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Second Opinions From Medical Oncologists for Early-Stage Breast Cancer
Prevalence, Correlates, and Consequences

Allison W. Kurian, MD, MSc; Christopher R. Friese, PhD, RN; Irina Bondarenko, MS; Reshma Jagsi, MD, DPhil; Yun Li, PhD; Ann S. Hamilton, PhD; Kevin C. Ward, PhD, MPH; Steven J. Katz, MD, MPH

IMPORTANCE Advances in the evaluation and treatment of breast cancer have made the clinical decision-making context much more complex. A second opinion from a medical oncologist may facilitate decision making for women with breast cancer, yet little is known about second opinion use.

OBJECTIVE To investigate the patterns and correlates of second opinion use and the effect on chemotherapy decisions.

DESIGN, SETTING, AND PARTICIPANTS A total of 1901 women newly diagnosed with stages 0 to II breast cancer between July 2013 and September 2014 (response rate, 71.0%) were accrued through 2 population-based Surveillance, Epidemiology, and End Results registries (Georgia and Los Angeles County, California) and surveyed about their experiences with medical oncologists, decision making, and chemotherapy use.

MAIN OUTCOMES AND MEASURES Factors associated with second opinion use were evaluated using logistic regression. Also assessed was the association between second opinion and chemotherapy use, adjusting for chemotherapy indication and propensity for receiving a second opinion. Multiple imputation and weighting were used to account for missing data.

RESULTS A total of 1901 patients with stage I to II breast cancer (mean [SD] age, 61.6 [11.0] years; 1071 [56.3%] non-Hispanic white) saw any medical oncologist. Analysis of multiply imputed, weighted data (mean n = 1866) showed that 168 (9.8%) (SE, 0.74%) received a second opinion and 54 (3.2%) (SE, 0.47%) received chemotherapy from the second oncologist. Satisfaction with chemotherapy decisions was high and did not differ between those who did (mean [SD], 4.3 [0.08] on a 1- to 5-point scale) or did not (4.4 [0.03]) obtain a second opinion (P = .29). Predictors of second opinion use included college education vs less education (odds ratio [OR], 1.85; 95% CI, 1.24-2.75), frequent use of internet-based support groups (OR, 2.15; 95% CI, 1.12-4.11), an intermediate result on the 21-gene recurrence score assay (OR, 1.85; 95% CI, 1.11-3.09), and a variant of uncertain significance on hereditary cancer genetic testing (OR, 3.24; 95% CI, 1.09-9.59). After controlling for patient and tumor characteristics, second opinion use was not associated with chemotherapy receipt (OR, 1.04; 95% CI, 0.71-1.52).

CONCLUSIONS AND RELEVANCE Second opinion use was low (<10%) among patients with early-stage breast cancer, and high decision satisfaction regardless of second opinion use suggests little unmet demand. Along with educational level and use of internet support groups, uncertain results on genomic testing predicted second opinion use. Patient demand for second opinions may increase as more complex genomic tests are disseminated.

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Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Allison W. Kurian, MD, MSc, Department of Medicine, Stanford University, HRP Redwood Building, Room T254A, 150 Governor's Ln, Stanford, CA 94305-5405 (akurian@stanford.edu).

Advances in the evaluation and treatment of breast cancer have made the clinical decision-making context much more complex.[1,2] Options for all modalities of treatment, including surgery, drug therapy, radiation, and reconstruction, have markedly expanded, as have preventive options for women at high genetic risk for second cancers. This is particularly true for decisions about systemic therapies because patients now must consider choices about 3 different medication categories: endocrine, chemotherapy, and biologic. Examples include whether to take tamoxifen or an aromatase inhibitor, with or without ovarian suppression, and for how long[3-6]; whether to take chemotherapy, with or without anthracyclines,[7-9] and before or after surgery[10,11]; and whether to take a new biologic agent, such as pertuzumab.[12,13] Moreover, diagnostic algorithms that guide treatment recommendations have become increasingly technical as genomic analyses, including germline genetic testing, are integrated into routine care.[14-18] This complicated decision context can quickly overwhelm a patient seeking to understand her new diagnosis and choose a comprehensive care plan. Furthermore, most patients have only recently met the specialist physicians who are now in charge of their cancer care. Thus, at the same time when she must deliberate between treatment options, a patient must also appraise the quality of one or more therapeutic relationships. These simultaneous demands may especially burden patients with limited educational, social, or financial resources.[19,20]

Second opinions can facilitate treatment decision making and should be encouraged when patients are uncertain about their options or lack confidence in the treatment decision process. Given the increasing complexity of treatment decision making, second opinions may be an increasingly important opportunity for patients to gain confidence in their physicians and the proposed management plan. It is possible that a second opinion may indicate poor communication or care coordination if, for instance, there are socioeconomic gradients in use, evidence of discordance in communication or decision making, or differential use of indicated treatments in patients who do vs do not obtain second opinions.

However, little is known about how patients are referred to a medical oncologist after diagnosis, and, surprisingly, virtually nothing is known about the patterns and correlates of second opinions in community practice or the implications for quality of care. Also unknown are the characteristics of the patient-oncologist encounter, whether related to the patient, physician, or clinical situation, that prompt patients to seek a second opinion. Understanding these aspects of treatment decision making is necessary to inform interventions that can improve breast cancer care delivery and outcomes. We examined the patterns and correlates of second medical oncology opinions and patients' perspectives on chemotherapy decision making and communication with oncologists in a large, diverse, contemporary population-based sample of patients newly diagnosed with breast cancer.

Key Points

Question As treatment decision making becomes more complex, is there an unmet need for second opinions from medical oncologists for the treatment of breast cancer?

Findings In this survey of a contemporary diverse population sample of 1901 patients newly diagnosed with breast cancer, 168 patients (9.8%) received a second opinion, and 54 (3.2%) received chemotherapy from a second medical oncologist. Second opinions were not associated with overall patient satisfaction or receipt of chemotherapy.

Meaning Use of second opinions from medical oncologists after diagnosis of breast cancer was low, but there was little evidence of unmet need.

Methods

Study Sample

We selected from the iCanCare study women aged 20 to 79 years diagnosed with stages 0 to II breast cancer who were reported to the Surveillance, Epidemiology, and End Results (SEER) registries of Georgia and Los Angeles County, California. Eligible patients were identified approximately 2 months after surgery via pathology reports from definitive surgical procedures (those intended to remove the entire tumor with clear margins). To ensure a relatively homogeneous sample of patients with early-stage disease, patients with stages III to IV metastatic disease, tumors larger than 5 cm, or more than 3 involved lymph nodes were excluded. Black, Asian, and Hispanic women were oversampled in Los Angeles as previously described.[21] Patients were selected between July 2013 and September 2014. This study was approved by the University of Michigan Institutional Review Board and received a waiver of documentation of informed consent. All data were deidentified before research use.

Questionnaire Design and Content

Questionnaire content was developed using a conceptual framework, research questions, and hypotheses. We developed measures by drawing from the literature and our prior research.[15,22] We used standard techniques to assess content validity, including systematic review by design experts, cognitive pretesting with patients, and pilot studies in relevant populations.

Data Collection

Surveys were mailed approximately 2 months after surgery. To encourage response, we provided a $20 cash incentive and used a modified Dillman method,[23] including reminders to nonrespondents. All materials were in English. We added Spanish-translated materials for all women with surnames that suggested Hispanic ethnicity.[21] Each SEER registry provided limited SEER data (stripped of all identifiers) for participants to the University of Michigan: these data were then merged to survey data under institutional review board approval from partnering universities and the public health departments of Georgia and California.

Measures

Patients provided information about chemotherapy decisions, including how strongly the oncologist recommended chemotherapy on a 1- to 5-point scale (1, very strongly; 2, weakly; 3, left it up to me; 4, weakly against it; and 5, very strongly against it), whether they saw a second oncologist (the question was worded as "Did you see a second medical oncologist for an opinion about chemotherapy?" [yes or no]), and, if so, whether that second oncologist administered chemotherapy (yes or no). Patients reported their satisfaction with their amount of involvement and information about chemotherapy decisions (on a 1- to 5-point scale, with 1 indicating not enough; 3, just right; and 5, too much) and the chemotherapy decision itself (on a 1- to 5-point scale, with 1 indicating not at all satisfied; 2, a little; 3, somewhat; 4, quite; and 5, totally). Patients rated their decision-making preferences on a 1- to 5-point scale (1 indicating not at all true; 2, a little; 3, somewhat; 4, quite; and 5, very) as follows: "preferred to be told what to do," "wanted my doctor to tell me," or "wanted to make my own decisions." Patients rated oncologists on a 1- to 5-point scale (1, not at all true; 2, a little; 3, somewhat; 4, quite; and 5, very) according to the Health Care Climate Questionnaire,[24] which measures perceived physician support of patient autonomy with questions as follows: "provided me with choices," "understood how I saw things," "expressed confidence in my decision making," "listened to how I would like to be treated," "encouraged me to ask questions," and "tried to understand how I saw things."

Patients provided information on the following: race/ethnicity, insurance, educational level, travel time to the nearest hospital, comorbidities, marital status, employment, and household income. Patients reported on whether they received germline genetic testing for the breast cancer 1 (*BRCA1*) (OMIM 113705) and breast cancer 2 (*BRCA2*) (OMIM 600185) genes (*BRCA1/2*) and/or other genes (yes or no) and results (positive, negative, or variant of uncertain significance [VUS]). Patients reported whether they received 21-gene recurrence score (RS) testing (yes or no) and results (low, intermediate, or high). Patients reported on use of internet-based support groups (1- to 5-point scale: 1, almost never; 2, rarely; 3, sometimes; 4, often; and 5, almost always). The SEER registries provided age (years), cancer stage (I, II), cancer grade (1-3), and biomarkers, including expression of estrogen receptor (ER), progesterone receptor (PR), and the erb-b2 receptor tyrosine kinase 2 gene/human epidermal growth factor receptor 2 gene (*ERBB2/HER2*) (OMIM 164870).

We constructed a measure of chemotherapy indication according to the guidelines of the National Comprehensive Cancer Network (eTables 1 and 2 in the Supplement).[25] Patients were categorized as having a high chemotherapy indication if they had a tumor larger than 1 cm and/or involved lymph nodes and also had ER- and PR-negative and/or *ERBB2*-positive disease. They were categorized as having a low chemotherapy indication if they had all of the following: age of 50 years or older, postmenopausal status, and stage I, grade 1, ER- and/or PR-positive, *ERBB2*-negative disease. All others were categorized as having an intermediate chemotherapy indication.

Statistical Analysis

Weights

Survey design and nonresponse weights were created to compensate for the differential probability of selecting patients by race, disease stage, and SEER site and to adjust for potential bias attributable to survey nonresponse. The weights were normalized to equal the observed sample size. Unless otherwise noted, all analyses were weighted so that statistical inferences are representative of our target population.[26]

Multiple Imputation

To account for item nonresponse and missing data, we multiply imputed data using a sequential regression multiple imputation framework.[26] We generated 5 independently imputed data sets and then computed inferential statistics that combined estimates across the data sets.[27]

Analyses

We described the unadjusted association of second opinion receipt with patient and tumor characteristics and patient appraisal of care yielded by observed unweighted data. A total of 436 patients (22.9%) had 1 or more missing values. We then multiply imputed data to which we applied inclusion and exclusion criteria to select an analytic sample (mean sample size, 1866 patients). We constructed a multivariable weighted logistic regression model to examine the association between the probability of second opinion receipt and SEER site, age at survey, race/ethnicity, comorbidities, educational level, employment, insurance, household income, marital status, travel time to nearest hospital, germline genetic testing receipt, 21-gene RS testing receipt, chemotherapy indication, internet-based support group use, and treatment decision-making preferences. We estimated the effect of second opinion receipt on the likelihood of chemotherapy receipt using an inverse probability of treatment weighting[28,29] approach, adopted to address confounding. For each patient, we estimated the propensity of receiving a second opinion. Weighting each patient by the inverse propensity of her second opinion receipt, we created a synthetic sample in which second opinion receipt is independent of patient characteristics. After examining the properties of the weights, we estimated the mean effect of second opinion receipt on the probability of chemotherapy receipt. In a separate model using the *F* test for multiply imputed data, we tested for the presence of a joint effect of second opinion receipt and its interaction with chemotherapy indication. Unless otherwise noted, results were generated using multiply imputed weighted data. All analyses were conducted using SAS statistical software, version 9.4 (SAS Institute Inc). $P < .05$ was considered statistically significant (2-sided joint Wald test). Reported results were generated using multiply imputed, weighted data.

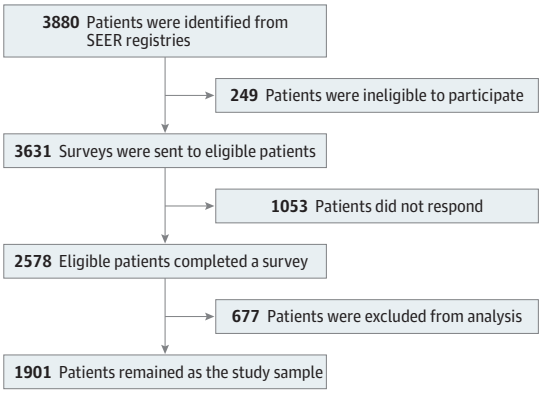
Results

Patient Characteristics

We selected 3880 women diagnosed with early-stage breast cancer (mean [SD] age, 61.6 [11.0] years), of whom 3631 (93.6%)

were eligible for the study. The survey response rate was 71.0% (N = 2578). We excluded 677 patients from this analysis (497 with noninvasive disease and 164 who never saw a medical oncologist) (**Figure 1**). eTable 3 in the Supplement indicates that the 1901 remaining patients were racially and socioeconomically diverse: 1071 (56.3%) were non-Hispanic white, 306 (16.1%) were non-Hispanic black, 328 (17.3%) were Hispanic, and 141 (7.4%) were Asian. For 1160 (61.0%), high school was the highest educational level (eTable 3 in the Supplement). A total of 1194 (62.8%) had stage I disease, 518 (27.2%) had grade 1 disease, and 471 (24.8%) had grade 3 disease. A total of 1597 (84.0%) had ER- and PR-positive tumors; 211 (11.1%) had *ERBB2*-positive tumors (eTable 1 in the Supplement). A total of 610 (32.1%) reported germline genetic testing, and 716 (37.7%) reported 21-gene RS testing.

Figure 1. Patient Flow Throughout the Study



Reasons for ineligibility include prior cancer diagnosis, Paget disease of nipple, disease stage of III or higher, residing outside Surveillance, Epidemiology, and End Results (SEER) registry region, unable to complete survey, and deceased. Reasons for exclusion include noninvasive (stage 0) disease and never having seen a medical oncologist.

Factors Associated With Receipt of Second Opinions

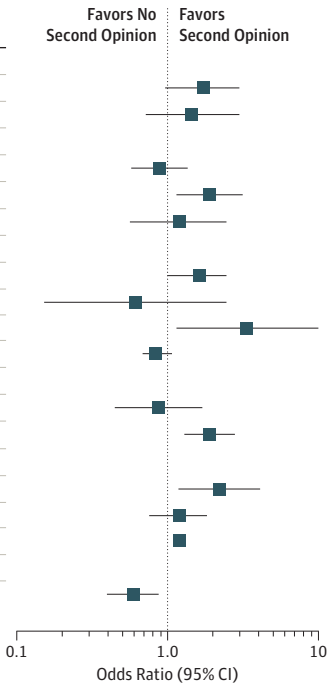
Multiple imputation (mean n = 1866 patients) yielded an estimated mean (SD) prevalence of second opinion receipt of 168 (9.8% [0.74%]). **Figure 2** shows that factors significantly associated with second opinion receipt were a college education vs less (odds ratio [OR], 1.85; 95% CI, 1.24-2.75), a preference for making one's own treatment decisions quite a bit of the time or always vs never or sometimes (OR, 1.15; 95% CI, 1.01-1.31), frequent use of internet-based support groups vs none (OR, 2.15; 95% CI, 1.12-4.11), an intermediate result on the 21-gene RS assay vs not tested (OR, 1.85; 95% CI, 1.11-3.09), and a VUS (OR, 3.24; 95% CI, 1.09-9.59) or negative result (OR, 1.58; 95% CI, 1.04-2.42) on germline genetic testing vs not tested. Odds of second opinion receipt were significantly lower in Georgia vs Los Angeles County (OR, 0.58; 95% CI, 0.39-0.87), but there were no interactions between site and other model covariates. No other factor, including comorbidities, employment, income, or race/ethnicity, was associated with second opinion receipt.

Receipt of Chemotherapy and Use of Second Opinions

Based on an analysis using multiply imputed, weighted data (average n = 1866), 823 patients (44.0% [SE, 1.2%]) reported chemotherapy receipt, with somewhat higher rates among patients who did (94 [52.1%]) vs did not (729 [43.2%]) receive a second opinion on univariate analysis (OR, 1.45; 95% CI, 1.07-1.97). However, several patient characteristics were corre-

Figure 2. Multivariable Model of Characteristics Associated With Receipt of a Second Opinion

Source	Odds Ratio (95% CI)
Chemotherapy indication (reference: weak)	
Intermediate	1.67 (0.93-3.00)
Strong	1.42 (0.69-2.94)
21-gene RS (reference: not tested)	
Low RS	0.87 (0.55-1.36)
Intermediate RS	1.85 (1.11-3.09)
High RS	1.15 (0.55-2.41)
BRCA1/2 test results (reference: not tested)	
Negative	1.58 (1.04-2.42)
Positive	0.60 (0.15-2.46)
Variant of uncertain significance	3.24 (1.09-9.59)
Age at survey (per 10 y)	0.83 (0.65-1.05)
Educational level (reference: high school diploma)	
No high school diploma	0.85 (0.43-1.68)
College	1.85 (1.24-2.75)
Internet-based support groups (reference: no use)	
Frequent use	2.15 (1.12-4.11)
Rare use	1.16 (0.74-1.82)
Preferred to make own decisions about treatment	1.15 (1.01-1.31)
Site differences (reference: Los Angeles County)	
Georgia	0.58 (0.39-0.87)



Squares indicate odds ratios; error bars, 95% CIs; and RS, recurrence score.

lated with second opinion and chemotherapy use, raising concern about confounding. To test whether second opinion use had a significant effect on chemotherapy use, we used an inverse probability of treatment weighting model to control for differences in the distribution of characteristics between patients who did vs did not receive a second opinion and thus reduce bias from confounding. We observed no significant interaction between second opinion receipt and chemotherapy indication on the probability of receiving chemotherapy (P = .45): high indication (OR, 0.42; 95% CI, 0.11-1.56), low indication (OR, 0.41; 95% CI, 0.06-2.77), and intermediate indication (OR, 1.28; 95% CI, 0.83-1.97). After controlling for patient and tumor characteristics, second opinion use was not associated with chemotherapy receipt (OR, 1.04; 95% CI, 0.71-1.52). Among patients who received a second opinion, 54 (3.2%) (SE, 0.47%) received chemotherapy from the second oncologist.

Patient Appraisal of Decision Making and Second Opinions

Satisfaction with chemotherapy decisions was high and did not differ between those who did (mean [SD], 4.3[.08] on a 1- to 5-point scale) or did not (4.4[.03]) obtain a second opinion (P = .29) (eTable 4 in the Supplement). Patients rated oncologists highly (mean score, 4.1 of 5) on the Health Care Climate Questionnaire, signifying perceived clinician support of patient autonomy (eTable 4 in the Supplement).

Discussion

Second opinions may substantially affect a breast cancer treatment plan. Recent studies[30-33] have focused on second opinions provided by one clinician to another: for example, indications that discordant reads in pathology and radiology reports change treatment in 10% to 25% of cases. Tumor boards, which enable clinicians to synthesize a combined multidisciplinary opinion, are associated with improved care quality.[34-36] We previously reported on the role of second opinions in surgical decision making.[37,38] However, despite this evidence of effect, little is known about the prevalence and consequences of second opinions that oncologists provide directly to patients.

In this large, diverse contemporary cohort, second opinion use was remarkably low: less than 10%, with less than 5% of all patients receiving chemotherapy from a second oncologist. There were regional differences, with second opinions less common in Georgia than Los Angeles County. Reassuringly, we did not observe racial/ethnic or socioeconomic gradients, patient-reported dissatisfaction with communication or decision making, or differential chemotherapy use by patients who did vs did not receive second opinions. We conclude that there is little evidence of unmet demand for second opinions and that their potential effect on chemotherapy decisions in community practice appears to be small.

Overall, our findings are encouraging with regard to the quality of breast cancer care. However, we identified key predictors of second opinion use that suggest opportunities for improvement. We observed a distinct profile of patients who were more likely to obtain second opinions. These patients were more often college educated, more frequently used internet-based support groups, and preferred to make their own treatment decisions. Such patients may desire greater engagement in their care and pursue second opinions for more information and support. This process may constitute an appropriate use of second opinions, yet interventions that enable the first oncologist to recognize and address these patients' needs may also be desirable.

Along with patient demographics and preferences, we identified a clinical predictor of second opinion use: uncertain results of genomic tests. Patients who reported having a VUS on germline genetic testing were 3 times more likely to obtain a second medical oncology opinion. These unclassified results may confuse patients; moreover, one study[39] found that few (<15%) physicians who order *BRCA1/2* testing understand how to manage a VUS. Oncologists confronted by VUSs may struggle to explain them to patients' satisfaction, prompting patients to seek another oncologist who can. Although VUS rates are low (2%-5%) when *BRCA1/2* are the only genes sequenced, they increase 10-fold (35%) with use of the multiple-gene panels that are rapidly emerging into breast cancer care.[40-44] Furthermore, VUS rates are significantly higher in racial/ethnic minorities than non-Hispanic whites.[45,46] Thus, the demand for second opinions may increase with dissemination of more comprehensive genetic testing and, to a greater extent, among vulnerable populations. This occurrence raises concern about future access disparities and emphasizes the need to follow trends in second opinion use over time. Studies are urgently needed to improve the interpretation of VUSs and physicians' ability to manage them.

Patients with intermediate results on the 21-gene RS assay were 2 times more likely than untested patients to receive a second opinion. Although the clinical utility of low and high RS is well established,[14,47-49] the appropriate management of intermediate RS remains unknown pending results of clinical trials.[14] A recent study[50] of oncologists reported low "genomic confidence," namely, the ability to use genomic testing results effectively for patient care. Some patients may perceive their oncologists' low confidence about treatment recommendations in the setting of uncertain germline or tumor genomic results and seek greater confidence through a second opinion. This finding underscores the need for educational interventions that help oncologists' knowledge and competence to keep pace with the rapid expansion of precision medicine technology.

Strengths and Limitations

Aspects of this study warrant comment. Its strengths include a large, racially/ethnically diverse, contemporary sample of patients with breast cancer enrolled from 2 population-based cancer registries; specific measures of patients' clinical decision making; and a high response rate. Furthermore, weighting and multiple imputation techniques were used to account for potential bias attributable to missing data and to ensure that results were representative of the overall population. Its limitations include restriction to 2 geographic areas (Georgia and Los Angeles County); thus, results may not apply fully to all US patients with breast cancer. Furthermore, the sample was se-

lected for earlier cancer stages (stages I-II) and had generally favorable tumor biology. The patterns, correlates, and outcomes of second opinion use may be different in patients whose stage or tumor biology renders them at higher risk for metastatic recurrence. We have not yet validated patients' reports of genetic testing or oncologists' perspectives on second opinions and other aspects of treatment. There has been insufficient follow-up time to ascertain long-term outcomes of cancer recurrence and survival. Nonetheless, this study offers a novel and clinically relevant view of breast cancer treatment decision making.

Conclusions

In an era of concern about the cost and value of cancer care, guidelines advise that we choose wisely before ordering diagnostic tests.[51] However, there are no guidelines as to whether a second opinion (with costs similar to those of diagnostic tests) is potentially valuable or merely redundant. Given the subjective and personal nature of the therapeutic encounter, second opinions may sometimes be necessary to address a poor fit between patient and physician. We were encouraged to find high endorsement of perceived autonomy supportiveness of medical oncologists, with few patients (<10%) seeking a second opinion and little evidence of an unmet need. Our results indicate that a patient's preference for greater engagement is one factor contributing to second opinion use, and uncertain results of diagnostic testing are another. As treatment options proliferate and molecular diagnostic tests expand, physicians may face increasing pressure to enable patients' preferences about treatment decision making and to navigate the increasingly murky landscape of genomic testing. These tasks demand effective physician-patient communication, and developing interventions to enhance the quality of such communication is a high priority.

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Author Affiliations: Department of Medicine, Stanford University, Stanford, California (Kurian); Departments of Health Research and Policy, Stanford University, Stanford, California (Kurian); Department of Systems, Populations, and Leadership and Institute for Healthcare Policy and Innovation, University of Michigan School of Nursing, Ann Arbor (Friese); Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor (Bondarenko, Li); Department of Radiation Oncology, Center for Bioethics and Social Science in Medicine, University of Michigan, Ann Arbor (Jagsi); Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles (Hamilton); Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia (Ward); Department of Health Management and Policy, University of Michigan, Ann Arbor (Katz); Department of Internal Medicine, School of Public Health, Division of General Medicine, Univeristy of Michigan, Ann Arbor (Katz).

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Study concept and design: Kurian, Bondarenko, Li, Ward, Katz.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Kurian, Friese, Bondarenko, Katz.
Critical revision of the manuscript for important intellectual content: All authors.
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