



Original Research

Risk of colorectal cancer and participation in fecal immunochemical test-based screening

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ARTICLE INFO

Keywords:

Colorectal cancer
Colorectal cancer screening
health inequities

ABSTRACT

Objectives: Participation rates in fecal immunochemical test (FIT)-based colorectal cancer (CRC) screening differ across socio-demographic subgroups. The largest health gains could be achieved in subgroups with low participation rates and high risk of CRC. We investigated the CRC risk within different socio-demographic subgroups with low participation in the Dutch CRC screening program.

Study design: Population-based cohort study.

Methods: All individuals invited for the Dutch CRC screening program in 2018 and 2019 were included. Data from a previous study, including screening data and demographic characteristics, were augmented with CRC diagnoses in 2018 and 2019. A multivariable logistic regression was used to assess the association between socio-demographic factors and risk of CRC.

Results: Overall participation was 72.3% and age-adjusted CRC incidence was 30.3 per 10,000 individuals. Males showed lower participation (69.7 %) but had a higher-than-average CRC risk (35.1). The difference in CRC risk between males and females was less pronounced among non-participants (OR: 1.28, 95% CI: 1.20–1.36) than participants (OR: 1.41, 95% CI: 1.35–1.47). Lower income groups also had lower participation (down to 60.0 %) and higher risk of CRC (down to 30.7), but the difference in CRC risk between low-income groups and high-income groups was only significant among participants (OR lowest vs highest quintile: 1.22, 95% CI: 1.14–1.32). Conversely, individuals with a Turkish/Moroccan migration background had lower participation (48.7 %), but their CRC risk was also lower (18.8; OR: 0.54, 95% CI: 0.46–0.63).

Conclusions: CRC risk varies significantly between low-participation groups in the Dutch CRC screening program. Interventions should prioritize the most vulnerable groups, considering both participation and risk of CRC.

1. Introduction

Colorectal cancer (CRC) is the second most commonly diagnosed cancer and the second most common cause of cancer death in Europe.¹ Aiming to strengthen prevention and early detection of CRC, the European Commission recommends CRC screening in all its member states.^{2,3} Organized screening is suggested, as it effectively reduces inequities in screening access compared to opportunistic screening.⁴ However, also in

organized CRC screening programs, participation is known to differ across socio-demographic and cultural subgroups.^{5–9} Previous research demonstrated that males, migrants, singles and individuals with low income are least likely to participate in the Dutch fecal immunochemical test (FIT)-based CRC screening program.⁹ The identification of non-participants and understanding of their characteristics can help tailor interventions to reach non-participants more effectively and increase the yield of screening.^{10,11} The health gains that can be achieved

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<https://doi.org/10.1016/j.puhe.2025.105938>

Received 20 February 2025; Received in revised form 2 July 2025; Accepted 22 August 2025

Available online 8 September 2025

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with such interventions depend not only on the participation rate of the target population, but also on their risk of CRC. Certain low-participation groups are known to have a higher risk of CRC, such as males or those with low socioeconomic status (SES).^{12,13} However, an extensive multifaceted analysis of both participation in screening and risk of CRC is lacking. We therefore investigated the risk of CRC within different socio-demographic subgroups of invitees to the Dutch CRC screening program, focusing on subgroups with low participation rates. In addition, we assessed the yield of screening in these subgroups.

2. Methods

2.1. The Dutch CRC screening program

In our study, data from the Dutch CRC screening program were used. In the Netherlands, individuals aged 55 to 75 are invited biennially for FIT-based CRC screening. Invitation packages include an invitation letter, information folder, reply envelope and a FIT kit. First-time invitees receive an advance notification letter three weeks prior to their invitation. Non-responders receive a reminder six weeks after the initial invitation. A detailed description of the Dutch CRC screening program can be found elsewhere.¹⁴

2.2. Study population

Data from a previous study on non-participation in CRC screening were used for the analyses.⁹ In brief, the data included information of all invitees to the Dutch CRC screening program in 2018 and 2019. Data on invitation and participation were selected in the Dutch national screening database (ScreenIT) and linked to demographic characteristics in Statistics Netherlands, such as sex, age, migration background, level of education, household characteristics, income and SES score. For the current study, these data were augmented with additional data from ScreenIT, including test results, yield of screening and screening history, and data from the Netherlands Cancer Registry (NCR), which included the incidence date, cancer stage and cancer location from all individuals aged 55 to 75 with a CRC diagnosis between 2018 and 2020. Diagnoses after 2019 were only used to determine the yield of screening among individuals invited in 2018 or 2019, as there is a delay between the date of invitation and diagnosis of CRC. Data from the NCR were linked to the original dataset using postal code, date of birth and sex. The linkage rate was 97.2%.

2.3. Definitions

A participant was defined as an invitee for CRC screening who returned a test kit. The participation rate was defined as the percentage of invitees who participated in the CRC screening program.

CRCs were categorized into cancers detected in participants (participant cancers) and non-participants (non-participant cancers). Participant cancers comprised screen-detected CRCs, FIT interval CRCs (cancers detected after a negative FIT and before the invitation to the next screening) and post-colonoscopy CRCs (cancers detected after a colonoscopy following a positive FIT). For individuals with multiple CRCs at diagnosis, the stage and location of the most advanced cancer was used.

CRC incidence per sociodemographic subgroup was defined as the number of CRC diagnoses divided by the number of individuals in that group. The detection rate was defined as the number of participants diagnosed with an advanced adenoma or CRC divided by the total number of participants in each subgroup.

Staging of CRCs was based on the American Joint Committee on Cancer TNM Classification, 8th edition.¹⁵

A more detailed description of the definitions, including the definitions of the sociodemographic variables, can be found in the [Supplementary Materials](#).

2.4. Analyses

CRC incidence in 2018 and 2019 was calculated per subgroup and age-standardized using the direct method, with the total study population as reference. The relative risk of non-participants compared to participants was calculated and tested using a Mid-p Fisher Exact test.

To investigate the yield of screening in different sociodemographic subgroups, the detection rate of participants in 2018 and 2019 was calculated per subgroup, including all screen-detected CRCs until the end of the follow-up period (i.e. December 31, 2020).

The effect of each sociodemographic factor on the risk of CRC was estimated in a multivariable logistic regression using CRC diagnosis in 2018 or 2019 as dependent variable. In the regression, strongly correlated variables (i.e., variables with Variance Inflation Factor >5) were not included simultaneously within one model; the model with the lowest Akaike Information Criterion was chosen. Relevant interaction terms based on literature were added to the model and tested using a likelihood ratio test. Odds ratios (ORs) were calculated for the final model, which included participation, sex, age, migration background, socioeconomic category, household type and household income as explanatory variables. Participation interacted significantly with both sex and household income. Therefore, ORs of these variables were calculated for participants and non-participants separately.

To further investigate the difference in risk of CRC between non-participants and participants, we built distinct models for both sexes and each income group (i.e., the variables that interacted significantly with participation). In each model, we calculated the OR of non-participants in reference to participants. These ORs were also corrected for confounding; only significant explanatory variables were included (OR females: corrected for age, migration background, level of education and household income; OR males: corrected for age, migration background, household size and household income; ORs for each income group: corrected for sex, age and migration background).

Statistical analyses were conducted in R, version 4.2.3.¹⁶ A significance level of 5% was used throughout. All data were analysed in a secure environment provided by Statistics Netherlands. Before exportation, the results were thoroughly checked for compliance with the most stringent requirements of the General Data Protection Regulation.

3. Results

3.1. Descriptive statistics

A total of 4,383,668 individuals were invited for CRC screening in 2018 and 2019, of which 3,167,680 (72.3%) participated. Males accounted for 49.3% of the sample and the mean age of invitees was 63.4 years (standard deviation 6.3 years). Irrespective of participation status, 13,302 invitees were diagnosed with CRC in 2018 or 2019. Of these cancers, 4148 (31.2%) were non-participant CRCs and 9154 (68.8%) were participant CRCs, of which 6757 (73.8%) screen-detected CRCs, 2278 (24.9%) FIT interval CRCs and 119 (1.3%) post-colonoscopy CRCs.

Screen-detected CRCs were diagnosed most often in stage I (47.4%), followed by post-colonoscopy CRCs (33.1%) and FIT interval CRCs (21.5%; [Table 1](#)). Non-participant CRCs were diagnosed least often in stage I (15.0%). Furthermore, screen-detected CRCs were diagnosed most often in the left side of the colon, while FIT interval CRCs and post-colonoscopy CRCs were more often detected right-sided. Non-participant CRCs were evenly distributed across the left colon, right colon or rectum.

Overall CRC risk was 30.3 per 10,000 individuals. Non-participants had a 1.16 times (95% confidence interval [CI]: 1.12–1.20, $p < 0.01$) higher risk of CRC than participants: 33.7 versus 29.0 per 10,000 individuals.

Table 1
Stage distribution and location of cancers.

	Screen-detected CRC	FIT interval CRC	Post-colonoscopy CRC	Non-participant CRC
	n = 6757	n = 2278	n = 119	n = 4148
Stage				
I	47.4%	21.5%	33.1%	15.0%
II	18.6%	23.5%	20.3%	23.3%
III	26.5%	31.2%	29.7%	33.9%
IV	6.4%	22.6%	15.3%	26.7%
Unknown	1.0%	1.1%	1.7%	1.1%
Location				
Right colon	30.9%	51.7%	46.6%	33.8%
Left colon	40.7%	20.3%	25.4%	34.5%
Rectum	27.1%	26.4%	24.6%	30.4%
Unknown	1.3%	1.6%	3.4%	1.4%

Abbreviations: CRC = colorectal cancer; FIT = fecal immunochemical test.

3.2. Risk of CRC in subgroups with low participation

Risk of CRC differed across the previously identified subgroups with low participation in screening. Individuals with a non-Western migration background had the lowest risk of CRC (e.g. age-standardized incidence per 10,000 individuals with a Turkish/Moroccan migration background: 18.8; see Fig. 1, Table 2) in the entire study population. Singles had a slightly lower risk of CRC compared to couples (29.8 vs 30.5). On the other hand, males had a higher risk of CRC compared to

females (35.1 vs 25.8) and CRC risk increased slightly with decreasing income (from 29.5 in the highest quintile to 30.2 in the lowest quintile) or SES (from 29.1 in the highest quintile to 31.1 in the lowest quintile). Notably, this pattern was only observed among participants; CRC risk decreased slightly with decreasing income among non-participants in screening (Table 2, Table S1).

The multivariable logistic regression model confirmed that individuals with a Dutch-Indian (OR: 0.80 [95% CI: 0.71–0.91], Table 3), Surinamese (OR: 0.70 [95% CI: 0.59–0.81]) or Turkish/Moroccan (OR: 0.54 [95% CI: 0.46–0.63]) migration background had a significantly lower risk of CRC compared to individuals with a Dutch background. Males had a higher risk of CRC than females, though the difference was less pronounced for non-participants (OR: 1.28 [95% CI: 1.20–1.36]) compared to participants (OR: 1.41 [95% CI: 1.35–1.47]). Low income was not significantly associated with risk of CRC among non-participants, only among participants (OR lowest vs highest quintile: 1.22 [95% CI: 1.14–1.32]).

The model also confirmed that non-participants had a significantly higher risk of CRC than participants (OR: 1.44 [95% CI: 1.29–1.60], Table 3). However, the extent of the risk difference varied across subgroups: the OR of CRC of non-participants compared to participants was 1.26 (95% CI: 1.18–1.33) among females, as opposed to 1.17 (95% CI: 1.11–1.23) among males. The risk difference increased with income, from an OR of 1.06 (95% CI: 0.98–1.15) for the lowest quintile to 1.34 (95% CI: 1.22–1.47) for the highest quintile.

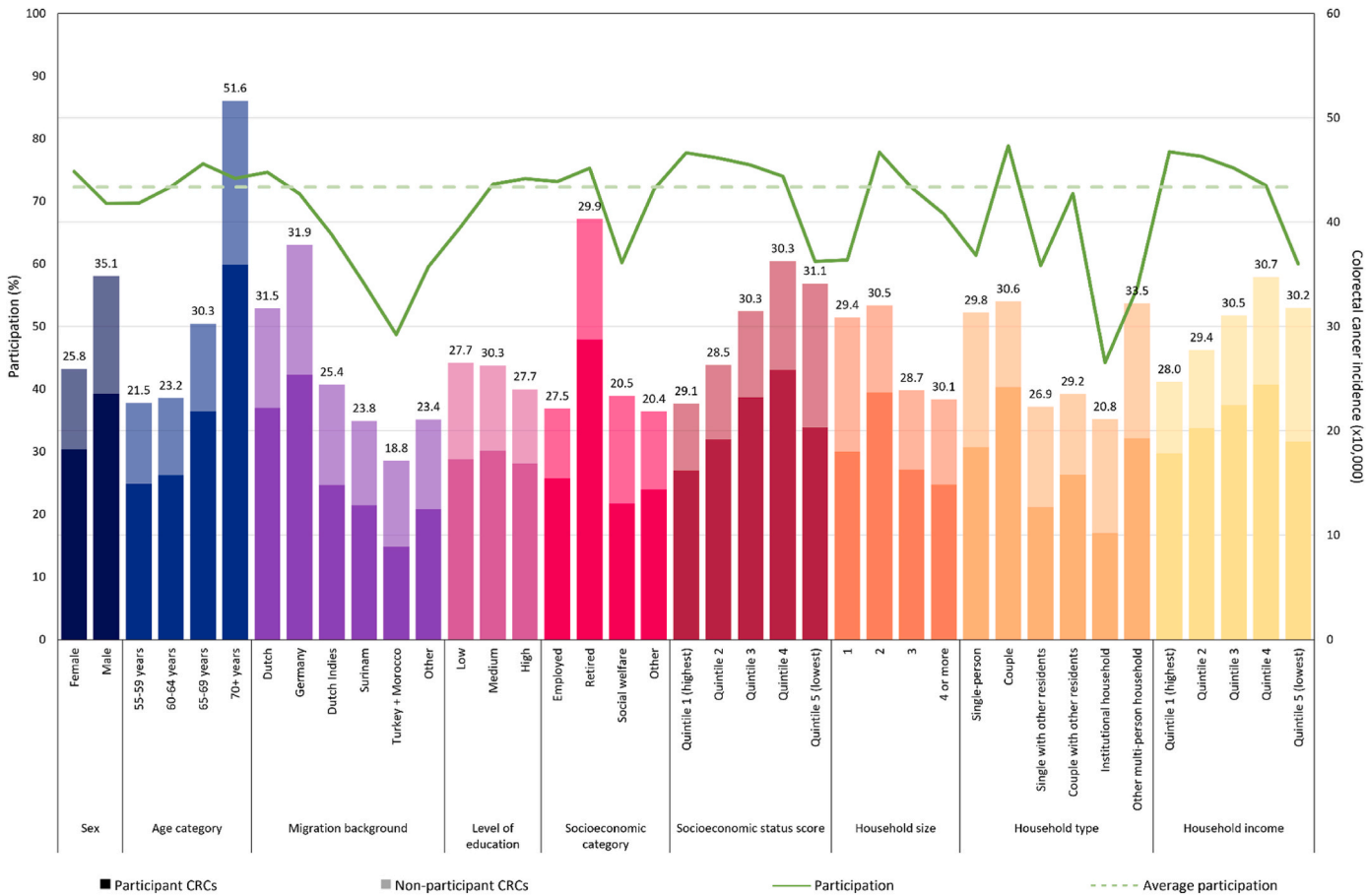


Fig. 1. Participation rate (green line) and CRC incidence per 10,000 individuals (coloured bars, split into unadjusted incidence in participants and unadjusted incidence in non-participants, labeled with age-standardized incidence rates) in different socio-demographic subgroups. Abbreviation: CRC = colorectal cancer.

Table 2
CRC incidence and yield of screening per sociodemographic subgroup.

	Incidence (x10,000)	Age-stand. incidence ^a (x10,000)	Age-stand. incidence ^a non- participants (x10,000)	Detection rate ^b
Population average	30.3	30.3	34.4	1.4%
Sex				
Female	26.0	25.8	30.2	1.0%
Male	34.8	35.1	38.5	1.8%
Age category				
55–59 years	21.5	21.5	24.0	1.4%
60–64 years	23.2	23.2	26.4	1.2%
65–69 years	30.3	30.3	34.5	1.3%
70+ years	51.6	51.6	58.9	1.9%
Migration background				
Dutch	31.7	31.5	37.4	1.5%
Germany	37.8	31.9	37.3	1.6%
Dutch Indies	24.4	25.4	29.1	1.3%
Surinam	21.0	23.8	21.0	1.0%
Turkey + Morocco	17.1	18.8	17.7	0.9%
Other	21.1	23.4	22.9	1.1%
Level of education				
Low	26.5	27.7	29.6	1.5%
Medium	26.3	30.3	34.2	1.4%
High	24.0	27.7	31.0	1.2%
Socioeconomic category				
Employed	22.1	27.5	31.2	1.3%
Retired	40.3	29.9	33.6	1.6%
Social welfare	23.4	20.5	20.0	1.4%
Other	21.9	20.4	32.3	1.0%
Socioeconomic status score				
Quintile 1 (highest)	22.6	29.1	37.5	1.1%
Quintile 2	26.3	28.5	34.3	1.3%
Quintile 3	31.5	30.3	33.7	1.5%
Quintile 4	36.3	30.3	34.7	1.6%
Quintile 5 (lowest)	34.1	31.1	32.6	1.6%
Household size				
1	30.9	29.4	31.7	1.5%
2	32.0	30.5	35.7	1.4%
3	23.9	28.7	32.2	1.3%
4 or more	23.0	30.1	29.2	1.3%
Household type				
Single-person	31.3	29.8	32.5	1.5%
Couple	32.4	30.6	36.4	1.4%
Single with other residents	22.3	26.9	28.7	1.2%
Couple with other residents	23.5	29.2	31.5	1.3%
Institutional household	21.1	20.8	18.5	1.1%
Other multi-person household	32.2	33.5	31.4	1.5%
Household income				
Quintile 1 (highest)	24.7	28.0	34.9	1.2%
Quintile 2	27.7	29.4	35.1	1.3%
Quintile 3	31.1	30.5	34.9	1.5%
Quintile 4	34.7	30.7	34.3	1.6%
Quintile 5 (lowest)	31.8	30.2	31.1	1.5%

Abbreviations: CRC = colorectal cancer; age-stand. = age-standardized.

^a Age-standardized incidence using the direct method, with the total study population as reference. Unadjusted incidence rates are used for the different age groups.^b The percentage of participants with an advanced adenoma or CRC.**Table 3**
Odds ratio per explanatory variable.

	Odds ratio (95%CI)
Participant	
Yes	ref
No	1.44 (1.29–1.60) ^a
Sex	
Non-participants	
Female	ref
Male	1.28 (1.20–1.36) ^a
Participants	
Female	ref
Male	1.41 (1.35–1.47) ^a
Age category	
55–59 years	ref
60–64 years	1.02 (0.97–1.08)
65–69 years	1.24 (1.15–1.34) ^a
70+ years	2.04 (1.88–2.21) ^a
Migration background	
Dutch	ref
Germany	1.00 (0.90–1.11)
Dutch Indies	0.80 (0.71–0.91) ^a
Surinam	0.70 (0.59–0.81) ^a
Turkey + Morocco	0.54 (0.46–0.63) ^a
Other	0.73 (0.67–0.78) ^a
Socioeconomic category	
Employed	ref
Retired	1.15 (1.07–1.23) ^a
Social welfare	1.10 (1.02–1.18) ^a
Other	1.13 (1.02–1.26) ^a
Household type	
Single-person	ref
Couple	1.02 (0.98–1.07)
Single with other residents	0.94 (0.84–1.06)
Couple with other residents	0.99 (0.93–1.05)
Institutional household	0.60 (0.48–0.74) ^a
Other multi-person household	1.11 (0.91–1.34)
Household income	
Non-participants	
Quintile 1 (highest)	Ref
Quintile 2	(0.90–1.13)
Quintile 3	1.00 (0.90–1.12)
Quintile 4	1.00 (0.90–1.11)
Quintile 5 (lowest)	0.96 (0.87–1.07)
Participants	
Quintile 1 (highest)	ref
Quintile 2	1.07 (0.99–1.14)
Quintile 3	1.12 (1.04–1.20) ^a
Quintile 4	1.15 (1.08–1.24) ^a
Quintile 5 (lowest)	1.22 (1.14–1.32) ^a

Abbreviation: CI = confidence interval.

^a significant at a 5% significance level.

3.3. Yield of screening in subgroups with low participation

The pattern of the detection rate in subgroups with low participation was similar to the pattern of overall CRC incidence: it was lower for individuals with a Turkish/Moroccan migration background (0.9%; Table 2, Fig. S3) and higher for males (1.8%) and individuals with low income (1.5% in the lowest quintile) or low SES (1.6% in the lowest quintile).

4. Discussion

Individuals with a Turkish/Moroccan migration background have both the lowest participation rates in CRC screening and the lowest risk of CRC within the entire study population. Males and low-income groups also have lower participation rates in screening, but they had a higher risk of CRC. For males, the difference was less pronounced, yet still significant for non-participants. For low-income groups, the difference was not significant for non-participants, only for participants.

The combination of lower participation and an increased CRC risk among males has been demonstrated previously.^{12,13} The risk of males

can be caused by biological and/or lifestyle-related factors. For example, males are more likely to accumulate abdominal visceral fat than females,¹⁷ which increases their risk of CRC.¹⁸ Moreover, males consume more red meat¹⁹ and alcohol,²⁰ and smoke more often than females.²¹ However, previous studies did not stratify results by participation status. We found that the difference in risk between males and females was less pronounced for non-participants compared to participants. The reason for this is not entirely clear, but our findings suggest a stronger healthy user bias in females compared to males. This would lead to a lower CRC risk among female participants, thus widening the gap between males and females among participants. Nonetheless, the higher risk of males implies that bigger health gains could be achieved if their screening rates would increase.

Overall risk of CRC increased slightly with decreasing income, in line with a previous Dutch publication.^{12,13} This can also be partly attributed to unhealthy behaviors, such as physical inactivity and smoking.²² In addition, unhealthy diets are more common in low-income groups as they are typically more affordable and accessible in low-SES neighborhoods.²² However, our analyses revealed that low income was not associated with higher CRC risk among non-participants, only among participants. This finding suggests the presence of complex interactions between income, screening participation and CRC risk factors; it appears that healthy user bias is primarily present in higher income groups. In addition, this finding demonstrates that non-participants constitute a selective subset of the target population.

Interestingly, some groups with low participation rates had a lower risk of CRC, such as those with a Dutch-Indian, Surinamese or Turkish/Moroccan migration background. The lower risk of non-Western immigrants has been confirmed in previous studies.^{23–25} Again, these differences are likely due to dietary and lifestyle differences.²⁶ Yet, it has also been shown that the risk of immigrants increases with time since immigration, as a consequence of adaptation to a Western lifestyle and increased exposure to risk factors.²⁴ This is consistent with the observed higher participation rates of second-generation migrants compared to first-generation migrants.⁹

Lastly, we showed that non-participants in the screening program have a significantly higher risk of CRC compared to participants. The difference can be explained by two main reasons. On the one hand, non-participants are more likely to have an unhealthy lifestyle, which increases their risk of CRC.²⁷ On the other hand, participants are more likely to have also participated in previous screening rounds, as reflected in the high rescreening rates in the Netherlands (92% in 2019), which decreases their risk of CRC.

Although we are not aware of other studies that investigate multiple sociodemographic and cultural risk factors for CRC and CRC screening rates simultaneously, our results are in line with existing literature regarding each factor individually. For example, male sex^{12,28} and low income²⁹ have been associated with an increased risk of CRC, and a non-Western migration background has been associated with a decreased risk of CRC.³⁰

A major strength of this study is the use of registry-based individual-level data, which enhanced the reliability of our results. We adopted a multifaceted approach, using data on both CRC incidence and participation in screening, and included numerous sociodemographic and cultural factors. With participation status being a potential mediator,⁹ adding it to our multivariable model accommodated a more accurate estimation of the direct effect of each sociodemographic factor on risk of CRC. A limitation of this study is that, due to its cross-sectional design, participation and CRC risk could not be fully disentangled, as participation in previous screening rounds also influences CRC risk. However, this effect is likely to be limited given the high rescreening rates in the Netherlands. Another limitation is that non-participants might have had a valid reason to not participate in screening, such as a previous CRC diagnosis, which might have led to a. In addition, the yield of screening was incomplete due to incomplete follow-up. Invitation data were available until December 31, 2019, whereas CRC data were available

until December 31, 2020, which implies that not all participants could be followed up until their next invitation for screening. However, since the average duration between a positive FIT result and subsequent colonoscopy is less than three weeks,³¹ the majority of screen-detected CRCs will have been included and only a small number of FIT interval CRCs and post-colonoscopy CRCs will be missing. Lastly, heterogeneity within different migrant groups because of unobserved variables such as time since immigration and degree of acculturation could not be accounted for. Although time since immigration is known to be related to risk of CRC,²⁴ we could not differentiate between first- and second-generation migrants due to small numbers.

For a screening program to be effective on a population level, high participation rates are essential.³² For that reason, interventions are being designed to reach out to non-participants. The largest health gains can be achieved in those subgroups that exhibit the lowest participation rates, as their potential for increasing participation is greatest, or in subgroups with the highest risk of CRC, as their yield of screening will be higher. Several interventions have been proven effective already. Examples among males include theory-based modifications of the advance notification letter,¹¹ reminder letters³³ and a brief informative phone call prior to the invitation.³⁴ Interventions among low-income groups also include reminders,³⁵ telephone support³⁶ and several other patient navigation initiatives.³⁷ Prioritizing the most vulnerable groups in terms of both participation and risk of CRC will improve the effectiveness of interventions. Nonetheless, this raises an ethical dilemma, where equity in screening outcomes may conflict with equal access to screening. Health inequity concerns should therefore be incorporated in the evaluation and optimization of screening, for instance using distributional cost-effectiveness analyses, which assesses both cost-effectiveness and the distribution of health effects across subpopulations.

To conclude, we investigated the risk of CRC across various sociodemographic and cultural subgroups with low participation rates in screening. We found that individuals with a non-Western migration background had a lower risk, whereas males had a higher risk of CRC. Individuals with low income did not have a higher risk among non-participants, only among participants. Targeted interventions should be designed to better reach the non-participants. Prioritizing those at higher risk of CRC would not only enhance more equitable access to CRC screening, but also contribute to reducing disparities in CRC outcomes.

Author statements

Ethical approval

Data for this study were obtained through the Dutch population-based national screening program, conducted under the authority of the Population Screening Act. The researchers were not involved in data collection and accessed only pseudonymised individual-level data. Participation in the screening program implies informed consent, with all individuals given the opportunity to opt out of the use of their data for scientific research.

Funding

Financial support for this study was provided by the Dutch Institute for Public Health and the Environment (contract number: 4410002642, PI: I. Lansdorp-Vogelaar). The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

Competing interests

ED: Received endoscopic equipment on loan of Olympus and FujiFilm and research grant from FujiFilm; received honorarium for consultancy from FujiFilm, Tillots, Olympus, GI Supply, Cancer Prevention Pharmaceuticals, PAION, and Ambu; and a speakers' fee from Olympus,

Roche, GI Supply, PAION, and IPSEN.

ILV: Associate editor at Gastroenterology; expert at the Health Council; panel member of the European Commission Initiative on Colorectal Cancer; visiting scientist at IARC.

MS: Received research support from Sentinel, Sysmex, Boston Scientific, Norgine, and Medtronic.

The other authors have no conflicts of interest to declare.

Author contributions

HJvdSV, ETZ and ILV conceptualized the study and contributed to the study design. HJvdSV accessed and verified the data and performed the analyses. LdJ supervised the data analysis. HJvdSV wrote the draft version of the manuscript, in close collaboration with ETZ. All authors contributed to reviewing drafts of the manuscript and approved the final manuscript draft.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhe.2025.105938>.

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