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Socioeconomic status, access to care, risk factor patterns and stage at diagnosis for head and neck cancer among Black and White patients

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Abstract

Background: Little is known about how factors combine to influence progression of squamous cell carcinoma of the head and neck (HNSCC). We aimed to evaluate multidimensional influences of factors associated with HNSCC stage by race.

Methods: Using retrospective data, patients with similar socioeconomic status (SES), access to care (travel time/distance) and behavioral risk factors (tobacco/alcohol use and dental care) were grouped by latent class analysis. Relative frequency differences (RFD) were calculated to evaluate latent classes by stage, race, and p16 status.

Results: We identified 3 latent classes. Advanced T-stage was higher for Black (RFD=$^{+}$20.2%; 95% CI: $^{-}$4.6–44.9) than White patients (RFD=$^{+}$10.7%; 95% CI: 2.1–19.3) in the low-SES/high-access/high-behavioral risk class and higher for both Black (RFD=$^{+}$29.6%; 95% CI: 4.7–54.5) and

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White patients (RFD=+23.9%; 95% CI: 15.2–32.6) in the low-SES/low-access/high-behavioral risk class.

Conclusion: Results suggest that SES, access to care, and behavioral risk factors combine to underly the association with advanced T-stage. Additionally, differences by race warrant further investigation.

Keywords

Head and neck cancer; latent class analysis; neoplasm stage; late stage; distance to care; socioeconomic status; HPV-related cancer; racial disparities

Introduction

In 2020, there were 10,750 estimated new deaths from squamous cell carcinoma of the head and neck (HNSCC) in the U.S. [1]. The stage at diagnosis is a strong predictor of HNSCC survival [2–4]. While the overall 5-year survival is poor (~65%), approximately 30% of the HNSCC cases are diagnosed at an early stage, for which the 5-year survival is 84%. Additionally, race appears to be associated with prognosis, with disproportionately lower survival rates among Black (48%) compared to White (67%) patients [1]. This discrepancy may be associated with the more frequent presentation at advanced stages (III/IV) for Black patients compared to White patients [5–8]. The presentation of advanced HNSCC has also been shown to be influenced by socioeconomic status (SES) [9–12], access to medical care [13, 14], behavioral risk factors such as tobacco and alcohol use [15–19], human papillomavirus (HPV) [20–22], and access to and use of dental care [23–27]. Furthermore, there is ample evidence that factors associated with advanced cancer presentation interact and that their interaction may vary according to race [16, 28, 29]. Thus, important gaps exist in understanding how individual factors combine or interact to influence the HNSCC stage at diagnosis.

Notably, previous studies addressing HNSCC risk have largely examined contributing factors individually as independent risk factors but have not accounted for the interdependence of different factors. For example, analyses of access to medical care typically have not accounted for SES, which has been shown to influence patients' timely interaction with medical care [14], or behavioral risk factors (e.g., tobacco, alcohol, and oral health) which are thought to interact with SES [16]. Overall, the existing literature provides associative data regarding the influence of individual components of SES, access, and behavioral risk factors on HNSCC and stage but fails to provide a more comprehensive and holistic assessment of how these factors may interact jointly to impact the HNSCC stage. Additionally, while there is limited data associating SES, HPV, and tobacco/alcohol with HNSCC incidence or survival differences by race [30–32], it is largely unknown how these factors may function together to influence stage differences in Black and White patients.

Given the poor understanding of how combinations of factors contribute to the disparity in HNSCC outcomes, we sought to extend the literature by performing latent class analysis (LCA) to create *a priori* person-centered groups (i.e., "latent classes") using the Carolina Head and Neck Cancer Epidemiology Study (CHANCE) as a population resource for ancillary retrospective analysis [26]. LCA identifies unobservable groups of individuals within

a population based on numerical responses to an observed set of factors [33]. This complex patterning provides an approach for understanding multidimensional effects that can be further stratified for a more holistic understanding of factors that contribute to disease presentation. Furthermore, LCA has been successfully applied to health equity-related epidemiology studies to describe the impact of SES and treatment timeliness on cancer outcomes [34, 35]. Thus, our primary purposes in this study were to 1) use LCA to categorize patients according to patterns of SES (based on the level of education, annual income, and insurance), access to care (based on geographic location); and behavioral risk factors (including tobacco and alcohol use and extent of dental care), and 2) evaluate the association of these categories with race and tumor characteristics. We hypothesized that these factors would have distinct associations with cancer presentation depending on the repertoire of factors within the latent class. Furthermore, because the T-stage (i.e., primary tumors) tends to be more observable than the N-stage (i.e., nodal metastases), we evaluated the T and N stages separately. Our results help to define the repertoire of associated factors that contribute to HNSCC stage by using LCA as an advanced approach to more comprehensive understanding of discrepancies in outcomes.

Methods

Data Source and Study Sample

The Carolina Head and Neck Cancer Epidemiology Study (CHANCE) is a population-based case-control study that prospectively identified patients aged ≥20 years with a first primary squamous cell carcinoma of the oral cavity, pharynx, or larynx who resided in the 46-county region of North Carolina between January 2002 and February 2006 [26]. For this study, we included all (n=895) cases with complete information on race, distance to medical care, and the pathology report for the initial biopsy leading to cancer diagnosis. In sensitivity analyses investigating the impact of cases missing these data (n=494) versus those with complete data (n=895), we found no differences in the presenting T-stage for the excluded patients missing information on race, addresses, or pathology report. All cases were identified by rapid case ascertainment via the North Carolina Central Cancer Registry. The collection of data on patients and the analysis of that data were approved by the University of North Carolina at Chapel Hill's Institutional Review Board.

Exposure assessment

Data on socioeconomic status (SES) and behavioral risk factor behavior were collected using a structured questionnaire during an in-home visit after diagnosis (average time=5.3 months). SES, which previously have been defined as: the social and economic factors that influence the position of individuals or groups within a societal structure [36], was determined according to the level of education (coded for this analysis as: some college or more, high school graduate, or less than high school), annual income (>$50,000, $20,000-$50,000, or <$20,000), and insurance (private, Medicaid/Medicare, or other). Behavioral risk factors included smoking status (never, ex-smoker, or current smoker), years smoked (never, 1–19, 20–39, or ≥40), pack-years smoking history (never, 1–19, 20–49, or ≥50), number of routine dental exam visits in past 10 years (0, 1–10, or ≥11), and alcohol use (never or ever). Total alcohol use was further defined among ever-drinkers as tertiles of cumulative

grams of lifetime ethanol consumption (never-drinker, 1–322,595; 322,596–1,422,084; or ≥1,422,085). In the U.S., one alcoholic drink equivalent contains 14 grams of alcohol [37]; thus, the highest level of consumption is equivalent to more than 35 drinks per week for 50 years.

Access to medical care factors included urban/rural residence, commute time, and Euclidean (linear) distance to biopsy [14]. Commute time and distance to biopsy were calculated in ArcMap 10.5 (ESRI 2017) from the residential address at in-home patient interview post-diagnosis and the geographic hospital location of initial biopsy, which were abstracted from the pathology report. Quartiles were calculated for commute time (<11.9 min, 11.9–22.5 min, 22.6–41.5 min, or ≥41.6 min) and distance to biopsy (<4.4 miles, 4.5–9.5 miles, 9.6–21.5 miles, or ≥21.6 miles). Urban/rurality of each address was defined by U.S. Department of Agriculture Economic Research Service rural-urban commuting area codes based on census tracts [38].

Covariates

Patient characteristics, including sex, race (White vs. Black), and age were ascertained through structured questionnaires at the in-home interview visit. The primary tumor site was abstracted from the patients' medical record, which was classified according to International Classification of Diseases for Oncology, 3rd edition (ICD-O-3). To assess tumor HPV-status cancer, p16 immunohistochemistry was retrospectively performed using a previously described protocol [24]. The P16 status was tested in oropharyngeal cancer cases (n=171) and a random sample of non-oropharyngeal cancer cases (n=109).

Outcome assessment

Data on T-stage and N-stage at diagnosis were abstracted from the patients' medical records specifying the initial treatment plan. T-stage at diagnosis was defined as 'early' (T1-T2) or 'advanced' (T3-T4). N-stage at diagnosis was defined as 'no nodes' (N0) or 'nodal metastases' (N1–3). All staging used 7th edition AJCC guidelines at the time data were collected.

Statistical analysis

We sought to extend understanding beyond isolated single-dimensional effects on advanced T-stage to the multidimensional effects of SES (including level of education, annual income, and insurance), access to medical care (including urban/rural residence, drive time and distance to first biopsy), and behavioral risk factors (including smoking, dental exam visits and alcohol use) by developing latent classes based on these variables that were then evaluated for their associations with advanced T-stage (Supplemental Figure). Latent class analysis (LCA) identifies unobservable groups of individuals who share common factors based on responses to an observed set of factors to describe underlying exposure patterns in the data. Once latent classes are accounted for, the variables are assumed to be conditionally independent [39]. Here, LCA probabilistically assigned each participant into a latent class based on item-response probabilities for each item. Continuous variables were transformed into categorical variables to be able to capture the individual patients in latent groupings. These groups were mutually exclusive and exhaustive. The latent variables in this analysis

represent the complex mixture of SES, access to medical care, and behavioral risk factor distributions that cannot be directly measured.

The optimal number of latent classes was determined by using an iterative approach, where models were performed starting with one class solution, and the number of classes was increased by one until the best model fit estimation was identified. The best model fit was determined by four goodness-of-fit criteria: 1) the G^2 likelihood ratio test statistic (produced using 100,000 sets of starting values), 2) the Akaike's Information Criterion, 3) the Bayesian Information Criterion, and 4) the entropy, the parameter estimation of correctly classified participants. Here, lower values indicated better model fitness. We compared a series of latent class models to determine the optimal model for model fit and parsimony using the criteria described above.

Separate generalized linear models were used to calculate relative frequency differences (RFDs) and 95% confidence intervals (95% CIs) as measures of association of the latent classes with T-stage, race, p16 status, or primary tumor site. RFD is interpretable as the percentage difference between the index and referent group. Latent class-T-stage models were further stratified by race. Race-stratified generalized linear models were adjusted for age, sex, and primary tumor site; and oropharynx site-specific models were adjusted for race and age. To understand latent class association with nodal involvement, we performed a secondary analysis according to the N-stage. All other models were adjusted for race, age, sex, and primary tumor site. Interval estimates calculated by confidence intervals were used to assess precision and summarize the results of the hypothesis tests. All analyses were done in SAS version 9.4 (SAS Institute, Cary, NC) and LCA was done using SAS package PROC LCA [40].

Results

The study population of 895 cases included 239 Black patients (26.7%) and 166 patients of younger age (<50 years; 18.5%). Advanced T-stage (n=340; 38%) was disproportionately reported among cases who were Black, younger age, lower education, lower income, uninsured, had a longer commute time/farther distance to biopsy, greater alcohol and tobacco use, or fewer number of dental exams in the last 10 years (Table 1).

Next, we determined groups of cases with similar patterns of covariates using LCA. Latent classes were defined by categorical variables describing education, income, insurance, commute time to biopsy, distance to biopsy, urban/rural residence, smoking status, pack-years smoking, alcohol use, and dental exams. We identified a 3-latent class model as the best model fit. This model had the lowest AIC, BIC, and likelihood-ratio G^2 statistic compared to one, two, four, five or six-class models. The resulting 3 latent classes were: 1) high SES/moderate access/low behavioral risk, 2) low SES/high access/high behavioral risk, and 3) low SES/low access/high behavioral risk (Figure 1). The characterization of the latent classes by individual probabilities of each variable are shown in Table 2.

For a more detailed understanding of how disease parameters differ for these three latent class groups, we separately evaluated their associations with T-stage, Black vs. White race,

p16 status and primary tumor site. The proportion of advanced T-stage cases increased across these latent classes: *high SES/moderate access/low behavioral risk* (24.2%), *low SES/high access/high behavioral risk* (37.0%), to *low SES/low access/high behavioral risk* (49.5%) (Table 3). Compared to the *high SES/moderate access/low behavioral risk* class, the *low SES/high access/high behavioral risk* (RFD: +12.8%, 95% CI 5.4 to 20.3) and *low SES/low access/high behavioral risk* classes (+25.3%, 95% CI 17.7 to 32.9) had statistically significantly higher frequency of advanced T-stage versus early T-stage prevalence, after adjustment for race, age, sex, and primary tumor site.

We also compared the racial distribution within the 3 latent classes. Black patients represented only 5.2% of the *high SES/moderate access/low behavioral risk* class, with the other 94.8% comprised of White patients. In contrast, the *low SES/high access/high behavioral risk* and *low SES/low access/high behavioral risk* classes each were comprised of more than 30% Black patients. The two low SES classes in combination constituted 94.6% (226/239) of the Black cases and 64.2% (421/656) of the White cases. Black race was statistically significantly associated with the *low SES/high access/high behavioral risk* class (RFD: +30.1%, 95% CI 23.3 to 37.8) and the *low SES/low access/high behavioral risk* class (RFD: +23.0%, 95% CI 15.9 to 30.2) versus the *high SES/moderate access/low behavioral risk* class, after adjusting for age, sex, and primary tumor site (Table 4).

Regarding p16 status, the relative frequency of the *low SES/high access/high behavioral risk* (RFD: −29.4%, 95% CI −45.3 to −14.6) and *low SES/low access/high behavioral risk* (RFD: −27.9%, 95% CI −43.5 to −12.2) classes were statistically significantly lower among p16-positive patients versus p16-negative patients, after adjusting for race, age, and primary tumor site (Table 5). When further considering the tumor site among oropharyngeal cancers, we observed similar patterns (Table 6).

Finally, to evaluate the association of race with the higher T-stage prevalence in the low SES classes, we compared the T-stage prevalence among Black and White patients in each class in a multivariate model. For the *low SES/high access/high behavioral risk* class relative to the *high SES/moderate access/low behavioral risk* class, advanced T-stage among Black patients (RFD = +20.2%; 95% CI: −4.6 to 44.9) was nearly twice as high as among White patients (RFD = +10.7%; 95% CI: 2.1 to 19.3), though the association with advanced T-stage (versus early T-stage) presentation was only statistically significant for White patients. Lastly, *low SES/low access/high behavioral risk* relative to *high SES/moderate access/low behavioral risk* was significantly associated with advanced T-stage presentation among both White patients (RFD = +23.9%; 95% CI: 15.2 to 32.6) and Black patients (RFD = +29.6%; 95% CI: 4.7 to 54.5) (Table 7). We also evaluated N-stage as a secondary analysis (N0 vs. N1–3) to assess whether HNSCC patients with more barriers to care may be more likely to present with nodal metastases. Yet, we observed that across latent classes, the association with N-stage was less strong and not statistically significant (Supplemental Table 1). Lastly, small subgroups precluded meaningful stratification by race.

Discussion

In a large, population-based study of 895 HNSCC cases, we performed a retrospective secondary latent class analysis (LCA), a data dimensionality reduction method, to identify patterns of unobserved groups. LCA has an advantage over other methodologies in that it considers many highly correlated variables together and produces discrete groupings that have higher capability to qualify the interrelated impact of these factors [39]. Many factors have been shown to be related to HNSCC outcomes, including SES, access to medical care, and behavioral risk factors [16, 41]; however, LCA describes the characteristics among samples rather than inferring associations among individual variables with statistical tests. In this respect, LCA is a more holistic and less biased than conventional statistical methodologies. LCA also avoids issues of collinearity and has been shown to provide a more nuanced fit than K-means clustering for characterizing the effects of SES and multipollutant exposure that underlie apparent cancer related disparities in Black populations [42].

Using LCA, we identified 3 latent classes that integrate SES (measured by individual-level education, income, and insurance type), access to medical care (measured by travel time/distance to care, and urban/rural residence), and other behavioral risk factors (measured by smoking status, pack-years smoking, alcohol use, total alcohol, and number of dental visits). These classes were: 1) *high SES/moderate access/low behavioral risk*, 2) *low SES/high access/high behavioral risk*, and 3) *low SES/low access/high behavioral risk*. Notably, Black patients had a higher prevalence in the two low SES classes (i.e., *low SES/high access/high behavioral risk* and *low SES/low access/high behavioral risk*). Compared to the *high SES/moderate access/low behavioral risk* class, both of the low SES classes were statistically significantly associated with advanced T-stage presentation, Black race, and p16-negative status. Furthermore, in race-stratified analyses that compared low SES classes to the referent high SES class within each race stratum, the pattern of lower SES, poorer access to care, and more behavioral risk factors in both White and Black patients was associated with advanced T-stage presentation. However, Black patients had greater frequency of these factors than White patients did in the two lower SES latent classes. These results are the first to elucidate the significance of these factors within meaningful and clinically relevant groupings and indicate that these factors may interact differentially by race in relation to late-stage presentation.

In the context of individual factors, our results are similar to those of previous studies that have found mostly independent associations among race, SES, and access to care factors with HNSCC stage. However, it is important to note that the specific variables for access to care (drive time to biopsy, distance to biopsy, and urban/rural residence) and SES (education, income, and insurance type) that we used to comprise the latent classes may be defined differently than in other studies and thus, may not be directly comparable. Previous studies have found associations between SES and stage [43, 44], while, another study found no evidence that lower SES HNSCC patients presented at a more advanced stage than patients with higher SES [45]. It is important to note that the distribution of SES factors and the health insurance systems in the countries in which the latter studies were performed (Denmark and Canada) differ from those in the U.S., which may influence outcomes [43, 45]. Furthermore, a previous analysis of CHANCE data showed stronger behavioral risk factor (tobacco and

alcohol use) associations in lower SES patients [16] but did not include the analysis of access to care or associations with stage. Annual dental exams have also been shown to be associated with early-stage disease in a CHANCE study [41], and HPV-positive oropharyngeal cancer has been associated with high SES in studies of other US cohorts [46, 47]. Overall, our current results are similar to those of other studies, but our integrative analysis has added to the understanding of HNSCC-associated factors by providing a more comprehensive overview that shows an association of SES, access to care, and other risk factors in combination within latent classes rather than as individual contributing components.

Interestingly, the grouping of two 'Low SES' classes underscores the idea that the interplay among SES, access to care, and alcohol and tobacco use is important. Previous research has demonstrated associations between low SES with the frequency of routine dental visits as well as tobacco and alcohol use [16]. We extended this by showing that access to care, while important, may be driving advanced T-stage presentation somewhat less among low SES patients with greater alcohol and tobacco use. We further examined these latent classes by race. Although not statistically significant, Black patients presented with much greater advanced T-stage than White patients within the "high access" group.

Notably, our multivariate analysis suggests that the association of Black race with T-stage is compounded by lower SES. More advanced stages at diagnosis of HNSCC for Black patients compared to White patients have been demonstrated in a previous study [48]. Furthermore, using Surveillance Epidemiology and End Results data, Arbes et al. found that lower SES, advanced stage, and differences in treatment prescribed accounted for an estimated 86% of the mortality from oral cancer disparity between Black and Whites [10]. While we did not investigate treatment or survival as an outcome, our finding is similar in that low SES and advanced stage was greater among Black patients compared to White patients. Despite our observed trend, we acknowledge that the relatively smaller number of Black patients in our study resulted in imprecise estimates (i.e., wide confidence intervals) for race analysis. Thus, application of the LCA methodology in a larger population with data on treatment history and other factors may help to elucidate additional factors that contribute to disease progression, recurrence, and survival. This is especially important in the context of the racial disparity in HNSCC outcomes, which is disproportionately worse among Black (5-year survival, 48%) compared to White patients (5-year survival, 67%) [1].

Consistent with our observations, previous studies have shown that reduced access to care, as measured by travel time to treating facility, is related to SES [49, 50]. One study found that access to care, as measured by insurance status, was the most important factor associated with racial differences in HNSCC 5-year survival [31]. Furthermore, previous analysis of CHANCE data demonstrated that longer drive time was associated with advanced T-stage in low income (<$20,000) patients [14]. Therefore, our findings are consistent with the findings of other studies in regards to the importance of treatment access. We acknowledge that some of these prior studies used the same data as the current investigation, however, we have extended these findings to multidimensional groupings that better quantify the significance of access according to other factors.

This study has some limitations that should be noted. First, small numbers resulted in imprecise estimates for some analyses, particularly when stratifying by race. In analysis examining associations of T-stage with latent class stratified by race, the high SES/moderate access/low behavioral risk group included only 3 (1.2%) of the 118 Black patients with advanced disease. This proportion may mirror the combination of the individual proportions of this latent class among black patients with advanced disease: high SES, moderate access, and low behavioral risks. Caution is need in the interpretation of these results and additional investigation is warranted. Though sparse membership in LCA can lead to uncertain conclusions, all individual level latent variables in our analysis had sufficient membership in all groupings that were inclusive of SES, access to care, and behavior risk factors (Figure 1). Yet, it would be of particular importance to verify racial correlations among latent classes in future studies. As an additional consideration, our cases when examined by site did not have sufficient data to examine nodal metastasis by tumor site, though we were able to account for primary tumor site in our analysis of latent classes by T-stage. Nodal metastasis is associated with the primary tumor site (e.g., subglottic tumors are less likely to have nodal metastases, despite stage at diagnosed; in contrast, p16-positive oropharyngeal cancers are more likely to have nodal metastases, even if they are diagnosed very early T-stage). For these reasons, T-stage may provide a surrogate endpoint that is more representative of advanced disease and has been the subject of many studies. Nevertheless, while N-stage and T-stage are helpful markers of disease and clinical presentation, they do not accurately portray the entire clinical picture, and future studies of survival and other disease parameters could be useful in extending our findings. Concerning missing information on race, behavioral risk factors, home addresses, and pathology report, we found no significant differences in the presenting T-stage for the excluded patients missing these data. Another limitation is our use of 7th edition AJCC staging guidelines. Information on depth-of-invasion and extranodal extension was not routinely included in the pathology reports during the study time-period; thus, we were not able to re-stage using the 8th edition guidelines. Furthermore, distance and time to biopsy is a proxy marker as many patients are subsequently referred to a tertiary facility after a biopsy with proven diagnosis of cancer. This may be ultimately confounding as more advanced primary disease is more likely to be referred, while less advanced disease may be less likely referred and treated in the community. Information on socioeconomic status was collected after diagnosis, which does not allow for a full temporal assessment for some factors and is another limitation. Furthermore, our use of questionnaires may not fully capture all dimensions of SES, alcohol and tobacco use. Lastly, these findings may not be generalizable to the U.S. population as this study was conducted in a single state. Caution is needed in interpreting these findings from secondary retrospective analyses, and replication using prospective study designs is needed. Despite these limitations, we believe that the strengths, such as the population-based study design, the unique integrative approach, the individual-level SES and other factors obtained via in-home interviews, support the value of our findings.

Conclusion

This study provides an integrative examination of SES, access to care, and other behavioral risk factors in association with T-stage at HNSCC diagnosis. Our study combine these

multiple factors into meaningful and clinically relevant groups and shows how the multidimensional interaction of these groups compounds to be differentially associated with advanced stage presentation by race, which extends our understanding beyond the single-dimensional effect of these factors alone. Notably, this study is unique in applying a methodology, LCA, that provides a more integrated approach to consider multiple factors simultaneously. The results of this study provide aggregated classifications of clinically and socially relevant factors that identify more 'at-risk' individuals for advanced presentation. These findings suggest that even with high access to care, Black patients present with much greater advanced T-stage than White patients. Targeting interventions may be challenging, but here we take a step toward capturing and comprehensively assessing patterns of important indicators for timely care. Future efforts to extend our approach to large diverse cohorts may help to verify and extend our findings to elucidate the contributions of factors that may contribute to differential disease presentation and associated treatment, recurrence, and survival outcomes for HNSCC and other cancers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. American Cancer Society. Cancer Facts & Figures 2020. Atlanta: American Cancer Society; 2020.;
2. Carvalho AL, Nishimoto IN, Califano JA, Kowalski LP. Trends in incidence and prognosis for head and neck cancer in the United States: a site-specific analysis of the SEER database. International Journal of Cancer. May 1 2005;114(5):806–16. doi:10.1002/ijc.20740 [PubMed: 15609302]
3. Kowalski LP, Carvalho AL. Influence of time delay and clinical upstaging in the prognosis of head and neck cancer. Oral Oncology. Jan 2001;37(1):94–8. doi:10.1016/s1368-8375(00)00066-x [PubMed: 11120489]
4. Du E, Mazul AL, Farquhar D, et al. Long-term survival in head and neck cancer: Impact of site, stage, smoking, and human papillomavirus status. The Laryngoscope. Nov 2019;129(11):2506–2513. doi:10.1002/lary.27807 [PubMed: 30637762]
5. Yu AJ, Choi JS, Swanson MS, et al. Association of race/ethnicity, stage, and survival in oral cavity squamous cell carcinoma: A SEER study. OTO open. Oct-Dec 2019;3(4):2473974×19891126. doi:10.1177/2473974x19891126
6. Ragin CC, Langevin SM, Marzouk M, Grandis J, Taioli E. Determinants of head and neck cancer survival by race. Head & Neck. Aug 2011;33(8):1092–8. doi:10.1002/hed.21584 [PubMed: 20967872]
7. Shiboski CH, Schmidt BL, Jordan RC. Racial disparity in stage at diagnosis and survival among adults with oral cancer in the US. Community Dentistry and Oral Epidemiology. Jun 2007;35(3):233–40. doi:10.1111/j.0301-5661.2007.00334.x [PubMed: 17518970]
8. Mahal BA, Inverso G, Aizer AA, Bruce Donoff R, Chuang SK. Impact of African-American race on presentation, treatment, and survival of head and neck cancer. Oral Oncology. Dec 2014;50(12):1177–81. doi:10.1016/j.oraloncology.2014.09.004 [PubMed: 25261298]

9. 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. Jul 2012;18(4):861–8. doi:10.1016/j.healthplace.2012.03.005 [PubMed: 22445028]
10. Arbes SJ Jr., Olshan AF, Caplan DJ, Schoenbach VJ, Slade GD, Symons MJ. Factors contributing to the poorer survival of black Americans diagnosed with oral cancer (United States). Cancer Causes Control. Dec 1999;10(6):513–23. doi:10.1023/a:1008911300100 [PubMed: 10616821]
11. Conway DI, Brenner DR, McMahon AD, et al. Estimating and explaining the effect of education and income on head and neck cancer risk: INHANCE consortium pooled analysis of 31 case-control studies from 27 countries. International Journal of Cancer. Mar 1 2015;136(5):1125–39. doi:10.1002/ijc.29063 [PubMed: 24996155]
12. Dalton SO, Olsen MH, Johansen C, Olsen JH, Andersen KK. Socioeconomic inequality in cancer survival - changes over time. A population-based study, Denmark, 1987–2013. Acta Oncol. May 2019;58(5):737–744. doi:10.1080/0284186x.2019.1566772 [PubMed: 30741062]
13. Adrien J, Bertolus C, Gambotti L, Mallet A, Baujat B. Why are head and neck squamous cell carcinoma diagnosed so late? Influence of health care disparities and socio-economic factors. Oral Oncology. Feb 2014;50(2):90–7. doi:10.1016/j.oraloncology.2013.10.016 [PubMed: 24268629]
14. Farquhar DR, Masood MM, Lenze NR, et al. Travel time to provider is associated with advanced stage at diagnosis among low income head and neck squamous cell carcinoma patients in North Carolina. Oral Oncology. Feb 2019;89:115–120. doi:10.1016/j.oraloncology.2018.12.029 [PubMed: 30732948]
15. Cohen N, Fedewa S, Chen AY. Epidemiology and demographics of the head and neck cancer population. Oral and Maxillofacial Surgery Clinics of North America. Nov 2018;30(4):381–395. doi:10.1016/j.coms.2018.06.001 [PubMed: 30078696]
16. Stanford-Moore G, Bradshaw PT, Weissler MC, et al. Interaction between known risk factors for head and neck cancer and socioeconomic status: the Carolina Head and Neck Cancer Study. Cancer Causes Control. Sep 2018;29(9):863–873. doi:10.1007/s10552-018-1062-8 [PubMed: 30069657]
17. Rettig EM, D'Souza G. Epidemiology of head and neck cancer. Surgical Oncology Clinics of North America. Jul 2015;24(3):379–96. doi:10.1016/j.soc.2015.03.001 [PubMed: 25979389]
18. Argiris A, Karamouzis MV, Raben D, Ferris RL. Head and neck cancer. Lancet. May 17 2008;371(9625):1695–709. doi:10.1016/s0140-6736(08)60728-x [PubMed: 18486742]
19. Kawakita D, Matsuo K. Alcohol and head and neck cancer. Cancer Metastasis Reviews. Sep 2017;36(3):425–434. doi:10.1007/s10555-017-9690-0 [PubMed: 28815324]
20. O'Rorke MA, Ellison MV, Murray LJ, Moran M, James J, Anderson LA. Human papillomavirus related head and neck cancer survival: a systematic review and meta-analysis. Oral Oncology. Dec 2012;48(12):1191–201. doi:10.1016/j.oraloncology.2012.06.019 [PubMed: 22841677]
21. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. The Lancet Oncology. Aug 2010;11(8):781–9. doi:10.1016/s1470-2045(10)70017-6 [PubMed: 20451455]
22. Mazul AL, Rodriguez-Ormaza N, Taylor JM, et al. Prognostic significance of non-HPV16 genotypes in oropharyngeal squamous cell carcinoma. Oral Oncology. Oct 2016;61:98–103. doi:10.1016/j.oraloncology.2016.08.019
23. Farquhar DR, Divaris K, Mazul AL, Weissler MC, Zevallos JP, Olshan AF. Poor oral health affects survival in head and neck cancer. Oral Oncology. Oct 2017;73:111–117. doi:10.1016/j.oraloncology.2017.08.009 [PubMed: 28939062]
24. Mazul AL, Taylor JM, Divaris K, et al. Oral health and human papillomavirus-associated head and neck squamous cell carcinoma. Cancer. Jan 1 2017;123(1):71–80. doi:10.1002/cncr.30312 [PubMed: 27571516]
25. Chang CC, Lee WT, Hsiao JR, et al. Oral hygiene and the overall survival of head and neck cancer patients. Cancer Medicine. Apr 2019;8(4):1854–1864. doi:10.1002/cam4.2059 [PubMed: 30865385]
26. Divaris K, Olshan AF, Smith J, et al. Oral health and risk for head and neck squamous cell carcinoma: the Carolina Head and Neck Cancer Study. Cancer Causes Control. Apr 2010;21(4):567–75. doi:10.1007/s10552-009-9486-9 [PubMed: 20049634]

27. 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. Nov 2012;23(11):1821–9. doi:10.1007/s10552-012-0061-4 [PubMed: 22961100]

28. Potter LN, Lam CY, Cinciripini PM, Wetter DW. Intersectionality and smoking cessation: exploring various approaches for understanding health inequities. Nicotine Tob Res. Jan 7 2021;23(1):115–123. doi:10.1093/ntr/ntaa052 [PubMed: 32208484]

29. Liang H, Beydoun MA. Modifiable health risk factors, related counselling, and treatment among patients in health centres. Health Soc Care Community. May 2019;27(3):693–705. doi:10.1111/hsc.12686 [PubMed: 30525260]

30. Cole L, Polfus L, Peters ES. Examining the incidence of human papillomavirus-associated head and neck cancers by race and ethnicity in the U.S., 1995–2005. PloS One. 2012;7(3):e32657. doi:10.1371/journal.pone.0032657 [PubMed: 22448226]

31. Gourin CG, Podolsky RH. Racial disparities in patients with head and neck squamous cell carcinoma. The Laryngoscope. Jul 2006;116(7):1093–106. doi:10.1097/01.mlg.0000224939.61503.83 [PubMed: 16826042]

32. Osazuwa-Peters N, Christopher KM, Hussaini AS, Behera A, Walker RJ, Varvares MA. Predictors of stage at presentation and outcomes of head and neck cancers in a university hospital setting. Head & Neck. Apr 2016;38 Suppl 1:E1826–32. doi:10.1002/hed.24327 [PubMed: 26695355]

33. Lanza ST, Collins LM, Lemmon DR, Schafer JL. PROC LCA: A SAS procedure for latent class analysis. Structural Equation Modeling : A Multidisciplinary Journal. 2007;14(4):671–94. [PubMed: 19953201]

34. Palumbo A, Michael Y, Hyslop T. Latent class model characterization of neighborhood socioeconomic status. Cancer Causes Control. Mar 2016;27(3):445–52. doi:10.1007/s10552-015-0711-4 [PubMed: 26797452]

35. Emerson MA, Golightly YM, Aiello AE, et al. Breast cancer treatment delays by socioeconomic and health care access latent classes in Black and White women. Cancer. Nov 15 2020;126(22):4957–4966. doi:10.1002/cncr.33121 [PubMed: 32954493]

36. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). J Epidemiol Community Health. Jan 2006;60(1):7–12. doi:10.1136/jech.2004.023531

37. The National Institute on Alcohol Abuse and Alcoholism. What is a standard drink? https://www.niaaa.nih.gov/what-standard-drink Accessed July 30 2020;

38. Wan N, Zhan FB, Lu Y, Tiefenbacher JP. Access to healthcare and disparities in colorectal cancer survival in Texas. Health Place. Mar 2012;18(2):321–9. doi:10.1016/j.healthplace.2011.10.007 [PubMed: 22118939]

39. Hagenaars JA, McCutcheon AL. Applied latent class analysis. Cambridge University Press; 2002.

40. PROC LCA, PROC LTA (Version 1.3.2) [Software], 2015. University Park: The Methodology Center, Penn State. Retrieved from http://methodology.psu.edu.

41. Farquhar DR, Lenze NR, Masood MM, et al. Access to preventive care services and stage at diagnosis in head and neck cancer. Head & Neck. Jul 3 2020;doi:10.1002/hed.26326

42. Larsen A, Kolpacoff V, McCormack K, Seewaldt V, Hyslop T. Using latent class modeling to jointly characterize economic stress and multipollutant exposure. Cancer Epidemiol Biomarkers Prev. Oct 2020;29(10):1940–1948. doi:10.1158/1055-9965.Epi-19-1365 [PubMed: 32856601]

43. Olsen MH, Bøje CR, Kjær TK, et al. Socioeconomic position and stage at diagnosis of head and neck cancer - a nationwide study from DAHANCA. Acta Oncol. May 2015;54(5):759–66. doi:10.3109/0284186x.2014.998279 [PubMed: 25734503]

44. Auluck A, Walker BB, Hislop G, Lear SA, Schuurman N, Rosin M. Socio-economic deprivation: a significant determinant affecting stage of oral cancer diagnosis and survival. BMC Cancer. Aug 2 2016;16:569. doi:10.1186/s12885-016-2579-4 [PubMed: 27480165]

45. Johnson S, Corsten MJ, McDonald JT, Chun J. Socio-economic factors and stage at presentation of head and neck cancer patients in Ottawa, Canada: a logistic regression analysis. Oral Oncology. May 2010;46(5):366–8. doi:10.1016/j.oraloncology.2010.02.010 [PubMed: 20308010]

46. Dahlstrom KR, Bell D, Hanby D, et al. Socioeconomic characteristics of patients with oropharyngeal carcinoma according to tumor HPV status, patient smoking status, and

sexual behavior. Oral Oncology. Sep 2015;51(9):832–8. doi:10.1016/j.oraloncology.2015.06.005 [PubMed: 26120093]

47. Peterson CE, Khosla S, Jefferson GD, et al. Measures of economic advantage associated with HPV-positive head and neck cancers among non-Hispanic black and white males identified through the National Cancer Database. Cancer Epidemiol. Jun 2017;48:1–7. doi:10.1016/j.canep.2017.02.011 [PubMed: 28282541]
48. Shavers VL, Harlan LC, Winn D, Davis WW. Racial/ethnic patterns of care for cancers of the oral cavity, pharynx, larynx, sinuses, and salivary glands. Cancer Metastasis Reviews. Mar 2003;22(1):25–38. doi:10.1023/a:1022255800411 [PubMed: 12716034]
49. Walker BB, Schuurman N, Auluck A, Lear SA, Rosin M. Socioeconomic disparities in head and neck cancer patients' access to cancer treatment centers. Rural and Remote Health. Jul-Sep 2017;17(3):4210. doi:10.22605/rrh4210 [PubMed: 28870083]
50. Massa ST, Liebendorfer AP, Zevallos JP, Mazul AL. Distance traveled to head and neck cancer provider: a measure of socioeconomic status and access. Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery. Feb 2020;162(2):193–203. doi:10.1177/0194599819892015 [PubMed: 31794337]

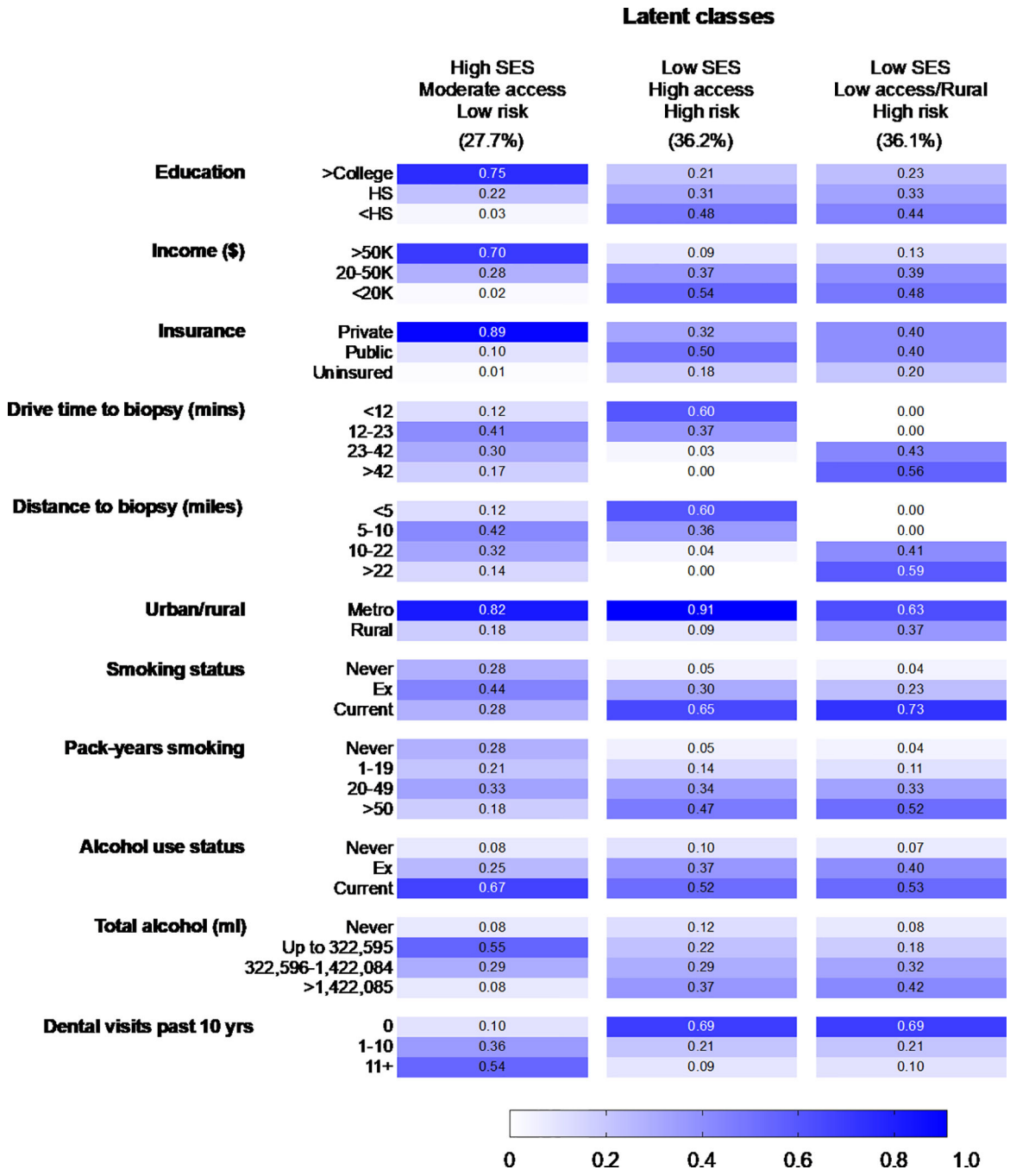

Figure 1.

Probabilities of responses to items for a three-class model measuring participant SES, access to medical care, oral health, and behavioral risk factors

Table 1.

Participant characteristics, access to medical care, oral health, and behavioral risk factors by t-stage

	Early T-stage (n=555)		Advanced T-stage (n=340)	
	No.	**(%)**	**No.**	**(%)**
Sex				
Male	424	(76.4)	271	(79.7)
Female	131	(23.6)	69	(20.3)
Race				
White	434	(78.2)	222	(65.3)
Black	121	(21.8)	118	(34.7)
Age				
20–49	84	(15.1)	82	(24.1)
50–59	181	(32.6)	109	(32.1)
60–69	170	(30.6)	102	(30.0)
70–80	120	(21.6)	47	(13.8)
Primary tumor site				
Larynx	222	(40.0)	123	(36.2)
Oropharynx	165	(29.7)	93	(27.4)
Oral cavity	57	(10.3)	41	(12.1)
Hypopharynx	23	(4.1)	24	(7.1)
Not otherwise specified	88	(15.9)	59	(17.4)
Education				
Less than high school	172	(31.0)	133	(39.1)
High school graduate	148	(26.7)	113	(33.2)
Some college and above	235	(42.3)	94	(27.7)
Income				
> $50,000	168	(30.3)	65	(19.1)
$20,000-$50,000	197	(35.5)	104	(30.6)
< $20,000	162	(29.2)	155	(45.6)
Missing	28	(5.1)	16	(4.7)
Insurance				
Private	221	(39.8)	96	(28.2)
Medicaid/Medicare	194	(34.9)	116	(34.1)
None	43	(7.8)	80	(23.5)
Other/combo	86	(15.5)	45	(13.2)
Missing	11	(2.0)	3	(0.9)
Urban/rural				
Metropolitan (>50,000)	443	(79.8)	259	(76.2)
Large rural (10,000–49,999)	74	(13.3)	59	(17.4)
Small rural (>10,000)	37	(6.8)	22	(6.5)
Commute time to biopsy (mins)				

	Early T-stage (n=555)		Advanced T-stage (n=340)	
	No.	(%)	No.	(%)
<11.9	149	(26.9)	74	(21.8)
11.9–22.5	148	(26.7)	75	(22.1)
22.6–41.5	138	(24.9)	84	(24.7)
>41.6	118	(21.3)	105	(30.9)
Missing	2	(0.4)	2	(0.6)
Distance to biopsy (miles)				
<4.4	145	(26.1)	77	(22.7)
4.5–9.5	144	(26.0)	75	(22.1)
9.6–21.5	141	(25.4)	80	(23.5)
>21.6	115	(20.7)	108	(31.8)
Missing	10	(1.8)	0	(0)
Smoking status				
Never-smoker	70	(12.6)	28	(8.2)
Ex-smoker	195	(35.1)	87	(25.6)
Current smoker	290	(52.3)	225	(66.2)
Years smoked				
Never-smoker	71	(12.8)	28	(8.2)
1–19	55	(9.9)	22	(6.5)
20–39	207	(37.3)	151	(44.4)
>40	219	(39.5)	136	(40.0)
Missing	3	(0.5)	3	(0.9)
Pack-years smoking history				
Never-smoker	70	(12.6)	28	(8.2)
1–19	88	(15.9)	45	(13.2)
20–49	176	(31.7)	121	(35.6)
>50	218	(39.3)	142	(41.8)
Missing	3	(0.5)	4	(1.2)
Alcohol use status				
Never-drinker	56	(10.1)	20	(5.9)
Ever-drinker	496	(89.4)	319	(93.8)
Missing	3	(0.5)	1	(0.3)
Total alcohol use (ml of ethanol)				
Never-drinker	56	(10.1)	20	(5.9)
Up to 322,595	176	(31.7)	74	(21.8)
322,596 to 1,422,084	159	(28.7)	91	(26.8)
1,422,085 and greater	129	(23.2)	122	(35.9)
Missing	35	(6.3)	33	(9.7)
Dental exams in past 10 years				
0	253	(45.6)	193	(56.8)
1 to 10	138	(24.9)	76	(22.4)

	Early T-stage (n=555)		Advanced T-stage (n=340)	
	No.	**(%)**	**No.**	**(%)**
11 and greater	150	(27.0)	43	(12.6)
Missing	14	(2.5)	28	(8.2)

Table 2.

Characterization of Latent Classes

Class	Class labels	Characterization
1	High SES, moderate access, low behavioral risk	Highest education and income, greatest private insurance, moderate distance to accessing care, low cigarette and alcohol use, most dental visits
2	Low SES, high access, high behavioral risk	Least education and income, most public insurance, closest to accessing care, heavy cigarette and alcohol use, less dental visits
3	Low SES, low access, high behavioral risk	Low education and income, furthest from accessing care, most rural, heavy cigarette and alcohol use, less dental visits

Abbreviations: SES, socioeconomic status

Table 3.

Frequency of advanced T-stage by latent classes in the Carolina Head and Neck Cancer Epidemiology Study*

	All cases (n=895)		Early T-stage (n=555)		Advanced T-stage (n=340)	
Latent classes	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
High SES, moderate access, low behavioral risk	248	(27.7)	188	(75.8)	60	(24.2)
Low SES, high access, high behavioral risk	324	(36.2)	204	(63.0)	120	(37.0)
Low SES, high access vs. High SES, RFD (95% CI)					**12.8**	**(5.4 to 20.3)**
Low SES, low access, high behavioral risk	323	(36.1)	163	(50.5)	160	(49.5)
Low SES, low access vs. High SES, RFD (95% CI)					**25.3**	**(17.7 to 32.9)**

Abbreviations: SES, socioeconomic status; RFD, relative frequency difference; “vs. High SES”, High SES, moderate access, low behavioral risk latent class

*Multivariate model adjusting for race, age, sex and primary tumor site. Referent group is early T-stage.

Table 4.

Distribution of latent classes by race *

	White (n=656)		Black (n=239)	
Latent classes	**No.**	**(%)**	**No.**	**(%)**
High SES, moderate access, low behavioral risk	235	(94.8)	13	(5.2)
Low SES, high access, high behavioral risk	198	(61.1)	126	(38.9)
Low SES, high access vs. High SES, RFD (95% CI)			**30.1**	**(23.3 to 37.8)**
Low SES, low access, high behavioral risk	223	(69.0)	100	(31.0)
Low SES, low access vs. High SES, RFD (95% CI)			**23.0**	**(15.9 to 30.2)**

Abbreviations: SES, socioeconomic status; RFD, relative frequency difference; “vs. High SES”, High SES, moderate access, low behavioral risk latent class

* Multivariate model adjusting for age, sex and primary tumor site. Referent group is white.

Table 5.

Distribution of latent classes by p16 status

	Negative* (n=153)		Positive† (n=127)	
Latent classes	**No.**	**(%)**	**No.**	**(%)**
High SES, moderate access, low behavioral risk	20	(23.0)	67	(77.0)
Low SES, high access, high behavioral risk	62	(68.9)	28	(31.1)
Low SES, high access vs. High SES, RFD (95% CI)			**−37.3**	**(−51.1 to −23.6)**
Low SES, low access, high behavioral risk	71	(68.9)	32	(31.1)
Low SES, low access vs. High SES, RFD (95% CI)			**−35.1**	**(−48.6 to −21.7)**

Abbreviations: SES, socioeconomic status; RFD, relative frequency difference; “vs. High SES”, High SES, moderate access, low behavioral risk latent class

*Adjusting for race and age. Referent group is negative p16 status

†p16 status was tested in cases with oropharyngeal cancers and a random sample of non-oropharyngeal cancer cases.

Table 6.

Distribution of latent classes by oropharynx site and p16 status *

	Oropharynx† (n=171)			
	p16 negative (n=62)		p16 positive (n=109)	
Latent classes	**No.**	**(%)**	**No.**	**(%)**
High SES, moderate access, low behavioral risk	6	(9.5)	57	(90.5)
Low SES, high access, high behavioral risk	24	(52.2)	22	(47.8)
Low SES, high access vs. High SES, RFD (95% CI)			**−29.5**	**(−46.4 to −12.8)**
Low SES, low access, high behavioral risk	32	(51.6)	30	(48.4)
Low SES, low access vs. High SES, RFD (95% CI)			**−21.1**	**(−36.6 to −5.6)**

Abbreviations: SES, socioeconomic status; RFD, relative frequency difference; “vs. High SES”, High SES, moderate access, low behavioral risk latent class

*Adjusting for race and age. Referent group is negative p16 status

†p16 status was tested in cases with oropharyngeal cancers and a random sample of non-oropharyngeal cancer cases. Subgroup analysis (n=171) is among p16 tested oropharyngeal cancers cases only.

Table 7.

Frequency of advanced T-stage by latent classes and race in the Carolina Head and Neck Cancer Epidemiology Study*

	T-stage and race							
	Early T-stage				Advanced T-stage			
	White (n=434)		Black (n=121)		White (n=222)		Black (n=118)	
Latent classes	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
High SES, moderate access, low behavioral risk	178	(71.7)	10	(4.0)	57	(23.0)	3	(1.2)
Low SES, high access, high behavioral risk,	135	(41.7)	69	(21.3)	63	(19.4)	57	(17.6)
Low SES, high access, high behavioral risk vs. High SES, RFD (95% CI)					**10.7**	**(2.1 to 19.3)**	**20.2**	**(−4.6 to 44.9)**
Low SES, low access, high behavioral risk	121	(37.5)	42	(13.0)	102	(31.6)	58	(18.0)
Low SES, low access, high behavioral risk, vs. High SES, RFD (95% CI)					**23.9**	**(15.2 to 32.6)**	**29.6**	**(4.7 to 54.5)**

Abbreviations: SES, socioeconomic status; RFD, relative frequency difference; “vs. High SES”, High SES, moderate access, low behavioral risk latent class

*Multivariate model adjusting for age, sex and primary tumor site. Referent group is early T-stage.