Service evaluation of faecal immunochemical testing introduced for use in North East London for patients at low risk of colorectal cancer

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Received 7 April 2020
Revised 7 June 2020
Accepted 9 June 2020
Published Online First 9 July 2020

To cite: Ayling RM, Machesney M. *J Clin Pathol* 2021;**74**:163–166.

ABSTRACT

Aims Colorectal cancer (CRC) is the fourth most common cancer in the UK. Following National Institute of Clinical Excellence (NICE) guidance for faecal immunochemical testing (FIT) (DG30), we introduced a service for the measurement of faecal haemoglobin (fHb) in symptomatic patients in line with the 2017 update of the NG12 guidance. The purpose of this study was to audit the use of FIT, focussing on the indication for request and referral for diagnostic tests as recommended in NICE guidance.

Methods Testing was rolled out after careful introduction with extensive education led by the local Cancer Alliance and reinforced by the laboratory. After 6 months, the outcomes of all patients tested were reviewed.

Results 1203 samples were received, of which 894 (74.3%) were suitable for analysis. Of these, 482 (53.9%) actually met the criteria for FIT analysis stipulated in our patient pathway. Eight patients were diagnosed with CRC; fHb was detectable in all and was ≥200 µg/g in seven and <10 µg/g in one. 217 patients underwent gastrointestinal investigations, and the sensitivity and specificity of FIT for CRC were found to be 87.5% (95% CI 46.6% to 99.7%) and 52.6% (95% CI 45.6% to 59.6%), respectively. Patients with anaemia were more likely to have fHb ≥10 µg/g.

Conclusions These findings suggest benefits from the introduction of FIT in terms of more efficient use of diagnostic investigations, while revealing initial problems relating to familiarity with a new test. This merits further intervention with education and awareness programmes for Primary Care and further audit.

INTRODUCTION

Colorectal cancer (CRC) is the fourth most common cancer in the UK. It accounts for 11% of all new cancer diagnoses, with approximately 43 000 patients diagnosed each year[1]; up to a quarter of these present as an emergency, often with advanced disease. A national Bowel Cancer Screening Programme was introduced in England in 2006 to aid earlier detection and has been associated with a 15% reduction in mortality.[2] In 2000, 2-week wait (2ww) pathways were established to facilitate early referral of patients presenting with symptoms suggestive of cancer. However, the cancer detection rate on such urgent pathways was <10%,[3] and in 2015, the National Institute for Health and Care Excellence (NICE) recommended modified pathways (NG12) indicating referral criteria with a proposed positive predictive value for cancer of 3%.[4] Faecal occult blood testing (FOBT) was recommended for patients at low risk (1%–3%) of CRC but this did not receive widespread support because of lack of sensitivity and specificity of the guaiac-based tests available at the time.[5] In 2017, NICE released its Diagnostic Guidance (DG30) on quantitative faecal immunochemical test (FIT)[6] for measurement of faecal haemoglobin (fHb) in patients without rectal bleeding, who have unexplained symptoms, but who do not meet the criteria for suspected cancer, and in the same year, this was incorporated into an updated version of the 2015 NG12 guidance.

In April 2019, we initiated a FIT service for primary care for use in symptomatic patients at low risk of CRC, using a cut-off of 10 µg/g, in line with the current NICE recommendations and this study was undertaken to audit its use.

METHODS

Service initiation

The FIT service was introduced in April 2019 in Newham, Tower Hamlets and Waltham Forest, an area with a combined population of about 950 000 (<10% over 65 years) and 128 Primary Care practices. Introduction was coordinated by a multidisciplinary team initiated by the North and East London Cancer Alliance. Prior to going live, education was provided to Primary Care colleagues by the Cancer Alliance, which included the nature and purpose of the test, the indications for its performance and its place within the referral pathway, together with practical aspects of how to perform it. At the same time, information about indications for performing the test and the container requirement were disseminated from the laboratory.

Each practice was sent a starter pack containing a supply of Eiken specimen collection devices, a pictorial patient information sheet and indications for 2ww referral and performance of FIT (table 1). This information was recirculated on two further occasions within the 6-month period and was reiterated opportunistically at all suitable occasions. A reminder of the container requirement and links to patient information sheets in 12 languages were arranged as a 'Pop-up box' at the time of electronic ordering of the test, via TQuest in Primary Care. Whenever an unsuitable sample was received, a message was returned via the laboratory reporting system alerting to the necessary preanalytical requirements.

Table 1 North East London lower gastrointestinal cancer referral pathway

Low (≤3%) risk offer FIT before referring for colorectal cancer in adults without rectal bleeding	Medium (3%–5%) and high (≥5%) risk 2ww referral without FIT
► ≥50 years with unexplained abdominal pain or weight loss ► <60 years with CIBH or IDA ► ≥60 years with anaemia without iron deficiency 2ww referral if fHb ≥10 µg/g or clinical suspicion persists	► Any age with unexplained rectal or abdominal mass ► Any age with unexplained anal mass or unexplained anal ulceration ► ≥40 years with unexplained weight loss and abdominal pain ► <50 years with rectal bleeding and any of: – Abdominal pain – CIHB – Weight loss – IDA ► ≥50 years with unexplained rectal bleeding ► ≥60 years with IDA ► ≥60 years with CIBH

CIBH, change in bowel habit; fHb, faecal haemoglobin ; FIT, faecal immunochemical testing; IDA, iron deficiency anaemia; 2ww, 2-week wait.

Sample analysis

Samples were returned to the Clinical Biochemistry Department at Barts Health NHS Trust by existing Primary Care transport and stored at 4°C before analysis, which took place within 1 week of receipt and 2 weeks of sampling. The laboratory is accredited by the UK Accreditation Service to ISO 15189 standards. Analysis was performed using a single OC-Sensor io (Eiken Chemical, Tokyo, Japan). Inter-run imprecision was assessed with quality control materials (Eiken) in each run. Coefficients of variation were 2.8% at 14 µg/g and 3.0% at 91 µg/g. External quality assurance was achieved via satisfactory performance in the UK National External Quality Assurance Scheme. The lower limit of quantification was 4 µg/g. The upper analytical limit was 200 µg/g and samples with a concentration above this were not diluted and reassayed but reported as >200 µg/g. A comment was appended to all results, which stated 'in line with NICE DG30 and local guidance suggest 2 week wait referral on lower gastrointestinal cancer pathway if FIT ≥10 µg/g'.

Data sources

All patients whose samples were analysed between 1 April and 30 September 2019 were included and outcomes were reviewed until 31 January 2020. Data about sample numbers and results were obtained from the Winpath laboratory information system. Patient information was obtained from the Cerner Millenium electronic primary and secondary care records. CRC and other diagnoses were determined by reviewing clinical notes and endoscopy, histology and radiology reports. All results were reviewed and information was obtained about the indication for the request, the date and nature of any subsequent referral, investigations performed and the final diagnosis. From this information, patients were categorised into those who, according to our local care pathway, required 2ww referral and those in whom FIT was recommended according to NICE guidance and our local pathway. Patients who fulfilled neither criteria comprised a third group.

Statistical analysis

Statistical analysis was performed using Analyse-it Software (Leeds, UK).

Table 2 Demographics of patients in whom faecal immunochemical testing was requested

	<40 years	40–49 years	50–59 years	≥60 years
n (%)	89 (10%)	120 (13.4%)	235 (26.2%)	450 (50.3%)
Male	35	44	114	2031
Female	54	76	121	247
Median age	33 years	46 years	55 years	71 years

RESULTS

Numbers of samples analysed and patient demographics

In the first 6 months of the service, 1203 requests for FIT analysis were received from 113 of 128 practices (88.3%). Of these, 309 (25.7%) were not able to be analysed; 17 samples were unlabelled, 37 were grossly overfilled with contamination of the collection device, 227 were in screw top pots rather than specimen collection devices and 13 requests had no accompanying sample. FIT analysis was performed in 894 patients (396 male), median age 60 years (range 23–98 years), 209 (23.4%) patients were younger than 50 years of age. Patient demographics are shown in table 2.

FIT results and clinical diagnoses

During the first 6 months of the service, 894 samples were analysed and fHb was ≥10 µg/g in 128 (14.3%). Of the 128 patients with a fHb result ≥10 µg/g, 115 (89.8%) were referred via the 2ww pathway as were 135 (17.6%) out of 766 patients with a fHb <10 µg/g. Figure 1 shows the distribution of requests by patient risk stratification and the number of subsequent referrals on the 2ww lower gastrointestinal cancer pathway.

Of the 894 patients whose samples were suitable for analysis, 250 (27.9%) were referred for, and 217 underwent investigation which included colonoscopy (195 patients) and CT pneumocolon alone (22 patients). No diagnosis was made in 26 patients who declined or failed to attend appointment for further investigation. Seven patients were not investigated under the 2ww referral pathway as they were already under the care of other gastrointestinal clinics.

Diagnoses are shown by patient risk stratification and FIT result in table 3. Of the patients referred and investigated, colon cancer was diagnosed in eight. fHb was detectable in all and was >200 µg/g in seven and 8 µg/g in one. One, aged 63 years, had previous iron deficiency anaemia alone as the presenting feature, three had iron deficiency anaemia and bowel symptoms, one had

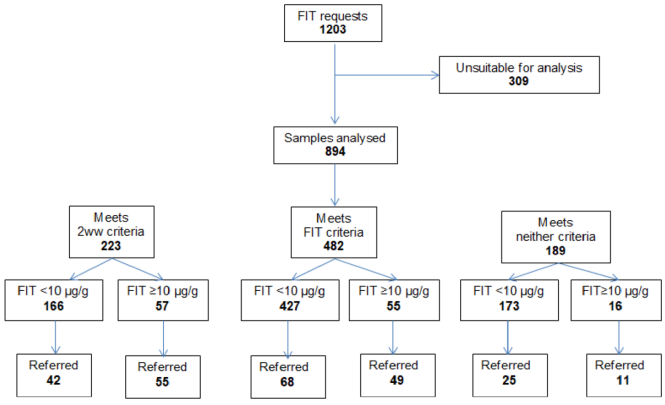

Figure 1 Distribution of requests and referrals by patient risk stratification. FIT, faecal immunochemical testing; 2ww, 2-week wait.

Table 3 Diagnosis by patient risk stratification and faecal haemoglobin (fHb) result

	Meets local criteria for 2ww referral		Meets local criteria for FIT		Meets neither criteria	
	fHb <10 µg/g	fHb ≥10 µg/g	fHb <10 µg/g	fHb ≥10 µg/g	fHb <10 µg/g	fHb ≥10 µg/g
CRC	1	7	–	–	–	–
HRA	1	8	–	4	1	–
LRA	9	10	16	16	5	4
Diverticular disease	6	8	4	5	–	1
Vascular ectasia	–	2	–	–	–	1
IBD	–	–	–	1	–	1
Other*	–	1*	–	–	–	–
Normal	19	14	38	20	11	3

*Whipworm infestation.
CRC, colorectal cancer; fHb, faecal haemoglobin; FIT, faecal immunochemical testing; HRA, high-risk adenoma; IBD, inflammatory bowel disease; LRA, low-risk adenoma; 2ww, 2-week wait.

change in bowel habit and one, aged 47 years, had unexplained weight loss and abdominal pain.

A decision was made in Primary Care to refer 59 patients before the FIT result was available, 19 meeting our 2ww referral criteria, 39 meeting our criteria for FIT and 9 meeting neither criteria.

Haemoglobin

Blood haemoglobin had been measured in 382 male and 472 female patients. A total of 170 male and 240 female patients were anaemic (Hb <130 g/L in males and <120 g/L in females[7]) at the time of their FIT test. For both male and female patients, haemoglobin was significantly lower in those with fHb ≥10 µg/g. The haemoglobin concentrations by sex and fHb result are shown in table 4.

Of the eight patients diagnosed with CRC, only three were anaemic at the time of FIT sampling.

Diagnostic accuracy

In the first 6 months of use, 217 patients underwent gastrointestinal investigations. The diagnostic accuracy of FIT for the diagnosis of CRC and high-risk adenomas[8] are shown in table 5.

DISCUSSION

We introduced FIT to be used in line with NICE guidance for symptomatic low-risk patients with suspected CRC. Our local pathway recommended Primary Care practitioners use FIT for patients to assess for colon cancer in adults of 50 years or over without rectal bleeding, considered to be at low risk, using the criteria previously suggested for guaiac FOBT in NG12 guidance, as shown in table 1, using a cut-off of ≥10 µg/g for referral. Only 54% of samples received met these criteria. Of note, in 59 patients, a referral was made before the FIT result was available and 209 samples were in patients <50 years old. Of these young patients, 12 had FIT≥10 µg/g, of whom 10 were referred; one had CRC but met the criteria for urgent 2ww referral without FIT, four had low-risk adenomas, six had unremarkable colonoscopies.

Twenty-five per cent of requests met the NG12 criteria for urgent referral rather than measurement of FIT. All the patients found to have CRC were in this group and all had detectable fHb, although in one, it was <10 µg/g. During the first 6 months of the service, 15 of our 128 practices (11.7%) did not send any samples for FIT.

There have been many studies investigating the performance of FIT in the diagnosis of CRC. The methodology has generally involved measurement of fHb in patients referred for colonoscopy. Interpreting the results is complicated by the use of different study populations and varying cut-offs for fHb. A meta-analysis of nine studies, involving 6755 patients, found a prevalence of CRC of 5.1%, and the pooled sensitivity and specificity of FIT for CRC were 90% (95% CI 87% to 92%) and 87% (95% CI 83% to 90%), respectively.[9] This study is different because in our pathway the result of the FIT is intended to inform the decision to refer from Primary Care. Although we have shown this was not always the case, our patient population was heterogeneous and represented those who are receiving the test in the community. Interestingly, an assessment of studies for inclusion in another meta-analysis noted that none was fully representative of patients with low-risk symptoms as in the amended NG12 guidance.[10] This meta-analysis did not include a study from Denmark specifically using FIT in Primary Care in patients with what were termed non-alarm symptoms.[11] The Danish study population was different from our own as it was left to GPs' judgement to decide when to request FIT, rather than using the recommendations of NICE DG30. It was found that 540 out of 3462 (15.6%) patients had fHb ≥10 µg/g. Of these, 51 (9.4%) were diagnosed with CRC and 73 (13.5%) with other significant bowel disease. Only 91 (2.4%) of samples were not viable. Both the infrastructure of Primary Care in Denmark and the patient demographics are very different from North East London and may have had a bearing on education and training aspects of using FIT. Despite its potential for use in high-risk patients and its incorporation into some clinical pathways,[12] a change in

Table 4 Haemoglobin concentrations of patients at the time of FIT analysis

Hb, g/L **median (range)**	fHb <10 µg/g	fHb ≥10 µg/g	
Male	133 (74–184)	126 (78–181)	p=0.004
Female	123 (82–158)	118 (72–160)	p=0.037

fHb, faecal haemoglobin; FIT, faecal immunochemical testing.

Table 5 Diagnostic accuracy for fHb at ≥10 µg/g (with 95% CIs)

	Colorectal cancer	Colorectal cancer and high-risk adenoma
Sensitivity, %	87.5 (47.4 to 99.7)	86.4 (65.1 to 97.1)
Specificity, %	52.6 (45.6 to 59. 6)	55.4 (48.1 to 62.5)
Positive predictive value, %	6.6 (5.0 to 8.7)	17.9 (14.8 to 21.5)
Negative predictive value, %	99.1 (94.6 to 99.9)	97.3 (92.6 to 99.1)

NICE guidance may require the accumulation of data from large National Institute for Health Research trials specifically in this group. We found the test to be more sensitive but less specific in this cohort of patients than when used in our previous study in a heterogeneous population of patients referred for colonoscopy solely on the basis of anaemia, in which the sensitivity and specificity were 71.4% and 95.9% respectively.[13] In this service evaluation, patients with anaemia were significantly more likely to have fHb ≥10 µg/g.

The NG12 2ww referral pathway was designed with the intention of capturing patients with a positive predictive value of at least 3%. In our study population, there were eight patients with CRC and all fulfilled the criteria for 2ww referral, giving an incidence of 3.6% in this group. At present, NICE guidance is to use FIT only in low-risk patients. Contrary to the recommendations of our pathway, we found that FIT had been performed in a number of patients at medium or high risk who met the criteria for a 2ww referral and they were not referred if fHb was <10 µg/g.

We introduced FIT into the North East London diagnostic pathway for use in patients aged 50 years and above at low risk of CRC, with the intention that the result could inform a Primary Care decision to refer. Despite an education programme sending starter packs containing written information to all practices prior to its introduction and the incorporation of guidance into our electronic test requesting system, in the first 6 months, 25.7% of samples were unsuitable for analysis, 34.2% did not meet our criteria for FIT testing and 15 of our 128 practices (11.7%) did not send any samples.

At this time, we tested 894 samples; eight patients were diagnosed with CRC, all of whom fitted the NG12 criteria for urgent 2ww referral without using FIT to inform the decision. However, assuming that all patients who underwent FIT testing would have been referred to specialist clinics or triaged straight to test colonoscopy services had the test not been available, of the 766 patients with a FIT <10 µg/g, only 135 (17.6%) were referred.

Take home messages

- Faecal immunochemical testing (FIT) is established for asymptomatic individuals as part of national Bowel Cancer Screening.
- FIT is also useful in Primary Care as a tool to prioritise referral for colonoscopy in symptomatic patients at low risk of colorectal cancer.
- Following the initiation of a FIT service in Primary Care, ensuring correct use of the referral guidelines and specimen collection device may require significant education and reinforcement.

Our evaluation suggests benefits from the introduction of a FIT service in line with the 2017 update of the NICE NG12 guidance, which incorporates DG30, with respect to more efficient use of diagnostic investigations. However, although there was significant investment in education and dissemination of information about the service, there were problems relating to familiarity with the test which require addressing and further audit.

Handling editor Tahir S Pillay.

Contributors RMA and MM were both involved in setting up the clinical service and in its evaluation and the authorship of this paper.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Deidentified patient data would be available on reasonable request from https://orcid.org/0000-0003-4662-2502.

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