






# Colorectal cancer screening with fecal immunochemical testing or primary colonoscopy: inequities in diagnostic yield

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## Abstract

**Background:** Socioeconomic inequalities in the uptake of colorectal cancer screening are well documented, but the implications on inequities in health gain remain unclear.

**Methods:** Sixty-year-olds were randomly recruited from the Swedish population between March 2014 and March 2020 and invited to undergo either 2 rounds of fecal immunochemical testing (FIT) 2 years apart ( $n = 60\,137$ ) or primary colonoscopy just once ( $n = 30\,400$ ). By linkage to Statistics Sweden's registries, we obtained socioeconomic data. In each defined socioeconomic group, we estimated the cumulative yield of advanced neoplasia in each screening arm (intention-to-screen analysis). In the biennial FIT arm, we predicted the probability of exceeding the yield in the primary colonoscopy arm by linear extrapolation of the cumulative yield to (hypothetical) additional rounds of FIT.

**Results:** In the lowest income group, the yield of advanced neoplasia was 1.63% (95% confidence interval [CI] = 1.35% to 1.93%) after 2 rounds of FIT vs 1.93% (95% CI = 1.49% to 2.40%) in the primary colonoscopy arm. Extrapolation to a third round of FIT implied a 86% probability of exceeding the yield in the primary colonoscopy arm. In the highest income group, we found a more pronounced yield gap between the 2 screening strategies—2.32% (95% CI = 2.15% to 2.49%) vs 3.71% (95% CI = 3.41% to 4.02%)—implying a low (2%) predicted probability of exceeding yield after a third round of FIT.

**Conclusions:** Yield of advanced neoplasia from 2 rounds of FIT 2 years apart was poorer as compared with primary colonoscopy, but the difference was less in lower socioeconomic groups.

**Clinical Trial Registration:** ClinicalTrials.gov identifier NCT02078804

The potential health benefit of colorectal cancer (CRC) screening depends on the screening mechanism's diagnostic yield, the effect of detecting a tumor earlier, and the long-term effect of polypectomy. Currently, the 2 most widely employed CRC screening strategies are fecal immunochemical testing (FIT) and primary colonoscopy. Workup colonoscopy after a positive FIT result or primary colonoscopy detects existing invasive cancers, and removal of premalignant lesions is crucial for preventing CRC (1).

Socioeconomic inequalities in the uptake of organized CRC screening are well documented (2-6). Investigators have reported a higher proportion of positive test results in lower socioeconomic groups among attendees in biennial guaiac fecal occult blood testing (7) and biennial FIT (5,6). In contrast, among the positive test results, lower uptake of workup colonoscopy among individuals in lower socioeconomic groups has been observed (5,6,8). One study has addressed socioeconomic inequality in the diagnostic yield of biennial FIT, and no clear socioeconomic gradient was found (6).

Our aim was to evaluate socioeconomic disparities in the yield of advanced neoplasia from screening with biennial FIT vs primary colonoscopy based on data from a nationwide randomized trial conducted in Sweden.

## Methods

### Intention-to-screen population

SCREENing of Swedish Colons (SCREESCO; ClinicalTrials.gov identifier NCT02078804) is a Swedish trial with randomized assignment of study individuals to 1 of 3 groups: invitations to 2 rounds of high-sensitivity FIT using a home test kit 2 years apart, once-only primary colonoscopy, or no intervention (control arm) (9). The Ethics Committee at Karolinska Institutet approved the trial (No. 2012/2058/31/3).

Sweden is divided into 21 regions, and each region is responsible for providing health-care services to its residents. Two of the regions started to implement CRC screening programs in 2008/2009 (10). Eighteen of the other 19 regions, all naive to organized

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CRC screening, participated in the trial. At the end of 2013, there were 437 000 registered inhabitants aged between 55 and 59 years (50.26% men) in the participating regions. SCREESCO started recruiting in March 2014 and concluded the recruitment phase (including both invitations to FIT) in March 2020. (In the period 2021-2023, the 19 regions in Sweden that were naive to organized CRC screening implemented a biennial FIT screening program for individuals aged 60-74 years.)

Sixty-year-olds born between 1954 and 1958 were randomly selected and invited to undergo either FIT or primary colonoscopy. A randomized block method allocated individuals to the respective arms (2:1 allocation). In total, 60 300 individuals were randomly assigned to the biennial FIT (2 rounds) arm and 31 440 were randomly assigned to the once-only primary colonoscopy arm. Ultimately, 60 137 (99.7%) and 30 400 (96.7%), respectively, were invited to each screening strategy. Further information about the invitation procedure can be found elsewhere (9).

## Diagnostic yield

In the FIT arm, a hemoglobin concentration of at least 10 µg/g of feces defined the cutoff for positivity (9).

The colonoscopy procedures have been described in detail elsewhere (9). In brief, 146 certified endoscopists (gastroenterologists, surgeons, and nurses) at 33 hospitals performed the colonoscopies and recorded the size and location of all lesions. Polyps were categorized as adenomas, serrated polyps, or inflammatory polyps (11). Advanced adenomas were adenomas measuring 10 mm or greater in diameter or those that had a villous component or high-grade dysplasia.

For the present analysis, we defined the primary outcome as screening-detected advanced neoplasm or not (ie, a binary outcome for each intention-to-screen individual). For the individuals invited to biennial FIT, advanced neoplasia was assessed based on the colonoscopy findings after 1) the first round of FIT (FIT 1) and 2) the 2 rounds of FIT (FIT 1 + 2 [ie, cumulative yield]). We also analyzed screening-detected CRC and advanced adenoma separately.

## Socioeconomic data

The Swedish Ethical Review Authority approved the linkage to Swedish population registers for obtaining sociodemographic data (No. 2022-01946-02).

Individual data registered in the SCREESCO database were sent to Statistics Sweden. Register holders in Sweden use the unique Swedish personal numbers for data linkage (12). Statistics Sweden's population registry data on household disposable income (disposable income per household per consumption unit, classified into national quartiles), education level (classified according to number of school years: >12 school years [corresponding to some education at university level] or ≤12 school years [no university education]), country of birth (Western vs non-Western [eastern Europe, Asia, Africa, and South America] countries), and residential neighborhood (see below) were linked to each 60-year-old individual allocated to the 2 screening arms. Time-varying data were assessed according to the year of invitation (first round in the biennial FIT arm). Statistics Sweden delivered a pseudo-anonymized data file for the present analysis.

Each intention-to-screen individual was geocoded to his or her residential neighborhood at the time of (first) invitation, according to a small-area division of Sweden referred to as *Demografiska StatistikOmråden*, or demographic statistics area. In December 2018, the number of inhabitants in each of the 5985 demographic statistics areas varied between 653 and 4243. It has been

demonstrated that these neighborhoods can be used in public health surveillance (13). In the present analysis, we considered the following neighborhood-level data for each calendar year of invitation: economic standard (neighborhoods classified into national quintiles, with Q1 being the richest and Q5 being the poorest, according to data on the proportions of households with disposable income in the lowest national quartile) and proportion of non-Western immigrants (proportion of inhabitants born in eastern Europe, Asia, Africa, or South America in each neighborhood assessed and, also classified into national quintiles 1-5).

## Statistical analysis

We calculated the proportion of intention-to-screen individuals according to each binary outcome, reflecting yields of advanced neoplasia. We evaluated heterogeneity in yield of advanced neoplasia across socioeconomic groups through exploratory subgroup analysis. Sampling uncertainty was evaluated using a nonparametric bootstrap method involving resampling of the entire study sample 5000 times with replacement. We then used this bootstrap approach, combined with the observed change in yield between the 2 FIT rounds, to estimate the probability of exceeding the yield of advanced neoplasia in the primary colonoscopy arm after 1 or 2 additional rounds of FIT. This estimation was made using linear extrapolation (see [Supplementary Methods](#) [available online] for technical details).

## Results

### Intention-to-screen population's socioeconomic characteristics

Two individuals had missing data on country of birth, and 215 individuals had missing data on educational attainment; these individuals were classified into the categories "Western" and "no university education," respectively. Hence, the individual-level analyses incorporated all invited persons (n = 60 137 in the FIT arm and n = 30 400 in the primary colonoscopy arm). For the analyses involving neighborhood characteristics, we excluded 24 individuals who could not be geocoded (14 in the biennial FIT arm and 10 in the primary colonoscopy arm).

[Table 1](#) shows the distributions of each socioeconomic covariate for the 2 intention-to-screen populations. This large randomized clinical trial (RCT) resulted in balanced covariate distributions between the 2 populations. The distributions of household income were concentrated to national quartiles 3 and 4 because 60-year-olds in Sweden generally have higher household incomes than do households with younger or older members.

### Yield of advanced neoplasia

In total, 170 instances of CRC and 2091 advanced adenomas were detected. Overall, the yield of advanced neoplasia was estimated at 3.23% (95% confidence interval [CI] = 3.03% to 3.43%) in the primary colonoscopy arm, which was greater than the yields of advanced neoplasia in the biennial FIT arm: 1.25% (95% CI = 1.16% to 1.34%) after FIT 1 and 2.13% (95% CI = 2.01% to 2.24%) after FIT 1 + 2 (test of equal yields, FIT 1 + 2 vs primary colonoscopy:  $P < .001$ ) ([Table 2](#)). Extrapolations to 2 additional rounds of FIT implied predicted probabilities of 0.05 and 1.0 for exceeding the yield of advanced neoplasia in the primary colonoscopy arm after a third and fourth round of FIT ([Table 2](#)).

The initial gain in the yield of advanced neoplasia by offering primary colonoscopy at the age of 60 years rather than biennial FIT was smaller in lower socioeconomic groups. After 2 rounds of

**Table 1.** Socioeconomic characteristics of the 60-year-olds invited to each screening arm

| Characteristic   | Fecal immunochemical test, No. (%) | Primary colonoscopy, No. (%) |
|--|------------------------------------|------------------------------|
| Household disposable income  |                                    |                              |
| National quartile 4  | 28 846 (48.0)                      | 14 604 (48.0)                |
| National quartile 3  | 15 869 (26.4)                      | 8108 (26.7)                  |
| National quartile 2  | 8200 (13.6)                        | 4120 (13.6)                  |
| National quartile 1  | 7222 (12.0)                        | 3568 (11.7)                  |
| University education   |                                    |                              |
| Yes  | 19 281 (32.1)                      | 9936 (32.7)                  |
| No   | 40 856 (67.9)                      | 20 464 (67.3)                |
| Region of country of birth   |                                    |                              |
| Western  | 56 084 (93.3)                      | 28 239 (92.9)                |
| Non-Western  | 4053 (6.7)                         | 2161 (7.1)                   |
| Neighborhood-level economic standard (neighborhoods classified into national quintiles 1-5)      |                                    |                              |
| 1 (richest)  | 9028 (15.0)                        | 4624 (15.2)                  |
| 2  | 12 373 (20.6)                      | 6270 (20.6)                  |
| 3  | 13 700 (22.8)                      | 6909 (22.7)                  |
| 4  | 13 776 (22.9)                      | 6900 (22.7)                  |
| 5 (poorest)  | 11 246 (18.7)                      | 5687 (18.7)                  |
| Neighborhood-level non-Western immigrants (neighborhoods classified into national quintiles 1-5) |                                    |                              |
| 1 (least)  | 15 378 (25.5)                      | 7818 (25.7)                  |
| 2  | 13 609 (22.6)                      | 6713 (22.1)                  |
| 3  | 11 257 (18.7)                      | 5619 (18.5)                  |
| 4  | 11 084 (18.4)                      | 5772 (19.0)                  |
| 5 (most)   | 8795 (14.6)                        | 4468 (14.7)                  |

FIT, 1.63% (95% CI = 1.35% to 1.93%) had advanced neoplasia detected among the intention-to-screen individuals with household disposable income in the lowest national quartile vs 1.93% (95% CI = 1.49% to 2.40%) in the primary colonoscopy arm ( $P = .30$ ) (Table 2). Extrapolation to a third round of FIT implied an 86% probability of an exceeding cumulative yield of advanced neoplasia from biennial FIT screening compared with once-only primary colonoscopy (Figure 1; Table 2). By contrast, 2.32% (95% CI = 2.15% to 2.49%) of individuals in the highest income quartile had an advanced neoplasm detected after 2 rounds of FIT vs 3.71% (95% CI = 3.41% to 4.02%) of individuals in the primary colonoscopy arm ( $P < .001$ ), implying a low (2%) predicted probability of exceeding the cumulative yield after a third round of FIT (Figure 1, A; Table 2). Similar patterns of advanced neoplasia yield were estimated across the population groups according to country of birth (Figure 2; Table 2).

The neighborhood-level socioeconomic gradients were less clear than the corresponding individual-level gradients (Table 2). For example, 1.91% (95% CI = 1.67% to 2.17%) and 2.05% (95% CI = 1.76% to 2.34%) of the invitees living in the poorest (Q5) and richest (Q1) neighborhoods, respectively, had advanced neoplasia detected after 2 rounds of FIT (Table 2; compare with the above-mentioned estimates of advanced neoplasia yield, reflecting the corresponding individual-level gradient [from 1.63% to 2.32%]). The difference in advanced neoplasia yield after 2 rounds of FIT between the invitees from the highest vs lowest income households was more pronounced among individuals living in the poorest neighborhoods (1.25 percentage points [95% CI = 0.56 to 1.95]) than among those individuals living in the richest neighborhoods (0.04 percentage points, 95% CI = -1.66 to 1.49), although the difference between these 2 differences (each reflecting the individual-level socioeconomic gradients in Q5 or Q1) was not statistically significant (1.21, 95% CI = -0.39 to 3.09). The analogous individual-level socioeconomic gradients for advanced neoplasia yield in the primary colonoscopy arm were

stronger and showed a reversed pattern across the Q5-Q1 strata: The difference in Q5 (1.46 percentage points, 95% CI = 0.28 to 2.63) was smaller than the difference in Q1 (2.46 percentage points, 95% CI = 0.86 to 3.82) but not statistically significantly (difference in difference = -1.10, 95% CI = -2.88 to 0.98).

Generally, yields of advanced neoplasia from FIT 2 years apart and primary colonoscopy, respectively, were poorer, but the difference was less among individuals in lower socioeconomic groups (Table 2).

We found analogous patterns when analyzing advanced adenoma separately (Supplementary Table 1, available online). The analyses of CRC provided no clear picture because there were few events (Supplementary Table 2, available online).

## Discussion

Based on the nationwide 2-arm SCREESCO RCT conducted in Sweden, including 60 137 60-year-olds invited to CRC screening with 2 rounds of biennial FIT and 30 340 invited to once-only primary colonoscopy, we found that the additional gain in the yield of advanced neoplasia by offering primary colonoscopy at the age of 60 rather than FIT (first round) was smaller in lower socioeconomic groups. Gradients in the yield of advanced neoplasia across variously defined socioeconomic groups were pronounced among the 60-year-olds invited to primary colonoscopy. We found weaker socioeconomic gradients in the cumulative yield of advanced neoplasia among the intention-to-screen individuals in the biennial FIT arm.

Two other RCTs (14,15) have been designed with separate FIT and primary colonoscopy arms, another RCT (16) allowed for crossover between FIT and primary colonoscopy, and 2 other RCTs (17,18) have been designed to compare hybrid screening strategies against either FIT or primary colonoscopy as the control arm. To our knowledge, the present analysis is the first to compare diagnostic yield between 2 large intention-to-screen populations randomly invited to biennial FIT and once-only primary colonoscopy, respectively, across socioeconomic strata.

It is difficult to explain the marginal socioeconomic gradients in the yield of advanced neoplasia among the intention-to-screen individuals in the biennial FIT arm, despite a strong socioeconomic gradient in the test uptake (5). We and others have found an increasing likelihood of a positive stool-based test in individuals from lower socioeconomic groups (5-7). The predictive values of a positive test result on the yield of advanced neoplasia may differ across socioeconomic groups (6). On the one hand, for example, the risk of comorbidities that require anticoagulation therapy may differ by socioeconomic group. On the other hand, the risk of CRC may differ between socioeconomic groups, which has been observed among people aged 55 to 74 years in Sweden (19). One should also bear in mind results that have shown a lower uptake of workup colonoscopy with decreasing socioeconomic status (5,6,8).

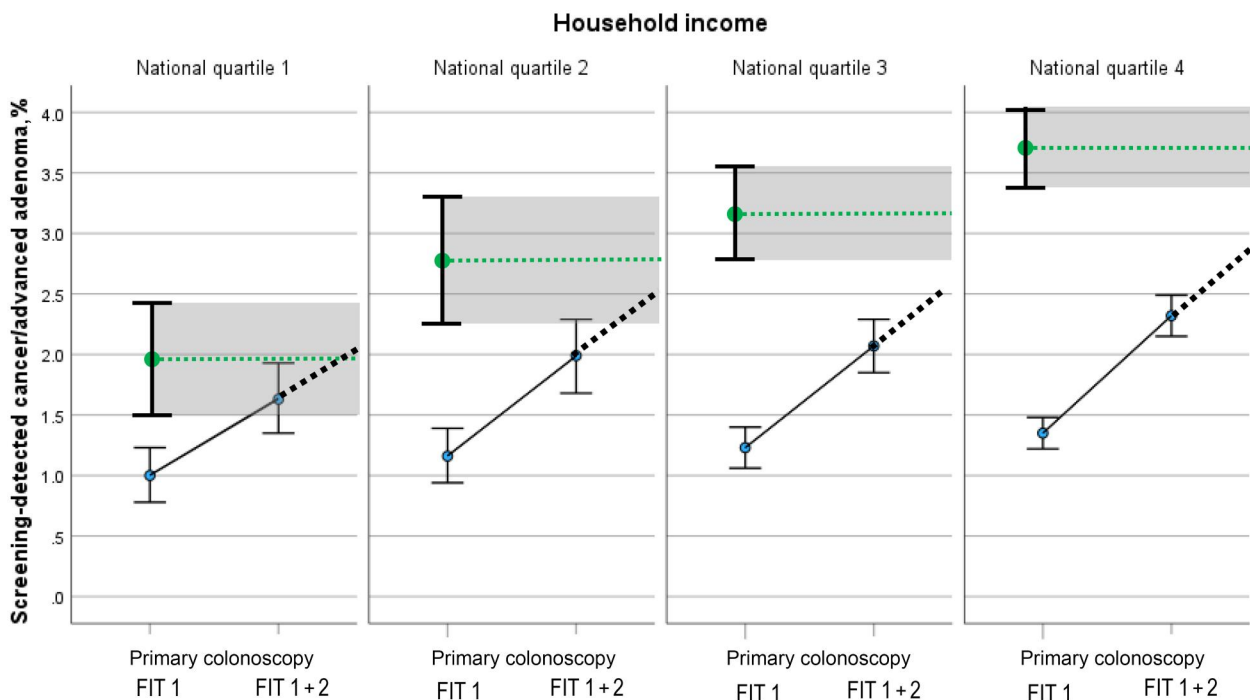
We employed linear extrapolation for the predictions of exceeding cumulative yields of advanced neoplasia from screening with biennial FIT vs primary colonoscopy at 60 years of age to third and fourth rounds of FIT at 64 and 66 years of age, respectively. A report from a biennial FIT screening program in northern Italy among individuals aged 50 to 69 years presented data on advanced neoplasia among individuals who had had a first FIT and were invited to up to 4 subsequent rounds of FIT (20). The proportions of individuals with detected advanced neoplasms out of the invited individuals per round were 0.84% (round 2), 0.80% (round 3), 0.86% (round 4), and 0.85% (round 5). Another

**Table 2.** Inequities in yield of advanced neoplasia from screening with biennial fecal immunochemical testing vs primary colonoscopy

| Characteristic   | Yield of advanced neoplasia vs primary colonoscopy, % (95% CI) | Yield of advanced neoplasia after FIT round 1, % (95% CI) | Yield of advanced neoplasia after FIT rounds 1 and 2, % (95% CI) | P <sup>a</sup> | Predicted probability of exceeding yield of advanced neoplasia after 1 and 2 additional rounds of FIT vs primary colonoscopy (linear extrapolation <sup>b</sup> ) |                                |
|--|--|---|--|----------------|---|--------------------------------|
|  |  |   |  |                | After FIT rounds 1 + 2 + 3  | After FIT rounds 1 + 2 + 3 + 4 |
| Overall  | 3.23 (3.03 to 3.43)  | 1.25 (1.16 to 1.34)                                       | 2.13 (2.01 to 2.24)  | <.001          | 0.05  | 1.00                           |
| Household disposable income  |  |   |  |                |   |                                |
| National quartile 4  | 3.71 (3.41 to 4.02)  | 1.35 (1.22 to 1.48)                                       | 2.32 (2.15 to 2.49)  | <.001          | 0.02  | 0.99                           |
| National quartile 3  | 3.17 (2.80 to 3.56)  | 1.23 (1.06 to 1.40)                                       | 2.07 (1.85 to 2.29)  | <.001          | 0.15  | 0.97                           |
| National quartile 2  | 2.77 (2.27 to 3.28)  | 1.16 (0.94 to 1.39)                                       | 1.99 (1.68 to 2.29)  | .007           | 0.56  | 0.98                           |
| National quartile 1  | 1.93 (1.49 to 2.40)  | 1.00 (0.78 to 1.23)                                       | 1.63 (1.35 to 1.93)  | .30            | 0.86  | 0.99                           |
| University education   |  |   |  |                |   |                                |
| Yes  | 3.71 (3.35 to 4.09)  | 1.32 (1.17 to 1.48)                                       | 2.16 (1.96 to 2.37)  | <.001          | 0.00  | 0.67                           |
| No   | 3.00 (2.76 to 3.23)  | 1.22 (1.11 to 1.33)                                       | 2.11 (1.97 to 2.25)  | <.001          | 0.54  | 1.00                           |
| Region of country of birth   |  |   |  |                |   |                                |
| Western  | 3.31 (3.10 to 3.53)  | 1.28 (1.18 to 1.37)                                       | 2.15 (2.03 to 2.27)  | <.001          | 0.02  | 1.00                           |
| Non-Western  | 2.13 (1.55 to 2.76)  | 0.89 (0.62 to 1.20)                                       | 1.83 (1.43 to 2.26)  | .47            | 0.92  | 1.00                           |
| Neighborhood-level economic standard (neighborhoods classified into national quintiles 1-5)      |  |   |  |                |   |                                |
| 1 (richest)  | 3.29 (2.79 to 3.83)  | 1.22 (0.99 to 1.44)                                       | 2.05 (1.76 to 2.34)  | <.001          | 0.11  | 0.85                           |
| 2  | 3.51 (3.06 to 3.97)  | 1.28 (1.08 to 1.47)                                       | 2.18 (1.92 to 2.43)  | <.001          | 0.08  | 0.91                           |
| 3  | 3.27 (2.85 to 3.70)  | 1.36 (1.17 to 1.55)                                       | 2.27 (2.03 to 2.52)  | <.001          | 0.39  | 0.99                           |
| 4  | 3.10 (2.71 to 3.52)  | 1.23 (1.05 to 1.42)                                       | 2.16 (1.92 to 2.41)  | <.001          | 0.51  | 1.00                           |
| 5 (poorest)  | 2.99 (2.56 to 3.43)  | 1.15 (0.96 to 1.34)                                       | 1.91 (1.67 to 2.17)  | <.001          | 0.15  | 0.91                           |
| Neighborhood-level non-Western immigrants (neighborhoods classified into national quintiles 1-5) |  |   |  |                |   |                                |
| 1 (least)  | 3.15 (2.76 to 3.54)  | 1.27 (1.10 to 1.45)                                       | 2.07 (1.84 to 2.30)  | <.001          | 0.15  | 0.95                           |
| 2  | 3.53 (3.09 to 3.97)  | 1.26 (1.08 to 1.46)                                       | 2.25 (2.00 to 2.50)  | <.001          | 0.16  | 0.97                           |
| 3  | 3.38 (2.91 to 3.86)  | 1.28 (1.07 to 1.50)                                       | 2.28 (2.02 to 2.56)  | <.001          | 0.40  | 0.99                           |
| 4  | 3.29 (2.85 to 3.75)  | 1.30 (1.09 to 1.51)                                       | 2.11 (1.84 to 2.38)  | <.001          | 0.11  | 0.89                           |
| 5 (most)   | 2.66 (2.21 to 3.14)  | 1.10 (0.89 to 1.32)                                       | 1.86 (1.59 to 2.15)  | .003           | 0.45  | 0.97                           |

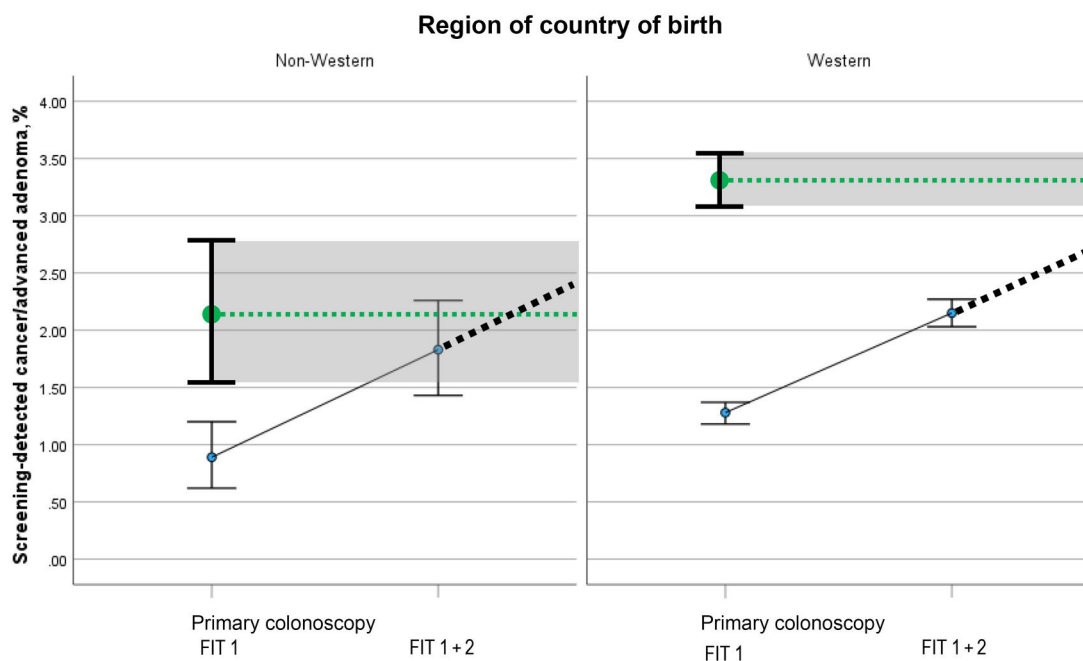
<sup>a</sup> Two-sided test of equal yields, primary colonoscopy vs FIT 1 + 2. CI = confidence interval; FIT = fecal immunochemical testing.

<sup>b</sup> Figure 1 illustrates the linear extrapolation of estimated yields of advanced neoplasia after FIT 1 and FIT 1 + 2, respectively, to additional FIT rounds.



**Figure 1.** Estimated cumulative yields of advanced neoplasia with 95% confidence intervals from screening with biennial fecal immunochemical testing (FIT) 2 years apart vs primary colonoscopy at the age of 60 years across population groups, stratified by household disposable income. The dotted line segments illustrate the linear extrapolation to additional FIT rounds.





**Figure 2.** Estimated cumulative yields of advanced neoplasia with 95% confidence intervals from screening with biennial fecal immunochemical testing (FIT) 2 years apart vs primary colonoscopy at the age of 60 years across population groups, stratified by region of country of birth. The dotted line segments illustrate the linear extrapolation to additional FIT rounds.

report from the Netherlands of a population-based study with random selection of individuals aged 50 to 74 years who were invited to undergo up to 4 rounds of biennial screening with 1-sample or 2-sample FIT (randomized allocation) showed the following proportions of advanced neoplasia out of the intention-to-screen individuals per round (pooled data from the 1-sample and 2-sample FIT arms): 2.13% (round 1), 1.15% (round 2), 0.82% (round 3), and 1.28% (round 4) (21). Hence, in those 2 studies, the cumulative yield showed a smaller increase between FIT rounds 2 and 3 than between the following consecutive rounds. One should bear in mind that 1) the referred studies included a substantial fraction of individuals aged 50 to 59 years at their first FIT (19) or at their first invitation to FIT (21), whereas our analysis considered fixed ages 60, 62, 64, and 66 years at invitations to FIT rounds 1 to 4, and 2) population incidence of CRC starts to increase rapidly from approximately 60 years of age (19). Taken together, we preferred to employ linear extrapolations for our predictions.

We had access to both individual-level and neighborhood-level socioeconomic data. Neighborhood-level data may be applicable in other countries where individual-level data are not available (22). Our analysis demonstrated the most distinct socioeconomic gradients in the yield of advanced neoplasia when the intention-to-screen populations were grouped according to household-level income (national quartiles) or individual-level country of birth (Western or non-Western).

The potential health benefit of CRC screening depends on the diagnostic yield, the effect of detecting a tumor earlier, and the long-term effect of polypectomy. Several observational studies have been conducted showing significant effects from screening on incidence and mortality (23–25), while systematic reviews of RCTs on the most widely employed screening strategies (26,27) and recent trial results (28) have produced inconclusive evidence regarding the screening impact on mortality and incidence. We have recently exploited the quasi-experimental setting in

Sweden, where 2 regions started to implement biennial stool-based screening for individuals aged 60 to 69 years in 2008/2009, while the other 19 regions in Sweden have started implementation of biennial FIT screening in recent years (29). We estimated the impact of such organized screening on population CRC incidence patterns over time and across age groups and found a change in age-specific incidence patterns, with a long-lasting incidence decrease in the population aged 70 to 74 years, implying reductions in the excess mortality and burden of the disease (29). Exploratory subgroup analyses did not reveal any significantly differential effect across population groups according to educational level or country of birth (29). Taken together with the present findings on the yield of advanced neoplasia in the biennial FIT arm of the SCREESCO RCT, the expectations for the nationwide organized biennial FIT screening in Sweden for individuals aged 60 to 74 years are reassuring: a reduced burden of CRC without unintentionally exacerbating inequalities in health.

Several interventional studies using social determinants of health have been conducted, aimed at improving uptakes of established screening programs (30,31). We question whether such interventional studies should be pursued for CRC screening based solely on observed inequalities in the uptake. Given that the potential health gain from CRC screening depends on the effect of detecting cancer earlier or a precancerous lesion, information about disparities in diagnostic yield across socioeconomic groups should be of more concern. Based on our findings, the incentive for pursuing interventional studies that use social determinants of health seems to be stronger for the primary colonoscopy strategy than for a biennial FIT strategy.

Furthermore, cost-effectiveness should be considered when evaluating screening strategies (30). Previous cost-effectiveness analyses of primary colonoscopy vs biennial FIT—based on early experiences in the SCREESCO RCT—has shown that screening with primary colonoscopy could be more cost-effective than FIT when lifelong effects and costs were

considered (32), although no considerations of equity implications were made. Our observations indicate that sociodemographic stratification of an intention-to-screen population could bring to the fore the choice among effectiveness, cost-effectiveness, and equal health distribution. Future economic evaluations incorporating information about the distributional impacts across sociodemographic subgroups, such as distributional cost-effectiveness analysis, will be important (33,34). Although such analyses have been made for targeted interventions for increased participation in organized CRC screening (35), no evaluation has been made regarding primary colonoscopy vs biennial FIT strategies. Hybrid strategies targeting interventions across sociodemographic groups may also be addressed. Given observed socioeconomic inequalities in the primary uptake but varying inequities in the diagnostic yield of alternative CRC screening strategies, such analyses will be crucial. An increased concern for equity aspects in cancer emphasizes the importance of such analyses.

This intention-to-screen analysis of a 2-arm RCT revealed inequities in the yields of advanced neoplasia. Pronounced socioeconomic disparities were found in the primary colonoscopy (at age 60) arm. Less pronounced socioeconomic disparities were found in the biennial FIT (2 rounds) arm. The present results will be valuable for comparative cost-effectiveness evaluations for considering equity in health gain from CRC screening.

## Data availability

Anonymized individual participant data that underlie the results reported in this article (text, tables, figures, and supplementary information) can be available to researchers after application to the SCREESCO Steering Committee. Researchers have to provide a methodologically sound proposal for a project that conforms with the Swedish Ethical Review Authority permit for the project. Researchers will have to sign a data access agreement. Data will be made available at a secure remote server to achieve the aims in the approved proposal. They will be available from 3 months after publication and end 3 years after article publication. Proposals regarding the data underlying this article may be submitted up to 2 years after publication. The SCREESCO study will not carry the costs of external projects. For data sharing questions, please contact [anna.forsberg@ki.se](mailto:anna.forsberg@ki.se).

## Author contributions

Carl Bonander, PhD (Conceptualization; Data curation; Formal analysis; Methodology; Resources; Visualization; Writing—review & editing); Marcus Westerberg, PhD (Data curation; Writing—review & editing); Gabriella Chauca Strand, MSc (Conceptualization; Writing—review & editing); Anna Forsberg, PhD (Investigation; Resources; Writing—review & editing); Ulf Strömberg, PhD (Conceptualization; Formal analysis; Methodology; Resources; Visualization; Writing—original draft; Writing—review & editing).

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## Conflicts of interest

All authors declare that they have no competing interests.

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