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

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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.
Advances in the evaluation and treatment of breast cancer have made the clinical decision-making context much more complex. 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; whether to take chemotherapy, with or without anthracyclines, and before or after surgery; and whether to take a new biologic agent, such as pertuzumab.

Moreover, diagnostic algorithms that guide treatment recommendations have become increasingly technical as genomic analyses, including germline genetic testing, are integrated into routine care. 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.

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, surprising, 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.

### Methods

#### Study Sample
We selected from the iCanCare study women ages 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.

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. 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, including reminders to nonrespondents. All materials were in English. We added Spanish-translated materials for all women with surnames that suggested Hispanic ethnicity. 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, germline genetic testing receipt, 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 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). Repotted 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.

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,
In an era of concern about the cost and value of cancer care, guidelines advise that we choose wisely before ordering diagnostic tests. 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.


44. Swisher EM. Usefulness of multigene testing: catching the train that’s left the station. JAMA Oncol. 2015;1(7):951-952.


