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Original Article

Faecal immunochemical testing in symptomatic patients to prioritize investigation: diagnostic accuracy from NICE FIT Study

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Abstract

Background: This study investigated whether a quantitative faecal immunochemical test (FIT) could be used to select patients with either high- or low-risk symptoms of colorectal cancer for urgent investigation.

Methods: A double-blinded diagnostic accuracy study was conducted in 50 hospitals in England between October 2017 and December 2019. Patients were eligible for inclusion if they had been referred to secondary care with suspected colorectal cancer symptoms meeting national criteria for urgent referral and triaged to investigation with colonoscopy.

Results: The study included 9822 patients, of whom 7194 (73.2 per cent) had high-risk symptoms, 1994 (20.3 per cent) low-risk symptoms, and 634 (6.5 per cent) had other symptoms warranting urgent referral. In patients with high-risk symptoms, the sensitivity of FIT for colorectal cancer at cut-off values of 2 and 10 μg haemoglobin per g faeces was 97.7 (95 per cent c.i. 95.0 to 99.1) and 92.2 (88.2 to 95.2) per cent respectively, compared with 94.3 (84.3 to 98.8) and 86.8 (74.7 to 94.5) per cent in patients with low-risk symptoms at the same cut-off points. At cut-off values of 2, 10, and 150 μg/g, the positive predictive value for colorectal cancer was 8.9, 16.2, and 30.5 per cent respectively for those with high-risk symptoms, and 8.4, 16.9, and 35.5 per cent for those with low-risk symptoms.

Conclusion: FIT safely selects patients with high or low risk symptoms of colorectal cancer for investigation.

Introduction

In the UK, faecal immunochemical test (FIT) is not currently recommended for selection of patients with high-risk symptoms of colorectal cancer for investigation, but is recommended to guide referral of patients with low-risk symptoms from primary care for urgent investigation on a 2-week wait (2WW) pathway[1]. These recommendations were based on studies that included patients with wide-ranging symptoms, not stratified by high- or low-risk symptoms in accordance with National Institute for Health and Clinical Excellence (NICE) criteria[2,3]. In the past 5 years, a growing body of evidence has suggested that FIT can be used in symptomatic patients to select for investigation. It may even be more accurate at detecting colorectal cancer than patient symptoms[2,4–6]. Nonetheless, the UK NICE does not recommend use of FIT in patients with high-risk symptoms, because of a lack of robust evidence for the diagnostic accuracy of FIT in this group[7,8].

Following expansion of referral criteria, the number of 2WW referrals for suspected colorectal cancer in England increased from 209 265 in 2013–2014 to 392 588 in 2018–2019[9]. Colorectal cancer detection rates on 2WW pathways have decreased, from 6.4 per cent (8985 of 140 259) in 2009 to 3.4 per cent (13 164 of 392 588) in 2018[10]. Most 2WW referrals for suspected colorectal cancer are investigated by colonoscopy[7] and, as a consequence of increased demand, only 55 per cent of endoscopy services in England are meeting cancer waiting targets[11]. The consumption of endoscopy capacity by 2WW investigations has prevented expansion of the Bowel Cancer Screening Programme in England[12]. Screen-detected colorectal cancers have a significantly better prognosis than those in symptomatic patients[13].

The NICE FIT study[14] investigated the diagnostic accuracy of FIT for colorectal cancer or other serious bowel disease in patients referred under the 2WW pathway. This further analysis aimed to compare the diagnostic accuracy of FIT for colorectal

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cancer in patients stratified by severity (high *versus* low risk), and to investigate the diagnostic accuracy of FIT for colorectal cancer by presenting symptom. Secondary aims of this study were to compare the incidence of serious bowel disease at different FIT cut-off values in patients with high- and low-risk symptoms.

Methods

The study was designed to meet STARD guidelines[15] and was registered prospectively (ISRCTN 49676259) after ethical approval had been obtained (IRAS 218404). The study was approved by the National Research Ethics Service Committee, London—South East (reference 16/LO/2174). Patients were recruited at 50 National Health Service hospitals across England. The study was designed with patient and public involvement, as reported previously[14].

Patient selection

Patients were eligible for inclusion if they were referred to secondary care with symptoms of suspected colorectal cancer that met NICE referral criteria under the 2WW pathway (*Table 1*)[1,7]. They were triaged to investigation by colonoscopy. Once vetted for colonoscopy, patients were invited by post or telephone to participate in the study by the central study team or local cancer research network team. Patients were posted a FIT specimen collection device and asked to collect one sample of faeces before commencing bowel preparation for colonoscopy, and to return the sample directly to the study laboratory with an enclosed stamped return envelope.

Patients were not eligible for inclusion if they withdrew consent, did not return a FIT sample, did not have a complete colonoscopy unless owing to colorectal cancer, or were retriaged to another investigation. Patients with low-risk symptoms were eligible for inclusion if they were not tested in primary care with guaiac faecal occult blood tests according to NG12 guidance, or FIT in accordance with DG30 guidance, and instead were referred to secondary care on a 2WW pathway for investigations. Patients who did not have symptoms that met NICE criteria and yet were referred urgently on a 2WW pathway because of clinical concern about suspected cancer by general practitioners (GPs) were assigned to an 'other' group.

Index and reference standard

A description of the methodology for the index test, reference standard, and sample size calculation has been reported previously[14]. The FIT assay used was HM-JACKarc (Hitachi Chemical Diagnostics Systems Co., Ltd, Tokyo, Japan), which has a limit of detection (LoD) of 2 μg haemoglobin per g faeces. In accordance with previous publications on FIT, the LoD and faecal haemoglobin (f-Hb) cut-off of 10 μg/g recommended in NICE DG30 was used as cut-off for investigation of high sensitivity[16,17]. To investigate the positive predictive value (PPV) at a higher f-Hb concentration, a higher cut-off of 150 μg/g was selected, which had been used previously in symptomatic patients[17]. Tests were deemed FIT-positive if equal to or above the described cut-off, or FIT-negative if below the cut-off.

Data analysis

Colorectal symptoms were classified by NICE NG12 2WW and DG30 referral criteria (*Table 1*)[1,7]. As patients are often referred with multiple symptoms, a hierarchy was created to assign one criterion to each patient. For NG12, the hierarchy of criteria was: abdominal or rectal mass, iron deficiency anaemia (patients 60 years or over), rectal bleeding, change in bowel habit (age 60 years or over), and abdominal pain and weight loss. DG30 criteria were ranked as: iron deficiency anaemia (aged less than 60 years), non-iron deficiency anaemia, abdominal pain or weight loss, change in bowel habit (aged less than 60 years).

Similarly, patients with multiple findings at colonoscopy were recategorized with one primary diagnosis in a hierarchy; colorectal cancer, higher-risk adenoma, inflammatory bowel disease, and low-risk adenoma were ranked above benign diagnoses including diverticular disease, microscopic colitis, benign perianal disease (haemorrhoids, anal fissures or fistulas, solitary rectal ulcers), or rarer findings such as angiodysplasia, melanosis coli, parasites or lipomas. Higher-risk adenoma were defined by the NICE FIT Steering Group as any polyp with high-grade dysplasia or polyps over 10 mm in size with low-grade dysplasia, and serrated lesions in the right colon. Other polyps were classified as low-risk adenomas. The term serious bowel disease was used to describe the three most significant diagnoses (colorectal cancer, higher-risk adenoma, inflammatory bowel disease) grouped together.

Statistical analysis

Normality of the data was assessed by the Shapiro test and Q–Q plot analysis. Categorical data were compared using χ^2 tests. Sensitivity, specificity, PPV, and negative predictive value (NPV) were reported for each f-Hb cut-off, with 95 per cent confidence intervals. Receiver operating characteristic (ROC) curves were plotted for f-Hb. These were done using an initial threshold of 0.1 to calculate sensitivity and specificity, and then recalculated

Table 1 Referral symptoms according to National Institute for Health and Care Excellence NG12 and DG30 guidance

Symptoms	2015 guidance (NG12)	2017 guidance (DG30)	Risk of colorectal cancer (%)
Mass IDA (age ≥ 60 years) RB (age ≥ 50 years) RB + IDA/CIBH/WL (age < 50 years) CIBH (age ≥ 60 years) AP *and* WL (age ≥ 40 years)	Refer		3–5
IDA (age < 60 years) Anaemia, non-IDA (age ≥ 60 years) AP *or* WL (age ≥ 50 years) CIBH (age < 60 years)	Test for occult blood (FOBT)	Test for occult blood (FIT)	1–3

Mass, abdominal or rectal mass; IDA, iron deficiency anaemia; RB, rectal bleeding; CIBH, change in bowel habit; WL, weight loss; AP, abdominal pain; FOBT, faecal occult blood test; FIT, faecal immunochemical test.

with increments of 0.1 to plot the ROC curve. To determine whether there were statistically significant differences in diagnostic accuracy, the equality of ROC curve areas was analysed using the χ^2 test. $P < 0.050$ was considered significant in all statistical analyses. Analyses were done using SAS® version 9.4 (SAS Institute, Cary, North Carolina, USA) and Stata® version 15 (StataCorp, College Station, Texas, USA).

Results

In total, 9822 patients were included, of whom 7194 (73.2 per cent) had high-risk symptoms meeting NG12 criteria, 1994 (20.3 per cent) had low-risk symptoms meeting DG30 criteria, and 634 (6.5 per cent) had other symptoms warranting urgent referral (*Fig. 1*). Patient demographics and colonoscopy findings in the three groups are described in *Table 2*. No colorectal disease was detected in 27.4 per cent of patients with high-risk symptoms and 44.3 per cent of those with low-risk symptoms ($P < 0.001$).

There was no difference in the diagnostic accuracy of FIT for colorectal cancer in high- and low-risk patients at any f-Hb cut-off (see confidence intervals) (*Table 3*). The proportion of patients with positive FIT tests at cut-off values of 2, 10, and 150 μg/g decreased in both high- and low-risk groups ($P < 0.001$). FIT sensitivity decreased at higher cut-off values, whereas specificity and PPV for both colorectal cancer and serious bowel disease increased. In ROC curve analysis the area under the curve of FIT for colorectal cancer was 0.94 (95 per cent c.i. 0.92 to 0.95) for patients with high-risk symptoms, 0.93 (0.89 to 0.97) for those with low-risk symptoms, and 0.91 (0.83 to 0.98) for the group with other symptoms (*Fig. 2*). The test of equality of the area under the curve for each group yielded a significance probability of 0.75, suggesting no significance difference between these areas.

The sensitivity and PPV of FIT for colorectal cancer at cut-off values of 2, 10, and 150 μg/g by presenting symptom is shown in *Table 4*. Complete diagnostic accuracy data on FIT for each referral symptom are available in *Tables S1–S3*. The NPV of FIT for colorectal cancer at cut-off values of 2 and 10 μg/g remained above 99 per cent for all NG12 and DG30 symptoms.

Table 2 Patient details

	NG12 (*n* = 7194)	DG30 (*n* = 1944)	Other* (*n* = 634)
Age (years)			
Mean(s.d.)	65.9 (11.1)	57.9 (11.3)	61.2 (14.6)
Median (range)	67 (20–97)	56 (22–94)	64 (17–91)
< 40	200 (2.8)	99 (5.0)	62 (9.8)
41–50	493 (6.9)	338 (17.0)	109 (17.2)
51–60	1172 (16.3)	951 (47.7)	103 (16.2)
61–70	2591 (36.0)	281 (14.1)	161 (25.4)
71-80	2293 (31.9)	256 (12.8)	157 (24.8)
≥ 80	445 (6.2)	69 (3.5)	42 (6.6)
Sex ratio (F : M)	3907 : 3287	1164 : 830	323 : 311
Ethnicity			
White	5693 (80.0)	1361 (70.7)	399 (67.2)
Asian	355 (5.0)	188 (9.8)	71 (12.0)
Black	253 (3.6)	90 (4.7)	22 (3.7)
Mixed	42 (0.6)	12 (0.6)	4 (0.7)
Chinese	27 (0.4)	11 (0.6)	4 (0.7)
Not specified	746 (10.5)	263 (13.7)	94 (15.8)
Index of Deprivation			
Mean(s.d.)	6.3 (2.6)	5.9 (2.6)	6.1 (2.6)
Median	7	6	6
Diagnosis at colonoscopy			
Colorectal cancer	257 (3.6)	53 (2.7)	19 (3.0)
Higher-risk adenoma	335 (4.7)	50 (2.5)	36 (5.7)
Inflammatory bowel disease	342 (4.8)	65 (3.3)	20 (3.2)
Serious bowel disease†	728 (10.1)	120 (6.0)	60 (9.5)
Normal	1973 (27.4)	884 (44.3)	222 (35.0)
Diverticular disease	1802 (25.0)	374 (18.8)	118 (18.6)
Low-risk adenoma	1730 (24.0)	435 (21.8)	156 (24.6)
Perianal disease	581 (8.1)	91 (4.6)	51 (8.0)
Microscopic colitis	125 (1.7)	20 (1.0)	7 (1.1)
Other	49 (0.7	22 (1.1	5 (0.8)

Values in parentheses are percentages unless indicated otherwise. Data were incomplete for ethnicity. * Other symptoms of suspected cancer that warrant urgent 2-week wait (2WW) referral, without meeting National Institute for Health and Care Excellence 2WW criteria. † Colorectal cancer, higher-risk adenomas or inflammatory bowel disease.

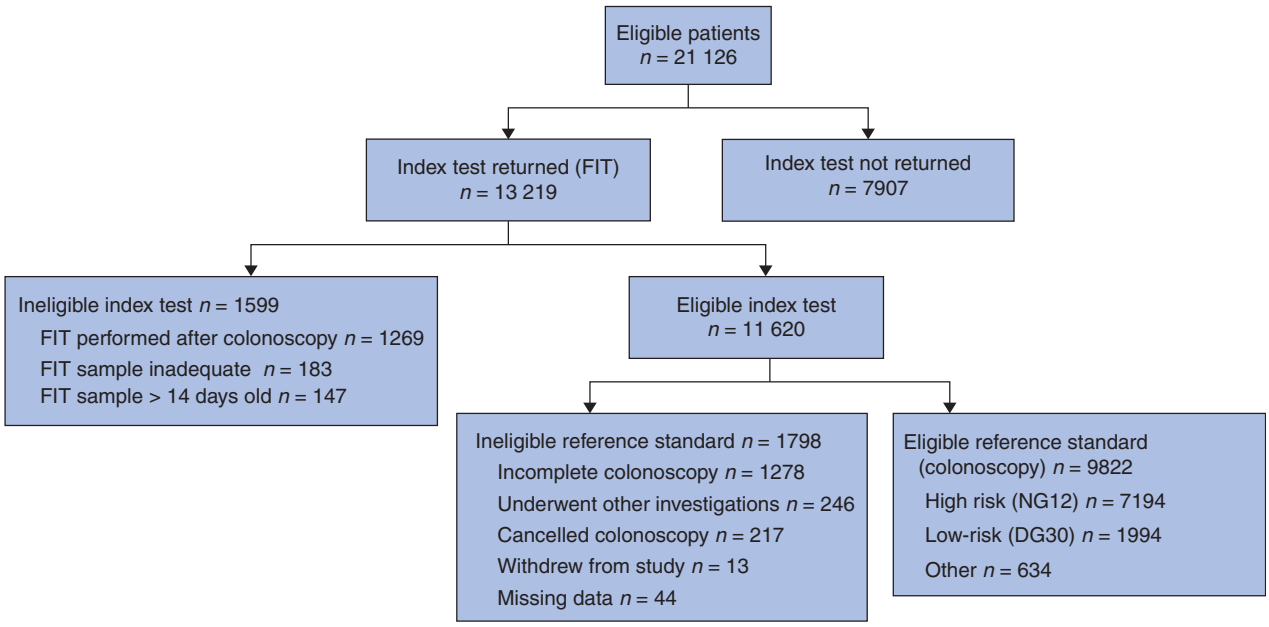

Fig. 1 Adapted STARD flow chart

FIT, faecal immunochemical test.

Table 3 diagnostic accuracy of faecal immunochemical test for colorectal cancer at different cut-off values by symptom risk category

Cut-off (μg/g)	FIT positivity (%)	Colorectal cancer				PPV for SBD (%)
		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	
High risk (NG12)						
≥ 2	39.2	97.7 (95.0, 99.1)	63.0 (61.8, 64.1)	8.9 (7.9, 10.0)	99.9 (99.7, 99.9)	25.8 (24.2, 27.5)
≥ 10	20.4	92.2 (88.2, 95.2)	82.3 (81.3, 83.2)	16.2 (14.3, 18.1)	99.7 (99.5, 99.8)	40.6 (38.0, 43.1)
≥ 150	8.4	72.0 (66.1, 77.4)	93.9 (93.3, 94.5)	30.5 (26.9, 34.4)	98.9 (98.6, 99.1)	64.5 (60.6, 68.3)
Low risk (DG30)						
≥ 2	29.9	94.3 (84.3, 98.8)	71.8 (69.8, 73.8)	8.4 (6.3, 10.9)	99.8 (99.4, 100)	20.1 (17.0, 23.5)
≥ 10	13.6	86.8 (74.7, 94.5)	88.4 (86.8, 89.8)	16.9 (12.7, 21.9)	99.6 (99.2, 99.8)	34.9 (29.3, 40.9)
≥ 150	4.7	62.3 (47.9, 75.2)	96.9 (96.0, 97.6)	35.5 (25.8, 46.1)	98.9 (98.4, 99.4)	64.5 (53.9, 74.2)
Other						
≥2	37.9	94.7 (74.0, 99.9)	63.9 (60.0, 67.7)	7.5 (4.5, 11.6)	99.7 (98.6, 100)	25.0 (19.7, 31.0)
≥ 10	19.4	84.2 (60.4, 96.6)	82.6 (79.4, 85.5)	13.0 (7.6, 20.3)	99.4 (98.3, 99.9)	38.2 (29.6, 47.4)
≥ 150	7.9	78.9 (54.4, 93.9)	94.3 (92.2, 96.0)	30.0 (17.9, 44.6)	99.3 (98.3, 99.8)	64.0 (49.2, 77.1)

Values in parentheses are 95 per cent confidence intervals. PPV, positive predictive value; NPV, negative predictive value; SBD, serious bowel disease.

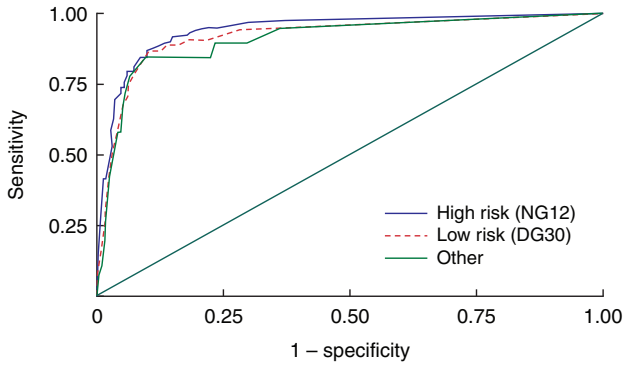

Fig. 2 Receiver operating characteristic (ROC) curve analysis of faecal immunochemical test for colorectal cancer in patient risk groups

Area under the curve: 0.94 (high-risk symptoms, NG12), 0.93 (low-risk symptoms, DG30), 0.91 (other symptoms).

To detect one colorectal cancer in patients referred by symptom-based criteria required 28.0–37.6 patients to undergo colonoscopy in each risk group (*Table 5*). The number needed to scope to detect one colorectal cancer ranged from 11.2–13.3 across each risk group at a cut-off of 2 μg/g, to 2.8–3.3 at a cut-off of 150 μg/g. The number needed to scope to detect one case of serious bowel disease ranged from 3.9–5.0 across each risk group at a cut-off of 2 μg/g, to 1.6 at a cut-off of 150 μg/g.

To detect one additional colorectal cancer in patients with high-risk (NG12) symptoms at a lower FIT cut-off of 2 μg/g instead of 10 μg/g required an additional 96.5 colonoscopies; to detect one additional case of serious bowel disease would require an additional 10.2 colonoscopies. To detect one additional colorectal cancer in patients with high-risk (NG12) symptoms in patients with undetectable *versus* detectable f-Hb (less than 2 μg/g *versus* 2 μg/g or higher) required an additional 729.3 colonoscopies; to detect one additional case of serious bowel disease would require an additional 21.2 colonoscopies.

Discussion

The results of this study support the use of FIT in patients with high-risk symptoms who meet NICE NG12 criteria, and those with low-risk symptoms in accordance with NICE DG30 recommendations. There was no difference in sensitivity or NPV of FIT for colorectal cancer in patients with high- and low-risk symptoms. The sensitivity of FIT for colorectal cancer was higher at the LoD (2 μg/g) for both risk groups than with 10 μg/g, the cut-off recommended in DG30, in keeping with other studies[4,17,18]. However, the difference in FIT sensitivity at a cut-off of 10 μg/g compared with the LoD (2 μg/g) will result in over three times as many colorectal cancers being undetected by FIT. This supports use of the LoD as the FIT cut-off for referral of symptomatic patients to maximize colorectal cancer detection while still reducing referral for investigations by 60 per cent compared with the current 2WW referral system. A negative FIT at the LoD rules out colorectal cancer with 99.7–99.9 per cent certainty in patients meeting NICE criteria for high- or low-risk symptoms. However, the NPV of FIT for colorectal cancer remains high at all FIT cut-off values investigated, owing to the low prevalence of colorectal cancer in the 2WW population. Higher f-Hb results were associated with increasing PPV for colorectal cancer and serious bowel disease, and could be used in secondary care to risk stratify referred symptomatic patients for urgent investigations alongside clinical history and examination.

It may be difficult to justify using the lower cut-off of 2 μg/g rather than 10 μg/g for referral of patients with high-risk NG12 symptoms when 96.5 patients need to undergo colonoscopy to detect one additional colorectal cancer. However, it is worth considering that additional patients with serious bowel disease will be detected in this group for every 10.2 colonoscopies at the lower cut-off. Furthermore, GPs are more likely to refer patients with a negative FIT for further investigation if higher f-Hb cut-off values are used because concerns about missed cancers[19]. Adoption of a lower cut-off at the LoD may ensure patient and clinician confidence in the rule-out value of the test, thus avoiding unnecessary investigation. The use of a risk score incorporating patient characteristics and FIT results, in conjunction with other novel biomarkers, may provide personalized colorectal cancer risk scores to determine appropriate referral[20,21].

Some specific referral criteria such as rectal bleeding have been excluded from FIT pathways in early service development projects in several regions of the UK[17]. These projects were initiated a few years ago when robust evidence of the diagnostic accuracy of FIT was not available. The present study has demonstrated that FIT can still detect colorectal cancer in patients with these symptoms. The sensitivity of FIT for colorectal cancer was surprisingly low, at 70.0 (95 per cent c.i. 34.8 to 93.3) per cent, in patients aged less than 60 years with a change in bowel habit; but given only 10 CRCs were detected in this group, no definite conclusion can be drawn given the wide confidence intervals.

Table 4 Diagnostic accuracy of faecal immunochemical test for colorectal cancer by symptom at different cut-off values

Symptom	No. of referrals	No. with colorectal cancer	Symptom PPV(%)	2 μg/g		10 μg/g		150 μg/g	
				Sensitivity (%)	PPV (%)	Sensitivity (%)	PPV (%)	Sensitivity (%)	PPV (%)
High risk (NG12)									
Mass	177 (1.8)	29	16.4	100.0	36.3	82.8	50.0	65.5	76.0
IDA (age ≥ 60 years)	299 (3.0)	26	8.7	100.0	17.0	100.0	28.6	76.9	50.0
CIBH (age ≥ 60 years)	3447 (35.1)	71	2.1	94.4	5.6	85.9	12.2	54.9	35.1
AP and WL (≥ 40 years)	225 (2.3)	4	1.8	100.0	6.6	75.0	11.1	75.0	33.3
RB (age ≥ 50 years, < 50 years with symptoms)	3046 (31.0)	127	4.2	98.4	9.4	96.9	15.3	81.9	24.7
Total high risk	7194 (73.2)	257	3.6	97.7	8.9	92.2	16.2	72.0	30.5
Low risk (DG30)									
AP (age ≥ 50 years)	341 (3.5)	9	2.6	100.0	10.5	88.9	23.5	77.8	58.3
WL (age ≥ 50 years)	168 (1.7)	4	2.4	100.0	8.5	75.0	13.6	25.0	20.0
CIBH (age < 60 years)	802 (8.2)	10	1.3	70.0	3.6	60.0	6.9	50.0	17.9
Anaemia (age ≥ 60 years)	503 (5.1)	23	4.6	100.0	10.7	95.7	21.0	60.9	37.8
IDA (age < 60 years)	180 (1.8)	7	3.9	100.0	13.5	100.0	29.2	85.7	54.5
Total low risk	1994 (20.3)	53	2.7	94.3	8.4	86.8	16.9	62.3	35.5
Other	634 (6.5)	19	3.0	94.7	7.5	84.2	13.0	78.9	30.0

Values in parentheses are percentages. PPV, positive predictive value; mass, abdominal or rectal mass; IDA, iron deficiency anaemia; CIBH, change in bowel habit; AP, abdominal pain; WL, weight loss; RB, rectal bleeding.

Table 5 Number of colonoscopies needed to detect one patient with colorectal cancer or serious bowel disease at different faecal haemoglobin cut-off values in each risk group

Cut-off (μg/g)	Number needed to scope to detect one cancer			Number needed to scope to detect one additional cancer or serious disease at a lower cut-off			
	NG12	DG30	Other	Cut-off (μg/g)	NG12	DG30	Other
Colorectal cancer							
None*	28.0	37.6	33.4				
≥ 2	11.2	11.9	13.3	None* *versus* ≥ 2	729.3	465.7	394.0
≥ 10	6.2	5.9	7.7	≥ 2 *versus* ≥ 10	96.5	81.3	58.5
≥ 150	3.3	2.8	3.3	≥ 10 *versus* ≥ 150	16.0	13.8	73.0
Serious bowel disease							
None*	7.7	11.9	8.5				
≥ 2	3.9	5.0	4.0	None* *versus* ≥ 2	21.2	29.1	26.3
≥ 10	2.5	2.9	2.6	≥ 2 *versus* ≥ 10	10.2	13.0	9.0
≥ 150	1.6	1.6	1.6	≥ 10 *versus* ≥ 150	4.2	5.1	4.9

* No cut-off (all patients on 2-week wait referral).

Clinical features, including abdominal mass, abdominal pain, weight loss or iron deficiency anaemia, may be caused by pathology outside of the bowel and therefore may warrant further diagnostic investigations regardless of the FIT result. In the present study, FIT was reliable at detecting colorectal cancer in patients with these symptoms (100 per cent sensitivity) at the LoD. Therefore, a negative FIT at the LoD may allow a more appropriate alternative 2WW investigation (such as CT or gastroscopy) for non-bowel pathology such as upper gastrointestinal, urological or gynaecological malignancy.

This study used double-blind diagnostic accuracy methodology designed using STARD guidelines to minimize bias and optimize generalizability. Nonetheless, the study had a degree of selection bias and excluded lower-risk patients. Even though these patients may have met NG12 or DG30 criteria, they may have not been included in this study and instead triaged to investigation by alternative modalities such as CT or flexible sigmoidoscopy, or even been discharged without investigation. The FIT return rate was 62.8 per cent, almost identical to the 62 per cent return rate in a previous diagnostic accuracy research study of FIT in symptomatic patients[22], whereas the FIT return rate in a service evaluation was notably higher (80.9 per cent)[17]. Reduced return rates may be due to the optional nature of participation in research, although an increased return rate was noted once logistical issues to deliver recruitment packets to patients with sufficient time before bowel preparation for colonoscopy had been addressed. Four FIT analysers are currently in use in clinical practice and the present results are based on the HM-JACKarc system with LoD of 2 μg/g. The other analysers have different LoDs and it is not known at present whether the different LoDs have a similar sensitivity for colorectal cancer. Extraction and classification of the heterogeneous collection of presenting symptoms in patients meeting 'other' criteria for referral was not feasible in a multicentre study at 50 sites.

Service evaluations from Scotland and Leicester have demonstrated a reduction in immediate referrals when FIT was used as a diagnostic adjunct to inform a GP's decision to refer for investigation[23,24]. When implemented in secondary care to triage referrals, FIT has not reduced referrals or colonoscopy demand, but has led to a rise in other investigations, including CT colonography[25]. Bowel symptoms are reported to account for 10 per cent of GP attendances[26]; unselective referral of symptomatic patients from primary care could overwhelm secondary care, even if only FIT-positive patients were investigated. This study was therefore

designed to examine the diagnostic accuracy of FIT in patients referred from primary care with suspected colorectal cancer symptoms rather than all bowel symptoms. However, there was no difference in the diagnostic accuracy of FIT between the high- and low-risk groups as classified by NICE as well as the group with other symptoms who were referred because of GP concerns. Furthermore, it is of interest that GP referral of other symptoms that did not meet NICE criteria yielded a colorectal cancer diagnosis rate of 3.0 per cent, not significantly different from the 3.6 per cent in high-risk patients or 2.7 per cent in low-risk patients, albeit in a small sample. This is an important finding supporting the clinical acumen of GPs, who still referred patients urgently, even if they did not meet specific NICE symptom criteria.

Even with a negative predictive value of 99.7 per cent or greater, a referral system based entirely on FIT will not detect all colorectal cancers. Clinical judgement and safety-netting pathways are therefore essential to avoid missing colorectal cancers in patients with negative FIT results. In service evaluations of FIT triage of higher-risk patients in Dundee and Nottingham, nearly all patients with FIT-negative cancers were referred on by GPs during longer-term follow-up[24,27]. Therefore, ongoing clinical concern warrants referral on routine or urgent pathways for assessment in secondary care.

Collaborators

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Supplementary material

Supplementary material is available at *BJS Open* online.

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