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.

We declare no competing interests.

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Faecal immunochemical testing in the COVID-19 era: balancing risk and costs

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The COVID-19 pandemic has dramatically reduced access to diagnostic endoscopy across the UK. As such, demand for timely investigation exceeds immediate National Health Service capacity. Referrals of people for investigation of lower gastrointestinal symptoms have dropped markedly, but as we move into a recovery phase, various methods are being explored to enable rebooting of clinical pathway services within the constraints of limited capacity. One challenge is detecting the minority of people with bowel symptoms who have colorectal cancer at a stage curable by surgery. In England, there are around 300 000 referrals for diagnostic endoscopy per year and this number is increasing.[1] Consideration is being given to ways to prioritise patients, including use of tests such as faecal immunochemical testing (FIT) for haemoglobin to diagnose colorectal cancer.

It has been suggested that red flag symptoms or faecal haemoglobin concentrations greater than 100 µg/g should prompt urgent referral, but both apply only to a minority of patients. The question is how to manage the majority who do not meet these criteria. National Institute for Health and Care Excellence (NICE) guidance recommends FIT for low-risk patients with lower gastrointestinal symptoms and faecal haemoglobin concentrations using a lower threshold of positivity of 10 µg/g.[2] Investigation of all individuals with results above that level would require very large numbers of colonoscopies or CT colonography, and most of these patients would be found not to have colorectal cancer. Risk stratification is required and studies[3] to address these knowledge gaps have been delayed because of COVID-19.

As a result, a particular area of contention is what FIT threshold to use and how best to implement this within a diagnostic pathway in the COVID-19 era. Faecal haemoglobin concentrations higher than 100 µg/g are suggestive of pathology,[4] mandating an urgent colonoscopy. However, individuals with faecal haemoglobin concentrations between 10 µg/g (or lower threshold) and 100 µg/g pose a challenge, because of a paucity of evidence on colorectal cancer risk and disease staging. The overall risk for these individuals is low, but there is probably a gradient of risk within this broad range, and the gradient might include individuals with resectable colorectal cancer or other clinically significant bowel disease. Current opinion (which varies by region) suggests that during COVID-19, those individuals who fall into this group have investigations (colonoscopy) deferred rather than omitted in order not to miss cancer. These deferrals are likely to be needed to release more capacity after the epidemic curve begins to fall.

A further group to consider is those individuals with faecal haemoglobin concentrations less than 10 µg/g (or lower than the detection limit). The evidence base

is limited for this group of patients, but the reported colorectal cancer risk is 1–2%.[5,6] Moreover, faecal haemoglobin concentrations are not specific to different cancer stages, with wide variation even with stage I disease.[7] Laboratory parameters might help to prioritise investigations. CT colonography is less costly than colonoscopy and would detect cancers and other diseases, such as adenomas (depending on size), inflammatory bowel disease, and some non-gastrointestinal cancers, but will miss conditions such as microscopic colitis, for which histological diagnosis is required. Other non-cancer diagnoses have been reported in patients with low faecal haemoglobin concentrations,[5] hence guidance for management during COVID-19 should suggest that individuals in this group are not discharged, but rather should include consideration for lower gastrointestinal endoscopy and other tests, albeit as a low priority (and requiring some resource allocation).

See Online for appendix

CT colonography could provide the added assurance of colorectal cancer exclusion, but capacity has been reduced because of long scanning times, and is likely to be between 50–75% of pre-COVID-19 levels, when approximately 120 000 CT colonographies were done annually in England. CT colonography could also miss about 4% of colorectal cancers,[8] similar to the proportion missed by colonoscopy.

Repeat FIT has been discussed within the bowel screening field,[9] but is subject to pre-analytical variation. Blood in stool might not be evenly distributed and stool sampling can vary with each attempt. Another option would be to add a second non-invasive test, such as urinary volatile organic compounds,[4] at the same time as FIT to risk stratify those at risk not only of colorectal cancer but also of other clinically significant bowel disease. However, to assess the diagnostic accuracy of other additional tests would require all patients to be tested irrespective of their FIT result.

Premature use of FIT for diagnosis of colorectal cancer during COVID-19 without appropriate safety measures in place will have unintended consequences, as demonstrated with faecal calprotectin and reflected in the NICE health technology assessment report.[10] General practitioners should still refer symptomatic patients for investigations, which might be more than colonoscopy, because other clinically significant pathologies could be detected.[5] Using FIT to triage timing of investigations could offer the opportunity to evaluate other technologies such as colon capsules, ideally in comparison with CT colonography. The costs and consequences of the various options for risk stratification of individuals with lower gastrointestinal symptoms are outlined in the appendix.

Only a small proportion of people investigated for lower gastrointestinal symptoms have colorectal cancer. There might be a cost-effectiveness threshold at which the benefits of detecting a tumour are outweighed by the disutility and costs of the very large number of colonoscopies required. Better non-invasive ways of determining risk are therefore needed. There is no simple or rapid solution, but patients might be harmed if proper evaluations of diagnostic tests are not done before clinical use. The precision of the test should guide clinical pathways, not the other way around.

A focus on colorectal cancer detection could also cause harm to patients if the main aim was excluding colorectal cancer rather than making a positive diagnosis and excluding other clinically significant bowel diseases. Patients without a positive diagnosis will be re-referred and will add to the existing service burden rather than reduce it. The evidence gaps with FIT in individuals with symptoms are: (1) diagnostic accuracy for colorectal cancer and clinically significant bowel disease when faecal haemoglobin concentrations are between the lowest threshold and 100 µg/g; (2) data on the occurrence of resectable colorectal cancer by bands of FIT score; and (3) cost savings and patient quality-adjusted life-years if fewer colonoscopies are done.

In summary, the distinction between a triage test and a diagnostic test must be clear. FIT during COVID-19 could be used as a triage tool to guide timing or prioritisation of investigations (to manage limited capacity) rather than replacing other investigations or discharging patients if their FIT results are below threshold.

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