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Race and age disparities in receipt of sentinel lymph node biopsy for early-stage breast cancer

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Abstract

To evaluate differences in use of sentinel lymph node biopsy (SLNB) by age and race in Medicare recipients with early-stage breast cancer, we examined Surveillance, Epidemiology and End Results—Medicare linked data for women undergoing breast conserving surgery for stage I or II breast cancer, including axillary staging, between January 2000 and December 2002.

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Multivariable generalized linear modeling with generalized estimating equations was used to identify predictors of receiving SLNB versus standard axillary lymph node dissection as the primary axillary staging modality. Women were significantly less likely to receive SLNB as their primary staging procedure if they were African American (OR 0.65), greater than 80 years of age (OR 0.71 vs. age <70), or dually eligible for Medicare and Medicaid (OR 0.61). Tumor characteristics, including well-differentiated histology and stage I disease, were associated with increased likelihood of SLNB, but estrogen receptor status was not a significant predictor. Women treated at an institution affiliated with an NCI cooperative research group had significantly greater likelihood of receiving SLNB (OR 2.31). Likelihood of receiving SLNB increased for women diagnosed in 2001 and 2002 compared with 2000. Significant disparities exist in receipt of SLNB in the Medicare population, with African Americans, the elderly, and economically disadvantaged patients being less likely to receive this innovative and morbidity-sparing procedure. These findings continue a previously observed pattern of reduced access to state of the art breast cancer care among underserved populations.

Keywords

Disparities; Sentinel lymph node biopsy; Breast cancer; Treatment; Surgery

Background and rationale

Axillary lymph node staging and treatment play a vital role in the prognosis and control of breast cancer. Metastasis to the regional lymph nodes is the most important prognostic factor for recurrence and mortality, and for some patients the removal of axillary nodes can improve local disease control and survival [1,2]. However, these benefits come at the price of considerable surgical morbidity, which has led to the development of innovative surgical techniques to replace traditional axillary lymph node dissection (ALND). Sentinel lymph node biopsy (SLNB) is an alternative staging method that enables the surgeon to sample and more thoroughly examine the lymph nodes most likely to contain metastases.

Sentinel lymph node biopsy has been widely adopted for clinical use in the United States beginning in the late 1990s. Although false negative results are possible [3], associated morbidities including lymphedema, wound infections, axillary seromas, and paresthesias are significantly less frequent than in ALND [4]. A recently reported clinical trial found no significant differences in regional control or survival between the two procedures [5,6].

Following the pattern of other treatments for early-stage breast cancer, SLNB has been underused in vulnerable populations [7,8]. Older age, ethnic minority status, and lower socioeconomic status have been associated with lower SLNB rates. Lack of health insurance, coverage by Medicare or Medicaid, and treatment at a non-academic facility have been associated with lower odds of receiving SLNB in early-stage breast cancer patients [8]. However, the effect of institutional characteristics on SLNB rates has yet to be well characterized, particularly in minorities.

Racial disparities exist in multiple other aspects of breast cancer treatment. African Americans experience lower rates of axillary lymph node staging [9], definitive local treatment [10,11], adjuvant radiation [10-14], chemotherapy and endocrine treatment [10], as well as post-treatment mammography surveillance [13,15]. Treatments are more likely to be delayed, and African-American woman are more frequently treated at hospitals with poor adherence to breast cancer treatment guidelines [15]. These disparities, along with lower screening rates, are widely believed to contribute to the racial gap in overall and stage-specific survival [16,17].

Similar patterns of disparities exist among elderly breast cancer patients. Older women are less likely to receive axillary lymph node staging [18,19], adjuvant radiation, and surveillance mammography, even after adjustment for co-morbidities [13]. Physician recommendations for adjuvant treatment [20], as well as chemotherapy rates, decrease with age [19,21], despite evidence that healthy older women derive significant benefit from standard adjuvant chemotherapy with reasonable toxicity [22-24]. Breast cancer-specific survival declines with advancing age, and this difference appears to be mediated by under treatment [21]. However, the racial gap in stage-specific survival appears to be attenuated in patients over age 65 [16], which may reflect improved access to care through Medicare coverage.

This study uses the Surveillance Epidemiology and End Results (SEER)-Medicare database to examine racial and age-related disparities in the use of SLNB. To our knowledge, this study is the first to examine disparities in SLNB among Medicare patients, who compose approximately 40% of new US breast cancer cases annually [25]. Further, this study controls at a more detailed level than previous analyses for institutional characteristics that have been previously suggested to influence cancer treatment disparities, including surgical volume, NCI affiliation, and involvement in cancer research networks [15,26-28]. In addition, the use of a Medicare patient sample enables examination of the hypothesis that increased access to health insurance may narrow breast cancer treatment disparities in this population.

Methods

Data

Data were obtained from the SEER-Medicare linked data, which have been previously described [29]. SEER-Medicare reflects the linkage of the SEER cancer registries program to administrative and claims data from Medicare. The SEER dataset represents roughly 25% of the US cancer population, and the Medicare data provides health insurance coverage information for 97% of Americans aged 65 and older. Together, these data include demographic characteristics, incident cancer information, and specific data on inpatient and outpatient cancer treatment and other health conditions. SEER-Medicare data offer a unique opportunity to study differences in cancer treatment and outcomes among a large population-based sample [29].

Study population

Data were extracted from SEER-Medicare linked data from January 2000 through December 2002. This time period was selected to permit examination of SLNB following its adoption by Medicare and prior to changes in AJCC cancer staging as recorded by SEER beginning in 2003. The sample was restricted to Caucasian or African-American women, diagnosed with stage I or II breast cancer as first or only primary cancer, aged 66 or older at date of diagnosis, and receiving breast conserving surgery (BCS) including axillary staging. Because we wished to examine racial disparities, only those SEER registries with 5% or greater African Americans were examined, including San Francisco, Detroit, Atlanta, Los Angeles, Rural Georgia, Louisiana, Kentucky and New Jersey. The sample included only women with complete claims from 12 months before diagnosis until 24 months after diagnosis. Claims were limited to procedures performed 1 month pre-diagnosis through 24 months post-diagnosis.

Independent and dependent variables

The primary outcome was receipt of SLNB. Patients were categorized as receiving SLNB if their scope of regional lymph node surgery in SEER indicated sentinel node removal with or without subsequent ALND, or if they had a Medicare CPT code for dye injection or

lymphoscintigraphy. Patients were categorized as receiving primary ALND if none of the above criteria for SLNB were met and if their scope of lymph node surgery in SEER-specified removal of regional lymph nodes with at least 10 nodes examined, or if analogous Medicare CPT codes were used. Patients who received SLNB followed by ALND were categorized as having received SLNB. In the case of discordance between SEER and Medicare, the patient was categorized as having SLNB if either database indicated that SLNB had been performed. Race was ascertained from SEER data. Due to extremely small sample sizes in other racial groups, the analysis was restricted to Caucasian and African-American women.

Covariates

Patient information included race, age at diagnosis and marital status. Clinical and tumor information included stage, grade, estrogen receptor status, and comorbidity index. Stage was determined according to the American Joint Committee on Cancer TNM staging system. Education level was assigned to each patient based on the 2000 census data for their area of residence, measured in quartiles within each registry and then combined across registries following previous methodology [15]. Medicare/Medicaid dual eligibility was included in the model as a patient-level indicator of SES. Due to high correlation between census level income and dual eligibility (Spearman correlation $P = 0.01$), only Medicaid eligibility was included in the final model. Building from previous work [30], an indicator variable was created to measure organizational affiliation with NCI Cooperative Groups having breast cancer research portfolios, including the American College of Surgeons Oncology Group, Eastern Cooperative Oncology Group, Cancer and Leukemia Group B, Southwest Oncology Group, and the National Surgical Adjuvant Breast and Bowel Project (ACOSOG, ECOG, CALGB, SWOG, NSABP, respectively).

Statistical analysis

To calculate the odds of receiving SLNB, a generalized linear model was fit using generalized estimation equations (GEE) as implemented in the GENMOD procedure (logit link function) in SAS 9.2 (SAS®, 2009). This procedure takes into account the clustering of observations within hospitals when calculating estimates of association between covariates. Receipt of SLNB was the dependent variable. Other variables in the final model are listed in Table 2. To specifically examine effect modification by race, models were stratified, and interaction terms between time and selected covariates were tested (data not presented). To illustrate time trends across the study period, predicted probabilities from these models were used to construct figures estimating the probability of SLNB over time by age and race (Figs. 1, 2). We included a quadratic time estimate to relax the restriction of linear effects by time and to facilitate better plotting of the estimates.

Results

Descriptive characteristics of the study sample are presented in Table 1. Although we specifically selected SEER regions with significant African-American populations, the percentage of such patients remained relatively low at 7.7%. The overall rate of SLNB was 68%. Case volume was distributed evenly over the 3-year study period. The overall sample was distributed evenly over the range of census tract income and education levels. 8.7% of patients were dually eligible for Medicare and Medicaid coverage. 80% were treated at an institution affiliated with at least one NCI cooperative group participating in breast cancer research.

In unadjusted analysis across all years, African Americans were roughly half as likely as Caucasians to receive SLNB (OR 0.54, 95% CI 0.42–0.69, data not presented). Results of

multivariable logistic regression modeling of potential predictors of SLNB are presented in Table 2. African-American patients remained significantly less likely to receive SLNB than white patients in adjusted analysis (OR = 0.65, 95% CI 0.50–0.85). There was an age-related decline in receipt of SLNB, with women age 80 and above having 0.71 times the odds of receiving the procedure compared to patients 65–69 (95% CI 0.57–0.87). Educational attainment was not significantly associated with likelihood of receiving SLNB; however, women enrolled in Medicaid had significantly lower odds of receiving the procedure (OR = 0.61, 95% CI 0.47–0.78). Medical co-morbidities as measured by Charlson index were not significantly associated with the likelihood of receiving SLNB.

In order to more fully understand the relationship among race, age, and the receipt of SLNB over time, additional modeling was performed with race-by-time and age-by-time interaction terms. Results of this analysis are presented in Figs. 1 and 2. Rates of SLNB among African Americans remained significantly lower than those for Caucasians throughout the study period; however, there was variability in the adjusted rate of SLNB among African-American woman over time, likely due to small sample size.

Tumor characteristics were significantly associated with use of SLNB, and overall, women with lower risk tumor characteristics were more likely to receive SLNB. Specifically, women with well-differentiated tumors were significantly more likely to receive the procedure than those with poorly differentiated tumors. Likewise, women with stage I or stage IIA tumors were more likely to undergo SLNB than those with IIB tumors. ER positivity did not meet significance.

Use of SLNB also varied significantly by institution and over time. Treatment at a cooperative group affiliated institution was associated with higher odds of receiving SLNB (OR 2.31, 95% CI 1.50–5.61). Other institutional factors previously reported to influence breast cancer care quality, including breast cancer-specific surgical volume and NCI center designation, were also examined in exploratory analysis to evaluate whether adjustment for these factors accounted for the observed racial disparities. These factors were not found to be significant confounders. To examine the possibility that the effect of institutional characteristics varied between African-Americans and Caucasians, interaction between race and cooperative group affiliation was assessed. No significant effect modification was found (data not presented).

Adoption of SLNB increased over time, with patients being significantly more likely to receive SLNB in 2001 and 2002 compared to 2000. Organizational predictors of use of SLNB were more closely examined in a separately published analysis using appropriate methods for organization-level analysis [30].

There was significant geographic variability in receipt of SLNB. The New Jersey SEER region had the highest rate of SLNB. Patients in the San Francisco, Detroit, Kentucky and Louisiana regions were significantly less likely to receive SLNB. Treatment in the Georgia or Los Angeles regions was not associated with a significant decrease in odds of receiving SLNB.

Discussion

This study found significant disparities in the receipt of SLNB, an innovative and morbidity-sparing procedure for early-stage breast cancer, among vulnerable populations including African-American women, those of low socioeconomic status, and the elderly. These disparities appear to persist over time, with only slight attenuation after controlling for geographic and institutional factors. Our work confirms that disparities in SLNB follow the

troubling pattern of reduced access to state of the art breast cancer care among underserved populations.

Prior work has suggested that racial disparities in stage-specific breast cancer survival may be narrowed in women over age 65 [16], presumably in part because Medicare eligibility reduces disparities in access to care. However, we found that even among a population composed entirely of Medicare recipients, African-American women were significantly less likely to receive SLNB than Caucasian women. Our analysis controlled for other known factors that might necessitate the more invasive ALND procedure in African-American women, such as more advanced stage at diagnosis [31] and higher rates of mastectomy [32,33], by limiting the sample to women undergoing breast conserving surgery and adjusting for tumor stage. After adjustment for these factors, African-American women remain significantly less likely to receive SLNB.

The omission of axillary staging in elderly women with breast cancer has been previously documented [11,13,18,21,34]. Our study shows further that even among those who receive axillary staging, very elderly women are less likely to receive SLNB. This finding is particularly troubling considering that the principal benefit of SLNB lies in its reduced morbidity, and the elderly are arguably the most in need of morbidity-sparing treatment.

This study found significantly lower rates of SLNB among Medicaid recipients, possibly indicating reduced access to this procedure. The patient population dually eligible for Medicare and Medicaid has been previously described to represent an extreme of low socioeconomic status, and to have disproportionate rates of disability and medical co-morbidity [35]. These patients may have a reduced choice of providers, may be poorly equipped to advocate for themselves, and may have reduced access to information regarding treatment options which could steer them toward institutions or physicians offering more innovative care. Future analyses should consider using this indicator to examine socioeconomic disparities in breast cancer care, and should continue to explore other innovative ways of defining socioeconomic status in SEER-Medicare data.

Institutional affiliation with cooperative research groups was significantly associated with a woman's likelihood of receiving SLNB. However, significant racial and age disparity remained after controlling for cooperative group affiliation, and exploratory analysis failed to show an effect of other institutional measures previously associated with quality and outcomes, including breast cancer surgical volume and NCI center designation. These findings suggest that choice of institution does not explain most or all of the racial and age disparities in receipt of SLNB.

During the period of early adoption covered by our study, the technical accuracy of SLNB as an axillary staging technique was well established through multiple single institution and multi-center studies [36], and guidance on learning and performing the technique was available in the surgical literature [37,38]. However, randomized data on the long term outcomes of SLNB were not yet mature during the study period, and two randomized trials of the technique by NCI cooperative groups were enrolling patients between 2000 and 2002. It is likely that this ongoing research influenced our results, either directly by enrollment of patients in the sample on SLNB clinical trials at participating institutions, or indirectly by earlier dissemination of SLNB expertise to surgeons at participating institutions. The decision by inexperienced surgeons and institutions to refrain from performing SLNB, as recommended by guidelines at the time [37,38], may in fact reflect responsible patient care.

The hypothesized gap in surgical experience between research and non-research institutions during the study period could disproportionately affect SLNB utilization among African Americans to the extent that physicians serving minority and underserved populations were

disproportionately affiliated with non-research institutions. Because the data in this analysis are de-identified, it is not possible to ascertain precisely which patients were treated at centers participating in ongoing SLNB trials. However, since the majority of clinical trial enrollment is through academic centers, which are commonly located in urban centers and disproportionately serve minority populations, it is a near certainty that minority populations were served in institutions sponsoring the trials. In the two randomized multicenter trials open during the study period, enrollment took place at 80 centers and 126 centers, respectively, including academic medical centers, teaching hospitals, and community centers, and 10% of participants were minorities [39,40]. It is clear that the number of minority patients at these participating institutions was considerable, particularly given the typically lower trial participation rates of minority populations compared to Caucasians.

The exclusion of women with no axillary staging, an omission which is known to occur more frequently in the oldest patients [34], may have selected a high-risk, healthy cohort of elderly women who can tolerate more extensive axillary surgery. However, multivariable analysis controlled for both tumor stage/grade and co-morbidity, which should attenuate any such selection bias. An initial sample was examined including stage I and II BCS patients reported as “no regional lymph nodes removed” as well as those for whom regional lymph node data was missing or unknown. This group comprised 15.9% of the initial sample (n = 732/4606), within the range of previously reported estimates of omission of axillary staging in breast conserving therapy patients in this age group [18]. To assess the risk of bias, preliminary modeling combined these women with the ALND group and found no significant changes in outcomes.

The inclusion of AJCC stage II patients presents a challenge for interpretation, due to the presence of node-negative and node-positive patients in the same subgroup. Because it is not possible to distinguish staging based on clinical versus pathologic information in this dataset, it is possible that some women had clinically detectable lymph node disease preoperatively and would be unlikely to be considered for SLNB. We therefore controlled for tumor stage using the most specific available subgroups and obtained a logical result showing decreased use of SLNB among women at higher risk of metastasis. Given that the majority of women with stage II breast cancers do not have clinically evident nodal disease prior to surgery, it is likely that other factors play a role in receipt of SLNB in this group.

Our findings for the most part mirror reports of race and age disparities in prior analysis of SLNB in other populations. Two prior studies of early-stage breast cancer patients in the National Cancer Database found a lower likelihood of SLNB among patients age 72 or older, African Americans, and those with Medicaid or no insurance, although dual eligibility was not specifically examined [7,8]. Examination of SLNB rates in melanoma found lower rates among patients older than 75 years, minority patients, and those with Medicaid [27]. The work presented here is the first to examine the Medicare population specifically and to establish that disparities in access to SLNB by race, age, and socioeconomic status do not appear to be significantly attenuated by access to Medicare coverage.

Despite the selection of SEER registries with relatively higher minority participation during the study period, the proportion of African-American patients in our sample remained relatively low. We chose to focus this manuscript on the critical period from 2000 to 2002 in order to capture patterns of use immediately after Medicare began reimbursing for the SLNB procedure but before changes in AJCC staging as recorded by the SEER registries in 2003, the inclusion of which would confound consistent inclusion criteria and sample selection. In the future, we plan to apply similar analytic techniques to data from 2003 forward. We anticipate that examination of newer data will provide a larger minority sample, and reflect maturing patterns of adoption of the SLNB technique.

This study demonstrates significant and troubling disparities in the receipt of SLNB among breast cancer patients. African-American women have significantly lower rates of SLNB, which are not fully explained by adjustment for disease characteristics, socioeconomic and institutional factors. Patients who stand to benefit substantially from reduced surgical morbidity, including the elderly and those with fewer economic resources, are paradoxically less likely to receive a procedure that offers them this benefit. In light of recent findings confirming that SLNB offers disease control and survival outcomes equivalent to those of axillary dissection, it is important to ensure appropriate use of this innovation which offers improved quality of life to breast cancer survivors. Given that Medicare coverage does not appear to resolve race and age-based disparities in receipt of this state of the art treatment, and that such disparities exist across a variety of institutions, providers should examine the decision-making process regarding SLNB in their own practice environments, and consider how best to deliver SLNB to the widest possible range of eligible patients.

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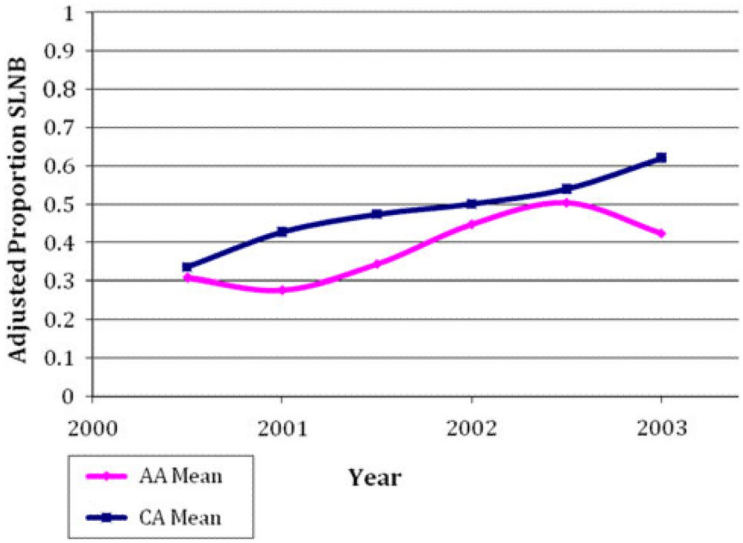

Fig. 1.

Estimated SLNB rates by race 2000–2002. *Adjusted for age, marital status, medicaid eligibility, comorbidity score, educational attainment, tumor grade and stage, ER status, institutional coop group affiliation, SEER region

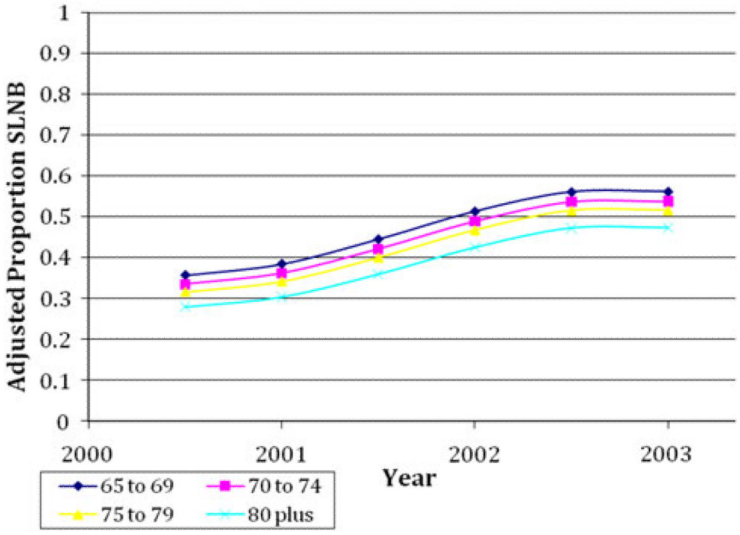

Fig. 2.

Estimated SLNB rates by age 2000–2002. *Adjusted for age, marital status, medicaid eligibility, comorbidity score, educational attainment, tumor grade and stage, ER status, institutional coop group affiliation, SEER region

Table 1

Characteristics of study patients

Patient characteristics	Frequency	%
Race		
Caucasian	3574	92.3
African American	300	7.7
Age		
65–69	941	24.3
70–74	1183	30.5
75–79	1071	27.7
80 plus	679	17.5
Marital status		
Unmarried	2102	54.3
Married	1772	45.7
Dual eligibility for medicare/medicaid		
No	3536	91.3
Yes	338	8.7
Comorbidity Score		
0	2578	66.6
1	1040	26.9
2	256	6.6
Educational attainment (census tract level)		
Above 75th percentile HS graduates	984	25.4
50–75th percentile	978	25.3
25–50th percentile	955	24.7
Below 25th percentile	952	24.6
Tumor Stage		
Stage I	2545	65.7
Stage IIA	986	25.5
Stage IIB or NOS	343	8.9
Tumor grade		
Well differentiated	961	24.8
Moderately differentiated	1586	40.9
Poorly differentiated	943	24.3
Unknown, not assessed	384	9.9
Estrogen receptor status		
Positive	2825	72.9
Negative	437	11.3
Unknown	612	15.8
Year of diagnosis		
2000	1279	33.0
2001	1281	33.1

Patient characteristics	Frequency	%
2002	1314	33.9
Region		
San Francisco	224	5.8
Detroit	683	17.6
Atlanta/rural Georgia	271	7.0
Los Angeles	591	15.3
Kentucky	470	12.1
Louisiana	328	8.5
New Jersey	1307	33.7
Treating institution affiliated with NCI cooperative group*		
No	774	20.0
Yes	3100	80.0

*CALGB, ECOG, SWOG, NSABP, ACOSOG

Table 2

Results of multivariate logistic regression

	OR	Lower 95% CI	Upper 95% CI
Race			
African American	0.65	0.50	0.85
Caucasian	1.00	N/a	N/a
Age (reference = 65–69)			
70–74	0.90	0.76	1.08
75–79	0.84	0.70	1.01
80 plus	0.71	0.57	0.87
Marital status (ref. = married)			
Unmarried	0.93	0.83	1.06
Dual medicare/medicaid eligible (ref. = no)			
Yes	0.61	0.47	0.78
Comorbidity Score (ref. = 2 or more)			
0	0.88	0.68	1.15
1	0.78	0.60	1.02
Census tract education (ref. = below 25th percentile)			
75th percentile HS graduates	1.14	0.94	1.37
50–74th percentile	1.17	0.98	1.40
25–49th percentile	1.09	0.91	1.31
Tumor AJCC stage (ref. = stage IIB)			
Stage I	1.90	1.50	2.40
Stage IIA	1.61	1.28	2.04
Tumor grade (ref. =poorly differentiated)			
Unknown/not assessed	1.16	0.92	1.47
Moderately differentiated	1.14	0.97	1.34
Well differentiated	1.29	1.05	1.58
Estrogen receptor status (ref. = positive)			
Negative	0.84	0.69	1.03
Unknown	0.98	0.80	1.19
Year of diagnosis (ref. = 2000)			
2001	1.59	1.32	1.92
2002	2.21	1.72	3.10
Region (ref. = New Jersey)			
San Francisco	0.44	0.22	0.89
Detroit	0.40	0.27	0.61
Atlanta/rural Georgia	0.70	0.39	1.26
Los Angeles	0.85	0.57	1.26
Kentucky	0.50	0.32	0.76
Louisiana	0.42	0.26	0.66
Treating institution affiliated with cooperative group*			

	OR	Lower 95% CI	Upper 95% CI
Yes	2.31	1.50	5.61

* CALGB, ECOG, SWOG, NSABP, ACOSOG