Familial Risk of Cancer and Knowledge and Use of Genetic Testing

Heather J. Baer, ScD[1,2,3], Phyllis Brawarsky, MPH[1], Michael F. Murray, MD[4], and Jennifer S. Haas, MD, MSPH[1,2,5]

[1]Division of General Medicine and Primary Care, Brigham and Women's Hospital, Boston, MA, USA; [2]Department of Medicine, Harvard Medical School, Boston, MA, USA; [3]Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA; [4]Division of Genetics, Brigham and Women's Hospital, Boston, MA, USA; [5]Department of Society, Human Development, and Health, Harvard School of Public Health, Boston, MA, USA.

BACKGROUND: Identification of genetic risk factors for common diseases, including cancer, highlights the importance of familial risk assessment. Little is known about patterns of familial cancer risk in the general population, or whether this risk is associated with knowledge and use of genetic testing.

OBJECTIVE: To examine the distribution of familial cancer risk and its associations with genetic testing in the United States.

DESIGN: Cross-sectional analysis of the 2005 National Health Interview Survey (NHIS).

PARTICIPANTS: 31,428 adults who completed the NHIS Cancer Control Supplement.

MAIN MEASURES: Familial cancer risk was estimated based on the number of first-degree relatives with a breast and ovarian cancer syndrome (BRCA)- or a Lynch-associated cancer, age of onset (<50 or ≥50 years), and personal history of any cancer. Outcomes included having *heard* of genetic testing, *discussed* genetic testing with a physician, been *advised* by a physician to have testing, and *received* genetic testing.

KEY RESULTS: Most adults (84.5%) had no family history of BRCA- or Lynch syndrome-associated cancer; 12.9% had a single first-degree relative (5.3% with early onset); and 2.7% had ≥2 first-degree relatives. Although 40.2% of adults had *heard* of genetic testing for cancer risk, only 5.6% of these individuals had *discussed* testing with a physician, and of these 36.9% were *advised* to be tested. Overall, only 1.4% of adults who had heard of genetic testing *received* a test. Familial risk was associated with higher rates of testing; 49.5% of participants in the highest risk group had *heard* of testing, of those 14.8% had *discussed* it with their physician, and 4.5% had *received* genetic testing.

CONCLUSIONS: These nationally representative data provide estimates of the prevalence of familial cancer risk in the US and suggest that information about genetic testing is not reaching many at higher risk of inherited cancer.

KEY WORDS: family history; primary care practice; cancer.
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INTRODUCTION

Growing evidence points to the role of genetic risk in common chronic conditions, including cancer. Although the majority of cases are sporadic, cancers of the breast, ovary, colorectum, and uterus may have a strong hereditary component and an available genetic test.[1] For this reason, collection of accurate information on familial risk can be an important tool for identifying individuals at elevated risk who may benefit from interventions such as risk factor modification, more frequent screening, and genetic testing.[2,3]

Although the importance of assessing familial risk of cancer is well recognized, family histories often are not obtained in clinical practice.[4] Barriers to the collection of family history include lack of time during a typical visit, as well as the concerns of clinicians about their ability to use this information to accurately counsel patients about their personal risk.[5,6] In addition, patient barriers are important in the communication of family history to clinicians. According to a survey conducted by the Centers for Disease Control (CDC), most Americans report that they have not actively collected health information from their relatives to develop a family history.[7]

As a result of these issues, there are sparse data on patterns of familial risk for cancer in the general US population. Furthermore, few studies have examined the relation between familial risk of cancer and awareness, referral, and use of genetic testing, which is currently available for several cancers associated with known genetic mutations. While there are a growing number of genetically defined cancer predisposition syndromes, breast and ovarian cancer syndrome (BRCA) and Lynch syndrome stand out as having well-defined strategies for testing. Therefore, the purpose of this investigation was to examine: (1) the distribution of estimated familial cancer risk for BRCA (breast and ovarian)- and Lynch-associated (colorectal and uterine) cancers, and (2) the association of these cancers with genetic testing, using data from a large, nationally representative sample.

METHODS

Study Population

This analysis is based on data from the 2005 National Health Interview Survey (NHIS). The NHIS, conducted by the National Center for Health Statistics and the CDC, is a national probability sample survey that collects information about the civilian, non-institutionalized US population through household interviews

(http://www.cdc.gov/nchs/nhis.htm). The NHIS includes a family component, which collects demographic and health status information for each family member, as well as a sample adult component, which collects additional information for a randomly selected adult. In 2005, the sample adult component included the Cancer Control Supplement, a series of questions that assessed personal and family history of cancer and knowledge and use of genetic testing. The population for the present study consisted of respondents to the sample adult component, who were 31,428 adults randomly selected from 39,284 families. The response rate for this sample was 69.0%.[8] The study protocol was approved by the Partners Institutional Review Board.

Independent Variables

We estimated participants' familial risk based on their reported number of first-degree relatives (i.e., parents, siblings, offspring) who had been diagnosed with cancers that are part of BRCA- or Lynch-associated cancer syndromes (including breast, ovary, colorectum, and uterus),[9–12] the age of each relative at diagnosis (<50 vs. ≥50 years), as younger age of onset is more likely associated with familial risk,[13] and participants' personal history of these cancers. We then categorized estimated familial risk of cancer as: (1) no first-degree relatives or personal history of one of these cancers; (2) one first-degree relative (or subject) diagnosed ≥ age 50 (average age of onset); (3) one first-degree relative (or subject) diagnosed < age 50 (early onset); or (4) ≥2 first-degree relatives (including subject) diagnosed at any age. Personal history of cancer also was categorized and examined as a separate independent predictor (no personal history of any cancer, personal history of a BRCA- or Lynch-associated cancer, or personal history of any other cancer).

We also assessed other participant characteristics, including age (18–39, 40–49, 50–59, 60–69, 70 or older), sex, race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic Black or other), whether US born, educational attainment (did not complete high school, high school graduate, some college, college graduate), marital status (married or living with partner vs. other), number of chronic medical conditions (including arthritis, peptic ulcer disease, chronic lung disease, cardiovascular disease, hypertension, and diabetes, categorized as none, one, two, three, or more), current smoking, self-rated poor health, body mass index (underweight or normal, overweight, obese), and region of the country (East, South, Midwest, West).

Outcome Variables

Four outcome variables pertaining to genetic testing for cancer were assessed in NHIS. Adults were asked whether they had ever *heard* of genetic testing for cancer. If they answered yes to this question, they were asked if they had *discussed* testing with their physician, and if discussed, whether their physician had *advised* them to have genetic testing. In addition, all participants who reported that they had heard of testing were asked if they had ever *received* genetic testing for cancer risk.

Statistical Analysis

We used bivariate analyses to compute percentages and to examine the associations of familial cancer risk with other characteristics and with each of the four genetic testing outcomes (*heard*, *discussed*, *advised*, and *received*); chi-square tests were used to determine statistical significance. We then used multivariate logistic regression models to estimate adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI) for the associations of familial cancer risk and other demographic and health variables with each of the four genetic testing outcomes. We included all factors that we believed, a priori, could potentially affect the genetic testing outcomes, based on previous literature. The final models included familial cancer risk, sex, age, race/ethnicity, education, marital status, BMI, self-perceived poor health, number of comorbid conditions, personal history of cancer, smoking status, US born and region of the US. We also conducted secondary analyses separately among individuals with and without a personal history of cancer. We used SUDAAN version 10.0 (RTI International, Research Triangle Park, NC), and incorporated the survey sample weights to account for the sampling strategy, non-response, and the potential design effect of cluster sampling of the NHIS.[8]

RESULTS

Most adults (84.5%) had no family or personal history of a cancer associated with BRCA or Lynch syndrome; 12.9% had a single first-degree relative or personal history (5.3% with early onset cancer); and 2.7% had ≥2 first-degree relatives (including personal history) (Table 1). A total of 342 participants (1.1% of the sample) had ≥2 first-degree relatives with BRCA-associated cancers, and 230 (0.7% of the sample) had ≥2 first-degree relatives with Lynch-associated cancers. Compared to those with no family history, participants in the highest familial risk group, with ≥2 first-degree relatives with a BRCA or Lynch-associated cancer, were older, more likely to be female, non-Hispanic white, born in the US, obese, and have ≥1 chronic disease, but less likely to be college graduates or current smokers. Even when personal history of breast or ovarian cancer was excluded, there was still a higher percentage of women in the strong familial risk group (66.9%) compared to the no family history category (50.1%).

Overall, 40.2% of participants had *heard* of genetic testing; of this group, however, only 5.6% had *discussed* testing with their physician, and 1.4% had *received* genetic testing (Table 2). Of those who had discussed it with their physician, 36.9% had been *advised* to have genetic testing. The percentage of participants who had *heard* of testing generally increased with stronger familial risk; of those with no family history, 38.6% had *heard* of genetic testing, compared to 49.5% of those in the highest familial risk group ($p<0.0001$). Those in the highest familial risk category also were most likely to have the other genetic testing outcomes, although the absolute percentages were still low.

Other participant characteristics also were related to the frequency of the genetic testing outcomes. Older participants (≥70 years) and males were less likely to have *heard* of genetic testing and to have *discussed* it. Hispanic and African-American participants were less likely to have *heard* of testing than white, non-Hispanic participants (17.7% and 28.8%, respectively, compared to 46.7%). However, among those who had *heard* of testing, Hispanics were more likely to report *discussion* with their physician, to have been *advised* to have

Table 1. Characteristics of the Sample by Family History of a Cancer Associated with an Inherited Syndrome[a]

	None	1 Relative or subject (age ≥50)	1 Relative or subject (age <50)	≥2 (including subject)	p-value
Sample N	26,341	2,448	1,721	918	
Weighted N	183,923,404	16,464,723	11,573,968	5,811,660	
	%	%	%	%	
Overall	84.5	7.6	5.3	2.7	
Sex					<0.0001
Male	49.9	43.2	37.9	27.7	
Female	50.1	56.8	62.1	72.3	
Age (years)					<0.0001
18–39	44.5	12.3	31.0	8.9	
40–49	20.5	20.2	23.7	14.0	
50–59	16.1	23.1	19.0	22.7	
60–69	9.3	20.8	13.0	21.8	
≥70	9.7	23.7	13.2	32.6	
Race/ethnicity					<0.0001
Hispanic	13.9	6.2	8.5	4.4	
African-American, Other non-Hispanic	16.9	9.7	12.5	9.7	
White, non-Hispanic	69.3	84.1	78.9	85.9	
Education[b]					<0.0001
<High school graduate	16.7	11.9	15.7	15.4	
High school graduate	29.5	29.0	30.7	34.8	
Some college	28.3	28.4	28.5	28.0	
College graduate	25.5	30.7	25.1	21.8	
Marital Status[b]					<0.0001
Married/ living with partner	62.6	68.0	65.0	62.4	
Not married	37.4	32.0	35.0	37.6	
Body mass index[b]					<0.0001
Underweight/normal	40.8	33.3	36.2	32.5	
Overweight	34.9	40.1	34.3	37.9	
Obese	24.3	26.5	29.5	29.6	
Number of comorbid conditions					<0.0001
None	50.0	29.1	35.0	20.5	
1	26.9	32.0	29.8	29.8	
2	14.1	21.2	19.8	25.1	
≥3	8.9	17.3	15.4	24.6	
Personal history of cancer					<0.0001
No cancer	96.4	81.0	84.2	65.4	
BRCA-/Lynch-associated cancer[a]	0	12.2	11.3	28.3	
Other cancer	3.6	6.8	4.5	6.3	
Current smoker[b]					<0.0001
Yes	21.5	15.8	22.9	14.2	
No	78.5	84.2	77.1	85.8	
Self-perceived poor health[b]					<0.0001
Yes	11.3	16.2	17.9	23.5	
No	88.7	83.8	82.1	76.5	
Born in US[b]					<0.0001
Yes	82.9	91.9	91.3	94.4	
No	17.1	8.1	8.7	5.6	
Region of US					0.0001
Northeast	18.2	19.9	16.2	20.8	
Midwest	24.3	27.5	26.2	27.6	
West	21.0	19.0	19.1	21.1	
South	36.5	33.6	38.4	30.5	

Percentages are weighted. P-values are from chi-square tests. [a]*Cancers included: breast, ovarian (BRCA), colorectal, uterine (Lynch)*
[b]*Missing: education, 355; marital status, 165; body mass index, 1,430; current smoker, 277; self-perceived poor health, 15; born in US, 27*

testing, and to have *received* it compared to the other racial/ethnic groups. The percentage of participants who had *heard* of genetic testing increased with education, although the other testing outcomes did not. Participants with a personal history of cancer were more likely to have all of the genetic testing outcomes. In addition, participants who were married or living with a partner or were born in the US were more likely to have *heard* of genetic testing, whereas those who were current smokers, had poor self-rated health, or lived in the South were less likely to have *heard* of testing.

After adjustment for other participant characteristics (Table 3), individuals with the highest familial risk (≥2 first-degree relatives) were more likely to have *heard* of genetic testing (OR=1.40, 95% CI: 1.17–1.68), to have *discussed* it with their physician (OR=4.05, 95% CI: 2.67–6.16), to have been *advised* to have testing (OR=1.58, 95% CI: 0.80–3.14), and to have *received* testing (OR=2.72, 95% CI: 1.45–5.11) compared to those with no family or personal history. However, the odds of having *heard* of genetic testing or being *advised* to have testing did not increase substantially across the familial risk groups.

Table 2. Characteristics of the Sample by Knowledge and Use of Genetic Testing for Cancer

	Heard of genetic testing	Discussed genetic testing with physician	Advised by physician to have genetic test	Received a genetic test
Sample (denominator)	29,326[a]	11,215[b]	640[c]	11,206[d]
Population (weighted) sample (denominator)	203,759,634	81,915,533	4,555,959	81,851,727
Overall	40.2%	5.6%	36.9%	1.4%
Number of first-degree relatives or subject with a BRCA- or Lynch-associated cancer (age of onset)[e]				
None	38.6%	4.2%	31.0%	1.0%
1 (age ≥50 years)	48.6%	9.1%	42.0%	2.1%
1 (age <50 years)	47.9%	12.1%	45.6%	3.8%
≥2	49.5%	14.8%	53.4%	4.5%
	<0.0001	<0.0001	0.005	<0.0001
Sex				
Male	36.5%	4.4%	32.0%	1.2%
Female	43.7%	6.5%	39.5%	1.5%
	<0.0001	0.0001	0.08	0.23
Age (years)				
18–39	36.7%	6.3%	33.0%	1.4%
40–49	44.5%	6.0%	37.3%	1.6%
50–59	48.1%	5.1%	42.6%	1.1%
60–69	45.4%	4.6%	36.5%	1.4%
≥70	28.8%	3.7%	46.8%	1.4%
	<0.0001	0.007	0.33	0.77
Race/ethnicity				
Hispanic	17.7%	10.9%	59.0%	4.4%
African-American, other non-Hispanic	28.8%	6.1%	32.3%	1.6%
White, non-Hispanic	46.7%	5.1%	34.5%	1.2%
	<0.0001	<0.0001	0.001	0.0005
Education[f]				
<High school grad	18.1%	7.3%	44.8%	2.2%
High school grad	31.7%	5.6%	42.2%	1.4%
Some college	45.5%	5.0%	34.2%	1.3%
College grad	58.6%	5.7%	33.8%	1.3%
	<0.0001	0.21	0.27	0.42
Marital status[f]				
Married/living with partner	43.0%	5.5%	35.7%	1.3%
Not married	35.6%	5.6%	39.2%	1.5%
	<0.0001	0.92	0.40	0.50
Body mass index[f]				
Underweight/normal	41.1%	5.8%	30.1%	1.1%
Overweight	40.7%	5.3%	40.0%	1.4%
Obese	39.0%	5.6%	43.6%	1.9%
	0.07	0.70	0.01	0.08
Number of comorbid conditions				
None	37.1%	5.4%	32.3%	1.2%
1	44.8%	6.3%	38.7%	1.6%
2	43.2%	5.4%	42.2%	1.2%
≥3	37.5%	4.5%	42.8%	1.8%
	<0.0001	0.14	0.27	0.36
Personal history of cancer				
No cancer	39.8%	5.0%	32.7%	1.1%
BRCA-/Lynch-associated cancer[e]	46.6%	18.9%	59.0%	9.6%
Other cancer	46.0%	9.4%	56.8%	3.5%
	<0.0001	<0.0001	0.0003	<0.0001
Current smoker[f]				
Yes	36.8%	5.9%	36.2%	1.3%
No	41.2%	5.5%	37.1%	1.4%
	<0.0001	0.53	0.85	0.59
Self-perceived poor health[f]				
Yes	29.8%	6.9%	49.6%	2.9%
No	41.7%	5.4%	35.4%	1.2%
	<0.0001	0.09	0.04	0.002
Born in US[f]				
Yes	43.6%	5.4%	35.9%	1.4%
No	21.9%	6.8%	45.3%	1.6%
	<0.0001	0.11	0.18	0.59
Region				
Northeast	43.2%	6.2%	41.0%	1.5%
Midwest	45.3%	5.3%	32.8%	1.4%
West	40.0%	6.6%	41.0%	1.5%

Table 2. (continued)

	Heard of genetic testing	Discussed genetic testing with physician	Advised by physician to have genetic test	Received a genetic test
South	35.4%	4.8%	34.3%	1.2%
	<0.0001	0.04	0.34	0.73

Percentages are weighted. P-values are from chi-square tests. [a]*2,102 missing from ever heard of genetic testing*
[b]*Denominator is subjects who heard of genetic testing, 6 missing*
[c]*Denominator is subjects who discussed genetic testing with a physician*
[d]*Denominator is subjects who had heard of genetic testing, 15 missing*
[e]*Cancers included: breast, ovarian (BRCA), colorectal, uterine (Lynch)*
[f]*Missing: education, 355; marital status, 165; BMI, 1,430; current smoker, 277; self-perceived poor health, 15; born in US, 27*

Table 3. Associations of Family History and Other Characteristics with Knowledge and Use of Genetic Testing for Cancer

	Heard of genetic test	Physician discussed genetic test	Physician advised genetic test	Received genetic test
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Number of first-degree relatives or subject with a BRCA- or Lynch-associated cancer (age of onset)				
None	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
1 (age ≥50 years)	1.26 (1.13–1.40)	2.74 (2.03–3.70)	1.49 (0.82–2.71)	1.95 (1.12–3.38)
1 (age <50 years)	1.30 (1.15–1.48)	2.80 (2.11–3.73)	1.50 (0.84–2.68)	2.98 (1.77–5.01)
≥2	1.40 (1.17–1.68)	4.05 (2.67–6.16)	1.58 (0.80–3.14)	2.72 (1.45–5.11)
Sex				
Female	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Male	0.71 (0.66–0.75)	0.73 (0.58–0.91)	0.68 (0.45–1.02)	0.95 (0.65–1.38)
Age (years)				
18–39	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
40–49	1.16 (1.06–1.27)	0.80 (0.63–1.00)	1.0 (0.63–1.59)	0.86 (0.54–1.38)
50–59	1.23 (1.12–1.35)	0.60 (0.45–0.81)	1.27 (0.75–2.15)	0.51 (0.29–0.91)
60–69	1.13 (1.01–1.28)	0.45 (0.30–0.67)	0.69 (0.32–1.47)	0.48 (0.23–1.00)
≥70	0.56 (0.49–0.63)	0.30 (0.19–0.48)	0.97 (0.44–2.16)	0.41 (0.18–0.93)
Race/ethnicity				
White, non-Hispanic	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Hispanic	0.48 (0.42–0.54)	2.33 (1.68–3.25)	3.37 (1.59–7.14)	4.73 (2.78–8.03)
African American, other non-Hispanic	0.59 (0.54–0.65)	1.39 (1.08–1.78)	1.03 (0.57–1.88)	1.65 (0.99–2.74)
Education				
Less than high school grad	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
High school grad	1.50 (1.33–1.68)	0.83 (0.55–1.24)	1.28 (0.63–2.60)	0.84 (0.45–1.55)
Some college	2.59 (2.32–2.90)	0.69 (0.46–1.03)	0.74 (0.36–1.51)	0.74 (0.40–1.39)
College grad	4.42 (3.95–4.95)	0.89 (0.62–1.29)	0.98 (0.48–1.98)	0.89 (0.50–1.59)
Married or living with partner				
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	1.14 (1.07–1.22)	0.98 (0.81–1.20)	0.76 (0.52–1.13)	0.96 (0.66–1.40)
Body mass index				
Underweight/normal	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Overweight	1.02 (0.95–1.10)	1.01 (0.79–1.29)	1.42 (0.90–2.25)	1.34 (0.89–2.00)
Obese	0.95 (0.87–1.03)	0.95 (0.73–1.24)	1.61 (1.00–2.61)	1.57 (0.96–2.59)
Self-perceived poor health				
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	0.74 (0.67–0.82)	1.23 (0.90–1.67)	1.05 (0.60–1.83)	1.84 (1.18–2.88)
No. comorbid conditions				
None	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
1	1.28 (1.18–1.38)	1.21 (0.97–1.52)	1.55 (0.98–2.45)	1.12 (0.71–1.78)
2	1.42 (1.28–1.58)	1.07 (0.79–1.44)	1.81 (0.99–3.32)	0.83 (0.44–1.54)
≥3	1.33 (1.18–1.51)	0.79 (0.51–1.21)	1.24 (0.59–2.63)	0.76 (0.38–1.52)
Personal history of cancer				
No cancer	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
BRCA-/Lynch-associated cancer[a]	1.03 (0.86–1.24)	2.48 (1.60–3.83)	2.33 (1.16–4.69)	6.72 (3.56–12.67)
Other cancer	1.28 (1.11–1.48)	2.47 (1.74–3.52)	2.93 (1.44–5.97)	4.19 (2.24–7.84)
Current smoker				
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	0.97 (0.89–1.06)	1.06 (0.82–1.36)	1.01 (0.64–1.61)	0.87 (0.54–1.41)
US born				
No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Yes	1.67 (1.48–1.87)	0.99 (0.72–1.36)	1.10 (0.54–2.28)	1.39 (0.80–2.40)
US region				
South	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Northeast	1.25 (1.12–1.39)	1.31 (0.97–1.77)	1.47 (0.82–2.64)	1.34 (0.80–2.22)
Midwest	1.29 (1.18–1.42)	1.17 (0.90–1.53)	0.89 (0.54–1.45)	1.39 (0.89–2.17)
West	1.28 (1.17–1.40)	1.36 (1.07–1.73)	1.07 (0.67–1.71)	1.19 (0.73–1.94)

[a]*Cancers included: breast, ovarian (BRCA), colorectal, uterine (Lynch)*

The associations of other participant characteristics, including race and ethnicity, with the genetic testing outcomes in the adjusted models were similar to results from the unadjusted analyses.

The odds ratios associated with familial risk generally were stronger among participants with a personal history of cancer than among those without (Table 4), although some of the confidence intervals were wide. For example, among those with a personal history of cancer, the odds ratio for receiving genetic testing was 6.08 (95% CI: 2.02–18.26) for those with ≥2 first-degree relatives; the comparable odds ratio among those with no personal history was 2.17 (95% CI: 0.77–6.11).

DISCUSSION

In this nationally representative sample of US adults, over 15% of participants, representing approximately 34 million US residents, reported having a family or personal history of a BRCA- or Lynch-associated cancer. Women were over-represented in the strong familial risk category even after excluding personal history of breast or ovarian cancer, suggesting that women may report their family histories of cancer more completely than men. Although greater familial risk was associated with increased awareness, referral, and use of genetic testing, the percentages of participants who had *heard* of genetic testing, *discussed* it with their physician, and *received* it were still low, even among those with the strongest familial risk. While many of these individuals may not have family histories strong enough to suggest hereditary cancer syndromes, our findings still suggest that information on genetic testing may not be reaching some appropriate individuals; this is consistent with results from another recent study that reported relatively low rates of awareness and utilization of genetic testing among women at high risk for hereditary breast and ovarian cancer.[14] In particular, only 50% of the 5.8 million US residents at highest risk of familial cancer had *heard* of genetic testing, and only 15% of these individuals had *discussed* testing with a physician. As expected, personal history of cancer was positively associated with testing. Interestingly, Hispanics and African Americans were less likely than non-Hispanic whites to have *heard* of genetic testing, but among those who had *heard*, Hispanics were more likely to have *discussed* testing with their physician, to have been advised to have it, and to have received it compared to non-Hispanic whites.

Very few studies have examined the prevalence of familial cancer risk in the general US population. A previous analysis that used data from the 2000 NHIS reported that approximately 25% of participants had a family history of any cancer,[15] but did not examine the association between familial risk and knowledge and use of genetic testing. Ours is one of the first studies to investigate the influence of familial risk of cancer on referral and use of genetic testing in the general population, although some previous studies have examined the association of familial risk with awareness or interest in genetic testing for specific populations. For example, a survey of 600 women from a mammography screening program found that awareness of genetic testing for breast cancer risk was significantly associated with family history of breast cancer, increasing from 35% in the lowest family history risk group to 67% in the group with strongest familial risk.[16] Several other studies focusing on general cancer risk or risk of breast or colon cancer have had similar findings.[17,18] An analysis of the 2000 NHIS found that awareness of genetic testing was higher for those with any family history of cancer (48.3%) than for those with no family history (37.5%),[19] and a subsequent study using data from the 2000 and 2005 NHIS found that women at high risk for hereditary breast and ovarian cancer were more likely than average risk women to have discussed genetic testing with a health professional and to have undergone testing.[14] Our finding that individuals with a personal history of cancer were generally more likely to report the genetic testing outcomes is not surprising, and may in fact signal an appropriate approach, as testing should begin with an affected proband.[10] In addition, educational efforts in the past decade have promoted improved recognition and counseling of cancer patients about hereditary cancer susceptibility.

Other studies have noted that awareness and use of genetic testing for cancer susceptibility is lower among minority US populations than among non-Hispanic whites.[19–23] This may be explained in part by factors such as education, acculturation, and region of residence, although differences remain apparent even after adjustment for many sociodemographic factors.[21] To

Table 4. Associations of Family History with Knowledge and Use of Genetic Testing for Cancer, Stratified by Personal History of Cancer[a]

	Heard of genetic testing	Discussed genetic testing with physician	Advised by physician to have genetic test	Received a genetic test
Personal history of cancer[a]–N	1,977	858	108	856
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Number of first-degree relatives or subject with a BRCA- or Lynch-associated cancer (age of onset)				
None	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
1 (age ≥50 years)	1.34 (1.01–1.78)	5.60 (2.57–12.24)	2.85 (0.50–16.22)	4.59 (1.66–12.66)
1 (age <50)	1.27 (0.89–1.80)	3.34 (1.45–7.70)	1.30 (0.21–8.13)	4.66 (1.45–14.94)
≥2 (any age)	1.49 (1.04–2.14)	6.44 (3.03–13.70)	1.88 (0.29–11.95)	6.08 (2.02–18.26)
No personal history of cancer-N	27,349	10,357	532	10,350
Number of first-degree relatives with a BRCA or Lynch-associated cancer (age of onset)[b]				
None	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
1 (age ≥50 years)	1.25 (1.12–1.40)	2.51 (1.82–3.48)	1.47 (0.74–2.91)	1.82 (0.91–3.64)
1 (age <50)	1.28 (1.11–1.46)	2.86 (2.10–3.89)	1.76 (0.92–3.34)	3.24 (1.88–5.59)
≥2 (any age)	1.37 (1.10–1.70)	3.81 (2.31–6.28)	1.48 (0.58–3.79)	2.17 (0.77–6.11)

[a] *Personal history of any cancer*
[b] *Cancers included: breast, ovarian (BRCA), colorectal, uterine (Lynch)*

our knowledge, however, this is the first study to report that Hispanics and African Americans who are aware of genetic testing are more likely to discuss it with their physicians or to undergo testing when advised by their physicians. This could be due to self-selection; members of these populations who have heard of genetic testing may represent an unusual and highly motivated subgroup of individuals who have reasons to be particularly concerned about cancer. These findings need to be confirmed in future studies.

A variety of evidence indicates that family history often is not explored or documented by primary care clinicians.[6] In a study of over 4,000 primary care visits, family history was discussed in 51% of new patient visits and 22% of follow-up visits, with substantial variation between physicians.[24] In a survey of primary care clinicians about breast cancer risk assessment, 30% reported that they do not elicit family history, and 58% reported that they do not communicate family history-based risk to patients.[25] Lack of time during visits and problems with current reimbursement policies are two important barriers to collection of family history information.[6,26] In addition, primary care physicians may lack confidence in their knowledge of familial risk and risk assessment,[25] or they may be discouraged by limited skills about how to use this information to counsel patients.[6] Another issue is that patients may not collect or report family history information to their physicians. In a 2004 survey of 4,345 adults conducted by the CDC, 96% of respondents considered family history to be important to their personal health, but only 30% had collected information to develop a family health history.[7] Patients may also avoid genetics consultations or genetic testing because they may be worried about privacy issues and potential adverse consequences, such as discrimination in insurance and employment.[27]

Primary care physicians also report that they lack sufficient knowledge and confidence about referral for genetic services.[27–29] In a survey of 82 physicians in a hospital-affiliated health system, including 51 primary care physicians, only 59% reported awareness of the hospital's cancer genetics program.[13] Studies in the United Kingdom have shown that referral guidelines and computerized decision support for general practitioners around familial risk assessment have facilitated appropriate referrals for genetic testing and improved clinician satisfaction with their ability to identify patients for genetic testing and manage familiar cancer risk.[30–32] A shortage of adult medical geneticists is another problem that has been reported.[27,33]

Our study has important clinical and policy implications. Family history has been identified as an important tool for risk stratification and improved disease prevention,[3] yet our results suggest that information about genetic testing may not be reaching those at highest familial risk. This may be due to issues with physicians' assessment of family history as well as their knowledge about familial risk and genetic services. Health professionals' lack of confidence in interpreting familial patterns of disease and lack of knowledge about genetics may limit their ability to appropriately counsel patients, order and accurately interpret genetic tests, and refer patients for genetic consultation.[27]

Although a number of questionnaires for assessing family history in clinical settings are available, few have been formally evaluated, and there are no simple, short generic family history questionnaires for use in primary care practice.[34] An important priority, therefore, is the development of such tools.[2] Computerized tools that collect family history data and utilize clinical decision support to help physicians evaluate risk, provide tailored prevention messages, and make appropriate referrals may be particularly useful.[4,6,31,35,36]

A major strength of our study is the use of a large, nationally representative dataset. The 2005 NHIS collected detailed information on family history of cancer, including both number of first-degree relatives and age of onset, allowing us to examine strength of familial risk in relation to awareness, referral, and use of genetic testing. We focused on familial risk of BRCA- or Lynch-associated cancers, because these are part of known inherited cancer syndromes for which genetic tests exist.[9–12] However, we were not able to conduct separate analyses among participants with family history of each of these syndromes, due to small numbers of the genetic testing outcomes within these subgroups. Our method of estimating familial cancer risk also was limited by the available data. The NHIS Cancer Control Supplement assessed history of cancer only among participants' first-degree relatives and did not ask about maternal or paternal lineage or whether a mutation had been identified in an affected family member. As a result, the familial risk categories are heterogeneous, and some individuals in the highest category may not have strong family histories suggesting hereditary cancer syndromes. In addition, since the data were cross-sectional, there is no way to determine for certain whether participants' knowledge of their family history of cancer actually preceded the genetic testing outcomes.

In conclusion, this study provides estimates of the prevalence of familial cancer risk in the general US population and suggests that information about genetic testing is not reaching some at high risk of inherited cancer. Advances in our understanding of genomics will likely make family history-based risk assessment and prevention more important over the coming decades, even for individuals with fewer affected family members. Future studies should explore methods for improving the collection and interpretation of family history information and for increasing knowledge about genetic testing, both for physicians and for patients at high familial cancer risk.

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Corresponding Author: *Jennifer S. Haas, MD, MSPH; Division of General Medicine and Primary Care, Brigham and Women's Hospital, 1620 Tremont Street, Boston, MA 02120, USA (e-mail: jhaas@partners.org).*

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