

Factors Associated With Receipt of Breast Cancer Adjuvant Chemotherapy in a Diverse Population-Based Sample

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Submitted January 24, 2012; accepted June 22, 2012; published online ahead of print at www.jco.org on August 6, 2012.

Supported by Grants No. R01 CA109696 and R01 CA088370 from the National Cancer Institute (NCI) to the University of Michigan; by Mentored Research Scholar Grant No. MRSG-09-145-01 from the American Cancer Society (R.J.); by Pathway to Independence Award No. R00NR010750 from the National Institute of Nursing Research (C.R.F.); and by Established Investigator Award No. K05CA111340 in Cancer Prevention, Control, Behavioral, and Population Sciences Research from the NCI (S.J.K.). The collection of Los Angeles County cancer incidence data used in this study was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code §103885; the NCI SEER Program under Contract No. N01-PC-35139 awarded to the University of Southern California, and Contract No. N01-PC-54404 and Agreement No. 1U58DP00807-01 were awarded to the Public Health Institute; the collection of metropolitan Detroit cancer incidence data was supported by NCI SEER under Contract No. N01-PC-35145.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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0732-183X/12/3025-3058/\$20.00

DOI: 10.1200/JCO.2012.41.9564

A B S T R A C T

Purpose

Disparities in receipt of adjuvant chemotherapy may contribute to higher breast cancer fatality rates among black and Hispanic women compared with non-Hispanic whites. We investigated factors associated with receipt of chemotherapy in a diverse population-based sample.

Patients and Methods

Women diagnosed with breast cancer between August 2005 and May 2007 (N = 3,252) and reported to the Detroit, Michigan, or Los Angeles County Surveillance, Epidemiology, and End Results (SEER) registry were recruited to complete a survey. Multivariable analyses examined factors associated with chemotherapy receipt.

Results

The survey was sent to 3,133 patients; 2,290 completed a survey (73.1%), and 1,403 of these patients were included in the analytic sample. In multivariable models, disease characteristics were significantly associated with the likelihood of receiving chemotherapy. Low-acculturated Hispanics were more likely to receive chemotherapy than non-Hispanic whites (odds ratio [OR], 2.00; 95% CI, 1.31 to 3.04), as were high-acculturated Hispanics (OR, 1.43; 95% CI, 1.03 to 1.98). Black women were less likely to receive chemotherapy than non-Hispanic whites, but the difference was not significant (OR, 0.83; 95% CI, 0.64 to 1.08). Increasing age (even in women age < 50 years) and Medicaid insurance were associated with lower rates of chemotherapy receipt.

Conclusion

In this population-based sample, disease characteristics were strongly associated with receipt of chemotherapy, indicating that clinical benefit guides most treatment decisions. We found no compelling evidence that black women and Hispanics receive chemotherapy at lower rates. Interventions that address chemotherapy use rates according to age and insurance status may improve quality of systemic treatment.

J Clin Oncol 30:3058-3064. © 2012 by American Society of Clinical Oncology

INTRODUCTION

Breast cancer fatality rates in the United States are higher among black and Hispanic women than among non-Hispanic whites.¹⁻⁴ Differences in outcomes have been attributed to more advanced stage and a higher likelihood of unfavorable tumor biology features, such as hormone receptor-negative disease and high-grade histology, among black women and Hispanics compared with non-Hispanic whites.⁵⁻²⁶ Lower average socioeconomic status (SES) among black women has been shown to account in part for the racial disparity in outcome.^{6,27-32} There is no corresponding information on Hispanics, but higher rates of poverty and lower rates of health insurance among Hispanics are

likely to contribute to poorer outcomes compared with non-Hispanic whites.³³ In particular, Hispanics with limited English proficiency face additional barriers to high-quality cancer information, decision support, and cancer care.³⁴⁻³⁷

Differences in the use of adjuvant chemotherapy have been proposed as another—and perhaps substantial—explanation for the outcome disparity among black women.³⁸ Studies of chemotherapy use among black women have yielded mixed results, with some studies reporting lower rates of chemotherapy among black women,^{8,16,39-41} and others demonstrating that blacks are at least as likely as whites to be administered chemotherapy.^{18,42-44} The inconsistent findings most likely arise from differences in patient sampling (hospital- or

clinic-based patient samples *v* population-based samples), method of assessing receipt versus nonreceipt of chemotherapy (registry data, claims data, medical record review, patient self-report), and time period and region under study. In contrast to the extensive research on patterns of care in blacks, population-based studies of chemotherapy receipt among Hispanics are extremely limited. Only one population-based study with a large number of Hispanics has been published; this study identified no evidence of undertreatment of Hispanics.⁴⁵ Another study of patients treated in the clinical setting of six hospitals in New York City demonstrated underuse of chemotherapy among Hispanics,³⁹ but other investigators employing clinical samples⁴⁶ or the National Cancer Database⁴⁷ have not shown underuse. Measures of acculturation, such as language preference, have not been included in any of the studies examining chemotherapy use rates among Hispanics.

Determining whether differences in chemotherapy receipt represent unwarranted disparities in chemotherapy is complicated. The higher prevalence of stages II and III disease and of unfavorable histologic features among blacks and Hispanics would increase the benefit of chemotherapy. On the other hand, the higher prevalence of comorbid illness, such as cardiovascular disease and diabetes among blacks^{48,49} and diabetes among Hispanics,^{50,51} could account for what is actually appropriate omission of chemotherapy, because competing causes of mortality decrease the marginal benefit of chemotherapy.^{52,53} In addition, nonclinical characteristics, such as insurance status⁵⁴ and marital status,^{55,56} which vary among racial and ethnic groups, have been associated with chemotherapy treatment patterns and could contribute to relative underuse of chemotherapy among minority women.

This study was designed to address gaps in the literature regarding the clinical and nonclinical factors associated with adjuvant chemotherapy receipt. We hypothesized that black and Hispanic women would be less likely to receive adjuvant chemotherapy than non-Hispanic whites after controlling for clinical and tumor characteristics. We were particularly interested in the role of acculturation and hypothesized that Hispanics who had low levels of acculturation would be at highest risk for omission of adjuvant chemotherapy. This hypothesis was informed by the work of other investigators who have demonstrated disparities in access to health care among Hispanics whose language preference is Spanish.^{34,35,57} In addition, we hypothesized that nonclinical factors, including SES (education, income, insurance status, employment status) and marital status, would contribute to racial and ethnic disparities in receipt of chemotherapy. Finally, we sought to characterize patient-reported reasons for nonreceipt of chemotherapy.

PATIENTS AND METHODS

Study Sample and Data Collection

Our sample included women age 20 to 79 years diagnosed with American Joint Committee on Cancer stages I to III breast cancer or ductal carcinoma in situ (DCIS) between June 2005 and May 2007 and reported to the Surveillance, Epidemiology and End Results (SEER) tumor registry in Los Angeles County or the tricity metropolitan Detroit catchment area. For this analysis, we excluded patients with DCIS (*n* = 458), because chemotherapy is not used in the treatment of noninvasive disease.

We recruited all eligible Hispanics in Los Angeles and all blacks in Los Angeles and Detroit, in addition to a random sample of non-Hispanic

whites. Asian women were not included, because they were being recruited by another investigator in Los Angeles, and the California Cancer Registry requires extensive coordination of patient recruitment between research groups when patients are being recruited to the studies of more than one investigator.

After physician notification of our intention to contact their patients, eligible patients were mailed a recruitment letter, survey, and \$10 cash gift. Patients who were likely to be Hispanic using a surname-based algorithm described previously⁵⁸ were mailed survey materials in English and Spanish. The modified Dillman method was used to maximize survey response. The Dillman method involves multiple methods of follow-up including postcard reminders, second mailing of questionnaires, and telephone calls.⁵⁹ Survey responses were then merged with demographic and clinical data from the SEER registries. The institutional review boards of the University of Michigan, University of Southern California, and Wayne State University approved all study procedures.

Measures

The dependent variable was patient report of receipt of chemotherapy. Patient self-report of chemotherapy has been shown to be highly accurate and valid when compared with medical record review⁶⁰⁻⁶² and superior to data from cancer registries.⁶³ Independent variables included clinical characteristics (age and comorbid conditions, both obtained from the patient survey), disease characteristics obtained from SEER (American Joint Committee on Cancer stage, estrogen receptor and progesterone receptor status, and histologic grade), and nonclinical factors obtained from the patient survey (race/ethnicity, educational attainment, insurance status, marital status, employment status, and income). For patients with missing income information, we assigned a value of "missing" and included the patients with missing income (but otherwise complete information) in the analyses. The SEER registries were not collecting information on human epidermal growth factor receptor 2 (HER2) status during the recruitment period of this study.

Acculturation in Hispanics was measured using the Short Acculturation Scale for Hispanics (SASH),^{64,65} a validated measure of acculturation in Hispanic populations.^{66,67} The SASH includes five questions based on the respondent's language preference, each of which is answered on a 5-point scale from 1 (only English) to 5 (only Spanish). Responses to the SASH were dichotomized into low (4 or 5) versus high acculturation (1, 2, or 3). Our previous work evaluated the performance of the SASH by comparing it with other measures of acculturation, including the number of years the respondent has lived in the United States and the countries of origin of the respondent's mother and father.⁵⁸

Patient race/ethnicity was then categorized into four groups: black, Hispanic with low acculturation, Hispanic with high acculturation, and non-Hispanic white. Respondents who did not receive chemotherapy were asked to select reasons from a list and could enter free text. Respondents could select more than one reason. Patients for whom any of the covariates were missing were excluded from the model, with the exception of income.

Statistical Analyses

Multivariable logistic regression analyses of chemotherapy receipt included all clinical and nonclinical factors as independent variables. We also controlled for registry (Detroit *v* Los Angeles). Population weights were included in the multivariable analyses to account for differential selection by race, ethnicity, and nonresponse. For patients with missing income information, we assigned a value of "missing" and included the 243 patients (17%) with missing income (but otherwise complete information) in the analyses. We did so because excluding these patients would reduce power and generalizability with regard to our focus on race/ethnicity and chemotherapy use. We tested for all two-way interactions; none significantly affected the main results we present here, and they are not included in the model.

Reasons for not receiving chemotherapy were tabulated under physician related or patient related. These results were then tabulated to present the

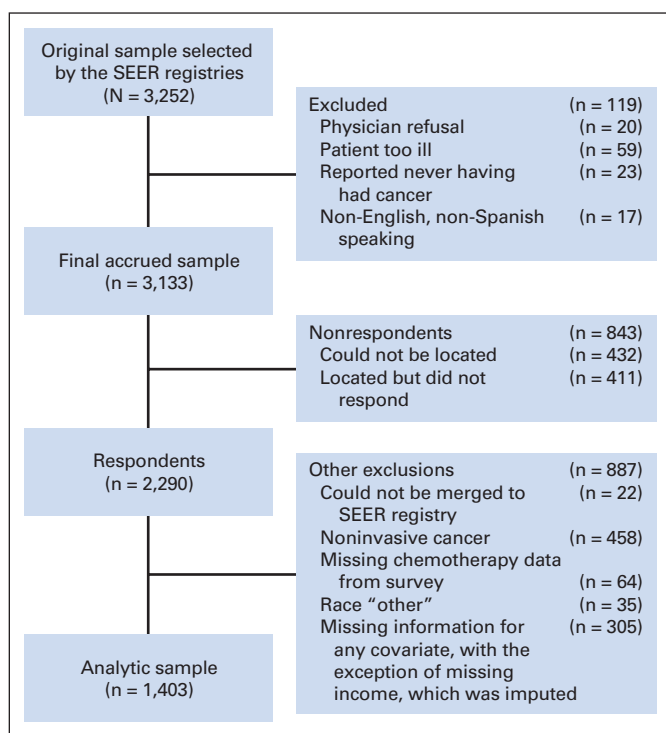


Fig 1. Study sample flow diagram.

frequency with which each reason was reported; reasons for not receiving chemotherapy were compared by race/ethnicity.

All statistical tests were two sided, and a P value less than .05 was considered statistically significant for bivariate and multivariate analyses. All analyses were performed using SAS software (SAS Institute, Cary, NC).

RESULTS

The original sample selected from the SEER registries included 3,252 patients. After physician and patient contact, 119 were excluded (Fig 1). Of the remaining patients, 2,290 (73.1%) returned a survey. After exclusions, most of which were because of a diagnosis of DCIS ($n = 458$) and missing information for any of the covariates ($n = 305$; range of missing covariates, 0% to 7%), the final analytic sample was 1,403 participants (Table 1). Fifty-seven percent of black women, 61% of Hispanics, and 69% of non-Hispanic whites returned a completed questionnaire ($P < .001$). The response rate did not differ by age.

Participant Characteristics and Factors Associated With Receipt of Chemotherapy

Compared with non-Hispanic whites, black women and Hispanics were more likely to have been diagnosed at a younger age ($P = .002$) and to have stage II or III disease ($P = .001$), hormone receptor–negative disease ($P < .001$), and higher-grade histology ($P < .001$), as has been seen in our previous studies and the work of other investigators.^{6-9,12,13,16-20,25,26} Black women and Hispanics were also significantly more likely to have a household income less than \$20,000 and to have less than a high school degree than non-Hispanic whites. In addition, black women were more likely than non-Hispanic whites and Hispanics to have two or more comorbid conditions and to

Table 1. Patient Demographic and Clinical Characteristics ($n = 1,403$)

Characteristic	No.	%
Age group, years		
< 40	103	7
40-49	299	21
50-59	401	29
60-69	366	26
≥ 70	234	17
Comorbid conditions		
None	584	42
One	398	28
≥ Two	421	30
Stage		
I	654	47
II	537	38
III	212	15
Hormone receptor status		
ER and/or PR positive	1,050	75
ER negative/PR negative	353	25
Histologic grade		
1	267	19
2	518	37
3	618	44
Income		
< \$20,000	246	18
\$20,000 to \$69,000	542	39
≥ \$70,000	372	26
Missing	243	17
Insurance status		
None	97	7
Other	827	59
Medicaid	132	9
Medicare	347	25
Education		
Not high school graduate	262	19
High school graduate	287	20
Some college	498	36
College graduate	356	25
Marital status		
Not married or partnered	603	43
Married/partnered	800	57
Employment status		
Employed	826	59
Not employed	577	41
Race/ethnicity		
Black	361	26
Low-accultured Hispanic	186	13
High-accultured Hispanic	183	13
Non-Hispanic white	673	48

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

be single. There was a nonsignificant difference in employment status among racial/ethnic groups.

Chemotherapy receipt was reported by 293 black women (65%), 172 low-accultured Hispanics (71%), 143 high-accultured Hispanics (65%), and 462 non-Hispanic whites (57%; $P < .001$). In multivariable analyses (Table 2), tumor characteristics (higher stage, negative hormone receptor status, and higher tumor grade), younger age (Fig 2), being Hispanic, and having insurance other than Medicaid were associated with receipt of chemotherapy.

Table 2. Logistic Regression Modeling of Factors Associated With Receipt of Chemotherapy (n = 1,403)

Factor	OR	95% CI	P*
Age, years	0.91	0.90 to 0.93	< .001
Comorbid conditions			.547
None	Referent		
One	0.95	0.75 to 1.21	
≥ Two	1.10	0.83 to 1.46	
Stage			< .001
I	Referent		
II	17.29	13.73 to 21.69	
III	52.29	33.67 to 81.22	
Hormone receptor status			< .001
ER and/or PR positive	Referent		
ER negative/PR negative	3.34	2.51 to 4.44	
Histologic grade			< .001
1	Referent		
2	2.91	2.24 to 3.78	
3	4.39	3.27 to 5.88	
Income			.908
< \$20,000	Referent		
\$20,000 to \$69,000	0.94	0.67 to 1.31	
≥ \$70,000	0.97	0.65 to 1.46	
Education			.440
Not high school graduate	Referent		
High school graduate	0.78	0.52 to 1.18	
Some college	1.17	0.77 to 1.77	
College graduate	0.73	0.47 to 1.14	
Insurance status			< .001
Medicare	Referent		
Medicaid	0.59	0.37 to 0.95	
Other	1.50	1.09 to 2.08	
None	1.77	0.98 to 3.19	
Marital status			.246
Married/partnered	Referent		
Not married or partnered	1.15	0.91 to 1.45	
Employment status			.092
Employed	Referent		
Not employed	1.23	0.97 to 1.57	
Race/ethnicity			< .001
Non-Hispanic white	Referent		
Black	0.83	0.64 to 1.08	
Low-acclulturated Hispanic	2.10	1.28 to 3.44	
High-acclulturated Hispanic	1.28	0.89 to 1.85	

NOTE. Model is adjusted for site (registry).
Abbreviations: ER, estrogen receptor; OR, odds ratio; PR, progesterone receptor.
*P values refer to tests for significance of the variables in the adjusted model.

Black women had an odds ratio (OR) of receiving chemotherapy of 0.83 (95% CI, 0.64 to 1.08), a difference that is not significant. Among Hispanics, low-acclulturated Hispanics (OR, 2.00; 95% CI, 1.31 to 3.04) and high-acclulturated Hispanics (OR, 1.43; 95% CI, 1.03 to 1.98) were both significantly more likely to receive chemotherapy than non-Hispanic white women. The odds of receiving chemotherapy decreased with increasing age (OR, 0.91; 95% CI, 0.90 to 0.92). That is, each additional year of age had 0.91 odds of receipt of chemotherapy compared with the age preceding it. Comorbidity, education, income, and marital status were not independently associated with receipt of chemotherapy. No meaningful interactions were identified in the fully interacted models,

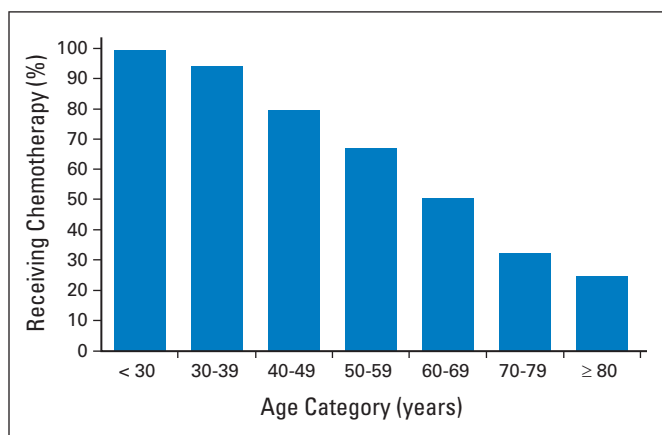


Fig 2. Percentage of patients receiving adjuvant chemotherapy by age category adjusted for comorbidity, stage, hormone receptor status, grade, income, insurance, education, marital status, employment status, registry (Detroit v Los Angeles), and race/ethnicity.

and as described, interaction terms were not included in the multivariable analyses.

Patient-Reported Reasons for Not Receiving Chemotherapy

Table 3 shows the reasons that patients reported for not receiving chemotherapy. Most patients attributed nonreceipt of chemotherapy to physician recommendation (74%) or lack of physician discussion about chemotherapy (3%).⁶⁸ Patient-related reasons for not receiving chemotherapy included a preference not to receive chemotherapy when the physician left it to the patient to make a decision (16%) and concerns about adverse effects or complications (9%), desire to avoid hair loss (3%), cost concerns (1%), and concern about chemotherapy being a burden to self or family (3%). The reasons for omission of chemotherapy did not differ by race/ethnicity.

DISCUSSION

In summary, in this large, diverse, population-based sample of women diagnosed with breast cancer between 2005 and 2007, we

Table 3. Patient-Reported Reasons for Not Receiving Chemotherapy (n = 633)*

Reason	No.	%
Physician related		
My physician(s) said I did not need it	471	74
My physician(s) did not discuss it with me	18	3
Patient related		
My physician(s) left it up to me and I chose not to	103	16
I was worried about side effects or complications	59	9
I did not want to lose my hair	18	3
I was worried about the cost	6	1
It would have been too much of a burden on me or my family	17	3
No reason selected	8	1

*Respondents could select more than one reason.

found no compelling evidence of adjuvant chemotherapy underuse among black or Hispanic women regardless of level of acculturation. In fact, Hispanics had statistically significantly higher odds of receiving chemotherapy than the other racial/ethnic groups after controlling for measurable factors. Low-acculturated Hispanics had the highest odds of receiving chemotherapy. These findings were contrary to our hypotheses and may be related to the types of facilities in which Hispanics receive specialty care. SES, measured via education attainment and income, and marital status were not associated with receipt of chemotherapy. With the exception of age and insurance, the only correlates of chemotherapy receipt were disease characteristics associated with a higher risk of distant recurrence and greater benefit of chemotherapy (higher stage, higher grade, negative hormone receptor status). Most patients who did not receive chemotherapy attributed omission to their physicians' recommendations (or perhaps their perceptions of physicians' recommendations).

The relationship between increasing age and decreasing use of chemotherapy (Fig 2) in our sample is consistent with previous research.⁶⁹⁻⁷² Despite the fact that older women with a life expectancy of 5 or more years reap the same degree of risk reduction with chemotherapy as younger women,^{73,74} increasing age was an independent factor associated with chemotherapy receipt. Rates of chemotherapy receipt in our sample of older patients were higher than those in earlier time periods,^{69,70} suggesting that dissemination regarding the benefits of chemotherapy in otherwise healthy older patients is taking place. There is, however, additional room for improvement in the care of older women.⁷⁵

The association between chemotherapy receipt and age among women younger than age 50 years is particularly notable. Although increasing age is associated with lower rates of chemotherapy receipt, as described, age has not been shown to play a role in receipt of chemotherapy in women younger than age 50 years. This novel finding suggests that in our sample, age was incorporated into chemotherapy decision making along the entire continuum of age. Unmeasured tumor features, such as HER2 positivity and presence of angiolymphatic invasion, have been shown to be more common in younger women in large, single-institution studies^{68,76} and may have been more common in our participants younger than age 50 years compared with older women. If present, such differences could account for the higher rates of chemotherapy receipt in the younger women in our sample.

The absence in our study of information on HER2 status and angiolymphatic invasion limits the ability to explain not only rates of chemotherapy among the younger patients but also the independent association between Hispanic ethnicity and chemotherapy receipt. HER2 status was not available in the SEER registries for patients in our sample. Treatment guidelines in place at the time our patients were diagnosed incorporated both HER2 status and the presence of angiolymphatic invasion (as a high-risk feature), and in fact, both features have been shown to predict use of chemotherapy in women with node-negative, estrogen receptor-positive disease.⁷⁷ Higher rates of angiolymphatic invasion or HER2-positive disease have been identified in some⁷⁶ but not all¹⁸ studies that included Hispanics. There is no evidence that HER2 status differs between black and non-Hispanic white women.^{18,78}

We also identified an association between insurance status and chemotherapy receipt. Patients with insurance indicated as "other"

most likely had private insurance, and these patients had higher odds of receiving chemotherapy compared with patients with Medicare; Medicaid insurance was associated with chemotherapy omission, as has been seen in other studies.⁴⁷

In addition to lacking data on angiolymphatic invasion and HER2 status, there are several other limitations of this study. We did not have information on chemotherapy regimen, dose or dose-intensity, or rates of completion of chemotherapy. Previous work has shown that black women and women of lower SES are more likely to receive nonstandard, often single-agent, chemotherapy regimens⁷⁹ and intentionally reduced doses of chemotherapy with the first cycle of chemotherapy.⁸⁰ Others have shown that black women participating in clinical trials receive lower doses of chemotherapy over the course of their chemotherapy than white women.⁸¹ Thus, although we have demonstrated no differences in the rate of chemotherapy according to race/ethnicity, we cannot state that the quality of chemotherapy is equivalent across different patient subgroups.

Another limitation of this study is that our sample was drawn from only two regions in the United States and included only patients who speak English or Spanish, so we cannot necessarily generalize our findings to other regions or other patient groups. Wu et al⁴⁵ recently demonstrated chemotherapy underuse according to area-level SES in seven state registries, whereas our study did not demonstrate SES disparities (using individual-level measures of SES). It is possible that the two regions we included in our study differ from care in those seven states in terms of urbanicity and availability of specialty cancer services. Finally, response bias may be playing a role in that those who participated in the study may differ in unmeasured ways from those who did not participate in the study.

In conclusion, it seems that race and ethnicity need not pose barriers to receipt of adjuvant chemotherapy. Such a finding is encouraging as we continue to address racial and ethnic disparities in the receipt of quality cancer care. Nonetheless, differences and disparities do exist in receipt of chemotherapy according to age, insurance, and employment status. These findings identify opportunities to continue to improve the quality of breast cancer care.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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

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Final approval of manuscript: All authors

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