Faecal Immunochemical Testing (FIT) for Screening and Symptomatic Patients

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What is FIT

• Type of Faecal Occult Blood test
  – Designed to look for small amounts of blood in stool
  – Uses antibodies specific to human haemoglobin
  – Quantitative result
  – Increased sensitivity and specificity
  – Automated
Current test - Guaiac FOB test

- Two separate smears per stool sample (– 3 stools in total)
- Reagent added to back side
- Built-in QC at bottom
- Kit develops between 30-60 seconds
Why should FIT be implemented?

• Guaiac FOB tests (gFOBt) relies on heme in faeces in a moderate quantity
  – Visable colour change
  – Analytically insensitive

• Dietary peroxidases can interfere
  – Myoglobin in meat, peroxidase in plants
  – Non specific test
Why should FIT be implemented?

• FIT uses antibodies specific for globin moiety of human Hb
  – More specific than gFOBt
  – Selective for colorectal bleeding
• Increase detection of cancers and advanced adenomas vs gFOBt
• Quantitative test = adjustable cut-off
• Single sample
faecal-Haemoglobin (f-Hb)

- f-Hb is directly related to severity of colorectal disease
- Median f-Hb is higher in CRC than no pathology or minor non-neoplastic pathology
- f-Hb higher in men
- f-Hb increases with age
- f-Hb increases as deprivation increases
Theoretical representation of distribution of fecal hemoglobin concentrations in normal subjects and cancer cases.
Young et al, Dig Dis Sci 2015; 60:609-22
The FIT test kit/device – which one?
The FIT test kit/device

• Small plastic bottle containing a stick with grooved tips.
• The grooved tips of stick are scraped along the bowel motion so that the grooves are covered.
• Stick is then returned to the bottle
  – Contains buffer to preserve the sample
• ‘wet’ faeces unstable
• Must use collection device specific for FIT analyser
Analysis

• Small amount of liquid is sampled from the test kit
  – Mixed with antibodies and latex reagent
  – Measures the amount of haemoglobin in the faeces (µg Hb/g faeces)
FIT & Screening

- FIT has been available for screening since early 1980s
- Research has shown that FIT provides superior sensitivity/selectivity for advanced colorectal neoplasia over gFOBt
- 2008 – randomised comparison between FIT and gFOBt
  - 2.5x advanced adenomas and cancer
  - 2.2x more cancers

Van Rossum et al. Gastroenterology 2008;135:82-90
FIT & English BCSP

• Pilot study 2014
  – Uptake 66.4% (vs 59.3%)
  – Significant increase in detection of cancers, advanced adenomas and all neoplasms
    • PPV lower for cancer, but similar to gFOBt for AA and higher for all neoplasms
    • Even at higher cut-offs

• Jan 2016, NSC recommended BCSP move from gFOBt to FIT
FIT & English BCSP

• ITT closed early October, evaluation of bids currently taking place
• Aim to start implementing FIT by end of 2018
• Phased roll out
• Working towards full roll out by April 2019
Symptomatic FIT

• In 2015, NG 12 Suspected cancer: recognition & referral

  “offer testing for occult blood in faeces to assess for CRC in adults without rectal bleeding who:
  - >50yrs unexplained abdo pain or weight loss
  - <60yrs with changes in bowel habit or IDA
  - >60yrs with anaemia even in the absence of iron deficiency

• Guidelines were considered ill advised
Symptomatic FIT

• Systematic review to analyse the clinical effectiveness of FIT for triaging referrals
  – FIT is a promising investigation to aid GPs determine which patients would benefit from referral for colonoscopy
  – Triage using FIT may reduce referral to colonoscopy

Westwood et al. BMC Medicine 2017;15:189
Symptomatic FIT

• NICE DG 30 “…faecal immunochemical tests are recommended for adoption in primary care to guide referral for suspected colorectal cancer in people without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer pathway referral outlined in NICE’s guideline on suspected cancer” (NG12)
Symptomatic FIT

• Studies on FIT so far have demonstrated:
  – Good rule in test for CRC. Positive FIT = referral for urgent colonoscopy
  – Good rule out test for significant bowel disease (SBD)
  – Better at detection of CRC than guidelines based on symptoms, age and other factors for referral
  – Some CRC, AA and IBD will be missed – Safety netting is mandatory
Symptomatic FIT

<table>
<thead>
<tr>
<th></th>
<th>Colorectal cancer</th>
<th>High Risk Adenoma (HRA)</th>
<th>Significant colorectal disease (CRC+HRA+IBD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>89.3%</td>
<td>50.0%</td>
<td>68.6%</td>
</tr>
<tr>
<td>Specificity</td>
<td>79.1%</td>
<td>78.0%</td>
<td>83.6%</td>
</tr>
<tr>
<td>PPV</td>
<td>14.2%</td>
<td>11.4%</td>
<td>39.8%</td>
</tr>
<tr>
<td>NPV</td>
<td>99.5%</td>
<td>96.5%</td>
<td>94.4%</td>
</tr>
</tbody>
</table>

Mowet et al. Faecal haemoglobin and faecal calprotectin as indicators of bowel disease in patients presenting to primary care with bowel symptoms. *Gut* 2016;65:1463-1469
Challenges with Symptomatic FIT

- Use of a single cut-off
- Lack of evidence of use in low risk patients in primary care
- Concern that colonoscopy referral may increase
- Missed CRC, HRA and IBD
Symptomatic FIT (North East)

• Pilot started in selected Northumbria GP practices
  – Low risk GI symptoms offered FIT test
• Northern Cancer Alliance are working with CCGs to roll out test across region
FIT current practice

• Use of FIT is increasing for both screening and symptomatic patients
  – FIT provides *ONE* test but in *TWO* different clinical settings
  – These applications have different
    • Target populations
    • Aims
    • Interpretation of results
    • Potential harms
    • Additional benefits
Target Populations

**To identify** – *in an age selected asymptomatic population* - those who are *most likely* to have colorectal neoplasia and would benefit most from colonoscopy.

**To assist in deciding** - *in a patient, of any age, presenting in primary care with lower abdominal symptoms* - who would be *unlikely* to benefit from referral to secondary care for colonoscopy.
Main Clinical Aims and f-Hb cut-off

To rule-in colorectal neoplasia.

Cut-off f-Hb may be high - depends on strategy of screening programme

To rule-out significant colorectal disease.

Cut-off f-Hb must be low.
Interpretation

A “positive” result means that an increased risk of CRC is present in that participant, and further investigation is warranted.

A “negative” result means the participant should be re-invited after the screening interval, currently two years.

If the result is “negative”, there is considerable reassurance that significant colorectal disease (CRC+ HRA + IBD) is not present.

A “detectable” f-Hb means that the patient warrants further investigation.
Problem Caused by Different Cut-offs

• may be instances when people, who have recently had a "negative" screening result (low risk of CRC), may get a "positive" result in primary care after reporting symptoms, simply because of the use of different f-Hb cut-offs in the two very different clinical settings.
### Differences between screening & symptomatic FIT

<table>
<thead>
<tr>
<th><strong>SCREENING</strong></th>
<th><strong>SYMPTOMATIC</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Offered through BCSP – 60-74yr olds, registered with a GP</td>
<td>Patients presenting to primary care with low risk GI symptoms</td>
</tr>
<tr>
<td>Kit sent to eligible participants by BCSP to patients home. Completed kit sent back to BCSP Hub</td>
<td>Likely that GP will hold stock of kits and then completed kit is returned to GP &amp; then referred to lab</td>
</tr>
<tr>
<td>Cut-off is high</td>
<td>Cut-off is low</td>
</tr>
<tr>
<td>GPs informed of results (Normal/abnormal)</td>
<td>GP gets normal/negative result and numerical value for results ≥ 10ug/g</td>
</tr>
<tr>
<td>Abnormal result = referred for SSP appointment by BCSP</td>
<td>Abnormal result = GP needs to refer</td>
</tr>
<tr>
<td>Normal result = invited to take part again in two years</td>
<td>Normal result – ensure safety netting procedures in place</td>
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Summary

• FIT is a more sensitive and specific test than gFOBt

• However, testing can be performed in two different clinical settings
  – Different cut-offs and thus interpretation

• Patients with symptoms should not be referred to BCSP
  – Should be offered symptomatic FIT or referred as appropriate
Any Questions?