Decreased overall survival in black patients with HPV-associated oropharyngeal cancer

Siddharth Sheth[1], Douglas Farquhar[1], Nicholas Lenze[1], Angela Mazul[2], Paul Brennan[3], Devasena Anantharaman [3], Behnoush Abedi-Ardekani [3], Jose Zevallos[2], Neil Hayes[4], and Andrew F. Olshan[5]

[1]University of North Carolina at Chapel Hill School of Medicine
[2]Washington University in Saint Louis School of Medicine
[3]International Agency for Research on Cancer
[4]The University of Tennessee Health Science Center
[5]University of North Carolina System

August 14, 2020

Abstract

Abstract Introduction: Racial disparities for overall survival (OS) in head and neck cancer have been well described. However, the extent to which these disparities exist for HPV-associated oropharyngeal squamous cell carcinoma (OPSCC), and the contribution of demographic, clinical, and socioeconomic status (SES) variables, is unknown. Methods: Patients were identified from the Carolina Head and Neck Cancer Epidemiology Study (CHANCE), a population-based study in North Carolina. Cox proportional hazards regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for OS in black versus white patients with sequential adjustment sets. Results: A total of 157 HPV-associated OPSCC patients were identified. Of these, 93% were white and 7% were black. Black patients with HPV-associated OPSCC were more likely to be younger, have an income <$20,000, live farther away from clinic where biopsy was performed, and have advanced T stage at diagnosis. Black patients had worse OS in the unadjusted analysis (HR 4.9, 95% CI 2.2-11.1, p<0.0001). The racial disparity in OS slightly decreased when sequentially adjusting for demographic, clinical, and SES variables. However, HR for black race remained statistically elevated in the final adjustment set which controlled for age, sex, stage, smoking, alcohol use, and individual-level household income, insurance, and education level (HR 3.4, 95% CI 1.1-10.1, p=0.028). Conclusion: This is the first population-based study that confirms persistence of racial disparities in HPV-associated OPSCC after controlling for demographic, clinical, and individual-level socioeconomic factors. Keywords: Head and neck neoplasms, disparities, race, survival, human papillomavirus, epidemiology

Structured Key Points:

- Black patients were more likely than white patients to present with advanced T stage at diagnosis for HPV-positive oropharyngeal squamous cell carcinoma
- Black patients had significantly worse overall survival than white patients in the unadjusted analysis
- The racial disparity in overall survival persisted when adjusting for age, sex, and tumor stage
- The racial disparity in overall survival persisted when adding alcohol and tobacco use to the previous adjustment set
- The racial disparity in overall survival remained significant in the final adjustment set which controlled for age, sex, tumor stage, smoking, tobacco use, and household income, insurance status, and education level

Introduction

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in the United States with 65,410 new diagnoses in 2019.(1) Over the past three decades, HNSCC epidemiology has changed significantly due to the rapidly increasing incidence of oropharyngeal squamous cell carcinoma (OPSCC).(2) This is primarily driven by rising exposure to the human papillomavirus (HPV) infection, which now accounts for 60-70% of incident OPSCC cases.(3) Compared to HPV-negative OPSCC, the demographic profile of patients with HPV-positive OPSCC tends to be younger, male, white, and non-smokers.(3) It is estimated that there are 3,500 new cases of HPV-associated OPSCC diagnosed in women and 15,500 in men each year in the United States.(4) In the United States, white patients with OPSCC are more likely than black patients to have HPV-positive tumors (67.6% vs. 42.3%, respectively; $p<0.001$).(5) Most studies evaluating the prognosis for patients with OPSCC have been composed of primarily of white patients. To date, there is limited information regarding the prognosis of black patients with HPV-associated OPSCC.

Racial disparities in HNSCC have been well described, but it is unknown if these findings translate to HPV-associated OPSCC, which is now recognized as a distinct clinicopathologic entity. Although black patients account for a minority of all HNSCC cases, they contribute disproportionately to the morbidity and mortality associated with this disease.(6,7) Black HNSCC patients are diagnosed at more advanced disease stage and have worse survival outcomes compared to white HNSCC patients.(8–10) Previous studies have suggested that lower socioeconomic status and differential access to care contribute to this disparity.(11,12) Some studies have shown that the racial disparities in HNSCC are largely driven by the OPSCC subsite, given that HPV-associated disease is more prevalent in white patients and has better prognosis.(13) However few studies have examined racial disparities in OPSCC while also assessing the relative influence of HPV-status.

A recent systematic review of studies assessing racial disparities in OS in OPSCC after adjusting for HPV-status (13) identified only 5 studies in the current literature that examined survival disparities by race after adjusting for HPV-status in OPSCC. None of these studies included measures of SES in the adjustment set. Furthermore, only one study included alcohol use in the adjustment set. These findings suggest that HPV-status accounts for much of the racial disparity in OS for OPSCC, but conclusions were limited by the small number of relevant studies and narrow adjustment sets.

To address this gap in current literature we examined racial differences in HPV-associated OPSCC outcomes using a population-based study with information on individual level-SES, as well as comprehensive demographic, clinical, and treatment variables. Previous studies examining racial disparities have relied either on single-institution data, clinical trial data, or cancer registry data, in which this information was not available.

Materials & Methods

Study Population

Data for this analysis was obtained from the [Blinded for peer review], a population-based study in [Blinded for peer review].(14) Eligible cases were diagnosed with their first primary squamous cell carcinoma of the oral cavity, pharynx, and larynx diagnosed between January 1st, 2002 and February 28th, 2006; were ages 20 to 80 years at diagnosis; and resided in [Blinded for peer review]. Case ascertainment relied on rapid identification of newly diagnosed cancer cases through the [Blinded for peer review]. The cancer registrars of 54 hospitals in the study area were contacted monthly to identify potentially eligible cases. Potentially eligible study subjects were mailed a brochure describing the purpose of the study, and upon consent, a study nurse conducted an at-home in-person interview. There were 1381 cases of HNSCC in [Blinded for peer review]. Our present analysis included only tumors that were p16+ and classified as oropharynx cancers (C01.9, C02.4, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0–C10.4, C10.8, and C10.9). Samples that failed p16 typing were not included. Staging classification was based on the American Joint Commission on Cancer (AJCC) 8th edition. This study was approved by the Institutional Review Board at [Blinded for peer review].

Questionnaire and Exposure Assessment

Demographic, lifestyle, oral health, diet, and other common risk factor information were collected using a

structured questionnaire during an in-home visit conducted by trained nurse-interviewers. Specific covariates obtained from the questionnaire included age, sex, race; pack-years of cigarette smoking; ever-consumption of alcohol products; whether the subject was covered by health insurance on diagnosis date, what type of insurance the subject was covered by; household income, and highest attained education level. Race was self-reported from a list of the following options: white, black, American Indian, Alaskan Native, Asian/Pacific Islander, other, and don't know. Given the low overall number of non-white or black patients (n=28), we focused our analysis on patients who self-identified as white or black. Clinical information such as TNM stage and primary treatment were abstracted from the subjects' medical record and reviewed by a pathologist and head neck cancer surgeon. Tumor HPV-status was assessed using p16 immunohistochemistry, and the full protocol has been previously reported in detail.(15)

Survival Assessment

[Blinded for peer review] data were linked to the National Death Index (NDI) based on name, social security number, date of birth, sex, race, and state of residence to identify deaths through December 31, 2013. The NDI is a national file of identified death record information, including cause of death compiled from computer files submitted by State Vital Statistics offices. Greater than 75% of the [Blinded for peer review] cases were perfect or near-perfect NDI matches on social security number, date of birth, and sex. The remaining near-matches were confirmed by examining the United States Social Security Death Index and obituaries on newspaper websites. We chose 5-year overall survival as our endpoint for this study, as there is a decreased contribution by the tumor to overall survival after this timepoint. Disease-specific survival was not available for this analysis secondary to lack of data on specific cause of death for patients in [Blinded for peer review].

Statistical Analysis

Descriptive statistics were calculated, and bivariate testing methods included t and chi-squared tests. Overall survival (OS) was calculated as time from diagnosis to either date of death due to any cause or censoring at 5 years post-diagnosis. Subjects who were still alive on December 31st, 2013 were censored on that date. Hazard ratios (HRs) and 95% confidence intervals (CI) for the independent effects of race on overall survival were estimated by Cox proportional hazards regression models. Sequential adjustment sets were used to examine the relative contribution of demographic, clinical and SES variables to the racial survival disparity. Variables that were missing >10% of observations were left out of the survival analysis, which was determined as an *a priori* threshold. These included rural/urban household designation (n=44 missing) and driving distance to clinic where biopsy was performed (n=49 missing). All variables were treated as categorical variables for the survival models. The proportional hazards assumption was met for all covariates and there was no evidence of multicollinearity on variance inflation factor testing. STATA 16 (StataCorp, College Station, TX) was used for all analyses.

Results

Baseline Characteristics

There were 157 patients diagnosed with HPV-positive OPSCC. Of these patients, 146 identified as white and 11 as black. Baseline characteristics are summarized **(Table I)** . The majority of patients were male (82%) and between 50 to 65 years of age (53%). Forty-two percent of individuals had an education of high school or less. Eleven percent had no medical insurance, and 18% had a household income of less than $20,000. The majority of patients reported at least a 10 pack-year smoking history (57%) and drinking alcohol (83%). The most common treatment modality was chemoradiation (39%), followed by surgery with adjuvant chemoradiation (26%). Twenty-nine percent of patients had advanced T stage at diagnosis. Only 2 out of the 157 patients presented with distant metastases.

Compared to white patients, black patients with OPSCC were significantly more likely to be younger, have an income <$20,000, live farther away from clinic where biopsy was performed, and have advanced T stage at diagnosis. Black patients were more likely to have at least a 10 pack-year smoking history (82%) compared to white patients (56%), although this difference was not statistically significant (p=0.228). There were

no significant differences by race in terms of treatment type (p=0.805) or number of treatment modalities received (p=0.472). No other baseline characteristics varied significantly by race.

5-year Overall Survival Analysis

In the unadjusted survival analysis, black HPV-positive OPSCC patients had significantly worse 5-year OS compared to white patients (HR 4.9, 95% CI 2.2-11.1, p<0.0001). We next sequentially adjusted for demographic, clinical, and SES variables. First, after adjustment for age, sex, T stage, N disease, and distant metastases, the racial disparity in 5-year OS remained statistically significant (HR 4.6, 95% CI 1.8-12.0, p=0.002) **(Table II)** . As expected, T4 disease was associated with significantly worse 5-year overall survival compared to T1 disease (HR 2.5, 95% CI 1.0-6.3). Nodal disease and the presence of distant metastases at diagnosis were associated with elevated but non-statistically significant risk of death.

Second, smoking and alcohol use were added to the previous adjustment set. The association between black race and worse 5-year overall survival persisted (HR 4.1, 95% CI 1.5-11.4, p=0.007) **(Table III)** . Neither smoking (>10 pack-years) nor alcohol use was significantly associated with worse overall survival (HR 1.0, 95% CI 0.5-2.2 and HR 1.6, 95% CI 0.5-4.6, respectively).

Finally, individual-level education, household income, and insurance status were added to the previous adjustment set, and the racial disparity remained statistically significant (HR 3.4, 95% CI 1.1-10.1, p=0.028) **(Table IV)** . Having no insurance (HR 3.0, 95% 0.9-9.8) and a household income <$20,000 (HR 1.9, 95% CI 0.5-6.6) were associated with non-significant trends towards worse overall survival in the fully adjusted model.

Discussion

This is the first population-based study that confirms worse HPV-associated OPSCC survival outcomes in black patients across a range of adjustment sets incorporating demographic, clinical, and individual-level SES variables. It has previously been documented that racial differences in SES and access to care are significant determinants of head and neck cancer disparities.(11,12,16) In OPSCC, racial differences in HPV tumor-status have been shown to contribute to the survival disparity.(17) However, the relative contribution of tobacco use, alcohol use, treatment, and SES to racial disparities in HPV-associated OPSCC has not been determined. Our analysis with sequential adjustment sets demonstrates that racial differences in SES contributes to some but not all of the disparity.

Our findings build upon the growing evidence in current literature for the presence of racial disparities in OPSCC. In a large database analysis of OPSCC stratified by HPV-status, Faraji et al. found that there was a weak but non-significant trend towards worse overall survival (OS) among black patients with HPV-associated OPSCC after adjusting for age, sex, race, year of diagnosis, insurance status, income, education, rural residence, facility region, TNM stage, Charlson-Deyo score, and treatment.(18) In an analysis of the SEER database among patients with HPV-associated OPSCC, black patients had significantly worse cancer-specific mortality than white patients even after adjusting for county-level indicators of SES.(19) In another study, no racial difference in OS was found when controlling for treatment received in the Veteran's Affairs medical system.(20) It is possible that the more homogenous care afforded by the VA system could have mitigated some of the racial disparity attributable to differences in SES and access to care.

There may be several explanations for the persistence of the racial disparity in OS after adjustment for clinical and socioeconomic factors. First, unmeasured confounders in socioeconomic factors, physician and system factors, and access to care may exist. We found that black patients were more likely to have a low income compared to white patients, but our sample lacked the power to adjust for other variables such as frequency of primary care visits or routine dental visits. Studies have found that patients lacking routine dental visits are diagnosed at more advanced stages of head and neck cancer,(21–23) although it is unknown if this pattern varies by race. In the past, racial disparities were largely attributed to genetic differences, but it is now recognized that race is a complex social construct and genetic factors are not likely to integrate with socially-defined racial groups as previously thought.(24)

Our study has several limitations. First, our study population had a small number of black patients with HPV-associated OPSCC. It should be noted that this is a limitation nationally, thereby limiting precise estimation of differences in this study population. Also, p16 testing was not routinely performed at the time of data collection for this study so our sample likely underestimates the true number of HPV-associated OPSCC patients in [Blinded for peer review]. Given the small sample size of our study, it is important to recognize that some of the non-significant findings may be due to lack of statistical power rather than a true non-effect. Efforts are being undertaken to combine databases to increase the sample size of black patients with HPV-associated OPSCC for future validation studies. Another limitation is that the [Blinded for peer review] database did not collect data on patient comorbidities, which may confound the relationship between race and OS. Disease specific mortality was not included in the analysis due to a lack of data on the specific cause of death for many of the [Blinded for peer review] patients.

Our findings may have implications for cancer treatment and future research directions. There is strong evidence to support that patients with HPV-associated OPSCC have improved treatment response and survival outcomes compared to patients with HPV-negative disease.(25) These findings have led to efforts to de-intensify treatment with the goal of alleviating therapy-related morbidity and mortality. Our results suggest that black patients with HPV-associated OPSCC may have worse outcomes despite their HPV-positive tumor status, and therefore, may not receive the same benefits from treatment deintensification. It is important to note that in our sample, we found no differences by race with regards to treatment type or number of treatments modalities received. Future de-intensification trials should closely monitor survival outcomes by race to ensure that this disparity is not being propagated.

Conclusions

There is a well-established correlation between race and survival outcomes in head and neck cancer. This population-based study demonstrated that the black versus white racial disparity in overall survival for HPV-associated OPSCC is only partially mediated by differences in SES. The persistence of the disparity after adjustment for demographic, clinical, and SES variables suggests the contribution of unmeasured confounders. Future research should seek to elucidate these determinants in order to fully address the racial disparity.

Conflicts of Interest Statement

The authors have no conflicts of interest to disclose.

Data Availability Statement Research data are not shared.

References

1. American Cancer Society. Cancer Facts & Figures 2019 [Internet]. Atlanta, GA: ACS; 2019. Report No.: 500819. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf

2. Marur S, Forastiere AA. Head and Neck Cancer: Changing Epidemiology, Diagnosis, and Treatment. Mayo Clinic Proceedings. 2008 Apr;83(4):489–501.

3. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. Lancet Oncol. 2010 Aug;11(8):781–9.

4. Viens LJ, Henley SJ, Watson M, Markowitz LE, Thomas CC, Thompson TD, et al. Human Papillomavirus-Associated Cancers - United States, 2008-2012. MMWR Morb Mortal Wkly Rep. 2016 Jul 8;65(26):661–6.

5. Liederbach E, Kyrillos A, Wang C-H, Liu JC, Sturgis EM, Bhayani MK. The national landscape of human papillomavirus-associated oropharynx squamous cell carcinoma. International Journal of Cancer. 2017;140(3).

6. Peterson CE, Khosla S, Chen LF, Joslin CE, Davis FG, Fitzgibbon ML, et al. Racial differences in head and neck squamous cell carcinomas among non-Hispanic black and white males identified through the National Cancer Database (1998-2012). J Cancer Res Clin Oncol. 2016 Aug;142(8):1715–26.

7. Gourin CG, Podolsky RH. Racial disparities in patients with head and neck squamous cell carcinoma. Laryngoscope. 2006 Jul;116(7):1093–106.

8. Ragin CC, Langevin SM, Marzouk M, Grandis J, Taioli E. Determinants of head and neck cancer survival by race. Head Neck. 2011 Aug;33(8):1092–8.

9. Mahal BA, Inverso G, Aizer AA, Bruce Donoff R, Chuang S-K. Impact of African–American race on presentation, treatment, and survival of head and neck cancer. Oral Oncology. 2014 Dec;50(12):1177–81.

10. Reitzel LR, Nguyen N, Zafereo ME, Li G, Wei Q, Sturgis EM. Neighborhood deprivation and clinical outcomes among head and neck cancer patients. Health Place. 2012 Jul;18(4):861–8.

11. Molina MA, Cheung MC, Perez EA, Byrne MM, Franceschi D, Moffat FL, et al. African American and poor patients have a dramatically worse prognosis for head and neck cancer: An examination of 20,915 patients. Cancer. 2008 Nov 15;113(10):2797–806.

12. Shin JY, Yoon JK, Shin AK, Diaz AZ. The influence of insurance status on treatment and outcomes in oral cavity cancer: an analysis on 46,373 patients. International Journal of Oral and Maxillofacial Surgery. 2018 Oct;47(10):1250–7.

13. Lenze NR, Farquhar DR, Mazul AL, Masood MM, Zevallos JP. Racial disparities and human papillomavirus status in oropharyngeal cancer: A systematic review and meta-analysis. Head Neck. 2018 Dec 18;

14. Divaris K, Olshan AF, Smith J, Bell ME, Weissler MC, Funkhouser WK, et al. Oral health and risk for head and neck squamous cell carcinoma: the Carolina Head and Neck Cancer Study. Cancer Causes Control. 2010 Apr;21(4):567–75.

15. D'Souza G, Anantharaman D, Gheit T, Abedi-Ardekani B, Beachler DC, Conway DI, et al. Effect of HPV on head and neck cancer patient survival, by region and tumor site: A comparison of 1362 cases across three continents. Oral Oncol. 2016;62:20–7.

16. Chu KP, Habbous S, Kuang Q, Boyd K, Mirshams M, Liu F-F, et al. Socioeconomic status, human papillomavirus, and overall survival in head and neck squamous cell carcinomas in Toronto, Canada. Cancer Epidemiology. 2016 Feb;40:102–12.

17. Stein E, Lenze NR, Yarbrough WG, Hayes DN, Mazul A, Sheth S. Systematic review and meta-analysis of racial survival disparities among oropharyngeal cancer cases by HPV status. Head & Neck. 2020 Jul 7;hed.26328.

18. Faraji F, Rettig EM, Tsai H-L, El Asmar M, Fung N, Eisele DW, et al. The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status. Cancer. 2019 01;125(5):761–9.

19. Pike LRG, Royce TJ, Mahal AR, Kim DW, Hwang WL, Mahal BA, et al. Outcomes of HPV-Associated Squamous Cell Carcinoma of the Head and Neck: Impact of Race and Socioeconomic Status. J Natl Compr Canc Netw. 2020;18(2):177–84.

20. Zevallos JP, Sandulache VC, Hamblin J, Skinner HD, Kramer J, Hartman CM, et al. Impact of race on oropharyngeal squamous cell carcinoma presentation and outcomes among veterans. Head Neck. 2016 Jan;38(1):44–50.

21. Langevin SM, Michaud DS, Eliot M, Peters ES, McClean MD, Kelsey KT. Regular dental visits are associated with earlier stage at diagnosis for oral and pharyngeal cancer. Cancer Causes Control. 2012 Nov;23(11):1821–9.

22. Groome PA, Rohland SL, Hall SF, Irish J, Mackillop WJ, O'Sullivan B. A population-based study of factors associated with early versus late stage oral cavity cancer diagnoses. Oral Oncol. 2011 Jul;47(7):642–7.

23. Gupta B, Kumar N, Johnson NW. Evidence of past dental visits and incidence of head and neck cancers: a systematic review and meta-analysis. Syst Rev. 2019 Feb 4;8(1):43.

24. American Association of Physical Anthropologists. AAPA Statement on Race & Racism [Internet]. Cleveland, Ohio; 2019 Mar [cited 2019 Oct 25]. Available from: https://physanth.org/about/position-statements/aapa-statement-race-and-racism-2019/

25. Wierzbicka M, Szyfter K, Milecki P, Składowski K, Ramlau R. The rationale for HPV-related oropharyngeal cancer de-escalation treatment strategies. Contemp Oncol (Pozn). 2015;19(4):313–22.

Tables and Figures:

Table I: Baseline characteristics in HPV-associated OPSCC stratified by race

Table II: 5-year Overall Survival in HPV-associated OPSCC adjusted for demographics and tumor stage

Table III: 5-year Overall Survival in HPV-associated OPSCC adjusted for demographics, tumor stage, tobacco, and alcohol

Table IV: 5-year Overall Survival in HPV-associated OPSCC adjusted for demographics, stage, tobacco, alcohol and SES

Table I: Baseline characteristics in HPV-associated OPSCC stratified by race

Race	White		Black	
	No.	%	No.	%
Age				
<50 (n=52)	49	34%	3	27%
50 - 65 (n=84)	76	52%	8	73%
>65 (n=21)	21	14%	0	0%
Sex				
Male (n=129)	120	82%	9	82%
Female (n=28)	26	18%	2	18%
Education				
<High school (n=25)	22	15%	3	27%
High school graduate (n=41)	35	24%	6	55%
>high school (n=91)	89	61%	2	18%
Insurance (relative to private)	**Insurance** (relative to private)			
Private (n=93)	90	62%	3	27%
Medicaid/Medicare (n=24)	21	14%	3	27%
None (n=18)	15	10%	3	27%
Other (n=22)	20	14%	2	18%
Income				
>$50,000 (n=75)	75	53%	0	0%
$20,000 - $50,000 (n=49)	45	32%	4	36%
<$20,000 (n=29)	22	15%	7	64%
Rural/Urban Household				
Metropolitan (n=90)	85	81%	5	62%
Micropolitan (n=11)	10	10%	1	12%
Rural (n=12)	10	10%	2	25%
Driving Time to clinic biopsy (1st quartile (Q) as baseline)				

Race	White		Black	
Q1 (n=20)	20	20%	0	0%
Q2 (n=31)	30	30%	1	14%
Q3 (n=27)	26	26%	1	14%
Q4 (n=30)	25	25%	5	71%
Smoking				
<10 Pack Years (n=66)	64	44%	2	18%
>10 Pack Years (n=90)	81	56%	9	82%
Alcohol use				
None (n=25)	24	17%	1	10%
Any (n=130)	121	83%	9	90%
T Stage				
T1 (n=43)	41	28%	2	18%
T2 (n=68)	66	45%	2	18%
T3 (n=24)	20	14%	4	36%
T4 (n=22)	19	13%	3	27%
Early (1-2) vs. Advanced T Stage (3-4)				
Early (n=111)	107	73%	4	36%
Advanced (n=46)	39	27%	7	64%
N stage				
N0 (n=29)	26	18%	3	27%
N1 (n=93)	88	60%	5	45%
N2 (n=20)	18	12%	2	18%
N3 (n=15)	14	10%	1	9%
M Stage				
M0 (n=155)	144	99%	11	100
M1 (n=2)	2	1%	0	0%
Treatment Category				
Chemotherapy Only (n=1)	1	1%	0	0%
Radiation Only (n=11)	10	7%	1	9%
Surgery Only (n=7)	7	5%	0	0%
Concurrent chemoradiation (n=61)	54	37%	7	64%
Surgery + adjuvant radiation (n=36)	34	23%	2	18%
Surgery + adjuvant chemoradiation (n=41)	40	27%	1	9%
Number of Treatment Modalities				
1 (n=19)	18	12%	1	9%
2 (n=97)	88	60%	9	82%
3 (n=41)	40	27%	1	9%

Table II: 5-year Overall Survival in HPV-associated OPSCC adjusted for demographics and tumor stage

	Adjustment with Demographics and Stage*	**Adjustment with Demogr**
	Hazard Ratio	95% CI
Black (vs. white)	4.6	1.8 - 12.0
Age Category (Relative to < 50)		
50-65	0.8	0.4 - 1.7
65+	1.3	0.5 - 3.5
Female sex (relative to male)	0.8	0.3 - 2.0
T Stage (relative to T1)		

	Adjustment with Demographics and Stage*	Adjustment with Demogr
T2	0.7	0.3 - 1.8
T3	1.6	0.6 - 4.2
T4	2.5	1.0 - 6.3
Nodal disease (relative to N0)	1.7	0.7 - 4.2
Distant Metastases (relative to M0)	5.2	0.7 - 41.7

*Model adjusted for race, age, sex, T stage, nodal disease, and distant metastases

Table III: 5-year Overall Survival in HPV-associated OPSCC adjusted for demographics, tumor stage, tobacco, and alcohol

	Addition of tobacco and alcohol use*	Addition of tobacco and alcohol
	Hazard Ratio	95% CI
Black (vs. white)	4.1	1.5 - 11.4
Age Category (Relative to < 50)		
50-65	0.9	0.4 - 2.0
65+	1.4	0.5 - 3.9
Female sex (relative to male)	0.8	0.3 - 2.0
T Stage (relative to T1)		
T2	0.8	0.3 - 1.9
T3	1.5	0.6 - 4.0
T4	2.5	1.0 - 6.3
Nodal disease (relative to N0)	1.7	0.7 - 4.2
Distant Metastases (relative to M0)	4.6	0.6 - 36.5
Smoking (> 10 pack-years)	1.0	0.5 - 2.2
Alcohol use (any vs. none)	1.6	0.5 - 4.6

*Model adjusted for race, age, sex, T stage, nodal disease, distant metastases, smoking, and alcohol use

Table IV: 5-year Overall Survival in HPV-associated OPSCC adjusted for demographics, stage, tobacco, alcohol and SES

	Addition of SES Variables*	Addition of SES Variables*	Additi
	Hazard Ratio	95% CI	P-Valu
Black (vs. white)	3.4	1.1 - 10.1	0.028
Age Category (Relative to < 50)			
50-65	0.8	0.4 - 1.9	0.698
65+	1.2	0.4 - 3.8	0.817
Female sex (relative to male)	0.5	0.2 - 1.5	0.223
T Stage (relative to T1)			
T2	1.0	0.4 - 2.6	0.985
T3	2.2	0.8 - 6.3	0.131
T4	2.4	0.9 - 6.3	0.081
Nodal disease (relative to N0)	1.2	0.5 - 3.1	0.705
Distant Metastases (relative to M0)	11.4	1.2 - 103.4	0.031
Smoking (> 10 pack-years)	0.6	0.3 - 1.4	0.221
Alcohol use (any vs. none)	1.3	0.4 - 4.0	0.672
Education (relative to less than high school)			

	Addition of SES Variables*	**Addition of SES Variables***	**Additi**
High school graduate	1.0	0.3 - 3.0	0.973
Additional education past high school	0.8	0.3 - 2.1	0.600
Insurance (relative to private insurance)			
Medicaid/Medicare	4.3	1.2 - 15.9	0.028
None	3.0	0.9 - 9.8	0.071
Other	2.5	0.8 - 7.6	0.118
Income (relative to $>$ 50 K)			
Income \$20,000 - \$50,000	0.8	0.3 - 2.2	0.683
Income $<$ \$20,000	1.9	0.5 - 6.6	0.313

*Model adjusted for race, age, sex, T stage, nodal disease, distant metastases, smoking, alcohol use, education, insurance status, and income