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Regional Disparities in the Use and Delivery of Adjuvant Radiation Therapy after Lumpectomy for Breast Cancer in the Medicare Population

Short title: Regional disparities in Radiation for Breast Cancer

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Declaration of interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abstract

Purpose:

We examined radiation therapy (RT) use among early-stage breast cancer patients and analyzed the contribution of patient, cancer, and regional factors on the likelihood of RT receipt across Health Service Areas (HSAs).

Methods:

We identified 13,176 patients aged 66-79 in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database diagnosed with lymph node negative breast cancer in 2007-2011 treated with breast-conserving surgery. Patients were stratified as "high-risk" or "low-risk" for recurrence based on National Comprehensive Cancer Network Guidelines. Receipt of radiation therapy was studied with 5 modelling approaches to determine whether RT use and regional variation in its use changed based on the risk-level of the cohort. Multivariable mixed-effects logistic regression was performed for each outcome. Chloropleth maps were used to describe patterns of RT use.

Results:

Among high-risk patients, 70.1% received RT, versus 72.6% of low-risk patients(p=0.002). Among patients receiving RT, 60.9% were classified as high-risk versus 63.0% of patients who did not receive RT (p=0.002). In multivariable analyses, patients in "all rural" areas had lower

odds of receiving RT among the entire cohort (OR=0.73, p<0.001) and had lower odds of being high-risk and receiving RT among the entire cohort (OR=0.69, p<0.001). Black patients (OR=0.73, p=0.001) and Asian patients (OR=0.74, p=0.004) had decreased likelihood of receiving RT among the entire cohort. The regional interclass correlation coefficient (ICC) for the model predicting receipt of RT among all patients was 0.05 and among low-risk patients was 0.06. The regional ICC dropped to 0.02 for the model predicting being both high-risk and receiving RT among all patients.

Conclusions:

We observed regional and racial/ethnic disparities in RT receipt among our cohort. Reassuringly, less regional variability was observed for RT receipt among those at high-risk. Future work is needed to understand the cause of these regional disparities to better serve patients who may benefit from treatment.

1.   Introduction

In 2020, the estimated number of new cases of invasive breast cancer in the US and estimated number of deaths are 279,100 and 42,690, respectively[1]. Most breast cancer deaths are due to recurrence of a previously treated early-stage cancer rather than a late-stage de novo metastatic cancer[2]. Adjuvant radiation therapy (RT) administered following breast-conserving surgery is known to substantially decrease the risk of loco-regional recurrence and improve survival rates for patients with invasive breast cancer[3]. However, for areas in which RT treatment is available, it is often delivered in suboptimal ways. For example, considerable disparities in time to starting RT after breast conserving surgery have been identified in certain

regions of the US[4]. Evidence shows that many breast cancer deaths may be attributable to disparities in cancer care rather than a lack of effective therapy[5], suggesting a need for identifying interventions to promote uniformity in more effective treatment methods . This is supported by an observed wide range of mortality rates among different counties. The fourfold difference in the minimum (11.2 deaths per 100,000 women) and maximum (51.6 deaths per 100,000 women) regional mortality highlights the need for intervention targeting healthcare delivery factors[6–8]. Regional variation can also be attributed to other factors including, but not limited to, age, race, ethnicity, social economic status, rurality, and insurance coverage which may be associated with breast cancer care and mortality[12]. As a result, regional differences in healthcare delivery are an important area of investigation for the US Medicare population, and geographical heterogeneity is often regarded as a marker for inefficiency of healthcare delivery[13].

In order to develop interventions to improve the quality of cancer care, we must first understand the extent and sources of these region-based disparities. With the main objective of formulating regional intervention strategies, we sought to understand geographic patterns of radiation treatment (RT) delivery to prioritize our effort for strategy execution. The focus of our current study was on examining RT use relative to breast cancer recurrence risk level across the United States among women with early-stage breast cancer treated with breast-conserving surgery. We analyzed the contribution of patient and cancer factors on the likelihood of receiving RT across Health Service Areas (HSAs) and well as the contribution of regional variation. HSAs are defined by the SEER-Medicare database as either a single county or cluster of counties that are self-contained with respect to hospital care. We performed multivariable

mixed-effects logistic regression on our data using 5 different approaches to evaluate the value of radiation and analyze whether RT receipt and regional variation in its use changed relative to risk for recurrence and the risk level of the cohort.

2.   Methods

This analysis used data derived from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. The population-based SEER database includes demographic and clinical characteristics for cancer cases and accounts for approximately 35% of the US population[14]. The Medicare database includes enrollment information and claims for approximately 97% of the US population aged 65 and older[15]. These files include information about inpatient, outpatient, durable medical equipment, home health, hospice, and physician services, and are used to examine health care patterns over time. Approximately 95% of the patients aged 65 and older that are included in the SEER database have been linked to Medicare data[15].

Our analysis focused on patients with lymph node negative breast cancer who had breast-conserving surgery within 12 months of diagnosis. Our cohort was obtained from the 2018 linkage of the SEER-Medicare dataset, which includes Medicare claims data up to December 31, 2016 for cancer cases diagnosed between 1991 and 2015. We included female patients diagnosed at age 66-79 between January 1, 2007 and December 31, 2011 with American Joint Committee on Cancer (AJCC) 6th edition stage lymph node negative I-III breast cancer as their first cancer. Patients with ductal carcinoma in situ (DCIS) or who had metastatic disease were not included in this analysis. Patients who had a second breast cancer within one year, were diagnosed at autopsy/death, or whose diagnosis was not pathologically confirmed

were excluded. Patients must have been eligible for Medicare due to age and had continuous enrollment in Medicare Parts A/B from 12 months prior to their month of diagnosis (for comorbidity score calculation) and for at least 60 months after diagnosis. Patients enrolled in a Health Maintenance Organization (HMO) plan during this period were excluded to ensure capture of complete claims for cancer treatment. Patients who had undergone mastectomy or who had not received breast-conserving surgery within 12 months of diagnosis were not included. Radiation therapy receipt was defined as treatment within 18 months of diagnosis.

Patients in our cohort were stratified into "high-risk" or "low-risk" categories based on NCCN 5.2021 Guidelines for Invasive Breast Cancer[16] . Radiation therapy receipt was defined as treatment within 18 months of diagnosis to ensure that patients who required multiple surgeries before RT were included in this analysis. Patients who were considered "low-risk" for recurrence had an option to omit breast irradiation in their treatment plan. These patients were defined by age 70, ER-positive tumors and who received adjuvant endocrine therapy as determined by claims. These criteria were also chosen to correspond with the entry criteria of the randomized CALGB 9343 study of radiation omission among women who intend to take endocrine therapy whose results were initially published in 2004 in manuscript form[17]. Patients whose cancer fell outside the low-risk criteria were considered "high-risk" and were recommended to undergo radiation therapy.

Choropleth maps to visually analyze regional radiation use for each of the five outcomes were created by diving the proportion of patients receiving RT into tertiles according to each individual model. For the choropleth map describing rurality, HSAs were classified as either "all

urban," "mostly urban," "mostly rural," or "all rural" based on where the majority of its contained patients were classified.

Multivariable mixed-effects logistic regression was performed using 5 approaches to study receipt of RT among different risk cohorts: Model 1) likelihood of receiving RT in the entire cohort, Model 2) likelihood of receiving RT and being high-risk among the entire cohort, Model 3) likelihood of receiving RT and being low-risk among the entire cohort, Model 4) likelihood of being high-risk among those patients who received RT, and Model 5) likelihood of receiving RT among those patients considered low-risk. Models 1, 2, and 3 were contained the entire cohort while Model 4 used the subset of patients who have received RT and Model 5 contained the subset of patients considered low risk for recurrence. The same regression was applied to all five models, but the patients in each of the cohorts used for modelling differed according to the outcome being measured. More details on the classification of these outcomes are shown in Table 1.

We controlled for covariates by treating them as fixed effects. Variables included in the multivariable regression as fixed effects were age, race/ethnicity (Non-Hispanic [NH] White, NH Black, Hispanic, NH Asian, NH Native American/Other/Unknown), rurality (all urban, mostly urban, mostly rural, all rural), ecological socioeconomic status (SES), education, and comorbidity score (0, 1, 2+). To calculate ecological SES, quintiles were derived using census tract median household income from US census data provided in the SEER-Medicare database; zip code median income was used for those patients without census tract information. To calculate ecological education level, quintiles were derived based on the percentage of households using the census and zip code files. Comorbidities scores were created using the

Deyo adaptation of the Charlson comorbidity index for the 12 month period prior to cancer diagnosis[18–20]. Odds ratios, 95% confidence intervals (CIs) and p-values were calculated for each variable in each of the five outcomes.

HSAs were added as random intercepts to each of the models. An HSA is defined by the National Center for Health Statistics as a geographic area containing one or more counties where most residents in the area obtain hospital care from the same hospitals[21]. An intraclass correlation coefficient (ICC)[22] was calculated by _____, which is the between-HSA variance on a log-odds scale estimated via the mixed-effect logistic regression model for each of the five outcomes. The ICC indicates how much of the total variation in the probability of receiving RT is accounted for by the HSAs on the logistic scale and ranges from 0 to 1. An ICC close to 1 indicates a great level of similarity between values in the same cluster, while an ICC close to 0 indicates that values in the same cluster differ and are not similar. In this study, the ICC values were used to compare the amount of regional variability effect on our stratified outcomes. All analyses were performed using R statistics package version 4.0.1.

4. Results

Our final cohort consisted of 13,176 patients diagnosed with lymph node negative breast cancer and breast-conserving surgery. The median (min, max) age at diagnosis in years was 71 (66, 78). Approximately 85.9% of patients were White, 5.1% were Black, 4.3% were Hispanic, and 4.1% were Asian. Approximately 61.7% lived in areas defined as "all urban" and 7.2% were defined as living in "all rural" areas. A greater proportion of minority patients (79.6% of Black patients, 77.2% of Hispanic patients, and 84.1% of Asian patients) lived in areas defined as "all urban" compared to the 58.9% of White patients. In addition, a larger proportion of

White patients lived in areas defined as "mostly urban," "mostly rural," and "all rural" compared to all other races. Among the groups, Black patients had greater frequency of being diagnosed with larger and poorly differentiated cancers. 51.0% of Black patients and 36.5% of Hispanic patients were in the lowest quintile of socioeconomic status. Descriptive statistics of our final cohort are further summarized in Table 2.

Table 3 displays recurrence risk level by RT receipt status. Of the patients classified as low-risk, 72.6% received RT versus the 70.1% of those meeting high-risk criteria (p=0.002). Table 4 shows receipt status by risk level for the entire cohort. Of the patients who received RT, a smaller proportion were classified as "high-risk" than those who did not receive RT (60.9% vs. 63.9%, p=0.002).

Figure 1 demonstrates that for certain regions, rurality and urbanity may have an impact the receipt of RT. In the choropleth map of Model 1, the likelihood of receiving RT regardless of risk level, most areas considered "all urban and "mostly urban" on the east and west coasts have high to medium radiation use. In the choropleth map of Model 2, among patients who are considered high risk for recurrence and have received RT, "all urban" and "mostly urban" HSAs reveal high to medium radiation use while those considered "all rural" and "mostly rural" reveal less RT use. In the choropleth map showing Model 3, among patients considered low risk for recurrence, there is higher radiation use in "all urban" or "mostly urban" HSAs in Washington and California. Meanwhile, radiation for those considered low risk is lower for HSAs on the East coast in this model. In the choropleth map of Model 5, among patients at low risk for recurrence, radiation usage is medium to high in areas considered "all urban" and "mostly urban."

Findings from the multivariable logistic regression analyses are summarized in Table 5, including ICCs to assess the contribution of regional variation towards the outcomes. Five modelling approaches were used to analyze whether the contribution of region to variation in RT use differs relative to level of risk for recurrence of the cohort. These analyses may identify patterns of disparity in the usage and delivery of RT. Models 1, 2, and 3 are multivariable analyses on the odds of receiving RT and either high or low risk status among all patients in the whole cohort. Models 4 and 5 address two different sub-populations of patients. Model 1 provides a benchmark for the odds of receiving RT regardless of risk status. Model 2 addresses whether patients at high-risk for local recurrence, for whom RT is highly recommended, are likely to receive RT. Model 4 addresses the odds of being high-risk among patients who have received RT, assessing whether appropriation of RT follows risk level or some other determinant. Model 3 addresses whether patients at low-risk for recurrence, for whom RT is discretionary, are likely to receive RT. Model 5 addresses the likelihood of receiving RT among patients considered low-risk. These models work together to address patterns of RT use relative to risk level.

Among the entire cohort, patients in "all rural" areas had decreased odds of receiving RT when compared to the "all urban" areas (OR=0.73, p<0.001) (Model 1). This was also true when predicting the odds of being high-risk and receiving RT among all patients (OR=0.69, p<0.001). We also observed differences in the odds of treatment among different race/ethnicity subgroups. Black patients (OR=0.73, p=0.001) and Asian patients (OR=0.74, p=0.004) had lower odds of receiving RT relative to White patients (Model 1). Asian patients (OR=0.72, p=0.001) and Hispanic patients (OR=0.76, P=0.003) also had lower odds of being high-risk and receiving

RT among the general cohort (Model 2). Patients with 2+ comorbidities had decreased odds of receiving RT (OR=0.81, p=0.001) (Model 1).

The regional ICC for HSA varied according to the outcome studied (Table 5). The overall ICCs were small as expected for a binary outcome. An ICC of 0.05 was observed for the likelihood of receiving RT among all patients regardless of risk level (Model 1). The observed ICC was 0.06 for the likelihood of receiving RT among low-risk patients (Model 5). However, the ICC dropped to 0.02 in the model predicting both receipt of RT and being high-risk (Model 2). The ICC was the lowest (0.01) for the model predicting being high-risk among patients who have all received RT (Model 4).

5. Discussion

We used the SEER-Medicare database to study the receipt of radiation therapy after breast-conserving surgery according to recurrence risk level and to assess the contribution of regional variation in its use. We found that the likelihood of receiving RT does not vary by recurrence risk level. Our study showed that Black and Asian race were both associated with lower odds of receiving RT after controlling for other covariates listed in Table 5. We also showed that patients living in "all rural" areas had lower odds to receive RT compared to patients living in "all urban" areas. Furthermore, we showed that there was regional variability in RT receipt.

Our finding that race/ethnicity and rurality were associated with decreased odds of receiving RT corroborates other examples of racial and ethnic disparities in cancer care delivery and outcomes demonstrated in existing literature[22–24]. An earlier study by Sail et al showed that

Black women had lower odds than White women of receiving adjuvant chemotherapy or radiation after breast-conserving surgery[24]. Our study using more recent data demonstrates that this disparity remains and is of similar magnitude noted by Sail.

Modelling of regional variation by including HSAs demonstrated that regional biases were more apparent when RT is discretionary (i.e. among the "low risk" patients). Our study showed that patients who received RT did not necessarily have features that increase the risk of cancer recurrence; in fact, high-risk patients represented a lower proportion of those who received RT versus those who did not. Additionally, we observed that a greater proportion of low-risk patients received RT compared to those who were high-risk. The choropleth maps suggest that urban areas have the greatest capacity for radiation and that rurality has an impact on receipt of RT regardless of risk status. Even for those patients in which RT is recommended, there are regional differences in the receipt of RT. The maps also demonstrate that patients considered "low risk" but receive RT tend to live in urban areas and that for many HSAs considered either "all urban" or "mostly urban" exhibit greater radiation use relative to those considered "low risk" corroborating our modelling results.

Evidence that the likelihood of receiving RT seems to be dictated by paradigms other than patient risk level suggests that other determinants of RT use may be more influential on the receipt of treatment. Likely examples could include referrals to RT and to a radiation oncologist, as well as the patient's access to RT facilities, which most likely differ based on region and urbanity.

Our study was conducted using the SEER-Medicare linked data which provided us with a large, population-based cohort, allowing us use HSAs to analyze regional variability of use of RT

among our cohort. However, our study is limited by the retrospective nature of claims data. Our cohort only includes patients who were 66-79, were enrolled in Medicare, and who lived in a SEER region. As such, it may not be generalizable to other populations. However, while absolute values may differ among younger patients, relative differences between regions would likely be similar. Treatment patterns and regional patterns observed may have changed over time, which would not be reflected in the data. Claims data does not include information on physician-patient communication or patient preferences, which could influence treatment decision making. Lastly, claims data does not provide the same granular clinical insight of a medical record chart review, but they are directly correlated with the costs of treatment which is salient in our current healthcare climate.

Disparities in breast cancer treatment by region, age, and race/ethnicity in breast cancer care are known to have significant effects on recurrence and survival rates. The greatest contributing factors to these differences in outcomes are not yet known. Understanding regional patterns of radiation therapy delivery will help identify areas which may benefit from intervention and provide the basis for actionable improvements in the US health care delivery system. Future work must be directed towards identifying the root causes of these observed regional disparities by performing analyses on variables of interest such as the density of radiation facilities and specialists per HSA.

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Figure 1 – Choropleth maps showing radiation usage and risk levels of each of the five outcomes in tertiles.
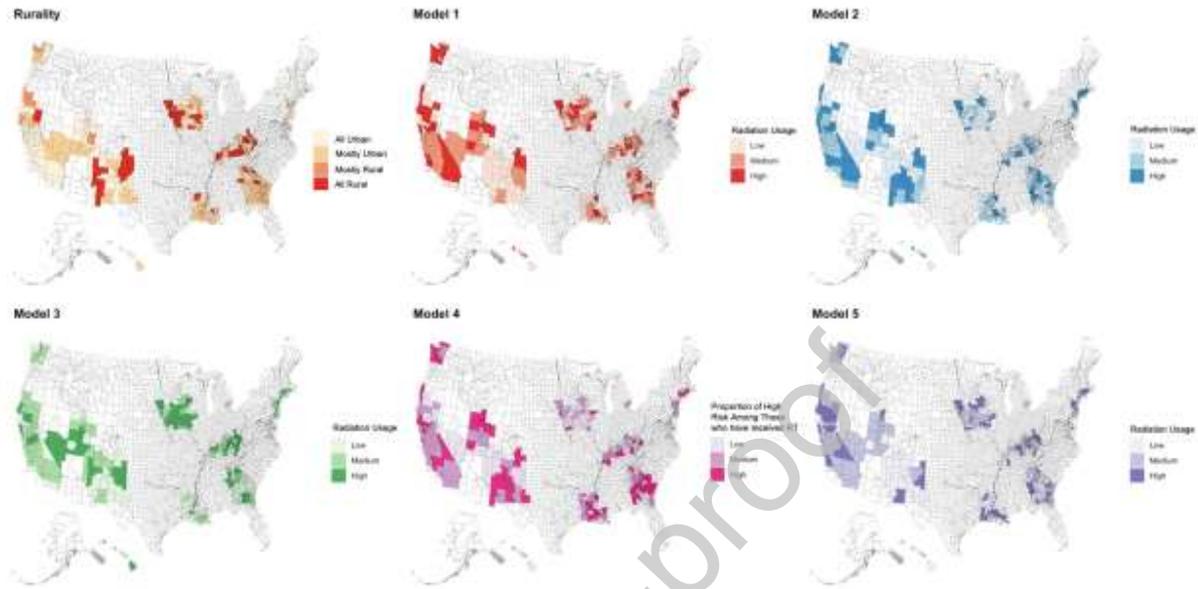
Table 1 - Descriptions of the five outcome variables

	RT Received	RT Not Received
High Risk	*A*	*B*
Low Risk	*C*	*D*

1	$\dfrac{\quad\quad}{\quad\quad}$	The likelihood of receiving RT in the entire population
2	$\dfrac{\quad\quad}{\quad\quad}$	The likelihood of receiving RT and being high risk in the entire population
3	$\dfrac{\quad\quad}{\quad\quad}$	The likelihood of receiving RT and being low risk in the entire population
4	$\dfrac{\quad}{\quad}$	The likelihood of being high risk in the sub-population of patients who have received RT
5	$\dfrac{\quad}{\quad}$	The likelihood of receiving RT in the sub-population of patients who are considered low risk

Table 2 - Descriptive statistics for patient and cancer factors*

	White (N=11322)	Black (N=672)	Hispanic (N=565)	Asian (N=536)	Other (N=81)	Overall (N=13176)
Attained diagnosis age in years (SEER)						
Mean (SD)	71.6 (3.66)	71.6 (3.57)	71.6 (3.75)	71.5 (3.65)	71.6 (3.93)	71.6 (3.66)
Median [Min, Max]	71.0 [66.0, 78.0]	72.0 [66.0, 78.0]	71.0 [66.0, 78.0]	71.0 [66.0, 78.0]	71.0 [66.0, 78.0]	71.0 [66.0, 78.0]
Rurality						
All Rural	894 (7.9%)	22 (3.3%)	20 (3.5%)	6 (1.1%)	11 (13.6%)	953 (7.2%)
Mostly Rural	958 (8.5%)	27 (4.0%)	22 (3.9%)	6 (1.1%)	12 (14.8%)	1025 (7.8%)
Mostly Urban	2807 (24.8%)	88 (13.1%)	87 (15.4%)	73 (13.6%)	12 (14.8%)	3067 (23.3%)
All Urban	6663 (58.9%)	535 (79.6%)	436 (77.2%)	451 (84.1%)	46 (56.8%)	8131 (61.7%)
Charlson Co-morbidity Index						
1 Comorbidity	2444 (21.6%)	182 (27.1%)	144 (25.5%)	157 (29.3%)	18 (22.2%)	2945 (22.4%)
2+ Comorbidities	1174 (10.4%)	148 (22.0%)	90 (15.9%)	67 (12.5%)	10 (12.3%)	1489 (11.3%)
No Comorbidities	7704 (68.0%)	342 (50.9%)	331 (58.6%)	312 (58.2%)	53 (65.4%)	8742 (66.3%)
Tumor Size						
<2 cm	9489 (83.8%)	527 (78.4%)	457 (80.9%)	457 (85.3%)	74 (91.4%)	11004 (83.5%)
2-5 cm	1797 (15.9%)	143 (21.3%)	107 (18.9%)	78 (14.6%)	7 (8.6%)	2132 (16.2%)
>5 cm	36 (0.3%)	2 (0.3%)	1 (0.2%)	1 (0.2%)	0 (0%)	40 (0.3%)
Tumor Grade						
Differentiated	3691 (32.6%)	146 (21.7%)	176 (31.2%)	167 (31.2%)	27 (33.3%)	4207 (31.9%)
Moderately Differentiated	5003 (44.2%)	300 (44.6%)	247 (43.7%)	240 (44.8%)	31 (38.3%)	5821 (44.2%)
Poorly Differentiated	2093 (18.5%)	188 (28.0%)	109 (19.3%)	107 (20.0%)	18 (22.2%)	2515 (19.1%)
Undifferentiated	39 (0.3%)	3 (0.4%)	4 (0.7%)	2 (0.4%)	2 (2.5%)	50 (0.4%)
Unknown	496 (4.4%)	35 (5.2%)	29 (5.1%)	20 (3.7%)	3 (3.7%)	583 (4.4%)
Education (Quintiles)						
Q1	2242 (19.8%)	125 (18.6%)	153 (27.1%)	125 (23.3%)	19 (23.5%)	2664 (20.2%)
Q2	2281 (20.1%)	110 (16.4%)	112 (19.8%)	120 (22.4%)	12 (14.8%)	2635 (20.0%)
Q3	2235 (19.7%)	111 (16.5%)	108 (19.1%)	106 (19.8%)	16 (19.8%)	2576 (19.6%)
Q4	2299 (20.3%)	134 (19.9%)	98 (17.3%)	94 (17.5%)	15 (18.5%)	2640 (20.0%)
Q5	2265 (20.0%)	192 (28.6%)	94 (16.6%)	91 (17.0%)	19 (23.5%)	2661 (20.2%)
Socioeconomic Status (Quintiles)						
Q1	1902 (16.8%)	343 (51.0%)	206 (36.5%)	108 (20.1%)	23 (28.4%)	2582 (19.6%)
Q2	2197 (19.4%)	140 (20.8%)	129 (22.8%)	125 (23.3%)	17 (21.0%)	2608 (19.8%)
Q3	2349 (20.7%)	73 (10.9%)	83 (14.7%)	109 (20.3%)	18 (22.2%)	2632 (20.0%)
Q4	2399 (21.2%)	65 (9.7%)	89 (15.8%)	106 (19.8%)	11 (13.6%)	2670 (20.3%)
Q5	2475 (21.9%)	51 (7.6%)	58 (10.3%)	88 (16.4%)	12 (14.8%)	2684 (20.4%)

Table 3 – Chi Square Test, risk level by RT status

	Received RT	Did not receive RT
Risk Level		
High Risk (N=8146)	5704 (70.1%)	2436 (29.9%)
Low Risk (N=5036)	3658 (72.6%)	1378 (27.4%)
Overall (N=13176)	9362 (71.1%)	3814 (28.9%)

P =.002

Table 4 – Chi Square Test , RT status by risk level

	High Risk	Low Risk
RT Status		
Received (N=9362)	5704 (60.9%)	3658 (39.1%)
Did not Receive (N=3814)	2436 (63.9%)	1378 (36.1%)
Overall (N=13176)	8140 (61.8%)	5036 (38.2%)

P =.002

Table 5 - Odd Ratios (ORs), 95% CIs, and p values from multivariate analysis are shown for variables associated with five outcomes of RT use based on risk level.

Predictors	Model 1 Receiving RT / All Odds Ratios	CI	p	Model 2 High Risk and Receiving RT / All Odds Ratios	CI	p	Model 3 Low Risk and Receiving RT / All Odds Ratios	CI	p	Model 4 High Risk / All having received RT Odds Ratios	CI	p	Model 5 Receiving RT / Low Risk Patients Odds Ratios	CI	p
Attained diagnosis age in years (SEER)	0.97	0.96 . 0.98	<0.001	1.01	1.00 . 1.02	0.269	0.96	0.95 . 0.97	<0.001	1.03	1.02 . 1.04	<0.001	0.96	0.94 . 0.98	<0.001
Years of Diagnosis (Year)	0.97	0.94 . 0.99	0.016	0.9	0.88 . 0.93	<0.001	1.09	1.06 . 1.12	<0.001	0.88	0.86 . 0.91	<0.001	0.99	0.95 . 1.04	0.653
Race/Ethnicity															
Black vs. White	_0.73_	0.62 . 0.88	**0.001**	0.95	0.80 . 1.12	0.536	0.74	0.60 . 0.90	**0.002**	1.2	0.97 . 1.49	0.099	0.88	0.64 . 1.22	0.451
Hispanic vs. White	0.91	0.75 . 1.11	0.346	_0.76_	0.63 . 0.91	**0.003**	1.23	1.02 . 1.49	**0.032**	0.75	0.60 . 0.92	**0.007**	1.1	0.81 . 1.50	0.537
Asian vs. White	_0.74_	0.61 . 0.91	**0.004**	_0.72_	0.59 . 0.87	**0.001**	1.08	0.88 . 1.33	0.446	0.77	0.61 . 0.97	**0.028**	0.81	0.59 . 1.12	0.203
Other vs. White	0.67	0.42 . 1.07	0.091	0.68	0.42 . 1.08	0.105	1.02	0.62 . 1.68	0.924	0.82	0.46 . 1.43	0.479	0.81	0.37 . 1.74	0.584
SES															
Q2 vs Q1	0.96	0.84 . 1.08	0.477	1.13	1.01 . 1.27	**0.039**	0.83	0.73 . 0.94	**0.003**	1.24	1.08 . 1.42	**0.002**	0.97	0.79 . 1.19	0.758
Q3 vs Q1	0.9	0.79 . 1.02	0.112	1.06	0.94 . 1.19	0.337	0.84	0.74 . 0.95	**0.006**	1.19	1.03 . 1.36	**0.017**	1.05	0.85 . 1.29	0.658
Q4 vs Q1	0.88	0.77 . 1.00	0.055	1.03	0.91 . 1.15	0.664	0.85	0.75 . 0.97	**0.014**	1.14	0.99 . 1.31	0.069	1.03	0.83 . 1.26	0.802
Q5 vs Q1	0.94	0.82 . 1.08	0.39	1.08	0.96 . 1.22	0.215	0.85	0.75 . 0.97	**0.016**	1.18	1.02 . 1.36	**0.022**	0.98	0.79 . 1.21	0.866
Education															
Q2 vs. Q1	0.96	0.85 . 1.09	0.548	1.02	0.91 . 1.14	0.776	0.95	0.84 . 1.07	0.375	1.06	0.93 . 1.22	0.381	0.96	0.78 . 1.16	0.648
Q3 vs. Q1	0.99	0.87 . 1.13	0.925	1.03	0.91 . 1.15	0.657	0.96	0.85 . 1.09	0.52	1.06	0.92 . 1.22	0.413	1.02	0.83 . 1.25	0.878
Q4 vs. Q1	0.97	0.86 . 1.11	0.689	1.12	1.00 . 1.26	0.052	0.85	0.75 . 0.96	**0.011**	1.22	1.06 . 1.40	**0.006**	1.04	0.84 . 1.29	0.703
Q5 vs. Q1	0.97	0.85 . 1.10	0.627	1.19	1.05 . 1.34	**0.005**	0.78	0.69 . 0.90	<0.001	1.33	1.15 . 1.54	<0.001	1.02	0.82 . 1.27	0.841
Rurality															
Mostly Urban vs. All Urban	0.85	0.77 . 0.94	**0.002**	0.95	0.86 . 1.04	0.232	0.91	0.82 . 1.01	0.068	1.03	0.92 . 1.15	0.594	0.76	0.64 . 0.90	**0.001**
Mostly Rural vs. All Urban	0.96	0.82 . 1.13	0.647	0.92	0.80 . 1.06	0.26	1.05	0.90 . 1.23	0.512	0.91	0.77 . 1.08	0.285	0.92	0.70 . 1.19	0.506
All Rural vs. All Urban	_0.73_	0.62 . 0.86	<0.001	_0.69_	0.59 . 0.80	<0.001	1.09	0.93 . 1.29	0.284	0.75	0.63 . 0.90	**0.002**	0.78	0.61 . 1.01	0.06
Charlson Co-morbidity Index															
1 Comorbidity vs. None	0.92	0.83 . 1.01	0.067	0.95	0.87 . 1.03	0.219	0.97	0.88 . 1.07	0.574	0.99	0.89 . 1.10	0.914	0.9	0.77 . 1.05	0.184
2+ Comorbidities vs. None	_0.81_	0.72 . 0.91	**0.001**	0.84	0.75 . 0.94	**0.003**	0.99	0.87 . 1.12	0.82	0.92	0.80 . 1.06	0.24	0.82	0.67 . 1.00	**0.05**
Tumor Size															
2-5cm vs. <2	0.87	0.78 . 0.97	**0.01**	0.85	0.77 . 0.93	**0.001**	1.06	0.95 . 1.18	0.284	0.87	0.77 . 0.98	**0.024**	1.02	0.85 . 1.22	0.843
>5cm vs. <2	0.84	0.43 . 1.66	0.618	1.32	0.70 . 2.50	0.389	0.51	0.21 . 1.23	0.131	2.03	0.80 . 5.15	0.136	0.41	0.13 . 1.32	0.136

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Tumor Grade

	OR	CI	p	OR	CI	p	OR	CI	p	OR	CI	p	OR	CI	p
Moderately Differentiated vs. Differentiated	1.15	1.05 . 1.25	**0.003**	1.04	0.96 . 1.13	0.31	1.09	1.00 . 1.19	0.056	0.96	0.87 . 1.06	0.423	1.14	0.99 . 1.31	0.069
Poorly Differentiated vs. Differentiated	1.39	1.24 . 1.56	**<0.001**	1.93	1.74 . 2.14	**<0.001**	0.59	0.53 . 0.67	**<0.001**	2.1	1.84 . 2.39	**<0.001**	1.33	1.07 . 1.65	**0.009**
Undifferentiated vs. Differentiated	0.97	0.53 . 1.79	0.93	1.53	0.86 . 2.71	0.145	0.5	0.23 . 1.07	0.075	2.27	1.01 . 5.11	**0.048**	1.93	0.40 . 9.35	0.415
Unknown vs. Differentiated	0.82	0.68 . 0.99	**0.043**	1.21	1.01 . 1.44	**0.04**	0.63	0.51 . 0.78	**<0.001**	1.58	1.25 . 2.00	**<0.001**	0.73	0.53 . 1.02	0.066
Random Effects															
ICC	0.05			0.02			0.02			0.01			0.06		
Total HSA (N)	187			187			187			184			183		
Cohort (N)	13176			13176			13176			9362			5036		

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