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The impact of gene expression profile testing on confidence in chemotherapy decisions and prognostic expectations

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Abstract

Purpose Little is known about whether gene expression profile (GEP) testing and specific recurrence scores (e.g., medium risk) improve women's confidence in their chemotherapy decision or perceived recurrence risk. We evaluate the relationship between these outcomes and GEP testing.

Methods We surveyed women eligible for GEP testing (stage I or II, Gr1-2, ER+, HER2−) identified through the Surveillance, Epidemiology, and End Results (SEER) Registry of Washington or Kaiser Permanente Northern California from 2012 to 2016, approximately 0–4 years from diagnosis ($N=904$, RR = 45.4%). Confidence in chemotherapy was measured as confident (Very, completely) versus Not Confident (Somewhat, A little, Not At All); perceived risk recurrence was recorded numerically (0–100%). Women reported their GEP test receipt (Yes, No, Unknown) and risk recurrence score (High, Intermediate, Low, Unknown). In our analytic sample ($N=833$), we propensity score weighted the three test receipt cohorts and used propensity weighted multivariable regressions to examine associations between the outcomes and the three test receipt cohorts, with receipt stratified by score.

Results 29.5% reported an unknown GEP test receipt; 86% being confident. Compared to no test receipt, an intermediate score (aOR 0.34; 95% CI 0.20–0.58), unknown score (aOR 0.09; 95% CI 0.05–0.18), and unknown test receipt (aOR 0.37; 95% CI 0.24–0.57) were less likely to report confidence. Most women greatly overestimated their recurrence risk regardless of their test receipt or score.

Conclusions GEP testing was not associated with greater confidence in chemotherapy decisions. Better communication about GEP testing and the implications for recurrence risk may improve women's decisional confidence.

Keywords Gene expression profile testing · Breast cancer · Chemotherapy

Introduction

Breast cancer clinical care guidelines recommend gene expression profile (GEP) tests in the diagnostic evaluation of women with newly diagnosed, early stage, hormone receptor positive breast cancer [1–3]. GEP tests such as Oncotype DX typically stratify women into low, intermediate, and high risk for cancer recurrence, and are intended to inform adjuvant chemotherapy decisions [4]. The initial ASCO and NCCN recommendations in 2009 were that women with low-risk scores (below 18) could forego chemotherapy. Publication of the TAILORx trial in 2018 demonstrated that women with Oncotype scores below 26 could safely omit chemotherapy without a decrease in invasive disease-free survival or freedom from distant recurrence [5]. These recent practice changing findings, together with direct-to-consumer

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marketing, are likely to significantly increase use of testing, and hopefully improve knowledge about recurrence risk and confidence regarding chemotherapy choice [6, 7].

Despite the promise and marketing claims, little is known about whether GEP risk recurrence scores actually improve women's estimation of their recurrence risk, or confidence in their treatment decisions, and past analyses did not consider how these patient-reported outcomes might vary by GEP results [8, 9]. Early research suggested that patients would have less confidence in intermediate recurrence scores, for which treatment recommendations have been largely uncertain until publication of the TAILORx results [10]. Women with intermediate recurrence scores who do not take active roles in their care (vs. those who do) have also been noted to report greater distress and lower quality of life [11]. This is likely related to observations that patients have difficulty in understanding uncertainty associated with treatment decisions [8, 12]. Finally, while TAILORx recently established treatment recommendations for intermediate risk scores, little is known about the experience of nearly a decade of patients who made their treatment decisions according to the previous guidelines, and how remaining unanswered questions about GEP scores and treatment may affect survivors.

To address these gaps in our understanding, we conducted a retrospective, population-based survey of two large cohorts of women with early stage, hormone receptor positive breast cancer to examine the relationships between GEP testing and two important patient-reported outcomes: confidence in chemotherapy decisions; and perceived risk of recurrence. We hypothesized that women with self-reported low- and high-risk GEP scores would have greater confidence in their chemotherapy decision, compared to women who reported they were not tested. Secondly, as the test score is intended to improve the accuracy of women's understanding of their recurrence risk, we hypothesized that perceived risk would align with their reported test scores. Our findings are intended to inform discussions between clinicians and breast cancer patients regarding the use of GEP testing and to highlight needs for future research on the impact of GEP testing on patient-facing survivorship outcomes.

Methods

The current report uses data from a larger multi-site, collaborative National Cancer Institute-funded study of GEP [13–15]. All participating site Institutional Review Boards approved the study.

Setting and population

The study included early stage, hormone receptor positive breast cancer survivors diagnosed between 2 January 2012 and 22 May 2016 identified from two populations: (1) residents of the SEER Western Washington State Cancer Surveillance System (WA-CSS) catchment area [part of the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute] and (2) survivors enrolled in Kaiser Permanente Northern California (KPNC) at the time of diagnosis. These populations were selected because they were representative of community practice, and included survivors of diverse race/ethnicity and a range of insurance types and health care settings. Breast cancer survivors were eligible if they met criteria in place at the time of the data collection for GEP testing [stage I or II, lymph node negative, estrogen-receptor positive, and human epidermal growth factor 2 negative (HER2)], ages 25–74 at diagnosis. Eligible women were identified from the KPNC tumor registry and electronic medical records and from the WA-CSS.

Data collection

At KPNC, we selected an age-stratified random sample of 800 test-eligible survivors, aiming for an equal proportion of tested versus non-tested survivors, as well as representation from varying age groups. In the WA-CSS region, there was no medical record data about GEP test receipt.

All participants were recruited using a mailed letter with information about the study, a URL address linked to a web-based questionnaire, and contact information for questions. At KPNC letter also included a postage-paid return postcard with options to request a paper survey or decline participation. Non-respondents were mailed a second recruitment letter; and follow-up courtesy calls were placed. At KPNC, participants who did not respond on-line were automatically sent paper surveys. At WA-CSS, survivors who did not complete the survey online received courtesy calls starting 1 week after mailing. WA-CSS survivors who informed study staff during courtesy calls that they wished to complete paper-based surveys were sent questionnaires by mail. At both sites, individuals who completed the survey received a $20 gift card. Surveys were collected between September 2015 and July 2016.

Information on age, AJCC tumor stage (I or II), ER and PR status, and diagnosis year (2012–2016) was captured from the SEER Registry in the WA-CSS sample and from medical records in the KPNC sample.

Measures

Confidence in the chemotherapy decision

The primary study outcome—confidence in the chemotherapy decision—was based on the following survey question, "How confident are you in the decision you and/or your doctor made about whether or not to have chemotherapy?"

Responses were grouped into Confident (Very or completely), Not Confident (Somewhat, A little, or Not at all), and Not Applicable (Chemotherapy was not offered as an option).

Perceived cancer recurrence risk

Estimated risk of cancer recurrence was recorded from a survey question asking, "What, in your personal opinion, is the chance of the breast cancer recurring in your lifetime?" Participants recorded their responses on a visual analog scale ranging from 0 ("No chance breast cancer will recur") to 100 ("Breast cancer definitely will recur").

Self-reported GEP test receipt and recurrence scores

Survivors were first categorized by self-reported GEP test receipt (Yes, No, I Don't Know). Those who indicated that they received a GEP test were also grouped by their self-reported recurrence risk scores [Low risk, Intermediate risk, High risk, I don't know, and Other (please explain)]. In eight cases, women provided their actual recurrence scores in the "Other" response category. These responses were reclassified into test risk categories based on the previous guideline-based test score cut-offs (low risk 0–17, intermediate risk 18–30, high risk 31–100) [1]. For the remainder who reported receiving a GEP test, we grouped "Other", "I don't know", and missing responses into a category labeled "Unknown risk".

Covariates

We measured several covariates that might affect the relationship between GEP test recurrence scores and our outcomes. Covariates included age, self-identified race (Non-Hispanic White, Asian, Other Single Race, Multiracial), education (High school or less, Some college, Associate degree, Bachelor degree, Graduate degree), and AJCC stage (I or II) at diagnosis [16]. We included an indicator for site to control for differences in care settings and regional practice patterns. The diagnosis year (2012–2016) was included to account for time trends.

Analysis

We first examined unadjusted descriptive statistics for the three cohorts of self-reported GEP test receipt (Yes, No, Unknown). To account for differences between the three test receipt cohorts, we used inverse propensity score weighting based on all the covariates [17, 18]. We estimated the likelihood of each cohort using a generalized boosted propensity model, which is augmented by machine learning [19]. A predetermined standardized mean difference of 0.2 was used to determine adequate balance between pairwise comparisons of the three test receipt cohorts [19]. After propensity score weighting, each covariate met this threshold (Appendix 1). We used propensity score weighted multivariable regressions to evaluate the associations between the outcomes and being in the three test receipt cohorts, with women who received the test further stratified by the recurrence score (high, intermediate, low, or unknown) [20]. A logistic model was used to evaluate a women's likelihood of reporting confidence in her chemotherapy decision; multivariable regression was used to test associations with perceived recurrence risk. We excluded the 204 women who answered the chemotherapy confidence question with "Not Applicable" because they were not offered chemotherapy.

We performed two sensitivity analyses: (1) excluded the 246 women with unknown GEP test receipt because they might have been different from the other two test receipt cohorts in unmeasured dimensions related to health literacy or other unmeasured covariates (Appendix 2) and (2) included the 204 women who answered the chemotherapy confidence question with "Not Applicable" because they were not offered chemotherapy and ran a propensity score weighted multinomial logistic regression with a three level dependent variable (Confident, Not Confident, and Not Applicable) (Appendix 3). Analyses were conducted using SAS version 9.4 (Cary, NC).

Results

Study population

There were a total of 1990 eligible survivors: 795 from northern California and 1195 from Washington State. The overall survey completion rate was 45.4% (53.1% from northern California and 40.3% from Washington, Fig. 1). Women who completed the survey were not significantly different from those who did not in terms of age, stage, and diagnosis year, except that non-responders were more likely than responders to be Non-White (20.2 vs. 12.2%, respectively) and from the WA-CSS sample (65.7 vs. 53.3%). From the sample of 904 respondents, we excluded 21 of the survivors with a missing response to the GEP test receipt item. We further excluded 48 with missing responses to the 2 outcome variables and an additional 2 with missing values for demographic questions, yielding an analytic dataset of 833 (92.1%) respondents.

The final sample of survivors was largely (80.1%) non-Hispanic White. Approximately half of the sample (49.3%) was at least 60 years old, and more than half (53.4%) had earned a college degree or higher. Most were diagnosed with stage I cancer (73.5%, Table 1).

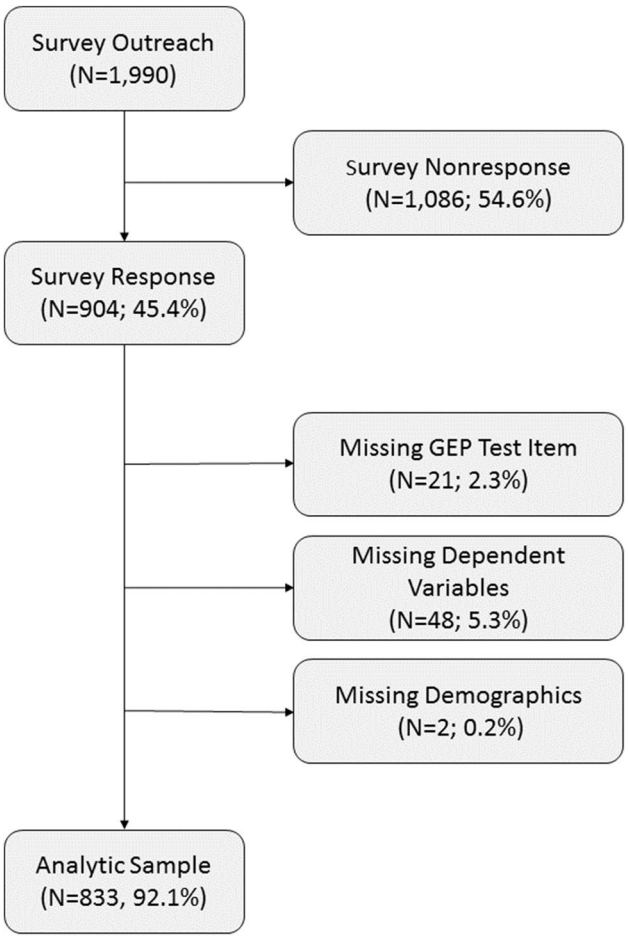

Fig. 1 Consort figure. Non-missing GEP test item responses included "Yes", "No", or "Unknown". Dependent variables included perceived cancer recurrence risk and confidence in the chemotherapy decision. Demographic included age, race, education, stage, and diagnosis year

Self-reported test receipt and recurrence scores

Nearly one-third (29.5%, 246/833) of women reported not knowing whether they had received a GEP test (Table 1). In unadjusted analyses, compared to those who reported test or no test receipt, women between the ages of 60–69 and those aged 70 years or older were more likely to report an unknown test receipt ($P<0.05$) as were those who reported Other Single Race ($P=0.01$), while those with a Bachelor's degree or a Graduate/Professional degree were less likely to report unknown test receipt ($P<0.01$). Among the 29.5% of women with an unknown test receipt, more were from KPNC (63.2%, $N=157$) than from WA (36.2%, $N=89$, $P<0.001$). Women were also more likely to report receiving a GEP test in the last 2 years of the sample. However, after propensity score weighting, the three test receipt cohorts were well balanced (Appendix 1).

The majority of respondents who reported receiving a test were able to report a specific recurrence score (e.g., low, intermediate, or high risk) (324/368 = 88.0%, Table 2).

Confidence in the chemotherapy decision

The majority of women (86.8%, 546/629) reported being confident in their chemotherapy choice (Women who answered "Not Applicable" to the Confidence in Chemotherapy item were excluded). Figure 2 displays the fully adjusted results of the association between confidence in the chemotherapy decision and self-reported GEP test receipt and recurrence scores. Confidence among women who reported high or low GEP scores was not significantly different than those who reported not having a GEP test. Compared to women who reported no test receipt, women who reported an intermediate score were less likely to report post-hoc confidence (aOR 0.34, 95% CI 0.20–0.58), as were women with an unknown recurrence score (aOR 0.09, 95% CI 0.05–0.18). Women who reported unknown test receipt were also less likely to report post-hoc confidence (aOR 0.37, 95% CI 0.24–0.57, Fig. 2).

Survivor's perceived cancer recurrence risk

The unadjusted estimated risk of recurrence among women with an unknown test receipt was higher than that of women who received the test and those who did not (31.4, 25.6, 27.8%, respectively; $P<0.01$). In fully adjusted analyses, respondents with high-risk scores reported higher estimates of recurrence risk than those who were not tested (63.1 vs. 38.3%; $P<0.001$), while respondents with low risk scores reported comparatively lower estimates than untested women (32.5 vs. 38.3%; $P<0.01$, Table 2). There was no difference in perceived risk between women who were not tested and those with an intermediate risk score, unknown risk score, or unknown test receipt.

In sensitivity analyses, excluding the 246 women with an unknown test receipt did not appreciably change the results (Appendix 2: Table 3, Fig. 3), and neither did including the 204 respondents who answered "Not Applicable" to the confidence in chemotherapy question (Appendix 3).

Discussion

In a population-based cohort study of early-stage breast cancer survivors, we found that almost one in three did not know whether they had received GEP testing. Those who reported receiving the test did not have more confidence in their chemotherapy decision than those who reported they were not tested. In addition, women who reported an intermediate risk score, as well as those who did not know

Table 1 Survivor characteristics by self-reported gene expression profile (GEP) test receipt

	Sample ($N=833$)	GEP test receipt ($N=368$)	No GEP test receipt ($N=219$)	Unknown GEP test receipt[a] ($N=246$)	*P*-values
Age					
25–49	169 (20.3%)	82 (22.3%)	51 (23.3%)	36 (14.6%)	0.05
50–59	253 (30.4%)	121 (32.9%)	58 (26.5%)	74 (30.1%)	
60–69	324 (38.9%)	135 (36.7%)	87 (39.7%)	102 (41.5%)	
70+	87 (10.4%)	30 (8.2%)	23 (10.5%)	34 (13.8%)	
Race					
White (Non-Hispanic)	667 (80.1%)	301 (81.8%)	181 (82.6%)	185 (75.2%)	0.09
Asian	61 (7.3%)	26 (7.1%)	16 (7.3%)	19 (7.7%)	
Other Single Race[b]	62 (7.4%)	21 (5.7%)	11 (5.0%)	30 (12.2%)	
Multiracial[c]	43 (5.2%)	20 (5.4%)	11 (5.0%)	12 (4.9%)	
Education					
High school	95 (11.4%)	36 (9.8%)	23 (10.5%)	36 (14.6%)	<0.01
Some college	187 (22.4%)	72 (19.6%)	43 (19.6%)	72 (29.3%)	
Associate degree	106 (12.7%)	46 (12.5%)	22 (10.0%)	38 (15.4%)	
Bachelor's degree	225 (27.0%)	109 (29.6%)	67 (30.6%)	49 (19.9%)	
Graduate or Professional degree	220 (26.4%)	105 (28.5%)	64 (29.2%)	51 (20.7%)	
Care setting					
Integrated Care California	391 (46.9%)	120 (32.6%)	114 (52.1%)	157 (63.8%)	<0.001
Washington SEER	442 (53.1%)	248 (67.4%)	105 (47.9%)	89 (36.2%)	
AJCC stage					
Stage I	612 (73.5%)	266 (72.3%)	170 (77.6%)	176 (71.5%)	0.26
Stage II	221 (26.5%)	102 (27.7%)	49 (22.4%)	70 (28.5%)	
Diagnosis year					
2012	33 (4.0%)	21 (5.7%)	8 (3.7%)	4 (1.6%)	<0.01
2013	144 (17.3%)	59 (16.0%)	38 (17.4%)	47 (19.1%)	
2014	454 (54.5%)	179 (48.6%)	122 (55.7%)	153 (62.2%)	
2015	183 (22.0%)	96 (26.1%)	49 (22.4%)	38 (15.4%)	
2016	19 (2.3%)	13 (3.5%)	2 (0.9%)	4 (1.6%)	

The results in this table are not propensity score weighted. Survey Item: "Did you have a multigene test (e.g., Oncotype DX, Mammaprint, Mammostrat, Rotterdam Signature 76-Gene Panel, or the Breast Cancer Index) of your breast cancer tumor at any time after you were diagnosed with breast cancer? This test is done by sending a small part of the tumor to the lab. These tests look at chances that the tumor could come back years after treatment. They are different than the hormone receptor (like ER) tests that are usually done or the BRCA multigene tests for cancers that run in families"

[a]Responded "I don't know"

[b]Includes Black ($N=21$), Hispanic ($N=29$), American Indian/Alaskan Native ($N=3$), Hawaiian/Pacific Islander ($N=4$), Other ($N=5$)

[c]Respondent checked more than one race category. The survey instructed respondents to "Check all that apply"

their risk score or did not know whether they had received the test, had lower confidence in their chemotherapy decision than those who were not tested. Overall, most women overestimated their recurrence risk regardless of their understanding of their GEP test receipt or recurrence scores.

Our finding that knowledge of recurrence scores did not increase confidence in the chemotherapy decision was unexpected. We framed confidence to be a measure of the individual's perception that they have made the right choice for their situation given the knowledge at hand. In a recent population-based study of GEP test use among early-stage breast cancer survivors demographically similar to our cohort, Friese et al. found that women were largely satisfied with their chemotherapy decisions, and that satisfaction did not differ substantively by receipt of either testing or chemotherapy [9]. Conceptually, satisfaction with and confidence in treatment decisions are distinct, but related concepts. Although Friese et al. also found that approximately one-third of women reported an unknown test receipt, the authors did not partition women by knowledge of their test receipt, which may account for the difference in our results.

We found that survivors who reported intermediate risk scores had lower confidence in their chemotherapy decision, which aligns with the uncertainty surrounding the

Table 2 Survivor's perceived cancer recurrence risk by self-reported GEP test receipt and score

	Sample ($N=833$)	Perceived probability of recurrence	
		Unadjusted risk of recurrence[a] (%)	Adjusted risk of recurrence[b] (%)
Self-report of GEP test result			
High risk score	16 (1.9%)	52.0	63.1[c]
Intermediate risk score	78 (9.4%)	31.3	42.4
Low risk score	230 (27.6%)	21.4	32.5[d]
Unknown risk score	44 (5.3%)	28.0	37.4
Unknown GEP test	246 (29.5%)	31.4	39.3
No GEP test (referent)	219 (26.3%)	27.8	38.3

Survey Item: "What, in your personal opinion, is the chance of the breast cancer recurring in your lifetime? (0–100%)?"

[a]Not propensity score weighted

[b]Propensity score weighted and adjusted for age, race, education, healthcare delivery site, AJCC stage, year. Model $R^2=0.081$

[c]$P<0.001$ compared to those reporting no GEP test

[d]$P<0.01$ compared to those reporting no GEP test

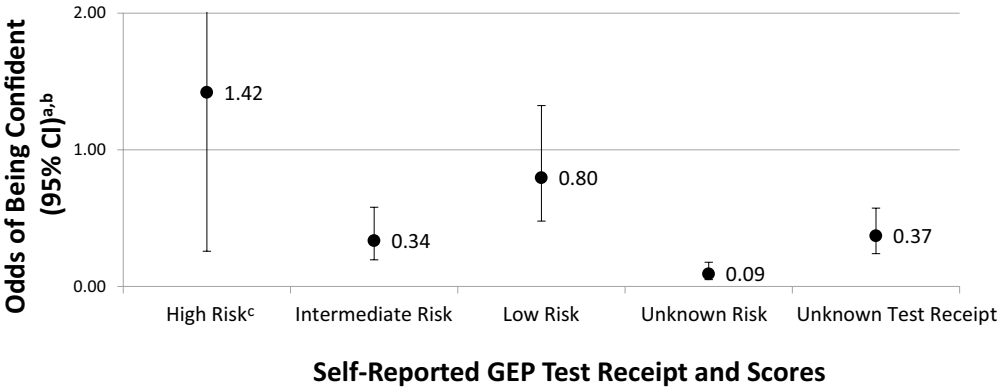

Fig. 2 Adjusted odds of being confident (Confident includes "Very" or "Completely" Confident. Not Confident includes "Somewhat", "A Little" or "Not At All" Confident) about the chemotherapy decision by self-reported GEP test receipt and score (Survey Item: "How confident are you in the decision you and/or your doctor made about whether or not to have chemotherapy?"). (Reference Group: no test receipt). [c]High risk: OR = 1.42, 95% CI (0.26, 7.83). [a]$N=629$ Respondents. We excluded 204 respondents who answered the question, "Not applicable (chemotherapy was not offered as an option)". [b]Propensity score weighted and adjusted for age, race, education, site, AJCC stage, and diagnosis year. Model AIC = 1177.8. Please note we conducted a sensitivity analysis with the additional 204 respondents who answered "Not applicable" to the Confident in Chemotherapy item and the results were similar

treatment recommendations for this test score. Our result is consistent with previous findings that patients have great difficulty understanding, accepting, and processing clinical risk information with relatively high levels of uncertainty [10, 12]. Now that the TAILORx trial has suggested that women with intermediate scores do not require chemotherapy, future research is warranted to understand whether the effect of intermediate scores on confidence changes, as well as whether testing affects longer term worry about recurrence and other survivorship outcomes.

We also found that perceived risk of recurrence was associated with high and low risk recurrence scores; however, survivors overall significantly overestimated their recurrence risk, even those with low risk recurrence scores. This is consistent with other studies of survivors [16, 21] and physicians [22]. Paradoxically, evidence suggests that inaccurate risk perception may be associated with poor treatment adherence and surveillance decisions in survivorship [23]. Following publication of the findings of the TAILORx study, future research should examine the role of GEP testing and risk perceptions on survivorship and surveillance outcomes.

Several limitations should be considered in evaluating our results. We relied on self-report of GEP test receipt and test scores to capture the respondent's understanding of their care. We did not have data on actual use of GEP testing or results to confirm the self-report. Many past studies have observed biases in who is selected for testing, including

lower rates of testing among women with co-morbidities, Non-White race, older age, geographic and practice organizational variations, and clinical factors that drive decisions regardless of GEP results [24–26]. We conducted propensity score weighting and included several of these factors as covariates in analyses. However, it is possible that residual confounding by unmeasured factors associated with both the probability of being tested and study outcomes could have biased our associations towards the null or produced spurious relationships. A second limit is that we used recurrence score cut-points recommended in the period of data collection, and it is possible that results might vary based on the categories used in TAILORx. Third, our finding that a lower proportion of women in KPNC recalled having the test could have stemmed from differences between this practice setting and Washington State, but might also reflect unmeasured differences between the two samples. The observed rate of test receipt in KPNC is similar to or higher than that in most other settings [13]. Fourth, our results are limited to two large geographic regions in the Western US. The respondents in this study were more likely to be White and more highly educated than women with breast cancer nationwide. Finally, when asking about GEP testing, we did not distinguish between different GEP testing platforms (e.g., Mammaprint vs. Oncotype DX). It is possible that differences in their presentation of the recurrence scores could systematically influence risk perceptions [16].

Despite these limitations, the findings have implications for clinical practice. First, some sites may need to redouble their efforts to inform breast cancer survivors about their GEP test receipt, results, and risk of recurrence. Second, women who reported intermediate recurrence scores had lower confidence in their chemotherapy decision than those with high or low RS. Recent findings from the TAILORx study suggest that patients with intermediate risk test results have low risk of recurrence without chemotherapy. This new data could lead to greater decisional confidence among future patients with these scores and could also improve the decisional confidence of past patients who omitted chemotherapy. However, the recent findings might also contribute to decision regret among the previous patients who chose chemotherapy [27]. These challenges could be addressed through the use of decision support tools that encourage communication, and help make informed patient decisions that align with patient treatment preferences [28].

We conclude that GEP testing may not be achieving its full potential to increase survivors' confidence in chemotherapy decisions and does not appear to improve the accuracy of survivors' estimates of their risk for cancer recurrence. The benefits of GEP testing could be enhanced via clearer communication to patients that they have been tested, and about what their test results mean regarding risk of recurrence.

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Data availability The datasets generated and analyzed during the current study are not publicly available due to IRB protocol, but may be available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Appendix 1: Post-propensity score weighted standardized mean differences of the three test receipt cohorts (yes, no, unknown)

We used inverse propensity score weighting for multiple treatments based on all the covariates to account for differences between the three cohorts [17, 18]. We estimated the likelihood of each cohort using a generalized boosted propensity model, which is augmented by machine learning [19]. A predetermined standardized mean difference of 0.2 was used to determine adequate balance between pairwise comparisons of the three test receipt cohorts [19]. After propensity score weighting, each covariate met this threshold.

Variables	Unweighted		Weighted	
	STD mean diff	*P*-values	STD mean diff	*P*-values
Test receipt versus no receipt				
AgeCat:1. 25–49	0.024	0.381	0.028	0.839
AgeCat:2. 50–59	0.139	0.381	0.054	0.839
AgeCat:3. 60–69	0.063	0.381	0.038	0.839
AgeCat:4. ≥ 70	0.082	0.381	0.062	0.839
RaceCat:1. White	0.022	0.98	0.077	0.836
RaceNewCat:2. Asian	0.009	0.98	0.053	0.836
RaceNewCat:3. Other Single Race	0.03	0.98	0.069	0.836
RaceNewCat:4. Multiracial	0.018	0.98	0.002	0.836
EducationCat:1. High school	0.024	0.932	0.023	0.984
EducationCat:2. Some college	0.002	0.932	0.002	0.984
EducationCat:3. Associate's degree	0.077	0.932	0.053	0.984
EducationCat:4. Bachelor's degree	0.021	0.932	0.005	0.984
EducationCat:5. Graduate/Professional degree	0.015	0.932	0.019	0.984
InstCat:1. Kaiser	0.397	0	0.068	0.463
InstCat:2. FH	0.397	0	0.068	0.463
StageCat:1. Stage I	0.122	0.153	0.035	0.71
StageCat:2. Stage II	0.122	0.153	0.035	0.71
DxYearCat:1. 2012	0.095	0.131	0.022	0.956
DxYearCat:2. 2013	0.036	0.131	0.03	0.956
DxYearCat:3. 2014	0.141	0.131	0.035	0.956
DxYearCat:4. 2015	0.086	0.131	0.015	0.956
DxYearCat:5. 2016	0.166	0.131	0.052	0.956
Test receipt versus unknown receipt				
AgeCat:1. 25–49	0.183	0.017	0.041	0.949
AgeCat:2. 50–59	0.061	0.017	0.014	0.949
AgeCat:3. 60–69	0.099	0.017	0.03	0.949
AgeCat:4. ≥ 70	0.198	0.017	0.031	0.949
RaceCat:1. White	0.172	0.038	0.047	0.878
RaceNewCat:2. Asian	0.026	0.038	0.064	0.878
RaceNewCat:3. Other Single Race	0.286	0.038	0.012	0.878
RaceNewCat:4. Multiracial	0.025	0.038	0.019	0.878
EducationCat:1. High school	0.172	0.038	0.051	0.966
EducationCat:2. Some college	0.244	0.001	0.039	0.966
EducationCat:3. Associate's degree	0.092	0.001	0.016	0.966
EducationCat:4. Bachelor's degree	0.212	0.001	0.027	0.966
EducationCat:5. Graduate/Professional degree	0.172	0.001	0.029	0.966
InstCat:1. Kaiser	0.637	0	0.068	0.472
InstCat:2. FH	0.637	0	0.068	0.472
StageCat:1. Stage I	0.017	0.842	0.008	0.926
StageCat:2. Stage II	0.017	0.842	0.008	0.926
DxYearCat:1. 2012	0.188	0	0.069	0.918
DxYearCat:2. 2013	0.083	0	0.01	0.918
DxYearCat:3. 2014	0.271	0	0.035	0.918
DxYearCat:4. 2015	0.247	0	0.003	0.918
DxYearCat:5. 2016	0.121	0	0.031	0.918
No test receipt versus unknown receipt				
AgeCat:1. 25–49	0.207	0.099	0.013	0.976
AgeCat:2. 50–59	0.078	0.099	0.04	0.976
AgeCat:3. 60–69	0.036	0.099	0.008	0.976
AgeCat:4. ≥ 70	0.116	0.099	0.031	0.976

Variables	Unweighted		Weighted	
	STD mean diff	*P*-values	STD mean diff	*P*-values
RaceCat:1. White	0.194	0.056	0.03	0.9
RaceNewCat:2. Asian	0.016	0.056	0.011	0.9
RaceNewCat:3. Other Single Race	0.316	0.056	0.081	0.9
RaceNewCat:4. Multiracial	0.006	0.056	0.018	0.9
EducationCat:1. High school	0.137	0.002	0.028	0.968
EducationCat:2. Some college	0.243	0.002	0.041	0.968
EducationCat:3. Associate's degree	0.169	0.002	0.037	0.968
EducationCat:4. Bachelor's degree	0.233	0.002	0.032	0.968
EducationCat:5. Graduate/Professional degree	0.188	0.002	0.048	0.968
InstCat:1. Kaiser	0.24	0.011	0	0.996
InstCat:2. FH	0.24	0.011	0	0.996
StageCat:1. Stage I	0.139	0.135	0.026	0.799
StageCat:2. Stage II	0.139	0.135	0.026	0.799
DxYearCat:1. 2012	0.094	0.18	0.048	0.977
DxYearCat:2. 2013	0.047	0.18	0.039	0.977
DxYearCat:3. 2014	0.13	0.18	0	0.977
DxYearCat:4. 2015	0.161	0.18	0.018	0.977
DxYearCat:5. 2016	0.045	0.18	0.021	0.977

Appendix 2: Chemotherapy decision and perceived cancer recurrence risk by self-reported GEP test receipt and score, by self-reported GEP test receipt and score: excluding the 246 women reporting unknown test receipt

We excluded the 246 women with unknown GEP test receipt because they may be different from the other two test receipt cohorts in unmeasured dimensions related to health literacy. This allows for a comparison of women who reported they received the test and those that did not receive the test (Table 3; Fig. 3).

Table 3 Survivor's perceived cancer recurrence risk by self-reported GEP test receipt and score

	Sample ($N=587$)	Perceived probability of recurrence	
		Unadjusted risk of recurrence[a] (%)	Adjusted risk of recurrence[b] (%)
Self-report of GEP test result			
High risk score	16 (2.7%)	52.0	63.8[c]
Intermediate risk score	78 (13.3%)	31.3	45.0
Low risk score	230 (39.2%)	21.4	38.3[d]
Unknown risk score	44 (7.5%)	28.0	32.1
No GEP test (referent)	219 (37.3%)	27.8	42.3

Survey Item: "What, in your personal opinion, is the chance of the breast cancer recurring in your lifetime? (0–100%)?"

[a]Not propensity score weighted

[b]Propensity score weighted and adjusted for age, race, education, healthcare delivery site, AJCC stage, year. Model $R^2=0.083$

[c]$P<0.001$ compared to those reporting no GEP test

[d]$P<0.01$ compared to those reporting no GEP test

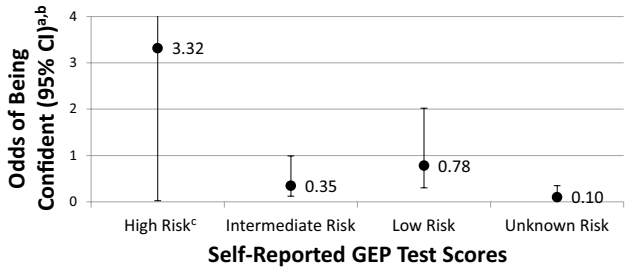

Fig. 3 Adjusted confidence about the chemotherapy decision by self-reported GEP test receipt and score (Survey Item: "How confident are you in the decision you and/or your doctor made about whether or not to have chemotherapy?"). [c]High risk: OR = 3.32, 95% CI (0.03, 9.46). [a]*N* = 456 Respondents. We excluded 131 respondents who answered the question, "Not applicable (chemotherapy was not offered as an option)". [b]Confident includes "Very" or "Completely" Confident. Not Confident includes "Somewhat", "A Little" or "Not At All" Confident. [c]Propensity score weighted and adjusted for age, race, education, site, AJCC stage, and diagnosis year. Model AIC = 229.0

Appendix 3: Logistic regression results for confidence in the chemotherapy decision by self-reported GEP test receipt and score

In this model, we included the *N* = 204 respondents who answered "Not applicable (chemotherapy was not offered as an option)". Confidence in chemotherapy (dependent variable) was specified with three levels: "Confident", "Not Confident" versus "Not Applicable".

Respondents (*N* = 587)	Dependent variable level	Adjusted odds ratio[a]	Confidence limits
GEP test receipt			
No receipt		Referent	
Yes receipt: high risk score	N/A	0.17	0.01–3.03
Yes receipt: high risk score	Confident	1.17	0.14–9.99
Yes receipt: intermediate risk score	N/A	0.01	0.001–0.09
Yes receipt: intermediate risk score	Confident	0.38	0.16–0.89
Yes receipt: low risk score	N/A	0.41	0.17–0.96
Yes receipt: low risk score	Confident	0.93	0.42–2.09
Yes receipt: other/missing/unknown	N/A	0.13	0.05–0.39
Yes receipt: other/missing/unknown	Confident	0.13	0.05–0.34
Unknown test receipt	N/A	0.37	0.17–0.82
Unknown test receipt	Confident	0.42	0.20–0.88

Reference was Not Confident

[a]Propensity score weighted and adjusted for age, race, education, site, AJCC stage, and diagnosis year. Model AIC = 1355.5

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