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Racial and Ethnic Variations in the Effects of Family History of Colorectal Cancer on Screening Compliance:

Family history and colorectal cancer screening

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Abstract

Background & Aims—Individuals with a family history of colorectal cancer (CRC) have a higher risk of developing CRC than the general population, and studies have shown that they are more likely to undergo CRC screening. We assessed the overall and race- and ethnic-specific effects of a family history of CRC on screening.

Methods—We analyzed data from the 2009 California Health Interview Survey to estimate overall and race- and ethnicity-specific odds ratios (ORs) for the association between family history of CRC and CRC screening.

Results—The unweighted and weighted sample sizes were 23,837 and 8,851,003, respectively. Individuals with a family history of CRC were more likely to participate in any form of screening (OR, 2.3; 95% confidence limit [CL], 1.7–3.1) and in colonoscopy screening (OR, 2.7; 95% CL, 2.2–3.4) than those without a family history, but this association varied among racial and ethnic groups. The magnitude of the association between family history and colonoscopy screening was highest among Asians (OR, 6.1; 95% CL, 3.1–11.9), lowest among Hispanics (OR, 1.4; 95% CL, 0.67–2.8), and comparable between non-Hispanic Whites (OR, 3.1; 95% CL, 2.6–3.8) and non-Hispanic Blacks (OR 2.6; 95% CL, 1.2–5.7) (*P* for interaction <0.001).

Conclusions—The effects of family history of CRC on participation in screening vary among racial and ethnic groups, and have the lowest effects on Hispanics, compared with other groups. Consequently, interventions to promote CRC screening among Hispanics with a family history should be considered.

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Keywords

population study; database analysis; early detection; colon cancer prevention

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the United States. Mortality from CRC has gradually decreased during the past decade,^{1, 2} which may be partially attributable to removal of adenomatous polyps or earlier stage at diagnosis of CRC as a result of screening.^{3, 4} Nonetheless, racial/ethnic disparities in CRC outcomes persist and minorities are less likely to be up-to-date on CRC screening.^{2, 5, 6}

Individuals with a family history of CRC have a higher risk of developing CRC than the general population.⁷⁻¹⁵ An estimated 30% of CRC cases may have an inherited component, of which approximately 5% constitute a well-defined genetic syndrome such as Lynch and polyposis syndromes. The remaining familial CRCs are likely due to multiple genetic factors and their interactions with the environment.^{9, 10} The risk of CRC in the latter group is between 2- and 6-fold compared to the general population depending on kinship, number of relatives, and age at diagnosis of affected family members.¹²⁻¹⁵ Siblings of patients with nonsyndromic CRC have recently been shown to have a higher prevalence of adenomas and advanced neoplasms.¹⁶ Risk stratification and screening recommendations for individuals with a family history of CRC depend on the details of the family history. Nevertheless, individuals with a family history of CRC should at the very least undergo average-risk screening, with colonoscopy being the preferred modality.¹⁷⁻¹⁹

Previous studies suggest that individuals with a family history of CRC are more likely to undergo CRC screening than those without a family history²⁰⁻²⁹ and that there may be racial/ethnic differences.³⁰⁻³² Nonetheless, previous studies generally compared racial/ethnic groups with (or without) a family history of CRC to Whites with (or without) a family history for the outcome of CRC screening. Although such comparisons provide evidence of differences *between* racial/ethnic groups, evidence of differences *within* racial/ethnic groups may be uniquely informative. Therefore, the aim of our study was to assess the impact of family history of CRC on CRC screening within racial/ethnic groups in a population-based sample.

Methods

Study population

We used data from the California Health Interview Survey (CHIS)³³ to assemble a study population for addressing our aim. CHIS is a population-based, random-digit dial telephone survey conducted in multiple languages among non-institutionalized California residents that uses a multistage sampling design to ensure that minority subgroups and rural populations are well-represented. The survey has been bi-annually administered since 2001 and queries information on a wide range of demographic and health-related topics, similar to the National Health Interview Survey (NHIS).³⁴

Our study used CHIS 2009 data³³ given the uniform availability of relevant exposure, covariate, and outcome information. All individuals aged between 50 and 75 years were eligible for our analysis because this group constitutes the generally accepted age range for average-risk CRC screening.^{17-19, 35} Although individuals with a family history of CRC may be recommended to initiate CRC screening prior to age 50 years, our objective was to compare the rate of CRC screening using average-risk guidelines so that we could compare

those with a family history to those without a family history of CRC. This study was approved by the Dana-Farber – Brigham and Women's Hospital Cancer Center Institutional Review Board.

Variables

Up-to-date average-risk CRC screening was defined as self-reported utilization of a fecal occult blood test (FOBT) within the past year, flexible sigmoidoscopy within the past 5 years, or colonoscopy within the past 10 years. We did not distinguish between screening and diagnostic tests, particularly considering that prior studies indicate self-reported reason for screening is often inaccurate.³⁶⁻³⁹ Family history of CRC was defined as having reported 1 first-degree relative diagnosed with colon or rectal cancer. The age at cancer diagnosis in the family member was not ascertained in the survey.

Self-reported race and ethnicity were categorized according to the Office of Management and Budget (OMB) Standards for Data on Race and Ethnicity,⁴⁰ which represent social rather than biologic measures.⁴¹ Briefly, race was categorized as American Indian or Alaska Native, Asian, Black, Native Hawaiian or Other Pacific Islander, and White. Ethnicity was categorized as Hispanic and non-Hispanic. Race/ethnicity was subsequently categorized for our analysis as Asian, Hispanic, non-Hispanic Black, non-Hispanic White, and Other. The "Other" category comprised American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals who reported multiple racial/ethnic categories. Additional information ascertained in the survey included age, gender, marital status, education, insurance status, and household income.

Data analysis

For descriptive analyses, we computed means (with standard deviations) and proportions while accounting for the complex survey design and population weights using PROC SURVEYMEANS and SURVEYFREQ in SAS 9.2 (SAS Institute, Cary, NC), respectively. We estimated overall and race/ethnicity-specific odds ratios (ORs) and 95% confidence limits (CL) for the association between family history of CRC (compared to no family history) and average-risk CRC screening as well as individual screening modalities. In addition, we explored potential statistical heterogeneity (i.e. third-order interaction) for the association between family history and CRC screening by race/ethnicity and insurance type (employer-based/private, Medicare only/Medicare and Medicaid, Medicaid only/Healthy Family/Other public program, or no insurance) given prior evidence that insurance type may be associated with CRC screening.⁴²

Odds ratios were adjusted to reduce confounding bias based on covariates identified in a directed acyclic graph (DAG).⁴³ Briefly, this graphical method is designed to identify of a minimal sufficient set of covariates for inclusion in a regression model to reduce confounding bias by applying an iterative algorithm (i.e. the back-door test).^{43, 44} One major advantage of this method is that it helps avoid overadjustment and unnecessary adjustment of covariates that may actually increase rather than reduce bias if inappropriately adjusted.⁴³⁻⁴⁵ Our DAG (Supplementary Figure 1) incorporated assumptions based on subject-matter knowledge⁴⁶ of dependencies between factors that influence CRC screening and family history of CRC. Application of the back-door test^{43, 44} indicated that adjustment for age and race/ethnicity in the overall model, and age in the race/ethnicity-specific models was minimally sufficient for reducing confounding bias in the association between family history of CRC and CRC screening. For comparison, we also estimated ORs and CL using all covariates in our graph that were not intermediates (i.e. age, race/ethnicity, gender, marital status, education, insurance status, and household income) rather than just the minimal sufficient set. CHIS uses a complex survey design and population weighting, which

if ignored, would bias variance estimates and compromise generalizability.⁴⁷⁻⁵² Therefore, we used PROC SURVEYLOGISTIC in SAS 9.2 (SAS Institute, Cary, NC) to estimate ORs and CL, which accounted for the complex survey design and population weights. In addition, effect heterogeneity by race/ethnicity was determined using interaction terms between family history and race/ethnicity in the models.

Sensitivity analysis

Given that self-reported family history may be inaccurate, we quantitatively explored the potential impact of misclassified self-reported family history of CRC in our study using a deterministic sensitivity analysis (Stata Corp, College Station, TX).^{53, 54} This type of analysis seeks to improve interpretation by quantifying the uncertainty in estimation.⁵⁴ Briefly, we used published values of sensitivity and specificity of self-reported family history from a validation study in the general population⁵⁵ as a starting point for exploring how classification errors in self-report could change our OR for the association between family history of CRC and CRC screening by any modality. We varied the paired-values of sensitivity and specificity to observe the change in OR from the original estimate. Of particular interest to us was the combination of sensitivity and specificity that could nullify our OR (i.e. the magnitude of misclassification would make our OR to equal 1.0). The results were subsequently used to interpret whether the values required for a null OR are plausible.

Results

The unweighted sample comprised 23,837 California residents aged 50 to 75 years (Table 1). Population-weighting yielded an evaluable sample size of 8,851,003 individuals representative of the California population, of whom approximately half were female. Non-Hispanic Whites were the largest racial/ethnic group (58%), followed by Hispanics (22%; 74% of whom were Mexican-origin), Asians (11%), and non-Hispanic Blacks (6%). The majority of individuals were insured and had household incomes of more than 100% of the federal poverty level.

Family history of CRC (defined as ≥ 1 first-degree relatives with CRC) was reported by 7% of respondents. Non-Hispanic Whites reported the highest proportion of individuals with a family history of CRC (8.2%) and Hispanics reported the lowest (4.2%) (Table 2). Any type of CRC screening was reported by 67% of respondents, of which colonoscopy was the most common. Non-Hispanic Whites had the highest frequency of any type of CRC screening (71%) and Hispanics had the lowest (57%). All of the racial/ethnic groups were more likely to have a colonoscopy than sigmoidoscopy or FOBT.

Individuals with a family history of CRC had higher odds of screening by any modality than those without a family history (OR 2.3, 95% CL: 1.7, 3.1) (Table 3). Among individuals with a family history of CRC, Hispanics were the least likely to undergo any form of CRC screening (61%), while the other three groups had similar frequencies of CRC screening (Asian 86%, non-Hispanic Black 87%, and non-Hispanic White 87%). We did not observe evidence of statistical interaction between race/ethnicity and insurance type (i.e. third-order interaction) for the association between family history and CRC screening (test for interaction, $P=0.56$).

With respect to specific screening modalities, individuals with a family history of CRC had higher odds of utilizing colonoscopy than those without a family history (OR 2.7, 95% CL: 2.2, 3.4) and lower odds of utilizing sigmoidoscopy (OR 0.72, 95% CL: 0.57, 0.93) or FOBT (OR 0.90, 95% CL: 0.75, 1.1). Hispanics with a family history were the least likely to undergo colonoscopy (44%), while Asians were the most likely to undergo colonoscopy

(83%), and non-Hispanic Blacks and non-Hispanic Whites had similar rates (72% and 79%, respectively) of colonoscopy.

The association between family history of CRC and colonoscopy use was highest among Asians (OR 6.1, 95% CL: 3.1, 11.9), lowest among Hispanics (OR 1.4, 95% CL: 0.67, 2.8), and comparable between non-Hispanic Whites (OR 3.1, 95% CL: 2.6, 3.8) and non-Hispanic Blacks (OR 2.6, 95% CL: 1.2, 5.7). The magnitude of association varied significantly between these racial/ethnic groups (test for interaction, $P<0.001$).

The overall and race-specific ORs were virtually unchanged when we adjusted for all covariates in our graph (Supplementary Table 1). For example, after adjustment for age, race/ethnicity, gender, marital status, education, insurance status, and household income, individuals with a family history had the same odds of having any colorectal cancer screening (OR=2.3, 95% CL: 1.8, 2.8) as estimated with our graph-based model which adjusted for only age and race/ethnicity. This lack of change in the estimate despite adjustment for additional covariates is consistent with the phenomenon of unnecessary adjustment⁴⁵ in which point estimates remain unchanged after adjustment for covariates that do not affect both the exposure and outcome, and thus do not satisfy criteria for confounding.

Table 4 summarizes ORs for the association between family history of CRC and CRC screening after adjustment for misclassification of family history using a range of paired-values of sensitivity and specificity derived from an external validation study⁵⁵ and hypothetical assumptions. Notably, the association between family history of CRC and CRC screening persisted over a wide range of sensitivity values for self-reported family history, except in scenarios of extreme differences in sensitivity values between screened and unscreened individuals. We observed inverse associations between family history and CRC screening only when we assumed greater than ~3-fold difference in sensitivity of self-reported family history between screened and unscreened individuals.

Discussion

The results of our population-based study suggest that the magnitude of association between family history of CRC and CRC screening, particularly colonoscopy use, varies substantially by racial/ethnic group. We observed a strong positive association between family history of CRC and colonoscopy use among Asians, whereas it was weakest among Hispanics. Notably, the magnitude of association between family history of CRC and colonoscopy use among non-Hispanic Whites and non-Hispanic Blacks was comparable.

A few prior studies have explored the association of family history of CRC and CRC screening by race/ethnicity. In contrast to our study, the primary comparison in these studies was CRC screening between racial/ethnic groups by subgroup of family history and used Whites as the reference group. For example, Murff et al. reported that African Americans with and without a family history of CRC were less likely to undergo colonoscopy screening compared to Whites.³⁰ In another study, Ponce et al. found that there was no difference in CRC screening between African Americans and Whites among those with and without a family history.³¹ However, Latinos were less likely than Whites to be screened for CRC in both family history subgroups, and this relative difference was greater among individuals with a family history than those without a family history. Unlike these studies, our study assessed the association between family history of CRC and CRC screening within racial/ethnic groups, which provides a unique perspective about the impact of family history on screening within these populations.

The strongest association between family history of CRC and colonoscopy use in our study is among Asians. Of note, the Asian American population is comprised of several subgroups that are known to have variable rates of CRC screening.^{56, 57} Therefore, further exploration of the association of family history of CRC and CRC screening among Asian subgroups is warranted.

Our results suggest that the impact of family history on CRC screening is similar among non-Hispanic Whites and non-Hispanic Blacks. This finding is consistent with the finding by Ponce et al.,³¹ but contrasts the report by Griffith et al. which concluded that risk-appropriate timely CRC screening rates did not differ between African-Americans with and without a family history, and were lower among African-Americans with a family history compared to non-Hispanic Whites with a family history.³² This discrepancy may be related to differences in outcome definition between studies. We defined CRC screening as adherence to average-risk screening as the basis for comparing individuals with and without a family history, whereas Griffith et al. used a definition consistent with ours for average-risk individuals but defined CRC screening individuals with a family history of CRC strictly as colonoscopy use within the past 10 years. Our finding may also indicate an improvement in CRC screening rates among non-Hispanic Blacks with a family history of CRC over the past several years.

We observed that Hispanics had the lowest prevalence of reported family history of CRC and of undergoing CRC screening among the general population and those with a family history, consistent with prior studies.^{31, 58} The association between family history of CRC and colonoscopy was also the weakest among Hispanics, suggesting the least impact of knowledge of family history on screening behavior. Our result is consistent with the finding by Ponce et al. that Latinos were less likely than Whites to be screened for CRC in both family history subgroups, and this difference was greater among individuals with a family history than those without a family history.³¹ The low prevalence of CRC screening and the minimal influence of family history on colonoscopy use among Hispanics is concerning. Consequently, promotion of CRC screening among Hispanics, particularly individuals with a family history of CRC, may need to be intensified.

Certain limitations of our analysis should be considered when interpreting our findings. Although prior studies have suggested that self-reported family history of CRC is modestly accurate for first-degree relatives,^{55, 59-61} we quantitatively explored the potential effect of potential misclassification on our estimate. The results of our sensitivity analysis illustrate that differences in the accuracy of family history would have to be rather extreme between screened and unscreened individuals for our observed association between family history of CRC and CRC screening to be nullified or reversed. Albeit informative, our sensitivity analysis is limited because we were unable to estimate classification errors in self-reported family history within the CHIS study population. The classification rates we used for adjustment were derived from other populations, which assumes applicability to our population. Furthermore, knowledge of family history may vary by race/ethnicity and immigration status, with racial/ethnic minorities and immigrants generally being less familiar with their family history,^{58, 62, 63} but limited external information on classification rates of family history by race/ethnicity precluded a more detailed sensitivity analysis. Future studies should emphasize accurate measurement of family history to reduce potential bias from self-report. A study with sufficient sample size to assess racial/ethnic variation would require considerable resources to accurately measure family history (e.g. if medical records of relatives were reviewed), but a validation sub-sample may be a feasible approach that would allow adjustment of the full-sample estimates for potential misclassification.⁵⁴

Another consideration is potential classification errors in self-report of CRC screening test use, particularly among racial/ethnic minorities.^{36, 37, 64-67} Misclassification of the outcome may exacerbate potential bias in our estimates, but the direction of this bias is difficult to speculate because of potential dependencies between misclassification of our exposure and outcome.⁶⁸ Lastly, variation in the prevalence of family history of CRC, CRC screening, or other characteristics between populations could vary the magnitudes of association observed in our study. For example, our estimates for CRC screening are higher than estimates based on the NHIS,⁶⁹ which may be attributable to differences in demographics, insurance coverage, or survey methods (e.g. CHS data are based telephone interview whereas NHIS data are based on in-person interview). Therefore, additional studies in other populations should be performed to explore the generalizability of our findings.

In summary, the results of our population-based study suggest considerable variation in the impact of family history of CRC on CRC screening by race/ethnicity, particularly colonoscopy use. Specifically, our results suggest that Hispanics with a family history of CRC may need to be targeted for CRC screening promotion. Prior studies have shown improvement in CRC screening among racial/ethnic minorities using patient navigator and other programs,⁷⁰⁻⁷⁴ but limited evidence is available about interventions aimed at those with a family history of CRC.^{75, 76} Future studies should explore the reasons for lack of CRC screening among racial/ethnic groups with a family history of CRC, and design interventions to improve CRC screening rates among this higher risk population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CHIS	California Health Interview Survey
CL	confidence limits
CRC	colorectal cancer
DAG	directed acyclic graph
FOBT	fecal occult blood testing
OMB	Office of Management and Budget
OR	odds ratio

Table 1

Characteristics of individuals aged 50 to 75 years in a representative sample of the California population.

Characteristic	N=8,851,003
Age (years); mean (SD)	59.9 (0.2)
Race/ethnicity; N (%)	
Asian	981,352 (11)
Hispanic	1,965,587 (22)
Non-Hispanic Black	519,525 (5.9)
Non-Hispanic White	5,166,464 (58)
Other	218,075 (2.5)
Female; N (%)	4,621,455 (52)
Marital status; N (%)	
Married or living with partner	6,387,410 (72)
Widowed, divorced, or separated	1,894,671 (21)
Never married	568,922 (6)
Education; N (%)	
High school diploma or less	3,358,279 (38)
Some college or vocational school	2,147,883 (24)
Bachelor's degree or more	3,344,841 (38)
Insurance N (%)	
Employer-based/private	4,810,682 (54)
Medicare only/Medicare and Medicaid	2,491,552 (28)
Medicaid only/Healthy Family/Other public	555,835 (6.3)
No insurance	992,934 (11)
Household income; N (%)	
0-99% FPL ^b	909,962 (10)
100-199% FPL	1,349,602 (15)
200-299% FPL	1,140,832 (13)
300% FPL	5,450,607 (62)
Family history of colorectal cancer; N (%)	610,520 (6.9)
Colon cancer screening; N (%)	
Fecal occult blood test (FOBT) within past year	2,241,502 (25)
Sigmoidoscopy within past 5 years	1,247,513 (14)
Colonoscopy within past 10 years	4,413,056 (50)
Any colon cancer screening ^a	5,950,664 (67)

^aFecal occult blood test (FOBT) within past year, sigmoidoscopy within past 5 years, or colonoscopy within past 10 years.

^bFederal poverty level (FPL).

Race-specific prevalence of family history of colorectal cancer and colorectal cancer screening^a for individuals aged 50 to 75 years in a representative sample of the California population.

Table 2

Race/ethnicity	Family history N (%)	FOBT N (%)	Sigmoidoscopy N (%)	Colonoscopy N (%)	Any screening N (%)
Asian	56,072 (5.7)	251,485 (26)	138,445 (14)	461,498 (47)	635,423 (65)
Hispanic	83,273 (4.2)	521,245 (27)	258,205 (13)	738,839 (38)	1,123,924 (57)
Non-Hispanic Black	31,784 (6.1)	141,189 (27)	95,974 (18)	243,233 (47)	348,300 (67)
Non-Hispanic White	422,315 (8.2)	1,251,364 (24)	722,414 (14)	2,857,777 (55)	3,687,661 (71)
Other	17,076 (7.8)	76,219 (35)	32,475 (15)	111,709 (51)	155,356 (71)

^aDefined as fecal occult blood test (FOBT) within past year, sigmoidoscopy within past 5 years; colonoscopy within past 10 years; any of these tests within their designated timeframes.

Table 3

Odds ratios for overall and race-specific associations between family history of colorectal cancer^a and colorectal cancer screening^b.

	FOBT (%)	FOBT Odds ratio ^c (95% CL ^d)	Sigmoidoscopy (%)	Sigmoidoscopy Odds ratio ^c (95% CL ^d)	Colonoscopy (%)	Colonoscopy Odds ratio ^c (95% CL ^d)	Any (%)	Any Odds ratio ^c (95% CL ^d)
Overall								
Family history (N=610,520)	24	0.90 (0.75, 1.1)	11	0.72 (0.57, 0.93)	73	2.7 (2.2, 3.4)	83	2.3 (1.7, 3.1)
No family history (N=8,240,483)	25	1.0	14	1.0	48	1.0	66	1.0
Asian								
Family history (N=56,072)	19	0.66 (0.30, 1.4)	13	0.92 (0.36, 2.3)	83	6.1 (3.1, 12)	86	3.5 (1.7, 7.4)
No family history (N=925,280)	26	1.0	14	1.0	45	1.0	64	1.0
Hispanic								
Family history (N=83,273)	26	1.0 (0.47, 2.1)	8.0	0.59 (0.26, 1.3)	44	1.4 (0.67, 2.8)	61	1.3 (0.41, 3.8)
No family history (N=1,882,314)	26	1.0	13	1.0	37	1.0	57	1.0
Non-Hispanic Black								
Family history (N=31,784)	25	0.80 (0.39, 1.6)	14	0.66 (0.25, 1.7)	72	2.6 (1.2, 5.7)	87	2.9 (1.2, 6.9)
No family history (N=487,741)	27	1.0	19	1.0	45	1.0	66	1.0
Non-Hispanic White								
Family history (N=422,315)	23	0.90 (0.75, 1.1)	11	0.73 (0.58, 0.91)	79	3.1 (2.6, 3.8)	87	2.7 (2.2, 3.2)
No family history (N=4,744,149)	24	1.0	14	1.0	53	1.0	70	1.0
Test of heterogeneity		<i>P</i> =0.90		<i>P</i> =0.96		<i>P</i> <0.001		<i>P</i> =0.21

^aFamily history of colorectal cancer defined as first-degree relative with colorectal cancer.

^bDefined as fecal occult blood test (FOBT) within past year; sigmoidoscopy within past 5 years; colonoscopy within past 10 years; any of these tests within their designated timeframes.

^cAdjusted for age and race for overall estimate, and age for race-specific estimates.

^dCL: Confidence limits.

Odds ratios (ORs) for the association between family history of colorectal cancer and colorectal cancer screening after adjustment for potential misclassification of family history using classification rates from an external validation study.^a.

Table 4

Scenario	Screened		Unscreened		Adjusted OR ^b
	Sensitivity	Specificity	Sensitivity	Specificity	
1 ^c	1.00	1.00	1.00	1.00	2.3
2	0.27	0.99	0.27	0.99	3.3
3	0.50	0.99	0.27	0.99	1.5
4	0.75	0.99	0.27	0.99	0.93
5	0.27	0.99	0.15	0.99	1.6
6	0.50	0.99	0.15	0.99	0.72
7	0.75	0.99	0.15	0.99	0.45

^aSensitivity and specificity based on estimates from a recent validation study in the general population.⁵⁵

^bAdjustment of the crude odds ratio for misclassification bias; not to be confused with adjustment for confounding bias.

^cSame as estimate reported in current study; assumes perfect sensitivity and specificity (i.e. no misclassification of family history).