WEO

The voice of world endoscopy

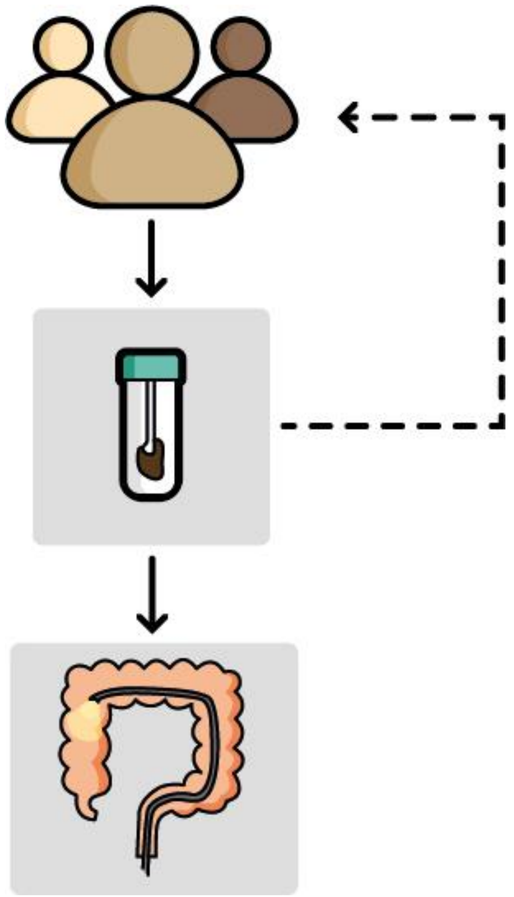
Risk model versus fecal immunochemical test for detecting advanced neoplasia:

A within-group comparison in a randomized controlled trial

Tim Kortlever, Manon van der Vlugt, Floor Duijkers, Ad Masclee, Roderik Kraaijenhagen, Manon Spaander, Iris Lansdorp-Vogelaar, Patrick Bossuyt, Evelien Dekker.

Advantages:

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

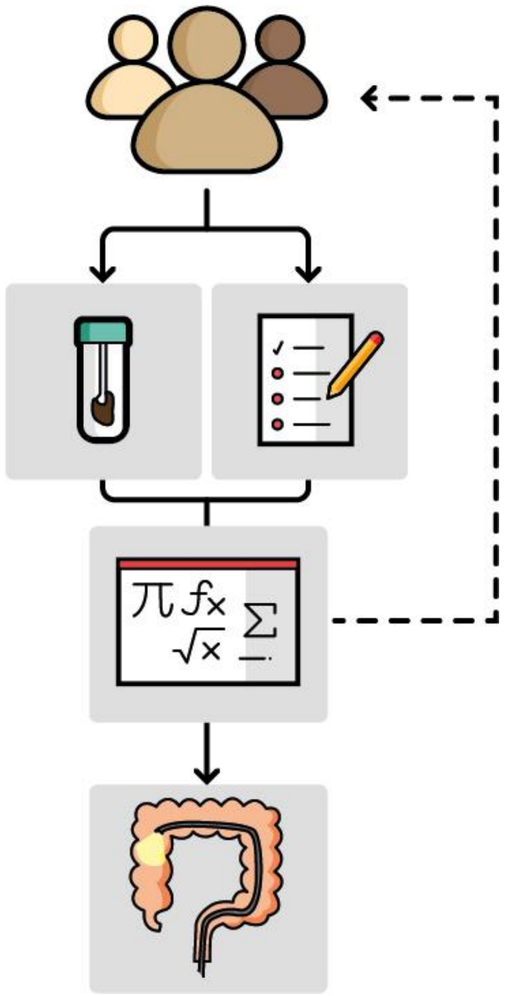


Disadvantages:

- Suboptimal sensitivity for advanced adenomas (20-30%)
- Suboptimal positive predictive value
- One-size-fits-all approach

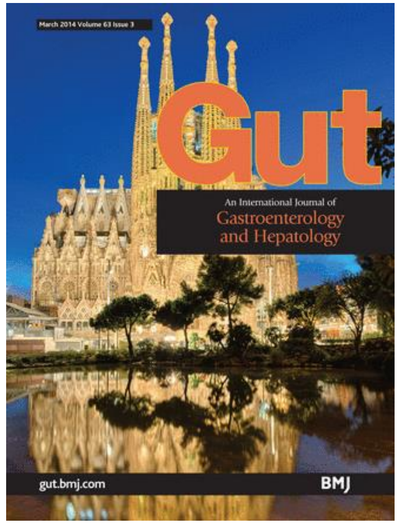
Imperiale et al, Ann Intern Med. DOI: 10.7326/M18-2390

National Monitoring of the CRC screening programme in the Netherlands 2019; https://www.rivm.nl/en/media/169811



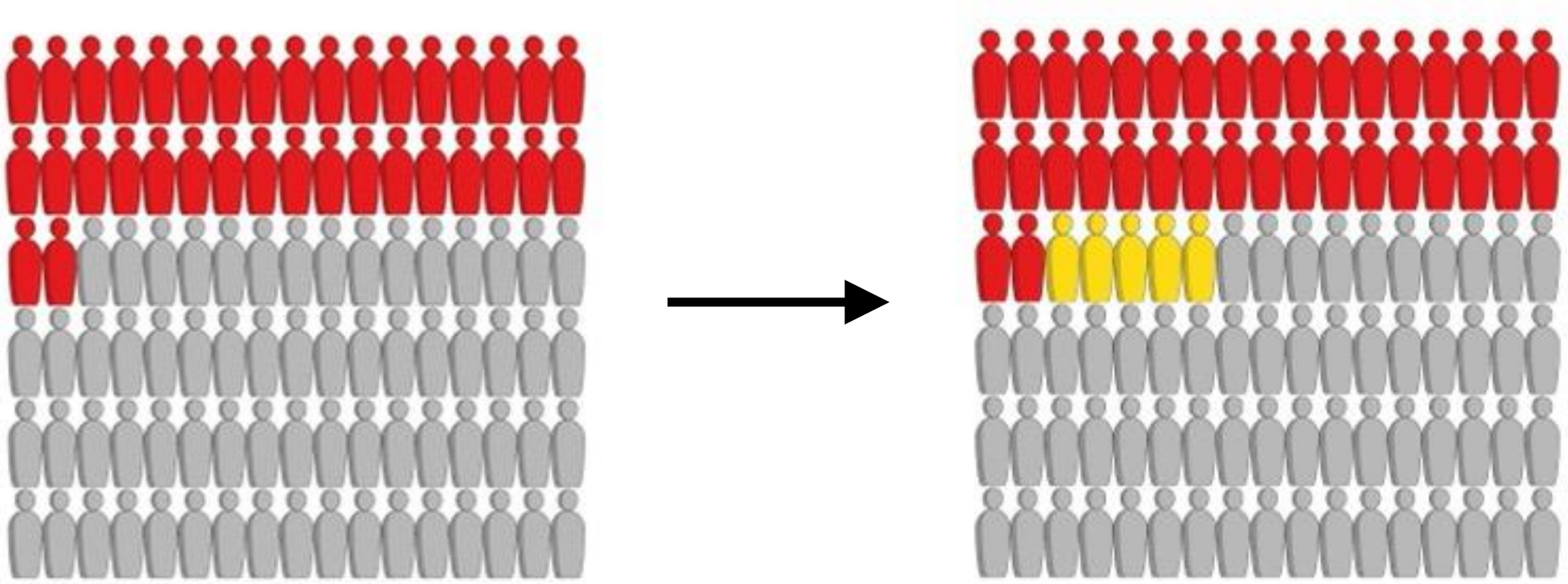
1. One-size-fits-all → Personalized screening

2. Potentially increases yield of advanced neoplasia (AN; CRC + advanced adenomas)



Stegeman et al, Gut. DOI: 10.1136/gutjnl-2013-305013

Background



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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

Stegeman et al, Gut. DOI: 10.1136/gutjnl-2013-305013

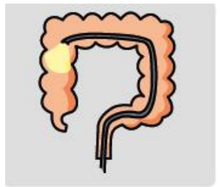
Randomized Controlled Trial

23,000 selected second-round invitees

Risk Model Group

Informed consent

Risk ≥ 0.10 and/or FIT ≥ 15 µg Hb/g



FIT Group

Informed consent

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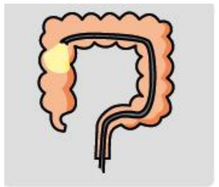

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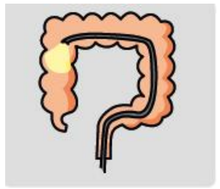

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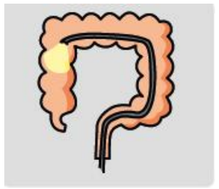
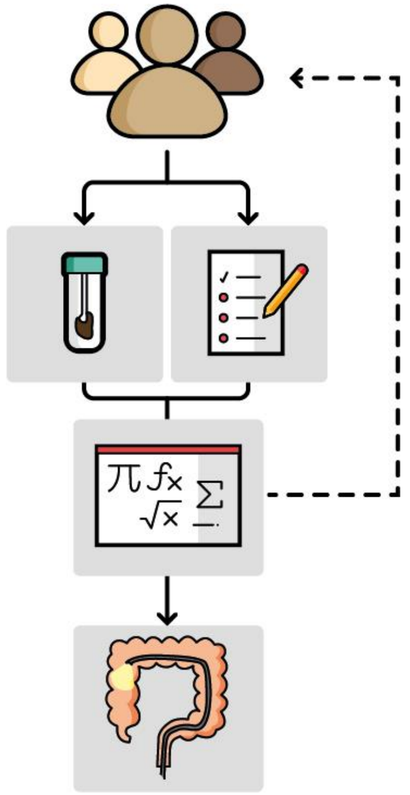


Risk model:

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



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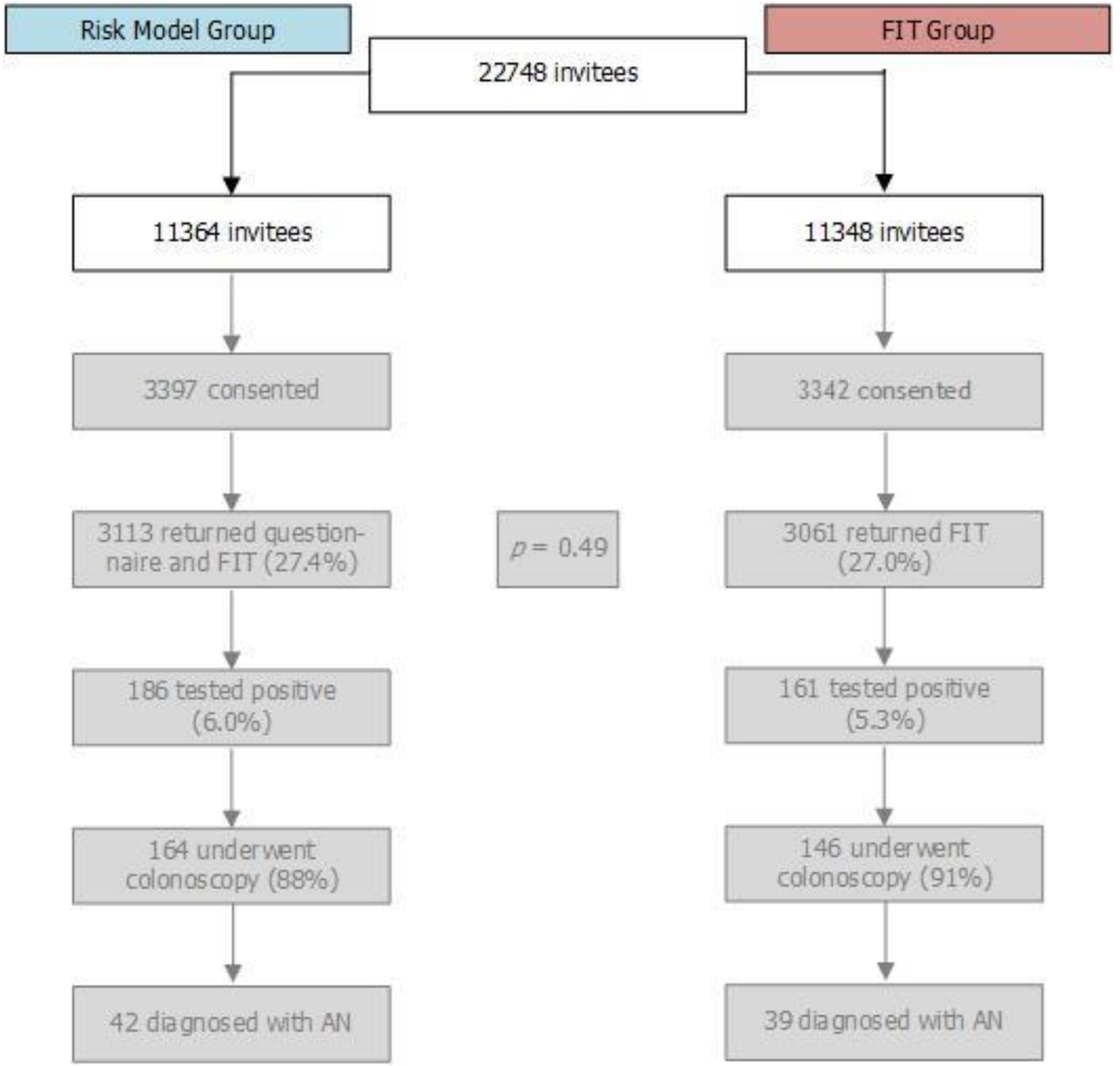
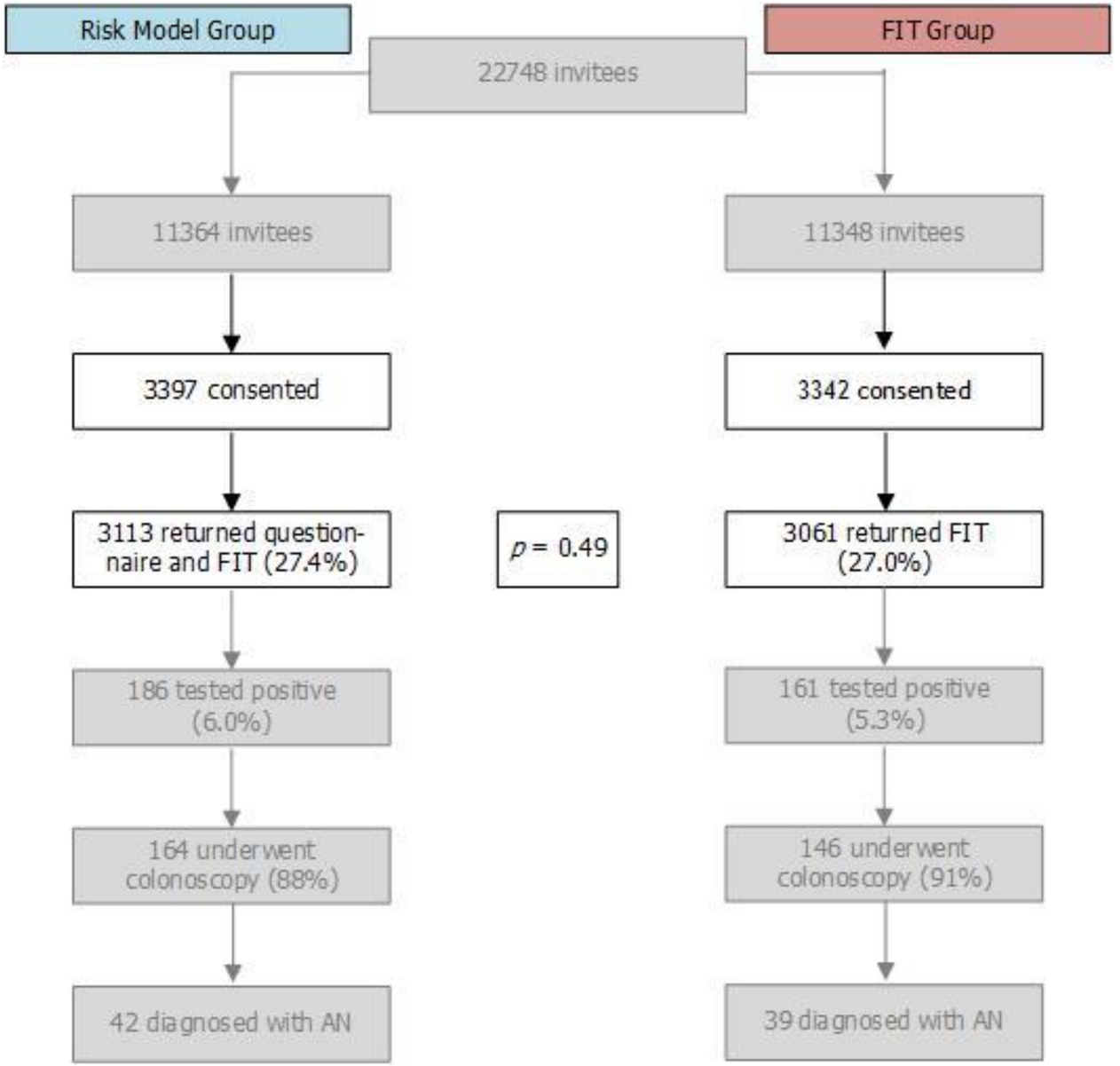

Risk Model Group
22748 invitees
FIT Group
11364 invitees
11348 invitees
3397 consented
3342 consented
3113 returned question-naire and FIT (27.4%)
p = 0.49
3061 returned FIT (27.0%)
186 tested positive (6.0%)
161 tested positive (5.3%)
164 underwent colonoscopy (88%)
146 underwent colonoscopy (91%)
42 diagnosed with AN
39 diagnosed with AN

Results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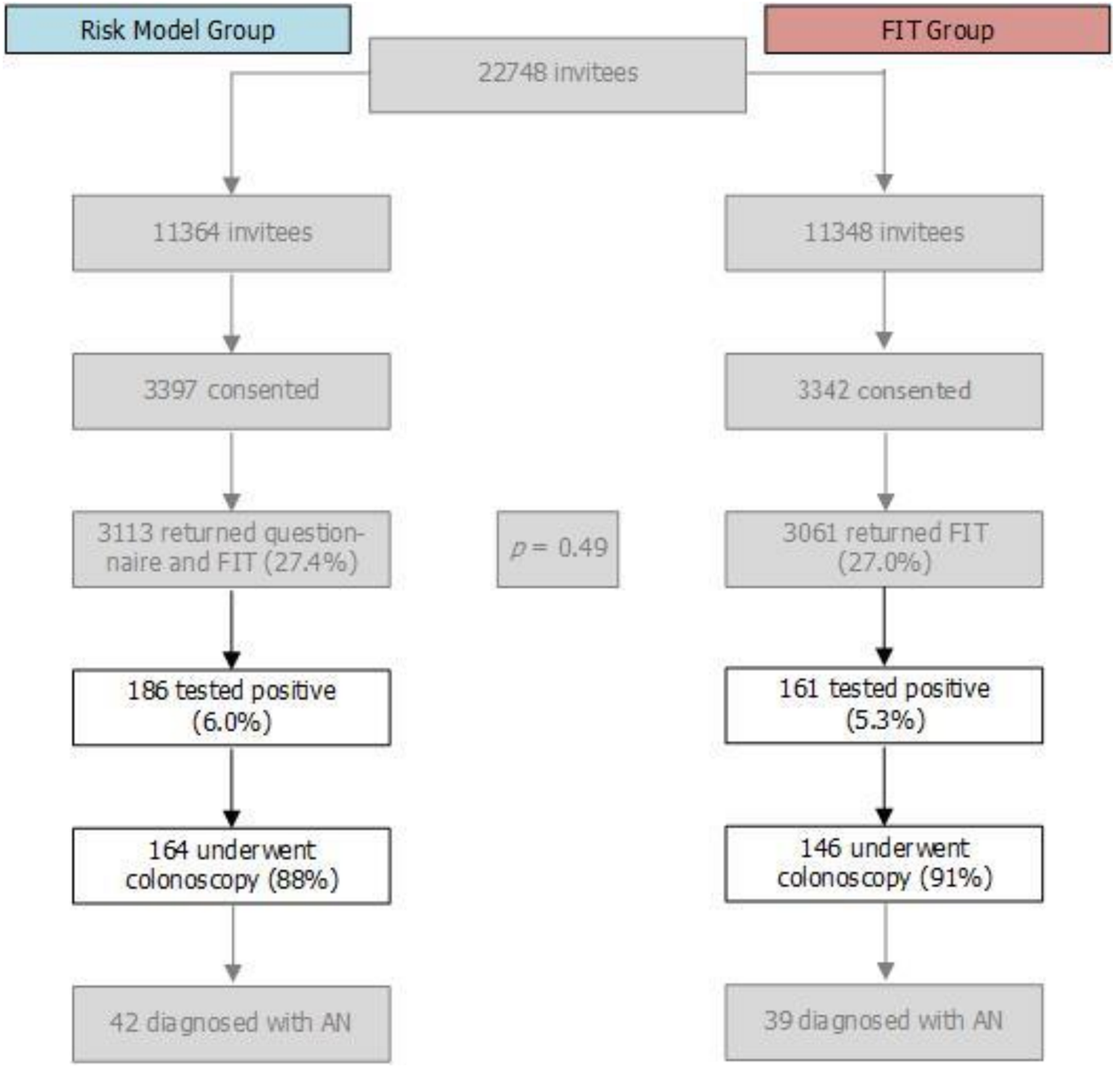
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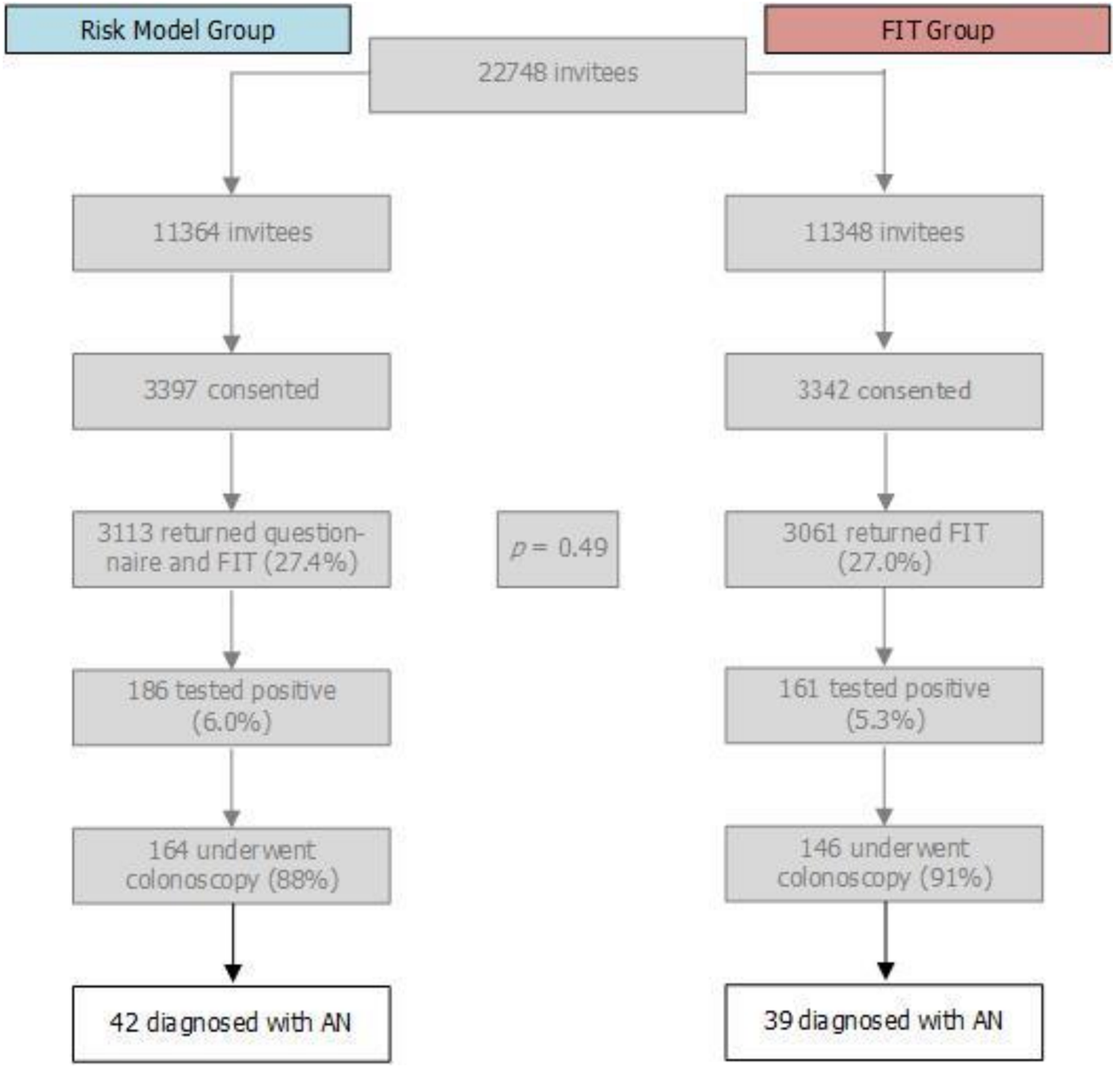
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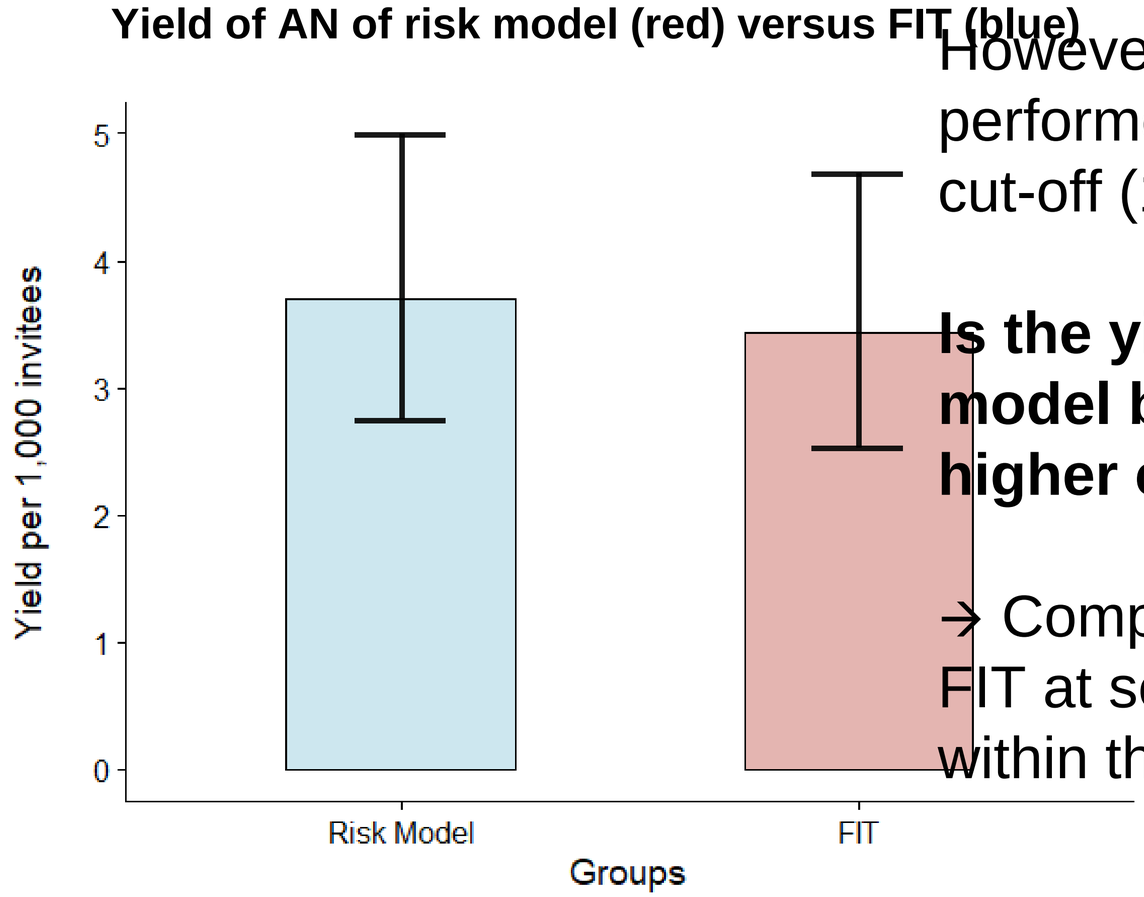


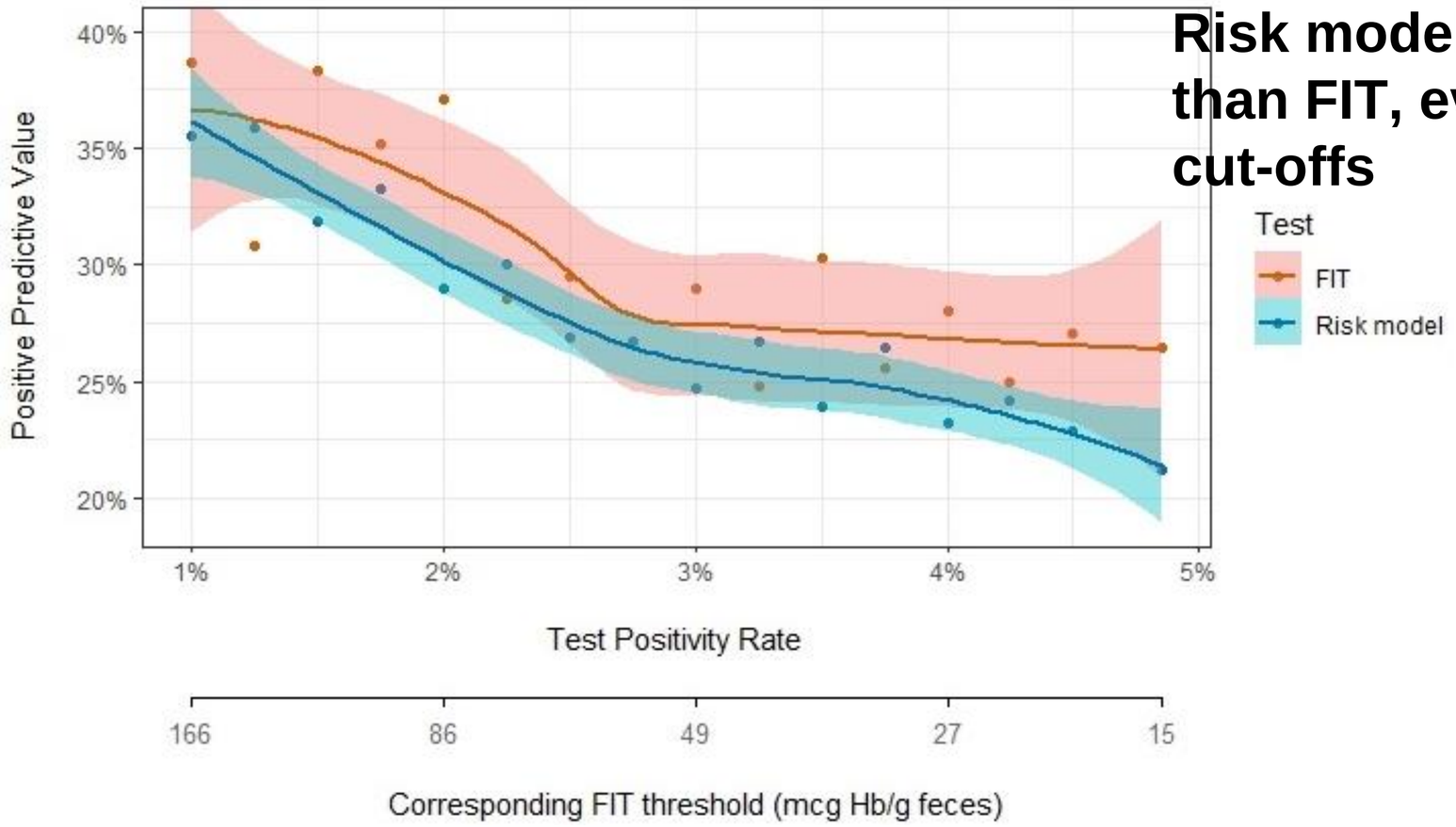
However, this analysis was performed at a relatively low cut-off (15 µg Hb/g feces)

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

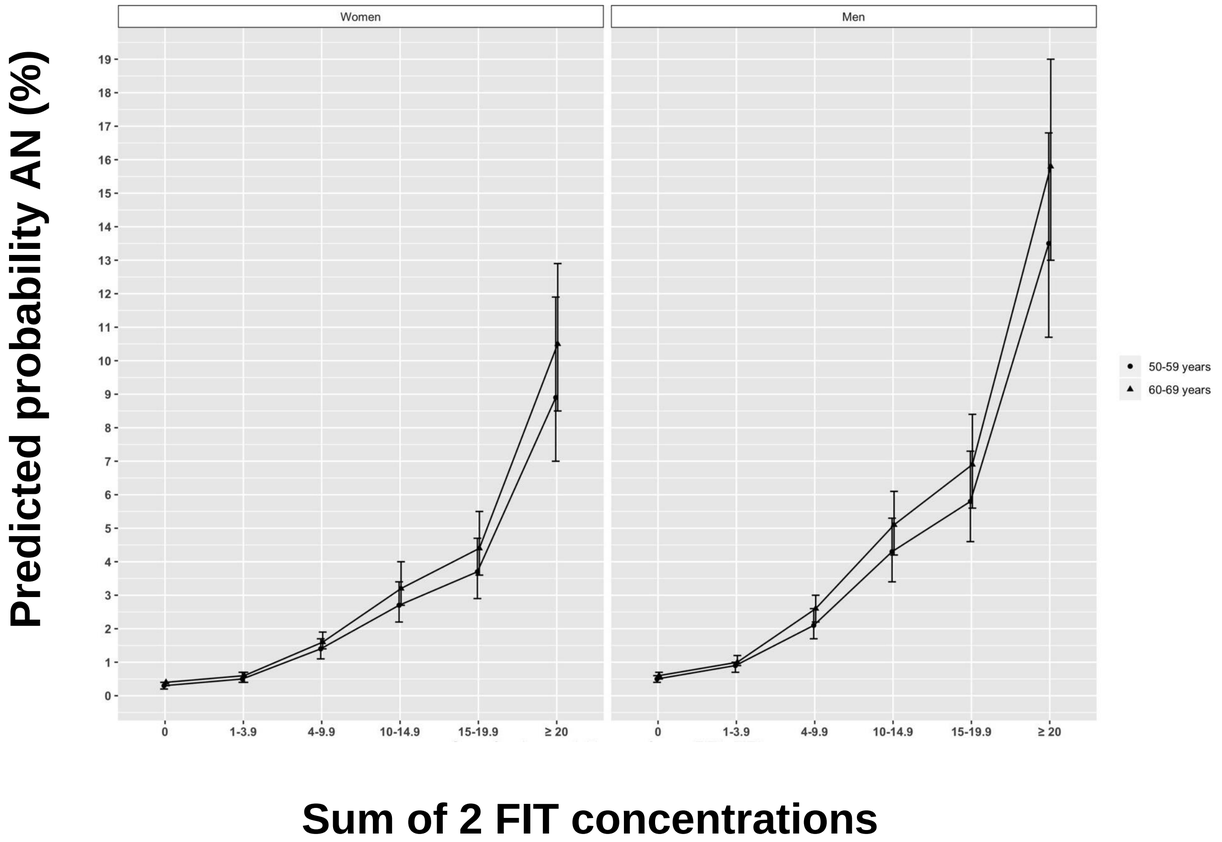
Results: risk-model versus FIT at higher cut-offs

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

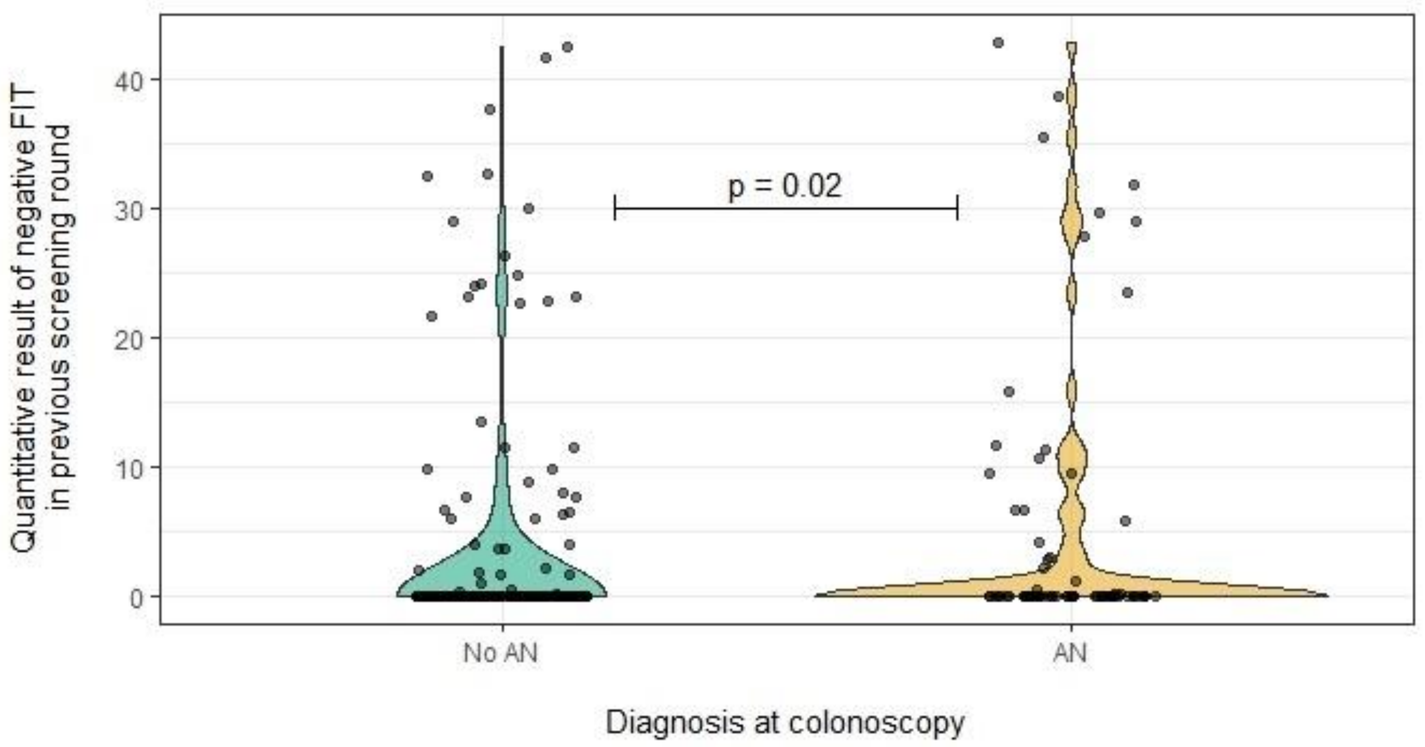
Is the FIT concentration of a previous negative FIT associated with detection of AN at colonoscopy in this trial?

Senore et al. Gut 2020. DOI: 10.1136/gutjnl-2018-318198

Meester et al. Gut 2022. DOI:10.1136/gutjnl-2022-327188

Results: FIT concentration of negative previous round

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

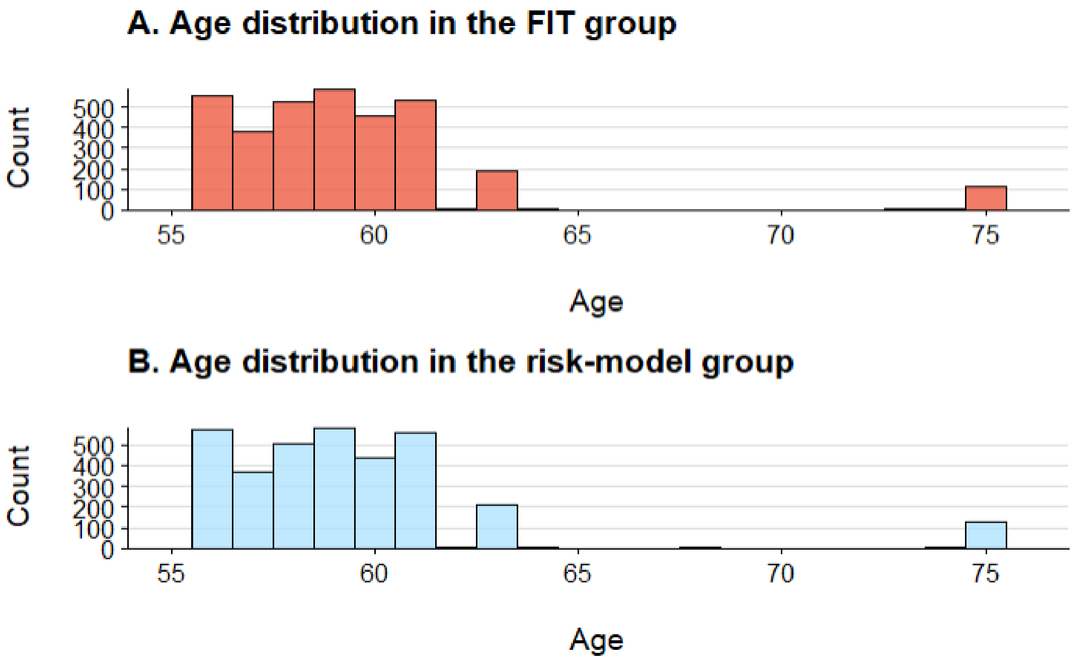
Previous FIT = risk factor

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