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Does Family History of Cancer Influence Undergoing Screening and Gastrointestinal Investigations?

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ABSTRACT

Background & Aims: Although a family history of cancer (FHC) can modify the lifestyle and attitudes towards participation in cancer screening programs, studies on this relationship show mixed results and vary across populations. The objectives of the study were to compare sociodemographic characteristics, history of gastrointestinal (GI) investigations and *Helicobacter pylori* eradication, and modifiable cancer risk factors between those with FHC and those with no FHC (NFHC), and to investigate the association between FHC and a history of GI investigations.

Methods: A total of 3,455 questionnaires from the pilot study of the "*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR study)" in Latvia were analysed. We compared sociodemographic characteristics and history of GI investigations between participants with self-reported FHC and NFHC. Binary logistic regression models adjusted for socio-demographic characteristics and modifiable cancer risk factors were built for a FHC and each GI investigation.

Results: Participants with a FHC were more likely to be women, have a higher education and less likely to have harmful habits (smoking, alcohol consumption) than those with NFHC. Participants with a FHC were approximately twice as likely to report recent colorectal investigations specifically for screening, than those with NFHC. In fully adjusted logistic regression models, FHC was significantly associated with a recent history of faecal occult blood tests (FOBTs), colonoscopies, and colorectal investigations (FOBT or colonoscopy) specifically for screening as part of the national organized screening programme.

Conclusion. Our results indicate that those with a FHC have different patterns of health-related behaviour than those with NFHC.

Key words: genetic predisposition to disease – early detection of cancer – screening-psychology – health behavior – lifestyle.

Abbreviations: CRC: colorectal cancer; FHC: family history of cancer; FOBT: faecal occult blood tests; GI: gastrointestinal; GP: general practitioners; *H. pylori: Helicobacter pylori*; NFHC: no family history of cancer.

INTRODUCTION

Family history is a simply obtainable, potentially useful but generally underused medical tool for identifying individuals at risk of cancer in a clinical setting [1]. Cancer risk tends to aggregate in families because of shared genetic, behavioural and environmental factors, which in the long term may play a substantial role in health outcomes [1]. Although an individual cannot modify genetic cancer risk, many behavioural risk factors can be modified to reduce the risk of cancer. It has been estimated that 30-50% of cancers can be prevented, and approximately one third of cancer deaths have been attributed to the five leading behavioural and dietary risk factors: high body mass index, low fruit and vegetable intake, physical inactivity, tobacco use, and alcohol consumption [2].

In previous studies, individuals with a family history of cancer (FHC) were more likely to participate in cancer screening than those with no family history of cancer (NFHC) [3, 5, 6]. However, these studies have shown inconsistent results pertaining to health-related behaviour among individuals with a family history of site-specific cancer, including both lower and higher odds of adherence to healthy lifestyle recommendations [3-5], as well as no significant differences [5, 6] between FHC and NFHC.

In Latvia, where cancer is often diagnosed in the late stages and participation in prophylactic measures and screening programmes remains low [7-9], investigating factors related to participation in preventive activities is of high relevance for cancer prevention. During the studied period, the response rate for the national screening programme for colorectal cancer (CRC) in Latvia ranged from 9.6% (2013) to 11.8% (2016) [7]. Prognosis for patients in Latvia remains exceedingly pessimistic, as 59% of CRC and 66% of gastric cancer cases are first diagnosed in the late stages (2016 data) [10]. Faecal occult blood tests (FOBT) within the national screening programme and colonoscopy for CRC, and endoscopy for gastric cancer are the primary modes for the early diagnosis of these cancers, which is why we have included these particular investigations in our study.

In this context, certain characteristics of people with a FHC, e.g. attitudes towards participation in cancer screening programmes and cancer preventive lifestyle behaviours, may provide valuable insight into cancer control measures.

We therefore aimed to compare sociodemographic characteristics (age, sex, nationality, level of education, employment status, income level), history of recent gastrointestinal (GI) investigations (upper endoscopy, colonoscopy, FOBT), history of *Helicobacter pylori* (*H. pylori*) eradication, and modifiable cancer risk factors between participants with a FHC and NFHC, as well as to investigate the association between FHC and a history of GI investigations, participation in CRC screening and a history of *H. pylori* eradication, while accounting for sociodemographic and modifiable cancer risk factors.

METHODS

Study population

A total of 3,455 participants aged 40 to 64 years (50% male) were enrolled in the pilot study of the "Multicentre randomized study of *H. pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality" (the GISTAR study) in four study centres in Latvia from October 2013 to December 2016. Individuals were invited using patients' lists of general practitioners (GPs) in the areas of local recruitment centres and contacted through phone and/or mail. Participants signed an informed consent form and were examined by a study physician at the time of enrolment. Participants were excluded if they had a personal history of gastric cancer, gastric resections due to benign disease, *H. pylori* eradication therapy within the last 12 months, presence of alarm symptoms of digestive or other diseases, as well as signs of serious disease requiring immediate management [11].

After completing a detailed questionnaire on socio-demographic characteristics, modifiable cancer risk factors and medical history, study participants were randomly allocated to intervention or control groups. The intervention group was tested for pepsinogens I and II by latex-agglutination test system (Eiken Chemical, Tokyo, Japan) and *H. pylori* IgG group antibodies by ELISA (Biohit, Finland). Those with pepsinogen PgI/PgII ≤2 and PgI≤30 ng/mL were referred for upper endoscopy. Those positive for *H. pylori* were offered eradication therapy as part of the intervention. For the current study, questionnaire data from both the control and intervention groups were used.

The GISTAR study protocol was approved by the Ethics Committee of the International Agency for Research on Cancer (IEC 12–36), and the Central Medical Ethics Committee of Latvia (01–29.1/11). The study protocol is registered in the clinicaltrials.gov database (NCT02047994) [11].

Survey

For the purpose of the current study, participants were divided into two groups based on self-reported family history of cancer (FHC and NFHC) among the 1st degree (parents, siblings, and children) and the 2nd degree (grandparents, aunts and uncles) relatives. Participants with a family history of any malignant neoplasm qualified for the FHC group. Data on the primary location of the neoplasm was also collected. Those that reported FHC in a specific relative but could not name its primary location were also included in the FHC group. Participants responding they did not know whether they had a family history of cancer were not included in the analysis.

The FHC and NFHC groups were characterised based on self-reported data obtained from the pilot study of the GISTAR questionnaires, including socio-demographic characteristics (age, sex, nationality, marital status, level of education, income level, employment status,), history of any cancer among 1st and 2nd degree relatives, medical investigations in the past three years (GI investigations in general, upper endoscopy, FOBT, colonoscopy, and FOBT or colonoscopy specifically for screening purposes as part of the organized national screening programme), history of *H. pylori* eradication, as well as the presence of modifiable cancer risk factors (smoking, alcohol consumption, dietary habits). Height and weight were measured. Modifiable cancer risk factors included in the analysis were chosen according to the recommendations of the World Health Organization [2, 12]. Although physical activity is also a modifiable risk factor, we could not assess it in our study due to limited data.

Body-mass index (BMI = weight (kg)/height (m)^2) was calculated and split into two categories: ≤ 24.9 kg/m^2 (normal or underweight) and > 25.0 kg/m^2 (overweight). Self-reported smoking habits were assessed according to the following categories: smoked at least 100 cigarettes in a lifetime (yes, no); and the number of cigarettes smoked per day (median, IQR). Alcohol consumption was assessed based on self-reports of having consumed alcohol (yes or never); consumption of alcohol at least once a week for more than 6 months (yes, no); 200g of liquor (alcohol content at least 40%) in one sitting during the past year (yes, no).

Dietary habits were assessed based on self-reports of a history of or current adherence to a special diet (including dieting for weight loss) (yes, no) as an indicator of attitudes towards health and general health awareness, and the consumption of at least 400g of fruit and vegetables daily during the past week (yes, no) according to WHO and FAO recommendations on minimum fruit and vegetable intake [13], assisted by visual representations of portions.

Statistical analysis

Descriptive statistics of participants with FHC and NFHC were performed on sociodemographic characteristics, history

of GI investigations, *H. pylori* eradication, and modifiable cancer risk factors, stratifying participants by sex. Pearson chi-square and Mann Whitney U tests were used to identify differences between the groups.

Binary logistic regression models were built for the association between FHC and GI investigations in general, FOBTs, upper endoscopy, colonoscopy, and a history of *H. pylori* eradication. We built a crude model (not adjusted for any covariate), a model adjusted for socio-demographic characteristics and a fully adjusted model adjusted for both socio-demographic characteristics and modifiable cancer risk factors that had shown statistical significance in univariate analysis. Statistical analysis was performed using the SPSS software, version 21.0 [14].

RESULTS

After excluding participants with missing data on FHC (n= 216), 3,239 participants were included in the analysis. The participants (men 47%) had a mean age of 51.5 years. FHC was reported by 1,827 (56.4%), of which 1,110 (60.8%) were women. Participants with a FHC were more likely to be female, of Latvian nationality, be currently employed and have a higher education than those with NFHC (Table I).

Participants with a FHC were significantly more likely to report a history of GI investigations in the past 3 years and *H. pylori* eradication than those with NFHC (Table II).

Participants with a FHC were less likely to have had alcohol at least weekly for more than six months, at least 200g of liquor in one sitting during the past year, and to have smoked at least 100 cigarettes in their lifetime, but more likely to have been on a diet than those with NFHC. FHC reported smoking an average of 5 cigarettes less per day than those with NFHC (Table III).

In the multiple logistic regression model, we observed an association between a FHC and a history of recent GI investigations (crude OR=1.23; 95%CI 1.04-1.44). Adjusting for personal covariates (gender, age, employment status, nationality, level of education) changed the result obtained in the crude model by 5% (OR=1.18; 95%CI 1-1.39) (Supplementary Table S.1). Additionally, adjusting for lifestyle factors (at least 100 cigarettes in lifetime, has consumed alcohol, 200g of liquor in one sitting during the past year, history of a special diet) did not affect the association (Fig. 1).

We observed significantly positive associations of FHC also with FOBTs, colonoscopies, and colorectal investigations for screening. Modifiable cancer risk factors did not further change the observed association for all these outcomes (Fig. 1, Supplementary Table S.1).

Table I. Sociodemographic characteristics of study participants by sex and self-reported family history of cancer (FHC)

Variable	All	FHC	NFHC	*p*	Men			Women		
					FHC	NFHC	*p*	FHC	NFHC	*p*
	3,239	1,827 (56.4%)	1,412 (43.6%)	< 0.01	717 (39.2%)	792 (56.1%)	< 0.01	1,110 (60.8%)	620 (43.9%)	< 0.01
Age (mean ± SD)**	51.5 ± 6.7	51.4 ± 6.6	51.8 ± 6.8	0.08	51.3 ± 6.6	51.6 ± 6.8	0.42	51.5 ± 6.7	52.1 ± 6.9	0.05
Nationality, N (%)*										
Latvian	2687 (39.1)	1476 (80.8)	1080 (76.5)	0.01	576 (80.3)	599 (75.6)	0.06	900 (81.1)	481 (77.6)	0.13
Russian	450 (6.5)	217 (11.9)	196 (13.9)		98 (13.7)	125 (15.8)		119 (10.7)	71 (11.5)	
Other	3,743 (54.4)	134 (7.3)	136 (9.6)		43 (6.0)	68 (8.6)		91 (8.2)	68 (11.0)	
Education, N (%)*										
Primary	141 (4.1)	57 (3.1)	77 (5.5)	< 0.01	40 (5.6)	52 (6.6)	0.02	17 (1.5)	25 (4.0)	0.01
Upper secondary	625 (18.3)	324 (17.8)	270 (19.2)		131 (18.3)	155 (19.7)		193 (17.5)	115 (18.6)	
Vocational technical	1590 (46.7)	817 (44.8)	682 (48.5)		374 (52.2)	443 (56.2)		443 (40.1)	239 (38.7)	
Higher	1051 (30.8)	624 (34.2)	377 (26.8)		171 (23.9)	138 (17.5)		453 (41.0)	239 (38.7)	
Income[a], N (%)*										
< 250 Eur	1,290 (37.7)	672 (40)	554 (42.8)	0.29	239 (36.9)	311 (43.3)	0.05	433 (41.9)	243 (42.3)	0.70
250-500	1,421 (41.5)	779 (46.3)	557 (43.1)		304 (46.9)	302 (42.1)		475 (46.0)	255 (44.3)	
>500 Eur	425 (12.4)	230 (13.7)	182 (14.1)		105 (16.2)	105 (14.6)		125 (12.1)	77 (13.4)	
Employment, N (%)*										
Unemployed	335 (9.8)	147 (8.0)	169 (12)	< 0.01	62 (8.6)	107 (13.5)	< 0.01	85 (7.7)	62 (10.0)	0.13
Employed	2709 (79.1)	1492 (81.7)	1076 (76.2)		573 (79.9)	588 (74.2)		919 (82.8)	488 (78.7)	
Retired	251 (7.3)	129 (7.1)	104 (7.4)		61 (8.5)	54 (6.8)		68 (6.1)	50 (8.1)	
Disabled	128 (3.7)	59 (3.2)	63 (4.5)		21 (2.9)	43 (5.4)		38 (3.4)	20 (3.2)	

*Differences obtained using $\chi 2$ test; **Differences obtained using T-test or Mann-Whitney U test; [a] monthly household income per family member after taxes; FHC: family history of cancer; NFHC: no family history of cancer.

Table II. Medical behaviour of study participants by sex and self-reported family history of cancer (FHC)

Variable, N (%)*	All N = 3,239	FHC N = 1,827	NFHC N = 1,412	p	Men			Women		
					FHC N = 717	NFHC N = 792	p	FHC N = 1,110	NFHC N = 620	p
Gastrointestinal investigations (last 3 years)	842 (24.6)	487 (26.7)	322 (22.9)	0.01	165 (23.0)	164 (20.8)	0.28	322 (29.0)	158 (25.5)	0.12
Upper endoscopy (last 3 years)	635 (18.6)	344 (18.8)	262 (18.6)	0.83	127 (17.7)	141 (17.8)	0.97	217 (19.6)	121 (19.5)	0.98
Colonoscopy (last 3 years)	185 (5.4)	117 (6.4)	60 (4.2)	0.01	45 (6.3)	30 (3.8)	0.03	72 (6.5)	30 (4.8)	0.16
Faecal occult blood test (last 3 years)	189 (5.5)	126 (6.9)	60 (4.2)	< 0.01	33 (4.6)	17 (2.1)	0.01	93 (8.4)	43 (6.9)	0.29
Colorectal investigations for screening purposes (last 3 years)	141 (4.1)	100 (5.5)	40 (2.8)	< 0.01	25 (3.5)	15 (1.9)	0.05	75 (6.8)	25 (4.0)	0.02
History of *HP* eradication	462 (13.8)	267 (15.0)	172 (12.4)	0.04	99 (14.3)	94 (12.2)	0.25	168 (15.4)	78 (12.7)	0.13

*All differences obtained using the $\chi 2$ test; *HP*: *Helicobacter pylori*

In the fully adjusted model for personal and lifestyle factors, the main factors affecting undergoing GI investigations were age (being older increased the probability) and alcohol consumption (reporting ever having consumed alcohol increased the probability, while having had at least 200g of liquor in one sitting in the past year decreased the probability thereof) (Supplementary Table S.2).

When grouping FHC by cancer site, it seems that the effect of FHC on health-seeking behaviour differs by the type of cancer (Supplementary Tables S.3, S.4). Individuals with a family history of gastric cancer were more likely to have a history of general GI investigations than those with a family history of CRC and any FHC. Participants with a family history of CRC were more likely to have undergone colonoscopies and FOBTs and curiously also more likely to have a history of *H. pylori* eradication than those with a family history of gastric cancer or any FHC. However, groups by cancer site were too small to draw convincing conclusions and perform further analysis.

DISCUSSION

Our study is one of the largest studies to investigate the role of FHC on lifestyle and medical behaviour. Participants with a FHC were 2.7 times more likely to have a recent history of FOBT than those with NFHC. Similar studies show that individuals with a FHC were more likely to participate in cancer screening than those with NFHC [3, 5, 6]. For example,

Table III. Modifiable cancer risk factors of study participants by sex and self-reported family history of cancer (FHC)

Variable	All N = 3,239	FHC N = 1,827	NFHC N = 1,412	p	Men			Women		
					FHC N = 717	FHC N = 792	p	FHC N = 1,110	NFHC N = 620	p
BMI, N (%)*				0.22			0.42			0.61
≤24.9 kg/m^2	866 (25.4)	480 (26.3)	344 (24.4)		177 (24.8)	182 (23.0)		303 (27.3)	162 (26.2)	
>25.0 kg/m^2	2550 (74.6)	1343 (73.7)	1065 (75.6)		536 (75.2)	608 (77.0)		807 (72.7)	457 (73.8)	
Smoked at least 100 cigarettes in lifetime, N (%)*	1,659 (48.6)	822 (45.1)	738 (52.3)	< 0.01	506 (70.7)	570 (72)	0.58	316 (28.5)	168 (27.1)	0.53
Cigarettes per day ** median (IQR)	15 (10)	10 (13)	15 (10)	0.01	17 (10)	15 (10)	0.52	8 (5)	8.5 (9)	0.99
Alcohol once a week for more than 6 months, N (%)*	559 (16.4)	273 (15.0)	258 (18.3)	0.01	201 (28.2)	224 (28.4)	0.94	72 (6.5)	34 (5.5)	0.41
200g of liquor (alcohol content at least 40%) in one sitting during the past year, N (%)*	1248 (36.5)	616 (33.7)	554 (39.2)	< 0.01	371 (51.7)	434 (54.8)	0.24	245 (22.1)	120 (19.4)	0.18
Adherence to a special diet, N (%)*	453 (13.2)	281 (15.4)	151 (10.7)	< 0.01	60 (8.4)	62 (7.8)	0.71	221 (19.9)	89 (14.4)	< 0.01
At least 400g of fruit/ vegetables daily, N (%)*	1832 (53.6)	1002 (54.9)	757 (53.6)	0.48	323 (45.0)	386 (48.8)	0.15	679 (61.3)	371 (59.8)	0.56

*Differences obtained using $\chi 2$ test; **Differences obtained using Mann-Whitney U test.

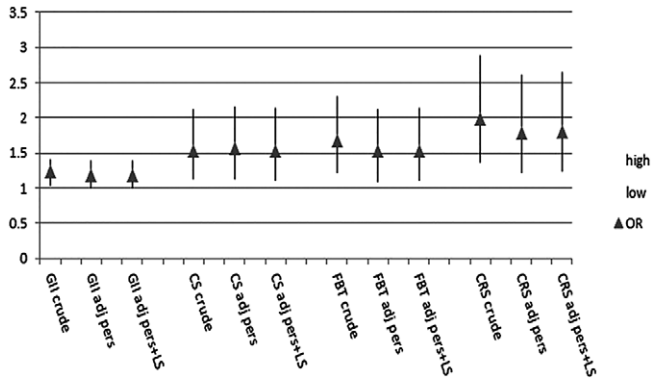

Fig. 1. Association between a family history of cancer and a history of gastrointestinal investigations, and a history of H. pylori eradication GII – gastrointestinal investigations, CS – colonoscopy, FBT – fecal blood test, CRS – colorectal investigations for screening purposes, adj pers – adjusted for personal factors, LS – lifestyle factors. OR – odds ratio, high – upper 95% confidence interval, low – lower 95% confidence interval. Personal factors: gender, age, employment status, nationality, level of education. Lifestyle factors: smoked at least 100 cigarettes in their lifetime, has consumed alcohol, 200 g of hard liquor in one sitting during the past year, history of or current adherence to a special diet.

in a cross-sectional study in Spain, individuals with a family history of CRC were twice more likely to participate in CRC screening than those with none [6].

Our results suggest that a FHC may be strongly associated with a history of recent GI investigations and CRC screening despite differences in socioeconomic status and lifestyle habits in the population. Although we cannot differentiate, to what extent this association is dependent on personal motivation, physician recommendations or a combination thereof, our findings suggest that individuals, when informed of a cancer risk associated with a FHC, may be more likely to participate in cancer screening programmes and other health related activities.

Female gender was the most consistently associated significant sociodemographic factor in determining participation in GI investigations, with women 2.5 times more likely than men to have had FOBTs. Several studies have shown that men are less inclined to participate in preventive healthcare than women [15-19]. According to the report on cancer screening practices in the European Union, women have a higher participation rate in CRC screening than men in all European countries implementing FOBTs [15]. In the UK, men are more likely to underestimate cancer incidence and the role of family history [17]. In a study conducted in the United States men were more willing to participate in cancer screening after receiving additional information than women, suggesting that the need for further explanation may be one of the reasons for their lower participation [19].

It is worth noting that gender disparities in health-seeking behaviour and cancer screening are reflected by cancer mortality rates, with the predicted total cancer related mortality rate in Europe 56% higher for men than women in 2017 [20]. Previous studies have found that health seeking behaviour and screening are influenced by the discussion of FHC among family members, which in turn is influenced by education and income [21]. Individuals with high levels of education may be more likely to associate their family history with an increased risk for disease. In a study in California, individuals reporting a FHC were more likely to have a college education and health insurance [5]. Bostean et al. [5] suggested that differences between those reporting a FHC and NFHC might to some extent be attributable to differences in health communication or health literacy rather than actual family cancer history. This may explain why a higher level of education was significantly associated with both reporting a FHC and having a history of FOBT in our study.

Other studies show that a low income and unemployment generally do not have an important role in the participation in screening programmes in European countries with nationwide population-based screening programmes [15, 22]. In Latvia, FOBT for CRC screening is state funded for ages 60-74 years, while further medical investigations such as colonoscopies and upper endoscopies are partly funded by the government if referred by GPs[15].This may explain why we did not observe significant differences in GI investigations and FOBTs across different categories of unemployment and income.

A study showed that approximately 23% of CRC cases could be prevented through the combination of no smoking, regular physical activity, limiting alcohol use, and maintaining a healthy diet and weight [23]. We found that participants with a FHC were generally more likely to avoid harmful habits. This may indicate increased awareness of modifiable risk factors in the FHC group, possibly making those with FHC more receptive to recommendations on adopting a healthier lifestyle. Similar studies show mixed results concerning health behaviours. In a cross-sectional study in California individuals with a family history of CRC were less likely to maintain a healthy weight and consume the recommended daily amount of fruit and vegetables, despite being more likely to be up-to-date with screening than those with NFHC [3]. Yet another similar study in California found no association between a FHC and better lifestyle behaviours [5].

A cross-sectional study in Oregon showed that only a small fraction of individuals with a family history of CRC reported discussing the risks of CRC and receiving recommendations on preventing CRC with their primary care provider [4]. The results of our study also suggest that many opportunities to educate those at increased risk on CRC prevention might have been missed.

CONCLUSIONS

Our results indicate that FHC is strongly associated with a history of recent GI investigations and CRC screening despite differences in socioeconomic status and lifestyle habits in the population. When informed of cancer risk associated with a FHC, individuals may be more likely to participate in cancer screening programmes and other health-related activities. In line with other studies, our findings suggest that efforts to increase prophylactic health behaviour and participation in cancer screening must be tailored to gender in order to decrease the gender gap. In addition, clinicians could play an essential role in emphasising health related behaviour counselling, especially targeting individuals with a FHC,

informing individuals of potentially shared behavioural risks in families and their major roles in the development of cancer.

Conflicts of interest: The authors declare no other conflicts of interest. Disclaimer: where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/World Health Organization.

Authors' contributions: J.Y.P, M.L., R.H., R.M. conceived and designed the study. I.P., S.P., D.S. data acquisition. D.R.E., I.Z. statistical analysis. D.R.E., I.Z., I.E., L.T. interpreted the results; D.R.E., I.E., L.T. drafted the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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