

Original Investigation

Characteristics Associated With Differences in Survival Among Black and White Women With Breast Cancer

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IMPORTANCE Difference in breast cancer survival by race is a recognized problem among Medicare beneficiaries.

OBJECTIVE To determine if racial disparity in breast cancer survival is primarily attributable to differences in presentation characteristics at diagnosis or subsequent treatment.

DESIGN, SETTING, AND PATIENTS Comparison of 7375 black women 65 years and older diagnosed between 1991 to 2005 and 3 sets of 7375 matched white control patients selected from 99 898 white potential controls, using data for 16 US Surveillance, Epidemiology and End Results (SEER) sites in the SEER-Medicare database. All patients received follow-up through December 31, 2009, and the black case patients were matched to 3 white control populations on demographics (age, year of diagnosis, and SEER site), presentation (demographics variables plus patient comorbid conditions and tumor characteristics such as stage, size, grade, and estrogen receptor status), and treatment (presentation variables plus details of surgery, radiation therapy, and chemotherapy).

MAIN OUTCOMES AND MEASURES 5-Year survival.

RESULTS The absolute difference in 5-year survival (blacks, 55.9%; whites, 68.8%) was 12.9% (95% CI, 11.5%-14.5%; $P < .001$) in the demographics match. This difference remained unchanged between 1991 and 2005. After matching on presentation characteristics, the absolute difference in 5-year survival was 4.4% (95% CI, 2.8%-5.8%; $P < .001$) and was 3.6% (95% CI, 2.3%-4.9%; $P < .001$) lower for blacks than for whites matched also on treatment. In the presentation match, fewer blacks received treatment (87.4% vs 91.8%; $P < .001$), time from diagnosis to treatment was longer (29.2 vs 22.8 days; $P < .001$), use of anthracyclines and taxols was lower (3.7% vs 5.0%; $P < .001$), and breast-conserving surgery without other treatment was more frequent (8.2% vs 7.3%; $P = .04$). Nevertheless, differences in survival associated with treatment differences accounted for only 0.81% of the 12.9% survival difference.

CONCLUSIONS AND RELEVANCE In the SEER-Medicare database, differences in breast cancer survival between black and white women did not substantially change among women diagnosed between 1991 and 2005. These differences in survival appear primarily related to presentation characteristics at diagnosis rather than treatment differences.

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For 20 years health care investigators in United States have been keenly aware of racial disparities in survival among women with breast cancer.¹⁻⁴ Numerous reports have not only identified and documented worse outcomes in black patients with breast cancer⁵⁻⁷ but have suggested potential reasons for the disparities based on differences in screening,^{5,8,9} presentation,^{5,10} comorbid conditions on presentation,^{5,10} tumor biology,^{5,11,12} stage,^{5,6} treatment,^{5,13,14} and socioeconomic status.^{7,15}

This study examined the extent of the racial disparity in breast cancer survival in the Medicare population, with the main goal of addressing why the disparity exists. The analysis used matching to compare the entire population of blacks in the Surveillance, Epidemiology and End Results (SEER)-Medicare database to 3 white populations individually paired to the black population to answer questions about the origins of the racial disparity, specifically, (1) are white women who present like black women treated in the same way as black patients, and if not, (2) to what extent does a difference in treatment explain the disparity in survival?

This study also examined the magnitude of the disparity; whether the disparity changed between the era before introduction of taxanes (1991-1998) and the era after introduction of taxanes (1999-2005); the relative contributions of presentation at diagnosis, and treatment after presentation, to differences in survival experienced by these groups; and how socioeconomic variables relate to the overall disparity.

Methods

Patient Population

The research protocol was approved by the institutional review board of The Children's Hospital of Philadelphia. We obtained the SEER-Medicare database for the years 1991-2005 for 16 SEER sites throughout the United States. For each patient, the entire SEER data set^{16,17} was merged with Medicare Part A, Part B, outpatient claims, and the Social Security denominator file, which was updated December 31, 2009, for this data set, providing a minimum of 4 years of follow-up for all patients.

For all analyses of trends over time, we analyzed the 12 SEER sites collecting data over the entire span of the study. For analyses not considering trends over time, we used all 16 sites.

Defining Patient Characteristics

We defined race using the SEER algorithm¹⁸ and compared black or African American with white non-Hispanic and white-Hispanic together for the primary analysis (results were similar if only non-Hispanic white patients were used as controls, because Hispanic white patients comprised only 3.8% of the total white population and because never more than 4.6% of any set of matched pairs included Hispanic whites). Patient comorbid conditions such as congestive heart failure, diabetes, past acute myocardial infarction, stroke, hypertension, and 21 other conditions noted in the eAppendix (Supplement) were defined with *International Classification of Diseases, Ninth Revision, Clinical Modification* codes¹⁹⁻²² and collected from Medi-

care claims (inpatient, outpatient, and physician bills) during a 3-month period prior to diagnosis.

Tumor Biology

Patient tumor characteristics, including stage, size, grade, estrogen receptor status, number of nodes dissected, and number of positive nodes, were obtained through the SEER database.

Treatment Variables

We defined treatment based on information from Medicare and SEER data. Surgery and chemotherapy were defined by billing codes in the Medicare claims; surgery was classified into conserving and nonconserving surgery types. Radiation therapy was determined by billing codes and SEER data. All definitions are provided in the eAppendix (Supplement).

Statistical Analysis

Matching Methodology

We included all black patients for each match, so the black study population was constant and fully representative of black patients in the SEER population. The white population changed according to the variables used in the match. We created 3 matched analyses, each using 1 white patient and 1 black patient in each matched pair. The demographics analysis matched white to black patients on age, year of diagnosis, and SEER site; the presentation analysis matched pairs of black and white patients on the demographics variables as well as presentation characteristics (comorbid conditions and tumor biology [stage, size, grade, and estrogen receptor status]); and the treatment analysis matched patients on demographics and presentation variables as well as relevant treatment variables such as surgery, radiation therapy, and chemotherapy, as well as individual types of surgery and chemotherapy.

As has been suggested by Rubin,²³⁻²⁵ matching was performed first, without viewing outcomes. All matching was implemented using the PROC ASSIGN²⁶ function in SAS, providing optimal matches that minimize the distance between cases and controls.²⁷ We used near-fine balance for SEER site in the treatment match.²⁸⁻³⁰ This meant that matches were geographically balanced, with each SEER site contributing almost identical numbers of white and black patients (eAppendix [Supplement]).

Matching on patient covariates in the presentation and treatment matches also included a score predicting black race (a propensity score), and a risk score based on a Charlson score.³¹⁻³⁴ The propensity scores used for the matches came from a logistic regression of black vs white race on the variables to be controlled in the match (eAppendix [Supplement]). Matching on a propensity score tends to balance variables in the score.^{27,35,36}

Statistical Tests

For each matching variable we verified that the match balanced the variables it intended to balance. We examined the standardized difference for each matching variable, which is the mean difference between black and white as a fraction of the standard deviation (SD) before matching.^{20,37,38} We aimed

to achieve standardized differences below 0.1 SDs.^{20,27,37,38} We also assessed how closely we achieved balance using 2-sample randomization tests, specifically the Wilcoxon rank-sum test for each continuous covariate, Fisher exact test for each binary covariate, and a single cross-match test for all covariates in a given match.³⁹ The cross-match test estimates a summary measure, ϵ (range, 0-1), that compares the actual match to the balance obtained by complete randomization. $\epsilon = 0.5$ suggests that the match resembled a randomized trial, indicating a successful match, whereas $\epsilon = 0$ signifies that the covariates always could be used to perfectly separate black patients from white patients—ie, a totally unsuccessful match—and $\epsilon > 0.5$ signifies better balance on observed covariates than expected by randomization.

When testing the hypothesis of no difference in outcomes between the matched black and white patients, the Wilcoxon sign-rank statistic⁴⁰ was used for continuous outcomes, the McNemar statistic⁴¹ for binary outcomes, and the Prentice-Wilcoxon statistic^{42,43} for survival outcomes. When modeling survival differences over time, we used the paired version of the Cox proportional hazards model.⁴⁴ We obtained standard errors for the white-black paired differences in survival utilizing the bootstrap method.⁴⁵ White-to-white comparisons were made using the same methods applied to the exterior match of nonoverlapping white control groups.^{42,43,46} $P \leq .05$ (2-tailed) was considered statistically significant. All tests were performed using SAS version 9.2 for UNIX (SAS Institute Inc)⁴⁷ or R version 2.13.1.⁴⁸

Results

Quality of Matches: Matching Results

A total of 107 273 patients were newly diagnosed with invasive breast cancer over all 16 sites, including 7375 black patients and 99 898 white patients from whom control patients were matched. **Table 1** reports the total black population and 3 white populations matched sequentially to the black population.

The 3 matched white groups sequentially remove aspects of the disparity while leaving other aspects in place so as to develop an understanding of how the disparity occurs. In each match, the variables controlled in that match were closely balanced, with no standardized difference ever exceeding 0.09 SDs. In a given match, unmatched variables exhibit differences that reveal aspects of the disparity. For example, among all black patients with breast cancer, 26% had a diagnosis of diabetes, whereas whites matched for age, year of diagnosis, and SEER site had a much lower rate of diabetes (15.3%). The presentation match then removed the difference in diabetes and many other characteristics describing patients at the time of cancer diagnosis; eg, in the presentation match, 25.9% of whites had diabetes, similar to the rate among blacks. The treatment match also identified whites with a similar rate of diabetes as blacks but also controlled for cancer treatment. Similar matching results for tumor biology and treatment variables were also achieved.

We checked the simultaneous balance of all matched covariates using the cross-match test and its summary measure ϵ .^{39,49} For each match, the multivariate imbalance in matched covariates was smaller than expected by random assignment to groups ($P > .99$, $\epsilon = 0.98$ for demographics; $P > .99$, $\epsilon = 0.65$ for presentation; $P > .99$, $\epsilon = 0.53$ for treatment). Thus, in each matched sample, using the matched covariates to identify black and white patients performed no better than chance.

Examining Treatment Differences by Race

Table 1 also reports information on differences in treatment by race. Overall, 12.6% of black patients did not have evidence of receiving any treatment for their breast cancer, compared with 5.9% of whites ($P < .001$, black patients vs demographics-matched white patients). However, even among whites who presented with the same patient and tumor characteristics as blacks, 8.2% did not have evidence of treatment ($P < .001$, blacks vs presentation-matched whites). Similarly, among those who did receive treatment, mean time from diagnosis to treatment was longer among blacks than among demographics-matched whites, 29.2 days vs 22.5 days ($P < .001$), and even among whites who presented like blacks, the delay was 22.8 days ($P < .001$). Blacks were also more likely to have very long delays in treatment. Whereas 5.8% of blacks did not initiate treatment within the first 3 months from diagnosis, only 2.5% of whites who presented like blacks displayed this gap ($P < .001$). Chemotherapy was also different for blacks and whites: 3.7% of blacks received both an anthracycline and a taxane, compared with 5.0% of whites matched to blacks at presentation ($P < .001$). Blacks also received breast-conserving surgery without any other treatment more often than presentation-matched whites (8.2% vs 7.3%, $P = .04$).

Survival Results

Figure 1 shows the survival of black patients and the corresponding white matched pairs for all 16 SEER sites in patients diagnosed with breast cancer between 1991 and 2005. Median follow-up time after diagnosis for censored patients was 7.6 years (interquartile range [IQR], 5.7-10.1) for blacks; 7.8 years (IQR, 5.8-10.5) for demographics-matched whites; 7.7 years (IQR, 5.8-10.4) for presentation-matched whites; and 7.6 years (IQR, 5.6-10.2) for treatment-matched whites. **Table 2** reports the 2- and 5-year survival differences, and median survival time, for the black and matched white populations. The absolute survival difference between blacks and demographics-matched whites at 5 years was 12.9% ($P < .001$).

Figure 1 also shows the white presentation match, representing white patients who had the age, year of diagnosis, and SEER site variables in the match but who also were matched on patient characteristics including comorbid conditions and tumor characteristics, including, but not limited to, stage, size, grade, and estrogen receptor status. The absolute difference in 5-year survival between the presentation-matched white population and the black total population was 4.4% ($P < .001$).

We also observed the treatment-matched white population, controlling all the variables in the presentation match as well as specific treatments including type of surgery, radiation therapy, and chemotherapy. The absolute difference in

Table 1. Quality of Matches^a

Variable	Matched White Patients, No. (%)				All Whites (Unmatched) (n = 99 898)
	Black Patients (n = 7375)	Treatment Match (n = 7375)	Presentation Match (n = 7375)	Demographics Match (n = 7375)	
Age at diagnosis, mean y	75.7	75.7	75.8	75.7	76.3 ^d
Year of diagnosis, mean	1999.3	1999.3	1999.3	1999.3	1999.0 ^d
CHF	710 (9.6)	654 (8.9)	675 (9.2)	435 (5.9) ^d	5785 (5.8) ^d
Diabetes	1917 (26.0)	1931 (26.2)	1908 (25.9)	1130 (15.3) ^d	12 762 (12.8) ^d
Stage					
I	2340 (31.7)	2282 (30.9)	2380 (32.3)	3359 (45.5) ^d	45 482 (45.5) ^d
II	2429 (32.9)	2461 (33.4)	2453 (33.3)	2195 (29.8) ^d	29 537 (29.6) ^d
III	800 (10.8)	826 (11.2)	736 (10.0)	507 (6.9) ^d	6427 (6.4) ^d
IV	676 (9.2)	676 (9.2)	676 (9.2)	376 (5.1) ^d	5023 (5.0) ^d
Missing	1130 (15.3)	1130 (15.3)	1130 (15.3)	938 (12.7) ^d	13 429 (13.4) ^d
Grade					
I	885 (12.0)	880 (11.9)	951 (12.9)	1304 (17.7) ^d	18 349 (18.4) ^d
II	2177 (29.5)	2205 (29.9)	2201 (29.8)	2724 (36.9) ^d	36 679 (36.7) ^d
III	2404 (32.6)	2343 (31.8)	2390 (32.4)	1813 (24.6) ^d	24 421 (24.4) ^d
IV	144 (2.0)	132 (1.8)	120 (1.6)	106 (1.4) ^b	1746 (1.7)
Missing	1765 (23.9)	1815 (24.6)	1713 (23.2)	1428 (19.4) ^d	18 703 (18.7) ^d
Estrogen receptor positive	3908 (53.0)	3878 (52.6)	3907 (53.0)	4759 (64.5) ^d	67 035 (67.1) ^d
Tumor size, cm					
3-<4	769 (10.4)	780 (10.6)	725 (9.8)	597 (8.1) ^d	8098 (8.1) ^d
≥4	1594 (21.6)	1516 (20.6)	1511 (20.5)	863 (11.7) ^d	11 616 (11.6) ^d
Unknown	900 (12.2)	913 (12.4)	911 (12.4)	647 (8.8) ^d	8652 (8.7) ^d
Nodes, mean					
Removed	7.7	7.5	8.3 ^d	8.3 ^d	8.2 ^d
Positive	1.7	1.6	1.9	1.3 ^d	1.3 ^d
Ratio of nodes positive to removed	0.16	0.15	0.16	0.11 ^d	0.11 ^d
No treatment	927 (12.6)	927 (12.6)	608 (8.2) ^d	433 (5.9) ^d	6487 (6.5) ^d
Mastectomy only	2221 (30.1)	2285 (31.0)	2239 (30.4)	2364 (32.1) ^c	32 913 (32.9) ^d
Breast-conserving surgery					
Plus radiation only	1067 (14.5)	1095 (14.8)	1215 (16.5) ^d	1584 (21.5) ^d	20 532 (20.6) ^d
Surgery only (without other treatment)	608 (8.2)	562 (7.6)	538 (7.3) ^b	542 (7.3) ^b	7553 (7.6) ^b
Chemotherapy					
Doxorubicin, no taxane	534 (7.2)	502 (6.8)	561 (7.6)	441 (6.0) ^c	5341 (5.3) ^d
Doxorubicin + taxane	273 (3.7)	303 (4.1)	367 (5.0) ^d	314 (4.3)	3122 (3.1) ^c
Days from diagnosis to treatment, of those who received treatment, mean	29.2	29.0	22.8 ^d	22.5 ^d	22.0 ^d
No treatment in 3 mo, %					
Of those who received treatment	1300 (5.8)	1291 (5.6)	780 (2.5) ^d	579 (2.1) ^d	8444 (2.1) ^d
All patients	1300 (17.6)	1291 (17.5)	780 (10.6) ^d	579 (7.9) ^d	8444 (8.5) ^d

Abbreviation: CHF, congestive heart failure.

^a The "Variable" column reports the variables controlled in some of the 3 matches but allowed to vary naturally in other matches. The 29 of a total of 140 variables used in the treatment match (which included all the variables in the study), along with all 140 variables, are described in the eAppendix. The "black patients" column reports the means for all black patients in the data set. The "Treatment Match" column reports the means for the closest white match, namely the treatment match (which also controls for presentation and demographics variables); the "Presentation Match" column also controls for demographics variables. The "All Whites (Unmatched)" column reports data for all whites in the data set, without control for age, year of diagnosis, or SEER site. Results for each variable that appear to the left of the bold red vertical line are for variables included in the match designated by the column. For cells to the left of the line, all *P* values were nonpaired *P* values as a test for balance,

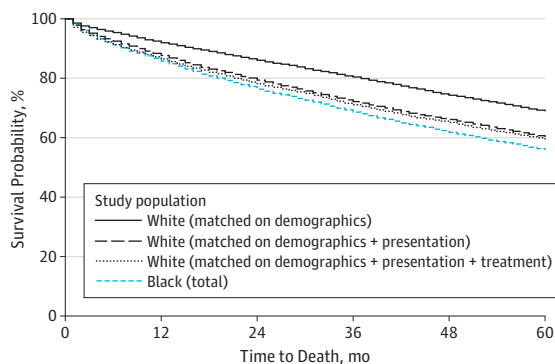
using Wilcoxon rank-sum for continuous variables and Fisher exact test for categorical variables; percentages or rates not displaying a *P* value designation imply nonsignificant differences between blacks and whites. Results to the right of the bold red vertical line are for variables not used in the match designated by the column. For cells to the right of the line (excluding the "All Whites" column, which is always nonpaired), all *P* values were paired values using Wilcoxon sign-rank for continuous variables and McNemar test for categorical variables; percentages or rates not displaying a *P* value designation imply nonsignificant differences between blacks and whites.

^b *P* < .05.

^c *P* < .01.

^d *P* < .001.

Figure 1. Kaplan-Meier Plot for Breast Cancer Survival for the Total Black Study Population and 3 Matched White Populations Diagnosed Between 1991-2005



No. at risk	7375	6822	6383	5958	5512	4721
White (matched on demographics)	7375	6517	5906	5362	4900	4142
White (matched on demographics + presentation)	7375	6432	5806	5280	4835	4075
White (matched on demographics + presentation + treatment)	7375	6394	5694	5113	4601	3823
Black (total)						

Demographics indicates age, year of diagnosis, and Surveillance, Epidemiology and End Results site; presentation indicates demographics variables plus comorbid conditions and tumor characteristics (stage, tumor size, tumor grade, and estrogen receptor status); treatment indicates presentation variables plus details of surgery, radiation, and chemotherapy. The extent of the difference between black patients and white patients is the vertical distance between the black and demographics-matched white curves.

Table 2. Breast Cancer Outcomes for All Matches^a

Outcome Measure	Black Patients (n = 7375)	Matched White Patients		
		Treatment Match (n = 7375)	Presentation Match (n = 7375)	Demographics Match (n = 7375)
Survival, median (IQR), mo	74 (71-77)	82 (79-85)	85 (82-88)	108 (104-110)
2-y survival, % (95% CI)	76.3 (75.3-77.3)	78.1 (77.2-79.1)	79.4 (78.4-80.3)	86.0 (85.2-86.8)
White - black difference	NA	1.8 (0.7-2.8)	3.1 (1.9-4.3)	9.7 (8.4-11.0)
P value		.006	<.001	<.001
No. of deaths	1681	1569	1469	992
5-y survival, % (95% CI)	55.9 (54.8-57.0)	59.5 (58.3-60.6)	60.3 (59.2-61.4)	68.8 (67.8-69.9)
White - black difference	NA	3.6 (2.3-4.9)	4.4 (2.8-5.8)	12.9 (11.5-14.5)
P value		<.001	<.001	<.001
No. of deaths	3207	2942	2888	2257
Paired Cox model HR, black:white (95% CI)	NA	1.11 (1.05-1.17)	1.18 (1.12-1.24)	1.54 (1.46-1.62)
P value		<.001	<.001	<.001

Abbreviations: HR, hazard ratio; IQR, interquartile range; NA, not applicable.

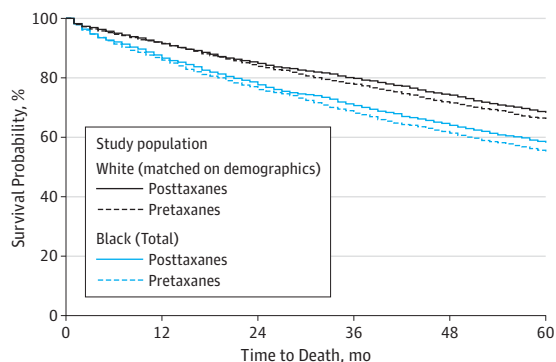
^a All P values for differences in survival between black patients and matched white patients use the Prentice-Wilcoxon test. Paired Cox Model P values use all follow-up data after diagnosis. All confidence intervals for white-black survival differences were based on bootstrapped standard errors.

5-year survival between the treatment-matched white population and the total black population was 3.6% ($P < .001$). Comparing the 5-year survival for whites who presented like blacks (ie, the whites matched to blacks on presentation and demographic variables) with whites who presented and were treated like blacks (ie, the whites matched to blacks on presentation and demographic variables as well as treatment variables), the absolute difference was small (0.81%) but statistically significant ($P = .04$). We further examined the causes of death determined by SEER based on death certificates for the treatment-matched pairs (eAppendix [Supplement]). Overall, about half of the deaths at 5 years were cancer related. Furthermore, about two-thirds of the difference in 5-year mortality between black and white patients was attributable to cancer-related causes, and one-third to noncancer causes of death.

Changes in Survival Differences Over Time

Figure 2 shows survival of all black patients and demographics-matched white patients in pairs of patients diagnosed in the era before the introduction of taxanes (pretaxanes; 1991-1998) and in the era after the introduction of taxanes (posttaxanes; 1999-2005) for just the 12 SEER sites that collected data in both periods. Both black and matched white survival improved slightly between eras, but the change in the black-white difference was small and not significantly different from zero (12.4% in the pretaxanes period and 12.2% in the posttaxanes period; $P = .65$). There also was no significant difference in the difference between blacks and whites matched on presentation or the treatment match between the eras before and after introduction of taxanes (eAppendix [Supplement]).

Figure 2. Breast Cancer Survival for Blacks and Demographics-Matched Whites for the Era Before Introduction of Taxanes (Pretaxanes; 1991-1998) and the Era After Introduction of Taxanes (Posttaxanes; 1999-2005)



No. at risk						
White (matched on demographics)						
Posttaxanes	2419	2247	2111	1992	1849	1495
Pretaxanes	2832	2616	2431	2255	2084	1925
Black (total)						
Posttaxanes	2419	2121	1902	1723	1564	1226
Pretaxanes	2832	2459	2181	1952	1754	1575

The overall survival difference did not change (blacks and demographics-matched whites each started with N = 2832 in the pretaxane era and N = 2419 in the post-taxane era).

Table 3. Primary and Preventive Care in the 6 to 18 Months Prior to Diagnosis, Across Matches

Measure	Black Patients (n = 7375)	Matched White Patients ^a		
		Treatment Match (n = 7375)	Presentation Match (n = 7375)	Demographics Match (n = 7375)
Any primary care				
No. evaluable ^e	5546	5388	5168	5546
Primary care, No. (%)	4463 (80.5)	4655 (86.4) ^b	4496 (87.0) ^b	4908 (88.5) ^b
Any breast cancer screening				
No. evaluable ^e	5546	5388	5168	5546
Screened, No. (%)	1304 (23.5)	1596 (29.6) ^b	1602 (31.0) ^b	1978 (35.7) ^b
Any cholesterol screening				
No. evaluable ^e	5546	5388	5168	5546
Screened, No. (%)	1870 (33.7)	2024 (37.6) ^b	1965 (38.0) ^b	2116 (38.2) ^b
Any colon cancer screening				
No. evaluable ^e	5546	5388	5168	5546
Screened, No. (%)	915 (16.5)	1115 (20.7) ^b	1101 (21.3) ^b	1313 (23.7) ^b

^aFor each match, pairs were only assessed if both members of the pair had 18 months of data to evaluate prediagnosis variables. This meant that for this table, we only analyzed patients who were diagnosed after age 66.5 years and diagnosed later than July 1, 1992. The paired P values are calculated between the black patients and matched white patients using McNemar Test.

^bP < .001.

Explaining Differences in Presentation

There were large differences in the way black and white patients presented. As a secondary analysis we studied differences in primary care well before diagnosis occurred in black and matched white populations. Table 3 describes preventive care indicators between 18 months to 6 months prior to diagnosis of breast cancer in the study's 3 matched pairs. (See eAppendix [Supplement] for coding definitions.) For the demographics match, blacks had significantly less evidence of at least 1 primary care visit^{50,51} than matched whites (80.5% vs 88.5%, respectively; P < .001); significantly lower rates of breast cancer screening (23.5% vs 35.7%; P < .001); and significantly lower rates of colon cancer and cholesterol screening. Smaller differences, still significant, were observed for presentation and treatment matches.

Examining the Relationship of Estrogen Receptor Status to the Survival Disparity

In this analysis we have reported the demographics match using only age, SEER site, and year of diagnosis that served as our base case for which we compared the role of presentation and then treatment. Because presentation comprises some variables that are potentially changeable (such as comorbid conditions and tumor size at time of diagnosis) and some that are biological and should not change (such as estrogen receptor status), we also present a secondary matching analysis that included the demographics matching variables plus estrogen receptor status (eAppendix [Supplement]). We found that 5-year survival in white patients matched to black patients for demographics plus estrogen receptor status decreased from 68.8% (95% CI, 67.8%-69.9%) to 67.1% (95% CI, 66.0%-68.1%)

($P < .001$). Hence, a portion of the survival difference between the demographics match and the presentation match was due to differences in estrogen receptor status, and as such should not be something that better screening or primary care could directly change, although improved preventive measures may potentially allow for earlier diagnosis.

Socioeconomic Status

As a final secondary analysis, using the treatment-matched pairs, we fit a paired Cox model to evaluate the influence of race before and after adjusting for dual eligibility status for both Medicare and Medicaid. Without adjustment, the black-vs-white hazard ratio for death was 1.11 (95% CI, 1.05-1.17) ($P < .001$). After adjusting for dual eligibility status, the hazard ratio was 1.02 (95% CI, 0.97-1.09) ($P = .41$). Using variables reflecting neighborhood poverty and education (Census 2000, databased on the patient's census tract) we observed findings similar to those obtained by adjusting for dual eligibility (eAppendix [Supplement]).

Discussion

The large racial difference in breast cancer survival from diagnosis did not change between 1991-1998 and 1999-2005. Most of the difference is explained by poorer health of black patients at diagnosis, with more advanced disease, worse biological features of the disease, and more comorbid conditions. The 5-year survival difference observed with whites matched for demographics (age, year of presentation, and SEER site) was 12.9%, or a difference in median survival time of nearly 3 years, whereas with whites matched for cancer and comorbid conditions (ie, the presentation match) the difference was 4.4%, or a median survival difference of less than 1 year. Compared with whites who both presented like blacks and were treated like blacks, (ie, the treatment match), the difference only changed by 3.6%; hence, treatment differences explained only 0.81% of the 12.9% difference in 5-year survival. Treatment disparities might matter more if blacks were diagnosed with less advanced cancers.

The 3.6% remaining racial difference in 5-year survival after matching on treatment was predominantly cancer related (eAppendix [Supplement]). However, given that racial and income disparities are seen throughout the US health care system,⁵² it would have been surprising to observe a complete elimination of the survival difference by matching for similar cancer presentation and treatment.

One important strength of our study was that 99 898 white patients were used as potential controls for 7375 black patients. This allowed us to achieve very close matches, generally avoiding the need for model-based analyses. A model fitted to 99 898 whites and 7375 blacks would be a model that mostly describes what happens to whites.⁵³

There were important limitations to this study. We did not have chart review to verify our definitions of treatment coded from Medicare bills or noted in SEER data. Hence, for example, we could not track the use of tamoxifen, although

other studies have suggested that black patients use tamoxifen in at least as high a rate as white patients when they have estrogen receptor-positive tumors.⁵⁴⁻⁵⁷ Nevertheless, it is possible that some portion of the residual unexplained difference after accounting for presentation and treatment relates to endocrine therapy not tracked in SEER. Furthermore, using SEER data we could not define triple-negative tumors.⁵⁸ However, triple-negative tumors are less common in postmenopausal than premenopausal blacks (14% vs 39%), and postmenopausal blacks and whites display no difference in their rates of triple-negative tumors.⁵⁸

Our results suggest that it may be difficult to eliminate the racial disparity in survival from diagnosis unless differences in presentation can be reduced. There is also a disparity in treatment, with blacks receiving treatment inferior to that received by whites with similar presentation, but this explains only a small part of the observed difference in survival. The disparity in treatment might matter more if the disparity in presentation were reduced, because blacks would then be diagnosed with less advanced disease, for which treatment is more effective.

Whether better screening for breast cancer would reduce the disparity in presentation is not known. Our data provide evidence suggesting that black patients diagnosed with breast cancer had previously received less adequate primary care than did white patients in the demographics match. Also, blacks were diagnosed with more advanced-stage disease and also with larger tumors. If a woman has limited primary care, then apart from screening, it may take longer before she seeks medical attention for a lump in her breast. Our data cannot distinguish the effects of screening from the effects of greater access to primary care. Screening and earlier diagnosis might be ineffective if black patients and white patients with similar cancer biology as measured by SEER had very different cancer biology if measured in much greater detail; however, in our population of elderly Medicare patients, differences in biology are smaller issues than in premenopausal patients.

Black patients are diagnosed not only with more advanced breast cancers but also with more unrelated comorbid conditions. Some of the effectiveness of cancer treatment for blacks may be blunted by other health problems. If the differences in comorbid conditions at diagnosis were reduced, it is possible that the differences in cancer treatment would matter more for the differences in survival.

Conclusions

In the SEER-Medicare database, racial differences in breast cancer survival did not substantially change among women diagnosed between 1991 and 2005. These differences in survival appear primarily related to presentation characteristics at diagnosis rather than treatment differences. In the presence of large racial differences in patient characteristics at presentation, treatment differences explained only a small portion of the survival difference, because

white women who presented like black women (ie, were matched on demographics and presentation) but who received treatment similar to that received by white women fared almost the same as white women who presented like black women and who were treated in the same way as black women.

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REFERENCES

- Haas JS, Earle CC, Orav JE, et al. Racial segregation and disparities in breast cancer care and mortality. *Cancer*. 2008;113(8):2166-2172.
- Ward E, Jemal A, Cokkinides V, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin*. 2004;54(2):78-93.
- Gorey KM, Luginaah IN, Schwartz KL, et al. Increased racial differences on breast cancer care and survival in America: historical evidence consistent with a health insurance hypothesis, 1975-2001. *Breast Cancer Res Treat*. 2009;113(3):595-600.
- Grann V, Troxel AB, Zojwalla N, Hershman D, Glied SA, Jacobson JS. Regional and racial disparities in breast cancer-specific mortality. *Soc Sci Med*. 2006;62(2):337-347.
- Curtis E, Quale C, Haggstrom D, Smith-Bindman R. Racial and ethnic differences in breast cancer survival: how much is explained by screening, tumor severity, biology, treatment, comorbidities, and demographics? *Cancer*. 2008;112(1):171-180.
- Ooi SL, Martinez ME, Li CI. Disparities in breast cancer characteristics and outcomes by race/ethnicity. *Breast Cancer Res Treat*. 2011;127(3):729-738.
- Cross CK, Harris J, Recht A. Race, socioeconomic status, and breast carcinoma in the U.S: what have we learned from clinical studies. *Cancer*. 2002;95(9):1988-1999.
- Smith-Bindman R, Miglioretti DL, Lurie N, et al. Does utilization of screening mammography explain racial and ethnic differences in breast cancer? *Ann Intern Med*. 2006;144(8):541-553.
- McCarthy EP, Burns RB, Coughlin SS, et al. Mammography use helps to explain differences in breast cancer stage at diagnosis between older black and white women. *Ann Intern Med*. 1998;128(9):729-736.
- Tammemagi CM, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and survival disparities among black and white patients with breast cancer. *JAMA*. 2005;294(14):1765-1772.
- Chagpar AB, Crutcher CR, Cornwell LB, McMasters KM. Primary tumor size, not race, determines outcomes in women with hormone-responsive breast cancer. *Surgery*. 2011;150(4):796-801.
- McBride R, Hershman D, Tsai WY, Jacobson JS, Grann V, Neugut AI. Within-stage racial differences in tumor size and number of positive lymph nodes in women with breast cancer. *Cancer*. 2007;110(6):1201-1208.
- Hershman D, McBride R, Jacobson JS, et al. Racial disparities in treatment and survival among women with early-stage breast cancer. *J Clin Oncol*. 2005;23(27):6639-6646.
- Gorin SS, Heck JE, Cheng B, Smith SJ. Delays in breast cancer diagnosis and treatment by racial/ethnic group. *Arch Intern Med*. 2006;166(20):2244-2252.
- Byers TE, Wolf HJ, Bauer KR, et al; Patterns of Care Study Group. The impact of socioeconomic status on survival after cancer in the United States: findings from the National Program of Cancer Registries Patterns of Care Study. *Cancer*. 2008;113(3):582-591.
- Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. *Med Care*. 2002;40(8)(suppl):IV-3-IV-18.
- SEER-Medicare Linked Database. National Cancer Institute website. <http://healthservices.cancer.gov/seermedicare>. Accessed August 8, 2012.
- Bach PB, Guadagnoli E, Schrag D, Schussler N, Warren JL. Patient demographic and socioeconomic characteristics in the SEER-Medicare database applications and limitations. *Med Care*. 2002;40(8)(suppl):IV-19-IV-25.
- Silber JH, Rosenbaum PR, Kelz RR, et al. Medical and financial risks associated with surgery in the elderly obese. *Ann Surg*. 2012;256(1):79-86.
- Silber JH, Rosenbaum PR, Trudeau ME, et al. Multivariate matching and bias reduction in the surgical outcomes study. *Med Care*. 2001;39(10):1048-1064.
- Volpp KG, Rosen AK, Rosenbaum PR, et al. Mortality among hospitalized Medicare beneficiaries in the first 2 years following ACGME resident duty hour reform. *JAMA*. 2007;298(9):975-983.
- Volpp KG, Rosen AK, Rosenbaum PR, et al. Mortality among patients in VA hospitals in the first 2 years following ACGME resident duty hour reform. *JAMA*. 2007;298(9):984-992.
- Rubin DB. For objective causal inference, design trumps analysis. *Ann Appl Stat*. 2008;2(3):808-840.

24. Rubin DB. The design versus the analysis of observational studies for causal effects: parallels with the design of randomized trials. *Stat Med*. 2007;26(1):20-36.
25. Rubin DB. Using propensity scores to help design observational studies: application to the tobacco litigation. *Health Serv Outcomes Res Methodol*. 2001;2(3-4):169-188.
26. SAS Institute Inc. *SAS/OR User's Guide: Mathematical Programming (Version 8)*. Cary, NC: SAS Institute Inc; 1999:39-54.
27. Rosenbaum PR. *Design of Observational Studies*. New York, NY: Springer; 2010.
28. Rosenbaum PR, Ross RN, Silber JH. Minimum distance matched sampling with fine balance in an observational study of treatment for ovarian cancer. *J Am Stat Assoc*. 2007;102(477):75-83.
29. Yang D, Small DS, Silber JH, Rosenbaum PR. Optimal matching with minimal deviation from fine balance in a study of obesity and surgical outcomes. *Biometrics*. 2012;68(2):628-636.
30. Rosenbaum PR. *Design of Observational Studies*. New York, NY: Springer; 2010:197-206.
31. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
32. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613-619.
33. Klabunde CN, Legler JM, Warren JL, Baldwin LM, Schrag D. A refined comorbidity measurement algorithm for claims-based studies of breast, prostate, colorectal, and lung cancer patients. *Ann Epidemiol*. 2007;17(8):584-590.
34. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *J Clin Epidemiol*. 2000;53(12):1258-1267.
35. Rosenbaum P, Rubin D. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55.
36. Joffe MM, Rosenbaum PR. Invited commentary: propensity scores. *Am J Epidemiol*. 1999;150(4):327-333.
37. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *Am Stat*. 1985;39(1):33-38.
38. Cochran WG, Rubin DB. Controlling bias in observational studies: a review. *Sankhyā*. 1973;35:417-446.
39. Heller R, Rosenbaum PR, Small D. Using the cross-match test to appraise covariate balance in matched pairs. *Am Stat*. 2010;64(4):299-309.
40. Hollander M, Wolfe DA. *Nonparametric Statistical Methods*. 2nd ed. New York, NY: John Wiley & Sons; 1999.
41. Bishop YMM, Fienberg SE, Holland PW. *Discrete Multivariate Analysis: Theory and Practice*. Cambridge: MIT Press; 1975:281-286.
42. Kalbfleisch JD, Prentice RL. *The Statistical Analysis of Failure Time Data*. New York, NY: John Wiley; 1980.
43. O'Brien PC, Fleming TR. A paired Prentice-Wilcoxon test for censored paired data. *Biometrics*. 1987;43(1):169-180.
44. Holt J, Prentice R. Survival analysis in twin studies and matched pair experiments. *Biometrika*. 1974;61(1):17-30.
45. Efron B, Tibshirani R. Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. *Stat Sci*. 1986;1(1):54-75.
46. Rosenbaum PR, Silber JH. Using the exterior match to compare two entwined matched control groups. *Am Stat*. 2013;67(2):67-75.
47. *Statistical Analytic Software System for UNIX (Version 9.2)*. Cary, NC: SAS Institute Inc; 2009.
48. R Development Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing website. www.R-project.org. 2012. Accessed May 14, 2013.
49. Rosenbaum PR. An exact distribution-free test comparing two multivariate distributions based on adjacency. *J R Stat Soc B*. 2005;67(part 4):515-530.
50. Pham HH, Schrag D, O'Malley AS, Wu B, Bach PB. Care patterns in Medicare and their implications for pay for performance. *N Engl J Med*. 2007;356(11):1130-1139.
51. Bach PB, Pham HH, Schrag D, Tate RC, Hargraves JL. Primary care physicians who treat blacks and whites. *N Engl J Med*. 2004;351(6):575-584.
52. 2011 National Healthcare Quality and Disparities Reports. Agency for Healthcare Research and Quality website. www.ahrq.gov/research/findings/nhqrd1/nhqrd11/qdr11.html. 2011. Accessed November 12, 2012.
53. Daniel SR, Armstrong K, Silber JH, et al. An algorithm for optimal tapered matching, with application to disparities in survival. *J Comput Graph Stat*. 2008;17(4):914-924.
54. Hershman DL, Kushi LH, Shao T, et al. Early discontinuation and nonadherence to adjuvant hormonal therapy in a cohort of 8,769 early-stage breast cancer patients. *J Clin Oncol*. 2010;28(27):4120-4128.
55. Kimmick G, Anderson R, Camacho F, Bhosle M, Hwang W, Balkrishnan R. Adjuvant hormonal therapy use among insured, low-income women with breast cancer. *J Clin Oncol*. 2009;27(21):3445-3451.
56. Ma AM, Barone J, Wallis AE, et al. Noncompliance with adjuvant radiation, chemotherapy, or hormonal therapy in breast cancer patients. *Am J Surg*. 2008;196(4):500-504.
57. Owusu C, Buist DS, Field TS, et al. Predictors of tamoxifen discontinuation among older women with estrogen receptor-positive breast cancer. *J Clin Oncol*. 2008;26(4):549-555.
58. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA*. 2006;295(21):2492-2502.