Choice of screening method-factors to take into account

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Conflicts of interest

• None
CRC incidence

- CRC is the most common type of GI cancer in Europe 447,000 new cases (13% of all cancers) in the EU in 2012
- Overall incidence rate: 68 per 100,000 population.
- Incidence in men: 79 per 100,000
- Incidence in women: 54 per 100,000

CRC mortality

- CRC is the second most common cause of cancer related death in Europe
- 215,000 cases in 2012 (12-13% of all cancer deaths)

CRC screening

CRC is very suitable for screening
- Detectable and treatable pre-malignant lesions (adenomas)
- Early detection of CRC improves the prognosis
- Benefits outweigh the potential harms

Cost-effectiveness of CRC screening

- CRC screening is cost-effective compared to no screening (cost-saving)
- No single strategy found to be the most effective or preferred for a given willingness to pay per LYG

Lansdorp-Vogelaar Epidemiol Rev 2011
Cost-effective Screening methods

**FOBT**
Chemical test (gFOBT)
Immunochemical test (FIT)
**Stool DNA tests**

**Endoscopy**
Sigmoidoscopy
Colonoscopy

**CTC**
Capsule endoscopy

Lansdorp-Vogelaar Epidemiol Rev 2011
Choice of methods of CRC screening

- Test features; invasiveness and diagnostic accuracy
- Uptake and adherence to repeated rounds
- Risks and burden
- Capacity
- Costs
- ........
Making screening effective depends also on;

- Solid organisation/ efficacy of the program
- Quality assurance on all levels
Screening methods

- Fecal tests
  - Chemical FOBT
  - Immunochemical FOBT

- Endoscopy
  - Sigmoidoscopie
  - Colonoscopie
Screening methods; FOBT

Guaiac FOBT (gFOBT)
2 fecal samples of 3 different stools

guaiac + H₂O₂ → Oxidation → Colour change

Catalysed by heme
Screening methods; FOBT

Immunochemical FOBT (FIT)
1 fecal sample

Fecal Hb + Latex anti-HbA  $\rightarrow$ Antigen-antibody complex
Screening methods; FOBT

Positive FOBT → Colonoscopy
Screening for colorectal cancer using the faecal occult blood test, Hemoccult (Review)

Hewitson P, Glasziou PP, Irwig L, Towler B, Watson E
CRC mortality; Hemoccult screening vs control

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Screening n/N</th>
<th>Control n/N</th>
<th>Peto Odds Ratio</th>
<th>Weight</th>
<th>Peto Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Randomised controlled trials</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Funen 2004</td>
<td>362/30967</td>
<td>431/30966</td>
<td></td>
<td>26.2%</td>
<td>0.84 [ 0.73, 0.96 ]</td>
</tr>
<tr>
<td>Goteborg 2005</td>
<td>252/34144</td>
<td>300/34164</td>
<td></td>
<td>18.3%</td>
<td>0.84 [ 0.71, 0.99 ]</td>
</tr>
<tr>
<td>Minnesota 1999</td>
<td>269/31157</td>
<td>177/15394</td>
<td></td>
<td>13.1%</td>
<td>0.74 [ 0.61, 0.90 ]</td>
</tr>
<tr>
<td>Nottingham 2002</td>
<td>593/76466</td>
<td>684/76384</td>
<td></td>
<td>42.4%</td>
<td>0.87 [ 0.77, 0.97 ]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>172734</strong></td>
<td><strong>156908</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.84 [ 0.78, 0.90 ]</strong></td>
</tr>
</tbody>
</table>

Total events: 1476 (Screening), 1592 (Control)
Heterogeneity: Chi² = 1.85, df = 3 (P = 0.60); I² = 0.0%
Test for overall effect: Z = 4.89 (P < 0.00001)
Test for subgroup differences: Not applicable

16% mortality reduction
gFOBT vs FIT

- FIT more likely to detect Hb from the lower GI tract
- FIT easier to use
- Higher uptake with FIT (UK; 59% → 66%)
  (NL; 50% → 62%)
- FIT enables quantitative measuring

- Uptake in subsequent rounds; gFOBT; between 39 - 44%
  FIT; between 56 – 72%

- Higher diagnostic yield of advanced neoplasia for FIT

Moss Gut 2016, Hol Gut 2010
Screening methods; endoscopy

**Sigmoidoscopy**
Anatomic extend: flexura hepatica
Preparation: phophate enema
Sedation: rare
Sigmoidoscopy

Positive test
1. Colorectal cancer
2. Advanced adenoma
3. ≥ 3 adenomas

Positive sigmoidoscopy $\rightarrow$ colonoscopy
CRC screening; proven effect on mortality

Flexible sigmoidoscopy versus faecal occult blood testing for colorectal cancer screening in asymptomatic individuals (Review)

Holme Ø, Bretthauer M, Fretheim A, Odgaard-Jensen J, Hoff G
CRC mortality; FS screening vs control

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Screening n/N</th>
<th>Control n/N</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Weight %</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexible sigmoidoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atkin 2010</td>
<td>221/57099</td>
<td>637/112939</td>
<td></td>
<td>47.3 %</td>
<td>0.69 [0.59, 0.80]</td>
</tr>
<tr>
<td>Hoff 2009</td>
<td>24/13653</td>
<td>99/41092</td>
<td></td>
<td>5.5 %</td>
<td>0.73 [0.47, 1.14]</td>
</tr>
<tr>
<td>Schoen 2012</td>
<td>252/77445</td>
<td>341/77455</td>
<td></td>
<td>37.7 %</td>
<td>0.74 [0.63, 0.87]</td>
</tr>
<tr>
<td>Segnan 2011 (1)</td>
<td>65/17136</td>
<td>83/17136</td>
<td></td>
<td>9.2 %</td>
<td>0.78 [0.57, 1.08]</td>
</tr>
<tr>
<td>Thiss-Evensen 1999</td>
<td>1/400</td>
<td>3/399</td>
<td></td>
<td>0.3 %</td>
<td>0.33 [0.03, 3.18]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>165733</td>
<td>249021</td>
<td></td>
<td>100.0 %</td>
<td>0.72 [0.65, 0.79]</td>
</tr>
</tbody>
</table>

2013
28% mortality reduction
18% incidence reduction
Colonoscopy
Anatomic extend: cecum
Preparation: 2-4L polyethylene glycol
Sedation: often
No data about the effect of colonoscopy screening yet

The expectation is that the incidence of CRC and the CRC related mortality will further decrease (around 70-90%)
Potential drawbacks of endoscopy screening

- Low uptake
  Netherlands; 22% uptake of colonoscopy screening
  32% uptake of sigmoidoscopy screening
- Complications
- Burden
- Capacity
- Costs

Stoop Lancet Oncology 2012, Hol Gut 2010
European Union???
Impact of CRC screening

It is unclear which modality has the largest effect on CRC–related morbidity and mortality in the population.

Kuipers EJ Nat Rev Clin Oncol 2013
The impact of a screening program is a function of **adherence** and the **efficacy** of that screening test.

Cost-effectiveness is **comparable** and other factors such as population preferences and colonosocpy resources might be more important in the decision for screening strategy.
Choice of methods of CRC screening

“The best test is the one that gets done, and done well”

S. Winawer
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Quality aspects

- Cancer registry
- IT system/Data warehouse
- Audit for the laboratories in case of FOBT
- Audit for the sigmoidoscopy/colonoscopy centers
- Quality assessment for all endoscopists
- Audit for the pathology centers
- Quality assessment throughout the program
Monitoring of a CRC screening program

- Monitor and evaluate process indicators
- Monitor and evaluate outcome indicators
- Monitor and evaluate quality indicators

- Indicators should be defined before the start