

Letter: extending FIT from DG30 to NG12 patients.

Letter: faecal immunochemical testing for adults with symptoms of colorectal cancer – ready for prime time?

Authors' reply: A unified approach to safety netting negative FITs is required.

Dear Editors,

We are extremely grateful to Turvill and Farrugia for their responses to our recent manuscript (1, 2). FIT is being rapidly but variably deployed across the NHS as a non-invasive triage test to prioritise symptomatic patients for colonoscopic investigation (3). This is a pragmatic approach to health service recovery following the drastic loss of endoscopy capacity caused by the COVID-19 pandemic.

We presented evidence from a symptomatic cohort, tested in primary care in the context of NICE DG30 guidance (4). Turvill rightly cautions against extrapolating estimates of risk associated with positive or negative test results from one population to another with a different disease prevalence. He illustrates this by comparing our “low-risk” symptomatic primary care population (DG30) with the “high-risk” symptomatic referred population (NG12) (1). A rapid update of the 2016 search performed for DG30 by NICE (to July 2020) found five articles reporting the diagnostic accuracy of FIT ≥ 10 μg Hb/g faeces in >1000 symptomatic patients (5). Additional large studies will provide us with greater confidence as, at present, “high-risk” symptomatic cohorts are not clearly associated with decreasing sensitivity (Table 1). Increasing cancer prevalence broadly aligns with increasing serious colorectal disease (SCD) but, as Farrugia points out (2), SCD detection is biased as all referred patients receive colonoscopy whilst primary care studies rely on observational follow-up for most.

Studies using sample collection devices excluded patients due to their faecal samples being unsuitable for analysis, particularly from older patients (6, 7). Farrugia et al highlight that sampling devices avoid haemoglobin degradation by suspending the stool into a buffer on collection (2). Sources of pre-analytical variation also include sampling quality and biological variability. Our laboratory staff sampled 33 faecal specimens in triplicate (8). 31 (93.9%) specimens were consistently positive or negative around ≥ 10 μg Hb/g. The variability of FIT results (median coefficient of variation, 27.8%, range 20.5% to 48.6%) reduced after specimens were homogenised (10.2%, 7.0% to 13.5%) and all specimens were consistently categorised. Of 225 patients with ≥ 3 consecutive specimens, 197 (87.6%) had concordant results (188 negative, 9 positive). We found no association between the likelihood of a positive result and the length of time it took the specimen to reach the laboratory ($p = 0.84$) or the order of specimens ($p = 0.21$). Whilst our approach, using standard faecal containers, risks haemoglobin degradation it improves precision through homogenisation, and avoids under-sampling that risks false negatives or over-sampling that risks rejection.

Whether dubbed a high, low, or intermediate risk symptomatic population, and regardless of sampling method, a unified approach to safety netting “negative” FITs is required to guard against false negative results. Patients with a negative FIT but persistent, worsening red flag, or new symptoms should be given rapid access back into clinical pathways. Debate continues about where the responsibility for this patient group should lie, which is reflected in the options of either primary or secondary care in NHS guidance. FIT provides an opportunity to improve lines of communication and patient safety between primary and secondary care.

Yours sincerely,

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Table 1: Studies published since NICE DG30 reporting the diagnostic accuracy of FIT ≥ 10 μ g Hb/g in more than 1000 symptomatic people. NPV: negative predictive value; CRC: colorectal cancer; SCD: serious colorectal disease = colorectal cancer, high-risk adenoma, and inflammatory bowel disease; CI: confidence interval; N/R: not reported.

Author (year) (ref)	Setting (N)	CRC n (%)	Sensitivity % (95% CI)	NPV % (95% CI)	SCD n (%)
Nicholson (2020) (4)	Primary Care (9896)	105 (1.1)	90.5 (84.9 to 96.1)	99.9 (99.8 to 100.0)	682 (6.9)
Juul (2018) (6)	Primary Care (3462)	53 (1.6)	~96 (N/R)	~99.9	105 (3.1)
Lazlo (2020) (7)	Referred (3596)	90 (2.5)	83.3 (75.6 to 91.0)	99.5 (N/R)	437 (12.2)
Quyn (2018) (9)	Referred (1514)	45 (3.0)	93.3 (80.7 to 98.3)	99.7 (99.2 to 99.9)	231 (15.3)
Mowat (2019) (10)	Referred (1447)	95 (6.5)	90.5 (N/R)	N/R	296 (20.5)

Declaration

The authors' declarations of personal and financial interests are unchanged from those in the original article (4).

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