Secondary Prevention of Colorectal Cancer – CRC (Screening)

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Screening & Case Finding

- Screening
  - Testing apparently healthy volunteers from the general population
  - The testing (screen; check-up) is initiated by those who do the tests
  - There is an inherent promise that those who volunteer shall benefit through early detection and treatment of disease

- Case-finding or ‘opportunistic screening’
  - Testing of patients (who have sought health care) for disorders unrelated to their chief complaints
  - The encounter is initiated by the patient, who receives a more comprehensive health assessment
The **presumptive** identification of **unrecognised** disease by application of tests, examinations or other procedures which can be applied rapidly, to sort out apparently well persons who **probably have** a disease from those who **probably do not**

A screening test is **not** intended to be diagnostic. Persons with positive or suspicious findings must be referred for diagnosis and necessary treatment
When can screening be useful?

- When primary prevention – taking away the causes of the disease – is not possible or limited in its effect

- When the criteria of Wilson and Jungner are met
**CRC: primary prevention**

- Healthy life style:
  - Eating healthy and balanced and exercise

- Don’t smoke
The Criteria of Wilson & Jungner*

- The disease
  - Must be a serious health problem
  - There must be a pre-clinical phase which can be detected
  - The natural history of the disease must be known
- The test must be
  - Sensitive and specific
  - Simple and cheap
  - Safe and acceptable for the target group
  - Reliable
- Diagnosis and treatment
  - Adequate facilities for diagnosis and treatment must be in place
  - An effective, acceptable and safe treatment must be present
- Cost-effectiveness

*Wilson JMG, Jungner G. The principles and practice of screening for disease, Public Health Papers 34, WHO 1968
Estimated numbers of cancer cases and cancer deaths in 40 European countries (in thousands)

Wilson & Jungner: the disease

Incidence of CRC

Source: Cancer Stats World
What is CRC?

Where does CRC occur?

60% in this part of the large bowel
Wilson & Jungner: Pre-clinical phase: Slow progression from adenoma (polyp) to cancer

- Colorectal cancer often starts with polyps
CRC as ideal candidate for screening: Survival according to stage

I  II  III  IV

Limited to the wall of the intestine  90 %
Through the wall of the intestine  20-40 %
Positive glands  20-40 %
Metastases  5 %
The success of a screening programme is for a great deal determined by:

- The efficiency of the used screening test
- The willingness to participate in the target group
Wilson & Jungner: The test
CRC – ideal candidate for screening

- High incidence and mortality in the Western world
- Slow progression from adenoma to carcinoma (large ‘window of opportunity’ (10-15 years) in which removing of the polyp or early CRC is resulting into recovery)
- High patient survival in case of early detection and removing of the polyps or the cancer by colonoscopy or surgery
- CRC-screening (FOBT) can reduce mortality by about 15%*

*Commission of the European Communities. Report from the commission to the council, the European parliament, the European economic and social committee and the committee of the regions. Contract No. 2003/878/EC. Brussels; 2008
"Men and women from 50 years of age should participate in colorectal screening. This should be within programmes with built-in quality assurance procedures"

"Faecal occult blood testing is actually the only recommended screening strategy"
European guidelines for quality assurance in colorectal cancer screening and diagnosis

First Edition

European Commission
FOBT

- FOBT means Faecal Occult Blood Test
- Since adenomas and CRC are bleeding regularly, the blood, which can not be seen with the naked eye, can be found in the stool when analysed properly
- There is a guajac based FOBT (gFOBT - Hemoccult) and an immunochemical FOBT (iFOBT)
- Until now, only for the gFOBT, there are Randomised Controlled Trials (RCTs) indicating a cause-specific mortality reduction
- However, since the iFOBT is based on the same mechanism, it is very plausible that it is also leading to a cause-specific mortality reduction
Which test?

Hemoccult®
(gFOBT)

Peroxidase
3 days
Manual

iFOBT

Human Hb
1 day
Automatic
**gFOBT versus iFOBT**

Prospect. Trial: 10,673 patients 50 - 75 y. gFOBT + iFOBT  
21 CRC, 149 advanced adenomas

<table>
<thead>
<tr>
<th></th>
<th>Pos. rate</th>
<th>Rel. sens. CRC</th>
<th>Rel. sens. Advanced adenomas*</th>
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<tbody>
<tr>
<td><strong>iFOBT</strong></td>
<td></td>
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</tr>
<tr>
<td>20 ng/ml</td>
<td>6.9%</td>
<td>1.50 (1.11-2.03)</td>
<td>3.56 (2.66-4.77)</td>
</tr>
<tr>
<td>50 ng/ml</td>
<td>3.3%</td>
<td>1.36 (0.99-1.87)</td>
<td>2.08 (1.63-2.64)</td>
</tr>
<tr>
<td>75 ng/ml</td>
<td>2.4%</td>
<td>1.14 (0.83-1.58)</td>
<td>1.70 (1.33-2.16)</td>
</tr>
<tr>
<td><strong>gFOBT</strong></td>
<td>2.4%</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Adenomas > 1 cm, high-grade dysplasia

Results of a study comparing participation (gFOBT vs. iFOBT) *

**gFOBT**
N=10,301

Participation
N=4,836 (47%)

<table>
<thead>
<tr>
<th>Age Range</th>
<th>N (Female)</th>
<th>N (Male)</th>
</tr>
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<tbody>
<tr>
<td>50-55</td>
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<tr>
<td>70-75</td>
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</table>

**iFOBT**
N=10,322

Participation
N=6,157 (60%)

<table>
<thead>
<tr>
<th>Age Range</th>
<th>N (Female)</th>
<th>N (Male)</th>
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*van Rossum L *et al.* Gastroenterology 2008;136:82-90
The iFOBT

The iFOB-test

Detection of occult blood
Symptomatic

General population 50 - 75 years

Symptomatic

Screening

Random sample 20,623

Randomisation

gFOBT

103

CRC

144

Age 69, 56% male

CRC

1130

CRC

144

CRC

11

Age 65, 56% male

CRC

280

CRC

30

*van Rossum L et al. Gastroenterology 2008;136:82-90
Stage distribution

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptomatic</th>
<th>Screening</th>
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<tbody>
<tr>
<td>I</td>
<td>93%</td>
<td>50%</td>
</tr>
<tr>
<td>IIA</td>
<td>85%</td>
<td>40%</td>
</tr>
<tr>
<td>IIB</td>
<td>72%</td>
<td>30%</td>
</tr>
<tr>
<td>IIIA</td>
<td>83%</td>
<td>20%</td>
</tr>
<tr>
<td>IIIB</td>
<td>64%</td>
<td>10%</td>
</tr>
<tr>
<td>IIIC</td>
<td>44%</td>
<td>10%</td>
</tr>
<tr>
<td>IV</td>
<td>8%</td>
<td>10%</td>
</tr>
</tbody>
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*van Rossum L et al. Gastroenterology 2008;136:82-90*
Results

**Symptomatic**

- CRC: 144
- Survival: 60%
- No surgery: 3%

**Screening**

- 41
- Survival: 77%
- No surgery: 27%

- p<0.0001

*van Rossum L et al. Gastroenterology 2008;136:82-90*
# Test performance alternatives

<table>
<thead>
<tr>
<th></th>
<th>gFOBT</th>
<th>iFOBT</th>
<th>Sigmo</th>
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<tbody>
<tr>
<td></td>
<td>50</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>Positive (%)</td>
<td>2.5</td>
<td>8.4</td>
<td>6.4</td>
</tr>
<tr>
<td>Colonoscopy (%)</td>
<td>2.3</td>
<td>7.2</td>
<td>5.5</td>
</tr>
<tr>
<td>Detection rate CRC</td>
<td>0.24</td>
<td>0.48</td>
<td>0.45</td>
</tr>
<tr>
<td>Detection rate adenomas</td>
<td>1.3</td>
<td>3.3</td>
<td>2.8</td>
</tr>
<tr>
<td>NNT scope</td>
<td>1.8</td>
<td>2.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>20</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Participation</td>
<td>47</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

Cost effectiveness*

- Once iFOBT versus
  - Once gFOBT
    - € 113,290,731
    - 12,043 life years gained

- No screening
  - € 403,653,983
  - 20,963 life years gained

*van Rossum L et al. Gastroenterology 2008;136:82-90
Conclusion gFOBT vs. iFOBT

- **iFOBT** is superior to gFOBT
  - High participation
  - High five year survival
  - Cost-effective
  - Other circumstances, cut-off point!
Summary: Why iFOBT?

- User-friendly
- High participation rate compared to gFOBT
- Ease/objectivity of the analysis
- No diet restrictions
- Only 1 stool sample needed
- Selectivity for colorectal bleeding
- Quality control on the assessment of the test results
- Automatic measuring/assessment
- Specific cut-off values
- High specificity and sensitivity
- Cost-effective
How to use the iFOBT?

Take a sample of your stool with the test kit.

There is also a collection paper. Put this in the lavatory bowl to collect your stool. **Be careful! Try to avoid contact with water as much as possible.**

Don’t wait too long to obtain the stool sample.

How to use the iFOBT?

Turn the cap and open the bottle.
Attached at the cap, there is a stick with small grooves.
Brush the grooves along the surface of your stool so that a little bit of stool sticks to the grooves.

Put the stick back into the bottle.
Push until you hear a click.

Put the bottle in the green bag and close it.
The collection paper with the stool can be flushed; it is biodegradable.
Follow-up examination: Colonoscopy

- Bowel has to be empty and clean
- Preparation needed:
  - Drinking a lot
  - Laxatives
- Complications:
  - 1 on 1,000 perforation
  - 1 on 10,000 decease
The Flanders case

The participation rate of the Flemish breast cancer screening programme is 48% after 10 years. This is very low compared to neighbouring countries.

The participation rate of the pilot trial for CRC screening was 64% (test kit by surface mail).

This participation rate is high and is rather unexpected, since a stool taboo could not be ruled out in advance.
Survey: A stool taboo?*

- Did you find it easy to obtain a stool sample? → Over 90% answered ‘yes’

- Non-participants:
  - Recent stool sample or colonoscopy (34.9%)
  - Not eligible (9.1%)
  - No complaints, feeling healthy (24.6%)
  - No one in neighbourhood with cancer (8.7%)
  - Prefer private examination (8.1%)

Survey: A stool taboo?

- Non-participants:
  - Annoying to obtain a stool sample (4.6%)
  - Obtaining a stool sample not practical (1.3%)
  - Afraid of the result (2.5%)
Conclusion

- iFOBT is a user friendly stool sampling device
- An information leaflet (user guide) offers sufficient information to obtain a proper sample of the stool when sending the test kit by regular mail
- The argument of feeling healthy is still showing up as a reason for non-participation → important role GP
- Only a very small minority gives as a reason for their non-participation that taking a stool sample is annoying or unpractical
- The non-participation seems not to be due to a ‘stool taboo’