Frequently Asked Questions:

NICaN Lower GI Suspected Cancer Pathway and implementation of the Quantitative Faecal Immunochemical Test (qFIT)

- **What if a patient has recently completed their Bowel Cancer Screening? (Updated Nov 21)**

What is qFIT?

The Quantitative Faecal Immunochemical Test (qFIT) is a test to detect blood in stool samples. Unlike faecal occult blood (FOB) tests, FIT uses antibodies that specifically recognise human haemoglobin released from lysed or broken down red cells. This means it is not affected by diet and medication or Upper GI pathology (as the globin protein is broken down and digested before it gets to the colon). Because qFIT relies on partial breakdown of the red bloods cells to release the globin protein, the test may be negative with intermittent benign anorectal/outlet bleeding where blood cells released are 'whole'. That being said it is still a very useful test in the investigation of rectal bleeding.

qFIT is much more sensitive than FOB and only 1 sample is required which improves patient compliance.

Further details can be found under the evidence related FAQ.

How is qFIT being used and why has the NICaN Red Flag Guidelines been amended for lower GI cancer?

Since the onset of the COVID pandemic, the quantitative result of the qFIT has been used to risk stratify the urgency of colorectal investigations for red flag and urgent referrals. There is national and regional support to use the qFIT result to stratify risk in primary care and direct the patient depending on the result (National Cancer Team update August 2020). The NICaN 'Lower GI Suspected Cancer Pathway' has been amended to include qFIT and can be found at the bottom of this document and on the NICaN website qFIT for lower GI symptoms | Northern Ireland Cancer Network (hscni.net). It is based on NICE and Scottish Referral Guidelines for Suspected Cancer and on validated studies on the use of qFIT for these symptoms.

qFIT is key to risk stratifying patients – it is a vital step to help you and secondary care prioritise your patient. We are recommending that qFITs are carried out on all patients with new lower GI symptoms as part of initial investigation in general practice.

Where referral is deemed necessary, urgency of investigation in secondary care will usually be based on the qFIT result. Patients should be made aware that qFIT speeds up the diagnostic process and therefore they should be aware of the importance of completing the test.

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What is the evidence on using qFIT in high risk symptomatic populations?

The most recent large scale study on the use of qFIT in patients with suspected colorectal cancer symptoms is the NICE FIT study (see references). This was powered to answer to the primary aim i.e. what is the sensitivity of qFIT in patients with a range of symptoms versus the reference standard, colonoscopy. The study was a prospective, double-blinded study which ultimately included many more patients than initially planned. This study demonstrates the accuracy of the test in patients with low and high risk lower GI symptoms including rectal bleeding. Key points include:

- qFIT has a negative predictive value (NPV) of 99.6% (at worst for all symptoms) for significant bowel disease (i.e. cancer, inflammatory bowel disease and large polyps ≥1cm) at thresholds of <2 and <10 µgHb/g. NB the limit of detection in the NI laboratory analyser is <7 µg Hb/g using the same HM-JACKarc system as used in this study. Therefore, in people with lower GI symptoms a qFIT result <7 µg Hb/g is likely to be wrong for significant bowel disease only c.4 out of 1000 times.

- Other studies have previously proven that where the qFIT has missed cancer the majority are picked up due to a co-existing anaemia. Therefore a negative qFIT result <7µg/g combined with the absence of anaemia, especially where symptoms are not persistent or progressive, can offer reassurance to both the patient and the GP and help avoid unnecessary referral usually for invasive tests for patients.

- The study demonstrates that the likelihood of colorectal cancer for patients with high risk symptoms increases depending on the level of the positive qFIT result i.e. a qFIT>150 µg Hb/g indicates a 30% chance of colorectal cancer and 65% risk of other significant bowel disease whereas a qFIT >400 µg Hb/g indicates an 80% chance of bowel cancer.

Why are you using a qFIT threshold of ≥7 µg Hb/g rather than ≥10 µg Hb/g referred to by NICE FIT and other studies?

7 µg Hb/g is the lowest numerical level that the laboratory analyser can give a value for. The aim is to maximise the sensitivity available.

How are qFIT results reported? (Updated Nov 21)

The qFIT results will be sent to the requesting GP via LABLINKS. The qFIT results will be reported with the statement 'unaccredited test'. This is because FIT is a new

test for the laboratory and is not yet included in their accreditation. Please be assured, this does not mean that there is anything wrong with the sample or it's processing so please ignore this statement. Remember a report <7 µg Hb/g is normal and any result ≥7 µg Hb/g is abnormal and requires a red flag referral.

From 23rd September 2021 abnormal results are identified with a red exclamation mark **!** and the upper range of normal.

There have been a few incidents reported by GPs whereby results have not been transmitted as expected. Results were on ECR but not on the GPs lab report. This has been investigated and a setting change was required. Labs have been contacting any practices where they have noticed a failure to transmit. In some instances, there may be a need for practices to contact their software provider.

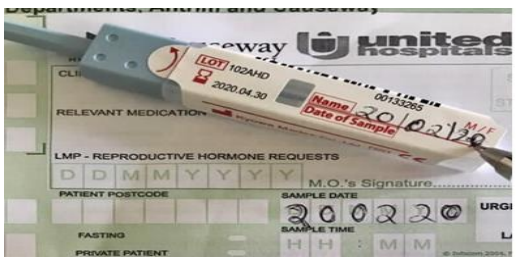
If in the rare case results are not returned when expected, please contact Clinical Biochemistry laboratory at Causeway 028 70346180 and select option 3 for specimen reception and test information.

Why might samples be rejected in the laboratory?

The sample will be rejected in the laboratory if the minimum data set has not been met i.e. no date of sample taken, missing patient details or if the sample is overfilled, absent or leaking.

During the first 12 weeks it has been reported that 9% of samples are unfortunately unable to be processed due to minimum dataset and other errors with the sample kit. Please ensure that the biochemistry forms are completed in full, these include the essential details on the patient and the request. Other samples have been received without an addressograph on the form and FIT kit. All practices should have a label printer. If your practice has no access to label printers please contact nican.office@hscni.net

In order to ensure an accurate result can be processed it is essential that the date of sample is correct. Therefore qFIT samples and forms received in the laboratory without 'date of sample' handwritten on the FIT kit and form (as below) will not be reported. A comment 'No sample date on form or sample, Please repeat' will be issued with no result.



What other investigations will be helpful for my decision making and for secondary care triage?

- Abdominal and more especially rectal examination are important. **A documented rectal examination may mean that your patient can be triaged direct to CTC (CT Colonography).**

Other Useful investigations	Rationale
Full Blood Count	Useful determinants of further investigations where qFIT is normal
Iron profile (including ferritin)*	Useful determinants of further investigations where qFIT is normal (see note below on iron deficiency anaemia)
U&E	Allows determination of renal risks of triaging direct to test hospital investigations
Coeliac profile	May be helpful if a patient has iron deficiency anaemia, weight loss or persistent loose motions.

***If referring with iron deficiency anaemia it is important that this is proven**. Iron deficiency anaemia is diminished red blood cell production due to low iron stores in the body**.** Anaemia is defined as a haemoglobin (Hb) level two standard deviations below the normal for age and sex. A serum ferritin level of less than normal range confirms iron deficiency (i.e. in the main iron store). Please refer to NICE guidance on diagnosis of iron deficiency anaemia for full information https://cks.nice.org.uk/topics/anaemia-iron-deficiency/diagnosis/investigations/

Please note:

- *Faecal calprotectin is NOT a diagnostic investigation if you suspect cancer.*
- *CEA is invariably used for post-op surveillance in patients with known bowel cancers and should NOT be used as a diagnostic tool in primary care.*

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Do I need to wait for the result before I send the referral?

Yes (other than for exception listed below). Red Flag referrals are often triaged within 24 hours of receipt, it is important that qFIT result is included as part of the referral as the result helps secondary care decisions around prioritisation of

investigation. **Exceptions** – **if a patient has rectal/anal or abdominal mass or proven iron deficiency anaemia DO NOT delay referral as secondary care may want to arrange other investigations while awaiting qFIT result. It is therefore important that you arrange a qFIT but proceed with referral and secondary care will look up the qFIT result on ECR when available. In the case of the latter please indicate on your referral that it has been sent.**

What happens if patient was referred as 'Routine' but later qFIT result is elevated?

For routine referrals made, where a later qFIT result is high, a new Lower GI suspect cancer/Red Flag referral must be made as this will not be picked up in the triage/vetting process.

Why is referrer's global impression of frailty important?

Referrers global impression of frailty; this is not a statement of "fitness for" procedures but rather an aide for hospital staff to know ceiling of investigation or treatment and whether the patient is suitable for bowel preparation etc. Issues that would be useful for GP to highlight are:

- **Overall frailty or very obviously diminished life-expectancy** (that might guide a palliative/curative decision),
- **Mobility issues** (that might make examination difficult),
- **Cognitive issues** (potentially affecting consent),
- **Cardiac or renal issues** (potentially affecting bowel prep).

In order to streamline the process for patients, fitter patients may be triaged direct to test. Patients who are not fit for colonoscopy may tolerate alternative radiological investigations e.g. CT or CTC if indicated on the referral letter. It is also important to know if the patient has been advised that further investigation may be required and appears agreeable to a direct to test option. Referrals will not be downgraded on the basis of fitness.

What do I need to do if a patient has a risk symptom on the pathway?

Please follow the NICaN Lower GI Suspected Cancer Pathway and use qFIT to ensure appropriate prioritisation of your patient. We would request the following steps are taken against relevant symptoms after assessment and investigation in primary care.

- **Rectal, Abdominal or Anal Mass:** Refer as red flag, arrange qFIT, mention qFIT requested on referral. Result will be picked up by secondary care.
- **Proven Iron Deficiency Anaemia:** Refer as red flag, arrange qFIT, mention qFIT requested on referral. Result will be picked up by secondary care.

- **Persistent Change in bowel habit towards looser stool for >4 weeks:** Arrange qFIT, await result and when referring, attach result with red flag referral – this will ensure the patient is appropriately prioritised at triage.
- **Rectal Bleeding:** Arrange a qFIT and if result is positive refer red flag. If result is negative consider referral on an urgent basis or as appropriate undertake safety netting considering red flag referral if persistent or progressive symptoms exist on primary care review.
- **Abdominal pain with weight loss: (***Please also consider if Upper GI referral might be more appropriate*.) Arrange a qFIT and if result is positive refer red flag. If result is negative, undertake appropriate safety netting and consider red flag referral if persistent or progressive symptoms exist on primary care review.
- **Normocytic anaemia + lower abdominal symptoms:** Arrange a qFIT and if result is positive refer red flag**.** If result is negative, undertake appropriate safety netting and consider red flag referral if persistent or progressive results/symptoms exist on primary care review.

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What about patients with lower GI symptoms but with qFIT<7 µg Hb/g?

NICE FIT study (see references) demonstrates the high negative predictive value of a qFIT result <7 µg Hb/g in patients with low and high risk lower GI symptoms including rectal bleeding (NPV = 99.6%). Benign conditions are a far more likely explanation for the patient's gastrointestinal symptoms. For patients without IDA, persistent change in bowel habit or persistent rectal bleeding and with normal examination including digital rectal examination, a negative qFIT (<7 µg Hb/g) can be used to support GPs in reassuring patients allowing appropriate use of a safety netting approach in primary care.

Nevertheless a very small proportion of patients with colorectal cancer will have a qFIT<7 µg Hb/g. Safety netting for symptoms and a negative test is important and guidelines are available on safety netting https://www.cancerresearchuk.org/health-professional/diagnosis/suspected-cancer-referral-best-practice/safety-netting

Please consider:

- Symptoms such as abdominal pain or weight loss may be caused by conditions arising outside the bowel and the patient may be more suitable for an alternative investigation.
- Investigating other concerning symptoms via alternative diagnostic pathway e.g. upper GI, urology, gynaecology. Consider checking CA125 in women.
- Safety netting, offer medical management if appropriate and offer review at 6-8 weeks to consider need for repeat/new investigation. Especially where symptoms are persistent, troublesome or at any point significantly deteriorate, repeating the

qFIT (earliest repeat qFIT interval permitted is 2 months), repeating the Hb and referring red-flag ideally with the results attached is appropriate in such cases.

- qFIT is an improvement on using NICE “high risk” criteria alone, which have much lower sensitivity than qFIT for detecting CRC. In this pathway qFIT should only be used in those who are symptomatic.
- Remember, even colonoscopy and CTC are not 100% sensitive for colorectal cancer.

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Is qFIT a useful test in patients with rectal bleeding?

Yes. Data from the NICE FIT study (Ref 1) showed that the high sensitivity of the FIT can be used to rule out CRC in patients with rectal bleeding and triage them more appropriately for investigation.

If a patient has rectal bleeding and a positive qFIT refer as red flag. Rectal bleeding with a qFIT <7 µg Hb/g is appropriate for urgent referral. Safety netting with any negative investigation is always important. If symptoms are persistent or progressive or if **blood is mixed with motions** or there are additional clinical concerns at review in primary care, then refer as red flag.

Please remember that rectal examination is essential as rectal / anal mass or ulceration consistent with colorectal cancer or anal squamous cell carcinoma require immediate referral.

When can qFIT be repeated?

qFIT should not be repeated any earlier than 2 months unless the sample was spoiled.

What if the patient refuses to do a qFIT or cannot produce a sample?

GPs are strongly encouraged to arrange qFIT before referring as this will greatly help stratify a patient’s risk. Consider reasonable adjustments that may be needed to support the patient. However if it is impossible to obtain a qFIT and there remain serious concerns, GPs may refer explaining the reasons why the test could not be done and why they feel the patient needs to be investigated.

What happens if a qFIT test is not arranged with the referral? (Updated Nov 21)

A qFIT result is now required information in the NICaN Primary Care Referral Guidance and must be included with referrals (other than the exception where it may follow). If you do not order a qFIT and await the result (incomplete information), this may delay access to the investigation your patient needs.

During the introduction of qFIT and NICaN Lower GI Suspected Cancer Pathway in July 2021, it was agreed that in order to allow the process to bed in, secondary care would continue to have access to qFIT for a period of three months, up to 5th October, enabling them to issue tests to patients referred without a qFIT result. We have managed to extend this by a further 6 weeks. **However, from 15th November we will need to move to a position whereby all referrals will require a qFIT to be included in the referral. Unfortunately referrals will be returned if a qFIT is not attached (exceptions listed in pathway).**

Secondary care clinicians can amend a referral's priority if insufficient information is contained within the referral or the information supplied does not confirm that the patient meets the NICaN Referral Guidance for Suspect Cancer.

Referrals which have had their prioritisation amended will be moved to the urgent or routine pathway as appropriate, based on clinical information contained within the referral letter. It has been agreed that the referring GP will be notified of any amended prioritisation.

What support and information will be available? (Updated Nov 21)

The following supporting documents are available on the NICaN website qFIT for lower GI symptoms | Northern Ireland Cancer Network (hscni.net)

- Frequently Asked Questions on implementation of qFIT and amended NICaN Lower GI Suspect Cancer Pathway
- NICaN Lower GI Suspected Cancer Pathway
- FIT Patient information leaflet
- Information for Treatment room staff on handing over FIT to patient
- Information for staff on ordering FIT kits and leaflets
- Links to recorded educational webinars from GPNI and NICaN are below. If password required please email nican.office@hscni.net or register to join GPNI mailing list
    - NICaN qFit for Primary Care a Pathway Fit for Purpose
    - Practice Nurses and Managers 'Get qFIT ready for July Fifth' | NICaN and GPNI.
    - Update on the Practical aspects of Quantitative Faecal Immunochemical Test (qFIT) and the new NICaN Lower GI Suspected Cancer Pathway (Nov21)

- Information video on collecting a sample link: https://vimeo.com/616801446

What if a patient has recently completed their Bowel Cancer Screening? (updated Nov 21)

Irrespective of how recently your patient was screened by the national screening programme, **their screening test result should be ignored in considering a patient presenting with new symptoms of concern.** The quantitative threshold for the Bowel Cancer Screening Programme qFIT is much higher than that used in our 'Symptomatic qFIT' testing, so a recent 'normal' or 'negative' from the screening programme should not be relied upon by GPs for reassurance.

There are some key differences in the use of Faecal Immunochemical Test (FIT) for screening asymptomatic people through the bowel screening programme, compared to it being used to investigate symptomatic patients. Cancer Research UK in collaboration with NICaN and the PHA, have developed a useful infographic to highlight the different uses of FIT for screening symptomatic people through bowel screening programme. The resource is now live on Cancer Research UK's health professional web page https://www.cancerresearchuk.org/health-professional/diagnosis/suspected-cancer-referral-best-practice/primary-care-investigations/fit-symptomatic#primarycareinvestigations2

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References

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Gut. 2021 Jun;70(6):1130-1138. https://gut.bmj.com/content/70/6/1130

Faecal immunochemical testing in symptomatic patients to prioritize investigation: diagnostic accuracy from NICE FIT Study
N D'Souza [1 2 3], T Georgiou Delisle [1 4], M Chen [5], S C Benton [6], M Abulafi [1], O Warren, S Ahmadi, C Parchment, A Shanmuganandan, N West, T Mitchell, S Sah, N Jackson, A Myers, P Ziprin, I Bloom, S Kaye, A Ramwell, J T Jenkins, K Monahan
Br J Surg 2021 Mar 23
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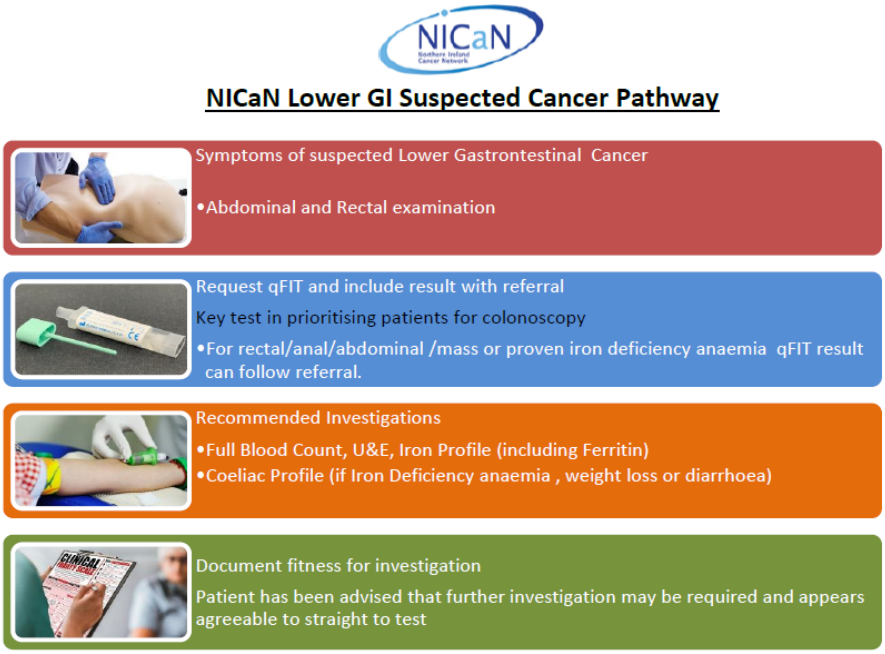
Using the faecal immunochemical test in patients with rectal bleeding: evidence from the NICE FIT study Georgina Hicks1 | Nigel D'Souza2,3,4 | Theo Georgiou Delisle2,4 | Michelle Chen5 | Sally C. Benton6 | Muti Abulafi2 | the NICE FIT steering group
Colorectal Dis. 2021 Feb 19
https://onlinelibrary.wiley.com/doi/10.1111/codi.15593

NICaN Lower GI Suspected Cancer Pathway



Version 22.6.21 – Pathway subject to review at 18 months following evaluation