# Patient Engagement With Clinicians and Family Members About Genetic Test Results Across Risk Groups in Women With Hereditary Cancer Susceptibility

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DOI https://doi.org/10.1200/OP-25-00776

## ABSTRACT

**PURPOSE** To examine patient report of engagement with clinicians and relatives about their germline genetic test results across risk groups in women diagnosed with cancer.

**PATIENTS AND METHODS** We surveyed women age 20-79 years diagnosed with breast, ovarian, or uterine cancer in 2018-19 in Georgia or California, in whom a germline genetic testing yielded a pathogenic variant (PV) in a breast, ovarian, or uterine cancer susceptibility gene (grouped by high *v* moderate risk) or a variant of unknown significance (VUS) about 4 years after diagnosis (N = 1,767, 52.4% response rate).

**RESULTS** Most patients with PVs (84.5%) had a genetic counseling visit to discuss test results, and a majority (70.6%) were encouraged to share results with relatives with no difference across PV risk groups. Half of the patients with PV reported that a genetic counselor gave them advice about how to talk to relatives and one third reported that a counselor talked directly with a relative. Physician engagement with patients about family communication of test results was low: one third of patients with high-risk PV reported that their oncologist encouraged them to share results with relatives. Patients with PV shared test results with 80% of first-degree relatives and one third of second-degree relatives. Compared with patients with PVs, those with VUS had less engagement with clinicians about sharing test results with relatives; were less likely to believe that they had a responsibility to share results with family; and were less likely to share results with relatives.

**CONCLUSION** Patients with PVs share results with many family members but clinician support is insufficient, especially among cancer doctors. A substantial proportion of patients with VUS-only engage relatives about results but more research is needed about the nature of the discussions regarding these indeterminate findings.

ACCOMPANYING CONTENT

Appendix

Accepted December 10, 2025
Published January 13, 2026

JCO Oncol Pract 00:1-8


View Online Article



## INTRODUCTION

Cascade genetic testing in families with hereditary cancer susceptibility (HCS) can reduce the burden of cancer through early detection and prevention.[1-3] Women in these families may benefit most because breast cancer, ovarian cancer, and uterine cancer are important targets for genetically informed risk-reducing strategies.[4-6] Despite this potential benefit, cascade testing is low in families with HCS. Cascade testing is challenging because patients diagnosed with cancer in whom a germline pathogenic variant (PV) is detected are responsible for engaging their relatives about these PV results, and clinical support for families is very limited. There are concerns that patients' engagement with their relatives, and clinician support, may not be well matched to the clinical relevance of the genetic test results.[2,7] In particular, the detection of a variant of uncertain significance (VUS) may foment strong reactions and responses from patients and their clinicians.[8-10] We identified a population-based sample of female cancer survivors who were diagnosed with breast cancer, ovarian cancer, or uterine cancer in 2018-19 and in whom a PV was detected on germline genetic testing within 2 years of diagnosis. We surveyed patients about 4 years after diagnosis. We examined patient attitudes about cascade genetic testing and report of engagement with relatives and clinicians, by test results groups. We hypothesized that,

## CONTEXT

**Key Objective**
Does patient engagement with clinicians and relatives about cascade genetic testing vary by genetic risk in families with hereditary cancer susceptibility?

**Knowledge Generated**
Patients with pathogenic variants (PVs) share their germline genetic test results with most first-degree relatives and many second-degree relatives. But clinician support for patient communication about family cascade testing is very low. Compared with patients with PVs, those with a variant of unknown significance communicate results with fewer relatives and with less support from clinicians.

**Relevance**
Results underscore the need for more effective engagement between clinicians and their patients who carry a PV about communication with families regarding cascade genetic testing.



compared with patients with clinically meaningful PVs, those with VUS-only findings would report less engagement about genetic test results with relatives, and less encouragement by clinicians to engage relatives.

## PATIENTS AND METHODS

We selected patients from the Georgia California SEER Genetic Linkage Initiative,[11] which identified all patients diagnosed with cancer in 2013-2019 who were linked to a germline genetic test result through 2021. We selected 3,869 women who were diagnosed with breast, ovarian, or uterine cancer in 2018-19 in Georgia or California, linked to a pathogenic or likely pathogenic or uncertain variant (PV or VUS-only) and alive at the time of selection. Most patients were tested near their diagnosis date (mean 2.5 days later), including 12.2% of patients tested before diagnosis. We oversampled nonbreast diagnoses in the VUS-only group to ensure adequate representation of these less prevalent cancers in the smallest genetic testing results group. We mailed a survey to these women about four and a half years after diagnosis (mean 1,665.4 days). The mode options were print or electronic survey. Surveys were translated into English and Spanish, and bilingual study information and surveys were sent to all patients identified as Hispanic in the SEER registry data system. Patients were mailed materials with a $20 in US dollars cash gift, and a modified Dillman method was used to encourage response.

### Outcome Measures

Outcome measures below were derived from the survey.

We first asked patients if "you have ever had a visit with a genetics expert to discuss cancer risk—that is, an appointment where the whole discussion is about genetic risk for cancer? (yes or no)." We categorized patients as having a genetic counseling visit if they responded yes to this question.

We then queried patients about their engagement with clinicians about cascade genetic testing (Fig 1): We queried patients about which clinicians: (1) encouraged you to talk about your genetic test results with your family members; (2) gave you advice or tips on how to talk with your family members about your genetic test results; and (3) talked directly with your family members about whether to get genetic testing for cancer risk. Clinician categories were (1) genetic counselor; (2) medical oncologist; and (3) cancer surgeon.

We then queried patients regarding their attitudes about talking with family about genetic testing for cancer risk (Fig 2): *Thinking about talking with your biological family about genetic testing for cancer risk, how true are each of the statements below?* Understand my results well enough to talk to my relatives; My results are useful to my family; It is my responsibility to share results with family. Responses were recorded on a five-point Likert scale ranging from not at all true to very true.

We determined adult family size by asking patients about the number of first- and second-degree adult relatives alive at the time of survey by family role (mother, father, brothers, sisters, aunts, uncles, nieces, and nephews). Half-siblings were included in the query. Additionally, for each relative category, we asked the patient "how many have you talked with about your cancer genetic test result?" We used the results from these two questions to calculate the proportion of adult relatives reported by the patient with whom the patient shared their test result (Fig 3).

### Independent Variables

Genetic testing results groups were categorized using the SEER GACA data set. We grouped linked test results into three categories for each cancer: (1) PV high-risk (breast: *BRCA1*, *BRCA2*, *CDH1*, *PALB2*, *PTEN*, *STK11*, and *TP53*; ovarian: *BRCA1*,

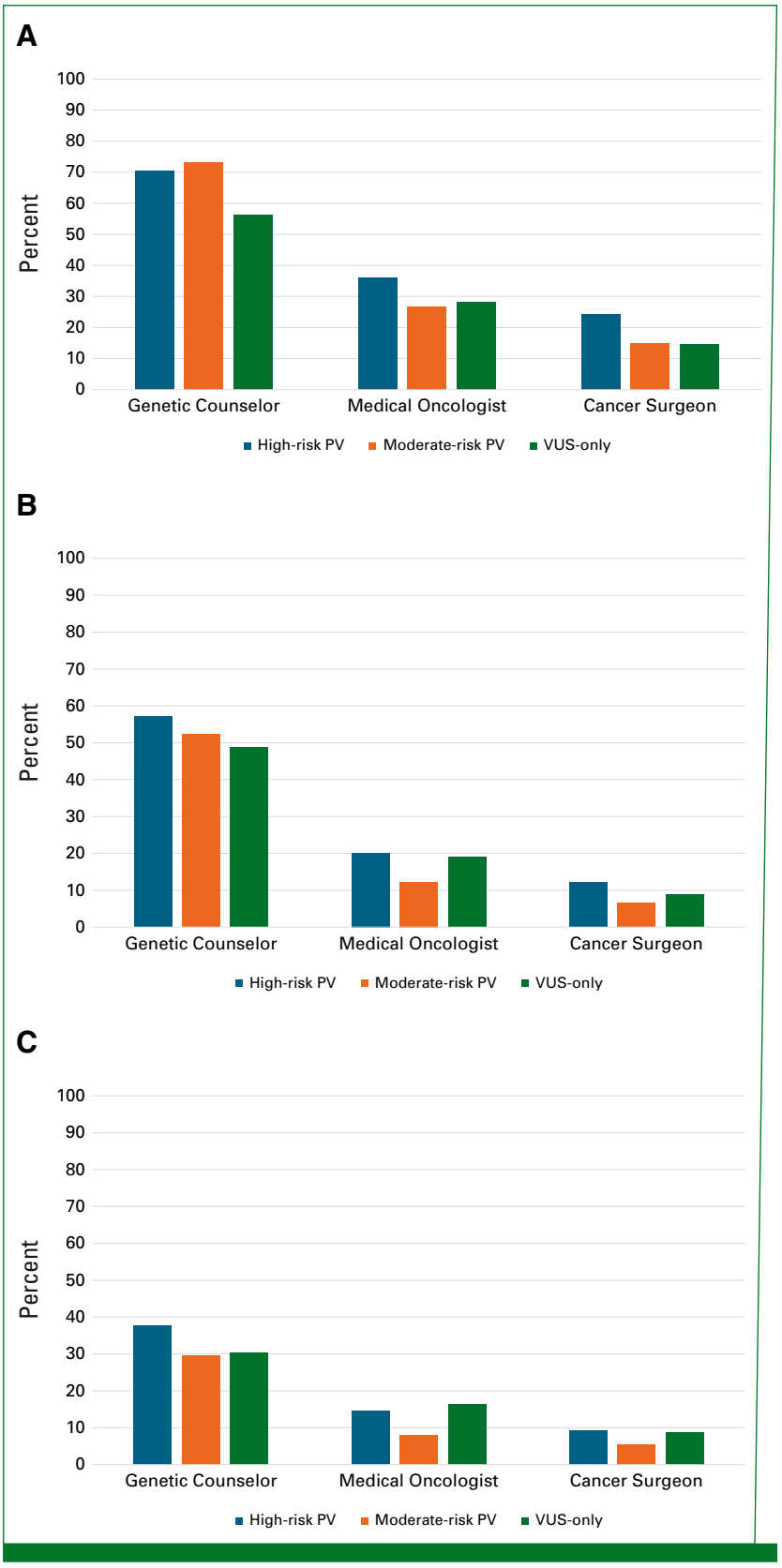


**FIG 1.** (A-C) Patient report of levels of engagement with their clinicians about communication with their relatives about genetic test results by clinician type and genetic testing results groups. (A) Encouraged you to talk about your genetic test results with your family members. (B) Gave you advice or tips on how to talk with your family members about your genetic test results. (C) Talked (continued on following page)

**FIG 1.** (Continued). directly with your family members about whether to get genetic testing for cancer risk. N = 1,767. PV, pathogenic variant; VUS, variant of uncertain significance.

*BRCA2*, *BRIP1*, *EPCAM*, *MLH1*, *MSH2*, *RAD51C*, and *RAD51D*; uterine: *EPCAM*, *MLH1*, *MSH2*, *MSH6*, and *PTEN*), (2) PV moderate-risk (breast*: ATM*, *BARD1*, *CHEK2*, *RAD51C*, and *RAD51D*; ovarian: *ATM*, *MSH6*, and *PALB2*; uterine: *BRCA1*) on the basis of guidelines published during the study period (Appendix Table A1, online only), and (3) VUS-only.[12]

Additional variables included age, cancer diagnosis date, cancer type (breast, uterine, or ovarian), race, and ethnicity, and state registry site, all from SEER registry data. Education level, total number of first-degree and second-degree relatives, and time from diagnosis to completion of the survey were derived from the survey.

### Statistical Analysis

We examined patient-reported outcomes by genetic test result groups using bivariate statistics. We created response weights to account for nonresponse bias and adjusted the bivariate results using these weights. In a secondary analysis, we examined potential confounders (patient age, race/ethnicity, education level, total number of first-degree and second-degree relatives, family size, cancer type, and survey completion time) using multiple logistic regression. We observed no significant or meaningful differences in the results from these adjusted analyses.

## RESULTS

Appendix Figure A1 shows the patient study flow: 11,256 female patients met the criteria for selection into the study (first cancer diagnosis of the selected cancer type, diagnosed in 2018-2019, alive on last SEER report with PV or VUS-only). We surveyed a weighted random sample of 4,263 (oversampling uterine and ovarian cancer patients with VUS-only to ensure adequate sample size); 394 patients were subsequently excluded after survey mailing because of death leaving 3,869, of whom 2027 returned completed surveys (52.4%). We subsequently excluded 87 respondents diagnosed with bilateral breast cancer (4.3%) and those with PV results other than primary breast or ovarian cancer genes or VUS (N = 173, 8.5%), yielding a final analytic sample of 1,767. Response to the survey was significantly lower for Hispanic and non-White patients (41.7%, 49.9%, and 59.8% for Hispanic, non-Hispanic non-White, and non-Hispanic White, respectively, $P < .001$) but there was no difference by age groups, cancer type, or gene groups. All analyses were run using the response weights to account for these differences.

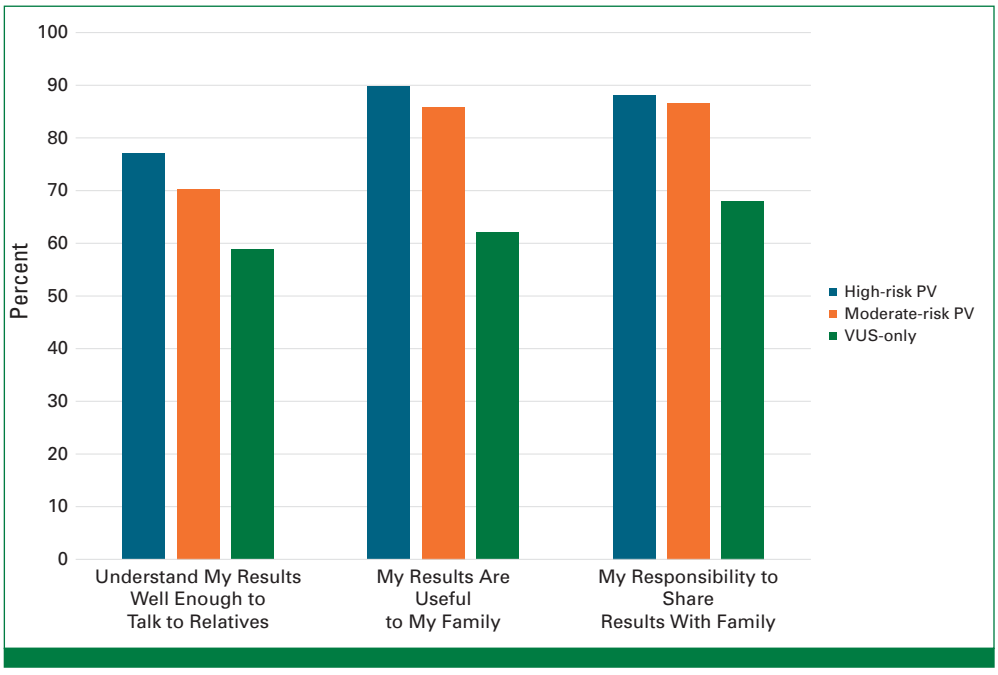


**FIG 2.** Patient attitudes about communication with relatives about genetic test results by genetic testing results groups. 5-Point Likert response categories from not at all true to very true. This figure shows percent of respondents indicating quite or very true for each selected item. N = 1,767. PV, pathogenic variant; VUS, variant of uncertain significance.

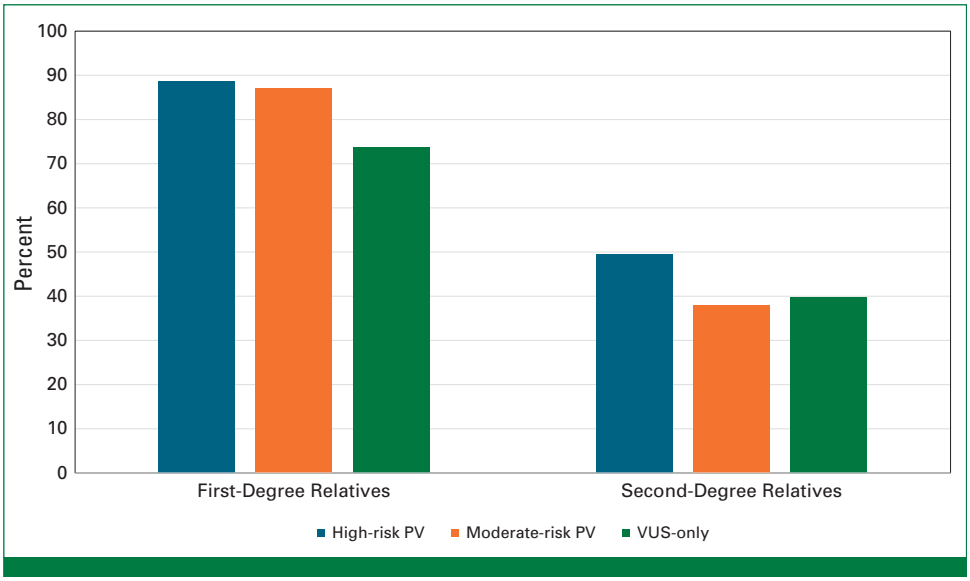


**FIG 3.** Proportion of relatives for whom patients shared their genetic test results by genetic test testing results groups. N = 1,767. PV, pathogenic variant; VUS, variant of uncertain significance.

Table 1 shows patient characteristics by genetic test results groupings (870 with high-risk PV; 477 with moderate-risk PV; 420 with VUS-only). Overall, 80.9% of the patients were diagnosed with breast cancer, 8.5% uterine, and 10.6% ovarian. Patients with VUS were more likely to have a nonbreast cancer diagnosis than the PV groups, which was the result of oversampling these less prevalent cancers in this smaller test result group to ensure adequate representation. The mean age was 52.4 years (standard deviation [SD], 12.6). The average family size was 5.5 (SD, 5.0). Over half were college graduates or higher and 28.6% lived in census tracts with 10% poverty level or higher. Age, education, family size, date range of diagnosis, time from diagnosis to survey completion, and state registry site were similar across test results groups.

Overall, 80.5% of patients reported that they received a visit with a genetic expert, such as a genetic counselor, to discuss genetic risk of cancer (84.5% of those with PV *v* 67.4% of those with VUS-only [$P < .001$]). Figures 1A-1C show patient reports of level of engagement with clinicians about their genetic test results. Patients were much more likely to engage with a genetic counselor versus physician for all levels of engagement. Among patients with high-risk PVs, 70.6%, 57.1%, and 37.8% of patients reported that a genetic counselor encouraged them to talk to family members, gave

**TABLE 1.** Characteristics of the Study Population by Genetic Test Results Group

| Variable | High-Risk PV, No. (%) | Moderate-Risk PV, No. (%) | VUS-Only, No. (%) |
|---|---|---|---|
| Cancer type | | | |
| Uterus | 62 (7) | 5 (1) | 93 (22) |
| Breast | 716 (82) | 456 (96) | 237 (56) |
| Ovary | 92 (11) | 16 (3) | 90 (21) |
| Age, years, mean (SD) | 50.6 (12.4) | 54.7 (12) | 53.6 (12.8) |
| Education (missing = 164) | | | |
| No high school | 27 (3) | 6 (1) | 3 (1) |
| Some high school | 25 (3) | 7 (2) | 14 (4) |
| High-school graduate or GED | 112 (14) | 41 (9) | 42 (12) |
| Some college or technical school | 233 (28) | 129 (30) | 117 (34) |
| College graduate | 216 (26) | 147 (34) | 77 (22) |
| Graduate degree | 210 (26) | 103 (24) | 94 (27) |
| Family size, mean (SD) | 5.25 (4.7) | 4.84 (4.29) | 6.77 (6.1) |
| Time from diagnosis to survey, days, mean (SD) | 1,649.9 (303) | 1,621.2 (261.9) | 1,748.8 (219.2) |

NOTE. See Appendix Table A1 for PV grouping.
Abbreviations: PV, pathogenic variant; SD, standard deviation; VUS, variant of uncertain significance.

advice about how to do so, or talked directly to a relative, respectively. These figures were much lower for physicians. Patient reports of level of engagement with genetic counselors were consistent across PV risk groups, but the level of engagement was lower in moderate-risk PV versus high-risk PV groups for medical oncologists and surgeons. Patients with VUS reported less engagement about genetic test results versus PV groups, across all clinician types.

Figure 2 shows patient attitudes about communication with relatives about genetic testing by results groups. Overall, 71.2% of patients believed that they understood their test results well enough to talk to relatives; 82.8% believed their results were useful for their family; and 83.5% believed it was their responsibility to share their results with family members. Patients with VUS were much less likely to believe that their results were useful to family members (62.1% *v* 89.8% and 85.8%, respectively [$P < .001$]) or believed it was their responsibility to share their results with family members (68.0% *v* 88.2% and 86.7% for high- and moderate-risk PV groups, respectively [$P < .001$]).

Figure 3 shows patient reports of the proportion of their first- and second-degree relatives with whom they shared test results. Patients with VUS were less likely to share results with family members compared with those with a PV. For first-degree relatives, the proportions were 88.7%, 87.0%, and 73.6% for high-risk PV, moderate-risk PV, and VUS-only ($P < .001$). For second-degree relatives, these proportions were 49.4%, 37.9%, and 39.8% ($P < .001$).

## DISCUSSION

Cascade genetic testing is a crucial aspect of population-level cancer prevention and control, but we know virtually nothing about whether patient engagement of family members or clinician support for cascade testing is personalized to the clinical importance of the patient's genetic test results. Previous published studies have been limited by small samples drawn from single clinical sites or online solicitation, narrow variability of the genetic risk (eg, BRCA1 and BRCA2 only), and little information from patients about their attitudes and experiences with cascade testing in their families.[13–15]

In this population-based study of female cancer survivors surveyed 4 years after diagnosis, we found that patients with PVs believed their test results were useful to their family members and that it was their responsibility to share results with them. These findings were consistent with PV carriers' report of the proportion of their relatives with whom they shared results: over 80% of first-degree relatives and over one third of second-degree relatives.

Despite the positive attitudes and substantial communication with relatives, patients with PVs reported low to moderate support from clinicians about communicating test results with relatives. Reassuringly, most patients with PVs (84.5%) reported that they had a genetic counseling visit to discuss test results, and most patients reported that a genetic counselor encouraged them to share test results with relatives. However, only about half of the patients reported that a genetic counselor gave them advice about how to talk to family members and about one third reported that a genetic counselor talked directly with a relative. Patient engagement about cascade testing was much lower with physicians. Additionally, physicians' engagement with patients was less guideline-aligned, because guidelines recommend cascade testing for all PVs studied, but clinicians were less likely to encourage patients with moderate-risk versus high-risk PVs to communicate results to their relatives.

Compared with patients with PVs, patients with VUS-only reported less engagement with clinicians about sharing test results with family members; were less likely to believe that their test results were useful to their family or that they had a responsibility to share results with family; and were somewhat less likely to share test results with relatives. These findings are consistent with our previous clinic-based study, in which patients received uniform genetic counseling across participating academic institutions.[16]

Patients with VUS-only results are a rapidly growing population as multigene panel testing increases. Although a VUS-only result does not contribute to patient cancer management, the implication for families is more complex: Up to 90% of VUS findings will ultimately be reclassified as negative but the remaining 10% will be reclassified as PV, with an increased risk of future cancers. A challenge is that reclassification of VUS is the responsibility of the testing laboratories—a process that occurs passively and over time as laboratories accumulate more information about tested family members and requires the ordering clinician to notify the tested patient when the VUS is reclassified. Additionally, other factors such as family history of cancer inform prevention and early detection strategies. Although the stakes are lower for a VUS-only finding versus a PV, patients and relatives may be vulnerable to misunderstanding about the implications of these indeterminate findings for personal risk or the recommendation for cascade testing. Thus, in many cases, there is need for discussion about the implications of VUS findings. Our results show that a substantial proportion of patients with VUS-only findings report engagement with clinicians and family members. Although this may be appropriate, given the complexity of the clinical context, it reinforces the need to ensure appropriate interpretation and responses from clinicians. More research is needed about the nature of these discussions and the level of understanding about indeterminate genetic results. However, given limited clinical resources—especially in genetic counseling—the target for quality improvement should be on closing the gap in genetic risk education and testing in families with HCS identified through detection of PVs.

The current findings reinforce the central role played by genetic counselors in implementing cascade genetic testing

in families with HCS: the great majority (85%) of patients with PVs consulted with a genetic counselor, and many patients reported that a genetic counselor encouraged them to share test results and advised them on how to do so. However, fewer patients reported that a genetic counselor talked directly to a relative, which reinforces insurance and practice-related barriers and may result from privacy concerns about clinician-mediated disclosure to family members.[17,18] Physicians, even those specialized in oncology, played a much smaller role in family communication. Our results suggest that physicians may insufficiently recognize the need to engage patients with PVs, especially those with moderate-risk PVs—or that such engagement is less prioritized amid many competing clinical concerns. Potential strategies to increase engagement between clinicians and patients could include integrating automated referral prompts, digital family-sharing tools, or genetics navigator programs.

Aspects of the study merit comment. Strengths include selection of adult patients from SEER state registries with a broad array of cancer types in whom a clinically meaningful PV was detected on germline testing and categorized by level of cancer susceptibility; a substantial response rate to the survey given the circumstances of this cancer survivorship population and the use of response weights in the analyses to account for potential bias in the results; valid measures of patient attitudes, and report of communication with family; and a rigorous analytic approach that assessed bias and confounding. Limitations include results limited to patients diagnosed in two large states; patient recall of engagement with relatives; and the duration from diagnosis to patient study participation.

This study's results inform strategies to increase cascade genetic testing in families with HCS. Genetic counselors are the gateway for quality improvement, and practice change is needed. First, there is a need to offload pretest communication with patients and channel genetic counselors' expertise to the growing demand to manage clinically relevant results. Second, it is essential to educate clinicians about indications for genetic testing, management of patients on the basis of genetic test results, and the implications of results for families. Third, there are opportunities emerging to facilitate clinicians' engagement of patients and their families through online tools at the point of care: we are currently developing and implementing tools for genetic risk education and the choice of clinical-grade, low-cost, at-home testing for relatives.[19] Such strategies could markedly reduce the gap in cascade genetic testing in families with HCS.



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## SUPPORT

Supported by the American Cancer Society RSG-20-025-01 and the National Cancer Institute (NCI) Grants U01CA254822 awarded to the University of Michigan and R01CA283207 to Stanford University. Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under Award Number P30CA046592 by the use of the following Cancer Center Shared Resource(s): Cancer Data Science. The collection of cancer incidence data in California was supported by the California Department of Public Health pursuant to California Health and Safety Code §103885 under cooperative agreement 5NU58DP006344 with the US Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries, contract HHSN261201800032I with the NCI's SEER program (awarded to the University of California, San Francisco), contract HHSN261201800015I with the NCI's SEER program (awarded to the University of Southern California), and contract HHSN261201800009I with the NCI's SEER program (awarded to the Public Health Institute, Cancer Registry of Greater California). The collection of cancer incidence data in Georgia was supported by contract HHSN261201800003I and task order HHSN26100001 from the NCI and cooperative agreement 5NU58DP006352-03-00 from the CDC. The ideas and opinions expressed herein are those of the authors. The State of California, Department of Public Health, the NCI, and the CDC and their contractors and subcontractors had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/OP-25-00776.

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**Final approval of manuscript:** All authors
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## ACKNOWLEDGMENT

The authors acknowledge the work of the project staff from the Georgia Cancer Registry, the University of Southern California, and the University of Michigan. The authors acknowledge with gratitude the patients with a history of cancer who responded to our survey.



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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

**Patient Engagement With Clinicians and Family Members About Genetic Test Results Across Risk Groups in Women With Hereditary Cancer Susceptibility**

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No other potential conflicts of interest were reported.

# APPENDIX

**TABLE A1.** High- and Moderate-Risk Genes by Cancer Site

| High-Risk Genes | Moderate-Risk Genes |
|---|---|
| Breast | |
| BRCA1 | ATM |
| BRCA2 | BARD1 |
| CDH1 | CHEK2 |
| PALB2 | RAD51C |
| PTEN | RAD51D |
| STK11 | |
| TP53 | |
| Ovary | |
| BRCA1 | ATM |
| BRCA2 | MSH6 |
| BRIP1 | PALB2 |
| EPCAM | |
| MLH1 | |
| MSH2 | |
| RAD51C | |
| RAD51D | |
| STK11 | |
| Uterine | |
| EPCAM | BRCA1 |
| MLH1 | |
| MSH2 | |
| MSH6 | |
| PTEN | |

NOTE. Genes by risk categories for each cancer type on the basis of NCCN guidelines published during the study period. Genetic/familial high-risk assessment: Breast, ovarian, and pancreatic (version 3.2024).[12]
Abbreviation: NCCN, National Comprehensive Cancer Network.

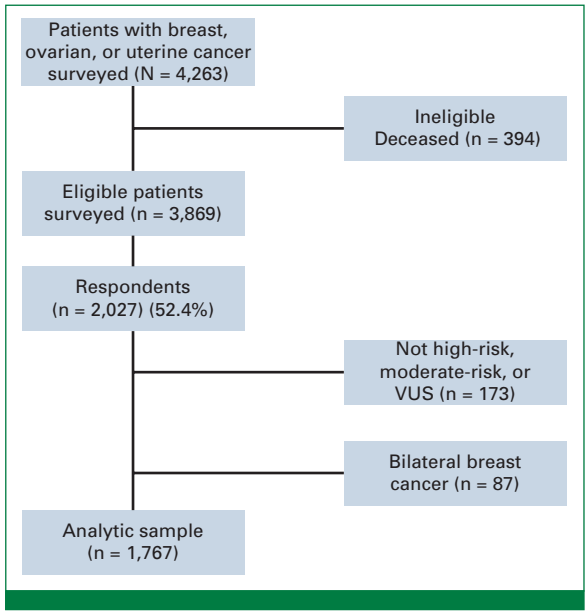


**FIG A1.** Patient study flow. VUS, variant of uncertain significance.