Risk model versus fecal immunochemical test for detecting advanced neoplasia: A within-group comparison in a randomized controlled trial

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Advantages:

- Reasonable sensitivity for CRC (74%) at high specificity (96%)
- Relatively cheap ($22)
- Easy to perform → high uptake
- Reduces demand on colonoscopy services

Disadvantages:

- Suboptimal sensitivity for advanced adenomas (20-30%)
- Suboptimal positive predictive value
- One-size-fits-all approach
1. One-size-fits-all → Personalized screening

2. Potentially increases yield of advanced neoplasia (AN; CRC + advanced adenomas)
Background
Design:
Prospective randomized controlled trial comparing a FIT-based risk model with FIT only

Primary outcome:
Yield of advanced neoplasia per 1,000 invitees

Secondary outcome:
Participation rate
Randomized Controlled Trial

Risk Model Group

Informed consent

Risk ≥ 0.10 and/or FIT ≥ 15 µg Hb/g

FIT Group

Informed consent

FIT ≥ 15 µg Hb/g

23,000 selected second-round invitees
Methods

Randomized Controlled Trial

Risk Model Group

- 23,000 selected second-round invitees

- Informed consent

- Risk ≥ 0.10 and/or FIT ≥ 15 µg Hb/g

FIT Group

- Informed consent

- FIT ≥ 15 µg Hb/g
Risk model:

\[
\ln(\text{odds AN}) = -4.96 + 0.34 \times \sqrt{\text{FIT}} - 0.01 \times \text{FIT} + 0.02 \times \text{age} + 0.07 \times \text{sex} + 0.92 \times \text{smoking status} + 0.37 \times \text{family history of CRC}
\]
Results

Risk Model Group

22748 invitees

11364 invitees

3397 consented

3113 returned questionnaire and FIT (27.4%)

186 tested positive (6.0%)

164 underwent colonoscopy (88%)

42 diagnosed with AN

FIT Group

11348 invitees

3342 consented

3061 returned FIT (27.0%)

161 tested positive (5.3%)

146 underwent colonoscopy (91%)

39 diagnosed with AN

$p = 0.49$
Results

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FIT Group

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3061 returned FIT (27.0%)

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39 diagnosed with AN

$p = 0.49$
Results

Risk Model Group

- 22748 invitees
- 11364 invitees
- 3397 consented
- 3113 returned questionnaire and FIT (27.4%)
- 186 tested positive (6.0%)
- 164 underwent colonoscopy (88%)
- 42 diagnosed with AN

FIT Group

- 11348 invitees
- 3342 consented
- 3061 returned FIT (27.0%)
- 161 tested positive (5.3%)
- 146 underwent colonoscopy (91%)
- 39 diagnosed with AN

$p = 0.49$
Results

Risk Model Group

22748 invitees

11364 invitees

3397 consented

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FIT Group

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p = 0.49
However, this analysis was performed at a relatively low cut-off (15 µg Hb/g feces).

Is the yield of AN of the risk model better than FIT at higher cut-offs?

→ Compare risk model and FIT at several positivity rates within the risk-model group.
Results: risk-model versus FIT at higher cut-offs

Positive predictive values at multiple possible cut-offs with positivity rates between 1-4.9%. Risk model (blue) vs FIT (red)

Risk model not better than FIT, even at higher cut-offs
Results: FIT concentration of a previous negative screening round

- FIT concentration of a previous negative result may be predictive of detection of AN at next round(s)

- May be used to improve future risk models

- Is the FIT concentration of a previous negative FIT associated with detection of AN at colonoscopy in this trial?
FIT concentration of previous negative screening round in those tested positive in the current round with no AN (green) and AN (yellow) at colonoscopy

Relative number of individuals with previous FIT >0 µg Hb/g feces

AN: 27/75 (33%)
No AN: 43/213 (20%)

\( p = 0.02 \)

Previous FIT = risk factor
Yield of advanced neoplasia of this risk model was not better than FIT, even at higher cut-offs compared to the original trial – despite promising results in development study.

Adding a questionnaire did not lead to a decrease in participation.

FIT concentration of a previous negative screening round is associated with detection of AN in those tested positive in a following screening round
1. Low participation compared to national CRC screening program
2. Fewer smokers compared to general population (10% versus 14%)
3. Limited variability age of study population

- Effect of risk model may be underestimated in the current trial.
- FITs of earlier screening round(s) should be considered in future risk models.
- More risk models should be evaluated in a screening setting.
WEO
World Endoscopy Organization