FIT for symptoms – evidence and future directions.

Mr Ayan Banerjea
Consultant Colorectal Surgeon
On behalf of
Nottingham Colorectal Service/ University of Nottingham
Nottinghamshire BCSP Hub
Nottinghamshire “Getting FIT” Collaboration

M25 Colorectal Diseases Masterclass
7th March 2018
How good is “Two week wait”?

Two week wait (2000)
- Cancer detection rate is 5-10%
- Massive resource allocation

Pathways to diagnosis
- Two week wait
- Routine
- Screening
- Emergency

Nottingham University Hospitals
Two week wait pathway

% Diagnosed in each pathway
- Routine: 38
- 2WW: 32
- Screening: 9
- Emergency: 21

We are here for you
“Early diagnosis”

- Two week referral guidelines do not promote detection of **early** stage CRC

Cancers diagnosed on Routine pathway

<table>
<thead>
<tr>
<th>Early (T1-T2 N0)</th>
<th>Not early</th>
</tr>
</thead>
</table>

Cancers diagnosed on 2WW pathway

<table>
<thead>
<tr>
<th>Early (T1-T2 N0)</th>
<th>Not early</th>
</tr>
</thead>
</table>

Cancers diagnosed by Screening

<table>
<thead>
<tr>
<th>Early (T1-T2 N0)</th>
<th>Not early</th>
</tr>
</thead>
</table>
Straight to test Colonoscopy (2014)

- Approximately 50% go STT
- Younger patients (mean 65.9 vs 78.7 years; p<0.0001)
- Reduced times to first test (13 vs 22 days; p<0.0001)
- Reduced times to tissue diagnosis (17 vs 24.5 days; p<0.0001)
- Improved 62 day compliance
- Lower cancer detection rate 5.2% STT vs 8.2% OPA
- Obviate “New” OPA = >£145000 p.a. for CCGs

Banerjea et al Col Dis (2017)

Prospective audit: understand your pathway
Understanding your pathway

Pre-NG12

2WW for CRC = “Symptomatic screening programme”


Pre NG12

Patients proven anaemic on 2WW referral are 3 times more likely to have CRC (OR 3.22, 95%CI 1.87-5.57) compared to non-anaemic patients.

WHO <120g/L in women or <130g/L in men

Hamilton et al BJC (2008)

Atkin et al HTA (2017)
Patients not referred with IDA

<table>
<thead>
<tr>
<th>Indication for referral</th>
<th>Number Referrals</th>
<th>Number anaemic</th>
<th>CRC %</th>
<th>Not anaemic</th>
<th>CRC %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIBH</td>
<td>436</td>
<td>109</td>
<td>8.3</td>
<td>327</td>
<td>1.8</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>113</td>
<td>36</td>
<td>8.3</td>
<td>77</td>
<td>3.9</td>
</tr>
<tr>
<td>CIBH &amp; Rectal bleeding</td>
<td>168</td>
<td>18</td>
<td>5.6</td>
<td>150</td>
<td>4.7</td>
</tr>
<tr>
<td>Rectal mass</td>
<td>31</td>
<td>9</td>
<td>33.3</td>
<td>22</td>
<td>18.1</td>
</tr>
<tr>
<td>Abdo mass</td>
<td>29</td>
<td>10</td>
<td>10</td>
<td>19</td>
<td>5.3</td>
</tr>
<tr>
<td>Other*</td>
<td>32</td>
<td>10</td>
<td>0</td>
<td>22</td>
<td>0</td>
</tr>
</tbody>
</table>

* Other: Weight loss, abnormal radiology

- FBC = <£3
- “Anaemia is a cheap & easy starting point for stratification”
NG12 - 2015

- Broadening of referral criteria
- Faecal Occult Blood Testing
  - "Rule in" low risk
    - Abdominal pain
    - Weight loss
    - Anaemia
    - Iron deficiency anaemia <60y
    - Non iron-deficient anaemia >60y

Which FOB test?? FIT >> gFOBT

What about “rule out”? Capacity???
Evidence for FIT

- **Jellema et al, BMJ 2010**
  - Meta analysis 47 studies
  - Family hx, IDA & weight loss
  - Good Sn but poor Sp
  - Age >50y & referral guidelines
  - Good Sn but poor Sp

- Only FIT had good Sn & Sp

- Evidence lacking

- **Cubiella et al, Col Dis 2014**
  - *Post hoc* COLONPREDICT
  - 97 CRC (12.3%) in 787 pts
    - 1179 referrals
    - Includes rectal bleeding
    - 100ng/ml = 20 µgHb/gFaeces
  - FIT significantly better than NICE 2011 (or SIGN)
    - Sn 87.6% vs 61.9%
    - Sp 77.4% vs 65.2%
    - Acc 0.88 (95% CI 0.84-0.92) vs 0.63 (0.58-0.69)
    - P<0.001
UK: Mowat et al., Gut 2015

- Includes Rectal bleeding & Faecal Calprotectin
- Not a “Two week pathway” for cancer
- 750 patients with colonoscopy and faecal haemoglobin concentration (f-Hb)
- 41.7% patients had undetectable f-Hb
- Test performance assessed for prediction of significant bowel disease (SBD)
- Colorectal cancer + high-risk adenoma + IBD

<table>
<thead>
<tr>
<th></th>
<th>SBD</th>
<th>No SBD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test +</td>
<td>90</td>
<td>347</td>
<td>437</td>
</tr>
<tr>
<td>Test -</td>
<td>12</td>
<td>301</td>
<td>313</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>648</td>
<td></td>
</tr>
</tbody>
</table>

PPV = 20.6%
NPV = 96.2%
Sensitivity = 88.2%
Specificity = 46.4%

2189 referrals
1043 FIT returns
750 with investigation results
33.9% rectal bleeding
Started with a cut-off of 20μgHb/gFaeces and then reduced.....
“Getting FIT” in Nottingham

Service Evaluation

• **Allow GPs** to access quantitative FIT for low risk
  – Cut off **150µgHb/gFaeces**

• **Postal FIT** within 2WW pathway

• **Patients with rectal bleeding excluded**

• **Prospective Audit**
  – 1000 tests commissioned by CCGs
  – Results available to study team
  – September 16 – August 17
Widlak et al., AP&T 2016

- 799 of 2822 referrals
- 430 completed investigations
- HMJack for FIT
- Includes Faecal Calprotectin
- 43% rectal bleeding
  - 3 CRC missed below 7µgHb/gFaeces

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Test</th>
<th>Normal</th>
<th>Abnormal</th>
<th>TPR</th>
<th>FPR</th>
<th>PPV</th>
<th>NPV</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC+HGD</td>
<td>FIT</td>
<td>405</td>
<td>25</td>
<td>0.84</td>
<td>0.07</td>
<td>44%</td>
<td>99%</td>
<td>84%</td>
<td>93%</td>
</tr>
<tr>
<td>CRC+HGD</td>
<td>FCP</td>
<td>405</td>
<td>25</td>
<td>0.84</td>
<td>0.16</td>
<td>21%</td>
<td>98%</td>
<td>68%</td>
<td>84%</td>
</tr>
<tr>
<td>CRC+HGD</td>
<td>Both</td>
<td>405</td>
<td>25</td>
<td>0.84</td>
<td>0.07</td>
<td>41%</td>
<td>99%</td>
<td>84%</td>
<td>93%</td>
</tr>
<tr>
<td>Adenoma</td>
<td>FIT</td>
<td>388</td>
<td>42</td>
<td>0.69</td>
<td>0.44</td>
<td>15%</td>
<td>94%</td>
<td>69%</td>
<td>56%</td>
</tr>
<tr>
<td>Adenoma</td>
<td>FCP</td>
<td>388</td>
<td>42</td>
<td>0.43</td>
<td>0.44</td>
<td>10%</td>
<td>90%</td>
<td>43%</td>
<td>56%</td>
</tr>
<tr>
<td>Adenoma</td>
<td>Both</td>
<td>388</td>
<td>42</td>
<td>0.69</td>
<td>0.44</td>
<td>15%</td>
<td>94%</td>
<td>69%</td>
<td>56%</td>
</tr>
</tbody>
</table>

FIT Cancer | Median | IQR   |
Left        | 713     | 142-998.5 |
Right       | 94      | 7.4-144   |

P < 0.05
“Getting FIT” pilot results

Table 2. Diagnosis and median FIT levels.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>2WW referrals n=810 (%)</th>
<th>Median FIT levels µgHb/gFaeces (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/Diverticulosis+/Haemorrhoids</td>
<td>476 (58.8)</td>
<td>1.2 (0-5.2)</td>
</tr>
<tr>
<td>Cancer</td>
<td>40 (4.9)</td>
<td>223 (34.8-1334.7)</td>
</tr>
<tr>
<td>Other cancer</td>
<td>18 (2.2)</td>
<td>15.4 (2-170.2)</td>
</tr>
<tr>
<td>High risk adenoma</td>
<td>45 (5.6)</td>
<td>20.6 (2.8-83.2)</td>
</tr>
<tr>
<td>LRA/benign UGI</td>
<td>168 (20.7)</td>
<td>2 (0-11.9)</td>
</tr>
<tr>
<td>SPECC</td>
<td>10 (1.2)</td>
<td>127 (17.4-898.6)</td>
</tr>
<tr>
<td>Colitis</td>
<td>22 (2.7)</td>
<td>42.2 (1.6-314.8)</td>
</tr>
<tr>
<td>Microscopic colitis</td>
<td>29 (3.6)</td>
<td>2 (0-6.2)</td>
</tr>
<tr>
<td>Complicated diverticular disease</td>
<td>2 (0.3)</td>
<td>17.7 (14-21.4)</td>
</tr>
</tbody>
</table>
Results

% of 891 FIT returns 81 DNA/declined

n=538 (60.4%)
1 Colorectal cancer
0.2%

n=83 (9.3%)
4 Colorectal cancers
3 IDA and 1 rectal mass
4.8%

n=198 (22.2%)
11 Colorectal cancers
5.5%

n=72 (8.1%)
26 Colorectal cancers
CRC detection rate 36.1%

n=810
"Getting FIT 2016-2017"

CRC detection rate n=810

<table>
<thead>
<tr>
<th>Category</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia (WHO criteria)</td>
<td>288</td>
</tr>
<tr>
<td>No anaemia</td>
<td>473</td>
</tr>
<tr>
<td>Hb unknown</td>
<td>49</td>
</tr>
</tbody>
</table>

Right sided cancers have sig lower FIT results
41.6 IQR 11.2-406.8 vs 286.8 IQR 142-5076.8
Kruskal Wallis p=0.0296

4 CRC’s picked up that were missed by our normal pathways because FIT >150

We are here for you
Performance characteristics

<table>
<thead>
<tr>
<th>Cut Off (µgHb/gFaeces)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4</td>
<td>97.5 (86.8-99.9)</td>
<td>64.5 (61.1-67.9)</td>
<td>12.5 (9.0-16.7)</td>
<td>99.8 (98.9-100)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>87.5 (73.2-95.8)</td>
<td>73.5 (70.2-76.6)</td>
<td>14.6 (10.4-19.8)</td>
<td>99.1 (98-99.7)</td>
</tr>
<tr>
<td>&gt;150</td>
<td>60.0 (43.3-75.1)</td>
<td>94.4 (92.6-95.9)</td>
<td>35.8% (24.5-48.5)</td>
<td>97.8 (96.5-98.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cut Off (µgHb/gFaeces) and/or anaemic</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4</td>
<td>100 (90.5-100)</td>
<td>45.3 (41.6-49)</td>
<td>8.6 (6.1-11.6)</td>
<td>100 (98.9-100)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>97.3 (85.8-99.9)</td>
<td>51.7 (47.9-55.4)</td>
<td>9.3 (6.6-12.7)</td>
<td>99.7 (98.5-100)</td>
</tr>
<tr>
<td>&gt;150</td>
<td>86.5 (71.2-95.5)</td>
<td>61.3 (57.7-64.9)</td>
<td>10.3 (7.12-14.2)</td>
<td>98.9 (97.4-99.6)</td>
</tr>
</tbody>
</table>

Better than NICE (2011) criteria – as per Jellema/Cubiella
## FIT and symptoms

<table>
<thead>
<tr>
<th>Referral symptom</th>
<th>% of referrals**</th>
<th>Overall risk of CRC (%)</th>
<th>CRC detection rate stratified by FIT cut offs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;4</td>
</tr>
<tr>
<td>Combined symptoms*</td>
<td>9.4</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>IDA</td>
<td>23.2</td>
<td>7.2</td>
<td>1.1</td>
</tr>
<tr>
<td>CIBH alone</td>
<td>57.5</td>
<td>2.9</td>
<td>0</td>
</tr>
<tr>
<td>Abdo mass</td>
<td>3.3</td>
<td>10.7</td>
<td>0</td>
</tr>
<tr>
<td>Rectal mass</td>
<td>4.1</td>
<td>5.9</td>
<td>0</td>
</tr>
<tr>
<td>Other”</td>
<td>2.4</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Includes IDA and CIBH combined with other sx
**As a proportion of all referrals without rectal bleeding
“Abdo pain/weight loss/abnormal imaging
FIT in practice…

- Who?
  - Primary care vs Secondary Care vs Both
- How?
  - Primary care handout
  - Secondary care handout
  - Postal
- When?
  - Before Referral 2WW clock starts
  - During 62 day clock
- What for?
  - All symptoms
  - Just Change In Bowel Habit

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**Clinical Governance**

NICE Guidance
NG12 & DG30

Valid Consent
Montgomery vs Lanarkshire 2015
Birch vs UCL 2008

BCSP – Cut offs vs Capacity

2WW pathway is about CRC
It can never detect every case!
5,660 FIT kits returned to laboratory

Referred to secondary care
n = 2,765

- Triaged to colonoscopy
  n = 1,392
  - Test not done
    n = 205

- Triaged to GI clinic
  n = 648

- Triaged to other assessment (sigmoidoscopy, OGD, CT etc.)
  n = 725
  - No colonoscopy required
    n = 435
  - Referred to colonoscopy, not done
    n = 21

Total with completed colonoscopy
n = 1,379
(1,187 referred straight to scope, 193 from clinic)

No referral
n = 2,680
Digby et al 2017

FIT usage increased from 22% to 66% of referrals in 6/12 (2016)

<table>
<thead>
<tr>
<th>Test +</th>
<th>Test -</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>241</td>
<td>38</td>
<td>279</td>
</tr>
<tr>
<td>514</td>
<td>586</td>
<td>1100</td>
</tr>
</tbody>
</table>

PPV = 32.0%
NPV = 93.9%
Sensitivity = 86.4%
Specificity = 53.2%

1,379 patients with f-Hb and colonoscopy outcome
Test performance characteristics assessed using cut-off of f-Hb > 10 µg Hb/g faeces
54.7% had a positive result
279 cases of significant bowel disease (SBD) colorectal cancer + high risk adenoma + IBD

6 patients with f-Hb < 10 µg Hb/g faeces had CRC...all had IDA
**Nottingham Rapid Colorectal Cancer Pathway**

**Patient with symptoms**

**Rectal bleeding or mass**
- Submit RCCD Form
- Immediate 2WW Clock start

**Other symptoms**
- Anaemia
- Abdominal mass
- **YES**
  - Whole Colon Investigation

**NO**
- Flexi sigmoidoscopy
- STT Flexi/ORB

**FIT required**
- GP requests FIT & interprets results independently
- GP requests FIT & submits RCCD form

**Submit RCCD Form with FIT result if appropriate**
- Immediate 2WW Clock start

**WINDOW**
- 2WW Clock on hold until FIT available

**Local Agreement with CCG’s/Primary care**
- FIT = £17.50
- Computerised requests
- Computerised support – F12
- Postal system from BCSP hub
- Every FIT request logged and audit ongoing
- November 2017 - now

We are here for you
## Interpreting FIT

<table>
<thead>
<tr>
<th>FIT &lt;4 CRC risk 0.2%</th>
<th>FIT 4-10 CRC risk 4.8%</th>
<th>FIT 10-150 CRC risk 5.5%</th>
<th>FIT &gt;150 CRC Risk 36.1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigate IDA only on 2WW CT Colon</td>
<td>Investigate in anaemia only (WHO criteria)</td>
<td>Investigate on 2WW pathway</td>
<td>Immediate 2WW clock start</td>
</tr>
</tbody>
</table>

**GP advised risk of CRC very low**

Options:
- Watch and wait
- Repeat FIT
- Refer on Routine pathway
- Refer on alternative urgent pathway

<table>
<thead>
<tr>
<th>CTC &gt; Colonoscopy</th>
<th>Colonoscopy or CTC</th>
<th>STT team contacts patient directly</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT AP for abdo mass/weight loss</td>
<td>?CT AP for abdo mass/weight loss</td>
<td>Fast track – STT Colonoscopy or CTC</td>
</tr>
</tbody>
</table>

OSCARS
# Impact of RCCD

<table>
<thead>
<tr>
<th></th>
<th>NUH RCCD Referrals</th>
<th>Window (%)</th>
<th>Window expired (%)</th>
<th>2WW Colonoscopy</th>
<th>Comparison to STT</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nov 17</strong>*</td>
<td>120</td>
<td>67 (55.8)</td>
<td>14 (20.9)</td>
<td>16</td>
<td>Nov 14</td>
<td>71</td>
</tr>
<tr>
<td><strong>Dec 17</strong></td>
<td>110</td>
<td>60 (54.5)</td>
<td>24 (40)</td>
<td>23</td>
<td>Dec 14</td>
<td>68</td>
</tr>
<tr>
<td><strong>Jan 18</strong></td>
<td>170</td>
<td>53 (31.1)</td>
<td>17 (32.1)</td>
<td>44</td>
<td>Jan 15</td>
<td>71</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>400</td>
<td>180 (45)</td>
<td>65 (36.7)</td>
<td>83</td>
<td>210</td>
<td>-60.5%</td>
</tr>
</tbody>
</table>

*ISTC not participating
Impact of RCCD

- 695 returns in 3 months (91.2%)
- 67 unreturned to date
- GPs requesting FIT in rectal bleeding
- 102 CRC detected
- 39.2% on 2WW
- 7 (6.9%) had colonoscopy in previous 3y

<table>
<thead>
<tr>
<th>Pilot (%)</th>
<th>RCCD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>60.4</td>
</tr>
<tr>
<td>4-10</td>
<td>9.3</td>
</tr>
<tr>
<td>10-150</td>
<td>22.2</td>
</tr>
<tr>
<td>&gt;150</td>
<td>8.1</td>
</tr>
</tbody>
</table>

Increase in returns <4 µgHb/gFaeces

**Opportunistic screening of a lower risk group**

One right colon lesion on CT AP with FIT <2 - ?cancer ?spasm
Pt co-morbid and frail – sx subsided
Declined further investigation
“Rule in”

FIT > 150µgHb/gFaeces
- Risk of CRC 1 in 3
- Risk of SBP 1 in 2

- Targeted to Consultant Colorectal Surgeons’ Colonoscopy lists

- CT/MRI slots held for staging

OSCARS
- One stop
- Surgical assessment
  - Fitness for surgery
  - Pre-optimisation
- Colonoscopy
  And
- Radiological Staging

We are here for you
Clinical effectiveness in 2WW

Additional data
• York
• Liverpool
• London

Feasible
• FIT
• Finger - DRE
• FBC & Ferritin
• Flexible sigmoidoscopy

• FAST score
  – Cubiella et al IJC (2017)
  – Anaemia?
    • Hogberg et al ScanJG (2016)

• Avoid colonoscopy in 75-80%
  – Capacity for BCSP??
Acknowledgements

Straight to test Team
• Sarah Thomson
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• Sara Blower
• Tara Dorn
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• Dr Nina Lewis & Gastroenterology Consultants

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• Dr Richard Rogers (GP)
• Dr Arun Tangri (GP)
• Nottingham North & East CCG
• Nottingham West CCG
• Rushcliffe CCG

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• Dr Jo Morling
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• Adam Barke
• Fiona McLeod
• Abby Duffin

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