Receipt of Guideline-Concordant Care Does Not Explain Breast Cancer Mortality Disparities by Race in Metropolitan Atlanta

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ABSTRACT

Background: Racial disparities in breast cancer mortality in the United States are well documented. Non-Hispanic Black (NHB) women are more likely to die of their disease than their non-Hispanic White (NHW) counterparts. The disparity is most pronounced among women diagnosed with prognostically favorable tumors, which may result in part from variations in their receipt of guideline care. In this study, we sought to estimate the effect of guideline-concordant care (GCC) on prognosis, and to evaluate whether receipt of GCC modified racial disparities in breast cancer mortality. **Patients and Methods:** Using the Georgia Cancer Registry, we identified 2,784 NHB and 4,262 NHW women diagnosed with a stage I–III first primary breast cancer in the metropolitan Atlanta area, Georgia, between 2010 and 2014. Women were included if they received surgery and information on their breast tumor characteristics was available; all others were excluded. Receipt of recommended therapies (chemotherapy, radiotherapy, endocrine therapy, and anti-HER2 therapy) as indicated was considered GCC. We used Cox proportional hazards models to estimate the impact of receiving GCC on breast cancer mortality overall and by race, with multivariable adjusted hazard ratios (HRs). **Results:** We found that NHB and NHW women were almost equally likely to receive GCC (65% vs 63%, respectively). Failure to receive GCC was associated with an increase in the hazard of breast cancer mortality (HR, 1.74; 95% CI, 1.37–2.20). However, racial disparities in breast cancer mortality persisted despite whether GCC was received (HR_{GCC}: 2.17 [95% CI, 1.61–2.92]; $HR_{non\text{-}GCC}$: 1.81 [95% CI, 1.28–2.91]). **Conclusions:** Although receipt of GCC is important for breast cancer outcomes, racial disparities in breast cancer mortality did not diminish with receipt of GCC; differences in mortality between Black and White patients persisted across the strata of GCC.

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Background

In the United States, racial disparities in breast cancer outcomes are well-documented, with non-Hispanic Black (NHB) women more likely to die of their disease than their non-Hispanic White (NHW) counterparts.[1–3] The disparity is in part attributed to stage and subtype—NHB women are more likely to be diagnosed with a metastatic cancer and/or a triple-negative subtype, both of which have a poor prognosis due to limited treatment options.[4,5] However, our group recently reported that the most pronounced racial disparities in breast cancer mortality were observed among women with nonmetastatic, estrogen receptor–positive (ER+) tumors.[6,7] Such tumors are known to have a favorable prognosis, given multiple highly effective biomarker-driven treatment regimens.[8] One explanation for such paradoxical findings is that disparities in survival outcomes among women with early-stage or ER+ disease may result from factors downstream of their cancer diagnosis, such as the failure to receive guideline-concordant care (GCC).[9]

Clinical guidelines for women diagnosed with stage I–III breast cancer have been developed based on results from multiple clinical trials, and failure to receive GCC has adverse effects on breast cancer outcomes.[10–13] Nonadherence to guidelines could arise from multiple factors, including structural racism, barriers to access, tumor and patient characteristics, or clinician and patient preferences.[11] Therefore, nonadherence to clinical guidelines may be a contributing factor to the observed race disparity in breast cancer mortality.[9,14] Observational studies assessing adherence to clinical guidelines are important in understanding patient outcomes; however, few studies have examined the receipt of GCC as a possible driver of disparate outcomes in a population-based setting.

To address this knowledge gap, we evaluated how failure to receive GCC contributes to breast cancer

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mortality overall and to disparities in breast cancer mortality among NHB and NHW women diagnosed with a first primary stage I–III breast cancer in metropolitan Atlanta, Georgia.

Patients and Methods

Study Population

Using the Georgia Cancer Registry (GCR), we identified women diagnosed with breast cancer between 2010 and 2014 while residing in metropolitan Atlanta (ie, Fulton, DeKalb, Gwinnett, Cobb, or Clayton counties). Patients with breast cancer were included if they were diagnosed with an invasive stage I–III first primary breast tumor and were classified as being NHW or NHB. Race was based on US Census Bureau definitions, and Hispanic ethnicity was determined by the North American Association of Central Cancer Registries Hispanic Identification Algorithm.[15,16] Additional criteria required that women had information available for assigning tumor subtype (ER, the progesterone receptor used to define women as hormone receptor–positive [HR+] or hormone receptor–negative [HR–], and HER2 expression) and had received surgery as part of their local therapy. Hormone receptor and HER2 status were used to assign women as HR+/HER2−, HR+/HER2+, HR−/HER2+, or HR−/HER2−. Detailed information on the differences between women who received surgery (94.6%) and those who did not (5.4%) are reported in supplemental eTables 1–3 (available with this article at JNCCN.org). Follow-up information was available on patients through December 31, 2016. The outcome of interest was breast cancer mortality (ICD-10-CM code C50), which was determined from death certificate data.

Exposure Assessment

Guideline Care

Receipt of guideline care was determined based on the 2011 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer (Table 1).[17] The NCCN Guidelines were used to inform the indication for each type of breast cancer therapy for every patient in our dataset. Information regarding the type of surgery received (mastectomy vs breast-conserving surgery), tumor receptor status (ER, progesterone receptor, and HER2 expression), tumor size, lymph node involvement, and 21-gene recurrence score data (obtained via direct linkage with Genomic Health Inc.) were ascertained from the GCR (supplemental eTables 4–7).

We first grouped women based on their breast cancer subtype as HR+/HER2−, HR+/HER2+, HR−/HER2+, or HR−/HER2−, as described in the previous section. These derived tumor subtypes informed the type of biomarker-driven therapies (endocrine therapy and anti-HER2 therapy) that a patient should receive. We then examined the possible combinations of surgery type, tumor size, lymph node status, and 21-gene recurrence score to determine treatment indications. Based on these patient-level data in the GCR, each woman was classified as indicated, discretionary, not indicated, or indeterminate (missing) for each type of therapy. The latter occurred among 6.6% of NHB women and 5.2% of NHW women.

Once the indication for each therapy was determined, we assessed whether the patient received therapy consistent with the NCCN Guidelines[17] using GCR treatment data. The GCR regularly collects information on surgery type and initiation of chemotherapy, radiation, and endocrine therapies. Anti-HER2 therapies were captured as chemotherapy in the GCR analytic database until 2013 and were coded as immunotherapy in subsequent years. Using natural language processing (NLP), we searched the treatment-related text fields of the GCR database for specific character strings related to an indication of trastuzumab receipt before 2013.[18] In addition, there were 271 women (3.6%) who did not have information available on the initiation of endocrine therapy. For these women, we used NLP to identify the receipt of endocrine therapy in treatment-related text fields.

Patients who were indicated for a treatment regimen and did not receive it, or those who received therapy without an indication, were classified as having received non-GCC for that treatment modality. Conversely, if a patient's indication was consistent with the receipt or nonreceipt of a specific therapy, then the patient was classified as guideline-concordant. Among women for whom a therapy was discretionary (based on the NCCN Guidelines[17]), any value (eg, receipt, nonreceipt, and missing/unknown value) resulted in a classification of guideline-concordant for that therapy.

Our primary exposure of interest was receipt of GCC across all treatment modalities and for each individual treatment modality. In a sensitivity analysis, we allowed for each patient to have any one therapy not meeting guideline care.

Covariates

We collected information on age at diagnosis (continuous), stage of disease (I–III), derived breast cancer subtype (HR+/HER2−, HR+/HER2+, HR−/HER2+, or HR−/HER2−), a US Census–derived area-based measure of socioeconomic status (SES; 0% to <5%, 5% to <10%, 10% to <20%, and 20%–100% below poverty level), marital status (single, married, divorced/separated/other), and insurance type (private, Medicare, Medicaid, military/other, and uninsured). SES status is based on census tract–level poverty data that are published annually from the American Community Survey[19] and have been used widely in population-based studies.[20,21]

Table 1. 2011 NCCN Guidelines[17] Recommendations

Tumor Subtype	Neoadjuvant	Surgery	Node Status	Tumor Size (cm)	Radiation	21-Gene Recurrence Score	Chemotherapy Recommendation	Anti-HER2 Indication	Endocrine Therapy Indication
ER−/HER2−	No	Mastectomy	Positive	<5	Discretionary	N/A	Yes	None indicated	None
				≥5	Yes				
			Negative	≤1	No		Discretionary		
				>1	No		Yes		
		BCS	Positive	All	Yes				
			Negative	≤1			Discretionary		
				>1			Yes		
	Yes	All	Positive/ Negative	All	Discretionary				
ER−/HER+	No	Mastectomy	Positive	<5	Discretionary	N/A	Yes	Yes	None
				≥5	Yes				
			Negative	≤1	No		Discretionary	Discretionary	
				1–5	No		Yes	Yes	
				>5	Yes				
		BCS	Negative	≤1	Yes		Discretionary	Discretionary	
				>5					
			Positive	All			Yes	Yes	
	Yes	All	Positive/ Negative		Discretionary				
ER+/HER2+	No	Mastectomy	Negative	≤0.5	No	N/A	Discretionary	Discretionary	Yes
		BCS			Yes				
		Mastectomy		0.6–1	No				
		BCS			Yes				
		Mastectomy		1–5	No		Yes	Yes	
				1–5	No				
				≥5	Discretionary				
				≥5	Discretionary				
		BCS		≥1	Yes				
				≥1	Yes				
		Mastectomy	Negative	1–5	Discretionary		Yes		
		Mastectomy		≥5	Yes				
		BCS		All	Yes				
	Yes	All	Negative	≤0.5	Discretionary	N/A	Discretionary	Yes	
				0.6–1					
				1–5			Yes		
				≥5					
			Positive	≤0.5					
				0.6–1					
				1–5					
				≥5					

(*continued*)

Statistical Methods

Descriptive statistics were calculated as median values with interquartile ranges or as n (%) for covariates of interest across the NHB and NHW population subgroups. We also report the frequency (%) of women who failed to receive GCC by treatment modality.

Follow-up was defined as time in months, from the date of surgery until whichever was first: (1) a mortality event, (2) the last date of contact in registry, or (3) December 31, 2016. We used multivariable-adjusted Cox proportional hazard models to calculate the hazard ratios (HRs) and 95% confidence intervals for the association

Table 1. 2011 NCCN Guidelines[17] Recommendations (cont.)

Tumor Subtype	Neoadjuvant	Surgery	Node Status	Tumor Size (cm)	Radiation	21-Gene Recurrence Score		Chemotherapy Recommendation	Anti-HER2 Indication	Endocrine Therapy Indication
ER+/HER2−	No	Mastectomy	Negative	≤0.5	No	N/A		No	None indicated	Yes
		BCS			Yes			No		
		Mastectomy		0.5–5	No	Consider Oncotype score	Low (<18)	Not indicated		
		BCS			Yes		Medium (18–30)	Discretionary		
		Mastectomy		≥5	Discretionary		High (>30)	Yes		
		BCS			Yes		Not done	Discretionary		
		Mastectomy	Positive	<5	Discretionary	N/A		Yes		
				≥5	Yes					
		BCS		All	Yes					
	Yes	All	Negative	≤0.5	Discretionary	N/A		No		
					Discretionary			No		
				0.5–5	Discretionary	Consider Oncotype score	Low (<18)	Not indicated		
					Discretionary		Medium (18–30)	Discretionary		
				≥5	Discretionary		High (>30)	Yes		
					Discretionary		Not done	Yes		
			Positive	<5	Discretionary	N/A		Yes		
				≥5	Discretionary					

Abbreviations: All, mastectomy or BCS; BCS, breast-conserving surgery; ER, estrogen receptor; N/A, not applicable.

between the receipt of GCC for joint concordance of all treatment modalities and each treatment modality independently with breast cancer mortality.

To address our second aim, we estimated the association between race and breast cancer mortality and whether this association was modified by the receipt of GCC (yes/no). Interaction describes the differences in the effect of one exposure across the strata of another exposure, which depends on the scale.[22,23] In this analysis, we assessed additive and multiplicative interaction for the effect of race on breast cancer mortality by receipt of GCC.[24] The presence of interaction between race and GCC was estimated with the common referent approach to calculate the relative excess risk due to interaction (RERI), evaluating the departure of the effect on the additive scale.[24,25] We calculated the 95% confidence interval for the RERI using the delta method.[23,26,27] The presence of multiplicative interactions, indicating whether the combined effect of race and GCC was greater than the product of the individual effects, was assessed by comparing stratum-specific effect estimates.[25]

We verified the proportional hazards assumption for all variables by checking the ln-ln survival curves for any gross violation.[28] Potential confounders included in the models were based on a priori knowledge and graphical-based methods (using a directed acyclic graph).[29] For the association between receipt of GCC and breast cancer mortality, confounders included race, disease stage, age at diagnosis, SES, derived breast cancer subtype, and insurance type (supplemental eFigure 1). For the interaction model including race and GCC, age at diagnosis was the only confounder identified, based on our graphical assessment (supplemental eFigure 2). The other covariates (eg, disease stage, SES, derived breast cancer subtype, and insurance type) are on the causal path between race and breast cancer mortality, and including them in the model could have potentially induced bias.[30] However, to be consistent with prior studies of race disparities in breast cancer outcomes, we present additional results from analyses adjusting for disease stage, SES, derived breast cancer subtype, and insurance type.

The association between GCC and breast cancer mortality may be susceptible to immortal person-time bias[31,32] because of exposure assignment after the initiation of follow-up, which could lead to a mortality event occurring before the start of an indicated treatment. To evaluate the potential bias, we performed landmark analyses. We extended the initiation of follow-up in 3-month intervals, up until 12 months after the recorded date of surgery for each treatment modality and combination. All analyses were conducted using R version 3.5 (R Foundation for Statistical Computing) and SAS 9.4 (SAS Institute Inc).

Results

We identified 7,046 (2,784 NHB and 4,262 NHW) study-eligible women treated with surgery in the metropolitan Atlanta area. On average, NHB women were younger (median age, 56 vs 60 years), less likely to have private health insurance (57% vs 64%), and less likely to live in a high-SES

Table 2. Patient Demographic, Clinicopathologic, and Treatment Characteristics

	NHB Median (IQR)	NHW Median (IQR)
Total, n	2,784	4,262
Age at diagnosis, y	56 (47–64)	60 (50–68)
Length of follow-up, mo	43 (28–59)	44 (29–61)
Time to event, mo	23 (15–37)	28 (14–42)
	NHB n (%)	**NHW n (%)**
Clinicopathologic characteristics		
Breast cancer–specific death	190 (6.8)	150 (3.5)
AJCC stage		
I	1,230 (44)	2,493 (58)
II	1,151 (41)	1,393 (33)
III	403 (14)	376 (8.8)
Tumor grade		
1	418 (15)	1,192 (28)
2	1,029 (37)	1,810 (42)
≥3	1,269 (46)	1,150 (27)
Unknown	68 (2.4)	110 (2.6)
Tumor size, cm		
≤0.5	231 (8.3)	471 (11)
0.6–1	382 (14)	813 (19)
>1 to <5	1,857 (67)	2,724 (64)
≥5	306 (11)	242 (5.7)
Unknown	8 (0.3)	12 (0.3)
Lymph node status		
Node-negative	1,741 (63)	2,986 (70)
Node-positive	919 (33)	1,122 (26)
1–3	617 (22)	830 (19)
≥4	216 (7.8)	238 (5.6)
Unknown number	86 (3.1)	54 (1.3)
No nodes examined	121 (4.4)	154 (3.6)
Unknown node status	3 (0.1)	0 (0.0)
ER status		
ER−	718 (26)	540 (13)
ER+	2,066 (74)	3,722 (87)
Derived tumor subtype		
HR+/HER2−	1,771 (64)	3,272 (77)
HR+/HER2+	341 (12)	482 (11)
HR−/HER2+	141 (5.1)	143 (3.4)
HR−/HER2−	531 (19)	365 (8.6)

(*continued*)

Table 2. Patient Demographic, Clinicopathologic, and Treatment Characteristics (cont.)

	NHB n (%)	NHW n (%)
Treatment characteristics		
Receipt of neoadjuvant therapy		
No	2,189 (79)	3,783 (89)
Yes	595 (21)	478 (11)
Surgery		
BCS	1,474 (53)	2,327 (55)
Mastectomy	1,309 (47)	1,933 (45)
Receipt of GCC		
21-gene recurrence score as indicated		
Not indicated and not received	1,300 (47)	1,520 (36)
Not indicated and received	414 (15)	621 (18)
Indicated and received		
<18	340 (12)	759 (18)
18–30	217 (7.8)	453 (11)
>30	59 (2.1)	93 (2.8)
Indicated and not received	391 (14)	697 (16)
Unknown (nodes/tumor size)	63 (2.3)	119 (2.8)
Chemotherapy as indicated		
Not indicated and not received	466 (17)	1,106 (26)
Not indicated and received	53 (1.9)	79 (1.9)
Not indicated and unknown	9 (0.3)	23 (0.5)
Discretionary		
No	361 (7.9)	905 (21)
Yes	301 (11)	326 (7.7)
Unknown	15 (0.5)	21 (0.5)
Indicated and not received	221 (7.9)	392 (9.2)
Indicated and received	1,287 (46)	1,292 (30)
Indicated and unknown	23 (0.8)	42 (1.0)
Cannot determine indication	48 (1.7)	75 (1.8)
Radiation as indicated		
Not indicated and not received	431 (15)	909 (21)
Not indicated and received	64 (2.3)	63 (1.5)
Not indicated and unknown	16 (3.1)	23 (0.5)
Discretionary		
No	281 (10)	440 (10)
Yes	550 (20)	509 (12)
Unknown	61 (2.2)	61 (1.4)
Indicated and not received	136 (4.9)	178 (4.2)
Indicated and received	1,131 (41)	1,971 (46)
Indicated and unknown	65 (2.3)	50 (1.2)
Cannot determine indication	49 (1.8)	58 (1.4)

(*continued on next page*)

Table 2. Patient Demographic, Clinicopathologic, and Treatment Characteristics (cont.)

	NHB n (%)	NHW n (%)
Receipt of endocrine therapy		
Not indicated and not received	647 (23)	491 (12)
Not indicated and received	25 (0.9)	17 (0.4)
Indicated and received	1,658 (60)	2,899 (68)
Indicated and not received	454 (16)	855 (20)
Receipt of anti-HER2 therapy[a]		
Not indicated and not received	2,263 (81)	3,597 (84)
Not indicated and received	39 (1.4)	40 (0.9)
Discretionary		
No	22 (0.8)	73 (1.7)
Yes	26 (0.9)	46 (1.1)
Indicated and received	335 (12)	388 (9.1)
Indicated and not received	99 (3.6)	118 (2.8)
Demographic characteristics		
Marital status		
Single	840 (30)	516 (12)
Married[b]	1,036 (37)	2,674 (63)
Other[c]	784 (28)	966 (23)
Unknown	124 (4.5)	106 (2.5)
Socioeconomic index		
0% to <5% poverty	173 (6.2)	1,344 (32)
5% to <10% poverty	360 (13)	1,265 (30)
10% to <20% poverty	1,030 (37)	1,130 (27)
20% to 100% poverty	1,221 (44)	523 (12)
Insurance type		
Uninsured	87 (3.1)	41 (1.0)
Private	1,596 (57)	2,735 (64)
Medicaid	376 (14)	111 (2.6)
Medicare	631 (23)	1,289 (30)
Military	47 (1.7)	35 (0.8)
Unknown	47 (1.7)	51 (1.2)

Abbreviations: BCS, breast-conserving surgery; ER, estrogen receptor; GCC, guideline-concordant care; GCR, Georgia Cancer Registry; HR, hormone receptor; IQR, interquartile ratio; NHB, non-Hispanic Black; NHW, non-Hispanic White.
[a]Data abstracted from text fields of GCR database.
[b]Common law and unmarried domestic.
[c]Divorced, widowed, separated.

neighborhood (6.2% vs 32%) compared with NHW women (Table 2). Receipt of overall GCC was comparable between NHB and NHW women (65% vs 63%, respectively; Table 3. Receipt of overall GCC was similar for NHB and NHW women with HR+/HER2−, HR+/HER2+, or HR−/HER2− breast cancer (68% vs 65%; 60% vs 60%; 82% vs 80%, respectively), whereas NHB women diagnosed with HR−/HER2+ breast cancer were less likely to receive GCC compared with NHW women (66% vs 72%, respectively). Across individual treatment modalities, NHB and NHW women were nearly equally likely to receive guideline-concordant radiation (88% vs 91%), chemotherapy (87% vs 86%), endocrine (83% vs 80%), and HER2-targeted (95% vs 96%) therapies (Table 3).

Table 3. Receipt of Overall GCC and Individual Treatment Modalities

Receipt of GCC	NHB n (%)	NHW n (%)
Total, N	2,784	4,262
Derived tumor subtype		
HR+/HER2−	1,125 (68)	2,046 (65)
HR+/HER2+	195 (60)	281 (60)
HR−/HER2+	88 (66)	100 (72)
HR−/HER2−	410 (82)	277 (80)
Individual treatment modalities		
All modalities		
Concordant	1,818 (65)	2,704 (63)
Discordant	791 (28)	1,346 (32)
Unknown	175 (6.3)	212 (5.0)
Radiation		
Concordant	2,454 (88)	3,890 (91)
Discordant	200 (7.2)	241 (5.7)
Unknown	130 (4.7)	131 (3.1)
Chemotherapy		
Concordant	2,430 (87)	3,651 (86)
Discordant	274 (9.8)	471 (11)
Unknown	80 (2.9)	140 (3.3)
Endocrine therapy		
Concordant	2,305 (83)	3,390 (80)
Discordant	479 (17)	872 (20)
Anti-HER2 therapy		
Concordant	2,646 (95)	4,104 (96)
Discordant	138 (5.0)	158 (3.7)

Abbreviations: GCC, guideline-concordant care; HR, hormone receptor; NHB, non-Hispanic Black; NHW, non-Hispanic White.

Main Effects

We observed an increase in the hazard of breast cancer mortality among women who did not receive GCC (HR, 1.74; 95% CI, 1.37–2.20) compared with those who did. We similarly found an increase in the hazard of breast cancer mortality among women who were discordant for chemotherapy (HR, 1.69; 95% CI, 1.24–2.31), radiation therapy (HR, 1.92; 95% CI, 1.36–2.71), endocrine therapy (HR, 1.70; 95% CI, 1.29–2.24), and anti-HER2 therapy (HR, 1.81; 95% CI, 1.21–2.71) (Table 4). Mutual

Table 4. Multivariable-Adjusted Association Between Receipt of GCC and Breast Cancer Mortality

Guideline Therapy	Events	HR (95% CI)[a]
GCC		
Discordant	128	1.74 (1.37–2.20)
Concordant	183	Ref
Chemotherapy		
Discordant	52	1.69 (1.24–2.31)
Concordant	272	Ref
Radiation		
Discordant	38	1.92 (1.36–2.71)
Concordant	284	Ref
Endocrine therapy		
Discordant	74	1.70 (1.29–2.24)
Concordant	266	Ref
Anti-HER2 therapy		
Discordant	31	1.81 (1.21–2.71)
Concordant	309	Ref
Any 3 modalities		
Discordant	39	2.43 (1.72–3.42)
Concordant	283	Ref

Abbreviations: GCC, guideline-concordant care; HR, hazard ratio.
[a]Adjusted for race, age, cancer stage, socioeconomic status, tumor subtype, and insurance type.

adjustment of the individual treatment modalities yielded similar results (data not shown).

In our sensitivity analysis, defining a patient with GCC as having received at least 3 treatment modalities consistent with guidelines, we observed a slightly more pronounced estimate of association (HR, 2.43; 95% CI, 1.72–3.42). These results suggest that the potential misclassification of GCC is not an explanation for our observed results. In our landmark analyses, we saw similar HR estimates as we increased the time since surgery for receipt of GCC. Our findings are thus robust to any potential immortal person-time bias (supplemental eTable 8).

Racial Disparities

The overall racial disparity in breast cancer mortality in our cohort was 1.98 (95% CI, 1.59–2.46),[7] which persisted even within the strata of the receipt of overall GCC (Table 5). Among women who received GCC across all treatment modalities, we observed a 2-fold increase in the NHB–NHW hazard of breast cancer mortality (HR, 2.17; 95% CI, 1.61–2.91). Among those who did not receive GCC, the NHB–NHW HR was similar, although less pronounced (HR, 1.81; 95% CI, 1.28–2.91; Table 5). In the common referent approach to assess departure on the additive scale, NHW women receiving discordant care had no greater risk of mortality compared with NHW women receiving concordant care. Conversely, NHB women had a 2-fold increased mortality rate regardless of whether they received overall concordant or discordant care.

Although NHB women were consistently more likely to die of their disease compared with NHW women, most pronounced race disparities were among those who received GCC for most independent therapeutic regimens (Table 5). Among women who were discordant for chemotherapy, radiation, or anti-HER2 therapy, the racial disparity in breast cancer mortality was attenuated and near-null. One exception was for endocrine therapy, with NHB women classified as receiving discordant care having a 2.35-fold increased hazard of breast cancer mortality compared with NHW women classified as received discordant care (95% CI, 1.48–3.73). The disparity among women concordant for endocrine therapy was less pronounced (NHB vs NHW HR, 1.92; 95% CI, 1.50–2.45). There was no evidence of additive or multiplicative interaction between race and receipt of GCC in breast cancer mortality. In models additionally adjusting for stage, insurance type, derived breast cancer subtype, and SES, we observed similar although attenuated associations in the disparities across treatment modalities (Table 5).

Discussion

We observed that as clinical guidelines would suggest, failure to receive GCC was associated with an increased hazard of breast cancer mortality. This was noted for the receipt of GCC overall and across each treatment modality. Despite the importance of GCC for health outcomes, the receipt of GCC did not seem to influence racial disparities in breast cancer mortality. Although NHB and NHW women were equally likely to receive care consistent with guidelines for all treatment modalities combined, NHB women had a nearly 2-fold increase in breast cancer mortality compared with their NHW counterparts within the strata of GCC receipt.

There are few previous population-based studies on receipt of GCC in relation to racial disparities in breast cancer mortality. Early investigations (circa 1990–2005) have reported that minority women are less likely to receive appropriate adjuvant therapy, although findings appear to be mixed and few studies report survival disparities.[33,34] The most recent, a study among women residing in rural Georgia, reported that NHB women were more likely to receive GCC compared with NHW women.[33] However, the authors of that study did not evaluate treatment modalities in combination with racial disparities in breast cancer mortality. Similarly, in the CDC's Patterns of Care Study, investigators likewise reported a greater proportion of NHB women received guideline care for chemotherapy.[36] Both of these previous studies included women diagnosed with invasive breast cancer prior to the introduction of the 21-

Table 5. Association Between Receipt of GCC and Breast Cancer Mortality

	Deaths, n		Common Referent HR (95% CI)			NHB vs NHW Stratified Effects	
Treatment Modality	NHW	NHB	NHW	NHB	RERI (95% CI)	HR (95% CI)[a]	HR (95% CI)[b]
Overall race disparity	136	173	—	—	—	1.98 (1.59–2.46)	—
Overall guideline care							
Discordant	62	66	1.53 (1.09–2.15)	2.77 (1.99–3.86)	0.07 (−0.82 to 0.97)	1.81 (1.28–2.91)	1.22 (0.84–1.77)
Concordant	75	108	Ref	2.17 (1.61–2.91)	—	2.17 (1.61–2.91)	1.24 (0.90–1.71)
Chemotherapy							
Discordant	28	24	1.94 (1.28–2.94)	2.92 (1.88–4.54)	−0.22 (−1.65 to 1.22)	1.51 (0.87–2.60)	1.19 (0.68–2.09)
Concordant	111	161	Ref	2.20 (1.72–2.81)	—	2.20 (1.72–2.81)	1.29 (0.98–1.69)
Radiation							
Discordant	17	21	2.41 (1.45–4.01)	3.15 (1.98–5.00)	−0.26 (−2.08 to 1.55)	1.31 (0.69–2.49)	0.95 (0.49–1.83)
Concordant	128	156	Ref	2.00 (1.58–2.53)	—	2.00 (1.58–2.53)	1.21 (0.93–1.58)
Endocrine therapy							
Discordant	33	41	0.95 (0.64–1.40)	2.24 (1.56–3.20)	0.36 (−0.47 to 1.19)	2.35 (1.48–3.73)	1.64 (1.01–2.64)
Concordant	117	149	Ref	1.92 (1.50–2.45)	—	1.92 (1.50–2.45)	1.14 (0.87–1.49)
Anti-HER2 therapy							
Discordant	15	16	2.87 (1.68–4.89)	3.43 (2.04–5.77)	−0.49 (−2.75 to 1.77)	1.19 (0.59–2.42)	1.03 (0.51–2.11)
Concordant	135	174	Ref	2.05 (1.63–2.57)	—	2.05 (1.63–2.57)	1.25 (0.97–1.62)
Any 3 modalities							
Discordant	19	20	2.21 (1.36–3.59)	3.61 (2.25–5.79)	0.43 (−1.47 to 2.33)	1.63 (0.88–3.06)	1.39 (0.73–2.65)
Concordant	126	157	Ref	1.96 (1.55–2.49)	—	1.96 (1.55–2.49)	1.18 (0.91–1.54)

Abbreviations: GCC, guideline-concordant care; HR, hazard ratio; NHB, non-Hispanic Black; NHW, non-Hispanic White; RERI, relative excess risk due to interaction.
[a]Adjusted for age.
[b]Adjusted for age, cancer stage, insurance type, socioeconomic status, and tumor subtype.

gene recurrence score and consideration of tumor subtype for chemotherapy, which may partially explain the differences.[37] Chemotherapy indication for women aged >70 years is subject to underlying comorbidities. The study in rural Georgia considered women aged >70 years to have a discretionary indication for chemotherapy, whereas the CDC study included chemotherapy indication for women aged >70 years because they were able to adjust for underlying comorbidities. In our study, we did not use age as an indicator for chemotherapy, but our results were similar in a sensitivity analysis excluding these women (data not shown). Another potential difference between our study and previous studies is that the metropolitan Atlanta area is a diverse population with approximately 50% NHB residents. This may mitigate some of the initial barriers in treatment initiation compared with rural regions in the southeast or other areas in the United States.

Although our study captured guideline care based on the indication and receipt of breast cancer therapies, we did not capture information on other aspects regarding quality of care, such as treatment facility characteristics or healthcare access, that may have influenced the observed results.[38] Higher-quality care may lead to additional workup by tumor boards or care coordination, leading to better treatment timelines, which may not be equitable across racial/ethnic groups.[39]

We acknowledge several limitations of this study. Our intent was to understand the association between receipt of guideline-concordant first-line therapy and breast cancer mortality and potential racial disparities in this mortality; however, we did not account for the timing of treatment initiation, duration, or completion of adjuvant therapies, which have been associated with patient outcomes and may vary by race.[40–42] We excluded women who did not receive surgery, which likely represents a population with poor outcomes compared with women who did receive surgery. Further exploration of the decision to forgo surgical treatment is important for future research. We similarly did not have information on adherence to endocrine therapy. In the United States, poor adherence and early discontinuation of endocrine therapy have been previously reported, with some studies suggesting racial differences.[43–45] These may be important considerations for future investigations as we work to identify multilevel targets for intervention. We assumed that women who were discretionary for a treatment modality received GCC, but further exploration of the decision to forgo adjuvant therapy (and potential

racial disparities within that decision) may be important for future research. Receipt of anti-HER2 therapy was determined using NLP from GCR treatment text fields among women diagnosed before 2013, which could result in misclassification of anti-HER2 therapy. To evaluate the ability of our NLP to correctly classify women as having received/not received anti-HER2 therapy, we compared results with the GCR treatment variable for women diagnosed after 2013. Results were largely consistent; we observed a 99% specificity and 97% sensitivity using the GCR treatment variable as the gold standard. Although treatment-related data in cancer registries are often underreported and may be subject to misclassification,[46] our findings are similar to those of Guy et al,[35] who used chart abstraction to identify first-line therapy. Finally, we were unable to collect information on comorbid conditions, which may impact both treatment adherence and efficacy.[32] Women with coronary artery disease or diabetes at diagnosis often have poor completion of taxane-based chemotherapy and are more likely to experience adverse effects from breast cancer treatments, which may affect prognosis.[48] Such comorbidities are more likely to present among NHB women, which could in part contribute to the observed disparity.[49]

Conclusions

Racial disparities in breast cancer survival outcomes are complex.[50] In this study, we observed that although GCC was important for patient prognosis overall, we did not find evidence that differences in receipt of GCC contributed to disparate cancer outcomes between NHB and NHW women with breast cancer. Rather, NHB women consistently had worse breast cancer survival outcomes than NHW women, regardless of GCC status. Future studies may be strengthened from a multilevel approach to incorporate information on healthcare access, neighborhood characteristics, characteristics of the treating facilities, treatment duration and completion, and the presence and management of comorbid conditions.

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Receipt of Guideline-Concordant Care Does Not Explain Breast Cancer Mortality Disparities by Race in Metropolitan Atlanta

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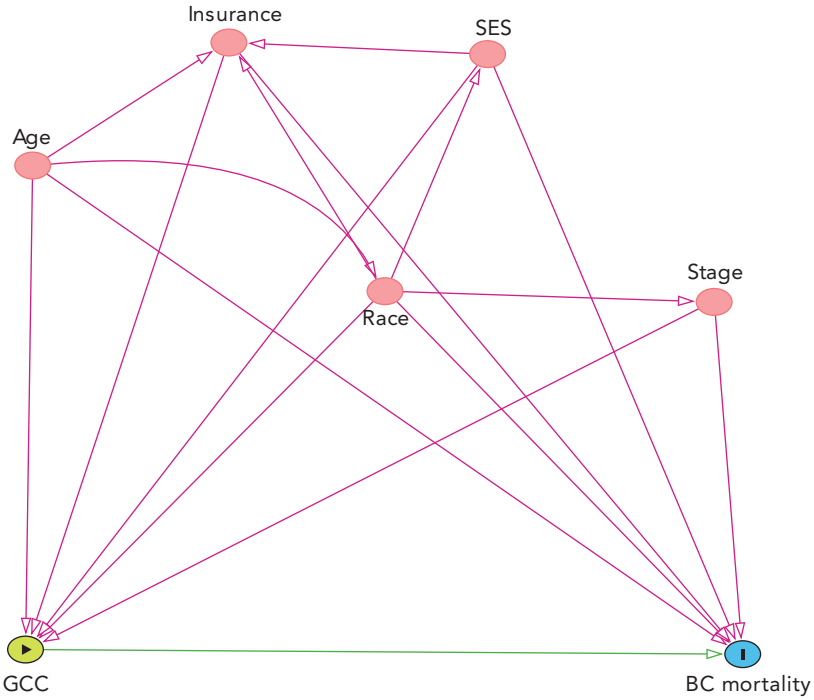
eAppendix 1. Supplemental Content

Exclusion of Women Who Did Not Receive Surgery

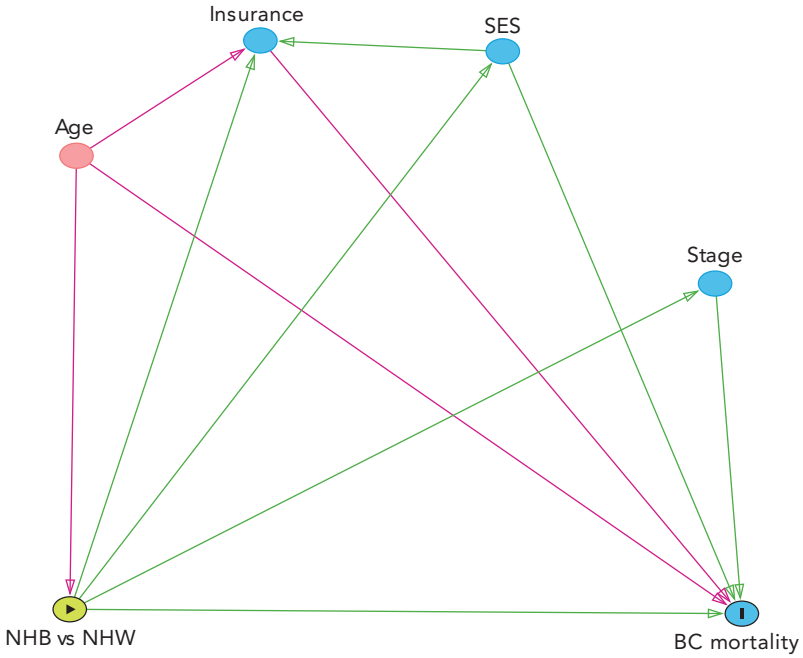
In this registry population-based study, we excluded women who did not receive surgery as part of their local therapy (n=402) because they were likely not representative of the women who went on to receive systemic therapies (see supplemental eTable 1). However, we describe the differences between women who did receive surgery and those who did not. Furthermore, we evaluated whether receipt of guideline-concordant surgical care modified the association between race and breast cancer mortality.

Results

Overall, among women who did not receive surgery we observed a higher mortality rate among both non-Hispanic White (NHW) and non-Hispanic Black (NHB) women compared with those who did receive surgery. Additionally, we observed a slight increase in hazard of breast cancer mortality among NHB women who did not receive surgery compared with NHW women (hazard ratio, 1.20; 95% CI, 0.80–1.82). Conversely, among women who did receive surgery, the racial disparity in breast cancer mortality was more pronounced (hazard ratio, 1.58; 95% CI, 1.26–1.97).



eFigure 1. Directed acyclic graph for the association for receipt of GCC and BC mortality. Colored arrows refer to direct (green) versus confounding (magenta) paths.
Abbreviations: BC, breast cancer; GCC, guideline-concordant care; SES, socioeconomic status.



eFigure 2. Directed acyclic graph for the association between race and BC mortality within strata of receipt of GCC. Colored arrows refer to direct (green) versus confounding (magenta) paths.
Abbreviations: BC, breast cancer; GCC, guideline-concordant care; NHB, non-Hispanic Black; NHW, non-Hispanic White; SES, socioeconomic status.

eTable 1. Distribution of Receipt of Overall GCC Including Surgery (N=7,448)

	NHB n (%)	NHW n (%)
GCC	1,636 (54)	2,278 (52)
No GCC	964 (32)	1,764 (40)
Missing	439 (14)	367 (8.3)

Abbreviations: GCC, guideline-concordant care; NHB, non-Hispanic Black; NHW, non-Hispanic White.

eTable 2. Comparison of Patient Demographic and Clinicopathologic Characteristics, by Receipt of Surgery[a]

	Received Surgery		Did Not Receive Surgery	
	NHW Median (IQR)	NHB Median (IQR)	NHW Median (IQR)	NHB Median (IQR)
Total, n	4,262	2,784	147	255
Age at diagnosis, y	60 (50–68)	56 (47–64)	73 (57–86)	61 (50–75)
Length of follow-up, mo	44 (30–61)	43 (28–59)	31 (15–47)	33 (15–55)
Time to event, mo	28 (14–42)	24 (16–37)	20 (10–31)	20 (9–31)
	Received Surgery		**Did Not Receive Surgery**	
	NHW n (%)	NHB n (%)	NHW n (%)	NHB n (%)
Clinicopathologic characteristics				
Breast cancer–specific death	150 (3.5)	190 (6.8)	35 (22)	73 (29)
AJCC stage				
I	2,493 (58)	1,230 (44)	43 (29)	53 (21)
II	1,393 (33)	1,151 (41)	66 (45)	129 (51)
III	376 (8.8)	403 (14)	38 (26)	73 (29)
Tumor grade				
1	1,192 (28)	418 (15)	33 (22)	25 (9.8)
2	1,810 (42)	1,029 (37)	44 (30)	84 (33)
≥3	1,150 (27)	1,269 (46)	42 (29)	109 (43)
Unknown	110 (2.6)	68 (2.4)	29 (19)	37 (15)
Tumor size, cm				
≤0.5	471 (11)	231 (8.3)	13 (8.8)	12 (4.7)
0.6–1	813 (19)	382 (14)	4 (2.7)	8 (3.1)
>1 to <5	2,724 (64)	1,857 (67)	12 (8.2)	11 (4.3)
≥5	242 (5.7)	306 (11)	100 (68)	161 (63)
Unknown	12 (0.3)	8 (0.3)	18 (12)	63 (25)
Lymph node status				
Node-negative	2,986 (70)	1,741 (63)	4 (2.7)	24 (9.4)
Node-positive	1,122 (26)	919 (33)	34 (8.5)	67 (26)
1–3	830 (19)	617 (22)	9 (2.2)	22 (5.5)
≥4	238 (5.6)	216 (7.8)	2 (0.5)	4 (1.0)
Unknown number	54 (1.3)	86 (3.1)	23 (5.70	41 (10)
No nodes examined	154 (3.6)	121 (4.4)	108 (73)	164 (64)
Unknown node status	0 (0)	3 (0.1)	0 (0)	0 (0)

(*continued*)

eTable 2. Comparison of Patient Demographic and Clinicopathologic Characteristics, by Receipt of Surgery[a] (cont.)

	Received Surgery		Did Not Receive Surgery	
	NHW n (%)	NHB n (%)	NHW n (%)	NHB n (%)
ER status				
ER−	540 (13)	718 (26)	30 (20)	77 (30)
ER+	3,722 (87)	2,066 (74)	117 (80)	178 (70)
Tumor subtype				
HR+/HER2−	3,272 (77)	1,771 (64)	104 (71)	147 (58)
HR+/HER2+	482 (11)	341 (12)	14 (9.5)	32 (13)
HR−/HER2+	143 (3.4)	141 (5.1)	12 (8.2)	16 (6.3)
HR−/HER2−	365 (8.6)	531 (19)	17 (12)	60 (26)
Treatment characteristics				
Chemotherapy				
Yes	1,715 (40)	1,662 (60)	42 (29)	102 (40)
No	2,459 (58)	1,073 (39)	89 (61)	129 (51)
Missing	88 (2)	49 (1.8)	16 (11)	24 (9.4)
Radiotherapy				
Yes	2,567 (60)	1,764 (63)	7 (4.8)	15 (5.9)
No	1,560 (37)	875 (31)	129 (88)	206 (81)
Missing	135 (3.2)	145 (5.2)	11 (7.5)	32 (13)
Demographic characteristics				
Marital status				
Single	516 (12)	840 (30)	26 (18)	90 (35)
Married[b]	2,674 (63)	1,036 (37)	56 (38)	46 (18)
Other[c]	966 (23)	784 (28)	55 (37)	103 (40)
Unknown	106 (2.5)	124 (4.5)	10 (6.8)	16 (6.3)
Socioeconomic index				
0% to <5% poverty	1,344 (32)	173 (6.2)	32 (22)	8 (3.1)
5% to <10% poverty	1,265 (30)	360 (13)	42 (29)	19 (7.5)
10% to <20% poverty	1,130 (27)	1,030 (37)	40 (27)	86 (34)
20%–100% poverty	523 (12)	1,221 (44)	33 (22)	142 (56)
Insurance type				
Uninsured	41 (1.0)	87 (3.1)	7 (4.8)	20 (5.0)
Private	2,735 (64)	1,596 (57)	45 (31)	104 (41)
Medicaid	111 (2.6)	376 (14)	5 (3.4)	40 (16)
Medicare	1,289 (30)	631 (23)	88 (60)	83 (33)
Military	35 (0.8)	47 (1.7)	0 (0)	3 (1.2)
Unknown	51 (1.2)	47 (1.7)	2 (1.4)	5 (2.0)

Abbreviations: ER, estrogen receptor; GCR, Georgia Cancer Registry; HR, hormone receptor; IQR, interquartile range; NHB, non-Hispanic Black; NHW, non-Hispanic White.
[a]Data abstracted from text fields of GCR database.
[b]Common law and unmarried domestic.
[c]Divorced, widowed, separated.

eTable 3. Association Between Receipt of Guideline Surgical Treatment and Breast Cancer Mortality

	Deaths, n		Common Referent HR (95% CI)		Stratified Effects[a] HR (95% CI)	Stratified Effects[b] HR (95% CI)
	NHW	NHB	NHW	NHB		
Surgery						
Discordant	35	73	9.35 (6.44–13.6)	11.1 (8.39–14.7)	1.19 (0.79–1.78)	1.20 (0.80–1.82)
Concordant	150	190	Ref	2.02 (1.63–2.51)	2.02 (1.63–2.51)	1.58 (1.26–1.97)

Abbreviations: HR, hazard ratio; NHB, non-Hispanic Black; NHW, non-Hispanic White.
[a]Adjusted for age.
[b]Adjusted for age, disease stage, insurance type, and socioeconomic status.

eTable 4. Guideline Care Indication Paths Among Women With Derived Tumor Subtype HR+/HER2−

	Subtype	Neo	Surgery	Node Status	Tumor Size	RT	21-Gene RS	Chemo	Tras	Endo		
					AND							
IF	HR+/HER2−	neo=no	surg=mast	node=neg	tumor size≤0.5	RT=no	SKIP	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≤0.5	RT=no	SKIP	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≤0.5	RT=yes	SKIP	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≤0.5	RT=yes	SKIP	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.5–5	RT=no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.5–5	RT=yes	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=yes or no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes

(*continued*)

eTable 4. Guideline Care Indication Paths Among Women With Derived Tumor Subtype HR+/HER2− (cont.)

	Subtype	Neo	Surgery	Node Status	Tumor Size	RT	21-Gene RS	Chemo	Tras	Endo		
					AND							
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥5	RT=yes	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size<5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size<5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size≥5	RT=yes	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size≥5	RT=yes	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=pos	tumor size=ALL	RT=yes	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=pos	tumor size=ALL	RT=yes	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≤0.5	RT=yes or no	SKIP	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≤0.5	RT=yes or no	SKIP	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.5–5	RT=yes or no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score≤18	chemo=no	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score=18–30	chemo=no or yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score>30	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≥5	RT=yes or no	score=missing	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=pos	tumor size<5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=pos	tumor size<5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=pos	tumor size≥5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=pos	tumor size≥5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=YES	THEN	guideline=yes
Among women aged ≥70 y												
IF		neo=no	surg=mast or BCS	node=98	tumor size≤0.5	RT=yes or no	SKIP	chemo=no	tras=no	endo=AI	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=98	tumor size≤0.5	RT=yes or no	SKIP	chemo=no	tras=no	endo=AI	THEN	guideline=yes

Abbreviations: AI, aromatase inhibitor; BCS, breast-conserving surgery; chemo, chemotherapy; endo, endocrine; HR, hormone receptor; mast, mastectomy; neg, negative; neo, neoadjuvant therapy; pos, positive; RS, recurrence score; RT, radiotherapy; surg, surgery; tras, trastuzumab.

eTable 5. Guideline Care Indication Paths Among Women With Derived Tumor Subtype HR+/HER2+

	Subtype	Neo	Surgery	Node Status	Tumor Size	RT	21-Gene RS	Chemo	Tras	Endo		
					AND							
IF	HR+/ HER2+	neo=no	surg=mast	node=neg	tumor size≤0.5	RT=no	SKIP	chemo=no or yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≤0.5	RT=no	SKIP	chemo=no or yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≤0.5	RT=yes	SKIP	chemo=no or yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≤0.5	RT=yes	SKIP	chemo=no or yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.6–1	RT=no	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=0.6–1	RT=no	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.6–1	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size=0.6–1	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=1–5	RT=no	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size=1–5	RT=no	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≥5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥1	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=neg	tumor size≥1	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=pos	tumor size<1	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=pos	tumor size<1	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size<1	RT=no	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size<1	RT=no	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size=1–5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size=1–5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size≥5	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size≥5	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=pos	tumor size=ALL	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=no	surg=BCS	node=pos	tumor size=ALL	RT=yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≤0.5	RT=no or yes	SKIP	chemo=no or yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size≤0.5	RT=no or yes	SKIP	chemo=no or yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.6–1	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=0.6–1	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=1–5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size=1–5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size>5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=neg	tumor size>5	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=pos	tumor size=ALL	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=pos	tumor size=ALL	RT=no or yes	SKIP	chemo=yes	tras=yes	endo=YES	THEN	guideline=yes

Abbreviations: BCS, breast-conserving surgery; chemo, chemotherapy; endo, endocrine; HR, hormone receptor; mast, mastectomy; neg, negative; neo, neoadjuvant therapy; pos, positive; RS, recurrence score; RT, radiotherapy; surg, surgery; tras, trastuzumab.

eTable 6. Guideline Care Indication Paths Among Women With Derived Tumor Subtype HER2+

	Subtype	Neo	Surgery	Node Status	Tumor Size	RT	21-Gene RS	Chemo	Tras	Endo		
IF	HER2	neo=no	surg=mast	node=pos	tumor size≤5	RT=no or yes	SKIP	chemo=yes	Tras=yes	endo=no	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size>5	RT=yes	SKIP	chemo=yes	Tras=yes	endo=no	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≤5	RT=no	SKIP	chemo=yes	Tras=yes	endo=no	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size>5	RT=yes or no	SKIP	chemo=yes	Tras=yes	endo=no	THEN	guideline=yes
IF		neo=no	surg=BCS	node=ALL	tumor size=ALL	RT=yes	SKIP	chemo=yes	Tras=yes	endo=no	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=ALL	tumor size=ALL	RT=no or yes	SKIP	chemo=yes	Tras=yes	endo=no	THEN	guideline=yes

Abbreviations: BCS, breast-conserving surgery; chemo, chemotherapy; endo, endocrine; mast, mastectomy; neg, negative; neo, neoadjuvant therapy; pos, positive; RS, recurrence score; RT, radiotherapy; tras, trastuzumab.

eTable 7. Guideline Care Indication Paths Among Women With Derived Tumor Subtype HR−/HER2−

	Subtype	Neo	Surgery	Node Status	Tumor Size	RT	21-Gene RS	Chemo	Tras	Endo		
					AND							
IF	HR−/HER2−	neo=no	surg=mast	node=pos	tumor size≤5	RT=no or yes	SKIP	chemo=yes	tras=no	endo=no	THEN	guideline=yes
IF		neo=no	surg=mast	node=pos	tumor size>5	RT=yes	SKIP	chemo=yes	tras=no	endo=no	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size≤5	RT=no	SKIP	chemo=yes	tras=no	endo=no	THEN	guideline=yes
IF		neo=no	surg=mast	node=neg	tumor size>5	RT=yes or no	SKIP	chemo=yes	tras=no	endo=no	THEN	guideline=yes
IF		neo=no	surg=BCS	node=ALL	tumor size=ALL	RT=yes	SKIP	chemo=yes	tras=no	endo=no	THEN	guideline=yes
IF		neo=yes	surg=mast or BCS	node=ALL	tumor size=ALL	RT=no or yes	SKIP	chemo=yes	tras=no	endo=no	THEN	guideline=yes

Abbreviations: BCS, breast-conserving surgery; chemo, chemotherapy; endo, endocrine; HR, hormone receptor; mast, mastectomy; neg, negative; neo, neoadjuvant therapy; pos, positive; RS, recurrence score; RT, radiotherapy; tras, trastuzumab.

eTable 8. Landmark Analyses to Explore Possible Influence of Immortal Person-Time Bias Among NHB and NHW Women

Treatment Modality	3-Month Landmark			6-Month Landmark			9-Month Landmark			12-Month Landmark		
	Deaths, n		Stratified Effects[a]	Deaths, n		Stratified Effects[a]	Deaths, n		Stratified Effects[a]	Deaths, n		Stratified Effects[a]
	NHW	NHB	HR (95% CI)	NHW	NHB	HR (95% CI)	NHW	NHB	HR (95% CI)	NHW	NHB	HR (95% CI)
Chemotherapy												
Discordant	32	25	1.39 (0.81–2.38)	30	24	1.45 (0.84–2.53)	29	24	1.56 (0.89–2.72)	26	22	1.54 (0.86–2.78)
Concordant	104	156	1.46 (1.10–1.92)	102	149	1.45 (1.09–1.92)	95	141	1.51 (1.13–2.03)	86	127	1.48 (1.09–2.00)
Radiation												
Discordant	16	19	1.14 (0.58–2.25)	16	18	1.10 (0.55–2.20)	14	18	1.30 (0.63–2.65)	12	16	1.27 (0.60–2.73)
Concordant	127	155	1.37 (1.05–1.80)	123	149	1.40 (1.06–1.83)	116	140	1.44 (1.09–1.91)	105	126	1.40 (1.04–1.88)
Endocrine therapy												
Discordant	31	39	1.60 (0.98–2.62)	31	36	1.52 (0.92–2.50)	26	34	1.78 (1.04–3.02)	24	34	1.89 (1.09–3.25)
Concordant	116	147	1.34 (1.02–1.76)	112	142	1.36 (1.03–1.80)	107	135	1.41 (1.06–1.87)	96	118	1.35 (0.99–1.82)
HER2 therapy												
Discordant	15	16	1.16 (0.57–2.37)	14	16	1.26 (0.61–2.60)	13	14	1.23 (0.57–2.64)	12	13	1.23 (0.56–2.72)
Concordant	132	170	1.41 (1.09–1.83)	129	162	1.40 (1.08–1.83)	120	155	1.50 (1.14–1.97)	108	139	1.47 (1.10–1.96)
GCC												
Discordant	61	65	1.38 (0.95–2.01)	59	61	1.38 (0.94–1.02)	55	58	1.45 (0.98–2.16)	50	54	1.43 (0.95–2.16)
Concordant	73	105	1.41 (1.02–1.96)	71	102	1.44 (1.04–2.01)	67	97	1.50 (1.07–2.11)	60	86	1.44 (1.01–2.06)

Abbreviations: GCC, guideline-concordant care; HR, hazard ratio; NHB, non-Hispanic Black; NHW, non-Hispanic White.
[a]Adjusted for age, disease stage, insurance type, and socioeconomic status.