



Racial and socioeconomic disparities associated with 90-day mortality among patients with head and neck cancer in the United States

Matthew E. Gaubatz^a, Aleksandr R. Bukatko^b, Matthew C. Simpson^b, Katherine M. Polednik^a, Eric Adjei Boakye^c, Mark A. Varvares^d, Nosayaba Osazuwa-Peters^{b,e,*}

^a Saint Louis University School of Medicine, Saint Louis, United States

^b Saint Louis University School of Medicine, Department of Otolaryngology-Head and Neck Surgery, Saint Louis, United States

^c Saint Louis University Center for Health Outcomes Research (SLUCOR), Saint Louis, United States

^d Harvard Medical School, Massachusetts Eye and Ear Infirmary, Department of Otolaryngology, Boston, United States

^e Saint Louis University Cancer Center, Saint Louis, United States

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ABSTRACT

Objectives: To quantify head and neck cancer (HNC) mortality rates and identify racial and socioeconomic factors associated with 90-day mortality.

Methods: The National Cancer Database (2004–2014) was queried for eligible HNC cases ($n = 260,011$) among adults treated with curative intent. Outcome of interest was any-cause 90-day mortality. Kaplan-Meier curves (Log-rank tests) estimated crude survival differences. A Cox proportional hazards model with further adjustments using the Šidák multiple comparison method adjusted for racial, socioeconomic and clinical factors.

Results: There were 9771 deaths (90-day mortality rate = 3.8%). There were crude differences in sex, race/ethnicity, comorbidity, distance, income, and insurance (Log-rank p -value < 0.0001). In the final model, blacks (aHR = 1.10, 95% CI 1.00, 1.21) and males (aHR = 1.07; 95% CI 1.00, 1.15) had greater 90-day mortality hazard, as did those uninsured (aHR = 1.72; 95% CI 1.48, 1.99), covered by Medicaid (aHR = 1.72; 95% CI 1.53, 1.93) or Medicare (aHR = 1.40; 95% CI 1.27, 1.53). Residence in lower median income zip code was associated with greater 90-day mortality [(aHR < \$30,000 = 1.30; 95% CI 1.18, 1.44); (aHR \$30,000–\$34,999 = 1.24; 95% CI 1.13, 1.36); (aHR \$35,000–\$45,999 = 1.18; 95% CI 1.08, 1.27)]; and farther travel distance for treatment was associated with decreased 90-day mortality [(aHR 50–249.9 miles = 0.86; 95% CI 0.77, 0.97); (aHR > 250 miles = 0.70; 95% CI 0.50, 0.99)].

Conclusions: There are significant race and socioeconomic disparities among patients with HNC, and these disparities impact mortality within 90 days of treatment.

Introduction

Currently, there are over 436,030 head and neck cancer (HNC) survivors in the United States with an estimated 64,690 new cases and 13,740 deaths from HNC in 2018, making HNC the 8th most common cancer and 14th most common cause of cancer death in the United States [1,2]. Known factors associated with long-term mortality include clinical factors such as tumor stage, anatomic site, and treatment modality as well as non-clinical factors such as gender, race, marital status, income, insurance status, and travel distance to treatment facility [3–9].

The above-named nonclinical factors impacting long-term mortality highlight the healthcare disparities and access to care problems faced

by the HNC population [10]. However, it is unknown how soon these disparities begin to exert an influence over patient mortality. While nonclinical factors are known to impact mortality in the long-term, there is a paucity of data on demographic and socioeconomic disparities associated with the short-term mortality, including 90-day mortality, among patients with HNC post-treatment. Eliminating health disparities, including those that are cancer-related, is a public health imperative and an overarching objective of the *Healthy People 2020* initiative [11]. Therefore, characterization of disparities associated with short-term mortality among patients with HNC, a well-known disparate population [12], is needed.

To our knowledge, no national cancer study has described 90-day mortality among patients with HNC in the United States. The aim of this

* Corresponding author at: Saint Louis University School of Medicine, Department of Otolaryngology-Head and Neck Surgery, 3635 Vista Avenue, 6th Floor Desloge Towers, Saint Louis, MO 63110-2539, United States.

E-mail address: nosazuwa@slu.edu (N. Osazuwa-Peters).

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study was to address this gap in the literature by quantifying 90-day mortality rates and by identifying racial and socioeconomic factors associated with 90-day mortality among patients with HNC in the United States.

Methods

Data source

In this retrospective analysis, we queried the National Cancer Database (NCDB) for adult cases of HNC diagnosed between 2004 and 2014. The NCDB is a joint project of the Commission on Cancer (CoC) between the American College of Surgeons and the American Cancer Society. The NCDB covers more than 70% of cancer incidence in the United States and is the largest clinical cancer registry in the world [13–15]. The CoC's NCDB and the hospitals participating in the CoC's NCDB are the source of the de-identified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Study sample

Patients with HNC who underwent at least part of their first treatment at the reporting facility were included in this study. The study sample was restricted to patients who presented with the American Joint Committee on Cancer (AJCC) stage I-IV HNC of squamous histology, received non-palliative treatment and were not missing information on first treatment, survival, or follow-up. See Fig. 1 for complete inclusion/exclusion criteria information. The following International Classification of Diseases for Oncology, third edition (ICD-O-3) topography codes were included in the study and used to categorize the primary cancer site variable: hypopharynx (C12.9, C13.0–C13.2, C13.8, C13.9); larynx (C32.0–C32.3, C32.8, C32.9); nasal (C30.0, C30.1, C31.0–C31.3, C31.8, C31.9); nasopharynx (C11.0–C11.3, C11.8, C11.9); oropharynx (C01.9, C02.4, C09.0, C09.1, C09.8, C09.9, C10.0–C10.3, C10.4, C10.8, C10.9, C14.0, C14.2); and oral cavity (C00.0–C00.6, C00.8, C00.9, C02.0–C02.3, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C05.0–C05.2, C05.8, C05.9, C06.0–C06.2, C06.8, C06.9, C07.9, C08.0, C08.1, C08.8, C08.9, C14.8). Histology was restricted to squamous cell carcinomas using the following ICD-O-3 histology codes: 8050–8076, 8078, 8083, 8084, 8094 [16].

Measures

Race/ethnicity was categorized as Non-Hispanic White, Non-Hispanic Black, Hispanic, and other/unknown. Sex was categorized as male or female. Household income quartiles were derived from the year 2000 US Census data and matched to each patient's area of residence by zip code with categories of: < \$30,000, \$30,000–\$34,999, \$36,000–\$45,999, and \$46,000+. Charlson-Deyo comorbidity scores were sums of individual comorbidities and were categorized as scores of 0, 1, 2, or 3+ [17]. Charlson-Deyo comorbidity scores were calculated from the following conditions: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, moderate or severe liver disease, and AIDS. Patient's comorbid conditions outside of this list did not contribute to the score. Cancer stage was assigned the value of the pathologic (if available) or clinical stage group per T, N, and M stages as defined by the AJCC. Distance to treating facility was the number of miles between the center of the patient's zip code (or city if zip code not available) and the street address of the facility. It was split into the following four categories: 0–12.49, 12.5–49.9, 50–249.9, and 250+ miles. Facility type classification was based on the CoC accreditation

statuses of academic/research, community, comprehensive community, and integrated network cancer programs [18]. Primary payor was defined as the patient's primary insurance at the time of diagnosis and/or treatment and was categorized as: private, Medicaid, Medicare, other government insurance, not insured, and insurance status unknown. Urbanization categories were based on the US Department of Agriculture (USDA) Economic Research Service 2003 data with matching stage and county FIPS code of the patient at time of diagnosis, and it was categorized as rural, urban, and metro counties.

Calculation of 90-day mortality

Post-treatment follow-up (in days) was defined as the start of first treatment to the last day of follow-up and was calculated as follows: [follow-up time (months) * 365.25 (days)/12(months)] – [time to first treatment(days)]. To identify censored or dead patients, vital status (alive or dead) at the date of last contact was used. Since the outcome of interest was 90-day mortality, estimated post-treatment follow-up time was capped at 90 days, and all surviving patients were censored after the 90th day.

Statistical analysis

Patient characteristics were described using descriptive statistics. Crude 90-day mortality rates and 95% confidence intervals (CI) were estimated under the assumption of a Poisson distribution (Table 1). Kaplan-Meier survival curves with a Log-rank test estimated unadjusted survival differences in our patient population based on sex, race/ethnicity, comorbidity score, distance, income, and insurance status. The adjusted Cox proportional hazard regression model estimated racial and socioeconomic factors associated with 90-day mortality and generated adjusted hazard ratios (aHRs) and 95% CI for variables of interest. The proportional hazards assumption was checked and satisfied via statistical significance of variable*survival time interaction variables at $\alpha = 0.1$. The final Cox model adjusted for time from diagnosis to treatment. The Šidák method was used for adjustment of α due to multiple comparisons for the overall model with an $\alpha = 0.05$ and an adjusted $\alpha = 0.00116507746$ for estimating 95% CI.

Results

Cohort characteristics and 90-day mortality rate

The study cohort consisted of 260,035 patients out of which 9771 died within 90 days of first treatment, yielding a 90-day mortality rate of 3.8%. The majority of the cohort were: Non-Hispanic Whites (83.08%), males (74.10%), diagnosed with oropharyngeal (33.03%) or oral cavity (30.28%) cancers, and with stage IV disease (44.24%, Table 1).

Kaplan-Meier (unadjusted) 90-day survival

There were differences in survival in our patient population based on sex, race/ethnicity, comorbidity, distance, income, and insurance (Fig. 2A–E). For each of these unadjusted associations, the log-rank test yielded a p -value of < 0.0001.

Socioeconomic factors associated with 90-day mortality

After adjusting for all clinical variables, including Charlson-Deyo comorbidity score, AJCC analytic stage group, primary tumor site, HPV status, facility type, days from diagnosis to treatment, and treatment type, we found that there were racial and socioeconomic factors associated with 90-day mortality. In our final model in which we accounted for multiple comparisons using the Šidák correction method, Non-Hispanic blacks (aHR = 1.10, 95% CI 1.00, 1.21) and males

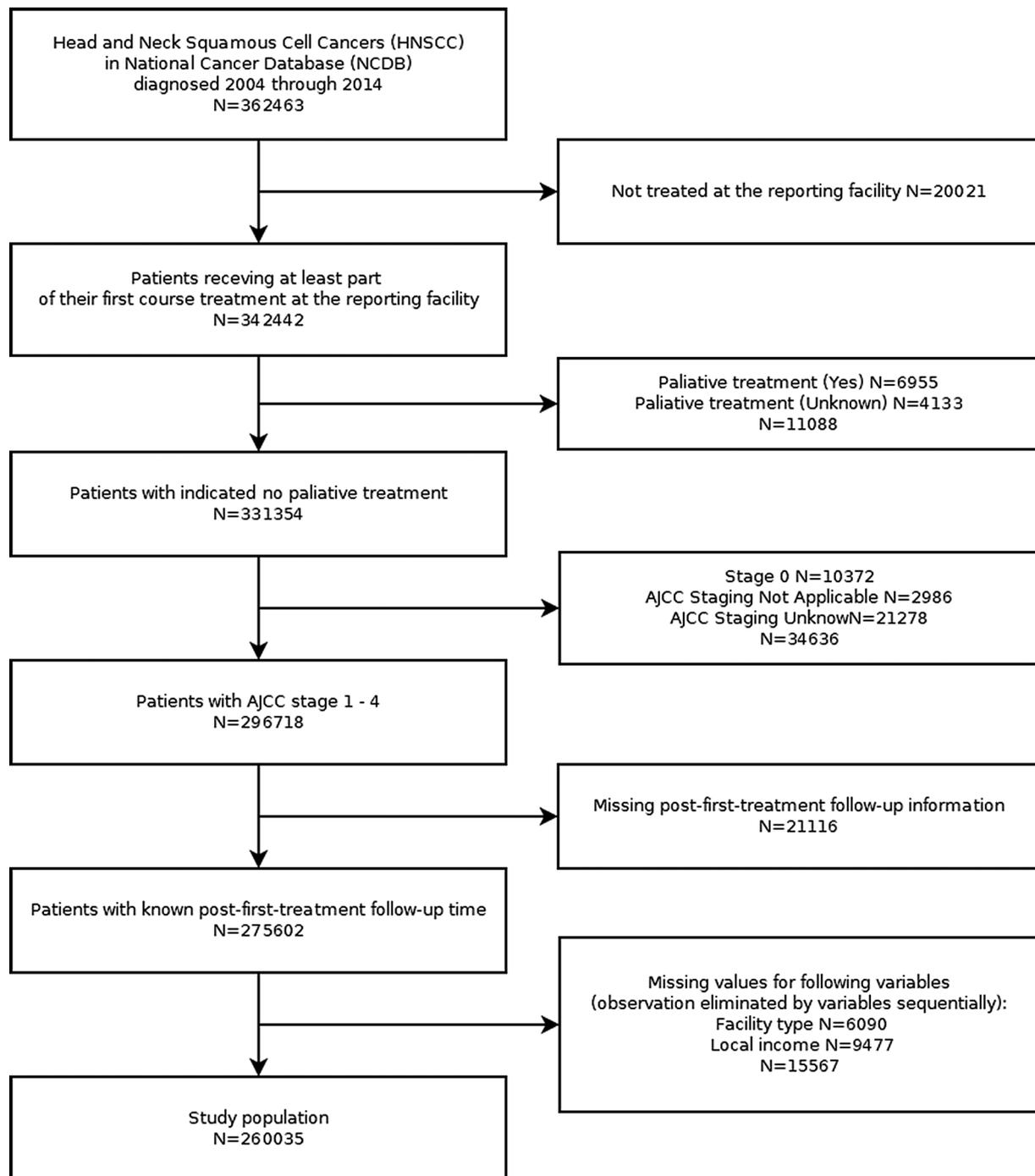


Fig. 1. Flowchart showing how final study sample ($n = 260,035$) was derived, and inclusion and exclusion criteria used in patient selection.

(aHR = 1.07; 95% CI 1.00, 1.15) were marginally more likely to die within 90 days of treatment (Table 2). The hazard of 90-day mortality was significantly greater among patients who were uninsured (aHR = 1.72; 95% CI 1.48, 1.99) or covered by Medicaid (aHR = 1.72; 95% CI 1.53, 1.93) or Medicare (aHR = 1.40; 95% CI 1.27, 1.53) compared to those with private insurance. Residence in a zip-code with lower median income was associated with greater hazard of 90-day mortality [(aHR < \$30,000 = 1.30; 95% CI 1.18, 1.44); (aHR \$30,000–\$34,999 = 1.24; 95% CI 1.13, 1.36); (aHR \$35,000–\$45,999 = 1.18; 95% CI 1.08, 1.27)]; while farther travel distance for treatment was associated with decreased hazard of 90-day mortality [(aHR 50–249.9 miles = 0.86; 95% CI 0.77, 0.97); (aHR > 250 miles = 0.70; 95% CI 0.50, 0.99)].

Discussion

This study sought to quantify 90-day mortality rate among patients with HNC in the United States and to identify associated racial and socioeconomic disparities in this population. We found that patients that were male, black, uninsured, with Medicaid or Medicare, and living in poorer zip-codes were more likely to die within 90 days of initial treatment. To our knowledge, this is the first study to establish racial and socioeconomic disparities associated with 90-day mortality post-treatment of patients with HNC in the United States.

Gender differences in HNC survival have been inconclusive in the literature, albeit for 5-year or longer-term survival [5,7,9,19–21]. In fact, one recent study reported that females have a higher mortality rate

Table 1
Descriptive statistics of study sample (n = 260,035).

	Distribution Count (percent)	90-day mortality Rate (95% CI)
<i>Primary tumor site</i>		
Hypopharynx	12,693 (4.88)	6.94 (6.48–7.40)
Larynx	71,688 (27.57)	3.56 (3.42–3.70)
Nasal	6310 (2.43)	4.26 (4.75–4.77)
Nasopharynx	4733 (1.82)	6.76 (6.02–7.50)
Oropharynx	85,883 (33.03)	3.24 (3.12–3.36)
Oral cavity	78,728 (30.28)	3.77 (3.63–3.90)
<i>AJCC analytic stage group</i>		
Stage I	62,934 (24.20)	1.05 (0.97–1.13)
Stage II	36,365 (13.98)	2.95 (2.77–3.12)
Stage III	45,700 (17.57)	3.89 (3.71–4.07)
Stage IV	115,036 (44.24)	5.44 (5.31–5.58)
<i>Charlson-Deyo comorbidity score</i>		
0	202,283 (77.79)	3.11 (3.03–3.18)
1	44,423 (17.08)	5.29 (5.08–5.51)
2	9906 (3.81)	7.92 (7.37–8.48)
3+	3423 (1.32)	10.25 (9.18–11.33)
<i>HPV test status</i>		
Positive (High risk types)	17,693 (6.80)	1.56 (1.38–1.74)
Positive (Low risk types)	4815 (1.85)	1.62 (1.26–1.98)
Negative	25,116 (9.66)	3.67 (3.43–3.91)
Unknown/not-tested	212,411 (81.69)	4.00 (3.91–4.08)
<i>Gender</i>		
Male	192,694 (74.10)	3.66 (3.57–3.74)
Female	67,341 (25.90)	4.05 (3.90–4.20)
<i>Race/ethnicity</i>		
Non-Hispanic white	216,033 (83.08)	3.58 (3.50–3.66)
Non-Hispanic black	25,745 (9.90)	5.41 (5.12–5.69)
Hispanic	9913 (3.81)	3.89 (3.51–4.28)
Other/unknown	8344 (3.21)	3.14 (2.76–3.52)
<i>Facility type</i>		
Community cancer program	21,401 (8.23)	4.11 (3.84–4.38)
Comprehensive community cancer program	95,429 (36.70)	3.91 (3.79–4.04)
Academic/research program	115,698 (44.49)	3.54 (3.43–3.65)
Integrated network cancer program	27,507 (10.58)	3.86 (3.63–4.09)
<i>Distance to facility (miles)</i>		
0–12.49	136,286 (52.41)	4.09 (3.98–4.20)
12.5–49.9	87,252 (33.55)	3.36 (3.24–3.48)
50–249.9	33203(12.77)	3.54 (3.33–3.74)
250 and over	3010 (1.16)	2.62 (2.05–3.20)
Unknown	284 (0.11)	4.58 (2.09–7.07)
<i>Primary payor</i>		
Not insured	13,598 (5.23)	4.11 (3.77–4.45)
Private insurance	102,634 (39.47)	1.80 (1.71–1.88)
Medicaid	24,540 (9.44)	4.57 (4.30–4.84)
Medicare	109,028 (41.93)	5.38 (5.24–5.52)
Other government	5589 (2.15)	3.20 (2.73–3.67)
Insurance status unknown	4646 (1.79)	4.41 (3.81–5.02)
<i>Median income quartiles</i>		
< \$30,000	40,564 (15.59)	4.80 (4.59–5.02)
\$30,000–\$35,999	51,133 (19.67)	4.16 (3.99–4.34)
\$36,000–\$45,999	74,346 (28.59)	3.84 (3.70–3.98)
\$46,000+	93,992 (36.15)	3.02 (2.91–3.13)
<i>Urbanization</i>		
Metro	203,206 (78.15)	3.77 (3.68–3.85)
Urban	45,862 (17.64)	3.77 (3.59–3.94)
Rural	6255 (2.41)	3.71 (3.23–4.19)
Unknown	4712 (1.81)	3.33 (2.81–3.85)
<i>Continuous variables</i>		
Age at diagnosis (years)	Mean (StDev)	Mean (StDev)
Diagnosis to first treatment (days)	63.15 (11.31)	68.88 (11.90)
	31.23 (35.00)	39.35 (53.39)

compared to males, possibly due to undertreatment [22]. We however found that males were more likely to die within 90 days of treatment than females. Potential explanations for our results are that males have a higher mortality rate since they also have greater incidence of the

disease and are more likely to smoke or drink, while females are more likely to present at an earlier stage of disease and have higher compliance to treatment [4,7,23]. These explanations, from longer-term survival studies, might also explain the gender differences we found in our 90-day mortality study. More research is needed however, to fully elucidate the factors underlying the difference in short-term mortality rates between male and female patients with HNC.

Black patients had a higher rate of 90-day mortality in our study. Numerous studies have also shown that Black patients die from HNC at higher rates than Whites; however, the results of this current study demonstrate that this disparity exists within 90 days of treatment and remains significant after adjusting for age, comorbidity score, stage of presentation, primary tumor site, HPV status, facility type, and treatment type. This is in contrast to several studies that have shown that racial disparities in long-term survival are eliminated after adjusting for factors including socioeconomic status, tumor characteristics, type of treatment, and comorbidity, which would suggest that when offered the same multidisciplinary cancer and medical care, race is not an independent factor in patient outcomes for HNC [3,4,6,24–27]. However, in our study, 81% of the disparities in mortality were accounted for by adjusting for covariates (data not published), highlighting that race is an independent risk factor for HNC mortality even in the short-term. While racial disparities are a known socioeconomic and access to care construct, some studies have suggested that it may be possible that biological/genetic differences may play some yet to be determined role in disparities seen among black patients [28,29]. There are however several other factors known to impact black patients with HNC, such as higher rates of tobacco and alcohol abuse, lower volume of minority patients at regionalized multidisciplinary treatment facilities, refusal of surgical treatment as well as other issues related to physician mistrust and poorer treatment compliance [5,6,12,24,29–37].

Several studies have established that patients with Medicaid or Medicare have worse outcomes compared to patients with private insurance [38–40]. This current study confirmed that this disparity exists even in the short-term, and the odds of worse outcomes when under Medicaid or Medicare persisted even after adjusting for clinical and nonclinical covariates. In fact, the adverse outcomes of having Medicaid or Medicare is highlighted by the fact that patients who had either Medicaid or Medicare were also more likely to have a greater comorbidity score, which is another independent, prognostic factor for mortality. Additionally, while the 90-day mortality rate for the entire cohort in our study was 3.8%, it was triple that (10.3%) among those with Medicaid. Thus, a driver of poor mortality rates among these patients with Medicaid is that they may have, pre-diagnosis, a greater disease burden. This, in addition to facing greater odds of experiencing longer treatment delays [41] create a disparate outcome for many of these patients with Medicaid even in the short-term.

Along with insurance status, we found an increasing likelihood of death within 90 days of death as median zip code income decreased from \$46,000+ to < \$30,000. A previous single-state study in the United States found that low income was an independent predictor of poor 5-year survival [4]. We showed that the same is true within 90 days of treatment. There is significant stress-related morbidity resulting from financial burdens of low income status, and this can be further exacerbated by the high financial toxicity associated with HNC care [42]. Even with possession of insurance, patients with HNC have significant out-of-pocket expenses, which is not helped by the significant loss of employment and job-related disability directly as a result of treatment, which, unfortunately, is quite common in this population [43,44]. As shown in our study, these financial toxicity factors could mortally impact patients even in the short-term after treatment.

A paradoxical finding from our study was that as travel distance to treatment facility increased, 90-day mortality post-treatment decreased. A recent study had a similar result [45]. The ability to travel long distance for care may be linked to financial power or socioeconomic status of patients as well as the willingness to receive and

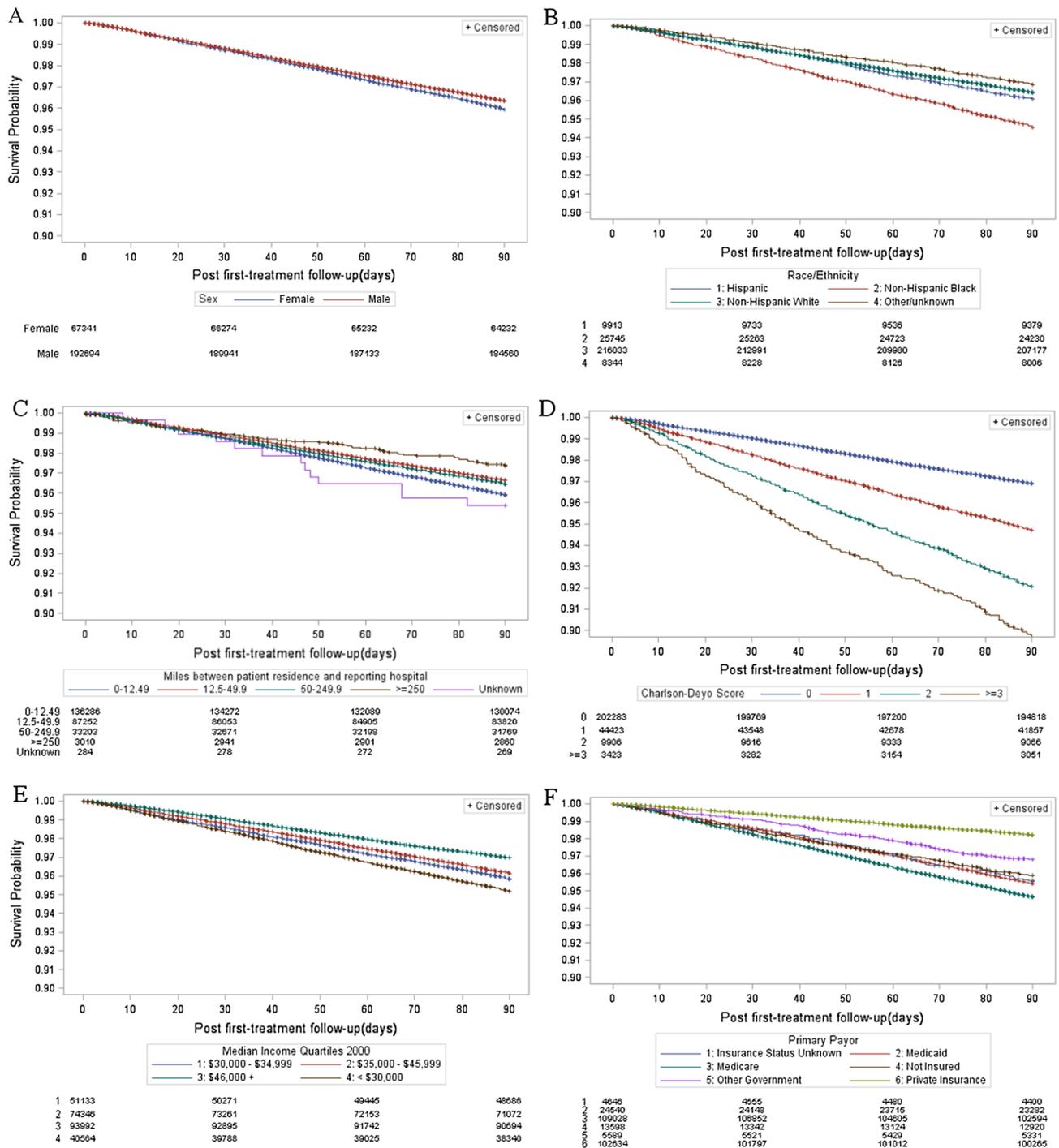


Fig. 2. Kaplan-Meier curves (A–E) shows unadjusted differences in survival of HNC based on several socioeconomic factors marital status A: sex; B: race/ethnicity; C: distance to treatment facility; D: comorbidity score; E: median zip code income; and F: insurance status. For each socioeconomic factor, Log-rank tests indicate that there was a significant difference in survival ($p < 0.0001$).

ability to afford the best cancer care available irrespective of distance. Most national or academic cancer centers are regionalized, necessitating travel for many patients. This is a disparity or an access to care issue. Travel for treatment could be expensive and time-consuming and thus potentially unaffordable to some patients with HNC. There may be other factors besides socioeconomic status, such as age, that might confound this association between mortality and travel distance, so further research is needed to determine the profile of the HNC patient that might benefit from traveling farther to receive cancer care.

Strengths and limitations

The strengths of this study include a large sample size on a national scale with diverse demographic and socioeconomic backgrounds, a variety of types of insurance and treatment facilities, and availability of clinical factors relevant to post-treatment survival outcomes such as comorbidity scores, staging, and HPV status. In addition, although 90-day mortality rates for patients with HNC have been reported in the United Kingdom [46], we believe the current study is the first to describe racial and sociodemographic factors associated with 90-day

Table 2
Racial and socioeconomic disparities associated with 90-day mortality.

	aHR (95% CI) ^{a,b}
Sex	
Female (ref)	–
Male	1.07 (1.00–1.15)
Race/ethnicity	
Non-Hispanic white (ref)	–
Non-Hispanic black	1.10 (1.00–1.21)
Hispanic	0.85 (0.72–0.99)
Other/unknown	0.79 (0.66–0.96)
Distance to facility (in miles)	
0–12.49 (ref)	–
12.5–49.9	0.92 (0.85–0.99)
50–249.9	0.86 (0.77–0.97)
250 and over	0.70 (0.50–0.99)
Unknown	0.92 (0.40–2.11)
Primary payor	
Private insurance (ref)	–
Not insured	1.72 (1.48–1.99)
Medicaid	1.72 (1.53–1.93)
Medicare	1.40 (1.27–1.53)
Other government	1.17 (0.92–1.48)
Insurance status unknown	1.57 (1.26–1.97)
Median income quartiles	
\$46,000+ (ref)	–
\$35,000–\$45,999	1.18 (1.08–1.27)
\$30,000–\$34,999	1.24 (1.13–1.36)
< \$30,000	1.30 (1.18–1.44)
Urbanization	
Metro (ref)	–
Urban	0.97 (0.88–1.07)
Rural	0.92 (0.74–1.13)
Unknown	0.94 (0.74–1.20)

^a Model adjusted for: age, Charlson-Deyo comorbidity score, AJCC analytic stage group, Primary tumor site, HPV status, facility type, days from diagnosis to treatment, and treatment type.

^b Šidák correction for multiple comparisons for overall $\alpha = 0.05$ and 19 CI estimates of interest in the model was used to obtain adjusted confidence interval estimates at individual $\alpha = 0.0026960063$.

mortality rates for patients with HNC receiving non-palliative treatment in the United States. However, the retrospective nature of this study, lack of cause-of-death information, lack of data on post-treatment complications, and residual confounding limited our ability to draw causal inference. In addition, our data lacked specific patient income or travel distance information, so data used were derived zip code-based demographics and treatment locations respectively. There may also be demographic differences by region and year that were outside the scope of this study.

Clinical and public health implications

While socioeconomic disparities are known to impact HNC outcomes in the long-term, we have characterized the impact of these disparities within 90 days of patients receiving treatment. We have also identified the characteristics of patients in the United States at greater risk of mortality due to these racial and socioeconomic disparities. Since healthcare disparities are modifiable barriers to health and well-being, there should be concerted efforts to mitigate these disparities and improve short-term HNC survival irrespective of race, gender, income, insurance status, or ability to travel long distance for care. Systemic efforts should be made to alleviate travel burden for patients who do not have access to regionalized multidisciplinary care centers or to eliminate the need to travel farther distance for better care, and

physicians should be cognizant of travel burden when creating a plan of treatment for HNC patients.

Conclusions

There are several racial and sociodemographic disparities that are associated with mortality among patients HNC in the United States including black race, male gender, low income, short travel distance, and being uninsured, or insured through Medicaid or Medicare. These disparities are present and impact mortality within 90 days post-treatment. While further research is warranted to determine the underlying mechanisms for these disparities; current efforts should focus on mitigating these disparities and access to care issues that impact HNC mortality even in the short-term.

Conflict of interest

None.

Funding sources

None.

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This study will be presented in part at the 11th American Association for Cancer Research (AACR) Conference on The Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved; November 2–5, 2018; New Orleans, LA.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.oraloncology.2018.12.023>.

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