



Cancer beliefs and participation in screening for colorectal cancer: A Danish cohort study based on data from the International Cancer Benchmarking Partnership and national registers



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ABSTRACT

Participation in screening for colorectal cancer (CRC) may be affected by general beliefs about cancer and about CRC screening. The aim of this population-based study was to examine prospectively the association between beliefs about cancer and CRC screening and later participation in screening for CRC. We included 1285 individuals who had answered 'the Awareness and Beliefs about Cancer (ABC) measure' in 2011 and who had been invited to CRC screening in 2014–2016. The ABC measure includes statements about six general beliefs about cancer and three beliefs about CRC screening. These data were combined with register-based information on CRC screening behaviour, which was obtained from the Danish Colorectal Cancer Screening Database. Multivariate analyses showed that individuals who tended to agree that they would worry about what might be found in the CRC screening (PR: 1.66, 95% CI: 1.24–2.23) and individuals who strongly agreed that screening is only necessary if symptoms are present (PR: 1.35, 95% CI: 1.05–1.75) were more likely to be non-participants than individuals who strongly disagreed with these beliefs. Included individuals were also more likely to be non-participants if they strongly agreed that they did not want to know about cancer (PR: 1.50, 95% CI: 1.09–2.07), whereas those who strongly agreed that screening could reduce their risk of dying from CRC were less likely to be non-participants (PR: 0.69, 95% CI: 0.49–0.97). This study shows that beliefs about CRC screening and, to a lesser extent, general beliefs about cancer are associated with participation in screening for CRC.

1. Background

Colorectal cancer (CRC) is the third most common type of cancer worldwide (Ferlay et al., 2015) and is currently the most common type in Denmark with approximately 5200 new cases diagnosed in 2016 (The Danish Health Data Authority, 2017). Danish CRC patients have a poor prognosis compared to CRC patients in countries with comparable healthcare systems (Coleman et al., 2011). This may be partly explained by later stage at diagnosis (Maringe et al., 2013). A number of initiatives have been carried out to improve the CRC prognosis in Denmark (Iversen et al., 2016). Latest, a national FIT-based CRC screening programme was introduced in 2014. When the programme is fully implemented in 2018, adults aged 50 to 74 years will be invited to an immunochemical faecal occult blood test (iFOBT) screening biennially (The Danish Health Authority, 2016). Although much debated (Ekelund et al., 2010; Riboe et al., 2013), screening with iFOBT has been

associated with a 16% reduced relative risk of CRC mortality for participants allocated to screening (Hewitson et al., 2011). However, as with any screening programme, the efficiency relies on high uptake in the target population. A recent analysis of the first 22 months of the Danish CRC screening programme showed an uptake of 64% (Danish Quality Database for Colon Cancer Screening, 2016).

A number of studies have explored factors associated with CRC screening participation, and many of these have focused on the association with socio-economic position (SEP). Living alone, being on social welfare and having lower income are all factors that have generally been associated with low uptake of CRC screening (Larsen et al., 2017; Lo et al., 2015; Power et al., 2009). Examination of SEP differences in screening uptake is important in order to identify segments of the population to target for intervention programmes aiming to increase the uptake. Moreover, it is important to identify modifiable factors that can be intervened upon (Power et al., 2009). Several studies have used

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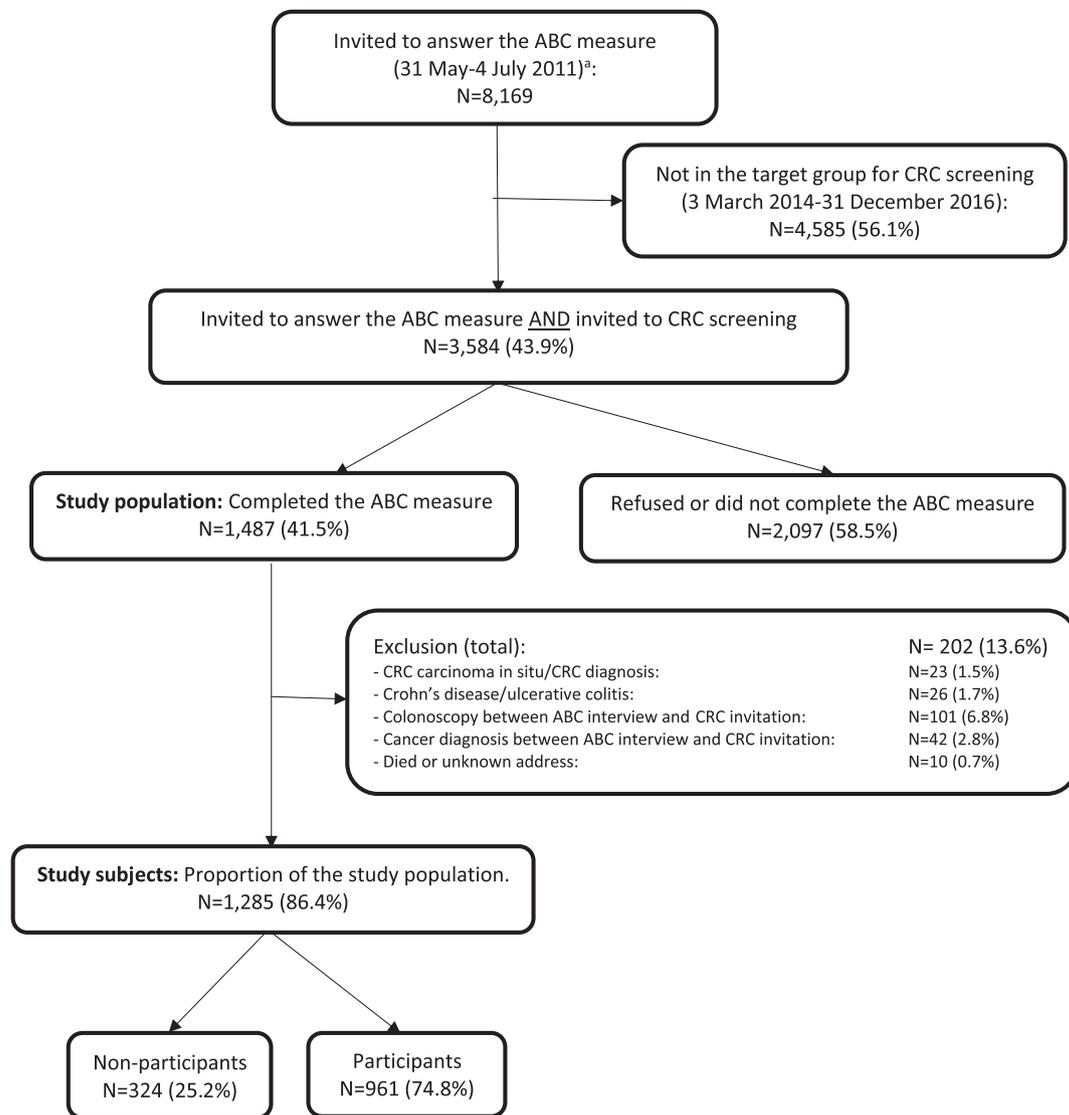


Fig. 1. Flowchart of the inclusion.

^aEligible and contacted to answer the ABC measure. For a more detailed description see (Hvidberg et al., 2015).

elements of social cognitive models e.g. the Health Belief Model (HBM) to identify factors associated with screening uptake (Janz et al., 2003; McCaffery et al., 2003; Power et al., 2008; Varlow et al., 2014). According to the HBM, important components for health preventive behaviors are ‘perceived susceptibility’ i.e. one’s belief regarding the chances of developing the condition. ‘Perceived severity’ is one’s belief regarding the seriousness of a condition. ‘Perceived benefits and barriers’ are one’s beliefs in the effectiveness of actions to reduce the potential threat to their health (i.e. benefits) and the costs of implementing the recommended action (i.e. barriers). The last key component, ‘self-efficacy’, refers to one’s confidence in the ability to take action (Rosenstock, 1974). In the studies that have used elements among other the HBM low uptake of CRC screening has been linked to negative attitudes toward the screening process, negative beliefs about cancer and lack of CRC knowledge (Janz et al., 2003; McCaffery et al., 2003; Power et al., 2008; Varlow et al., 2014). However, much of this previous research has used the intention to be screened or self-reported screening behaviour as outcomes (Janz et al., 2003; McCaffery et al., 2003; Varlow et al., 2014), and this approach has shown only moderate validity (Lofters et al., 2015; Sheeran, 2002). The Danish Colorectal Cancer Screening Database (Thomsen et al., 2017) offers a unique opportunity to accurately identify participants and non-participants and

research based on such reliable and valid data has been called for in the CRC screening literature (Power et al., 2008). Therefore, the aim of this study was to examine the association between beliefs about cancer, beliefs about CRC screening and later participation in screening for CRC as recorded in national registers.

2. Methods

2.1. Setting

The healthcare system in Denmark is based on the principle of equal access to healthcare, and CRC screening is offered free-of-charge to Danish residents (Ministry of Health, 2016). In the first screening round (i.e. prevalence round 2014–2017), individuals aged 50–74 years were invited randomly according to month of birth, whereas individuals turning 50 and 75 years of age within the four-year prevalence round were invited just before their birthday (The Danish Cancer Society, 2017).

2.2. Study design and population

This study was performed as a historical cohort study and the study

base was 60,000 individuals aged 30 years of age and older residing in Denmark, who was randomly selected through the Danish Civil Registration System (CRS) in 2011 (Schmidt et al., 2014). The following two inclusion criteria were applied for the historical cohort: Firstly, eligible individuals should have been invited to answer the Awareness and Beliefs about Cancer (ABC) measure. The data on the ABC measure was collected from 31 May to 4 July 2011 and was carried out as computer-assisted telephone interview undertaken by trained native-language interviewers (Hvidberg et al., 2014). Secondly, these individuals should have been invited to participate in CRC screening between 3 March 2014 and 31 December 2016.

This applied to 3584 individuals in total, and 1487 (41.5%) of these had completed the ABC measure. Individuals were excluded if registered with CRC carcinoma in situ (D010, D012, D013, D014) or a CRC diagnosis (C18, C19, C20) in the Danish Cancer Registry (DCR) (Gjerstorff, 2011) ($n = 23$), Crohn's disease (K50) or ulcerative colitis (K51) ($n = 26$) in the Danish National Patient Register (NPR) (Lyng et al., 2011) before the date of the screening invitation. This approach was taken because specific recommendations for screening apply to these groups. Individuals who had received colonoscopy ($n = 101$) recorded in the NPR or were registered with any other cancer diagnosis in the DCR ($n = 42$) between the date of the ABC interview and the screening invitation were also excluded due to potential effect modification. Lastly, individuals were excluded if they had died before receiving the invitation to screening or in case of unknown address ($n = 10$). Thus, in total 1285 (86.4%) were included in the analyses (Fig. 1).

2.3. Data

All Danish citizens are assigned a unique ten-digit number in the CRS (Schmidt et al., 2014). We used this number to link all data at the individual level.

2.4. Screening participation

Invitations for CRC screening were sent from a central office in each of the five Danish Regions and were delivered by post (surface mail) along with a home sampling screening kit (FIT), instructions and a prepaid return envelope. A reminder was sent after 45 days if the screening kit had not been returned. An individual was categorised as a non-participant if the screening kit had not been returned within three months after receipt of the reminder. This information was obtained from the Danish Colorectal Cancer Screening Database (Thomsen et al., 2017).

2.5. Beliefs about cancer and about CRC screening

Data on beliefs about cancer and beliefs about CRC screening were obtained from the ABC measure that was developed as part of Module 2 of the International Cancer Benchmarking Partnership (ICBP) (Simon et al., 2012). The Danish data were collected as computer-assisted telephone interviews from 31 May to 4 July 2011. This interview was completed by 3000 persons (response rate: 36.7%) aged 30 years or older. The methodology has been described elsewhere (Hvidberg et al., 2014).

The ABC measure has shown acceptable reliability and validity in both a Danish and an international context (Hvidberg et al., 2017; Simon et al., 2012). The ABC measure included six statements on beliefs about cancer and three statements on beliefs about CRC screening. The beliefs about cancer and CRC screening included both positively and negatively framed statements, and the order of these was rotated to minimise order-effect bias (Allen & Yen, 2002). Response options were measured on a 4-point scale (strongly agree, tend to agree, tend to disagree and strongly disagree). If the respondent did not want to answer or answered 'don't know' to a statement, such statement was

classified as missing.

2.6. Statistical analyses

To study whether beliefs about cancer and beliefs about CRC screening were associated with non-participation in screening for CRC, we calculated prevalence ratios (PRs) using generalised linear models (GLM) (Barros & Hirakata, 2003). The analyses were adjusted for age, gender, marital status, educational level, disposable household income as per 1 January 2011 (Statistics Denmark, 2018) and cancer diagnosis before the ABC interview (Storm et al., 1997) as these variables have shown to be associated with beliefs about cancer and non-participation in screening for CRC (Hvidberg et al., 2015; Larsen et al., 2017). Age, gender and marital status were derived from the Danish CRS (Schmidt et al., 2014). Information on educational level and disposable income was obtained from Statistics Denmark (Statistics Denmark, 2018) and grouped in accordance with the International Standard Classification of Education (UNESCO, 2018) and into tertiles, respectively.

We tested for trends in screening non-participation across response categories (i.e. strongly disagree, tend to disagree, tend to agree and strongly agree) for beliefs about cancer and about CRC screening using the non-parametric test described by Cuzick (Cuzick, 1985). Statistical significance was set at 0.05. Data were analysed using Stata 14.2.

3. Results

The overall screening non-participation rate was 25.2%. The characteristics of participants and non-participants in screening for CRC are shown in Table 1. A higher proportion of non-participants than participants were males, in the youngest age group, living alone and had a low disposable household income.

Table 1

Characteristics of eligible individuals who were invited to participate in CRC screening and who had answered the ABC measure ($n = 1285$), divided into CRC screening participants or non-participants.

	Participants		Non-participants		p-Value ^a
	%	(n)	%	(n)	
Eligible individuals	74.8	(961)	25.2	(324)	
Gender					0.045
Female	57.0	(548)	50.6	(164)	
Male	43.0	(413)	49.4	(160)	
Age group (years)					0.028
49–54	23.6	(227)	32.1	(104)	
55–59	18.5	(178)	18.2	(59)	
60–64	17.2	(165)	15.1	(49)	
65–69	18.4	(177)	13.6	(44)	
70–75	22.3	(214)	21.0	(68)	
Age, mean (SD)	61.7	(8.2)	60.2	(8.7)	
Marital status					0.003
Married/cohabiting	80.4	(773)	72.5	(235)	
Living alone	19.6	(188)	27.5	(89)	
Educational level					0.392
≤ 10 years	20.3	(193)	22.7	(72)	
11–15 years	46.9	(447)	48.3	(153)	
> 15 years	32.8	(313)	29.0	(92)	
Disposable household income					< 0.001
Low	29.9	(386)	42.3	(137)	
Middle	34.1	(327)	29.6	(96)	
High	36.0	(345)	28.1	(98)	
Cancer diagnosis before ABC interview					0.110
Yes	8.6	(83)	5.9	(19)	
No	91.4	(878)	94.1	(305)	

Numbers vary due to missing data.

Significant results in bold.

^a Chi-square test.

Table 2
Unadjusted and adjusted prevalence ratios (PRs) with 95% confidence intervals (CI) for the association between beliefs about cancer and non-participation in CRC screening.

	Participants		Non-participants		Unadjusted PR	Adjusted PR	Trend
	%	(n)	%	(n)	PR (95%CI)	PR ^a (95% CI)	p-Value
Positively framed beliefs							
People with cancer can expect to continue with normal activities							0.207
Strongly disagree	64.7	(22)	35.3	(12)	1.00	1.00	
Tend to disagree	71.6	(83)	28.5	(33)	0.81 (0.47–1.38)	0.97 (0.54–1.72)	
Tend to agree	75.6	(450)	24.4	(145)	0.69 (0.43–1.11)	0.84 (0.50–1.42)	
Strongly agree	75.6	(381)	24.4	(123)	0.69 (0.43–1.12)	0.88 (0.51–1.49)	
Cancer can often be cured							0.279
Strongly disagree	62.9	(22)	37.1	(13)	1.00	1.00	
Tend to disagree	76.2	(64)	23.8	(20)	0.64 (0.36–1.14)	0.66 (0.37–1.17)	
Tend to agree	74.5	(414)	25.5	(142)	0.69 (0.44–1.08)	0.73 (0.47–1.15)	
Strongly agree	75.6	(444)	24.4	(143)	0.66 (0.42–1.03)	0.73 (0.46–1.16)	
Going to the doctor as quickly as possible after noticing a symptom of cancer could increase the chances of surviving							0.368
Disagree ^b	64.3	(18)	35.7	(10)	1.00	1.00	
Tend to agree	75.0	(87)	25.0	(29)	0.70 (0.39–1.26)	0.82 (0.46–1.44)	
Strongly agree	75.0	(855)	25.0	(285)	0.70 (0.42–1.16)	0.77 (0.48–1.26)	
Negatively framed beliefs							
Most cancer treatment is worse than the cancer itself							0.924
Strongly disagree	74.0	(111)	26.0	(39)	1.00	1.00	
Tend to disagree	73.4	(174)	26.6	(63)	1.02 (0.73–1.44)	0.99 (0.70–1.40)	
Tend to agree	75.1	(347)	24.9	(115)	0.96 (0.70–1.31)	0.96 (0.70–1.33)	
Strongly agree	73.8	(234)	26.2	(83)	1.01 (0.73–1.40)	0.96 (0.68–1.36)	
I would not want to know if I have cancer							0.001
Strongly disagree	76.8	(773)	23.2	(233)	1.00	1.00	
Tend to disagree	73.7	(101)	26.3	(36)	1.13 (0.84–1.53)	1.08 (0.80–1.45)	
Tend to agree	60.0	(30)	40.0	(20)	1.73 (1.21–2.47)	1.58 (1.11–2.27)	
Strongly agree	62.7	(42)	37.3	(25)	1.61 (1.16–2.24)	1.50 (1.09–2.07)	
A diagnosis of cancer is a death sentence							0.184
Strongly disagree	76.4	(360)	23.6	(111)	1.00	1.00	
Tend to disagree	74.7	(333)	25.3	(113)	1.08 (0.86–1.35)	1.07 (0.85–1.34)	
Tend to agree	74.3	(199)	25.8	(69)	1.09 (0.84–1.42)	1.00 (0.77–1.31)	
Strongly agree	68.1	(47)	31.9	(22)	1.35 (0.92–1.98)	1.30 (0.90–1.88)	

Numbers vary due to missing data.

Significant results in bold.

^a Adjusted for gender, age (numeric), marital status, educational level, income and cancer diagnosis before ABC interview.

^b Tend to disagree and strongly disagree are combined due to few observations in each cell.

3.1. Associations between beliefs about cancer and non-participation in CRC screening

Associations between beliefs about cancer and non-participation in CRC screening are presented in Table 2. In both the unadjusted and adjusted analyses, individuals that tended to agree or strongly agreed that they 'would not want to know if they have cancer' were more likely to be non-participants than individuals who strongly disagreed. For this belief, a statistically significant trend was found in non-participation across the responses categories. No significant associations were seen between the other general beliefs about cancer and non-participation in screening for CRC.

3.2. Associations between beliefs about CRC screening and non-participation in CRC screening

After adjustments, individuals who tended to agree or strongly agreed that 'bowel cancer screening could reduce my risk of dying from bowel cancer' were less likely to be non-participants than individuals who strongly disagreed (Table 3).

Individuals who strongly agreed that 'bowel cancer screening is only necessary if I have symptoms' and individuals who tended to agree that 'I would be so worried about what might be found that I would prefer not to do it' were more likely to be non-participants than individuals who strongly disagreed with these two statements and a statistical significant trend was found in non-participation for these two groups (Table 3).

4. Discussion

4.1. Main findings

In this historical cohort study, we examined the association between beliefs about cancer and about CRC screening and later participation in screening for CRC. We found that individuals who agreed that they would not want to know if they had cancer, that bowel cancer screening is only necessary if symptoms are present, and that they would be worried about what might be found at screening were more likely to be CRC screening non-participants in 2014–2016 than individuals who strongly disagreed with these statements. Finally, individuals who agreed that CRC screening could reduce their risk of dying from CRC were less likely to be non-participants than individuals who strongly disagreed with this statement.

4.2. Strengths and limitations

This study used a prospective design. The participants' beliefs about cancer and about CRC screening were measured before the introduction of a national CRC screening programme in Denmark. Thus, a key strength of the study was that the participants' beliefs were unlikely to be biased by past CRC screening experience (Lechner et al., 1997). Moreover, the data on beliefs about cancer and CRC screening were assessed by the ABC measure, which has been found to have satisfactory measurement properties (Hvidberg et al., 2017; Simon et al., 2012). Another key strength of the study was the use of register-based data on screening participation. Lofters et al. (Lofters et al., 2015) evaluated the

Table 3

Unadjusted and adjusted prevalence ratios (PRs) with 95% confidence intervals (CI) for the association between beliefs about CRC screening and non-participation in CRC screening.

	Participants		Non-participants		Unadjusted PR	Adjusted PR	Trend
	%	(n)	%	(n)	PR (95% CI)	PR ^a (95% CI)	p-Value
Positively framed beliefs							
Bowel cancer screening could reduce my risk of dying from bowel cancer							0.345
Strongly disagree	64.5	(40)	35.5	(22)	1.00	1.00	
Tend to disagree	72.7	(32)	27.3	(12)	0.77 (0.43–1.38)	0.72 (0.40–1.29)	
Tend to agree	77.7	(234)	22.3	(67)	0.63 (0.42–0.93)	0.60 (0.41–0.87)	
Strongly agree	74.4	(620)	25.6	(213)	0.72 (0.51–1.03)	0.69 (0.49–0.97)	
Negatively framed beliefs							
Bowel cancer screening is only necessary if I have symptoms							
Strongly disagree	78.2	(372)	21.9	(104)	1.00	1.00	0.005
Tend to disagree	76.7	(188)	23.3	(57)	1.06 (0.80–1.41)	1.04 (0.79–1.39)	
Tend to agree	74.2	(204)	25.8	(71)	1.18 (0.91–1.54)	1.13 (0.87–1.47)	
Strongly agree	68.6	(168)	31.4	(77)	1.44 (1.12–1.85)	1.35 (1.05–1.75)	
I would be so worried about what might be found that I would prefer not to do it							
Strongly disagree	77.3	(760)	22.7	(223)	1.00	1.00	< 0.001
Tend to disagree	70.4	(112)	29.6	(47)	1.30 (1.00–1.70)	1.29 (0.99–1.68)	
Tend to agree	58.3	(42)	41.7	(30)	1.84 (1.37–2.47)	1.66 (1.24–2.23)	
Strongly agree	65.3	(32)	34.7	(17)	1.53 (1.02–2.28)	1.34 (0.88–2.03)	

Numbers vary due to missing data.

Significant results in bold.

^a Adjusted for gender, age (numeric), marital status, educational level, income and cancer diagnosis before ABC interview.

self-reported screening behaviour for cervical, breast and colorectal cancer and found that the sensitivity of self-reported CRC screening was particularly low. The low sensitivity could be caused by social desirability bias (tendency to respond in culturally or socially sanctioned ways) and acquiescence bias (tendency to agree with questions, particularly when in doubt). These types of bias constitute a problem for both self-reported screening behaviour and screening intentions (de Vet et al., 2011). Furthermore, factors influencing screening intentions have shown to differ from factors influencing behaviour (Gregory et al., 2011; Power et al., 2008); this stresses the importance of using register data to explore screening participation.

However, it is a limitation that beliefs about cancer and beliefs about CRC screening were measured at least three years before the individuals received an invitation for CRC screening. Therefore, beliefs about cancer and cancer screening may have changed in some individuals during this period. If the beliefs changed over time in some individuals, this is likely to be non-differential and independent of individual participation in CRC screening. Yet, it could be argued that the information bias was stronger for individuals who merely tended to agree/disagree with the different statements as less strongly held beliefs are more susceptible to change and therefore less stable over time (Howe & Krosnick, 2017). If this was the case, this could have led to an underestimation of the association between less strongly held beliefs (i.e. tend to agree/disagree) and non-participation in CRC screening.

Selection bias might exist as the participation rate was higher in this cohort (74.8%, Table 1) than has been reported overall for CRC screening in the period between March 2014 and December 2016 (62.6%) (de Vet et al., 2011). The difference in participation rate is likely to be affected by the fact that respondents of the ABC measure were more often ethnic Danes, were more often married/cohabiting and had a high household income. These socioeconomic factors have also been associated with participation in CRC screening (Hvidberg et al., 2014; Larsen et al., 2017). However, as the results are adjusted for these characteristics, this is not likely to have affected the reported associations. Yet, it is likely that negative beliefs about cancer and CRC screening were stronger among individuals who declined to participate in a telephone interview on cancer (i.e. the ABC measure) and among non-participants in screening. If this is the case, this could mean that the observed associations represent a minimum estimate of the true difference.

4.3. Comparison with other studies

The only general belief about cancer that was associated with non-participation in this study was 'not wanting to know if one has cancer'. The preference to remain oblivious of a cancer diagnosis could be related to cancer fatalism, i.e. the belief that events are out of individual control, and hence cancer cannot be prevented, and death is inevitable (Powe & Finnie, 2003). Previous studies have found that such beliefs are negatively associated with preventive behaviour such as screening (Powe, 1995; Schueler et al., 2008). Each of the three beliefs about CRC screening was associated with participation. We found that individuals who strongly agreed that 'bowel cancer screening is only necessary in case of symptoms' were more likely not to participate in CRC screening than individuals who strongly disagreed with this belief. Lack of symptoms has also consistently been associated with lower uptake of screening for both CRC, breast cancer and cervical cancer (Marlow et al., 2015; Power et al., 2009; Schueler et al., 2008), which could be related to the concept of perceived susceptibility, i.e. people perceive a lower risk of CRC in the absence of symptoms (Power et al., 2009). Other studies have also reported significant associations between the perception of personal susceptibility and participation in screening (Atkinson et al., 2015; Janz & Becker, 1984).

In order to increase the screening participation, future information leaflets and campaigns should target the individuals who do not want to know about cancer. Among other, these may remind individuals that early detection improves survival and that treatments for CRC have improved over time. In line with this, survivor role models, have also been stated as playing an essential role in modifying the belief of not wanting to know about cancer (Gregory et al., 2011). Moreover, a target group for the interventions is the individuals who believe that screening is only necessary if symptoms are present. Such campaigns should emphasise that CRC and precancerous polyps can be asymptomatic and that this is targeted in the screening (Atkinson et al., 2015; Powe & Finnie, 2003). The emphasis on precancerous polyps may also help allay the worry about what might be found in a CRC screening; this belief was also associated with non-participation. However, the screening literature has reported contradictory findings on the influence of worry or fear on screening participation, i.e. motivating, inhibiting and no effect (Janz & Becker, 1984). These conflicting findings may occur because different aspects of fear or worry influence the

screening behaviour in different ways (Hall et al., 2015).

In accordance with the HBM (Rosenstock, 1974), we found that the individual's perceived benefit of CRC screening was associated with participation. Hence, individuals who agreed that CRC screening could reduce the risk of dying from CRC were less likely to be non-participants. This factor has also shown to be among the few factors that rather consistently affect not only intentions but also actual screening behaviour (Gregory et al., 2011; Power et al., 2008). The HBM is one of the most used theoretical frameworks to guide interventions aiming to increase participation in CRC screening (Rawl et al., 2012). Wardle et al. (Wardle et al., 2003) developed an educational booklet based on the model, which was sent to individuals with low interest in screening. Individuals who received the booklet reported more positive beliefs and had a higher participation rate. However, multifactorial interventions focusing on the individual, the healthcare professionals and the organisational level have shown to have the best effect on the screening participation rate (Hay et al., 2005; Power et al., 2009).

5. Conclusion and implications

This is one of the first studies to explore the association between beliefs about cancer, beliefs about CRC screening and non-participation in screening for CRC. We used a prospective design and included register-based information on screening participation. Negative beliefs about CRC screening and not wanting to know about cancer strongly predicted non-participation in CRC screening. Exploring these beliefs for actual screening behaviour is important because many of these are potentially modifiable, and future interventions may profit from focusing on the cancer-specific screening beliefs.

Declarations

Ethics approval

ICBP Module 2 with ID 166 has been approved and is registered in the Record of Processing Activities at the Research Unit for General Practice in Aarhus in accordance with the provisions of the General Data Protection Regulation (GDPR).

Author contributions

LH, LJV, AFP and PV conceived the idea for the study. All authors contributed to the design of the study. LH performed the statistical analyses in consultation with the other authors. LH drafted the manuscript, and all authors contributed with input and critical revisions. Finally, all authors read and approved the final version of the manuscript.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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