Urban density differences in colorectal cancer screening participation and screening yield in The Netherlands

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ABSTRACT

Lower socioeconomic status has been associated with higher colorectal cancer incidence and lower participation in population-based screening with faecal immunochemical testing (FIT) but regional variations in participation may also exist. We analysed differences in participation and yield in colorectal cancer screening by urban density level.

Data of all invitees to the Dutch colorectal cancer screening programme in 2014–2015 were included. Primary outcomes were participation (returning FIT), FIT positive predictive value, and screening yield (advanced neoplasia detected in invitees). Differences were explored across five levels of urban density.

In total 1,873,639 screening invitees were included. FIT participation was 77.3% in the lowest versus 62.8% in the highest urban areas (RR 1.23; 95%CI 1.23–1.24). FIT positive predictive value was 58.6% in the lowest versus 55.2% in the highest urban areas (RR 1.06; 95% CI 1.04–1.09). Screening yield was also higher in the lowest (2.1%-2.3%) compared to the highest urban areas (1.8%). Compared to socioeconomic status, differences in urban density were associated with larger differences in screening participation.

In conclusion, participation is lower and fewer cases of advanced neoplasia are detected in areas with a high urban density in the Dutch colorectal cancer screening programme. Differences in urban density could be used in tailoring regional strategies to target barriers in colorectal cancer screening.

1. Introduction

Colorectal cancer (CRC) is the second most common cause of cancer-related death. (Ferlay et al., 2018) Population screening for CRC is effective in reducing CRC-related morbidity and mortality by the detection of CRC in an early stage and the removal of its precursor lesions. (Shaukat et al., 2013) Organised screening programmes have been implemented across the world. Most of these use faecal immunochemical tests (FIT) as triage for colonoscopy. (Schreuders et al., 2015) Key performance indicators of organised CRC screening programmes are participation and screening yield (Malila et al., 2012;44 Suppl 3:SE31-48.). Participation rates have been shown to vary both between

countries as well as across subpopulations within countries, a clear example being groups varying in socioeconomic status. (de Klerk et al., 2018).

The Dutch nationwide CRC screening programme started in 2014. Two years after its implementation, continuous monitoring showed that participation with FIT was 72% (AvLEM, 2016). Despite this high participation rate, differences in participation within the population have been observed. Recent data of the Dutch CRC screening programme showed, for example, that participation differs by socioeconomic status. In the population with the highest socioeconomic status (quintile 1) 73.9% participated, versus 75.1% in quintiles 2 and 3, and 73.0% in quintile 4. Participation was distinctly lower in the subpopulation with

the lowest socioeconomic status: 67.0% in quintile 5. (Unpublished results of co-authors IL and ET). Socioeconomic status has also been associated with a higher CRC incidence (Oliphant et al., 2011; Tweed et al., 2018). A lower participation rate among specific groups, in combination with a higher CRC incidence, may lead to a widening of health inequalities within a population when implementing a screening programme. To avert this, tailored invitation strategies for CRC screening may be considered, removing barriers towards participation.

Socioeconomic status is not the only identifiable determinant of participation differences in screening populations. (Deding et al., 2017; Jäntti et al., 2021) Population density, for example, has also been related to screening participation and yield. In England, screening participation was lowest in the most urban regions while the proportion of positive faecal tests in urban regions was higher compared with more rural areas. (Hirst et al., 2018) In contrast, screening participation in major cities in Australia exceeded participation in remote areas. (Sun et al., 2018) Data from The Netherlands, a small country with nearby healthcare facilities available for most inhabitants, could add relevant insights on associations between urban density on screening participation and yield.

We analysed data collected in the Dutch population CRC screening programme to assess if population density levels are associated with screening uptake, FIT positive predictive value (PPV), and screening yield. We additionally compared these differences with the observed variation by socioeconomic status.

2. Methods

2.1. Study design

In the Netherlands, the national CRC screening programme using biennial FIT started in 2014, with a gradual roll-out by age within a period of five years. The target population eventually consists of individuals aged 55 to 75 years.. Data were collected between 2014 and 31 March 2016 and included only first-time invited individuals aged 63, 65, 67, 75 and 76 years old in 2014 and individuals aged 61, 63, 65, 67, 69 and 75 years old in 2015 were invited, due to the gradual roll-out of the programme.

All invitees received a FIT at home (FOB-Gold, Sentinel, Italy). Initially, FITs were analysed at a cutoff of 15 µg Hb/g faeces. Based on real-time monitoring results during the first half year of the programme, the cutoff was changed from 15 µg Hb/g to 47 µg Hb/g faeces halfway through 2014. (Toes-Zoutendijk et al., 2017) To increase homogeneity, early invitees were included in our analysis at a cutoff of 47 µg Hb/g faeces. Data collection took place through the information system of the national screening programme ("ScreenIT"). Collected data include postal code, FIT participation and colonoscopy and pathology results. Postal codes were provided in a four-digit fashion, without the two additional letters used in the Netherlands..

2.2. Urban density

Statistics Netherlands is an organisation that provides demographic data which are publicly available. For this study, information was selected on urban density (downloaded Oct 26th, 2018 from https://www.cbs.nl). All invitees were assigned to urban density quintiles, based on the urban density level of their postal code area, with quintile UD1 referring to areas with a very high urban density ($\geq 2,500$ addresses/km^2) and quintile UD5 to the least urban areas (with ≤ 500 addresses/km^2).

2.3. Socioeconomic status

Socioeconomic status levels are developed by The Netherlands Institute for Social Research (https://www.scp.nl); they are a composite score considering income, employment status and education.

Socioeconomic status scores were provided for each four-digit postal code area in 2014. All invitees were also assigned to socioeconomic status quintiles, based on the socioeconomic status level of their postal code area, with quintile SES1 representing areas with the highest socioeconomic status and quintile SES5 the lowest socioeconomic status.

2.4. Statistical analysis

We focused on participation, FIT PPV, and screening yield. Participation rates were calculated by taking the number of invitees returning a FIT relative to the total number of invitees. FIT PPV for advanced neoplasia (AN) was defined as the number of participants in whom AN was detected after a positive FIT relative to the total number of participants undergoing colonoscopy after a positive FIT. AN included advanced adenoma and/or CRC. Advanced adenoma are adenomas with $\geq 25\%$ villous component, high-grade dysplasia and/or size ≥ 10 mm. Screening yield was defined as the number of screening invitees in whom AN was detected at colonoscopy relative to the total number of invitees.

We calculated estimates of participation rates, FIT PPV and screening yield in the respective quintiles, defined by urban density. Differences in participation rates, PPV and screening yield were tested for statistical significance using Chi-square test statistics. P-values of < 0.05 were considered to indicate statistically significant differences. Relative differences between areas varying in urban density were expressed as risk ratios, with corresponding 95% confidence intervals (CI).

To assess whether urban density level better explains differences in screening participation and PPV, compared with socioeconomic status, we composed two 5×5 tables. In addition, we built two logistic models, one with urban density as the predictor and a second model with socioeconomic status as the predictor, using indicator variables. We compared goodness-of-fit of the two models, as expressed in the Akaike Information Criterion (AIC). The statistical software package SPSS (IBM Corp., New York; version 25) was used for all analyses.

2.5. Visualization

Combining our data with publicly available geoinformation systems data, or shapefiles, enabled us to visualize regional differences in a map of the Netherlands (downloaded on 30th August 2019) using ArcGIS version 10.3.1 software (ESRI, United States). Color-coded maps were created to visualize regional differences in urban density.

2.6. Ethics approval and consent to participate

No ethical approval was required for using the national screening monitoring data. All data are anonymous. All invitees to the Dutch national CRC screening programme consented to the use of their data for monitoring the programme and for scientific research, unless they had explicitly opted out (9.2% in 2014 and 8.8% in 2015). (Bevolkingsonderzoek darmkanker: Monitor, 2014; Darmkanker, 2015).

3. Results

3.1. Invitees, urban density levels and socioeconomic status

A total of 1,873,639 invitees were included. Fig. 1 shows the urban density level per postal code area. Table 1 shows the number of postal code areas, number of invitees and socioeconomic status per quintile of urban density level.

3.2. Differences by urban density level

Participation with FIT was higher in the most rural area UD5 (77.3%) than in areas with a very high urban density UD1 (62.8%) (RR 1.23; 95% CI 1.23 to 1.24; Table 2). Screening yield was significantly higher in all
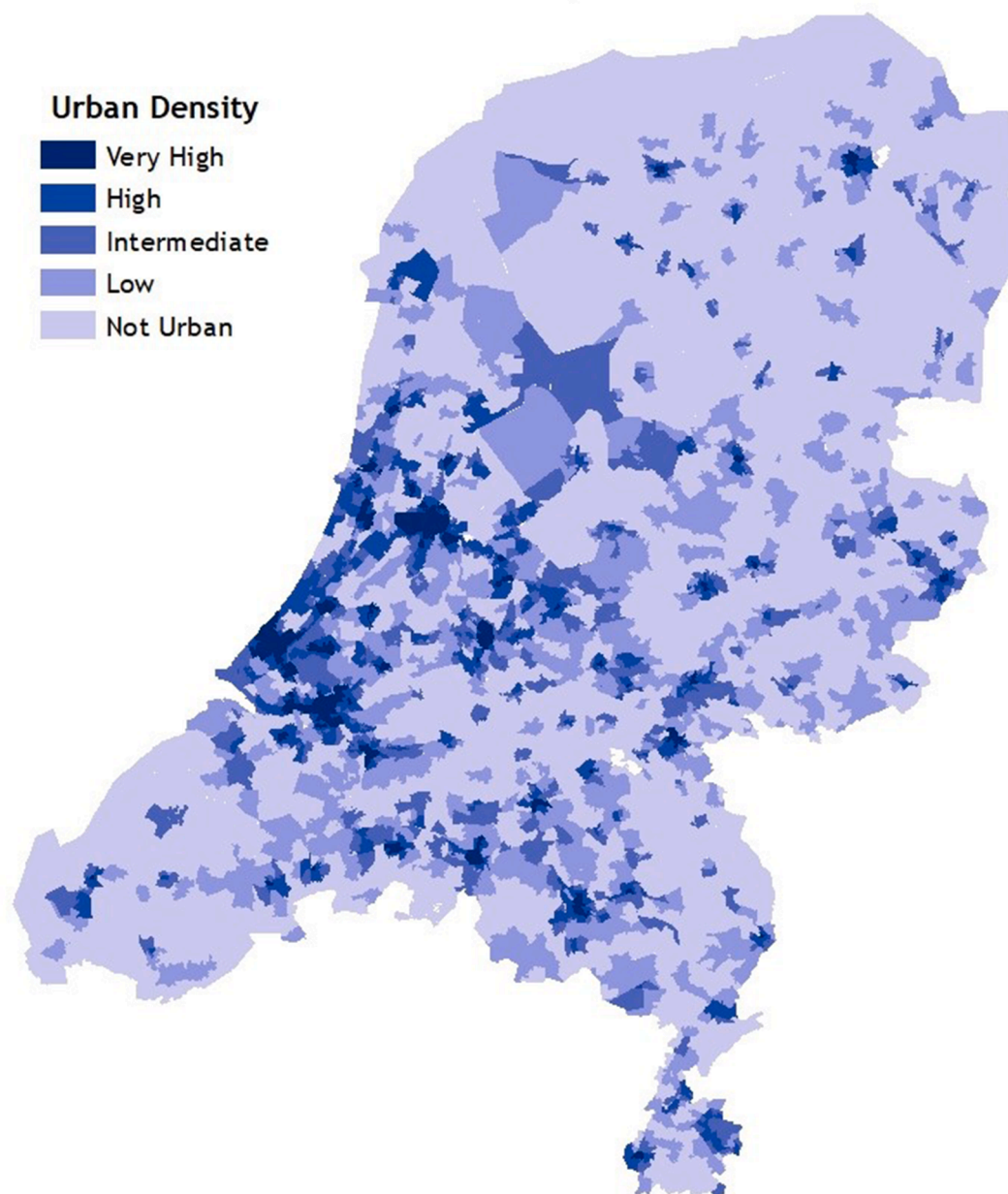
Fig. 1. Urban density level per postal code in The Netherlands.

Table 1
Invitees and socioeconomic status per urban density level.

		Number of postal code areas	Number of invitees	Mean SES level
Urban density level	UD1	387	320,791	3.35
	UD2	552	471,773	3.22
	UD3	475	362,928	2.71
	UD4	566	375,663	2.63
	UD5	2037	342,509	2.67

UD1 Very high urban density ($\geq$2500 addresses/km^2)
UD2 High urban density (1500–2500 addresses/km^2)
UD3 Intermediate urban density (1000–1500 addresses/km^2)
UD4 Low urban density (500–1000 addresses/km^2)
UD5 Very low urban density ($\leq$500 addresses/km^2)
*SES: socioeconomic status (Quintile 1 is the highest SES level and 5 is the lowest SES level)

regions (2.1–2.3%) compared to the region with the highest urban density UD1 (1.8%) (2.1–2.3%) (RR 1.31; 95% CI 1.27 to 1.36; Table 2). A comparable trend was seen in FIT PPV (Table 2). In areas with a very low urban density the PPV was 58.6% compared to 55.2% in areas with a very high urban density (RR 1.06; 95% CI 1.04 to 1.09). The PPV trend is reflected in the proportion of invitees in whom AN is detected.

3.3. Participation differences: Urban density level versus socioeconomic status

Table 3 (and absolute data in Supplementary table A.1) shows the gradient in participation level with urban density, across levels of socioeconomic status. At each urban density level, the lowest participation level was observed in the group with the lowest socioeconomic status. Similarly, in each socioeconomic status category, the lowest participation level was seen in the group with the highest urban density levels. Nevertheless, the gradient over levels of socioeconomic status within

Table 2
Participation and yield of AN by urban density level.

| | Participation | | | | Screening yield and PPV of AN | | | | | |
	Total FIT invitees	Participants	Participation	RR (95% CI)	Colonoscopies	AN	AN yield	RR (95%CI)	AN PPV	RR (95% CI)
UD1	320,791	201,475	62.8%	*Ref*	10,291	5681	1.8%	*Ref*	55.2%	*Ref*
UD2	471,733	338,656	71.8%	1.14 (1.14–1.15)	17,725	10,065	2.1%	1.21 (1.17–1.25)	56.8%	1.03 (1.01–1.05)
UD3	362,928	271,576	74.8%	1.19 (1.19–1.20)	14,103	8187	2.3%	1.27 (1.23–1.32)	58.1%	1.05 (1.03–1.08)
UD4	375,663	289,216	77.0%	1.23 (1.22–1.23)	14,906	8707	2.3%	1.31 (1.27–1.35)	58.4%	1.06 (1.045–1.08)
UD5	342,509	264,845	77.3%	1.23 (1.23–1.24)	13,578	7952	2.3%	1.31 (1.27–1.36)	58.6%	1.06 (1.04–1.09)

UD1 Very high urban density ($\geq$2500 addresses/km^2)
UD2 High urban density (1500–2500 addresses/km^2)
UD3 Intermediate urban density (1000–1500 addresses/km^2)
UD4 Low urban density (500–1000 addresses/km^2)
UD5 Very low urban density ($\leq$500 addresses/km^2)
FIT: fecal immunochemical test; AN: advanced neoplasia; PPV: positive predictive value; RR: risk ratio; CI: confidence interval

Table 3
Participation by five levels of urban density and socioeconomic status.

Participation %	SES1	SES2	SES3	SES4	SES5
UD1	65.5	64.4	63.8	64.1	58.6
UD2	73.4	73.0	72.6	71.1	67.6
UD3	75.8	75.4	75.0	74.9	70.0
UD4	76.7	77.2	77.7	76.9	73.3
UD5	76.6	77.7	77.7	76.5	73.8

UD1 Very high urban density ($\geq$2500 addresses/km^2)
UD2 High urban density (1500–2500 addresses/km^2)
UD3 Intermediate urban density (1000–1500 addresses/km^2)
UD4 Low urban density (500–1000 addresses/km^2)
UD5 Very low urban density ($\leq$500 addresses/km^2)
*SES: socioeconomic status:
SES1 Very high socioeconomic status to SES 5 Very low socioeconomic status

separate urban density categories is less pronounced. When a logistic model was fitted to these data, using urban density as the explanatory variable (five levels), the Akaike Information Criterion (AIC) was 850. When a similar model was fitted using only socioeconomic status as the explanatory variable (five levels), the AIC was 3450. The better fit of the urban density model indicates that urban density is better able to explain differences in participation than socioeconomic status.

3.4. FIT positive predictive value: Urban density level versus socioeconomic status

In Table 4 (and Supplementary table A.2) we see a comparable pattern. When a logistic model was fitted to these data, using only urban density as the explanatory variable (five levels), the AIC was 234. When a similar model was fitted using only socioeconomic status as the explanatory variable (five levels), the AIC was 243. This indicates a

Table 4
FIT positive predictive value by five levels of urban density and socioeconomic status.

PPV %	SES1	SES2	SES3	SES4	SES5
UD1	54.6	57.4	58.3	55.8	53.2
UD2	55.2	56.2	58.3	57.3	56.6
UD3	57.1	58.7	58.9	57.4	58.4
UD4	58.2	57.7	58.0	60.0	58.1
UD5	60.1	57.3	58.6	60.2	55.9

UD1 Very high urban density ($\geq$2500 addresses/km^2)
UD2 High urban density (1500–2500 addresses/km^2)
UD3 Intermediate urban density (1000–1500 addresses/km^2)
UD4 Low urban density (500–1000 addresses/km^2)
UD5 Very low urban density ($\leq$500 addresses/km^2)
*SES: socioeconomic status:
SES1 Very high socioeconomic status to SES 5 Very low socioeconomic status

slightly better explanatory power of urban density. Adding socioeconomic status to urban density as an additional predictor did not significantly improve goodness-of-fit (AIC 236, p = 0.84).

4. Discussion

In this study, invitees living in areas with a high urban density were less likely to participate in screening, compared to invitees living in more rural areas. This lower participation rate is reflected in a lower detection rate of AN in urban areas. In those undergoing colonoscopy after a positive FIT, slightly fewer AN were detected in urban areas compared with rural areas.

The following limitations should be considered when interpreting our results. We used continuously gathered monitoring data from the first two years of the Dutch national CRC screening programme (2014–2015) which included invitees aged 61, 63, 65, 67, 69, 75 and 76 years old. We cannot exclude that differences in participation have changed since, for example due to an increased awareness and more knowledge about screening after implementation of the programme or by inviting younger age groups. Participation in younger age groups is generally slightly lower, while overall participation in the recent years is relatively stable. (Bevolkingsonderzoek darmkanker: Monitor, 2014; Bevolkingsonderzoek darmkanker: Monitor, 2020).

Both socioeconomic status and urban density may influence – and are influenced by - personal and contextual factors, all of which might impact differently on our outcome measures. In The Netherlands detailed sociodemographic individual data is not available on this scale and could therefore not be used in this study. As discussed previously, area-based scores, as used here, may therefore not well reflect the personal situation of each screening invitee living in that area. (Hirst et al., 2018; Demissie et al., 2000).

A small proportion of screening invitees could not be included in our analyses of socioeconomic status because their postal code was not included in the Dutch social status scores, leading to a discrepancy between the total number of invitees in Table 2 and the numbers in Supplementary table 1 and 2.

The 14.5% difference in participation between the most urban and rural regions exceeds the recently shown participation differences in England. (Hirst et al., 2018) In the study from Hirst et al, the most densely populated area, London, witnessed a screening uptake of 42.3%, compared with 50.2% to 54.5% in the other four English screening regions. A contrasting trend was observed in Australia, where participation in major cities (33.4%) was higher than in remote (27.9%) or very remote areas (25.0%), although this effect was strongly related to a lower uptake among indigenous populations who predominantly live in the remote regions of Australia. (Sun et al., 2018) Large differences in the definition of 'remote area' in Australia and 'rural area' in The

Netherlands make meaningful comparisons between these two countries hazardous. Differences associated with urban density, as observed here, also go beyond that of other known factors associated with lower uptake in The Netherlands, such as socioeconomic status. (Hirst et al., 2018; von Wagner et al., 20112011).

Relatively reassuring is the fact that in the areas with the lowest participation, the urban areas, the screening yield of AN is lower than in the rural areas in The Netherlands. This is in contrast to previous evidence from England where the proportion of positive faecal tests was higher in London: 2.6% versus 1.7% to 2.1% in other English regions. (Hirst et al., 2018) Moreover, in Ireland CRC risk was higher in urban than in rural areas (males RR 1.14, 95% CI 1.09 to 1.18; females RR 1.04, 95% CI 1.00 to 1.09). (Sharp et al., 2014) Although The Netherlands is a relatively small country, with limited travel times and nationwide access to healthcare, urban areas have more health care facilities. In Amsterdam for example, there are six hospitals and several commercial colonoscopy clinics. We can therefore not exclude that individuals with gastrointestinal symptoms in large cities seek medical care more often, and at an earlier stage, compared to those in rural districts, leading to a lower yield in screening.

The differences reported here are most likely not a causal effect of density itself, but of factors associated with it. Urban populations vary more in ethnicity, (cultural) beliefs, trust in government, and education levels. All these factors have been shown to be associated with CRC incidence and health behaviors. (Bryant and McGregor, 2008; Honein-AbouHaidar et al., 2013) The widely used area-based data on socioeconomic status lacks the possibility to adjust for individual confounding factors for participation differences in CRC screening. A promising approach for future interventions in CRC screening might be geodemographic segmentation to identify urban 'hotspots' of low screening uptake. Other than classifying subgroups with similar individual characteristics, such as age, gender and socioeconomic status, geodemographic segmentation is closely linked to social marketing principles. It includes a wide range of selected contextual variables, such as preferences, beliefs and behaviors. (Nnoaham et al., 2010) By identifying one or more predominant characteristics in areas with the smallest uptake, a more robust insight in local conditions could be achieved, and more effective strategies could be designed, to target screening barriers. (Nnoaham et al., 2010; Openshaw and Blake, 1995).

The relative impact of geodemographic segmentation on CRC screening uptake was compared to the index of multiple deprivation (IMD) in a study in the South of England. Participation differences could be better characterized by geodemographic factors, such as high ethnic variability, a high proportion of single pensioner households, and more rental houses than by the IMD alone. (Nnoaham et al., 2010) Recently, Ramai et al used geospatial segmentation in Brooklyn (New York) to identify and characterize small urban areas with the lowest uptake of FIT-screening. (Ramai et al., 2019) Using a 'hot-spot analysis' they identified three clusters of very low uptake. On this small level, interventions such as promotion by community health workers or interactive telephone calls might be effective and feasible, in contrast to comparable strategies on national level. (Schaefer Solle et al., 2017; Wong et al., 2017).

5. Conclusion

We observed that urban density is associated with differences in participation and yield in CRC screening, and that these differences exceed those associated with postal code differences in socioeconomic status. In the future, targeted strategies could be developed, focusing on urban hot spots of low uptake, possibly identified by methods that include multiple geodemographic variables known to affect CRC screening participation behavior.

6. Data availability

Data are held by the Dutch Foundation of Population Screening, delegated by the Dutch Ministry of Public Health, Welfare and Sport in a database 'ScreenIT'. Access to the monitoring data by external parties is governed by the Foundation of Population Screening, see: https://www.rivm.nl/bevolkingsonderzoek-darmkanker/professionals/wetensc happelijk-onderzoek.

CRediT authorship contribution statement

Clasine M. de Klerk: . **Manon van der Vlugt:** Supervision. **Bente A. Smagge:** . **Esther Toes-Zoutendijk:** . **Iris Lansdorp-Vogelaar:** Supervision. **Evelien Dekker:** Supervision. **Patrick M. Bossuyt:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2022.101791.

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