Issues and unknowns when comparing FIT tests

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Erasmus MC
Look-alikes?
The importance

• Should we be worried? Yes!
• Effects on population level
• Endoscopy resources
• Small differences = enormous effect
• Screening in the Netherlands¹
Issues when comparing FITs

• Design of the study
• Quantitative vs. qualitative
• Number of tests
• Cut-off
• Non-analyzable tests
Design of a study

• Population based vs. opportunistic
  • Participation levels
• Quantitative vs. qualitative
  • Rely on the reported cut-off by manufacturer
  • Limits research
• Follow-up by colonoscopy for all?
  • Enables sensitivity and specificity
  • Decreases participation rates
  • Limits effect of FIT to one round

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Two samples: one stool?

- Head-to-head comparison
- Makes comparing participation rates impossible
- Be aware of different collection methods
  - Two separate information folders
  - Risk of confusion
- Choosing a cut-off
  - One positive FIT
  - Two positive FITs
Issues with using a cut-off

- Fecal Hb concentration
- Wide range of units
- Proposal to standardize reporting units\(^1\)
  \[\mu g \text{ hemoglobin per g feces} = \frac{(\text{ng hemoglobin per mL} \times \text{mL buffer})}{(\text{mg feces collected})}\]
- Differences remained

\(^1\) Fraser et al., J Natl Cancer Inst 2012
Differences despite standardization

• 10 µg Hb/g feces
  – FOB-Gold 12.8% vs. OC-sensor 8.3% (P<0.01)\(^1\)
  – FOB-Gold 6.5% vs. OC-sensor 7.9% (P<0.01)\(^2\)

• 20 µg Hb/g feces
  – OC-sensor 3.8% vs. HM-Jack 3.9% (NS)

Limitations to the formula

- Based on manufactures information
- Changes in buffer
- Variations in consistency of stool
- Variations in human ‘stool collecting skills’
- Proposal of a new formula in µg Hb per ml feces

2. Fraser et al., J Natl Cancer Inst 2016
From analytical to clinical

• Strategies not based on mass of feces

• Strategies based on clinical outcomes
  • Positivity rate
  • Positive predictive value
Adjusting for positivity rate

• Results in equal number of colonoscopies
• Outcome positive predictive value
• Similar diagnostic yield
• Takes into account endoscopy resources
## Positivity rate vs. positive predictive value

<table>
<thead>
<tr>
<th>Cut-off 10 $\mu$g Hb</th>
<th>OC-sensor</th>
<th>FOB-Gold</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positivity rate</td>
<td>7.9%</td>
<td>6.5%</td>
<td>0.002</td>
</tr>
<tr>
<td>PPV*†</td>
<td>31%</td>
<td>32%</td>
<td>0.86</td>
</tr>
<tr>
<td>Detection rate†</td>
<td>2.3%</td>
<td>1.9%</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* PPV= positive predictive value  
† outcome is advanced neoplasia

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**Grobbee et al. Gut 2016**
Positivity rate vs. positive predictive value

- OC-sensor
- FOB-Gold

Grobbee et al. Gut 2016
Non-analyzable tests

- Reflection of usability
- Often not reported in articles
- Impact on costs
- Effect on participation
- Burden for screenees
Take home messages (I)

- Different FIT-brands do not perform the same
- Improvements by reporting μg Hb/g feces
- The need for protocols on (pre)analytical variation remains
- Standardize reporting clinical outcomes
Take home messages (II)

• Report positivity rate versus positive predictive value
• Report FITs that could not be analyzed

More research comparing FITs head-to-head in one population is highly warranted