Colorectal cancer - recognition and referral
Cancer cascade workshop

Michael Machesney BSc MD FRCS
Colorectal surgeon
Chair of the Colorectal Cancer Clinical Expert Group for NHSE

RCGP
Royal College of General Practitioners
A human being should be able to change a diaper, plan an invasion, butcher a hog, conn a ship, design a building, write a sonnet, balance accounts, build a wall, set a bone, comfort the dying, take orders, give orders, cooperate, act alone, solve equations, analyze a new problem, pitch manure, program a computer, cook a tasty meal, fight efficiently, die gallantly. Specialization is for insects.

- Robert A. Heinlein -
Networks to alliances

Cancer Networks as at 1st October 2008

Cancer alliances 2017
Diagnosing cancer: a needle in a haystack

UK population: 66,850,000
494,100,000 health service interactions

42,100
13.8% colorectal
UK Bowel cancer statistics

- 42,100 new cases per year
- 3rd most common cancer in females, approx. 18,600 new cases per year
- 3rd most common cancer in males, approx. 23,500 new cases per year
- Over half of bowel cancers are diagnosed at a late stage
- Bowel cancer is the 2nd most common cause of cancer death (10%)
- Since the 1970s bowel cancer mortality rates have decreases by 44%
- Bowel cancer deaths are most common in the most deprived areas
The problem
The survival gap—international variation

5-year net survival(%) 

Australia(A), Canada(C), Denmark(D), England(E), Norway(N) and Sweden(S)

Walters et al. BJC 2015
Unwarranted national variation
Survival 1 year

Figure 5A: One-year age-standardised net survival (%) from colon cancer for patients diagnosed 2011, by NHS England Area Teams and sex
Variations in the proportion of patients diagnosed in stage 1 & 2 by CCG

Early diagnosis has a lower cost for treatment

<table>
<thead>
<tr>
<th>Stage</th>
<th>Colon cancer</th>
<th>Rectal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>£3,373</td>
<td>£4,449</td>
</tr>
<tr>
<td>Stage 2</td>
<td>£7,809</td>
<td>£6,944</td>
</tr>
<tr>
<td>Stage 3</td>
<td>£9,220</td>
<td>£8,302</td>
</tr>
<tr>
<td>Stage 4</td>
<td>£12,519</td>
<td>£11,815</td>
</tr>
</tbody>
</table>

£24M if all CCGs had best performance
What’s best for the patient?

• Early diagnosis

• Removal of unwarranted variation

• Safer more effective treatment

• High quality complete data
Targets
Lower GI suspected cancer referral
(2 Week Wait Referral) CG27 2005

Please FAX within 24 hours to Cancer Two Week Wait Office

<table>
<thead>
<tr>
<th>All ages</th>
<th>Over 40 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] Definite, palpable, right sided, abdominal mass</td>
<td>[ ] Rectal bleeding WITH a change of bowel habit towards looser stools &amp;/or increased frequency ≥6 wks</td>
</tr>
<tr>
<td>[ ] Definite, palpable, rectal (not pelvic) mass</td>
<td>Over 60 years</td>
</tr>
<tr>
<td>[ ] Unexplained iron deficiency anaemia</td>
<td>[ ] Rectal bleeding persisting ≥6wks WITHOUT a change in bowel habit or anal symptoms (e.g. soreness, discomfort, itching, prolapse, pain)</td>
</tr>
<tr>
<td><strong>AND:</strong></td>
<td>[ ] Change in bowel habit to looser stools &amp;/or more frequent stools persisting ≥6 wks WITHOUT rectal bleeding</td>
</tr>
<tr>
<td>[ ] Male with a Hb of &lt; 11g/dl</td>
<td></td>
</tr>
<tr>
<td>[ ] Non menstruating female with a Hb of &lt; 10g/dl</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical History, Known Allergies</th>
<th>All Medication</th>
<th>Mandatory Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIABETIC: YES/NO</td>
<td>WARFARIN: YES/NO</td>
<td>[ ] PR examination</td>
</tr>
<tr>
<td></td>
<td>CLOPIDROGREL: YES/NO</td>
<td>[ ] Abdo examination</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Findings:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[ ] FBC: Hb: _____ MCV ___ Date: __ /<strong>/</strong></td>
</tr>
</tbody>
</table>
Lowering the threshold for referral

5. HOW SHOULD WE IMPROVE SURVIVAL?

- We need to shift behaviours so that GPs are encouraged to refer for tests at a lower threshold of suspicion of cancer, and try new approaches for patients to access tests.

- We will have to invest to increase our diagnostic capacity. Otherwise, the system will be unable to cope with current requirements, let alone increased demand.
Suspected cancer: recognition and referral
NICE guidelines [NG12] Published 23 June 2015

• NG12 replaces NICE clinical guideline CG27 (published June 2005)
• nice.org.uk/guidance/ng12
• Recommendations developed using a ‘risk threshold’
• Risk of symptoms being caused by cancer at this level triggers referral
• Threshold defined as positive predictive value (PPV)
• Reduction of PPV from 5% to 3% for suspected cancer pathway referrals and urgent direct access investigations such as endoscopy
Positive predictive value (PPV)

- The percentage of patients with a positive symptom who have the disease
- PPV = a (true positives) / a (true positives) + b (false positives)
- How good is the evidence for symptoms that may be caused by cancer?
- Do they facilitate preventing late diagnosis?
Suspected cancer: recognition and referral

Colorectal cancer

1.3.1 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer if:

- they are aged 40 and over with unexplained weight loss and abdominal pain or
- they are aged 50 and over with unexplained rectal bleeding or
- they are aged 60 and over with:
  - iron-deficiency anaemia or
  - changes in their bowel habit, or
- tests show occult blood in their faeces (see recommendation 1.3.4 for who should be offered a test for occult blood in faeces). [new 2015]
1.3.2 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in people with a rectal or abdominal mass. [new 2015]

1.3.3 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults aged under 50 with rectal bleeding and any of the following unexplained symptoms or findings:

- abdominal pain
- change in bowel habit
- weight loss
- iron-deficiency anaemia. [new 2015]

1.3.4 Offer testing for occult blood in faeces to assess for colorectal cancer in adults without rectal bleeding who:

- are aged 50 and over with unexplained:
  - abdominal pain or
  - weight loss, or
- are aged under 60 with:
  - changes in their bowel habit or
  - iron-deficiency anaemia, or
- are aged 60 and over and have anaemia even in the absence of iron deficiency. [new 2015]
1.3.4 This recommendation has been replaced by our diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care (http://www.nice.org.uk/guidance/dg30). The diagnostics guidance recommends tests for occult blood in faeces, for people without rectal bleeding but with unexplained symptoms that do not meet the criteria for a suspected cancer pathway referral in recommendations 1.3.1 to 1.3.3.
Discrepancy

- Nice Clinical Knowledge Summaries
- The cause of iron deficiency anaemia should be determined and treated
- Men of any age should be referred for upper and lower GI endoscopy
- Post menopausal women should be referred for upper and lower GI endoscopy
- People with unexplained iron deficiency anaemia who don’t fit the criteria should be referred on the 18 week pathway
FIT recommended to assist GPs to triage referral to secondary care

DG30

• Test intended for low risk but not no risk
• Age and symptoms with a positive predictive value of between 0.1% and 3% for colorectal cancer
• If positive FIT for 2 week wait referral for a colonoscopy or CTC
More simple or more complex?
Gut feeling?

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

BMJ Open  Determinants of general practitioner’s cancer-related gut feelings—a prospective cohort study  2016

Gé A Donker,¹ Eva Wiersma,² Lucas van der Hoek,¹ Marianne Heins¹
Has it made enough of a difference?
How are bowel cancer patients diagnosed?
Does the 2WW improve outcome for bowel cancer?
Do we investigate enough?


Figure 3.3. International comparisons – crude colonoscopy rates per 1,000 in 2010/11
Solution

Reduce emergency presentation

Increase screening participation
5 year forward view

‘faster diagnosis for cancer’

‘We will expand access to screening’

‘in Denmark reducing by two thirds the number of hospitals that perform colorectal cancer surgery has improved post-operative mortality’
Can we afford not to address the cost of emergency presentation?

One year survival for colorectal cancer:
All routes of diagnosis: 73%
Emergency presentation: 48%
Impact of bowel cancer screening on emergency surgery

- Before screening 24%
- After screening 16%
- Screening age 12%
- Increase in elective surgery

Hwang et al. Colorectal Dis 2014
Missed opportunity for earlier diagnosis of bowel cancer in 50-59 year olds in England

Lucy Ironmonger\textsuperscript{1}, Michael Machesney\textsuperscript{2}, Nick Ormiston-Smith\textsuperscript{1}, Aaron Quyn\textsuperscript{3} & Robert Steele\textsuperscript{3}

\textsuperscript{1}Cancer Research UK \textsuperscript{2}Barts Health NHS Trust \textsuperscript{3}University of Dundee
Results

- Difference in stage distribution for Scotland & England

Bowel Cancer in 50-59s, all routes

Proportion of cases

Scotland (2011-13)
England (2012)
### Results

**EXTRAPOLATING TO ENGLAND:**

- Number of additional cases that could have been diagnosed at stage I & II:

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-54s</td>
<td>4</td>
<td>22</td>
<td>26</td>
<td>90</td>
<td>117</td>
<td>123</td>
<td>78</td>
</tr>
<tr>
<td>55-59s</td>
<td>27</td>
<td>56</td>
<td>99</td>
<td>125</td>
<td>181</td>
<td>205</td>
<td>163</td>
</tr>
<tr>
<td>50-59s</td>
<td>31</td>
<td>78</td>
<td>125</td>
<td>215</td>
<td>298</td>
<td>328</td>
<td>241</td>
</tr>
</tbody>
</table>

3-year average

- 105
- 185
- 290

June 2016

Bowel screening in 50-59s
Comparing Costs
Screening strategy England v’s Scotland 50-59 years

• 5xFOBT+2% colonoscopy £61
• Flexible sigmoidoscopy £351

“PM David Cameron has announced £60m over the next four years to introduce the latest cancer screening technology” Oct 2010

Is there a need for a Plan B?
FIT from 50?

GI cancer in the UK – can we do better, RCP 7th December 2015
Colonoscopy capacity – a major constraint?
Traditional colorectal pathway
Triaged straight to test
Triaged straight to test pilot 2014

- GP choose and book appointment
- Nurse telephone triage. Check indication and fitness for bowel prep
- Investigations: Colonoscopy (81%), colonoscopy & gastroscopy (9%), flexible sigmoidoscopy (6%) or clinic (3%)
- Mean total wait for 18WW: 32 days (67% reduction)
- Mean total wait for 2WW: 13.6 days (51% reduction)
- Refer back to GP after results review ‘virtual clinic’


Straight to test colonoscopy-a viable means of shortening time to a definitive diagnosis
Gut 2014;63 (suppl 1) A27
Faster diagnostic standard
28 day pathway - deliver definitive diagnosis

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 0 to 3</th>
<th>Day 3 to 14</th>
<th>Day 14</th>
<th>Day 21</th>
<th>Day 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent GP referral^1 Including locally mandated information</td>
<td>Clinical triage (with telephone consultation)</td>
<td>Straight to test (STT) Colonoscopy or CT Colon / CT / Flexi Sig +/- OGD</td>
<td>Staging Investigations Contrast CT Chest / Abdo / Pelvis MRI +/- TRUS (rectal cancer) Bloods (incl. CEA)</td>
<td>MDT^2</td>
<td>Communication to patient on outcome (cancer confirmed or all-clear provided)</td>
</tr>
<tr>
<td>Patient information Provided in primary care</td>
<td></td>
<td></td>
<td>Cancer unlikely Patient informed; management according to local protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinic review With CNS support</td>
<td></td>
</tr>
</tbody>
</table>
Risk assessment
Faecal immunological test for haemoglobin
FIT

Studies found FIT approaches 100% negative predictive value, (NPV) for colorectal cancer

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Sample number</th>
<th>Cut off (µg Hb/g faeces)</th>
<th>Missed CRC/HRA</th>
<th>Analyser</th>
<th>Return rate</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>96.7%</td>
<td>79.9%</td>
<td>5.2%</td>
<td>100%</td>
<td>1003</td>
<td>10</td>
<td></td>
<td>OC Sensor</td>
<td>n/a</td>
<td>Rodriguez-Alonso et al 2015</td>
</tr>
<tr>
<td>87.5%</td>
<td>67.4%</td>
<td>5.6%</td>
<td>99.6%</td>
<td>373</td>
<td>25-50</td>
<td></td>
<td>Medix Biochemica</td>
<td>n/a</td>
<td>Hogberg et al 2017</td>
</tr>
<tr>
<td>100%</td>
<td>43.4%</td>
<td>6.4%</td>
<td>100%</td>
<td>755</td>
<td>10</td>
<td>3 CRC</td>
<td>OC-Sensor</td>
<td>47.9%</td>
<td>Mowat et al 2015*</td>
</tr>
<tr>
<td>68.9% a</td>
<td>80.2% a</td>
<td>26.3% a</td>
<td>96.2% a</td>
<td>484</td>
<td>10-(40)</td>
<td>0 CRC 9 HRA</td>
<td>JM Jack</td>
<td>55.7%</td>
<td>Godber et al 2016*</td>
</tr>
<tr>
<td>84%</td>
<td>93%</td>
<td>44%</td>
<td>99%</td>
<td>430</td>
<td>7</td>
<td></td>
<td>JM Jack</td>
<td>62%</td>
<td>Widlak et al 2017**</td>
</tr>
</tbody>
</table>

* values only given for ‘significant colorectal disease’ and include combined CRC, high risk adenoma, irritable bowel syndrome and colitis
*Scottish pilots
** Coventry pilot

NHS England FIT conference- 26 Feb 2019
qFIT pilot

- NIHR study led by UCLH Cancer Collaborative
- Can FIT ‘rule-out’ test of significant bowel disease for high risk symptomatic patients in primary care?
- April 2017 – Feb 2019 → 20+ hospitals and 70+ GP practices recruiting in NCEL & England

- Primary & secondary care
- FIT handed out in parallel to 2WW pathway
- Results compared with colonoscopy and CTC
- OC-Sensor
qFIT pilot – Preliminary results

- Over 4000 viable samples collected
- Test uptake varies regionally, 30-50%
- 81% of viable samples <6µg/g
- 76 cancers in 2801 fully coded cases
- 704 polyps (95% >10µg/g)
- Cancer prevalence lower than in Scotland
- FIT NPV is over 99.4% (cancer)
- 9 cancer cases (12%) had FIT <10µg/g
- 7 cancer cases had FIT <6µg/g

### Reason for referral

<table>
<thead>
<tr>
<th>Indication</th>
<th>Second Indication</th>
<th>Third Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in bowel habit</td>
<td>Weight loss</td>
<td></td>
</tr>
<tr>
<td>Abnormal Imaging</td>
<td>Rectal bleeding</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Rectal bleeding</td>
<td></td>
</tr>
<tr>
<td>Change in bowel habit</td>
<td>Abdominal pain</td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in bowel habit</td>
<td>Weight loss</td>
<td>Positive Faecal Occult Blood test</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Weight loss</td>
<td>Right or Left Iliac Fossa Pain/ Tenderness</td>
</tr>
</tbody>
</table>
There is time: Probability of undiagnosed disease progression

Table 32: Probability of progression for undiagnosed colorectal cancer

<table>
<thead>
<tr>
<th>Colorectal Stage</th>
<th>Annual probability of progression for undiagnosed CRC (95% CI)</th>
<th>PSA Distribution</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dukes A – Dukes B</td>
<td>0.58 (0.57-0.59)</td>
<td>Uniform</td>
<td>Tappenden et al 2004</td>
</tr>
<tr>
<td>Dukes B – Dukes C</td>
<td>0.66 (0.64-0.67)</td>
<td>Uniform</td>
<td>Tappenden et al 2004</td>
</tr>
<tr>
<td>Dukes C – Dukes D</td>
<td>0.87 (0.85-0.88)</td>
<td>Uniform</td>
<td>Tappenden et al 2004</td>
</tr>
</tbody>
</table>

Safety netting by referral on routine referral pathway for patients with persistent symptoms and FIT below threshold
Sir Mike Richards  
Chief Inspector of Hospitals  
March 2017  

“The NHS now stands on a burning platform - the need for change is clear, but finding the resources and energy to deliver that change while simultaneously providing safe patient care can seem almost impossible.”
Will it deliver for bowel cancer?

“By 2028, the proportion of cancers diagnosed at stages 1 and 2 will rise from around half now to three-quarters”

“We will lower the starting age for [bowel cancer] screening from 60 currently to 50”

This will need performance targets for the NBCSP

Colonoscopy not mentioned...
We will have to fix it
If liberty means anything at all, it means the right to tell people what they do not want to hear.