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Type 2 diabetes and colorectal cancer screening: Findings from the English Longitudinal Study of Ageing

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Abstract

Objectives. While previous studies have identified type 2 diabetes (T2D) as a risk factor for colorectal cancer (CRC), little is known about whether T2D influences participation in CRC screening programmes. This study tested the extent to which Type 2 Diabetes is negatively associated with colorectal cancer screening uptake.

Methods. In this study, we analysed individual data of screening-eligible men and women aged 60 to 75 without cancer diagnosis from wave 6 of the English Longitudinal Study of Ageing (collected 2012-2013) to investigate whether T2D influences CRC screening behaviour independently of demographic characteristics, body mass index, socio-economic status, and other chronic diseases.

Results. Using both self-reported T2D diagnosis and glycated haemoglobin (HbA1c), individuals who reported to have been diagnosed with T2D or had HbA1c levels of 48 mmol/mol or higher were less likely to have ever completed a screening test (faecal occult blood test; 62.8% vs 75.8%, $p<0.01$) or to be up-to-date with their biennial screening invitation (60.2% vs 72.0%, $p<0.05$). The negative associations of T2D on CRC screening were found both in unadjusted and adjusted regression models.

Conclusions. Future qualitative and quantitative research should identify reasons for this discrepancy to inform interventions to increase screening uptake in this high-risk population.

Introduction

Individuals with type 2 diabetes (T2D) are at higher risk of developing cancer, including kidney cancer, non-small-cell lung, pancreas, early gastric, breast, ovarian and colorectal cancer (CRC) [1-7] potentially due to insulin resistance and compensatory hyperinsulinemia [8].

As the number of T2D patients worldwide has consistently increased [9] and CRC is among the most frequently diagnosed cancers [10], it is important to investigate the role of T2D in CRC preventive behaviours such as CRC screening uptake. Individuals with T2D are at higher CRC risk, and therefore regular participation in CRC screening programmes is particularly recommended [11]. So far, studies have shown that women with T2D are less likely to undergo cervical screening [12-15] and breast cancer screening [13,14, 16], although support for this has not been completely consistent [12].

Findings for CRC screening are equivocal. Two US studies, looking at samples of women aged 40 or older, demonstrated that those with T2D were more likely to be screened for CRC than those without [12,17]. Similarly, a recent US study looking at men and women aged 50 or older showed that those with T2D were more likely to be up-to-date with the recommended CRC screening [18]. In contrast, another US study, of older women (≥67 years), found a negative association [15]. All of the aforementioned studies were based in the US and looked at opportunistic rather than organised CRC screening programmes.

The only non-US study of is an English prospective survey of 55-year olds intending to have flexible sigmoidoscopy screening [19]. The study found an independent negative association between reporting T2D and screening attendance. However, the study was limited to people who had already expressed an intention to attend. Currently, there is a lack of studies looking

at the association for men and women in the context of an organised population-based CRC screening programme.

To address this limitation, the current study used data from the English Longitudinal Study of Ageing (ELSA; a nationally representative study of community-dwelling English adults aged ≥50 years that started in 2002-2003 (wave 1) [20]) to examine the role of T2D in CRC screening in a screening-eligible sample of English adults aged 60 to 75 years. In England, the National Health Service (NHS) invites people in that age range to complete a home-based stool test (faecal occult blood test; FOBt) every two years. We tested the hypothesis that people who reported having been diagnosed with diabetes or had elevated HbA1c levels at wave 6 are less likely to have ever been screened and less likely to be up to date with CRC screening.

Methods

Study population

We used individual data of screening-eligible men and women aged 60 to 75 without cancer diagnosis from ELSA's wave 6 questionnaire and nurse visit, which was collected in 2012 and 2013. All participants gave informed consent at each wave of data collection. ELSA was approved by the London Multicentre Research Ethics Committee (MREC/01/2/91), and informed consent was obtained from all participants. All study methods were performed in accordance with the Helsinki Declaration and good clinical and scientific practice.

Screening uptake

Ever screening was measured from the individual questionnaire in wave 6 of ELSA 'Have you ever completed the NHS bowel cancer screening test using the home test kit?' with response options being 'yes' or 'no'. Individuals who reported to have completed the

screening test were then asked to indicate the date of their most recent bowel cancer screening test. The response to this follow-up question was used to determine whether individuals followed the recommended biennial screening interval. Out of the 5160 participants in the screening-eligible age range of 60 to 75 without cancer diagnosis, 4925 (95.4%) responded to the date of the screening question.

Type 2 diabetes

T2D was measured using the question 'Has a doctor ever told you that you have diabetes or high blood sugar?' from the individual wave 6 questionnaire and from the glycated haemoglobin (HbA1c) level measured in the blood sample taken by the nurse during the wave 6 nurse visit. HbA1c values, ranging from 15-137 mmol/mol were dichotomised into two categories; those below 48 mmol/mol and those with values of 48 mmol/mol or higher [21]. The question about having a diabetes diagnosis was answered by 4882 participants in the eligible age range, while blood samples were obtained from 3270 participants. For the purpose of this study, we only considered respondents who answered the self-reported question and had a blood sample result recorded. Individuals were classified as having diabetes if they either reported a diabetes diagnosis or had an HbA1c value of 48 mmol/mol or higher.

Body Mass Index (BMI) and other comorbidities

Objective BMI measurements (height in m^2/weight in kg) were taken from the wave 6 nurse visit and categorised into normal weight (BMI<25), overweight (BMI 25–29.9), class I obesity (BMI 30–34.9), class II obesity (BMI 35–39.9) and class III obesity (BMI>=40) [22].

Assessments of coronary heart diseases, such as angina or myocardial infarction, depression, respiratory diseases like asthma and lung disease and stroke were based on the questions from

the individual questionnaires 'What type of emotional, nervous or psychiatric problems do you have?' and "Has a doctor ever told you that you have any of the conditions on this card?'

Covariates

We included gender, age, living arrangement, education and household non-pension wealth as socio-demographic covariates from the individual questionnaire. Living arrangement was coded as in binary as either living alone or with somebody.

Education was assessed in 4 categories ranging from 0 = "no formal education" to 3 = "university degree or higher".

Non-pension wealth is an indicator of socio-economic status (SES) in older people [23]. Non-pension wealth was measured at the family level, and this is the sum of net primary housing wealth, net physical wealth (other property wealth, business wealth and other physical assets) and net financial wealth. It included saving accounts, ISAs, TESSAs, premium bonds, national savings, PEPs, shares, trusts, bonds, other savings minus credit card, private and other debt. Quintiles of non-pension wealth (1 = low, 5 = high) were used for the analysis [24].

Statistical analysis

Characteristics of the sample were described using mean scores (standard deviations) for continuous variables and numbers (percentages) for categorical variables. We used unadjusted and adjusted multivariate logistic regression models to investigate whether T2D was associated with CRC screening behaviour.

The adjusted model controlled for demographic characteristics, BMI, SES, chronic heart disease, depression, respiratory problems and stroke. Note that we do not adjust for ethnicity, as the vast majority (97.2%) of the analytic sample reported a white ethnic background. All

statistical analyses were conducted with Stata/SE version 15.1 (StataCorp LP, College Station, TX).

Results

Descriptive characteristics

The analytic sample comprised of 3270 participants. The characteristics of the sample are presented in Table 1. The mean age of the participants was 66.7 years, and the majority fell into the overweight and obesity categories. 422 participants (12.9%) were classified as having T2D. Most of them reported a diabetes diagnosis and had an elevated HbA1c level of 48 mmol/mol or higher (N=235; 55.7%). 104 (24.6%) of the diabetic group (N= 422) who did not report a diagnosis were classified as having T2D because of their HbA1c level. Finally, 83 (19.7%) self-reported a diagnosis but had an HbA1c level below 48 mmol/mol.

Using the alternative classification of diabetes, 108 were classified as having undiagnosed diabetes, while 83 were classified as diabetes patients who control their diabetes well and 235 who control their diabetes poorly.

Ever uptake of CRC screening

Table 2 shows that individuals were less likely to have ever done CRC screening if they had T2D in both the unadjusted and the adjusted regression models (62.8% vs 75.8%,Odds Ratio (OR) 0.54, 95% confidence interval (CI) 0.43-0.67, $p<0.01$ and adjusted Odds Ratio (aOR) 0.70, 95% CI 0.56-0.89, $p<0.01$, see Table 3 for full results of the univariate and multivariate analysis). Class III obesity and increasing age were negatively associated with self-reported ever uptakes. Reporting a coronary heart disease or respiratory disease were also negatively associated with CRC screening in the unadjusted but not the adjusted regression. In contrast, women and participants who were cohabiting, respondents with

formal education and from a higher income group were more likely to have done the stool test.

Being up-to-date with CRC screening

T2D was also negatively associated with being up-to-date with the recommended CRC screening interval in both the unadjusted and adjusted regression models (60.2% vs 72.0%, OR 0.59, 95% CI 0.48-0.73, $p<0.01$ and aOR 0.74, 95% CI 0.59-0.94, $p<0.05$).

Similarly, to the results for ever uptake, age and Class III obesity were negatively associated with being up-to-date with CRC screening. While diagnosis of chronic heart diseases and respiratory diseases were again negatively associated with CRC screening in the unadjusted regressions, only the association for respiratory diseases remained statistically significant in the fully adjusted model. In contrast, relative affluence, being female, and having A-levels or a university degree were positively associated with screening.

Discussion

In this study, diabetes was negatively associated with CRC screening behaviour, independently whether it was defined by self-reported diabetes alone or in combination with HbA1c. Individuals with diabetes were less likely to have ever done CRC or be up-to-date with their biennial CRC screening invitation. These findings are particularly concerning as people with diabetes are at a moderately increased risk of developing CRC [24].

In line with a recent US study looking at individuals with diabetes which found that those who had an HbA1c level of 48 mmol/mol or higher were less likely to have been screened for CRC [25]. The present study adds to the literature by looking at the link between diabetes and CRC screening behaviour in an organised population-based CRC programme with routine

call and recall. Previous research has focused on the US [12, 15, 17, 18], while the one previous study of men and women in the UK included only those who had already expressed an intention to attend flexible sigmoidoscopy screening, limiting the generalisability of the findings to the population at large [19].

Nevertheless, the results of this earlier UK based study [19] are in keeping with the present analysis whereby those with diabetes were less likely to report being up to date with the recommended biennial screenings. Our study findings are also consistent with studies showing lower cervical [12-15] and breast-screening uptake [13, 14, 16] in people with diabetes. Given that the association we found was independent of several potential confounders, particularly the level of obesity, SES, and other comorbidities, indicates that there is a need to explore the diabetes specific barriers to screening.

Diabetes treatment guidelines highlight the importance of engaging in positive health behaviours [26] and attending CRC and other population-based cancer screenings are a part of engaging in proactive behaviours to benefit one's long-term health. Awareness of a chronic condition such as T2D could be considered a trigger for positive lifestyle change [27]. However, the findings of this study support research suggesting lower levels of engagement with positive health behaviour may be habitual in this population and difficult to modify [28]. Furthermore, there could be a common underlying mechanism in how individuals engage in unhealthy lifestyle leading to increased risk of diabetes, cancer or other chronic conditions [29]. These mechanisms could extend to the perceived susceptibility of subsequent associated risks and cues to action (e.g. CRC screening) [30, 31]. Low SES could exert a strong influence on these complex mediating pathways via low literacy, healthcare access, healthy food options etc. and our results for education and wealth seem to support this mechanism. A recent study, using the ELSA cohort, demonstrated that limited positive

behaviour change appears to occur following the diagnosis of T2D, with no changes in physical activity, fruit and vegetable intake and alcohol consumption detected [32].

Furthermore, a recent conceptual framework describing the potential influence of comorbidities on the timely diagnosis of cancer described mechanisms through which comorbid conditions could either facilitate help seeking and screening, or be associated with delays [34]. In the case of cancer screening, individuals with diabetes might have competing demands, as the management of diabetes can take priority (for both patients and healthcare providers) and this might interfere with participating in screening [34, 35].

The competing demands mechanism has been reported to interfere with help-seeking for symptomatic patients with serious comorbidities [36]. It can be even more relevant in the context of screening, where individuals are not experiencing cancer symptoms and instead have other more urgent healthcare needs.

Our study had several limitations. First, we used self-reported measures for CRC screening participation and comorbidities which may be subject to recall bias. However, a recent study that compared self-reported CRC screening behaviour with participation recorded by the programme found that more than 90% were able to accurately report whether they had ever completed a FOB test [33]. Secondly, this cross-sectional study does not look at the date of diabetes diagnosis, making the direction of the association between diabetes and CRC screening unclear.

In conclusion, we found evidence that people with T2D are less likely to undergo CRC screening in England. Further research is required to understand how to motivate and facilitate CRC screening in this and other groups at moderately increased CRC risk.

Conflict of Interest statement

The authors have declared that no competing interests exist in relation to the findings presented in this manuscript. However, Stacy Bailey has served as a consultant to Merck, Sharp & Dohme Corp, Northwestern University/Gordon and Betty Moore Foundation, Pfizer, Inc and Luto LLC for work unrelated to this manuscript. She has also received funding support via her institution from Merck, Sharp & Dohme Corp and Eli Lilly and Company. Michael Wolf has served as a consultant to Merck, Sharp & Dohme Corp, Abbvie, Vivus, Inc., Luto LLC, Pfizer, Inc, Anheuser Busch Imbev, DenverHealth, and Teva Pharmaceuticals for work unrelated to this manuscript. He also has received funding support via his institution from Merck, Sharp & Dohme Corp, Eli Lilly and Company, Abbvie, and UnitedHealthcare.

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Authors' contributions

STS, CvW, DC, RAH and PD developed the study concept and design. STS and CW performed the data analysis and interpretation. SS drafted the manuscript, and all authors provided critical revisions. All authors approved the final version of the manuscript for submission.

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Table 1. Participant characteristics (N=3270)

	N	(%)
Age (Mean and SD)	66.7	4.5
Gender		
Male	1500	(45.9%)
Female	1770	(54.1%)
Living arrangement		
Alone	832	(25.4%)
With somebody	2438	(74.6%)
Education		
No formal education	733	(22.4%)
Foreign or other	392	(12.0%)
A-levels or equivalent	1641	(50.2%)
University degree	504	(15.4%)
Non-pension wealth category		
5 (Most affluent)	716	(21.9%)
4	678	(20.7%)
3	670	(20.5%)
2	645	(19.7%)
1 (least affluent)	561	(17.2%)
BMI categories		
Normal weight (<25)	906	(27.7%)
Overweight (25-29.9)	1381	(42.2%)
Class I obesity (30-34.9)	681	(20.8%)
Class II obesity (35-39.9)	231	(7.1%)
Class II obesity (>40)	71	(2.2%)
Coronary heart diseases		
No	3040	(93.0%)
Yes	230	(7.0%)
Depression		
No	3047	(93.2%)
Yes	223	(6.8%)
Respiratory diseases		
No	2807	(85.8%)
Yes	463	(14.2%)
Stroke		
No	3171	(97.0%)
Yes	99	(3.0%)
Diabetes		
No	2848	(87.1%)
Yes	422	(12.9%)

BMI= body mass index; HbA1c= glycated haemoglobin; SD standard deviation

Table 2. Screening uptake according to demographics (N=3270)

	Ever uptake of CRC screening				Being up-to-date with CRC screening			
	No	**Yes**	**(% Yes)**	**p-value***	**No**	**Yes**	**(% Yes)**	**p-value***
Overall uptake	846	2424	(74.1)		966	2304	(70.5%)	
Gender								
Male	423	1077	(71.8%)	0.005	464	1036	(69.1%)	0.108
Female	423	1347	(76.1%)		502	1268	(71.6%)	
Living arrangement								
Alone	276	556	(66.8%)	<0.001	320	512	(61.5%)	<0.001
With somebody	570	1868	(76.6%)		646	1792	(73.5%)	
Education								
No formal education	267	466	(63.6%)		296	437	(59.6%)	
Foreign or other	88	304	(77.6%)	<0.001	108	284	(72.5%)	<0.001
A-levels or equivalent	385	1256	(76.5%)		436	1205	(73.4%)	
University degree	106	398	(79.0%)		126	378	(75.0%)	
Non-pension wealth category								
5 (Most affluent)	120	596	(83.2%)		143	573	(80.0%)	
4	137	541	(79.8%)		163	515	(76.0%)	
3	190	480	(71.6%)	<0.001	216	454	(67.8%)	<0.001
2	210	435	(67.4%)		236	409	(63.4%)	
1 (least affluent)	189	372	(66.3%)		208	353	(62.9%)	
BMI categories								
Normal weight (<25)	233	673	(74.3%)		277	629	(69.4%)	
Overweight (25-29.9)	310	1071	(77.6%)		365	1016	(73.6%)	
Class I obesity (30-34.9)	197	484	(71.1%)	<0.001	211	470	(69.0%)	<0.001
Class II obesity (35-39.9)	73	158	(68.4%)		79	152	(65.8%)	
Class II obesity (>40)	33	38	(53.5%)		34	37	(52.1%)	
Coronary heart diseases								
No	771	2269	(74.6%)	0.016	884	2156	(70.9%)	0.035
Yes	75	155	(67.4%)		82	148	(64.4%)	
Depression								
No	792	2255	(74.0%)	0.558	898	2149	(70.5%)	0.747
Yes	54	169	(75.8%)		68	155	(69.5%)	
Respiratory diseases								
No	703	2104	(75.0%)	0.008	796	2011	(71.6%)	<0.001
Yes	143	320	(69.1%)		170	293	(63.3%)	
Stroke								
No	818	2353	(74.2%)	0.578	933	2238	(70.6%)	0.401
Yes	28	71	(71.7%)		33	66	(66.7%)	
Diabetes								
No	689	2159	(75.8%)	<0.001	798	2050	(72.0%)	<0.001
Yes	157	265	(62.8%)		168	254	(60.2%)	

BMI= body mass index; HbA1c= glycated haemoglobin; SD standard deviation

*p-value refers to Chi-square test

Table 3. Predictors of CRC screening

		Ever uptake of CRC screening					Being up-to-date with CRC screening			
		Unadjusted model		Adjusted model			Unadjusted model		Adjusted model	
Variable	(%)	OR	95% CI	OR	95% CI	(%)	OR	95% CI	OR	95% CI
Overall uptake	(74.1%)					(70.5%)				
Age		0.934	0.918 - 0.951**	0.942	0.924 - 0.960**		0.919	0.903 - 0.935**	0.926	0.909 - 0.943**
Gender										
Male	(71.8%)	Ref.		Ref.		(69.1%)	Ref.		Ref.	
Female	(76.1%)	1.251	1.069 - 1.463**	1.471	1.243 - 1.741**	(71.6%)	1.131	0.973 - 1.315	1.341	1.140 - 1.577**
Living arrangement										
Alone	(66.8%)	Ref.		Ref.		(61.5%)	Ref.		Ref.	
With somebody	(76.6%)	1.627	1.370 – 1.932**	1.514	1.132 - 2.027**	(73.5%)	1.734	1.468 – 2.047**	1.338	1.014 - 1.765*
Education										
No formal education	(63.6%)	Ref.		Ref.		(59.6%)	Ref.		Ref.	
Foreign or other	(77.6%)	1.979	1.495 - 2.621**	1.514	1.132 - 2.027**	(72.5%)	1.781	1.365 – 2.324**	1.338	1.014 - 1.765*
A-levels or equivalent	(76.5%)	1.869	1.548 – 2.258**	1.427	1.164 - 1.748**	(73.4%)	1.872	1.558 – 2.250**	1.408	1.155 - 1.715**
University degree	(79.0%)	2.151	1.656 - 2.795**	1.666	1.264 - 2.196**	(75.0%)	2.032	1.583 - 2.609**	1.558	1.196 - 2.030**
Non-pension wealth category										
5 (Most affluent)	(83.2%)	Ref.		Ref.		(80.0%)	Ref.		Ref.	
4	(79.8%)	0.795	0.606 - 1.043	0.873	0.662 - 1.153	(76.0%)	0.788	0.612 - 1.017	0.869	0.669 - 1.128
3	(71.6%)	0.509	0.393 - 0.659**	0.602	0.461 - 0.787**	(67.8%)	0.525	0.411 - 0.670**	0.631	0.489 - 0.813**
2	(67.4%)	0.417	0.323 - 0.539**	0.529	0.403 - 0.695**	(63.4%)	0.433	0.339 - 0.552**	0.546	0.421 - 0.708**
1 (least affluent)	(66.3%)	0.396	0.305 - 0.515**	0.476	0.361 - 0.628**	(62.9%)	0.424	0.330 - 0.544**	0.507	0.389 - 0.661**
BMI categories										
Normal weight (<25)	(74.3%)	Ref.		Ref.		(69.4%)	Ref.		Ref.	
Overweight (25-29.9)	(77.6%)	1.196	0.984 - 1.454	1.251	1.021 - 1.533*	(73.6%)	1.226	1.019 - 1.475*	1.277	1.052 - 1.549*
Class I obesity (30-34.9)	(71.1%)	0.851	0.681 - 1.063	0.975	0.771 - 1.232	(69.0%)	0.981	0.791 - 1.217	1.114	0.887 - 1.398
Class II obesity (35-39.9)	(68.4%)	0.749	0.547 - 1.023	0.845	0.607 - 1.177	(65.8%)	0.847	0.624 - 1.151	0.939	0.680 - 1.297
Class II obesity (>40)	(53.5%)	0.399	0.244 - 0.650**	0.473	0.282 - 0.796**	(52.1%)	0.479	0.295 - 0.780**	0.562	0.335 - 0.941*
Coronary heart diseases										
No	(74.6%)	Ref.		Ref.		(70.9%)	Ref.		Ref.	
Yes	(67.4%)	0.702	0.527 – 0.936*	0.968	0.711 - 1.318	(64.4%)	0.740	0.559 – 0.980*	1.013	0.749 - 1.369
Depression										
No	(74.0%)	Ref.		Ref.		(70.5%)	Ref.		Ref.	
Yes	(75.8%)	1.099	0.801 - 1.509	1.195	0.858 - 1.666	(69.5%)	0.952	0.709 - 1.280	1.007	0.738 - 1.373
Respiratory diseases										
No	(75.0%)	Ref.		Ref.		(71.6%)	Ref.		Ref.	
Yes	(69.1%)	0.748	0.603 – 0.927**	0.853	0.681 - 1.069	(63.3%)	0.682	0.555 - 0.838*	0.776	0.625 - 0.963*
Stroke										
No	(74.2%)	Ref.		Ref.		(70.6%)	Ref.		Ref.	
Yes	(71.7%)	0.882	0.565 – 1.375	1.295	0.812 - 2.066	(66.7%)	0.834	0.545 - 1.275	1.228	0.785 - 1.920
Diabetes										
No	(75.8%)	Ref.		Ref.		(72.0%)	Ref.		Ref.	
Yes	(62.8%)	0.539	0.434 - 0.668**	0.703	0.557 - 0.887**	(60.2%)	0.589	0.476 - 0.727**	0.744	0.592 - 0.936*
N		3270		3270			3270		3270	
R^2				0.096					0.102	

* p<0.05; ** p<0.01 BMI= body mass index; CI= confidence interval; CRC= colorectal cancer; OR= odds ratio