Risk stratified intervals for FIT screening

Iris Lansdorp-Vogelaar
Disclosures

No conflicts to disclose
Balance between benefits and harms

• Benefits
  Lower mortality
  Lower morbidity

• Harms
  False-positives
  Complications
  Overdiagnosis
Balance between benefits and harms

- **Benefits**
  - Lower mortality
  - Lower morbidity

- **Harms**
  - False-positives
  - Complications
  - Overdiagnosis

Balance between benefits and harms
Personalization to further improve?

- Participants to CRC screening
  - 1,000

- 97.5%: No relevant findings at FIT
  - 975

- Relevant findings at repeat FIT
  - 24

- No relevant findings at repeat FIT
  - 950

- Interval cancers
  - 1
Possibilities for risk-stratification

- Individual risk factors: Sex, race and ethnicity, lifestyle, family history, SNPs
- Risk prediction models combining individual risk factors
- Screening history
Feasibility of risk-stratified screening

• Idea introduced >25 years ago by David Lieberman, yet still not implemented

• Potential reasons:
  • (Extensive) additional data collection required
  • Modest discriminatory accuracy of ~63%; Odds Ratio of max 14
  • Complex: participation, informed decision making, stigmatization and discrimination
Prior fecal Hb concentration as the solution?

- Advantages of prior fecal Hb concentration:
  - No need for additional data collection
  - Promising predictive performance, with anticipated improvements with data over multiple screening rounds
  - Linking screening recommendations to test result rather than individual characteristics more acceptable?
Evidence for predictive performance of fecal Hb concentration
Taiwan and Scotland: Single FIT

Chen, Lancet Oncology 2011

Digby, J Med Screen 2017
Netherlands and Italy: Consecutive FITs

Grobbee, Gastro 2017

Senore, Gut 2020

Cumulative fHb concentration (µg Hb/g feces)
Spain: Consecutive FITs

Odds ratios for advanced neoplasia or interval cancer after second screen

<table>
<thead>
<tr>
<th>FIT, 1st screen</th>
<th>FIT, 2nd screen</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-detectable</td>
<td>Non-detectable</td>
<td>1.00</td>
<td>4.02 (3.12–5.19)</td>
</tr>
<tr>
<td>Low negative FIT</td>
<td>Low negative FIT</td>
<td>4.00 (2.99–5.35)</td>
<td>10.79 (6.97–16.72)</td>
</tr>
<tr>
<td>High negative FIT</td>
<td>High negative FIT</td>
<td>6.99 (5.06–9.65)</td>
<td>19.64 (11.95–32.26)</td>
</tr>
</tbody>
</table>

Buron, Eur J Cancer 2019
Multiple rounds of FIT statistically and clinically superior

Single FIT

Consecutive FITs

Meester, WEO 2021
Improved performance with increasing screening rounds?

Multivariate joint models for individual dynamic prediction
Conclusion

• Prior fecal Hb concentration is a promising means for introducing risk-stratified colorectal cancer screening:
  • Good predictive performance, anticipated to further improve with increasing screening rounds
  • No need for additional data collection
• Time is now to perform studies to address other barriers to risk-stratified screening and start implementing it!
  • Initiatives in the Netherlands, Italy and Spain
Thank you

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