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Racial Disparities in Time to Treatment Initiation and Outcomes for Early-Stage Anal Squamous Cell Carcinoma

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Abstract

Objectives: Although cure rates for early stage anal squamous cell cancer (ASCC) are overall high, there may be racial disparities in receipt of treatment and outcome precluding favorable outcomes across all patient demographics. Therefore, we aimed to assess the time to treatment initiation and overall survival (OS) in Black and white patients receiving definitive chemoradiation for early stage ASCC.

Methods: We identified patients diagnosed with early-stage (stage I-II) ASCC and treated with chemoradiation diagnosed between 2004–2016 in the National Cancer Database. Clinical and treatment variables were compared by race using chi-square, and OS assessed via Cox regression with 1:1 nearest neighbor propensity score matching.

Results: Among 9,331 patients, 90.6% were white. Black patients had longer median time to treatment initiation as compared to white patients (47 vs. 36 days, $p<.001$), and on multivariable analysis, the Black race was associated with higher odds of > 6 weeks of time to treatment initiation. (HR 1.78 [1.53–2.08], $p<.001$). Furthermore, Black patients had worse OS (5-year survival 71% vs. 77%, $p<.001$), which persisted after propensity score matching ($p=.007$).

Conclusions: Black patients had a longer time to treatment initiation and worse OS as compared to white patients with early-stage ASCC treated with chemoradiation. Further research is needed to better elucidate the etiologies of these disparities.

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Keywords

Anal Neoplasms; Time to Treatment; Healthcare Disparities; Propensity Score; Race Factors

INTRODUCTION

Although anal cancer is a rare disease, with 8,300 new cases diagnosed annually in the United States, both the incidence and mortality of anal cancer has been increasing over the last two decades, with an annual percentage change of 1.9% and 3.6%, respectively¹. According to the American Cancer Society, there are approximately 1000 deaths attributed to anal cancer annually². Anal squamous cell cancer (ASCC) is the most common histologic subtype of anal cancer, constituting about 80% of cases^{3,4}. Although the underlying causes of the rising rates are unclear, the most common hypotheses include increased prevalence of human papillomavirus (HPV), changing sexual practices, increasing prevalence of human immunodeficiency virus (HIV), among other factors that cause immunodeficiency⁵. In particular, ASCC is strongly associated with HPV, with 90% of cases caused by infection with oncogenic HPV strains^{6,7}. In addition, patients with HIV have a 40 to 80 times greater risk for developing ASCC as compared to the general population⁸.

The current standard treatment for ASCC is chemoradiotherapy (CRT) with 5-Fluorouracil (5-FU) and mitomycin⁹. Cure rates for localized ASCC are overall high, with a 5-year survival rate of approximately 81%². Therefore, early diagnosis and treatment of ASCC are critical for achieving a good prognosis. Disparities based upon sociodemographic characteristics, including race, have been reported for several other malignancies^{10–13}, however have not recently been studied for early stage ASCC, despite the high relative prevalence of traditionally medically disadvantaged populations diagnosed with ASCC.

As such, we assessed racial disparities in presentation and overall survival (OS) in patients undergoing definitive CRT for early-stage (stage I and II) ASCC using the National Cancer Database (NCDB).

MATERIALS AND METHODS

The NCDB is a hospital-based database, including more than 1,500 Commission on Cancer (CoC)-accredited facilities in the US and provides de-identified data on approximately 70% of cancer cases, including patient demographics, tumor characteristics, the first course of treatments and survival outcomes (<https://www.facs.org/quality-programs/cancer/ncdb>).

Study Population

We identified 56,426 adult patients (18–90 years) with anal cancer diagnosed between 2004 and 2016. We used the “C21.0-C21.2” ICD-O-3/WHO 2008 site recode and “8070–8078” ICD-O-3 histologic codes to limit to patients with ASCC histology^{14–17}. We included early stage (I-II) American Joint Committee on Cancer (AJCC)¹⁸ patients with ASCC who received concurrent CRT (defined as the start date of chemotherapy and radiotherapy within 14 days of each other)¹⁷. The staging was defined using the AJCC clinical stage group, which includes the 6th and 7th editions wherein there were no changes^{19,20}. The majority of

the patients did not undergo surgery; therefore, the clinical AJCC stage was combined with the pathological AJCC stage to determine the most accurate overall AJCC stage^{21,22}. Patients with other histologies, those who had more than one primary tumor, with unknown follow-up, non-white or Black race, and those who did not receive CRT and the first course of treatment at the reporting facility (N=46,612) were excluded (Figure 1).

Statistical analysis

Chi-square test or Fisher's exact test was used to compare baseline categorical variables by race. We used the two-sample T-test for continuous variables. Overall survival was evaluated using the Kaplan-Meier method and compared between white and Black patients with the log-rank test. Cox proportional regression method was used for multivariable survival analysis with race (Black vs. white) as the primary independent variable of interest adjusting the effect of other risk factors described below. Patients were censored if still alive at the date of the last follow-up. Multivariable logistic regression analysis was also used to assess the relationship between race and time to treatment initiation (≤ 6 weeks vs. > 6 weeks). We defined time to treatment initiation as days between diagnosis and CRT initiation¹⁹, which was stratified as ≤ 6 weeks versus > 6 weeks. Other variables included in the model were demographics, socioeconomic status, and staging [AJCC stage I-II]. Patient demographics include age [< 50 , 50–64, ≥ 65 years], sex [male, female], facility type [academic, non-academic, other], Charlson-Deyo Score [0–2+], facility location [New England, Middle Atlantic, South Atlantic, East North Central, East South Central, West North Central, West South Central, Mountain, Pacific]. Comorbid conditions defined as Charlson-Deyo score, which is calculated based on disease severity²³. Socioeconomic status contains rurality [metropolitan, non-metropolitan], insurance status [uninsured, private insurance, Medicaid, Medicare, other government insurance], education level [rates of patients without high school level $\geq 17.6\%$, 10.9% – 17.5%, 6.3% – 10.8%, $< 6.3\%$], travel distance to treatment facility [< 12.5 , 12.5–49.9, ≥ 50 miles], and median income quartiles [$< \$40,227$, $\$40,227$ – $50,353$, $\$50,354$ – $63,332$, $\geq \$63,333$]. Patients with missing data for each variable were categorized as “unknown” and were included in multivariable analyses as such.

We used 1:1 nearest neighbor propensity score matching (PSM) in an attempt to reduce confounding effects²⁴. R software version 3.6.2 with MatchIt package was performed for PSM with sex, age, year of diagnosis, comorbidity score, facility type, facility location, insurance status, income, education, rurality, travel distance, stage, and grade as matching variables²⁵. Survival analyses were reanalyzed after propensity matched using Kaplan Meier and Cox regression methods.

P-values were two-tailed considered statistically significant if $< .05$. All statistical analyses were performed using SPSS version 25.0. This study was deemed exempt from the Institutional Review Board at the University of Texas Southwestern, given the use of de-identified data.

RESULTS

Baseline Characteristics

Among 9,311 patients who met inclusion criteria, 8,451 (90.6%) were white, and the median age was 58 years. White patients were more likely to be female (67% vs. 51%), older age (65 years) (31% vs. 17%), of higher education level (25% vs. 7%), have private insurance (50% vs. 39%), and report higher income (35% vs. 16%), as compared to Black patients (*all* $p<.001$). In contrast, Black patients were more likely to live in metropolitan areas (92% vs. 81%), have comorbidity scores ≥ 2 (18% vs. 6%), receive treatment at an academic center (46% vs. 28%), live in the Southern Atlantic, (32% vs. 23%), and travel shorter distance for care (80% vs. 61%) (*all* $p<.001$) (Table 1). Black patients were more likely to have Medicaid insurance as compared to white patients (19% vs. 8%, $p<.001$). In addition, black patients had longer median time to treatment initiation (47 vs. 36 days, $p<.001$) and on multivariable logistic regression, the Black race was associated with higher odds of > 6 weeks of time to treatment initiation (HR 1.78 [1.53–2.08], $p<.001$) (Figure 2). Other variables positively associated with ≥ 6 weeks until treatment initiation included high comorbidity score (≥ 2) and long travel distance (≥ 50 miles) (Table 2).

Survival analyses

Without propensity score matching, Black patients had worse OS compared to white patients (HR 1.18 [1.02–1.36], $p=.03$), 5-year survival rate 71% vs. 77%, $p<.001$) (Table 1, Figure 3A). After propensity score matching, the Black race remained associated with worse overall survival (5-year survival rate 71% vs. 75%, $p=.007$) (Table 1, Figure 3B). After multivariable analysis, this difference has remained as Black patients had decreased overall survival than white patients (HR 1.25 [1.02–1.52], $p=.03$) (Table 3).

DISCUSSION

In this comprehensive nationwide study of patients with early-stage ASCC, we observed socioeconomic and racial disparities in treatment and outcome. In particular, Black patients had a worse OS. The etiologies of this disparity are likely multifactorial, including both patient and systems-level factors such as insurance status, income, education, and access to timely and high quality cancer care^{26–28}. Indeed, we also found that the Black race was associated with greater time to treatment initiation. These findings are consistent with prior reports such as by Ramsey et al., showing that among patients with ASCC, Black patients with public insurance and lower education levels experienced greater treatment initiation delays as compared to their white counterparts¹⁹. Notably, Black patients were more likely to be treated at academic cancer centers. It is possible that some of the delays in treatment initiation for Black patients could be due to difficulties in obtaining timely work-up and care at academic centers due to longer wait times at such centers, although we controlled for facility type in our analyses. Prior studies have also demonstrated an association between racial disparities and delay to treatment initiation in breast, colorectal, prostate, lung, and head & neck cancers^{29–33}. Accordingly, research on cancer outcomes has demonstrated that delays in the initiation of cancer treatment appear to be associated with worse survival^{29,30,34,35}.

Several prior studies have also demonstrated a higher incidence and mortality of ASCC among Black patients^{14,36,37}. In a study using the SEER database, Arora et al. reported that white women and Black men had the highest rate of increase in the incidence of ASCC³⁸. Another study showed that Black patients have higher annual percentage increases in incidence and mortality of ASCC compared to whites and that 5-year relative survival was significantly lower in Black patients (56% vs. 67%)³⁹. Indeed, multiple studies have demonstrated that Black patients with ASCC have higher mortality as compared to whites^{14,21,38,40}. In a large cohort, Fields et al. found that the Black race was significantly associated with unfavorable survival in stage I, II, and III diseases but not for stage IV disease⁴⁰. Furthermore, a combined analysis of two studies using the SEER database between 1973 to 2005 and 1988 to 2012 showed the Black race as an independent predictor of worse survival^{41,42}. Our study adds to the literature by demonstrating this disparity among early stage ASCC patients, who have the highest chance for disease cure.

Our study has several limitations inherent to large cancer registries, including lack of information on treatment completion, details on radiotherapy fields, treatment toxicities, chemotherapy dosage and regimens, details of staging (endoscopy, biopsy, specific imaging studies, etc.), and missed appointments. In addition, there was no information on HIV status, which would have been helpful to include as a covariable. Also, NCDB only includes overall survival, and there is no information on cancer-specific outcomes.

Black patients with early stage ASCC had greater time to treatment initiation and worse OS as compared to white patients. Further research is needed to elucidate the underpinnings of these disparities.

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Abbreviations:

CRT	Chemoradiation therapy
ASCC	anal squamous cell cancer
NCDB	National Cancer Database
OS	Overall survival
NS	not significant

REFERENCES

1. Sites A SEER cancer statistics review 1975–2011. Bethesda, MD: National Cancer Institute 2014.
2. Howlader N, Noone A, Krapcho M, et al. SEER Cancer Statistics Review, 1975–2013, National Cancer Institute Bethesda, MD In:2016.

3. Nelson RA, Levine AM, Bernstein L, et al. Changing patterns of anal canal carcinoma in the United States. *J Clin Oncol*. 2013;31(12):1569–1575. [PubMed: 23509304]
4. Valvo F, Ciurlia E, Avuzzi B, et al. Cancer of the anal region. *Crit Rev Oncol Hematol*. 2019;135:115–127. [PubMed: 30819440]
5. Shiels MS, Pfeiffer RM, Chaturvedi AK, et al. Impact of the HIV epidemic on the incidence rates of anal cancer in the United States. *J Natl Cancer Inst*. 2012;104(20):1591–1598. [PubMed: 23042932]
6. Hoots BE, Palefsky JM, Pimenta JM, et al. Human papillomavirus type distribution in anal cancer and anal intraepithelial lesions. *Int J Cancer*. 2009;124(10):2375–2383. [PubMed: 19189402]
7. Alemany L, Saunier M, Alvarado-Cabrero I, et al. Human papillomavirus DNA prevalence and type distribution in anal carcinomas worldwide. *Int J Cancer*. 2015;136(1):98–107. [PubMed: 24817381]
8. Melbye M, Rabkin C, Frisch M, et al. Changing patterns of anal cancer incidence in the United States, 1940–1989. *Am J Epidemiol*. 1994;139(8):772–780. [PubMed: 8178790]
9. Shridhar R, Shibata D, Chan E, et al. Anal cancer: current standards in care and recent changes in practice. *CA Cancer J Clin*. 2015;65(2):139–162. [PubMed: 25582527]
10. Khawja SN, Mohammed S, Silberfein EJ, et al. Pancreatic cancer disparities in African Americans. *Pancreas*. 2015;44(4):522–527. [PubMed: 25872128]
11. Newman LA. Disparities in breast cancer and african ancestry: a global perspective. *Breast J*. 2015;21(2):133–139. [PubMed: 25639288]
12. Berger M, Lund MJ, Brawley OW. Racial disparities in lung cancer. *Curr Probl Cancer*. 2007;31(3):202–210. [PubMed: 17543948]
13. Bhardwaj A, Srivastava SK, Khan MA, et al. Racial disparities in prostate cancer: a molecular perspective. *Front Biosci (Landmark Ed)*. 2017;22:772–782. [PubMed: 27814645]
14. Bojko MM, Kucejko RJ, Poggio JL. Racial Disparities and the Effect of County Level Income on the Incidence and Survival of Young Men with Anal Cancer. *Health Equity*. 2018;2(1):193–198. [PubMed: 30283867]
15. Goffredo P, Robinson TJ, Frakes JM, et al. The impact of location on the prognosis of squamous cell carcinomas of the anorectal region. *Journal of surgical research*. 2018;231:173–178. [PubMed: 30278926]
16. Goffredo P, Garancini M, Robinson TJ, et al. A national-level validation of the new American Joint committee on cancer 8th edition subclassification of stage IIA and B Anal squamous cell cancer. *Annals of surgical oncology*. 2018;25(6):1654–1660. [PubMed: 29572706]
17. Youssef I, Osborn V, Lee A, et al. Survival benefits and predictors of use of chemoradiation compared with radiation alone for early stage (T1–T2N0) anal squamous cell carcinoma. *Journal of Gastrointestinal Oncology*. 2019;10(4):616. [PubMed: 31392041]
18. Hauerstock D, Ennis RD, Grossbard M, et al. Efficacy and toxicity of chemoradiation in the treatment of HIV-associated anal cancer. *Clinical colorectal cancer*. 2010;9(4):238–242. [PubMed: 20920996]
19. Ramey SJ, Rich BJ, Kwon D, et al. Demographic disparities in delay of definitive chemoradiation for anal squamous cell carcinoma: a nationwide analysis. *Journal of gastrointestinal oncology*. 2018;9(6):1109–1126. [PubMed: 30603130]
20. Elson JK, Kachnic LA, Kharofa JR. Intensity-modulated radiotherapy improves survival and reduces treatment time in squamous cell carcinoma of the anus: A National Cancer Data Base study. *Cancer*. 2018;124(22):4383–4392. [PubMed: 30329160]
21. Bilimoria KY, Bentrem DJ, Rock CE, et al. Outcomes and prognostic factors for squamous-cell carcinoma of the anal canal: analysis of patients from the National Cancer Data Base. *Dis Colon Rectum*. 2009;52(4):624–631. [PubMed: 19404066]
22. Bilimoria KY, Bentrem DJ, Ko CY, et al. Squamous cell carcinoma of the anal canal: utilization and outcomes of recommended treatment in the United States. *Annals of surgical oncology*. 2008;15(7):1948. [PubMed: 18414951]
23. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *Journal of clinical epidemiology*. 1992;45(6):613–619. [PubMed: 1607900]
24. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate behavioral research*. 2011;46(3):399–424. [PubMed: 21818162]

25. Ho DE, Imai K, King G, et al. MatchIt: nonparametric preprocessing for parametric causal inference. *Journal of Statistical Software*. <http://gkingharvard.edu/matchit> 2011.
26. Williams DR, Priest N, Anderson NB. Understanding associations among race, socioeconomic status, and health: Patterns and prospects. *Health Psychol*. 2016;35(4):407–411. [PubMed: 27018733]
27. Chaudhry SI, Herrin J, Phillips C, et al. Racial disparities in health literacy and access to care among patients with heart failure. *J Card Fail*. 2011;17(2):122–127. [PubMed: 21300301]
28. Rikard RV, Thompson MS, McKinney J, et al. Examining health literacy disparities in the United States: a third look at the National Assessment of Adult Literacy (NAAL). *BMC Public Health*. 2016;16:975. [PubMed: 27624540]
29. Naghavi AO, Echevarria MI, Strom TJ, et al. Treatment delays, race, and outcomes in head and neck cancer. *Cancer Epidemiol*. 2016;45:18–25. [PubMed: 27664388]
30. Liederbach E, Sisco M, Wang C, et al. Wait times for breast surgical operations, 2003–2011: a report from the National Cancer Data Base. *Ann Surg Oncol*. 2015;22(3):899–907. [PubMed: 25234018]
31. Halpern MT, Holden DJ. Disparities in timeliness of care for U.S. Medicare patients diagnosed with cancer. *Curr Oncol*. 2012;19(6):e404–413. [PubMed: 23300364]
32. Gwyn K, Bondy ML, Cohen DS, et al. Racial differences in diagnosis, treatment, and clinical delays in a population-based study of patients with newly diagnosed breast carcinoma. *Cancer*. 2004;100(8):1595–1604. [PubMed: 15073845]
33. Elmore JG, Nakano CY, Linden HM, et al. Racial inequities in the timing of breast cancer detection, diagnosis, and initiation of treatment. *Med Care*. 2005;43(2):141–148. [PubMed: 15655427]
34. Colleoni M, Bonetti M, Coates AS, et al. Early start of adjuvant chemotherapy may improve treatment outcome for premenopausal breast cancer patients with tumors not expressing estrogen receptors. The International Breast Cancer Study Group. *J Clin Oncol*. 2000;18(3):584–590. [PubMed: 10653873]
35. Colleoni M, Gelber RD. Time to initiation of adjuvant chemotherapy for early breast cancer and outcome: the earlier, the better? *J Clin Oncol*. 2014;32(8):717–719. [PubMed: 24516011]
36. Shiels MS, Kreimer AR, Coghil AE, et al. Anal Cancer Incidence in the United States, 1977–2011: Distinct Patterns by Histology and Behavior. *Cancer Epidemiol Biomarkers Prev*. 2015;24(10):1548–1556. [PubMed: 26224796]
37. Johnson LG, Madeleine MM, Newcomer LM, et al. Anal cancer incidence and survival: the surveillance, epidemiology, and end results experience, 1973–2000. *Cancer*. 2004;101(2):281–288. [PubMed: 15241824]
38. Arora N, Gupta A, Zhu H, et al. Race- and Sex-Based Disparities in the Therapy and Outcomes of Squamous Cell Carcinoma of the Anus. *J Natl Compr Canc Netw*. 2017;15(8):998–1004. [PubMed: 28784861]
39. Baughman DM, Shah BK. Disparities in receipt of radiotherapy and survival by age, sex, and race among patients with non-metastatic squamous cell carcinoma of the anus. *J Gastrointest Oncol*. 2016;7(6):968–973. [PubMed: 28078120]
40. Fields AC, Welten VM, Lu P, et al. Does race impact survival for patients with anal squamous cell carcinoma? *J Surg Oncol*. 2019;120(7):1201–1207. [PubMed: 31549446]
41. Kim E, Kim JS, Choi M, et al. Conditional Survival in Anal Carcinoma Using the National Population-Based Survey of Epidemiology and End Results Database (1988–2012). *Dis Colon Rectum*. 2016;59(4):291–298. [PubMed: 26953987]
42. Metildi C, McLemore EC, Tran T, et al. Incidence and survival patterns of rare anal canal neoplasms using the surveillance epidemiology and end results registry. *Am Surg*. 2013;79(10):1068–1074. [PubMed: 24160801]

Figure 1.
Flow chart showing patient selection

Figure 2.
Histogram to display time to treatment initiation (≤ 6 weeks vs. > 6 weeks) in white and Black patients with anal squamous cell carcinoma

Figure 3. Overall survival in white and Black patients with anal squamous cell carcinoma (**A**) unmatched groups (**B**) propensity matched groups

Table 1.

Baseline characteristics

Characteristics	Unmatched		<i>p-value</i>	Propensity Matched		<i>p-value</i>
	White (%)	Black (%)		White (%)	Black (%)	
	8, 451 (90.6)	880 (9.4)		880 (50.0)	880 (50.0)	
Sex			<i><.001</i>			<i>NS</i>
Male	2,789 (33)	428 (48.6)		433 (49.2)	428 (48.6)	
Female	5,662 (67)	452 (51.4)		447 (50.8)	452 (51.4)	
Age			<i><.001</i>			<i>NS</i>
None						
< 50 years	1,675 (19.8)	329 (37.4)		290 (33.0)	329 (37.4)	
50–64 years	4,125 (48.8)	397 (45.1)		447 (50.8)	397 (45.1)	
65 years	2,651 (31.4)	154 (17.5)		143 (16.3)	154 (17.5)	
Year of diagnosis			<i>NS</i>			<i>NS</i>
2004–2006	1,440 (17.0)	148 (16.8)		145 (16.5)	148 (16.8)	
2007–2009	1,863 (22.0)	190 (21.6)		194 (22.0)	190 (21.6)	
2010–2012	2,320 (27.5)	241 (27.4)		261 (29.7)	241 (27.4)	
2013–2015	2,828 (33.5)	301 (34.2)		280 (31.8)	301 (34.2)	
Comorbidity Score			<i><.001</i>			<i>NS</i>
0	6,936 (82.1)	607 (69.0)		612 (69.5)	607 (69.0)	
1	1,016 (12.0)	115 (13.1)		125 (14.2)	115 (13.1)	
2+	499 (5.9)	158 (18.0)		143 (16.3)	158 (18.0)	
Facility Type			<i><.001</i>			<i><.001</i>
Academic	2,386 (28.2)	402 (45.7)		354 (40.2)	402 (45.7)	
Non-academic	5,822 (68.9)	398 (45.2)		494 (56.1)	398 (45.2)	
Others	243 (2.9)	80 (9.1)		32 (3.6)	80 (9.1)	
Facility Location			<i><.001</i>			<i><.001</i>
New England	596 (7.1)	32 (3.6)		53 (6.0)	32 (3.6)	
Middle Atlantic	1,057 (12.5)	143 (16.3)		138 (15.7)	143 (16.3)	
South Atlantic	1,923 (22.8)	282 (32.0)		210 (23.9)	282 (32.0)	
East North Central	1,474 (17.4)	141 (16.0)		183 (20.8)	141 (16.0)	
East South Central	641 (7.6)	60 (6.8)		70 (8.0)	60 (6.8)	
West North Central	596 (7.1)	37 (4.2)		47 (5.3)	37 (4.2)	
West South Central	508 (6.0)	60 (6.8)		59 (6.7)	60 (6.8)	
Mountain	410 (4.9)	4 (0.5)		26 (3.0)	4 (0.5)	
Pacific	1,003 (11.9)	41 (4.7)		62 (7.0)	41 (4.7)	
Unknown	243 (2.9)	80 (9.1)		32 (3.6)	80 (9.1)	
Insurance status			<i><.001</i>			<i>.03</i>
Uninsured	417 (4.9)	67 (7.6)		74 (8.4)	67 (7.6)	
Private	4,197 (49.7)	346 (39.3)		402 (45.7)	346 (39.3)	
Medicaid	645 (7.6)	164 (18.6)		128 (14.5)	164 (18.6)	
Medicare	2,892 (34.2)	262 (29.8)		246 (28.0)	262 (29.8)	
Other Government	127 (1.5)	17 (1.9)		9 (1.0)	17 (1.9)	

Characteristics	Unmatched		<i>p-value</i>	Propensity Matched		<i>p-value</i>
	White (%)	Black (%)		White (%)	Black (%)	
	8, 451 (90.6)	880 (9.4)		880 (50.0)	880 (50.0)	
Unknown	173 (2.0)	24 (2.7)		21 (2.4)	24 (2.7)	
Income			<i><.001</i>			<i>.001</i>
< \$40,227	1,432 (16.9)	401 (45.6)		364 (41.4)	401 (45.6)	
\$40,227 - \$50,353	1,977 (23.4)	206 (23.4)		237 (26.9)	206 (23.4)	
\$50,354 - \$63,332	1,977 (23.4)	122 (13.9)		148 (16.8)	122 (13.9)	
\$63,333	2,939 (34.8)	139 (15.8)		131 (14.9)	139 (15.8)	
Unknown	126 (1.5)	12 (1.4)		0 (0)	12 (1.4)	
Education[‡]			<i><.001</i>			<i>.01</i>
17.6%	1,512 (17.9)	355 (40.3)		342 (38.9)	355 (40.3)	
10.9% - 17.5%	2,197 (26.0)	269 (30.6)		294 (33.4)	269 (30.6)	
6.3% - 10.8%	2,485 (29.4)	179 (20.3)		177 (20.1)	179 (20.3)	
<6.3	2,143 (25.4)	65 (7.4)		67 (7.6)	65 (7.4)	
Unknown	114 (1.3)	12 (1.4)		0 (0)	12 (1.4)	
Rurality			<i><.001</i>			<i>.03</i>
Metropolitan	6,878 (81.4)	811 (92.2)		809 (91.9)	811 (92.2)	
Non-metropolitan	1,368 (16.2)	55 (6.3)		67 (7.6)	55 (6.3)	
Unknown	205 (2.4)	14 (1.6)		4 (0.5)	14 (1.6)	
Travel distance			<i><.001</i>			<i>NS</i>
<12.5 miles	5,143 (60.9)	705 (80.1)		694 (78.8)	705 (80.1)	
12.5–49.9 miles	2,654 (31.4)	137 (15.6)		158 (18.0)	137 (15.6)	
50 miles	630 (7.5)	37 (4.2)		28 (3.2)	37 (4.2)	
Unknown	24 (0.3)	1 (0.1)		0 (0)	1 (0.1)	
Stage			<i>NS</i>			<i>NS</i>
I	2,420 (28.6)	227 (25.8)		228 (25.9)	227 (25.8)	
II	6,031 (71.4)	653 (74.2)		652 (74.1)	653 (74.2)	
Grade			<i>.003</i>			<i>NS</i>
I-II	4,253 (50.3)	420 (47.7)		423 (48.1)	420 (47.7)	
III-IV	2,106 (24.9)	197 (22.4)		191 (21.7)	197 (22.4)	
Unknown	2,092 (24.8)	263 (29.9)		266 (30.2)	263 (29.9)	
Overall Survival			<i><.001</i>			<i>.007</i>
5-year survival rate	77 %	71 %		75 %	71 %	

[‡] Education: percentage of patients without high school level

Table 2.

Multivariable Logistic regression analysis for time to treatment initiation (≤ 6 weeks vs. > 6 weeks)

Characteristics	OR (95% CI)	<i>p-value</i>
Race		
White	Ref	
Black	1.78 (1.53–2.08)	<.001
Sex		
Male	Ref	
Female	0.72 (0.65–0.79)	<.001
Age		
<50 years	Ref	
50–64 years	1.03 (0.91–1.16)	<i>NS</i>
65 years	1.06 (0.91–1.24)	<i>NS</i>
Comorbidity Score		
0	Ref	
1	1.07 (0.94–1.23)	<i>NS</i>
2+	1.28 (1.08–1.53)	.004
Facility Type		
Academic	Ref	
Non-academic	0.62 (0.56–0.68)	<.001
Other	0.76 (0.58–0.98)	.03
Travel distance		
<12.5 miles	Ref	
12.5–49.9 miles	1.02 (0.92–1.13)	<i>NS</i>
50 miles	1.25 (1.04–1.51)	.02
Unknown	1.08 (0.43–2.71)	<i>NS</i>
Income		
< \$40,227	Ref	
\$40,227 - \$50,353	0.98 (0.85–1.12)	<i>NS</i>
\$50,354 - \$63,332	0.96 (0.84–1.10)	<i>NS</i>
\$63,333	0.89 (0.78–1.01)	<i>NS</i>
Unknown	1.61 (1.08–2.40)	.02
Insurance status		
Uninsured	Ref	
Private	0.62 (0.51–0.76)	<.001
Medicaid	1.17 (0.93–1.49)	<i>NS</i>
Medicare	0.71 (0.57–0.88)	.002
Other/Unknown	0.95 (0.71–1.27)	<i>NS</i>
Rurality		
Metropolitan	Ref	
Non-metropolitan	0.80 (0.70–0.93)	.003
Unknown	0.99 (0.73–1.33)	<i>NS</i>

Characteristics	OR (95% CI)	<i>p-value</i>
Stage		
I	Ref	
II	0.53 (0.48–0.58)	<i><.001</i>
Grade		
I-II	Ref	
III-IV	0.82 (0.74–0.92)	<i>.001</i>
Unknown	1.02 (0.92–1.14)	<i>NS</i>

Note: The multivariable logistic regression predicted the probability of time to treatment initiation: > 6 weeks

Table 3.

Multivariable Cox regression analysis for overall survival

Characteristics		Unmatched		Propensity matched	
		HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Race					
	White	Ref		Ref	
	Black	1.18 (1.02–1.36)	.03	1.25 (1.02–1.52)	.03
Sex					
	Male	Ref		Ref	
	Female	0.64 (0.58–0.70)	<.001	0.62 (0.50–0.76)	<.001
Age					
	< 50 years	Ref		Ref	
	50–64 years	1.28 (1.12–1.46)	<.001	1.16 (0.91–1.47)	<i>NS</i>
	65 years	2.00 (1.71–2.35)	<.001	1.66 (1.21–2.28)	.002
Comorbidity Score					
	0	Ref		Ref	
	1	1.34 (1.19–1.51)	<.001	1.37 (1.04–1.81)	.02
	2+	2.27 (1.98–2.59)	<.001	2.44 (1.94–3.08)	<.001
Facility Type					
	Academic	Ref		Ref	
	Non-academic	1.12 (1.01–1.24)	.03	0.97 (0.79–1.20)	<i>NS</i>
	Unknown	1.69 (1.28–2.24)	<.001	1.47 (0.95–2.28)	<i>NS</i>
Travel distance					
	<12.5 miles	Ref		Ref	
	12.5–49.9 miles	0.91 (0.82–1.01)	<i>NS</i>	0.87 (0.65–1.16)	<i>NS</i>
	50 miles	0.91 (0.76–1.10)	<i>NS</i>	0.84 (0.49–1.44)	<i>NS</i>
	Unknown	1.31 (0.50–3.50)	<i>NS</i>	N/A	
Income					
	< \$40,227	Ref		Ref	
	\$40,227 - \$50,353	0.86 (0.76–0.98)	.02	1.03 (0.81–1.31)	<i>NS</i>
	\$50,354 - \$63,332	0.86 (0.76–0.98)	.02	1.14 (0.86–1.51)	<i>NS</i>
	\$63,333	0.77 (0.68–0.87)	<.001	0.87 (0.64–1.18)	<i>NS</i>
	Unknown	0.79 (0.53–1.17)	<i>NS</i>	0.51 (0.18–1.43)	<i>NS</i>
Insurance status					
	Uninsured	Ref		Ref	
	Private	0.63 (0.52–0.78)	<.001	0.76 (0.51–1.14)	<i>NS</i>
	Medicaid	1.10 (0.87–1.38)	<i>NS</i>	1.04 (0.68–1.59)	<i>NS</i>
	Medicare	0.93 (0.76–1.15)	<i>NS</i>	1.26 (0.84–1.90)	<i>NS</i>
	Other/Unknown	0.97 (0.75–1.31)	<i>NS</i>	1.45 (0.84–2.53)	<i>NS</i>
Rurality					
	Metropolitan	Ref		Ref	
	Non-metropolitan	1.20 (1.05–1.37)	.006	1.65 (1.11–2.45)	.01

Characteristics	Unmatched		Propensity matched	
	HR (95% CI)	<i>p-value</i>	HR (95% CI)	<i>p-value</i>
Unknown	1.15 (0.86–1.54)	<i>NS</i>	3.18 (1.44–7.01)	<i>.004</i>
Stage				
I	Ref		Ref	
II	1.66 (1.49–1.85)	<i><.001</i>	1.59 (1.24–2.04)	<i><.001</i>
Grade				
I-II	Ref		Ref	
III-IV	0.99 (0.89–1.09)	<i>NS</i>	1.00 (0.78–1.29)	<i>NS</i>
Unknown	0.89 (0.80–0.99)	<i>.03</i>	0.79 (0.63–0.99)	<i>.04</i>