Incorporating demographic information

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Disclosures

No conflicts to disclose
Take-home Message

Using different FIT positivity thresholds, based on demographic information would reduce differences in FIT performance and restore equity and efficiency in CRC screening.
Demographic information is known: Age and Sex
Age and Sex in FIT screening: Illustration

- population-based invitational screening pilot
- 1,121 asymptomatic screen-naïve participants (50-75 years)
  - Screening Colonoscopy
  - One sample FIT (OC-Sensor)
- Blinded evaluation
- Advanced Neoplasia: Carcinoma & Advanced Adenoma
  (≥ 10 mm, villous histology (≥ 25 % villous), high-grade dysplasia)

Netherlands Trial Register 1829
Participants: Age and Sex

The bar chart shows the number of participants in different age groups (50, 55, 60, 65, 70, 75) divided into females (light blue) and males (dark green). The number of participants increases with age, particularly for females, with a peak at age 60. Males also show an increase with age, but the difference is not as pronounced as that of females. The number of participants drops significantly at age 75.
Participants with Advanced Neoplasia by Sex

Proportion of Participants

Females

Males
Participants with Advanced Neoplasia by Age
FIT: Single Positivity Threshold

FIT

0 5 10 15 20 25 30 35 40 µg / g
FIT: Single Positivity Threshold

μg / g
FIT: Single Positivity Threshold
FIT: Single Positivity Threshold

FIT

μg / g

0  5  10  15  20  25  30  35  40
FIT positivity by Sex

Threshold 10 μg / g

Proportion of Participants

Females

Males
FIT positivity by Age

Threshold 10 μg / g

Proportion of Participants

0 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08 0.09 0.1 0.11 0.12 0.13 0.14 0.15 0.16 0.17 0.18 0.19

50 55 60 65 70 75
Distribution of FIT results
Participants with advanced neoplasia: Q3 by Sex

FIT (μg / g)

Females

Males
Participants without advanced neoplasia: Q3

FIT (ng/ml)

- Females: 0.4 ng/ml
- Males: 1.2 ng/ml
Participants without advanced neoplasia: Q3
FIT: Sensitivity & Specificity by Sex

- **AN Sensitivity**
- **AN Specificity**

Threshold 10 μg / g
FIT: Sensitivity & Specificity by Age

Threshold 10 μg / g

50 55 60 65 70 75
FIT: Positive Predictive Value by Sex

Positive Predictive Value

Threshold 10 μg / g
FIT: Positive Predictive Value by Age

Positive Predictive Value

Threshold 10 μg / g

NNS: 1.75 (4/7)

NNS: 3.5 (2/7)
FIT-screening: Yield by Sex

- Females: 0.02
- Males: 0.04

Threshold: 10 μg / g
FIT-screening: Yield by Age

Proportion of Participants

Threshold 10 μg / g

NNT: 60

NNT: 10
We observe differences by Age and Sex

• ... in risk of having advanced neoplasia
• ... in distribution of FIT results

• ... in FIT positivity (proportion positives)
• ... in FIT sensitivity and specificity
• ... in FIT positive predictive value (positive colonoscopies)
• ... in yield of FIT-based screening (adv neoplasia detected)
• ... in total number of life years gained by FIT-based screening
Equity? Efficiency?

- ... in risk of having advanced neoplasia
- ... in distribution of FIT results

- ... in FIT positivity (proportion positives)
- ... in FIT sensitivity and specificity
- ... in FIT positive predictive value (positive colonoscopies)
- ... in yield of FIT-based screening (adv neoplasia detected)
- ... in total number of life years gained by FIT-based screening
We can change FIT performance…

• ... in risk of having advanced neoplasia
• ... in distribution of FIT results

• ... in FIT positivity (proportion positives)
• ... in FIT sensitivity and specificity
• ... in FIT positive predictive value (positive colonoscopies)
• ... in yield of FIT-based screening (adv neoplasia detected)
• ... in total number of life years gained by FIT-based screening
FIT: Single Positivity Threshold
FIT: Different Positivity Thresholds

- Females: 7 out of 25
- Males: 8 out of 25
FIT: Equity in Positive Predictive Value
Example: Equity in Positive Predictive Value

Combinations of Age and FIT threshold to yield similar positive predictive values
Which differences should be reduced first?

- ... in risk of having advanced neoplasia
- ... in distribution of FIT results
- ... in FIT positivity (proportion positives)
- ... in FIT sensitivity and specificity
- ... in FIT positive predictive value (positive colonoscopies)
- ... in yield of FIT-based screening (adv neoplasia detected)
- ... in total number of life years gained by FIT-based screening
Which differences should be reduced first?

[Zoom Poll]
Equity in Positive Predictive Value

- Ethics: comparable Benefit / Burden balance when undergoing colonoscopy
- Efficiency: comparable number needed to scope (colonoscopy resources)
- Can be objectified (e.g. logistic regression modeling)
Challenges

• Have to consider differential participation
• Have to consider differential colonoscopy acceptation
• Have to consider multiple rounds
• More complex = More errors?
• Acceptability?
Key Messages:

• Most FIT-based screening programs use a single FIT positivity threshold.

• But CRC risk and FIT results vary with sex and age.

• This leads to differences by sex and age in FIT performance and screening yield.

• Using different FIT positivity thresholds, based on sex and age, could reduce differences and restore equity and efficiency.
ONE SIZE DOES NOT FIT ALL

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