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# Black-white differences in receipt and completion of adjuvant chemotherapy among breast cancer patients in a rural region of the US

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# Abstract

Recent breast cancer treatment studies conducted in large urban settings have reported racial disparities in the appropriate use of adjuvant chemotherapy. This article presents the first focused evaluation of black-white differences in receipt and completion of chemotherapy for breast cancer in a primarily rural region of the United States. We performed chart abstraction on initial therapy received by 868 women diagnosed with Stages I, IIA, IIB, or IIIA breast cancer in 2001-2003 in southwest Georgia (SWGA). For chemotherapy, information collected included treatment plan, dates of delivery, concordance between therapy planned and received, and date and reasons for end of treatment. The patient's age at diagnosis, race, marital status, insurance coverage, hormone receptor status, comorbidities, socioeconomic status, urban/rural status, treatment site, and distance to the site were also collected. Following univariate analyses, we used multivariable logistic regression modeling to examine the impact of race on the likelihood of (1) receiving chemotherapy and (2) completing planned chemotherapy. For patients terminating chemotherapy prematurely, the reasons were documented. The results showed that the unadjusted black-white difference in receipt of chemotherapy (48.3 vs. 36.0%) was significant, but in the multivariable analysis the black – white odds ratio (OR = 1.18) was not. While the unadjusted black–white difference (92.0 vs. 87.8%) in completing chemotherapy was not significant, in multi-variable models black race was positively associated with completing care (p ranging from 0.032 to 0.087 and OR, correspondingly, from 2.16 to 2.64). The impact of race on completing chemotherapy was influenced by marital status, with a significant black-white difference for patients not married (OR = 4.67), but no difference for those married (OR = 1.06). We find compelling racial differences in this largely rural region—with black breast cancer patients receiving or completing chemotherapy at rates that equal or exceed white patients. Further investigation is warranted, both in SWGA and in other rural regions.

#### Keywords

Cancer health disparities; Adjuvant chemotherapy; Racial differences in cancer care; Cancer care in rural regions

# Introduction

The effectiveness of adjuvant chemotherapy in reducing disease recurrence and improving overall and disease- free survival in early stage breast cancer has been demonstrated over time in multiple-randomized trials [1–5] and recent population-based studies [6, 7]. For maximum impact, the planned course of treatment should be delivered until completion, unless there are clinically sound reasons for stopping or delaying therapy [1, 3].

Previous studies have found that incomplete treatment with adjuvant chemotherapy in breast cancer is associated with poorer survival and, in addition, a higher percentage of black women received less than expected treatment compared with whites [8–10]. While compelling, these findings must be interpreted through the prism of the patient populations studied, as well as the information available for defining and evaluating cancer care receipt and completion. Relevant investigations to date include clinical trials [9], observational studies using linked registry-administrative data files [6, 7], at least one statewide analysis

[11], and studies of specific urban–suburban populations [8, 10–12]. With rare exception [13], little attention has been directed to non-metropolitan areas. Consequently, our current knowledge is limited regarding the delivery of chemotherapy for breast cancer in rural America.

Equally important are the methods that investigators have adopted for defining and evaluating chemotherapy completion. Whether using data from clinical trials [9], medical records [8], or linked registry-administrative data [14], studies have typically needed to employ empirically based algorithms or decision rules (e.g., "actual vs. expected" care) to define incomplete treatment. To our knowledge, no population-based study has attempted to adjudicate incomplete chemotherapy based on *joint consideration* of the (a) therapy recommended in the treatment plan, (b) course of treatment actually received, and (c) documented reasons for treatment discontinuation.

This article presents the first focused evaluation of both the receipt and the completion of adjuvant chemotherapy for breast cancer in a primarily rural region of the United States—specifically, a 33-county area in the southwest portion of the state of Georgia (southwest Georgia—SWGA). Specifically, we examine (1) the extent to which early stage breast cancer patients in SWGA received adjuvant chemotherapy, and the factors associated with receipt of therapy; and (2) the extent to which patients who had a plan to start chemotherapy completed recommended treatment, and the factors associated with successful completion.

Of particular interest is whether the type of black–white differences found in urban and suburban populations of breast cancer patients are likewise evident in this largely rural region of the US.

# Materials and methods

#### Patients and geographic setting

The study population included all women residing in SWGA<sup>1</sup> diagnosed with a first primary, early stage breast cancer between January 1, 2001 and December 31, 2003, and who received at least their first 12 months of therapy post diagnosis entirely within the region. Incident breast cancer cases were identified through the Georgia Comprehensive Cancer Registry. Early stage breast cancer was defined to include diagnosis at American Joint Committee on Cancer (AJCC) stages I, II, or IIIA<sup>2</sup>. Receipt of neoadjuvant chemotherapy (prior to surgery) can impact decisions about the amount and timing of adjuvant chemotherapy, and may also have implications for the patient's propensity to complete adjuvant therapies. Consequently, we excluded (as have others [7, 11]) those patients receiving neoadjuvant chemotherapy.

<sup>&</sup>lt;sup>1</sup>The 33 counties comprising SWGA had a census-estimated population near the time of this study of about 724,000. About 82% of SWGA residents live in non-metropolitan areas. The median household income is about 72% of the U.S. average, and about 21% of the population lives below the Federal poverty line, compared with 12.4% nationally. About 38% of the population is African-American [15].

<sup>&</sup>lt;sup>2</sup>While characterizations of invasive "early stage" breast cancer vary in the literature, with some papers including only stages I and II, the definition here is consistent with current National Cancer Institute terminology (http://www.cancer.gov/dictionary?expand=E). Throughout, we combine stages IIA and IIB into a single stage II, given sample size constraints.

Roughly 80–85% of cancer patients treated in SWGA receive care at one (or more) of four American College of Surgeons' Commission on Cancer (CoC)-approved cancer centers<sup>3</sup>.

The study was approved by the institutional review boards at Emory University, the Centers for Disease Control and Prevention, and the Georgia Department of Community Health, and by committees at the four main cancer centers in SWGA.

# Data collection and specification of variables

To meet study objectives, we developed a customized electronic data collection instrument and trained onsite abstractors to identify and code information from medical records. For each major type of cancer treatment, including chemotherapy, the electronic instrument guided the abstractor through a sequence of study-relevant inquiries on treatments planned, delivered, and discontinued. Data abstraction was conducted by five teams: one for each cancer center study site, and a fifth team assigned to 23 smaller hospitals and free-standing clinics operating across SWGA during the study period<sup>4</sup>.

While identifying patients who began adjuvant chemotherapy was relatively straightforward, determinating whether, when, and why a patient with a chemotherapy plan failed to complete treatment required a case-by-case examination. To proceed, all study-included cases were reviewed in detail by two of the authors (KCW and TWG), focusing on these two questions in the instrument: "Did the chemotherapy received match the plan?" and "If not, what were the reasons for not matching the plan?". Each affirmative response ("Yes") was validated by examining the recorded treatments given, their dates, and the overall degree of agreement between treatment plan and chemotherapy actually received. Each negative response ("No") was evaluated similarly, but with additional assessment of the reason(s) recorded for not matching the planned care.

For our base-case analyses of chemotherapy completion, we excluded patients for whom the recorded reason for not matching planned care was death, from any cause. The discontinuation of cancer care in such cases was regarded as the (necessary) consequence of a change in treatment plan, rather than as a "discretionary" decision involving some assessment of the benefits and harms of continuing care. We tested the impact of this assumption through sensitivity analyses, as reported below.

Explanatory variables for analyses of both chemotherapy initiation and chemotherapy completion included age at diagnosis, race, marital status, insurance status, socio-economic status, rural status, comorbidity status, AJCC stage at diagnosis, estrogen receptor/ progesterone receptor (ER/PR) status, primary treatment site where care was received in SWGA, and the distance (in miles) between the patient's residence and the primary

<sup>&</sup>lt;sup>3</sup>These study sites and their approximate total annual case volume (all cancer types) during the study period are as follows: Phoebe Cancer Center in Albany, 1,000–1,100; Pearlman Cancer Center at South Georgia Medical Center in Valdosta, 400–600; Singletary Oncology Center at Archhold Medical Center in Thomasville, 400–600; and Tift Regional Oncology Center at Tift Medical Center in Tifton, 300–400 [16]. During the study period, the nearest National Cancer Institute-designated cancer center was at least 180 miles away for virtually any SWGA resident. <sup>4</sup>The Southwest Georgia Cancer Coalition, based in Albany, assisted Emory University investigators in developing effective working

<sup>&</sup>lt;sup>4</sup>The Southwest Georgia Cancer Coalition, based in Albany, assisted Emory University investigators in developing effective working relationships with the four cancer centers. The fifth study team was managed by the GCCR Regional Coordinator for Southwest Georgia.

#### Statistical analyses

For the two study outcomes of interest—receipt of adjuvant chemotherapy and successful completion of chemotherapy—we conducted univariate analyses with each of the explanatory variables, in turn, using  $\chi^2$  tests accompanied by 2-sided *p* values. Guided by these findings, we estimated multivariable logistic regression models for each study outcome, with a focus on race and with the other explanatory variables regarded as potential con-founders. We tested for clinically and behaviorally plausible interaction effects. Logistic regression results were expressed as adjusted odds ratios, with corresponding 95% confidence intervals (CI). For the one predictor variable with a significant number of missing values, ER/PR status, we re-estimated the relevant model(s) omitting this variable, as a sensitivity analysis. To guard against overfitting the regressions, we adopted a commonly embraced guidepost<sup>5</sup>.

For patients who discontinued care prior to its scheduled completion we provide a descriptive summary of the reasons, as coded by the abstractors.

Analyses were conducted with SAS Version 9.2 (SAS Institute, Cary, NC).

# Results

Of the 1,289 women diagnosed with breast cancer from January 1, 2001 through December 31, 2003 in the 33-county region of SWGA, 1,096 (85%) were treated in SWGA (Fig. 1). Of these, 908 were diagnosed with early stage invasive disease. Excluding the 40 women who received neoadjuvant chemotherapy leaves 868 patients meeting study inclusion criteria.

#### Receipt of adjuvant chemotherapy

Overall, 344 of the 868 SWGA patients (39.6%) received adjuvant chemotherapy (Fig. 1).

In univariate analyses (Table 1), the percent of black women receiving chemotherapy was significantly greater than for whites (48.3 vs. 36.0%, p = 0.001). Receipt of chemotherapy was also positively and significantly associated with younger age at diagnosis, being married, having no comorbid conditions at time of diagnosis, later stage of diagnosis, and being ER/PR negative. There was a significant univariate insurance effect, with patients who had Medicaid or Medicaid/pending having the highest rate of chemotherapy use. Patients treated at CoC-approved hospitals had an overall higher prevalence of chemotherapy use than those treated at non-CoC facilities. In these unadjusted analyses, receipt of chemotherapy was positively (not inversely) related to distance from the patient's home to her primary treatment facility.

<sup>&</sup>lt;sup>5</sup>Specifically, we adhered to Harrell's recommendation that for models with a binary response variable, the number of predictors should generally not exceed m/10, where  $m = \min(N_1, N_2)$ , and  $N_1$  and  $N_2$  are the marginal frequencies of the binary outcome [18].

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Our estimated base-case multivariable logistic regression model is reported in Table 2. After controlling for other demographic factors (e.g., age, marital status, insurance status), clinical factors (stage, ER/PR status, comorbidities), and provider factors (treatment site and the patient's distance to it), there was no significant black– white difference in predicted receipt of chemotherapy. Receipt of chemotherapy was positively and significantly associated with younger age at diagnosis, a higher stage at diagnosis, and being ER/PR negative. Having Medicaid or Medicaid Pending was positively associated with receipt of chemotherapy, but no other insurance variable was significant. Patients living in a census tract with <10% of the population below the Federal poverty line were more likely to receive chemotherapy. The patient's distance to the treatment site was not significant in this multivariable analysis, but site-of-care remained a significant predictor of receiving chemotherapy<sup>6</sup>.

While ER/PR status was an important predictor of receiving chemotherapy, observations on this variable were missing for 131 of our 868 patients (Table 1). In a sensitivity analysis (not shown), we re-estimated the logistic regression model excluding ER/PR status, thereby increasing the available sample from 721 to 846. There were no changes in sign or patterns of statistical significance for the remaining variables in the model.

In additional multivariable modeling (not shown), we found no significant interaction effects between race and the other predictor variables.

The model in Table 2 and its variants exhibited high goodness-of-fit, with a *c index* (probability of concordance) of 0.907 in the base case and above 0.886 in all variants.

#### Completion of planned adjuvant chemotherapy

In addition to the 344 patients who began chemotherapy, three additional patients had a treatment plan but did not start (Fig. 1). Of these 347 patients, 310 (89.3%) completed *planned* chemotherapy, so that 37 (10.7%) did not.

We note in passing that of the 310 patients who completed planned adjuvant chemotherapy, 270 had no recorded change in plan; the 40 who did included also the four patients who died during the initial treatment period.

In univariate analyses (Table 3), the percentage of patients completing planned chemotherapy was higher for blacks than whites (92.0 vs. 87.8%), but the difference was not statistically significant (p = 0.227). There was an age effect, with patients under age 65 completing chemotherapy at a higher rate, but no other significant effects.

<sup>&</sup>lt;sup>6</sup>Because the patient's distance from her home to primary site of treatment may be regarded as an important attribute of the site itself, we estimated alternative versions of the model that excluded, in turn, the distance variables and the site-of-care variables. The results (available from the authors upon request) confirmed the robustness of the model reported in Table 2. The site-of-care variables remained significant when distance was omitted; the distance variables remained insignificant when the site-of-care variables were omitted; and the statistical performance of the other variables in these model variants were consistent with the results in Table 2. The persistence of this site-of-care effect, after controlling for multiple patient-level factors, is noteworthy and suggests that the style of medical oncology practice may have differed systematically across these CoC-approved cancer centers during the 2001–2003. However, the fact that only four cancer centers (plus 23 smaller hospitals) are involved inherently limits our ability to generalize about site effects.

While the sample size limited the number of variables that could be simultaneously included in a multivariable regression model here, we did identify robust interaction effects involving race, the presence of comorbid conditions, and marital status (Table 4).

In the direct-effects specification (Table 4, Model 1), the adjusted black–white odds ratio for completing planned chemotherapy was 2.36 [p = 0.052, CI (0.99–5.62)], while the odds ratio associated with 1 or more comorbid conditions, 0.53, trended toward significance [p = 0.085, CI (0.26–1.09)], controlling for marital status. Additional insight into how marital status appears to mediate the impact of both race and comorbidity status on the likelihood of completing chemotherapy is revealed in Model 2, where race and comorbidity status are each interacted with marital status. Conditional on being unmarried, the black:white odds ratio for completing planned therapy was 4.67 and highly significant [CI (1.36–16.04)]<sup>7</sup>. Similarly, conditional on being unmarried, patients with 1 or more comorbidities were significantly less likely to complete planned therapy. For married patients, there was no race or comorbidity effect on the likelihood of completing chemotherapy.

In additional regressions not reported here, the overall trends concerning the impact of race, comorbidity, and marital status on the likelihood of completing chemotherapy were not affected when additional candidate predictors were included in the model, either singly or in combination (e.g., age, insurance status, socioeconomic status). Good-ness-of-fit for the regressions in Table 4 was only modest (c = 0.627 and 0.676), reflecting in part our adherence to guidelines against overfitting.

Finally, recall that patients who died while still undergoing adjuvant chemotherapy were not counted in the group that "discontinued" planned care. This is consistent with Ramsey et al. [19], though other analyses have not made death during the period of adjuvant therapy an exclusion criterion [8, 9]. To investigate the robustness of our base-case results, we reassigned the four patients who stopped adjuvant chemotherapy because of death to the group classified as having not completed planned chemotherapy. This increased the total who failed to complete planned therapy from 37 to 41 (see Fig. 1 note), and the corresponding percent who failed to complete from 10.7 to 11.8% ( $41/347 \times 100$ ). We then repeated all univariate and multivariable analyses related to completion of chemotherapy. The results (available upon request) were virtually unchanged from the base-case findings reported in Tables 3 and 4 in terms of the algebraic sign and statistical significance of individual variable effects.

#### Reasons for early termination of planned adjuvant chemotherapy

For each of the 37 patients not completing planned chemotherapy in the base case, we assigned a primary reason based on the abstracted medical records. The results are noted in Fig. 1 and summarized in Fig. 2. About two-thirds of these patients failed to complete chemotherapy for clinical reasons (toxicity, 54%; disease progression, 3%; and other clinical reasons, 8%). The remaining one-third did not complete for "other patient-related reasons"

<sup>&</sup>lt;sup>7</sup>For logistic models with interaction terms, SAS 9.2 computes a 95% confidence interval for the odds ratio for the variable of interest in the interaction term (e.g., race), conditional on the assumed value of the other variable in the (two-way) interaction term (e.g., marital status), rather than p values for the individual direct effect and interaction terms included in the regression. See note c in Table 4.

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(patient decision to stop, 16%; started, then no show, 5%; other patient reasons, 6%; and had plan but did not start, 8%). Of note, 16 of 27 (59%) white patients and 8 of 10 (80%) black patients stopped care for clinical reasons, though in this modest-size sample, the difference by race across the seven defined primary reasons for termination was not significant (p = 0.694)<sup>8</sup>.

# Discussion

Given the important findings by Hershman et al. [8] that among breast cancer patients in a large urban–suburban population and in randomized trials [9], blacks were significantly less likely than whites to complete adjuvant chemotherapy, we asked whether there were similar racial differences in SWGA. What we found was strikingly different:

- Regarding receipt of chemotherapy, the unadjusted difference between blacks and whites was highly significant (Table 1); but in the multivariable analysis (Table 2), the black-white odds ratio was not. The latter finding of no significant difference is consistent with multivariable modeling results reported by Elkin et al. [6] in a SEER-Medicare sample, Kimmick et al. [20] among North Carolina Medicaid enrollees, and Lund et al. [12] in Metropolitan Atlanta. However, in another multivariable analysis using SEER-Medicare data, Giordano et al. [7] found that white breast cancer patients were significantly more likely than black patients to receive chemotherapy, as did Bickell et al. [10] in their New York City study and, most recently, Freedman et al. [21] in a National Cancer Data Base Study (which did not distinguish patients by urban/rural status). These studies controlled for many of the same key factors, e.g., stage, ER/PR status, as did our analyses. But they also differed (from our work and among each other) in terms of population studied and data resources, time period examined, and statistical modeling approaches. Future work to sort out these contrasting findings will need to account for differences in data and methods.
- While the difference between blacks and whites in completing chemotherapy was not significant in a univariate analysis (Table 3), black race was positively associated with completing care in multivariable models (Table 4). Moreover, the impact of race on completing chemotherapy appears to be influenced by the patient's marital status—with a significant black—white difference for patients who are not married patients, but no difference for those married. This interplay between marital status and race (and also marital status and comorbidity status) on patterns of care in cancer has not been previously reported, to our knowledge, and merits further investigation.
- The overall rate of premature discontinuation of chemotherapy for breast cancer in SWGA was 10.7%. This is similar to the Hershman et al. [9] calculation of 9% based on a synthesis of clinical trials data, and to the estimate of 13.5% by Buist et al. [22] based on data from several large HMOs. These estimates contrast sharply

<sup>&</sup>lt;sup>8</sup>When the 7 primary reasons for termination were collapsed into clinical reasons (3) and other patient-related reasons (4), there was still no significant black-white difference (p = 0.241, using Pearson's exact test, and p = 0.432 after application of the Yates correction for small expected cell sizes).

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with the 28% figure reported for the Metropolitan Detroit area [8]. Both Hershman et al. analyses define discontinuation by comparing actual care with guidelinedriven expected care, while Buist et al. rely on medical chart abstraction and physician notes, similar to the approach taken in this study.

#### Strengths, limitations, and matters for further investigation

This article provides the most comprehensive examination to date of factors associated with receipt and successful completion of adjuvant chemotherapy for breast cancer in a primarily rural region of the U.S. The analyses draw from virtually a complete census of patients diagnosed and treated for early stage breast cancer in the 33-county area of SWGA over the 3-year period 2001–2003.

However, the study has some important limitations. First, it focuses on one particular geographic area. It remains to be seen whether similar findings would emerge in other rural regions, particularly in other parts of the country. Over 80% of the cancer care in SWGA is rendered at four CoC-approved cancer centers, which are expected to promote evidenced-based multidisciplinary care. Rural regions with a smaller percentage of breast cancer care at CoC-approved facilities could yield different findings. Second, our results necessarily reflect the patterns of care for breast cancer cases diagnosed in SWGA during 2001–2003, thus, raising questions about generalizability over time. However, we are unaware of changes in breast cancer treatment guidelines or third-party reimbursement policies over the past decade that would have significantly altered the environment for decision making about adjuvant chemotherapy for breast cancer.

A third and more fundamental limitation of our analyses, and the others discussed here, is the absence of the patient's own perspective on the decision to begin or to discontinue therapy, including the impact of treatment (actual or anticipated) on health-related quality of life [23]. This severely limits our ability *ex post facto* to develop a satisfactory explanation for these black–white differences (or the lack thereof) and for the evident interplay between marital status, race, and completion of therapy.

Regarding the effect of race on receipt and completion of care, our discussions (in 2009) with providers and administrators at the 4 cancer centers in SWGA pointed to two general considerations. First, during 2001–2003 (and subsequently) each center provided free transportation services to patients who petitioned for help; and each was a federally designated "disproportionate share" hospital— implying that admission and treatment decisions were not to be influenced by the patient's ability to pay. It is possible these center-specific factors served to attenuate race-based differences in patterns of care. Second, to the extent that social support networks that are anchored through churches and extended families are more extensively developed in the black community, this could influence the propensity to undergo and stay the course with cancer therapy.

In a similar vein, it is conceivable that the patients who were unmarried (and among those in Table 3, this includes 59.8% of blacks compared to 29.0% of whites) and had strong ties within such a network thereby had a "social support" advantage over unmarried patients

with fewer social ties. If so, this could shed light on the race-marital status interaction effect on the propensity to complete adjuvant chemotherapy.

Regarding matters for further investigation, the first follows directly from above: the need for patient-reported information that can help identify the full set of factors influencing the patient's treatment decisions. Second, our findings on the impact of health insurance are generally contrary to expectations [24]. Women with Medicaid/ Medicaid Pending were more likely to receive chemotherapy compared with the privately insured, and there were no other significant insurance effects. Although it is not clear why the impact of insurance is relatively muted here, the strong Medicaid effect may be explained, in part, by the launch of the CDC's Breast and Cervical Cancer Prevention and Treatment Act (BCCPTA) program in July 2001. Georgia was one of 12 states adopting the most expansive BCCPTA enrollment option, which resulted in a significant increase in the Medicaid enrollment rate for women diagnosed with breast cancer [25]<sup>9</sup>.

Third, a centrally important matter is the impact of failing to complete chemotherapy on survival. Most patients in our analyses received multi-modality care, including radiation therapy or hormonal therapy, in additional to adjuvant chemotherapy, following surgery. A survival analysis that accounts for the joint impact of these treatment modalities—while adjusting for patient, provider, and health system factors [26]—is an important next step but beyond the scope of this article.

As Hassett and Griggs [27] note, the assessment of racial disparities in adjuvant chemotherapy for breast cancer has come to focus increasingly on black–white differences not only the receipt of care, but its timely and dose-appropriate delivery—and its successful completion. This article contributes to that expanding discussion by asking whether the differences by race found in previous US studies likewise surface when the geographic focus shifts to a primarily rural region of the country. On balance, we find compelling black–white differences—but with black patients receiving and completing care at rates that equal or exceed those for white patients. Further investigation is warranted, both in SWGA and other rural areas of the US.

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# References

 Bonadonna G, Valagussa P. Dose-response effect of adjuvant chemotherapy in breast cancer. NEJM. 1981; 304:10–15. [PubMed: 7432433]

<sup>&</sup>lt;sup>9</sup>Adams et al. [25] found that enrollment rates in the Georgia Medicaid program for women diagnosed with breast cancer increased from 2.8 per 1,000 person-months in the pre-BCCPTA period (January 1999–June 2001) to 4.5 per 1,000 person-months post-BCCPTA (July 2001–December 2005). Georgia's relatively expansive program provides Medicaid coverage for uninsured women under age 65 regardless of whether they are diagnosed with breast (or cervical) cancer through the CDC's National Breast and Cervical Cancer Early Detection Program or by non-NBCCEDP providers.

- Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomized trials Lancet. 2005; 365:1687–1717. [PubMed: 15894097]
- Clinical Practice Guidelines in Oncology. [Accessed 26 February 2011] Breast Cancer (version 3.2009). National Comprehensive Cancer Network. 2011. http://www.nccn.org/professionals/ physician\_gls?PDF/breast.pdf.
- National Cancer Institute, Physician Data Query. [Accessed 17 June 2010] Breast Cancer Treatment. http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional.
- Muss HB, Berry DA, Cirrincione CT, et al. Adjuvant chemotherapy in older women with earlystage breast cancer. NEJM. 2009; 360:2055–2065. [PubMed: 19439741]
- Elkin EB, Hurria A, Mitra N, et al. Adjuvant chemotherapy and survival in older women with hormone-receptor breast cancer: assessing the outcome in a population-based, observational cohort. J Clin Oncol. 2006; 24:2757–2764. [PubMed: 16782916]
- 7. Giordano SH, Duan Z, Kuo Y-F, et al. Use and outcomes of adjuvant chemotherapy in older women with breast cancer. J Clin Oncol. 2006; 24:2750–2756. [PubMed: 16782915]
- Hershman D, McBride R, Jacobson JS, et al. Racial disparities in treatment and survival among women with early-stage breast cancer. J Clin Oncol. 2005; 23:6639–6646. [PubMed: 16170171]
- Hershman D, Unger JM, Barlow WE, et al. Treatment quality and outcomes in African-American versus white breast cancer patients: retrospective analysis of southwest oncology studies S8814/ S8897. J Clin Oncol. 2009; 27:2157–2162. [PubMed: 19307504]
- Bickell NA, Wang JJ, Oluwole S, et al. Missed opportunities: racial disparities in adjuvant breast cancer treatment. J Clin Oncol. 2006; 24:1357–1362. [PubMed: 16549830]
- Richardson LC, Tian L, Voti L, et al. The roles of teaching hospitals, insurance status, and race/ ethnicity in receipt of adjuvant therapy for regional-stage breast cancer in Florida. Am J Public Health. 2006; 96:160–166. [PubMed: 16317209]
- Lund MJ, Brawley OP, Ward KC, et al. Parity and disparity in first course treatment of invasive breast cancer. Breast Cancer Res Treat. 2008; 109(3):545–557. [PubMed: 17659438]
- Tropman SE, Ricketts TC, Paskett E, et al. Rural breast cancer treatment: evidence from the Reaching Communities with Cancer Care (REACH) project. Breast Cancer Res Treat. 1999; 56:59–66. [PubMed: 10517343]
- 14. Dobie SA, Baldwin L-M, Dominitz JA, et al. Completion of therapy by Medicare patients with stage III colon cancer. J Natl Cancer Inst. 2006; 98:610–619. [PubMed: 16670386]
- 15. U.S. Census Bureau. PHC-1–12, Georgia. Washington, DC: 2002. 2000 Census of population and housing, summary population and housing characteristics.
- Goodman M, Almon L, Bayakly R, et al. Cancer outcomes research in a rural area: a multiinstitutional partnership model. J Community Health. 2009; 34(1):23–32. [PubMed: 18850070]
- U.S. Department of Agriculture, Economic Research Service. [Accessed on 18 July 2010] Measuring rurality: rural–urban continuum [Beale] codes. 2010. http://www.ers.usda.gov/Briefing/ Rurality/RuralUrbCon/.
- Harrell, FE, Jr. Springer Series in Statistics. New York: Springer-Verlag; 2001. Regression modeling strategies, with applications to linear models, logistic regression, and survival analysis; p. 61
- Ramsey SD, Zeliadt SB, Richardson LC, et al. Discontinuation of radiation treatment among Medicaid-enrolled women with local and regional stage breast cancer. Breast J. 2009; 15:1–8. [PubMed: 19141129]
- Kimmick G, Camacho F, Foley KL, et al. Racial differences in patterns of care among Medicaidenrolled patients with breast cancer. J Oncol Pract. 2006; 2(5):205–213. [PubMed: 20859339]
- 21. Freedman RA, Virgo KS, He Y, et al. The association of race/ethnicity, insurance status, and socioeconomic factors with breast cancer care. Cancer. 2011; 117:180–189. [PubMed: 20939011]
- 22. Buist DSM, Chubak J, Prout M, et al. Referral, receipt, and completion of chemotherapy in patients with early-stage breast cancer older than 65 years at high risk of breast cancer recurrence. J Clin Oncol. 2009; 27:4508–4514. [PubMed: 19687341]

- Richardson LC, Wang W, Hartzema AG, et al. The role of health-related quality of life in early discontinuation of chemotherapy in breast cancer. Breast J. 2007; 13(6):581–587. [PubMed: 17983400]
- 24. Ward E, Halpern M, Schrag N, et al. Association of insurance with cancer care utilization and outcomes. CA Cancer J Clin. 2008; 58:9–31. [PubMed: 18096863]
- Adams EK, Chien L-N, Florence CS, et al. The Breast and Cervical Cancer Prevention and Treatment Act in Georgia: effects on time to Medicaid enrollment. Cancer. 2009; 115:1300–1309. [PubMed: 19189369]
- Komenaka IA, Martinez ME, Pennington RE Jr, et al. Race and ethnicity and breast cancer outcomes in an underinsured population. J Natl Cancer Inst. 2010; 102:1178–1187. [PubMed: 20574040]
- 27. Hassett MJ, Griggs JJ. Disparities in breast cancer adjuvant chemotherapy: moving beyond Yes and No (editorial). J Clin Oncol. 2009; 27(13):2120–2121. [PubMed: 19307493]



\*Includes 36 patients who survived the initial treatment phase, had at least one change in treatment plan, and completed therapy according to the last available plan, and also 4 patients whose chemotherapy necessarily terminated during the initial treatment phase due to death.

#### Fig. 1.

Breast cancer patients diagnosed and treated in SWGA, 2001–2003: receipt and completion of adjuvant chemotherapy in the study sample



Reasons for early termination of adjuvant chemotherapy (N = 37)

#### Table 1

Receipt of adjuvant chemotherapy, by demographic and clinical characteristics, among women with early stage invasive breast cancer diagnosed and treated in SWGA, 2001–2003

Characteristic	No. of patients <sup>j</sup> (N = 868)	% of Sample	% Received adjuvant chemo (N = 344)	χ <sup>2</sup> p
Age at diagnosis (years)				
<50	177	20.3	72.3	< 0.0001
50-64	323	37.2	49.2	
65–74	167	19.2	29.9	
75+	201	23.1	3.5	
Race <sup><i>a</i></sup>				
White	611	70.4	36.0	0.001
Black	257	29.6	48.3	
Marital status <sup>b</sup>				
Married	439	51.2	46.7	< 0.0001
Not married	418	48.8	32.3	
Insurance status <sup>C</sup>				
Private (FFS, HMO) + Medicare	606	70.0	38.8	< 0.0001
w/supplemental + VA/CHAMPUS				
Medicare Only (no supplemental)	122	14.1	23.8	
Medicaid or Medicaid Pending	78	9.0	69.2	
Uninsured (self- Pay/charity)	62	7.1	41.9	
Socioeconomic status: % in census tract below	poverty level <sup>d</sup>			
>20	443	51.7	38.8	0.447
10–20	292	34.1	39.3	
<10	122	14.2	45.1	
Rural status $(\%)^e$				
Metro	162	18.7	44.4	0.165
Non-metro	706	81.3	38.5	
Comorbid conditions <sup>f</sup>				
None	451	52.0	44.1	0.005
1 or more	417	48.0	34.8	
AJCC stage at diagnosis				
Ι	445	51.2	19.8	< 0.0001
п	327	37.7	59.3	
IIIA	96	11.1	64.6	

 ${\it Estrogen/progesterone\ status}^g$ 

Characteristic	No. of patients <sup>j</sup> (N = 868)	% of Sample	% Received adjuvant chemo (N = 344)	χ <sup>2</sup> p
ER- and PR-	167	22.7	64.7	< 0.0001
ER+ or PR+	570	77.3	36.5	
Treatment site <sup>h</sup>				
А			47.7	< 0.0001
В			45.4	
С			34.5	
D			29.7	
Other			21.2	
Distance to treatment site (miles) <sup>i</sup>				
<5	293	33.8	34.1	0.025
5–22	292	33.6	39.7	
>22	283	32.6	45.2	

Early stage invasive refers to breast cancer diagnosed at AJCC stages I, IIA, IIB, or IIIA, and aligns with the National Cancer Institute's definition of "early stage" breast cancer (see http://www.cancer.gov/dictionary?expand=E)

<sup>a</sup>Defined as 2-level variable that includes non-Hispanic whites (White) and non-Hispanic blacks (Black), since all other racial/ethnic groups, including Hispanics, together constituted only 0.8% of the incident breast cancer cases in SWGA in 2001–2003

 $^{b}$ Not married includes women who are single, separated, divorced, or widowed

<sup>C</sup>This 4-level variable was constructed from the coverage options in a drop-down box in the electronic data collection instrument as follows: uninsured (no insurance, self-pay, or charity); Medicaid (either enrolled in Medicaid or application for enrollment pending); Medicare only (enrolled in fee-for-service Medicare and without supplemental private insurance); and private insurance/managed care (private insurance, health maintenance organization/independent practice association (HMO/IPA), Medicare advantage or fee-for-service Medicare with supplemental private insurance, and CHAMPUS or VA coverage). The inclusion of military service-related options in the final category assumes that cancer care provided by the Department of Defense and the Department of Veterans Affairs is delivered in a "managed care" type of environment. Consistently, the intent was to capture insurance status at time of diagnosis, to the extent possible

 $^{d}$ Based on whether the patient's residential address lies in a US census tract where greater than 20%, between 10 and 20%, or fewer than 10% of the population is classified as living below the Federal poverty line in 2000

<sup>e</sup> To index the degree of rurality (Rural Status) associated with the patient's residential address, she was designated as metro if she lived in a county that met any of the Beale Code's 3 conditions for being a "metro county"; otherwise, she was assigned non-metro status. The formulas and rationale for the Beale Code classification of urban/rural status are provided by the US Department of Agriculture [17]

<sup>f</sup>As coded at the time of diagnosis, based on the following menu of options built into the project's electronic data reporting instrument: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, ulcer disease, dementia, hemiplegia, AIDS, diabetes, diabetes with end organ damage, mild liver disease, moderate/severe liver disease, moderate/ severe renal disease, any tumor, leukemia, lymphoma, metastatic solid tumor (Note also that any patient with a recorded previous cancer was excluded from these analyses)

<sup>g</sup>Hence, patients are classified as double-negative versus ER positive or PR positive or both

<sup>h</sup>Sites of care A–D are the four CoC-approved hospitals in SWGA, while other indicates the patient received her cancer care primarily at some other treatment facility in SWGA

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# Table 2

Multivariable logistic regression analysis of factors associated with receipt of adjuvant chemotherapy

Characteristic	Odds ratio	95% CI	р
Age at diagnosis (years)			
<50	1.000		
50-64	0.297	0.167-0.529	< 0.0001
65–74	0.124	0.060-0.257	< 0.0001
75+	0.006	0.002-0.016	< 0.0001
Race			
White	1.000		
Black	1.178	0.712-1.948	0.524
Marital status			
Married	1.000		
Not married	0.693	0.427-1.125	0.138
Insurance status			
Private (FFS, HMO)+ Medicare w/supplemental + VA/CHAMPUS	1.000		
Medicare Only (no supplemental)	1.310	0.639–2.685	0.462
Medicaid or Medicaid Pending	3.176	1.407-7.170	0.005
Uninsured (self-pay/charity)	0.741	0.315-1.741	0.491
Census tract % below poverty lev	vel		
>20	1.000		
10–20	1.326	0.802-2.192	0.271
<10	2.078	1.009-4.277	0.047
Rural status			
Metro	1.000		
Non-metro	1.194	0.547-2.606	0.657
Comorbid conditions			
None	1.000		
1 or more	1.293	0.809-2.065	0.283
AJCC stage at diagnosis			
Ι	1.000		
II	12.961	7.983-21.043	< 0.0001
IIIA	25.135	10.474-60.318	< 0.0001
Estrogen/progesterone status			
ER- and PR-	1.000		
ER+ or PR+	0.388	0.228-0.661	0.001
Treatment site			
А	1.000		
В	0.692	0.321-1.493	0.349

Characteristic	Odds ratio	95% CI	р
С	0.410	0.191-0.878	0.022
D	0.268	0.117-0.611	0.002
Other	0.400	0.157-1.015	0.054
Distance to treatment site (miles)			
<5	1.000		
5–22	0.846	0.482-1.485	0.560
>22	1.125	0.561-2.257	0.740
N = 721; <i>c</i> index (probability of con	ncordance	0 = 0.907	

# Table 3

Completion of planned adjuvant chemotherapy, by demographic and clinical characteristics

Characteristic	No. of patients who began or had Tx plan for adj chemo (N = 347)	No. of patients (%) who completed adj chemo (N = 310)	χ <sup>2</sup> p
Age at diagnosis (years)			
<50	128	115 (89.8)	0.012
50-64	160	149 (93.1)	
65–74	52	40 (76.9)	
75+	7	6 (85.7)	
Race			
White	222	195 (87.8)	0.227
Black	125	115 (92.0)	
Marital Status			
Married	206	188 (91.3)	0.372
Not married	137	121 (88.3)	
Insurance status			
Private (FFS, HMO) + Medicare w/supplemental + VA/CHAMPUS	238	213 (89.5)	0.906
Medicare Only (no supplemental)	29	25 (86.2)	
Medicaid or Medicaid Pending	54	48 (88.9)	
Uninsured (self-pay/charity)	26	24 (92.3)	
Census tract % poverty			
>20	175	153 (87.4)	0.278
10-20	115	107 (93.0)	
<10	55	48 (87.3)	
Rural status (%)			
Metro	73	65 (89.0)	0.927
Non-metro	274	245 (89.4)	
Comorbid conditions			
None	199	182 (91.5)	0.138
1 or more	148	128 (86.5)	
AJCC stage at diagnosis			
Ι	89	77 (86.5)	0.387
II	196	175 (89.3)	
IIIA	62	58 (93.5)	
Estrogen/progesterone status			
ER- and PR-	108	97 (89.8)	0.748
ER+ or PR+	211	187 (88.6)	
Treatment site			
А		(87.5)	0.124
В		(93.7)	
С		(83.3)	

-

Characteristic	No. of patients who began or had Tx plan for adj chemo (N = 347)	No. of patients (%) who completed adj chemo (N = 310)	χ <sup>2</sup> p
D		(100.0)	
Other		(88.0)	
Distance to treatment site (miles)			
<5	101	94 (93.1)	0.151
5–22	116	105 (90.5)	
>22	130	111 (85.4)	

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Multivariable logistic regression analysis of the impact of race, comorbidity status, and marital status on completion of planned adjuvant chemotherapy

Characteristic	$(1)^{a}$			(2)b			
	Odds ratio	95% CI	d	Odds ratio <sup>c</sup> (married = 1 for race and comorbidity)	95% CI	Odds ratio <sup>c</sup> (married = 0 for race and comorbidity)	95% CI
Race							
White	1.000			1.000		1.000	
Black	2.364	0.994-5.619	0.052	1.062	0.331–3.411	4.673	1.361-16.039
Comorbid conditions							
None	1.000			1.000		1.000	
1 or more	0.531	0.258 - 1.092	0.085	1.411	0.506-3.938	0.138	0.036-0.525
Marital status							
Married	1.000			1.000		1.000	
Not married	0.591	0.280 - 1.249	0.168	0.968	0.396–2.368	0.968	0.396–2.368
	N = 343 (with discontinuing	h 309 completing z); $c = 0.627$	g and 34	N = 343; c = 0.676			

probability of completing) is modeled as a function of race, the presence of comorbid conditions, and marital status. In Model 1, all variables represent direct effects (Hence, Model 1 is structually similar to Model 1 is a multivariable logistic regression model in which the likelihood that the patient completed planned adjuvant chemotherapy (expressed operationally as the log odds ratio, or logit, of the the base-case logistic regression model for receipt of adjuvant chemotherapy, summarized in Table 2)

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 $b_{\rm Model 2}$  is simply Model 1 with the addition of 2 interaction terms: race by marital status, and comorbidity status by marital status

computed at the sample means of NONWHITE (=0.356) and COMORBID (=0.426) for the observations used in the regressions. Calculations were carried out through the ODDSRATIO option available in <sup>c</sup>Odds ratios for both race and comorbidity status are computed conditional on whether the patient is married (NOTMARRI = 0) or not married (NOTMARRI = 1). Odds ratios for marital status are SAS 9.2 version of PROC LOGISTIC, which computes 95% CIs for variables included in interaction terms