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The results of this controlled study show that abdominal pain/discomfort, diarrhea and chronic fatigue (31.7% vs. 13.7%; P<0.001). The frequency of IBS according to the Rome was greater in patients than in controls (Table 1) as was the frequency of patients with loss of smell and taste, fatigue, muscle pain, diarrhea, weight loss and antibiotic treatment was evaluated by both univariate (chi-squared and Mann-Whitney tests) and multivariate were also recorded. Association between exposure to SARS-CoV-2 infection and symptoms and chronic fatigue persist after the infection has not been fully established. We have investigated the prevalence of gastrointestinal symptoms and chronic fatigue by means of a structured questionnaire after the resolution of SARS-CoV-2 infection. Methods: 378 subjects, age range 18-80 years, were studied. 177 patients had a molecular diagnosis of SARS-CoV-2 infection at our hospital in Feb-Apr 2020; 201 subjects, who had been tested because living in the same house as other infected people or working at the hospital, had a negative test in current period (control group). 13 symptoms were respectively excluded because of a previous gastrointestinal disease, 9 and 16 of them with Irritable Bowel Syndrome (IBS). All the subjects filled in a web-based structured questionnaire about 5 months after infection. 164 patients (mean age 44 years, 40% female) and 183 control subjects (mean age 40 years, 61% female) completed the study. These clinical data, acute SARS-CoV-2 related symptoms, the presence and severity of 22 gastrointestinal symptoms grouped in five symptom domains and the presence of six extra-intestinal symptoms including chronic fatigue were recorded according to the Structured Assessment of Gastrointestinal Symptoms (SAGIS) questionnaire. The Rome IV criteria for IBS, Bristol Stool scale, SCL-12 for somatization and of Hospital Anxiety and Depression Scale (HADS) for anxiety and depression were also recorded. Association between exposure to SARS-CoV-2 infection and symptoms was evaluated by both univariate (chi-squared and Mann-Whitney tests) and multivariate analysis (linear and robust Poisson regression models). Results: Fever, shortness of breath, loss of smell and taste, fatigue, muscle pain, diarrhea, weight loss and antibiotic treatment were more frequent in patients during the infection (results not shown) after the infection resolving, the severity of abdominal pain/discomfort and diarrhea/incontinence symptoms was greater in patients than in controls (Table 1) as was the frequency of patients with Rome IV criteria, loose stools, SCL-12 for somatoform disorders and HADS-A and -D for anxiety and depression scores tended to be greater in patients than in controls (Table 2). Conclusions: The results of this controlled study show that abdominal pain/discomfort, diarrhea and chronic fatigue persist after the infection has not been fully established. We have investigated the prevalence of gastrointestinal symptoms and chronic fatigue by means of a structured questionnaire after the resolution of SARS-CoV-2 infection. Measurement of recovery period.

Table 2. Frequency of patients with IBS and loose stools and scores of Symptom Check List (SCL)-12 for somatization and of Hospital Anxiety and Depression Scale (HADS) according to previous SARS-CoV-2 infection.

| Symptom Domain | Negative (n=183) | Positive (n=164) | p-value |
|----------------|-----------------|-----------------|---------|
| Abdominal pain/discomfort | 0.33 (0.53) | 0.49 (0.60) | 0.0092 |
| Diarrhea/incontinence | 0.28 (0.60) | 0.41 (0.55) | 0.0310 |
| Diarrhea/repetition | 0.56 (0.44) | 0.39 (0.51) | 0.0617 |
| Nausea/vomiting | 0.17 (0.25) | 0.2 (0.35) | 0.7016 |
| Constipation | 0.35 (0.68) | 0.31 (0.82) | 0.8211 |

Table 1. Gastrointestinal symptoms in the five domains of the Structured Assessment of Gastrointestinal Symptoms Scale (SAGIS) according to SARS-CoV-2 infection.

| Symptom Domain | Negative (n=183) | Positive (n=164) | p-value |
|----------------|-----------------|-----------------|---------|
| Irritable Bowel Syndrome (Rome IV), r (%) | 46 (25.1%) | 43 (26.2%) | 0.81 |
| Loose stool defined as Bristol 6, n (%) | 17 (9.9%) | 29 (17.8%) | 0.02 |
| SCL-12, somatization (mean ± SD) | 56.5 ± 10.4 | 54.6 ± 10.8 | 0.001 |
| HADS-A, anxiety (mean ± SD) | 4.47 ± 3.38 | 4.64 ± 3.97 | 0.87 |
| HADS-D, depression (mean ± SD) | 3.53 ± 3.34 | 3.81 ± 3.53 | 0.47 |

Impact of COVID-19 related disuctions to colorectal cancer screening programs in three countries: A comparative modelling study

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Background: Colorectal cancer (CRC) screening programs worldwide have been disrupted during the COVID-19 pandemic. CRC screening has been well-established to reduce long-term CRC incidence and mortality. Any disruption to screening would reduce these health benefits. This study aimed to estimate the impact of disruption to organized CRC screening programs on short- and long-term CRC incidence and mortality in three countries using microsimulation modelling.

Methods: Using well-calibrated and validated CRC microsimulation models for Australia (Policy1-Bowel), Canada (OncoSim) and the Netherlands (ASCCA and MISCAN-Colon) participating in the COVID-19 and Cancer Global Modelling Consortium (CGMC), we simulated a range of hypothetical scenarios to assess the potential impact of disruptions to screening on CRC incidence and mortality. All models simulate the adenoma-carcinoma pathway, and ASCCA and Policy1-Bowel additionally summarise the serrated pathway. Modelled scenarios varied by disruption duration (3-, 6- and 12-months), post-disruption participation reduction (3-months -50% and 3-months -25%, and 6-months -50%), and catch-up screening strategies (no catch-up, immediate, and 6-months delayed catch-up).

Results: Without catch-up screening, CRC incidence would increase by 0.1-0.3%, 0.2-0.6%, and 0.4-1.2% over 2020-2050 among individuals aged 50 years and older in the three modelled countries after 3-, 6-, and 12-month disruptions, respectively (Figure 1). CRC mortality would increase by 0.2-0.5%, 0.4-1.0%, and 0.8-2.0% over 2020-2050 among individuals aged 50 years and older in the three modelled countries after 3-, 6-, and 12-month disruptions, respectively, compared to undisrupted screening (Figure 2). A 6-month disruption without catch-up would result in an estimated 3,552, 2,844 and 803-1,803 additional CRC diagnoses and an estimated 1,964, 1,319, and 676-856 additional CRC-related deaths in Australia, Canada and the Netherlands, respectively, compared to undisrupted screening. A post-disruption reduction in participation could increase CRC diagnoses by 0.2-0.9% and CRC-related deaths by 0.5-1.6% compared to undisrupted screening depending on the size of the reduction in participation. Providing catch-up could minimize the impact of the disruption to an increase of 0.0-0.2% in CRC diagnoses and CRC-related deaths.

Conclusion: Although the relative impact of the modelled CRC screening disruptions (when considered over the long-term, 30 years) due to the COVID-19 pandemic appears modest, given a high burden of CRC, there is a substantial impact on CRC diagnoses and deaths across all countries considered. It is crucial that, if disrupted, screening programs ensure participation rates return to previously observed rates and provide catch-up screening whenever possible, as the impact of any disruption could be considerably larger.

Change in CRC incidence relative to the comparator scenario (no disruption) by MISCAN-Colon, ASCCA, Policy1-Bowel and OncoSim Abbreviations: CRC, Colorectal Cancer. Note: the base case scenario is the scenario in which a 6-month disruption period from April to September 2020 was assumed, with no catch-up or changes to participation in the recovery period.

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Impact of COVID-19 related disruptions to colorectal cancer screening programs in three countries: A comparative modelling study

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Background: The impact of SARS-CoV-2 infection on patients with IBD is still not fully understood. We aimed to evaluate the clinical course of pediatric IBD patients with positive COVID-19 antibody titers. Methods: This is a single-center, retrospective study of pediatric (<18y) IBD patients with positive COVID-19 Antibody Testing, using a serological enzyme-linked immunosorbent assay developed at Mount Sinai, Icahn School of Medicine. A COVID-19 Antibody Titer was sent routinely at time of biologic infusion or clinic visit between April and November 2020 to better understand IBD patients’ seroconversion and long-term response to COVID-19.

Data on demographics, disease behavior, location and activity (Harvey Bowes index or partial Mayo score) and treatment were gathered at time of antibody testing. Data were collected on antibody titer level (Amanat, F et al. Nat Med (2020) 26, 1033–1036) and, if available, on presence of symptomatic COVID-19 illness, worsening of IBD following SARS-CoV-2 infection, and changes to medications due to illness. Associations of COVID-19 symptom severity with biologic use and COVID-19 antibody titers were assessed with chi-square and Pearson product-moment correlation respectively. Results: Twenty-six children had a positive COVID-19 antibody test between May 6, 2020 and November 5, 2020; demographic, phenotype, and medication data are in Table 1. A majority (86%) of CD patients were in clinical remission, compared to only 1 (20%) UC patient. Median [IQR] antibody titer was 960 [320-1440]. Nineteen children (73%) had documentation regarding...
their COVID-19 course; 68% with symptoms consistent with COVID-19 and 32% asymptomatic. All but two patients (89%) identified a known exposure from a family member or a close contact. One recently diagnosed CD male had a complicated course of COVID-19 with Multisystem Inflammatory Syndrome in children (MIS-C); all other cases were outpatient and uncomplicated. Four (13%) children were diagnosed with IBD with IBD symptoms starting shortly (Mean: 4.75 [Range: 2-8] weeks) following their SARS-CoV-2 infection. A further 4 with established IBD had a subjective worsening of IBD symptoms during or immediately following infection and none had IBD medications held due to COVID-19. There was no association between biologic use and symptomatic infection with SARS-CoV-2 (r = -0.56, P = 0.02). Conclusions: Despite biologic exposure, many antibody positive pediatric IBD patients did not have any active COVID-19 symptoms and their treatment continued without interruption. There were a significant number of patients diagnosed with IBD following their course of COVID-19, warranting further study into the downstream effects of SARS-CoV-2 infection.

### Table 1: Patient Demographics

| Males (N/%) | 17 (66%) |
|------------|----------|
| Median [IQR] Age | 14 (11-16) years |
| Phenotype | |
| Crohn’s Disease N (%) | 21 (81%) |
| Disease location | |
| Ileal | 3 (14%) |
| Colonic | 3 (14%) |
| Ileocelecal | 13 (66%) |
| Isolated Upper Tract | 2 (10%) |
| Disease behavior | |
| Non-penetrating, Non-stricturing | 100% |
| Penetrating Disease | 3 (14%) |
| Ulcerative colitis N (%) | 5 (19%) |
| Disease extent | |
| Rectosigmoiditis | 1 (20%) |
| Extensive/Pancolitis | 4 (80%) |
| Medications at time of COVID-19 Antibody Test N (%) | |
| Biologics | |
| Infliximab | 17 (65%) |
| Adalimumab | 11 (65%) |
| Ustekinumab | 3 (18%) |
| Veddolizumab | 2 (12%) |
| S-aminosalicylate | 1 (6%) |
| Ciprotroloxin/Metronidazole | 3 (12%) |
| No medications (%) | 5 (19%) |
| No medications with new diagnosis IBD (%) | 4 (80%) |
| Median [IQR] height | 63.0 (55-69) inches |
| Median [IQR] weight | 109 (74-153) pounds |
| Median [IQR] BMI | 18.9 (16.7-24.3) |

**Methods:** Small intestinal biopsies from patients who underwent clinically indicated endoscopic procedures after a positive SARS-CoV-2 nasopharyngeal swab (n=27) or were found to have positive serology (n=2) were analyzed by immunofluorescence (IF) (n=25) and electron microscopy (EM) (n=14) for the presence of virus. Clinical details were also collected (Table 1).

**Results:** Patients were between 15 days and 7 months of symptom onset. Sixteen of 29 patients had detectable SARS-CoV-2 antigen by either IF or EM (Figure 1). Virus was restricted to the epithelium and patchy in distribution. It was detected as soon as 15 days after symptom onset and persisted up to 7 months following symptom resolution. This persistence is not associated with an overt inflammatory infiltrate and does not appear to correlate with presence of GI symptoms in the acute COVID-19 setting.

**Discussion:** SARS-CoV-2 infects enterocytes in humans in vivo and can persist up to 7 MONTHS FOLLOWING RESOLUTION OF SYMPTOMS. There was a moderate negative correlation of tier level with symptomatic infection with SARS-CoV-2 (r = -0.56, P = 0.02). Conclusions: Despite negative nasopharyngeal swab tests at symptom onset, 37.5% (6 of 16) of patients with virus detected in the small bowel had GI symptoms (diarrhea, nausea or vomiting) during their acute COVID-19 illness. Interestingly, only 37.5% (6 of 16) of patients with virus detected in both patients and both patients were nasopharyngeal swab negative for all procedures. Interestingly, only 37.5% (6 of 16) of patients with virus detected in the small bowel had GI symptoms (diarrhea, nausea or vomiting) during their acute COVID-19 illness as compared to 46.1% (6/13) of patients where no virus could be detected in the intestines. Conclusions: SARS-CoV-2 infects enterocytes in humans in vivo and can persist in the intestines up to 7 months following symptom resolution. This persistence is not associated with an overt inflammatory infiltrate and does not appear to correlate with presence of GI symptoms in the acute COVID-19 setting.