HHS Public Access

Author manuscript

Am J Clin Oncol. Author manuscript; available in PMC 2021 February 01.

Published in final edited form as:

Am J Clin Oncol. 2020 February ; 43(2): 101–106. doi:10.1097/COC.0000000000000638.

Association of diabetes and other clinical and sociodemographic factors with guideline-concordant breast cancer treatment for breast cancer

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Abstract

Background—Women with breast cancer have worse health outcomes with co-occurring type 2 diabetes, possibly due to suboptimal breast cancer treatment.

Methods—We created a cohort of women ages 66–85 with stage I-III breast cancer from 1993–2012 from an integrated healthcare delivery system (n=1,612) and fee-for-service Medicare beneficiaries (n=98,915), linked to Surveillance, Epidemiology, and End Results (SEER) data (total n=100,527). We evaluated associations between type 2 diabetes and other factors with undergoing guideline-concordant cancer treatment. We estimated relative risks (RR) using

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AUTHOR CONTRIBUTIONS

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Conflicts of interest: The authors declare no potential conflicts of interest.

multivariable log-binomial models for outcomes of 1) overall guideline-concordant treatment, 2) definitive surgical therapy (mastectomy or lumpectomy with radiation), 3) chemotherapy, if indicated, and 4) endocrine therapy.

Results—Overall, 23% had diabetes, 35% underwent overall guideline-concordant treatment, 24% chemotherapy, and 83% endocrine therapy. Women with diabetes were less likely to undergo overall guideline-concordant treatment (RR:0.96;95%CI:0.94–0.98), and only slightly less likely to undergo guideline-concordant definitive surgical therapy (RR:0.99,95%CI:0.99–1.00). No differences were found for chemotherapy or endocrine therapy. Other factors significantly associated with lower risk of guideline-concordant care were cancer stages II-III (vs I; RR=.47-.69,p<0.0001), older age (vs 66–69; RR=.56-.90,p<0.0001), higher comorbidity burden, and Medicaid dual-eligibility.

Conclusions—Diabetes was associated with lower adherence to overall guideline-concordant breast cancer treatment. However, higher stage, older age, higher comorbidity burden, and Medicaid insurance were more strongly associated with lower use of guideline-concordant treatment. Given the heavy burden of breast cancer and diabetes, long-term outcomes analysis should consider guideline-concordant treatment.

Impact—Other factors besides diabetes are more strongly associated with guideline-concordant breast cancer treatment.

Introduction

Breast cancer is the most frequently diagnosed cancer in women, with over 252,000 new diagnoses in 2017[1] and increasing incidence with age (the median age at diagnosis is 61 years[2]). The prevalence of type 2 diabetes also increases with age (14% at age 60, rising to 27% by age 65,[3]), and type 2 diabetes and breast cancer are diagnosed more frequently in the same individual than would be expected,[4] which may be due to shared risk factors such as obesity, poor diet, and physical inactivity.[5] Furthermore, women with breast cancer have worse health outcomes if they have type 2 diabetes.[6] Multimorbidity may affect treatment benefits and adherence to care,[7–12] and the presence of diabetes at the time of a cancer diagnosis may influence treatment patterns and complications.[13] Patients with cancer are at risk for hyperglycemic excursions from glucocorticoids,[14,15] chemotherapeutic agents,[15,16] high body mass index,[17] nutritional imbalances,[18–21] physical inactivity,[22–24] stress,[16,18,25] and/or infections.[16] The relationship between diabetes and breast cancer is complex, with each affecting the other condition and their treatments in potentially problematic ways.

The mechanism whereby diabetes might worsen health outcomes in patients with breast cancer is unclear, and this study focuses on one aspect of the clinical pathway: adherence to clinical treatment guidelines for breast cancer. With the goal of treatment guidelines to optimize outcomes, guideline-discordant care may have a negative effect on health outcomes. To identify variations in breast cancer treatment patterns, we evaluated whether diabetes and other clinical and health system characteristics and patient demographics were associated with receipt of clinical-guideline-concordant treatment for stages I-III breast cancer in a large cohort of older women.

Data and Methods

We created a cohort of 100,527 women ages 66–85 diagnosed from 1993–2012 with stages I-III breast cancer from two sources, a large, integrated healthcare delivery system in Washington state (Kaiser Permanente Washington (KPWA)) with linkage to the Surveillance, Epidemiology, and End Results (SEER) tumor registry (n=1,612), and the linked SEER-Medicare claims data (n=98,915). The KPWA data included demographics, enrollment, inpatient and outpatient diagnoses and procedures, breast care services and results, pharmacy dispensings, laboratory results, vital signs, and death.[26] Treatment information for patients at KPWA was collected from medical chart abstraction, electronic health records, and claims data. The KPWA pharmacy database included all medications dispensed at its outpatient pharmacies and claims from contracting pharmacies. Pharmacy data are estimated to be 97% complete. Automated death data were from an on-going link to Washington State death records. The SEER-Medicare data included Medicare physician, hospital, outpatient, and Part D drug benefit claims data to identify treatment. Part D data for medications were from 2007–2012 only, and for only the 53–57% of subjects subscribed in any given year. All patients had at least 1 year of data before breast cancer diagnosis to identify diabetes and other comorbidities that were used in the calculation of a modified Klabunde index that excluded diabetes.[27] The Klabunde index is a refined comorbidity algorithm that uses the same comorbid conditions identified by Charlson et al,[28] but which is specific to breast cancer and uses estimated coefficients for mortality as unique weights for each condition.

We had several exclusions, including Medicare beneficiaries not having Parts A and B or enrolling in health maintenance organizations, or KPWA patients disenrolling from the health plan during the treatment period. We also excluded patients who had no surgery or died within 1 year of breast cancer diagnosis due to the possibility of missing treatment information.

Treatment could include mastectomy or lumpectomy, radiation, endocrine therapy, and/or chemotherapy. Whether a subject's treatment was considered guideline-concordant depended on whether these components matched clinical guidelines from the National Comprehensive Cancer Network.[29,30] Guideline-concordant breast cancer treatment was determined by the following factors: 1) disease stage (stages I, II or III); 2) diagnosis year (1993–2012); 3) estrogen receptor (ER) status and having at least two years of follow-up for those patients with medication data; and 4) age (70+) for radiation guidelines,[31] using the diagnosis year-concordant guidelines from the National Comprehensive Cancer Network.[29,30] Guidelines changed in 2006 to incorporate HER-2 expression tests and treatment with trastuzumab,[32] but due to low uptake of HER-2 testing in the cohort overall, treatment with trastuzumab was not required for guideline-concordant therapy in this study. If patients had no medication data available, for example, if they did not have Part D Medicare benefits, we could not require them to have endocrine therapy if their tumors were ER-positive. Our outcomes were overall guideline-concordant treatment (n=100,527) and each of the 3 components of guideline-concordant treatment: 1) definitive surgical therapy (mastectomy or lumpectomy with radiation, n=100,527), 2) chemotherapy, if indicated (n=77,406), and 3) endocrine therapy among women with ER-positive tumors and medication data (n=15,140).

Model covariates included diabetes and other clinical and demographic information. Diabetes was considered present if a subject had 1 inpatient claim or 2 outpatient claims with an International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) diagnosis code for diabetes (codes in Appendix) in the year prior to incident breast cancer diagnosis. We did not include diabetes medication as an indicator of having diabetes (i.e., oral medications or insulin), because we only had medication information from Part D claims data from 2007, and not for the entire cohort. Other model variables included age at cancer diagnosis (66–69, 70–74, 75–79, 80–85 years), tumor stage (I-III), ER status (for consideration of endocrine therapy in those with medication data), Klabunde comorbidity index as defined previously (0, >0 & <1, ≥1), Medicaid beneficiary status in the year prior to breast cancer diagnosis, race/ethnicity (White, Black, Asian, Hispanic, Other), high poverty level (>20%) in the Census tract, urban or rural Census tract, and diagnosis year. We also included SEER registry area and site of care (KPWA or SEER).

Using chi-squared tests, we assessed the association between diabetes and each of the demographic and other clinical variables with guideline-concordant treatment in effect in the diagnosis year. Multivariable log-binomial models were estimated[30] to obtain relative risks (RR) and 95% confidence intervals for overall guideline-concordant treatment and for each of 3 components of guideline-concordant treatment: 1) definitive surgical therapy (mastectomy or lumpectomy with radiation), 2) chemotherapy, if indicated, and 3) endocrine therapy among women with ER-positive tumors. We used this model because of the high occurrence of the outcome of interest, guideline-concordant care, and we incorporated the same covariates in each model to allow for qualitative comparisons across outcomes. Analyses used SAS version 9 (Cary, NC).

Results

Overall, 23% (n=22,707) of women in the cohort had type 2 diabetes, and women with diabetes were less likely to undergo guideline-concordant breast cancer care (36% vs 33%, p<0.01). (Table 1) Sixty percent of the cohort had stage I breast cancer, 34% had stage II, and the remainder had stage III, similar to the overall breast cancer population in the United States.[35–38] Forty-seven percent of the cohort was between the ages 75–85, 89% was White, 6% was Black/African American, 11% was dually eligible for Medicare and Medicaid in the year prior to diagnosis, 10% lived in a rural Census tract, and 13% lived in a high poverty area. For guideline-concordant care, 35% had overall guideline-concordant treatment, with 92% undergoing guideline-concordant definitive surgical therapy (mastectomy or lumpectomy with radiotherapy), 24% chemotherapy, 73% radiotherapy, and 83% endocrine therapy.(Table 2)

Multivariable analysis showed that compared to women without diabetes, women with diabetes were slightly less likely to receive overall guideline-concordant treatment for breast cancer (RR: 0.96; 95%CI: 0.94–0.98)(Table 3). No associations were found between diabetes and risks of guideline-concordant definitive surgical therapy or receipt of chemotherapy or endocrine therapy after adjustment for other covariates.(Table 3) Other factors significantly associated with a lower risk of undergoing overall guideline-concordant care were higher cancer stage (stage II RR: 0.47, 95%CI:0.46–0.48; stage III RR: 0.69;

95%CI:0.66–0.72 versus stage I), older age (age 75–79 RR: 0.75; 95%CI:0.74–0.77; age 80–85 RR: 0.56; 95%CI: 0.54–0.57 versus age 66–69), higher (non-diabetes) comorbidity burden (e.g., comorbidity score≥1 RR: 0.80; 95%CI: 0.76–0.84), and Medicaid dual-eligibility (RR: 0.83; 95%CI: 0.81–0.86). Over this period, the adjusted relative risk of guideline concordance generally increased, that is, there was more adherence to guidelines over time, after adjusting for other covariates.

For the individual components of guideline-concordant therapy, higher stage was associated with an increased risk of receiving guideline-concordant chemotherapy or endocrine therapy, whereas older age and higher comorbidity burden were associated with lower use.(Table 3)

Discussion

Overall guideline-concordant therapy comprises all possible therapies a patient should receive, which includes a multidisciplinary approach to treatment that requires careful consideration and appropriate specialty referrals and follow-up. This complex constellation of care may be more difficult to optimize than each individual treatment a patient may be eligible for. Therefore, while we saw a high proportion, 92%, of subjects undergoing optimal definitive surgical therapy (i.e., mastectomy or lumpectomy with radiotherapy), we saw a lower proportion, 35%, undergoing the optimal composite of guideline-concordant care. We hypothesized that diabetes would be associated with lower use of guideline-concordant breast cancer therapy, and this was true for the overall treatment outcome, but not for the individual components. In particular, we expected lower guideline concordance for chemotherapy use, because chemotherapy often is infused concurrently with steroids, which could negatively impact diabetes control. Chemotherapy side effects, such as neutropenia, infection, anemia, and possible effects on liver and kidney function, might also be more concerning for breast cancer patients with diabetes and lead to lower use of chemotherapy. Research has shown mixed results related to this association, especially when adjusting for other factors besides diabetes.[13,39,40]

Statistically significant results in our models may be due to our large sample size of more than 100,000 subjects. Some of the adjusted relative risks did not appear clinically significant independently, but could have a meaningful contribution in combination with other factors. We required that all subjects must at minimum have had surgery, because we were leveraging previously-collected data for a subgroup in our study; this may have led to overestimates of the proportion of women receiving guideline-concordant care, because subjects were required to have surgery to enter the cohort as a method to ensure they were being treated with curative intent.[41]

There were changes in treatment guidelines over the 20-year study period from 1993–2012. Most important was the incorporation in 2006 of HER2 testing, when HER2-targeted therapy with trastuzumab was indicated for HER2-positive breast cancer.[42] Uptake of trastuzumab use in clinical practice was slow despite guideline recommendations. Another relevant guideline change in 2004 was the recommendation for use of a genomic assay, OncotypeDX, which helps define which individual patients could benefit from the addition of chemotherapy to hormonal therapy in early stage ER (+) breast cancer.[42] Our database did

not include OncotypeDX Recurrence Scores, making it impossible to predict the influence that this assay may have had on treatment choices. It is possible that our observation of decreasing chemotherapy use over time may have reflected the increased utilization of OncotypeDX to define patients who do not need chemotherapy. Use of OncotypeDX and other similar genomic assays will most likely be more relevant to findings in the years after our study period.[43,44] There were occasional cases where we saw unusually aggressive treatment patterns beyond guideline indications, which may be due to variables we did not have, in particular, margin width (how far tumor is from edge of excision), family history, and multifocal disease (i.e, more than one site of cancer in the breast). For example, patients may receive post-mastectomy radiotherapy for close margins, multifocal disease, or positive axillary nodes.

There could be some misclassification of diabetes. To define diabetes, we relied only on ICD-9-CM codes for type 2 diabetes. Well-controlled patients not requiring specific visit interventions for diabetes treatment could have been missed. Including all diabetes medications in the definition of disease may have resulted in wider inclusion of patients. Similarly, data regarding insulin use was not available for all patients, therefore making it difficult to assess disease severity or duration of diabetes diagnoses. Finally, some patients may have been misclassified as having type 1 diabetes, when they actually had type 2 diabetes, particularly for those individuals treated with insulin.

The 2013 Institute of Medicine (IOM) report, *Delivering High Quality Cancer* Care, calls for evidence-based cancer care based on expanded breadth of data on cancer management for older adults and those with comorbid conditions.[45] Our study focused on the unique association of diabetes with breast cancer treatment adherence, and it did not yield strong findings related to that specific factor. We were limited to using a simple definition of diabetes linked only to ICD9 diagnosis codes because laboratory data were not available in the linked SEER-Medicare data. Diabetes severity, including duration of diabetes and insulin use, was not included in this study, also due to lack of availability in the linked SEER-Medicare data. Others have found that diabetes severity and other comorbidities were inversely related to guideline-concordant treatment.[46,47] Future work may address the question of how severity and diabetes control may influence treatment choice, particularly when “severe” diabetes may be well controlled and therefore have less influence on treatment and vice versa. In addition, this study did not evaluate how breast cancer treatment affected diabetes management or outcomes, which are also important questions. Future work should focus on whether variations in treatment patterns for breast cancer and diabetes are associated with breast cancer-related outcomes and overall mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This work was supported by the National Institutes of Health, National Cancer Institute, through grant numbers R01CA188353 (Gold) and R01CA120562 (Boudreau).

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Table 1.

Cohort characteristics, by receipt of guideline concordant breast cancer therapy (n=100,527, row %)

	Guideline concordant breast cancer treatment, n (%)	
	No (n=64,941, 64.6%)	**Yes (n=35,586, 35.4%)**
Type 2 diabetes in year before breast cancer diagnosis		
No	49,667 (63.8)	28,153 (36.2)
Yes	15,274 (67.3)	7,433 (32.7)
AJCC stage		
I	33,195 (55.1)	27,064 (44.9)
II	27,514 (80.1)	6,820 (19.9)
III	4,232 (71.3)	1,702 (28.7)
Year of diagnosis		
1993	2,578 (72.8)	963 (27.2)
1994	2,475 (71.9)	967 (28.1)
1995	2,495 (70.5)	1,044 (29.5)
1996	2,364 (69.9)	1,020 (30.1)
1997	2,374 (68.4)	1,099 (31.6)
1998	2,125 (64.1)	1,192 (35.9)
1999	2,205 (64.1)	1,234 (35.9)
2000	4,347 (64.7)	2,374 (35.3)
2001	4,361 (63.4)	2,518 (36.6)
2002	4,259 (63.6)	2,439 (36.4)
2003	4,008 (63.1)	2,342 (36.9)
2004	3,807 (62.1)	2,320 (37.9)
2005	3,478 (61.2)	2,201 (38.8)
2006	3,360 (60.8)	2,169 (39.2)
2007	3,628 (67.3)	1,767 (32.8)
2008	3,457 (64.6)	1,893 (35.4)
2009	3,473 (64.2)	1,935 (35.8)
2010	3,379 (62.8)	1,998 (37.2)
2011	3,420 (62.4)	2,057 (37.6)
2012	3,348 (62.0)	2,054 (38.0)
Age at diagnosis		
66–69 years	13,014 (59.4)	10,689 (45.1)
70–74 years	17,812 (60.6)	11,602 (39.4)
75–79 years	17,905 (67.9)	8,462 (32.1)
80–85 years	16,210 (77.0)	4,833 (23.0)
Race		
White	57,402 (64.4)	31,758 (35.6)
Black	4,270 (69.4)	1,886 (30.6)

	Guideline concordant breast cancer treatment, n (%)	
	No (n=64,941, 64.6%)	**Yes (n=35,586, 35.4%)**
Asian	1,218 (61.0)	778 (39.0)
Hispanic	741 (69.4)	327 (30.6)
Others/Unknown	1,310 (61.0)	837 (39.0)
Comorbidity index in year before breast cancer diagnosis		
0	50,835 (63.2)	29,544 (36.8)
>0 & <1	10,212 (68.1)	4,783 (31.9)
≥1	3,894 (75.6)	1,259 (24.4)
Medicaid status in year before breast cancer diagnosis		
No	57,021 (63.6)	32,652 (36.4)
Yes	7,920 (73.0)	2,934 (27.0)
Urban/Rural		
Urban	57,989 (64.4)	32,046 (35.6)
Rural	6,939 (66.3)	3,535 (33.8)
Census tract poverty indicator		
<=20% poverty	47,907 (63.1)	27,963 (36.9)
>20%	8,620 (68.1)	4,031 (31.9)
Unknown	8,414 (70.1)	3,592 (29.9)
SEER Registry		
Connecticut	5,209 (64.4)	2,883 (35.6)
Detroit	5,464 (64.7)	2,986 (35.3)
Hawaii	891 (57.6)	655 (42.4)
Iowa	5,610 (64.0)	3,151 (36.0)
New Mexico	1,737 (69.4)	767 (30.6)
Seattle	5,576 (65.3)	2,969 (34.8)
Utah	2,069 (65.5)	1,091 (34.5)
Kentucky	3,593 (65.3)	1,908 (34.7)
Louisiana	3,215 (66.4)	1,629 (33.6)
New Jersey	6,326 (61.8)	3,909 (38.2)
Georgia	6,843 (63.6)	3,920 (36.4)
California	18,408 (65.5)	9,718 (34.6)
Cohort		
SEER-Medicare	63,838 (64.5)	35,077 (35.5)
KPWA	1,103 (68.4)	509 (31.6)
Estrogen receptor (ER) status		
Positive	49,255 (64.1)	27,596 (35.9)
Negative	13,048 (62.0)	7,990 (38.0)
Unknown	2,638 (100%)	0 (0.0%)

Table 2.

Proportion of subjects undergoing each component of guideline-concordant breast cancer therapy, 1993–2012.

Component of guideline-concordant therapy	No	Yes	Total eligible
Definitive surgical therapy[&]	7,926 (7.9)	92,601 (92.1)	100,527
Chemotherapy[$]	59,215 (76.5)	18,191 (23.5)	77,406
Endocrine therapy[*]	2,540 (16.8)	12,600 (83.2)	15,140

Notes:

[&] Defined as mastectomy or lumpectomy with radiation

[$] Restricted to 77,406 patients who should receive chemotherapy according to NCCN guidelines.

[*] For SEER-Medicare, restricted to subjects diagnosed with breast cancer starting in 2007, enrolled in Medicare Part D, and whose tumors were estrogen-receptor positive.

Table 3.

Adjusted relative risk (RR) and 95% confidence interval (CI) for overall guideline-concordant breast cancer therapy and each of three components.*

	Overall (n=100,527)		Definitive surgical therapy** (n=100,527)		Chemotherapy (n=77,406)		Endocrine therapy (n=15,140)	
	RR	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
Type 2 diabetes								
No	Ref		Ref		Ref		Ref	
Yes	0.957	0.94–0.98	0.996	0.99–1.00	1.00	0.98–1.02	1.00	0.99–1.01
AJCC stage								
I	Ref		Ref		Ref		Ref	
II	0.47	0.46–0.48	0.997	0.99–1.00	1.74	1.71–1.77	1.06	1.05–1.07
III	0.69	0.66–0.72	1.011	1.01–1.02	2.40	2.35–2.45	1.08	1.06–1.10
Year of diagnosis								
1993	Ref		Ref		Ref		-	
1994	1.04	0.97–1.12	0.99	0.98–1.01	1.01	0.93–1.09	-	-
1995	1.08	1.00–1.16	1.00	0.99–1.02	1.06	0.98–1.15	-	-
1996	1.11	1.02–1.21	0.99	0.97–1.01	1.14	1.03–1.25	-	-
1997	1.16	1.06–1.26	0.98	0.96–0.99	1.22	1.12–1.34	-	-
1998	1.31	1.20–1.43	0.98	0.97–1.00	1.41	1.29–1.54	-	-
1999	1.31	1.20–1.42	0.97	0.96–0.99	1.45	1.32–1.58	-	-
2000	1.33	1.23–1.44	0.98	0.96–0.99	1.50	1.38–1.63	-	-
2001	1.37	1.27–1.49	0.98	0.97–1.00	1.53	1.41–1.66	-	-
2002	1.37	1.26–1.48	0.97	0.96–0.99	1.50	1.39–1.63	-	-
2003	1.37	1.27–1.49	0.98	0.97–1.00	1.53	1.40–1.66	-	-
2004	1.38	1.28–1.50	0.98	0.96–0.99	1.49	1.37–1.62	-	-
2005	1.43	1.32–1.55	0.99	0.98–1.01	1.47	1.35–1.59	-	-
2006	1.41	1.31–1.53	0.98	0.97–1.00	1.48	1.36–1.60	-	-
2007	1.19	1.10–1.30	1.00	0.98–1.01	1.40	1.29–1.52	Ref	
2008	1.27	1.17–1.37	1.00	0.99–1.02	1.43	1.32–1.56	0.99	0.97–1.01
2009	1.28	1.18–1.39	1.00	0.98–1.01	1.42	1.31–1.55	0.99	0.97–1.01
2010	1.32	1.22–1.44	0.99	0.98–1.01	1.39	1.28–1.51	1.00	0.98–1.02
2011	1.33	1.23–1.44	0.99	0.98–1.01	1.36	1.25–1.48	1.01	0.99–1.03
2012	1.36	1.27–1.46	0.99	0.98–1.00	1.42	1.32–1.52	1.01	0.99–1.03
Age at diagnosis								
66–69	Ref		Ref		Ref		Ref	
70–74	0.90	0.88–0.92	1.01	1.01–1.01	0.85	0.83–0.86	0.99	0.97–1.00
75–79	0.75	0.74–0.77	0.99	0.99–1.00	0.67	0.65–0.68	0.95	0.94–0.97
80–85	0.56	0.54–0.57	0.93	0.93–0.94	0.48	0.46–0.49	0.91	0.89–0.92
Race								

	Overall (n=100,527)		Definitive surgical therapy** (n=100,527)		Chemotherapy (n=77,406)		Endocrine therapy (n=15,140)	
	RR	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
White	Ref		Ref		Ref		Ref	
Black	0.96	0.93–1.00	0.971	0.96–0.98	1.02	0.99–1.05	1.00	0.98–1.03
Asian	1.05	1.00–1.11	1.011	1.00–1.02	1.05	1.00–1.10	1.00	0.96–1.04
Hispanic	1.06	0.97–1.16	0.998	0.98–1.02	1.10	1.02–1.18	1.04	1.00–1.09
Others	1.13	1.07–1.19	1.016	1.01–1.03	1.08	1.03–1.13	1.04	1.01–1.08
Comorbidity index in year before diagnosis								
0	Ref		Ref		Ref		Ref	
>0 & <1	0.93	0.91–0.96	0.985	0.98–0.99	0.95	0.92–0.97	0.99	0.97–1.00
≥1	0.80	0.76–0.84	0.95	0.94–0.96	0.87	0.84–0.91	0.97	0.95–1.00
Medicaid in year before diagnosis								
No	Ref		Ref		Ref		Ref	
Yes	0.83	0.81–0.86	0.97	0.97–0.98	0.90	0.88–0.93	0.99	0.98–1.01
Rural/Urban								
Rural	Ref		Ref		Ref		Ref	
Urban	1.03	1.00–1.06	1.01	1.00–1.01	0.96	0.94–0.99	1.00	0.97–1.00
Census tract poverty indicator								
≤20%	Ref		Ref		Ref		Ref	
>20%	0.96	0.93–0.98	1.00	0.99–1.00	0.98	0.96–1.01	1.01	0.99–1.02
Unknown poverty	1.01	0.95–1.06	0.99	0.98–1.00	1.01	0.96–1.07	1.00	0.97–1.03

*Adjusted for registry and site

**Defined as mastectomy or lumpectomy with radiotherapy