Guidelines for Genetic Risk Assessment of Hereditary Breast and Ovarian Cancer: Early Disagreements and Low Utilization

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BACKGROUND: *BRCA1/2* testing is one of the most well-established genetic tests to predict cancer risk. Guidelines are available to help clinicians determine who will benefit most from testing.

OBJECTIVE: To identify women at high risk of hereditary breast and ovarian cancer and estimate their awareness of and experience with genetic testing for cancer risk.

DESIGN: Analyses of the 2000 and 2005 National Health Interview Surveys.

PARTICIPANTS: Women with no personal history of breast or ovarian cancer (n=35,116).

MEASUREMENTS: Risk of hereditary breast or ovarian cancer based on self-reported family history of cancer and national guidelines; self-reported awareness of genetic testing for cancer risk; discussion of genetic testing for cancer risk with a health professional; having undergone genetic testing for breast/ovarian cancer risk.

RESULTS: Using guideline criteria, 0.96% of women were identified as being at high risk of hereditary breast and ovarian cancer. Among high-risk women, 54.04% were aware of genetic testing for cancer risk, 10.39% had discussed genetic testing with a health professional, and 1.41% had undergone testing for breast/ovarian cancer risk. Adjusting for survey year, high-risk women were more likely than average-risk women to have heard of genetic testing for cancer risk (RR, 1.3, 95% CI 1.2-1.4), to have discussed genetic testing with a health professional (RR 5.2, 95% CI 3.6-7.4), and to have undergone genetic testing for breast/ovarian cancer risk (RR 6.8, 95% CI 2.6-18.0).

CONCLUSIONS: We find low provision of guideline-recommended advice to women for whom testing may be appropriate and of significant clinical benefit.

KEY WORDS: guidelines; genetic risk assessment; hereditary; breast cancer; ovarian cancer; BRCA1/2 testing.
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INTRODUCTION

Testing for hereditary breast/ovarian cancer (HBOC) susceptibility, commercially available since 1996, is one of the most well-established[1–3] and widely ordered genetic tests for cancer risk in the United States. Most health insurers reimburse at least partially for *BRCA1/2* genetic testing for women with strong personal and/or family histories of breast or ovarian cancers.[4] Five to ten percent of breast cancers and 10% of ovarian cancers, or 18,000 new cases of breast cancer and 1,900 new cases of ovarian cancer per year, are believed to be hereditary.[5–7] *BRCA1/2* mutations confer remarkable risks through age 75 of breast (35-84%) and ovarian (6-55%) cancers,[5,8,9] and prompt recommendations for aggressive surveillance and risk-reducing interventions[2,3] to lower cancer incidence or improve life expectancy.[10] A negative test result in a member of a family in which a disease-associated mutation has been identified should provide great reassurance.

Currently, genetic testing is only recommended for women at increased risk for mutations. For example, 1 in 12 women with a strong family history of breast or ovarian cancer may carry a *BRCA1/2* mutation.[11,12] General population screening for *BRCA1/2* mutations has not been recommended by cancer experts due to the low population prevalence of *BRCA1/2* mutations (estimated to be only 1 in 300 to 500) and concerns regarding the potential physical and psychological consequences of difficult to interpret test results.[1–3,8]

A number of clinical practice guidelines have emerged providing specific criteria clinicians may use in determining whether referral for genetic counseling, identification and *BRCA1/2* testing of affected family members, and/or *BRCA1/2* testing for individual patients is appropriate. Three early sets of guidelines were developed as commercial and academic laboratories were making *BRCA1/2* testing widely available. Two guidelines were developed by committees consisting primarily of oncologists, geneticists, and genetics counselors and disseminated to organizations of oncologists: the American Society of Clinical Oncologists published guidelines in 1996 (ASCO, 1996),[13] and the National Comprehensive Cancer Network published guidelines in 1999 (NCCN, 1999).[14] New York State and the American College of Medical Genetics (NYS/ACMG, 1999) published guidelines on the New York State website that were developed under the guidance of a broader range of health professionals, including oncologists, geneticists, genetic counselors, and representatives of primary care physician and public health groups.[15] These guidelines were subsequently disseminated in *American Family Physician*, a peer-reviewed publication of the American Academy of Family

Physicians.[16] Each of these guidelines sets minimum criteria based on patients' personal and family histories of breast and ovarian cancer that identify patients at sufficiently high risk for HBOC to warrant genetic counseling and possible testing. ASCO formally updated its guidelines in 2003,[1] and the NCCN has updated its guidelines annually.[2] NYS/ACMG informally updated their guidelines in 2007.[17] In 2005, the United States Preventive Services Task Force issued a set of practice guidelines focused on women without a personal history of breast/ovarian cancer.[3]

To our knowledge, there is no information in the published literature assessing the degree of compliance with these guidelines. In this study, we identify women in the 2000 and 2005 National Health Interview Survey (NHIS) Cancer Control Supplements at high risk for HBOC based on pre-2000 guideline criteria and develop national estimates of the proportion of women at high risk who have discussed the possibility of genetic testing with their doctor or another health-care professional, as suggested by these guidelines. We focus on women with a family rather than personal history of breast or ovarian cancer in order to concentrate on the implications of genetic risk assessment for cancer prevention in the primary care setting.

Table 1. Main Outcome Measures: Survey Questions on Genetic Testing for Cancer Risk from 2000 and 2005 NHIS Cancer Control Supplements (n=35,116)

Question	NHIS 2000	NHIS 2005	Relative change (%)
1. Have you ever heard of genetic testing to determine if a person is at greater risk of developing cancer? (% "yes")	43.56	40.71	−6.5‡
2. Have you ever discussed the possibility of getting a genetic test for cancer risk with a doctor or other health professional? (% "yes")	1.79	2.38	33.0†
3. Did the doctor or other health professional advise you to have such a test? (% "yes")	0.62	0.87	40.3†
4. Please think about your most recent genetic test for cancer risk. Which kinds of cancer was it for? (% responding "yes" to breast or ovarian)	0.20	0.24	20.0

*$p<0.05$, †$p<0.01$, ‡$p<0.001$

METHODS

Data

The NHIS is an in-person survey conducted annually by the National Center for Health Statistics to monitor the health of the US population. It uses a cross-sectional multistage area probability design to allow calculation of statistics representative of the US non-institutionalized population. In 2000 and 2005, 36,054 female respondents 18 and older participated in Cancer Control Supplements to the NHIS (combined final response rate of 71%). Respondents self-reported whether they or their first-degree relatives had ever been diagnosed with cancer, and if so, the type(s) and whether the cancer was diagnosed at age 50 or younger. Table 1 lists questions asked regarding awareness of and experience with genetic testing for cancer risk. Responses to these items are our main outcome measures.

Application of Guideline Criteria

We first used the 1996 ASCO, 1999 NYS/ACMG, and 1999 NCCN guidelines to categorize respondents as being at high risk (meeting at least one guideline criterion) or average risk (meeting no guideline criteria) for HBOC. These guidelines have explicit criteria, and all were available prior to the first year of our data, 2000 (Table 2). Family members' *BRCA1/2* mutation status, HBOC-relevant ethnicity (e.g., Ashkenazi Jewish), breast cancer diagnoses in family members prior to age 45, diagnoses of multiple primary breast cancers (including bilateral cancer), and cancer diagnoses among second- and third-degree relatives are unavailable in the NHIS. Thus, our approach to identifying respondents at high risk of HBOC—women meeting guideline criteria for potential counseling and testing—is based solely on the cancer histories of first-degree relatives, underestimating the prevalence of individuals who are candidates for testing in this population-based study. Having assessed risk, we then determined whether our main outcomes varied by risk status.

Our second analysis assessed how well the above guidelines agreed with one another in determining high HBOC risk. Further, we determined whether guideline updates over time improved inter-guideline agreement by comparing agreement among the 2005 USPSTF guidelines, the 2007 NCCN guidelines, and the 2007 informal update to the NYS/ACMG guidelines. The 2003 ASCO guidelines were not included because that update did not include explicit criteria for recommending HBOC risk assessment.

Statistical Analysis

Bivariate analyses were used to track changes in respondents' awareness of and experience with genetic testing for cancer risk from 2000 to 2005, to compare the characteristics of women at high and average risk for HBOC, and to compare respondents' awareness of and experience with genetic testing for HBOC risk. Statistically significant differences were identified using Pearson's chi-squared statistics. Given that characteristics of women at high and average risk for HBOC did not change significantly from 2000 to 2005, our descriptive statistics are based on data pooled across the two survey years.

Poisson regression was used to calculate relative risks (RRs)[18] describing the differences in the main outcome measures detailed in Table 1 for women at high versus average risk of HBOC, controlling for survey year. We tested an interaction term to determine whether the association between risk status and outcomes changed from 2000 to 2005. Similar regressions were used to assess changes in the main outcome measures as a function of the number of guidelines for which a respondent met at least one criterion indicating high risk of HBOC.

Agreement among the guidelines was assessed using the kappa statistic of interrater agreement.

All analyses were conducted using Intercooled Stata 9.2 for Windows (Stata Corporation, College Station, TX) taking account of NHIS design characteristics.

Table 2. Pre-2000 National Guideline Criteria for High Risk of HBOC (n=35,116)

Guidelines	NHIS 2000, 2005 respondents meeting criteria
ASCO 1996	
>2 Relatives with breast cancer and ≥1 relatives with ovarian cancer	0.01% (n=2)
>3 Relatives with breast cancer before age 50	0.01% (n=2)
Sister pairs with ≥2 breast and/or ovarian cancer cases before age 50	0.12% (n=43)
Meets ≥1 ASCO 1996 criteria	0.12% (n=45)
NCCN 1999	
≥2 Close relatives with breast cancer, especially if ≥1 is ≤50 years of age	0.62% (n=213)
≥2 Close relatives with ovarian cancer	0.09% (n=31)
≥1 Close relative with breast cancer at age ≤40 or bilateral breast cancer	N/A*
A family member is known to have a *BRCA1/2* mutation	N/A*
≥1 Close relative diagnosed with breast cancer and ≥1 close relative diagnosed with ovarian cancer	0.26% (n=100)
≥2 Male relatives with breast cancer	0.00% (n=0)
Of Ashkenazi Jewish descent with ≥1 close relative with breast or ovarian cancer	N/A*
Meets ≥1 NCCN 1999 criteria	0.92% (n=323)
NYS/ACMG 1999	
≥3 Family members† with diagnoses of breast or ovarian cancer‡	0.07% (n=24)
Multiple primary or bilateral breast cancers in a family member	N/A*
A family member is known to have a *BRCA1/2* mutation	N/A*
≥1 Family member† diagnosed with breast cancer and ≥1 family member diagnosed with ovarian cancer‡	0.257% (n=93)
≥1 Male relative with breast cancer	0.05% (n=24)
High-risk ethnic background§ and ≥1 family member with breast or ovarian cancer	N/A*
Meets ≥1 NYS/ACMG criteria	0.35% (n=135)
Number of guidelines with ≥1 criteria met	
1	0.56% (n=192)
2	0.35% (n=136)
3	0.04% (n=13)

*N/A = information not available in the NHIS Cancer Supplements
†Family members must be from the same side of the family
‡Excludes male breast cancer
§For example, Ashkenazi Jewish

RESULTS

Knowledge of and Experience with Genetic Testing

Of the 36,054 female respondents to the NHIS Cancer Control Supplements, 35,116 (97%) met our inclusion criterion of no personal history of breast or ovarian cancer. From 2000 to 2005, the fraction of these women who had heard of genetic testing for cancer risk declined three percentage points, from approximately 44% to 41% ($p<0.001$) (Table 1). Nevertheless, the proportion of women in our study population who reported having discussed the possibility of genetic testing with a health professional increased by a third, from 1.79% to 2.38% ($p=0.002$), and the number advised by a health profession to get tested increased by 40%, from 0.62% to 0.87% ($p=0.01$) over that same time period. We did not have power to detect significant changes over time in genetic testing rates for breast/ovarian cancer.

Prevalence of Family History

Based on the history of breast or ovarian cancer among first degree relatives, high risk of HBOC was identified for 0.12% of respondents according to the 1996 ASCO guidelines, 0.92% of respondents according to the 1999 NCCN guidelines, and 0.35% of respondents according to the 1999 NYS/ACMG guidelines (Table 2). The majority of these women met criteria based on having relatives diagnosed with breast cancer. Overall, 0.96% of respondents were deemed at high risk of HBOC according to at least one guideline: 0.56% met the criteria for one set of guidelines, 0.35% met the criteria of two sets of guidelines, and 0.04% met the criteria for all three guidelines.

Interguideline Agreement

The 1996 ASCO guidelines were in poor agreement with the 1999 NCCN and the 1999 NYS/ACMG guidelines, with kappas of 0.24 and 0.14, respectively. Agreement between the 1999 NCCN and 1999 NYS/ACMG guidelines was fair at 0.51. Among the more recent guidelines, there was poor agreement between the 2007 NYS criteria and both the 2005 USPSTF guidelines and the 2007 NCCN guidelines (kappas≤0.27). A kappa of 0.76 indicated good agreement between the 2005 USPSTF guidelines and the 2007 NCCN guidelines. High risk according to at least one pre-2000 guideline agreed well with the 2007 NCCN guidelines and 2005 USPSTF guidelines (kappas≥0.70), suggesting the newer guidelines would identify most of the same high-risk individuals as the earlier guidelines in aggregate.

Characteristics of the Sample

Characteristics of our study population are summarized in Table 3. Women meeting at least one criterion for high risk of HBOC according to any of the three pre-2000 guidelines tended to be older than average-risk women, as would be expected. High-risk women were less likely to self-identify as Hispanic and more likely to have had a clinical breast exam, a mammogram, or a diagnosis of cancer somewhere other than the breast or ovaries than average-risk women. Race, education, poverty status, having a usual source of care, and having had a visit to a health professional in the past year were not significantly associated with being at high risk for HBOC according to at least one guideline.

Women's Awareness of and Experience with Genetic Testing for Cancer Risk

Women's reported awareness of and experience with genetic testing was similar regardless of which guideline was used to identify them as being at high risk for HBOC, both in terms of the proportion of women responding "yes" on the main outcome measures and the relative difference between those deemed at high versus average risk of HBOC (Table 4). Among women deemed at high risk of HBOC according to at least one guideline criterion, 54% had heard of genetic testing for cancer risk, just over 10% had discussed genetic testing for cancer risk with a health professional, fewer than 5% were advised by a health professional to be tested, and fewer than 2% actually underwent testing.

Table 3. Characteristics of Women at High Versus average risk of HBOC

	High risk* n= 341 (%)	Average risk† n =34,775 (%)	Chi-squared statistic p-value
Age			<0.001
18-30	7.0	23.8	
31-50	22.8	40.2	
51-70	40.5	24.7	
71+	29.8	11.3	
Race			0.24
White	86.1	81.2	
Black	9.0	12.3	
Asian	2.1	3.4	
Other	2.8	3.1	
Hispanic ethnicity	4.8	11.3	<0.001
Highest education completed			0.08
<8th grade	8.6	6.0	
Some high school	9.9	10.8	
High school/GED	35.4	30.3	
Some college or Associates degree	27.6	29.6	
Bachelor's degree or higher	18.5	23.3	
Income <100% federal poverty level	14.2	18.0	0.07
Has usual source of care	93.5	89.8	0.07
Visited health professional in last 12 months (yes)	91.5	89.4	0.31
Clinical breast exam	82.1	61.1	<0.001
Ever mammogram	80.8	51.9	<0.001
History of other cancer (yes)	12.1	5.3	<0.001

High risk is defined as meeting at least one criterion from any one guideline in Table 2
†*Average risk is defined as not meeting any criteria from any guideline in Table 2*

Women at high risk of HBOC according to any guideline were 29% more likely to have heard of genetic testing for cancer risk than women at average risk of HBOC, controlling for survey year (RR 1.3, 95% CI 1.2-1.4, p<0.001). Women at high risk for HBOC were five times as likely to have discussed genetic testing for cancer risk with a health professional compared to women at average risk, controlling for survey year (RR 5.2, 95% CI 3.6-7.4, p<0.001). Women at high risk of HBOC were over six times more likely to have been advised by a health professional to be tested (RR 6.4, 95% CI 3.4-11.9, p< 0.001), and nearly seven times more likely to have been tested specifically for breast/ovarian cancer risk (RR 6.8, 95% CI 2.6-18.0, p<0.001) than average-risk women, controlling for survey year. Based on statistical tests of the interaction between HBOC risk and year, there was no evidence that the relative difference in outcomes between those at high and average risk for HBOC changed between survey years, indicating similar changes over time for both high- and average-risk women.

Awareness of genetic testing for cancer risk was similar whether criteria for 1, 2, or 3 guidelines were met (Table 5). However, discussion of genetic testing for cancer risk with a health professional increased monotonically with increasing agreement among the guidelines. While only 8% of women meeting criteria for high risk of HBOC on just one set of guidelines discussed testing, more than 32% of women deemed high-risk by all three guidelines had such discussions. Advice to undergo genetic testing was also highest among women deemed high risk according to all three guidelines.

DISCUSSION

Using nationally representative survey data, our analysis indicates that only 10% of women nationally who met guideline criteria for consideration of genetic counseling for breast/ovarian cancer risk report having discussed such a possibility with a health professional. Though 10% is low in absolute terms, it is reassuring to note that high risk women were five times as likely as average risk women to have had such a discussion and more than six times as likely to have been advised to seek testing. This suggests that while discussions of

Table 4. Awareness of and Experience with Genetic Testing for Cancer Risk by Risk of HBOC

	High risk* (% "yes")	Average risk† (% "yes")	RR‡ (95% CI)
ASCO 1996	n=45	n=35,071	
Heard of genetic testing for cancer risk	47.46	42.08	1.1 (0.8-1.6)
Discussed testing with health professional	14.11	2.08	7.0 (3.1-15.5)
Advised by health professional to be tested	7.89	0.74	10.9 (3.1-38.2)
Had a genetic test for breast or ovarian cancer risk	0.00	0.22	NA§
NCCN 1999	n=323	n=34,793	
Heard of genetic testing for cancer risk	53.64	41.98	1.3 (1.2-1.4)
Discussed testing with health professional	10.27	2.02	5.1 (3.5-7.3)
Advised by health professional to be tested	4.21	0.72	5.8 (3.1-11.1)
Had a genetic test for breast or ovarian cancer risk	1.47	0.21	7.1 (2.7-18.7)
NYS/ACMG 1999	n=135	n=34,981	
Heard of genetic testing for cancer risk	59.16	42.03	1.4 (1.2-1.6)
Discussed testing with health professional	15.16	2.05	7.4 (4.7-11.6)
Advised by health professional to be tested	5.18	0.74	7.0 (2.7-17.9)
Had a genetic test for breast or ovarian cancer risk	2.65	0.21	12.5 (4.3-36.3)
≥1 guideline criterion	n=341	n=34,775	
Heard of genetic testing for cancer risk	54.04	41.97	1.3 (1.2-1.4)
Discussed testing with health professional	10.39	2.01	5.2 (3.6-7.4)
Advised by health professional to be tested	4.57	0.71	6.4 (3.4-11.9)
Had a genetic test for breast or ovarian cancer risk	1.41	0.21	6.8 (2.6-18.0)

High risk is defined as meeting at least one criterion from any one guideline in Table 2
†*Average risk is defined as not meeting any criteria from any guideline on Table 2*
‡*RR = relative risk adjusted for survey year*
§*Statistic not available due to 0 cell count among high-risk women*

Table 5. Guideline Agreement and Experience with Genetic Testing for Cancer Risk (n=35,116)

	Number of guidelines for which a woman was defined as high risk (% affirmative response)				RR (95% CI) *		
	0	1	2	3	1 vs 0	2 vs 0	3 vs 0
Heard of genetic testing for cancer risk	42	53	55	58	1.3 (1.1-1.5)	1.3 (1.1-1.6)	1.4 (0.9-2.2)
Discussed testing with health professional	2.0	8.4	10.9	32.4	4.2 (2.5-7.2)	5.4 (3.3-8.8)	16.1 (7.4-35.0)
Advised by health professional to be tested	0.71	4.79	3.07	14.29	6.7 (2.9-15.4)	4.3 (1.8-10.2)	20.0 (3.5-114.3)
Had a genetic test for breast or ovarian cancer risk	0.21	0.73	2.65	0	3.5 (0.5-26.0)	12.7 (4.4-36.8)	NA †

RR = relative risk adjusted for survey year
†Statistic not available due to 0 cell count

genetic assessment are being targeted correctly, many high-risk women are not being reached. Discussions of possible genetic testing are an important step in identifying an affected family member who may be a candidate for testing. Legitimate differences in preference may drive decisions to pursue genetic testing, but women at high risk of HBOC should at least discuss the possibility of testing with a health professional. Because *BRCA1/2* testing is so well known, has well-accepted clinical utility, and has been around for so long, our findings provide nationally representative empirical evidence for the challenges involved in widespread dissemination of genetic medicine, particularly in primary care settings.

The implications of low utilization of this effective cancer prevention strategy are not insignificant. Our analysis indicates that at least 0.96% of the population of women with no personal history of breast or ovarian cancer—or approximately 1,000,000 women—meet at least one guideline criterion suggesting they may be candidates for *BRCA1/2* testing. Based on estimates of prevalence for deleterious *BRCA1/2* mutations in this group (8.7%),[8] average penetrance (55% for breast cancer and 25% for ovarian cancer),[8] and our estimate that only 10.8% of high-risk women discuss the possibility of genetic testing with a health professional, we estimate that over 60,000 women may have missed an opportunity to reduce their cancer risk. Given that our analysis addressed the family history of first-degree relatives only and did not include other family history, ethnicity, or clinical criteria indicated in the guidelines, these estimates are very conservative. Other sources indicate that the prevalence of high risk for HBOC in this population may be as high as 2%[3] or even 4%.[19] The high agreement between risk defined collectively by the pre-2000 guidelines and current guidelines (2005 USPSTF and 2007 NCCN) provides confidence in our identification of high-risk women. Our results suggest that a substantial number of high-risk women are unaware that they carry a deleterious mutation and are thus unlikely to avail themselves of recommended prevention strategies, ranging from aggressive screening to prophylactic surgery,[2,3,20] which have been shown to be effective at reducing mortality among *BRCA1/2* mutation carriers.[10]

The low proportion of women at high risk for HBOC that report discussing genetic testing for cancer risk with their health professionals suggests a substantial disconnect between available clinical evidence and practice. Implementation of HBOC genetic screening guidelines has likely been hampered by several factors identified by physicians as common barriers to guideline compliance, including lack of awareness and familiarity with guidelines, lack of self-efficacy, and external barriers,[21,22] as well as low levels of physician knowledge of clinical genetics and confidence counseling patients about genetic testing.[23–26] Lack of awareness may stem from the fact that two out of three early guidelines were directed at oncologists rather than primary care providers (PCPs), those most likely to interact with women who have no personal history of breast or ovarian cancer. While the NYS/ACMG guidelines were disseminated to PCPs, they were not distributed through maximally visible channels. The high-profile publication of the 2005 USPSTF guidelines,[3,8,27–30]—which was specifically aimed at PCPs, although available too late for physicians to apply in this population—was an important step forward, and future research should address the impact of these guidelines on primary care practice.

The lack of consensus across guidelines may also be contributing to low rates of discussion. Our analyses indicate poor to fair agreement across the pre-2000 guidelines. However, women deemed at high risk of HBOC according to multiple guidelines were far more likely to have discussed genetic testing for cancer risk and been advised to seek such testing. This finding suggests that the intersection of agreement among these guidelines identifies a truly high-risk group and that the threshold for discussing/advising is high. It may also indicate that greater guideline concordance will lead to the identification of a higher proportion of high-risk women. Additional research is needed to assess whether recent increases in guideline concordance will improve identification of high-risk women in the future.

Although collection of family history data is the cornerstone of genetic risk assessment and is routinely collected at intake for new patients, it is rare for family history data to be recorded in adequate detail to implement practice guidelines.[24] The average PCP visit is 20 min in duration.[31] Physicians may be inadequately reimbursed to conduct a full family history. Acute concerns may also take precedence over prevention measures.[32] Federal plans to invest $19 billion in health information technology, including the mass implementation of electronic health records (EHRs),[33] may help PCPs collect and access family history data. Statutary requirements for certified EHRs and "meaningful use" will encourage the implementation of computerized decision support (CDS) tools linked to EHRs. CDS could be programmed to evaluate family history information, identify women at high risk for HBOC, and list actionable recommendations for follow-up, a particularly helpful feature for PCPs, the majority of whom are likely to see very few high-risk women.[34–38] However, this application of CDS has not yet been proven in clinical practice. Absent technological support

for processing the information requirements of current guidelines, appropriate rates of discussion for genetic risk assessment may ultimately be improved by reducing the number and complexity of guideline criteria.

Patient preference, family preference, expense, stigma, and potential discrimination by employers and insurers have all been identified as reasons patients do not undergo genetic testing. [39–45] If these factors lead patients to withhold family history information from relevant health professionals (though not from survey interviewers), that would help explain the low rate of discussions we observe among our high-risk women. The study data were collected prior to the 2008 Genetic Information Nondiscrimination Act (GINA), during a time when virtually all protections from genetic discrimination existed in state law. Few states had laws comprehensive enough to allay the full spectrum of patient concerns.[46,47] The extent to which GINA alleviates patient unease is an important area for future investigation.

Our findings must be considered in light of certain limitations. As noted, we were only able to ascertain family history of breast and ovarian cancer for primary relatives. The exclusion of higher degree relatives reduces our ability to capture the full population of high-risk women. We were also unable to identify high-risk ethnic groups, for example, Ashkenazim; discussions of genetic counseling and testing are likely much more common in this group. However, less than 3% of the US population is of Ashkenazi Jewish ancestry, so the bias from misclassifying respondents' risk status as a result of missing ethnicity data is apt to be minimal. An additional limitation is the self-reported nature of NHIS data and the fact that the NHIS questions were not designed with this specific study in mind. We believe it unlikely that systematically inaccurate responses would induce a strong enough bias to explain the low rate of discussions we observe.

We found that through 2005, women meeting national guideline criteria for high HBOC risk rarely reported having had discussions of genetic counseling or testing with their health professionals, though they were much more likely to have such discussions than average risk women. Genetic testing for HBOC is one of the longest standing and best understood applications of clinical genetics. The failure to adequately capitalize on this beneficial genetic application places in stark relief the challenges associated with translating emerging genomics applications into broad clinical practice. Additional guideline dissemination efforts directed towards the primary care community, expanded use of CDS tools, or simplified guidelines are needed to assist PCPs and other providers in incorporating genetic strategies for risk assessment, prevention, and treatment into clinical practice. Addressing specific barriers to guideline implementation will help ensure that thousands of women get the information they need to address a potentially deadly threat to their health.

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