Title

National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer

Journal

Journal of Clinical Oncology, 35(34)

ISSN

0732-183X

Authors

Childers, Christopher P
Childers, Kimberly K
Maggard-Gibbons, Melinda
et al.

Publication Date

2017-12-01

DOI

10.1200/jco.2017.73.6314

Peer reviewed

VOLUME 35 · NUMBER 34 · DECEMBER 1, 2017

JOURNAL OF CLINICAL ONCOLOGY

RAPID COMMUNICATION

National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer

Christopher P. Childers, Kimberly K. Childers, Melinda Maggard-Gibbons, and James Macinko

Author affiliations and support information (if applicable) appear at the end of this article.

Published at jco.org on August 18, 2017.

Processed as a Rapid Communication manuscript.

Corresponding author: Christopher P. Childers, MD, Department of Surgery, David Geffen School of Medicine at University of California, Los Angeles, Ronald Reagan UCLA Medical Center, 10833 Le Conte Ave, CHS 72-247, Los Angeles, CA 90095; e-mail: cchilders@mednet.ucla.edu.

0732-183X/17/3534w-3800w/$20.00

ABSTRACT

Purpose

In the United States, 3.8 million women have a history of breast (BC) or ovarian cancer (OC). Up to 15% of cases are attributable to heritable mutations, which, if identified, provide critical knowledge for treatment and preventive care. It is unknown how many patients who are at high risk for these mutations have not been tested and how rates vary by risk criteria.

Methods

We used pooled cross-sectional data from three Cancer Control Modules (2005, 2010, 2015) of the National Health Interview Survey, a national in-person household interview survey. Eligible patients were adult females with a history of BC and/or OC meeting select 2017 National Comprehensive Cancer Network eligibility criteria on the basis of age of diagnosis and family history. Outcomes included the proportion of individuals reporting a history of discussing genetic testing with a health professional, being advised to undergo genetic testing, or undergoing genetic testing for BC or OC.

Results

Of 47,218 women, 2.7% had a BC history and 0.4% had an OC history. For BC, 35.6% met one or more select eligibility criteria; of those, 29.0% discussed, 20.2% were advised to undergo, and 15.3% underwent genetic testing. Testing rates for individual eligibility criteria ranged from 6.2% (relative with OC) to 18.2% (diagnosis ≤ 45 years of age). For OC, 15.1% discussed, 13.1% were advised to undergo, and 10.5% underwent testing. Using only four BC eligibility criteria and all patients with OC, an estimated 1.2 to 1.3 million individuals failed to receive testing.

Conclusion

Fewer than one in five individuals with a history of BC or OC meeting select National Cancer Comprehensive Network criteria have undergone genetic testing. Most have never discussed testing with a health care provider. Large national efforts are warranted to address this unmet need.

J Clin Oncol 35:3800-3806. © 2017 by American Society of Clinical Oncology

INTRODUCTION

Up to 10% of breast and 15% of ovarian cancers are attributable to hereditable mutations, most commonly mutations in *BRCA1/2*.[1,2] In the United States, 316,120 women will be diagnosed with breast cancer and 22,440 with ovarian cancer this year.[3] Identifying which of these patients carries heritable mutations can direct cancer treatment[4,5] and alter surgical decision making.[6,7] Recent estimates suggest that rates of genetic testing in newly diagnosed patients meeting National Comprehensive Cancer Network (NCCN) criteria are up to 53%.[8]

Although patients should undergo genetic testing at the time of diagnosis, there is likely a large cohort of breast and ovarian cancer survivors for whom testing was not offered, pursued, or even available. Indeed, the number of new diagnoses this year accounts for less than 10% of the 3.8 million women living with a history of breast or ovarian cancer.[9] Of these women, 70% were diagnosed 5 years ago, and half were diagnosed more than 10 years ago.[10] The importance of identifying heritable mutations extends beyond the initial treatment period, enabling cancer prevention and early detection for patients and their family members.[11] Single-site studies provide some insight into rates of testing for cancer survivors, with estimates as low as 25% for breast cancer and 10% for ovarian cancer,[12,13] but it is unknown how often genetic testing is performed at a population level.

This study used a nationally representative sample to quantify the unmet need for genetic testing in patients with a history of breast and/or

ASSOCIATED CONTENT

See accompanying Editorial on page 3789

Appendix

DOI: https://doi.org/10.1200/JCO.2017.73.6314

DOI: https://doi.org/10.1200/JCO.2017.73.6314

ovarian cancer meeting select NCCN eligibility criteria and determined how rates differed across cancer type and risk criteria. Understanding these deficits can guide policy priorities and inform providers about which patients are most at risk for being overlooked.

METHODS

The data source was the National Health Interview Survey (NHIS), a multistage cross-sectional in-person household interview that gathers self-reported health data for the civilian noninstitutionalized US population.[14] Since 1987, a Cancer Control Module (CCM) has been administered approximately every 5 years. This study merged the Person, Sample Adult, and Sample Adult Cancer files with subsequent pooling of the 2005, 2010, and 2015 data sets. Pooling increased precision and allowed assessment of longitudinal trends. Reliable estimates (relative SE $<$ 30%) were rarely available for subpopulations in individual years.[15] The overall response rate ranged from 70.1% to 86.5%.[14,16,17]

The population of interest was adult women with a history of breast and/or ovarian cancer. Although males with a history of breast cancer were included in NHIS, the population was too small to generate reliable estimates. Questions related to genetic encounters were prefaced with the following phrase: "The following questions refer to genetic testing for cancer risk. That is, testing your blood to see if you carry genes which may predict a greater chance of developing cancer at some point in your life." Genetic encounters included the proportion of individuals self-reporting (1) a history of discussing the possibility of getting a genetic test for cancer risk with a doctor or other health professional (referred to as discussing hereafter); (2) a history of being advised to undergo a genetic test by a doctor or other health professional (referred to as advising hereafter); or (3) a history of having a genetic test to determine future breast/ovarian cancer risk (referred to as testing hereafter). Responses to (2) required an affirmative response to (1), whereas responses to (3) were independent of the other two.

Subpopulations were defined using 2017.2 NCCN Genetic/Familial High-Risk Assessment for Breast and Ovarian Cancer Guidelines.[19] The NHIS Cancer Control Module collects sufficient personal and family history to evaluate the following eligible breast cancer populations: (1) diagnosis 45 years of age or younger, (2) diagnosis 50 years of age or younger with one or more first-degree relatives (FDRs) with breast cancer, (3) diagnosis at any age with one or more FDRs with breast cancer 50 years of age or younger, and (4) diagnosis at any age with one or more FDRs with ovarian cancer. Patients with breast cancer not meeting one of these criteria were considered eligibility unknown. NHIS does not collect, and therefore we were unable to estimate rates for, other testing criteria, including those that rely on cancer diagnoses in second- or third-degree relatives, multiple primaries, family history of pancreatic or Gleason score $\geq$ 7 prostate cancer, Ashkenazi Jewish ancestry, or triple-negative tumor pathology (Appendix Table A1, online only). Individuals with breast cancer who met one of these criteria but did not meet the four available criteria were included in the eligibility unknown category. All individuals with a history of ovarian cancer were considered eligible for testing.

STATA software (v14.2; STATA, College Station, TX) was used for all analyses. Sample weights were divided by 3 to adjust for pooling of multiple years. Unique identifiers were created for the 2005 strata before merging with the 2010/2015 data files because of a shift in sample design periods. Analyses were adjusted for complex survey weights using *svy* and *subpop* commands. SEs were calculated using the Taylor series linearization method. An alpha of .05 was used for statistical significance.

Data set calibration was assessed by comparing the sample with summary statistics from the 2000 and 2010 US Census.[19a,19b] Of 92,257 total survey respondents, 84,746 (92%) had complete data for all three genetic encounters (discussed, advised, and tested). Covariable means and proportions were compared for individuals with and without genetic encounter data using adjusted Wald and χ^2 tests. Individuals with data were, on average, 2 years younger than those without data, but were no different with respect to sex, survey year, or history of breast or ovarian cancer (Appendix Table A2). All further analysis was conducted on complete cases, with count estimates scaled to the population with known outcomes. Encounter rates were calculated for risk pools defined by NCCN criteria and compared using χ^2 tests. An estimate for the national unmet need was generated by multiplying the weighted total number of patients with eligible breast or ovarian cancer by 1 minus the 95% CI of rate of testing.

RESULTS

Database Calibration and Population Demographics

The data set included 92,257 observations representing 229,926,502 adults in the noninstitutionalized civilian US population. Age and racial distributions closely approximate estimates from the 2000 and 2010 US Census, with 17.4% of the sample $\geq$ 65 years of age, 14% Hispanic/Latino, and 11.7% non-Hispanic Black (Table 1).

Genetic Encounter Availability and Cancer Prevalence

Of 92,257 survey respondents, 84,746 (92%) had complete data for all three genetic encounters, including whether the individual had (1) discussed genetic testing with a health care provider, (2) been advised to undergo genetic testing, and (3) undergone genetic testing. Of the individuals with complete data (referred to as population hereafter), 51.7% were female; of these, 2.7% had a history of breast cancer, and 0.4% had a history of ovarian cancer (Table 2).

Identification of Individuals With Breast or Ovarian Cancer Meeting Eligibility Criteria

For women with a history of breast cancer, four eligibility criteria, as defined by NCCN guidelines,[19] were identified on the

Table 1. Demographic Comparison Between NHIS Sample and 2000/2010 US Census

Characteristic	NHIS		Census	
	Proportion (SE)	Population Equivalent, No.	2000, No. or %	2010, No. or %
Adults, years				
$\geq$ 18	100	229,926,502	209,128,094	234,564,071
18-24	12.7 (0.2)	29,222,958	27,143,454	30,672,088
25-44	35.7 (0.2)	82,045,758	85,040,251	82,134,554
45-64	34.2 (0.2)	78,577,896	61,952,636	81,489,445
$\geq$ 65	17.4 (0.2)	40,079,890	34,991,753	40,267,984
Race				
Non-Hispanic White*	68.3 (0.3)		69.1	63.7
Non-Hispanic Black*	11.7 (0.2)		12.1	12.2
Hispanic/Latino*	14.0 (0.1)		12.5	16.3

NOTE. Data sources: NCHS, National Health Interview Survey; US Census Bureau, 2010 Briefs and Reports.
Abbreviation: NHIS, National Health Interview Survey.
*NHIS proportions are based on population $\geq$ 18 years of age, whereas Census proportions are based on all ages.

Table 2. Descriptive Summary of the NHIS Sample, Cancer Prevalence, Genetic Testing Eligibility Criteria, and Genetic Encounter Rates With Population Equivalence and Trends Over Time

Characteristic	Proportion, % (SE)[a]	NHIS Sample Size for Estimation, No.	Population Equivalent, No.	Discussed Genetic Test With Provider (pooled sample including 2005/2010/2015 data), % (SE)	Advised to Undergo Genetic Test (pooled sample including 2005/2010/2015 data), % (SE)	Overall Tested (pooled sample including 2005/ 2010/2015 data), % (SE)	Tested 2005/ 2010, % (SE)	Tested 2015, % (SE)
Complete Sample		92,257	229,926,502					
All outcome variables known	92	84,746	211,155,613					
Females[b]	51.7 (0.2)	47,218	109,114,838					
Personal history of breast cancer[c]	2.7 (0.1)	1,383	2,922,050	18.6 (1.4)	12.3 (1.2)	10.1 (1.1)	7.9 (1.2)	13.2 (2.0)
Personal history of ovarian cancer[c]	0.4 (0.0)	206	449,640	15.1 (3.0)	13.1 (2.9)	10.5 (2.6)	9.7 (3.4)[d]	11.6 (4.4)[d]
Breast cancer eligibility criteria								
Personal history of breast cancer, and:[f]								
Diagnosis ≤ 45 years of age	25.0 (1.5)	325	731,631	31.9 (3.3)	22.8 (3.1)	18.2 (2.9)	14.7 (3.2)	23.3 (5.4)
≥ 1 FDR with breast cancer ≤ 50 years of age	9.8 (1.1)	127	287,333	30.7 (5.3)	19.9 (4.7)	14.6 (4.1)	16.3 (5.8)[d]	11.9 (5.4)[d]
Diagnosis ≤ 50 years of age and ≥ 1 FDR with breast cancer	9.1 (0.9)	125	264,451	43.3 (5.3)	24.8 (5.3)	15.4 (4.3)	12.9 (5.5)[d]	19.7 (7.4)[d]
≥ 1 FDR with ovarian cancer	3.8 (0.6)	53	109,645	17.9 (6.8)[d]	14.1 (6.4)[d]	6.2 (4.0)[e]	[j]	[j]
Summary values								
Personal history of breast cancer, eligibility unknown[g]	64.4 (1.7)	910	1,882,819	12.8 (1.6)	8.0 (1.4)	7.2 (1.2)	5.6 (1.3)	9.5 (1.9)
Personal history of breast cancer, eligible[h]	35.6 (1.7)	473	1,039,232	29.0 (2.7)	20.2 (2.5)	15.3 (2.2)	12.1 (2.4)	20.0 (4.2)
Eligible breast cancer and ovarian cancer	NA	671[i]	1,471,279	25.0 (2.2)	18.1 (2.0)	13.8 (1.7)	11.3 (1.9)	17.6 (3.4)

NOTE. data source: NCHS, National Health Interview Survey.
Abbreviations: FDR, first degree relative; NA, not applicable; NHIS, National Health Interview Survey.
[a]Denominator varies across rows; proportions adjusted for complex survey design and include weights.
[b]Denominator is all individuals with known outcomes.
[c]Denominator is females with known outcomes.
[d]Estimates are considered unreliable when the SE is ≥ 30%.
[e]SE > 50%.
[f]Only includes FDRs, specifically mother, sister(s), and/or daughter(s); denominator is females with known outcomes and personal history of breast cancer.
[g]Eligibility unknown defined as meeting none of the four eligibility criteria.
[h]Eligible defined as meeting one or more of the four eligibility criteria. Patients may meet more than one eligibility criterion; for details, see Appendix Table A3.
[i]Eight observations reported a personal history of both breast and ovarian cancer.
[j]Sample size too small to estimate.

basis of age of diagnosis and family history of breast and/or ovarian cancer. Thirty-six percent of individuals with a history of breast cancer met one or more of the criteria, representing 1,039,232 people (Table 2). Individuals were most likely to meet criteria for having the diagnosis at 45 years of age or younger (25.0%). Smaller proportions were eligible because of having ≥ 1 FDR diagnosed with breast cancer at 50 years of age or younger (9.8%), having a personal diagnosis at 50 years of age or younger with ≥ 1 FDR with a history of breast cancer (9.1%), and ≥ 1 FDR with a history of ovarian cancer (3.8%; Table 2). Of individuals with a history of breast cancer, 64.4% did not meet one of the four eligibility criteria and were considered eligibility unknown. All women with a history of ovarian cancer were considered eligible, representing 449,640 individuals[19] (Table 2). Of eligible patients, 83% met only one criterion, whereas 10%, 6%, and 1% met two, three, and four criteria, respectively (Appendix Table A3).

Genetic Encounter Rates for Breast Cancer, Stratified by Risk-Profile

For women with a history of breast cancer meeting one or more eligibility criteria, outcomes of the pooled sample were as follows: discussed, 29.0%; advised, 20.2%; and tested, 15.3%. The rate of testing was 12.1% in 2005/2010 and 20% in 2015. The rate of testing in individuals with a history of breast cancer who did not meet any of the eligibility criteria (eligibility unknown) was 7.2% (Table 2; Fig 1). Of the women with a history of breast cancer who underwent genetic testing, 54% (SE = 5.4%) met one or more eligibility criteria.

Genetic Encounter Rates for Breast Cancer, Stratified by Eligibility Criteria

Stratifying by individual criteria, rates of discussing ranged from 17.9% (≥ 1 FDR with ovarian cancer) to 43.3% (personal diagnosis at 50 years of age or younger, ≥ 1 FDR with breast cancer) and rates of advising ranged from 14.1% (≥ 1 FDR with ovarian cancer) to 24.8% (personal diagnosis at 50 years of age or younger, ≥ 1 FDR with breast cancer). Rates of testing ranged from 6.2% (≥ 1 FDR with ovarian cancer) to 18.2% (personal diagnosis at 45 years of age or younger). Because of small samples, the only reliable estimates over time were in individuals with a diagnosis at 45 years of age or younger, where the rate of testing was 14.7% in 2005/2010 and 23.3% in 2015 (Table 2; Fig 1).

Genetic Encounter Rates for Ovarian Cancer

In women with a history of ovarian cancer, outcome rates for the pooled sample were as follows: discussed, 15.1%; advised, 13.1%; and tested, 10.5%. Testing rates were 9.7% in 2005/2010 and 11.6% in 2015.

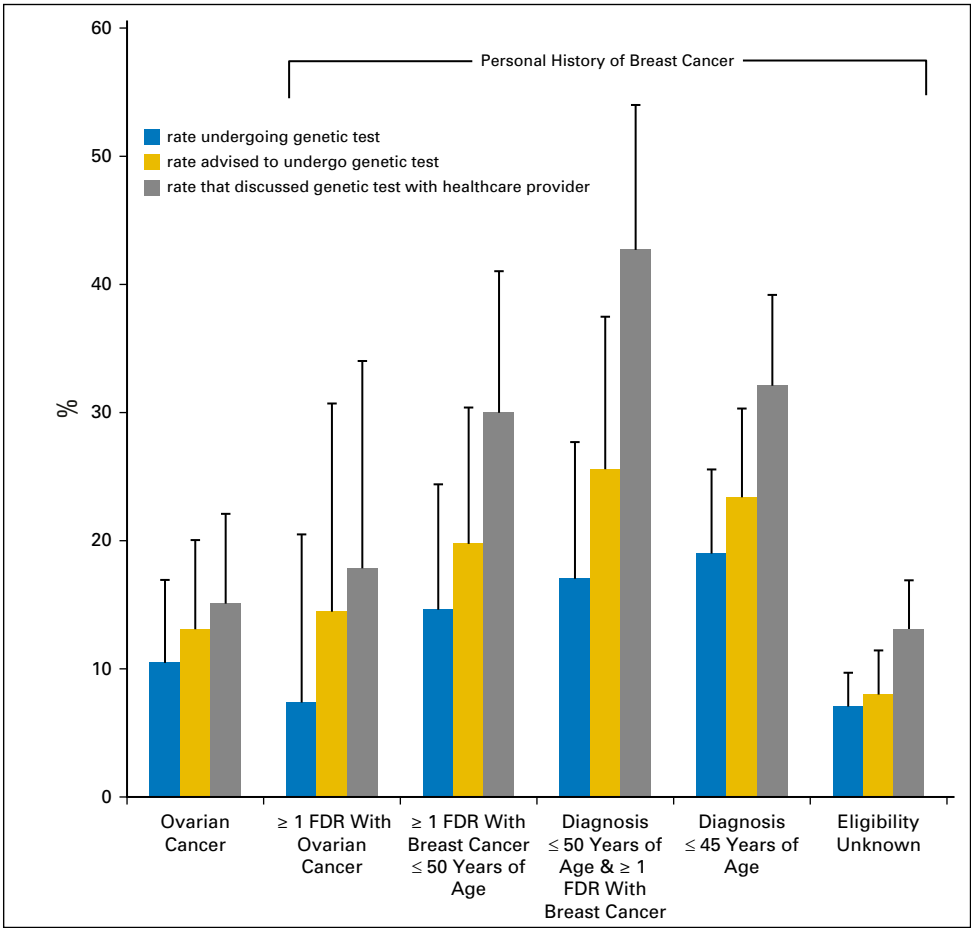

Fig 1. Genetic encounter rates for women with a history of breast or ovarian cancer, stratified by cancer type and eligibility criteria. FDR, first-degree relative. Data source: NCHS, National Health Interview Survey.

Population Estimates of Untested Individuals Meeting One or More Eligibility Criteria

In the pooled sample, an estimated 1,471,279 women with a history of breast and/or ovarian cancer met one or more of the identifiable eligibility criteria. In this population, the rate of genetic testing was 13.8% (95% CI, 10.8% to 17.6%). Using only these five criteria, this generates a population-based estimate of unmet need of genetic testing for breast and ovarian cancer survivors between 1,212,334 and 1,312,381.

DISCUSSION

This study estimates that 1.2 to 1.3 million women with a history of breast and/or ovarian cancer have not undergone genetic testing despite evidence-based guidelines supporting this as the standard of care. This includes 800,000 women with breast cancer and 400,000 women with ovarian cancer. Furthermore, over 70% of eligible patients with breast cancer and 80% of patients with ovarian cancer have never discussed genetic testing with a health care provider.

Although rates of testing are low across the entire study, ovarian cancer seems to be a particularly unrecognized indication for genetic testing. NCCN guidelines have recommended genetic testing for patients with a history of ovarian cancer since at least 2010.[20] Previous studies have shown this discrepancy, but the magnitude of this deficit was not previously known.[12,21]

The rates of genetic testing in this study population differ dramatically from recent reports, with estimates of discussing and testing as high as 71% and 53%, respectively.[8] Although some of this difference may reflect NHIS data being outdated, the rate of testing in 2015 in this study was still only 20%. Much of this difference can be attributed to a focus on women with new diagnoses, a small fraction of the population that lives with a history of breast or ovarian cancer. Women with diagnoses 5, 10, or even 20 years ago are likely susceptible to much lower rates of testing due to a lack of awareness or availability, yet may still benefit significantly from genetic testing. There are other reasons to believe our estimates are more representative—the NHIS samples from the entire US noninstitutionalized civilian population, instead of focusing on academic centers, single or regional (often urban) sites, or unique populations such as those diagnosed at particularly young ages or participating in advocacy groups. Furthermore, the in-person nature of the NHIS may help mitigate the self-selection bias inherent in mailed surveys; however, responses are still limited by self-report and potential recall bias.

Analyzing the steps a patient must take before undergoing genetic testing can provide insight into the barriers of care. Seventy-five of every 100 eligible patients with a history of breast or ovarian cancer have never discussed genetic testing with a health care provider. An additional seven patients are lost between discussing and advising, and four more between advising and testing.

These first two gaps (before discussing and between discussing and advising) reflect a lack of patient identification and perhaps a lack of provider awareness and knowledge. A number of women now eligible for testing would not have been identified at the time of their diagnosis because of the rapid evolution of NCCN guidelines over the past number of years.[19,20] This may also reflect changes in care; as patients move away from their initial cancer providers, new providers may overlook these remote histories or may not be aware of contemporary guidelines. Although most primary care providers are aware of *BRCA* mutations, as few as 20% could accurately identify NCCN guidelines in a 2011 study.[22]

Previous studies have documented the importance of provider recommendation on patients' pursuit of genetic testing[8,23] and have shown a lack of recommendation as the primary reason for many untested women.[8] Thus, it becomes important for all providers to make note of those with a personal history and inquire about prior genetic testing. All women with a history of ovarian cancer should be identified and referred. For breast cancer, three pieces of information—age at diagnosis, FDR with breast cancer (with age of diagnosis), and FDR with ovarian cancer—can identify a large population of women at risk for carrying a heritable gene mutation. Using these four questions as part of each routine visit could identify over 1 million women eligible for genetic testing.

The final gap in the continuum is between advising and testing. This discrepancy may reflect a myriad of health care challenges, such as availability of providers (including genetic counselors,[24,25] certified advanced practice nurses, and physicians), out-of-pocket expenses to the patient,[26] and patient preference.[27] The availability of genetic counselors is especially problematic and is currently being addressed by the National Society of Genetic Counselors. The American Board of Genetic Counseling lists approximately 4,000 board-certified genetic counselors (CGCs), but a 2011 survey suggests that only two thirds of these CGCs practice in clinical settings (one third work in industry), and only 25% of clinical CGCs specialize in cancer.[28] The geographic distribution of CGCs is not uniform, with 500 located in California, whereas states such as Missouri, Wyoming, Mississippi, and Alaska each have five or fewer CGCs. Possible solutions include expanding the CGC workforce,[25] integrating CGCs into multidisciplinary clinic workflows,[29] and the use of telemedicine.[30] Education focused on increasing the number of advanced practice nurses and physicians who are comfortable initiating genetic testing could also help alleviate the burden from this overstretched workforce, but would require that insurers eliminate a recent change to prerequisite genetic counseling.[31] Although the cost of genetic testing has decreased significantly over recent years, cost still remains a barrier for underinsured individuals. Providers and patients should also be reminded of the numerous provisions that protect patients from discrimination on the basis of genetic information.[32]

Given the low testing rate and large impact of identifying a heritable mutation, aggressive solutions should be considered. These may include universal testing for women with breast and/or ovarian cancer or other select populations,[33] directed patient education for self-referral, or modified direct-to-consumer testing. As the cost of testing continues to decline, there is evidence that universal screening of adult women older than 30 years of age may fall below $100,000 per quality-adjusted life-year.[34]

Increasing the rate of genetic testing in affected women is critical to enable subsequent cancer prevention and early detection in patients and their family members.[4-7,11] The ultimate impact of genetic testing is to identify all individuals at high-risk for cancer before they are affected to maximize the opportunity for prevention and early detection. This effort will be challenging if we

cannot first identify affected individuals with hereditary cancer gene mutations.

This study has several limitations. First, NHIS only collects self-reported data and is not validated against the medical record. Recall bias as it relates to advising, discussing, and testing are all possible and are likely magnified as patients become more removed from their treatment. Patients may confuse other pathologies with cancer diagnoses or report inaccurate ages at diagnosis for themselves or their relatives. Second, survivorship bias may result in under-representation of aggressive tumor pathologies, such as triple-negative breast cancer or epithelial ovarian cancer. Third, low event rates and small subpopulations limit precision. Pooling data improve these estimates but at the expense of information being outdated. Fourth, NHIS only collects data to estimate four eligible breast cancer subpopulations, whereas NCCN outlines over a dozen (Appendix Table A1). Patients who would have otherwise met criteria (eg, if their eligibility was dependent on second- or third-degree relatives) would be included in our eligibility unknown population. To our knowledge, an empirical estimate of the significance of this is not available. However, studies suggest that age at diagnosis and family history of breast and ovarian cancer account for the majority of all eligible individuals.[29,35] Further support that these limited criteria capture the majority of eligible women is the comparability between the proportion of individuals eligible in our study with recent studies with access to more granular data[36] and the significant difference in rates of testing between our eligible patients with breast cancer (15.3%) and the eligibility unknown patients (7.2%). Given this lower rate in the eligibility unknown patients, if additional criteria expanded the pool, our estimate for the number of patients needing testing would actually increase, suggesting our estimates are conservative.

Future research should focus on understanding the characteristics of the eligible population that has not been tested, with an emphasis on measures of access to care. Further research should also assess the patient and provider factors that contribute to decreasing rates of patients discussing, being advised to undergo, and actually undergoing genetic testing.

In conclusion, in a nationally representative sample, fewer than one in five women with a history of breast and/or ovarian cancer meeting select NCCN eligibility criteria have undergone genetic testing. This represents a deficit of 1.2 to 1.3 million women. Most women meeting criteria have never even discussed genetic testing with a health care provider. Large national efforts are needed to address this unmet need.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

AUTHOR CONTRIBUTIONS

Conception and design: All authors
Collection and assembly of data: Christopher P. Childers, James Macinko
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

REFERENCES

1. American Cancer Society: Breast cancer facts & figures 2015-2016. Atlanta, GA, American Cancer Society, 2015 https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2015-2016.pdf
2. Norquist BM, Harrell MI, Brady MF, et al: Inherited mutations in women with ovarian carcinoma. JAMA Oncol 2:482-490, 2016
3. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2017. CA Cancer J Clin 67:7-30, 2017
4. Byrski T, Huzarski T, Dent R, et al: Response to neoadjuvant therapy with cisplatin in BRCA1-positive breast cancer patients. Breast Cancer Res Treat 115: 359-363, 2009
5. Fong PC, Boss DS, Yap TA, et al: Inhibition of poly(ADP-ribose) polymerase in tumors from BRCA mutation carriers. N Engl J Med 361:123-134, 2009
6. Evans DG, Ingham SL, Baildam A, et al: Contralateral mastectomy improves survival in women with BRCA1/2-associated breast cancer. Breast Cancer Res Treat 140:135-142, 2013
7. Heemskerk-Gerritsen BA, Rookus MA, Aalfs CM, et al: HEBON: Improved overall survival after contralateral risk-reducing mastectomy in BRCA1/2 mutation carriers with a history of unilateral breast cancer: A prospective analysis. Int J Cancer 136: 668-677, 2015
8. Kurian AW, Griffith KA, Hamilton AS, et al: Genetic testing and counseling among patients with newly diagnosed breast cancer. JAMA 317:531-534, 2017
9. American Cancer Society: Cancer treatment & survivorship facts & figures 2016-2017. Atlanta, GA, American Cancer Society, 2016 https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/cancer-treatment-and-survivorship-facts-and-figures/cancer-treatment-and-survivorship-facts-and-figures-2016-2017.pdf
10. Howlader N, Noone AM, Krapcho M, et al (eds): SEER Cancer Statistics Review, 1975-2014, Bethesda, MD, National Cancer Institute. https://seer.cancer.gov/csr/1975_2014/
11. Scheuer L, Kauff N, Robson M, et al: Outcome of preventive surgery and screening for breast and ovarian cancer in BRCA mutation carriers. J Clin Oncol 20:1260-1268, 2002
12. Febbraro T, Robison K, Wilbur JS, et al: Adherence patterns to National Comprehensive Cancer Network (NCCN) guidelines for referral to cancer genetic professionals. Gynecol Oncol 138:109-114, 2015
13. Stuckey A, Febbraro T, Laprise J, et al: Adherence patterns to National Comprehensive Cancer Network guidelines for referral of women with breast cancer to genetics professionals. Am J Clin Oncol 39: 363-367, 2016
14. National Center for Health Statistics: National Health Interview Survey, 2015. Public-use data file and documentation. https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm
15. NCHS: Technical Notes for Summary Health Statistics Tables: National Health Interview Survey https://www.cdc.gov/nchs/data/nhis/2015_shs_hb_tech_notes.pdf
16. National Center for Health Statistics: Data file documentation, National Health Interview Survey, 2010 (machine readable data file and documentation), Hyattsville, Maryland, National Center for Health Statistics, Centers for Disease Control and Prevention, 2011 https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm
17. National Center for Health Statistics: Data File Documentation, National Health Interview Survey, 2005 (machine readable data file and documentation). Hyattsville, Maryland, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006 https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm
18. Reference deleted
19. Daly MB, Pilarski R, Berry M, et al: NCCN guidelines insights: Genetic/familial high-risk assessment: Breast and ovarian, version 2.2017. J Natl Compr Canc Netw 15:9-20, 2017
19a. Howden LM, Meyer JA: Age and Sex Composition: 2010, US Census Bureau, 2010 Census Briefs, C2010BR-03, https://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf
19b. Humes KR, Jones NA, Ramirez RR: Overview of Race and Hispanic Origin: 2010, US Census

Bureau, 2010 Census Briefs, C2010BR-02, https://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf

20. Daly MB, Axilbund JE, Buys S, et al: Genetic/familial high-risk assessment: Breast and ovarian. J Natl Compr Canc Netw 8:562-594, 2010

21. Powell CB, Littell R, Hoodfar E, et al: Does the diagnosis of breast or ovarian cancer trigger referral to genetic counseling? Int J Gynecol Cancer 23:431-436, 2013

22. Bellcross CA, Kolor K, Goddard KA, et al: Awareness and utilization of BRCA1/2 testing among U.S. primary care physicians. Am J Prev Med 40:61-66, 2011

23. Rosenberg SM, Ruddy KJ, Tamimi RM, et al: BRCA1 and BRCA2 mutation testing in young women with breast cancer. JAMA Oncol 2:730-736, 2016

24. Haga SB, Burke W, Agans R: Primary-care physicians' access to genetic specialists: An impediment to the routine use of genomic medicine? Genet Med 15:513-514, 2013

25. Pan V, Yashar BM, Pothast R, et al: Expanding the genetic counseling workforce: Program directors' views on increasing the size of genetic counseling graduate programs. Genet Med 18:842-849, 2016

26. Matro JM, Ruth KJ, Wong YN, et al: Cost sharing and hereditary cancer risk: Predictors of willingness-to-pay for genetic testing. J Genet Couns 23:1002-1011, 2014

27. Schlich-Bakker KJ, ten Kroode HF, Wárlám-Rodenhuis CC, et al: Barriers to participating in genetic counseling and BRCA testing during primary treatment for breast cancer. Genet Med 9:766-777, 2007

28. American Board of Genetic Counseling: Practice analysis and information. http://www.abgc.net/Certification/practice_analysis_and_information.asp

29. Kishan AU, Gomez CL, Dawson NA, et al: Increasing appropriate BRCA1/2 mutation testing: The role of family history documentation and genetic counseling in a multidisciplinary clinic. Ann Surg Oncol 23:634-641, 2016 (suppl 5)

30. Bradbury A, Patrick-Miller L, Harris D, et al: Utilizing remote real-time videoconferencing to expand access to cancer genetic services in community practices: A multicenter feasibility study. J Med Internet Res 18:e23, 2016

31. Whitworth P, Beitsch P, Arnell C, et al: Impact of payer constraints on access to genetic testing. J Oncol Pract 13:e47-e56, 2017

32. Gammon A, Neklason DW: Confidentiality & the risk of genetic discrimination: What surgeons need to know. Surg Oncol Clin N Am 24:667-681, 2015

33. King MC, Levy-Lahad E, Lahad A: Population-based screening for BRCA1 and BRCA2: 2014 Lasker Award. JAMA 312:1091-1092, 2014

34. Long EF, Ganz PA: Cost-effectiveness of universal BRCA1/2 screening: Evidence-based decision making. JAMA Oncol 1:1217-1218, 2015

35. Lim GH, Borje E, Allen JC Jr: Evaluating the performance of National Comprehensive Cancer Network (NCCN) breast and ovarian genetic/familial high risk assessment referral criteria for breast cancer women in an Asian surgical breast clinic. Gland Surg 6:35-42, 2017

36. Kurian AW, Li Y, Hamilton AS, et al: Gaps in incorporating germline genetic testing into treatment decision-making for early-stage breast cancer. J Clin Oncol 35:2232-2239, 2017

Affiliations

Christopher P. Childers and **Melinda Maggard-Gibbons**, David Geffen School of Medicine at University of California-Los Angeles; **Christopher P. Childers** and **James Macinko**, Fielding School of Public Health at University of California-Los Angeles; and **Kimberly K. Childers**, Providence Health & Services Southern California, Los Angeles, California.

Support

C.P.C. is funded by Agency for Healthcare Research and Quality Grant No. F32HS025079. The Agency for Healthcare Research and Quality had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Christopher P. Childers
No relationship to disclose

Kimberly K. Childers
No relationship to disclose

Melinda Maggard-Gibbons
No relationship to disclose

James Macinko
No relationship to disclose

Appendix

Table A1. NCCN *BRCA1/2* Testing Criteria for Women With a History of Breast or Ovarian Cancer

Included/Not Included	Criteria
Included in study	Personal history of ovarian cancer
	Personal history of breast cancer diagnosed ≤ 45 years of age
	Personal history of breast cancer diagnosed ≤ 50 years of age with ≥ 1 FDR with breast cancer at any age
	Personal history of breast cancer diagnosed at any age with ≥ 1 FDR with breast cancer diagnosed ≤ 50 years of age
	Personal history of breast cancer diagnosed at any age with ≥ 1 FDR with ovarian cancer
Not included in study	Personal history of breast cancer diagnosed ≤ 50 years of age with an additional breast cancer primary
	Personal history of breast cancer diagnosed ≤ 50 years of age with ≥ 1 second- or third-degree relative with breast cancer
	Personal history of breast cancer diagnosed ≤ 50 years of age with ≥ 1 close relative with pancreatic cancer
	Personal history of breast cancer diagnosed ≤ 50 years of age with ≥ 1 close relative with prostate cancer (Gleason score ≥ 7)
	Personal history of breast cancer diagnosed ≤ 50 years of age with unknown/limited family history
	Personal history of breast cancer diagnosed ≤ 60 years of age with triple-negative breast cancer
	Personal history of breast cancer diagnosed at any age with ≥ 2 close relatives with breast cancer, pancreatic cancer, or prostate cancer (Gleason score ≥ 7)
	Personal history of breast cancer diagnosed at any age with ≥ 1 second- or third-degree relative with breast cancer ≤ 50 years of age
	Personal history of breast cancer diagnosed at any age with ≥ 1 second- or third-degree relative diagnosed with ovarian cancer
	Personal history of breast cancer diagnosed at any age with a close male relative with breast cancer
	Personal history of breast cancer diagnosed at any age for individuals of ethnicity associated with higher mutation frequency (ie, Ashkenazi Jewish)

NOTE. Additional *BRCA1/2* testing criteria exist for patients with prostate/pancreatic cancer and in select unaffected individuals with family history alone. Data source: National Cancer Comprehensive Network.
Abbreviations: FDR, first-degree relative; NCCN, National Comprehensive Cancer Network.

Table A2. Summary Statistics for Individuals With and Without Genetic Encounter Data

	All Outcomes Available		Outcomes Not Available		
Characteristic	Mean/ Proportion	SE	Mean/ Proportion	SE	*P*
Age (years)	46.2	0.11	48.2	0.27	< .01
Gender (%)					
Male	48.3	0.2	47.2	0.7	.16
Female	51.7	0.2	52.8	0.7	
Survey year (%)					
2005	31.7	0.3	29.8	0.7	.06
2010	33.2	0.3	33.7	0.8	
2015	35.0	0.3	36.4	0.8	
Breast cancer (%)					
Yes	2.7	0.1	3.1	0.3	.20
No	97.3	0.1	96.9	0.3	
Ovarian cancer (%)					
Yes	0.4	0.0	0.4	0.1	.80
No	99.6	0.0	99.6	0.1	

NOTE. Data source: NCHS, National Health Interview Survey.

Table A3. Population Weighted Estimates of Individuals Meeting One or More Eligibility Criteria

Criteria	NHIS Sample Size for Estimation	Proportion, % (SE)*
Met 1 criteria		
Total meeting 1 criteria	554	82.7 (1.7)
Personal history of ovarian cancer	198	29.4 (2.3)
Personal history of breast cancer, and:		
Diagnosis ≤ 45 years of age	232	36.1 (2.4)
Diagnosis ≤ 50 years of age and ≥ 1 FDR with breast cancer	26	3.1 (0.7)
≥ 1 FDR with breast cancer ≤ 50 years	63	9.4 (1.5)
≥ 1 FDR with ovarian cancer	35	4.8 (1.0)
Met 2 criteria	72	10.0 (1.3)
Met 3 criteria	42	6.5 (1.2)
Met 4 criteria	3	†
Met 5 criteria	0	NA
Total individuals meeting one or more criteria	671	

NOTE. data source: NCHS, National Health Interview Survey.
Abbreviations: FDR, first-degree relative; NA, not applicable; NHIS, National Health Interview Survey.
*Proportions adjusted for complex survey design and include weights.
†Sample size too small to estimate.