ELSEVIER

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr



The association between health literacy and colorectal cancer screening uptake in a publicly funded screening program in Denmark: Cross-sectional study

Petricia Marie Horshauge^{a,b,*}, Pernille Gabel^a, Mette Bach Larsen^a, Pia Kirkegaard^a, Adrian Edwards^{a,c}, Berit Andersen^{a,b}

ARTICLE INFO

Keywords: Health literacy Mass screening Colorectal cancer Patient participation

ABSTRACT

There are multiple reasons for not participating in colorectal cancer screening, but the role of health literacy in screening uptake is not well understood.

The aims of this study were to determine the association between health literacy and colorectal cancer screening uptake and to explore whether socioeconomic and -demographic characteristics and worry and attitude variables modify this association.

In a cross-sectional study, 10,030 53–74-year-old randomly selected citizens resident in Central Denmark Region received a questionnaire assessing health literacy using the European Health Literacy Survey Short Scale 16-item. Data on colorectal cancer screening uptake were obtained from the Danish Colorectal Cancer Screening database, and socioeconomic and -demographic data were linked from Statistics Denmark.

The response rate was 71% (n = 7142). Odds ratio (OR) for uptake was 1.06 (95% confidence interval (CI): 0.96, 1.19) for problematic health literacy and 1.00 (95% CI: 0.87, 1.16) for inadequate health literacy, when using adequate health literacy as the reference value. The association was not modified by socioeconomic or -demographic characteristics, worry or attitude.

No association was found between health literacy and colorectal cancer screening uptake. Future research needs to clarify which dimensions of health literacy may predict screening uptake and how it is best measured.

1. Introduction

Colorectal cancer (CRC) represents a substantial part of the global cancer burden. It is currently the third most common type of cancer among men and the second most common type of cancer among women. In developed countries the age-standardized mortality rate is 12.8 and 8.5 per 100,000 men and women per year, respectively (Bray et al., 2018).

CRC screening programs have been widely implemented across the world as screening for CRC can detect precancerous polyps and early-stage cancers, and thereby reduce CRC mortality (Maida et al., 2017). CRC screening based on the Fecal Occult Blood Test (FOBT) reduces mortality by 25% among those participating at least once (Levin et al., 2018; Zhang et al., 2017). However, the Fecal Immunochemical Test

(FIT) is superior to the FOBT in detecting CRC and is now the favored screening test (Parra-Blanco et al., 2010).

The overall efficiency of screening relies on high uptake in the target population (Sundhedsstyrelsen, 2014). The minimal desirable CRC screening uptake is considered to be 65% by the European Commission (Moss et al., 2012) and 80% by the American Cancer Society (American Cancer Society, 2017). CRC screening uptake in screening programs across the world varies between 16 and 68% (Njor et al., 2018; Hirst et al., 2018; de Moor et al., 2018; Navarro et al., 2017 May 28) and thus, CRC screening uptake remain below the desired standards.

Screening non-participation is associated with lower socioeconomic status as assessed by dimensions such as income, educational level, and employment status (Gimeno Garcia, 2012; Wools and Dapper, 2015;

E-mail address: pehors@rm.dk (P.M. Horshauge).

^a Department of Public Health Programmes, Randers Regional Hospital, Denmark

^b Department of Clinical Medicine, Aarhus University, Denmark

^c Division of Population Medicine, School of Medicine, Cardiff University, UK

^{*}Corresponding author at: Department of Public Health Programmes Randers Regional Hospital, Central Denmark Region Skovlyvej, 15 8930 Randers NØ,

Von Wagner et al., 2011; Larsen et al., 2017). Likewise, other sociodemographic characteristics including younger age, male sex, living alone, and belonging to an ethnic minority are also associated with lower CRC screening uptake (Gimeno Garcia, 2012; Wools and Dapper, 2015; Von Wagner et al., 2011; Larsen et al., 2017).

In recent years, health literacy has been suggested as a possible factor influencing CRC screening uptake (White et al., 2008; Arnold et al., 2012; Kobayashi et al., 2014; Solmi et al., 2015; Guerra et al., 2005; Miller et al., 2007; Peterson et al., 2007; Wangmar et al., 2018). "Health literacy is linked to literacy and entails people's knowledge, motivation and competences to access, understand, appraise, and apply health information in order to make judgments and take decisions in everyday life concerning healthcare, disease prevention and health promotion to maintain or improve quality of life during the life course" as defined by Sørensen et al. (2012). The concept of health literacy is of particular interest as health literacy has been suggested as a potential modifiable factor by which health disparities, such as inequalities in CRC screening, can potentially be reduced (Mantwill et al., 2015; Stormacq et al., 2018). However, literature regarding the association between health literacy and CRC screening uptake is inconsistent. Some studies conclude that inadequate/limited health literacy is associated with lower screening uptake (White et al., 2008; Arnold et al., 2012; Kobayashi et al., 2014; Solmi et al., 2015), whereas other studies find no association (Guerra et al., 2005; Miller et al., 2007; Peterson et al., 2007; Wangmar et al., 2018). Most of the previous research was based on small study populations and was primarily conducted in the US (Arnold et al., 2012; Guerra et al., 2005; Miller et al., 2007; Peterson et al., 2007), where CRC screening is not publicly funded and not organized in a national screening program with regular screening invitations. Furthermore, most previous studies use self-reported screening behavior as their outcome (White et al., 2008; Arnold et al., 2012; Kobayashi et al., 2014; Solmi et al., 2015; Guerra et al., 2005; Miller et al., 2007; Peterson et al., 2007), and this approach has shown only moderate validity (Dodou and de Winter, 2015) as it is potentially vulnerable to recall bias and tends to overestimate screening uptake (Lofters et al., 2015). Only one large study conducted in Sweden used registry-based data on CRC screening uptake (Wangmar et al., 2018).

We sought to determine the association between health literacy and CRC screening uptake in the FIT-based CRC screening program in Denmark and to explore whether socioeconomic and -demographic characteristics and worry and attitude modify this association.

2. Methods

2.1. Setting

This study was conducted during the implementation phase of the national FIT-based CRC screening program which was introduced in Denmark in 2014 and fully implemented at the end of 2017. All citizens were scheduled to be invited once during 2014–2017. Invitation order of those who were 50–74 years on January 1st 2014 was decided by randomization of birth months. Citizens who turned 50 or 75 years during the implementation phase were invited within a few months before their birthday if not invited earlier. Along with the screening invitation, citizens received a screening kit for home-based self-sampling and a pre-stamped return envelope. Screening reminders were sent out to non-participants after 45 days.

The screening program is organized nationally and administered by each of the five Danish regions. This study was conducted in the Central Denmark Region which is the second largest region in Denmark with approximately 1.3 million citizens, corresponding to 23% of the total Danish population (Statistics Denmark, 2019a). Central Denmark Region hosts the second largest city in Denmark and more rural areas.

2.2. Study design and population

A cross-sectional study among citizens about to be invited for CRC screening during the implementation phase of the Danish CRC screening program was conducted based on baseline data from a randomized controlled trial (Gabel et al., 2019). A random sample of 10,030 residents in Central Denmark Region aged 53–74 years and randomized to be invited to CRC screening from October to December 2017 was provided by the Danish Health Data Authority on August 8th 2017. Citizens aged 50–52 years by August 2017 had been invited just before their birthday and were therefore not included in the sample.

2.3. Data collection

The population sample was identified from the Danish Civil Registration System (Pedersen, 2011), and contained information on the unique civil registration number (CPR-number) which includes information on birthday and sex.

A web-based questionnaire assessing health literacy, worries about CRC and CRC screening and attitudes toward CRC screening, was distributed to all included citizens via digital mail along with the invitation for CRC screening. A digital reminder was sent to non-respondents after two weeks, and if the citizen had not returned the questionnaire within four weeks, the citizen was offered to complete the questionnaire via the telephone (Gabel et al., 2019).

By completing the questionnaire, respondents consented to the collection of individual screening data from the Danish Colorectal Cancer Screening Database by the research group.

Questionnaire data and data on CRC screening uptake were linked with registry-based background data on socioeconomic and -demographic characteristics from Statistics Denmark using the individual CPR-number (Statistics Denmark, 2019b).

2.4. Variables

2.4.1. Questionnaire data

Health literacy was assessed using the European Health Literacy Survey Short Scale 16-item (HLS-EU-Q16) which is based on the original European Health Literacy Survey 47-item (HLS-EU-Q47) (Sørensen et al., 2015). The HLS-EU-Q47 is considered too long for screening purposes, and hence a shortened version was developed based on Item Response Theory and Rash Analysis (Okan et al., 2019). The questionnaire is based on the HLS-EU consortium's model of health literacy capturing four dimensions of health literacy; the way people access, understand, appraise and apply information (Sørensen et al., 2012). However, this short version measures overall health literacy and not each sub-dimension.

According to the manual, health literacy was categorized as 'in-adequate' (0–8 points), 'problematic' (9–12 points), or 'adequate' (13–16 points). Missing items were scored 0, and the total score was coded as missing if more than two items were missing and hence, excluded from the analyses. The manual and the translated scale were obtained from another research group who had previously translated the scale into Danish using forward–backward translation (Beaton et al., 2000). The Danish version of HLS-EU-Q16 is currently under validation as an independent scale.

Worries about CRC and CRC screening were assessed by three statements "I get worried when I think of CRC", "I get scared when I think of CRC" and "I am afraid they will find cancer if I participate in CRC screening" to which the citizens answered on a five-point Likert scale ranging from strongly disagree to strongly agree. This approach has been used previously to assess cancer worries (Hay et al., 2005). Scoring ranged from 3 to 15 points with higher scores indicating higher levels of worry. The total score was coded missing if one or more answers were missing.

Attitudes toward CRC screening were assessed in four items

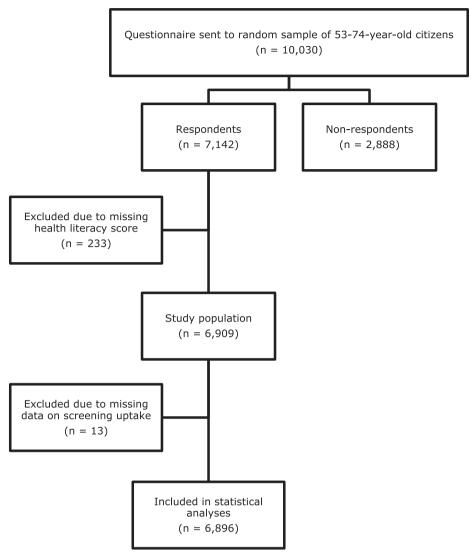


Fig. 1. Inclusion flow chart.

formulated as statements "For me, having the screening test for CRC will be..." followed by a seven-point scale with answers ranging from beneficial to harmful (item 1), important to unimportant (item 2), good thing to bad thing (item 3), pleasant to unpleasant (item 4). The total score ranged from 4 to 28 points with higher scores indicating more positive attitudes toward CRC screening. If one or more items were missing the total score was coded as missing, according to the manual (Marteau et al., 2001). The scale was translated into Danish by the research group using forward-backward translation (Beaton et al., 2000).

2.4.2. CRC screening uptake

Individual level data on CRC screening uptake were obtained from the Danish Colorectal Cancer Screening Database (Thomsen et al., 2017). Uptake was determined at 45 days after receiving the screening invitation because the intervention in the randomized controlled trial from which these data originates, was distributed to approximately half of this study population along with the screening reminder at this time (Gabel et al., 2019).

2.4.3. Background data

Ethnicity was categorized as Danish, Western immigrant (EU, Andorra, Australia, Canada, Iceland, Lichtenstein, Monaco, New Zealand, Norway, San Marino, Switzerland, USA, and the Vatican

state), or Non-Western immigrant (others) according to the classification defined by Statistics Denmark (Statistics Denmark, 2019c). Marital status was dichotomized into married/cohabitant or living alone. Based on tertiles, the equivalent disposable income (Statistics Denmark, 2019d) was categorized as < €30,000 (lowest 33%), €30,000–€43,000 (33-66%) or ≥€43,000 (highest 33%). Education was categorized 10 years (lower educational attainment; 1–2), $> 10-\le 15$ years (medium educational attainment; level 3–5), or > 15 years (higher educational attainment; level 6-8) according to the International Standard Classification of Education (ISCED 2011) (UNESCO Institute for Statistics, 2011). Occupation was categorized as self-employed/Chief executive, employed, not employed/welfare benefits, retired, or others. According to the classification defined by Statistics Denmark, population area was categorized as densely populated area, intermediately populated area, or thinly populated area (Statistics Denmark, 2019e).

2.5. Statistical analysis

Differences between questionnaire respondents and non-respondents were tested using Pearson's Chi^2 test for categorical variables and Kruskal Wallis' non-parametric test for mean of age since age was not normally distributed.

The association between health literacy and CRC screening uptake

was assessed by logistic regression analyses, using uptake as the dichotomous dependent outcome and health literacy as the categorical independent outcome. Analyses were adjusted for sex, age, ethnicity, and marital status. Both crude and adjusted Odds ratios (OR) with 95% confidence intervals (CI) was presented, using adequate health literacy as the reference value.

To determine if the association between health literacy and CRC screening uptake was modified by sex, marital status, education, occupation or worry and attitude variables, stratified ORs (crude and adjusted) were calculated and the hypothesis of no effect modification was tested using the Wald test.

All statistical analyses were undertaken with Stata/SE 15.1 (StataCorp LP, College Station, Texas, USA) at a 5% significance level.

Ethical approvals

Collection of survey and registry data was permitted by the Danish Data Protection Agency (Journal no.: 2012-58-006/Case no.: 1-16-02-94-16). Ethical clearance was achieved by the Central Denmark Region Committee on Health Research Ethics (143/2016) and the Danish Patient Safety Authorities allowed for the collection of data (Journal no.: 3-313-1729-1).

3. Results

In total, 7142 citizens (71%) answered the questionnaire of which 721 (10%) responded via telephone. A total of 6896 were included in the analyses (Fig. 1). Questionnaire respondents were more often females, of younger age and Danish ethnicity, married or cohabitant, with a higher income, 10–15 years of education, employed, and living in thinly populated areas compared to non-respondents. Differences between respondents and non-respondents were statistically significant in all background variables (Table 1).

Approximately half of the included citizens lacked adequate health literacy skills (3600/6896; 52%).

The overall CRC screening uptake among questionnaire respondents was 61% (data not shown). The OR for CRC screening uptake was not statistically significantly different between those with problematic health literacy (adjusted OR = 1.06; 95% CI: 0.96, 1.19) or inadequate health literacy (adjusted OR = 1.00; 95% CI: 0.87, 1.16) compared to those with adequate health literacy. However, there may be a tendency for those with problematic health literacy to take up screening slightly more than citizens with adequate health literacy (Table 2).

In the stratified analyses only one statistically significant association was observed. In the group "other occupation" citizens with inadequate health literacy participated less in CRC screening than citizens with adequate health literacy (adjusted OR = 0.16; 95% CI: 0.03, 0.79). No modification of the association between health literacy and CRC screening uptake was observed by sex, marital status, education or occupation or by either worry or attitude (p-values > 0.05) (Table 3).

4. Discussion

4.1. Main findings

In this study among 6896 individuals having a FIT-based CRC screening offer as part of a publicly funded screening program, less than half of the participants demonstrated adequate health literacy. Our results indicate that citizens with problematic health literacy might be more likely to take up screening compared with those with adequate and inadequate health literacy. However, the results are not statistically significant. The association between health literacy and CRC screening uptake was not modified by socioeconomic or -demographic characteristics, worry or attitude.

Table 1Socioeconomic and -demographic characteristics for questionnaire respondents and non-respondents.

	Respondents (N = 7,142; 71%) n (%) ^a	Non-respondents (N = 2,888; 29%) n (%) ^a	p-value ^b
Sex			
Male	3316 (46)	1426 (49)	
Female	3826 (54)	1462 (51)	0.007
Age (years)			
Median	63.63	63.66	0.009 ^c
Ethnicity			
Danish	6854 (96)	2611 (91)	
Western immigrant	159 (2)	87 (3)	
Non-Western immigrant Marital status	122 (2)	183 (6)	≤ 0.001
Married/Cohabitant	5484 (77)	1689 (59)	
Single	1651 (23)	1192 (41)	≤0.001
Income	1031 (23)	11)2 (41)	≥ 0.001
< €30,000	1955 (27)	1401 (49)	
€30,000-€43,000	2406 (34)	779 (27)	
≥€43,000	2781 (39)	708 (25)	≤0.001
Education	2,01 (0))	, 00 (20)	_ 0.001
≤10 years	1679 (24)	1023 (37)	
> 10-≤15 years	4849 (69)	1597 (57)	
> 15 years	530 (8)	181 (7)	≤0.001
Occupation		,	
Self-employed/Chief executive	498 (7)	182 (6)	
Employed	3135 (44)	903 (31)	
Not employed/welfare	230 (3)	155 (5)	
benefits	` '	, ,	
Retired	3194 (45)	1579 (55)	
Other	82 (1)	66 (2)	\leq 0.001
Population area			
Densely populated area	1423 (20)	651 (23)	
Intermediately populated area	2085 (29)	822 (29)	
Thinly populated area	3634 (51)	1415 (49)	0.013

^a Some columns do not sum up to 7142 due to missing values, and some percentages do not sum up to 100 because of roundings.

Table 2 Association between health literacy and CRC screening uptake (N = 6,896).

		Screening OR uptake (CI) uptake		
	n_{total}	n (%ª)	Crude ^b	Adjusted ^{c,d}
Health literacy				
Adequate	3296	1985 (60)	1 (ref)	1 (ref)
Problematic	2515	1553 (62)	1.07 (0.96, 1.19)	1.06 (0.96, 1.19)
Inadequate	1085	656 (61)	1.01 (0.88, 1.16)	1.00 (0.87, 1.16)

^a Proportion taking up screening.

4.2. Strengths and limitations

The main strength of this study was the individual level registry-based information on screening uptake from the Danish Colorectal Cancer Screening Database to avoid information bias (Thomsen et al., 2017 Feb). However, we had to rely on screening uptake within 45 days and before any reminder was received since the study was a part of a

^b Pearson's Chi² test for difference between groups.

 $^{^{\}rm c}$ Kruskall Wallis' non-parametric test for difference of means between groups.

^ь R² 0.02%.

 $^{^{\}rm c}$ Logistic regression analyses adjusted for sex, age, ethnicity, and marital status.

^d R² 2.37%.

Table 3
Stratified analyses of associations between CRC screening uptake and health literacy according to socioeconomic and -demographic characteristics and worry and attitude variables and test of effect modification.

	Adequate vs. problematic health literacy			Adequate vs. inadequate health literacy		
	n _{total}	OR uptake (CI)			OR uptake (CI)	
		Crude	Adjusted	n _{total}	Crude	Adjusted
Sex						
Male	2626	0.88 (0.76, 1.03)	0.88 (0.75, 1.03) ^a	2018	1.07 (0,88, 1.29)	1.08 (0.89, 1.32) ^a
Female	3185	0.97 (0.84, 1.12)	1.00 (0.86, 1.16) ^a	2363	0.84 (0.69, 1.04)	0.88 (0.71, 1.09) ^a
p-value ^d		0.388			0.108	
Marital status						
Married/Cohabitant	4485	0.91 (0.81, 1.03)	$0.92 (0.81, 1.04)^{b}$	3367	0.97 (0.82, 1.14)	0.96 (0.81, 1.13) ^b
Single	1320	1.01 (0.82, 1.26)	1.00 (0.80, 1.25) ^b	1011	1.05 (0.79, 1.39)	$1.04 (0.78, 1.40)^{b}$
p-value ^d		0.416			0.646	
Education						
≤10 years	1269	1.01 (0.81, 1.27)	1.02 (0.81, 1.28) ^c	986	0.98 (0.74, 1.29)	0.95 (0.72, 1.27) ^c
> 10-≤15 years	3992	0.91 (0.80, 1.04)	0.91 (0.80, 1.04) ^c	2988	1.02 (0.86, 1.21)	1.00 (0.84, 1.20) ^c
≥15 years	484	1.03 (0.71, 1.52)	1.01 (0.68, 1.50) ^c	358	0.65 (0.31, 1.38)	0.70 (0.32, 1.53) ^c
p-value ^d		0.650			0.519	
Occupation						
Self-employed/Chief executive	443	1.09 (0.74, 1.61)	1.08 (0.73, 1.61) ^c	305	1.37 (0.78, 2.40)	1.35 (0.76, 2.41) ^c
Employed	2636	0.96 (0.82, 1.12)	0.95 (0.81, 1.11) ^c	1965	1.05 (0.85, 1.31)	1.01 (0.81, 1.26) ^c
Not employed/welfare benefits	189	1.10 (0.62, 1.96)	1.00 (0.54, 1.84) ^c	135	1.20 (0.57, 2.55)	1.10 (0.49, 2.46) ^c
Retired	2497	0.92 (0.78, 1.09)	$0.93~(0.78,~1.10)^{\circ}$	1921	1.01 (0.82, 1.24)	0.97 (0.79, 1.20)°
Other	63	0.51 (0.18, 1.43)	$0.56 (0.18, 1.72)^{c}$	53	0.24 (0.06, 0.88)	$0.16 (0.03, 0.79)^{c}$
p-value ^d		0.675			0.200	
Worry score ^e						
1. quartile; 3–7	1678	0.90 (0.74, 1.10)	$0.91~(0.74,~1.12)^{c}$	1253	1.03 (0.75, 1.40)	1.01 (0.74, 1.38) ^c
2. quartile; 8–9	1701	0.91 (0.75, 1.11)	$0.92~(0.75,~1.12)^{c}$	1269	1.05 (0.80, 1.37)	1.03 (0.78, 1.36) ^c
3. quartile; 10	796	0.95 (0.71, 1.28)	0.94 (0.70, 1.26)°	569	0.96 (0.64, 1.43)	0.97 (0.64, 1.47) ^c
4. quartile; 11–15	1579	1.08 (0.88, 1.32)	1.08 (0.87, 1.33) ^c	1246	1.10 (0.87, 1.40)	1.10 (0.86, 1.41) ^c
p-value ^d		0.614			0.945	
Attitude score ^f						
1. quartile; 4–18	492	0.90 (0.73, 1.10)	$0.90 (0.73, 1.11)^{c}$	1145	0.89 (0.68, 1.16)	$0.88 (0.67, 1.16)^{c}$
2. quartile; 19–22	1565	0.90 (0.73, 1.10)	0.89 (0.73, 1.10) ^c	1169	0.96 (0.74, 1.24)	0.92 (0.70, 1.21) ^c
3. quartile; 23–24	705	0.86 (0.63, 1.17)	0.82 (0.60, 1.13) ^c	505	0.97 (0.63, 1.49)	0.93 (0.60, 1.45) ^c
4. quartile; 25–28	2005	1.00 (0.82, 1.22)	1.02 (0.83, 1.25) ^c	1531	1.04 (0.80, 1.36)	1.05 (0.80, 1.38) ^c
p-value ^d		0.792	, , ,		0.869	, , ,

^a Logistic regression analyses adjusted for age, ethnicity, and marital status.

randomized controlled trial with an intervention provided along with the reminder. If we had been able to measure CRC screening uptake after the reminder, those still not taking up screening may have been different from those included in the study. Those still not taking up screening may have been those with lower health literacy, and thus our sample formation at 45 days may partly explain why we found no association between health literacy and CRC screening uptake.

Another strength of this study was the use of individual level registry-based data of high validity from Statistics Denmark (Statistics Denmark, 2019b). Statistical analyses were adjusted for important socioeconomic and -demographic characteristics in order to remove the effect of possible confounders. The analyses were not adjusted for education due to the strong correlation between health literacy and educational attainment (Paasche-Orlow et al., 2005). Hence, adjusting for education would entail a potential risk of over-adjustment bias. Nevertheless, the risk of residual confounding cannot be ruled out due to the study design.

The questionnaire response rate of 71% and few missing values contributed to a low risk of selection bias. Nevertheless, non-respondents differed from respondents in background variables. If citizens with inadequate/problematic health literacy tend to be non-respondents and screening non-participants, the potential association between lower levels of health literacy and lower CRC screening uptake may not be detected due to selection bias.

Health literacy was assessed using a continuous scale and subsequently categorized into three groups according to the HLS-EU-Q16 manual. This approach was used to facilitate comparisons with previous studies. However, categorizing health literacy as adequate, problematic or inadequate using arbitrary cut-offs might be problematic. The limit between adequate, problematic, and inadequate health literacy might differ between individuals, and defining arbitrary cut-offs might indicate that a true cut-off exists. Instead, it has been suggested to use continuous scales to measure variables like health literacy in order to reflect a continuous spectrum of the truth (Ghanouni et al., 2016). Further, HLS-EU-Q16 is a subjective measure of health literacy providing a measure influenced, for example, by how exposed the respondent has been to the complexity of the health care system and how self-confident they are in their own abilities as compared to cognitive measures that provide a direct measure of the individual's skills. However, objective measures often require in-person tests which were not feasible in this large-scale study. Further, subjective measures are better suitable for assessing if the healthcare system serves the population well which was the aim of this study (Nguyen et al., 2017).

The random selection of the population sample supports representativeness. Central Denmark Region resembles the general Danish population because it consists of both urban and rural areas, and the results can thus be generalized nationally. Further, the results may be generalized to other countries with comparable socioeconomic and

^b Logistic regression analyses adjusted for sex, age, and ethnicity.

^c Logistic regression analyses adjusted for sex, age, ethnicity, and marital status.

^d Wald test for difference between groups.

^e Higher scores indicate higher levels of worry.

f Higher scores indicate more positive attitudes toward CRC screening.

-demographic characteristics, similar screening culture and a publicly funded FIT-based CRC screening program.

4.3. Interpretation of results

Previous research of the association between health literacy and CRC screening uptake have been inconsistent. Those not reporting an association suffers from small study populations (N < 150) (Guerra et al., 2005; Miller et al., 2007; Peterson et al., 2007) and underrepresentation of individuals with inadequate health literacy (Wangmar et al., 2018). However, a large study found a significant association between lower health literacy and lower screening uptake among those older than 65 years (White et al., 2008). Three other previous studies likewise reported a statistically significant association between limited/ inadequate health literacy and lower CRC screening uptake (Arnold et al., 2012; Kobayashi et al., 2014; Solmi et al., 2015). Our results indicate a possible U-shaped association with the middle group (problematic health literacy) being those most likely to take up screening compared to those with adequate and inadequate health literacy. This is consistent with the pattern demonstrated for the association of educational attainment and CRC screening uptake (Larsen et al., 2017). However, reasons for this U-shaped pattern remain unexplored. It is known that some of those with lower educational attainment prefer a clear recommendation from the health authorities about CRC screening uptake and consider the directly mailed invitation with a screening kit a request for participation (Kirkegaard et al., 2015). Due to the association between education and health literacy (Paasche-Orlow et al., 2005); this may explain why those with problematic health literacy tend to participate more, but it does not explain why those with adequate and inadequate participate less. Furthermore, reasons are likely to differ between the two groups.

Health literacy is a complex concept which makes it difficult to measure comprehensively. Different methodological approaches covering different dimensions of health literacy have been used in previous research including both non-validated tests (Kobayashi et al., 2014; Solmi et al., 2015) and validated tests (White et al., 2008; Arnold et al., 2012; Guerra et al., 2005; Miller et al., 2007; Peterson et al., 2007; Wangmar et al., 2018) like the National Assessment of Adult Literacy (NAAL) (White et al., 2008), the Rapid Estimate of Adult Literacy in Medicine (REALM) (Arnold et al., 2012; Miller et al., 2007; Peterson et al., 2007) and the Short-Test of Functional Health Literacy in Adults (S-TOFHLA) (Guerra et al., 2005). However, because of the varying methodological approaches comparison of results across studies might be difficult and future research is needed to clarify which dimensions of health literacy may help explain screening uptake and other preventive health behaviors.

Based on our results, health literacy was not associated with CRC screening uptake. However, this may be because other important factors mediate the association. For example, cancer fatalism, the belief that death is inevitable when cancer is present, has been associated with lower CRC screening uptake (Miles et al., 2011) and lower levels of health literacy (Fleary et al., 2019). Likewise, lower self-efficacy for participation in CRC screening has been associated with lower health literacy (Von Wagner et al., 2009). Therefore, is seems plausible that future studies need to take psychological factors into consideration when assessing the association between health literacy and screening uptake.

The only significant finding in this study was in the stratified analyses among citizens with "other occupation". Within this small subgroup, inadequate health literacy was associated with lower CRC screening uptake. "Other occupation" is a category formed by a process of elimination, containing individuals that does not fit in any of the other categories. Thus, the most marginalized individuals are in this category indicating that health literacy may be an important resource among those most vulnerable. However, it cannot be ruled out that this result represents a random finding due to the number of statistical

analyses conducted in Table 3.

5. Conclusion

Based on our results, health literacy may not represent as fertile an area for future interventions aiming to increase CRC screening uptake as previously considered. At least, future research needs to clarify which dimensions of health literacy may predict screening uptake and how it is best measured. However, less than half of the general population eligible for CRC screening demonstrated adequate health literacy which is important to take into account when communication with participants about the pros and cons of CRC screening.

Funding

This study was supported by grants from the Danish Cancer Society, Denmark (grant ID: R146-A9555).

CRediT authorship contribution statement

Petricia Marie Horshauge: Methodology, Data curation, Writing original draft, Writing - review & editing. Pernille Gabel: Conceptualization, Methodology, Investigation, Writing - review & editing, Supervision. Methodology, Writing - review & editing, Supervision. Pia Kirkegaard: Conceptualization, Writing - review & editing, Supervision. Pia Kirkegaard: Conceptualization, Writing - review & editing, Supervision. Adrian Edwards: Writing - review & editing, Supervision. Berit Andersen: Conceptualization, Methodology, Resources, Writing - review & editing, 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.

References

- Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R.L., Torre, L.A., Jemal, A., 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 68 (6), 394–424.
- Maida, M., Macaluso, F.S., Ianiro, G., Mangiola, F., Sinagra, E., Hold, G., et al., 2017.
 Screening of colorectal cancer: present and future. Expert Rev. Anticancer Ther. 17 (12), 1131–1146.
- Levin, T.R., Corley, D.A., Jensen, C.D., Schottinger, J.E., Quinn, V.P., Zauber, A.G., et al., 2018. Effects of organized colorectal cancer screening on cancer incidence and mortality in a large community-based population. Gastroenterology 155 (5), 1383–1391 e5.
- Zhang, J., Cheng, Z., Ma, Y., He, C., Lu, Y., Zhao, Y., et al., 2017. Effectiveness of screening modalities in colorectal cancer: a network meta-analysis. Clin. Colorectal Cancer 16 (4), 252–263.
- Parra-Blanco, A., Gimeno-García, A.Z., Quintero, E., Nicolás, D., Moreno, S.G., Jiménez, A., et al., 2010. Diagnostic accuracy of immunochemical versus guaiac faecal occult blood tests for colorectal cancer screening. J. Gastroenterol. 45 (7), 703–712.
- Sundhedsstyrelsen [The Danish Health Authority]. Anbefalinger vedrørende nationale screeningsprogrammer [Danish]. 2014.
- Moss, S., Ancelle-Park, R., Brenner, H. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition Evaluation and interpretation of screening outcomes. Endoscopy 2012;44(S 03):SE49–SE64.
- American Cancer Society. Colorectal Cancer Facts & Figures 2017-2019. 2017.
- Njor, S.H., Friis-Hansen, L., Andersen, B., Søndergaard, B., Linnemann, D., Jørgensen, J.C.R., et al., 2018. Three years of colorectal cancer screening in Denmark. Cancer Epidemiol. 57, 39–44.
- Hirst, Y., Stoffel, S., Baio, G., McGregor, L., von Wagner, C., 2018. Uptake of the English Bowel (Colorectal) Cancer Screening Programme: an update 5 years after the full rollout. Eur. J. Cancer 103, 267–273.
- de Moor, J.S., Cohen, R.A., Shapiro, J.A., Nadel, M.R., Sabatino, S.A., Yabroff, K.R., et al., 2018. Colorectal cancer screening in the United States: trends from 2008 to 2015 and variation by health insurance coverage. Prev. Med. 112, 199–206.
- Navarro, M., Nicolas, A., Ferrandez, A., Lanas, A., 2017 May 28. Colorectal cancer population screening programs worldwide in 2016: an update. World J. Gastroenterol. 23 (20), 3632–3642.
- Gimeno Garcia, A.Z., 2012. Factors influencing colorectal cancer screening participation.

 Gastroenterol Res Pract 2012, 483417.

- Wools, A., Dapper, E., 2015. Leeuw Jd. Colorectal cancer screening participation: a systematic review. Eur. J. Public Health 26 (1), 158–168.
- Von Wagner, C., Baio, G., Raine, R., Snowball, J., Morris, S., Atkin, W., et al., 2011. Inequalities in participation in an organized national colorectal cancer screening programme: results from the first 2.6 million invitations in England. Int. J. Epidemiol. 40 (3), 712–718.
- Larsen, M.B., Mikkelsen, E.M., Rasmussen, M., Friis-Hansen, L., Ovesen, A.U., Rahr, H.B., et al., 2017. Sociodemographic characteristics of nonparticipants in the Danish colorectal cancer screening program: a nationwide cross-sectional study. Clin. Epidemiol. 9, 345.
- White, S., Chen, J., Atchison, R., 2008. Relationship of preventive health practices and health literacy: a national study. Am. J. Health Behav. 32 (3), 227–242.
- Arnold, C.L., Rademaker, A., Bailey, S.C., Esparza, J.M., Reynolds, C., Liu, D., et al., 2012. Literacy barriers to colorectal cancer screening in community clinics. J. Health Commun. 17 (3), 252–264.
- Kobayashi, L.C., Wardle, J., von Wagner, C., 2014. Limited health literacy is a barrier to colorectal cancer screening in England: evidence from the English Longitudinal Study of Ageing. Prev. Med. 61, 100–105.
- Solmi, F., Von Wagner, C., Kobayashi, L.C., Raine, R., Wardle, J., Morris, S., 2015. Decomposing socio-economic inequality in colorectal cancer screening uptake in England. Soc. Sci. Med. 134, 76–86.
- Guerra, C.E., Dominguez, F., Shea, J.A., 2005. Literacy and knowledge, attitudes, and behavior about colorectal cancer screening. J. Health Commun. 10 (7), 651–663.
- Miller, D.P., Brownlee, C.D., McCoy, T.P., Pignone, M.P., 2007. The effect of health literacy on knowledge and receipt of colorectal cancer screening: a survey study. BMC Family Practice 8 (1), 16.
- Peterson, N.B., Dwyer, K.A., Mulvaney, S.A., Dietrich, M.S., Rothman, R.L., 2007. The influence of health literacy on colorectal cancer screening knowledge, beliefs and behavior. J. Natl Med. Assoc. 99 (10), 1105.
- Wangmar, J., Jervaeus, A., Fritzell, K., Wångdahl, J., Hultcrantz, R., Wengström, Y., 2018. Health literacy levels and views about being invited to a colorectal cancer screening program. Acta Oncol. 57 (6), 743–749.
- Sørensen, K., Van den Broucke, S., Fullam, J., Doyle, G., Pelikan, J., Slonska, Z., et al., 2012. Health literacy and public health: a systematic review and integration of definitions and models. BMC Public Health 12 (1), 80.
- Mantwill, S., Monestel-Umaña, S., Schulz, P.J., 2015. The relationship between health literacy and health disparities: a systematic review. PLoS ONE 10 (12), e0145455.
- Stormacq C, Van den Broucke S, Wosinski J. Does health literacy mediate the relationship between socioeconomic status and health disparities? Integrative review. Health Promot Internation 2018.
- Dodou, D., de Winter, J., 2015. Agreement between self-reported and registered colorectal cancer screening: a meta-analysis. European J. Cancer Care 24 (3), 286–298.
- Lofters, A., Vahabi, M., Glazier, R.H., 2015. The validity of self-reported cancer screening history and the role of social disadvantage in Ontario, Canada. BMC Public Health 15 (1), 28.
- Statistics Denmark. FOLK1A: Population at the first day of the quarter by sex, age and marital status (2019Q2). Available at: https://www.statistikbanken.dk/statbank5a/SelectVarVal/Define.asp?MainTable = FOLK1A&PLanguage = 1&PXSId = 0&wsid = cftree. Accessed 05/24, 2019.
- Gabel, P., Edwards, A., Kirkegaard, P., Larsen, M.B., Andersen, B., 2019. The LEAD trial-The effectiveness of a decision aid on decision making among citizens with lower educational attainment who have not participated in FIT-based colorectal cancer

- screening in Denmark: a randomised controlled trial. Patient Educ. Couns. Pedersen, C.B., 2011. The Danish civil registration system. Scand J Public Health 39 (7),
- Pedersen, C.B., 2011. The Danish civil registration system. Scand J Public Health 39 (7) 22–25.
- Statistics Denmark. The division of research services, Statistics Denmark [Available in English]. Available at: www.dst.dk. Accessed 04/29, 2019.
- Sørensen, K., Pelikan, J.M., Röthlin, F., Ganahl, K., Slonska, Z., Doyle, G., et al., 2015. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health 25 (6), 1053–1058.
- Okan O, Bauer U, Levin-Zamir D, Pinheiro P, Sørensen K. International Handbook of Health Literacy – Research, practice and policy across the lifespan: Policy Press; 2019
- Beaton, D.E., Bombardier, C., Guillemin, F., Ferraz, M.B., 2000. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 25 (24), 3186–3191.
- Hay, J.L., Buckley, T.R., Ostroff, J.S., 2005. The role of cancer worry in cancer screening: a theoretical and empirical review of the literature. Psycho-Oncol.: J. Psychol., Social Behav. Dimens. Cancer 14 (7), 517–534.
- Marteau, T.M., Dormandy, E., Michie, S., 2001. A measure of informed choice. Health Expect. 4 (2), 99–108.
- Thomsen, M.K., Njor, S.H., Rasmussen, M., Linnemann, D., Andersen, B., Baatrup, G., et al., 2017 Feb Feb. Validity of data in the Danish colorectal cancer screening database. Clin. Epidemiol. 17 (9), 105–111.
- Statistics Denmark. Begreber Vestlige lande [Danish]. Available at: https://www.dst.dk/da/Statistik/dokumentation/hvadbetyder. Accessed 04/29, 2019.
- Statistics Denmark. Ækvivaleret disponibel indkomst (AEKVIVADISP_13) [Danish]. Available at: https://www.dst.dk/da/Statistik/dokumentation/Times/personindkomst/aekvivadisp-13. Accessed 04/29, 2019.
- UNESCO Institute for Statistics. International Standard Classification of Education ISCED 2011 ISBN 978-92-9189-123-8. 2012.
- Statistics Denmark. Urbaniseringsgrad (DEGURBA) [Danish]. Available at: https://www.dst.dk/da/Statistik/dokumentation/nomenklaturer/urbaniseringsgrad-degurba—danmarks-statistik. Accessed 04/29, 2019.
- Paasche-Orlow, M.K., Parker, R.M., Gazmararian, J.A., Nielsen-Bohlman, L.T., Rudd, R.R., 2005. The prevalence of limited health literacy. J. General Internal Med. 20 (2) 175–18.
- Ghanouni, A., Renzi, C., Meisel, S.F., Waller, J., 2016. Common methods of measuring 'informed choice'in screening participation: challenges and future directions. Preventive Med. Rep. 4, 601–607.
- Nguyen, T.H., Paasche-Orlow, M.K., McCormack, L.A., 2017. The state of the science of health literacy measurement. Inf. Services Use 37 (2), 189–203.
- Kirkegaard, P., Mortensen, G.L., Mortensen, S.L., Larsen, M.B., Gabel, P., Andersen, B., 2015. Making decisions about colorectal cancer screening. A qualitative study among citizens with lower educational attainment. Eur. J. Public Health 26 (1), 176–181.
- Miles, A., Rainbow, S., von Wagner, C., 2011 Oct Oct. Cancer fatalism and poor self-rated health mediate the association between socioeconomic status and uptake of colorectal cancer screening in England. Cancer Epidemiol. Biomarkers Prev. 20 (10), 2132–2140.
- Fleary, S.A., Paasche-Orlow, M.K., Joseph, P., Freund, K.M., 2019. The relationship between health literacy, cancer prevention beliefs, and cancer prevention behaviors. J. Cancer Educ. 34 (5), 958–965.
- Von Wagner, C., Semmler, C., Good, A., Wardle, J., 2009. Health literacy and self-efficacy for participating in colorectal cancer screening: the role of information processing. Patient Educ. Couns. 75 (3), 352–357.