Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

R. BALFOUR SARTOR, MD
Center for Gastrointestinal Biology and Disease
Division of Gastroenterology and Hepatology
Department of Medicine
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

References

1. Sartor RB, Wu GD. Roles for intestinal bacteria, viruses, and fungi in pathogenesis of inflammatory bowel diseases and therapeutic approaches. Gastroenterology 2017;152:327–339 e4.
2. Rath HC, Herfarth HH, Ikeda JS, et al. Normal luminal bacteria, especially Bacteroides species, mediate chronic colitis, gastritis, and arthritis in HLA-B27/human beta2 microglobulin transgenic rats. J Clin Invest 1996; 98:945–853.
3. Round JL, Palm NW. Causal effects of the microbiota on immune-mediated diseases. Sci Immunol 2018;3.
4. Frank DN, St Amand AL, Feldman RA, et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci U S A 2007;104:13780–13785.
5. Gevers D, Kugathasan S, Denson LA, et al. The treatment-naive microbiome in new-onset Crohn's disease. Cell Host Microbe 2014;15:382–392.
6. Landers CJ, Cohavy O, Misra R, et al. Selected loss of tolerance evidenced by Crohn's disease-associated immune responses to auto- and microbial antigens. Gastroenterology 2002;123:689–699.
7. Hegazy AN, West NR, Stubbington MJT, et al. Circulating and tissue-resident CD4(+) T cells with reactivity to intestinal microbiota are abundant in healthy individuals and function is altered during inflammation. Gastroenterology 2017;153:1320–1337 e16.
8. Lodes MJ, Cong Y, Elson CO, et al. Bacterial flagellin is a dominant antigen in Crohn disease. J Clin Invest 2004; 113:1296–1306.
9. Targan SR, Landers CJ, Yang H, et al. Antibodies to CBir1 flagellin define a unique response that is associated independently with complicated Crohn's disease. Gastroenterology 2005;128:2020–2028.
10. Kugathasan S, Denson LA, Walters TD, et al. Prediction of complicated disease course for children newly diagnosed with Crohn's disease: a multicentre inception cohort study. Lancet 2017;389:1710–1718.
11. Calderon-Gomez E, Bassolas-Molina H, Mora-Buch R, et al. Commensal-specific CD4(+) cells from patients with Crohn's disease have a T-helper 17 inflammatory profile. Gastroenterology 2016;151:489–500 e3.
12. Cook L, Lisko DJ, Wong MQ, et al. Analysis of flagellin-specific adaptive immunity reveals links to dysbiosis in patients with inflammatory bowel disease. Cell Mol Gastroenterol Hepatol 2020;9:485–506.
13. Feng T, Wang L, Schoeb TR, et al. Microbiota innate stimulation is a prerequisite for T cell spontaneous proliferation and induction of experimental colitis. J Exp Med 2010;207:1321–1332.
14. Alexander KL, Zhao Q, Reif M, et al. Human microbiota flagellins drive adaptive immune responses in Crohn's disease. Gastroenterology 2021;161:522–535.
15. Schmitz JM, Tonkonogy SL, Dogan B, et al. Murine adherent and invasive E. coli induces chronic inflammation and immune responses in the small and large intestines of monoassociated IL-10-/- mice independent of long polar fimbriae adhesin A. Inflamm Bowel Dis 2019;25:875–885.
16. Eun CS, Mishima Y, Wohlgemuth S, et al. Induction of bacterial antigen-specific colitis by a simplified human microbiota consortium in gnotobiotic interleukin-10-/- mice. Infect Immun 2014;82:2239–2246.
17. Furusawa Y, Obata Y, Fukuda S, et al. Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. Nature 2013;504:446–450.
18. Torres J, Petralia F, Sato T, et al. Serum biomarkers identify patients who will develop inflammatory bowel diseases up to 5 years before diagnosis. Gastroenterology 2020;159:96–104.
19. Zhao Q, Duck LW, Huang F, et al. CD4(+) T cell activation and concomitant mTOR metabolic inhibition can ablate microbiota-specific memory cells and prevent colitis. Sci Immunol 2020;5.

Correspondence:
Address correspondence to: R. Balfour Sartor, MD, Midget Distinguished Professor of Medicine, Microbiology & Immunology, Division of Gastroenterology and Hepatology, 7309A MBRB, CB#7032, Chapel Hill, NC 27599-7032. e-mail: rbs@med.unc.edu.

Conflicts of interest
The author has made the following disclosures: Dr Sartor has no conflicts directly related to this editorial, but has current consulting agreements or is on advisory boards with Vedanta, SERES, Second Genome, BioMx, Biomica, Otsuka, Takeda, Qu Biologics, and Bridge Biotherapeutics, and has research grant support from Takeda, Vedanta, SERES, BioMx, Biomica, and Artizan.

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2021.05.031

Re-FIT-ting Colorectal Cancer Screening During and Beyond COVID

See "Noninvasive colorectal cancer screening tests help close screening gaps during coronavirus disease 2019 pandemic," by Myint A, Roh L, Yang L, et al, on page 712.

Behind the tragic global crisis caused by the response to COVID-19, there lies another, silent, health crisis: that of the undiagnosed cancers and unattended chronic diseases. Around the world, routine ambulatory care and

screening have been put on the back burner, or into ever-expanding backlogs which are expected to linger for several years to come.

While it is impossible to fully measure the impact of the pandemic response on cancer burden at this time, several modeling studies indicate that even short-term interruptions of screening may have significant consequences. In the United Kingdom, a national population-based modeling study estimated that the delay in colorectal cancer (CRC) diagnosis induced by a 12-month disruption in screening and usual care could give rise to up to 16.6% more CRC-related deaths at 5 years.[1] Another modeling study of organized fecal immunochemical test (FIT)–based screening predicted that much of the excess mortality they found could be avoided if interventions to "catch up" on missed screening are undertaken in the near future,[2] which would require additional FIT and colonoscopy resources.

With every day of this pandemic, every wave, and every return to lockdown, the tension between this overt COVID crisis and the growing, silent, pandemic of unattended care and unaddressed diagnoses grows. Confronted with these pressures, the need to find efficiencies within the system is imperative. Solutions are required imminently, but it is predicable that the effects of the COVID-19 response will remain with us for a long time and that we may not ever return to the pre-COVID status quo. In other words, the delivery of GI care will have to adapt to a new normal.

In the United States, the National Cancer Institute's Population-Based Research to Optimize the Screening Process (PROSPR) consortium estimated that CRC screening rates dropped by 82% in 2020.[3] How have health organizations reacted to the abrupt and drastic disruption, and are there examples of adaptability and innovation that we can learn from?

In the United States Veterans Affairs (VA) hospitals, multilevel interventions were performed to help alleviate the consequences of the March 2020 directive to cease all elective and nonurgent procedures.[4] Guidances to primary care and endoscopy services were promptly released to encourage the use of FIT instead of colonoscopy for CRC screening and on the prioritization of endoscopic procedures. Preexisting IT tools were also adapted to default to FIT instead of colonoscopy as first-line CRC screening test and to assign a priority level to each postponed or incoming request for procedure; the system was also able to measure the backlog and categorize it by indication and priority level.

This month's issue of *Gastroenterology* features another example of prompt service adaptation. Myint et al demonstrate how purposefully encouraging the use of stool-based CRC screening modalities among patients and providers of the University of California Los Angeles (UCLA) health system allowed screening to continue despite the temporary cessation of elective endoscopies.[5] In the months following resumption of elective endoscopy, the authors also observed a dramatic increase in overall screening test utilization, with a predominant rise in utilization of noninvasive screening modalities (ie, FIT and stool DNA) whereas the use of colonoscopy approached but did not match pre-pandemic volumes.

These examples highlight that, in this new reality imposed by the COVID pandemic, the ideal CRC screening test is one that does not require a procedure or a visit to a health facility, that is easy to use, and that is accessible and yet effective, such as FIT. In fact, in response to the COVID pandemic, the PROSPR consortium recommended increasing the use of established methods of remote testing, such as mailed FIT kits, to improve outcomes of screening and decrease disparities.[3]

Not only could FIT allow screening to continue during the pandemic, it also represents an effective strategy to debulk the endoscopy backlog. Tinmouth et al have shown that redirecting requests for either average-risk colonoscopy or surveillance in people with low-risk adenoma to FIT can substantially reduce the colonoscopy backlog and its recovery time.[6] To achieve a similar effect, colonoscopy capacity would need to exceed mean historical volumes by as much as 45%. This approach effectively "converts" procedures with a low yield for advanced colorectal neoplasia (such as average-risk colonoscopy) into "high-yield" ones, as about one-third of colonoscopies performed in FIT-positive individuals will reveal advanced colorectal neoplasia, including CRC in about 1 in every 19 such colonoscopies.[7]

In many parts of the world, the pandemic has strained health care systems which were already saturated, pushing innovation and rapid changes. It has also exposed blatant flaws and inefficiencies that may have been tolerated in the past and which may no longer be considered acceptable. It behooves us to critically appraise the effectiveness of the millions of procedures performed each year.[8] The realization that CRC screening through a FIT-based model is a safer, more accessible, more equitable evidence-based model than a colonoscopy-based model, as made obvious during the pandemic, is likely to drive permanent changes in the delivery of GI care. One can expect that the nature of colonoscopy will evolve to become primarily a diagnostic and interventional procedure, rather than a screening modality.[8,9]

The ease and rapidity by which this change occurs within a health care system will likely depend on its level of organization, integration, and the adequacy of its IT infrastructure, as illustrated by the examples from the VA hospitals and UCLA health system, which were both able to swiftly and effectively implement changes to reduce the impact of endoscopy closures.[4,5]

Opportunities abound to create centralized processes for evidence-based triage, prioritization, and procedure booking with the use of a single queue.[10] In such models, the conversion of referrals for screening colonoscopy may easily be redirected to an FIT test, and referring physicians may be educated about the benefits of this new strategy. This promotes equity and reduces the use of scarce endoscopy resources for procedures of questionable benefit, or procedures that could safely be avoided and substituted for noninvasive tests, such as FIT for CRC screening.

CATHERINE DUBÉ
Prevention and Cancer Control, Ontario Health (Cancer Care Ontario), Toronto, Ontario, Canada *and*

Department of Medicine, The Ottawa Hospital, Ottawa, Ontario, Canada *and*
Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada

References

1. Maringe C, Spier J, Morris M, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol 2020; 21:1023–1034.
2. de Jonge L, Worthington J, van Wifferen, et al. Impact of the COVID-19 pandemic on faecal immunochemical test-based colorectal cancer screening programmes in Australia, Canada, and the Netherlands: a comparative modelling study. Lancet Gastroenterol Hepatol 2021; 6:304–314.
3. Corley D, Sedki M, Ritzwoller DP, et al. Cancer screening during the coronavirus disease-2019 pandemic: a perspective from the National Cancer Institute's PROSPR Consortium. Gastroenterology 2021; 160:999–1002.
4. Gawron AJ, Kaltenbach T, Dominitz JA. The impact of the coronavirus disease-19 pandemic on access to endoscopy procedures in the VA healthcare system. Gastroenterology 2020;159:1216–1220.e1.
5. Myint A, Roh L, Yang L, Connolly L, Esrailian E, May FP. Noninvasive colorectal cancer screening tests help close screening gaps during coronavirus disease 2019 pandemic. Gastroenterology 2021;161:712–714.
6. Tinmouth J, Dong S, Stogios C, Rabeneck L, Rey M, Dube C. Estimating the backlog of colonoscopy due to coronavirus disease 2019 and comparing strategies to recover in Ontario, Canada. Gastroenterology 2021; 160:1400–1402.
7. Quintero E, Castells A, Bujanda L, et al. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. N Engl J Med 2012;366(8):697–706.
8. Leiman DA, Weinstein ML, Adams MA. An impetus for change: How coronavirus disease 2019 will transform the delivery of gastroenterology health care. Clin Gastroenterol Hepatol 2021 Apr 2 [e-Pub ahead of print].
9. Gupta S, Lieberman D. Screening and surveillance colonoscopy and COVID-19: avoiding more casualties. Gastroenterology 2020;159:1205–1208.
10. Rouillard S, Liu VX, Corley DA. COVID-19 and long-term planning for procedure-based specialties during extended mitigation and suppression strategies. Gastroenterology 2021;160:4–9.

Correspondence
Address correspondence to: Catherine Dubé MD, MSc, FRCPC, The Ottawa Hospital Civic Campus, 1053 Carling Avenue, Ottawa, ON, K1Y 4E9, Canada. e-mail: cdube@toh.ca.

Conflicts of interest
The author is employed by Ontario Health (Cancer Care Ontario) and declares no conflicts.

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2021.05.004

More Testosterone, Less Aggression…At Least in the Stomach

See "Glucocorticoids and androgens protect from gastric metaplasia by suppressing group 2 innate lymphoid cell activation," by Busada JT, Peterson KN, Khadka S, et al, on page 637.

Chronic inflammation contributes to the development of several types of cancer, including gastric cancer. Gastric cancer is the fifth most common neoplasm and fourth leading cause of cancer-associated deaths.[1] Although many people develop chronic gastritis as a result of infection with *Helicobacter pylori* and autoimmune gastritis, only a subset of those affected will develop gastric cancer.[2] Individuals who develop atrophy and metaplasia have a much higher risk of developing gastric cancer than those with mild gastritis. In the stomach, at least 2 types of metaplasia develop, spasmolytic polypeptide-expressing metaplasia and intestinal metaplasia, and both may be precursors of gastric cancer.[3,4] There are many risk factors that influence the progression from gastritis to gastric cancer, including infection with pathogenic strains of *H pylori*, genetics, environment, and chronic inflammation.[5,6]

The article by Busada et al[7] featured in this issue of *Gastroenterology* investigates the role of androgens and glucocorticoids in the development of gastritis and gastric metaplasia.[7]

The fact that sex hormones influence immune cell function and inflammation may account for differences in inflammatory diseases that develop in males and females. For example, it is well-established that the incidence of many autoimmune diseases is much higher in females than males.[8,9] Glucocorticoids and androgens are reported to have anti-inflammatory effects, so differences in the levels of either or both may contribute to inflammatory diseases.[9–12] Busada et al7 studied the role of an androgen (testosterone) in protecting from the development of gastritis and gastric metaplasia. To induce disease, cohorts of male and female mice were adrenalectomized (ADX) to remove endogenous glucocorticoids, leading to gastritis. By 2 months of age, females developed gastritis and gastric metaplasia, whereas male mice remained normal. To investigate whether testosterone was responsible for protecting male mice from disease, male mice underwent ADX and a subset were castrated to remove sex hormones. ADX and castrated males developed gastritis that appeared identical