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Breast Cancer Treatment among Older Women in Integrated Health Care Settings

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Abstract

Purpose—A substantial literature describes age-dependent variations in breast cancer treatment, showing that older women are less likely to receive standard treatment than are younger women. We sought to identify patient and tumor characteristics associated with the non-receipt of standard primary tumor and systemic adjuvant therapies.

Methods—We studied 1,859 women aged 65 years or older with stage I and II breast cancer diagnosed between 1990 and 1994 who were cared for in six geographically dispersed community-based health care systems. We collected demographic, tumor, treatment, and comorbidity data from electronic data sources, including cancer registry, administrative, and clinical databases, and from subjects' medical records.

Results—Women 75 years of age or older and those with higher comorbidy indices were more likely to receive non-standard primary tumor therapy; to not receive axillary lymph node dissection; and to not receive radiation therapy following breast conserving surgery. Asian women were less likely to receive breast conserving surgery and African American women were less likely to be prescribed tamoxifen. Although non-receipt of most therapies was associated with a lower baseline risk of recurrence, an important minority of high risk women (16–30%) did not received guideline therapies.

Conclusions—Age is an independent risk factor for non-receipt of effective cancer therapies, even when comorbidity and risk of recurrence are taken into account. Information regarding treatment

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effectiveness in this age group and tools that allow physicians and patients to estimate the benefits versus the risks of therapies, taking into account age and comorbidity burden, are critically needed.

Keywords

breast cancer; older women; patterns of care

INTRODUCTION

A substantial literature describes age-dependent variations in breast cancer treatment, consistently showing that older women are less likely to receive standard treatments than are younger women. Past investigations have examined factors that might explain these age-dependent treatment variations, including patients' health and functional status;[1,2,3,4,5] patient-physician communication;[1,3,6,7,8] and patients' and their families' treatment preferences and support.[3,5,9,10] Race- and socioeconomic status-dependent variations in breast cancer treatment have also been reported.[11,12] In integrated health care settings (networks of care providers and organizations that offer coordinated health care services to a defined population and assume clinical and fiscal accountability for clinical outcomes[13]) where cost and access barriers to care are reduced, a small number of studies indicate that older women and minority women are more likely to receive breast conserving surgery and to receive radiation therapy following breast conserving surgery than are their counterparts treated in fee-for-service settings.[14,15,16,17]

We studied 1,859 women aged 65 years or older with early stage breast cancer that received care in six geographically dispersed community-based integrated health care systems whose care is not accessible for study using Medicare data. We sought to identify patient and tumor characteristics associated with the non-receipt of standard primary tumor and systemic adjuvant therapies. We extend previous investigations by the inclusion of a substantial number of the oldest women and by focusing on both primary and adjuvant therapies in integrated health care settings.

METHODS

Setting

The Cancer Research Network (CRN) consists of the research programs and enrollee populations of 12 integrated health systems, including Group Health Cooperative, Harvard Pilgrim Health Care, Henry Ford Health System/Health Alliance Plan, HealthPartners Research Foundation, Lovelace Health Plan, the Meyers Primary Care Institute of Fallon Community Health Plan/Fallon Foundation/University of Massachusetts Medical School, and Kaiser Permanente in six regions: Colorado, Georgia, Hawaii, Northwest (Oregon and Washington), Northern California, and Southern California. The overall goal of the CRN is to increase the effectiveness of preventive, curative and supportive interventions that span the natural history of major cancers among diverse populations and health systems through a program of collaborative research.[18]

Study Sample Eligibility

We identified potentially eligible subjects at six of the CRN members: Group Health Cooperative (GHC), Western Washington; Kaiser Permanente (KPSC), Southern California; Lovelace (L), New Mexico; Henry Ford Health System (HF), Detroit, Michigan; HealthPartners (HP), Minnesota; and Fallon Community Health Plan (F), Massachusetts. These six were chosen to achieve diversity in geography, system size, and patient populations while maintaining study feasibility. We used population-based cancer registry databases at four

participating sites (GHC, KPSC, L, HF) and administrative databases at two participating sites (HP, F) to identify potentially eligible subjects. Eligible subjects were all women aged 65 years or older and diagnosed for the first time with histologically confirmed, early stage breast cancer (American Joint Commission on Cancer [AJCC] TNM stage[19] I, IIA, or IIB) between January 1, 1990 and December 31, 1994. Women were ineligible if they had another clinically active malignancy, except non-melanoma skin cancer, diagnosed within five years before, or 30 days after, their breast cancer diagnosis. We also excluded women with simultaneously diagnosed bilateral breast cancer.

At sites with Surveillance, Epidemiology and End Results (SEER) cancer registries, we identified women with ICD-Oncology codes indicating a breast cancer diagnosis (C50.0 – C50.9). At sites without cancer registries, we reviewed claims and other administrative databases for ICD-9 or -10 codes 174–174.9 and ICD-9 and CPT codes for excisional biopsy; breast biopsy; mastectomy; partial mastectomy with lymphadenectomy; partial mastectomy with breast cancer diagnosis; and partial mastectomy with radiotherapy or chemotherapy.

Medical record abstractors verified (at sites with cancer registries) or determined (at sites without cancer registries) each subject's primary cancer site and stage at diagnosis, breast cancer diagnosis date, age at diagnosis, and the absence of other clinically active malignancies.

Sampling

We included all eligible subjects from all sites except KPSC, the largest site, where we sampled 10% of the subgroup of non-Hispanic white subjects younger than age 80 with stage I breast cancer, since including the complete sample of these subjects would only marginally increase the statistical power of the study, but would substantially decrease its cost-efficiency.

Protection of Human Subjects

The protocol for this study was approved by the Institutional Review Boards at each participating institution.

Data Collection

We collected demographic, tumor, treatment, and comorbidity data from electronic data sources — including cancer registry, administrative, and clinical databases — and from subjects' medical records. An automated Data Collection System (DCS) was preloaded with electronically available data from each site. We verified all preloaded data against medical records, except cancer registry data elements for sites with SEER registries. The SEER data items for demographic information, tumor characteristics, and primary tumor therapy were considered the gold standard.[20]

Standardized medical record reviews were conducted at each site and the data were entered directly into the DCS. We assessed intra-rater and inter-rater reliability twice during the one and one-half year data collection period. The intra-rater reliability rates were 93% for both time periods, and the inter-rater reliability rates were 91% for time period one and 88% for time period two.

Demographic Information—We ascertained each woman's date of birth, race, and ethnicity.

Comorbidity—Comorbid conditions present during the one year before breast cancer diagnosis, as reflected in the medical record, were used to calculate the Charlson Comorbidity Index.[21]

Tumor Characteristics—We collected date of diagnosis and stage at diagnosis, laterality, tumor size, lymph node evaluation, estrogen/progesterone receptor protein (ERP/PRP) status, and histology type and grade.

Breast Cancer Treatment—We collected the specific type of surgery performed, and if done, the results of axillary lymph node dissection (ALND) or sentinel node biopsy. The number of courses and dosages for radiation, hormonal therapy, and chemotherapy, and the specific hormonal and chemotherapeutic agents prescribed were ascertained from the medical record.

Analytic Variables

Independent Variables

Demographic Characteristics We categorized age as 65–69, 70–74, 75–79, and 80+ years of age. We grouped race/ethnicity as Non-Hispanic white, Hispanic, African-American, and Asian/Pacific Islander. We classified the small number of other/unknown race (n=5) as non-Hispanic white. For the 19% of the sample with missing ethnicity information, we applied a validated adaptation of the GUESS (Generally Useful Ethnic Search System) computer program to assign ethnicity based on a subject's last name.[22,23]

Comorbidity We calculated the weighted Charlson Index (0, 1–2, 3–4, 5+), using the original algorithm.[21] Because of small numbers, we collapsed scores of 3 or greater into one group.

Tumor Characteristics/Risk of Recurrence We categorized stage as I and II pathologically when the data were available (80% of the time) and clinically in the remainder. Histologic grade was categorized as well differentiated, intermediate/moderately differentiated, poorly/undifferentiated/anaplastic, or not determined/stated. ERP and PRP status were classified as positive, negative, or indeterminate/other. Together these data were combined to categorize risk of recurrence as minimal, intermediate, or high using the 1992 St. Gallen criteria.[24]

Dependent Variables

Other than Standard Primary Tumor Therapy We compared those who received other than standard primary tumor therapy to those who received it, with standard primary tumor therapy defined as either breast conserving surgery (BCS) with axillary lymph node dissection followed by radiation therapy, or modified radical mastectomy, in accordance with the 1990 NIH Consensus Development Conference recommendations.[25] To better understand specific patterns of care, we examined the components of standard primary tumor therapy, comparing (1) those who did not receive an ALND to those who did (only two subjects underwent sentinel node biopsy), and (2) those who did not receive radiation therapy following breast conserving surgery to those who did. We also compared those who received mastectomy to those who received BCS.

Non-receipt of Systemic Adjuvant Therapy We compared those who did not receive a tamoxifen prescription to those who did, and those who did not receive chemotherapy to those who did.

Data Analysis—We calculated the frequency and proportions of patient, tumor, and treatment characteristics in the four age groups. To identify factors associated with non-receipt of treatments, we compared the patient and tumor characteristics of subjects who received treatments and those who did not. We used the Pearson chi-square to test the homogeneity of the proportions of patients receiving treatments in categories of the independent variables.

All factors found to be associated with treatments at the bivariate level ($p<0.1$) were entered into multivariable logistic regression models (one for each dependent variable). These models were adjusted for age, race/ethnicity, comorbidity, and risk of recurrence, regardless of whether these variables met the model entry criterion of $p<0.1$. We used Generalized Estimating Equations (GEE) in SAS version 9 to account for clustering by surgeon. The odds ratios represent the odds of not receiving indicated treatment if the patient was in the target category, relative to the reference category, adjusted for the other variables. Type 3 GEE analysis was performed to compute a score statistic to test for homogeneity of null odds ratios across covariate categories.[26]

Because of the differences in case ascertainment at sites with and without cancer registries, we conducted analyses including and not including the non-cancer registry sites. As the results were comparable, we present the overall results only.

RESULTS

We confirmed eligibility for 1,859 women, excluding 257 whose medical records were not available. The 257 did not differ systematically from the 1859. The cohort was predominantly non-Hispanic white and one-fifth of subjects were 80 years of age or older (Table 1). Subjects were generally healthy and most had tumors with favorable prognostic characteristics. The majority (80%) received standard primary tumor therapy. Approximately equal numbers of women received either a mastectomy or BCS and most underwent ALND. Although only 39% of all study patients received radiation therapy, when the denominator was restricted to just those who received BCS, the proportion increased to 77%. Two-thirds received a prescription for tamoxifen, while only 10% received adjuvant chemotherapy. The oldest women had, in general, tumors with more favorable prognostic characteristics.

Receipt of Non-standard Primary Tumor Therapy

In both the bivariate (Table 2) and multivariable analyses (Table 3), women 75 years of age or older, those with higher Charlson Comorbidity Index scores, and those at low or intermediate risk of recurrence were more likely to receive non-standard primary therapy. Sixteen percent of women at high risk of recurrence received nonstandard therapy. The predictors we observed for non-standard primary therapy overall were the same predictors for non-receipt of ALND, although association between age and non-receipt of ALND was greater. Women 75 years or older were more likely not to receive radiation therapy, as were those with more comorbidity, but baseline risk of recurrence was not associated with receipt of radiation. In contrast to these observations, age and comorbidity were not associated with receipt of mastectomy in comparison to BCS. Rather, being Asian/Pacific Islander was associated with receipt of mastectomy, as was being at higher risk of recurrence.

Non-Receipt of Systemic Adjuvant Therapy

Among all women at high risk of recurrence at baseline, 85% did not receive chemotherapy, 30% did not receive tamoxifen, and 24% received no systemic adjuvant therapy. Nonetheless, 99% of women who received chemotherapy were at high risk of recurrence. African American women and those at low risk of recurrence were less likely to be prescribed tamoxifen. The African American association was confined to those whose ERP status was undetermined, but whose other tumor characteristics put them at low or intermediate risk of recurrence.

DISCUSSION

In this study, conducted in a demographically and geographically diverse group of women diagnosed with early stage breast cancer, older age and greater comorbidity burden were

independently and inversely related to the receipt of standard primary therapy. Our findings are consistent with other recent studies,[3,4,27,28] and extend them to integrated health care delivery system settings.

Baseline risk of recurrence was associated with the receipt of standard primary therapy, with women at lower initial risk being more likely to receive less than standard therapy. While this may be appropriate, it is concerning that 16% of those at high risk did not receive standard primary tumor therapy. Considering risk of recurrence in older women is important because gains in life expectancy have occurred at the end of life: the average life expectancy of a 75 year old woman is nearly 12 years (17 years if healthy), and that of an 85 year old woman is 5.9 years (9.6 years if healthy).[29] These gains mean that older women with breast cancer have, on average, longer periods of time when they are at risk for recurrences than breast cancer patients diagnosed in the past.

Age and comorbidity were also associated with non-receipt of ALND. These patterns are consistent with data from a similar time frame demonstrating that rates of ALND decreased sharply with age, with women 80+ years of age being nearly six times less likely to receive ALND than those 55 years of age or younger.[30] The arguments for or against ALND in early stage breast cancer have shifted focus with the advent of sentinel node biopsy (SNB). Although the evidence supporting its use is based on only one published clinical trial, the American Society of Clinical Oncology has determined that SNB "is an appropriate initial alternative to routine staging ALND for patients with…clinically negative axillary nodes."[31] The expert panel also observed that the odds of successful SNB decreases with increasing age.[32] It is unclear how the decreasing accuracy of SNB with age will affect older women's treatment patterns and outcomes.

While increasing age and comorbidity were also associated with the non-receipt of radiation therapy, it is noteworthy that baseline recurrence risk was not. This difference may stem from the perception that older women, in general, are at lower risk of recurrence than are younger women and thus derive less benefit from radiation therapy. Clinical trial evidence supports this perception, but only among node negative women with small ERP positive tumors.[33]

Asian women were more likely to undergo mastectomy compared with white women. Recent studies of BCS in early-stage breast cancer patients[34,35,36,37] suggest that both patient and physician factors may account for the differences in mastectomy vs. BCS between Asian/Pacific Islanders and non-Hispanic white women. These factors include poor cosmetic outcome, language barriers, physician concern regarding adherence to radiation therapy regimens, and patient preference. Those at highest risk of recurrence were also more likely to undergo mastectomy, perhaps due to the recognition that BCS even when followed by radiation therapy is associated with an increased risk of recurrence relative to mastectomy.

We found that age and comorbidity were not related to receipt of BCS. Comorbidity has not consistently been considered as a covariate in prior studies in integrated health care settings[e.g.,15,38] Although previous studies have reported an inverse association of age with BCS among women with early stage breast cancer,[4,39,40] at least two found that women with private insurance were more likely to have received BCS than women without private insurance.[5,39] Riley et al's study of HMO and fee-for-service came from a slightly earlier time frame than our study found that older women cared for in HMO settings were modestly more likely to undergo BCS and radiation therapy following BCS than women in fee-for-service settings (38.4% vs. 36.8% for BCS and 69% vs. 63.7% for radiation therapy).[15] Our figures were 46% and 77%, respectively.

We observed a reduced receipt of chemotherapy among the oldest women compared with the youngest, consistent with available guidelines at the time of our study enrollment.[24]

Differences in chemotherapy use by age in early stage breast cancer have been well-documented,[4,27,41,42] and among those who do receive chemotherapy, older women are more likely to receive lower dose intensity.[43] The absence of sufficient clinical trial data among women over the age of 70 and worries about toxicity have undoubtedly influenced clinical practice.

In contrast to the findings for chemotherapy, most studies, including ours, have not found an association between age and receipt of hormonal therapy,[4,27,41] suggesting that patients and their physicians agree that the benefits of hormonal therapy outweigh the risks.[44] In this study, however, 30% of women at high risk of recurrence at baseline did not receive tamoxifen.

An important limitation of this study was our inability to measure important factors in the treatment decision-making process. We were only able to collect information from automated data and medical records, typically poor sources of information about treatment decision-making. Another limitation of our study is that our subjects were diagnosed in the early to mid 1990s. Although care patterns have changed in the intervening years, with increasing use of BCS, radiation therapy following BCS, tamoxifen, and chemotherapy among older women,[27,45] age remains a strong predictor of how older women are treated to the present.[46,47] Thus, our data remain relevant in three ways: (1) they provide comprehensive information about all aspects of breast cancer treatment received by older women in community settings not available for study using Medicare data; (2) age-dependent variations in care persist and we still do not know how much of the variation is warranted; and (3) the variations in care observed have substantial relevance to the surviving women from this cohort, and women like them who were diagnosed in the same timeframe, all of whom continue to be at risk for recurrence and breast cancer mortality. A strength of our work is that we were able to study a relatively unselected sample of older women with complete treatment data in integrated health care systems, where barriers to care have been minimized.

Our work demonstrates that age is an independent risk factor for non-receipt of effective therapies, even when comorbidity and risk of recurrence are considered. To reduce these disparities will require high quality evidence regarding treatment efficacy in older and sicker populations. Efficacy information, coupled with accurate tools that allow physicians and older patients to estimate the benefits versus the risks of therapies, are critically needed. Older persons are very heterogeneous with respect to functional reserve, comorbidity burden, and preferences, all of which need to be considered in the treatment decision-making process.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of the Study Sample, Overall and by Age at Breast Cancer Diagnosis.

	Total		Age			
			65–69	70–74	75–79	80+
	N=1859	%	N=632 %	N=548 %	N=313 %	N=366 %
Race/Ethnicity	1523	82	75	81	85	91
White (non-Hispanic)	93	5	7	6	4	2
Hispanic	190	10	13	11	8	7
African American	53	3	5	2	3	<1
Asian/Pacific Islander						
Charlson Comorbidity Index	1264	68	76	66	62	62
0	507	27	22	29	31	32
1–2	88	5	2	5	7	6
3+						
Stage	1049	56	51	55	59	67
I	810	44	49	45	41	33
II						
Estrogen Receptor Status	1331	72	70	73	76	69
Positive	300	16	20	16	13	11
Negative	228	12	10	11	11	20
Indeterminate/other						
Progesterone Receptor Status	1060	57	57	57	61	54
Positive	524	28	33	29	25	23
Negative	275	15	11	14	14	24
Indeterminate/other						
Histologic Grade	299	16	16	18	13	16
Well differentiated	684	37	39	35	35	37
Intermediate/moderate	434	23	24	25	24	19
Poorly/Undifferentiated/Anaplastic	442	24	21	22	27	28
Not determined/stated						
Risk of Recurrence	320	17	16	19	16	17
Low	269	14	12	13	15	20
Intermediate	1270	68	72	68	69	63
High						
Primary Therapy	1492	80	89	89	71	60
(Mast) or (BCS+AND+RT)*	367	20	11	11	29	40
Other than primary therapy						
Surgery	977	53	54	55	49	50
Mastectomy	860	46	45	45	48	48
Breast Conserving Surgery	22	1	1	<1	3	2
Other						
Axillary Node Dissection	1497	81	91	90	73	55
Yes	362	19	9	10	27	45
No						
Radiation Therapy Received	716	39	45	43	37	22
Yes	1143	61	55	57	63	68
No						
Chemotherapy Received	188	10	19	10	4	1
Yes	1671	90	81	90	96	99
No						
Tamoxifen Prescribed	1222	66	66	67	68	62
Yes	637	34	34	33	32	38
No						

*Mastectomy or Breast Conserving Surgery with Axillary Node Dissection and Radiation Therapy

Table 2

Bivariate Associations of Patient and Tumor Characteristics with Non-Receipt of Treatments.

	Other than Standard Primary Therapy* (N= 367/1859)	Axillary Node Dissection not Performed (N=344/1837)##	Radiation Therapy not Received after BCS** (N=197/860)#	Mastectomy Received (N=977/1837)##	Tamoxifen not Prescribed (N= 637/1859)	Chemotherapy not Received (N=1671/1859)
Age (years)						
65–69	67 (11%)	51 (8%)	26 (9%)	341 (54%)	217 (34%)	515 (81%)
70–74	62 (11%)	56 (10%)	25 (10%)	299 (55%)	181 (33%)	493 (90%)
75–79	90 (29%)	78 (26%)	47 (31%)	154 (51%)	101 (32%)	301 (96%)
80+	148 (40%)	159 (44%)	99 (56%)	183 (51%)	138 (38%)	362 (99%)
	p<.0001	p<.0001	p<.0001	p=.5	p=.4	p<.0001
Race/Ethnicity						
White (non-Hispanic)	319 (21%)	296 (20%)	162 (22%)	771 (51%)	527 (35%)	1364 (90%)
Hispanic	12 (13%)	12 (13%)	8 (27%)	63 (68%)	24 (26%)	85 (91%)
African American	32 (17%)	30 (16%)	23 (27%)	103 (55%)	73 (38%)	173 (91%)
Asian/Pacific Islander	4 (8%)	6 (11%)	4 (31%)	40 (76%)	13 (25%)	49 (92%)
	p=.02	p=.1	p=.6	p=.0001	p=.08	p=.8
Charlson Comorbidity Index						
0	207 (16%)	183 (15%)	107 (18%)	668 (53%)	428 (34%)	1113 (88%)
1–2	132 (26%)	130 (26%)	75 (32%)	260 (52%)	178 (35%)	471 (93%)
3+	28 (33%)	31 (36%)	15 (39%)	49 (56%)	31 (35%)	87 (99%)
	p<.0001	p<.0001	p<.0001	p=.5	p=.9	P=.0002
Risk of Recurrence						
Low	96 (30%)	84 (27%)	47 (22%)	104 (33%)	178 (56%)	319 (99%)
Intermediate	67 (25%)	65 (25%)	35 (23%)	110 (42%)	81 (30%)	268 (99%)
High	204 (16%)	195 (16 %)	115 (23%)	763 (61%)	378 (30%)	1084 (85%)
	p<.0001	p<.0001	p=.95	p<.0001	p<.0001	p<.0001

*Standard Primary Therapy refers to receipt of Mastectomy or Breast Conserving Surgery with Axillary Node Dissection and Radiation Therapy

**Breast Conserving Surgery

#Denominator of 860 refers to the subjects who had Breast Conserving Surgery

##Denominator of 1837 refers to sample size after excluding 22 cases receiving other than Breast Conserving Surgery or Mastectomy.

Table 3

Adjusted Odds Ratios and 95% Confidence Intervals from Multivariable Models Relating Patient Characteristics to Breast Cancer Care.

	Other than Standard Primary Therapy*	Axillary Node Dissection not Performed	Radiation Therapy not Received After BCS**	Mastectomy Received@	Tamoxifen not Prescribed
Age (years)					
65–69	1	1	1	1	1
70–74	0.9 (0.6, 1.4)	1.1 (0.8, 1.6)	1.2 (0.7, 2.0)	1.2 (0.9, 1.5)	0.9 (0.7, 1.1)
75–79	2.9 (1.9, 4.3)	3.3 (2.3, 4.9)	4.0 (2.2, 7.0)	1.0 (0.7, 1.2)	0.9 (0.7, 1.2)
80+	5.8 (3.9, 8.6)	8.7 (5.8, 13.2)	11.1 (6.8, 18.2)	0.9 (0.7, 1.3)	1.1 (0.8, 1.5)
	Overall p <.0001	Overall p <.0001	Overall p <.0001	Overall p = .3	Overall p = .3
Race/Ethnicity					
White (non-Hispanic)	1	1	1	1	1
Hispanic	1.1 (0.6, 2.1)	1.2 (0.6, 2.2)	1.6 (0.7, 3.8)	1.3 (0.8, 2.0)	0.8 (0.4, 1.6)
African American	1.0 (0.6, 1.6)	1.0 (0.6, 1.7)	1.5 (0.8, 2.7)	0.8 (0.6, 1.2)	1.4 (1.0, 2.0)
Asian/Pacific Islander	0.5 (0.2, 1.4)	1.1 (0.5, 2.5)	2.1 (0.8, 6.0)	2.3 (1.3, 4.1)	0.8 (0.4, 1.6)
	Overall p = .5	Overall p = .9	Overall p = .3	Overall p = .03	Overall p = .3
Charlson Comorbidity Index					
0	1	1	1	1	1
1–2	1.5 (1.2, 2.0)	1.8 (1.4, 2.3)	1.5 (1.1, 2.0)	1.0 (0.8, 1.3)	1.0 (0.8, 1.2)
3+	2.1 (1.2, 3.8)	3.2 (1.8, 5.6)	1.9 (1.0, 3.6)	1.0 (0.7, 1.6)	1.1 (0.7, 1.8)
	Overall p = .01	Overall p =.0001	Overall p = .06	Overall p = .9	Overall p = .9
Risk of Recurrence					
Low	2.4 (1.8, 3.4)	2.1 (1.5, 2.8)	1.1 (0.7, 1.6)	0.4 (0.3, 0.5)	2.8 (2.2, 3.6)
Intermediate	1.6 (1.1, 2.3)	1.5 (1.0, 2.1)	0.8 (0.5, 1.1)	0.5 (0.4, 0.6)	0.97 (0.7, 1.3)
High	1	1	1	1	1
	Overall p <.0001	Overall p = .0009	Overall p = .3	Overall p <.0001	Overall p <.0001

* Standard Primary Therapy refers to receipt of Mastectomy or Breast Conserving Surgery with Axillary Node Dissection and Radiation Therapy

** Breast Conserving Surgery

Due to small sample sizes, Charlson Comorbidity Indices of 1+ were compared to 0 group in the model for non-receipt of Chemotherapy @ 22 cases with surgery other than Mastectomy or Breast Conserving Surgery were excluded in the model