain settings, personal protective equipment (PPE). Combined with the need to conserve health system capacity, these measures have changed how healthcare is being delivered in both the inpatient and ambulatory care spaces. This change has spurred rapid and widespread implementation of innovative healthcare delivery models that may not have been possible in the pre-pandemic era.² These dramatic shifts, supported by a collective sense of urgency, motivation, and shared objectives across government and healthcare sectors, have provided valuable insights and lessons related to how IBD care is delivered and what clinicians and individuals with IBD value in healthcare services delivery. These lessons will have an enduring influence on models of IBD care delivery beyond the SARS-CoV-2 pandemic.



Changes in Healthcare Delivery

The SARS-CoV-2 pandemic has had a dramatic impact on the delivery of healthcare services both for persons living with and without IBD. Most outpatient care has shifted to virtual care, with elective and semi-elective **endoscopy** and bowel resection surgery volumes dramatically decreased globally at most centres during the pandemic.³ In most cases, these reductions were due to government and institutional policy decisions either to minimize potential patient and healthcare worker exposure to SARS-CoV-2 (especially at the start of the pandemic when personal protective equipment was limited) or to facilitate redeployment of staff to other essential services, such as intensive care units, emergency departments (ED), and medical wards.

Outpatient Visits Replaced by Virtual Care

Perhaps one of the most impressive, rapidly adopted, and far-reaching changes in how IBD care has been delivered during the SARS-CoV-2 pandemic relates to a wholesale adoption of eHealthcare delivery options to reduce the risk of transmission of SARS-CoV-2 associated with in-person clinical visits. eHealth includes the use of both synchronous (telephone consults or follow-up visits, video visits) as well as asynchronous (text messaging, eConsultation, healthcare delivery via social media) virtual delivery healthcare modalities.⁴ The convergence of government and healthcare system information technology infrastructure support (financial support, fast tracking privacy and security threat assessments, reduction in innovation resistance), patient and provider acceptance, and rapid adoption as a result of the mandatory restrictions imposed during the pandemic, led to unprecedented health system change on a global scale.

Gastroenterologists around the world have reported dramatic reductions in the use of in-person clinics for the delivery of outpatient care.⁴⁻⁸ The literature has overwhelmingly demonstrated that providers and persons living with IBD feel that virtual care is an acceptable, feasible, and safe method of healthcare delivery.⁹ Evaluations have demonstrated consistently high levels of satisfaction among persons living with IBD.¹⁰⁻¹³ In fact, several studies have observed that the majority of individuals surveyed would prefer virtual visits versus in-person clinics, particularly for matters of routine follow-up (for information on this matter specific to children/adolescents with IBD and their families, see the [Health System Impact section](#) of the Children and Expectant Mothers with IBD chapter).^{11, 14} In a survey study of 115 individuals with IBD in Italy (of whom 100 completed the questionnaire), trust in **telemedicine** services for consultation and desire to continue to use **telemedicine** services was >90%.¹⁵ Additionally, in a Portuguese survey study of 973 individuals with IBD, 88.8% supported remote consultations and 77.3% were satisfied with this type of appointment.¹⁶ Although less commonly reported, some centres even utilized social media and alternate communication platforms (e.g. WeChat) in order to facilitate the delivery of virtual care.⁸ Mastronardi *et al.* conducted a single-centre study in Castella Grottem, Italy between March and April 2020.¹⁷ They allocated 1,038 persons with IBD that they were previously followed into two groups: (1) 421 individuals who they continued to assess in-person (chosen because they required **biologic** transfusions) and (2) 617 individuals who received tele-monitoring (chosen because they were able to self-administer their therapy [oral or subcutaneous

therapies)). Tele-monitoring was scheduled every three days, either by remote video call or telephone. They observed significantly more clinical relapses, based on Mayo Score or Harvey-Bradshaw Index, in the telemonitoring group (23.5%) compared to the in-person control group (18.3%). However, there were no significant differences observed in quality of life (assessed using the IBD32Q) between the groups. Since clinical disease activity is poorly correlated with endoscopic disease activity, these data should be interpreted with caution. Additionally, those being seen in person may have a greater disease burden since they were on **biologic** therapy. Therefore, a comparable relapse rate between the groups suggests that in-person may be preferred for certain patient groups. However, some individuals remain concerned about missed findings without a physical examination and may prefer in-person care.¹⁷

Endoscopy and Disease Monitoring

Monitoring IBD disease activity during the pandemic has been challenging with the rapid reduction in the number of colonoscopies being performed at medical centres globally. The Netherlands reported a 14.7% net decrease in **endoscopy** over the course of the pandemic, with some centres reporting much higher decreases;¹⁸ this has forced many IBD centres to be creative in their approach to monitoring disease activity. In an international survey, 52 gastroenterologists from 33 countries reported using blood testing, **fecal calprotectin**, and cross-sectional imaging when **endoscopy** was not available.⁵ However, access to cross-sectional imaging was limited in some countries (e.g. Brazil, Canada, and the U.S.). Even as we begin to emerge

from the third wave of the pandemic, it is highly likely that access to cross-sectional imaging will become even more limited due to the cumulative backlog of tests. Although some Canadian centres had no barriers to accessing **fecal calprotectin** testing, some centres identified limited access and funding for **fecal calprotectin**, including the use of at home **fecal calprotectin** kits. All Canadian centres had access to standard blood testing, and most had usual access to basic diagnostic imaging (e.g. x-rays). The Endoscopic Healing Index (EHI) is a serum test composed of 13 protein biomarkers to produce a quantitative score ranging from 0–100, which was validated against colonoscopy in individuals with Crohn's disease and may provide another metric for disease monitoring.¹⁹

Hospital and Surgical Care

In some COVID-19 hot spots, hospitals have come under considerable strain as persons who contract COVID-19 fill hospital beds and increase overall hospital admission volumes. For example, at the height of the pandemic in New York City, individuals with COVID-19 occupied more than 50% of acute care beds.²⁰ In many areas with lower COVID-19 rates, however, the increase in number of hospitalizations for COVID-19 has been offset by reductions on non-COVID-19 hospitalizations, often resulting in overall reductions in hospitalization burden as many individuals elect to administer self-care at home so as to avoid potential exposure. The rates of ICU admission have increased in most regions as a result of COVID-19, particularly in hot spots. As critical illness cannot be deferred, COVID-19 has compounded general ICU admissions, leading many centres to develop

ancillary ICU beds in other parts of the hospital. Some regions, such as Italy and India, have had to implement rationing of ICU beds, ventilators, and oxygen due to overwhelming demands at pandemic peaks.

Similar to trends in the general population, hospitalizations for IBD declined following the onset of the pandemic.^{10, 21} In Madrid, the rate of IBD-related hospitalizations and visits to the emergency department decreased by 50% and 58%, respectively, compared with rates in the same period the previous year.¹⁰ In a nationwide Dutch study, combined IBD-related endoscopic and surgical services decreased by 59.7% at the national peak of the pandemic in April 2020 as compared to pre-pandemic rates in the preceding year. Over the duration of the pandemic, endoscopic and surgical procedures showed a net decrease of 14.7% (1,443 procedures) and 5.5% (33 procedures), respectively.¹⁸ In Alberta, 5.7% of patients reported a delay of surgery by a median of 10 weeks.²²

The inevitable hurdle that will be faced by practitioners and institutions once elective services resume to normal capacity will be managing the backlog of cases that have accumulated, most of which would likely still have an active indication for intervention, and which may have become more urgent due to delays in investigation and treatment.

Multidisciplinary Care

Complex medical, surgical, and psychosocial issues associated with IBD often require specialized expertise from a multidisciplinary team that includes gastroenterologists, pharmacists, surgeons, psychologists, and dietitians.^{23, 24} This type of multidisciplinary care delivery is often restricted to large academic centres.²⁴⁻²⁶ An integrated

model of care in IBD has the potential to improve the quality of care, patient satisfaction, mental and physical health, and to reduce healthcare costs.^{23, 27, 28} During the pandemic, multidisciplinary visits have often been continued virtually with the individual seen on same day by different members of the multidisciplinary team in order to make joint treatment decisions.^{29, 30}

Before the **SARS-CoV-2** pandemic began, it was recognized that IBD specialist nurses, the main point of access for persons with IBD, played a pivotal role in providing education about disease; medications; monitoring of therapy; basic dietary advice; within-scope psychological and emotional support; access to service; and telephone advice, particularly during periods disease flares.^{25,31,32} The **SARS-CoV-2** pandemic has led to a significant increase in the reliance on IBD nurses to provide essential services to persons with IBD remotely. Both synchronous and asynchronous virtual care through telephone and email have been provided by IBD nurses as an important communication pathway for people with IBD needing access to specialist support/advice and facilitating avoidance of clinic appointments and hospital admission.^{24, 33, 34} IBD nurses have also played an important role in the identification of high levels of distress (already common in people with IBD and exacerbated by the pandemic) through their remote interactions with patients and have been able to offer virtual modes of psychologic support. Digital eHealth systems have enabled screening of psychologic well-being and delivery of solutions such as app-based, cognitive-behavioral therapy.⁹

Medical Therapy during the Pandemic

Immunomodulatory Therapy and Risk of Severe COVID-19

At the beginning of the pandemic, there was concern among people with IBD that being on immunosuppressive medications might enhance the risk for either acquiring SARS-CoV-2 infection or having more severe COVID-19. Hence, there was concern for individuals with IBD either not being adherent with medications or not accessing them at appropriate intervals due to fear about attending infusion centres or even going into public pharmacies to fill prescriptions. Early assurances from the **SECURE-IBD** registry regarding the use of **anti-TNFs** helped to reduce anxiety related to IBD **biologic** use, but concerns remain for other therapies (e.g. steroids). The risk of severe COVID-19 across medication groups are reviewed in detail in the chapter on [Clinical Risk Factors and IBD Medications](#). The IBD population was advised early in the pandemic not to interrupt their medication, as this may lead to disease relapse, which could necessitate a new prescription of **corticosteroids** or hospitalization. These events were considered to pose a greater risk than the medications used to treat IBD.³⁵

Provider Prescribing and Treatment Adherence

While data were emerging from the **SECURE-IBD** registry and experts were providing guidance on medication usage during the pandemic, little information relating to what individuals with IBD and their providers actually did with IBD-specific medications during the pandemic exists. In a Vancouver, BC general gastroenterology clinic, a retrospective chart review of 241 people with IBD compared medication adherence rates after telehealth visits ($n=113$ individuals) with in-person visits ($n=128$ individuals). The majority of individuals

had IBD as their primary gastrointestinal problem and two thirds were using biological therapy. Prescription fill rates for individuals seen through telehealth (98.2%) were higher than in-person visits (89.1%, $p=0.004$). Excluding **biologic** therapies, the prescription fill rate was 94.7% in telehealth group and 81.4% in in-person group (**OR**: 4.11; 95% **CI**: 0.88, 19.27). Reasons for this difference were not clear but may include the process of getting the prescriptions to the pharmacies (i.e. electronically faxed directly to pharmacies versus individuals being handed a prescription during the in-person visit forcing another visit to a public establishment [the pharmacy]) or systematic differences between those people seen in person versus those seen via telehealth, which may influence medication adherence. In a study out of Denmark, 14.3% of 400 participants using IBD medication paused or stopped their IBD treatment during the initial phase of the pandemic. The majority (61.4%) discontinued IBD medications either due to remission or because of side-effects;³⁶ however, **corticosteroids** were the most frequently discontinued medication, and it is not clear if discontinuation was due to completion of a short-course of steroids or in response to risks associated with SARS-CoV-2 infection. Only five respondents stated that the pandemic contributed to their decision to discontinue therapy.

Access to Biologic Therapies

While adherence to medications may not have changed significantly, there were concerns that public health policies might limit access to **biologic** therapies due to a reduction in infusion capacity or closure of infusion clinics. In a study of 398 patients attending University of Alberta or

University of Calgary IBD clinics from March 2020 through July 2020, only 2.2% reported a delay in **biologic** infusions for a median of two weeks; it is unknown how representative this is of other clinic models across Canada.²² As a result of concerns about attending health clinics for infusions at two hospitals in the U.K. in March 2020, a program was implemented in which all hospital-based intravenous infusions of **infliximab** were switched to home-based, self-administered, subcutaneous injections of CT-P13, an **infliximab** biosimilar, with all but three of 163 patients tolerating the switch without early flares or intolerance.³⁷

IBD Care Delivery: Lessons for the Future

The rapid and transformative healthcare delivery changes that have been made and lessons learned throughout the SARS-CoV-2 pandemic to date have facilitated fast-paced innovation that has leveraged and built upon previous eHealth implementation success in the IBD space. These innovations will need to continue well beyond the current pandemic to improve access to quality care for persons living with IBD.

Another area of healthcare delivery in the ambulatory IBD space that will be transformed in the future relates to remote monitoring of clinical factors proven to impact disease-related outcomes. Remote monitoring of patient-reported outcomes, disease activity, medication adherence, nutritional status, mental health, and well-being through the use of digital health technology will facilitate implementing a more comprehensive and holistic care model; one that has historically been difficult, if not impossible, to implement through traditional clinic-based models of care and with limited IT infrastructure. These models will also serve to engage and empower many people living

with IBD with respect to self-management and autonomy. Apps on mobile devices or web-based programs through which individuals can report symptoms to providers who then respond with a timely intervention have the potential to improve health outcomes. Only a few randomized trials have evaluated such digital health technology and its potential impact on health outcomes. So far, improved disease specific quality of life and reduced healthcare utilization including outpatient visits and hospitalizations have been reported.³⁸⁻⁴⁰

The future model of IBD care will almost certainly include a hybrid of in-person and virtual care delivery strategies, supported by synchronous and asynchronous eHealth technology. These eHealth platforms will be integrated within the electronic medical record along with clinical data (i.e. symptoms, laboratory and biomarker data) derived from both active and passive (e.g. smart watches) digital remote monitoring tools.⁴¹ Given the exponential rise in the routine collection of clinical data through remote monitoring activities, artificial intelligence (AI) algorithms based on evidence-based care pathways will be needed in order to gather, classify, and interpret data, as well as support clinicians (i.e. clinical decision supports through embedded smart algorithms). These eHealth and digital monitoring tools will ideally be applied within the context of a multidisciplinary care setting in which the ability to respond to the data and to adequately address individual needs will be facilitated. How these technologies are designed and implemented within clinical care settings as well as the individuals' lives will need to be balanced by a patient-centred approach, informed by extensive stakeholder engagement.

Much work in relation to healthcare delivery advocacy and policy is needed now and into the future. Pre-existing barriers in access to high quality, multidisciplinary care have been exacerbated by the SARS-CoV-2 pandemic. National guidelines for the use and implementation of virtual care, digital remote monitoring, and the application of AI will need to be developed and standardized, while taking into account the unique environmental considerations of each province, institution, and clinic. As technology evolves, integration of all eHealth platforms within an Electronic Medical Record will allow for more seamless tracking of data and, therefore, a greater likelihood of technology adoption.

Several initiatives that were being developed in the Canadian landscape prior to the pandemic have evolved and will play an important role in the future of IBD care (Table 5). Developed by Crohn's and Colitis Canada, the Promoting Access and Care

through Centres of Excellence (PACE) Telemedicine Program in Ontario has already demonstrated that use of video consultation for geographic areas with minimal access to specialized IBD care was feasible, reduced wait times, and was cost-saving.⁴² These benefits were realized while maintaining high value care. Teleconsultation through the PACE program has been successful in Ontario and will be expanded across Canada in the near future. MyGut, a mobile app inaugurated in 2020, is a platform for healthcare provider-patient interaction, remote monitoring, and tele-education. Also being implemented is the IBD Global Rating Scale, a web-based, periodic self-reporting system for IBD care providers to help improve and standardize the quality of IBD care across Canada. The Crohn's and Colitis Canada COVID-19 and IBD Task Force should remain as a general IBD **knowledge translation** channel even after the pandemic.

Table 5:

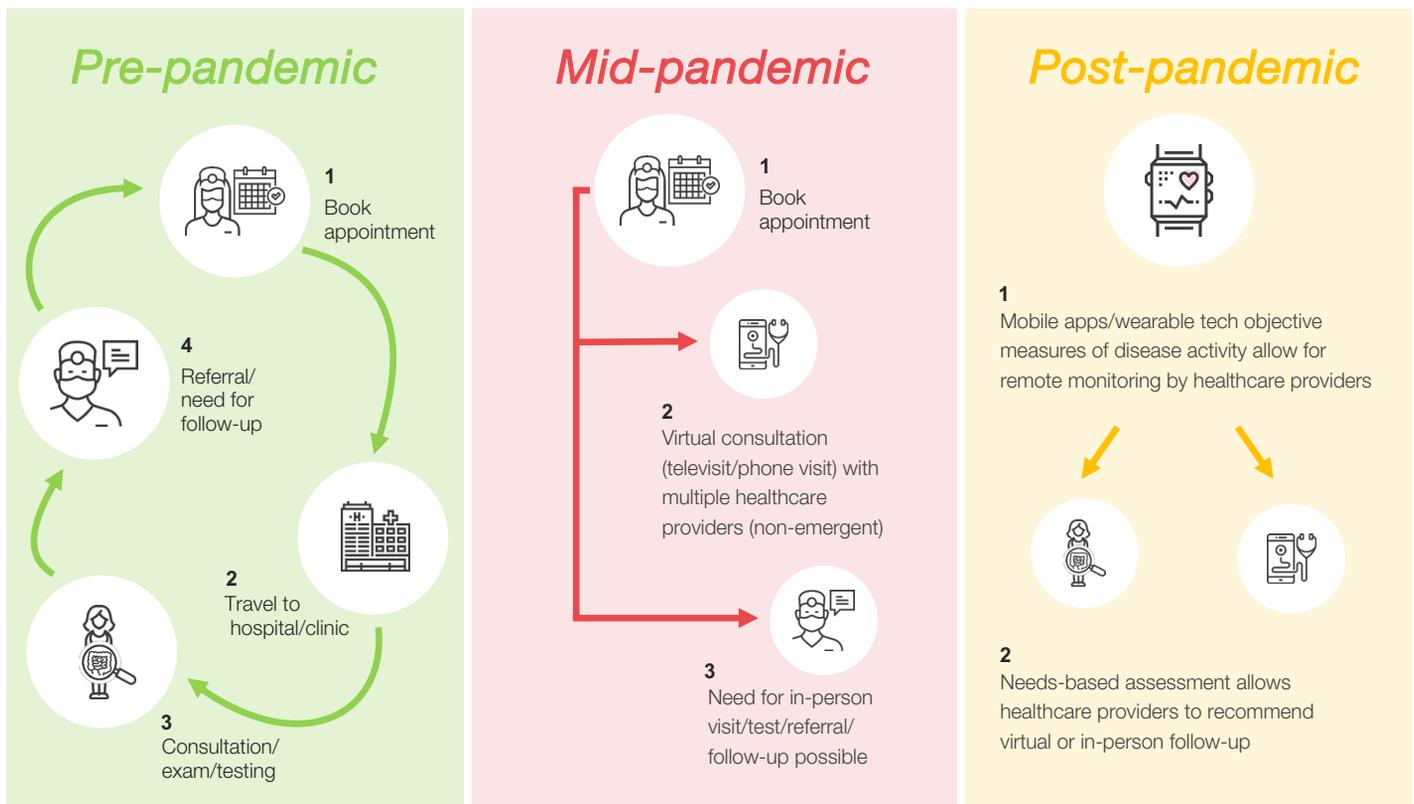
Post-pandemic care in IBD: Canadian initiatives.

Activity	Current	Future
Teleconsultation	PACE* Telemedicine Program	Expansion across Canada
Telemonitoring	MyGut mobile device application	MyGut implementation
IBD Quality of Care	Guidelines, IBD GRS*** PACE IBD care pathways	Implementation of IBD GRS and PACE IBD care pathways
Knowledge Translation	CCC*** COVID-19 and IBD Task Force	Dedicated long-term Knowledge Translation Committee

*Promoting Access and Care through Centres of Excellence.

**Inflammatory Bowel Disease Global Rating Scale.

***Crohn's and Colitis Canada.



An increasing amount of health research utilizes patient partners as invaluable resources in defining the research questions, participating in literature reviews, and providing stakeholder assessments and feedback. As the new models of care first introduced during the pandemic continue to evolve in the post-pandemic era, they must do so with users at top of mind. Specifically, people with IBD need to be partners in the design of the post-pandemic multidisciplinary care models, including synchronous and asynchronous care, data tracking (e.g. wearable technology or mobile apps), and in training and testing AI algorithms for care pathways. Individual preferences should also be incorporated in the type and location of care provided. A critical component of this patient-centred approach are integrated **knowledge translation** strategies where end-stage users are included in the research.

The COVID-19 pandemic is a global crisis that will leave its imprint for years to come and will reshape the way medicine is practiced. The medical community has had to respond, adapt, and effect change rapidly. This change will pave the way for a transformed and enhanced model of IBD care and will bring about reflection on our readiness for future challenges of such magnitude as the COVID-19 pandemic. Rapidly emerging literature in relation to the widespread implementation of virtual care modalities in combination with the use of non-invasive disease monitoring strategies have demonstrated the acceptability, feasibility, and safety of these approaches during the pandemic.

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