Implementing a CRC screening program using sex-specific positivity cut-off: the Finnish experience

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Outline

- Colorectal cancer screening in Finland – change from FOBT to FIT test
- Three-year pilot with gender-specific cut-offs

✓ **National program with similar cut-offs since 2022**

History of CRC screening in Finland

- Randomised, gradually implemented program with a guaiac fecal occult blood test (gFOBT), 2004-2016
  - 40 % of municipalities in 2014
- Men and women aged 60-69 years; test package mailed home biennially
- Effect on CRC mortality evaluated in 2015; no difference between invitees and non-invitees (Pitkäniemi et. Al. 2015)
  - Non-significant reduction in men
  - Non-significant increase in women

✓ **Screening was suspended in 2016**

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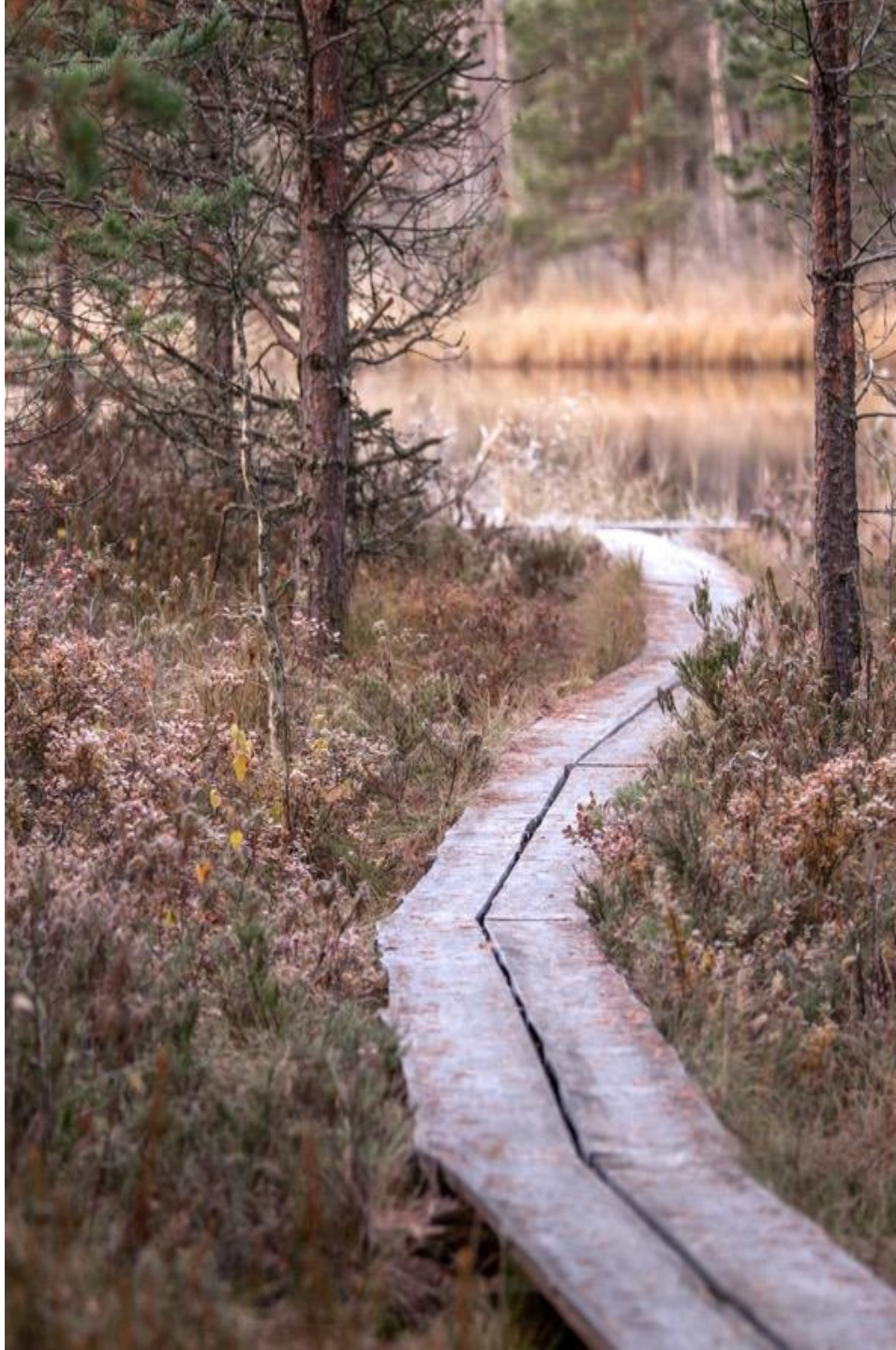

Screening with a faecal immunochemical test (FIT)

✓ **FIT had replaced gFOBT as a primary test to detect blood from stool**

- Higher yield of colorectal neoplasms*
- Higher acceptance (easy to use, only one test needed)

- Non-fixed haemoglobin concentration cut-off
- Specificity to detect human haemoglobin*

- Higher sensitivity, positive predictive value and effectiveness in men than in women*

✓ Sex-specific cut-offs to account for the plausible variation in carcinogenic pathways and the difference in CRC incidence levels, and to reach comparable relative reduction in CRC mortality

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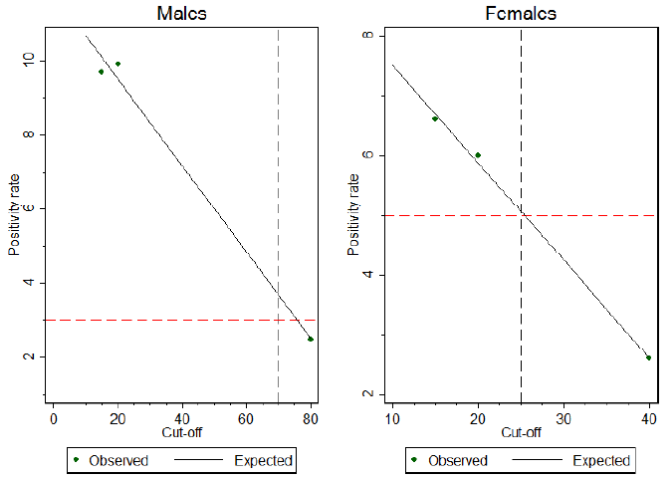
*Brenner et. al. 2010, 2013; Shaukat et. al. 2013, 2018; Stegeman et. al. 2013; Young et. al. 2015

Pilot study with sex-specific cutt-offs (n=30 000, 60-66 yrs)

- **2019***
- **25 µg/g in women, 70 µg/g in men**

✓ Compared to previous gFOBT screening, performance improved slightly in men and clearly in women

  - Participation 80 %
  - Positivity rates low (2.4 %, 2.8 %)
  - Detection rates of CRC and AA moderate



Colonoscopy resources and previous results:
- Positivity rates 3% and 5%

FIT cut-offs, positivity rates:
- Sweden, Denmark, Norway

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*Sarkeala et. al. 2021

Pilot study with sex-specific cutt-offs (n=30 000, 60-66 yrs)

- **2020***
- **15 µg/g in women, 50 µg/g in men**

✓Compared to 2019:

- Participation 79 %
- Positivity rates increased (RR 1.50; 1.29)
- Detection rates of advanced tumours improved (RR 1.57; 1.25)
- No changes in PPV of test or PPV of colonoscopy

- Still suboptimal results in men since PPVs did not change even though detection rates improved and were clearly higher than those of women

*Kuoppa et. al. 2022 (in Finnish)

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Cost-effectiveness analysis in 2020 – a window for a national program

- **MISCAN-modelling with Erasmus University** using pilot data (2019), and registry data on CRC incidence, CRC mortality, and population*
- Restrictions due to colonoscopy capacity (5%)

- **Same target age and screening interval by sex**
  - Target age, interval and cut-off refined
    - 56-74, 2 years, 25 µg/g
  - CRC mortality will reduce by 30-50%
    - 150 CRCs prevented annually
    - 170 deaths due to CRC prevented annually
  - Price of a life-year gained < 10 000 euros

ABSTRACT

A faecal immunochemical test (FIT) screening pilot was introduced in Finland in 2019 with sex-specific screening strategies. This study aims to model cost-effectiveness of sex-specific strategies for the whole population, and to assess whether the current strategies are optimal.

We developed separate MISCAN-Colon models, including different FIT performances, for the Finnish men and women using the first-year data of the FIT screening pilot. We evaluated 180 FIT strategies varying in FIT cut-off, screening interval, age to start, and age to stop screening, and compared them to no-screening by sex. We used incremental cost-effectiveness ratios (ICERs) to identify the optimal strategy after combining all male and female strategies and restricting the analysis by costs and referral rate to diagnostic colonoscopies.

Offering annual FIT screening with a cut-off of 25 µg/g at 50–79 years in men and with a cut-off of 10 µg/g at 55–69 years in women was optimal. This combined strategy prevented 28% of colorectal cancer (CRC) cases and 55% of CRC deaths with acceptable costs (ICER = 9000€/life-years gained). Screening at the current target age of 60–74 years was suboptimal for both sexes. Among strategies with the same target age and interval for both sexes, expected benefits from optimal screening were lower but still reasonable.

Our results support a wider age range of screening in men, and a lower cut-off for a positive test in women when restrictions on colonoscopy capacity and costs are in place. National FIT screening program should start at younger age.

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*Heinävaara et. al. 2022

Expansion matrix

	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
1975	47	48	49	50	51	52	53	54	55	56
1974	48	49	50	51	52	53	54	55	56	57
1973	49	50	51	52	53	54	55	56	57	58
1972	50	51	52	53	54	55	56	57	58	59
1971	51	52	53	54	55	56	57	58	59	60
1970	52	53	54	55	56	57	58	59	60	61
1969	53	54	55	56	57	58	59	60	61	62
1968	54	55	56	57	58	59	60	61	62	63
1967	55	56	57	58	59	60	61	62	63	64
1966	56	57	58	59	60	61	62	63	64	65
1965	57	58	59	60	61	62	63	64	65	66
1964	58	59	60	61	62	63	64	65	66	67
1963	59	60	61	62	63	64	65	66	67	68
1962	60	61	62	63	64	65	66	67	68	69
1961	61	62	63	64	65	66	67	68	69	70
1960	62	63	64	65	66	67	68	69	70	71
1959	63	64	65	66	67	68	69	70	71	72
1958	64	65	66	67	68	69	70	71	72	73
1957	65	66	67	68	69	70	71	72	73	74
1956	66	67	68	69	70	71	72	73	74	
1955	67	68	69	70	71	72	73	74		
1954	68	69	70	71	72	73	74			
1953	69	70	71	72	73	74				

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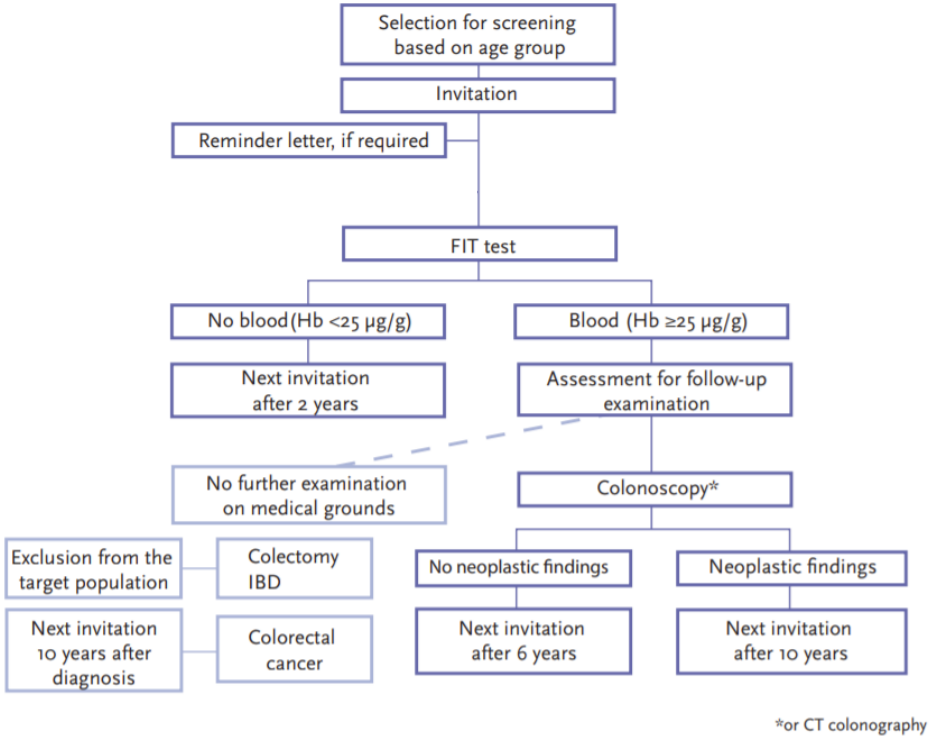
National program 2022 onwards – cut-off 25 µg/g

- Statistics from 2022, published in 06/2022
- Preliminary statistics from 2023

✓ **Coverage 100%**

✓ **Participation 77% (81/73)**

✓ **Test positives 5.1% (3.9/6.1)**



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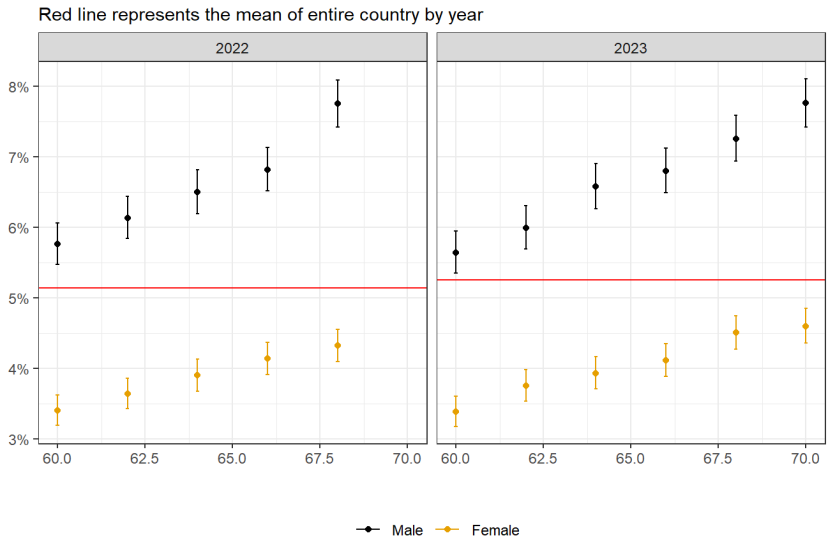
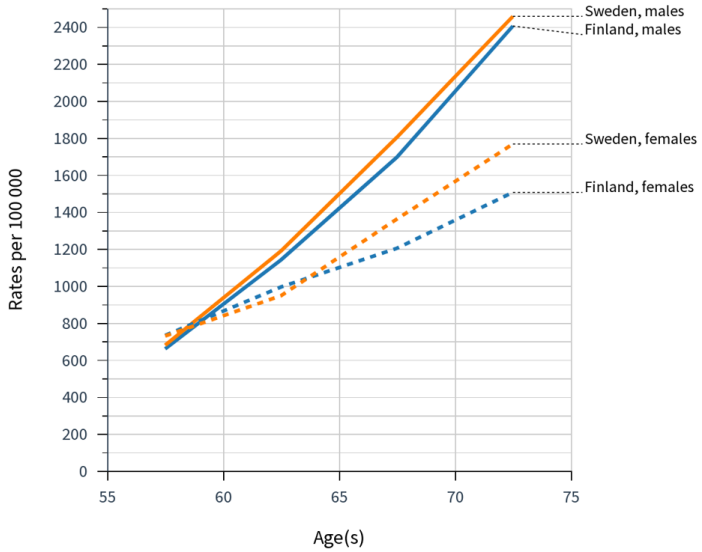
National program (2022-23) – cut-off 25 µg/g





Positivity rates differ by sex and age -- Similar pattern in CRC incidence rates

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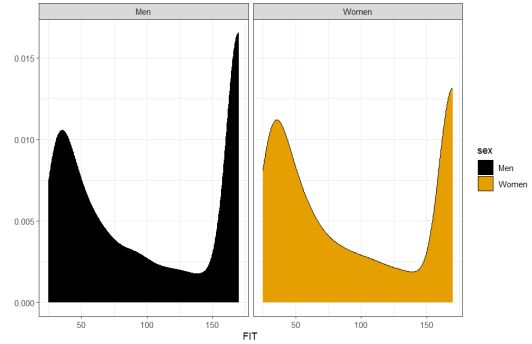
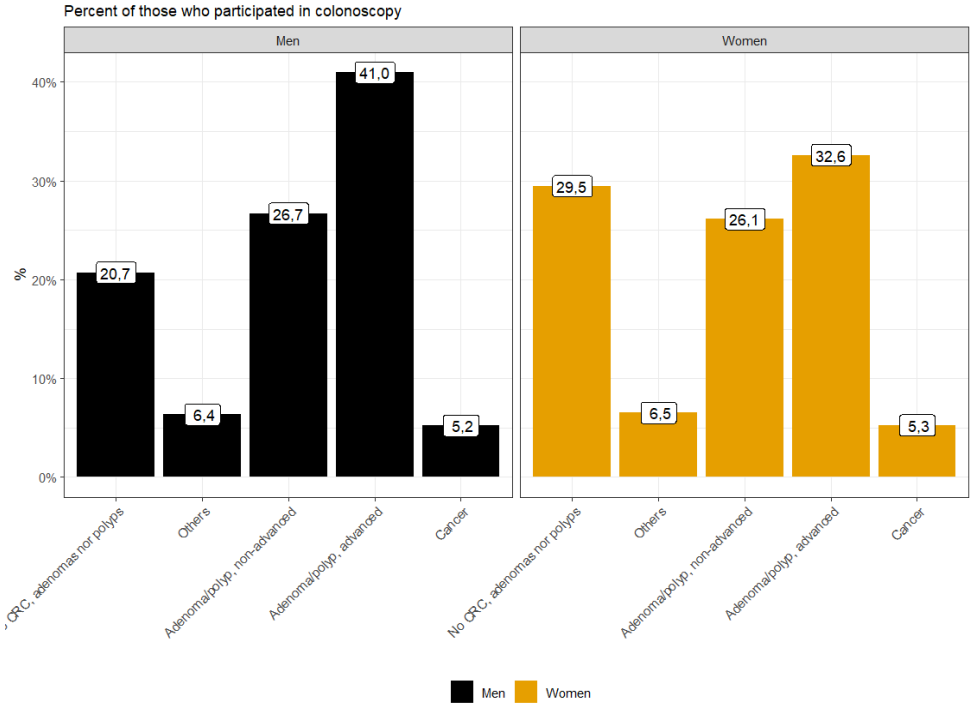
National program (2022-23) – cut-off 25 µg/g





- Data from 23882 individuals (14095 men, 9787 women) who underwent colonoscopy after a positive FIT

✓ **Distribution of findings in men (somewhat) corresponds to that in women**

- Proportion of advanced adenomas higher
  - Proportion of indolent findings higher in women

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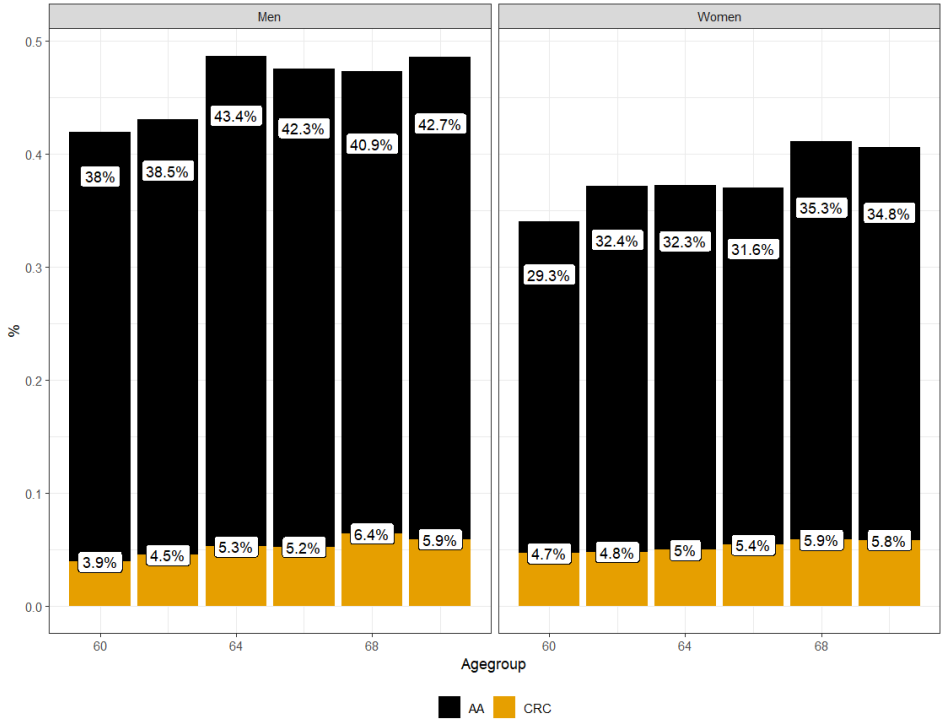
National program (2022-23) – cut-off 25 µg/g



- Data from 23882 individuals (14095 men, 9787 women) who underwent colonoscopy after a positive FIT

✓ **A notable age-gradient in the proportion of advanced adenomas (AA) and colorectal cancers (CRC) in both sexes**

- Age-specific cut-offs?

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Conclusions

- The lower FIT cut-off for women narrowed the performance gap between genders. Even then, the detection rates were much higher in men
- Current similar cut-off for both sexes, 25 µg/g, produces +/- similar distribution of findings with a preferred 5% positivity rate
  - Proportion of indolent findings higher in women, proportion of advanced adenomas higher in men
  - Proportion of cancers similar
- There is a notable age-gradient in the proportion of findings – age-specific cut-offs?

✓ **The greatest benefit from FIT screening is obtained by screening men. Efforts should be put on methodologies better detecting advanced tumors in women**

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