

Supplement Article

Crohn's and Colitis Canada's 2021 Impact of COVID-19 and Inflammatory Bowel Disease in Canada: Mental Health and Quality of Life

Lesley A. Graff, CPsych, PhD^{1,2}, Sharyle Fowler, MD³, Jennifer L. Jones, MD, MSc⁴, Eric I. Benchimol, MD, PhD^{5,6,7,8}, Alain Bitton, MD⁹, James Guoxian Huang, MBBS⁵, M. Ellen Kuenzig, PhD^{5,6}, Gilaad G. Kaplan, MD, MPH^{10,11}, Kate Lee, MBA, PhD¹², Mariam S. Mukhtar, MD¹³, Parul Tandon, DO¹⁴, Laura E. Targownik, MD, MSc¹⁴, Joseph W. Windsor, PhD¹⁰, Charles N. Bernstein, MD^{2,15}

¹Department of Clinical Health Psychology, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; ²University of Manitoba IBD Clinical and Research Centre, Winnipeg, Manitoba, Canada; ³Department of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; ⁴Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada; ⁵SickKids Inflammatory Bowel Disease Centre, Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, Ontario, Canada; ⁶Child Health Evaluative Sciences, SickKids Research Institute, Toronto, Ontario, Canada; ⁷ICES, Toronto, Ontario, Canada; ⁸Department of Paediatrics and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; ⁹Department of Medicine, McGill University Health Centre, McGill University, Montreal, Quebec, Canada; ¹⁰Department of Medicine, University of Calgary, Calgary, Alberta, Canada; ¹¹Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; ¹²Crohn's and Colitis Canada, Toronto, Ontario, Canada; ¹³Department of Internal Medicine, King Abdulaziz University Hospital, Jeddah, Saudi Arabia; ¹⁴Division of Gastroenterology and Hepatology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada; ¹⁵Department of Internal Medicine, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

Correspondence: Charles N. Bernstein, MD, Rady Faculty of Health Sciences, University of Manitoba, 804-715 McDermot Avenue, Winnipeg, Manitoba R3E3P4, Canada, e-mail: Charles.bernstein@umanitoba.ca

ABSTRACT

There has been a dramatic rise in mental health difficulties during the coronavirus disease 2019 (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. Somewhat of 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 elevated anxiety symptoms 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 inflammatory bowel disease (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 prevalent 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 COVID-19 or a worse outcome if acquired. Concerns about access to health care add to mental distress. People with IBD generally report lower quality of life (QOL) compared to community controls. Psychological interventions, in addition to adequate disease control, have been shown to improve health-related QOL. Uncertainty is another factor associated with reduced

Received: June 25, 2021; Accepted: August 11, 2021.

© The Author(s) 2021. Published by Oxford University Press on behalf of the Canadian Association of Gastroenterology. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

Key Messages

- 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.
- During the COVID-19 pandemic, the general population has experienced an increase in distress and mental health disorders.
- Several factors contribute to mental health disorders during the pandemic, including uncertainty regarding risks for morbidity and mortality if COVID-19 is acquired, and uncertainty as to prevention optimization, social isolation and financial stressors from workplace changes.
- 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 health care.
- The COVID-19 pandemic has had a significant negative impact on the quality of life of persons with IBD.

health-related QOL. Most studies suggest that persons with IBD have suffered QOL impairment 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.

Keywords: *Coronavirus; Crohn's disease; Mental health; Quality of life; SARS-CoV-2; Ulcerative colitis*

MENTAL HEALTH IN THE GENERAL POPULATION DURING THE PANDEMIC

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak has had widespread health, economic and social impact. Health care systems have been challenged to manage an onslaught of severely ill individuals; deaths due to the coronavirus disease 2019 (COVID-19) are now in the millions worldwide; and governments have imposed restrictive measures, including lockdowns and business closures to slow transmission. With pandemic sequelae of 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 elevated anxiety symptoms early in the pandemic compared to pre-pandemic levels (5% compared to 20% as of April, 2020) and a doubling of those with pervasive elevated depressive symptoms (4% compared 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 of clinically significant distress in the United Kingdom, measured through their national longitudinal household survey, identified a significant escalation from 2018 to 2019 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 United States (also using a probability-based representative sample comparing participants over time) 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 for acquiring COVID-19 or being financially impacted (16). While evidence of population adaptation to the pandemic challenges are 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 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 (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, Middle East respiratory syndrome and COVID-19 found high point prevalence rates post-illness for post-traumatic stress disorder (32%) as well as depression and anxiety (14%), with mental illness post-SARS persisting up to 4 years (21). An epidemiologic study in the United States 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 6-month period for more than 236,000 persons with a COVID-19-positive diagnosis, they found that one in three (33% incidence rate) COVID-19-positive persons had neurological or psychiatric diagnoses, with anxiety disorder (17%) being most common (23).

MENTAL HEALTH IN PERSONS WITH INFLAMMATORY BOWEL DISEASE DURING THE PANDEMIC

Persons with inflammatory bowel disease (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 psychological distress (24). Anxiety and depression have been found to be more prevalent in persons with IBD compared to healthy controls, with rates of anxiety and depression ranging from 19% to 28% during remission and 34% to 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 health care costs (30).

Many potential factors could contribute to the increased psychological 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 3815 participants from 51 countries around the world. Most respondents feared contracting COVID-19 (3242, 85%) or infecting other people (3330, 87%). Just under a third of respondents believed that IBD predisposed them to an increased risk of COVID-19 (1150, 30%) and nearly

two-thirds believed that immunosuppressive drugs were associated with a higher risk of infection (2427, 64%). Similar concerns were identified in a study from China, in which 2277 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 psychological 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 United Kingdom (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 (QOL). Anxiety or depression were the most common comorbidities, 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 psychological impact of COVID-19 on people with IBD in Saudi Arabia through a validated Arabic version of the Hospital Anxiety and Depression Scale (36). Of the 1156 persons with IBD assessed, normal, borderline and Hospital Anxiety and Depression Scale–Anxiety subscale 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 Scale (38). This study showed that people with higher scores on the Patient Health Engagement scale had significantly lower levels of the perceived risk of COVID-19 emergency; they also 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.

QOL IN PERSONS WITH IBD

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 and Prevention 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 and morbidity 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 psychologic 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 health care resource use, including IBD-related hospital admissions, emergency department visits, use of psychologic services, telephone calls to clinicians, gastroenterology 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 1 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, psychologic distress as part of a transdisciplinary care approach.

HRQOL 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 to have the largest reductions in QOL given significant uncertainty relating to the morbidity and mortality of 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 health care providers and health care 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

Table 1. 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 • Reduced energy • Impaired body image • Maladaptive coping mechanisms • Social isolation
Psychologic distress	Negative	Negative	
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
Parental stress	Negative	Unknown	<ul style="list-style-type: none"> • Disease-related psychologic distress
Effective medical therapy	Positive	Positive	<ul style="list-style-type: none"> • Perceived difficulty of medical stressors
Health information gathering from internet	Negative	Negative	<ul style="list-style-type: none"> • Induction of long-term remission • Reduced certainty
Poor sleep quality	Negative	Negative	<ul style="list-style-type: none"> • Fatigue • Daytime dysfunction

IBD, Inflammatory bowel disease; QOL, Quality of 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 UK survey was performed with moderate- and high-risk IBD populations (IBD populations deemed to be at high risk of morbidity from COVID-19) (33). Out of 685 respondents, the majority reported a negative impact of the pandemic on QOL as well as significant increases in perceived stress. Many respondents identified remote health care 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 reductions 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.

Funding

This supplement is sponsored by Crohn's and Colitis Canada and a Canadian Institutes of Health Research (CIHR) COVID-19 Rapid Research Funding Opportunity (Funding Reference Number – VR5 172684). Crohn's and Colitis Canada received partial funding support from Pfizer Canada, AbbVie Corporation (Canada), and Takeda Canada Inc. after completing the draft of the impact of COVID-19 and IBD report. Only Crohn's and Colitis Canada was involved in the research, writing, and conclusions of this report. The other sponsors had no role in the development or conclusions of this report.

CONFLICT OF INTEREST

E.I.B. has acted as a legal consultant for Hoffman La-Roche Limited and Peabody & Arnold LLP for matters unrelated to medications used

to treat inflammatory bowel disease and has received honoraria from McKesson Canada. He is Chair of the Scientific and Medical Advisory Council of Crohn's and Colitis Canada. C.N.B. is supported in part by the Bingham Chair in Gastroenterology. He is on Advisory Boards for AbbVie Canada, Amgen Canada, Bristol Myers Squibb, Janssen Canada, Pfizer Canada, Roche Canada, Sandoz Canada and Takeda Canada. He is a Consultant for Mylan Pharmaceuticals and Takeda. He has received educational grants from AbbVie Canada, Pfizer Canada, Takeda Canada and Janssen Canada. He is on the speaker's panel for AbbVie Canada, Janssen Canada, Pfizer Canada, Takeda Canada and Medtronic Canada and received research funding from AbbVie Canada, Pfizer Canada and Sandoz Canada. A.B. has participated in advisory boards with AbbVie, Janssen, Pfizer, Takeda, Hoffman-LaRoche and Amgen. He has received research support from AbbVie. He has received educational support from Fresenius Kabi and Takeda. L.A.G. has served as a consultant for Roche Canada. S.F. has received honoraria for speaking and consulting for AbbVie, Janssen, Pfizer, Shire, Takeda, Roche and Novartis. J.L.J. has received honoraria for speaking and consulting for AbbVie, Janssen, Pfizer, Shire and Takeda. G.G.K. has received honoraria for speaking or consultancy from AbbVie, Janssen, Pfizer and Takeda. He has received research support from Ferring, Janssen, AbbVie, GlaxoSmith Kline, Merck and Shire. He has been a consultant for Gilead. He shares ownership of a patent: Treatment of Inflammatory Disorders, Autoimmune Disease, and PBC. UTI Limited Partnership, assignee. Patent WO2019046959A1. PCT/CA2018/051098. 7 September 2018. L.E.T. has received research funding from AbbVie Canada, Takeda Canada, Sandoz Canada, Amgen Canada, Gilead Canada, Roche Canada and Pfizer Canada, and has been on Advisory Boards for Janssen Canada, AbbVie Canada, Takeda Canada, Pfizer Canada, Merck Canada, Roche Canada, Sandoz Canada and Amgen Canada. The authors M.E.K., K.L., J.G.H., M.S.M., P.T. and J.W.W. declare no conflict of interest.

Supplement sponsorship. This supplemental issue was produced with support from Pfizer Canada. Pfizer Canada had no role in the creation of the Impact of COVID-19 & IBD Report, nor did it influence its contents. This supplemental issue was also produced with support from Crohn's and Colitis Canada and a Canadian Institutes of Health Research (CIHR) COVID-19 Rapid Research Funding Opportunity grant (Funding Reference Number – VR5 172684).

References

1. Moreo C, Wykes T, Galderisi S, et al. How mental health care should change as a consequence of the COVID-19 pandemic. *Lancet Psychiatry* 2020;7(9):813–24.
2. Holmes EA, O'Connor RC, Perry VH, et al. Multidisciplinary research priorities for the COVID-19 pandemic: A call for action for mental health science. *Lancet Psychiatry* 2020;7(6):547–60.
3. Pfefferbaum B, North CS. Mental health and the COVID-19 pandemic. *N Engl J Med* 2020;383(6):510–2.
4. Li J, Yang Z, Qiu H, et al. Anxiety and depression among general population in China at the peak of the COVID-19 epidemic. *World Psychiatry* 2020;19(2):249–50.
5. González-Sanguino C, Ausin B, Castellanos MÁ, et al. Mental health consequences during the initial stage of the 2020 coronavirus pandemic (COVID-19) in Spain. *Brain Behav Immun* 2020;87:172–6.
6. Czeisler ME, Lane RI, Petrosky E, et al. Mental health, substance use, and suicidal ideation during the COVID-19 pandemic—United States, June 24–30, 2020. *Morb Mortal Weekly Rep.* 2020;69(32):1049–57.
7. Fisher JR, Tran TD, Hammarberg K, et al. Mental health of people in Australia in the first month of COVID-19 restrictions: A national survey. *Med J Aust* 2020;213(10):458–64.
8. Niedzwiedz CL, Green MJ, Benzeval M, et al. Mental health and health behaviours before and during the initial phase of the COVID-19 lockdown: Longitudinal

- analyses of the UK Household Longitudinal Study. *J Epidemiol Community Health* 2021;75(3):224–31.
9. Jenkins EK, McAuliffe C, Hirani S, et al. A portrait of the early and differential mental health impacts of the COVID-19 pandemic in Canada: Findings from the first wave of a nationally representative cross-sectional survey. *Prev Med* 2021;145:106333.
 10. Pierce M, McManus S, Jessop C, et al. Says who? The significance of sampling in mental health surveys during COVID-19. *Lancet Psychiatry* 2020;7(7):567–8.
 11. Mental Health Research Canada. Mental health in crisis: How COVID-19 is impacting Canadians. April 2020. <<https://www.mhrc.ca/national-polling-covid>> (Accessed May 5, 2021).
 12. Mental Health Research Canada. Mental health in crisis: How COVID-19 is impacting Canadians. December 2020. <<https://www.mhrc.ca/national-polling-covid>> (Accessed May 5, 2021).
 13. Mental Health Research Canada. Mental health in crisis: How COVID-19 is impacting Canadians. February 2021. <<https://www.mhrc.ca/national-polling-covid>> (Accessed May 5, 2021).
 14. Daly M, Sutin AR, Robinson E. Longitudinal changes in mental health and the COVID-19 pandemic: Evidence from the UK Household Longitudinal Study. *Psychol Med* 2020;1–10. Online ahead of print. doi:10.1017/S0033291720004432.
 15. Daly M, Robinson E. Longitudinal changes in psychological distress in the UK from 2019 to September 2020 during the COVID-19 pandemic: Evidence from a large nationally representative study. *Psychiatry Res* 2021;300:113920.
 16. Robinson E, Daly M. Explaining the rise and fall of psychological distress during the COVID-19 crisis in the United States: Longitudinal evidence from the Understanding America Study. *Br J Health Psychol* 2021;26(2):570–87.
 17. Holland KM, Jones C, Vivolo-Kantor AM, et al. Trends in US emergency department visits for mental health, overdose, and violence outcomes before and during the COVID-19 pandemic. *JAMA Psychiatry* 2021;78(4):372–9.
 18. O'Connor RC, Wetherall K, Cleare S, et al. Mental health and well-being during the COVID-19 pandemic: Longitudinal analyses of adults in the UK COVID-19 Mental Health & Wellbeing study. *Br J Psychiatry* 2020;218(6):326–33. Online ahead of print. doi:10.1192/bjp.2020.212.
 19. Qiu J, Shen B, Zhao M, et al. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: Implications and policy recommendations. *Gen Psychiatr* 2020;33(2):e100213.
 20. Wang Y, Kala MP, Jafar TH. Factors associated with psychological distress during the coronavirus disease 2019 (COVID-19) pandemic on the predominantly general population: A systematic review and meta-analysis. *PLoS One* 2020;15(12):e0244630.
 21. Rogers JP, Chesney E, Oliver D, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: A systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry* 2020;7(7):611–27.
 22. Taquet M, Luciano S, Geddes JR, et al. Bidirectional associations between COVID-19 and psychiatric disorder: Retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry* 2021;8(2):130–40.
 23. Taquet M, Geddes JR, Husain M, et al. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: A retrospective cohort study using electronic health records. *Lancet Psychiatry* 2021;8(5):416–27.
 24. Graff LA, Walker JR, Lix L, et al. The relationship of inflammatory bowel disease type and activity to psychological functioning and quality of life. *Clin Gastroenterol Hepatol* 2006;4(12):1491–501.
 25. Mikocka-Walus A, Knowles SR, Keefer L, et al. Controversies revisited: A systematic review of the comorbidity of depression and anxiety with inflammatory bowel diseases. *Inflamm Bowel Dis* 2016;22(3):752–62.
 26. Kochar B, Barnes EL, Long MD, et al. Depression is associated with more aggressive inflammatory bowel disease. *Am J Gastroenterol* 2018;113(1):80–5.
 27. Nigro G, Angelini G, Grosso SB, et al. Psychiatric predictors of noncompliance in inflammatory bowel disease: Psychiatry and compliance. *J Clin Gastroenterol* 2001;32(1):66–8.
 28. van Langenberg DR, Lange K, Hetzel DJ, et al. Adverse clinical phenotype in inflammatory bowel disease: A cross sectional study identifying factors potentially amenable to change. *J Gastroenterol Hepatol* 2010;25(7):1250–8.
 29. Park KT, Ehrlich OG, Allen JJ, et al. The cost of inflammatory bowel disease: An initiative from the Crohn's & Colitis Foundation. *Inflamm Bowel Dis* 2020;26(1):1–10.
 30. Mittermaier C, Dejaco C, Waldhoer T, et al. Impact of depressive mood on relapse in patients with inflammatory bowel disease: A prospective 18-month follow-up study. *Psychosom Med* 2004;66(1):79–84.
 31. D'Amico F, Rahier JF, Leone S, et al. Views of patients with inflammatory bowel disease on the COVID-19 pandemic: A global survey. *Lancet Gastroenterol Hepatol* 2020;5(7):631–2.
 32. Chen Y, Hu S, Wu H, et al. Patterns of care for inflammatory bowel disease in China during the COVID-19 pandemic. *Lancet Gastroenterol Hepatol* 2020;5(7):632–4.
 33. Harris RJ, Downey L, Smith TR, Cummings JRF, Felwick R, Gwiggner M. Life in lockdown: Experiences of patients with IBD during COVID-19. *BMJ Open* 2020;7(1):e000541.
 34. Goodday SM, Travis S, Walsh A, Friend SH. Stress-related consequences of the coronavirus disease 2019 pandemic on symptoms of Crohn's disease. *Eur J Gastroenterol Hepatol* 2021. Online ahead of print. doi:10.1097/MEG.0000000000002081.
 35. Clara I, Lix LM, Walker JR, et al. The Manitoba IBD Index: Evidence for a new and simple indicator of IBD activity. *Am J Gastroenterol* 2009;104(7):1754–63.
 36. Mosli M, Alourfi M, Alamoudi A, et al. A cross-sectional survey on the psychological impact of the COVID-19 pandemic on inflammatory bowel disease patients in Saudi Arabia. *Saudi J Gastroenterol* 2020;26(5):263–71.
 37. Trindade IA, Ferreira NB. COVID-19 pandemic's effects on disease and psychological outcomes of people with inflammatory bowel disease in Portugal: A preliminary research. *Inflamm Bowel Dis* 2021;27(8):1224–9.
 38. Castellini G, Savarese M, Leone S, et al. Italian IBD patients coping with Covid-19 emergency: The mitigating role of psychological readiness to engage in self-care. *Inflamm Bowel Dis* 2020;26(10):e130–1.
 39. Centers for Disease Control and Prevention. Health related quality of life (HRQL). 2018. <<https://www.cdc.gov/hrqol/concept.htm>> (Accessed May 5, 2021).
 40. World Health Organization. Quality of Life Assessment (WHOQOL): Development and general psychometric properties. *Soc Sci Med* 1998;46(12):1569–85.
 41. Gandek B, Sinclair SJ, Kosinski M, et al. Psychometric evaluation of the SF-36 Health Survey in Medicare managed care. *Health Care Financ Rev* 2004;25(4):5–25.
 42. Selim AJ, Rogers W, Fleishman JA, et al. Updated U.S. population standard for the Veterans RAND 12-item Health Survey (VR-12). *Qual Life Res* 2009;18(1):43–52.
 43. Dominick KL, Ahern FM, Gold CH, et al. Relationship of health-related quality of life to health care utilization and mortality among older adults. *Aging Clin Exp Res* 2002;14(6):499–508.
 44. DeSalvo KB, Blosner N, Reynolds K, et al. Mortality prediction with a single general self-rated health question. A meta-analysis. *J Gen Intern Med* 2006;21(3):267–75.
 45. Cámara RJ, Ziegler R, Bégre S, et al.; Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS) Group. The role of psychological stress in inflammatory bowel disease: Quality assessment of methods of 18 prospective studies and suggestions for future research. *Digestion* 2009;80(2):129–39.
 46. Maunder RG, Levenstein S. The role of stress in the development and clinical course of inflammatory bowel disease: Epidemiological evidence. *Curr Mol Med* 2008;8(4):247–52.
 47. Mawdsley JE, Rampton DS. Psychological stress in IBD: New insights into pathogenic and therapeutic implications. *Gut* 2005;54(10):1481–91.
 48. Bitton A, Sewitch MJ, Peppercorn MA, et al. Psychosocial determinants of relapse in ulcerative colitis: A longitudinal study. *Am J Gastroenterol* 2003;98(10):2203–8.
 49. Bernklev T, Jahnson J, Lygren I, et al. Health-related quality of life in patients with inflammatory bowel disease measured with the short form-36: Psychometric assessments and a comparison with general population norms. *Inflamm Bowel Dis* 2005;11(10):909–18.
 50. Hoivik ML, Bernklev T, Solberg IC, et al.; IBSEN Study Group. Patients with Crohn's disease experience reduced general health and vitality in the chronic stage: Ten-year results from the IBSEN study. *J Crohns Colitis* 2012;6(4):441–53.
 51. Hoivik ML, Moum B, Solberg IC, et al.; IBSEN Study Group. Health-related quality of life in patients with ulcerative colitis after a 10-year disease course: Results from the IBSEN study. *Inflamm Bowel Dis* 2012;18(8):1540–9.
 52. Otley AR, Griffiths AM, Hale S, et al.; Pediatric IBD Collaborative Research Group. Health-related quality of life in the first year after a diagnosis of pediatric inflammatory bowel disease. *Inflamm Bowel Dis* 2006;12(8):684–91.
 53. Casellas F, Arenas JI, Baudet JS, et al. Impairment of health-related quality of life in patients with inflammatory bowel disease: A Spanish multicenter study. *Inflamm Bowel Dis* 2005;11(5):488–96.
 54. Pallis AG, Vlachonikolis IG, Mouzas IA. Assessing health-related quality of life in patients with inflammatory bowel disease, in Crete, Greece. *BMC Gastroenterol* 2002;2:1.
 55. Vidal A, Gómez-Gil E, Sans M, et al. Health-related quality of life in inflammatory bowel disease patients: The role of psychopathology and personality. *Inflamm Bowel Dis* 2008;14(7):977–83.
 56. Pizzi LT, Weston CM, Goldfarb NI, et al. Impact of chronic conditions on quality of life in patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2006;12(1):47–52.
 57. Gumidyala AP, Greenley RN. Correlates of health-related quality of life in pediatric inflammatory bowel disease: A cumulative risk model approach. *J Pediatr Psychol* 2014;39(1):55–64.
 58. Cunningham CL, Drotar D, Palermo TM, McGowan K, Arendt R. Health-related quality of life in children and adolescents with inflammatory bowel disease. *Children's Health Care* 2007;36(1):29–43.
 59. Greenley RN, Hommel KA, Nebel J, et al. A meta-analytic review of the psychosocial adjustment of youth with inflammatory bowel disease. *J Pediatr Psychol* 2010;35(8):857–69.

60. Kunz JH, Hommel KA, Greenley RN. Health-related quality of life of youth with inflammatory bowel disease: A comparison with published data using the PedsQL 4.0 generic core scales. *Inflamm Bowel Dis* 2010;16(6):939–46.
61. Ryan JL, Mellon MW, Junger KW, et al. The clinical utility of health-related quality of life screening in a pediatric inflammatory bowel disease clinic. *Inflamm Bowel Dis* 2013;19(12):2666–72.
62. Lix LM, Graff LA, Walker JR, et al. Longitudinal study of quality of life and psychological functioning for active, fluctuating, and inactive disease patterns in inflammatory bowel disease. *Inflamm Bowel Dis* 2008;14(11):1575–84.
63. van Erp SJ, Brakenhoff LK, Vollmann M, et al. Illness perceptions and outcomes in patients with inflammatory bowel disease: Is coping a mediator? *Int J Behav Med* 2017;24(2):205–14.
64. Kiebles JL, Doerfler B, Keefer L. Preliminary evidence supporting a framework of psychological adjustment to inflammatory bowel disease. *Inflamm Bowel Dis* 2010;16(10):1685–95.
65. Devlen J, Beusterien K, Yen L, et al. Barriers to mesalamine adherence in patients with inflammatory bowel disease: A qualitative analysis. *J Manag Care Spec Pharm* 2014;20(3):309–14.
66. Mikocka-Walus AA, Turnbull DA, Moulding NT, et al. Controversies surrounding the comorbidity of depression and anxiety in inflammatory bowel disease patients: A literature review. *Inflamm Bowel Dis* 2007;13(2):225–34.
67. Mussell M, Böcker U, Nagel N, et al. Reducing psychological distress in patients with inflammatory bowel disease by cognitive-behavioural treatment: Exploratory study of effectiveness. *Scand J Gastroenterol* 2003;38(7):755–62.
68. von Wietersheim J, Kessler H. Psychotherapy with chronic inflammatory bowel disease patients: A review. *Inflamm Bowel Dis* 2006;12(12):1175–84.
69. IsHak WW, Pan D, Steiner AJ, et al. Patient-reported outcomes of quality of life, functioning, and GI/psychiatric symptom severity in patients with inflammatory bowel disease (IBD). *Inflamm Bowel Dis* 2017;23(5):798–803.
70. Holdam AS, Bager P, Dahlerup JF. Biological therapy increases the health-related quality of life in patients with inflammatory bowel disease in a clinical setting. *Scand J Gastroenterol* 2016;51(6):706–11.
71. Vogelaar L, Spijker AV, van der Woude CJ. The impact of biologics on health-related quality of life in patients with inflammatory bowel disease. *Clin Exp Gastroenterol* 2009;2:101–9.
72. Xu J, Lin H, Feng X, et al. Different therapeutic approaches on quality of life in patients with inflammatory bowel disease. *BMC Gastroenterol* 2014;14:199.
73. LeBlanc K, Mosli MH, Parker CE, MacDonald JK. The impact of biological interventions for ulcerative colitis on health-related quality of life. *Cochrane Database Syst Rev* 2015;9:CD008655.
74. Feagan BG, Patel H, Colombel JF, et al. Effects of vedolizumab on health-related quality of life in patients with ulcerative colitis: Results from the randomised GEMINI 1 trial. *Aliment Pharmacol Ther* 2017;45(2):264–75.
75. Niv G, Bar Josef S, Ben Bassat O, et al. Quality of life and uncertainty in Crohn's disease. *Qual Life Res* 2017;26(6):1609–16.
76. Azzam NA, Aljebreen A, Almuhabeb A, et al. Disability and quality of life before and during the COVID-19 outbreak: A cross-sectional study in inflammatory bowel disease patients. *Saudi J Gastroenterol* 2020;26(5):256–62.
77. Grunert PC, Reuken PA, Stallhofer J, Teich N, Stallmach A. Inflammatory bowel disease in the COVID-19 pandemic—the patients' perspective. *J Crohns Colitis* 2020;14(12):1702–8. Online ahead of print. doi:10.1093/ecco-jcc/jjaa126.
78. Martinelli M, Strisciuglio C, Fedele F, et al. Clinical and psychological issues in children with inflammatory bowel disease during COVID-19 pandemic. *Inflamm Bowel Dis* 2020;26(9):e95–6.
79. Rogerio P, Marley F, Sandro F, Hugo C, Joaquim RJ, Omar F. Measuring patient-reported outcomes in Crohn's disease patients during the outbreak of COVID-19. *Am J Gastroenterol* 2021;115:S15.