The FIT Revolution

CS case study

RM Partners
Accountable Cancer Network

Coming to Your Practice Soon

The NICE FIT Study is a research project in Bowel Cancer Care that has been initiated by the department of Colorectal Surgery at Croydon University Hospital together with RM Partners Accountable Cancer Network in South and West London.

Evidence from studies conducted around the world indicate that faecal immunochemical testing (FIT) could rule out bowel cancer in symptomatic patients, thus avoiding the need for invasive and costly colonoscopy. Following a review of these studies, NICE[1] in 2017 recommended using FIT in primary care for patients presenting to their GPs with low risk symptoms (cancer risk <3%) before referral to secondary care.

However, there has never been a large research study on FIT published in England, that looks at faecal haemoglobin level variation by age, sex, ethnicity and deprivation. Large scale diagnostic studies are required to create reference values for the English population with the defined symptom spectrum recommended for referral under the NICE suspected cancer referral guidelines (NICE NG12 2015[2]).

The NICE FIT study is the largest study in England investigating whether FIT can be used as a triage tool in primary care to guide referrals for colonoscopy.

Figure 1. *Mr Muti Abulafi, (5th from the left) and his team at Croydon University Hospital.*

The initial aim was to test a minimum of 5500 patients in London, and further patients across the UK to create a robust evidence base that patients, GPs and hospital doctors can use with confidence. NHS England is funding the work through RM Partners and all hospitals that manage referrals for suspected colorectal cancer are eligible to join the study.

When Alpha Laboratories previously reported on progress of the NICE FIT study (Focus on FIT 2018), 1000 patients had been recruited. Earlier this year Mr Muti Abulafi, consultant colorectal surgeon and chief investigator at Croydon University Hospital [Figure1], presented an update at the Royal College of Physicians with some of the interim results from the study. He reported that 12 months on, over 11,000 patients had now been recruited in sites right across England [Figure 2].

Figure 2. *As of February 2019, 11523 patients across England had been recruited to the NICE FIT Study*

Although recruitment has now finished for the main study, there are still some sub-studies ongoing; a review of the patient and GP experience, a multi sampling study as well as an additional biomarker study.

The presentation reviewed data from 4,069 patients with both FIT and colonoscopy results and where the clinical data had been thoroughly checked for correct coding of data entry. The number of cancers in this data set was 105 (2.5%) [Figure 3].

This interim data was similar in number to the 10 studies across two technologies that were reviewed by the NICE DG30[1] committee and used to generate their recommendation on the applications of FIT.

Optimised Cut-Off of 2 μg Hb/g faeces

Mr Abulafi presented a case that compared the NICE DG30 guideline cut-off of 10 μg Hb/g faeces where 94 out of the 105 cancers were positive, to an optimised cut-off of 2 μg Hb/g faeces where 101 out of 105 cancers were positive.

Mr Abulafi suggested that identification of patients with cancer was a priority and hence FIT should be used as a rule in rather than the original NICE proposal of a rule out test. He suggested that using the test in this way would reduce missing cancer by two thirds.

> ***"FIT should be used as a rule in rather than the original NICE proposal of a rule out test.***
>
> ***Using the test in this way would reduce missing cancer by two thirds."***

The evidence that supports this proposal was then used to model what impact this would have on colonoscopy resources if a 2 μg Hb/g faeces cut-off was applied [Figure 4].

Mr Abulafi suggested that for every 1000 patients tested, 300 would be positive, of which 25 would have cancer (PPV 8%), 28 HRA and 35 IBD (PPV 28%)

Of the 700 negative FIT results two will be missed cancers (NPV 99.8%). Safety Netting would result in additional secondary care referrals from this group. However it is estimated that the overall referrals for colonoscopy would result in a reduction between 30-50 % of the original 1,000.

Of course there is still another 7,500 patient FIT and colonoscopy results yet to be reviewed. This would add to the statistical significance of the findings as in total it would double the data reviewed by NICE in 2017.

However, the conclusion of the presentation suggested that there was definitely a revolution in progress with FIT. The early results have proved promising especially in view of the optimised cut-off of 2 μg Hb/g faeces proposed by Mr Abulafi for the symptomatic population, but that additional work on evidence base and safety netting pilots should be implemented to complete the proposed patient pathway.

RM Partners Accountable Cancer Network

Interim analysis of NICE FIT Study

Croydon Health Services NHS NHS Trust

4069 patients and 105 (2.6%) cancers diagnosed

Using 10 μg/g (LoQ) as a cutoff threshold

FIT positive:	741 (18%)	TP 94	FP 647	PPV 12.7%
FIT negative:	3328	FN 11	TN 3317	NPV 99.7%

Using 2 μg/g (LoD) as a cutoff threshold

FIT positive:	1251 (31%)	TP 101	FP 1152	PPV 8.1%
FIT negative:	2818	FN 4 (p=0.06)	TN 2814	NPV 99.85%

Figure 3. *Using the Limit of Detection as a cut-off threshold would reduce missing cancer by two thirds*

RM Partners Accountable Cancer Network

Interim analysis of NICE FIT Study

What it means in real practice

Croydon Health Services NHS NHS Trust

@ a threshold of 2 μg/g

- **Out of a 1000 patients with both high and low risk symptoms tested with FIT :**
  - **300 will be positive of which 25 will have cancer (PPV 8%)**
    - **28 HRA and 35 IBD (PPV 28%)**
  - **700 will be negative of which 2 will have cancers (NPV 99.8%) and initially will not be referred but it is estimated that 20-40% will be referred through Safety Netting (SN). It is expected that colonoscopy reduction is between 30 – 50%**

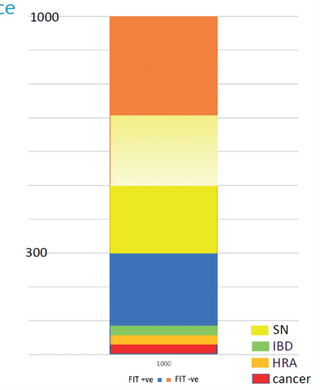

Figure 4. *Using FIT to triage symptomatic patients could reduce colonoscopy requirements by 30-50%*

Figure 5. *Sally Benton (left) with staff at the Bowel Cancer Screening Hub - South of England*

Alpha Laboratories is proud to be supporting the NICE FIT study by providing the FIT analyser (HM_JACKarc), the FIT kits, the raw materials and patient instruction leaflets.

Expertise and experience in both the logistics and analysis of FIT specimens is provided by the team at the Bowel Cancer Screening Hub-South of England, led by Sally Benton [Figure 5].

The study team has created a website where full details can be found at **www.nicefitstudy.com**

References

1. NICE DG30 (2017), Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care. Section 4 – Evidence. www.nice.org.uk/guidance/dg30/chapter/4-Evidence
2. NICE NG12 (2015), Suspected cancer: recognition and referral. www.nice.org.uk/guidance/ng12

alpha laboratories supplying quality to science

Find out more about FIT at www.faecal-immunochemical-test.co.uk