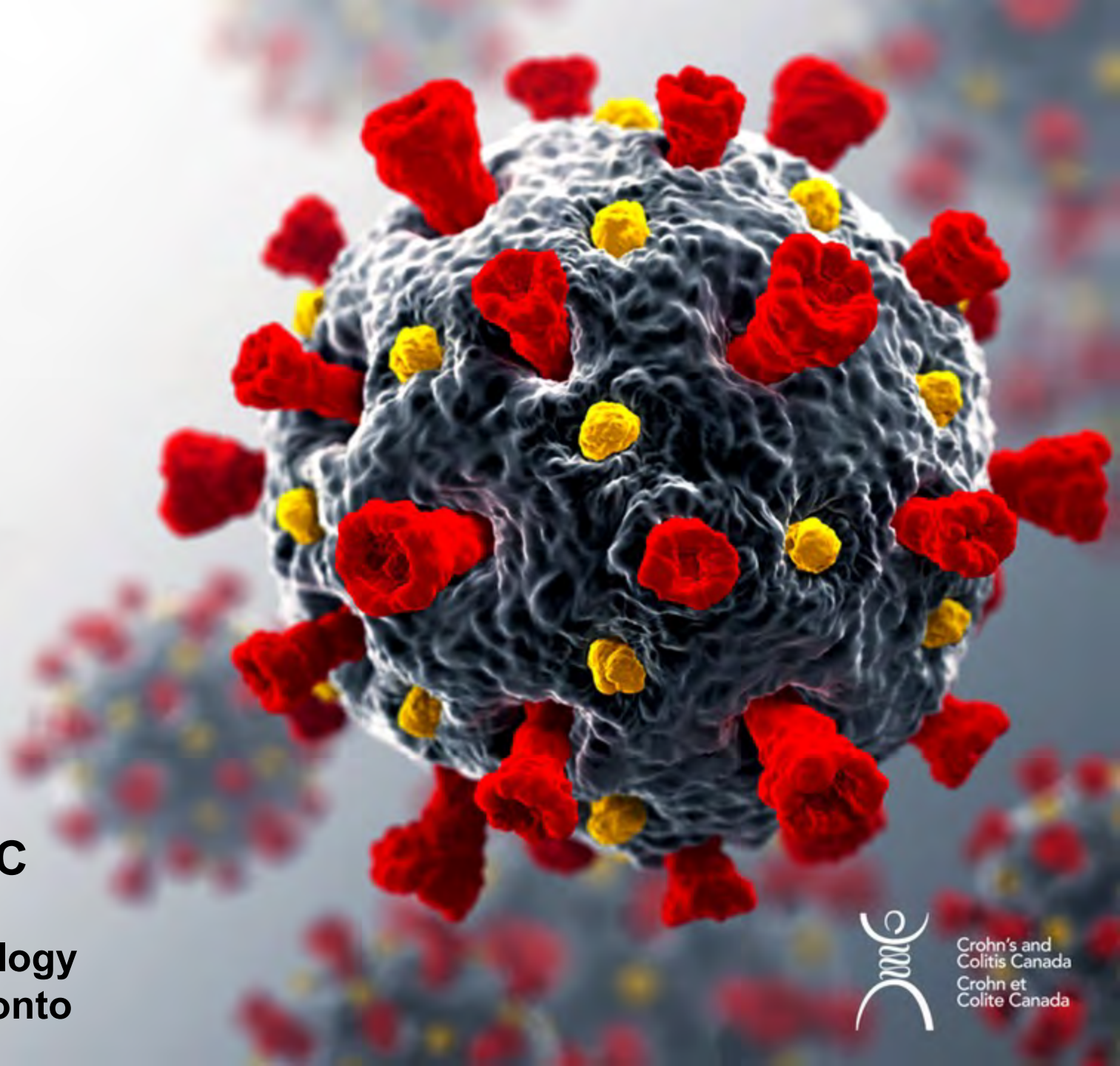
COVID-19 & Inflammatory Bowel Disease

2021 Impact of COVID-19 & Inflammatory Bowel Disease in Canada Report



Eric Benchimol, MD, PhD, FRCPC
Co- Chair, COVID-19 & IBD Task Force
Professor of Paediatrics and Epidemiology
SickKids IBD Centre, University of Toronto

Crohn's and Colitis Canada
Crohn et Colite Canada

TIMELINE OF EVENTS (2020)

- **January:**
  - Jan 9: WHO announces Coronavirus-related pneumonia in Wuhan, China
  - Jan 21: CDC confirms first US case
  - Jan 23: Wuhan under quarantine
  - Jan 25: First Canadian case of infection in Toronto
  - Jan 31: WHO issues Global Health Emergency
- **March**
  - Mar 11: WHO declares COVID-19 a Pandemic
  - Mar 12: CCC SMAC discusses impact on people with IBD
  - Mar 16: Canada closes international borders
  - Mar 17: First COVID-19 & IBD Taskforce meeting
  - Mar 19: First CCC COVID-19 & IBD webinar

How should we manage the COVID-19 pandemic for IBD patients living in Canada?

CCC COVID-IBD Task Force Recommendations:
https://crohnsandcolitis.ca/covid-19

CROHN'S AND COLITIS CANADA COVID-19 TASK FORCE:

Dr. Gil Kaplan, University of Calgary

Dr. Eric Benchimol, University of Toronto

Dr. Lisa Barrett, Dalhousie University

Dr. Charles Bernstein, University of Manitoba

Dr. Marc Bradette, Université Laval

Usha Chauhan, RN, NP, McMaster University

Dr. Sharyle Fowler, University of Saskatchewan

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Dr. Deanna Gibson, UBC

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Dr. Cynthia Seow, University of Calgary

Dr. Laura Targownik, University of Toronto

Ms. Sandra Zelinsky, Patient Advisor

Dr. Kate Lee, Crohn's and Colitis Canada

Angie Specic, Crohn's and Colitis Canada

SCAN ME

2021 Impact of COVID-19 & Inflammatory Bowel Disease in Canada: **Objectives**

1. Create an up-to-date relevant overview on the burden of COVID-19 on IBD in Canada
2. Raise awareness of the impact of COVID-19 on IBD for the general public, patients, healthcare providers, administrators, and policy makers
3. Provide guidance to the special needs in the delivery of care for those with IBD during the pandemic.

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SCAN ME

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CANGIEC
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JCAG

JOURNAL OF THE
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OF GASTROENTEROLOGY

VOLUME 4 NUMBER S2 December 2021 academic.oup.com/jcag

2021 Impact of COVID-19 and Inflammatory Bowel Disease in Canada

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Canadian Association of Gastroenterology
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www.cag-acg.org

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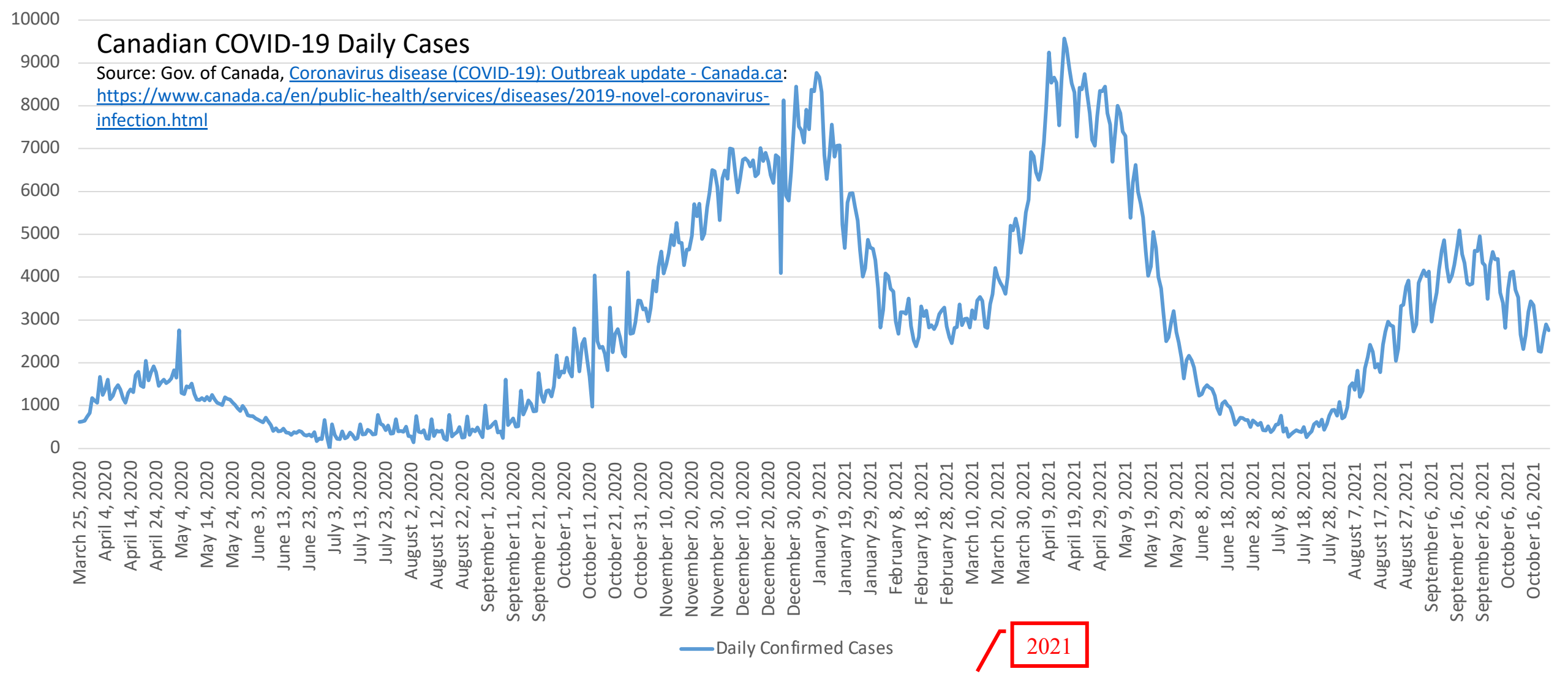
Impact of COVID-19 & IBD in Canada
LAUNCHED July 7, 2021

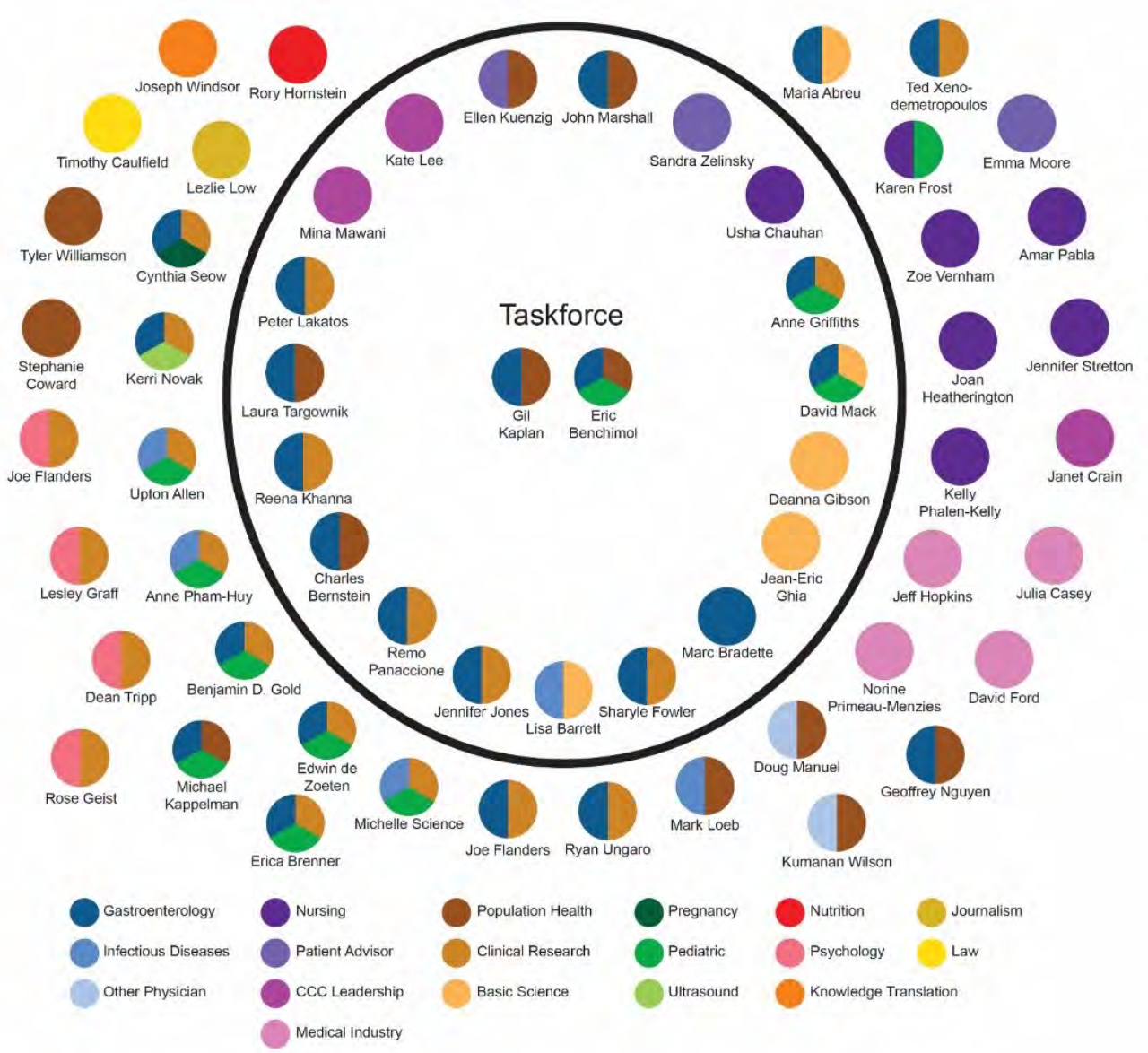
Journal of the Canadian Association of Gastroenterology

9 Articles in a Supplemental Issue

Epidemiology & Knowledge Translation



Date	Mar 19	Mar 26	Apr 2	Apr 16	May 7	May 14	May 21	June 25	Sept 10	Oct 8	Nov 19	Dec 17	Jan 21	Feb 18	Mar 18	Apr 28	May 27	June 27	Sept 9	Oct 25
World Cases	230,055	521,086	1.002m	2.101m	3.809m	4.405m	5.047m	9.506m	27.933m	36.234m	56.421m	75.014m	97.008m	110.02m	121.37m	149.74m	168.54m	181.19m	222.21m	243.87m
Canada Cases	782	3,409	11,067	28,893	63,895	72,538	80,142	102,573	134,294	173,123	311,714	488,636	725,495	834,197	919,244	1.202m	1.375m	1.413m	1.525m	1.699m
SECURE-IBD	21	102	255	547	996	1,104	1,242	1,570	2,323	2,559	3,195	3,905	4,578	5,202	5,596	5,959	6,176	6,278	6,562	6,635



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	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,	Hours Watched:	Registrants: 3,112	Total Views: 7,468
	COVID-19 F Factors: Live Q&A				Total Views: 3,470
	Infusion Clin Pregnancy & Newborns	March 26, 2020	Watched: 435.0	1,269	Total Views: 3,364
	Vaccines and “Home” for the Holidays	Released: December 17, 2020	Hours Watched: 423.2	Registrants: 2,606	Total Views: 4,280

- Total registrants: >31,000;
- Total live audience: >15,000;
- Total archived video views: >40,000
- Visitors to web pages: >480,000

SECURE-IBD DATABASE

Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

COVID-19 in People with Inflammatory Bowel Disease

Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

Country Breakdown: World

Please use the following citation if referencing the data on this page. Also see the Publications tab of this window.
Brenner EJ, Ungaro RC, Colombel JF, Kappelman MD. SECURE-IBD Database Public Data Update. covidibd.org. Accessed on MM/DD/YY.

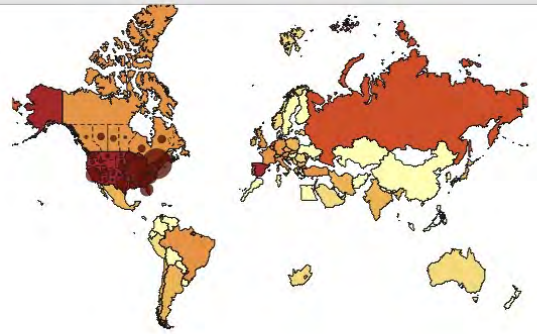
About

Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE-IBD) is an international, pediatric and adult registry to monitor and report on outcomes of COVID-19 occurring in IBD patients. The SECURE-IBD registry is funded by the Helmsley Charitable Trust.

We encourage IBD clinicians worldwide to report ALL cases of COVID-19 in their IBD patients, regardless of severity (including asymptomatic patients detected through public health screening). Reporting a case to this Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE)-IBD registry should take approximately 5 minutes. Please report only confirmed COVID-19 cases, and *report after sufficient time has passed to observe the disease course through resolution of acute illness and/or death*. **To report a case of coronavirus, click here.**

Interactive Data Visualization Reference:
Windsor JW, Underwood FE, Brenner E, Colombel J-F, Kappelman MD, Ungaro R; Zhang X, Kaplan GG. Data Visualization in the Era of COVID-19: An Interactive Map of the SECURE-IBD Registry. The American Journal of Gastroenterology 2020;115 (11):1923-1924. doi: 10.14309/ajg.0000000000000953.

About | Publications | Directions



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October 6, 2021

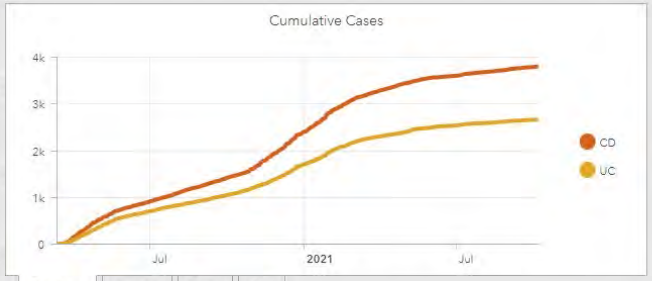
No legend

Cases
6,635

Hospitalizations
996

Deaths
105

As of Oct. 6th.



Timeline | Activity | Type | Sex

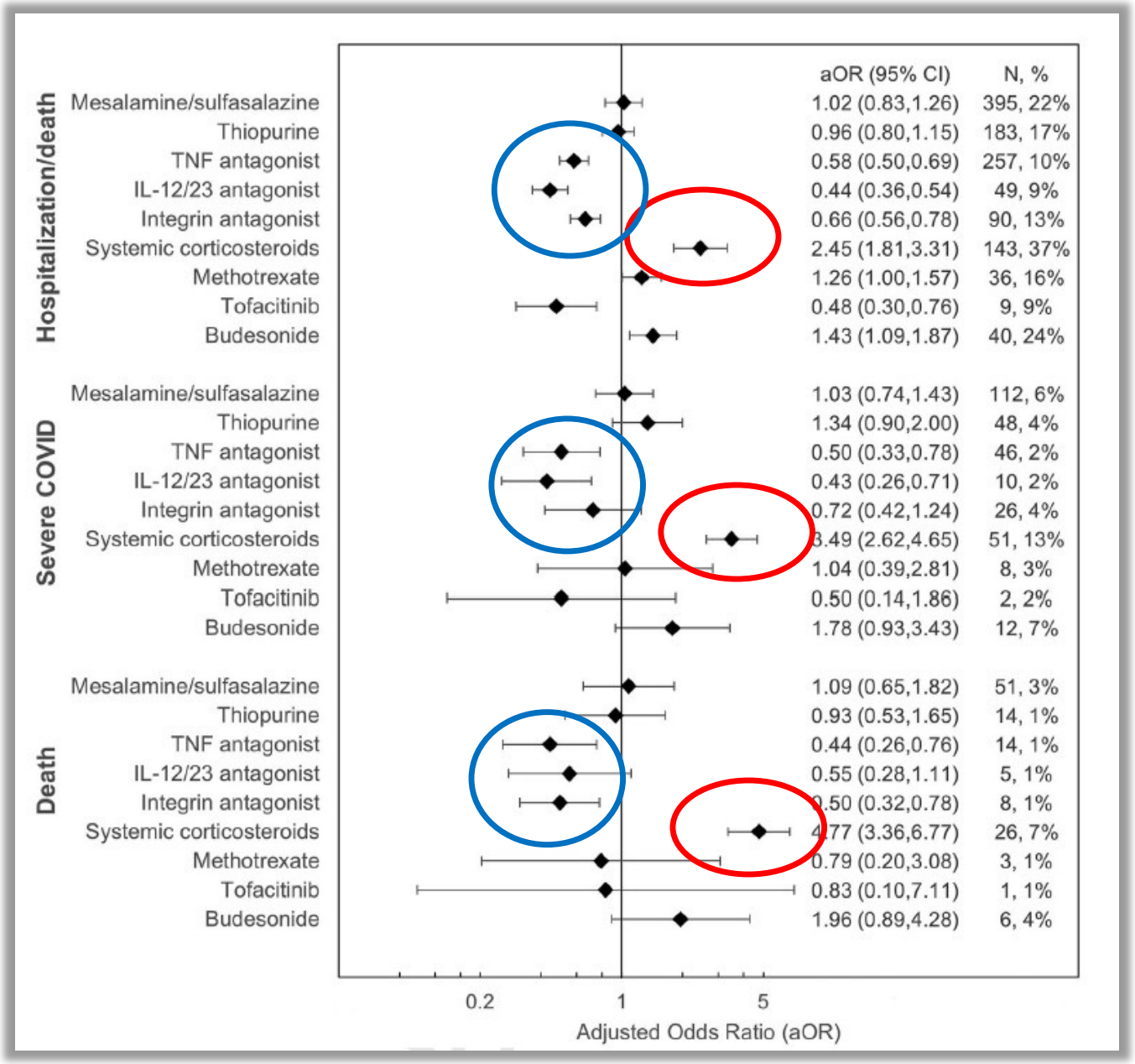
Age | Treatment | Country | US State | Canadian Province

Visuals prepared by the research lab of Dr. Gilaad G. Kaplan (Twitter), a gastroenterologist and epidemiologist in the Cumming School of Medicine at the University of Calgary. For more maps of digestive diseases, visit Kaplan Lab.

Windsor JW, Underwood FE, Brenner E, Colombel J-F, Kappelman MD, Ungaro R; Zhang X, Kaplan GG. Data Visualization in the Era of COVID-19: An Interactive Map of the SECURE-IBD Registry. The American Journal of Gastroenterology 2020;115 (11):1923-1924. doi: 10.14309/ajg.0000000000000953.

SECURE-IBD DATABASE

Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion



Ungaro et al., Gastroenterology ePublication ahead of print 2021 Sept 13. Doi 10.1053/j.gastro.2021.09.011 – PMID 34529987

JAMA Network Open.

Original Investigation | Infectious Diseases

Association Between Tumor Necrosis Factor Inhibitors and the Risk of Hospitalization or Death Among Patients With Immune-Mediated Inflammatory Disease and COVID-19

Zara Izadi, MPharm, MAS; Erica J. Brenner, MD; Satveer K. Mahil, PhD; Nick Dand, PhD; Zenas Z. N. Yiu, MBChB; Xian Zhang, PhD; Manasi Agrawal, MD; Jean-Frederic Colombel, MD; Milena A. Gianfrancesco, MPH, PhD; Kim Loreto Carmona, MD, PhD; Elsa F. Mateus, PhD; Saskia Lawson-Tovey, BA; Eva Klingberg, MD, PhD; Giovanna ... Ana Rita Cruz-Machado, MD; Ana Carolina Mazeda Pereira, MD; Rebecca Hassell, MD; Alexander Pfeil, MD; Ha... Laura Trupin, MPH; Stephanie Rush, BA; Patricia Katz, PhD; Gabriela Schmajuk, MD, MS; Lindsay Jacobsohn, B... Leanna Wise, MD; Emily L. Gilbert, MD, PhD; Ali Duarte-Garcia, MD, MSc; Maria O. Valenzuela-Almada, MD; Ca... Enrique R. Soriano, MD, MSc; Tiffany Y-T. Hsu, MD, PhD; Kristin M. D'Silva, MD; Jeffrey A. Sparks, MD, MMSc; ... Claudia Diniz Lopes Marques, PhD; Adriana Maria Kakehasi, MD, PhD; René-Marc Flipo, MD, PhD; Pascal Claud... Philippe Goupille, MD, PhD; Zachary S. Wallace, MD, MSc; Suleman Bhana, MD; Wendy Costello; Rebecca Grai... Jonathan S. Hausmann, MD; Jean W. Liew, MD, MS; Emily Sirotich, BSc; Paul Sufka, MD; Philip C. Robinson, M... Christopher E. M. Griffiths, MD; Jonathan N. Barker, MD; Catherine H. Smith, MD; Jinoos Yazdany, MD, MPH; ... for the Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 Infection (PsoProtect... Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD); and the COVID-19 Global Rheumat...

Abstract

IMPORTANCE Although tumor necrosis factor (TNF) inhibitors are widely prescribed globally because of their ability to ameliorate shared immune pathways across immune-mediated inflammatory diseases (IMIDs), the impact of COVID-19 among individuals with IMIDs who are receiving TNF inhibitors remains insufficiently understood.

OBJECTIVE To examine the association between the receipt of TNF inhibitor monotherapy and ... risk of COVID-19–associated hospitalization or death compared with other commonly prescribed ... immunomodulatory treatment regimens among adult patients with IMIDs.

DESIGN, SETTING, AND PARTICIPANTS This cohort study was a pooled analysis of data from 3 ... international COVID-19 registries comprising individuals with rheumatic diseases, inflammatory bowel disease, and psoriasis from March 12, 2020, to February 1, 2021. Clinicians directly reporte... COVID-19 outcomes as well as demographic and clinical characteristics of individuals with IMIDs ... confirmed or suspected COVID-19 using online data entry portals. Adults (age ≥18 years) with a ... diagnosis of inflammatory arthritis, inflammatory bowel disease, or psoriasis were included.

EXPOSURES Treatment exposure categories included TNF inhibitor monotherapy (reference ... treatment), TNF inhibitors in combination with methotrexate therapy, TNF inhibitors in combina... with azathioprine/6-mercaptopurine therapy, methotrexate monotherapy, azathioprine/6-mercaptopurine monotherapy, and Janus kinase (Jak) inhibitor monotherapy.

MAIN OUTCOMES AND MEASURES The main outcome was COVID-19–associated hospitalizati... or death. Registry-level analyses and a pooled analysis of data across the 3 registries were condu... using multilevel multivariable logistic regression models, adjusting for demographic and clinical characteristics and accounting for country, calendar month, and registry-level correlations.

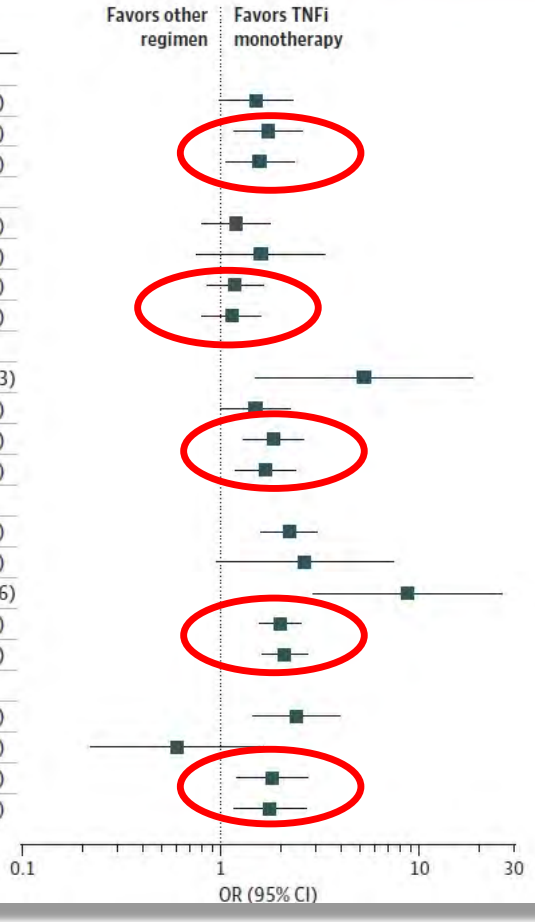
RESULTS A total of 6077 patients from 74 countries were included in the analyses; of those, 32... individuals (52.9%) were from Europe, 3563 individuals (58.6%) were female, and the mean (SD) age

(continued)

Author affiliations and article information are listed at the end of this article.

Figure. Adjusted Odd Ratios (ORs) of COVID-19–Associated Hospitalization or Death Among Patients Receiving Immunomodulatory Treatment Regimens vs Tumor Necrosis Factor Inhibitor (TNFi) Monotherapy

Treatment regimen	OR (95% CI)
TNFi plus AZA/6MP vs TNFi monotherapy	
SECURE-IBD registry	1.51 (0.98-2.31)
Pooled estimate (primary analysis)	1.74 (1.17-2.58)
Pooled estimate (sensitivity analysis)	1.57 (1.06-2.35)
TNFi plus MTX vs TNFi monotherapy	
GRA registry	1.20 (0.80-1.79)
SECURE-IBD registry	1.59 (0.76-3.34)
Pooled estimate (primary analysis)	1.18 (0.85-1.63)
Pooled estimate (sensitivity analysis)	1.14 (0.81-1.60)
AZA/6MP monotherapy vs TNFi monotherapy	
GRA registry	5.28 (1.51-18.43)
SECURE-IBD registry	1.50 (1.00-2.24)
Pooled estimate (primary analysis)	1.84 (1.30-2.61)
Pooled estimate (sensitivity analysis)	1.69 (1.19-2.39)
MTX monotherapy vs TNFi monotherapy	
GRA registry	2.21 (1.59-3.08)
SECURE-IBD registry	2.66 (0.95-7.43)
PsoProtect registry	8.76 (2.94-26.06)
Pooled estimate (primary analysis)	2.00 (1.57-2.56)
Pooled estimate (sensitivity analysis)	2.10 (1.62-2.72)
JAKi monotherapy vs TNFi monotherapy	
GRA registry	2.41 (1.46-3.99)
SECURE-IBD registry	0.60 (0.22-1.64)
Pooled estimate (primary analysis)	1.82 (1.21-2.73)
Pooled estimate (sensitivity analysis)	1.77 (1.16-2.69)

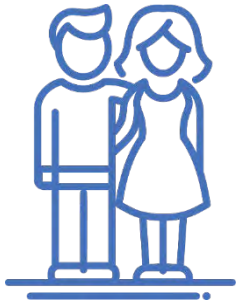


Children with IBD, Expectant Mothers AND Seniors

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+



Low risk of severe COVID-19

Increased risk among people with multiple chronic health conditions

Vaccines against COVID-19 recommended for all adults

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

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

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

Risk Profiles

IBD Profile

RISK

65+ years OR Under 65 years old , AND

- On systemic steroids
- Moderate/Severe active inflammation
- Moderate or severe malnutrition
- Requirement of parenteral nutrition

HIGH RISK

- Self isolate
- Refer to considerations for other family members and people who live with high-risk individuals

Under 65 years old *AND u*sing immunosuppressives or biologics

- Immunomodulators
- Anti-TNF biologics
- Anti-IL12/23 biologics
- Anti-leukocyte migration biologics
- JAK inhibitor small molecules

MEDIUM RISK

- Avoid indoor in-person meetings
- Wear a mask indoors or outdoors if close to others
- Follow local public health guidance for your community

<65 y AND NOT TAKING immunosuppressives, AND

- IBD in remission, no active inflammation
- Not malnourished
- No comorbidities (respiratory, cardiac, hypertension, diabetes)

Follow Public Health (PHAC) Guidelines

Follow public health guidelines for general population (physical distancing, hand hygiene, self-monitoring, etc.)

- Physical distancing
- Wear a mask indoors or outdoors if close to others
- Wash hands frequently
- Do not go to work/school if you have symptoms of COVID-19.

SECURE-IBD DATABASE

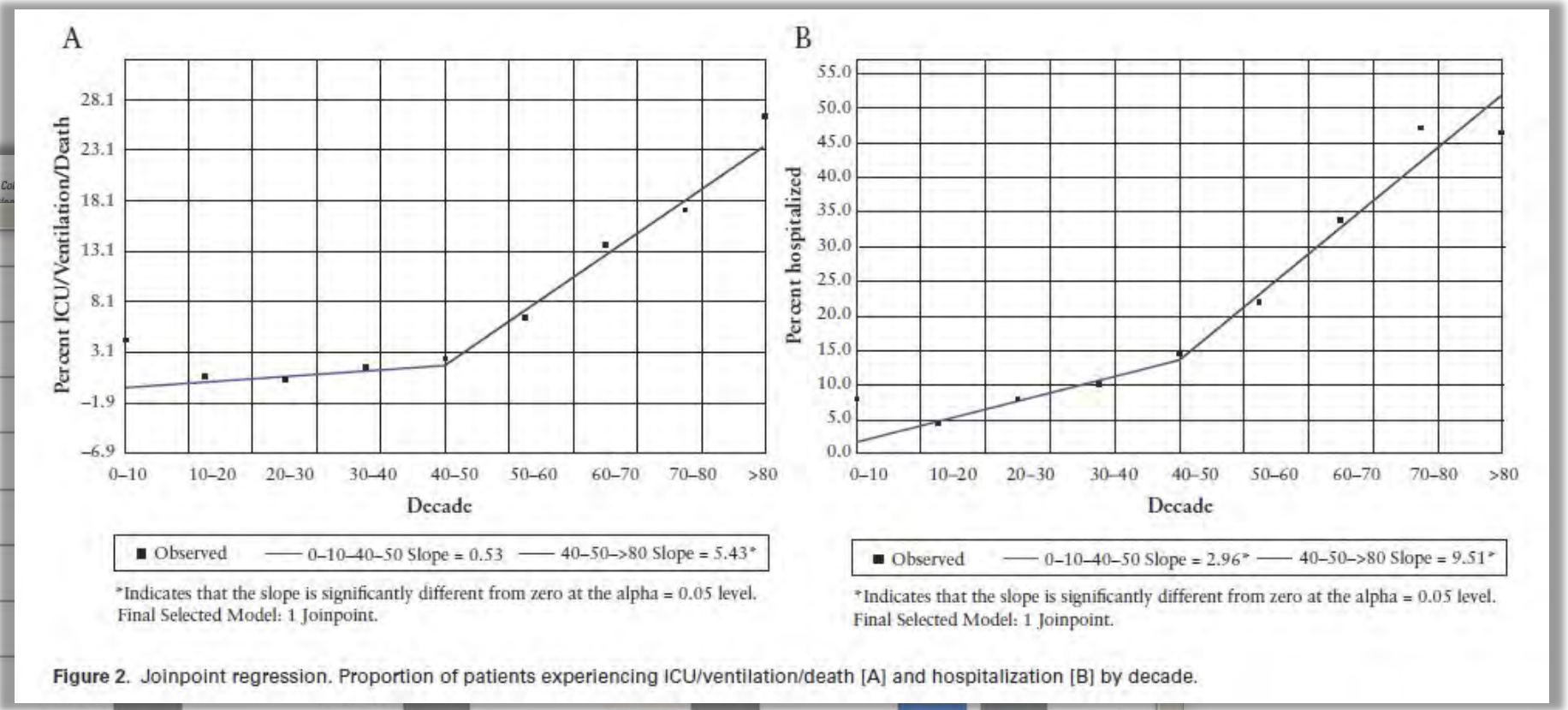


Figure 2. Joinpoint regression. Proportion of patients experiencing ICU/ventilation/death [A] and hospitalization [B] by decade.

Journal of Crohn's and Co

Original Article

Inflammatory Bowel Dise Associated with COVID-1 Younger Patients

Amanda Ricciuto,[a,b,c] Christopher A. L Gareth J. Walker,[h,i] Nicholas A. Kenne Gilaad G. Kaplan,[k] Michael D. Kappelr Jean-Frederic Colombel,[m,n] Erica. J. Br Walter Reinisch,[n] Anne M. Griffiths,[a,c,f]

[a]SickKids IBD Centre, Division of Gastroenterology, He [b]Child Health Evaluative Sciences, SickKids Research In Paediatrics, University of Toronto, Toronto, ON, Canada University, Newcastle upon Tyne, NE2 4HH, UK [g]Departme NHS Foundation Trust, Newcastle upon Tyne, NE1 4LP, UK University of Toronto, Toronto, ON, Canada [j]ICES, Toronto and South Devon NHS Foundation Trust, Torquay, TQ2 7AA Exeter NHS Foundation Trust, Exeter, EX2 5DW, UK [l]Exeter IB UK [k]Department of Medicine, University of Calgary, Calgary Chapel Hill, NC, USA [m]Icahn School of Medicine at Mount Vienna, Austria [o]Department of Gastroenterology, Hull Uni [p]Faculty of Health Sciences, University of Hull, Hull, HU6 7R

Corresponding author: Amanda Ricciuto, MD, PhD, The Hospit 813-7733; Fax: 416-813-4972; Email: amanda.ricciuto@sickkids.

Abstract

Background and Aims: Age is a major prognost inflammatory bowel disease [IBD] activity on CO between IBD activity and COVID-19 severity accor
Methods: We included IBD patients diagnosed w March 13, 2020 and August 3, 2021. Clinical IBD activi [PGA]. COVID-19-related outcomes were [1] inte death, and [2] hospitalization. Using generalized odds ratios [aOR, 95% confidence interval] for mo PGA, controlling for demographics, medications stratified analyses by age [≤50 vs >50 years].
Results: Among 6078 patients, adverse COVID-19 outcomes were more common with active IBD: ICU/ventilation/death in 3.6% [175/4898] of remission/mild, 4.9% [45/920] of moderate and 8.8% [23/260] of severe [$p < 0.001$]; and hospitalization in 13% [649/4898] of remission/mild, 19% [178/920] of moderate and 38% [100/260] of severe [$p < 0.001$]. Stratified by decade, effect sizes were larger for younger patients. In patients ≤50 years, severe PGA was independently associated with ICU/ventilation/death (aOR 3.27 [1.15–9.30]) and hospitalization (aOR 4.62 [2.83–7.55]). In

Ricciuto et al., J Crohn Colitis ePublication ahead of print 2021 Sept 27. doi 10.1093/ecco-jcc/jjab172 – PMID 34570886

PGA	ICU/Vent/death aOR (95% CI)		Hospitalization aOR (95% CI)	
	<50 y	≥50 y	<50 y	≥50 y
Remission/ mild	REF	REF	REF	REF
Moderate	1.62 (0.74 to 3.59)	1.10 (0.94 to 1.29)	1.44 (1.02 to 2.03)	1.53 (1.14 to 2.06)
Severe	3.27 (1.15 to 9.30)	0.89 (0.37 to 2.15)	4.62 (2.83 to 7.55)	0.90 (0.39 to 2.09)

Adjusted for: time period, sex, comorbidities, ethnicity, IBD type, medications (systematic steroids, anti-TNF monotherapy, anti-TNF combo therapy, IMM mono therapy, 5-ASA/SASP)

Ricciuto et al., J Crohn Colitis ePublication ahead of print 2021 Sept 27.
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Ricciuto et al., J Crohn Colitis ePublication ahead of print 2021 Sept 27. doi 10.1093/ecco-jcc/jjab172 – PMID 34570886

Changing Care Paradigms & Mental Health

Pre-pandemic

1
Book appointment

4
Referral/ need for follow-up

2
Travel to hospital/clinic

3
Consultation/ exam/testing

Mid-pandemic

1
Book appointment

2
Virtual consultation (televisit/phone visit) with multiple healthcare providers (non-emergent)

3
Need for in-person visit/test/referral/ follow-up possible

Post-pandemic

1
Mobile apps/wearable tech objective measures of disease activity allow for remote monitoring by healthcare providers

2
Needs-based assessment allows healthcare providers to recommend virtual or in-person follow-up

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)

Youth in Canada have experienced the highest impact to mental health

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

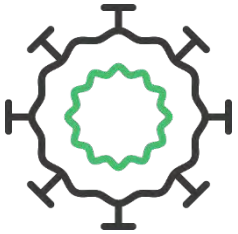

2021
IMPACT OF
COVID-19 &
INFLAMMATORY
BOWEL DISEASE
IN CANADA
Crohn's and Colitis Canada
Crohn et Colite Canada

Vaccines

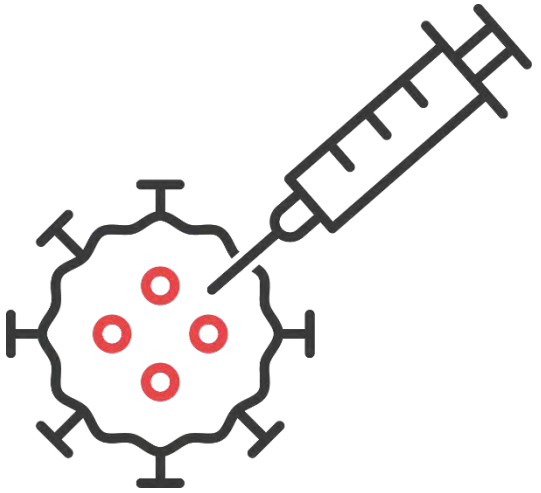
mRNA
(messenger ribonucleic acid)

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)

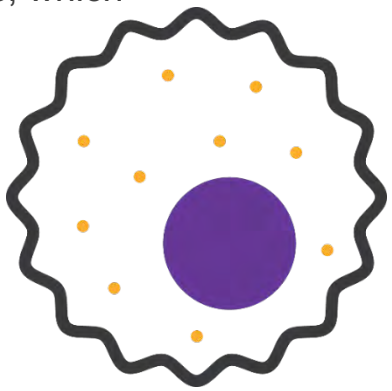


A non-infectious virus is engineered to be harmless to humans, but to carry genetic material for the spike protein from the SARS-CoV-2 virus to host cells



Once injected into the muscle, these non-infectious vaccines teach the host's cells to produce only the SARS-CoV-2 spike protein, which is harmless on its own

The body recognises the foreign spike proteins and mounts an immune response to eradicate them, resulting in memory T and B lymphocyte cells, which remain in the bloodstream to quickly and efficiently fight off any future infections



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.

Gastroenterology 2021;161:827–836

Effectiveness of SARS-CoV-2 Vaccination in a Veterans Affairs Cohort of Patients With Inflammatory Bowel Disease With Diverse Exposure to Immunosuppressive Medications

Nabeel Khan[1,2,*] and Nadim Mahmud[1,2,3,4,*]

[1]Division of Gastroenterology, Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, Pennsylvania; [2]Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [3]Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania, Philadelphia, Pennsylvania; and [4]Leonard Davis Institute of Health Economics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania

BACKGROUND & AIMS: Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly expanded; however, clinical trials excluded patients taking immunosuppressive medications such as those with inflammatory bowel disease (IBD). Therefore, we explored real-world effectiveness of coronavirus disease 2019 (COVID-19) vaccination on subsequent infection in patients with IBD with diverse exposure to immunosuppressive medications. **METHODS:** This was a retrospective cohort study of patients in the Veterans Health Administration with IBD diagnosed before December 18, 2020, the start date of the Veterans Health Administration patient vaccination program. IBD medication exposures included mesalamine, thiopurines, anti-tumor necrosis factor biologic agents, vedolizumab, ustekinumab, tofacitinib, methotrexate, and corticosteroid use. We used inverse probability weighting and Cox's regression with vaccination status as a time-updating exposure and computed vaccine effectiveness from incidence rates. **RESULTS:** The cohort comprised 14,697 patients, 7321 of whom received at least 1 vaccine dose (45.2% Pfizer, 54.8% Moderna). The cohort had median age 68 years, 92.2% were men, 80.4% were White, and 61.8% had ulcerative colitis. In follow-up data through April 20, 2021, unvaccinated individuals had the highest raw proportion of SARS-CoV-2 infection (197 [1.34%] vs 7 [0.11%] fully vaccinated). Full vaccination status, but not partial vaccination status, was associated with a 69% reduced hazard of infection relative to an unvaccinated status (hazard ratio, 0.31, 95% confidence interval, 0.17–0.56; $P < .001$), corresponding to an 80.4% effectiveness. **CONCLUSIONS:** Full vaccination (> 7 days after the second dose) against SARS-CoV-2 infection has an ~80.4% effectiveness in a broad IBD cohort with diverse exposure to immunosuppressive medications. These results may serve to increase patient and provider willingness to pursue vaccination in these settings.

Keywords: SARS-CoV-2 Vaccine; Inflammatory Bowel Disease; Effectiveness; Immunosuppressive Medications; Veterans Affairs Healthcare System.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is a grave threat to public health, with more than 28 million people reported to have been infected and more than half a million deaths in the United States alone as of April 2, 2021.[1] Inflammatory bowel disease (IBD), consisting of ulcerative colitis (UC) and Crohn's disease (CD), is a chronic inflammatory disorder of the gastrointestinal tract of unknown etiology. The pathophysiology of IBD involves dysregulation of the mucosal immune system and is usually treated with immunomodulatory and/or immunosuppressive medications, which can lead to an increased risk of infection.[2–4] To date, however, the incidence of SARS-CoV-2 among all patients with IBD appears to be comparable to that observed in the general population.[5–8]

To curb the ongoing pandemic caused by SARS-CoV-2 infection, vaccine development has been undertaken at an unprecedented pace, and numerous candidates have been authorized or are under development.[9] At present, 2 vaccines are in wide clinical use in the US, the BNT162b2 messenger RNA coronavirus disease 2019 (COVID-19) vaccine from Pfizer and the messenger RNA-1273 SARS-CoV-2 vaccine from Moderna.[10,11] Both vaccines have been shown to have greater than 90% efficacy, and to date, more than 100 million vaccines have been administered in the US. However, the seminal clinical trials excluded patients taking immunosuppressive medications or those with immunosuppressive conditions, thus the effectiveness in the population of patients with IBD is unknown.

To evaluate the effectiveness of SARS-CoV-2 vaccination in the IBD population and the potential impact of immunosuppressive medications, we identified in the Veterans Health Administration (VHA) a national cohort of patients with IBD. Our secondary aims were to evaluate the impact of vaccination on severe SARS-CoV-2 infection and all-cause mortality. The VHA is the largest integrated health care system in the US, serving more than 9 million veterans every year.[12] As of April 22, 2021, more than 2.1 million veterans have been fully vaccinated.[13] The VHA has also

*Authors share co-first authorship.

Abbreviations used in this paper: CD, Crohn's disease; CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; IBD, inflammatory bowel disease; IPW, inverse probability weight(s) (ed) (ing); IQR, interquartile range; NLP, natural language processing; PS, propensity score; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SMD, standardized mean difference; TNF, tumor necrosis factor; UC, ulcerative colitis; VHA, Veterans Health Administration.

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2021.05.044

Gastroenterology 2021;161:1715–1717

RESEARCH LETTERS

BNT162b2 Messenger RNA COVID-19 Vaccine Effectiveness in Patients With Inflammatory Bowel Disease: Preliminary Real-World Data During Mass Vaccination Campaign

A 2-dose regimen of the BNT162b2 messenger (m) RNA COVID-19 vaccine (Pfizer-BioNTech; Pfizer, New York, NY) has demonstrated 95% efficacy in preventing COVID-19 in a phase III placebo-controlled randomized clinical trial[1] and in real-world data analyses.[2,3]

Patients with inflammatory bowel disease (IBD) treated with immune-modifying agents are considered partially immunosuppressed, and thus, the International Organization for the Study of Inflammatory Bowel Disease (IOIBD) recommends that patients with IBD should be vaccinated against COVID-19 and that vaccination should not be deferred in patients receiving immune-modifying therapies.[4] Because patients with immune conditions (including IBD) were excluded from the COVID-19 vaccine clinical trials, it is important to describe accumulating real-world data.[5]

In Israel, patients with IBD were given priority for early vaccination in the campaign, which is, as of June 23, 2021, the most extensive worldwide (63.6% of the total population received at least 2 doses, and 59.5% of the population was fully vaccinated).[6]

This study is a preliminary report of the effect of mass vaccination in patients with IBD.

This retrospective cohort study was conducted using data from the Maccabi Healthcare Services (MHS) central computerized database. MHS is the second largest state-mandated health care provider in Israel, covering >2.5 million members (25% of the population) and is a representative sample of the Israeli population.

To evaluate vaccine effectiveness, this study included individuals from the MHS IBD registry aged ≥16 years who received the BNT162b2 mRNA COVID-19 vaccine and matched patients (1:3) who were vaccinated between December 19, 2020 and March 10, 2021. Individual matching was performed based on sex, birth year, coexisting comorbidities, and month of the first vaccination dose. IBD status was defined according to the MHS IBD registry based on physician diagnosis and dispensed medications.[7]

The analysis excluded patients with a history of a positive polymerase chain reaction (PCR) result or a diagnosis of COVID-19 any time before the first BNT162b2 vaccination. All eligible patients were required to have a minimum of 30 days of follow-up after the second vaccine dose date, referred to as the "index date," to observe study outcomes. Retrospective follow-up lasted from the index date until April 11, 2021 (details are provided in the Supplementary Text). The MHS Ethics Committee approved the study protocol.

The study included 12,231 patients with IBD and 36,254 matched patients. Overall, 50.0% were women, and the mean age was 47 ± 17 years in both groups. Follow-up was a median of 71 days (interquartile range, 52–80 days), and the interval between vaccines was a median of 21 days (interquartile range, 20–21 days). Baseline characteristics and positive PCR result by disease type and treatment are presented in Supplementary Table 1.

Breakthrough infection rates >7 days after the second dose were 0.19 % in patients with IBD and 0.15% in matched patients and after >14 days after the second dose were 0.14% and 0.10%, respectively. The calculated relative risk (RR) for IBD was 1.21 (95% confidence interval [CI], 0.74–1.97) >7 days after the second dose and 1.26 (95% CI, 0.71–2.23) >14 days after the second dose. The Mantel-Cox log-rank test from the Kaplan-Meier survival analysis (Figure 1*A*) was not statistically significant ($P = .430$). Of 23 patients with IBD who had a positive PCR result >7 days after the second dose, 9 had symptoms, 2 were hospitalized, and 1 died (details in Supplementary Table 2*a*).

Compared with their matched patients, patients with Crohn's disease (CD) were at a greater risk for breakthrough infection ($P = .055$), while no significant difference ($P = .310$) was shown among patients with ulcerative colitis (UC) (Figure 1*B* and *C*). The RR for CD and matched patients was 1.52 (95% CI, 0.69–3.28) >7 days after the second dose and 1.82 (95% CI, 0.69–4.79) >14 days after the second dose, whereas for UC and matched patients, the RR was 0.53 (95% CI, 0.18–1.58) >7 days after the second dose and 0.95 (95% CI, 0.28–3.81) >14 days after the second dose.

In multivariable Cox proportional hazard models, patients with CD had an elevated risk for breakthrough infection compared with patients with UC >7 days and >14 days after the second dose, with hazard ratios of 3.56 (95% CI, 1.29–9.83) and 3.38 (95% CI, 1.07–10.64), respectively. No increased risk was demonstrated for patients treated with immune-modifying therapies (Supplementary Table 2*a* and *b*).

In this study, we describe the effectiveness of the BNT162b2 mRNA COVID-19 vaccine in patients with IBD. As demonstrated in the general population, the vaccine is highly efficient, with a very low absolute breakthrough infection rate (0.1%) for fully vaccinate patients.

Our large cohort allowed us to explore the effect of immune-modifying treatments in patients with IBD on the risk for COVID-19 infection after vaccination. A publication by the IOIBD recommended that patients with IBD vaccinated against COVID-19 be counseled that vaccine efficacy may be decreased when receiving systemic corticosteroids.[4] Despite the wide use of immune-modifying medications,

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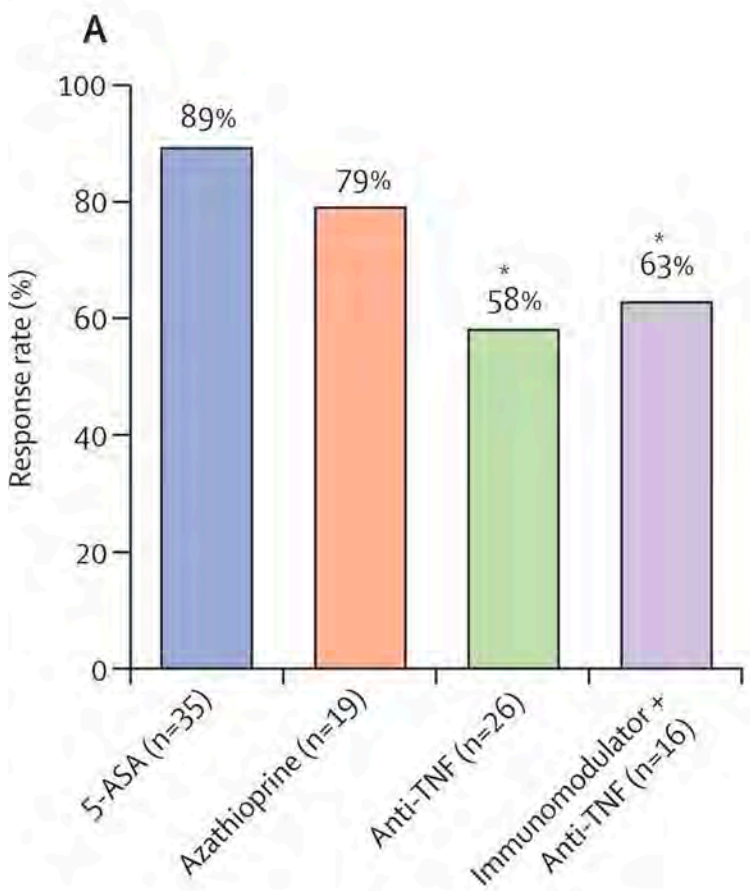
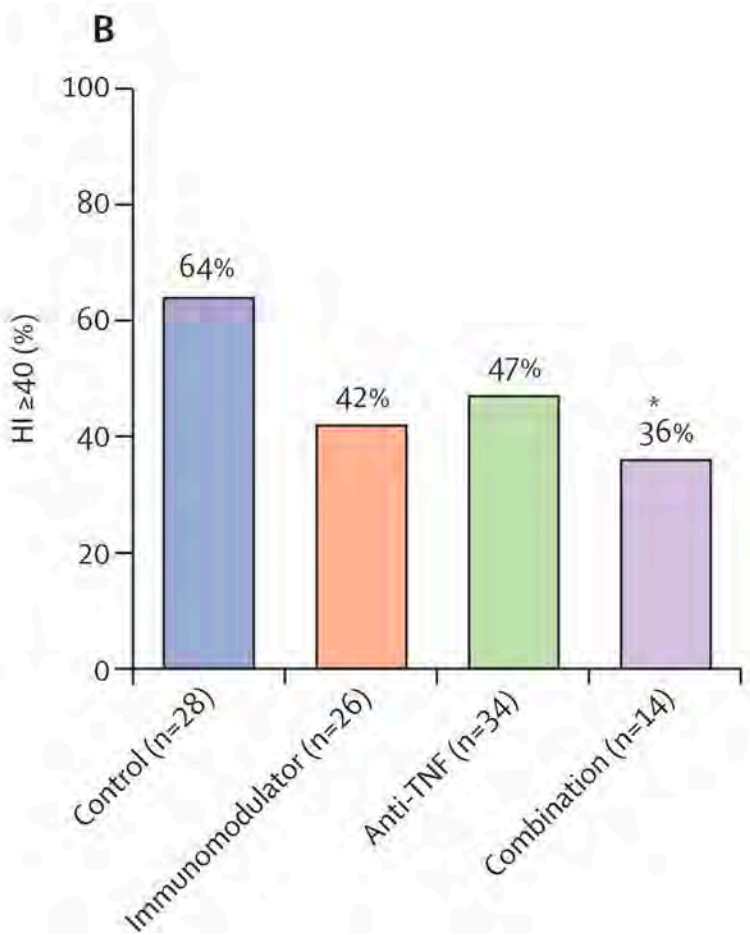
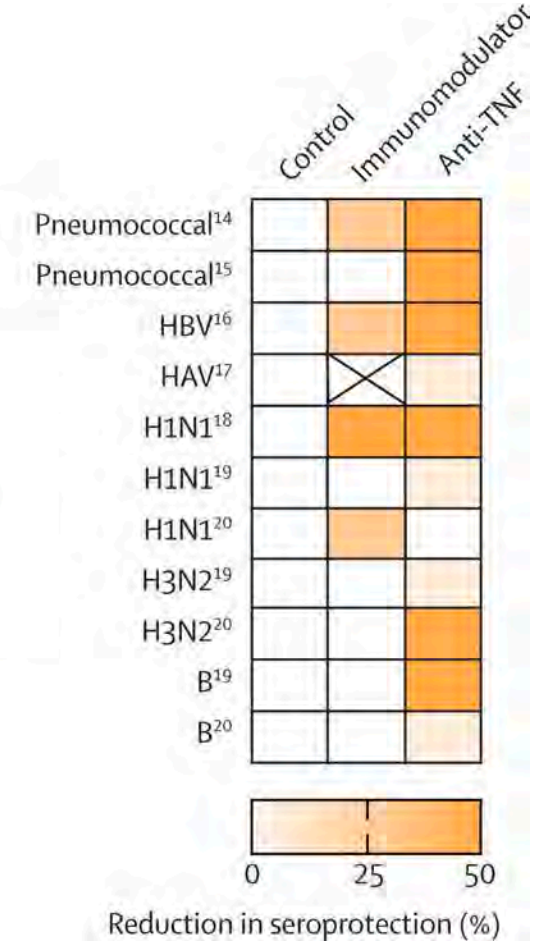
0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2021.06.076

Impaired vaccination responses in immunosuppressed IBD patients[1–7]

Slide courtesy of
Dr. Charlie Lees,
CCC COVID-19 Webinar,
April 29, 2021





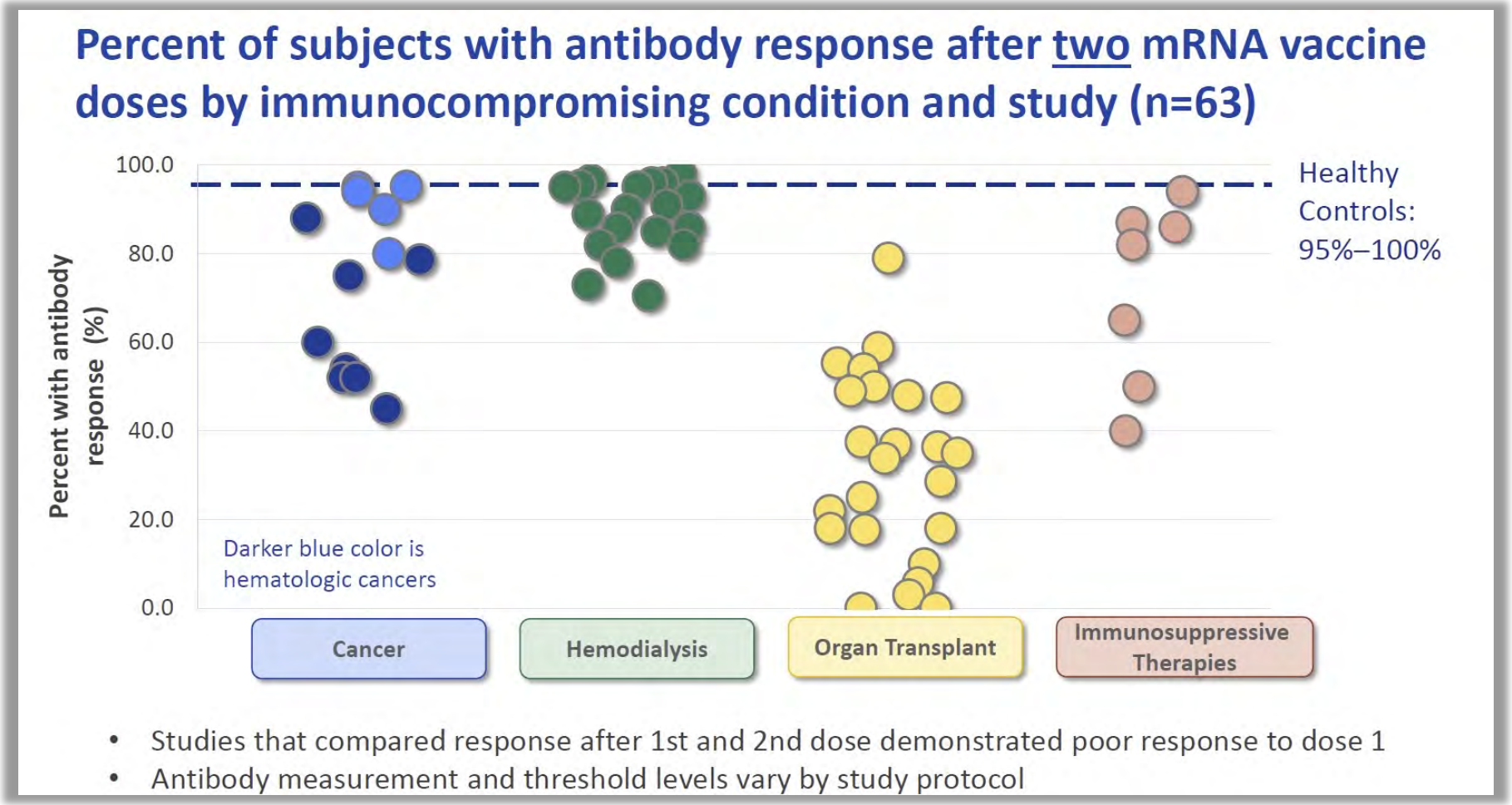


*p<0.05 for anti-TNF/combined response vs controls.

5-ASA, 5-aminosalicylic acid; H1N1, influenza A subtype H1N1; H3N2, influenza A subtype H3N2; HAV, hepatitis A virus; HBV, hepatitis B virus; IBD, inflammatory bowel disease; IM, immunomodulator; TNF, tumour necrosis factor.

1. Adapted from Fiorino G, et al. *Inflamm Bowel Dis*. 2012;18:1042–7; 2. Lee CK, et al. *J Crohns Colitis*. 2014;8:384–91; 3. Pratt PK, et al. *Inflamm Bowel Dis*. 2018;24:380–6; 4. Park SH, et al. *Inflamm Bowel Dis*. 2014;20:69–74; 5. Adapted from Cullen G, et al. *Gut*. 2012;61:385–91; 6. Lu Y, et al. *Am J Gastroenterol*. 2009;104:444–53; 7. Hagihara Y, et al. *J Crohns Colitis*. 2014;8:223–33.

IMMUNOCOMPROMISED PEOPLE



Slide from:
Sara Oliver MD, MSPH - ACIP Meeting, July 22, 2021

IMMUNOCOMPROMISED PEOPLE

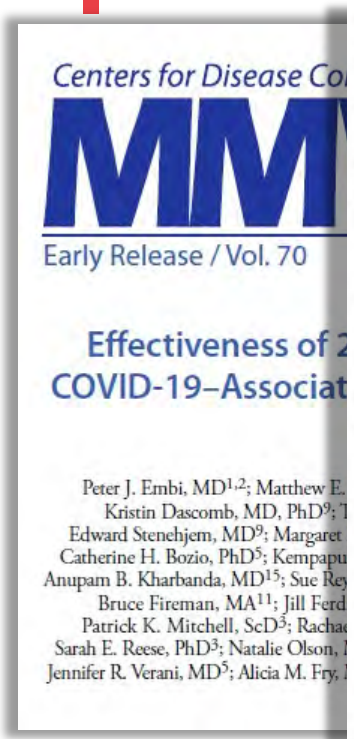
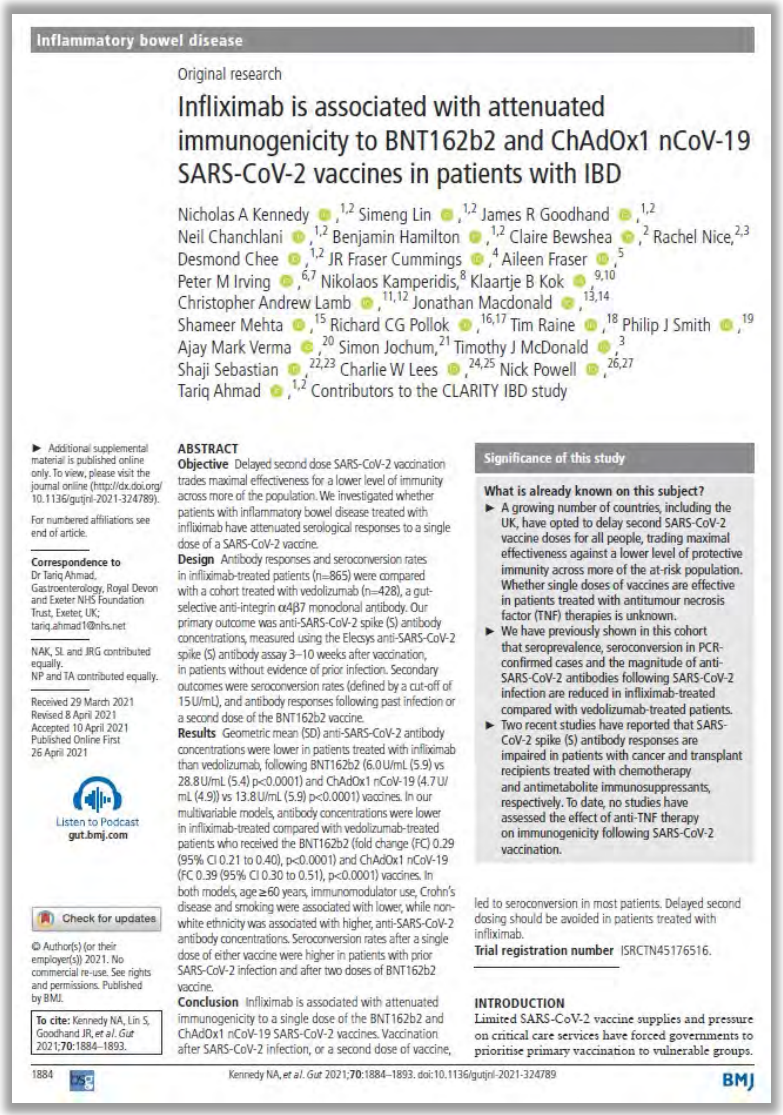


TABLE 3. Two-dose mRNA COVID-19 vaccine effectiveness* against laboratory-confirmed COVID-19–associated hospitalization† among subgroups of adults aged ≥18 years with specific types of conditions and presumed to be immunocompromised (20,101)§ — nine states,¶ January–September 2021

Condition (no. of adults)	Total	SARS-CoV-2–positive tests, no. (row %)	VE,** % (95% CI)
Solid malignancy†† (8,887)			
Unvaccinated	3,986	304 (7.6)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	4,901	106 (2.2)	79 (73–84)
Vaccinated with 2 Moderna (mRNA-1273) vaccine doses§§	2,053	30 (1.5)	85 (76–91)
Vaccinated with 2 Pfizer-BioNTech (BNT162b2) vaccine doses§§	2,848	76 (2.7)	72 (62–80)
Hematologic malignancy¶¶ (2,790)			
Unvaccinated	1,156	130 (11.2)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	1,634	86 (5.3)	74 (62–83)
Vaccinated with 2 Moderna vaccine doses§§	660	26 (3.9)	85 (74–92)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	974	60 (6.2)	62 (42–75)
Rheumatologic or inflammatory disorder* (5,024)**			
Unvaccinated	2,380	383 (16.1)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	2,644	123 (4.6)	81 (75–86)
Vaccinated with 2 Moderna vaccine doses§§	1,053	48 (4.6)	78 (65–86)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	1,591	75 (4.7)	78 (69–84)
Other intrinsic immune condition or immunodeficiency††† (6,380)			
Unvaccinated	3,418	429 (12.6)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	2,962	137 (4.6)	73 (66–80)
Vaccinated with 2 Moderna vaccine doses§§	1,199	42 (3.5)	81 (71–87)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	1,763	95 (5.4)	64 (50–74)
Organ or stem cell transplant§§§ (1,416)			
Unvaccinated	607	92 (15.2)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	809	80 (9.9)	59 (38–73)
Vaccinated with 2 Moderna vaccine doses§§	337	31 (9.2)	70 (46–83)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	472	49 (10.4)	45 (13–66)

Embi PJ, et al., MMWR 2021; ePublication 2 Nov 2021

IBD PATIENTS ON INFLIXIMAB HAVE ATTENUATED REPONSE AND ANTIBODIES DECAY MORE RAPIDLY



Inflammatory bowel disease

Original research

Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD

Nicholas A Kennedy [1,2] Simeng Lin [1,2] James R Goodhand [1,2] Neil Chanchlani [1,2] Benjamin Hamilton [1,2] Claire Bewshea [2] Rachel Nice [2,3] Desmond Chee [1,2] JR Fraser Cummings [4] Aileen Fraser [5] Peter M Irving [6,7] Nikolaos Kamperidis [8] Klaartje B Kok [9,10] Christopher Andrew Lamb [11,12] Jonathan Macdonald [13,14] Shameer Mehta [15] Richard CG Pollok [16,17] Tim Raine [18] Philip J Smith [19] Ajay Mark Verma [20] Simon Jochum [21] Timothy J McDonald [3] Shaji Sebastian [22,23] Charlie W Lees [24,25] Nick Powell [26,27] Tariq Ahmad [1,2] Contributors to the CLARITY IBD study

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/gutjnl-2021-324789).

For numbered affiliations see end of article.

Correspondence to
Dr Tariq Ahmad, Gastroenterology, Royal Devon and Exeter NHS Foundation Trust, Exeter, UK; tariq.ahmad1@nhs.net

NAK, SL and JRG contributed equally.
NP and TA contributed equally.

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ABSTRACT

Objective Delayed second dose SARS-CoV-2 vaccination trades maximal effectiveness for a lower level of immunity across more of the population. We investigated whether patients with inflammatory bowel disease treated with infliximab have attenuated serological responses to a single dose of a SARS-CoV-2 vaccine.

Design Antibody responses and seroconversion rates in infliximab-treated patients (n=865) were compared with a cohort treated with vedolizumab (n=428), a gut-selective anti-integrin α4β7 monoclonal antibody. Our primary outcome was anti-SARS-CoV-2 spike (S) antibody concentrations, measured using the Elecsys anti-SARS-CoV-2 spike (S) antibody assay 3–10 weeks after vaccination, in patients without evidence of prior infection. Secondary outcomes were seroconversion rates (defined by a cut-off of 15 U/mL), and antibody responses following past infection or a second dose of the BNT162b2 vaccine.

Results Geometric mean (SD) anti-SARS-CoV-2 antibody concentrations were lower in patients treated with infliximab than vedolizumab, following BNT162b2 (6.0 U/mL (5.9) vs 28.8 U/mL (5.4) p<0.0001) and ChAdOx1 nCoV-19 (4.7 U/mL (4.9)) vs 13.8 U/mL (5.9) p<0.0001) vaccines. In our multivariable models, antibody concentrations were lower in infliximab-treated compared with vedolizumab-treated patients who received the BNT162b2 (fold change (FC) 0.29 (95% CI 0.21 to 0.40), p<0.0001) and ChAdOx1 nCoV-19 (FC 0.39 (95% CI 0.30 to 0.51), p<0.0001) vaccines. In both models, age ≥60 years, immunomodulator use, Crohn's disease and smoking were associated with lower, while non-white ethnicity was associated with higher, anti-SARS-CoV-2 antibody concentrations. Seroconversion rates after a single dose of either vaccine were higher in patients with prior SARS-CoV-2 infection and after two doses of BNT162b2 vaccine.

Conclusion Infliximab is associated with attenuated immunogenicity to a single dose of the BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines. Vaccination after SARS-CoV-2 infection, or a second dose of vaccine, led to seroconversion in most patients. Delayed second dosing should be avoided in patients treated with infliximab.

Trial registration number ISRCTN45176516.

Significance of this study

What is already known on this subject?

- A growing number of countries, including the UK, have opted to delay second SARS-CoV-2 vaccine doses for all people, trading maximal effectiveness against a lower level of protective immunity across more of the at-risk population. Whether single doses of vaccines are effective in patients treated with antitumour necrosis factor (TNF) therapies is unknown.
- We have previously shown in this cohort that seroprevalence, seroconversion in PCR-confirmed cases and the magnitude of anti-SARS-CoV-2 antibodies following SARS-CoV-2 infection are reduced in infliximab-treated compared with vedolizumab-treated patients.
- Two recent studies have reported that SARS-CoV-2 spike (S) antibody responses are impaired in patients with cancer and transplant recipients treated with chemotherapy and antimetabolite immunosuppressants, respectively. To date, no studies have assessed the effect of anti-TNF therapy on immunogenicity following SARS-CoV-2 vaccination.

INTRODUCTION

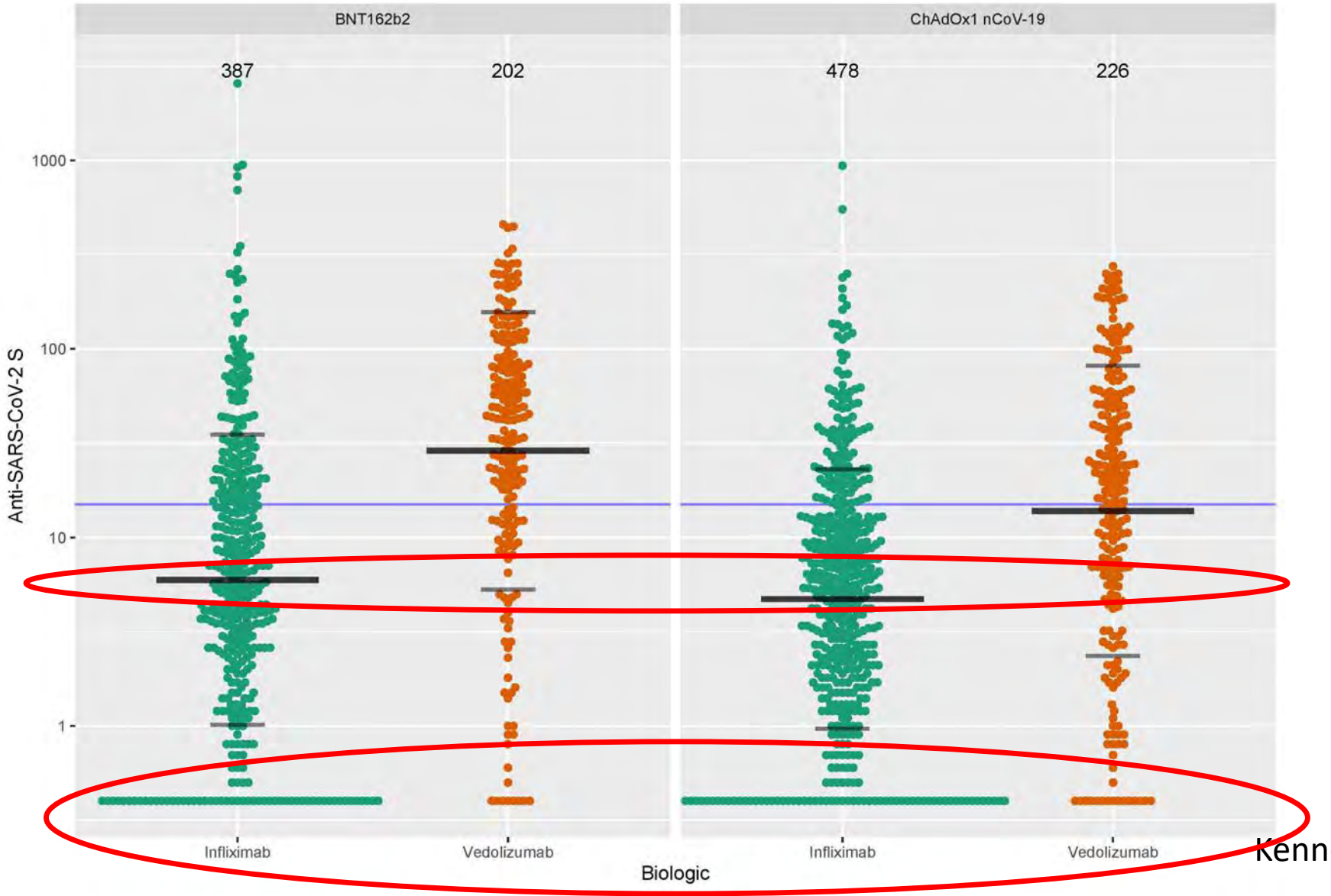
Limited SARS-CoV-2 vaccine supplies and pressure on critical care services have forced governments to prioritise primary vaccination to vulnerable groups.

CLARITY IBD

Kennedy et al., Gut 2021; 70: 1884-93

How does Spike antibody concentration compare in patients on infliximab and vedolizumab?

Slide courtesy of
Dr. Charlie Lees,
CCC COVID-19 Webinar,
April 29, 2021



Increasing protection

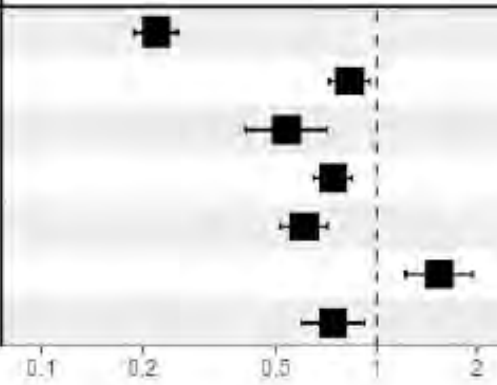
Decreasing protection

Kennedy et al., Gut 2021; 70: 1884-1893

WHAT ABOUT OTHER IMMUNOMODULATORS?

All

Variable	N	Fold change (95% CI)	p
Infliximab (vs vedolizumab)	2034/2950	0.22 (0.19, 0.26)	<0.0001
Thiopurine	1231/2950	0.83 (0.72, 0.95)	0.0090
Methotrexate	165/2950	0.54 (0.41, 0.71)	<0.0001
Crohn's disease (vs UC or IBDU)	1699/2950	0.74 (0.65, 0.85)	<0.0001
Age ≥ 60	571/2950	0.61 (0.52, 0.71)	<0.0001
Non-white ethnicity	241/2950	1.54 (1.22, 1.94)	0.00023
Current smoker	283/2950	0.74 (0.60, 0.92)	0.0062



Extended Data Figure 1: Exponentiated coefficients of linear regression models of log(anti-S RBD antibody concentration)

Kennedy et al., Gut 2021; 70: 1884-93

VACCINE RECOMMENDATIONS FOR GOVERNMENT

Crohn's and Colitis Canada
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Apr 7, 2021

PEOPLE ON IMMUNOSUPPRESSION THERAPIES REQUIRE TIMELY ACCESS TO THE SECOND DOSE OF COVID-19 VACCINES

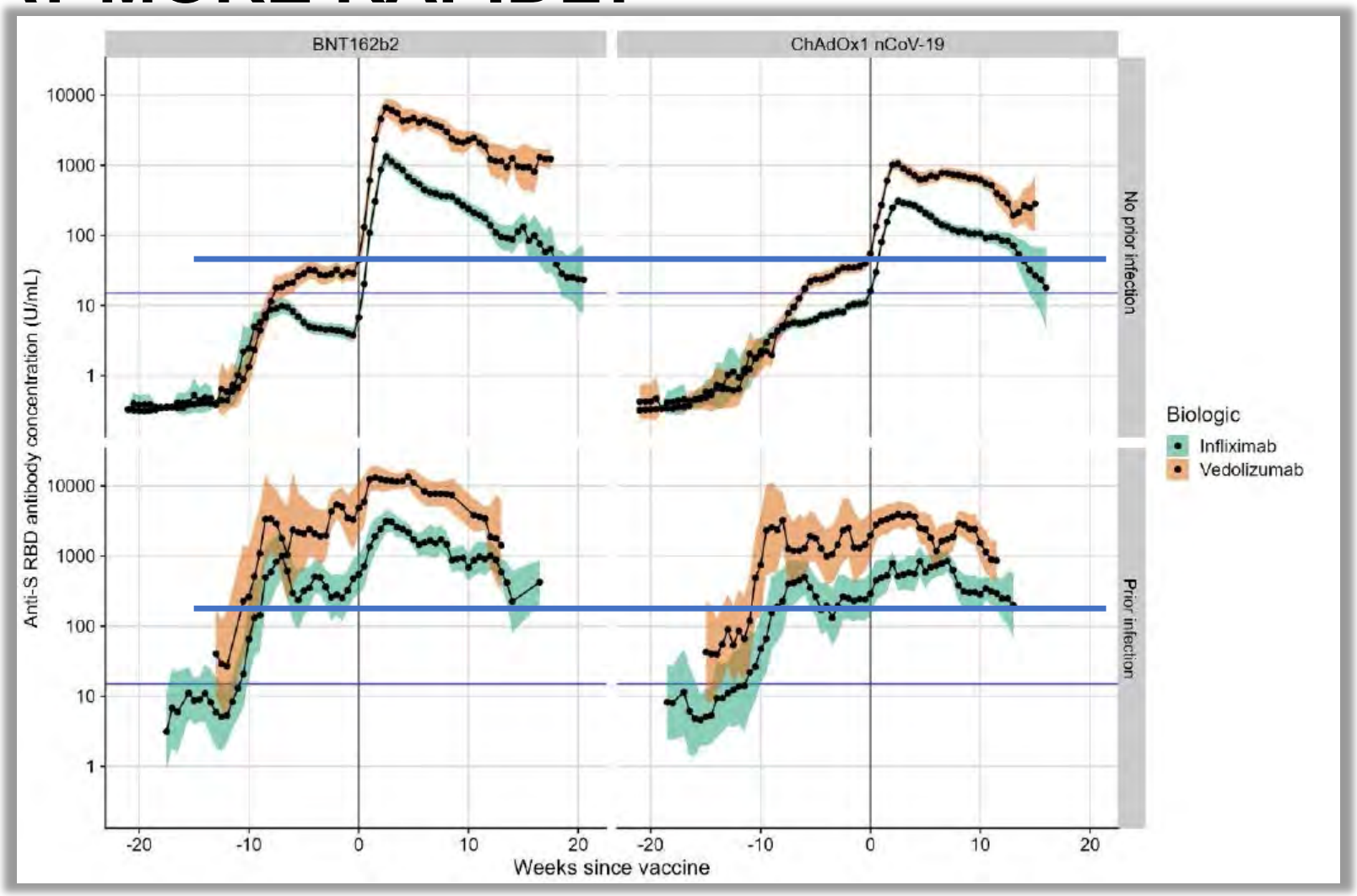
RESEARCH RAISES QUESTIONS OVER SAFETY OF DELAYING THE SECOND VACCINE DOSE

The COVID-19 & IBD Task Force calls on the National Advisory Committee on Immunization (NACI) to include IBD patients on immunosuppression therapies on the list of exceptions for extended

crohnsandcolitis.ca/About-Crohn-s-Colitis/COVID-19-and-IBD/Vaccines

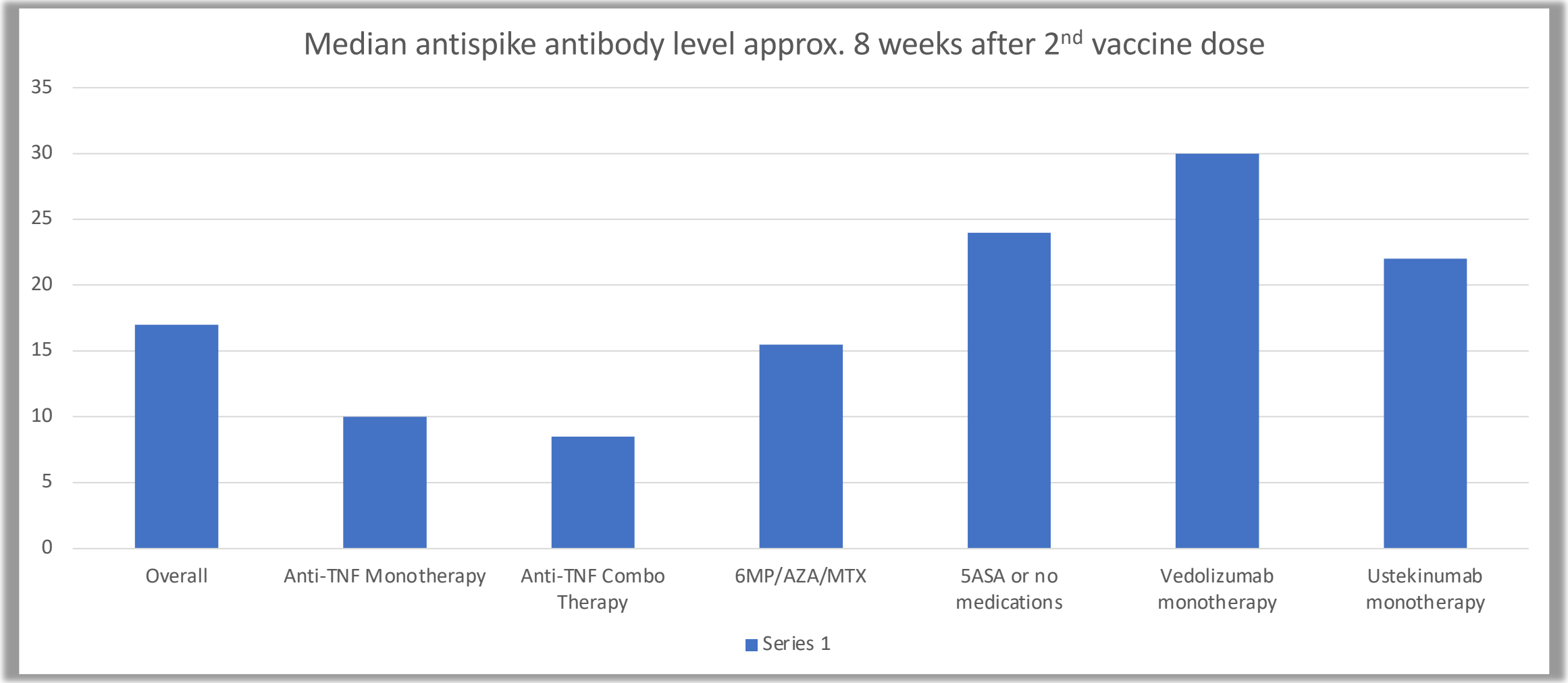
Crohn's and Colitis Canada
Crohn et Colite Canada

IBD PATIENTS ON INFLIXIMAB HAVE ATTENUATED REPONSE AND ANTIBODIES DECAY MORE RAPIDLY



Kennedy et al., Gut 2021; 70: 1884-93

WHAT ABOUT OTHER IMMUNOMODULATORS?



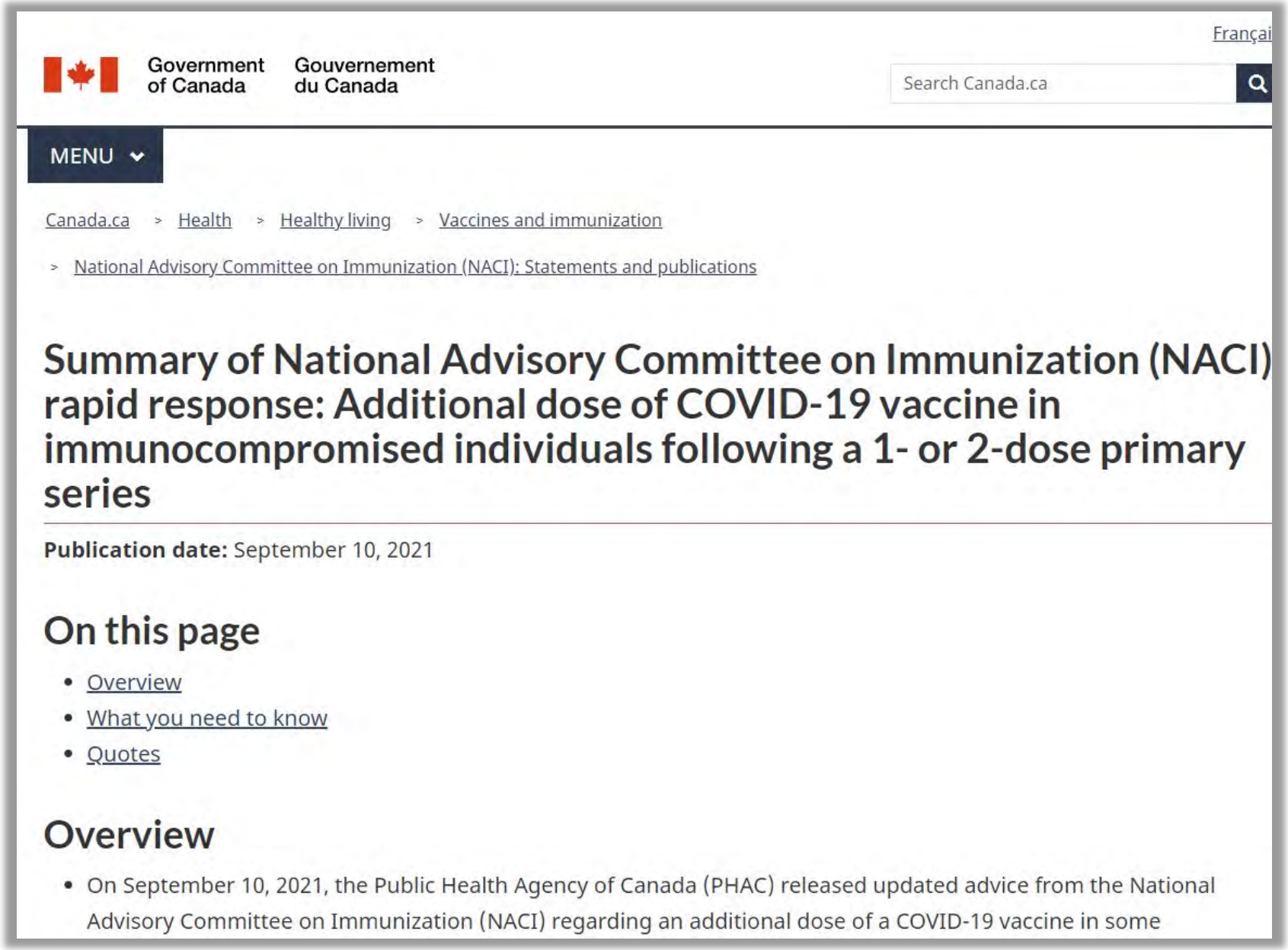
Kappelman MD et al., *Gastroenterology* 2021; 161(4): 1340-43

COVID-19 TASK FORCE RECOMMENDATIONS (August 24, 2021)

1. We recommend that people with IBD who are receiving medications that suppress their immune system (systemic corticosteroids, thiopurines, methotrexate, and biologics) have access to a 3rd COVID-19 vaccine dose between 14–18 weeks after their second vaccine dose.

2. We recommend that unimmunized people with IBD receive the COVID-19 vaccine as soon as possible.

3. We strongly encourage employers and schools to consider **mandatory vaccination policies** so as to minimize the risk of serious and deadly COVID-19 in people living with Crohn's disease and ulcerative colitis.



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> National Advisory Committee on Immunization (NACI): Statements and publications

Summary of National Advisory Committee on Immunization (NACI) rapid response: Additional dose of COVID-19 vaccine in immunocompromised individuals following a 1- or 2-dose primary series

Publication date: September 10, 2021

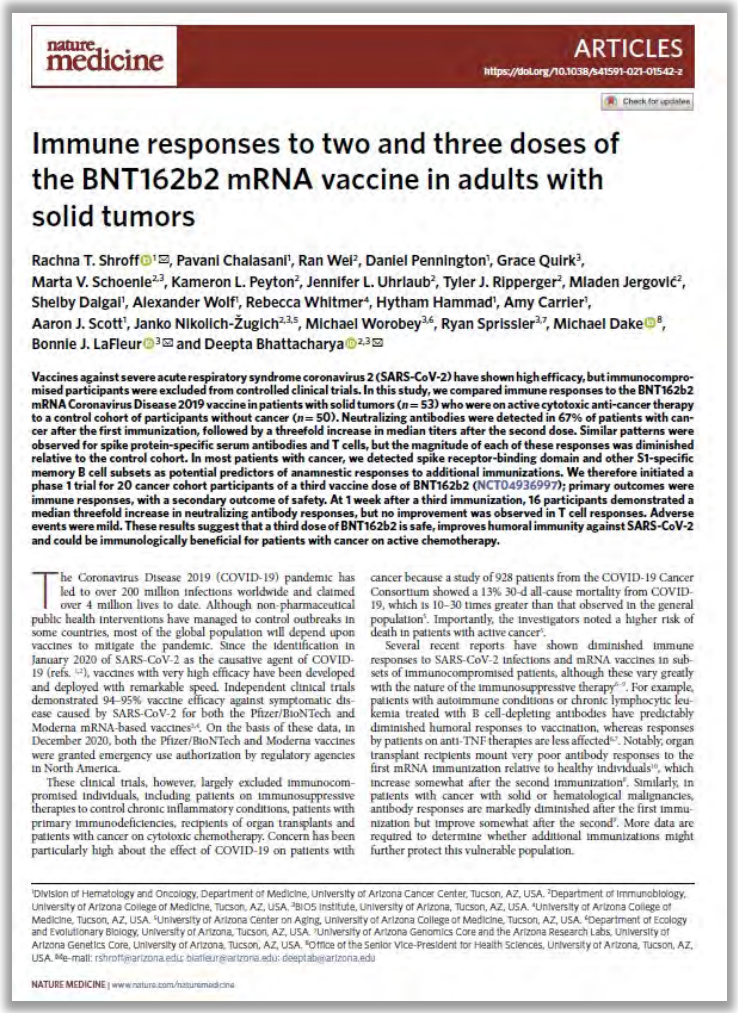
On this page

- Overview
- What you need to know
- Quotes

Overview

- On September 10, 2021, the Public Health Agency of Canada (PHAC) released updated advice from the National Advisory Committee on Immunization (NACI) regarding an additional dose of a COVID-19 vaccine in some

3rd VACCINE DOSE: EVIDENCE IN IMMUNOSUPPRESSED PEOPLE



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ARTICLES

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Immune responses to two and three doses of the BNT162b2 mRNA vaccine in adults with solid tumors

Rachna T. Shroff[1]✉, Pavani Chalasani[1], Ran Wei[2], Daniel Pennington[1], Grace Quirk[3], Marta V. Schoenle[2,3], Kameron L. Peyton[2], Jennifer L. Uhrlaub[2], Tyler J. Ripperger[2], Mladen Jergovic[2], Shelby Dalgal[1], Alexander Wolf[1], Rebecca Whitmer[4], Hytham Hammad[1], Amy Carrier[1], Aaron J. Scott[1], Janko Nikolich-Žugich[2,3,5], Michael Worobey[3,6], Ryan Sprissler[3,7], Michael Dake[8], Bonnie J. LaFleur[3]✉ and Deepta Bhattacharya[2,3]✉

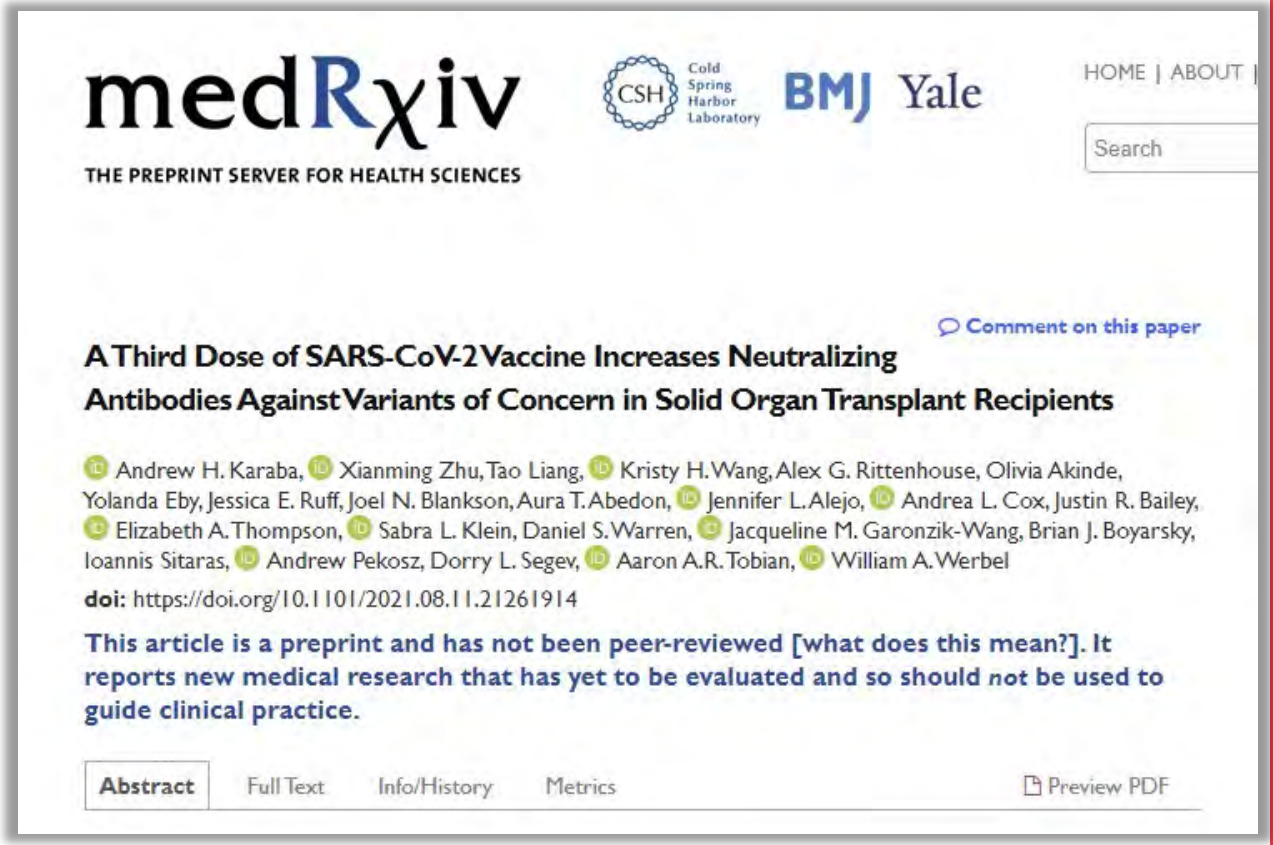
Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have shown high efficacy, but immunocompromised participants were excluded from controlled clinical trials. In this study, we compared immune responses to the BNT162b2 mRNA Coronavirus Disease 2019 vaccine in patients with solid tumors ($n = 53$) who were on active cytotoxic anti-cancer therapy to a control cohort of participants without cancer ($n = 50$). Neutralizing antibodies were detected in 67% of patients with cancer after the first immunization, followed by a threefold increase in median titers after the second dose. Similar patterns were observed for spike protein-specific serum antibodies and T cells, but the magnitude of each of these responses was diminished relative to the control cohort. In most patients with cancer, we detected spike receptor-binding domain and other S1-specific memory B cell subsets as potential predictors of anamnestic responses to additional immunizations. We therefore initiated a phase 1 trial for 20 cancer cohort participants of a third vaccine dose of BNT162b2 (NCT04936997); primary outcomes were immune responses, with a secondary outcome of safety. At 1 week after a third immunization, 16 participants demonstrated a median threefold increase in neutralizing antibody responses, but no improvement was observed in T cell responses. Adverse events were mild. These results suggest that a third dose of BNT162b2 is safe, improves humoral immunity against SARS-CoV-2 and could be immunologically beneficial for patients with cancer on active chemotherapy.

The Coronavirus Disease 2019 (COVID-19) pandemic has led to over 200 million infections worldwide and claimed over 4 million lives to date. Although non-pharmaceutical public health interventions have managed to control outbreaks in some countries, most of the global population will depend upon vaccines to mitigate the pandemic. Since the identification in January 2020 of SARS-CoV-2 as the causative agent of COVID-19 (refs. [1,2]), vaccines with very high efficacy have been developed and deployed with remarkable speed. Independent clinical trials demonstrated 94–95% vaccine efficacy against symptomatic disease caused by SARS-CoV-2 for both the Pfizer/BioNTech and Moderna mRNA-based vaccines[3,4]. On the basis of these data, in December 2020, both the Pfizer/BioNTech and Moderna vaccines were granted emergency use authorization by regulatory agencies in North America.

These clinical trials, however, largely excluded immunocompromised individuals, including patients on immunosuppressive therapies to control chronic inflammatory conditions, patients with primary immunodeficiencies, recipients of organ transplants and patients with cancer on cytotoxic chemotherapy. Concern has been particularly high about the effect of COVID-19 on patients with cancer because a study of 928 patients from the COVID-19 Cancer Consortium showed a 13% 30-d all-cause mortality from COVID-19, which is 10–30 times greater than that observed in the general population[5]. Importantly, the investigators noted a higher risk of death in patients with active cancer[5].

Several recent reports have shown diminished immune responses to SARS-CoV-2 infections and mRNA vaccines in subsets of immunocompromised patients, although these vary greatly with the nature of the immunosuppressive therapy[6–9]. For example, patients with autoimmune conditions or chronic lymphocytic leukemia treated with B cell-depleting antibodies have predictably diminished humoral responses to vaccination, whereas responses by patients on anti-TNF therapies are less affected[6,7]. Notably, organ transplant recipients mount very poor antibody responses to the first mRNA immunization relative to healthy individuals[10], which increase somewhat after the second immunization[8]. Similarly, in patients with cancer with solid or hematological malignancies, antibody responses are markedly diminished after the first immunization but improve somewhat after the second[9]. More data are required to determine whether additional immunizations might further protect this vulnerable population.

[1]Division of Hematology and Oncology, Department of Medicine, University of Arizona Cancer Center, Tucson, AZ, USA. [2]Department of Immunobiology, University of Arizona College of Medicine, Tucson, AZ, USA. [3]BIO5 Institute, University of Arizona, Tucson, AZ, USA. [4]University of Arizona College of Medicine, Tucson, AZ, USA. [5]University of Arizona Center on Aging, University of Arizona College of Medicine, Tucson, AZ, USA. [6]Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, AZ, USA. [7]University of Arizona Genomics Core and the Arizona Research Labs, University of Arizona Genetics Core, University of Arizona, Tucson, AZ, USA. [8]Office of the Senior Vice-President for Health Sciences, University of Arizona, Tucson, AZ, USA. ✉e-mail: rshroff@arizona.edu; blafleur@arizona.edu; deepta@arizona.edu



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Karaba et al., MedRxiv 2021. doi 10.1101/2021.08.11.21261914. PMID 34671774

SUMMARY & CONCLUSIONS

CONCLUSIONS

SCAN ME

1. COVID-19 was of great concern to IBD patients, their families, and their health care providers
2. Crohn's and Colitis Canada's COVID-19 & IBD Task Force quickly formed and moved to synthesize rapidly evolving knowledge about the impact of COVID-19 on people living with IBD
3. The 2021 Impact of COVID-19 & Inflammatory Bowel Disease in Canada summarizes the scientific knowledge, recommendations, and knowledge translation activities of the Task Force

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