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Race as a social construct in head and neck cancer outcomes

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Abstract

Objective—We examined ancestry informative markers (AIMs) to estimate the amount of population admixture and control for this heterogeneity for stage and survival in a primary head and neck squamous carcinoma (HNSCC) cohort.

Study Design—Historical cohort study

Setting—Integrated health care system.

Subjects—The cohort comprised 358 HNSCC who self-reported race as Caucasian American (CA), African American (AA), or Other.

Methods—DNA was interrogated for West African (WA) and European genetic background by genotyping AIMs. Associations of race (self-report or WA ancestry) with stage and survival were analyzed using logistic regression and Cox regression modeling. A subgroup analysis for diagnosis (late versus early stage) and survival (time to death) and WA ancestry was performed for self-reported AAs.

Results—There were significant associations between stage and self-reported race ($p=0.04$ {univariate}) and with cancer site (OP: $p=0.014$; HP: $p=0.026$ {multivariate}). For prognosis, there were significant multivariate associations between stage ($p=0.002$), age (>65 years, $p<.001$), and cancer site (HP: $p<0.001$; OC: $p=0.049$), but self-reported race was not associated with overall survival. Interestingly, there was no association with degree of WA ancestry and stage or survival. In the sub-group analysis of genetic ancestry among self-reported AAs, cancer site remained an independent risk factor for stage (other site: $p=0.026$) and survival (OP: $p=0.036$). Late stage persisted as an independent variable for poor survival ($p=0.032$).

Conclusions—Stratification within AAs by WA ancestry revealed no correlation with stage or survival suggesting that HNSCC outcomes with race may be due to social/ behavior factors rather than biological differences.

Introduction

Cancer rates of the head and neck are traditionally linked to public health issues. In the United States ¹, approximately 35,720 new cases of head and neck squamous cell carcinoma

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(HNSCC) are expected in 2009 with an estimated 7,600 deaths². . Despite considerable efforts, the 5-year survival rate for HNSCC has not changed significantly. In addition to tobacco and alcohol^{3,4}, epidemiological and laboratory evidence now warrant the conclusion that, the human papilloma virus (HPV) is a causative agent for some HNSCC^{5,6} and an independent risk factor for oropharyngeal HNSCC⁷⁻⁹. The biologic significance of HPV as another independent risk factor, is underscored by the improved prognosis for patients with HPV-positive (+ve) HNSCC relative to HPV-negative (-ve) HNSCC^{6,7,10,11}, due in part to a better therapeutic response to chemoradiotherapy¹².

HNSCC remains a disfiguring disease with a high mortality rate and disparate unfavorable diagnosis and prognosis outcomes for African Americans (AA)^{13,14}. There is no consensus on the causes of the differences in the higher incidence of and the mortality from HNSCC for AA when compared to Caucasian Americans (CA)¹⁵, but they may include differences in access to care, stage at diagnosis, insurance status, attitudes of health providers, as well as HPV infection status¹⁶. A recent study found that poorer survival outcomes for AA versus CA with oropharyngeal tumors was attributable to racial differences in the prevalence of HPV-positive tumors. HPV positivity was higher in CA (34%) as compared to 4% in AA and HPV-negative AA and CA patients had similar survival outcomes¹⁶.

Recent genetic association studies have recommended adjusting for population stratification as a strategy for minimizing spurious association^{17,18}. Racial categories are usually based on self-reports, and, although this standard is appropriate for studying race and ethnicity as social phenomena, it does not allow for the critical scientific investigation of their biological accuracy.

Over the past ten years, many groups have developed and characterized sets of single nucleotide polymorphism (SNP) markers that can distinguish genetic ancestry among major ethnic groups (called ancestry informative markers [AIMs])¹⁹. These studies also showed the ability of small sets of AIMs to separate a variety of self-identified subjects of European, Amerindian, East Asian, and West African ancestry. Using these SNPs many are able to provide admixture information for West African, European and Amerindian admixed populations, and perform structured association testing in the context of mixed or admixed population groups²⁰⁻²³.

Using genetic markers to probe ancestry in cancer studies affords increased statistical power permitting inclusion of biologically ill-defined notions of race or ethnicity as a continuous variable rather than a single choice²⁴. It is cautioned however, that race is not equal to genetics and that genetic markers don't define specific races; but are proxies for shared ancestry²⁴. Therefore, the finding of racial differences is simply a first clue for follow-up studies to disentangle whether the differences have biological or environment underpinnings²⁴.

Given the heterogeneity in the AA population, for evaluation of health disparities, genetic ancestry rather than self-reported racial designation can reduce potential confounding effects due to population admixture. In this study, we examined diagnosis (late versus early stage) and prognosis (over all survival) outcomes for AAs with HNSCC based on self-reported race and genetic markers of West African ancestry based on a panel of 100 previously validated ancestry informative markers to estimate and control for differences in genetic background.

Material and Methods

Study Population

The study cohort of 358 primary HNSCC was drawn from a multi-ethnic (37% African American), primary care patient population. Cases were diagnosed by surgical biopsies in the Henry Ford Health System between 1988 and 2005, and followed from 4-21 years (through August of 2009)²⁵. Eligibility into the study required that patients have tumor DNA available for the examination of the molecular characteristics of the tumor.

Self-reported race as Caucasian American (CA), African American (AA), or Other was obtained from the Henry Ford Health System Corporate Data Store and/or the medical record. This study was approved by the Henry Ford Health System Institutional Review Board (IRB#2218).

Genetic markers of ancestry

DNA from paraffin-embedded tissue blocks was genotyped using 100 carefully selected ancestry informative markers for all samples. These autosomal markers have previously been used to extract continental ancestry information in AAs and genotyped using published methods^{26,27}

Variables of Interest

Of particular interest are associations between variables reflecting “race” (either self-report or the West African genetic ancestry (0-100%) based on AIMs, and as outcomes, stage at diagnosis (**AJCC**) and survival time.

Statistical Considerations

Individual genetic ancestry was determined for each person using 100 ancestry informative markers for West African (WA) and European genetic ancestry²⁷⁻³⁰. Individual ancestry was estimated from the genotype data using the Bayesian Markov Chain-Monte Carlo method implemented in the program STRUCTURE 2.1³¹. STRUCTURE 2.1 was run under the admixture model using prior population information and independent allele frequencies. We ran the Bayesian Markov Chain-Monte Carlo method using K = 2 parental populations and a burn-in length of 30,000 for 70,000 repetitions²⁷. Each participant was then scored from 0% to 100% on individual ancestry estimates of WA ancestry.

The associations with stage and with time to death were assessed using logistic and Cox regression models, respectively, for inferences about the relationship of gender, age (3 categories: 50, >50<65, >65), smoking (never smokers, past smokers, current smokers), marital status, race, genetic race (continuous variable), and tumor site (5 sites: larynx, oral cavity, oropharynx (OP), hypopharynx (HP), and site as other (lip-external, nose maxilla, nasopharynx, sinonasal). Associations with self-reported race were tested with t-tests (or Wilcoxon rank test tests) and with chi square tests. Subgroup analyses for diagnosis (late versus early stage) and survival (time to death) were performed for African-Americans with WA genetic ancestry values >15%.

Results

Final Cohort

Of the 358 primary HNSCC, 13 were subsequently found to not meet eligibility criteria (not primary HNSCC), leaving 345 for analysis. Based upon “self-report” 136 were classified by as AA, 204 as CA and 5 were of “Other” race. A summary of patient characteristics by race

is shown in **Table 1**. The characteristics of the 321 for whom stage at diagnosis is available are shown by stage (early or late) in **Table 2**.

Ancestry informative markers (AIMs)

The distributions of West African and European genetic ancestry for self-reported CA, AA, and Other are shown in **Figures 1 and 2**, respectively. The range of West African genetic ancestry for our entire cohort was 0.004-0.992. Given misclassifications and the historical classification of AA in the US we included all African Americans with 15% or more West African ancestry in our statistical analyses³². Four of 136 subjects who self-reported African-American race had WA genetic ancestry under 15% (0.4%, 1.5%, 5.9%, and 6.8%), leaving 132 for sub-analysis of genetic race.

Results for “self reported” subjects analyses

The associations with stage shown in **Table 2** were assessed using logistic regression models. The odds ratios and p-value for these models are shown in **Table 3**. There were significant univariate associations for site ($p<0.001$), and (self-reported) race ($p=0.04$). In the multivariate model, site as OP (OR=2.72, 95% CI 1.22, 6.06, $p=0.014$) and HP (OR=3.36, 95% CI 1.16, 9.76, $p=0.026$) remained an independent factor for late stage. However, the adjusted odds ratio for self-reported African-American race 1.46 ($p=0.163$) in the multivariate analysis was reduced from 1.64 ($p=0.040$) in the univariate analysis, without statistical significance.

Associations with time to death using Cox regression models are shown in **Table 4**. There were significant univariate associations with stage ($p=0.002$), age ($p<0.001$), and cancer site as ($p<0.001$). Self-reported race was not associated with time to death ($p=0.386$). In the multivariable model, the overall p-value for site was not quite significant ($p=0.007$), however, three of the individual site-to-site comparisons versus larynx had hazard ratios large enough to be clinically important (OP: HR=2.24, $p=0.036$, HP: HR=1.92, $p=0.054$, and OC: HR=1.81, $p=0.074$). Late stage (HR=1.63 95% CI 1.20, 2.22, $p=0.002$), age > 65 (HR=2.28, 95% CI 1.51, 3.46, $p<0.001$), and site as OC and HP (OC: HR=1.48, 95% CI 1.00, 2.19, $p=0.049$; HP: HR=2.35, 95% CI=1.46, 3.76, $p<0.001$) were independent variables for poor prognosis.

Results for AA subgroup analyses using WA genetic ancestry

The subgroup logistic regression odds ratio estimates for late vs. early stage are shown in **Table 5**. Gender was a significant variable (univariate analysis), with male AA more likely to present with late stage than female AA (OR 2.35, 95% CI 1.04, 5.30, $p=0.039$) without statistical significance in the multivariate model ($p=0.070$). Cancer site in the univariate analysis ($p=0.118$) emerged as an independent variable in the multivariable model for site as other (OR=0.12, 95% CI 0.02-0.78, $p=0.026$), indicating a reduced risk of late stage for site as other when compared to larynx.

Hazard ratios from Cox survival models are shown in **Table 6**. Significant univariate risk factors, late stage ($p=0.02$) and site ($p=0.002$), remained in the multivariate model. Self-reported AAs with 15% or more West African ancestry with site in the oropharynx cancer was an independent predictor of poorer survival (OR=2.24, 95% CI 1.06, 4.76, $p=0.036$). Site as HP and OC had hazard ratios large enough to be clinically important (HP: HR=1.92, $p=0.054$, and OC: HR=1.81, $p=0.074$). Late stage persisted as an independent variable for poor survival (OR=1.84, 95% CI=1.06, 3.22, $p=0.032$).

There is little evidence of an association between WA genetic ancestry and mortality in either univariate (HR=0.92, $p=0.878$) or multivariable (HR=1.02, $p=0.974$) analysis.

However, the hazard ratio confidence intervals were wide, with large upper bounds (2.59 and 3.06, respectively), so an association with WA genetic ancestry cannot be definitively ruled out.

Discussion

We found no association between WA genetic ancestry and diagnosis (early versus late stage) and prognosis (overall survival) outcomes among HNSCC patients who identified themselves as African American. The rationale for the cut-off of >15% WA genetic ancestry includes the misclassification of study subjects³² and the historical classification schema of the one-drop rule to denote AAs. The wide range of West African genetic ancestry for our cohort (39% self-reported AAs), illustrated in **Figure 1**, is similar to previous findings by us and others^{27,28,33}. Only 5% of self-reported AA had over 95% West African ancestry with 27% having less than 60% WA ancestry. The latter contrasted with more than 48% of Whites with over 95% European American ancestry. Our figures highlight that variation within so-called “racial groups” deconstruct traditional racial categorization³⁴.

The lack of association with HNSCC outcomes for AA based on genetic ancestry contrasted with that of race as self-classified AA. For our primary HNSCC cohort, self-reported AA ethnicity revealed a univariate risk factor for late stage (OR=1.64, $p=0.040$), but in the **multivariable** model it had a reduced adjusted odds ratio (1.46 $p=0.163$). Thus our data may be consistent with a reduced, but still clinically important association between AA ethnicity and stage. For overall survival, neither self-report nor genetic ancestry was associated with mortality.

For WA genetic ancestry and self-report as AA, cancer site remained a uniformly independent risk factor for both late stage and survival. HNSCC, often treated as a single entity, is in fact a heterogeneous group of tumors and outcome of both diagnosis and prognosis is strongly influenced by the anatomic site of the primary tumor^{25,35}. In our study, among all HNSCC cohort patients, influence of location of the primary tumor on late stage diagnosis, with larynx as the reference site was the highest for cancer site as HP, followed by OP. Both OC and HP (and not OP) were predictors of poorer survival.

When we stratified the AA group by WA genetic ancestry, site as other had a reduced risk of late stage when compared to larynx. Interestingly, for survival, site as OP was independently associated with poorer survival (OP: HR=2.24, $p=0.036$) and may reflect a likely lower prevalence of HPV infection among AAs with oropharyngeal cancer¹⁶. The Settle et al. 2009¹⁶ study found that poorer survival outcomes for AA versus CA with oropharyngeal tumors were attributable to racial differences in the prevalence of HPV-positive tumors; HPV prevalence in AA was significantly lower than CA with similar survival outcomes for HPV-negative AA and CA patients. Our data on site concur with previously reported HNSCC diagnosis and prognosis outcomes from our group²⁵.

There is abundant epidemiological evidence that self-identified race/ethnicity is associated with differences in cancer incidence and mortality. Some examples include prostate cancer³⁶ and early-onset breast cancer³⁷. In analyses by race and ethnicity³⁸, AA men and women have 40% and 18% higher death rates from all cancers combined than CA men and women, respectively.

Increase in the incidence of cancer of the head and neck among minority groups³⁹ complement the 1998 NCDB Report on Cancer of the Head and Neck¹³, which showed a 10.0% proportionate increase in AA (from 8.0% to 8.8%) and a 21.4% proportionate increase in Hispanic patients (from 2.8% to 3.4%). The disproportionate increase in the

number of head and neck mucosal cancers in AA as compared to CA is supported by other studies. In HNSCC, racial disparity also extended to disease stage with a greater proportion of advanced-stage cancers (stages III and IV) occurring among lower-income groups, the geographic region of the Southeast, and AA^{13,14}.

Variance in genetic background of study subjects is becoming more of an issue with the increasing number of genetic association studies on complex disease. Differences in genetic background among study individuals may impact the power and reliability of genetic association studies^{24,32,40}. Methods to detect and control for differences in ancestry in genetic association studies utilize AIMs. AIMs have high utility in biomedical research because they can be used to accurately measure individual ancestry (IA) of subjects enrolled in studies. Most importantly these IA estimates can be used to control for heterogeneity in genetic studies in recently admixed populations like African Americans and Hispanic Americans.

We believe that this is the first report to look at diagnosis and prognosis outcomes in HNSCC based on genetic race. In this study, only self-reported race was associated with stage. Stratification within the AA group by West African genetic ancestry revealed no correlation with stage or survival pointing to the causes of HNSCC disparities as likely due to social rather than biological factors. These findings have clinical relevance for evaluation of health disparities. Given the heterogeneity in the AA population, genetic ancestry rather than self-reported racial designation can reduce potential confounding effects due to population admixture and control for heterogeneity, bringing into sharper focus, ethnic differences for cancer risk and prognosis in HNSCC.

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References

1. Edwards BK, Brown ML, Wingo PA, et al. Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. *J Natl Cancer Inst.* 2005; 97:1407-27. [PubMed: 16204691]
2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2009. *CA Cancer J Clin.* 2009; 59:225-49. [PubMed: 19474385]
3. Hashibe M, Brennan P, Benhamou S, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *J Natl Cancer Inst.* 2007; 99:777-89. [PubMed: 17505073]
4. Hashibe M, Boffetta P, Zaridze D, et al. Contribution of tobacco and alcohol to the high rates of squamous cell carcinoma of the supraglottis and glottis in Central Europe. *Am J Epidemiol.* 2007; 165:814-20. [PubMed: 17244634]
5. Gillison ML, Lowy DR. A causal role for human papillomavirus in head and neck cancer. *Lancet.* 2004; 363:1488-9. [PubMed: 15135592]
6. Gillison ML, Koch WM, Capone RB, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. *J Natl Cancer Inst.* 2000; 92:709-20. [PubMed: 10793107]
7. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med.* 2010; 363:24-35. [PubMed: 20530316]
8. D'Souza G, Kreimer AR, Viscidi R, et al. Case-control study of human papillomavirus and oropharyngeal cancer. *N Engl J Med.* 2007; 356:1944-56. [PubMed: 17494927]

9. Chen AA, Marsit CJ, Christensen BC, et al. Genetic variation in the vitamin C transporter, SLC23A2, modifies the risk of HPV16-associated head and neck cancer. *Carcinogenesis*. 2009; 30:977–81. [PubMed: 19346260]
10. Schwartz SRYB, McDougall JK, Daling JR, Schwartz SM. Human papillomavirus infection and survival in oral squamous cell cancer: a population-based study. *Otolaryngol Head Neck Surg*. 2001; 125:1–9. [PubMed: 11458206]
11. Weinberger PMYZ, Haffty BG, Kowalski D, Harigopal M, Brandsma J, Sasaki C, Joe J, Camp RL, Rimm DL, Psyrri A. Molecular classification identifies a subset of human papillomavirus—associated oropharyngeal cancers with favorable prognosis. *J Clin Oncol*. 2006; 24:736–47. [PubMed: 16401683]
12. Fakhry C, Westra WH, Li S, et al. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst*. 2008; 100:261–9. [PubMed: 18270337]
13. Hoffman HT, Karnell LH, Funk GF, et al. The National Cancer Data Base report on cancer of the head and neck. *Arch Otolaryngol Head Neck Surg*. 1998; 124:951–62. [PubMed: 9738803]
14. Shavers VL, Harlan LC, Winn D, et al. Racial/ethnic patterns of care for cancers of the oral cavity, pharynx, larynx, sinuses, and salivary glands. *Cancer Metastasis Rev*. 2003; 22:25–38. [PubMed: 12716034]
15. Ryerson AB, Peters ES, Coughlin SS, et al. Burden of potentially human papillomavirus-associated cancers of the oropharynx and oral cavity in the US, 1998–2003. *Cancer*. 2008; 113:2901–9. [PubMed: 18980273]
16. Settle K, Posner MR, Schumaker LM, et al. Racial survival disparity in head and neck cancer results from low prevalence of human papillomavirus infection in black oropharyngeal cancer patients. *Cancer Prev Res (Phila Pa)*. 2009; 2:776–81.
17. Kittles RA, Weiss KM. Race, ancestry, and genes: implications for defining disease risk. *Annu Rev Genomics Hum Genet*. 2003; 4:33–67. [PubMed: 14527296]
18. Elbein SC, Das SK, Hallman DM, et al. Genome-wide linkage and admixture mapping of type 2 diabetes in African American families from the American Diabetes Association GENNID (Genetics of NIDDM) Study Cohort. *Diabetes*. 2009; 58:268–74. [PubMed: 18840782]
19. Seldin MF. Admixture mapping as a tool in gene discovery. *Curr Opin Genet Dev*. 2007; 17:177–81. [PubMed: 17466511]
20. Collins-Schramm HE, Chima B, Operario DJ, et al. Markers informative for ancestry demonstrate consistent megabase-length linkage disequilibrium in the African American population. *Hum Genet*. 2003; 113:211–9. [PubMed: 12783300]
21. Collins-Schramm HE, Phillips CM, Operario DJ, et al. Ethnic-difference markers for use in mapping by admixture linkage disequilibrium. *Am J Hum Genet*. 2002; 70:737–50. [PubMed: 11845411]
22. Kosoy R, Nassir R, Tian C, et al. Ancestry informative marker sets for determining continental origin and admixture proportions in common populations in America. *Hum Mutat*. 2009; 30:69–78. [PubMed: 18683858]
23. Seldin MF, Morii T, Collins-Schramm HE, et al. Putative ancestral origins of chromosomal segments in individual african americans: implications for admixture mapping. *Genome Res*. 2004; 14:1076–84. [PubMed: 15140829]
24. Beckman M. The race for ancestral genetics in clinical trials. *J Natl Cancer Inst*. 2006; 98:1270–1. [PubMed: 16985243]
25. Sethi S, Lu M, Kapke A, et al. Patient and tumor factors at diagnosis in a multi-ethnic primary head and neck squamous cell carcinoma cohort. *J Surg Oncol*. 2009; 99:104–8. [PubMed: 19034903]
26. Tian C, Hinds DA, Shigeta R, et al. A genomewide single-nucleotide-polymorphism panel with high ancestry information for African American admixture mapping. *Am J Hum Genet*. 2006; 79:640–9. [PubMed: 16960800]
27. Giri VN, Eggleston B, Ruth K, et al. Race, genetic West African ancestry, and prostate cancer prediction by prostate-specific antigen in prospectively screened high-risk men. *Cancer Prev Res (Phila Pa)*. 2009; 2:244–50.

28. Hooker S, Hernandez W, Chen H, et al. Replication of prostate cancer risk loci on 8q24, 11q13, 17q12, 19q33, and Xp11 in African Americans. *Prostate*. 2010; 70:270–5. [PubMed: 19902474]
29. Kupfer SS, Anderson JR, Hooker S, et al. Genetic Heterogeneity in Colorectal Cancer Associations in Americans of African vs. European Descent. *Gastroenterology*. 2010
30. Kupfer SS, Torres JB, Hooker S, et al. Novel single nucleotide polymorphism associations with colorectal cancer on chromosome 8q24 in African and European Americans. *Carcinogenesis*. 2009; 30:1353–7. [PubMed: 19520795]
31. Falush D, Stephens M, Pritchard JK. Inference of population structure using multilocus genotype data: linked loci and correlated allele frequencies. *Genetics*. 2003; 164:1567–87. [PubMed: 12930761]
32. Torres JB, Kittles RA. The relationship between “race” and genetics in biomedical research. *Curr Hypertens Rep*. 2007; 9:196–201. [PubMed: 17519124]
33. Robbins C, Torres JB, Hooker S, et al. Confirmation study of prostate cancer risk variants at 8q24 in African Americans identifies a novel risk locus. *Genome Res*. 2007; 17:1717–22. [PubMed: 17978284]
34. Keita SO, Kittles RA, Royal CD, et al. Conceptualizing human variation. *Nat Genet*. 2004; 36:S17–20. [PubMed: 15507998]
35. Medow MA, Weed HG, Schuller DE. Simple predictors of survival in head and neck squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg*. 2002; 128:1282–6. [PubMed: 12431171]
36. Weir HK, Thun MJ, Hankey BF, et al. Annual report to the nation on the status of cancer, 1975-2000, featuring the uses of surveillance data for cancer prevention and control. *J Natl Cancer Inst*. 2003; 95:1276–99. [PubMed: 12953083]
37. O'Malley CD, Le GM, Glaser SL, et al. Socioeconomic status and breast carcinoma survival in four racial/ethnic groups: a population-based study. *Cancer*. 2003; 97:1303–11. [PubMed: 12599239]
38. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2006. *CA Cancer J Clin*. 2006; 56:106–30. [PubMed: 16514137]
39. Kosary, CLRL.; Miller, BA.; Hankey, BF.; Harras, A.; Edwards, BK. SEER Cancer Statistics Review, 1973-1992: Tables and Graphs. National Cancer Institute; Bethesda, Md: 1995. NIH publication 96-2789 1995
40. Aldrich MC, Selvin S, Hansen HM, et al. Comparison of statistical methods for estimating genetic admixture in a lung cancer study of African Americans and Latinos. *Am J Epidemiol*. 2008; 168:1035–46. [PubMed: 18791191]

Distribution of West African Ancestry Percentages by Self-Report Group
N=345

Figures 1.

The percentage of African ancestry as estimated by means of genetic markers in the HNSCC cohort is shown in Figure 1

Distribution of European Ancestry Percentages by Self-Report Group N=345

Figure 2.

The percentage of European ancestry as estimated by means of genetic markers in the HNSCC cohort is shown in Figure 2

Table 1

Summary by Self-Reported Race

Variable	Response	White	Black	Other
		(N=204)	(N=136)	(N=5)
Gender	Male	154 (75%)	99 (73%)	4 (80%)
	Female	50 (25%)	37 (27%)	1 (20%)
age category	c) >65	96 (47%)	48 (35%)	3 (60%)
	b) 51-65	77 (38%)	57 (42%)	1 (20%)
	a) ≤50	31 (15%)	31 (23%)	1 (20%)
married	0-No	58 (30%)	66 (51%)	1 (20%)
	1-Yes	136 (70%)	63 (49%)	4 (80%)
smokecategory	0:Never Smk	30 (15%)	12 (9%)	1 (20%)
	1:Past Smk	79 (40%)	39 (30%)	2 (40%)
	2:Current Smk 1-15 py	6 (3%)	17 (13%)	0 (0%)
	3:Current Smk 15-25 py	37 (19%)	42 (33%)	0 (0%)
	4:Current Smk 25-35 py	18 (9%)	10 (8%)	0 (0%)
	5:Current Smk >35 py	28 (14%)	8 (6%)	2 (40%)
site groups	Oral cavity (OC)	55 (27%)	26 (19%)	2 (40%)
	Oropharynx (OP)	35 (17%)	24 (18%)	0 (0%)
	Hypopharynx (HP)	16 (8%)	18 (13%)	2 (40%)
	Larynx	67 (33%)	51 (38%)	1 (20%)
	* Other	31 (15%)	17 (13%)	0 (0%)
stage groups	Early	80 (39%)	41 (30%)	1 (20%)
	Late	106 (52%)	89 (65%)	4 (80%)
	Unknown	18 (9%)	6 (4%)	0 (0%)
race-BlackWhite	1	204 (100%)	0 (0%)	0 (%)
	2	0 (0%)	136 (100%)	0 (%)
%European	N Mean ± SD (Min - Max)	204 0.85 ± 0.21 (0.1 - 1.0)	136 0.26 ± 0.22 (0.0 - 1.0)	5 0.73 ± 0.35 (0.1 - 1.0)
%WestAfrican	N Mean ± SD (Min - Max)	204 0.12 ± 0.20 (0.0 - 0.8)	136 0.70 ± 0.22 (0.0 - 1.0)	5 0.06 ± 0.07 (0.0 - 0.2)

py=pack years

* lip-external, nose maxilla, nasopharynx, sinonasal, smk=smoker, Min= minimum, Max=maximum

Table 2

Summary by Stage

Variable	Response	Early	Late
		(N=122)	(N=199)
Gender	Male	84 (69%)	153 (77%)
	Female	38 (31%)	46 (23%)
age category	c) >65	61 (50%)	73 (37%)
	b) 51-65	40 (33%)	85 (43%)
	a) <=50	21 (17%)	41 (21%)
married	0-No	40 (35%)	77 (41%)
	1-Yes	74 (65%)	113 (59%)
smoke (smk) category	0:Never Smk	15 (13%)	25 (13%)
	1:Past Smk	46 (39%)	62 (33%)
	2:Current Smk 1-15 py	9 (8%)	13 (7%)
	3:Current Smk 15-25 py	30 (25%)	47 (25%)
	4:Current Smk 25-35 py	8 (7%)	19 (10%)
	5:Current Smk >35 py	10 (8%)	24 (13%)
site group	Oral cavity (OC)	30 (25%)	46 (23%)
	Oropharynx (OP)	12 (10%)	45 (23%)
	Hypopharynx (HP)	5 (4%)	27 (14%)
	Larynx	55 (45%)	61 (31%)
	* Other	20 (16%)	20 (10%)
race group	White	80 (66%)	106 (53%)
	Black	41 (34%)	89 (45%)
	Other	1 (1%)	4 (2%)

py=pack years

* lip-external, nose maxilla, nasopharynx, sinonasal, smk=smoker

Table 3

Logistic regression for Late stage (versus Early)

N	Effect	Univariate		Multivariate (N=292)		
		Odds Ratio and C.I.	p-value	Odds Ratio and C.I.	p-value	Overall p-value
321	Gender: Male vs Female	1.50 (0.91,2.49)	0.113	0.70 (0.39,1.26)	0.237	0.234
321	Age 51-65 vs <=50	1.09 (0.57,2.08)	0.797	1.26 (0.61,2.59)	0.532	0.242
	65 vs <=50	0.61 (0.33,1.15)	0.126	0.77 (0.38,1.54)	0.454	
304	Married vs unmarried	0.79 (0.49,1.28)	0.346	0.83 (0.48,1.43)	0.454	0.485
308	Smoking: Past vs Never	0.81 (0.38,1.70)	0.576	0.62 (0.26,1.45)	0.271	0.429
	Current vs Never	1.08 (0.53,2.22)	0.825	0.83 (0.36,1.92)	0.660	
321	Site: OC vs Larynx	1.38 (0.77,2.49)	0.279	1.25 (0.66,2.38)	0.495	0.017
	OP vs Larynx	3.38 (1.62,7.04)	0.001	2.72 (1.22,6.06)	0.014	
	HP vs Larynx	4.87(1.75, 13.5)	0.002	3.36 (1.16, 9.76)	0.026	
	* Other vs Larynx	0.90 (0.44,1.85)	0.778	0.78 (0.35,1.73)	0.537	
321	Race: Black vs White	1.64 (1.02,2.62)	0.04	1.48 (0.86,2.50)	0.163	0.310
	Other vs White	3.02 (0.33,27.5)	0.327	2.36 (0.25,22.7)	0.457	

* lip-external, nose maxilla, nasopharynx, sinonasal

Table 4

Time to Death-Survival Estimates

Variable/Category	Univariate			Multivariable (N=292)		
	N	HR_CI	0.906	Overall p_value	HR_CI	p_value
Gender: Male vs female	345	0.98 (0.73,1.31)	<.001	0.895	0.98 (0.70,1.37)	0.904
Age: 51-65 vs <=50	345	1.23 (0.82,1.85)		<.001	1.05 (0.68,1.63)	0.826
>65 vs <=50		2.14 (1.45,3.16)	0.002		2.28 (1.51,3.46)	<.001
Stage: Late vs Early	321	1.55 (1.17,2.05)	0.507	0.002	1.63 (1.20,2.22)	0.002
Married vs unmarried	328	0.85 (0.65,1.12)	0.119	0.247	0.92 (0.68,1.24)	0.580
Smoking: Past vs Never	331	1.35 (0.86,2.11)		0.367	1.30 (0.77,2.19)	0.325
Current vs Never		1.35 (0.88,2.08)	0.009		1.63 (0.98,2.72)	0.060
Site: OC vs Larynx	345	1.62 (1.15,2.28)		<0.001	1.48 (1.00,2.19)	0.049
OP vs Larynx		1.25 (0.85,1.85)			1.38 (0.87,2.17)	0.172
HP vs Larynx		2.62 (1.73,3.97)	0.977		2.35 (1.46,3.76)	<0.001
* Other vs Larynx		1.22 (0.81,1.85)			1.53 (0.95,2.47)	0.083
Race: Black vs White	345	1.12 (0.86,1.46)	0.386	0.573	1.03 (0.76,1.40)	0.841
Other vs White		1.49 (0.47,4.68)	0.463		1.07 (0.33,3.48)	0.916

* lip-external, nose maxilla, nasopharynx, sinonasal

Table 5

Logistic Regression Statistics for Late Stage (Versus Early)

Restricted to African-Americans with a West African AIMS Score $\geq 15\%$

N	Effect	Univariate			Multivariable (N=112)		
		Odds Ratio and C.I.	p-value	Overall p-value	Odds Ratio and C.I.	p-value	Overall p-value
126	Gender Male vs Female	2.35 (1.04,5.30)	0.039	0.039	2.41 (0.93,6.24)	0.070	0.070
126	Age 51-65 vs ≤ 50	0.74 (0.26,2.07)	0.566	0.149	0.51 (0.15,1.73)	0.282	0.224
	>65 vs ≤ 50	0.39 (0.14,1.10)	0.075		0.33 (0.09,1.16)	0.084	
119	Married vs unmarried	0.61 (0.28,1.33)	0.216	0.216	0.50 (0.19,1.31)	0.158	0.151
118	Smoking: Past vs Never	0.51 (0.09,2.80)	0.435	0.681	0.11 (0.01,1.23)	0.074	0.159
	Current vs: Never	0.66 (0.13,3.45)	0.625		0.08 (0.01,1.02)	0.052	
126	Site OC vs Larynx	3.15 (0.93,10.7)	0.065	0.118	3.25 (0.78,13.6)	0.107	0.059
	Site OP vs Larynx	1.70 (0.57,5.104)	0.344		0.91 (0.24,3.41)	0.885	
	Site HP vs Larynx	1.56 (0.48,5.10)	0.462		0.98 (0.25,3.82)	0.979	
	Site * Other vs Larynx	0.43 (0.12,1.55)	0.197		0.12 (0.02,0.78)	0.026	
126	WestAfrican	0.98 (0.13,7.25)	0.984		1.14 (0.10,12.3)	0.916	0.922

* lip-external, nose maxilla, nasopharynx, sinonasal

Table 6

Time to Death - Survival Estimates: African Americans WA=>15%

Variable/Category	Univariate			Multivariable (N=112)		
	N	HR_CI	p_value	Overall p_value	HR_CI	p_value
Gender: Male vs female	132	1.22 (0.76,1.96)	0.405	0.405	1.11 (0.65,1.90)	0.704
Age: 51-65	132	0.90 (0.53,1.53)	0.693	0.884	0.86 (0.48,1.54)	0.618
>65		0.88 (0.51,1.50)	0.63		1.19 (0.64,2.21)	0.618
Stage: Late vs Early	126	1.74 (1.09,2.76)	0.02	0.02	1.84 (1.06,2.21)	0.032
Married vs unmarried	125	0.85 (0.56,1.30)	0.456	0.456	0.88 (0.56,1.39)	0.58
Smoking: Past vs Never	124	1.85 (0.76,4.50)	0.173	0.393	1.23 (0.42,3.64)	0.71
Current vs Never		1.63 (0.70,3.82)			1.10 (0.36,3.43)	0.865
Site: OC vs Larynx	132	2.21 (1.24,3.93)	0.007	0.002	1.81 (0.94,3.47)	0.074
OP vs Larynx		2.09 (1.17,3.73)	0.012		2.24 (1.06,4.76)	0.036
HP vs Larynx		2.12 (1.15,3.91)	0.017		1.92 (0.99,3.72)	0.054
* Other vs Larynx		0.61 (0.28,1.34)	1.51		0.91 (0.32,2.61)	0.856
West African	132	0.92 (0.33,2.59)	0.878		1.02 (0.34,3.06)	0.974
						0.934

* lip-external, nose maxilla, nasopharynx, sinonasal