Bowel cancer risk in the under 50s

Greg Rubin
Professor of General Practice and Primary Care
Prevalence of GI problems in the consulting population
Thompson et al, Gut 2000

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of patients</th>
<th>% of patients with gut problems (255)</th>
<th>% of all screened patients (3111)</th>
</tr>
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<tbody>
<tr>
<td>Functional</td>
<td>112</td>
<td>43.9</td>
<td>3.6</td>
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<tr>
<td>IBS</td>
<td>76</td>
<td>29.8</td>
<td>2.4</td>
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<tr>
<td>Organic</td>
<td>100</td>
<td>39.2</td>
<td>3.2</td>
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<tr>
<td>IBD</td>
<td>12</td>
<td>4.7</td>
<td>0.4</td>
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<tr>
<td>Coeliac disease</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unknown</td>
<td>43</td>
<td>16.9</td>
<td>1.4</td>
</tr>
</tbody>
</table>
## Prevalence of GI problems in the consulting population

Thompson et al, Gut 2000

<table>
<thead>
<tr>
<th>Type of GI Problem</th>
<th>Number of Patients</th>
<th>% of Patients with gut problems (255)</th>
<th>% of all screened patients (3111)</th>
<th>Incidence in UK, per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional</td>
<td>112</td>
<td>43.9</td>
<td>3.6</td>
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<tr>
<td>IBS</td>
<td>76</td>
<td>29.8</td>
<td>2.4</td>
<td>200</td>
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<tr>
<td>Organic</td>
<td>100</td>
<td>39.2</td>
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<tr>
<td>IBD</td>
<td>12</td>
<td>4.7</td>
<td>0.4</td>
<td>22</td>
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<tr>
<td>Coeliac disease</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24*</td>
</tr>
<tr>
<td>Unknown</td>
<td>43</td>
<td>16.9</td>
<td>1.4</td>
<td></td>
</tr>
</tbody>
</table>
Average Number of New Cases of Colorectal Cancer Per Year and Age-Specific Incidence Rates per 100,000 Population, UK, 2012-2014

Source: cruk.org/cancerstats
Coeliac disease: incidence in the UK

(West et al, AJ Gastroenterol 2014)
54% of men referred after 1 or 2 appointments

37% of women consulted 5 times or more before referral

34% of respondents were happy with the level of GP support
Delays in diagnosis of IBD

(Vavricka et al, Inf Bowel Dis 2012)

• Diagnostic delay in CD patients was 9 months, compared to 4 months in UC patients.

• Seventy-five percent of CD patients were diagnosed within 24 months compared to 12 months for UC.

• Age <40 years at diagnosis and ileal disease are independent risk factors for long diagnostic delay in CD (>24 months).

• Nonsteroidal anti-inflammatory drug and male gender were associated with long diagnostic delay in UC (>12 months).
Delays to coeliac disease diagnosis
Norstrom et al, BMC Gastroenterology 2011

• Mean total diagnostic interval 9.7 years
• Mean diagnostic interval 5.8 years
Effects of delay in diagnosis


Patients with coeliac disease with a diagnostic delay shorter than 2 years were significantly less often in need of steroids and/or immunosuppressants, substitution for any nutritional deficiency but more often free of symptoms 6 and 12 months after diagnosis.

Patients with delayed diagnosis of IBD require more complex treatment (UC) and are more likely to undergo surgical resection (CD)
Diagnosing IBS: the Rome IV criteria

Lacy et al, Gastroenterology 2016

• Recurrent abdominal pain, on average, at least 1 day/week in the last 3 months, associated with two or more of the following criteria:
  • Related to defecation
  • Associated with a change in frequency of stool
  • Associated with a change in form (appearance) of stool.
• Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.
IBS diagnosis: NICE guidance (CG61)

Consider diagnosing IBS only if the person has abdominal pain or discomfort that is:

• relieved by defaecation, or
• associated with altered bowel frequency or stool form

and at least 2 of the following:

• altered stool passage (straining, urgency, incomplete evacuation)
• abdominal bloating (more common in women than men), distension, tension or hardness
• symptoms made worse by eating
• passage of mucus.

Lethargy, nausea, backache and bladder symptoms may be used to support diagnosis.
Diagnostic testing in patients with suspected IBS (CG61)

- Prior assumption is that patients with alarm symptoms for colorectal cancer are directed down the 2WW pathway
- Priority is to exclude inflammatory causes for symptoms
  - FBC
  - ESR
  - C Reactive protein
  - *Faecal Calprotectin*
  - Tests to exclude coeliac disease
Urgent referral for suspected colorectal cancer

**Colorectal cancer**

1.3.1 Refer adults 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. [new 2015]

1.3.2 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults 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]
IBD Standards (2013): Diagnosis of IBD

- Guidance should be developed for the identification and referral of symptomatic patients in whom IBD is suspected. GPs should be prepared to periodically review their diagnosis in patients with unresponsive, atypical or troublesome abdominal symptoms.

- Faecal biomarkers such as faecal calprotectin may be useful in primary care, in association with clinical assessment.

- A communication pathway must be agreed for referral of possible IBD patients to the IBD service for rapid consultation and assessment. Such patients should be contacted within two weeks of referral and seen within four weeks, or more rapidly if clinically necessary.
NICE guidance on coeliac disease diagnosis (NG20, 2015)

Offer serological testing for coeliac disease to:
people with any of the following:
• persistent unexplained abdominal or gastrointestinal symptoms
• faltering growth
• prolonged fatigue
• unexpected weight loss
• severe or persistent mouth ulcers
• unexplained iron, vitamin B12 or folate deficiency
• type 1 diabetes, at diagnosis
• autoimmune thyroid disease, at diagnosis
• irritable bowel syndrome (in adults)

first-degree relatives of people with coeliac disease.
Testing for coeliac disease (NG20)

• Explain that any test is accurate only if a gluten-containing diet is eaten during the diagnostic process.

• When healthcare professionals request serological tests to investigate suspected coeliac disease in young people and adults, laboratories should:
  • test for total immunoglobulin A (IgA) and IgA tissue transglutaminase (tTG) as the first choice.
  • use IgA endomysial antibodies (EMA) if IgA tTG is weakly positive.
  • consider using IgG EMA, IgG deamidated gliadin peptide (DGP) or IgG tTG if IgA is deficient.

• Refer people with negative serological test results to a gastrointestinal specialist for further assessment if coeliac disease is still clinically suspected.
## Unrestricted use of faecal calprotectin in primary care: poor test performance

Conroy et al, J Clin Path 2017

<table>
<thead>
<tr>
<th>Current Study</th>
<th>Pavlidisa 2013&lt;sup&gt;6&lt;/sup&gt;</th>
<th>Turvill 2016&lt;sup&gt;3&lt;/sup&gt;</th>
<th>NICE DG11&lt;sup&gt;3&lt;/sup&gt;: Secondary Care Meta-Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease differentiation</strong></td>
<td>For IBD vs no IBD</td>
<td>Organic v non-organic</td>
<td>Organic v non-organic</td>
</tr>
<tr>
<td><strong>Primary or secondary care setting</strong></td>
<td>Primary</td>
<td>Primary</td>
<td>Primary</td>
</tr>
<tr>
<td><strong>Threshold for positive faecal calprotectin (µg/g faeces)</strong></td>
<td>&gt;50</td>
<td>&gt;50</td>
<td>&gt;50</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>72.7%</td>
<td>77.8%</td>
<td>82%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>64.9%</td>
<td>66.8%</td>
<td>77%</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>5.41%</td>
<td>14.2%</td>
<td>28%</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>98.9%</td>
<td>97.7%</td>
<td>98%</td>
</tr>
</tbody>
</table>

*Table 2. Summary of sensitivity and specificity of faecal calprotectin testing in current study and other studies in primary and secondary care. (IBD = inflammatory bowel disease; PPV positive predictive value; NPV negative predictive value)*
Faecal immunochemical tests (FIT) to rule out colorectal cancer in patients presenting in primary care with lower abdominal symptoms

Triage using quantitative FIT, at a faecal haemoglobin concentration cut-off of 10 μg Hb/g faeces, has the potential to avoid colonoscopy in 75–80% of symptomatic patients for whom a general practitioner is considering a referral to secondary care, but who do not meet the criteria for 2-week wait suspected cancer referral.

Westwood et al, BMC Med 2017
Adding FIT and calprotectin to clinical assessment for significant colorectal disease

Elias et al BMC Med 2016

Patients were eligible if suspected of SCD, defined by lower abdominal complaints for at least 2 weeks, combined with rectal bleeding, change in bowel habit, abdominal pain, fever, diarrhoea, weight loss, and/or a sudden onset of abdominal complaints at > 50 years of age. The basic diagnostic model consisted of: Age, Abdominal pain, Rectal blood loss, Rectal mucus, Weight loss, Change in bowel habit, Abdominal bloating, Constipation, Abnormal digital rectal examination, CRP in mg/L
PPVs (95% CI) for colorectal cancer (CRC) or inflammatory bowel disease (IBD) in males and females aged 18–49 years for individual risk markers and for pairs of risk markers in combination.

<table>
<thead>
<tr>
<th>Rectal bleeding</th>
<th>Change in bowel habit</th>
<th>Diarrhoea</th>
<th>Abdominal pain</th>
<th>Low mean red cell volume</th>
<th>Raised white cell count</th>
<th>Raised platelets</th>
<th>Abnormal liver function</th>
<th>Low haemoglobin</th>
<th>Raised inflammatory markers</th>
<th>PPV as a single symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 (1.1 to 1.4)</td>
<td>1.8 (0.8 to 1.3)</td>
<td>0.5 (0.5 to 0.6)</td>
<td>0.3 (0.2 to 0.2)</td>
<td>0.4 (0.3 to 0.4)</td>
<td>0.3 (0.3 to 0.3)</td>
<td>0.8 (0.7 to 0.9)</td>
<td>0.1 (0.1 to 0.1)</td>
<td>0.3 (0.3 to 0.3)</td>
<td>0.5 (0.5 to 0.6)</td>
<td></td>
</tr>
<tr>
<td>2.4 (1.9 to 3.7)</td>
<td>2.6 (0.9 to 4.4)</td>
<td>3.7 (0.7 to 6.3)</td>
<td>1.5 (1.1 to 2.2)</td>
<td>3.2 (1.3 to 7.4)</td>
<td>2.7 (1.3 to 5.3)</td>
<td>5.3 (1.4)</td>
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<td>3.3 (1.7 to 6.2)</td>
<td>5.2 (2.9 to 9.1)</td>
<td>Rectal bleeding</td>
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<tr>
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<td>1.4 (0.8 to 2.5)</td>
<td>1.0 (0.6 to 1.6)</td>
<td>5.5 (1.1)</td>
<td>2.1 (1.0)</td>
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<td>1.0 (0.5 to 1.9)</td>
<td>0.6 (1.1)</td>
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<td>Change in bowel habit</td>
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<tr>
<td>1.5 (1.2 to 1.9)</td>
<td>0.9 (0.7 to 1.1)</td>
<td>2.1 (1.3 to 3.5)</td>
<td>2.8 (1.9 to 4.2)</td>
<td>6.9 (3.7 to 13)</td>
<td>6.9 (3.7 to 13)</td>
<td>1.1 (0.8 to 1.5)</td>
<td>2.1 (1.5 to 3.1)</td>
<td>2.8 (2.0 to 3.7)</td>
<td></td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>0.4 (0.4 to 0.5)</td>
<td>1.0 (0.7 to 1.4)</td>
<td>0.7 (0.4 to 0.9)</td>
<td>2.7 (1.0 to 4.8)</td>
<td>0.3 (0.3 to 0.4)</td>
<td>0.8 (0.6 to 1.0)</td>
<td>1.2 (1.0 to 1.5)</td>
<td>0.9 (1.0 to 1.3)</td>
<td>1.3 (1.8 to 1.8)</td>
<td>0.4 (0.3 to 0.6) 0.6 (0.5 to 0.7) 1.7 (1.2 to 2.3)</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>1.3 (1.0 to 1.7)</td>
<td>0.4 (0.3 to 0.5)</td>
<td>0.5 (0.4 to 0.6)</td>
<td>1.0 (0.8 to 1.2)</td>
<td>1.0 (1.0 to 1.5)</td>
<td>1.2 (1.0 to 1.5)</td>
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<td></td>
<td>1.3 (1.8 to 1.8)</td>
<td>0.4 (0.3 to 0.6) 0.5 (0.4 to 0.6) 1.0 (0.8 to 1.2)</td>
<td>Raised white cell count</td>
</tr>
<tr>
<td>1.0 (0.7 to 1.4)</td>
<td>1.2 (0.9 to 1.5)</td>
<td>2.0 (1.5 to 2.6)</td>
<td>1.0 (0.7 to 1.4)</td>
<td>0.5 (0.4 to 0.6)</td>
<td>0.5 (0.4 to 0.6)</td>
<td>1.4 (1.1 to 1.7)</td>
<td>0.5 (0.4 to 0.6) 0.5 (0.4 to 0.6) 1.4 (1.1 to 1.7)</td>
<td>Low haemoglobin</td>
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</tr>
</tbody>
</table>

Sally A Stapley et al. Br J Gen Pract  
doi:10.3399/bjgp17X690425

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Patient with persistent symptoms (>3 weeks) referable to the lower GI tract

FBC, ESR, CRP, Coeliac screen, Faecal calprotectin, FIT

Diagnosis not clear

Risk assessment tool

Risk >3%
Refer

Risk 1-3%
Calprotectin if not already done

Risk <1%
Manage expectantly
Conclusions

• Significant colonic disease, including colorectal cancer, is not rare and should be borne in mind when patients present with persistent GI symptoms
• Selecting those patients who need specialist assessment could take a ‘significant colorectal disease’ perspective
• The Risk Assessment Tool allows estimation of risk based on symptoms / signs
• FIT Hb adds to symptom assessment in prioritising endoscopy (and possibly in case selection)
• Calprotectin has a role, but may not perform as well as NICE suggest, and not in ruling CRC in or out.