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ORIGINAL ARTICLE

The effects of reminders for colorectal cancer screening: participation and inequality

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Abstract

Purpose To investigate the effect of sending out reminders for colorectal cancer screening on socioeconomic and demographic inequalities in screening uptake.

Methods All citizens aged 50–74 in Denmark are invited every 2 years for colorectal cancer screening. Non-participants receive an electronically distributed reminder. Data for these analyses were derived from national registers. Socioeconomic status was measured by income and educational level. Demographic variables included age, gender and marital status, and the analyses were stratified by immigration status. Logistic regression analyses were conducted to estimate the odds of non-participation for invited citizens and for reminded citizens divided by socioeconomic and demographic predictors.

Results Of 763,511 native Danes invited for screening from 2014 to 2015, 387,116 (50.70%) participated after the initial invitation and 133,470 after receiving a reminder. Differences in participation were present in relation to all subgroups among both the invited citizens and reminded citizens. Differences persisted after full model adjustments with reductions for demographic variables. Odds ratio (OR) for non-participation in the eldest age group was 0.32 (95% CI, 0.32; 0.33) before and 1.11 (95% CI 1, 0.08; 1.14) after the reminder, compared to those under 55 years. OR for the 4th income quartile was 0.54 (95% CI, 0.53; 0.55) before and 0.44 (95% CI, 0.43; 0.45) after the reminder, compared to 1st quartile.

Conclusions Reminders increased the overall participation, and the inequalities in participation in relation to demographic factors were reduced after the distribution of reminders. The age differences were especially reduced. The inequalities in participation related to socioeconomic status were, however, slightly increased after reminder distribution.

Keywords Colorectal cancer screening · Reminder · Socioeconomic status · Inequality · Screening

Background

The Danish national colorectal cancer screening program was introduced in 2014. Citizens aged 50–74 were invited to participate in an initial screening by receiving an envelope with a kit for collecting a faeces sample. The kit was returned by mail to a laboratory and tested for blood. Non-participants, who did not return the kit, received a reminder electronically after 6 weeks. The use of reminder letters for non-participating individuals in the colorectal cancer screening has been previously proven effective in increasing the overall participation proportion [1–4]. Socioeconomic and demographic differences in participation for colorectal cancer screening have also been established in several national screening interventions [5–11]. Factors such as immigration status, age, gender, marital status, income and educational level are associated with differences in the participation

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proportions [5]. The effects of sending reminder letters on the socioeconomic differences have not yet been established. A socioeconomic gradient in participation may be reduced by an enhanced reminder letter [4]; however, if a gradient is also present in populations receiving reminder letters for participation, the social inequality could be increased by the use of reminder letters.

Therefore, we examined the socioeconomic and demographic differences in participation for colorectal cancer screening in the population of invited citizens, as well as in the population receiving a reminder.

Methods

Invitations for colorectal cancer screening were distributed to citizens based on their month of birth. The invitation included an invitation letter, an information leaflet from the Danish National Health Authority, a sample kit and a manual on the completion of the sample. An electronic reminder letter was sent to non-participants after a median of 46 days. The reminder letter included instructions on how to acquire a new sample kit if needed. Citizens participated by mailing a faeces sample in a prepaid envelope to a hospital laboratory in their region. Information on invited citizens, electronically mailed reminders and participation registration were linked with existing administrative registers holding information on gender, age, education, income, immigration status and marital status. Registers were linked using encrypted unique personal identification numbers [12].

Registers

The Danish Colorectal Cancer Screening Database holds information on dates of invitations for screening, dates of reminders and dates of faecal sample reception at laboratories. The data in the Danish Colorectal Cancer Screening Database were derived from the National Patient Register, the National Pathology Registry and the Invitation and Administration Module for the national colorectal cancer screening [13].

The Population's Education Register holds individual information on the highest achieved level of education for each citizen living in Denmark [14]. The Income Statistics Register holds information on annual personal and household income as well as registered partners [15]. The Danish Civil Registration System holds information on the date of birth, gender and country of origin [12]. The Danish Register of Causes of Death holds information on dates of death [16]. The National Patient Register holds information on all diagnoses provided in Danish hospitals [17].

Participation in colorectal cancer screening

Individuals were registered as participants in the colorectal cancer screening when their completed stool samples were received at the hospitals, even if the completion of the stool sample was faulty. The study population included individuals with an initial invitation in 2014–2015. Follow-up for submitted samples and reminders continued until July 6, 2016. Passive and active non-participants should not be investigated as a homogeneous group in the analysis, as they differ in characteristics [18]. Therefore, individuals actively deregistering from screening were excluded from the study as we aimed to explore differences between passive non-participants and participants.

Socioeconomic status

Educational level and economic income were used as measures of socioeconomic status in this study. Data on the highest completed educational level was derived from the Population's Education Register. The highest completed educational level at the end of 2013 was used for citizens invited in 2014 and at the end of 2014 for those invited in 2015. Invited citizens were divided into three groups based on the International Standard Classification of Education level of highest completed education: basic school (primary); high school or vocational education (secondary); and short, medium or long length higher education (higher).

Income was derived from the Income Statistics Register as annual household income in the year 2013 for those invited in 2014 and in the year 2014 for those invited in 2015. Income was adjusted for inflation and was divided by 1.5 if the individual was living with a partner [19]. Income was divided into four groups based on quartiles: first quartile < 235,820 DKK (< 39,476 USD/< 31,684 Euro), second quartile 235,820–354,014 DKK (39,476–59,261 USD/31,684–47,565 Euro), third quartile > 354,014–507,479 DKK (59,261–84,951 USD/47,565–68,184 Euro), and fourth quartile > 507,479 DKK (> 84,951 USD/> 68,184 Euro) (exchange rate date: February 2, 2018).

Demographic variables

Information on gender, date of birth and country of origin was derived from the Danish Civil Registration System. Date of birth was used to calculate the age at the date of invitation for each individual. Age was

divided into groups of 5-year intervals. Marital status was defined as "with a partner" or "single" based on registered partners in the Income Statistics Register. Individuals were registered as having a partner if they were married, were registered partners, were cohabiting with their child's other parent or were cohabiting with an individual of the opposite gender whose age differed by no more than 15 years from their own. Immigration status was grouped as native Danes, Western immigrants and non-Western immigrants. Immigrants were categorised as Western if their country of origin was one of the following: Andorra, Australia, Canada, Iceland, Liechtenstein, Monaco, New Zealand, Norway, San Marino, Switzerland, Czechoslovakia, the United States of America, Vatican state and all 28 member countries of the European Union by October 2017 [20] (for results on Western and non-Western immigrants, see appendix).

Statistical analyses

The main analyses consisted of univariate and multivariate logistic regression models, comparing participants after the initial invitation and participants after the reminder with passive non-participants. Using univariate logistic regression models, we estimated the odds ratios of non-participation as a result of each socioeconomic and demographic variable. Using multivariate logistic regression models, we estimated the odds ratios of non-participation as a result of each socioeconomic and demographic variable through the inclusion of all of the variables in the same models. The group of citizens who participated after the initial invitation and the group of citizens participating after being reminded were both compared to the same group consisting of all passive non-participants. As interactions were present, stratification by immigration status and the inclusion of design variables combining marital status and gender were performed. The results from the analyses of Western and non-Western immigrants are included in appendix. Multivariate logistic regression models were conducted for all citizens invited from 2014 to 2015 and for all citizens subsequently receiving a reminder. Data management was conducted using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA), and all statistical analyses were performed using the R statistical software package, version 3.3.2 [21].

Results

A total of 886,088 individuals were invited for colorectal cancer screening from 2014 to 2015. As shown in Fig. 1, 70,632 were excluded, 22,133 (2.5%) of which were due to missing data (covariate data and faulty date registrations). The analyses were stratified by immigration status, and 20,696 Western immigrants and 31,249 non-Western immigrants were excluded from the main analyses (see results from analyses of Western and non-Western immigrants in appendix). Of all of the invited native Danes, 387,116 (50.70%) individuals participated in colorectal cancer screening after the initial invitation. Reminders were sent to 376,395 individuals during follow-up. Of all native Danes receiving a reminder, 133,470 (35.46%) subsequently participated (Fig. 1). Of all of the reminders, 94.21% were sent within 46 days after the initial invitation and 99.98% of reminders were sent within the first 3 months after the initial invitation.

In total, including Western and non-Western immigrants, 550,698 (67.53%) participated in colorectal cancer screening during follow-up. The mean time from the invitation to participation was 35.23 days with a median of 24 days and a mode of 22 days. Within 42 days after the initial invitation, 95% of participants had participated and 90% had participated within 36 days.

Overall participation among native Danes was 520,586 (68.18%) with 133,470 (17.48%) participating after receiving a reminder. Non-participation by subgroups varied from 25.3% (aged > 65–70 years) to 43.4% (singles). Subgroups with the highest participation before reminders were those aged > 65–70 (61.8%) and those aged > 70 (61.0%). Subgroups with the highest participation after reminders were those aged 55 or younger (24.3%) and those in the fourth income quartile (24.0) (Table 1).

Among the native Danes participating after the initial invitation compared to non-participants ($n = 630{,}041$), the odds of non-participation were higher in males and singles, decreased with increasing income quartiles and were lower for individuals with secondary or higher educational level and increased age before and after full model adjustment (Fig. 2). In our sample of native Danes receiving a reminder ($n = 376{,}395$), the odds of non-participation were higher in males, singles and in the age groups > 55–60 to > 70, and the odds decreased with increasing income quartile and educational level in univariate regression models. After full model adjustment, the odds of non-participation were higher in males, singles and in the age groups > 55–60, > 60–65 and > 70, and the odds decreased with increasing income quartile and educational level and were lower in those aged > 65–70 (Fig. 2). Patterns of OR in the socioeconomic and demographic subgroups were not identical in the group of invited citizens and in the group of reminded citizens. Differences between educational levels and incomes were slightly larger among reminded citizens, with the exception of a slight

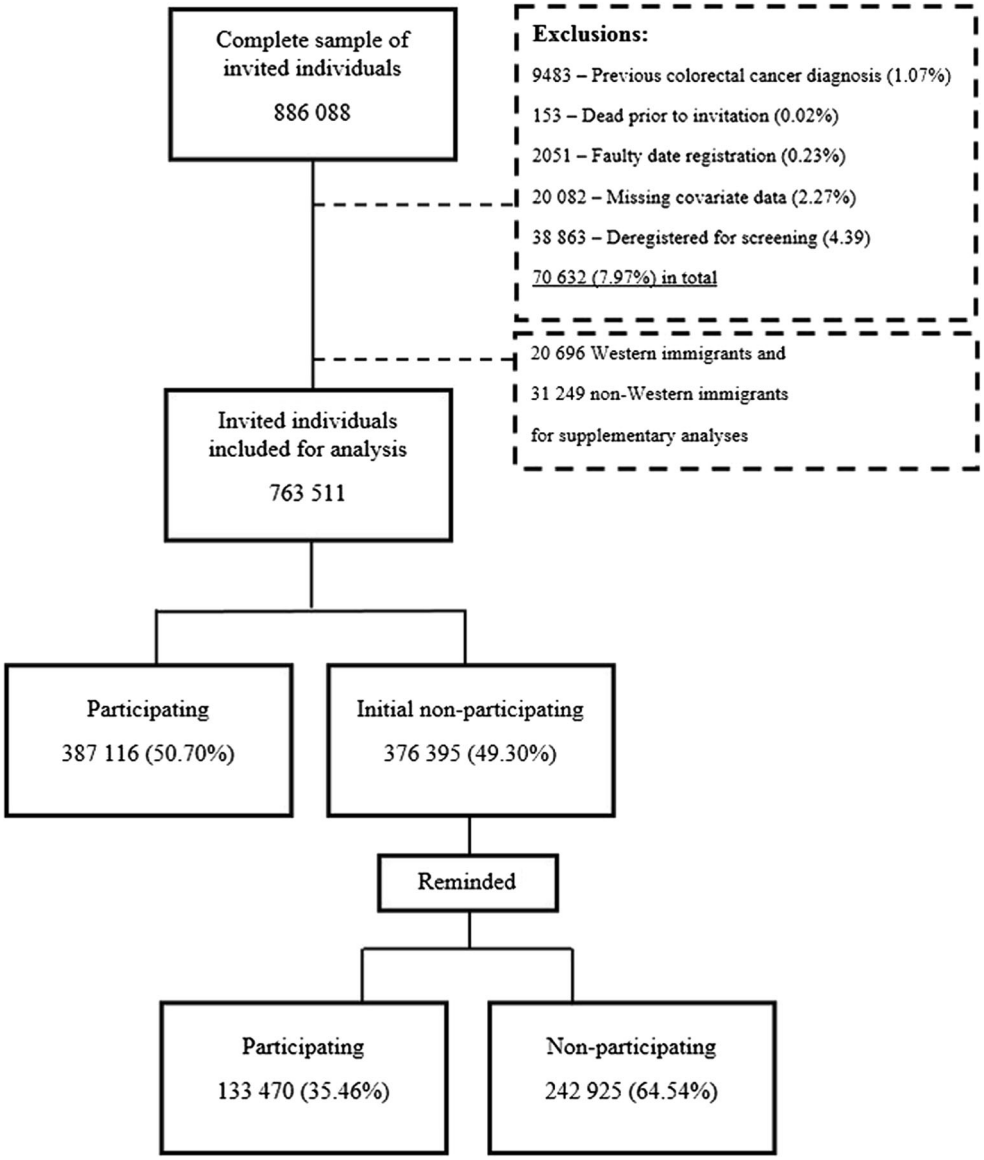

Fig. 1 Flowchart of invited citizens for colorectal cancer screening, Denmark 2014–2015

reduction in the gap between the first and second income quartiles, whereas differences in the subgroups of marital status, gender and especially between the age groups were smaller among the reminded citizens, compared to the invited citizens. Patterns of the OR's were similar among Western and non-Western immigrants (with the exception of a U-shaped pattern for the age groups among the non-Western immigrants after the initial invitation), although the OR sizes varied between the immigrant status populations (the results from the analyses of Western and non-Western immigrants are provided in the appendix).

Discussion

After the distribution of reminders, the overall participation rose by 17.48%. This increase indicates that reminders can increase adherence with low associated costs as the reminders were distributed electronically. The risk of non-participation decreased with age at the initial invitation. This effect was not present for individuals receiving reminders, indicating that older age groups decided whether to participate after the initial invitation, whereas the younger age groups may benefit more from receiving reminders. The effects of socioeconomic status on non-participation were maintained or even increased with reminders, as those in a higher position were more inclined to participate after both the initial invitation and the subsequent reminder, indicating that social inequality may be increased by distributing reminders. The effects of the demographic variables were maintained or even decreased with reminders, as males and individuals without a partner were less inclined to participate after the initial

Table 1 Participation proportions by socioeconomic and demographic subgroups, colorectal cancer screening, Denmark 2014–2015, $n = 763,511$, native Danes

Variable	Participating after first invitation ($n = 387,116$)	Participating after reminder ($n = 133,470$)	Non-participating ($n = 242,925$)	Total ($n = 763,511$)
Gender				
Female	215,231 (55.5)	65,920 (17.0)	106,691 (27.5)	387,842
Male	171,885 (45.7)	67,550 (18.0)	136,234 (36.3)	375,669
Age groups				
<=55	96,813 (37.7)	62,291 (24.3)	97,376 (38.0)	256,480
>55–60	59,428 (49.3)	22,149 (18.4)	38,949 (32.3)	120,526
>60–65	64,664 (55.9)	17,778 (15.4)	33,160 (28.7)	115,602
>65–70	73,985 (61.8)	15,377 (12.9)	30,306 (25.3)	119,668
>70	92,226 (61.0)	15,875 (10.5)	43,134 (28.5)	151,235
Income				
1st quartile	84,132 (48.9)	19,906 (11.5)	68,150 (39.6)	172,188
2nd quartile	100,126 (53.9)	25,931 (14.0)	59,818 (32.1)	185,875
3rd quartile	103,260 (51.6)	38,224 (19.1)	58,535 (29.3)	200,019
4th quartile	99,598 (48.5)	49,409 (24.0)	56,422 (27.5)	205,429
Educational level				
Primary	101,645 (48.7)	28,447 (13.6)	78,775 (37.7)	208,867
Secondary	175,704 (51.3)	61,767 (18.1)	104,786 (30.6)	342,257
Higher	109,767 (51.7)	43,256 (20.3)	59,364 (28.0)	212,387
Marital status				
With a partner	298,788 (54.7)	98,960 (18.1)	148,565 (27.2)	546,313
Single	88,328 (40.7)	34,510 (15.9)	94,360 (43.4)	217,198

All proportions are described using frequencies with row percentages in parenthesis

invitation than after the reminders. The effect of age was nearly eliminated with the use of reminding, indicating that socioeconomic inequality may be especially increased when distributing reminders. These results suggest that it may be possible to reduce the inequality in participation by the demographic subgroups, but possibly not by socioeconomic status when using a standard reminder. An enhanced reminder letter has been shown elsewhere to reduce the socioeconomic gradient defined by a deprivation score [4, 22]. Enhancing and developing the reminders used in relation to our population may change the effects of the reminders by socioeconomic status. The results of this study indicate that the existing reminders are increasing the gap between the socioeconomic population groups. As the reminders did, in fact, increase overall participation, it is recommended to continue to distribute reminders to non-participants. Enhancing the reminder or developing subgroup-specific reminder letters could be of interest in reducing social inequality and increasing participation, although relying on only written information in decreasing inequalities may be challenging [4]. Furthermore, simplified information for individuals with lower literacy may not decrease a social gradient in uptake [23]. The addition of a second reminder letter has increased participation in another population [3], but in Denmark, individuals are invited every second year, and the next invitation may also act as a reminder. The addition of a postal reminder for non-participants after the electronic reminder may be beneficial to some subgroups if there are differences in attitudes towards technology between the socioeconomic and demographic groups. Mailed non-electronic reminders have proven cost-effective elsewhere [24]. Text-message reminders have also increased uptake in breast cancer screening [25] but may not have the same effect in socioeconomically deprived populations for colorectal cancer screening [26]. Therefore, there is a risk that text-message reminders would increase the social inequality even further. Barriers perceived by early, late and non-participants in colorectal cancer screening may be similar but could differ in strength [27]. Reminders may, therefore, benefit from focusing on barriers to the faeces test. If these barriers are stronger in populations of low socioeconomic status, such a change in focus could help decrease the observed inequality. As socioeconomic and

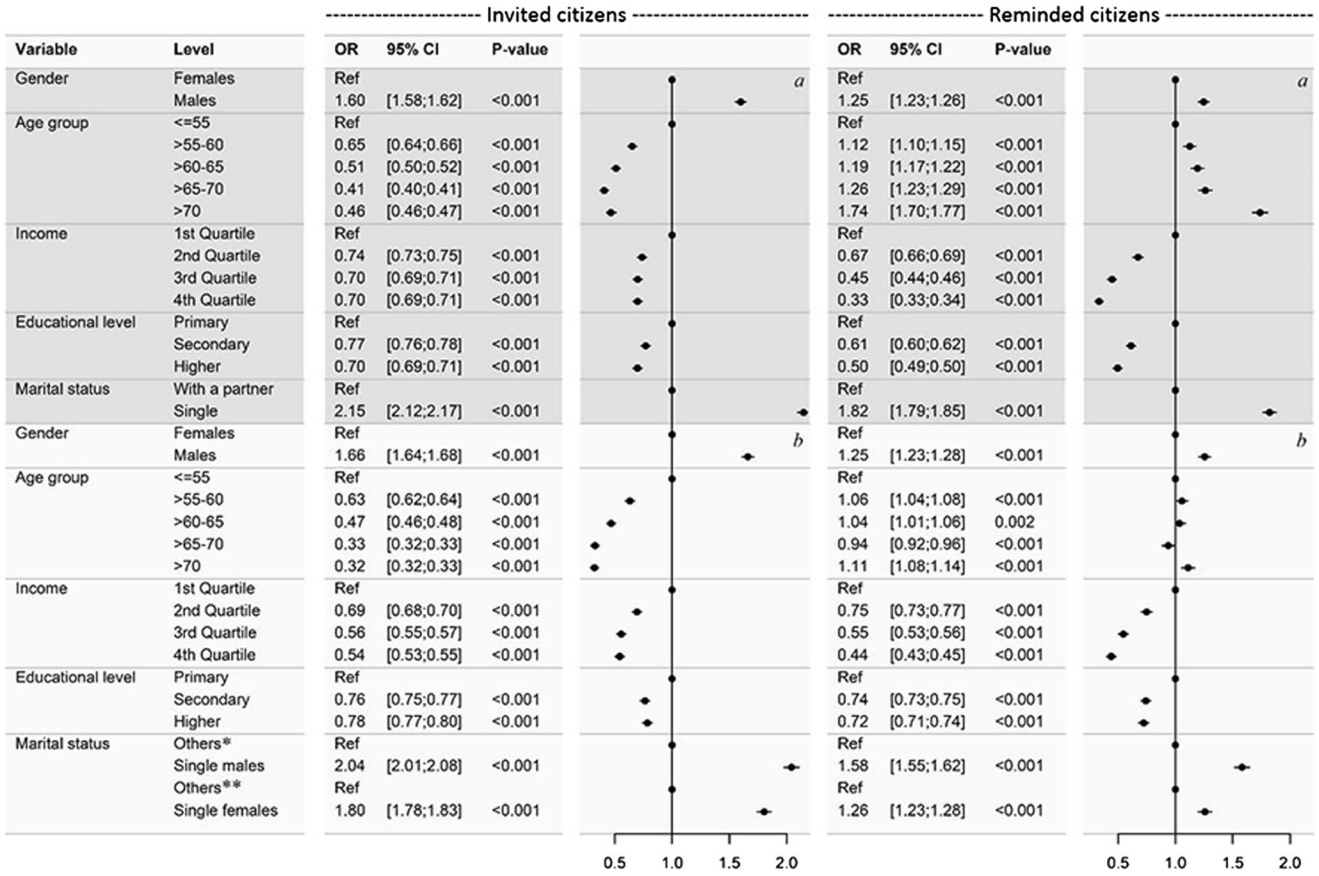

Fig. 2 Odds ratios (OR) and 95% confidence intervals (95% CI) for non-participation based on socioeconomic and demographic variables in ten univariate and two multivariate logistic regression models, among 630,041 invited and 376,395 reminded native Danes in the colorectal cancer screening program, 2014–2015. **a** Univariate logistic regression models. **b** Multivariate logistic regression model including gender, age group, income, educational level and design variables combining gender and marital status. *Others as a reference for single males include single women, women with a partner and men with a partner. **Others as a reference for single females include single men, men with a partner and women with a partner

demographic subgroups respond differently to invitations and reminders, colorectal cancer screening programmes may benefit from targeting the type of invitation and reminders to sociodemographic groups of recipients. Even though interactions were present, and immigrant populations were therefore analysed separately, the patterns of odds were similar in those populations, compared to native Danes.

Strengths and limitations

The information used in this study origins from administrative registers. Due to the quality and validity of these registers [12–17], the risk of information bias is limited, and the registers made it possible to include individual data for demographic and socioeconomic variables. The sample size ensured precise risk estimates, as it included all individuals invited in 2014–2015 with complete information. The fact that only 2.50% were excluded due to missing data, the inclusion of the complete population of invited citizens in the years of 2014–2015 and the complete follow-up using the registers limit the risk of selection bias substantially. To limit the risk of overadjustment and unidentified effect modifications, interactions were investigated, stratification by immigration status was performed and marital status was included as design variables combined with gender. Individuals were registered as participating when a sample was received at the hospital laboratory; therefore, individuals submitting samples ineligible for analysis were still registered as participating, reflecting the intention to participate.

As invited citizens are not required to submit their sample within a specific timeframe, there is a risk of misclassification, as they could participate with a long latency. However, this is unlikely to be the case as individuals were invited during 2014–2015 and follow-up for participation continued until 6 July 2016. This timeline gave invited citizens at least 5 months to submit their sample. There is a possibility that some of the

reminded individuals would have participated even without the reception of a reminder, but the median reaction time was 24 days from the invitation to participation, and the reminders were scheduled 46 days after invitation. Within 42 days after the initial invitation, 95% of participants had participated, suggesting that this problem may be limited. Furthermore, those who did not participate before they had received a reminder, but did so after, were not included as non-participants in the analyses of invited citizens and should, therefore, not affect those results. The reference group in the regression models for invited citizens with no reminder was identical with the reference group in the regression models for reminded citizens.

Conclusion

The distribution of electronic reminders for colorectal cancer screening increased overall participation. The inequalities in participation based on socioeconomic status were all increased except for a minor reduction in the gap between the first and second income quartiles. Demographic inequalities were, on the contrary, maintained or were reduced; furthermore, especially the inequalities in participation based on age were substantially reduced. Electronic reminders are an effective way to increase participation, but differences related to income and education are increased after reminders, increasing overall social inequality. Enhanced or subgroup-targeted reminder letters should be considered to help reduce the social inequalities.

Compliance with ethical standards

The current study was approved by the Danish Data Protection Agency (Ref. 2008-58-0028, 2016-34). All data in the study were linked and stored in computers held by Statistics Denmark. Data were made available with de-identified personal information. This study only publishes aggregated statistical analyses and results.

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval Retrospective anonymized register-based studies do not require written informed consent and ethical approval [28]. This article does not contain any studies with human participants or animals performed by any of the authors.

Appendix

Table 2 Participation proportions by socioeconomic and sociodemographic subgroups, Western immigrants

Variable	Participating after first invitation ($n = 9668$)	Participating after reminder ($n = 3591$)	Non-participating ($n = 7437$)	Total ($n = 20,696$)
Gender				
Female	5412 (49.6)	1931 (17.7)	3561 (32.7)	10,904
Male	4256 (43.4)	1660 (17.0)	3876 (39.6)	9792
Age groups				
< =55	2333 (36.2)	1473 (22.8)	2645 (41.0)	6451
> 55–60	1489 (44.6)	606 (18.1)	1248 (37.3)	3343
> 60–65	1639 (49.3)	511 (15.4)	1172 (35.3)	3322
> 65–70	1753 (53.9)	478 (14.7)	1021 (31.4)	3252
> 70	2454 (56.7)	523 (12.1)	1351 (31.2)	4328
Income				
1st quartile	2526 (42.4)	818 (13.7)	2614 (43.9)	5958
2nd quartile	2554 (50.6)	739 (14.6)	1756 (34.8)	5049
3rd quartile	2313 (48.8)	937 (19.8)	1488 (31.4)	4738
4th quartile	2275 (45.9)	1097 (22.2)	1579 (31.9)	4951
Educational level				
Primary	1359 (46.0)	424 (14.4)	1171 (39.6)	2954
Secondary	4341 (47.3)	1534 (16.7)	3296 (36.0)	9171
Higher	3968 (46.3)	1633 (19.0)	2970 (34.7)	8571
Marital status				
With a partner	6855 (49.8)	2516 (18.3)	4395 (31.9)	13,766
Single	2813 (40.6)	1075 (15.5)	3042 (43.9)	6930

All proportions are described using frequencies with row percentages in parenthesis

Table 3 Participation proportions by socioeconomic and sociodemographic subgroups, non-Western immigrants

Variable	Participating after first invitation ($n = 11,903$)	Participating after reminder ($n = 4950$)	Non-participating ($n = 14,396$)	Total ($n = 31,249$)
Gender				
Female	6107 (40.1)	2577 (16.9)	6555 (43.0)	15,239
Male	5796 (36.2)	2373 (14.8)	7841 (49.0)	16,010
Age groups				
< =55	6165 (36.8)	2825 (16.9)	7761 (46.3)	16,751
> 55–60	2368 (41.9)	875 (15.5)	2410 (42.6)	5653
> 60–65	1543 (41.1)	550 (14.6)	1664 (44.3)	3757
> 65–70	973 (37.9)	366 (14.3)	1228 (47.8)	2567
> 70	854 (33.9)	334 (13.2)	1333 (52.9)	2521
Income				
1st quartile	4150 (32.7)	1745 (13.7)	6805 (53.6)	12,700
2nd quartile	4221 (41.1)	1578 (15.3)	4483 (43.6)	10,282
3rd quartile	2346 (42.7)	1056 (19.2)	2087 (38.0)	5489
4th quartile	1186 (42.7)	571 (20.6)	1021 (36.8)	2778
Educational level				
Primary	3839 (35.5)	1441 (13.3)	5525 (51.1)	10,805
Secondary	4813 (39.1)	2019 (16.4)	5484 (44.5)	12,316
Higher	3251 (40.0)	1490 (18.3)	3387 (41.7)	8128
Marital status				
With a partner	8847 (40.7)	3577 (16.4)	9323 (42.9)	21,747
Single	3056 (32.2)	1373 (14.4)	5073 (53.4)	9502

All proportions are described using frequencies with row percentages in parenthesis

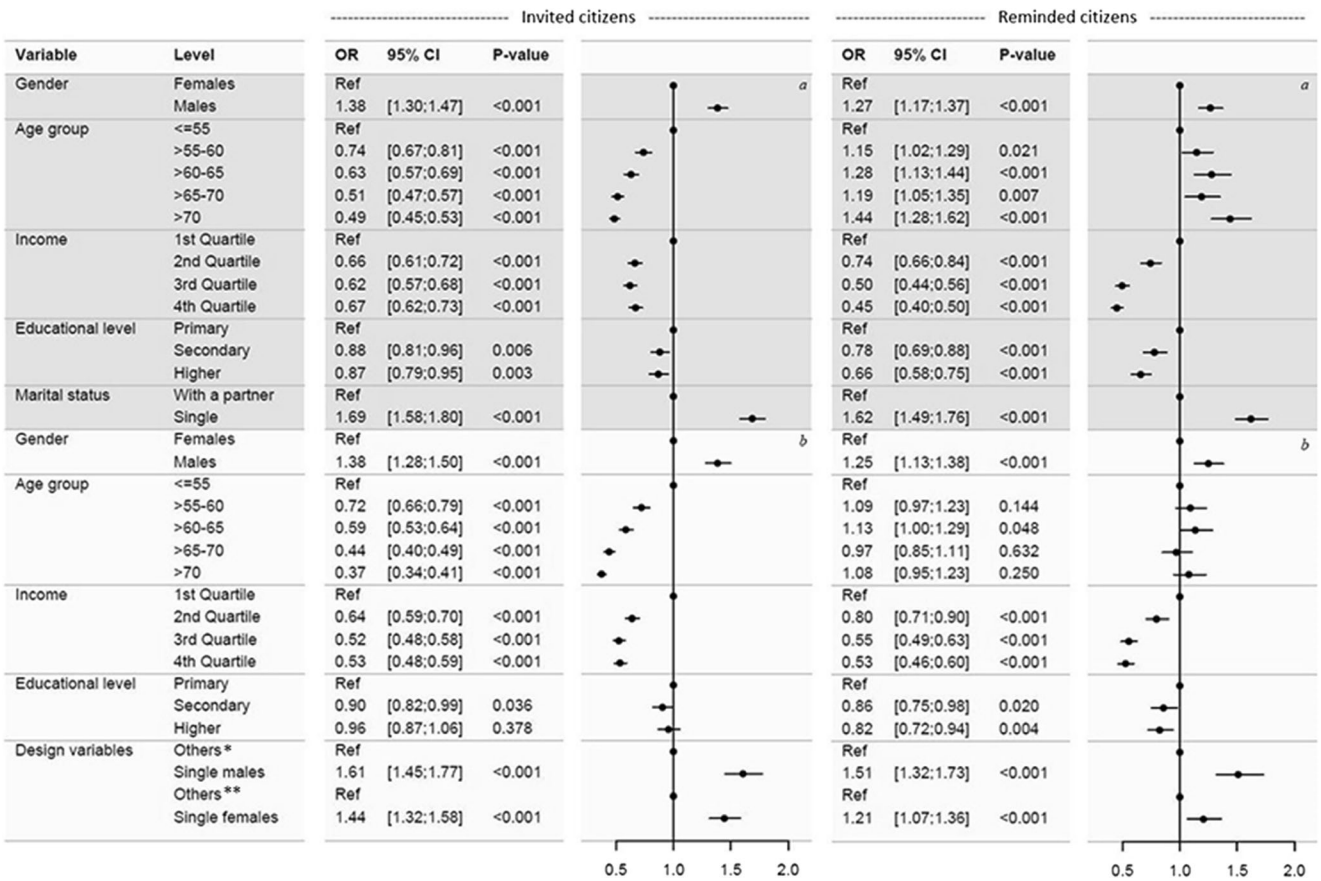

Fig. 3 Odds ratios (OR) and 95% confidence intervals (95% CI) for non-participation based on socioeconomic and demographic variables in ten univariate and two multivariate logistic regression models, among 17,105 invited and 11,028 reminded Western immigrants in the colorectal cancer screening program, 2014–2015. **a** Univariate logistic regression models. **b** Multivariate logistic regression model including gender, age group, income, educational level and design variables. *Others as a reference for single males include single women, women with a partner and men with a partner. **Others as a reference for single females include single men, men with a partner and women with a partner

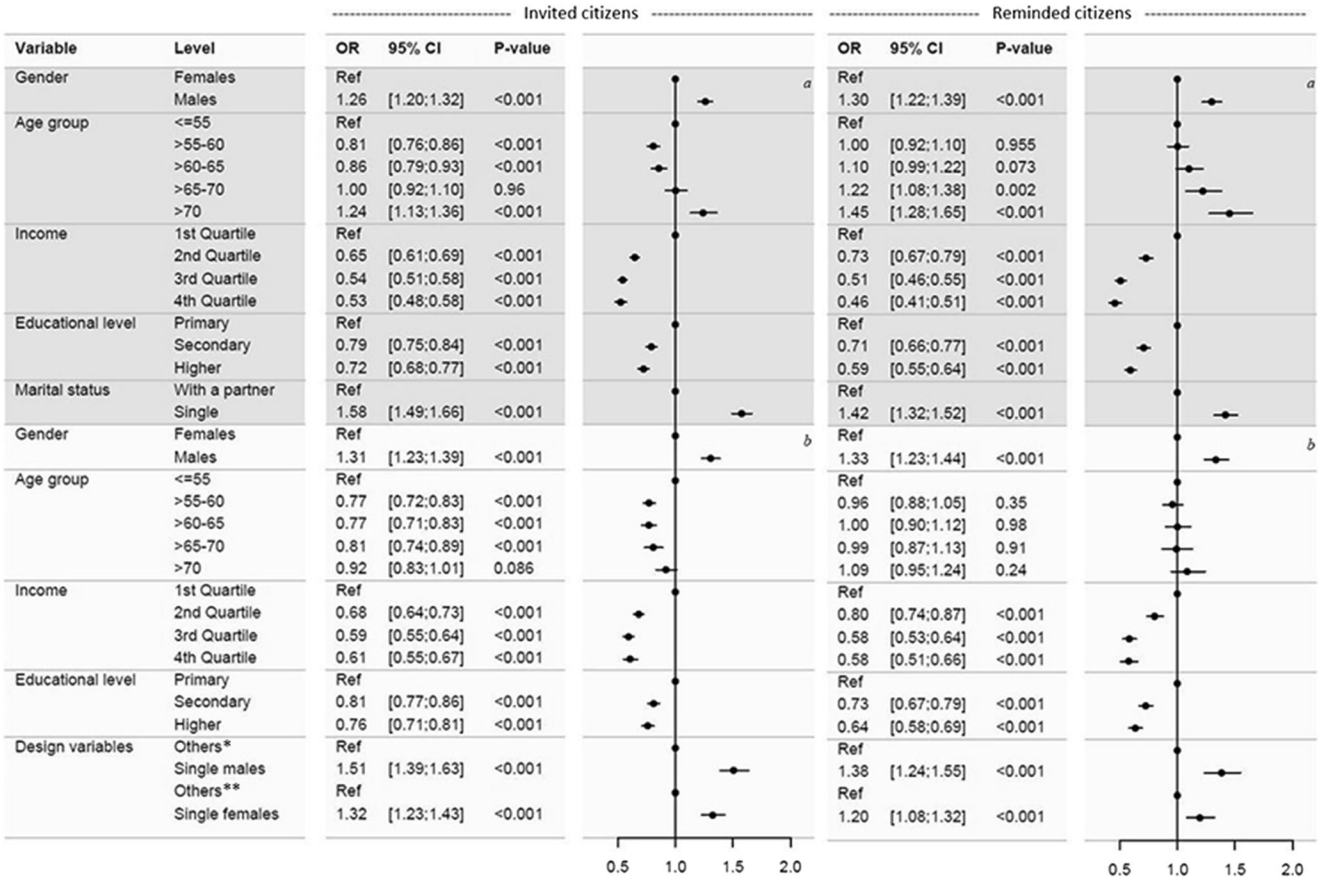

Fig. 4 Odds ratios (OR) and 95% confidence intervals (95% CI) for non-participation based on socioeconomic and demographic variables in ten univariate and two multivariate logistic regression models, among 26,299 invited and 19,346 reminded non-Western immigrants in the colorectal cancer screening program, 2014–2015. **a** Univariate logistic regression models. **b** Multivariate logistic regression model including gender, age group, income, educational level and design variables. *Others as a reference for single males include single women, women with a partner and men with a partner. **Others as a reference for single females include single men, men with a partner and women with a partner

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