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## Colorectal Cancer Screening in the Novel Coronavirus Disease-2019 Era



*“All major population-based screening programs will shortly grind to an unseemly halt.”*

If this had been the title of a WEO Screening Committee meeting presentation in October 2019, it would have been described as sensationalist, an exaggeration, perhaps even fiction. However, in the context of the impact that the novel coronavirus disease-2019 (COVID-19) pandemic has had on endoscopic services over the last months, it can no longer be dismissed. But will we be prepared for the next pandemic? Will lessons have been learned?

The COVID-19 pandemic is an unprecedented global health crisis that has so far led to the deaths of more than half a million people. It has severely challenged the provision of routine health care, including screening for colorectal cancer (CRC).<sup>1</sup> Many countries curtailed CRC screening, in the face of staff relocation, diminishing health care resources, government-imposed isolation measures, and the fear of spreading the virus during endoscopic procedures. Although an effective response to the COVID-19 pandemic is of utmost importance, failing to screen will in itself increase mortality. In regions where the spread of the virus is under control, the focus needs to extend to responsibly restoring screening. This article explores the impact that the pandemic has currently had on CRC screening, it identifies issues that need to be addressed to successfully resume screening, and it describes how to transform CRC screening to mitigate the adverse clinical impact of future outbreaks of COVID-19 and other infectious agents.

## Effects of the COVID-19 Pandemic on CRC Screening and Diagnosis

### *Impact of the Pandemic on Screening and Diagnosis of CRC*

The COVID-19 pandemic has challenged the provision of routine health care, resulting in a temporary curtailment of many CRC screening programs. The WEO Colorectal Cancer Screening Committee focuses on the science and practice of CRC screening and has a large membership from all parts of the world. A survey of selected members of this committee showed that most national and regional screening programs paused or markedly curtailed their provision of screening during the pandemic. This was influenced by national and regional policies, differences in health-care systems and the structure and methodology adopted by the different screening programs. Although many programs were forced to pause all screening-related activities, including the provision of colonoscopy for fecal immunochemical test (FIT)-positive individuals, others maintained a colonoscopy service with markedly reduced capacity. Some centers in the United States used FIT positivity to prioritize colonoscopies for symptomatic patients. Some countries that successfully contained the spread of severe acute respiratory syndrome novel coronavirus-2 (SARS-CoV-2), such as Taiwan and Australia, continued CRC screening. Others with stringent and effective lockdowns, such as New Zealand, were able to pause for a short period.

As screening programs around the world were forced to constrain their routine services, many people found themselves unable to participate in screening or subject to long delays for colonoscopy after a positive FIT or guaiac fecal occult blood test and therefore the possibility of later stage cancer diagnosis. Previous studies have shown that delaying colonoscopy by >9 months after a positive FIT can

lead to increased risk of CRC and advanced stage CRC.<sup>2,3</sup>

### *Risk of SARS-CoV-2 Infection during Colonoscopies*

Performing a colonoscopy during the pandemic has been associated with SARS-CoV-2 infection, albeit in only a few cases. Endoscopists in Northern Italy reported a 1% rate of SARS-CoV-2 infection among endoscopy patients, and a lower rate of infection among endoscopy personnel (4.3%) than among all health care workers (10%).<sup>4</sup> In the United States, colonoscopy is considered a potential aerosol-generating procedure and the presence of SARS-CoV-2 RNA in fecal samples has been reported in a marked proportion of infected patients.<sup>5-8</sup>

To decrease the risk of infection, preprocedure testing of patients or regular testing of staff for SARS-CoV-2 can be considered, after factoring in the availability of testing material, the local case rates of COVID-19, and the limited yield of testing in asymptomatic individuals. Also, personal protective equipment (eg, gloves, gowns, glasses, and face masks) should be worn during a screening colonoscopy or sigmoidoscopy.<sup>9</sup> Standard surgical face masks can be used during the endoscopy of a patient with a negative SARS-CoV-2 test or a patient without COVID-19 symptoms, not having been in close unprotected contact with an infected individual, and not having recently (<14 days) traveled to an area with a relatively high infection rate. If these criteria are not met, it is advised to use additional protective measures, including a N95/FFP2 mask. Crowding at medical facilities may compromise the safety of both health care personnel and CRC screening participants and should also be avoided. For this reason, centers in the United States (Veteran's Affairs Health System) and Taiwan have accelerated plans to augment existing kit distribution with mailed FIT.

## How to Restart Screening after a Shut Down

### *Planning a Restart*

As the burden of the pandemic in many regions abates, screening jurisdictions are considering how to recommence or scale-up their screening programs. Limited resources may constrain the rate of return to full screening capacity. Compliance with jurisdictional guidance on the reintroduction of scheduled surgical and procedural work will be important, given the downstream impacts of CRC screening on diagnostic (imaging, pathology, colonoscopy) and treatment services, particularly surgery. Beyond alignment, a thoughtful, phased approach is recommended.

The jurisdictions responsible for each of the steps in the screening pathway vary widely between countries and institutions.<sup>10</sup> Some programs manage the entire process of screening, from offering the screening test to managing the colonoscopy with a central coordinated system, whereas others manage the initial screening test, and leave follow-up colonoscopy to their health care provider systems. Consequently, the return to normal activities can be complex and subject to multiple levels of control. Bottlenecks in screening can occur at one or more of the multiple steps in the screening process, which include primary care, the postal service, laboratory, preprocedure testing appointments, colonoscopy, pathology, and cancer treatment. In the short term, it is important that the number of invitations to participate in screening aligns with the service capacity that presents the largest bottleneck. Waiting for colonoscopy or cancer treatment for several months after a positive primary screening test undermines the benefit of screening and raises ethical concerns.

### *How to Address a Backlog*

For organized CRC screening programs based on either FIT or guaiac fecal occult blood test (referred to here as FIT), there will likely be a backlog of persons waiting to be screened. It may be necessary to delay resumption of

screening invitations until the backlog in colonoscopy is cleared. Persons with a positive FIT or symptoms suspicious for CRC who have not yet had colonoscopy should be the first priority. The backlog of persons who are overdue for receipt of a FIT need next to be considered and prioritization can be based on their known CRC risk characteristics. Priority groups could be defined based on age and screening history (no prior screening, overdue for screening, number of recent negative FITs or potentially previous fecal hemoglobin concentration[s]). Priority could also be given to those at lower risk of adverse effects of COVID-19 exposure. Although no prioritization is the easiest solution because it requires no program infrastructure changes, it may decrease the potential number of prevented CRC cases and deaths compared with a prioritization strategy. The size of the backlog and resources available to undertake prioritization will influence the preferred approach.

For CRC screening programs using endoscopy (colonoscopy or flexible sigmoidoscopy) as the initial screening test, a combined approach, offering FIT to those who refuse primary endoscopy screening could be considered. If endoscopy resources are significantly constrained, FIT screening could be adopted as a short-term alternative to colonoscopy.<sup>11</sup> FIT screening may be more appealing for those who fear hospital visits and increased risk of SARS-CoV-2 infection, and it may extend the reach of screening to a larger proportion of the target population.

### *How to Address Limited Resources*

In the lockdown and post-lockdown phases of COVID-19, most endoscopy services have substantially reduced capacity.<sup>12-14</sup> This reality creates a tension between organized screening and other clinical activity, both of which will be competing for the same or similar endoscopy resources. To maximize the benefit of the reduced endoscopy capacity, prioritization as described above may offer a solution. Conversely, cohorts at low risk of

advanced neoplasia, such as low-risk surveillance cohorts, or persons already examined through opportunistic colonoscopy screening, could be postponed until capacity is restored.<sup>15-18</sup> Surveillance using FIT for these low-risk cohorts could be a practical alternative, although the evidence base is sparse. Surveillance using colonoscopy could be limited to cohorts with higher expected benefit and diagnostic yield, for example, completion of polypectomy, short-term follow-up of piecemeal resection of large polyps, patients who are overdue for follow-up of high-risk adenomas (large adenomas or with villous features or high-grade dysplasia),<sup>9</sup> and those with high-risk familial syndromes, such as the Lynch syndrome. Diagnostic colonoscopy for symptoms could be postponed for those without alarm symptoms (ie, recent-onset rectal bleeding in a person >40 years old and iron deficiency anemia in nonmenstruating persons). Finally, efforts made to minimize a decrease in endoscopic capacity will mean that doctors have to work more hours and will inevitably also compete with time consuming academic, teaching and research activities.

### *How to Maintain Screening Participation*

An important concern when resuming screening is the potential disruptive impact that the COVID-19 pandemic might have on participation. Fear of contracting SARS-CoV-2 from health care settings has been widely reported and has resulted in delayed presentations of patients with a cardiovascular emergency.<sup>19</sup> This fear may affect screening, especially with primary endoscopic screening or after FIT-positive colonoscopy. In addition, loss of employment-linked insurance due to a pandemic-induced economic crisis may lead to a decrease in screening participation, especially among minority groups. Many studies have demonstrated that public awareness and the way screening services are provided significantly influences screening uptake.<sup>20</sup> When resuming CRC screening after an outbreak of SARS-COV-2,

**Table 1.** Proposed Indicators to Assess the Impact of the COVID-19 Pandemic on Screening and Outcomes for Colorectal Cancer

Process Indicators	Outcome Indicators
Percentage of delayed screening invitations (3–6, 6–12 months and $\geq 12$ months)	Response rate to screening invitation
Positivity rate of FIT/gFOBT	Detection rate of CRC and advanced adenomas
Interval between positive FIT/gFOBT result and colonoscopy	Stage distribution of detected cancers
Proportion of refused/rescheduled appointments related to COVID-19	Interval cancer rate
Rate of SARS-CoV-2 infections associated with CRC screening and diagnostic follow-up	CRC-related mortality

COVID-19, coronavirus disease-2019; CRC, colorectal cancer; FIT, fecal immunochemical test; gFOBT, guaiac fecal occult blood test.

various approaches might encourage CRC screening participation. In regions where participants collect their kits from family practitioners, pharmacists, or hospitals, direct mailing of the FIT screening kit could be considered and might even increase uptake in both organized and opportunistic screening programs. Leading screening physicians, but also (well-known) patients, could consider promoting public awareness of CRC screening and its importance in local and national media during the pandemic.<sup>21</sup> A centralized communication team could exploit telemedicine or telephone communication instead of physical appointments to invite and encourage

screening participation and colonoscopy attendance. It might also be worthwhile offering multiple screening choices to facilitate screening compliance.<sup>22</sup> Last, public confidence in safety of attending colonoscopy units could be restored by promoting regular testing of staff as well as patients.<sup>23</sup>

### *Monitoring the Restart of Screening*

To measure the impact of the pandemic and the effect of measures taken to restart CRC screening, various indicators seem relevant (Table 1). Established measures of the early impact of screening, such as the

detection rate of neoplastic lesions, stage distribution of screen detected cancers and interval cancer rate, allow us to assess the impact of the delay on these outcomes. We should consider the rate of COVID-19 infections associated with colonoscopies performed in screening programs and its impact on diagnostic follow-up for CRC. This will provide information about the actual risk associated with these procedures, as well as about the effectiveness of protective measures.

To ensure successful operation of the program during the transition to routine screening, indicators of short-term screening activity are useful. The response rate of people invited for

**Table 2.** Observations of the Impact of the COVID-19 Pandemic on Colorectal Cancer Screening

Health care resources can be rapidly overwhelmed during a pandemic.
If screening is not considered to be of high priority, it may be ignored by policymakers responding to a pandemic, especially if prior planning is lacking or delegation ineffective.
Available screening staff will quickly be diminished, be redeployed to acute services, or be indisposed due to personal or family illness or enforced isolation.
Without a plan, FIT-kit distribution, laboratory analysis and endoscopic activity can be uncoordinated and disrupted.
Without previously prepared media releases or personal communications, the public will not be adequately informed about screening arrangements.
Public anxiety can grow about missed tests, positive FIT results without a colonoscopy appointment, cancelled appointments and fear of contracting COVID-19 in an endoscopy unit.
Personal Protective Equipment may not be available for (screening) endoscopy.
Screening IT and communication systems may not be supported owing to staff shortages or modified priorities.
Without prior planning, it will not be clear how to prioritize a backlog of FIT-kits awaiting distribution or testing and many months of delayed endoscopy and associated surgery.
New or existing endoscopy units may be unsuited to social distancing and may compromise the safety of patients and staff not wearing protective gear.

COVID-19, coronavirus disease-2019; FIT, fecal immunochemical test; gFOBT, guaiac fecal occult blood test.

primary screening or to colonoscopy following a positive FIT test, should be monitored so that organizational barriers and subjects' fears and concerns about the potential risk of infection can be addressed in a timely fashion. This could also include the possibility to stratify the data based on postal code or ethnicity to detect general disparities in health access between social groups. Consideration should be given to introducing a new indicator designed to measure the proportion of refusals or rescheduled appointments for colonoscopy after a positive screening test related to COVID-19 (mainly fear of being infected when attending an examination in an endoscopy center<sup>24,25</sup>).

In addition to existing indicators of screening activity (eg, invitation coverage and wait time for diagnostic colonoscopy), new indicators based on the observed trends are needed to support decisions on recovery plans. Strict and continuous real-time monitoring of the number of procedures performed in each program/ or , as well as of the backlog, provides the necessary information to estimate the expected time to a complete recovery, to assess the ability of the program to achieve the expected targets and to make quick adjustments as problems became apparent. Ideally, continuous rather than categorical data should be collected to assess the association between the delay and the outcome.

### Modelling Scenarios and Outcomes

Because the COVID-19 pandemic is unprecedented, there are no clinical studies to inform decision making for our screening programs. That is where well-established and validated decision models using closely monitored outcomes from existing and new indicators come into play. Modelers from all around the world have joined forces in the COVID-19 and Cancer Global Modelling Consortium ([ccgmc.org](http://ccgmc.org)) to simulate different scenarios of disruption and recovery strategies and predict both long-term outcomes of CRC cases and deaths as well as short-term and long-term costs and

savings. Comparing the benefits, harms, and costs of the different scenarios, policymakers can decide on the best recovery strategy for their programs.

### Lessons to Be Learned

Will we be prepared for the next pandemic? Will lessons have been learned? We, as an expert working group, describe the following observations from which lessons are to be learned (Table 2).

The multiple steps in the CRC screening process make it a complex enterprise that can be easily affected if one component fails. The observations described in Table 2 could inform plans to strengthen screening programs and decrease the risk of major service disruption in future pandemic waves.

Policymakers must recognize that cancer screening is an important component of modern health care. The COVID-19 pandemic provides an opportunity for screening programs to reflect on their current arrangements and decide whether, if reorganized, they could increase coverage, uptake, and clinical effectiveness, as well as being more robust to a future disruption. Considerations should include what proportion of endoscopy capacity is allocated to screening, and how to maximize its yield with limited capacity (eg, by moving from colonoscopy to a noninvasive screening test or adjusting the positivity cut-off for FIT-screening). Finally, we should reflect on how well we communicate with the public, ensure safety for patients and staff during endoscopic procedures, and strengthen communication and collaboration between screening, surgery, and oncology. These plans can be made and implemented with the help of sound evidence from the current crisis. Extensive monitoring and review of the current restart and upscaling efforts of CRC screening is therefore of vital importance.

Already in the pre-COVID era, health care systems worldwide were forced to deal with increasing demands, shortage in workforce, and

budget constraints. These factors all strengthened the need for prevention, such as with relevant cancer screening programs. These programs reduce the need for intense treatments of patients with advanced disease. The COVID-19 pandemic has markedly increased the constraints as discussed elsewhere in this Commentary and thus makes CRC screening far more instead of less relevant.

We are presented with an opportunity to strengthen CRC screening programs as we resume services blighted by the pandemic. By learning from this crisis, we can have a robust plan for the next!

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