The Dutch bowel cancer screening program

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Volkskrant 26-05-2011

NRC 25-05-2011
Guiac FOBT RCTs: mortality-reduction 16%

![Graph showing the effects of screening with Hemoccult on mortality from CRC (fixed effects model).]

**Figure 1.** Effects of screening with Hemoccult on mortality from CRC (fixed effects model).

**Table:**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Screening n/N</th>
<th>Control n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minnesota 1999</td>
<td>269/31157</td>
<td>177/15394</td>
<td>14.34</td>
<td>0.75</td>
<td>[0.62, 0.91]</td>
</tr>
<tr>
<td>Nottingham 2002</td>
<td>593/76466</td>
<td>684/76384</td>
<td>41.42</td>
<td>0.87</td>
<td>[0.78, 0.97]</td>
</tr>
<tr>
<td>Funen 2004</td>
<td>362/30967</td>
<td>431/30966</td>
<td>26.09</td>
<td>0.84</td>
<td>[0.73, 0.96]</td>
</tr>
<tr>
<td>Goteborg 2005</td>
<td>252/34144</td>
<td>300/34164</td>
<td>18.15</td>
<td>0.84</td>
<td>[0.71, 0.99]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>172734</strong></td>
<td><strong>156908</strong></td>
<td></td>
<td><strong>100.00</strong></td>
<td><strong>0.84 [0.78, 0.90]</strong></td>
</tr>
<tr>
<td><strong>Total events:</strong></td>
<td><strong>1476 (Screening), 1592 (Control)</strong></td>
<td></td>
<td></td>
<td><strong>100.00</strong></td>
<td><strong>0.84 [0.78, 0.90]</strong></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 1.65, df = 3 (P = 0.65), P = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 4.89 (P &lt; 0.00008)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Hewitson, Am J Gastro 2008*
Fecal Immunochemical Test: FIT

- Quantitative test for human blood
- Automated
- Variable cut-off
First 2 RCTs FIT vs gFOBT (2006-2007)

- Tests sent to patients by postal mail
- FIT cut-off 10 μg Hb/g feces\(^1\) & FIT cut-off 20 μg Hb/g feces\(^2\)
- FIT: - Higher participation rates: 60% vs. 47%\(^1\), 61,5 vs 49,5%\(^2\)
  - Higher detection rate advanced neoplasia (AN)
  - More user-friendly
- -> FIT best option for FOBT-screening!

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\(^1\) van Rossum, Gastro 2008
\(^2\) Hol, Gut 2010
Other screening pilots in NL

- Sigmoidoscopy: participation 32%
- Colonoscopy vs CT-colonography: COCOS-study
  - Colonoscopy: participation 22%
  - CT-colonography: participation 33%
## COCOS: information on sens & spec FIT

<table>
<thead>
<tr>
<th>FIT 50:10 μgHb/g feces¹</th>
<th>Sens (CI)</th>
<th>Spec (CI)</th>
<th>PPV (CI)</th>
<th>NPV (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC</td>
<td>88 (47-99)</td>
<td>91 (89-92)</td>
<td>6 (3-12)</td>
<td>100 (99-100)</td>
</tr>
<tr>
<td>Advanced neoplasia</td>
<td>38 (29-47)</td>
<td>93 (92-95)</td>
<td>37 (29-46)</td>
<td>93 (92-95)</td>
</tr>
<tr>
<td>FIT 75:15 μgHb/g feces¹</td>
<td>Sens (CI)</td>
<td>Spec (CI)</td>
<td>PPV (CI)</td>
<td>NPV (CI)</td>
</tr>
<tr>
<td>CRC</td>
<td>75 (36-96)</td>
<td>93 (92-95)</td>
<td>7 (3-15)</td>
<td>100 (99-100)</td>
</tr>
<tr>
<td>Advanced neoplasia</td>
<td>33 (25-42)</td>
<td>96 (94-97)</td>
<td>44 (34-55)</td>
<td>93 (92-95)</td>
</tr>
<tr>
<td>FIT 100:20 μgHb/g feces¹</td>
<td>Sens (CI)</td>
<td>Spec (CI)</td>
<td>PPV (CI)</td>
<td>NPV (CI)</td>
</tr>
<tr>
<td>CRC</td>
<td>75 (36-96)</td>
<td>95 (93-96)</td>
<td>8 (3-18)</td>
<td>100 (99-100)</td>
</tr>
<tr>
<td>Advanced neoplasia</td>
<td>31 (23-40)</td>
<td>97 (96-98)</td>
<td>52 (40-64)</td>
<td>93 (91-94)</td>
</tr>
</tbody>
</table>

¹ De Wijkerslooth, Am J Gastro 2012
Biennial FIT-screening in both A’dam & R’dam

   RCT FIT vs gFOBT


3. April 2011-Feb 2012
   RCT 2 types FIT

   RCT 2 types FIT

Participation remained high in consecutive rounds: ≈ 60%
Increases participation 3.3%
Advice health council 2009

National BCSP for 55-75 yr improves health
Advice health council 2009

Tabel 5 geeft de relatieve waardering in plussen en minnen weer die de commissie toekent aan de verschillende screeningsmethoden. Op basis van eenvoud, acceptatie, testeigenschappen en veiligheid vindt de commissie iFOBT-screening de meest geëigende strategie voor bevolkingsonderzoek naar darmkanker.

<table>
<thead>
<tr>
<th></th>
<th>gFOBT</th>
<th>iFOBT&lt;sub&gt;75&lt;/sub&gt;</th>
<th>Sigmoidoscoopie</th>
<th>Coloscopie</th>
<th>CT-colografie</th>
<th>Moleculaire markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opkomst</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Bewijskracht</td>
<td>++</td>
<td>+</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Testprestaties</td>
<td>±</td>
<td>++</td>
<td>±±</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Weinig belastend</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>--</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td>Weinig riskant</td>
<td>++</td>
<td>++</td>
<td>±</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Kosteneffectiviteit</td>
<td>+</td>
<td>++</td>
<td>+?</td>
<td>+?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Minder beslag op curatieve zorg</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>?</td>
</tr>
</tbody>
</table>
Biennial FIT-program at 15 μg Hb/g feces¹:

- 2,2 million invitations per yr: 1,3 mln participants (60%)
- 6% positives
- 72.000 coloscopies per yr (baseline 190.000)
  - 6-7% CRC
  - 38% advanced adenomas
  - PPV 45%
- Cost-effective
- Can save 2400 CRC-deaths per year (>5000 before)
Long road to a national program in 2014

- International data on RCTs with guiac FOBT
- 2005 Dutch consensus meeting
- Dutch pilot RCTs guiac FOBT vs FIT
- Other screening-pilots in NL
- 2009 Positive advice health Council
- 2010-11 “Exploratory phase of national program”
- 2011 Positive Decision Minister of Health of NL
- 3 years of preparation of logistics & monitoring process
Nation-wide implementation in 2014

- Biennial FIT
- Invitational: by postal mail, including the test
- Population 55-75 yrs
- Different FIT (*FOB-Gold*), cut-off 15 μg Hb/g feces¹
Phased start: 5 year roll-out
Governance
Workflow & monitoring process
Results of first 6 months 2014

- High participation-rate (68%) -> many colonoscopies
- High positivity rate (12%) -> more colonoscopies
- 763 (7%) CRC & 3832 (33%) advanced adenomas
- 40% “true positives”: PPV slightly lower than expected (45%)
- Colonoscopy capacity -> waiting-lists..

NB results mainly in older age-group!
Action needed!

2 options:

• Increase cut-off: to increase specificity, but will also slightly lower sensitivity

• Adjust roll-out scheme: delay certain birth-cohorts
July 2014: Decision Minister of Health

- Increase cut-off of FIT to 47 μg Hb/g feces:
  - As modelled (iMGZ) will meet expectations

- Lots of lay press discussion on brand of FIT:
  - Studies needed to compare FIT-brands
Het bevolkingsonderzoek darmkanker loopt goed. In het eerste jaar namen zelfs meer mensen deel aan het bevolkingsonderzoek dan verwacht. Bijna 2.500 van hen is darmkanker gevonden. Door de onverwacht hoge deelname blijft de coloscopie capaciteit in sommige gebieden een aandachtspunt.
2014: Participation 71%!

<table>
<thead>
<tr>
<th>Geboortecohort</th>
<th>Man</th>
<th>Vrouw</th>
<th>Totaal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1938</td>
<td>35.614</td>
<td>39.625</td>
<td>75.239</td>
</tr>
<tr>
<td></td>
<td>65,1%</td>
<td>63,3%</td>
<td>64,1%</td>
</tr>
<tr>
<td>1939</td>
<td>37.459</td>
<td>41.636</td>
<td>79.095</td>
</tr>
<tr>
<td></td>
<td>67,5%</td>
<td>66,7%</td>
<td>67,1%</td>
</tr>
<tr>
<td>1947</td>
<td>69.367</td>
<td>72.315</td>
<td>141.682</td>
</tr>
<tr>
<td></td>
<td>73,3%</td>
<td>75,6%</td>
<td>74,5%</td>
</tr>
<tr>
<td>1949</td>
<td>57.237</td>
<td>59.761</td>
<td>116.998</td>
</tr>
<tr>
<td></td>
<td>72,1%</td>
<td>76,5%</td>
<td>74,3%</td>
</tr>
<tr>
<td>1951</td>
<td>44.235</td>
<td>45.185</td>
<td>89.420</td>
</tr>
<tr>
<td></td>
<td>71,7%</td>
<td>76,8%</td>
<td>74,2%</td>
</tr>
<tr>
<td>1954</td>
<td>12.825</td>
<td>13.797</td>
<td>26.622</td>
</tr>
<tr>
<td></td>
<td>66,1%</td>
<td>73,1%</td>
<td>69,5%</td>
</tr>
<tr>
<td><strong>Totaal</strong></td>
<td><strong>256.737</strong></td>
<td><strong>272.319</strong></td>
<td><strong>529.056</strong></td>
</tr>
<tr>
<td></td>
<td><strong>70,3%</strong></td>
<td><strong>72,3%</strong></td>
<td><strong>71,3%</strong></td>
</tr>
</tbody>
</table>
2014: Positivity-rate 12.2 \rightarrow 6.3\%
2014: Yield

PPV 41 -> 48%
2014: 2483 “extra” CRCs
Real-Time Monitoring of Results During First Year of Dutch Colorectal Cancer Screening Program and Optimization by Altering Fecal Immunochemical Test Cut-Off Levels

Esther Toes-Zoutendijk, Monique E. van Leeram, Evelien Dekker, Frank van Hees, Corine Penning, Iris Nagtegaal, Miriam P. van der Meulen, Anneke J. van Vuuren, Ernst J. Kuipers, Johannes M. G. Bonfrer, Katharina Biermann, Maarten G. J. Thomeer, Harriet van Veldhuizen, Sonja Kroep, Marjolein van Ballegooijen, Gerrit A. Meijer, Harry J. de Koning, Manon C. W. Spaander, and Iris Lansdorp-Vogelaar, on behalf of the Dutch National Colorectal Cancer Screening Working Group

CONCLUSIONS: Close monitoring of the implementation of the Dutch national CRC screening program allowed for instant adjustment of the FIT cut-off levels to optimize program performance.
2015

Participation remains high
6.4% FIT-positives: 42,405 extra colonoscopies
2015

FIT-positives: only 17.8% no findings..

Challenging colonoscopies!
Quality in screening program
What have we learned?

- Slow but well-studied & organized implementation of national BCSP
- Pilot-studies have provided basis & expectations
- Good start
  - Organisation, support
  - High participation rate, high detection rate
- However .. results ≠ all expectations
- ScreenIT & short-term monitoring has great value
What have we learned?

- Further optimization of program
  - Cut-off FIT? FIT-brand? Other (fecal) test?
  - Use of other risk-factors?
- Research within the national program should be facilitated
You should send this one for the screening program!