ORIGINAL REPORT

Adjuvant Chemotherapy Use and Health Care Costs After Introduction of Genomic Testing in Breast Cancer

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A B S T R A C T

Purpose

We assessed the associations between the 21-gene recurrence score assay (RS) receipt, subsequent chemotherapy use, and medical expenditures among patients with early-stage breast cancer.

Patients and Methods

Data from the Pennsylvania Cancer Registry were used to assemble a retrospective cohort of women with early-stage breast cancer from 2007 to 2010 who underwent initial surgical treatment. These data were merged with administrative claims from the 12-month periods before and after diagnosis to identify comorbidities, treatments, and expenditures (n = 7,287). Propensity score–weighted regression models were estimated to identify the effects of RS receipt on chemotherapy use and medical spending in the year after diagnosis.

Results

The associations between RS receipt and outcomes varied markedly by patient age. RS use was associated with lower chemotherapy use among women younger than 55 (19.2% lower; 95% CI, 10.6 to 27.9). RS use was associated with higher chemotherapy use among women 75 to 84 years old (5.7% higher; 95% CI, 0.4 to 11.0). RS receipt was associated with lower adjusted 1-year medical spending among women younger than 55 ($15,333 lower; 95% CI, $2,841 to $27,824) and with higher spending among women who were 75 to 84 years old ($3,489 higher; 95% CI, $857 to $6,122).

Conclusion

RS receipt was associated with reduced use of adjuvant chemotherapy and lower health care spending among women with breast cancer who were younger than 55. Conversely, among women 75 and older, RS testing was associated with a modest increase in chemotherapy use and slightly higher spending. From a population perspective, the impact of RS testing on breast cancer treatment and health care costs is much greater in younger women.

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INTRODUCTION

Adjuvant chemotherapy is used in selected patients with early-stage breast cancer after initial surgical therapy to reduce the risk of cancer recurrence and to improve long-term survival. Historically, this decision has been based on relatively crude, population-based clinical and histopathologic predictors of cancer recurrence risk. However, adjuvant chemotherapy carries the risk of drug-associated toxicity, and, because most women with localized breast cancer will never have recurrent disease,[1-4] they would receive no benefit from adjuvant chemotherapy despite being exposed to the toxicity risk. Therefore, a more precise "personalized" cancer recurrence prediction better informs the chemotherapy decision, both by reducing the use of chemotherapy in patients at low risk of recurrence and by identifying patients at high risk of recurrence who would clearly benefit from chemotherapy.

The 21-gene recurrence score assay (RS; Oncotype DX; Genomic Health, Redwood City, CA) was developed in 2004 to predict the risk of cancer recurrence in women with early-stage breast cancer.[5-9] Continuous recurrence scores generated by the test are categorized into low, intermediate, and high risk of recurrence. A validation study determined that the marginal benefit of chemotherapy was minimal among women with low RS, indeterminate among women with intermediate

RS, and high among women with a high RS.[10] In 2007, the American Society of Clinical Oncology recommended RS testing in women with estrogen receptor/progesterone receptor–positive, node-negative breast cancers to identify appropriate chemotherapy candidates.[11] RS use was also recommended in the National Comprehensive Cancer Network and St. Gallen practice guidelines.[12]

The impact of RS on health care spending is uncertain. Several economic analyses have modeled the cost consequences of testing.[13-16] Most predicted RS would be either cost saving or modestly cost increasing and would improve population-based outcomes by reducing the number of patients experiencing adverse effects of chemotherapy. However, it is unknown whether these anticipated costs and benefits have been realized in practice. Therefore, the goal of this research was to assess the associations between receipt of RS testing and subsequent chemotherapy use and medical expenditures in a population-based cohort of patients with early-stage breast cancer during years when RS testing became widespread (2007 to 2010). Because adjuvant chemotherapy use is strongly correlated with patients' age,[17-19] we also investigated whether the association between RS testing and chemotherapy use varied with age.

PATIENTS AND METHODS

Patients

We used the Pennsylvania Cancer Registry (PCR), a medical provider–mandated database of cancer cases in Pennsylvania, to identify 51,385 Pennsylvania residents with breast cancer diagnosed between January 1, 2007, and December 31, 2010. We selected patients who had T-stage I to IV, node-negative, nonmetastatic, estrogen receptor/progesterone receptor–positive breast cancer. We excluded patients with more than one contemporaneously reported tumor (n = 5,620) or who had noninvasive cancer (n = 9,126). We also excluded patients who lacked clinical pathology data confirming the cancer diagnosis (n = 210), died before definitive diagnosis (n = 372), lacked cancer histology information (n = 776), had metastatic, node-positive, or node-status-unknown disease (n = 13,026), or were male (n = 184). There were 22,071 patients meeting the initial inclusion criteria.

Using Social Security numbers, we linked PCR records to administrative claims from fee-for-service Medicare, which comprised approximately two-thirds of Pennsylvania's Medicare beneficiaries during 2007 to 2010,[20] as well as to claims from Independence Blue Cross (Independence), one of Pennsylvania's largest commercial health insurers.[21] Both payers covered RS testing fully during the study period. To ensure a complete set of cost and outcomes data, we included only the 7,687 patients who had had continuous enrollment in either Medicare or Independence for at least 365 days before and after diagnosis, and who had made a claim for breast surgery within the postdiagnosis 1-year period. We excluded patients whose total medical spending was zero (n = 22), because this suggested the primary insurance coverage was provided by another insurer. Patients who did not have at least 365 days of continuous enrollment in either Medicare or Independence prior to diagnosis were also excluded (n=378). The final study cohort consisted of 7,287 patients with breast cancer (ie, 33% of the 22,071 Pennsylvanians meeting the initial selection criteria).

Predictor Variables

Patients' demographic information and detailed clinical information (eg, cancer stage, tumor size, and so forth) were obtained from the PCR. Clinical comorbidities were abstracted from administrative claims in the year before breast cancer diagnosis using the Elixhauser classification system.[22] To control for each patient's baseline level of health care spending, prediagnosis health care costs were obtained from payment amounts as recorded on claims in the year before cancer diagnosis. Receipt of RS testing was identified in claims via Current Procedural Terminology codes and/or the National Provider Identifier of the RS manufacturer, which billed Medicare directly for the testing.

The University of Pennsylvania's Institutional Review Board approved the study.

Chemotherapy Use and Total Spending

Receipt of chemotherapy within 1 year of diagnosis was determined from each patient's claims via Healthcare Common Procedure Coding System codes indicating chemotherapy, using a previously validated search algorithm.[23] Total 1-year medical spending was measured from the all-payer perspective, including insurer payments as well as copayments and deductibles assigned to patients from the date of cancer diagnosis through 1 year after diagnosis. Expenditures for chemotherapy drugs and their administration were calculated based on the drugs identified in the administrative claims after a classification algorithm devised by Hassett et al.[23] Because we did not have access to prescription drug data, supportive care costs (eg, antiemetics or colony-stimulating factors dispensed by outpatient pharmacies, and so forth) were excluded from our cost estimates. Costs were inflated to 2010 dollars using the Gross Domestic Product price index.[24]

Statistical Analysis

Patients' baseline characteristics were compared by RS receipt using t tests for continuous variables and χ^2 tests for categorical variables. To control for observed confounders, we used a two-stage propensity score framework. First, we estimated the predicted probability that each patient received RS from a logistic regression model that controlled for age, insurer, tumor stage/grade/size, year of diagnosis, patient minority status, total spending in the year before diagnosis, comorbidity burden in the year before diagnosis, and the patient's geographic region[25] (ie, nine clusters of contiguous counties defined by the Pennsylvania Department of Health).

Subsequently, we modeled the associations between RS receipt and both chemotherapy receipt and medical spending with models weighted by the inverse probability of treatment derived from the propensity score.[26] Because we anticipated that age would modify the effect of RS on costs and chemotherapy use because of the strong a priori association between age and chemotherapy use,[17-19] our model specification included a binary indicator variable for RS receipt, indicators for the patient's age category, and interactions between age and RS receipt. We modeled the association between RS receipt and chemotherapy receipt using logistic regression. To facilitate interpretation, we converted the results to predictive margins on the zero-to-one probability scale; this well-validated method produces more clinically interpretable results as compared with odds ratios.[27] Average marginal effects of RS receipt were computed as arithmetic differences between predictive margins within each age category. SEs were calculated using the delta method and Wald tests were used to assess statistical significance.

Total 1-year medical spending and non-chemotherapy-related spending were modeled using generalized linear models with a log link. For all spending models, we ascertained the best-fitting error distribution as the γ distribution by means of the modified Park test,[28] and we reported results on the dollar scale. Because a high proportion of patients did not receive chemotherapy, we modeled chemotherapy spending using a two-part model.[29] The first part was a logistic regression predicting any chemotherapy spending, and the second part was a log-γ generalized linear model of non-zero chemotherapy spending. To enhance interpretation of the interaction between age and RS receipt, we then re-estimated the propensity score–weighted models of chemotherapy receipt and total medical spending, with age entering the model as a quadratic term rather than as a categorical variable. This model's results generated a graphic display of average marginal effects of RS receipt at each decade of age.

All statistical analyses were performed using STATA 13.1 (STATA, College Station, TX).

RESULTS

Cohort Characteristics

Of the 7,287 patients in the final analytic sample, 74% were insured by fee-for-service Medicare and 26% by Independence (Table 1). The mean age of the cohort was 71.6 years; 81% of the cohort was white non-Hispanic; and 45% of patients were residents of Philadelphia or its surrounding counties (Fig 1). The proportion of patients undergoing RS testing increased from 16% among patients diagnosed in 2007 to 28% of patients in 2010 ($P < .001$ for the difference). Relative to patients not receiving RS testing, patients receiving RS testing were younger, were more likely to have

Independence coverage, had fewer comorbidities, and were more likely to have stage I cancer.

RS Testing and Age

The proportion of patients with breast cancer in our cohort who were undergoing RS testing declined with advancing age. Thirty-nine percent of women younger than 55 underwent RS testing, as did 42% of women 55 to 64. However, the percentage of women 65 to 74 undergoing RS testing was lower (28%), whereas only 12% of women 75 to 84 underwent RS testing, and just 1.4% of women 85 and older underwent RS testing ($P < .001$ for the difference across ages).

RS Testing, Age, and Chemotherapy Use

The association between RS testing and chemotherapy use varied markedly by age (Table 2). After adjustment, RS testing was

		RS Testing		
Variable Name	Overall (N = 7,287)	No (n = 5,678)	Yes (n = 1,609)	P
Age at diagnosis, mean (SD), years	71.6 (11.6)	73.4 (11.2)	65.3 (10.8)	< .001
Age category, years				
< 55	733 (10)	447 (7.9)	286 (18)	< .001
55-64	762 (10)	445 (7.8)	317 (20)	
65-74	2,526 (35)	1,831 (32)	695 (43)	
75-84	2,479 (34)	2,179 (38)	300 (19)	
≥ 85	787 (11)	776 (14)	11 (0.7)	
Race/ethnicity				
White, non-Hispanic	5,896 (81)	4,572 (81)	1,324 (82)	.22
Nonwhite or Hispanic	612 (8.4)	481 (8.5)	131 (8.1)	
Race/ethnicity missing	779 (11)	625 (11)	154 (9.6)	
Payer				
Medicare	5,407 (74)	4,453 (78)	954 (59)	< .001
Independence	1,880 (26)	1,225 (22)	655 (41)	
Cancer stage				
I	5,542 (76)	4,280 (75)	1,262 (78)	< .001
II	1,550 (21)	1,224 (22)	326 (20)	
III	87 (1.2)	83 (1.5)	4 (0.2)	
Missing	108 (1.5)	91 (1.6)	17 (1.1)	
Tumor grade				
1	2,018 (28)	1,622 (29)	396 (25)	< .001
2	3,190 (44)	2,331 (41)	859 (53)	
3	1,628 (22)	1,350 (24)	278 (17)	
4	41 (0.6)	39 (0.7)	2 (0.1)	
Missing	410 (5.6)	336 (5.9)	74 (4.6)	
Tumor size, cm				
< 1	2,261 (31)	1,904 (34)	357 (22)	< .001
1-2	3,919 (54)	2,813 (50)	1,106 (69)	
> 2	797 (11)	680 (12)	117 (7.3)	
Missing	310 (4.3)	281 (4.9)	29 (1.8)	
Diagnosis year				
2007	1,876 (26)	1,573 (28)	303 (19)	< .001
2008	1,831 (25)	1,421 (25)	410 (25)	
2009	1,819 (25)	1,408 (25)	411 (26)	
2010	1,761 (24)	1,276 (22)	485 (30)	
Prior year health care spending, $				
Mean (SD)	6,028 (12,400)	6,261 (12,993)	5,205 (9,993)	.003
Median (IQR)	2,244 (4632)	2,288 (4,784)	2,144 (4,192)	.25
Elixhauser[22] comorbidity count				
0	1,388 (19)	989 (17)	399 (25)	< .001
1-3	4,087 (56)	3,157 (56)	930 (58)	
≥ 4	1,812 (25)	1,532 (27)	280 (17)	

NOTE. Data are presented as No. (% of the column's total patients) unless otherwise specified.
Abbreviations: RS, 21-gene recurrence score assay; IQR, interquartile range.
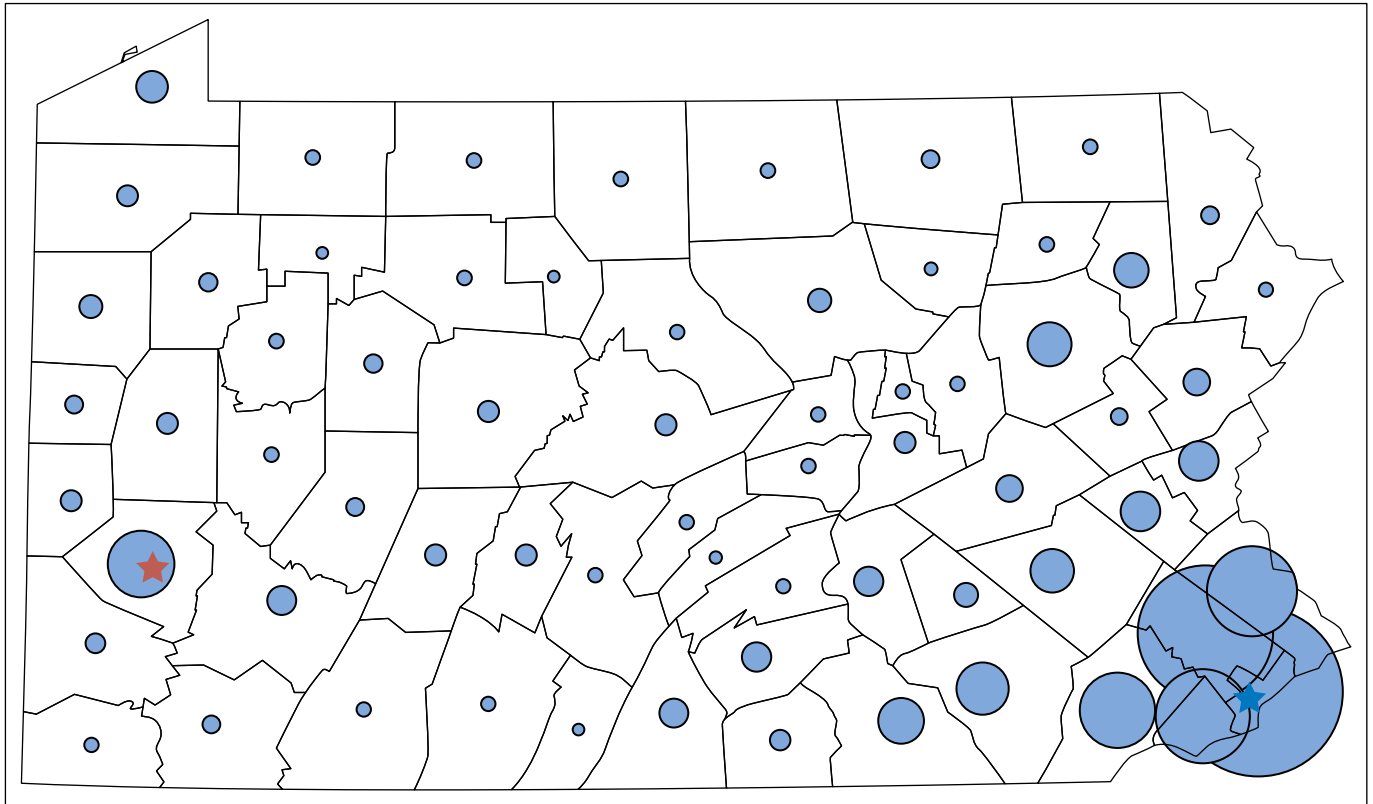
Fig 1. Number of patients in study cohort, by Pennsylvania county of residence. Pennsylvania county borders are indicated in black. The area of the blue circles indicates the relative numbers of patients in the study cohort from each county. The stars indicate the locations of Pennsylvania's two largest cities: Pittsburgh (red) and Philadelphia (blue).

associated with lower chemotherapy use among women younger than 55 (41.5% *v* 60.8%; difference, 19.2% ; 95% CI, 10.6 to 27.9). However, RS testing was associated with higher chemotherapy use among women 75 to 84 (14.4% *v* 8.7%; difference, 5.7% ; 95% CI, 0.4 to 11.0).

The adjusted probability of RS-tested women who received adjuvant chemotherapy also decreased with age. The risk-adjusted probability of an RS-tested woman younger than age 55 years proceeding to adjuvant chemotherapy was 41.5%. This proportion declined to just 14.4% among RS-tested women 75 to 84, and

further declined to 0% among the 11 women 85 and older who underwent RS testing.

Medical Spending

The association between RS testing and spending also varied by age (Table 3). Testing was associated with lower total adjusted 1-year medical spending among women younger than 55 years old ($81,334 *v* $96,667; difference, −$15,333; 95% CI, −$27,824 to −$2,841) and with higher total spending among women who

Age Category, years	Received RS Testing	Percentage of Subgroup Receiving Chemotherapy	Percentage Point Difference in Chemotherapy Receipt Between RS Recipients and Nonrecipients (95% CI)	P
< 55	Yes (n = 286)	41.5	−19.2 (−27.9 to −10.6)	< .001
	No (n = 447)	60.8		
55-64	Yes (n = 317)	35.0	−5.9 (−13.6 to 1.8)	.13
	No (n = 445)	41.0		
65-74	Yes (n = 695)	21.3	1.1 (−3.0 to 5.3)	.59
	No (n = 1,831)	20.2		
75-84	Yes (n = 300)	14.4	5.7 (0.4 to 11.0)	.036
	No (n = 2,179)	8.7		
≥ 85	Yes (n = 11)	0.0	−2.3 (−3.4 to −1.3)	< .001
	No (n = 776)	2.3		

Table 2. Adjusted Percentage of Patients Receiving Chemotherapy, by Age and RS Testing Receipt Status

Abbreviation: RS, 21-gene recurrence score assay.

Table 3. Adjusted Mean 1-Year Health Care Spending after Breast Cancer Diagnosis, by Age and RS Testing Receipt Status

Age, years	Received RS Testing	Total Spending			Chemotherapy Spending			Nonchemotherapy Spending		
		Mean 1-Year Spending ($)	Difference Between RS Recipients and Nonrecipients (95% CI)	P	Mean 1-Year Spending ($)	Difference Between RS Recipients and Nonrecipients (95% CI)	P	Mean 1-Year Spending ($)	Difference Between RS Recipients and Nonrecipients (95% CI)	P
<55	Yes (n = 286)	81,334	−15,333 (−27,824 to −2,841)	.002	16,101	−21,396 (−30,701 to −12,091)	< .001	65,233	6,063 (305 to 11,821)	.04
	No (n = 447)	96,667			37,497			59,170		
55-64	Yes (n = 317)	72,785	−1,733 (−10,561 to 7,095)	.70	10,535	−9,675 (−15,450 to −3,901)	.001	62,251	7,943 (2,225 to 13,660)	.006
	No (n = 445)	74,518			20,210			54,308		
65-74	Yes (n = 695)	39,090	2,442 (−233 to 5,118)	.07	3,905	−2,171 (−3,542 to −800)	.002	35,184	4,613 (2,514 to 6,713)	< .001
	No (n = 1,831)	36,647			6,076			30,571		
75-84	Yes (n = 300)	33,209	3,489 (857, 6,122)	.009	2,093	206 (−1,238 to 1,650)	.78	31,116	3,283 (1,275 to 5,292)	.001
	No (n = 2,179)	29,720			1,887			27,832		
≥85	Yes (n = 11)	32,402	9,788 (−375 to 19,950)	.06	54	−132 (−273 to 9)	.07	32,402	9,974 (−185 to 20,132)	.054
	No (n = 776)	22,614			186			22,428		

NOTE. Data reported are 2010 dollars.
Abbreviation: RS, 21-gene recurrence score assay.

were 75 to 84 years old ($33,209 *v* $29,720; difference, $3,489; 95% CI, $857 to $6,122). Similar to the observed patterns of chemotherapy use by patient age, adjusted 1-year chemotherapy spending was also lower among women who underwent the RS test, with marked variations by age. Chemotherapy costs were lower among RS-tested women younger than 55 ($16,101 *v* $37,497; difference, −$21,396; 95% CI, −$30,701 to −$12,091), RS-tested women 55 to 64 ($10,535 *v* $20,210; difference, −$9,675; 95% CI, −$15,450 to −$3,601), and RS-tested women 65 to 74 ($3,905 *v* $6,076; difference, −$2,171; 95% CI, −$3,542 to −$800). However, there was no statistically significant difference in chemotherapy costs between RS-tested and non-RS–tested women older than 75.

Replacing the age categories in our primary analytic model with age modeled as a quadratic term enabled calculations of the marginal probability of chemotherapy use and the marginal health care cost related to RS testing along the full age continuum. As demonstrated graphically (Fig 2), reduced chemotherapy use and concomitant health care cost savings related to RS testing were restricted to patients younger than 65.

DISCUSSION

In this cohort of Pennsylvania patients with breast cancer treated between 2007 and 2010, we found that, among patients younger than 65, RS testing was associated with lower use of adjuvant chemotherapy as well as lower overall medical expenditures and lower chemotherapy spending in the year after diagnosis. These lower medical costs included the cost of RS testing itself (Medicare's 2010 reimbursement for RS was $3,416); thus, there was strong evidence that the RS test was, on average, cost saving in younger patients. However, among patients 75 to 84, RS testing was associated with increased use of adjuvant chemotherapy and increased overall costs.

There are several possible explanations for the strong modifying effect of age on the relationships among RS testing, chemotherapy use, and costs. A fundamental goal in the development and clinical implementation of "personalized" genomic testing is to reduce the use of unnecessary treatment in patients who are unlikely to benefit. This concept is consistent with our finding that, among younger patients, RS testing was associated with a reduction of adjuvant chemotherapy use, lower total medical spending, and lower chemotherapy spending. We conclude that there is strong evidence that RS testing is meeting this important therapeutic goal among younger women.

However, our findings in older patients likely reflect a more complicated phenomenon with important ramifications for the economic impact of high-cost genomic tests. Compared with younger patients, older patients are less likely to have tumors with high RS scores[10] and are more likely to have chronic medical conditions, frailty, and so on, that would complicate the receipt of chemotherapy. Hence, RS testing may be commonly used among younger patients to "rule out" patients for chemotherapy, but conversely, it may be used among older patients to "rule in" the use of chemotherapy in patients who would otherwise be considered borderline treatment candidates but who had high-risk RS results. In the latter scenario, neither a reduction in chemotherapy use nor a decrease in health care costs would be expected (on average) from the use of RS testing. Hence, at the population level, the impact of RS testing on breast cancer treatment and costs seems to be influenced greatly by patient age.

Limitations

Our results should be interpreted in the context of several limitations. First, because our data did not include results of RS testing, we could not discern whether RS recipients were treated with chemotherapy in a manner consistent with the test results. Second, we excluded patients with node-positive breast cancer
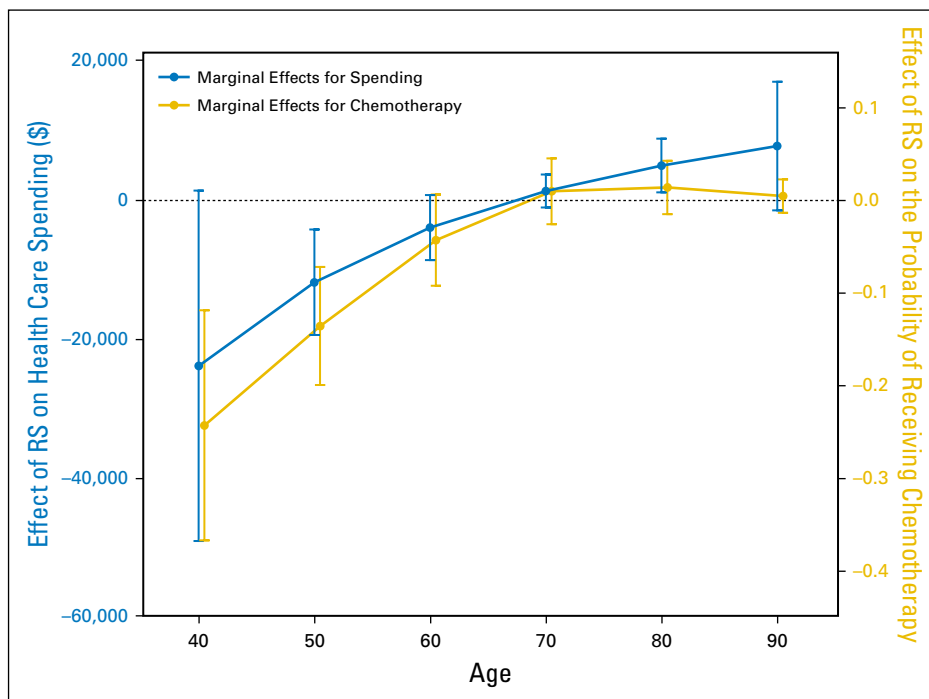

Fig 2. Incremental effect of RS receipt on probability of chemotherapy receipt and incremental effect of RS receipt on total spending. The *x*-axis indicates patient age. The gold dots and connecting lines represent the difference in probability (0 to 1 scale) of chemotherapy use among RS recipients, with probability change plotted on the right-side *y*-axis. The blue dots and connecting lines represent the change in total health care costs (2010 $US) among RS recipients, with cost change plotted on the left-side *y*-axis. The vertical lines indicate 95% CIs for the point estimates. Note that the blue and gold plots are "jittered" slightly along the *x*-axis to avoid overlap. RS, 21-gene recurrence score assay.

because the clinical trials reporting the usefulness of RS testing in these patients were not published until midway through our study period.[30] Third, our cohort undoubtedly included patients who were human epidermal growth factor receptor 2 (HER2 neu) positive, because the PCR did not begin collecting data on HER2 neu status until 2010. Adjuvant chemotherapy is recommended for women with HER2 neu positive breast cancer regardless of RS results,[31] and younger women have a higher incidence of HER2 neu positive breast cancer.[32] Hence, some of the cost differences between RS-tested and non–RS-tested younger women may be a result of the higher costs in HER2 neu–positive patients who did not undergo RS testing and were treated with high-cost (ie, trastuzumab-based) adjuvant chemotherapy. However, the age variation in HER2 neu prevalence is not large enough to explain our findings to entirely.[33] Fourth, our data did not include outpatient prescription drug claims, and therefore, we could not measure supportive care costs derived from high-cost pharmaceuticals dispensed by outpatient pharmacies. Therefore, the chemotherapy-related cost differences we reported may underestimate the true cost differences among groups with differing rates of chemotherapy receipt. Finally, contemporary clinical use of RS testing may differ from use in the period of 2007 to 2010, although marked changes in practice patterns are unlikely.

The follow-up period (median, 3.9 years from diagnosis) was relatively short. Although it is possible that increases in the fraction of high-risk patients treated with adjuvant chemotherapy may have produced a survival benefit, it was not observable in this short time period. Longer follow-up times would be necessary to determine whether RS testing resulted in improved survival.

We do not know which unmeasured patient and physician characteristics may have motivated the decision to pursue RS testing or the use of adjuvant chemotherapy, particularly in elderly patients. We observed that only 11 of the 787 patients older than 84 received RS testing, and none of these 11 patients received chemotherapy. Because chemotherapy was used rarely (ie, < 3%) in the "oldest old," it is unclear if RS testing in these patients influenced clinical decision-making meaningfully.

Because the majority of elderly patients in our cohort were covered by Medicare, whereas most of the younger patients were insured by Independence, it is possible that the age effect that we observed was confounded by insurance type or other (unmeasured) factors. However, our sample included 344 Medicare beneficiaries under 65, as well as 690 Independence patients older than 65, so our statistical models retained substantial ability to control for confounding by insurance type.

Strengths and Contributions

Our cohort was a large, diverse, population-based sample of patients undergoing breast cancer treatment in multiple non-experimental clinical settings, including patients covered by Medicare as well as privately insured patients. We combined clinically detailed cancer registry data with administrative claims data to examine treatment trends across a wide age range of patients, in contrast to studies involving SEER/Medicare data that are generally restricted to patients of at least 65 years of age.

Published cost models for RS testing have hinged on whether the cost of genomic testing outweighed the savings from reduced chemotherapy use. Unsurprisingly, models derived from health systems with low chemotherapy costs found RS testing to be cost increasing,[34-36] whereas studies that assumed higher chemotherapy costs found the RS test to be cost saving.[37,38] Among our study's subcohort of younger women treated in Pennsylvania, RS receipt was related to substantially lower medical spending, thus supporting the predictions of models in which chemotherapy was high cost.

Policy Implications

Our findings have important policy implications for genomic testing. It is encouraging that RS testing was associated with substantial reductions in the use of chemotherapy and medical spending among a population of younger women in real-world practice settings, because this implies that RS testing reduced unnecessary treatment—a critical goal of personalized medicine. However, among the elderly, RS testing may be less likely to rule out potential candidates for chemotherapy, but more likely to provide impetus to use chemotherapy among patients with comorbidities. This scenario is consistent with our finding that—at the population level—RS had minimal influence on overall chemotherapy rates among elderly women. Because the clinical benefit of RS testing is less clear in any patient for whom chemotherapy would be inappropriate, our results highlight the importance of careful selection of older candidates for high-cost testing.

Summary

Among women under 65 with nonmetastatic breast cancer, RS testing was associated with a lower likelihood of chemotherapy and lower medical spending in the year after cancer diagnosis. However, among women 65 or older, RS testing was associated with minimal differences in chemotherapy rates and higher medical spending. From a population perspective, RS testing has a much greater effect on clinical practice patterns and health care costs among younger women.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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