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Racial Disparities in Diagnostic Delay Among Women with Breast Cancer

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Summary Sentence

We observed racial disparities in delays in the diagnostic process for screen detected breast cancer (BC) malignancies and total delay in diagnosis was associated with an increase in BC mortality.

Introduction

In the U.S, breast cancer (BC) mortality rates have been declining, with an average annual decrease of 1.4% over the last decade[1]. This decline is largely attributed to national screening programs, resulting in detection of BC at earlier, treatable stages, and the development of targeted therapies[2]. However, substantial barriers to primary care and screening programs still exist. These barriers to initial diagnosis can lead to delays in treatment and result in poor outcomes.

In addition, while overall mortality rates are decreasing, Black-White mortality disparities 30 years of national efforts to reduce the mortality gap[3]. Efforts to increase screening among

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Black women have resulted in similar mammography rates, with 77% of Black and 72% of White women reportedly receiving a mammogram in the last two years[4]. However, these data may represent only a select subset of women and fail to capture the type, frequency, and completeness of BC screening[5–7].

The screening mammogram is only the first step in the BC diagnostic process. Abnormal findings on screening require further diagnostic evaluation and subsequent biopsy if deemed suspicious, each with an interval of time in between. At each stage of this multi-step process, there is potential for the patient to experience a prolongation of an interval (*i.e.*, delay) that would impact their overall time to diagnosis. While there are no national guidelines or recommendations on follow-up time for abnormal screening results, the Breast Cancer Surveillance Consortium reports that approximately 90% of diagnostic imaging and 81% of biopsy or surgical consultation occur within 30 days of recommendation[8]. Previous studies have investigated the impact of patient characteristics, such as race, socioeconomic status, insurance type, and distance from screening facility, on diagnostic delay[9–11]. Still, others have estimated the association between screening and tumor characteristics (e.g., stage and subtype)[12,13]. However, there has been no study to date that has evaluated these collective factors in a cohort of women diagnosed with breast cancer, examining the impact of delay from screening to diagnosis at each interval beyond the initial screen. We sought to not only address this knowledge gap but understand how delays in diagnosis contribute to tumor characteristics and BC mortality among Black and White women diagnosed with BC in a metro-Atlanta hospital system.

Methods

Sample Population

Data for this study were obtained from the Emory University Breast Imaging Centers, which includes four sites in the Emory University Healthcare system that provide BC screening services throughout the metropolitan-Atlanta area. We first identified 806 women with a screening mammography date between 01 January 2010 and 31 December 2014, and who had a confirmed BC diagnosis. Race was self-reported. Of the 806 BC patients identified in the Emory University Healthcare screening database, we were able to validate BC diagnosis by linking to the Georgia Cancer Registry (GCR) for a final retrospective cohort[14] of 730 (91%) BC patients. Reasons for not linking to the GCR included: BC diagnosis before initial screening date, diagnosed with BC outside of Georgia, not a first primary BC, or invalid patient identifier.

Diagnostic Delay

Delays leading up to a BC diagnosis were defined based on dates of mammography screening, diagnostic evaluation, and biopsy. We defined diagnostic delay as the number of days between screening mammography and diagnostic evaluation, biopsy delay as the number of days between diagnostic evaluation and biopsy, and total delay as the number of days between initial screening mammogram and biopsy. As no clinical guidelines exist on the recommended timeline from screening to diagnostic evaluation to biopsy for breast cancer, we established cut-points to define delay vs. no delay based on the distribution of

the number of days in each of the intervals (screening to diagnostic evaluation, diagnostic evaluation to biopsy and screening to biopsy) along with clinical input by a breast radiologist (RS) and medical oncologist (KG). Diagnostic delay was categorized as ≥30 days vs. <30 days; biopsy delay was categorized as ≥15 days vs. <15 days, and total delay was categorized as ≥45 days vs. <45 days. The median and IQR were calculated for the total sample population for diagnostic evaluation delay, biopsy delay, and total delay (Supplemental Table 1) to confirm utility of the cut-points.

Predictors of Delay

Patient demographic information was collected from the GCR and was considered as possible predictors of delays in diagnosis. We included patient race (Black and White), age at BC diagnosis (<55, 55– <65, 65– <75, 75 or older), a census-derived area-based measure of socioeconomic status [SES] (0%– <10%, 10%– <20%, 20%–100% below poverty), insurance status (uninsured, private, Medicaid, Medicare, Military, unknown), and marital status (single, married, or other). Due to small sample size, we categorized insurance status as private vs. Medicare and marital status as partnered vs. other for the purposes of the analysis. We calculated geographical distance to screening facilities based on both the patient's address at time of screening and the address of the screening hospital. Distance was derived based on the centroid of the census tract for both the patient and screening facility address using the SAS Macro Distance. The geographical distance to facility was subsequently categorized into quartiles (0 to 5.8 miles; 5.8 to 10.8 miles; 10.8 to 18.95 miles; ≥18.95). The quartiles for distance correspond to approximately 30 additional minutes of drive time, which could correspond to barriers in access to care. There were 6 women who lived >200 miles from the facility where they received screening. We excluded these women in a sensitivity analysis.

Tumor Characteristics

Information on the tumor characteristics at diagnosis were abstracted from the GCR. We collected information on stage (0–IV), tumor grade (I–III), lymph node involvement (none, 1–3, 3+, or unknown/unexamined), tumor size (≤1cm, 1–5cm, ≥5cm), and derived BC subtype (Luminal A, Luminal B, HER2-overexpressing, or triple negative breast cancer [TNBC]) based on estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) status. We additionally collected information on BC mortality (ICD10-C50), which was determined using ICD-10 codes from death certificate data.

Statistical Analysis

Descriptive statistics were calculated as frequency and proportion for covariates of interest across delay categories.

We used multivariable-adjusted logistic regression models to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) associating the demographic predictors with diagnostic delay, biopsy delay, and total delay. We additionally explored the association between each predictor and delay using quantile regression, as the distribution of each category of delay was right-skewed. We report multivariable-adjusted estimates for the average diagnostic,

biopsy and total delay days by each predictor with corresponding 95%CI at the 50th percentile of the distribution of the outcome.

To estimate the associations between delay and tumor characteristics, we used multivariable-adjusted ordinal logistic regression models to compute the ORs and 95%CIs associating diagnostic, biopsy and total delay with stage (I, II, III) and grade (I, II, III). We used logistic regression to compute the ORs and 95%CIs associating delay with lymph node involvement (positive vs negative), tumor size (≥1cm vs <1 cm), ER status (ER+ vs ER−), and BC mortality (BC mortality event vs. alive or other cause of death). Analyses examining the association between delay and tumor characteristics were restricted to those diagnosed with invasive, non-metastatic, BC (n=505).

For all analyses, potential confounders included in the models were based on a literature review and graphical assessment[15]. Graphical assessment for all models is provided in the online supplementary materials (Supplemental Figure 1). All analyses were carried out in SAS v9.4 (Cary, NC).

Results

We identified 730 women (362 White and 368 Black women) who underwent BC screening prior to a BC diagnosis at an Emory University Breast Imaging Center (Table 1). The median number of days for each time interval was approximately 60% greater for Black women than White women (for total delay: 42 vs. 26 days). Similarly, women residing in lower SES neighborhoods (20%–100% poverty) had longer median number of days of total delay to diagnosis (42 vs 28 days) compared with women residing in higher SES neighborhoods (0%–10% poverty). Uninsured women also experienced the longest median number of days of total delay (44.5 days). Approximately half of uninsured women experienced diagnostic, biopsy and total delays (Supplemental Table 1). In addition, compared with White BC patients, Black women were more likely to experience longer total delay to diagnosis (≥45 days: 28% vs 46%, respectively). With respect to tumor characteristics, women with later stage (stage IV: 90 days), larger tumor size (>5cm: 43 days), and triple-negative tumors (43 days) had longer median number of days of total delay to diagnosis (Table 1).

Patient Characteristics

Associations between patient demographic characteristics and diagnostic delay are provided in Table 2. In quantile regression models, we observed that Black women experienced an average 10-day delay in diagnosis compared with White women (β=10.1; 95%CI=7.62, 12.6). Black women were also more likely to experience a biopsy delay (β=3.38; 95%CI=2.10, 4.67), and total delay ≥45 days (β=16.3; 95%CI=11.6, 21.0). Neighborhood-level SES was also associated with delays in diagnosis. Women residing in the lowest SES neighborhoods had a slight increase in delays in biopsy (β=1.63; 95%CI=0.10, 3.17) and total delay of ≥45 days (β=6.79; 95%CI=0.22, 13.4), although the estimates were imprecise. In logistic regression models, we observed that Black women were at least twice as likely to experience diagnostic delays (OR=1.98; total 95%CI=1.45, 2.71), biopsy delays (OR=2.41; 95%CI=1.67, 3.41), and delays ≥45 days (OR=2.22; 95%CI=1.63, 3.02) compared with

White women [Supplemental Table 2]. Among women who resided in neighborhoods with low SES, we observed a 1.69 times increase in the odds of diagnostic delay compared with women who resided in neighborhoods with high SES (OR=1.69; 95%CI=1.12, 2.57).

Tumor Characteristics

When considering the association between delay and tumor characteristics, we observed that women with a total delay of ≥45 days were more likely to have a later stage tumor compared with women who did not experience a total delay (OR=1.72; 95%CI=1.17, 2.53) (Figure 1). In multivariable-adjusted models, women who experienced a diagnostic delay were less likely to be diagnosed with ER+ disease compared with women who did not experience a diagnostic delay (OR=0.61; 95%CI=0.36, 0.99).

Breast Cancer Mortality

Among women who experienced a total diagnostic delay of ≥45 days, we observed 1.57 times increase in the odds of BC mortality compared with women who did not experience a delay (OR=1.57, 95%CI=0.96, 2.58) (Figure 1). We additionally explored how delay contributed to racial disparities in BC mortality. Among women who experienced a total diagnostic delay, Black women had a 1.6 times increased odds of BC mortality compared with White women (OR=1.61, 95%CI=0.77, 3.37). Among women who did not experience a total diagnostic delay the estimate was attenuated (OR=1.22, 95%CI=0.63, 2.34).

Discussion

In our study, we examined delays in diagnosis of screen detected malignancies including delays in diagnostic evaluation and biopsy, ultimately leading to a total delay to diagnosis. We explored the contribution of patient demographic characteristics to delay, and the contribution of delay to tumor characteristics and BC mortality, potentially identifying stages of the diagnostic process that may benefit from intervention. Our results showed the most pronounced associations with delay among Black women and women living in lower SES neighborhoods. For Black women, association with delay was observed in each stage of the diagnostic process. In contrast, associations with delay among women residing in lower SES neighborhoods were driven by delay to diagnostic evaluation. Delay was associated with more advanced stage of BC diagnosis, with the most pronounced association for delay to diagnostic evaluation. Additionally, we observed an association between total delay and BC mortality, underscoring the importance of early detection.

Our results are consistent with studies that have reported pronounced racial disparities in delays between an abnormal screening mammogram to definitive BC diagnosis[9,16–19]. When compared with White women, Black women had longer times between a provider recognized abnormality to BC diagnosis, with one study reporting delays up to twice that of White women[20]. Consistent with these studies, we found that Black women were at least twice as likely to experience delays at each stage of the diagnostic process compared with White women. Interestingly, in our study, race was the only patient characteristic associated with delay to biopsy; Black women had a 2.4 times increase in the odds of delay to biopsy compared with White women [OR=2.41; 95%CI=1.67, 3.41].

Our results also suggest that area-level SES is an important factor driving delays in BC diagnostic evaluation. Previous studies have reported that lower income is associated with both incomplete diagnostic work-up and delays from abnormal mammogram to diagnosis[21,22]. In addition to SES as a contributor to delay in BC diagnosis, type of insurance has also been considered[10,23,24]. We observed that half of uninsured patients experienced diagnostic and total screening delays, but numbers were too few to estimate associations in multivariable models. A previous study among uninsured women <65 years of age in North Carolina reported that women experienced a longer time to initial diagnostic evaluation after positive screening mammography [HR=0.47; 95%CI=0.25–0.89] compared with women who had private insurance[10]. Another study found that having private health insurance did not eliminate race-associated delays in BC diagnosis, with insured Black women having more than twice as many days between a suspicious finding during a physical exam, mammography, or ultrasound and diagnosis than insured White women[24]. These findings may suggest that systemic inequities (*i.e.*, provider biases, discrimination, social and physical environments), rather than race itself, are fundamental drivers of delay, as observed in the present study. Understanding what barriers contribute to Black women receiving delays in diagnostic evaluation requires further study and is necessary for determining what interventions are required to reduce this disparity.

Tumor characteristics are an important consideration in this study, as prognosis for certain aggressive tumors may be more sensitive to delays, and still other tumor characteristics (e.g., stage) are directly related to timeliness of diagnosis. Women diagnosed with late stage BC (III and IV) have worse prognosis compared with women diagnosed with early stage BC[4]. Black women are more likely to present with late stage tumors at diagnosis[25]. In our study, we found that there was an increased odds of being diagnosed with a late-stage tumor among women who experienced a total delay >45 days compared with women who did not experience a total delay to diagnosis. Our findings are supported by other studies that have shown an association between diagnostic delay and late stage BC diagnosis[20,26,27]. Women diagnosed with TNBC were more likely to have a diagnostic delay, compared with women diagnosed with hormone receptor positive disease. In multivariable models we report a 40% lower odds of ER+ disease among women with a diagnostic delay after adjusting for age, race, and area-level SES. Few studies have examined the relationship between delays and tumor markers but, given that ER− tumors (particularly TNBC) are more likely to have an aggressive phenotype and poorer prognosis compared with ER+ tumors, it is imperative to ensure women at highest risk for aggressive tumor types (namely Black and young women) are evaluated in a timely manner.

The deleterious impact of delaying BC diagnosis and subsequent treatment, including neoadjuvant and adjuvant systemic therapy, surgery, and radiation on mortality has been well-documented[28–35]. After adjusting for age, race, and area-level SES, we found a positive association between total delay and BC-specific mortality. While we were underpowered to perform formal mediation analyses, it is likely that the associations between delay and BC mortality are driven primarily by tumor stage and reinforces that efforts to reduce overall BC mortality also include strategies to reduce delays in diagnosis.

The major strengths of our study include the comprehensive evaluation of patient characteristics, our diverse study population, ability to study multiple delay intervals, the inclusion of important tumor characteristics, and long-term follow-up for mortality. However, our study was restricted to looking at women who were diagnosed with BC within one healthcare system in the metropolitan Atlanta area. The selected healthcare system services the diverse population of metro-Atlanta and, while the proportion of patients varied by race, each center reflected the surrounding neighborhood composition. The advantage of using a single hospital system is that the processes for screening and follow up are consistent across sites, with each site having adequate capacity for care. We acknowledge that women in our study may not represent the larger population of women that are receiving screening mammograms without abnormal results or women that receive abnormal results but are not diagnosed with BC. However, the primary aim of our study was to understand the diagnostic process, both with assessment of patient characteristics related to delay and assessment of delay on tumor characteristics and BC mortality, we believe our population was appropriate for this study. Additionally, we were unable to assess all potential contributors of delay, primarily the role of family history of BC[36], BRCA1/2 status, screening mammography usage, or reason for diagnostic evaluation, for example self-detected or system detected[18,37]. Furthermore, our study population received their screening and diagnosis at private care facilities and the distribution of insurance types was limited and did not allow us to look at the 3-way interaction between race, screening, insurance and BC disparities. As the expansion of Medicaid in recent years has contributed to a decrease in uninsured patients and a reduction in late-stage breast cancer diagnosis[38], it is important to include Medicaid coverage in future analyses. Finally, due to our limited sample size, some of our estimates were imprecise and we were unable to fully explore the association between diagnostic delay and racial disparities in BC mortality. Future studies may benefit from a formal mediation analysis to understand the contribution of diagnostic delay on racial disparities in BC mortality. Our results suggest that race is the most pronounced driver of delays in the diagnosis of screen detected breast cancers. As such, necessary steps must be taken to identify the personal and structural barriers that influence timely receipt of care for Black women. Further understanding the contribution of delays in BC diagnosis to racial disparities in BC outcomes is needed to inform strategies to reduce the mortality gap.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Take-home points

- Race is the most pronounced driver of delays in the diagnosis of screen detected breast cancers.
- Total delay to diagnosis is associated with an increase in breast cancer mortality
- Intervention strategies are needed to reduce delays among Black women at all stages of the diagnostic process.
- Additional research is required to understand whether these delays contribute to racial disparities in BC mortality.

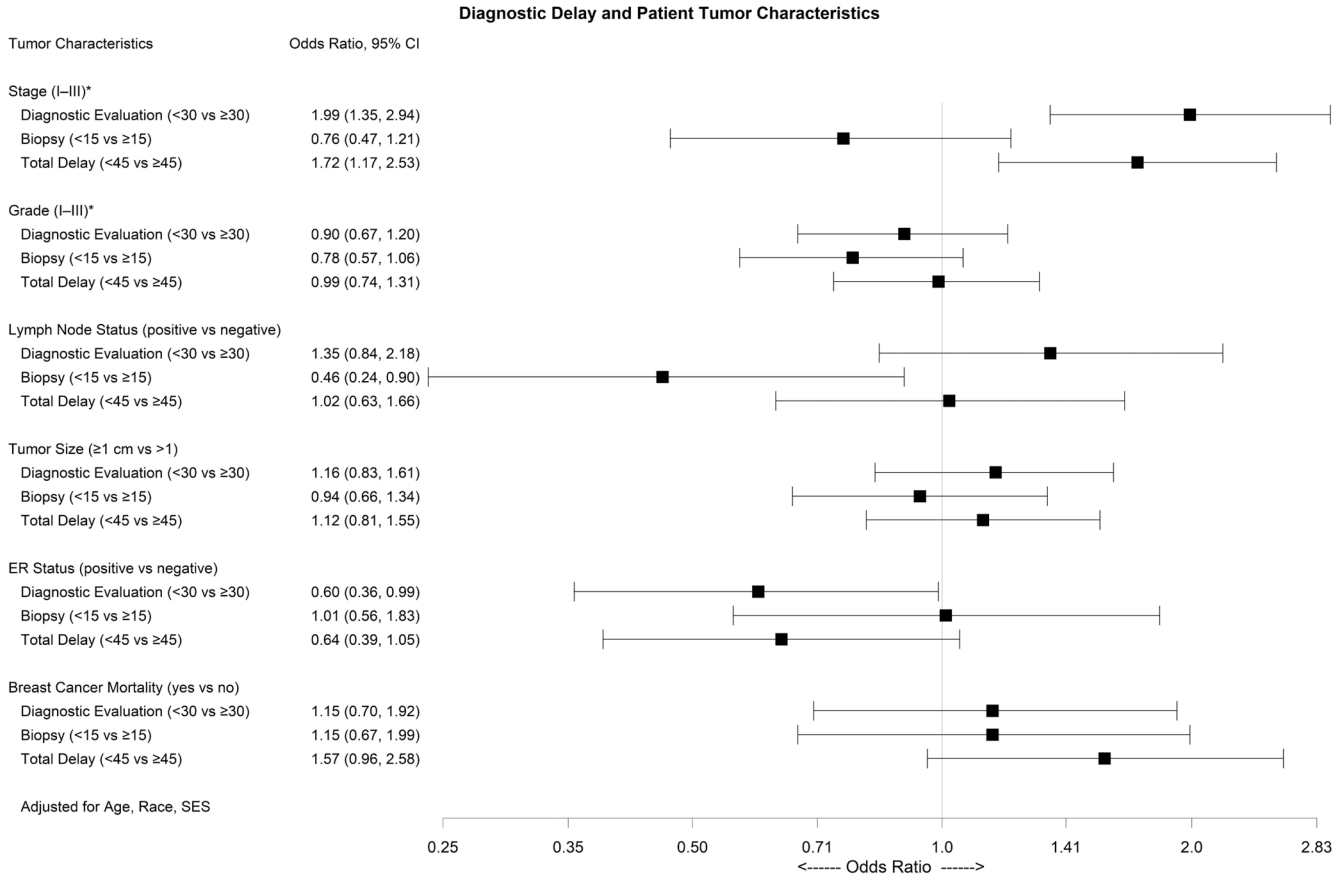

Figure 1.

Multivariable-adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for the association between diagnostic delay and patient tumor characteristics among 730 Black and White women with screen-detected breast cancer at an Emory University Breast Imaging Center (2010–2014). *Ordinal logistic regression

Table 1.

Demographic and tumor characteristics by diagnostic delay (median diagnostic evaluation, biopsy, and total delay days) among 730 Black and White women who underwent breast cancer screening prior to a breast cancer diagnosis at an Emory University Breast Imaging Center (2010–2014).

Demographic Characteristics	Diagnostic Evaluation Delay Median (IQR)	Biopsy Delay Median (IQR)	Total Delay Median (IQR)
Total Patient Population	22 (13, 38)	7 (3, 15)	33 (20, 59)
Race			
White	17 (9, 32)	6 (2, 11)	26 (15, 49)
Black	27 (18, 42)	9.5 (5, 19)	42 (26, 67)
Age Category			
<55	21 (15, 41)	7 (3, 13)	34 (23, 56)
55–64	21 (14, 39)	6 (2, 15)	30 (19, 56)
65–74	24 (13, 40.5)	7 (3, 15)	37 (20, 63)
>=75	21 (12, 37)	8 (4, 15)	33 (20, 59)
Socioeconomic Status			
0% – <10% poverty	20 (13, 31)	6 (2, 13)	28 (18, 51)
10% – <20% poverty	22 (13, 38)	7 (3, 15)	34 (19, 59)
20% – 100% poverty	27 (14, 43)	10 (4, 18)	42 (24, 69)
Insurance Status			
Uninsured	28.5 (24, 49)	13.5 (9, 27)	44.5 (33, 62)
Private	22 (13, 39)	7 (2, 14)	32 (19, 58)
Medicaid	29 (24, 47)	11 (6, 17)	39 (29, 84)
Medicare	21 (12, 36)	8 (3, 16)	33 (19, 16)
Military	28 (20, 48)	6 (3, 21)	43 (26, 54)
Unknown	13 (10, 37.5)	6.5 (3.5, 12.5)	21 (14, 50)
Geographical Distance to Screening Facilities			
Range 1 (0–5.8 miles)	21 (12, 40)	7 (2, 16)	33 (19, 16)
Range 2 (5.8–10.8)	25 (16, 37)	8 (5, 15)	37 (25, 60)
Range 3(10.8–18.95)	26 (13, 35.5)	7 (3, 17)	35 (20, 57.5)
Range 4(18.95–2180.5)	18 (8, 42)	6 (3, 13)	26 (15, 58)
Marital Status			
Single	24 (14, 37)	9 (4, 21)	40.5 (21, 63)
Married (common law and unmarried domestic)	21 (13, 36)	7 (3, 16)	31 (19.58)
Other (divorced, widowed, separated	25 (13, 42)	7 (3, 16)	35.5 (20, 60)
Unknown	15 (9, 28.5)	6.5 (1, 9)	23 (17, 38.5)
Tumor Characteristics			
Stage			
0	25 (14, 37)	10 (6, 20)	37 (22, 61)
I	20 (12, 32.5)	7 (3, 14)	29 (17, 49.5)
II	26 (13, 68)	6 (2, 13)	39 (21, 109)

Demographic Characteristics	Diagnostic Evaluation Delay Median (IQR)	Biopsy Delay Median (IQR)	Total Delay Median (IQR)
III	21 (14, 62)	6 (1, 10)	29.5 (20, 87)
IV	52 (19, 203)	6 (0, 11)	90 (19, 273)
Unknown	63.5 (47, 179.5)	9 (2.5, 16.5)	80 (56, 189.5)
Grade			
I	21 (13, 39)	7 (3, 17)	34.5 (19, 56)
II	22 (13, 36)	7 (3, 15)	33 (20, 58)
III	22 (13, 42)	7 (2, 14)	33.5 (20, 62)
Other/unknown	25 (13, 45)	6 (2, 18)	36 (18, 61)
Lymph Node Involvement			
1–3 positive	25 (13, 52)	5 (2, 9)	32 (17, 87)
3+	20 (15, 47)	7 (3, 11)	28 (22, 58)
Negative	22 (13, 37)	7 (3, 14)	32 (20, 58)
Unknown/no nodes examined	22 (12, 37)	8 (5, 19)	37 (20, 62)
Tumor Size			
≤1 cm	22 (13, 34)	8 (4, 15)	34 (20, 54)
1–5 cm	21 (13, 40)	6 (2,13)	31 (19, 58)
≥5 cm	27 (13, 45)	10.5 (6, 20)	43 (21, 72)
Subtype			
Luminal A	21 (12, 37)	6.5 (3, 13)	31 (18, 53.5)
Luminal B	22.5 (16, 53)	6.5 (2, 11)	34.5 (22, 89)
HER2-overexpressing	21 (18, 71)	7 (2, 14)	31 (20, 93)
TNBC	28 (17, 54)	7 (1, 14)	43 (21, 68)
Unknown	23 (13, 36)	10 (6, 20)	36 (22, 61)
ER Status			
ER+	21 (13, 38)	6.5 (3, 13)	31 (18, 56)
ER−	28 (17. 56)	7 (1, 14)	42 (21, 69)

Table 2:

Age and multivariable-adjusted Quantile Regression β coefficient and 95% confidence intervals for diagnostic delay (diagnostic evaluation, biopsy, and total delay) according to patient demographic characteristics among 730 Black and White women who underwent breast cancer screening prior to a breast cancer diagnosis at an Emory University Breast Imaging Center (2010–2014).

Demographic Characteristics	Diagnostic Evaluation Delay (30≥ vs <30) β (95% CI)	Biopsy Delay (15≥ vs <15) β (95% CI)	Total Delay (45≥ vs <45) β (95% CI)
Race *			
White	Reference	Reference	Reference
Black	10.10 (7.62, 12.60)	3.38 (2.10, 4.67)	16.30 (11.6,21.00)
Age Category			
<55	Reference	Reference	Reference
55–65	0.00 (−6.09, 6.09)	−1.00 (−3.03, 1.03)	−4.00 (−14.4, 6.39)
66–75	3.00 (−2.96, 8.96)	0.00 (−1.99, 1.99)	2.00 (−8.17, 12.20)
>75	0.00 (−5.93, 5.93)	1.00 (−0.98, 2.98)	−1.00 (−11.1, 9.1)
Socioeconomic Status **			
0% – <10% poverty	Reference	Reference	Reference
10% – <20% poverty	1.69 (−1.48, 4.87)	−0.39 (−1.84, 1.05)	2.89 (−3.27, 9.06)
20% – 100% poverty	1.64 (−1.74, 5.02)	1.63 (0.10, 3.17)	6.79 (0.22, 13.40)
Insurance Status ***			
Private(BLUE CROSS, HMO PPO)	Reference	Reference	Reference
MEDICARE	−2.26 (−6.40, 1.88)	1.00 (−0.40, 2.4)	−3.31 (−9.82, 3.60)
Geographical Distance to Screening Facilities ****			
Range 1 (0–5.8 miles)	Reference	Reference	Reference
Range 2 (5.8–10.8)	1.00 (−2.43, 4.43)	0.40 (−1.46, 2.26)	3.07 (−3.85, 10.00)
Range 3(10.8–18.95)	0.00 (−3.56, 3.56)	0.10 (−1.83, 2.03)	0.85 (−6.33, 8.04)
Range 4(18.95–2180.5)	−3.00 (−6.50, 0.50)	−0.85 (−2.76, 1.06)	−3.93 (−11.0, 3.16)
Marital Status *****			
Married (common law and unmarried domestic)	Reference	Reference	Reference
Other (single, divorced, widowed, separated)	0.30 (−2.36, 2.96)	0.50 (−0.87, 1.87)	1.36(−4.09, 6.81)

Adjustments

* age

** age, race

*** age, SES

**** age, SES, race