Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____Hiba Ahmed_____ _____

Date

Guideline concordant care improves overall survival for locally advanced non-small cell lung carcinoma patients: a National Cancer Data Base analysis.

By

Hiba Zara Ahmed
MD, MPH

Global Epidemiology

_____

Dr. Michael Goodman
Faculty Thesis Advisor

_____

Dr. Kristin Higgins
Thesis Field Advisor

Guideline concordant care improves overall survival for locally advanced non-small cell lung carcinoma patients: a National Cancer Data Base analysis.

By

Hiba Zara Ahmed

BS
University of Notre Dame
2012

MD
Emory University
2017

Faculty Thesis Advisor: Michael Goodman MD, MPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Epidemiology
2017

Abstract

Guideline concordant care improves overall survival for locally advanced non-small cell lung carcinoma patients: a National Cancer Data Base analysis.

By Hiba Zara Ahmed

Introduction: Current evidence-based guideline-concordant care (GCC) for locally advanced non-small cell lung cancer (NSCLC) in patients with good performance status includes platinum-based chemotherapy during thoracic radiotherapy (TRT). This study evaluates factors associated with lack of GCC.

Patients and methods: Unresected stage III NSCLC patients, diagnosed from 2005 – 2013 with a Charlson-Deyo Score 0, were identified from the National Cancer Data Base. Primary outcomes were receipt of GCC, defined as administration of chemotherapy with TRT commencing within 2 weeks of each other and minimum TRT dose of 60 Gy, and overall survival (OS). Multivariable logistic regression modeling identified variables associated with non-GCC. Cox proportional hazard modeling examined OS.

Results: About 23% of patients (n=45,825) received GCC. Uninsured patients were more likely to receive non-GCC (odds ratio [OR]=1.54, $p<0.001$) compared to privately-insured patients. Other groups with greater odds of receiving non-GCC included: patients treated in the western, southern, or northeastern U.S. (ORs=1.39, 1.37, 1.19, respectively, all p values <0.001) compared to patients treated in the Midwest; those with adenocarcinoma (OR=1.48, $p<0.001$) compared to those with squamous cell carcinoma ; and women (OR=1.08, $p=0.002$) compared to men. Every one-year increase in age, increased a patient's odds of not receiving GCC by 4% ($p<0.001$). Those receiving non-GCC had higher death rates compared to those receiving GCC (hazard ratio [HR]=1.42, $p<0.001$). Other groups with lower survival for non-GCC versus GCC included: the uninsured (HR=1.53, $p<0.001$), patients treated in the western, southern, or northeastern US (HRs= 1.56, 1.41, 1.34, respectively, all $p<0.001$), adenocarcinomas (HR=1.39, $p<0.001$), and women (HR=1.44, $p<0.001$).

Conclusion: Socioeconomic factors, including lack of insurance and geography, are associated with lack of GCC. Patient/disease specific factors, including increasing age, adenocarcinoma histology, and sex, are also associated with non-GCC.

Guideline concordant care improves overall survival for locally advanced non-small cell lung carcinoma patients: a National Cancer Data Base analysis.

By

Hiba Zara Ahmed

BS
University of Notre Dame
2012

MD
Emory University
2017

Faculty Thesis Advisor: Michael Goodman MD, MPH

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Epidemiology
2017

Table of Contents

BACKGROUND

Lung cancer is the leading cause of cancer-related mortality in the US with an estimated 158,040 deaths in 2015[1]. Lung cancer is the second most common newly diagnosed cancer per year, with a projected 221,200 individuals to be newly diagnosed in 2016[1]. Of these newly diagnosed lung cancers, approximately 85% are classified as non-small cell lung carcinoma (NSCLC). Despite the high incidence of this disease, 5-year survival rates range from 49% for Stage IA disease to 1% for stage IV disease[1]. The outcomes for locally advanced cases are particularly dismal, with a 5-year survival rate for stage IIIA NSCLC at approximately 14% and at 5% for stage IIIB[2].

According to the American College of Radiology (ACR) Appropriateness Criteria[3], the American Society for Radiation Oncology (ASTRO)[4], and the American Society of Clinical Oncology (ASCO)[5], the current evidence-based clinical practice guidelines recommend concurrent administration of platinum-based chemotherapy during thoracic radiotherapy (TRT) for locally advanced NSCLC [6]. All three organizations independently assembled multidisciplinary expert panels that performed extensive reviews of the current medical literature in order to develop evidence-based recommendations for the treatment of locally advanced NSCLC.

Several sentinel studies contributed to establishing these current guidelines. Perez et al. established the minimally sufficient radiation dose for stage III NSCLC as 60 Gy[7]. The Radiation Therapy Oncology Group (RTOG) 94-10, a randomized phase III trial also comparing concurrent versus sequential chemoradiation[8], showed that once-daily concurrent chemoradiation was significantly better than sequential chemoradiation and that twice-daily concurrent chemoradiotherapy was not statistically different from once-daily chemoradiotherapy. Additional

studies were also published between the years of 1999-2005 showing superiority of concurrent chemotherapy to sequential chemotherapy[9-12]. Additionally, Aupérin et al. performed a meta-analysis of six randomized control trials specifically comparing the outcomes of concomitant versus sequential chemoradiotherapy and demonstrated that concomitant chemoradiation resulted in better overall survival[13].

Despite standardized treatment regimens, there are barriers to delivery of guideline concordant care (GCC). In a systematic review and meta-analysis of socioeconomic status (SES) and receipt of lung cancer treatment, Forrest et al. demonstrated statistically significant associations between lower SES and the likelihood of receiving surgical interventions and chemotherapeutic regimens[14].Furthermore, a study looking specifically at race and sex as effect modifiers of receiving appropriate treatment for NSCLC showed that African American patients with Stage III disease were 34% less likely to receive standard treatment[15]. In a previous study of NCDB data, Khullar et al. analyzed the association of long-term survival of NSCLC patients undergoing pulmonary resection with various socioeconomic factors[16], and found that Caucasians received lung resections at significantly greater rates than African Americans[16].

Despite established evidence-based guidelines, ones that the American Society of Clinical Oncology has officially endorsed, patients do not receive guideline concordant care. This is especially true for NSCLC treatment. In order to work toward closing this chasm, the academic community needs to understand the reasons for these disparities, which remain largely unexplored. This research attempts to examine this disparity and elucidate possible contributors to not receiving guideline-concordant care, specifically for unresected, stage III NSCLC patients of good performance status. Unlike previous analyses though, which primarily focus on receipt of surgery or chemotherapy, this study assesses receipt of radiotherapy in addition to

chemotherapy. The NCDB NSCLC data have not, to our knowledge, been previously analyzed for the effect of socioeconomic risk factors on stage III treatment, thus making this study one of the largest with a cohort of 45,825 patients

METHODS

This study utilizes the National Cancer Data Base (NCDB), a clinical oncology database containing both clinical and demographic information collected from patients treated at over 1,500 Commission on Cancer (CoC)-accredited institutions, which is jointly supported by the American College of Surgeons and the American Cancer Society. Unresected stage IIIA/IIIB NSCLC patients, diagnosed from 2005 – 2013 and with a Charlson-Deyo Score of 0, were identified. Exclusion criteria included patients with any distant metastases, who received any surgical intervention, who received any form of radiotherapy other than photon therapy, who received TRT for palliative purposes or anywhere other than the lungs/chest, and patients who received treatment for a non-primary tumor.

Primary outcomes of interest were receipt of GCC, defined as administration of chemotherapy with TRT commencing within 2 weeks of each other and minimum TRT dose of 60 Gy, and overall survival (OS). Patient- and facility-level variables examined included facility type, facility location, sex, race/ethnicity, insurance status, income, education, and distance to treatment facility labeled as great circle distance in the NCDB. Facility type was characterized according to CoC accreditation criteria, which are based on an institution's caseload and services offered. Race was defined as Caucasian, African American (AA), or other based on patient self-identification. Hispanic ethnicity was also categorized based on self-identification. Insurance type was grouped as no insurance, government insurance (including Medicare, Medicaid, and other government insurance programs), or private insurance. Patient income and education levels were estimates based on US Census Bureau average incomes/high school diplomacy rates for patients' zip codes. NCDB presented income data as median quartiles and education was represented by median quartiles of the percentage of patients without high school degrees. In

addition to these socioeconomic variables, the researchers controlled for year of diagnosis, tumor histology, tumor grade, and age.

Statistical Analyses

All statistical analyses were performed using SAS version 9.4 (Cary, NC). The threshold for statistical significance for all tests was set at the two sided alpha error of 0.05. Multivariable logistic regression modeling identified variables associated with delivery of GCC. The results of logistic regression models were expressed as adjusted odds ratios (OR) and the corresponding 95% confidence intervals. For survival analyses, the sample size was further limited to those diagnosed between 2005 and 2012, since survival data for patients diagnosed after 2012 were unavailable. To minimize lead-time bias, survival analyses only considered patients surviving more than 3 months from time of diagnosis. Once factors associated with receiving non-GCC were identified, two-way interaction testing was performed to detect any conditional interdependence among variables. Hazard ratios (HR) and the 95% CI estimates were calculated for individuals receiving non-GCC within each high-risk demographic group using Cox proportional hazard modeling.

Lastly, propensity score matched (PSM) analyses were performed. A logistic regression model predicting GCC status was used to calculate propensity scores factoring in facility location, facility geographical region, sex, race/ethnicity, insurance type, geographic area, income, education, year of diagnosis, histology, grade, great circle distance, and age at diagnosis. Patients from the GCC and non-GCC groups were matched based on the propensity scores using a greedy matching algorithm. The effectiveness of the PSM was evaluated by calculating the standardized differences of the covariates on the matched sample. The effects of non-GCC on OS were recalculated using the matched sample.

RESULTS

Patient Characteristics

A total of 45,825 unresected stage IIIA and IIIB NSCLC patients with Charlson-Deyo score of 0 diagnosed between 2005 and 2013 met inclusion criteria (Figure 1). Patient characteristics are represented in Table 1. Overall, 23% of patients were treated with GCC. Approximately 28% of patients received neither chemotherapy nor TRT; 23% received chemotherapy but no TRT; 13% received chemotherapy and TRT to < 60 Gy; 5% received sequential chemoradiation to ≥ 60 Gy; 4% received no chemotherapy but received TRT to < 60 Gy; and 4% received no chemotherapy but TRT to ≥ 60 Gy.

Factors Associated with Patients Receiving Guideline-Concordant Care

Crude analysis showed statistically significant differences between patients receiving GCC versus non-GCC for all included socioeconomic variables (Table 1). Due to missing data for at least one of the variables of interest, only 39,232 observations out of the 45,825 eligible were included in further analyses. Multivariable logistic regression (MLR) modeling showed that several demographic groups were at higher risk of receiving non-GCC, even after controlling for all other socioeconomic and clinical factors included in the study (Table 2). For example, women were more likely to receive non-GCC with an adjusted OR of 1.08 (95% CI 1.03 – 1.14; p = 0.002) when compared to men. Differences were also seen in terms of race/ethnicity when compared to Caucasians as the reference group; the odds of receiving non-GCC for AA were 1.13 (95% CI 1.05 – 1.21, p = 0.002) and 1.24 (95% CI 1.07 – 1.43, p = 0.004) for the "other" category. Hispanics were also at increased risk of receiving non-GCC (OR = 1.30, 95% CI 1.11 – 1.51, p = 0.001) compared to non-Hispanics. Insurance type also influenced receipt of GCC; in comparison to privately insured patients, the uninsured had an odds ratio of 1.54 for not getting

GCC (95% CI 1.37-1.75, p < 0.001). Patients treated in the western, southern, or northeastern U.S. were more likely to receive non-GCC (OR= 1.39, 95% CI 1.28 – 1.50; OR = 1.37, 95% CI 1.29 – 1.46; OR = 1.19, 95% CI 1.10 – 1.28; each p value <0.001) compared to patients treated in the Midwest. Adenocarcinoma and large-cell/other histological types were more likely to receive non-GCC (OR = 1.48, 95% CI 1.40 – 1.57; OR = 1.30, 95% CI 1.22 – 1.39; both p<0.001) compared to squamous cell carcinoma histology. Lastly, for every one-year increase in age, patients had a 4% increased odds of not receiving GCC (OR = 1.04, 95% CI 1.03 – 1.04, p < 0.001). Interaction testing revealed interaction between geographical region and Hispanic ethnicity and insurance status and between race and gender (Table 3).

Survival Analyses

On Cox proportional hazard modeling, the overall cohort consisting of those who did not receive GCC had higher death rates compared to those who received GCC (HR = 1.42, 95% CI 1.38 – 1.47, p < 0.001) (Table 4). In a head to head comparison, women receiving non-GCC had death rates 1.44 times that of women receiving GCC (95% CI 1.38 – 1.51, p < 0.001). Other groups with lower OS for non-GCC versus GCC included: AAs (HR = 1.57, 95% CI 1.45 – 1.70, p < 0.001), the uninsured (HR=1.53, 95% CI 1.33 – 1.77, p<0.001), treatment in the western, southern, or northeastern US [HRs= 1.56 (1.43 – 1.69), 1.41 (1.35 – 1.48), 1.34 (1.26 – 1.44), respectively, p<0.001], adenocarcinomas and large cell/other histologies [HRs=1.39 (1.32 – 1.46), 1.47 (1.39 – 1.54), respectively, p<0.001). PSM data showed comparable hazard ratios for most groups (Table 5). Before PSM, 10,476 patients received GCC and 35,349 patients received non-GCC across the entire study population. Afterwards, 7,626 patients were in each cohort. These results are illustrated in the form of Kaplan Meier curves with log-rank testing in Figure 2.

DISCUSSION

Despite gains in knowledge regarding optimal treatment regimens, utilization of GCC was only 23% in this study using a large database that contains approximately 70% of cancer cases in the United States. This study shows a that receipt of GCC was associated with certain socioeconomic risk factors, including insurance status and facility geographical location, as well as other patient and disease related characteristics, such as sex, race/ethnicity, age, and tumor histology. It also shows better overall survival for those receiving GCC.

The relationship between socioeconomic risk factors and receipt of GCC was observed after controlling for a number of confounders. The cause of these disparities in treatment is likely multifaceted including possible environmental, patient-associated, and healthcare system-associated variables. But even if disadvantaged patients have equal access to care, it may not translate into optimal treatment provided. Patient-associated factors also influence whether or not a patient receives optimal treatment. There may be other factors influencing treatment options, such as underlying deficits in health literacy[19-21]. Another factor at play, perhaps related to deficits in health literacy, may be suboptimal patient-physician interactions. Even patients' perceptions about treatment can lead to differential treatment refusal rates across socioeconomic factors, which would then influence which groups of patients end up receiving the GCC[22-24]. There are differences in attitudes, beliefs, and knowledge about lung cancer risk, treatment, and mortality across the various socioeconomic strata and racial/ethnic groups[22-24]. For example, one study found an increased prevalence of fatalism and denial in African American patients versus Caucasian patients, adding an additional barrier to receiving the appropriate care[25].

Some studies have demonstrated that when socioeconomic risk factors are minimized and access to care is equitable, patients receive the appropriate care at the right time with very

few racial differences[26-28]. Most of these studies examined Veterans Affairs facilities' patients. Most importantly, these studies eliminate any disparities across insurance status, which was the strongest predictive variable of receipt of non-GCC in this study. Controlling for this single factor eliminated most differences observed across racial/socioeconomic lines[26-28].

One of the more unexpected findings was evidence of sex disparities. Women were at a risk 1.08 times that of men for receiving non-GCC. This is a relatively novel finding as typically many studies find no gender difference in the receipt of therapy[29]. For example, Bista et al. found no disparities in the receipt of radiotherapy by sex among patients with stage I follicular lymphoma[29]. The few studies that do find sex disparities in receipt of treatment have varying explanations for this phenomenon. In one particular study, women were less likely to receive systematic chemotherapy for their advanced bladder cancer when compared to men, which was attributed to a variety of factors, including tumor biology, i.e. histology and staging, and health-care related factors, i.e. differential time to diagnosis and surgical mortality[30]. There is also evidence of decreased chemotherapy use for women with pancreatic cancer, Hodgkin lymphoma, renal cell carcinoma, and colon cancer[31-34].

Another significant finding was the strong influence of geographic region of treatment facility on receipt of GCC. There have been several studies examining geographic disparities for vaccine coverage, incidence of childhood diabetes/obesity, HIV treatment, and surgery for pituitary tumors[35-40], yet very few provide any reasoning as to what drives these disparities. The general pattern of disparity in these studies is similar to what is seen in this study: the west and especially the south have the largest gaps in healthcare coverage. Heumann et al. suggested that these disparities are due to a lack of awareness and understanding in these regions[35]. Lee et al., in an analysis of childhood diabetes and obesity rates, suggested that the disparate incidence of

these diseases could in part be due to geographic disparities in physician and, more specifically, endocrinologist supply[36]. Lastly, Svider et al. emphasized that areas like the south/west are slower to adapt changes in technique/recommendations for treatment[40]. Although similar studies have not been performed for stage III NSCLC treatment, comparable factors could be influencing the disparate delivery of GCC observed in this study.

One potential explanation for the low proportion of patients receiving GCC (23%) may be related to a lag time in utilization of concurrent chemoradiation relative to publication of sentinel studies showing a clear benefit.

Our data show that the use of GCC increased significantly since 2005 and appears to have reached the present levels around 2010. These findings indicate that concurrent chemoradiotherapy was relatively slow to be adopted within the U.S. population, despite several large randomized trials showing a survival benefit to this regimen relative to sequential chemoradiotherapy[8-13]. Reasons for this delay in adopting concurrent therapy are unclear, but may be a result of concerns about toxicities, particularly given that supportive care platforms for management of combined modality treatment toxicities were likely less developed in the early years of this study period. Similar uptake of evidence-based care over time has been reported in other cancers[41-48].

Perhaps the most important finding of this study is the significantly worse overall survival for those who do not receive GCC versus those receiving GCC. The association was evident for every identified high-risk group.. This key finding underscores previous work with similar findings related to lung cancer and other types of cancers, derived from a variety of sources, including population-based cancer surveillance data, NCDB, and national patterns of care studies[41-48].

Unlike previous analyses though, which primarily focus on receipt of surgery or chemotherapy, this study assesses receipt of radiotherapy in addition to chemotherapy[14,15,17,49]. The NCDB NSCLC data have not, to our knowledge, been previously analyzed for the effect of socioeconomic risk factors on stage III treatment, thus making this study one of the largest with a cohort of 45,825 patients.

Limitations of this study include the inherent retrospective nature of NCDB data. The information on patient income/education status is limited to area-based census data, which limits the ability to apply on an individual patient level. Race can sometimes represent not measurable or poorly measured socioeconomic risk factors, including income/education status; thus, it is possible that any racial differences in outcomes observed in this study may, in fact, be due to underlying undetectable financial/educational differences. NCDB also does not provide patient performance status, which, if used in lieu of Charlson-Deyo score, would have added accuracy to our results. Better patient-level data on income, education, and performance status would be needed to address these possible sourcees of bias. This study was also intentionally limited to stage III NSCLC patients eligible for concurrent chemoradiation. Further studies can be done to identify who is at high-risk of receiving guideline discordant care for other treatment options/stages of NSCLC. This study can also not comment on treatment toxicities nor determine the exact cause of death in our patient population. Furthermore, this study could not examine exactly where in the process, from diagnosis to treatment initiation, the opportunity is being lost to improve the rates of guideline concordance related to treatment. Further studies are needed to elucidate specific areas where interventions to improve guideline-concordant care might be most effectively implemented.

Even though GCC was associated with significant differences in overall survival, only 23% of patients received GCC. Socioeconomic factors, including lack of insurance and geography, are associated with non-GCC. Patient specific factors, including sex, race/ethnicity, and increasing age are also associated with non-GCC, as are disease specific factors, such as adenocarcinoma histology. Future interventions might target these groups as an opportunity to improve provision of GCC, as it is so crucial to improving survival.

References

1. *Cancer Facts & Figures.* Atlanta, Ga: American Cancer Society;2015.
2. *Cancer Treatment & Suvivor Facts & Figures 2014-2015.* Atlants, Ga: American Cancer Society;2015.
3. Chang JY, Kestin LL, Barriger RB, et al. ACR Appropriateness Criteria(R) nonsurgical treatment for locally advanced non-small-cell lung cancer: good performance status/definitive intent. *Oncology (Williston Park, N.Y.).* 2014;28(8):706-710, 712, 714 passim.
4. Rodrigues G, Choy H, Bradley J, et al. Definitive radiation therapy in locally advanced non-small cell lung cancer: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based clinical practice guideline. *Practical radiation oncology.* 2015;5(3):141-148.
5. Bezjak A, Temin S, Franklin G, et al. Definitive and Adjuvant Radiotherapy in Locally Advanced Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the American Society for Radiation Oncology Evidence-Based Clinical Practice Guideline. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2015;33(18):2100-2105.
6. O'Rourke N, Roque IFM, Farre Bernado N, Macbeth F. Concurrent chemoradiotherapy in non-small cell lung cancer. *The Cochrane database of systematic reviews.* 2010(6):Cd002140.
7. Perez CA, Pajak TF, Rubin P, et al. Long-term observations of the patterns of failure in patients with unresectable non-oat cell carcinoma of the lung treated with definitive

radiotherapy. Report by the Radiation Therapy Oncology Group. *Cancer.* 1987;59(11):1874-1881.

8. Curran WJ, Jr., Paulus R, Langer CJ, et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. *Journal of the National Cancer Institute.* 2011;103(19):1452-1460.

9. Furuse K, Fukuoka M, Kawahara M, et al. Phase III study of concurrent versus sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-small-cell lung cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 1999;17(9):2692-2699.

10. Fournel P, Robinet G, Thomas P, et al. Randomized phase III trial of sequential chemoradiotherapy compared with concurrent chemoradiotherapy in locally advanced non-small-cell lung cancer: Groupe Lyon-Saint-Etienne d'Oncologie Thoracique-Groupe Francais de Pneumo-Cancerologie NPC 95-01 Study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2005;23(25):5910-5917.

11. Belani CP, Wang W, Johnson DH, et al. Phase III study of the Eastern Cooperative Oncology Group (ECOG 2597): induction chemotherapy followed by either standard thoracic radiotherapy or hyperfractionated accelerated radiotherapy for patients with unresectable stage IIIA and B non-small-cell lung cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2005;23(16):3760-3767.

12. Wolski MJ, Bhatnagar A, Flickinger JC, Belani CP, Ramalingam S, Greenberger JS. Multivariate analysis of survival, local control, and time to distant metastases in patients with unresectable non-small-cell lung carcinoma treated with 3-dimensional conformal

radiation therapy with or without concurrent chemotherapy. *Clinical lung cancer.* 2005;7(2):100-106.

13. Auperin A, Le Pechoux C, Rolland E, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2010;28(13):2181-2190.

14. Forrest LF, Adams J, Wareham H, Rubin G, White M. Socioeconomic inequalities in lung cancer treatment: systematic review and meta-analysis. *PLoS medicine.* 2013;10(2):e1001376.

15. Shugarman LR, Mack K, Sorbero ME, et al. Race and sex differences in the receipt of timely and appropriate lung cancer treatment. *Medical care.* 2009;47(7):774-781.

16. Khullar OV, Gillespie T, Nickleach DC, et al. Socioeconomic risk factors for long-term mortality after pulmonary resection for lung cancer: an analysis of more than 90,000 patients from the National Cancer Data Base. *Journal of the American College of Surgeons.* 2015;220(2):156-168.e154.

17. Coughlin SS, Matthews-Juarez P, Juarez PD, Melton CE, King M. Opportunities to address lung cancer disparities among African Americans. *Cancer medicine.* 2014;3(6):1467-1476.

18. Gould MK, Schultz EM, Wagner TH, et al. Disparities in lung cancer staging with positron emission tomography in the Cancer Care Outcomes Research and Surveillance (CanCORS) study. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer.* 2011;6(5):875-883.

19. Kamimura A, Chernenko A, Nourian MM, Aguilera G, Assasnik N, Ashby J. The Role of Health Literacy in Reducing Negative Perceptions of Breast Health and Treatment Among Uninsured Primary Care Patients. *Journal of community health.* 2016;41(4):858-863.

20. Poureslami I, Nimmon L, Rootman I, Fitzgerald MJ. Health literacy and chronic disease management: drawing from expert knowledge to set an agenda. *Health promotion international.* 2016.

21. Pakhale S, Baron J, Armstrong M, et al. Lost in translation? How adults living with Cystic Fibrosis understand treatment recommendations from their healthcare providers, and the impact on adherence to therapy. *Patient education and counseling.* 2016;99(8):1319-1324.

22. Landrum MB, Keating NL, Lamont EB, Bozeman SR, McNeil BJ. Reasons for underuse of recommended therapies for colorectal and lung cancer in the Veterans Health Administration. *Cancer.* 2012;118(13):3345-3355.

23. Rutten LF, Hesse BW, Moser RP, McCaul KD, Rothman AJ. Public perceptions of cancer prevention, screening, and survival: comparison with state-of-science evidence for colon, skin, and lung cancer. *Journal of cancer education : the official journal of the American Association for Cancer Education.* 2009;24(1):40-48.

24. George M, Margolis ML. Race and lung cancer surgery--a qualitative analysis of relevant beliefs and management preferences. *Oncology nursing forum.* 2010;37(6):740-748.

25. Aberle DR, Abtin F, Brown K. Computed tomography screening for lung cancer: has it finally arrived? Implications of the national lung screening trial. *Journal of clinical*

oncology : official journal of the American Society of Clinical Oncology. 2013;31(8):1002-1008.

26. Zullig LL, Carpenter WR, Provenzale DT, et al. The association of race with timeliness of care and survival among Veterans Affairs health care system patients with late-stage non-small cell lung cancer. *Cancer management and research.* 2013;5:157-163.
27. Ganti AK, Subbiah SP, Kessinger A, Gonsalves WI, Silberstein PT, Loberiza FR, Jr. Association between race and survival of patients with non--small-cell lung cancer in the United States veterans affairs population. *Clinical lung cancer.* 2014;15(2):152-158.
28. Zullig LL, Carpenter WR, Provenzale D, Weinberger M, Reeve BB, Jackson GL. Examining potential colorectal cancer care disparities in the Veterans Affairs health care system. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2013;31(28):3579-3584.
29. Bista A, Sharma S, Shah BK. Disparities in Receipt of Radiotherapy and Survival by Age, Sex, and Ethnicity among Patient with Stage I Follicular Lymphoma. *Frontiers in oncology.* 2016;6:101.
30. Rose TL, Deal AM, Nielsen ME, Smith AB, Milowsky MI. Sex disparities in use of chemotherapy and survival in patients with advanced bladder cancer. *Cancer.* 2016.
31. Khanal N, Upadhyay S, Dahal S, Bhatt VR, Silberstein PT. Systemic therapy in stage IV pancreatic cancer: a population-based analysis using the National Cancer Data Base. *Therapeutic advances in medical oncology.* 2015;7(4):198-205.
32. Olszewski AJ, Shrestha R, Castillo JJ. Treatment selection and outcomes in early-stage classical Hodgkin lymphoma: analysis of the National Cancer Data Base. *Journal of*

clinical oncology : official journal of the American Society of Clinical Oncology. 2015;33(6):625-633.

33. Smaldone MC, Handorf E, Kim SP, et al. Temporal trends and factors associated with systemic therapy after cytoreductive nephrectomy: an analysis of the National Cancer Database. *The Journal of urology.* 2015;193(4):1108-1113.

34. Paulson EC, Wirtalla C, Armstrong K, Mahmoud NN. Gender influences treatment and survival in colorectal cancer surgery. *Diseases of the colon and rectum.* 2009;52(12):1982-1991.

35. Heumann C, Cohn SE, Krishnan S, et al. Regional variation in HIV clinical trials participation in the United States. *Southern medical journal.* 2015;108(2):107-116.

36. Lee JM, Davis MM, Menon RK, Freed GL. Geographic distribution of childhood diabetes and obesity relative to the supply of pediatric endocrinologists in the United States. *The Journal of pediatrics.* 2008;152(3):331-336.

37. Barker LE, Chu SY, Li Q, Shaw KM, Santoli JM. Disparities between white and African-American children in immunization coverage. *Journal of the National Medical Association.* 2006;98(2):130-135.

38. Hirth JM, Rahman M, Smith JS, Berenson AB. Regional variations in HPV vaccination among 9-17 year old adolescent females from the BRFSS, 2008-2010. *Human vaccines & immunotherapeutics.* 2014;10(12):3475-3483.

39. Rahman M, McGrath CJ, Berenson AB. Geographic variation in human papillomavirus vaccination uptake among 13-17 year old adolescent girls in the United States. *Vaccine.* 2014;32(21):2394-2398.

40. Svider PF, Keeley BR, Husain Q, et al. Regional disparities and practice patterns in surgical approaches to pituitary tumors in the United States. *International forum of allergy & rhinology.* 2013;3(12):1007-1012.

41. Inwald EC, Ortmann O, Zeman F, et al. Guideline concordant therapy prolongs survival in HER2-positive breast cancer patients: results from a large population-based cohort of a cancer registry. *BioMed research international.* 2014;2014:137304.

42. Denu RA, Hampton JM, Currey A, et al. Influence of patient, physician, and hospital characteristics on the receipt of guideline-concordant care for inflammatory breast cancer. *Cancer epidemiology.* 2016;40:7-14.

43. Nadpara P, Madhavan SS, Tworek C. Guideline-concordant timely lung cancer care and prognosis among elderly patients in the United States: A population-based study. *Cancer epidemiology.* 2015;39(6):1136-1144.

44. Nadpara PA, Madhavan SS, Tworek C, Sambamoorthi U, Hendryx M, Almubarak M. Guideline-concordant lung cancer care and associated health outcomes among elderly patients in the United States. *Journal of geriatric oncology.* 2015;6(2):101-110.

45. Guy GP, Jr., Lipscomb J, Gillespie TW, Goodman M, Richardson LC, Ward KC. Variations in Guideline-Concordant Breast Cancer Adjuvant Therapy in Rural Georgia. *Health services research.* 2015;50(4):1088-1108.

46. Stitzenberg KB, Sanoff HK, Penn DC, Meyers MO, Tepper JE. Practice patterns and long-term survival for early-stage rectal cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2013;31(34):4276-4282.

47. Punglia RS, Hughes ME, Edge SB, et al. Factors associated with guideline-concordant use of radiotherapy after mastectomy in the national comprehensive cancer network. *International journal of radiation oncology, biology, physics.* 2008;72(5):1434-1440.

48. Slatore CG, Au DH, Gould MK. An official American Thoracic Society systematic review: insurance status and disparities in lung cancer practices and outcomes. *American journal of respiratory and critical care medicine.* 2010;182(9):1195-1205.

49. Hardy D, Liu CC, Xia R, et al. Racial disparities and treatment trends in a large cohort of elderly black and white patients with nonsmall cell lung cancer. *Cancer.* 2009;115(10):2199-2211.

Table 1. Descriptive statistics of study population and univariate association analysis.

Variable	Level	N = 45825 (col %)	Guideline concordant care[1]		Parametric p-value*
			No (col %)	Yes (col %)	
Guideline concordant care[1]	No	35349 (77.1)		-	-
	Yes	10476 (22.9)		-	-
Guideline concordant care: expanded breakdown	No chemo or radiation	12718 (27.8)		-	-
	No chemo, radiation ≥ 60 Gy	1636 (3.6)		-	-
	Chemo, no radiation	10504 (22.9)		-	-
	Chemo, radiation < 60 Gy	6157 (13.4)		-	-
	No chemo, radiation <60 Gy	1951 (4.3)		-	-
	Sequential chemoradiation: chemo radiation ≥e60 Gy; lagtime[2] between 14 - 121 days	2383 (5.2)		-	-
	Concurrent chemoradiation: chemo, radiation ≥o60 Gy; lagtime within 14 days	10476 (22.9)		-	-
Facility type	Academic/research program	13140 (28.9)	28.95	28.6	**<0.001**
	Community cancer program/other	6885 (15.1)	15.09	15.26	
	Comprehensive community cancer program	22915 (50.3)	50.08	51.24	
	Integrated network cancer program	2575 (5.7)	5.88	4.89	
	Missing	310			
Geographical region	West	6707 (14.7)	15.39	12.53	**<0.001**
	South	18194 (40.0)	40.71	37.49	
	Northeast	8886 (19.5)	19.54	19.46	
	Midwest	11728 (25.8)	24.36	30.53	
	Missing	310			
Sex	Male	25360 (55.3)	54.51	58.15	**<0.001**
	Female	20465 (44.7)	45.49	41.85	

Variable	Level	N = 45825 (col %)	Guideline concordant care[1]		Parametric p-value*
			No (col %)	Yes (col %)	
Race	Caucasian	37761 (83.1)	82.87	84.06	**<0.001**
	African American	6064 (13.4)	13.39	13.23	
	Other	1594 (3.5)	3.75	2.71	
	Missing	406			
Hispanic ethnicity	No	40934 (96.8)	96.51	97.64	**<0.001**
	Yes	1369 (3.2)	3.49	2.36	
	Missing	3522			
Insurance type	Not insured	2014 (4.5)	4.56	4.27	**<0.001**
	Government insurance	29263 (65.3)	67.01	59.47	
	Private insurance	13548 (30.2)	28.43	36.26	
	Missing	1000			
Geographic area type	Rural	1128 (2.6)	2.48	2.89	**<0.001**
	Urban	7879 (17.9)	17.4	19.77	
	Metro	34892 (79.5)	80.12	77.34	
	Missing	1926			
Median income quartiles 2000	Not available	1934			**0.032**
	< $30,000	7355 (16.8)	16.79	16.64	
	$30,000 - $35,999	8899 (20.3)	20.23	20.42	
	$36,000 - $45,999	12715 (29.0)	28.67	29.97	
	$46,000 +	14922 (34.0)	34.3	32.97	
Percent no high school degree quartiles 2000	Not available	1939			**<0.001**
	>=29%	9024 (20.6)	20.92	19.37	
	20-28.9%	11433 (26.1)	25.7	27.24	
	14-19.9%	10489 (23.9)	23.66	24.7	
	< 14%	12940 (29.5)	29.72	28.69	

Variable	Level	N = 45825 (col %)	Guideline concordant care[1]		Parametric p-value*
			No (col %)	Yes (col %)	
Year of diagnosis	2005	6547 (14.3)	14.65	13.05	**<0.001**
	2006	5873 (12.8)	12.9	12.54	
	2007	5692 (12.4)	12.49	12.19	
	2008	5974 (13.0)	13.47	11.58	
	2009	5835 (12.7)	13.08	11.55	
	2010	4195 (9.2)	8.74	10.55	
	2011	4023 (8.8)	8.38	10.12	
	2012	3926 (8.6)	8.36	9.26	
	2013	3760 (8.2)	7.92	9.16	
Histology	Adenocarcinoma	16536 (36.1)	37.35	31.82	**<0.001**
	Other	14076 (30.7)	31.16	29.23	
	Squamous cell carcinoma	15213 (33.2)	31.49	38.96	
Grade	Well differentiated, differentiated, NOS	1144 (2.5)	2.67	1.9	**<0.001**
	Moderately differentiated, moderately well differentiated, intermediate differentiation	5893 (12.9)	12.5	4.06	
	Poorly differentiated	14020 (30.6)	30.04	32.47	
	Undifferentiated, anaplastic	767 (1.7)	1.7	1.58	
	Cell type not determined, not stated or not applicable, unknown primaries, high grade dysplasia	24001 (52.4)	53.08	49.99	
Great circle distance (units = 50 mi)	Mean	0.45	0.46	0.43	**0.048**
	Median	0.17	0.17	0.19	
	Minimum	0.00	0	0	
	Maximum	54.34	54.34	50.19	
	Std dev	1.66	1.71	1.47	
	Missing	1126.00	0.46	0.43	

Variable	Level	N = 45825 (col %)	Guideline concordant care[1]		Parametric p-value*
			No (col %)	Yes (col %)	
Age at diagnosis (years)	Mean	67.62	68.52	64.6	**<0.001**
	Median	68.00	69	65	
	Minimum	18.00	18	27	
	Maximum	90.00	90	90	
	Std dev	11.49	11.65	10.39	
	Missing	0.00	68.52	64.6	

Table 2. Multiple logistic regression to predict odds of getting non-guideline-concordant care

		Non-guideline-concordant care		
Covariate	**Level**	**Odds ratio (OR) (95% CI)**	**OR p-value**	**Type 3 p-value**
Facility type	Integrated network cancer program	1.14 (1.01-1.28)	0.034	**<.001**
	Comprehensive community cancer program	0.88 (0.83-0.93)	<.001	
	Community cancer program/other	0.99 (0.91-1.07)	0.796	
	Academic/research program	-	-	
Facility geographical region	West	1.39 (1.28-1.50)	<.001	**<.001**
	South	1.37 (1.29-1.46)	<.001	
	Northeast	1.19 (1.10-1.28)	<.001	
	Midwest	-	-	
Sex	Female	1.08 (1.03-1.14)	0.002	**0.002**
	Male	-	-	
Race	Other	1.24 (1.07-1.43)	0.004	**<.001**
	Black	1.13 (1.05-1.21)	0.002	
	White	-	-	
Hispanic ethnicity	Yes	1.30 (1.11-1.51)	0.001	**0.001**
	No	-	-	
Insurance type	Not insured	1.54 (1.37-1.75)	<.001	**<.001**
	Government insurance	1.03 (0.97-1.09)	0.390	
	Private insurance	-	-	
Geographic area	Rural	0.84 (0.72-0.97)	0.020	**0.004**
	Urban	0.92 (0.86-0.98)	0.008	
	Metro	-	-	

Covariate	Level	Non-guideline-concordant care Odds ratio (OR) (95% CI)	OR p-value	Type 3 p-value
Year of diagnosis	2005	1.34 (1.21-1.49)	<.001	**<.001**
	2006	1.22 (1.10-1.36)	<.001	
	2007	1.21 (1.09-1.35)	<.001	
	2008	1.37 (1.23-1.52)	<.001	
	2009	1.32 (1.19-1.46)	<.001	
	2010	1.01 (0.91-1.12)	0.873	
	2011	1.00 (0.90-1.11)	0.989	
	2012	1.06 (0.95-1.18)	0.314	
	2013	-	-	
Histology	Adenocarcinoma	1.48 (1.40-1.57)	<.001	**<.001**
	Squamous cell carcinoma	1.30 (1.22-1.39)	<.001	
	Other	-	-	
Grade	Well differentiated, differentiated, NOS	1.26 (1.06-1.50)	0.009	**0.002**
	Moderately differentiated, moderately well differentiated, intermediate differentiation	0.93 (0.86-1.00)	0.060	
	Poorly differentiated	0.93 (0.88-0.98)	0.011	
	Undifferentiated, anaplastic	1.05 (0.86-1.28)	0.637	
	Cell type not determined, not stated or not applicable, unknown primaries, high grade dysplasia	-	-	
Great circle distance (units = 50 mi)		1.02 (1.00-1.04)	0.021	**0.021**
Age at diagnosis (years)		1.04 (1.03-1.04)	<.001	**<.001**

* Number of observations in the original data set = 45825. Number of observations used = 39232.
** Backward selection with an alpha level of removal of .2 was used. The following variables were removed from the model: Median income quartiles 2000, and percent no high school degree quartiles 2000.

Table 3. Results of statistically significant interaction testing between variables found to be significantly associated with receipt of guideline concordant care on multivariable logistic regression analysis

		Guideline concordant care = no		
Covariate	**Level**	**Odds ratio (OR) (95% CI)**	**OR p-value**	**Type 3 p-value**
Stratified comparisons by geographical region:				
				0.033
West	Non-Hispanic vs. Hispanic ethnicity	0.79 (0.61-1.02)	0.066	-
South	Non-Hispanic vs. Hispanic ethnicity	0.61 (0.46-0.81)	**<.001**	-
Northeast	Non-Hispanic vs. Hispanic ethnicity	1.15 (0.84-1.57)	0.381	-
Midwest	Non-Hispanic vs. Hispanic ethnicity	0.74 (0.43-1.27)	0.269	-
				0.009
West	Government insurance vs. not insured	0.43 (0.29-0.64)	<.001	-
	Private insurance vs. not insured	0.40 (0.27-0.60)	<.001	
South	Government insurance vs. not insured	0.63 (0.54-0.75)	<.001	-
	Private insurance vs. not insured	0.66 (0.55-0.78)	<.001	
Northeast	Government insurance vs. not insured	0.93 (0.66-1.32)	0.691	-
	Private insurance vs. not insured	0.95 (0.67-1.35)	0.781	
Midwest	Government insurance vs. not insured	0.79 (0.62-1.01)	0.061	-
	Private insurance vs. not insured	0.70 (0.55-0.90)	0.006	

Table 4. Overall survival (months) comparison between patients receiving non-guideline-concordant care versus patients receiving guideline concordant care

Population	Hazard ratio (HR) (95% CI)	HR p-value
Total cohort	1.42 (1.38-1.47)	**<.001**
Women	1.44 (1.38-1.51)	**<.001**
Men	1.40 (1.35-1.46)	**<.001**
Other race/ethnicity	1.13 (0.95-1.35)	0.180
African American	1.57 (1.45-1.70)	**<.001**
Caucasian	1.41 (1.37-1.46)	**<.001**
Hispanic ethnicity	1.27 (1.05-1.54)	**0.014**
Non-Hispanic ethnicity	1.43 (1.38-1.47)	**<.001**
Uninsured	1.53 (1.33-1.77)	**<.001**
Privately insured	1.35 (1.29-1.43)	**<.001**
West	1.56 (1.43-1.69)	**<.001**
South	1.41 (1.35-1.48)	**<.001**
Northeast	1.34 (1.26-1.44)	**<.001**
Midwest	1.42 (1.35-1.50)	**<.001**
Adenocarcinoma histology	1.39 (1.32-1.46)	**<.001**
Other histology	1.47 (1.39-1.54)	**<.001**

Population	Hazard ratio (HR) (95% CI)	HR p-value
Squamous cell carcinoma histology	1.41 (1.33-1.48)	**<.001**

*Variables controlled for in this analysis include facility type, geographical region, sex, race, Hispanic ethnicity, insurance type, geographical area type, income, education, year of diagnosis, histology, grade, great circle distance, and age of diagnosis.

Table 5. Overall survival (months) comparison between patients receiving non-guideline-concordant care versus patients receiving guideline-concordant care (GCC) for various socioeconomic risk factors represented by hazard ratios with propensity score matching

	Overall survival		
Population	**N**	**Hazard Ratio (95% CI)**	**HR P-value**
Guideline concordant care	7626	1.42 (1.37-1.47)	**<.001**
Women	3190	1.41 (1.33-1.49)	**<.001**
Men	4433	1.39 (1.33-1.46)	**<.001**
Other race/ethnicity	192	1.13 (0.89-1.44)	0.299
African American	1005	1.54 (1.40-1.71)	**<.001**
Caucasian	6424	1.39 (1.34-1.45)	**<.001**
Hispanic ethnicity	174	1.42 (1.10-1.84)	**0.007**
Non-Hispanic ethnicity	7446	1.41 (1.36-1.46)	**<.001**
Uninsured	313	1.64 (1.36-1.98)	**<.001**
Privately insured	2761	1.33 (1.26-1.42)	**<.001**
West	1018	1.52 (1.38-1.68)	**<.001**
South	2888	1.38 (1.30-1.46)	**<.001**
Northeast	1483	1.27 (1.17-1.37)	**<.001**
Midwest	2200	1.37 (1.28-1.46)	**<.001**

	Overall survival		
Population	**N**	**Hazard Ratio (95% CI)**	**HR P-value**
Adenocarcinoma histology	2375	1.35 (1.26-1.44)	**<.001**
Other histology	2951	1.42 (1.34-1.51)	**<.001**
Squamous cell carcinoma histology	2295	1.38 (1.29-1.47)	**<.001**

*Variables controlled for in this analysis include facility type, geographical region, sex, race, Hispanic ethnicity, insurance type, geographical area type, income, education, year of diagnosis, histology, grade, great circle distance, and age of diagnosis.

Stratified comparison by race:				**0.009**
Other	Male vs. female	0.79 (0.58-1.06)	0.110	-
African American	Male vs. female	1.11 (0.97-1.27)	0.124	-
Caucasian	Male vs. female	0.90 (0.85-0.95)	**<.001**	-

* Number of observations in the original data set = 45825. Number of observations used = 38542.
** Backward selection with an alpha level of removal of .2 was used. No variables were removed from the model.
*** The estimated stratified treatment effect was controlled by: age at diagnosis, great circle distance (units = 50 mi), grade, Hispanic ethnicity, sex, year of diagnosis, facility type, geographical region, histology, race, and insurance.

Figure 1

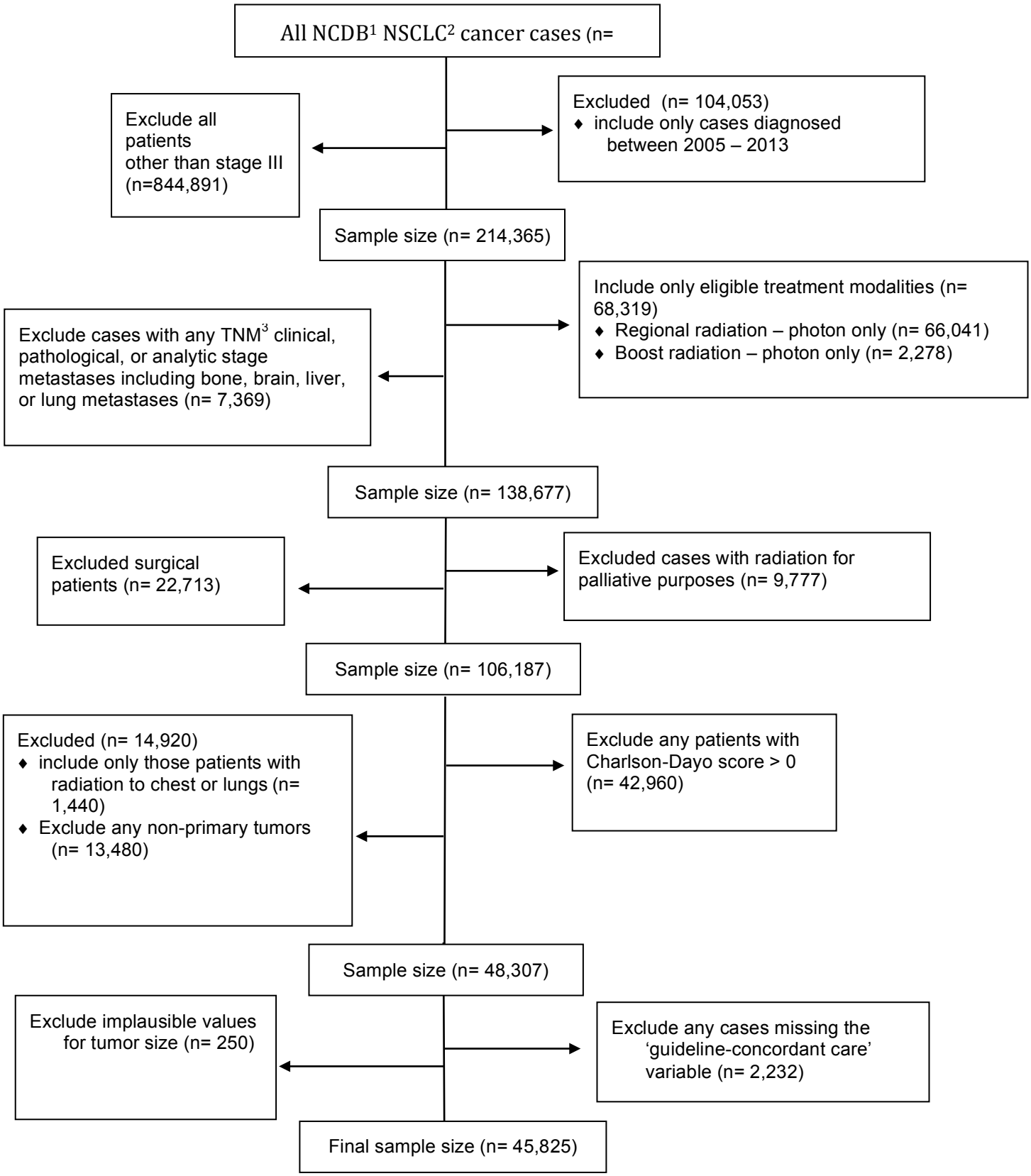
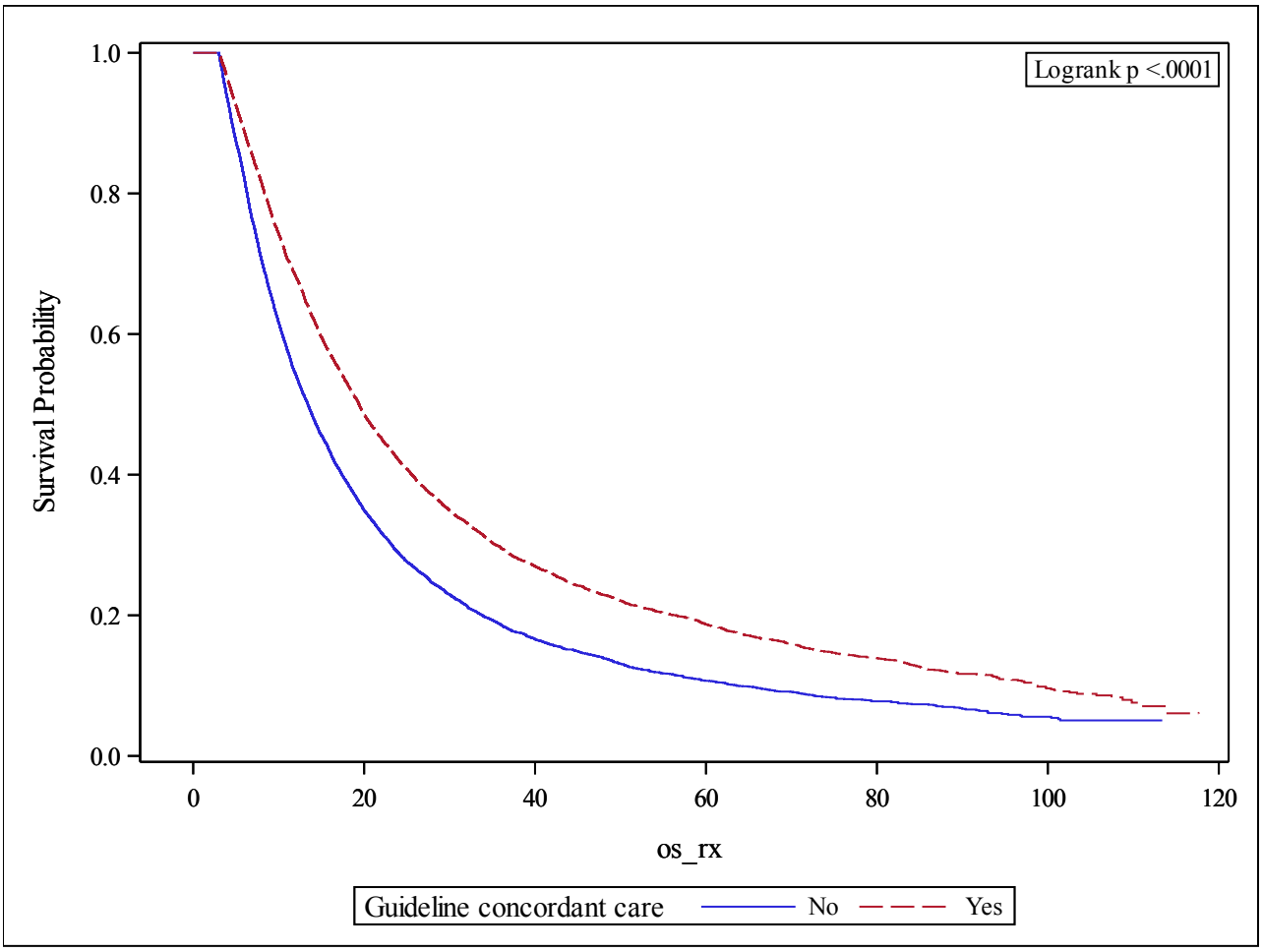

All NCDB[1] NSCLC[2] cancer cases (n=
Exclude all patients other than stage III (n=844,891)
Excluded (n= 104,053)
♦ include only cases diagnosed between 2005 – 2013
Sample size (n= 214,365)
Include only eligible treatment modalities (n= 68,319)
♦ Regional radiation – photon only (n= 66,041)
♦ Boost radiation – photon only (n= 2,278)
Exclude cases with any TNM[3] clinical, pathological, or analytic stage metastases including bone, brain, liver, or lung metastases (n= 7,369)
Sample size (n= 138,677)
Excluded surgical patients (n= 22,713)
Excluded cases with radiation for palliative purposes (n= 9,777)
Sample size (n= 106,187)
Excluded (n= 14,920)
♦ include only those patients with radiation to chest or lungs (n= 1,440)
♦ Exclude any non-primary tumors (n= 13,480)
Exclude any patients with Charlson-Dayo score > 0 (n= 42,960)
Sample size (n= 48,307)
Exclude implausible values for tumor size (n= 250)
Exclude any cases missing the 'guideline-concordant care' variable (n= 2,232)
Final sample size (n= 45,825)

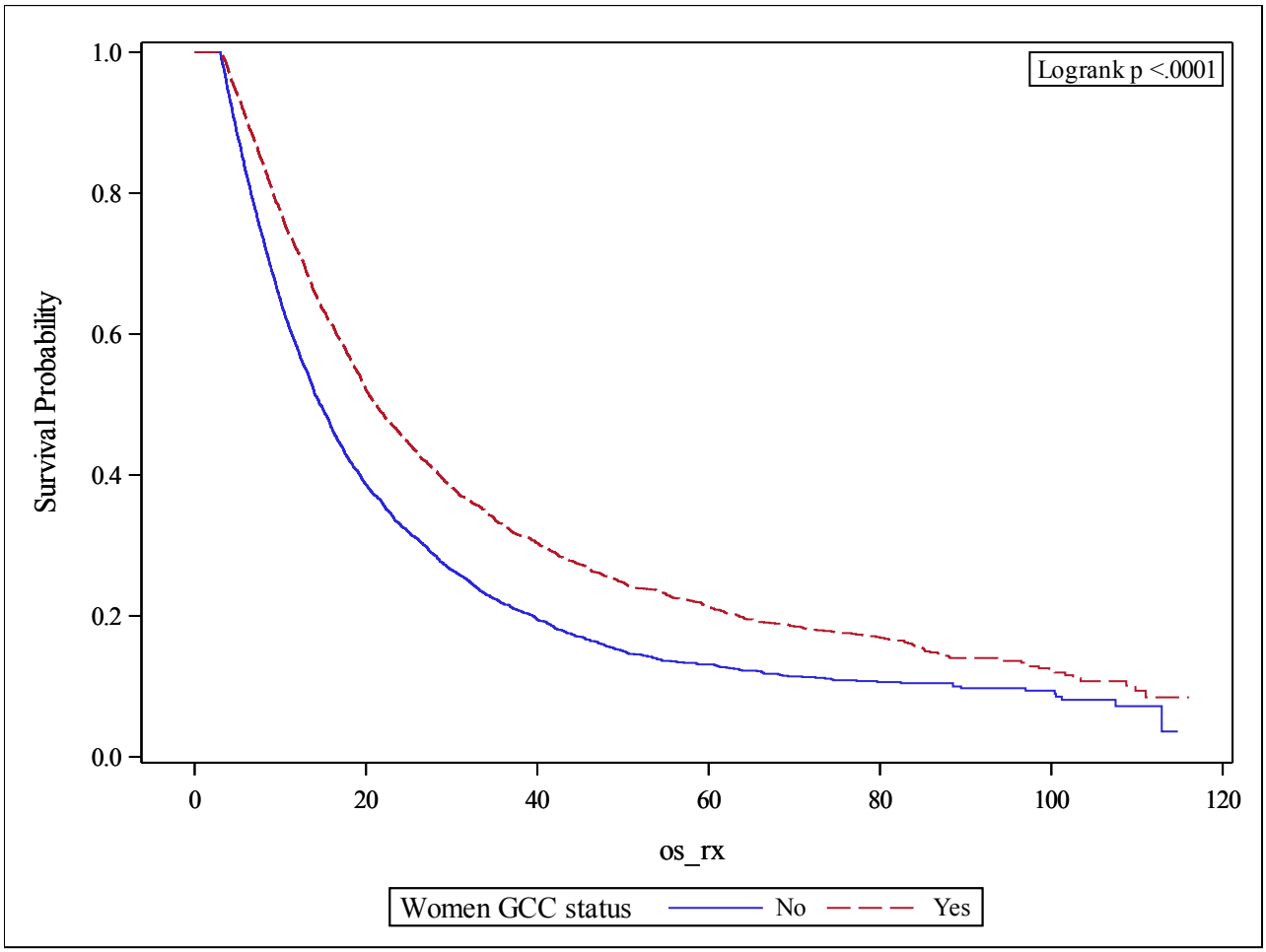
Figure 2. Kaplan-Meier curves of patients receiving guideline concordant care versus those receiving non-guideline-concordant care with propensity score matching for overall cohort and subgroups

a)



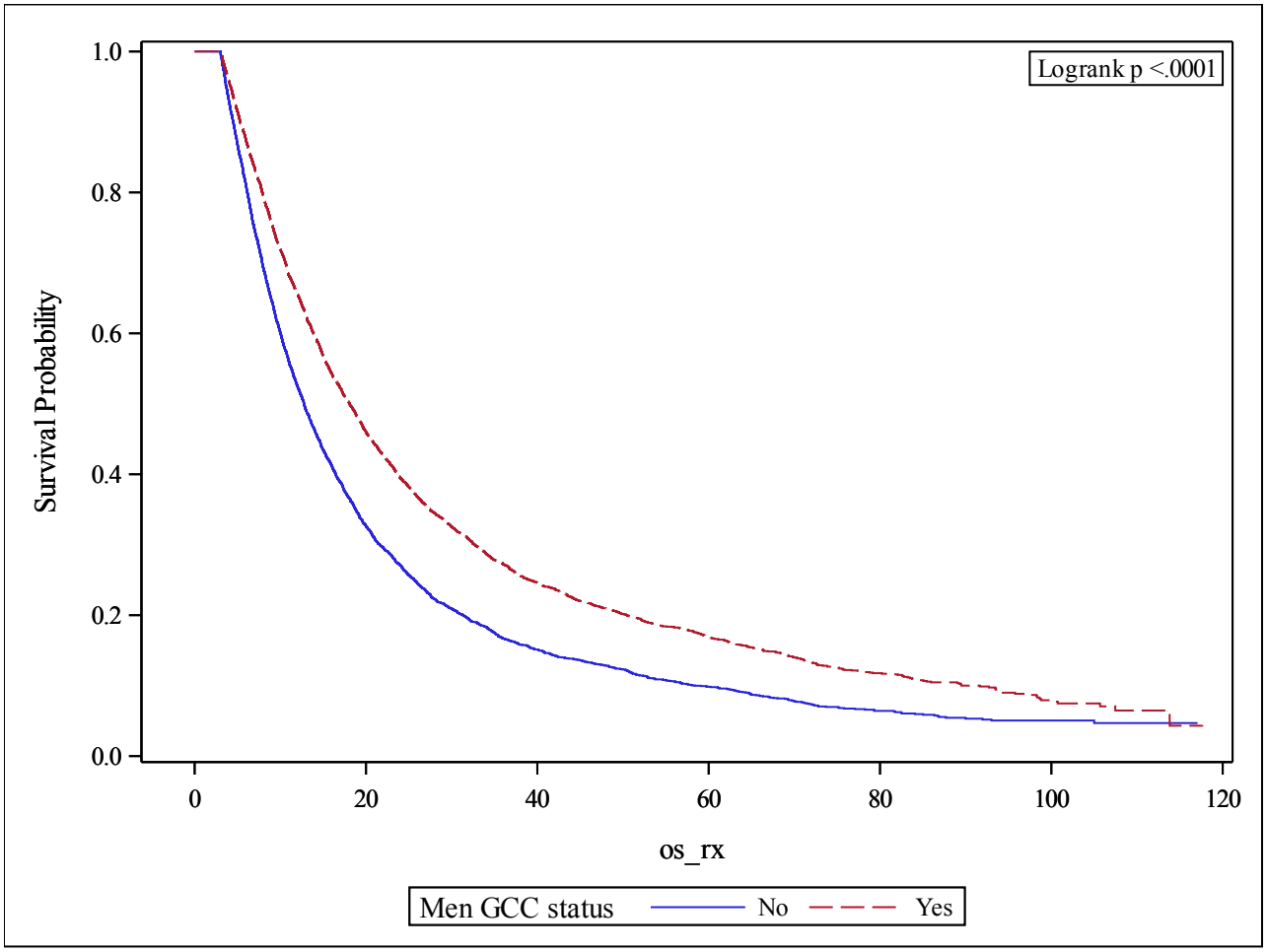
Guideline concordant care	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	7626	6323 (83%)	1303 (17%)	13.4 (13, 13.8)	54.2% (53.1%, 55.4%)	10.7% (9.9%, 11.5%)
Yes	7626	5819 (76%)	1807 (24%)	19.4 (18.9, 19.9)	68.3% (67.2%, 69.3%)	18.7% (17.7%, 19.7%)

b)



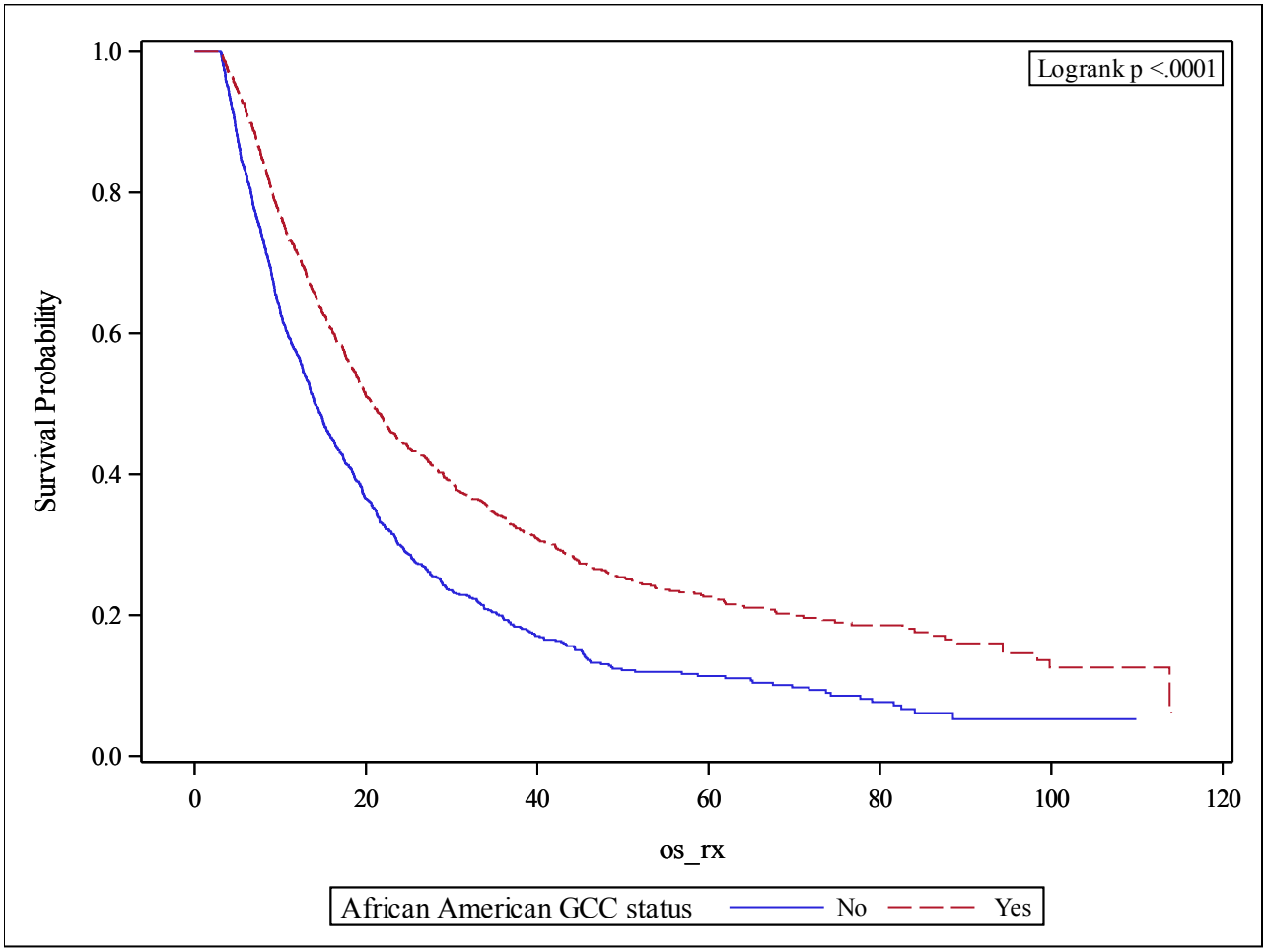
Women GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	3190	2527 (79%)	663 (21%)	14.6 (14, 15.4)	57.9% (56.2%, 59.6%)	13.1% (11.7%, 14.6%)
Yes	3190	2335 (73%)	855 (27%)	21.2 (20.2, 22.2)	71.9% (70.3%, 73.4%)	21.2% (19.6%, 22.9%)

c)



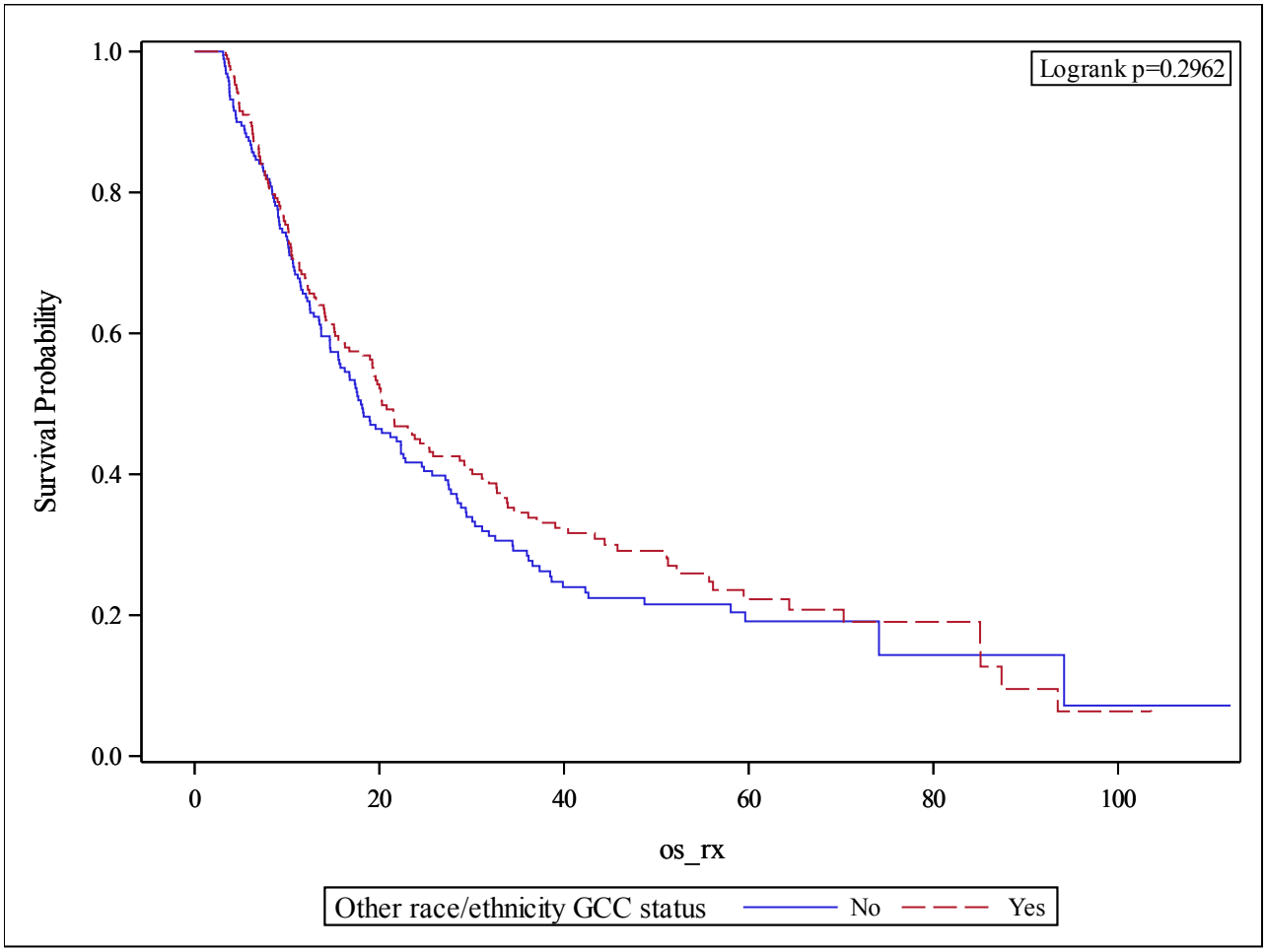
Men GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	4433	3732 (84%)	701 (16%)	12.8 (12.3, 13.2)	52.5% (51.0%, 54.0%)	9.8% (8.8%, 10.9%)
Yes	4433	3482 (79%)	951 (21%)	18.1 (17.3, 18.8)	65.7% (64.2%, 67.0%)	16.9% (15.7%, 18.2%)

d)



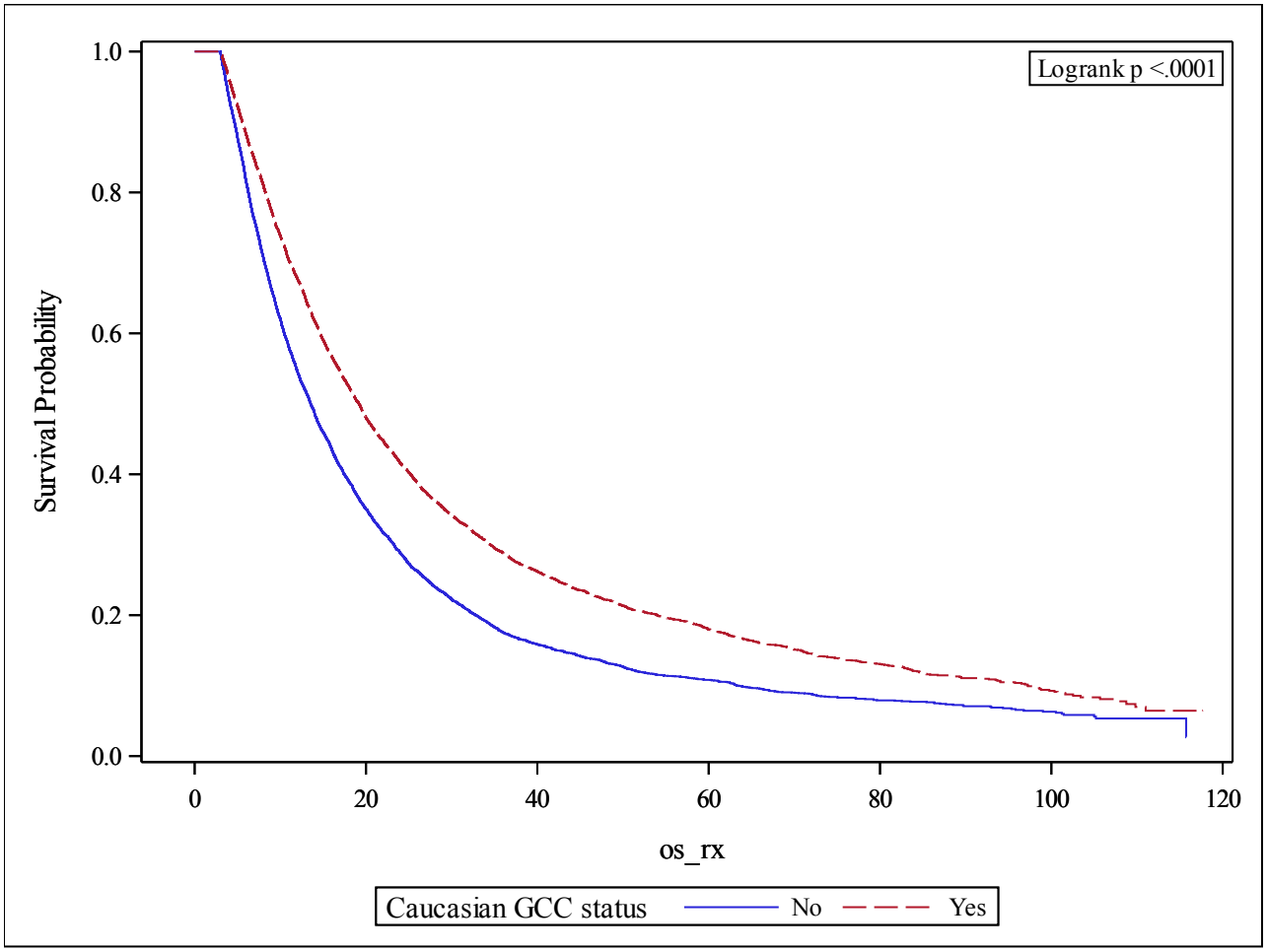
African American GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	1005	807 (80%)	198 (20%)	14 (13.2, 15.2)	57.0% (53.8%, 60.0%)	11.4% (9.0%, 14.0%)
Yes	1005	723 (72%)	282 (28%)	20.8 (19.2, 22.4)	71.4% (68.5%, 74.1%)	22.6% (19.7%, 25.7%)

e)



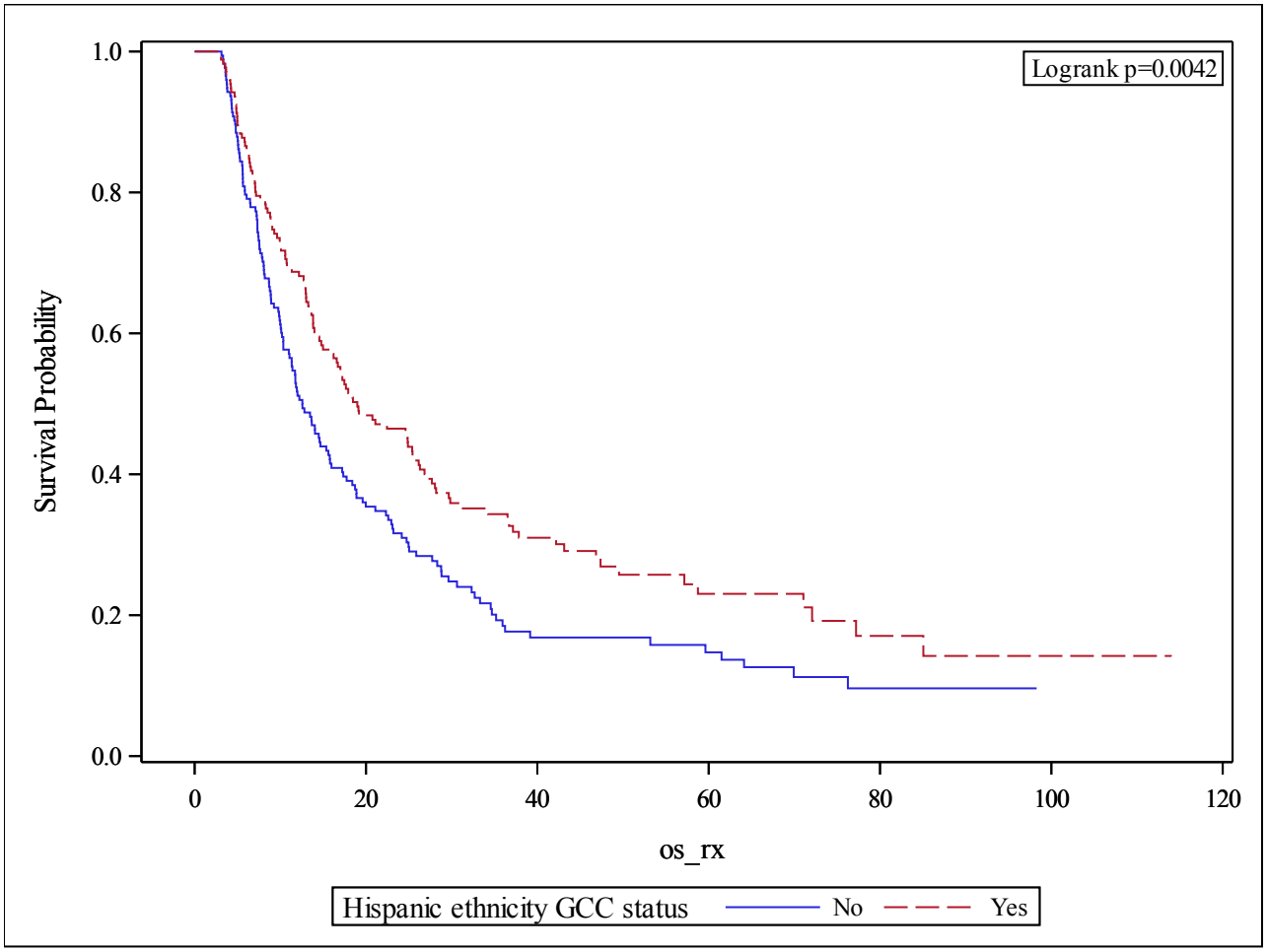
Other race ethnicity GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	192	139 (72%)	53 (28%)	18 (14.7, 22.3)	65.6% (58.3%, 72.0%)	19.1% (13.0%, 26.1%)
Yes	192	135 (70%)	57 (30%)	20.3 (16.7, 25.8)	67.3% (60.0%, 73.5%)	22.3% (15.4%, 29.9%)

f)



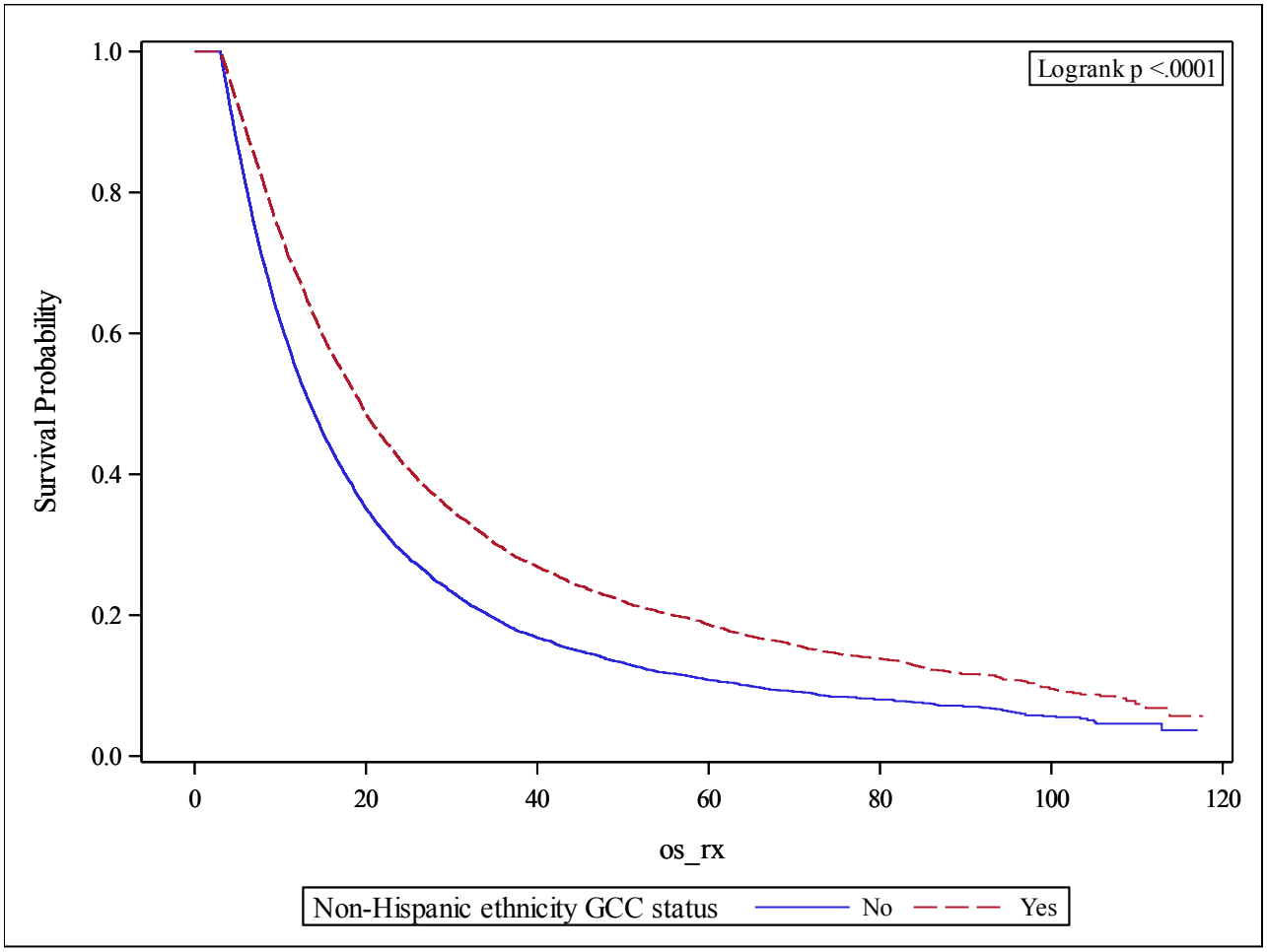
Caucasian GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	6424	5356 (83%)	1068 (17%)	13.5 (13.2, 14)	54.6% (53.4%, 55.8%)	10.8% (10.0%, 11.7%)
Yes	6424	4958 (77%)	1466 (23%)	19.2 (18.6, 19.7)	67.8% (66.6%, 68.9%)	18.0% (16.9%, 19.1%)

g)



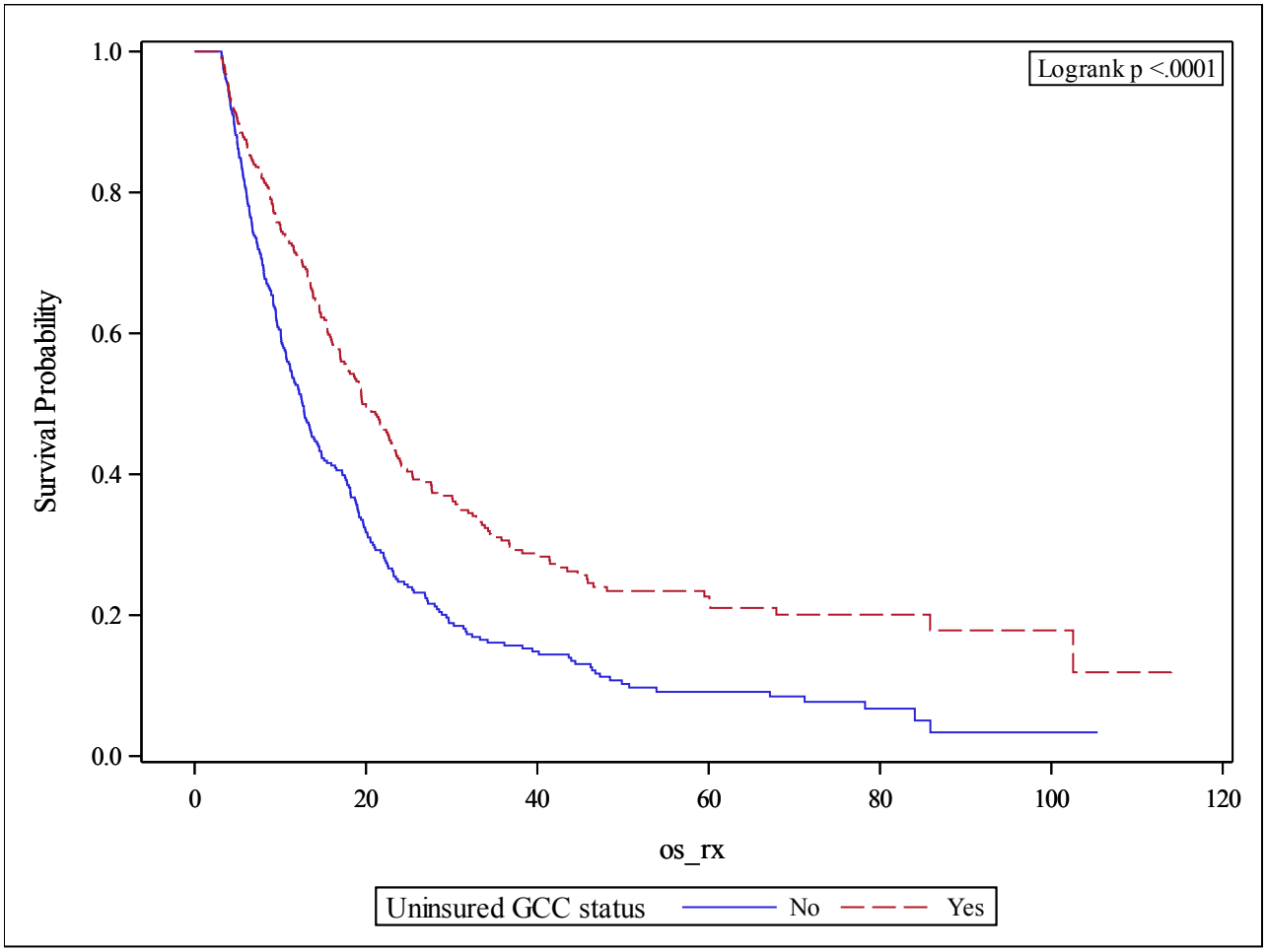
Hispanic ethnicity GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	174	141 (81%)	33 (19%)	12.6 (10.4, 15.8)	51.1% (43.4%, 58.4%)	14.7% (9.4%, 21.3%)
Yes	174	122 (70%)	52 (30%)	19 (15, 25.4)	68.7% (61.2%, 75.1%)	23.0% (15.9%, 30.9%)

h)



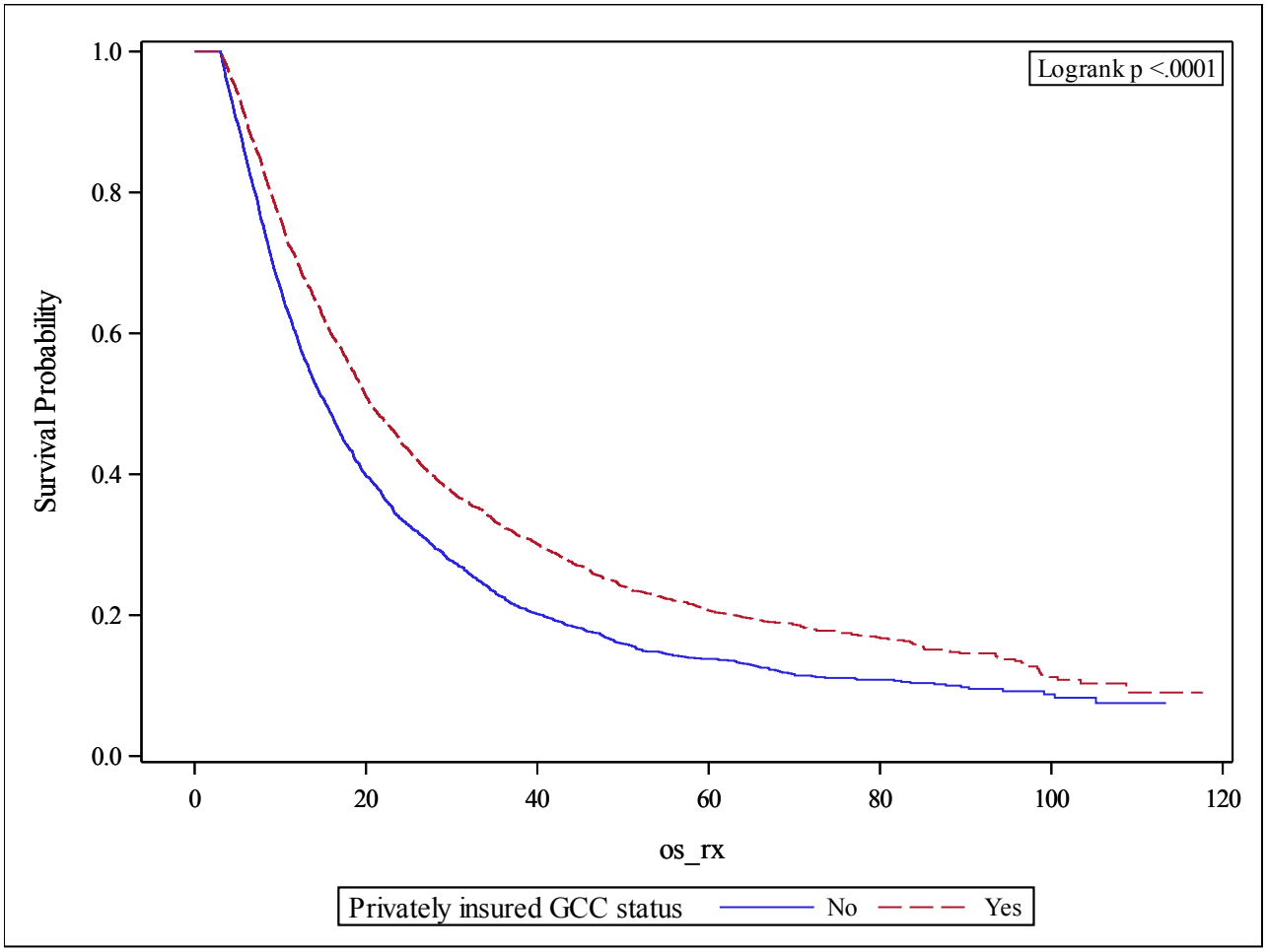
Non-Hispanic ethnicity GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	7446	6153 (83%)	1293 (17%)	13.5 (13.1, 13.9)	54.4% (53.3%, 55.6%)	10.8% (10.0%, 11.7%)
Yes	7446	5694 (76%)	1752 (24%)	19.4 (18.9, 19.9)	68.2% (67.1%, 69.3%)	18.6% (17.6%, 19.7%)

i)



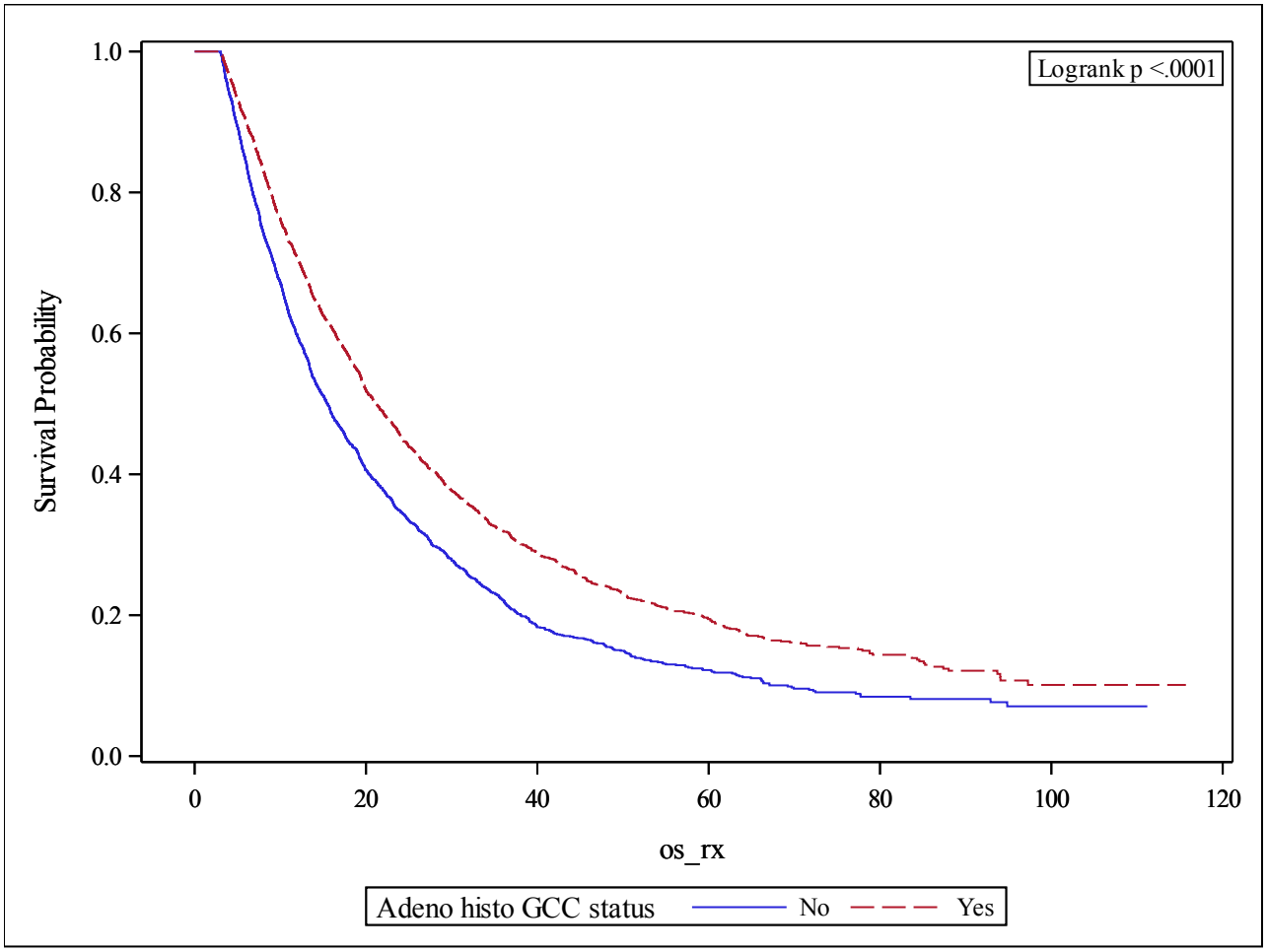
Uninsured GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	313	268 (86%)	45 (14%)	12.6 (11, 14.3)	52.7% (46.9%, 58.1%)	9.1% (5.9%, 13.2%)
Yes	313	220 (70%)	93 (30%)	19.6 (17.5, 23)	71.1% (65.7%, 75.8%)	22.6% (17.5%, 28.2%)

j)



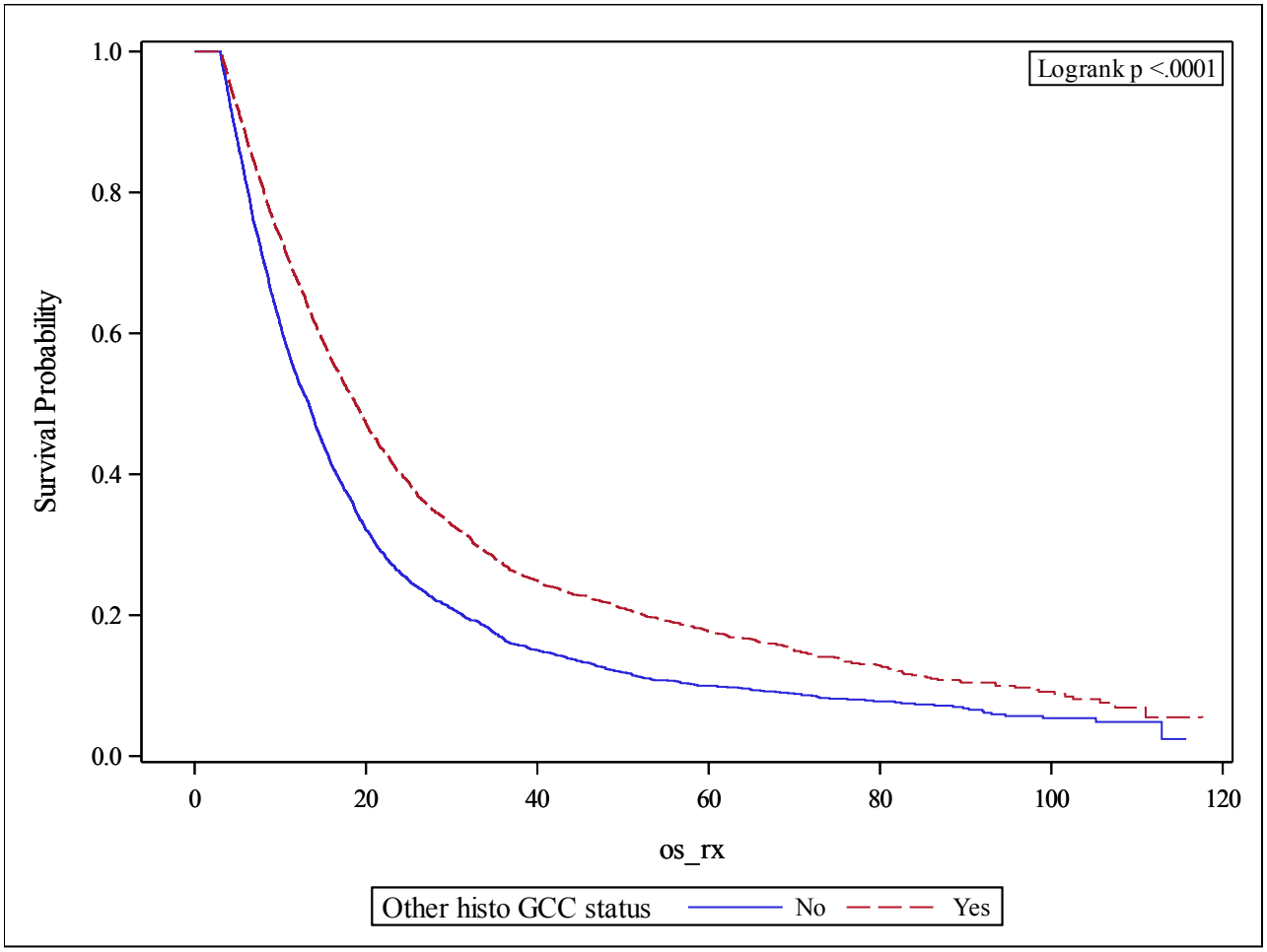
Privately insured GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	2761	2191 (79%)	570 (21%)	15.3 (14.5, 16.1)	59.3% (57.4%, 61.1%)	13.8% (12.3%, 15.4%)
Yes	2761	2059 (75%)	702 (25%)	20.6 (19.7, 21.8)	70.1% (68.4%, 71.8%)	20.7% (19.0%, 22.4%)

k)



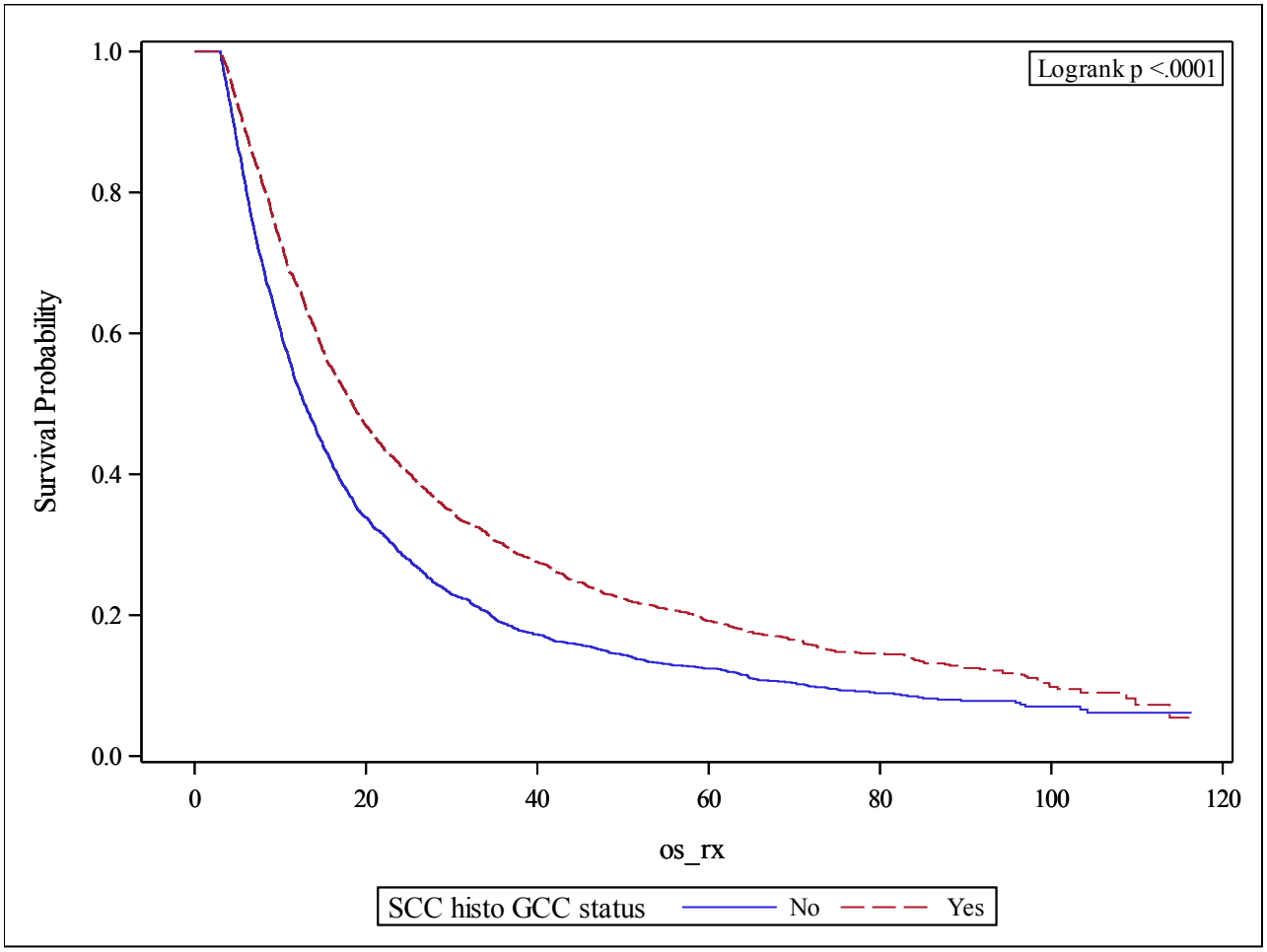
Adeno histo GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	2375	1853 (78%)	522 (22%)	15.5 (14.5, 16.3)	59.6% (57.5%, 61.5%)	12.2% (10.6%, 14.0%)
Yes	2375	1728 (73%)	647 (27%)	21.2 (20, 22.5)	70.8% (68.9%, 72.6%)	19.5% (17.6%, 21.4%)

I)



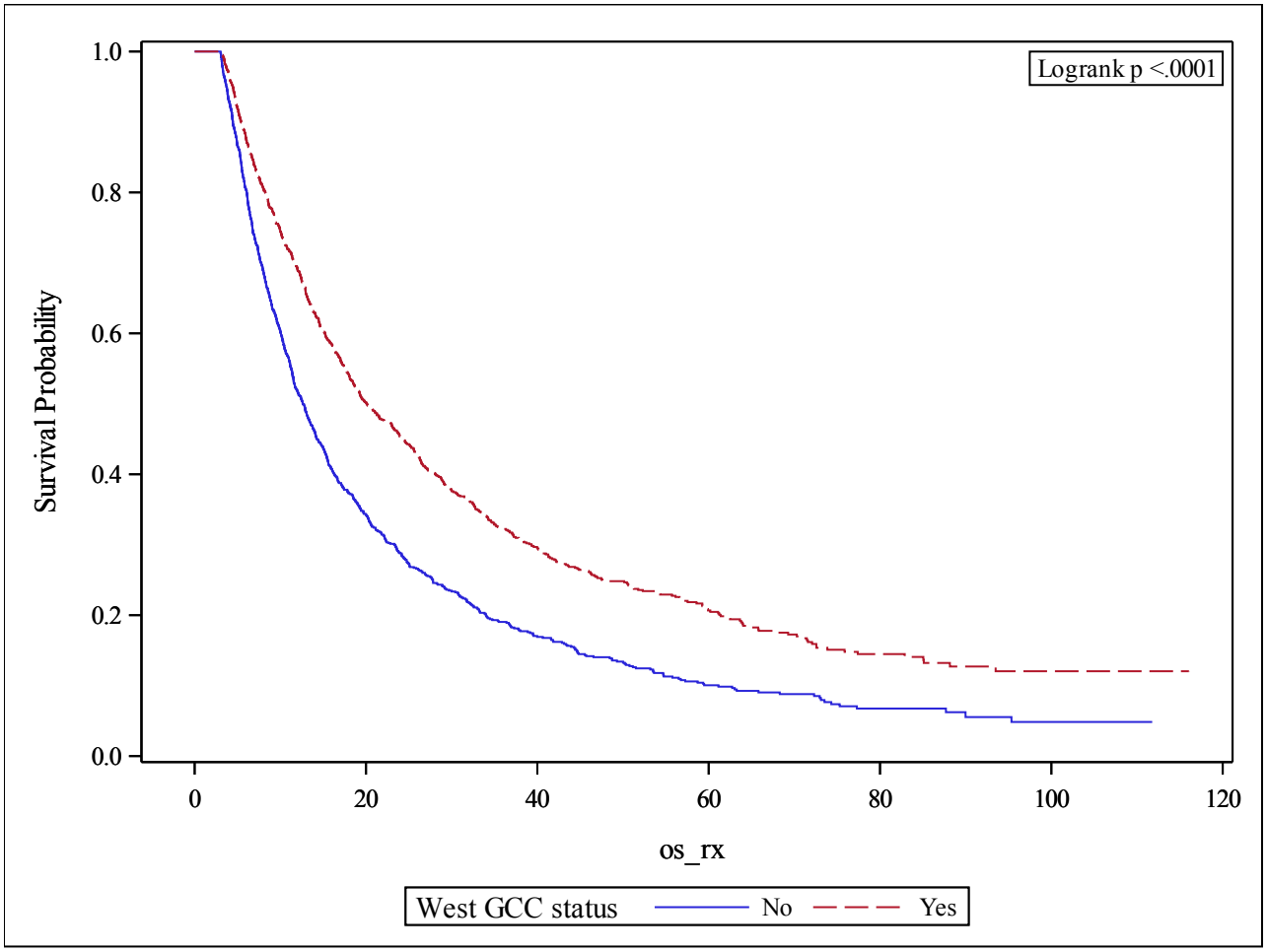
Other histo GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	2951	2461 (83%)	490 (17%)	13.3 (12.6, 13.8)	53.6% (51.8%, 55.4%)	10.0% (8.7%, 11.3%)
Yes	2951	2267 (77%)	684 (23%)	18.8 (17.9, 19.6)	67.4% (65.7%, 69.1%)	17.7% (16.1%, 19.3%)

m)



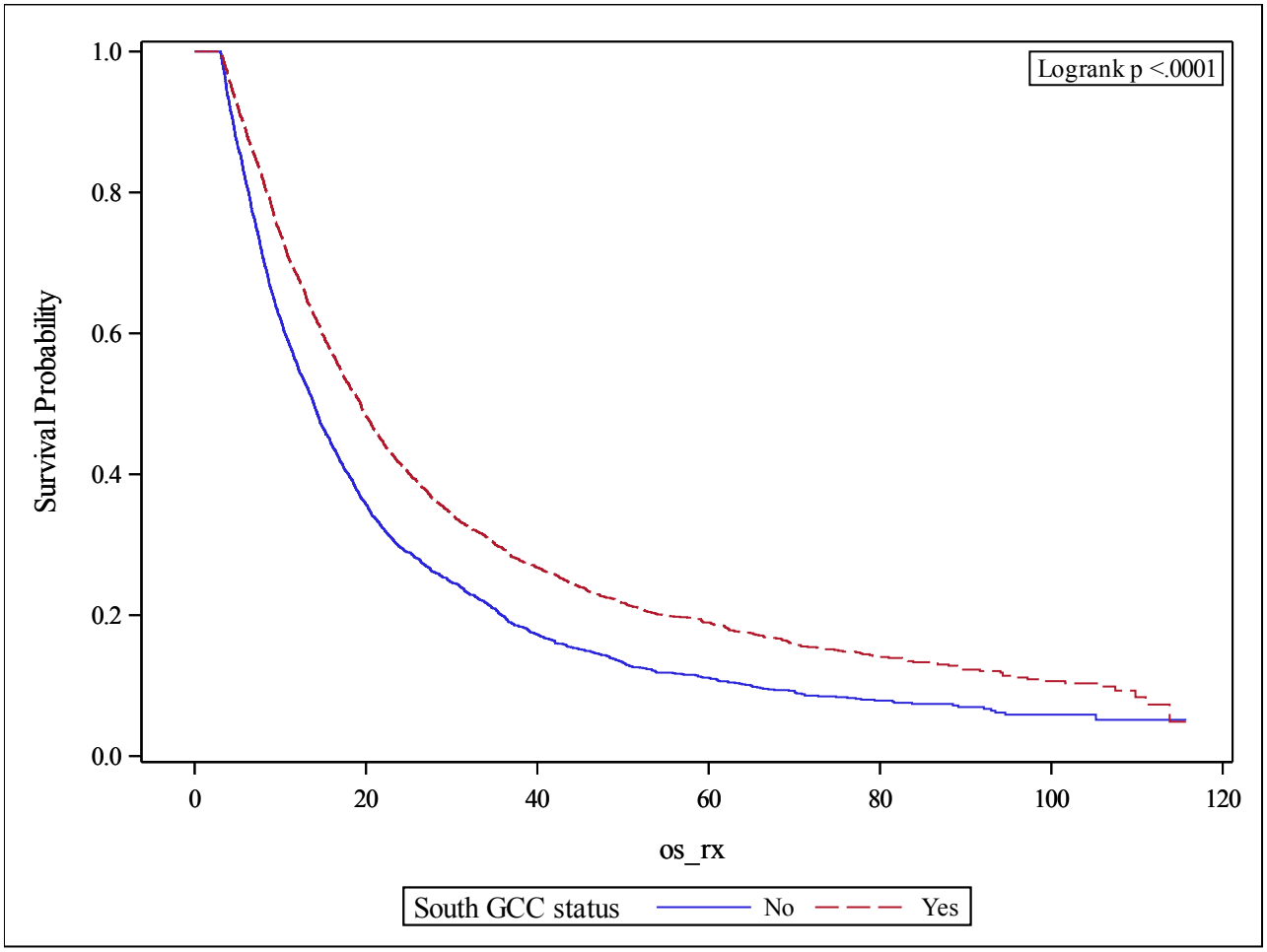
SCC histo GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	2295	1940 (85%)	355 (15%)	12.8 (12.2, 13.6)	52.6% (50.6%, 54.7%)	12.4% (11.0%, 14.0%)
Yes	2295	1820 (79%)	475 (21%)	18.4 (17.5, 19.4)	66.8% (64.8%, 68.7%)	19.2% (17.5%, 21.0%)

n)



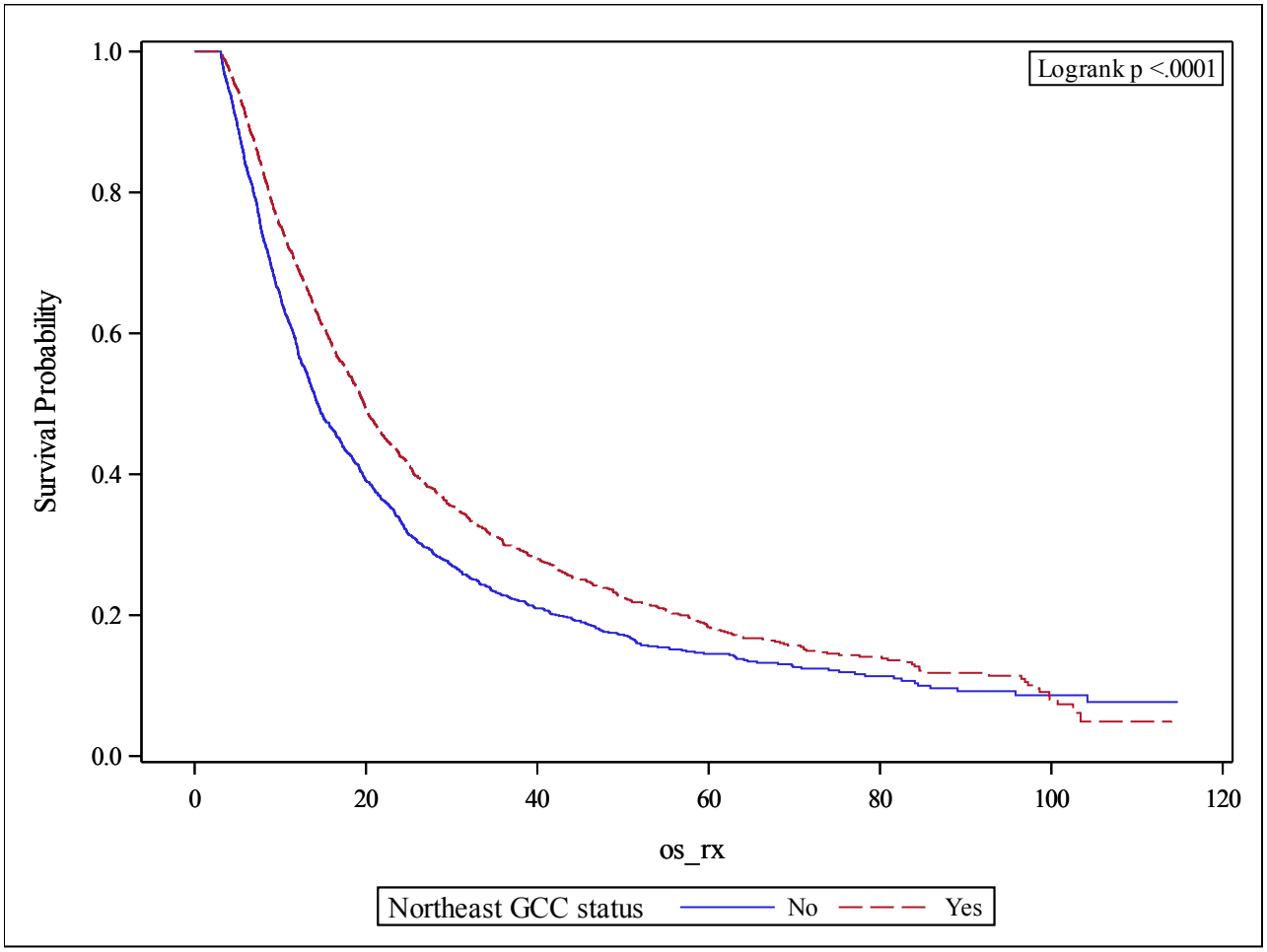
West GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	1018	857 (84%)	161 (16%)	12.6 (11.6, 13.7)	51.7% (48.6%, 54.8%)	10.1% (8.0%, 12.4%)
Yes	1018	764 (75%)	254 (25%)	20.1 (18.5, 23)	69.0% (66.1%, 71.8%)	20.7% (17.9%, 23.6%)

o)



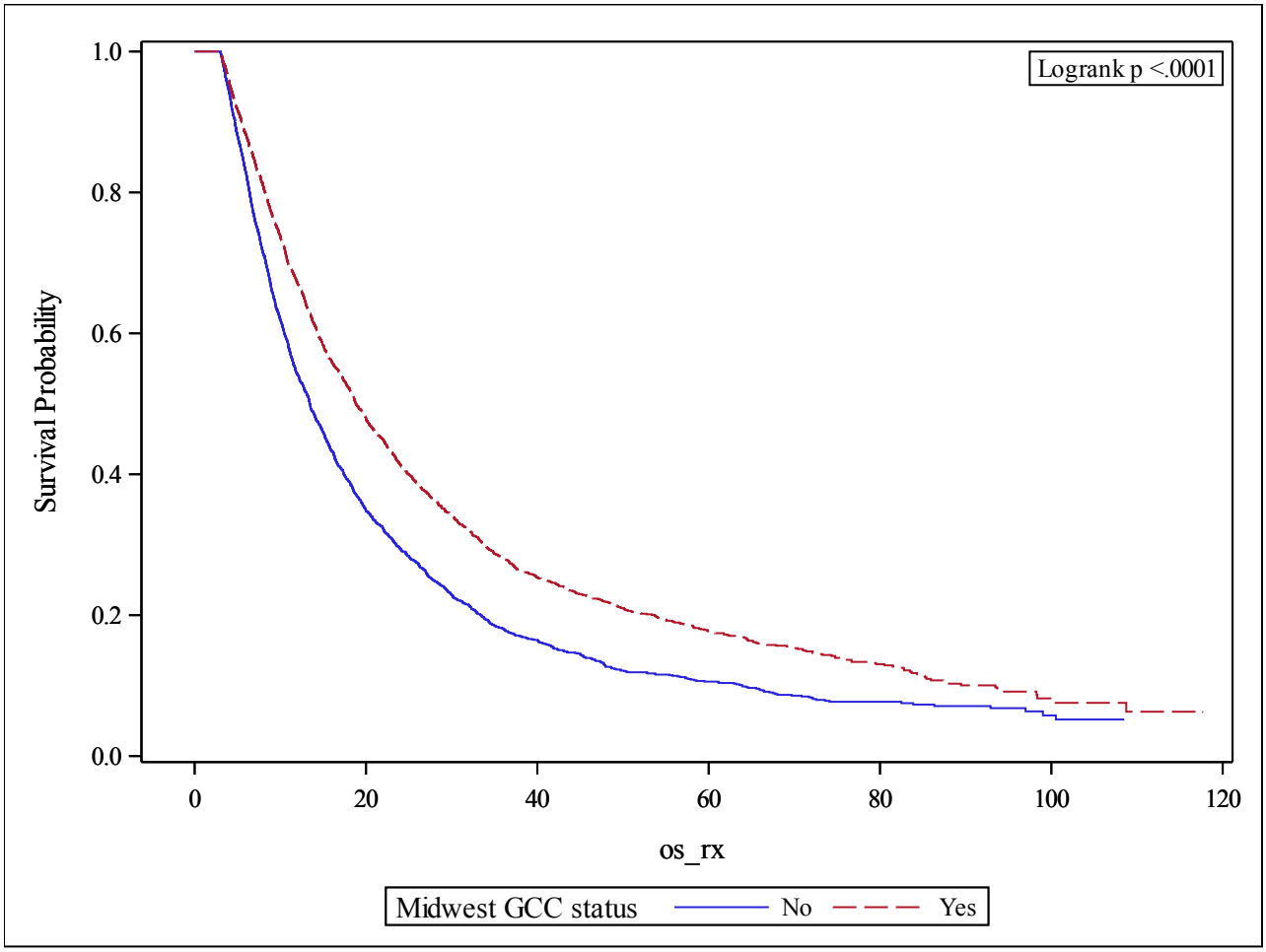
South GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	2888	2368 (82%)	520 (18%)	13.9 (13.3, 14.5)	55.5% (53.6%, 57.3%)	11.1% (9.8%, 12.6%)
Yes	2888	2200 (76%)	688 (24%)	19.4 (18.4, 20)	68.2% (66.5%, 69.9%)	19.0% (17.3%, 20.6%)

p)



Northeast GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	1483	1156 (78%)	327 (22%)	14.4 (13.6, 15.4)	57.9% (55.3%, 60.4%)	14.5% (12.4%, 16.8%)
Yes	1483	1126 (76%)	357 (24%)	19.8 (18.8, 20.9)	69.4% (67.0%, 71.7%)	18.3% (16.0%, 20.7%)

q)



Midwest GCC status	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	60 Mo Survival
No	2200	1835 (83%)	365 (17%)	13.4 (12.8, 14.2)	54.1% (52.0%, 56.2%)	10.6% (9.1%, 12.1%)
Yes	2200	1703 (77%)	497 (23%)	18.8 (18.1, 20)	67.2% (65.2%, 69.1%)	17.7% (15.9%, 19.6%)

Figure Legends

Figure 1. Patient selection algorithm. [1]NCDB, National Cancer Data Base. [2]Non-small cell lung cancer. [3]Tumor, nodes, metastases staging system.

Table 1. Descriptive statistics of study population and univariate association analysis. [1]Guideline concordant care = concurrent chemoradiation. [2]Lagtime = time between start of chemo and radiation. *The parametric p-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.

Table 2. Multiple logistic regression to predict odds of getting non-guideline-concordant care. Reported as risk odds ratios of not getting GCC. * Number of observations in the original data set = 45,825. Number of observations used = 39,232. ** Backward selection with an alpha level of removal of .2 was used. *** The following variables were removed from the model: median income quartiles 2000 and percent no high school degree quartiles 2000.

Table 3. Overall survival (months) comparison between patients receiving non-guideline-concordant care versus patients receiving guideline concordant care for various socioeconomic risk factors represented by hazard ratios. Reported as hazard ratios (HR).

Figure 2. Kaplan-Meier curves of patients receiving guideline concordant care versus those receiving non-guideline-concordant care with propensity score matching for overall cohort and subgroups. Survival probabilities across time (months).

a) Overall cohort
b) Women
c) Men
d) African American race/ethnicity

e) Other race/ethnicity
f) Caucasian race/ethnicity
g) Hispanic ethnicity
h) Non-Hispanic ethnicity
i) Uninsured
j) Privately-insured
k) Adenocarcinoma histology
l) Large cell/other histology
m) Squamous cell carcinoma histology
n) Western US
o) Southern US
p) Northeastern US
q) Midwest US

Table 4. Overall survival (months) comparison between patients receiving non-guideline-concordant care versus patients receiving guideline concordant care for various socioeconomic risk factors represented by hazard ratios with propensity score matching. Reported as hazard ratios (HR).

Table 5. Results of statistically significant interaction testing. Reported as odds ratios. Tested only on a multiplicative scale. * Number of observations in the original data set = 45825. Number of observations used = 38542. ** Backward selection with an alpha level of removal of .2 was used. No variables were removed from the model. *** The estimated stratified treatment effect was controlled by: age at diagnosis, great circle distance (units = 50 mi), grade, Hispanic ethnicity, sex, year of diagnosis, facility type, geographical region, histology, race, and insurance.