

Women's Interest in Gene Expression Analysis for Breast Cancer Recurrence Risk

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A B S T R A C T

Purpose

Genomic and other technologies are improving the accuracy with which clinicians can estimate risk for recurrence (RFR) of breast cancer and make judgments about potential benefits of chemotherapy. Little is known of how patients will respond to genomic RFR testing or interact with their physicians to make informed decisions regarding treatment. We assessed interest in genomic RFR testing and patient preferences for incorporating results into treatment decision making.

Patients and Methods

One hundred thirty-nine women previously treated for early-stage breast cancer completed surveys that presented hypothetical scenarios reflecting different test outcomes and potential decisions. We assessed women's attitudes toward RFR testing, how results would affect their choices about adjuvant treatment, and potential concerns about and perceived benefits of testing.

Results

The majority of participants said they would "definitely" want to be tested (76%), receive their results (87%), and discuss these results with their physicians. They were willing to pay, on average, \$997 for testing. Those who expressed more concerns about testing were less interested in testing and in incorporating results into treatment decision making. Participants were more likely to want chemotherapy when presented with high-risk results and would worry more about those results. They were least likely to trust and most likely to express potential anticipated regret in response to intermediate RFR results.

Conclusion

Participants expressed strong interest in testing. Although these decisions were sensitive to RFR, participants' complex reactions to intermediate RFR suggest care is needed when communicating such results.

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INTRODUCTION

In 2007, an estimated 178,480 women in the United States will be diagnosed with breast cancer.¹ Although effective treatments for breast cancer are increasingly available,² decisions about which treatment options to pursue are complex³ and often produce anxiety.⁴ Currently, estimates of risk for recurrence (RFR) of breast cancer and benefits of adjuvant therapy are based on clinical characteristics, such as disease stage, tumor pathology, estrogen and progesterone receptor status, human epidermal growth factor (HER-2) status, and patients' overall health.^{5,6} Recent studies suggest that gene expression analysis of breast cancer tumors can categorize RFR,⁷ aid prognosis,⁸⁻¹³ and predict response to chemother-

apy.^{7,14} Gene expression analysis offers the potential to identify women who are at greatest RFR and therefore are likely to receive the greatest benefit from chemotherapy.^{3,7} Ultimately, genomic RFR testing could reduce the need for additional treatments for some women with early-stage, node-negative, and estrogen- and progesterone-positive breast cancers. Two clinical trials^{15,16} will provide a better understanding of the potential clinical impact of these methods.

Few studies have assessed either physicians' or patients' interest in genomic RFR testing or how it may affect decision making regarding chemotherapy. Cognitive and affective factors—such as perceived benefits of treatment, concerns about the toxicities of treatment, and related worry—are known to influence adjuvant treatment

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decision making by patients.¹⁷ Similar factors could affect response to RFR testing.

Studying potential responses to clinical innovations before they become part of routine practice allows for the identification of important patient or physician concerns.¹⁸⁻²¹ Therefore, our study assessed breast cancer patients' attitudes toward genomic RFR testing, interest in testing had it been available when they were diagnosed, and potential response to the receipt of test results. We also examined how varying the magnitude of RFR would influence patients' preferences for chemotherapy and their anticipated emotional responses.

PATIENTS AND METHODS

Participants

Study methods are described elsewhere.²² In brief, eligible patients met the following criteria: English-speaking, previously diagnosed with stage I/II primary breast cancer, completed surgery, and either had not received or had completed adjuvant chemotherapy. Patients were ineligible if they had a life-threatening comorbid disease, second primary cancer, cancer recurrence or metastasis, or history of serious psychiatric illness.

In 2005, eligible patients were mailed invitation letters 2 weeks before their appointments and were approached by trained research assistants in the University of North Carolina Breast Clinic (Chapel Hill, NC). Participants were read, and were provided a paper copy of, a brief description of genomic RFR testing (Appendix, online only), and completed self-administered questionnaires. Study protocol and materials were approved by the University of North Carolina institutional review board.

Measures

Participant characteristics. We assessed age, race, education, and financial status. To minimize typically high levels of nonresponse to questions about income, we assessed financial status using an item previously shown to have high levels of completion: "Without giving exact dollars, how would you describe your household's financial situation right now?"²³ A dichotomous variable indicated sufficient/limited financial status. Because just over half of the participants reported at least a college education (54%), we dichotomized educational attainment. We asked whether participants had heard of genomic RFR testing before participation. We reviewed the medical records of those who completed HIPAA authorization to assess years since diagnosis, tumor stage and grade, receptor status, primary therapy and adjuvant therapy. We computed participants' 10-year RFR using a validated tool that provides objective risk estimates using clinical parameters.²⁴

Being tested. Two items assessed interest in testing: willingness to be tested if it were free, accompanied by a 5-point scale labeled "definitely would not" to "definitely would," and willingness to pay out of pocket for testing, accompanied by a 6-point scale labeled, "Nothing," "\$1 to 99," "\$100 to 499," "\$500 to 999," "\$1,000 to 2,499," and "\$2,500 or more." We coded responses to the latter with the value of each category's midpoint, with zero as the lowest response and \$2,500 as the highest response.

Attitudes about testing. We adapted 11 items from the literature to assess participants' attitudes toward genomic RFR testing,^{20,21,25} accompanied by a 5-point scale labeled "strongly disagree" to "strongly agree." We obtained a two-factor solution using principal axis factoring and created two scales by averaging these items. The first scale, "concerns," had seven items that shared the common theme of concerns about testing and how it would affect treatment ($\alpha = 0.78$). The second scale, "benefits," had four items that shared the common theme of benefits of testing and how it would affect treatment ($\alpha = 0.80$).

Preferences about decision making. Two items assessed participants' preferred decision-making style regarding involvement in the decision to be tested and in how the test results would influence treatment. Each was accompanied by a response scale adapted from the Control Preferences Scale.²⁶ Consistent with common practice,^{27,28} responses were recoded as a "passive," "active," or "shared" decision-making styles.

Using test results. Three items assessed participants' preferences for incorporating RFR test results into treatment planning. Three items assessed whether participants would want to know RFR test results, whether they would want to discuss the results with their doctors, and whether they would want the results incorporated in treatment decision making, accompanied by a 5-point scale labeled from "definitely would not" to "definitely would."

We used hypothetical scenarios to assess potential responses to testing, similar to what was done in early studies undertaken to understand the potential uptake of and response to cancer susceptibility testing.²¹⁻²³ All participants viewed scenarios that described hypothetical test results yielding high and then low RFR. For each vignette, we assessed participants' interest in chemotherapy given the results alone and in combination with the advice of their physician to get chemotherapy, accompanied by 5-point scales from "definitely would not" to "definitely would." We assessed trust in test results and worry and regret about results in response to scenarios describing high, low, and then intermediate (ie, "in-between") RFR results, accompanied by 5-point scales labeled "not at all" to "extremely."

Statistical Analyses

Data were analyzed using SPSS 13.0 (SPSS Inc, Chicago, IL). To identify potential covariates, we examined bivariate correlations between our outcomes and age; race; education; financial status; concerns about and perceived benefits of testing; completion of chemotherapy and radiotherapy and use of hormone therapy; stage of disease; years since diagnosis; having heard of RFR testing; and the participant's own RFR. This analysis identified all but completion of radiotherapy, use of hormone therapy, and the participant's years since diagnosis and RFR as covariates. Covariates were included in all subsequent analyses. Multiple linear regressions were used to examine predictors of the amount participants would be willing to pay for RFR testing and their preferred decision-making roles. Multiple logistic regressions were used to examine predictors of interest in testing and incorporating results into treatment decision making. Repeated measures analysis of covariance was used to examine differences in response to varied RFR magnitudes and the impact of covariates.

RESULTS

We present our findings in separate sections on participants' characteristics, perceived concerns and benefits, interest in testing, preferred decision-making role, potential response to test results, and the impact of RFR on treatment decisions. Overall, we found very strong interest in genomic RFR testing. However, we also identified some concerns about trust in testing and test results.

Study Participants

We approached 231 women; 166 (72%) agreed to participate. Twenty-one women had heard of RFR testing; one indicated that it was used for decision making during her initial diagnosis. She was removed from further analysis to allow for greater comparability among participants. We report findings on 139 participants (60%) with complete data on all dependent variables. Mean age was 58 years; 86% were white, 11% African American, and 3% Asian American. We combined African American and Asian American participants into one group to simplify data analyses. Participants were, on average, 4 years postdiagnosis (range, 0 to 14 years). Fifty-six percent were diagnosed with stage I cancer; 48% had received chemotherapy (Table 1).

Concerns About and Perceived Benefits of RFR Testing

Participants rated the potential benefits of the genomic RFR test higher than they did potential concerns (3.13 v 1.33, respectively, on a 5-point scale; $t = 18.97$; $P < .001$). Participants, on average, strongly disagreed with concerns about testing, and they were more balanced in

Table 1. Participant Characteristics

| Characteristic | No. | % |
|--------------------------------|-------|------|
| Age, years | | |
| Mean | 58.07 | |
| SD | 10.03 | |
| Years since diagnosis | | |
| Mean | 3.89 | |
| SD | 3.12 | |
| Race/ethnicity | | |
| White | 120 | 86.3 |
| African American | 15 | 10.8 |
| Asian American | 4 | 2.9 |
| Education | | |
| Less than a college degree | 65 | 46.8 |
| At least a college degree | 74 | 53.2 |
| Self-reported financial status | | |
| Sufficient | 124 | 65.5 |
| Limited | 15 | 34.5 |
| Breast cancer stage | | |
| I | 78 | 56.1 |
| IIa | 41 | 29.5 |
| IIb | 20 | 14.4 |
| Received radiation | | |
| Yes | 90 | 64.7 |
| No | 49 | 35.3 |
| Received chemotherapy | | |
| Yes | 67 | 48.2 |
| No | 72 | 51.8 |
| Received hormonal therapy | | |
| Yes | 97 | 69.8 |
| No | 42 | 30.2 |

Abbreviation: SD, standard deviation.

their response to potential benefits, tending neither to agree nor disagree with these statements. Concerns and perceived benefits were uncorrelated ($r = -.13$; $P = .13$), suggesting that they were distinct constructs. Women with limited finances expressed significantly greater concerns, as did those without college degrees (Table 2).

Interest in Testing

The majority of women stated they would “definitely” want to be tested (76%). Responses were categorized as “definitely” and “other” for statistical analyses. “Definitely” wanting to be tested was inversely related to age and concerns about testing. Women who reported more perceived benefits of and fewer concerns about testing were more likely to say that they would “definitely” want to be tested (Table 3).

Women said they were willing to pay, on average, \$997 (95% CI, \$840 to \$1,155) out of pocket for testing. Those who had heard of genomic RFR testing before the study were willing to pay more for testing (Table 2).

Preferred Decision-Making Role

Most women preferred to be involved in the decision-making process both before RFR testing and after results were available. Most participants preferred shared (39%) or active (56%) decision making about whether to receive RFR testing. Younger participants and those with fewer concerns were more likely to prefer active involvement in the decision to be tested (Table 2). The majority also preferred shared (45%) or active participation (44%) in the decision regarding how test

results would be incorporated into treatment decision making. Participants who were younger, had earlier-stage tumors at initial diagnosis and had fewer concerns preferred greater involvement in treatment decision making (Table 2).

Potential Use of Test Results

We examined how participants said they would have responded to genomic RFR results if they were tested. Most women (87%) stated that they would “definitely” want to know their RFR. Women who had received chemotherapy to treat their breast cancers reported less interest in discussing RFR test results with their physicians (Table 3). Most participants indicated that they would have wanted to include RFR information in decision making about treatment (84%). Women who perceived greater benefits of and fewer concerns about testing were also more likely to prefer using the test information in their treatment decisions (Table 2).

Impact of Risk for Recurrence Results on Response to Testing

We examined how RFR magnitude (low *v* high) and physician recommendations affected women’s self-reported interest in having chemotherapy. Participants were significantly more willing to have chemotherapy if test results indicated high RFR [$F(1,129) = 186.68$; $P < .001$] and if their physicians advised them to do so [$F(1,129) = 169.55$; $P < .001$]. RFR had much less impact on interest in chemotherapy if a physician recommended it, as shown in Figure 1 [$F(1,129) = 68.04$; $P < .001$]. Younger people expressed greater interest in chemotherapy, but only when RFR was high and in the absence of physician advice [ie, three-way interaction; $F(1,129) = 4.02$; $P = .04$]. Having received chemotherapy to treat their breast cancer was not a significant covariate of women’s reported preferences for chemotherapy.

RFR magnitude affected anticipated emotional responses (Fig 2). Participants’ worry would increase as a function of RFR [$F(2,129) = 80.19$; $P < .001$]. They would regret an intermediate RFR result the most [$F(2,129) = 11.13$; $P < .001$], with those expressing more concerns about testing anticipating greater regret [$F(2,129) = 3.90$; $P = .02$]. They also trusted an intermediate RFR result the least [$F(2,129) = 24.37$; $P < .001$]. Women who perceived more benefits were more trusting of test results [$F(2,129) = 4.36$; $P = .02$], as were those who had received chemotherapy [$F(2,129) = 4.27$; $P = .02$] and those with sufficient finances [$F(2,129) = 4.75$; $P = .01$].

We considered that participants with high RFR at their initial diagnosis might express systematically different responses to testing and to decisions about treatment. Sensitivity analyses indicated that participants’ own RFR was not a significant covariate or interaction term in any analysis.

DISCUSSION

Most participants indicated that they would have been interested in genomic RFR testing at the time they were treated for early-stage breast cancer had it been available. Most women preferred an active role in decision making about treatment and would have wanted the results incorporated into treatment planning.

Women said they would be willing to pay approximately \$1,000 for genomic RFR testing. Currently, the out-of-pocket costs for OncotypeDx (Genomic Health, Redwood City, CA) range from a few

Recurrence Risk Testing

Table 2. Predictors of Attitudes Toward Genomic Risk for Recurrence Testing

| Predictor | Perceived Benefits of Testing | | Concerns About Testing | | Amount Willing to Pay for Testing (\$US) | | Prefers To Be Involved In Decision To Test | | Prefers to be Involved in How to Use Results | | Prefers to Use Results to Guide Treatment | |
|--------------------------|-------------------------------|------|------------------------|------|--|-------|--|------|--|------|---|------|
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Age | | | | | | | | | | | | |
| < Median (57) | 3.07 | 0.69 | 1.40 | 0.80 | 1,160 | 937 | 3.61* | 0.64 | 3.39* | 0.81 | 4.17 | 0.81 |
| ≥ Median | 3.19 | 0.58 | 1.27 | 0.85 | 930 | 939 | 3.44 | 0.66 | 3.22 | 0.76 | 4.37 | 0.74 |
| Race | | | | | | | | | | | | |
| White | 3.18 | 0.64 | 1.29 | 0.81 | 1,009 | 923 | 3.56 | 0.63 | 3.33 | 0.78 | 4.26 | 0.76 |
| African/Asian American | 3.18 | 0.66 | 1.64 | 0.89 | 926 | 1,045 | 3.32 | 0.75 | 3.16 | 0.83 | 4.32 | 0.95 |
| Education | | | | | | | | | | | | |
| < College degree | 3.11 | 0.70 | 1.55* | 0.88 | 853 | 922 | 3.41 | 0.71 | 3.16 | 0.94 | 4.13 | 0.85 |
| ≥ College degree | 3.15 | 0.58 | 1.15 | 0.73 | 1,124 | 938 | 3.62 | 0.59 | 3.43 | 0.60 | 4.38 | 0.70 |
| Financial status | | | | | | | | | | | | |
| Limited | 3.11 | 0.70 | 1.94* | 1.01 | 1,029 | 1,108 | 3.27 | 0.88 | 2.77 | 0.93 | 3.93 | 0.83 |
| Sufficient | 3.13 | 0.64 | 1.26 | 0.77 | 994 | 919 | 3.56 | 0.62 | 3.37 | 0.75 | 4.30 | 0.77 |
| Had chemotherapy | | | | | | | | | | | | |
| No | 3.21 | 0.61 | 1.29 | 1.01 | 1,010 | 930 | 3.61 | 0.62 | 3.37 | 0.68 | 4.32 | 0.71 |
| Yes | 3.14 | 0.67 | 1.38 | 0.88 | 984 | 950 | 3.44 | 0.68 | 3.25 | 0.88 | 4.20 | 0.85 |
| Stage | | | | | | | | | | | | |
| I | 3.14 | 0.63 | 1.35 | 1.01 | 1,009 | 939 | 3.55 | 0.66 | 3.44* | 0.77 | 4.25 | 0.78 |
| II | 3.12 | 0.66 | 1.31 | 0.78 | 983 | 941 | 3.50 | 0.65 | 3.14 | 0.78 | 4.29 | 0.79 |
| Heard of RFR test | | | | | | | | | | | | |
| No | 3.13 | 0.62 | 1.36 | 1.83 | 882* | 895 | 3.53 | 0.68 | 3.28 | 0.79 | 4.23 | 0.80 |
| Yes | 3.08 | 0.77 | 1.22 | 0.81 | 1,649 | 915 | 3.52 | 0.51 | 3.45 | 0.76 | 4.48 | 0.68 |
| Benefits | | | | | | | | | | | | |
| < Median | | | | | 922 | 905 | 3.52 | 0.66 | 3.30 | 0.77 | 4.08† | 0.80 |
| ≥ Median | | | | | 1,064 | 964 | 3.53 | 0.65 | 3.32 | 0.80 | 4.43 | 0.73 |
| Concerns | | | | | | | | | | | | |
| < Median | | | | | 1,106 | 935 | 3.73† | 0.53 | 3.52† | 0.59 | 4.48† | 0.66 |
| ≥ Median | | | | | 897 | 933 | 3.33 | 0.70 | 3.10 | 0.89 | 4.06 | 0.83 |

NOTE. Variables for age, benefits, and concerns were continuous in regression analyses, but dichotomized at the median to make the clinical significance of the findings easier to interpret.

Abbreviations: SD, standard deviation; RFR, risk for recurrence.

* $P \leq .05$.

† $P \leq .001$.

dollars for some insured women up to \$3,287 for some uninsured women.^{29,30} Although the highest option on our scale assessing willingness to pay was less than some women might pay (an artifact of the

test's cost being unknown when we planned our study), only a handful of women used this highest option. This gives us confidence that \$1,000 offers a realistic early estimate of women's willingness to pay for

Table 3. Predictors of Attitudes Toward Receiving Genomic Risk for Recurrence Testing and Discussing the Results

| Predictor | If the Recurrence Test Were Free, Would You Agree to Have It? | | Would You Want to Discuss the Result With Your Doctor? | |
|-------------------|---|--------------|--|---------------|
| | OR | 95% CI | OR | 95% CI |
| Age | 0.95* | 0.90 to 0.99 | 0.99 | 0.92 to 1.06 |
| White race | 0.78 | 0.21 to 2.86 | 2.96 | 0.59 to 14.91 |
| College degree | 0.66 | 0.24 to 1.75 | 3.23 | 0.70 to 15.01 |
| Financial status | 0.58 | 0.14 to 2.46 | 2.41 | 0.18 to 31.72 |
| Had chemotherapy | 0.80 | 0.28 to 2.26 | 0.19* | 0.03 to 0.99 |
| Stage | 0.94 | 0.48 to 1.83 | 1.71 | 0.70 to 4.16 |
| Heard of RFR test | 2.02 | 0.43 to 9.44 | 1.96 | 0.31 to 12.43 |
| Benefits | 2.38* | 1.18 to 4.75 | 0.65 | 0.26 to 1.68 |
| Concerns | 0.36† | 0.20 to 0.65 | 1.35 | 0.60 to 3.06 |

Abbreviations: OR, odds ratio; RFR, risk for recurrence.

* $P \leq .05$.

† $P \leq .001$.

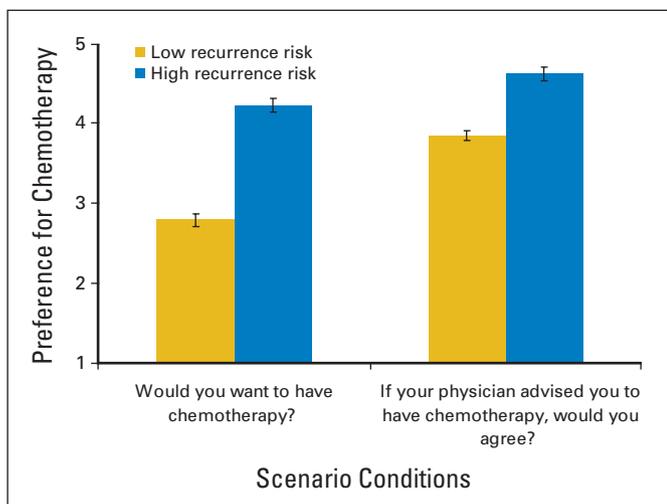


Fig 1. Participants were more likely to choose chemotherapy in response to genomic test results indicating high than low risk for recurrence. However, risk magnitude had a weaker effect in the presence of a physician's recommendation to have chemotherapy. Error bars show SEs.

the test, an amount that is lower than some women would, in practice, pay out of pocket.

Participants' expectations regarding chemotherapy preferences, worry and regret about test results, and trust in test results were all sensitive to RFR magnitude. This is important, because one potential benefit of this technology is the ability to more accurately predict recurrence and tailor adjuvant care for some women.³ Previous studies indicate that many early-stage breast cancer patients prefer chemotherapy even if it will offer little benefit.^{31,32} For the potential benefits of RFR testing to be fully realized, patients and their physicians must recognize that not all patients require adjuvant chemotherapy. Patients, in turn, must be willing to forgo chemotherapy based on the combination of their physicians' recommendations, RFR test results, and other relevant clinical information.

Patient's chemotherapy preferences were sensitive to low and high RFR magnitudes, even when a physician counseled them to have chemotherapy. Some of the scenarios that we presented are likely to happen frequently in practice, such as a physician's recommendation to have chemotherapy in response to a high RFR result. Other scenarios are less likely, such as a recommendation to have chemotherapy in response to a low RFR result. In practice, few physicians would advocate chemotherapy in light of indicators that a woman's RFR was low. We used this scenario to elicit participants' reactions to a situation presenting conflicting information rather than to suggest that it mirrored common clinical practice. Our results underscore the comparable weight that participants placed on their physicians' recommendations and the importance of patient education regarding how clinicians incorporate genomic RFR information into treatment decision making. Indeed, the value placed on testing by the physician and how this is conveyed will likely be critical to patients' decision-making processes.

Although it is promising that participants' hypothetical decisions about chemotherapy were sensitive to RFR and physician recommendations, participants trusted high RFR results most and intermediate RFR results least. Although the clinical significance of these findings on trust is unclear given their small magnitude, one potential expla-

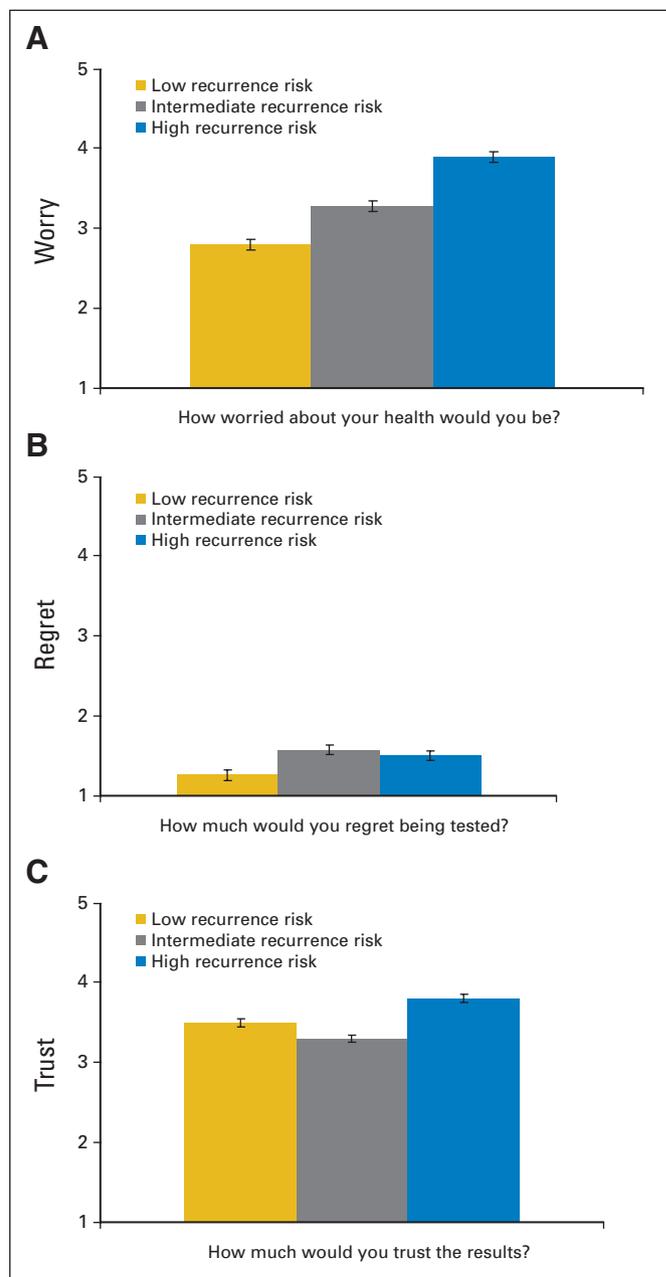


Fig 2. Anticipated (A) worry, (B) regret, and (C) trust differed significantly in response to low, intermediate, and high recurrence risk results. Error bars show SEs.

nation is that a high RFR result would suggest a clearer path of action (chemotherapy), whereas a result indicating an intermediate RFR would involve greater ambiguity, thus changing the acceptability of the result.³³ Medical decision making in response to results conferring an intermediate RFR, along with results that are not concordant with clinical parameters, would convey the greatest uncertainty and require the most deliberation. Our results suggest that patients may have the greatest difficulty in accepting the validity of such results, mirroring findings regarding the difficulties inherent in understanding, accepting and processing clinical risk information that confers higher than expected levels of ambiguity.³⁴⁻³⁸

Participants' concerns about testing were unrelated to their treatment decisions in the context of a hypothetical scenario about chemotherapy. In contrast, participants with more concerns reported lower willingness to be tested and to have the results used to guide treatment decisions. One explanation for these apparently conflicting results is that some participants were unable to integrate their reservations about the test into their hypothetical treatment decisions. It remains possible that patient concerns may affect treatment decisions in a clinical setting.

This study has several limitations, including a cross-sectional design and a sample limited to women who were post-treatment for breast cancer and who received follow-up care at one clinical center. Only 60% of the women approached during the study were included in our analysis. The combination of these factors suggests that our results may not reflect the attitudes of all women who will qualify for RFR testing. Because we conducted this study as RFR testing was moving into clinical use, we could not interview similar groups of women who had received genomic RFR testing. Responses of actual patients and clinicians may depart from our findings. Also, hypothetical scenarios cannot fully capture the complexities of decision making before the commencement of adjuvant treatment. The scenarios did not specify a timeframe for recurrence, and we did not counterbalance to distribute any potential order effects across the scenarios. However, the employment of hypothetical scenarios allowed us to systematically examine participants' responses under different conditions relevant to decision making about adjuvant care.³⁹⁻⁴¹

Unlike people with strong family histories of cancer proactively seeking cancer susceptibility testing⁴² (which they can do without referral from their health care provider), breast cancer RFR testing likely will be integrated into the routine care of women with early-stage, node-negative, estrogen- and progesterone-positive breast cancers. Just as early studies examining potential response to cancer susceptibility testing employed hypothetical scenarios, our research took this approach to allow us to obtain critical early information on women's preferences. Although we have since learned that those stud-

ies overestimated uptake^{20,21,43} and emotional distress,^{21,44} they were an important step in understanding how best to communicate with patients about testing.

Several studies have examined adjuvant treatment preferences^{32,45,46} and their relation to RFR was assessed using standard clinical indicators.⁴⁰ To our knowledge, our study is the first to demonstrate patients' interest in genomic RFR testing and how these results might influence decisions about adjuvant care. Overall, our results indicate that patients will welcome this information, that they prefer to be involved in how their test results will guide treatment choices, and that they will be sensitive to results when making decisions about their treatment. These findings have important implications for communicating with patients newly diagnosed with breast cancer as RFR testing transitions into clinical care.^{15,16}

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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REFERENCES

1. American Cancer Society: Cancer Facts and Figures. Atlanta, GA, American Cancer Society, 2007
2. Jemal A, Clegg LX, Ward E, et al: Annual report to the nation on the status of cancer, 1975-2001, with a special feature regarding survival. *Cancer* 101:3-27, 2004
3. Swain S: A step in the right direction. *J Clin Oncol* 24:3717-3718, 2006
4. Whelan T, Levine M, Willan A, et al: Effect of a decision aid on knowledge and treatment decision making for breast cancer surgery: A randomized trial. *JAMA* 292:435-441, 2004
5. Early Breast Cancer Trialists' Cooperative Group: Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: An overview of the randomised trials. *Lancet* 365:1687-1717, 2005
6. Early Breast Cancer Trialists' Collaborative Group. Tamoxifen for early breast cancer. Oxford, United Kingdom, Cochrane Library, 1, CD000486
7. Paik S, Tang G, Shak S, et al: Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. *J Clin Oncol* 24:3726-3734, 2006

8. Perou CM, Sorlie T, Eisen MB, et al: Molecular portraits of human breast tumours. *Nature* 406:747-752, 2000
9. Sorlie T, Perou CM, Tibshirani R, et al: Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc Natl Acad Sci U S A* 98:10869-10874, 2001
10. Sorlie T, Tibshirani R, Parker J, et al: Repeated observation of breast tumor subtypes in independent gene expression data sets. *Proc Natl Acad Sci U S A* 100:8418-8423, 2003
11. van't Veer L, Dai H, van de Vijver MJ, et al: Gene expression profiling predicts clinical outcome of breast cancer. *Nature* 415:530-536, 2002
12. Carey L, Perou CM, Livasy CA, et al: Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA* 295:2492-2502, 2006
13. Perreard L, Fan C, Quackenbush JF, et al: Classification and risk stratification of invasive breast carcinomas using a real-time quantitative RT-PCR assay. *Breast Cancer Res* 8:R23, 2006
14. Buchholz TA, Stivers DN, Stec J, et al: Global gene expression changes during neoadjuvant chemotherapy for human breast cancer. *Cancer J* 8:461-468, 2002

15. Sparano J, Hayes D, Dees EC, et al: Phase III randomized study of adjuvant combination chemotherapy and hormonal therapy versus adjuvant hormonal therapy alone in women with previously resected axillary node-negative breast cancer with various levels of risk for recurrence. <http://www.cancer.gov/clinicaltrials/ECOG-PACCT-1>
16. MINDACT Design and MINDACT overview. <http://www.breastinternationalgroup.org/TransBIG/Mindact.aspx>
17. Jansen S, Otten W, Stiggelbout AM: Review of determinants of patients' preferences for adjuvant therapy in cancer. *J Clin Oncol* 22:3181-3190, 2004
18. Croyle RT, Lerman C: Interest in genetic testing for colon cancer susceptibility: Cognitive and emotional correlates. *Prev Med* 22:284-292, 1993
19. Smith KR, Croyle RT: Attitudes toward genetic testing for colon cancer risk. *Am J Public Health* 85:1435-1438, 1995
20. Lerman C, Daly M, Masny A, et al: Attitudes about genetic testing for breast-ovarian cancer susceptibility. *J Clin Oncol* 12:843-850, 1994
21. Struewing J, Lerman C, Kase RG, et al: Anticipated uptake and impact of genetic testing in hereditary breast and ovarian-cancer families. *Cancer Epidemiol Biomarkers Prev* 4:169-173, 1995

22. Lillie SE, Brewer NT, O'Neill SC, et al: Retention and use of breast cancer recurrence risk information from genomic tests: The role of health literacy. *Cancer Epidemiol Biomarkers Prev* 16:249-255, 2007
23. Rimer BK, Halabi S, Skinner CS, et al: Effects of a mammography decision-making intervention at 12 and 24 months. *Am J Prev Med* 22:247-257, 2002
24. Olivetto IA, Bajdik CD, Ravdin PM, et al: Population-based validation of the prognostic model ADJUVANT! for early breast cancer. *J Clin Oncol* 23:2716-2725, 2005
25. Jacobsen PB, Valdimarsdottir HB, Brown KL, et al: Decision-making about genetic testing among women at familial risk for breast cancer. *Psychosom Med* 59:459-466, 1997
26. Degner L, Sloan JA, Venkatesh P: Control preferences scale. *Can J Nurs Res* 29:21-43, 1997
27. Bruera E, Sweeney C, Calder K, et al: Patients preferences versus physician perceptions of treatment decisions in cancer care. *J Clin Oncol* 19:2883-2885, 2001
28. Grunfeld E, Maher EJ, Browne S, et al: Advanced breast cancer patients' perceptions of decision making for palliative chemotherapy. *J Clin Oncol* 24:1090-1098, 2006
29. Harvard Pilgrim Healthcare: TA 6.35 Oncotype DX Recurrence Score Assay for Predicting Breast Cancer Recurrence. http://www.harvardpilgrim.org/portal/page?_pageid=253,214340&_dad=portal&_schema=PORTAL#635
30. Genomic Health: Medicare Contractor Establishes Reimbursement Coverage Policy for Genomic Health's Oncotype DX Breast Cancer Test. <http://investor.genomichealth.com/ReleaseDetail.cfm?ReleaseID=184309>
31. Ravdin PM, Siminoff IA, Harvey JA: Survey of breast cancer patients concerning their knowledge and expectations of adjuvant therapy. *J Clin Oncol* 16:515-521, 1998
32. Duric VM, Stockler MR, Heritier S, et al: Patients' preferences for adjuvant chemotherapy in early breast cancer: What makes AC and CMF worthwhile now? *Ann Oncol* 16:1786-1794, 2005
33. Cioffi D: Asymmetry of doubt in medical self-diagnosis: The ambiguity of "uncertain wellness." *J Pers Soc Psychol* 61:969-980, 1991
34. Cioffi D: When good news is bad news: Medical wellness as a nonevent in undergraduates. *Health Psychol* 13:63-72, 1994
35. van Zuuren FJ, van Schie ECM, van Baaren NK: Uncertainty in the information provided during genetic counseling. *Patient Educ Couns* 32:129-139, 1997
36. Press NA, Yasui Y, Reynolds S, et al: Women's interest in genetic testing for breast cancer susceptibility may be based on unrealistic expectations. *Am J Med Genet* 99:99-110, 2001
37. Lloyd FJ, Reyna VF, Whalen P: Accuracy and ambiguity in counseling patients about genetic risk. *Arch Intern Med* 161:2411-2413, 2001
38. Peters E, McCaul KD, Stefanek M, et al: A heuristics approach to understanding cancer risk perception: Contributions from judgment and decision-making research. *Ann Behav Med* 31:45-52, 2006
39. Palda VA, Llewellyn-Thomas HA, Mackenzie RG, et al: A breast cancer patients' attitudes about rationing postlumpectomy radiation therapy: Applicability of trade-off methods to policy-making. *J Clin Oncol* 15:3192-3200, 1997
40. Chao C, Studts JL, Abell T, et al: Adjuvant chemotherapy for breast cancer: How presentation of recurrence risk influences decision-making. *J Clin Oncol* 21:4299-4305, 2003
41. Grunfeld EA, Ramirez AJ, Maher EJ, et al: Chemotherapy for advanced breast cancer: What influences oncologists' decision-making? *Br J Cancer* 84:1172-1178, 2001
42. US Preventive Services Task Force: Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility. *Ann Intern Med* 143:355-361, 2005
43. Ropka M, Wenzel J, Phillips EK, et al: Uptake rates for breast cancer genetic testing: A systematic review. *Cancer Epidemiol Biomarkers Prev* 15:840-855, 2006
44. Schlich-Bakker K, ten Kroode HFJ, Ausems MGEM: A literature review of the psychological impact of genetic testing on breast cancer patients. *Patient Educ Couns* 62:13-20, 2006
45. Jansen SJ, Otten W, Baas-Thijssen MC, et al: Explaining differences in attitude toward adjuvant chemotherapy between experienced and inexperienced breast cancer patients. *J Clin Oncol* 23:6623-6630, 2005
46. Jansen SJ, Otten W, van de Velde CJ, et al: The impact of the perception of treatment choice on satisfaction with treatment, experienced chemotherapy burden and current quality of life. *Br J Cancer* 91:56-61, 2004

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Appendix

The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).