Investigating faecal immunochemical tests (FITs) for symptomatic primary care patients in the South West of England

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## NG12 versus DG30 symptom criteria for gFOBT/FIT

<table>
<thead>
<tr>
<th>NG12 gFOBT criteria</th>
<th>DG30 FIT criteria</th>
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<tbody>
<tr>
<td>Aged ≥50 years with abdominal pain or weight loss</td>
<td>Patients without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer</td>
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<tr>
<td>Aged &lt;60 years with changes in bowel habit or iron deficiency anaemia</td>
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<tr>
<td>Aged &gt;60 years and with anaemia (in absence of iron deficiency)</td>
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*FIT = faecal immunochemical test. gFOBT = guaiac-based faecal occult blood test.*

The detection of invisible blood in faeces to diagnose colorectal cancer (CRC) has evolved with the introduction of the faecal immunochemical test — commonly referred to as FIT. It will soon replace the guaiac-based faecal occult blood test (gFOBT) in the NHS Bowel Cancer Screening Programme and has been recommended by the National Institute for Health and Care Excellence (NICE) for use in low-risk symptomatic patients with suspected CRC. There is tremendous enthusiasm to introduce FIT into 2-week wait (2WW) pathways to reduce referrals of patients without significant bowel disease and improve patient experience, free up overstretched endoscopy capacity, and save costs. But FIT is not without its shortcomings, and GPs will need to be aware of the limitations of this test, in addition to its exciting potential.

FIT BENEFITS

The clear and overriding benefit of FIT is its precision to detect the degradation products of blood in faeces, measured in μg of blood per gram of faeces (μg/g). Consequently, its sensitivity for CRC is significantly better than gFOBT in NICE modelling, at 92-100% vs 50% countries and therefore data from studies outside of England may not be applicable to an English population.8

Despite the lack of evidence, the HTA and DG30 committee concluded that FIT could be used in low-risk patients with a cut-off of 10 μg/g but recommended that further large-scale studies were needed to fully evaluate the diagnostic accuracy of FIT in low-risk patients. Without this research, implementation of FIT across the board in all low-risk symptomatic patients may lead to an endoscopy capacity crisis because of patients with false-positive FIT results, but more seriously may lead to delayed diagnosis for patients with false-negative FIT results.

FALSE-POSITIVE FIT

DG30 recommended that FIT is performed in ‘patients without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer’.3 Literal interpretation of the guidance will lead to the eligibility of patients with any bowel or abdominal symptom (in the absence of rectal bleeding), of any age, who do not meet 2WW criteria. Previous data reported in 2007 positive gFOBT from this group were referred for further investigations.

FIT has now supplanted gFOBT in the pathway for symptomatic patients. At 76.6–85.8%,1 the specificity of FIT at a cut-off of 10 is relatively high but this means that up to 25% of patients will have a false-positive result. As the broader DG30 criteria create a potentially enormous pool of low-risk patients, triage with FIT may lead to an overall increase in patients with false-positive results, and a higher number of referrals for further investigation. Limiting this pool of patients to specific symptom criteria (for example, the same low-risk criteria for gFOBT in NG12 guidance [Box 2]), also recommended by CRUK, would prevent a surge in referrals.

FALSE-NEGATIVE FIT

Although false-positive referrals from DG30 have worrying implications for endoscopy service provision and costs, false-negative results will have the more devastating clinical impact on patients.

The sensitivity of FIT is very high, but not 100%:7 up to 10% of patients with CRC will have a false-negative FIT result.
FALSE-POSITIVE FIT

DG30 recommended that FIT is performed in ‘patients without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer’.³ Literal interpretation of the guidance will lead to the eligibility of patients with any bowel or abdominal symptom (in the absence of rectal bleeding), of any age, who do not meet 2WW criteria. Previous data reported in 2007 estimated that approximately 10% of primary care consultations were for gastrointestinal symptoms.⁹,¹⁰ The pool of eligible patients with gastrointestinal symptoms is therefore unquantified, but possibly enormous. Referral of these patients to secondary care would overwhelm endoscopy services, and many patients would undergo unnecessary investigation.
D’Souza and colleagues underestimate GPs’ clinical judgement in selecting patients for a faecal immunochemical test (FIT). NICE may recommend FIT for ‘low-risk’ symptomatic patients ‘without rectal bleeding who have unexplained (abdominal) symptoms but do not meet the criteria for a suspected cancer’, but this has not led to the ‘deluge’ of referrals or worsening of the ‘endoscopy capacity crisis’ in the centres where FIT has been adopted.

The majority of the estimated 10% of consulting patients with abdominal complaints will not be referred for colonoscopy. GPs conduct a careful triage using history and examination, an understanding of their patients’ consulting patterns and comorbidity, preferences for testing, and by deciding when to respond to a positive result. Only a highly selected group of those tested and with a positive FIT are referred.

The NICE positive predictive value (PPV) threshold to rule in patients for urgent referral is 3%: the PPV for a low-risk symptom such as abdominal pain is 2% (increasing with age) compared with 5% for rectal bleeding. The PPV of a positive FIT in the low-risk symptomatic population is estimated at 13%. If FIT is positive, referral is uncontroversial; if negative, the PPV falls to <1%, making colonoscopy non-referral reasonable. FIT is more likely to result in a reduction of unnecessary (routine) endoscopy referrals for low-risk symptoms.
Evaluation plan

• Primary outcome – colorectal cancer (C18.0 – C21)

• Analysis:
  • Diagnostic performance statistics
  • Number of routine and 2WW referrals to endoscopy
  • A (series of) Receiver Operating Characteristic (ROC) curve analysis
  • 3500 test results needed

| Aged 50-60 with: changes in bowel habit or iron deficiency anaemia |
| Aged over 50 with: unexplained abdominal pain or weight loss |
| Aged 60 or over and have anaemia without iron deficiency |
Early findings

• Data collection ongoing

• As of March 2019: 7,073 samples received at the two labs

• 1,079 positive (15.3%)

• We have data on 517 of these... and 308 have complete follow up SO FAR
Early findings

- 24 cancers diagnosed - 9 early, 9 late, 6 unknown

- Including all patients: the PPV is 4.6% (95% CI 3.0 – 6.8) (based on entire sample of 517).

- The positive predictive value (PPV) was 7.8% (95% CI 5.1 – 11.4) including only 308 patients with complete outcome data.

- Next year: more results
Challenges and difficulties

- Missing data
- Variation in recording and reporting
- Data access
What next?

- Continue data quest – missing data

- Parallel studies:
  - East of England collaboration with Cambridge
  - Qualitative work
  - Health economics study

- Talk to everyone else who is trying to do this
Thank you

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