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The state of the faecal immunochemical test in symptomatic patients in the UK

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The use of the faecal immunochemical test (FIT) to guide referral of patients with suspected bowel cancer symptoms is yet to be widely adopted in the UK. FIT has been used extensively over the last 20 or so years, in bowel cancer screening programmes all over the world, as a surrogate marker to detect bowel cancer in unsuspecting and asymptomatic individuals. In its 2015 NG12 guidance, NICE recommended the use of guaiac-based faecal occult blood test (gFOBT) and not FIT in primary care to triage patients with low-risk symptoms for cancer, due to paucity of evidence on FIT diagnostic accuracy at the time.[1] But as evidence on FIT efficacy in symptomatic patients continued to emerge, gFOBT was replaced with FIT in NICE 2017 DG30 guidance.[2] However, this recommendation was not extended to patients with high-risk symptoms for cancer or rectal bleeding.[2] Since then, several pioneering centres in the UK, including centres in Nottingham, Oxfordshire and Tayside in Scotland, introduced FIT in patients with high and low risk symptoms using record linkage as part of service development projects, and reported promising results.[3–5] At the same time, three large research studies were conducted in England, investigating the diagnostic accuracy of FIT in high and low risk symptomatic patients and reporting similar results.[6–8] Two recent meta-analyses evaluated this and other evidence of the diagnostic accuracy of FIT.[9,10] The key message from these studies remains remarkably consistent:

- FIT is sensitive for the detection of colorectal cancer. The summary sensitivity at a cut-off of 10 ug/g was 87.2% (95% CI 81.0% to 91.6%, 15 studies; *n*=48,872), which increased to 93.4% (95% CI 88.0% to 96.4%, 11 studies; *n*=41,338 patients) at the lower cut-off of detectable blood, known as the limit of detection (LoD).[9]
- Colorectal cancer and serious bowel pathology detection rates rise with higher faecal haemoglobin concentrations.[3–8]
- When FIT is "negative" below a concentration of 10 ug/g, the negative predictive value of FIT is high; above 99.5% in most published studies, due largely to the low prevalence of colorectal cancer in most patients with bowel symptoms.[10] Thus, in symptomatic patients with a negative FIT, the chance of having a cancer is 0.5% and the number needed to investigate/scope to detect

one cancer would be over 200. This is compared to 6-10 patients with FIT above 10ug/g and 4-5 patients with FIT above 100ug/g.[6–8]

- The diagnostic accuracy of this test is, counter-intuitively, barely improved by the addition of other clinical characteristics into a risk-score.[3,11]

Despite these encouraging results, there has been reluctance on the part of some groups in the UK, including NHS England, to recommend the use of FIT in the high-risk symptomatic patients because of concerns about missing cancer. However, COVID-19 shifted the paradigm, forcing services in all four home nations to introduce FIT into referral pathways to suit local needs, reduce inappropriate referrals and prioritise investigations.[3,12–14] An unpublished ACPGBI survey of UK regions conducted between 4 October and 8 November 2021 showed that 94.5% of UK regions are using FIT in triaging high risk symptomatic patients with 69% of the regions introducing FIT after the COVID-19 pandemic. Some regions have incorporated FIT for selected symptoms (eg change in bowel habit in patients older than 60 in Leicester),[15] while other regions are awaiting guidance from NICE before incorporating FIT in their own pathways. However, such guidance is not forthcoming soon and, to address this unmet need and bring consistency to all four home nations, the ACPGBI and BSG have joined forces to develop national guidelines on this topic with expected release in the second quarter of 2022.

While diagnostic accuracy of FIT remains consistently high, there are a few minor but important issues the upcoming guidelines should address. Chief among them is the main concern of clinicians of how to identify and manage the small number of FIT negative cancers. When considering this issue, it is important to note that the UK post-colonoscopy cancer rate varies from 3.2%-7.6%.[16] Like colonoscopy, FIT sensitivity is not 100% and therefore cancers will be missed by relying solely on the outcome of the test. Unlike colonoscopy, which is a diagnostic test, FIT is simply a triage test which should be used alongside clinical acumen, especially in FIT negative patients. The number of missed cancers will be reduced when patients are appropriately assessed and referred (eg when a rectal mass is found on digital examination), or safety netted by general practitioners (due to worrying, persistent or deteriorating symptoms), as confirmed in service evaluations from England and Scotland.[3,5] Already, safety netting has been implemented in existing FIT pathways; lessons from these pathways are essential to manage FIT negative patients, which should be an integral part of any FIT implementation programme.

The inevitable direction of travel will be to use FIT as a triage tool to decide which patients to investigate, and how urgently to investigate them. FIT's sensitivity, and positive and negative predictive values make it a once-in-a-lifetime tool that could revolutionise the way bowel symptoms are investigated. To fully exploit the potential of this test would require a major overhaul of the referral pathways for suspected colorectal cancer, including referral criteria, treatment targets and safety netting pathways. While this may be a radical step, a revolution to the way suspected bowel cancer symptoms are investigated is long overdue.

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