Using prior Hb concentration for risk-stratified intervals of FIT screening
Rationale for and design of a randomized controlled trial in the Netherlands

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Disclosures

No conflicts to disclose
Dutch CRC screening program

• First 4 years of colorectal cancer (CRC) screening in the Netherlands:
  • 14,000 CRCs
  • 76,000 advanced adenomas (AA)
  • 12-18% of CRCs are missed by the program
Balance between benefits and harms

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

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

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Personalization to further improve?

• Risk prediction model based on genetic predisposition, lifestyle, family history and sex:
  • Complex, requiring extensive additional data
  • Discriminatory accuracy of ~63%; Odds Ratio of max 14.
• Previous presentation: quantitative FIT-result much better predictor
Dutch program in numbers

- **2.200.000**
  - Participants CRC screening program

- **2.068.000**
  - 95.5%: Negative FIT <47 ug/g feces

- **1.500.000**
  - 75% participants ~0 ug/g feces

- **1.470.000**
  - 98% no findings at repeat screening

- **200.000**
  - 10%: Participants just below cutoff (15-47 ug/g feces)

- **1000 iCRCs**
  - 50% of interval cancers found in individuals just below cutoff
Interval CRCs to be prevented?

Screening population

50% of interval CRC

- 10% Non-detectable Hb
- 2.6-15 µg Hb/g feces
- 15-47 µg Hb/g feces

- 67% 1st year
- 33.3% 2nd year

- Screening 10% of individuals earlier
- CRCs prevented

200,000

33.3%
Screening burden reduced

- Prolonging interval of individuals with non-detectable Hb → reduction of 40% of burden of screening on population level

- **Low-risk** (non-detectable Hb): interval of 3 years
- **Medium-risk** (2.6-15 µg Hb/g feces): interval of 2 years
- **High-risk** (15-47 µg Hb/g feces): interval of 1 year
Aim

• To evaluate whether personalized screening based on fecal Hb is feasible and acceptable and leads to a superior balance in benefits versus harms
Randomized controlled trial

Randomized trial to evaluate feasibility, acceptability and superiority of risk-based screening, embedded in existing screening program

20,000 individuals with ≥1 screening round

10,000 usual care: interval of 2 years;

10,000 intervention: interval of
- 3 years: <2.6µg
- 2 years: 2.6-15µg
- 1 year: 15-47µg

Comparison between arms of:
- Yield per screen
- Participation
Outcomes

- **Primary:**
  - Detection rate (AA and CRC) per screened individual and colonoscopy
  - Referral rate for colonoscopy

- **Secondary:**
  - Acceptability of and adherence to personalized screening - participation rate
  - Cost-effectiveness using the MISCAN-Colon simulation model
Implementation within the program
Implementation within the program

• Invite >50,000 individuals to participate in the study; more if needed to reach 20,000 inclusions
• Obtain informed consent of 20,000 individuals
• Randomize 10,000 each to either control or intervention group, and invite according to randomization
• After participation, all participants return to current screening interval (2 years)
• Close collaboration with all stakeholders involved
Focus groups

• **Set-up of focus groups**
  • Before start of the study
  • In screenees with interval of 1 year
  • In screenees with interval of 3 years

• **To study:**
  • Information needs of participants
  • Thoughts and feelings when assigned 1- or 3-year interval
### Time line

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- ✔️ indicates tasks that are scheduled for completion.
Thank you
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