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Breast Cancer Survival among Economically Disadvantaged Women: The Influences of Delayed Diagnosis and Treatment on Mortality

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Abstract

Breast cancer affects thousands each year in the United States, and disproportionately affects certain subgroups. For example, the incidence of breast cancer in South Carolina is lower in African American compared with European American women by ~12% to 15%, but their mortality rate is twice as high as in European American women. The purpose of the study was to assess factors associated with breast cancer mortality between African American and European American women. Participants (n = 314) in South Carolina's Breast and Cervical Cancer Early Detection Program (SCBCCEDP), which provides breast cancer screening and treatment services, during the years 1996-2004 were included in the study. Data, including tumor characteristics, delay intervals, and race, were examined using the χ^2 test and the Wilcoxon rank-sum test. Cox regression modeling was used to assess the relationship between delay intervals and other factors. No racial differences were found in age at diagnosis, tumor characteristics, or delay intervals. Time delay intervals did not explain differences and mortality rates by race. Survival, however, was affected by prognostic factors as well as by a significant interaction between hormone-receptor status and race. Despite the excellent record of the SCBCCEDP in screening and diagnostic or treatment referrals, the racial disparities in breast cancer mortality continue to exist in South Carolina. These findings highlight the need for future research into the etiology of racial differences, and their impact on breast cancer survival.

Introduction

In the United States, and more prominently in South Carolina, a large and widening disparity in breast cancer mortality rates has been reported between African American and European American women (1-3). The cause(s) of this disparity has been attributed to factors ranging from differences in tumor biology, to environmental factors, to socioeconomic and cultural differences between the groups (2-5). Socioeconomic status and cultural beliefs could affect a woman's survival through certain time intervals across the breast cancer diagnosis continuum, resulting in delays in detection, diagnosis, and treatment. Subsequently, the timeliness of

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detecting a breast abnormality may result in an earlier stage of disease, thereby improving a woman's prognosis and clinical outcomes (3,6-13). Likewise, prompt follow-up of an abnormality with diagnostic testing and appropriate and timely treatment may reduce mortality (14-25).

Numerous studies have assessed delays in screening, diagnosis, and treatment, and their effects on breast cancer mortality, as summarized in a systematic review conducted by Richards and colleagues (19). Overall, they found that patients experiencing delays of three or more months had lower 5-year survival than did patients with shorter delays. Very few studies (26,27), however, have examined the combination and interplay of these intervals. To our knowledge, no study has examined the connection between breast cancer mortality and prolonged intervals (i.e., intervals longer than those recommended by the health care provider), alone or in combination with one another, among medically under-served African American and European American women.

The present study used data from the Best Chance Network (BCN), a South Carolina program that is part of the National Breast and Cervical Cancer Early Detection Program. The BCN provides comprehensive screening services to economically disadvantaged women through the Breast and Cervical Cancer Mortality Prevention Act of 1990 (Public Law 101-354). Because of their low socioeconomic status, these women are at high risk for delays in breast cancer detection, diagnosis, and treatment (28). Little is known, however, about their patterns in delay and the effects on their survival. We analyzed two time intervals for which data were available, the time from the first examination in which a breast abnormality was found to breast cancer diagnosis and the time from diagnosis to the initiation of first treatment, and examined racial inequalities along the time continuum. We also examined racial differences in the relationship between breast cancer mortality and the diagnosis and treatment delay intervals.

Materials and Methods

Setting

The setting for this study was the BCN of South Carolina. The BCN is implemented through the South Carolina Department of Health and Environmental Control and funded by the Centers for Disease Control and Prevention. The program provides services for underserved women ages 47 to 64 years, who are at or below 200% of the Federal poverty level, and do not have insurance or have insurance that covers only hospital care. The BCN provides screening services, such as mammo-grams and clinical breast exams, diagnostic procedures, case management, and community education on breast cancer and early detection. Eligible women are recruited into the BCN through active in-reach efforts by primary care providers from federally qualified health centers, outreach through the American Cancer Society, South-Atlantic Division, and various media mechanisms. This study was approved by the Institutional Review Boards of the South Carolina Department of Health and Environmental Control and the University of South Carolina.

Study Population

Female beneficiaries of the BCN who were diagnosed with pathologically confirmed breast cancer from 1996 to 2004 were linked with data from the South Carolina Central Cancer Registry (SCCCR). All BCN participants who were screened and had a histopathologically confirmed incident breast cancer diagnosed through BCN and had a corresponding record in the SCCCR were included ($n = 323$). Exclusions were made for the following reasons: missing or incomplete diagnostic information ($n = 6$) and ethnicity other than African American or European American ($n = 3$).

Definition of Delay Intervals

The primary exposures of interest were delays in three time intervals: diagnostic delay, treatment delay, and total delay (see Fig. 1). The diagnostic delay was defined as the time between the first screening examination (clinical breast exam or mammography) that found an abnormality and the date of the pathologic diagnosis of breast cancer within that screening cycle. The date of the first examination of an abnormal screening was defined as the first date when a “suspicious” clinical breast exam (CBE) result or a mammography result of category 4, category 5, or category 0 was reported and diagnostic work-up was planned. CBE and mammography results were obtained from the BCN. Screening mammography is done on all eligible BCN participants annually for women ages 47 to 64 years and as recommended for those women who require follow-up. Mammography and CBE performance and results, and the performance and results of diagnostic procedures are reported by the providers to the BCN. CBE results are categorized according to the established criteria of the Minimum Data Elements of the National Breast and Cervical Cancer Early Detection Program. Mammography results are categorized according to the American College of Radiology/Breast Imaging Reporting and Data System's Final Assessment Categories (29).

Every eligible woman in the BCN that presented with a clinical problem such as a palpable mass, nipple discharge, nipple scaliness, or skin dimpling/retraction underwent diagnostic work-up. Additionally, those patients who had an abnormality detected on a screening mammogram that required further investigation also underwent diagnostic work-up. Diagnostic work-up may include additional mammographic views, ultrasound, fine-needle aspiration, and image-guided biopsy.

Treatment delay was defined as the time between the date of the pathologic diagnosis of breast cancer and the date of the initiation of the first course of treatment. For both diagnostic delay and treatment delay intervals, the date of the pathologic diagnosis was classified as the date of diagnosis obtained from the SCCCR, which maintains records for all cancers diagnosed in South Carolina. Hospitals with existing tumor registries submit >80% of the reported cases electronically. The remaining data are collected from hospitals without registries, and from pathology laboratories, treatment centers, and physician offices. Quality control measures, such as visual reviews of 100% of collected data, and computerized data edits are done periodically to ensure the completeness and quality of data. The SCCCR has met the highest rating (Gold) given by the North American Association of Central Cancer Registries to cancer registries seeking certification, with both completeness and accuracy rates exceeding the national standard of >97.5%.

The date of treatment initiation was considered as the date of the start of the first course of treatment obtained from the SCCCR. Treatment included surgery with or without radiation or chemotherapy, or with neoadjuvant chemotherapy/radiation followed by surgery and again with radiation/chemotherapy, hormonal therapy, and immunotherapy. The date of treatment initiation was not found for 20 women. Due to the fact that treatments for all stages of breast cancer (i.e., *in situ* and invasive) are reported to the SCCCR, these women were assumed to have never had treatment for breast cancer. Thus, their treatment delay interval was censored at the date of death or at the end of the study period, whichever came first. Analyses were run to evaluate if these women were significantly different from the rest of the study population;there were no significant differences between the 20 women without treatment dates and the women with treatment dates. Total delay was defined as the time between the first screening examination that found an abnormality and the date of the initiation of treatment. All delay intervals were treated as continuous, not categorical, variables to maximize the study power and to ensure that residual confounding within categories did not occur. Categories of delay intervals were used in the interpretation of the final models. This was to allow for

comparisons across studies. The categorization of time delays was similar to the ones previously used in other studies, especially the Richards meta-analysis (19).

After reviewing the distributions for each delay interval, several extreme outliers were eliminated which negatively impacted the skewness and kurtosis measures. Although a normal distribution is not an assumption of the Cox modeling used for this analysis, the authors were concerned that a few outlier measures (possibly attributable to incomplete or missing data) might distort measures of association. It should be noted that all models were run with and without the outlier values, and the results remained unchanged.

Covariates

Demographic characteristics such as income and age were self-reported by the BCN participants upon enrollment into the program. Complete annual household income and age were obtained from the BCN. Data regarding tumor size, classified into categories of 0-1, >1-2, >2-5, and >5 cm, were collected by the BCN and reported to the SCCCR. Thus, only additional tumor characteristics, such as stage, grade, behavior, and hormone receptor status were requested from the SCCCR. Tumor stage was classified according to the Surveillance, Epidemiology, and End Results summary stages as *in situ*, localized, regional, and distant (30). *In situ* and localized cancers were combined to form a category of early-stage cancers, which category was compared with a category of late-stage cancers that comprised regional and distant cancers. This collapsing was due to small cell frequencies for both African American and European American women in our study. Due to small cell frequencies, the degree of differentiation of the reported tumor was dichotomized into categories of well differentiated or moderately differentiated versus poorly or undifferentiated (and unknown) for the purposes of the survival analyses. Tumor type was classified as *in situ* disease versus invasive disease. Data on estrogen (ER) and progesterone (PR) hormone receptor status were combined to categories of “positive/positive,” “negative/negative,” “other combinations,” and “unknown.” Tumors with unknown ER/PR status included categories of tests not done and tests that were ordered but results were not recorded in the medical charts. First course of treatment type included surgery, chemotherapy, or radiation, or not reported. Date of initial treatment is the date of the first course of therapy for the tumor being reported.

Survival time was defined as the time from the date of diagnosis to the date of death or the time from diagnosis to the end of follow-up.

Statistical Analyses

All analyses were done using SAS software, version 9.1 (31). Descriptive characteristics of the study population, including tumor characteristics, were compared between African American women and European American women using the χ^2 test for categorical data and the Wilcoxon rank-sum test for continuous variables, due to the nonnormal distribution of biological data (32). All P values were two-tailed, and P values <0.05 were considered statistically significant.

Kaplan-Meier survival curves were used to examine all-cause and disease-specific survival (33). Associations among mortality rates, race, delay intervals, and all covariates were estimated using the Cox proportional-hazards model (34). The final model was obtained by including all covariates and all interaction terms into a multivariate backward elimination process. Significant covariates and interaction terms made up the final models whose results are tabulated. Follow-up mortality information was ascertained annually at the end of the year by the SCCCR through a variety of data sources, including the Department of Motor Vehicles registration files, hospital cancer registries and discharge data sets, death records, and the Social Security Death Index. The last day of the follow-up period, December 31, 2004, was chosen

as the censoring date used in our analyses, as that was the last day complete follow-up could be ensured for all of the previous sources. Mortality information was obtained from the death certificate and included whether breast cancer was a primary cause of death, contributing cause of death, or neither. The other causes of death included all primary causes of death that were not breast cancer. If breast cancer was noted as a contributing cause of death on the death certificate, then it was considered to be a death from breast cancer. The specific causes of death, other than breast cancer, were not known. Competing risk models also were estimated using the death certificate as a means to identify if breast cancer was a primary or contributing cause of death.

Hazard functions for all Cox proportional hazards models were checked, and no violations of proportionality were noted (35).

Results

Table 1 reports the descriptive characteristics of the study population. The mean income for African American women was lower than that for European American women ($P < 0.05$). No other racial differences were noted. Additionally, no differences between races were noted in the method in which the breast abnormality was detected (data not shown).

Among women diagnosed with breast cancer after an abnormal CBE or mammogram screening, the mean or median time from the first abnormal screening to diagnosis was similar between African American and European American women (data not shown). Likewise, no racial differences were observed with regard to the time from diagnosis to the initiation of treatment according to the mean or the median time. In contrast, a statistically significant difference in the total delay interval was noted. African American women had a mean total interval of 9 days longer ($P < 0.05$) and a median total interval 5 days longer ($P = 0.08$) than did European American women. The distribution of the delay intervals was similar when plotted and examined visually.

For all women who were diagnosed with breast cancer from 1996 to 2004, 39 European American women and 34 African American women died during the follow-up time period. Among European American women, 2 died after a diagnosis of *in situ* breast cancer whereas 37 died after a diagnosis of invasive breast cancer. Among African American women, 3 died after a diagnosis of *in situ* breast cancer whereas 32 died after a diagnosis of invasive breast cancer. In all five *in situ* cases, breast cancer was not the primary cause, but a contributing cause of death. Thus, the five cases were contributors to the all-cause survival analyses but not the breast cancer– specific analyses. We evaluated the survival times, hypothesizing that shorter survival times might be related to treatment toxicity or surgery. However, all five cases had longer treatment delays and total delays, suggesting this hypothesis was not the case. Additional survival analyses were run to evaluate if the deletion of the five deaths affected our results. In both the all-cause and breast cancer – specific survival analyses, this deletion did not significantly affect any of our results;therefore, the data from these women were left in the analyses. According to the log-rank statistic ($P = 0.94$), overall survival did not differ by race (Fig. 2). The 5-year survival rates were 82% in European American women and 75% in African American women.

Table 2 summarizes the multivariate models with each delay interval defined as the main exposure. Step-wise regression techniques initially included all variables and interaction terms, and the final models were constructed using only significant variables and/or interaction terms. Four models were run that treated each delay interval (i.e., diagnosis delay, treatment delay, total delay, and the joint effects of diagnosis delay and treatment delay) as the main exposure. In all models, a significant association between the risk of death and the delay intervals was

not found (data not shown). In all four models, however, a significant association between the risk of death and the interaction of race and hormone receptor status was noted. Table 3 summarizes the interaction term for total delay. Estimated hazard ratios (HR) were reported for each combination of race and ER/PR status. Analyses were conducted to disentangle the interaction term by comparing African American and European American women within each ER/PR category. In all four models, African American women with ER/PR– positive receptor tumors were found to have a greater risk of death (all HRs > 4; $P < 0.001$) compared with European American women with ER/PR – positive tumors. Furthermore, in all models African American women with ER/PR– negative tumors were found to have an even greater risk of death compared with European American women with ER/PR – negative tumors (HRs between 36% and 50% higher than those observed in comparing ER/PR– positive tumors; $P < 0.001$). The risk was greatest in model 1, which treated diagnosis delay as the main exposure (HR, 9.67), and in model 4, which treated both individual delay intervals as the main exposure (HR, 9.13). European American women with ER/PR– negative tumors were found to have a greater risk of death compared with European American women with ER/PR – positive tumors (HR, 6.68). In all models, women diagnosed with later-stage disease had a higher risk of death compared with women diagnosed with earlier-stage disease ($P < 0.001$;data not shown). No other covariates adjusted for in the models were significant.

Women with breast cancer as a primary or contributing cause of death reported on their death certificates were considered to have died from breast cancer. Using this definition, 34 European American women and 25 African American women died of breast cancer during the follow-up time period. According to the log-rank statistic ($P = 0.53$), survival from disease-specific causes did not differ by race (Fig. 3).

Table 4 summarizes the Cox proportional breast cancer – specific mortality multivariate hazard models of the main covariates of delay intervals and race. Step-wise regression techniques initially included all variables and interaction terms, and the final models were constructed using only those variables and/or interaction terms found to be statistically significant. In all models, no association between the risk of death and delay intervals or race was noted. Similar to the results seen in the all-cause survival analyses, all models showed that women diagnosed with later-stage disease had a significantly greater risk of death compared with women diagnosed with earlier-stage disease ($P < 0.0001$;data not shown). This risk was marginally more pronounced in the model with total delay than the other models (HR, 4.82 versus HRs, 4.05 and 3.68). Furthermore, in all models women with ER/PR –negative tumors were found to have a greater risk of death ($P < 0.001$) compared with women with ER/PR – positive tumors. This increase was more pronounced in the model treating diagnosis delay as the main exposure (HR, 4.42) than the models with a main exposure of treatment delay (HR, 3.49), total delay (HR, 4.01), or joint delay intervals (HR, 4.09). Unlike the analyses done with all-cause survival, an interaction of race and ER/PR status was not found in any of the models (data not shown). No other covariates in the models were significant.

Discussion

In this study, African American women with later-stage disease at diagnosis and those with negative ER/PR hormone receptor status were at increased risk of mortality compared with European American women. The study is unique in that it examines mortality experiences in a group of women who, due to their socioeconomic status, were shown to have longer delays between detecting a breast abnormality to diagnosing breast cancer and between diagnosis to treatment initiation (8,26,36-40). Both of these delays impact stage at diagnosis and breast cancer outcomes, whereby women with delayed evaluation and treatment are more likely to be diagnosed at a later stage and ultimately experience a higher risk of mortality (15,17,19, 20,23). Additionally, the BCN participants studied represent two racial groups that, in previous

studies, exhibited a difference in time-delay intervals, breast tumor characteristics, and cancer mortality (27,41-44). Thus, our finding that delays were not different between African American and European American women is particularly encouraging and interesting. The finding that race and total delay were not significant independent risk factors for breast cancer survival in our study suggests that the targeted efforts seen through the BCN to an otherwise high-risk group is proving beneficial in shortening the racial disparity gap in breast cancer mortality. This is a testament to the National Breast and Cervical Cancer Early Detection Program, whose aim is to assure equal access to timely and quality cancer screening and diagnosis among medically underserved women.

By contrast, the molecular markers of ER/PR that were found to impact mortality and shown to differ by race indicate an etiologic difference in tumor aggressiveness by race. As such, they cannot be controlled through interventions aimed at early detection, diagnosis, and treatment. This study contributes to a growing body of research, including those conducted in South Carolina, that have also noted differences in the presence of prognostic molecular markers by race such that African American women are significantly more likely to have ER/PR – negative tumors than European American women, even after controlling for tumor stage (41-47). For example, Cunningham found that in South Carolina, African Americans had more aggressive diseases with ER-negative tumors compared with their European American counterparts (42). On a national level, using the Surveillance, Epidemiology, and End Results database, Morris and colleagues observed that African American women were more likely to have ER-negative tumors and breast cancers found at later stage and higher grade (47). It is interesting to note the significant interaction between race and ER/PR receptor status that was noted for all-cause, but not disease-specific, survival. Further studies are needed to understand the interaction between race and hormone receptor status. These findings may have implications for basic/etiologic research as well as for targeted cancer treatment.

In the analyses of factors influencing the exposure-delay intervals and mortality, stage of disease was significantly associated with the risk of mortality. This result was observed when deaths were attributed to all-cause mortality and when deaths were attributed to breast cancer, further highlighting the impact that disease stage plays on survival. The HR increased in all breast cancer –specific survival analyses when the interaction term between race and hormone-receptor status was included in the model. The most pronounced increase in the HR for stage was seen in the model that considered treatment delay as the main exposure in which the hazard increased from 3.7 to 4.6.

Researchers have found that African American women have longer delays than European American women whereas other researchers did not note a significant difference (26,37,39, 48-51). Thus, diagnosis and treatment delays may be affected by other factors. Psychosocial factors, such as having higher levels of cancer-specific anxiety, fatalistic beliefs, misconceptions about cancer, cultural beliefs, and sociodemographic variables also have been found to influence patient delay (39,52-55). Sociodemographic factors include having a low household income, poor health status, no history of previous screening mammographies, and transportation problems (36,40,53).

Our study has several limitations. Data quality was not assessed on ER/PR status and treatment type, and interpretation of the study findings needs to be made in lieu of this limitation. We were unable to identify ER/ PR status on 42% of the women and treatment type on 10% of the women. ER/PR information is not required to be reported to the SCCCR. The women without ER/PR status, however, did not differ significantly from those with ER/PR status on important background factors such as race, treatment type, income, or tumor stage. In further examination by hospital type, a comparison of American College of Surgeons – approved hospitals versus non – American College of Surgeons hospitals showed no differences in reporting ER/PR or

treatment type. After further analysis, treatment type did not differ between African American and European American women. Furthermore, the type of treatment was not different by tumor type, size, or stage. The type of treatment, however, did differ by tumor grade, with persons having poorly/undifferentiated tumors being more likely to receive chemotherapy/radiation and surgery compared with persons having well/moderately differentiated tumors. No treatment or an unknown treatment type was more likely to be found among women with unknown ER/PR status compared with women with known ER/PR status.

Information regarding other factors that have been shown to impact the risk of breast cancer, such as parity, menopausal status, body mass index, the presence of *BRCA1* or *BRCA2*, and age at menarche also were not available (56). Similarly, information concerning her-2/ neu, a known prognostic risk factor for more aggressive breast cancer and a marker for resistance to adjuvant therapy that is associated with breast cancer recurrence and mortality, also was not available (57–61). Her-2/neu expression and ER/PR status act as prognostic factors for breast cancer and, taken together with other known effects on breast cancer recurrence and mortality, may have impacted our study (62). Another limitation of our study is the possibility of residual confounding due to the collapsing of small cell frequencies found among some variables, particularly stage and grade of disease. This could have resulted in some confounding factors not being accounted for in the model.

On the other hand, our study has several strengths. To our knowledge, this is the first study to examine racial disparities, the timeliness of diagnosis and treatment, and their collective effect on mortality among medically underserved women. Although the results of the present study may not be generalizable to other programs due to demographic differences, the findings can inform other organizations and programs aimed at targeting patients who are economically disadvantaged and from racial minority groups. Also, it may have special relevance to the 55% of all African Americans who live in the Southeast.

In summary, these findings suggest the usefulness of targeted efforts through programs, such as the BCN, to ensure prompt follow-up of breast abnormalities and treatment initiation among economically disadvantaged women and racial groups. Additionally, these findings highlight the need for future research into the etiology of racial differences, particularly regarding prognostic molecular markers, and their impact on the survival of patients with breast cancer.

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Figure 1.
Schematic of primary exposures of interest.

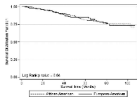

Figure 2.
Kaplan-Meier survival curves: All cause-survival analysis, Best Chance Network, South Carolina, 1996-2004.

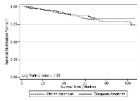

Figure 3.
Kaplan-Meier survival curves: breast cancer specific– survival analysis, Best Chance Network, South Carolina, 1996-2004.

Table 1

Demographic and clinical characteristics of the study population by race (n = 314), Best Chance Network, South Carolina, 1996-2004

	African American (n = 164)	European American (n = 150)
Demographic characteristics	Mean (SD)	Mean (SD)
Income (U.S. dollars)*	3,682 (5, 539)	5,434 (6, 491)
Age at abnormality detection, y	55 (8.5)	55 (8)
Age at diagnosis, y	55 (7.6)	55 (8)
Tumor characteristics	% (Count)	% (Count)
Tumor type		
In situ	14 (23)	11 (16)
Invasive	86 (141)	89 (134)
Tumor grade		
Well/moderately differentiated	35 (57)	43 (64)
Poorly differentiated/undifferentiated	44 (73)	40 (63)
Not determined/unknown	21 (34)	17 (26)
Tumor stage (SEER summary stage)		
In situ/localized	60 (97)	54 (80)
Regional/distant	40 (64)	46 (68)
Tumor size (cm)		
0-1	12 (17)	18 (24)
>1-2	27 (39)	28 (36)
>2-5	38 (54)	37 (48)
>5	15 (21)	11 (14)
Unknown	8 (11)	6 (8)
ER/PR status		
+/+	27 (44)	34 (51)
–/–	20 (32)	16 (24)
All other combinations	8 (13)	10 (15)
Not done/unknown	45 (74)	40 (60)
Treatment type		
Chemotherapy/radiation	8 (13)	8 (12)
Surgery	79 (130)	84 (127)
Not reported	13 (21)	8 (11)

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.

* $P < 0.05$ based on Wilcoxon rank-sum test between African American and European American.

Table 2

Definitions of delay intervals, best chance network, South Carolina 1996-2004

Model: Main exposure	Delay interval	Definition
Model 1	Diagnosis delay	Diagnosis delay was defined as the time between the first examination that found an abnormality by CBE or a mammogram and the diagnosis of breast cancer.
Model 2	Treatment delay	Treatment delay was defined as the time between diagnosis of breast cancer and initiation of treatment.
Model 3	Total delay	Total delay was defined as the time between the first examination that found an abnormality by CBE or a mammogram and the initiation of treatment.
Model 4	Diagnosis delay and treatment delay	Model with both delays included diagnosis delay and treatment delay as separate variables.

Table 3

Multivariate analysis of factors influencing total delay and all cause-survival, Best Chance Network, South Carolina 1996-2004

	African American	European American
ER/PR (+/+)		
Cases	12	4
Person-months	44	51
HR (95% CI)	4.30* (1.34, 13.82)	1.00 (Referent)
ER/PR(–/–)		
Cases	1	6
Person-months	39	45
HR (95% CI)	7.16* (2.29, 22.33)	6.68* (1.65, 27.06)
ER/PR (+/– or –/+)		
Cases	13	11
Person-months	64	48
HR (95% CI)	1.25 (0.14, 11.45)	1.3 (0.41, 3.92)
ER/PR (unknown)		
Cases	13	13
Person-months	296	240
HR (95% CI)	2.68 (0.84, 8.64)	0.61 (0.16, 1.66)

NOTE: Model adjusted for total delay, race, income, age, tumor type, tumor grade, tumor stage, tumor size, treatment type, ER/PR status, and interaction between race and ER/PR status. Total delay was defined as the time between the first examination which found abnormality by CBE or a mammogram and the initiation of treatment. Total delay was the combination of diagnosis delay and treatment delay. Survival was measured from the date of histologic diagnosis of breast cancer.

* $P < 0.05$.

Table 4

Multivariate analyses of factors influencing delay intervals and breast cancer-specific survival, Best Chance Network, South Carolina, 1996-2004

Model: main exposure	Variables	HR (95% CI) or (*P*)	Cases	Person-months
Model 1*	Diagnosis delay	1.00 (0.98-1.00)		11,641
	Race			
	African American	1.12 (0.63-1.98)	25	
	European American	1.00	34	
Model 2†	Treatment delay	1.00 (0.97-1.00)		6,159
	Race			
	African American	1.12 (0.65-1.94)	25	
	European American	1.00	34	
Model 3‡	Total delay	1.00 (0.99-1.00)		18,154
	Race			
	African American	1.12 (0.64-1.94)	25	
	European American	1.00	34	
Model 4§	Diagnosis delay	1.00 (0.99-1.00)		11,641
	Treatment delay	1.00 (0.97-1.01)		6,159
	Race			
	African American	1.16 (0.65-2.08)	25	
	European American	1.00	34	

NOTE: All models were adjusted for total delay, race, income, age, tumor type, tumor grade, tumor stage, tumor size, treatment type, ER/PR status, and interaction between race and ER/PR status. Survival was measured from the date of histologic diagnosis of breast cancer.

Abbreviations: HR, hazard ratio; CI, confidence interval; ND, not defined; ER, estrogen receptor; PR, progesterone receptor; CBE, clinical breast exam.

*Model 1 treated diagnosis delay as the main exposure. Diagnosis delay was defined as the time between the first examination which found abnormality by CBE or a mammogram and the diagnosis of breast cancer.

†Model 2 treated treatment delay as the main exposure. Treatment delay was defined as the time between diagnosis of breast cancer and initiation of treatment.

‡Model 3 treated total delay as the main exposure. Total delay was defined as the time between the first examination which found abnormality by CBE or a mammogram and the initiation of treatment. Total delay was the combination of diagnosis delay and treatment delay.

§Model 4 treated diagnosis delay and treatment delay as the main exposures. Model with both delays included diagnosis delay and treatment delay as separate variables.