Diagnosing colorectal cancer in primary care; *can we do better?*

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**Agenda**

- Colorectal cancer; *the need for early diagnosis*
- Role of the GP in diagnosing CRC; *how are we doing now?*
- How can we improve?
Colorectal cancer; baseline data

- Second most frequent type of cancer
- Incidence 80/100,000 (3-4 per GP practice)
- 14% of all cancer incidence

- Lifetime risk 5-6%
- 90% of patients > 50 years
- 5 years survival 61-65%

CRC survival is improving

But…differences between countries, health systems and professionals!
Overall cancer survival is improving

- Between 2003-2013: 53 new cancer drugs
- Mean 3.4 extra months survival (range 0-8.5)
- 50% of new drugs no survival benefit

*Probably improved survival is more due to earlier diagnosis than to better chemotherapy*

Earlier diagnosis; better prognosis?

Difference in 5 year survival between early detection (stage I or II) versus late detection (stage III or IV)
CRC; stage at diagnosis

<table>
<thead>
<tr>
<th>stage</th>
<th>5-year survival</th>
<th>Distribution at diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>93%</td>
<td>22%</td>
</tr>
<tr>
<td>2</td>
<td>78%</td>
<td>34%</td>
</tr>
<tr>
<td>3</td>
<td>61%</td>
<td>25%</td>
</tr>
<tr>
<td>4</td>
<td>9%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Agenda

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Colorectal cancer screening; results 2015

Invited: 848,761 (55-75 years)

Response rate: 72.6%

Pos FIT: 6.7%

Colonoscopy rate: 79.4%

Cancer: 4.3 per 1000 FIT screened

Adenoma: 34.4 per 1000 screened

PPV for cancer positive FIT: 8.7%

Estimated net benefit: 2400 (50%) CRC deaths
Where is cancer diagnosed?

90% of cancers diagnoses are symptom based

80% are seen in general practice

- Alarming symptoms: 48%
- Serious, aspecific: 20%
- Vague symptoms: 32%

15% of patients had a potential cancer symptom in the past year

The cancer pathway; from symptom to treatment
Dickens project

Duration and determinants of the diagnostic interval in cancer

Linking 6 academic routine primary care networks with Dutch Cancer registry

Duration and determinants of intervals in 10 cancer types

Pilot: colorectal cancer

309 symptomatic patients

Median duration (IQR)

<table>
<thead>
<tr>
<th>Symptom(s)</th>
<th>Consultation</th>
<th>Referral</th>
<th>Diagnosis</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>IP</td>
<td>22 (8-62)</td>
<td>8 (1-60)</td>
<td>26 (13-54)</td>
<td>27 (15-39)</td>
</tr>
<tr>
<td>IPC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISD</td>
<td>54 (21-116)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IT</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ID</td>
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</tbody>
</table>
Determinants of prolonged PC interval

Associated with relatively long duration were:

- Patients younger than 50 years
- *Female gender*
- History of malignancy
- *Non-alarming GI symptoms*
- *Presence of hemorroids*
- Additional investigations performed by GP
Agenda

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Interventions for more timely diagnosis

Organisational level:
- Public awareness campaigns on CRC symptoms
- Improving guideline adherence through cancer pathways (ACE, CPP’s)
- Desk top decision aids
- Rapid access to colonoscopy (2 weeks rule)
- Diagnostic centers for cancer suspicion (MDC’s)

*GP: Improving personalised risk assessment!*
Diagnostic process GP

1. Age, gender
   Medical history
   Family history

   Prior risk of cancer

2. Symptoms
   Physical examination
   Laboratory tests

   Personalised risk
   (Individual cut-off point?)

The importance of family history

1. Sporadic CRC (85%)

2. Hereditary CRC (5%)
   - Hereditary Non Polyposis CRC/Lynch syndrom (3%)
   - Familial Adenomatosis Polyposis (1%)

3. Familial CRC (> 3 population risk) (10%)
Familial CRC: cumulative lifetime risk (%)

Meta-analyses Johns, Baglietto en Butterworth

Importance of alarm symptoms

Interval between registration of alarm symptom and referral

<table>
<thead>
<tr>
<th>Alarm Symptom</th>
<th>N (%)</th>
<th>Median (IQR)</th>
<th>Mean (± SD)</th>
<th>Range</th>
<th>N (%) &gt; 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal bleeding</td>
<td>115 (37.2)</td>
<td>1 (1-10)</td>
<td>4.2 (10.9)</td>
<td>1-686</td>
<td>30 (26.1)</td>
</tr>
<tr>
<td>Rectal bleeding and altered defecation pattern</td>
<td>94 (30.4)</td>
<td>1 (1-3)</td>
<td>4.0 (10.7)</td>
<td>1-686</td>
<td>29 (30.9)</td>
</tr>
<tr>
<td>Rectal bleeding without perianal abnormalities</td>
<td>110 (35.6)</td>
<td>1 (1-13)</td>
<td>3.3 (10.3)</td>
<td>1-686</td>
<td>26 (23.6)</td>
</tr>
<tr>
<td>2 or more alarm symptom categories at first consultation</td>
<td>99 (32.0)</td>
<td>1 (1-2)</td>
<td>3.1 (10.2)</td>
<td>1-686</td>
<td>24 (24.2)</td>
</tr>
</tbody>
</table>

“In cases with RBL and “perianal abnormalities present”, median duration was 47 days (IQR: 1 to 117).”

Hamilton et al BJGP 2011, Shapely et al BJGP 2010, Mowat GUT, Helsper, submitted

Note: 2 Two-week (or more) wait for referral after registration of alarm symptom

Note: 3 Definition: any combination of alarm symptom categories at first consultation
Predictive value of symptoms

Hamilton et al, BJGP 2011

CEDAR-study: discriminating organic and functional bowel disease in primary care

990 patients with complaints suggestive for OBD in primary care (with need for referral for endoscopy)

Patient history, phys ex, Rome Criteria
Blood tests (gliadine, ESR, WBC)
-Fecal tests on POC Calprotectin and FIT

Reference test:
Endoscopy and/or histology

Elias et al, BMC Medicine 2016
## Results

### Basic model

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<thead>
<tr>
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<th>OR</th>
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<tbody>
<tr>
<td>Age, per 5 years</td>
<td>1.1 (1.1-1.2)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0.6 (0.4-1.0)</td>
</tr>
<tr>
<td>Rectal blood loss</td>
<td>2.6 (1.7-4.0)</td>
</tr>
<tr>
<td>Rectal mucus</td>
<td>1.6 (1.1-2.5)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1.4 (0.9-2.3)</td>
</tr>
<tr>
<td>Change in bowel habit</td>
<td>1.3 (0.8-2.1)</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>0.7 (0.4-1.0)</td>
</tr>
<tr>
<td>Constipation</td>
<td>0.7 (0.5-1.1)</td>
</tr>
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</table>

**Physical examination**

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<tbody>
<tr>
<td>Abnormal digital rectal examination</td>
<td>1.9 (0.8-4.4)</td>
</tr>
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</table>

**Blood tests**

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<tbody>
<tr>
<td>C-reactive protein in mg/L, per log(CRP+1)</td>
<td>1.2 (1.0-1.6)</td>
</tr>
</tbody>
</table>

### Integrated risk model

- Basic model: 0.74 (95%CI: 0.70-0.79)
- Extended:
  - Calprotectin POC test: 0.77 (95%CI: 0.73-0.82) (95%CI: 0.79-0.87);
  - IFOBT POC test: 0.83 (95%CI: 0.79-0.87);
  - Both fecal POC tests: 0.84 (95%CI: 0.80-0.88).
Care as usual

of 1,000 primary care patients referred for colonoscopy

174 have serious colorectal disease
826 do not
of 174 cases:
46 colorectal cancer
60 advanced polyps
46 inflammatory bowel disease
22 diverticulitis

New diagnostic strategy

Simple diagnostic strategy including faecal test

300 have low risk: no referral
288 correctly not referred

700 have high risk: referral for colonoscopy
12 with delay in diagnosis
1 colorectal cancer
5 advanced polyps
6 diverticulitis

162 have serious colorectal disease
538 do not

Elias et al., BMC Medicine 2016

comment

The mantra “early diagnosis” is like “free money”—it sounds great, but there’s a catch. Patients will be short changed unless it’s fairly explained

How low should we go?

People’s willingness to accept overdetection in cancer screening: population survey

Van den Bruel senior clinical research fellow, Caroline Jones senior researcher, Yaling Yang senior researcher in health economics, Jason Oke medical statistician, Paul Hewitson senior researcher

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Diagnosing CRC in primary care; we can do better

- Increasing public awareness
- Health system interventions

The GP has a key role:
- Guideline compliance
- Action on family history and alarmsymptoms
- Personalised, integrated risk assessment

Research
- Identify 10% ‘high risk to miss’ patients
- Evaluation of simple additional testing