

Developing an Evidence Base for NHS England

The NICE FIT Study – 6 Months on...

RM Partners

Accountable Cancer Network

The NICE FIT study was launched through Croydon University Hospital in early 2017, as a diagnostic accuracy study for faecal immunochemical testing (FIT). Following the introduction of NICE DG30¹ the study has grown significantly in size. After the first pilot, the study, based initially at Croydon University Hospital, was expanded under the direction of chief investigator Mr Muti Abulafi and co-investigator, Mr Nigel D'Souza. Working with Royal Marsden Partners (RM Partners) the aim is for multi-centre recruitment throughout England. As one of the largest studies conducted on FIT, Alpha Laboratories' Senior Product Manager, Matthew Davis, spoke with Mr D'Souza to find out about the latest progress with the NICE FIT Study.



The NICE FIT Study Team:

Left to Right: Dr John Chang, Croydon University Hospital R&D Director
Mrs Carlene Parchment, NICE FIT Trial Manager
Mr Muti Abulafi, Chief Investigator
Mrs Antoinette Dzakpasu, NICE FIT Coordinator
Dr Michelle Chen, RM Partners R&D Manager
Mr Nigel D'Souza, Co-Investigator

What prompted the initial push for the NICE FIT Study?

The colorectal department at Croydon screens all two-week-wait (2WWW) referrals for symptomatic patients with suspected bowel cancer. While referrals have been steadily increasing over the last 10 years, they have doubled since 2015. The change in NICE NG12 to include more low risk patients could be a source of rising referrals.

The decision within London not to test these patients for FOBt prior to referral may be another reason. Due to the low sensitivity of FOB, it was considered a 'coin-toss test' – with a 50:50 chance of going to colonoscopy.

How did you obtain the funding for the study?

The initial pilot had no funding. It was only possible with a lot of goodwill from many parties. Patients were recruited through the endoscopy department, and analysis was performed by Sally Benton's team in the Bowel Cancer Screening Southern Hub (Guildford). Kits were supplied free-of-charge by Alpha Laboratories Ltd who also arranged sample transport. I screened patients and coordinated this in my own time.

Now the study is expanding, what helped you to obtain new funding?

A combination of factors; first of all, early diagnosis is key to the "Five Year Forward View" for early cancer diagnosis. This makes FIT very attractive as a simple dipstick test to rule out bowel cancer, instead of putting all these patients onto the two week wait pathway.

The Sustainability and Transformation Plan (STP4) for saving money was also a major benefit factor: comparing a £9.00 FIT to a £375 colonoscopy¹ makes the argument easier to emphasize. We submitted the bid on behalf of RM Partners and with their support, they submitted the bid as part of the STP funding.

So RM Partners did the pitch to NHS England?

Yes – we drew up the basic cost savings, projections, and methodology for the project. We couldn't have done it without their support. Dr Michelle Chen and Professor Stan Kaye from the R&D team have been instrumental in supporting our initial roll-out and subsequent expansion.

The study has been running some months, and now you've recruited additional hospitals: how is that progressing?

When we first designed our study, we weren't sure we would achieve NIHR badge approval. The initial model involved recruiting patients directly from RM Partner sites in London, using our own research nurses, who would be hired with funding. However, when we were awarded badge approval onto the NIHR portfolio, Dr Michelle Chen recommended recruitment via a colorectal nurse (CRN), to facilitate recruitment to more sites both in and outside of London.

As a portfolio study, hospitals are awarded funding for each patient recruited to the study. So with the high volume this was an attractive proposition for hospitals.

By recruiting patients from outside London, has the thrust of the study changed at all?

Our main goal is (and will remain) to recruit 5,500 patients from London to prove the diagnostic accuracy of FIT in diverse populations.

This is the main thrust of the study.

Portfolio adoption enables additional (non-London) recruitment, because NHS England wants as much data on FIT as possible.

Fortunately, our study methodology for London recruitment can be scaled to recruit across sites throughout England. The work was within our scope, so we could support the additional roll out. The local hospitals, R&D departments and CRNs will play a larger role in recruitment, but ultimately we remain responsible for the data management and quality assurance.



Logistically, how does this work with the London and non-London sites?

For London sites, the hospital sends the patient information to us, and we arrange to have the FIT kit sent to the patient. Outside London the hospitals do the recruitment work themselves. The samples, regardless of where they were sent from, are all returned to Sally's team at the Guildford Hub, and the data generated is sent straight back to us at Croydon.

Why is it so important for the data to come straight to you?

It's very important that the data come back to us. When examining a colonoscopy report, it can be challenging for a non-clinician to accurately classify the findings. During the pilot, we noticed many coding errors on the system, where findings had been incorrectly coded on the system.

To ensure the data is as accurate as possible, the findings are logged onto our bespoke system by a member of the local CRN.

All data points are double-checked by the central study team. A senior clinician then checks every single colonoscopy and histopathology report. With the three layers of checks, we can be as sure as reasonably possible that the result on the system is correct.

This study appears to have become multi-faceted: examining the use of FIT and its implementation and the improvement of colonoscopy/histopathology reporting services.

Are there any other branches to this study you are thinking of including?

We're working on funding for a research fellow for a number of sub-studies. One will focus on the process of sampling and pre-analytics (e.g. whether accuracy improves with multiple samples from the same or different stool). Another is the polygenic risk score; combining a faecal test with other tests such as; blood, saliva, and breath tests, to develop a broader risk score for patients and other cancer markers. Lastly, we're also looking to qualitatively assess and improve the patient experience with FIT.

You've worked with Sally Benton and her team in Guildford, do you have any comments on her 'essentialism vs. consequentialism' views? Are you finding much evidence of this with your implementation of FIT?

FIT can miss some cancers, we know this.

We're working on a way to make FIT as safe as possible, and identify whether it misses cancer in a predictable way. We believe in FIT, and find it a very attractive test for managing patients with GI symptoms.

However, a large part of the project aims to prevent FIT being used indiscriminately without awareness of its limitations. This could result in more cancers being missed, and if this came to the attention of the clinicians, GPs, press or patients, the faith in FIT would be completely undermined. We're putting a significant amount of effort into ensuring the data is as good as it can be, so NHS England can map the limitations of FIT, to provide a safe and reliable evidence base for FIT implementation.

Congratulations on the 1,000 patient uptake! Is there anything specific you can attribute this increase to?

A thousand is good but I'd hoped for more and we still have a few hurdles to overcome.

What is your current return rate for the test?

It varies greatly – between 25 and 50%.

One of our main questions is, what's limiting the uptake? Each site is different, some patients are seen in clinics, and some are triaged straight to test based on the referral letter, so there isn't a one-size-fits-all approach.

In Croydon, a triage nurse calls every patient referred for colonoscopy. In the conversation with the patient, the nurse informs them about the NICE FIT Study, and we've found this is a good way of introducing them to it.

There is a lot of evidence from screening programmes showing that London has a significantly lower uptake than the national average – could this be a factor?

I remember calling our first patient, and the call was not well received! The main question the patient asked was, "what's in it for me?" At the time, my response could only be, "well... nothing directly!" I think this may be one of the key problems for the recruitment of patients – there is no immediate, obvious benefit to doing it as they are still referred for colonoscopy, and the FIT result does not affect their management.

Do you now explain any potential future benefits to FIT when talking to patients?

We do try to emphasize that based on the study data we collect, we could in the future improve the process for patients being referred with GI symptoms.

Mr Abulafi was keen to develop a patient pathway tailored specifically for London. Does this come into your study?

Not quite. We're mainly looking at the diagnostic accuracy of FIT, and the sub-studies will work on ways to improve diagnostic accuracy. The positioning of FIT in primary or secondary care is being examined in other studies and service improvement projects in England and Scotland.

Other sites, such as Nottingham and Leicester, have very different pathways and decision making processes. What are your thoughts on the development of a pathway?

Hopefully, once the process is complete, we can combine information on diagnostic accuracy and decision making pathways from all the studies to construct an evidence based patient pathway. We are providing the diagnostic accuracy portion of the evidence base.

Roughly when do you think you'll have sufficient data for a summary on the project?

The recruitment rate continues to increase so it is adaptive. With our aim to recruit the 5,500 London patients, and the additional national patients, I believe we should have some initial data by December 2018.

I think there would be an interesting comparison between those inside London and those outside? Another potential study arm?

Yes definitely, we've already seen differences in recruitment method and patient response, so yes, I think it would be valuable information.

What happens with the data you collect?

We will conduct a primary data analysis based on, "F-Hb depending on; age, sex, ethnicity and deprivation, and also NICE criteria on patients referral. We will then pool data with NHS England, to create a database for the safe utilisation of FIT.

It has been intimated by some key opinion leaders (WAGE) that NICE was 'wrong' with DG30 and that FIT should not be used solely for the 'low-risk' patients, but all patients with GI symptoms. What are your thoughts on this?

I have grounds to agree and disagree. Firstly, I do not believe these patients are necessarily low risk based on the data we've collected. NICE are encouraging this process using the terms 'low-risk' and 'high-risk' for cancer. The category divisions may not be black and white – GPs may not always have time to assess for all symptoms prior to referral, so the high- and low-risk classification may be inappropriate.

Previous work by our team has found that "low risk" symptoms may have a higher rate of cancer than that which has been predicted by NICE.

Secondly, I do not believe there is sufficient evidence upon which the recommendations are based. We will shortly be publishing our own analysis of DG30. I worry still about the test being used without full understanding of the limitations and the safety netting requirements, and resulting in missed cancers. This could result in this great test being pulled off the table before it's had chance to be used.

Ultimately, we will hopefully use FIT for all symptomatic patients, however I think there should be a larger evidence base for the recommendations and so work is still to be done.

The NICE FIT Study has a dedicated website which provides further information:

www.nicefitstudy.com

This information is for both clinicians and patients and provides ongoing updates on participating sites as well as recruitment numbers.

Reference:

1. NICE (2017) "Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care" Diagnostics guidance DG30. Section 4 – Evidence [Online] Available at: www.nice.org.uk/guidance/dg30/chapter/4-Evidence