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It's More than Just Cancer Biology: Health Disparities in Patients with Pancreatic Neuroendocrine Tumors

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Abstract

Background and Objectives: Pancreatic neuroendocrine tumors (PNETs) represent a rare form of pancreatic cancer. Racial/ethnic disparities have been documented in pancreatic ductal adenocarcinoma, but health disparities have not been well described in patients with PNETs.

Methods: A retrospective review of patients with PNETs in the National Cancer Database was performed for 2004–2014. 16,605 patients with PNETs and available vital status were identified. Survival was compared by race/ethnicity and socioeconomic status using Kaplan-Meier methods and Cox regression.

Results: There were no significant differences in survival between Non-Hispanic, White; Hispanic, White; or Non-Hispanic, Black patients on univariate analysis. Kaplan-Meier analysis showed that patients from communities with lower median household income and education level had worse survival ($p<0.001$). Patients age <65 without insurance, similarly, had worse survival ($p<0.001$). Multivariable modeling found no association between race/ethnicity and risk of mortality ($p=0.37$). Lower median household income and lower education level were associated with increased mortality ($p<0.001$).

Conclusions: Unlike most other malignancies, race/ethnicity is not associated with survival differences in patients with PNETs. Patients with lower socioeconomic status had worse survival. The presence of identifiable health disparities in patients with PNETs represents a target for intervention and opportunity to improve survival in patients with this malignancy.

Keywords

healthcare disparities; neuroendocrine carcinoma; pancreas cancer

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Introduction

Primary pancreatic neuroendocrine tumors (PNETs) represent a rare form of pancreatic cancer, comprising only 1–3% of pancreatic neoplasms.[1,2] The incidence of PNETs is approximately 0.82 per 100,000 persons, as of 2012. This represents a greater than fourfold increase from 20 years prior[3], which is thought to be partially due to the increase in incidental, non-functional PNETs diagnosed on Computed Tomography (CT) imaging. PNETs exhibit varied malignant potential[2] and treatment options include hormonal or chemotherapeutic agents, radiation/nuclear medicine therapies, and surgical intervention. Treatment patterns and outcomes vary by provider and institution and the optimal treatment of PNETs remains controversial.[1,4,5] Tumor size and functionality are important clinical factors that affect treatment decisions. Nevertheless, PNETs prove deadly, with a five-year overall survival of 52%.[6]

Health disparities are known to underlie outcomes in nearly every malignancy.[7,8,9] Racial/ethnic and other socioeconomic disparities exist for patients with pancreatic ductal adenocarcinoma (PDAC), the most common type of pancreatic cancer.[10,11,12,13] Incidence and survival with PDAC vary by race/ethnicity, with Non-Hispanic, Black (NHB) patients having higher incidence and worse overall survival compared to Non-Hispanic, White (NHW) patients. Hispanic patients have the best overall survival, which appears to be independent of socioeconomic status. Other socioeconomic factors such as lower income, urban/rural residence, geographic location, and insurance status are also associated with survival in PDAC across racial/ethnic groups, but these factors do not fully explain the observed disparities, suggesting biologic differences across races/ethnicities that drive tumor pathogenesis.[14] However, the presence of these disparities remains underexplored in PNETs. A single study of disparities in PNETs in the Surveillance, Epidemiology, and End Results (SEER) database exists, but only compares Black patients to all others, rather than comparing data across races/ethnicities.[15]

Further exploration into health disparities in PNETs is needed and may help elucidate optimal management, as well as improve outcomes. This work seeks to evaluate the presence of health disparities in patients with PNETs captured in the National Cancer Database (NCDB), as well as to characterize these disparities. The objective of this study is to examine survival by race/ethnicity and other socioeconomic factors in patients diagnosed with PNETs. We hypothesize that health disparities exist in patients with PNETs.

Materials and Methods

Data source and study population

An application was submitted to the National Cancer Database (NCDB) for a Participant User File (PUF) for all cases of pancreatic malignancies diagnosed between 2004–2014. The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. It includes data from more than 1,500 Commission-accredited cancer programs in the United States. The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology

employed, or the conclusions drawn from these data by the investigator. The database includes about 70% of all newly diagnosed cancers in the United States [16]. The data are de-identified and IRB exempt. The PUF was queried for all cases of PNETs. The following International Classification of Diseases for Oncology (ICD-O) codes were used to identify these cases: 8150, 8151, 8152, 8153, 8155, 8156, 8240, 8243, 8246, and 8249. There were 20,601 identified cases. Vital status was missing for 2,991 patients. An additional 1,022 patients were excluded because their case counts by race/ethnicity were too low for inclusion; their race/ethnicity was listed as American Indian/Native Alaskan (N=49), Asian (N=448), Hispanic, Black (N=318), Native Hawaiian/Pacific Islander (N=36) or other/unknown (N=171), leaving 16,605 cases for analysis.

Variables and outcomes

Patient characteristics and socioeconomic variables included age, sex, race, ethnicity, Charlson/Deyo score (a comorbidity index), insurer (private, Medicare/Medicaid, or uninsured), distance lived from the hospital that reported the case, urban vs rural geographic location, median household income and percentage of population without a high school degree in the patient's ZIP code, whether surgery was performed, facility type, histology, and presence of metastasis. The median household income for patients' area of residence at the time of diagnosis was determined by ZIP code and 2012 American Community Survey data. Race (black, white, etc.) was combined with ethnicity (Hispanic vs Non-Hispanic). Patients were classified as Non-Hispanic, White; Non-Hispanic, Black; or Hispanic, White. Tumors were classified as secretory (ICD-O codes 8150 or 8246), non-secretory (8151, 8152, 8153, 8155, 8156) or carcinoid (8240, 8243, 8249) as recommended by the Neuroendocrine Tumor Task Force of the National Cancer Institute GI Steering Committee.[17] Pathologic T, N, and M stage are reported. The primary outcome of interest was survival across race/ethnicity. Secondary outcomes included survival by other socioeconomic factors.

Statistical analysis

Statistical analysis was conducted using the R statistical software package (V.3.6.3, The R Foundation for Statistical Computing).[18] Descriptive statistics were calculated from variables of interest noted above. P-values are the results of Fisher's exact or chi-square tests (categorical variables) or Mann-Whitney tests (continuous variables). Kaplan-Meier methods were used for univariate analysis of survival by patient variables. Pairwise comparisons were calculated for variables with >2 groups and reported when significant.

Mixed-effects Cox proportional hazards models were used for multivariable analysis of long-term survival. A random effect for hospital was included to account for the clustering of observations by medical center. Facility type was excluded as a covariate because it was a marker for severity of case (patients needing surgery tended to be reported by academic centers and patients with more advanced disease more often were reported by community centers). Similarly, N stage was excluded as it was highly correlated with T stage. After exclusions, covariates for all models included gender, age, geographic region (East, Midwest, New England or Pacific), population (metro, metro adjacent, non-metro adjacent or rural), race, distance from center reporting the case, Charlson/Deyo score, year

of diagnosis, tumor type (secretory, non-secretory or carcinoid), tumor site (C250, C251, C252, C258, C259 or other), tumor grade (well-differentiated, moderately differentiated, poor or undifferentiated, or undetermined), tumor size, T stage (T0/T1, T2, T3, or T4/TX), and metastasis. The relationship between age and mortality was non-linear, with risk increasing rapidly for older patients, so a quadratic term was included in the models. The increasing risk of tumor size plateaued at 39mm. Therefore, the model assumed a linear effect for tumors <39mm and static effect for tumors >39mm.

Education and income levels were highly correlated (78% of those in the highest income bracket were also in the highest education bracket, while only 3% of those in the lowest two income brackets were in the highest education bracket). To avoid possible masking of effects introduced by collinearity, we ran two models, one with all covariates above plus income, and a second replacing income with education. Also, because Medicare causes insurance status to be highly correlated with age, the effect of insurance status was estimated in two subanalyses that included all covariates above plus income, but considered patients <65 and 65 and older separately. The non-linear age terms were dropped from these models because it did not improve model fit.

Most covariates were 100% complete (gender, age, race, Charlson/Deyo score, year of diagnosis, metastasis, tumor type, site and grade) or had missingness rates <3% (income, education, insurance, population area and distance from reporting center). Only region (8%), tumor size (13%) and T stage (13%) had higher missingness rates. All missing data was multiply imputed (10 iterations) via the R package “mice”, which draws values for missing data from a likely distribution given the patient’s values on other variables and the distribution of the data across all patients [19]. Results of the 10 model runs were pooled according to the methods of Barnard and Rubin to yield final effect estimates[20].

Results

Patient characteristics

There were 16,605 patients with PNETs meeting inclusion criteria in the NCDB from 2004–2015 (Table 1). Of those, 13,095 were NHW; 2,061 were NHB; 1,449 were Hispanic, White (HW). The patient characteristics for these populations are displayed in Table 1. The average age at diagnosis (mean ± standard deviation) for NHW patients was higher (61 ± 13.6 years) than for all other groups. Black patients were younger (57 ± 13.3 years) and more often female (58.9%, compared to < 47.9% for all other groups). NHB and HW patients had higher uninsured rates (5.6% and 7.4%, respectively) compared to NHW (2.3%). NHW patients more often lived in ZIP codes with median income > $63,000 (38%), compared to 17.9% of NHB and 28.8 % of HW. Additionally, NHB and HW patients more often lived in ZIP codes with greater than 21% of the population lacking a high school degree (32.1% and 29.3%, respectively) compared to NHW (10.5%). NHB and HW more often lived in metro locations (91.1% and 89.8%, respectively) compared to NHW (82.7%). NHW patients lived a closer distance to the hospital compared to NHB and HW (61.2 ± 170 miles vs 35.0 ± 121 miles and 38.1 ±115 miles, respectively). There were significant differences by race/ethnicity for a number of oncologic factors including disease site (p<0.0001), tumor size (p<0.0001), grade (p=0.006), type (p=.005), T stage (p=0.0003), and N stage (p=0.002).

There were not significant differences by race/ethnicity on the presence of metastasis at diagnosis (p=0.10).

Patient characteristics and survival

As a preliminary step prior to risk-adjustment using Cox regression models, Kaplan-Meier analysis was performed to assess the effect of individual socioeconomic parameters on overall survival. Fig. 1 demonstrates that there is no significant difference in overall survival by race/ethnicity (log-rank p=0.151). Median survival times in months (95% CI) were 78.8 (75.6–82.0), 84.0 (74.0–93.1), and 95.6 (87.5–110.8) in the NHW, HW, and NHB groups, respectively.

The effect of socioeconomic factors on survival were similarly evaluated using Kaplan-Meier analysis. Fig. 2 shows that there is a significant difference in survival by median household income in patient area of residence (log-rank p<0.001). Pairwise comparisons show that patients living in ZIP codes with median household income of > $63,000 live significantly longer than all other groups. Median survival times in months (95% CI) were 74.8 (66.9–81.0), 74.2 (67.3–79.4), 78.8 (73.2–86.1) and 95.0 (87.7–104.2) in the <$38,000, $38,000-$47,999, $48,000-$62,999 and ≥$63,000 groups, respectively. Fig. 3 demonstrates that there is a significant difference in survival by percentage of the population without a high school diploma in the patient's area of residence (log rank p<0.001). Pairwise comparisons show that patients living in ZIP codes with <7% of the population without a high school diploma live significantly longer than all other groups. Median survival times in months (95% CI) were 76.4 (69.8–85.0), 77.4 (72.4–85.8), 76.0 (70.8–81.8), and 100.1 (91.3–107.1) in the >21%, 13–20.9%, 7–12.9%, and <7% groups, respectively. Finally, the effect of insurer on overall survival was evaluated (Fig. 4). Because of the age restriction for Medicare, we considered the effect of insurance for patients 65 or older (N=6,674) and those <65 (N=9,931) separately. Among patients 65 or older, there were no significant survival differences among those on public, private or no insurance. Median survival times in months (95% CI) were 36.7 (CI non-estimable because of small group size) for uninsured, 51.3 (48.1–55.7) for Medicare/Medicaid, and 53.5 (45.8–61.3) for private insurance. In contrast, for patients <65, those on private insurance had better survival than those on public insurance or those uninsured (p<.0001 for both pairwise comparisons). Median survival times in months (95% CI) were 65.4 (56.7–100.7) for uninsured, 80.3 (73.0–95.7) for Medicare/Medicaid, and 116.7 (109.7–130.4) for private insurance.

Multivariable analysis of patient characteristics and survival

The effect of covariates on survival was evaluated using mixed-effects Cox proportional hazards models. Because of their high correlation, the effects of income and education level were estimated in two otherwise identical models. Table 2 shows the results of these models, each pooled over 10 multiply imputed datasets. Similarly, because of the Medicare-induced confounding of age and insurance status, the effect of insurance was estimated in two models, one including only patients 65 and older and an otherwise identical model including only younger patients (Table 3). Notably, despite the large sample size, race/ethnicity was not significantly associated with survival in any of the four models (overall p>0.50 for all), although there was marginal evidence that HW have a slight survival advantage over NHW.

As expected, as age increased, the risk of mortality also increased (p <0.0001). Male patients had significantly higher risk of mortality than female patients (p<.002 in all models). There was a significant difference in mortality by median household income (p<.0002 in all three models that included income as a covariate) and by education level (p<.0001). Patients who live in ZIP codes with median household income >$63,000 and/or in the highest education bracket (<7% without high school diploma) had significantly lower risk of mortality compared to those with lowest income and/or education (p<.0001). Insurance status had a significant effect for patients <65, with those on private insurance having better survival than those on public insurance, presumably largely Medicaid (p<.0001); however, this effect disappeared for patients 65 and older, where there was no difference in outcome between those with private insurance and those with public insurance, presumably mostly Medicare (p=.792). Other notable clinical and pathologic variables that were associated with increased mortality include lesion in the head or body of the pancreas, worse tumor grade, increased tumor size, increased T stage, and the presence of metastasis. Race, year of diagnosis and population area were not significantly associated with survival in any of the four models.

Discussion

The extent of health disparities underlying outcomes in pancreatic neuroendocrine tumors has not been described. This work represents an in-depth evaluation of the impact of a number of socioeconomic factors on survival at the national level. There were no differences in univariable or multivariable analysis of survival by race/ethnicity. Patients who were uninsured or who resided in communities with lower median household income and lower education level had worse overall survival. The evidence in this study demonstrates that while race/ethnicity is not associated with survival, patients from disadvantaged socioeconomic backgrounds are at risk of worse survival. Clinical factors that increased the risk of death from PNETs included larger tumor size, increased T stage, and the presence of metastasis.

A single national study using the SEER database evaluated for health disparities in patients with PNETs.[15] This study found that Black patients had worsened overall survival and disease specific survival compared to “White/Other” patients. Unfortunately, making significant conclusions about race-specific survival when comparing Black patients to all other patients is difficult. Further, it is important to understand the differences between the NCDB and SEER database. The advantage of the SEER database is the ability to derive population level data and disease specific survival. The advantage of the NCDB is that it captures about 70% of all new cancer cases compared to 28% of cancer cases captured by SEER. We chose to perform this study using the NCDB due to the rarity of PNETs and desire for increased samples size. No conclusions can be made about how the differences in the databases may account for observed differences between studies. Importantly, provided a large database with robust race/ethnicity data, studies to evaluate for racial/ethnic disparities should avoid combining large, diverse groups together to make conclusions about a single race.

Our results differ significantly from many other malignancies. For instance, Black patients with invasive breast cancer are more likely to die from stage 1 disease than non-Hispanic, White, and Asian women, even after adjustment for income.[21] Similar trends have been observed in Black men with prostate cancer.[22] In lung cancer, 5-year survival is lower among Black patients than White patients.[23] In evaluating other GI malignancies, Black patients have been found to have worsened survival in gastric, colorectal, liver cancer, and the most common pancreatic cancer, pancreatic ductal adenocarcinoma[14,24,25,26,27,28] In our study, there were not significant differences in unadjusted or adjusted survival in NHW, NWB, and HW patients. A study using the NCDB to evaluate for racial/ethnic disparities in pancreatic ductal adenocarcinoma found that Hispanic patients, particularly those of Dominican descent, had improved survival.[28] Due to sample size limitations among Hispanic patients with PNETs, further subpopulation analysis was not feasible. Similar to our study, other studies in the NCDB have found socioeconomic factors such as median household income, education, insurance status, and urban/rural residence to be associated with survival in pancreatic, colorectal, lung, and oral cancer[14,29,30,31]

There are a number of important limitations to note about our study. Although it utilizes a national database with a large sample set, it is retrospective in nature. Misclassification bias may occur. There is no ability to classify multi-racial persons in the NCDB, although they are certainly present, thus the extent of misclassification of race/ethnicity, particularly for patients of diverse ancestry, is unknown. Additionally, analysis of all reported racial/ethnic groups was not feasible due to low case counts for certain groups. Since ZIP codes are used to determine median household income, these are not representative of an individual's socioeconomic status, but reflect the community in which the patient resides. Finally, some variables that may affect disease stage at presentation and overall survival had incomplete or unavailable data. While these limitations are important to understand, given the large patient population in the NCDB, the results reported remain valuable to understanding how socioeconomic status affects survival in patients with PNETs.

Conclusion

In conclusion, unlike many other malignancies, there were not significant survival differences by race/ethnicity in patients with PNETs. More importantly, socioeconomic factors are associated with survival. Patients who come from disadvantaged backgrounds have worse survival. Further work to identify factors contributing to these health disparities, such as barriers to follow-up surveillance, or ability to adhere to recommended treatment plans, may further characterize possible access-related issues associated with these socioeconomic factors. Identifying patients at risk of poorer outcomes and implementing mechanisms to overcome these disparities represent important next steps in improving survival in PNETs.

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Data availability statement

The primary dataset (National Cancer Database) is publicly available by request through the American College of Surgeons (https://www.facs.org/quality-programs/cancer/ncdb). The dataset analyzed for this study may be made available by the corresponding author upon request.

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Synopsis:

Race/ethnicity is not associated with survival differences in patients with PNETs. Patients with lower socioeconomic status had worse survival. The presence of identifiable health disparities in patients with PNETs represents a target for intervention and opportunity to improve survival.

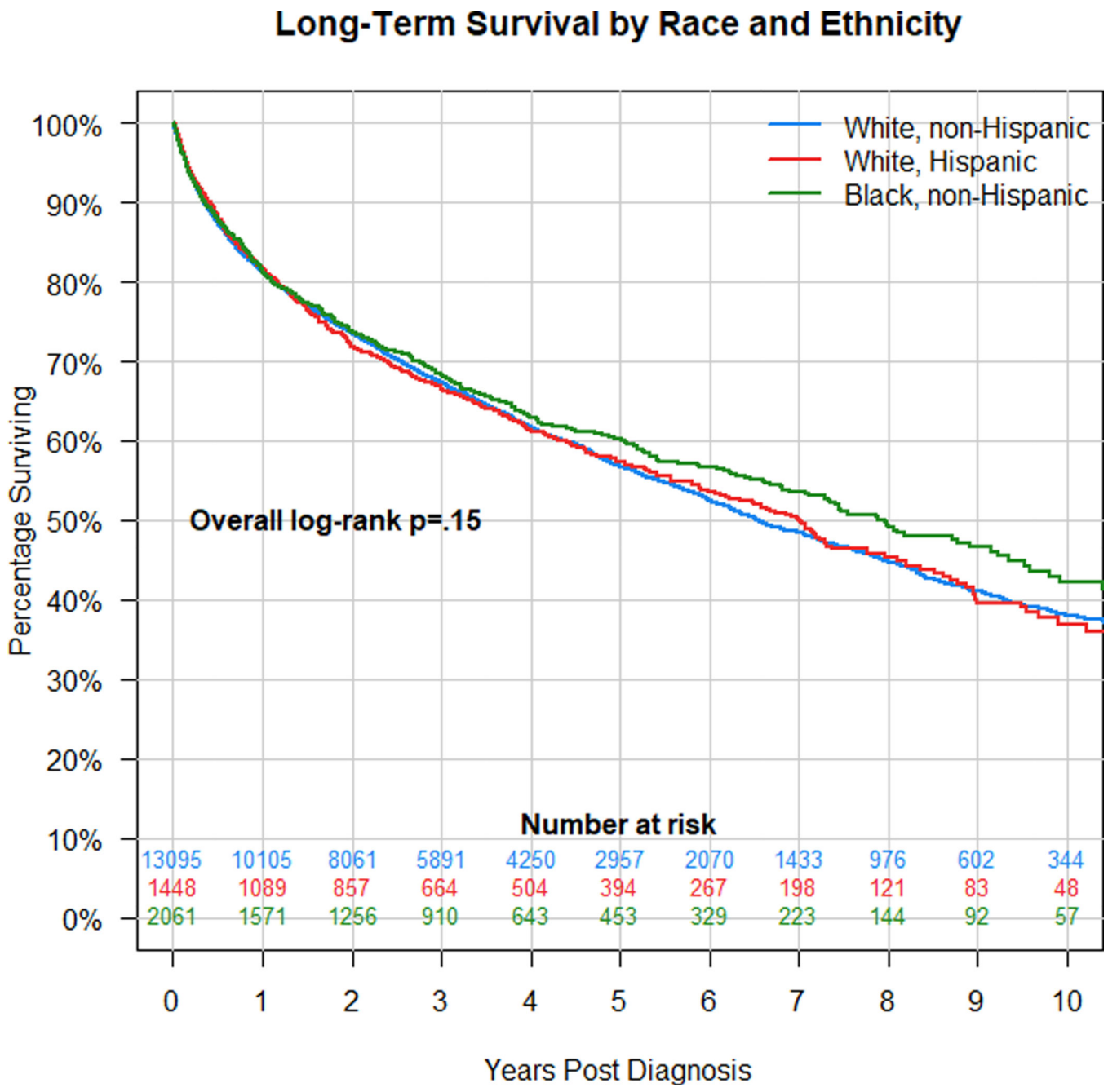

Figure 1.

Kaplan-Meier analysis of survival in patients with PNETs by race/ethnicity. There is no significant difference in survival by race/ethnicity, overall log-rank p=0.151.

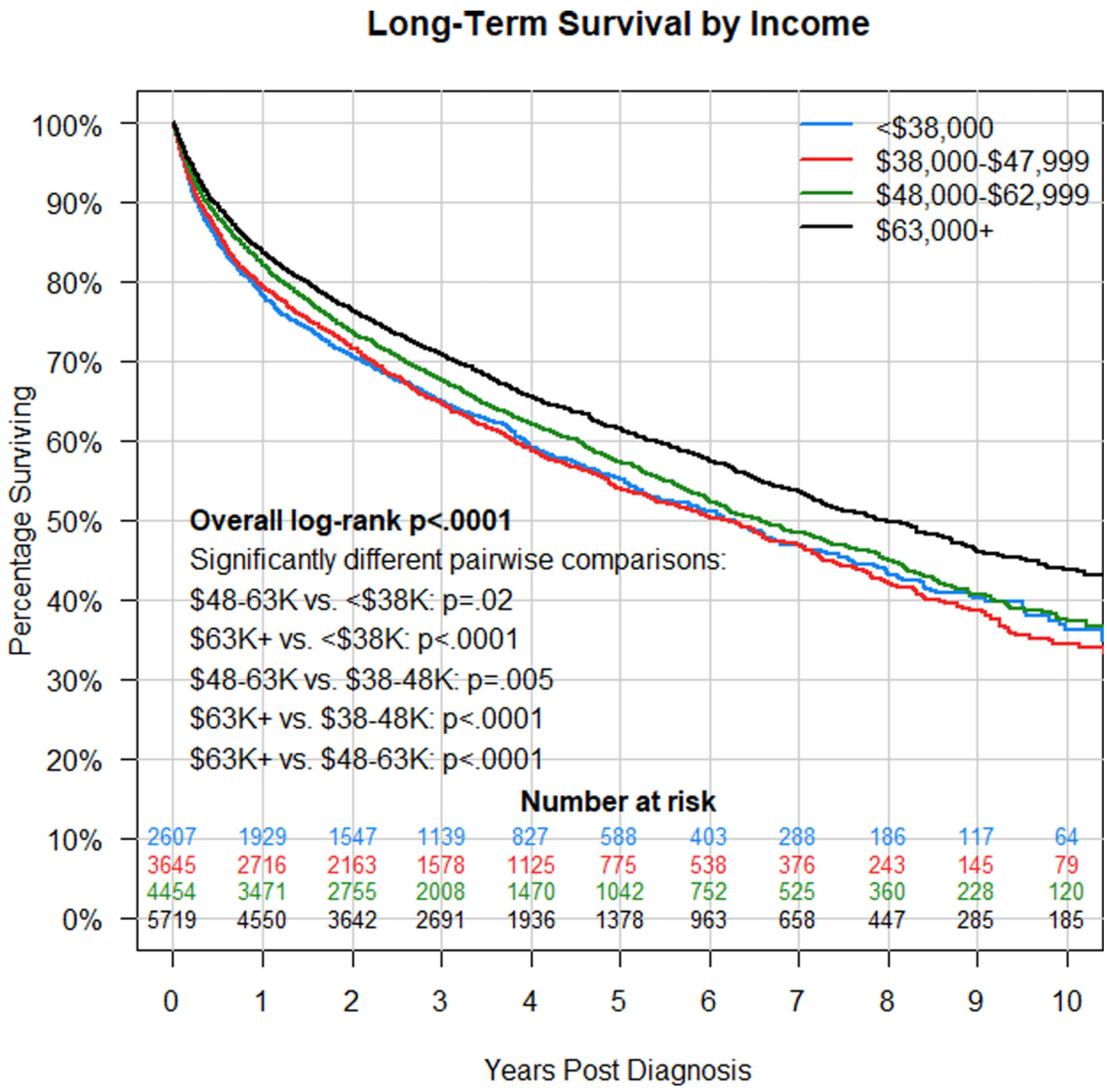

Figure 2.

Kaplan-Meier analysis of survival in patients with PNETs by median household income in patients' area of residence. There is a significant difference in survival by median household income (log-rank p<0.001). Pairwise comparisons demonstrated that patients residing in ZIP codes with median household income > $63,000 had significantly longer survival than all other groups (p<0.001).

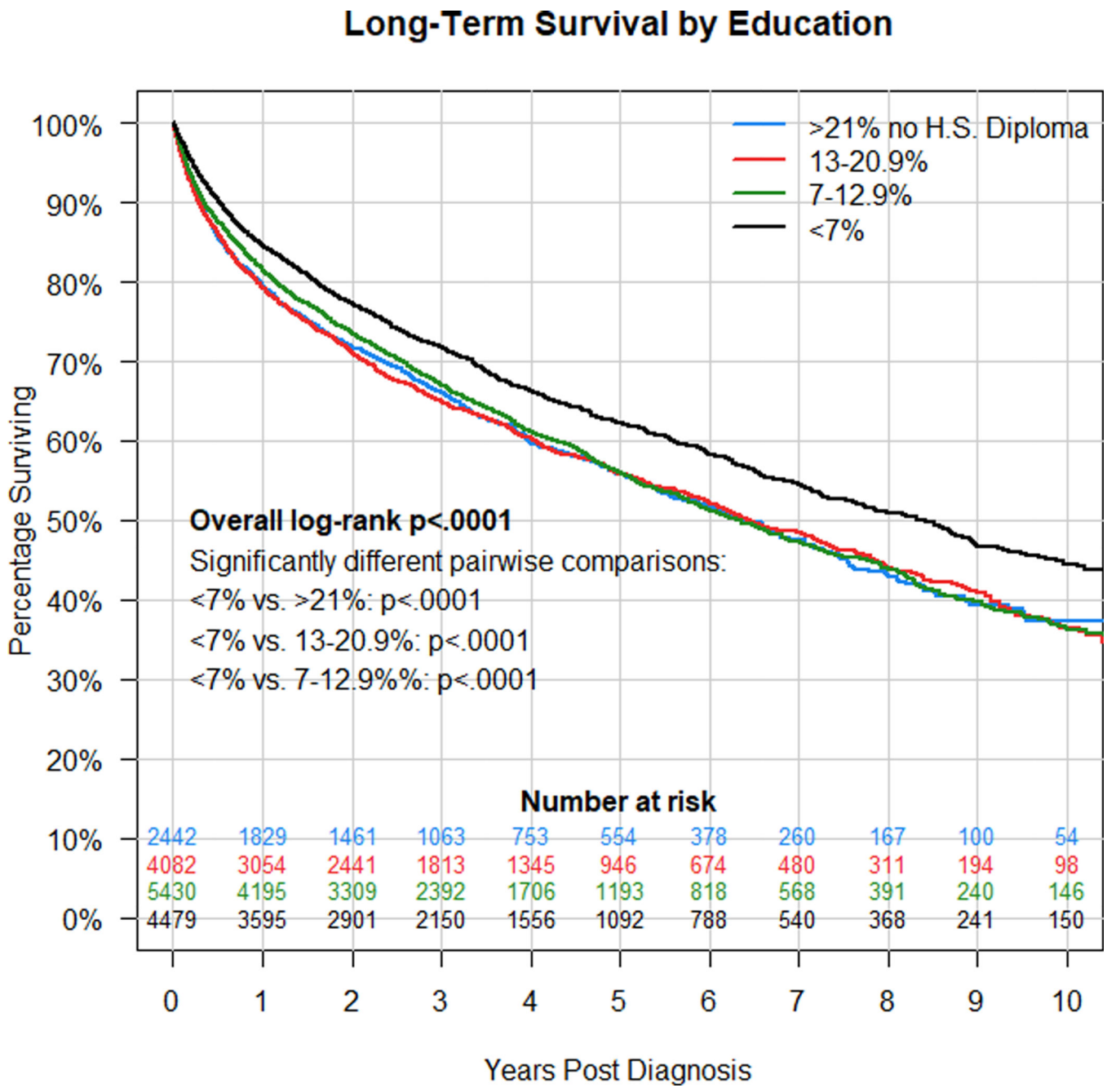

Figure 3.

Kaplan-Meier analysis of survival in patients with PNETs by percentage of population without a high school diploma in patients' area of residence. There is a significant difference in survival by percentage without high school diploma (log-rank p<0.001). Pairwise comparisons demonstrated that patients residing in ZIP codes with <7% of the population without a high school diploma had significantly longer survival than all other groups (p<0.001).

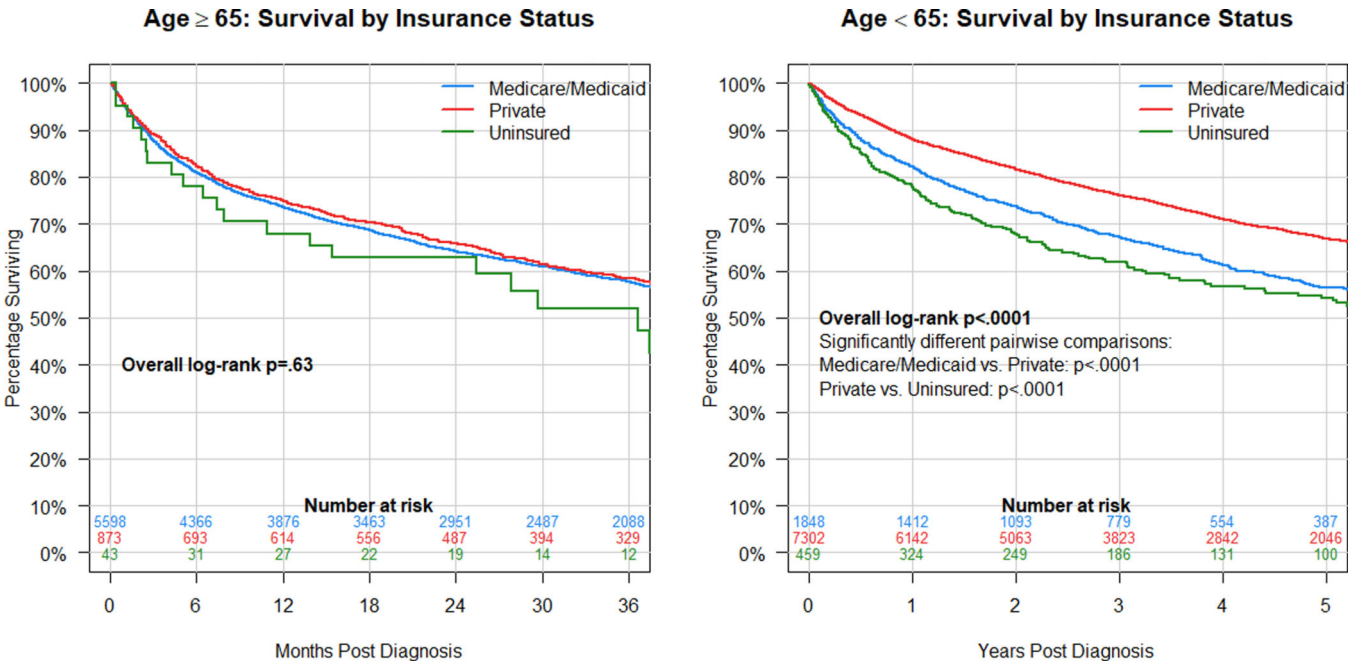

Figure 4.

Kaplan-Meier analysis of survival in patients with PNETs by insurance type. Among patients 65 or older at diagnosis, there is no significant difference in survival by insurance type (p=.625), but among patients <65, those with private insurance have better survival than those on public insurance or without insurance (p<.0001).

Table 1.

Patient Characteristics

	White, Non-Hispanic (N = 13,095)	Black, Non-Hispanic (N = 2,061)	White, Hispanic (N = 1,449)	p-value
Age	61.0 (13.6)	56.9 (13.3)	58.2 (14.7)	<0.0001
Male	7311 (55.8)	848 (41.1)	755 (52.1)	<0.0001
Charlson/Deyo Score				<0.0001
0	9648 (73.7)	1367 (66.3)	1060 (73.2)	
1	2650 (20.2)	533 (25.9)	312 (21.5)	
2	556 (4.2)	105 (5.1)	52 (3.6)	
3+	241 (1.8)	56 (2.7)	25 (1.7)	
Surgery	7163 (55.9)	1101 (54.9)	782 (55.1)	0.667
Distance from Hospital	61.1 (170)	35.0 (120)	38.1 (115)	<0.0001
Insurer				<0.0001
Medicare/Medicaid	5879 (46.2)	964 (47.9)	603 (43.5)	
Private	6557 (51.5)	937 (46.5)	681 (49.1)	
None	288 (2.3)	112 (5.6)	103 (7.4)	
Median Income				<0.0001
< $38,000	1490 (11.5)	824 (40.3)	293 (20.4)	
$38,000 – $47,999	2869 (22.2)	441 (21.6)	335 (23.4)	
$48,000 – $62,999	3648 (28.2)	413 (20.2)	393 (27.4)	
> $63,000	4942 (38.2)	365 (17.9)	413 (28.8)	
% of Population with Less than High School Education				<0.0001
>21%	1366 (10.5)	656 (32.1)	420 (29.3)	
13–21%	3039 (23.5)	689 (33.7)	355 (24.8)	
7–13%	4567 (35.3)	486 (23.8)	377 (26.3)	
<7%	3984 (30.8)	213 (10.4)	282 (19.7)	
Facility Location				<0.0001
Midwest	2148 (17.6)	279 (15.1)	304 (23.7)	
East	2925 (24.0)	471 (25.6)	248 (19.4)	
New England	5178 (42.4)	1001 (54.3)	478 (37.3)	
Pacific	1960 (16.1)	91 (4.9)	251 (19.6)	
Facility Type				<0.0001
ARP	6797 (55.7)	1086 (59.0)	604 (47.2)	
CCCP	554 (4.5)	66 (3.6)	45 (3.5)	
CCP	3650 (29.9)	429 (23.3)	459 (35.8)	
INCP	1210 (9.9)	261 (14.2)	173 (13.5)	
Urban/Rural				<0.0001
Metro	10475 (82.7)	1834 (91.1)	1269 (89.8)	
Metro adjacent	1362 (10.8)	114 (5.7)	81 (5.7)	

	White, Non-Hispanic (N = 13,095)	Black, Non-Hispanic (N = 2,061)	White, Hispanic (N = 1,449)	p-value
Non-metro adjacent	572 (4.5)	40 (2.0)	48 (3.4)	
Rural	260 (2.1)	26 (1.3)	15 (1.1)	
Tumor Type				0.005
Secretory	9964 (76.1)	1562 (75.8)	1161 (80.1)	
Non-secretory	284 (2.2)	37 (1.8)	31 (2.1)	
Carcinoid	2847 (21.7)	462 (22.4)	257 (17.7)	
Disease Site				<0.0001
Head of pancreas	3842 (29.3)	668 (32.4)	468 (32.3)	
Body of pancreas	1759 (13.4)	325 (15.8)	189 (13.0)	
Tail of pancreas	4196 (32.0)	497 (24.1)	426 (29.4)	
Pancreatic duct	8 (0.1)	4 (0.2)	1 (0.1)	
Islets of Langerhans	415 (3.2)	54 (2.6)	38 (2.6)	
Other	271 (2.1)	56 (2.7)	29 (2.0)	
Overlapping	854 (6.5)	131 (6.4)	85 (5.9)	
Pancreas, NOS	1750 (13.4)	326 (15.8)	213 (14.7)	
Tumor Size (mm)	43.6 (59.9)	41.3 (49.8)	46.2 (53.3)	<0.0001
Grade				0.006
Poor	841 (6.4)	113 (5.5)	104 (7.2)	
Moderate	1375 (10.5)	177 (8.6)	155 (10.7)	
Well	5711 (43.6)	947 (45.9)	578 (39.9)	
Undifferentiated	165 (1.3)	21 (1.0)	21 (1.4)	
Undetermined	5003 (38.2)	803 (39.0)	591 (40.8)	
T Stage				0.0003
T0	17 (0.1)	3 (0.2)	2 (0.2)	
T1	1892 (16.6)	278 (15.8)	166 (13.0)	
T2	1845 (16.2)	326 (18.5)	215 (16.9)	
T3	1745 (15.3)	257 (14.6)	181 (14.2)	
T4	136 (1.2)	23 (1.3)	32 (2.5)	
TX	5737 (50.4)	875 (49.7)	677 (53.2)	
N Stage				0.002
N0	3479 (30.8)	533 (30.5)	336 (26.6)	
N1	1698 (15.0)	305 (17.4)	205 (16.2)	
NX	6106 (54.1)	912 (52.1)	724 (57.2)	
Distant Metastasis				0.096
No	7820 (59.7)	1264 (61.3)	836 (57.7)	
Yes or unavailable	5275 (40.3)	797 (38.7)	613 (42.3)	

[a]Categorical variables displayed as N (%); Continuous variables are displayed as mean (SD)

[b]P-values are the results of chi-square tests (categorical variables) or Kruskal-Wallis tests (continuous variables).

[c]ARP: Academic/Research Program; CCCP: Comprehensive Community Cancer Program; CCP: Community Cancer Program; INCP: Integrate Network Cancer Program; NOS: Not otherwise specified

Table 2.

Multivariable results for Income and Education level: Pooled effects from two mixed-effects Cox models for long-term survival[a,b]

Factor	Model 1: HR (95% CI), p-value	Model 2: HR (95% CI), p-value
Education (vs. ≥21% no high school diploma)		Overall p<.0001
13–20.9%	NA	0.98 (.903,1.06), .572
7–12.9%	NA	0.97 (.894,1.05), .399
<7%	NA	0.81 (.742,.877), <.0001
Race (vs. White, non-Hispanic)	Overall p=.565	Overall p=.666
White, Hispanic	0.92 (.843,1.00), .055	0.92 (.840,1.00), .051
Black, Non-Hispanic	1.0 (.938,1.11), .656	1.0 (.956,1.12), .381
Male gender (vs. female)	1.1 (1.09,1.20), <.0001	1.1 (1.09,1.20), <.0001
Age overall p-value (for combined linear and non-linear terms)	<.0001	<.0001
Age (linear component)	0.97 (.955,.979), <.0001	0.97 (.955,.979), <.0001
Age (quadratic component)	1.1 (1.04,1.06), <.0001	1.1 (1.04,1.06), <.0001
Year of diagnosis (HR multiplies per year)	1.0 (.990,1.01), .797	1.0 (.990,1.01), .827
Income (vs. <$38K/year)	Overall p<.0001	
$38,000-$47,999	0.94 (.870,1.02), .145	NA
$48,000-$62,999	0.90 (.829,.973), .009	NA
$63,000+	0.80 (.738,.867), <.0001	NA
Charlson/Deyo score (HR multiplies by per unit increase)	1.2 (1.13,1.21), <.0001	1.2 (1.12,1.20), <.0001
Miles from hospital (HR multiplies by per 10-mile increment)	0.99 (.993,.998), .0001	0.99 (.994,.998), .0001
Region (vs. West)	Overall p<.0001	Overall p<.0001
East	1.2 (1.06,1.24), .001	1.1 (1.06,1.24), .001
New England	1.0 (.952,1.10), .515	1.0 (.935,1.08), .866
Pacific/mountain	1.1 (1.01,1.20), .031	1.1 (.993,1.19), .070
Population area (vs. Rural)	Overall p=.119	Overall p=.086
Metro	1.1 (.904,1.31), .376	1.1 (.884,1.27), .527
Metro adjacent	1.2 (.969,1.43), .102	1.2 (.965,1.42), .109
Not metro adjacent	1.0 (.813,1.26), .921	1.0 (.815,1.26), .907
Disease site (vs. Other)	Overall p<.0001	Overall p<.0001
C250	1.5 (1.29,1.64), <.0001	1.5 (1.29,1.64), <.0001
C251	1.2 (1.05,1.37), .009	1.2 (1.05,1.37), .008
C252	1.1 (.969,1.24), .141	1.1 (.969,1.24), .143
C258	1.2 (.990,1.33), .067	1.2 (.988,1.33), .071
C259	1.4 (1.23,1.59), <.0001	1.4 (1.22,1.58), <.0001
Tumor type (vs. carcinoid)	Overall p<.0001	Overall p<.0001
Non-secretory	1.2 (1.01,1.45), .037	1.2 (1.01,1.44), .041
Secretory	1.4 (1.30,1.54), <.0001	1.4 (1.30,1.53), <.0001

Factor	Model 1: HR (95% CI), p-value	Model 2: HR (95% CI), p-value
Tumor grade (vs. well-differentiated)	Overall p<.0001	Overall p<.0001
Poor/Undifferentiated	3.8 (3.46,4.10), <.0001	3.8 (3.46,4.10), <.0001
Moderately differentiated	1.4 (1.25,1.53), <.0001	1.4 (1.25,1.53), <.0001
Undetermined	1.7 (1.63,1.85), <.0001	1.7 (1.63,1.85), <.0001
Tumor size ≤39mm (HR multiplies per mm increase)	1.01 (1.005,1.015), .0003	1.01 (1.005,1.016), .0002
Tumor >39mm	1.5 (1.26,1.70), <.0001	1.5 (1.27,1.71), <.0001
T stage (vs. 0/1)	Overall p<.0001	Overall p<.0001
T2	1.0 (.844,1.21), .903	1.0 (.840,1.21), .946
T3	1.2 (1.00,1.43), .048	1.2 (1.00,1.43), .051
T4/X	1.9 (1.57,2.18), <.0001	1.8 (1.56,2.17), <.0001
Metastasis	2.9 (2.72,3.06), <.0001	2.9 (2.72,3.07), <.0001

[a]Model 1=All covariates+income (pooled adjusted R2=0.34, pooled AUC=0.79)

[b]Model 2=All covariates+education (pooled adjusted R2=0.34, pooled AUC=0.79)

Table 3.

Multivariable results for Insurance Status: Pooled effects from two mixed-effects Cox models for long-term survival.

Factor	Model 1: HR (95% CI), p-value	Model 2: HR (95% CI), p-value
Insurance (vs. Medicare/Medicaid)	Overall p=.335	Overall p<.0001
Private	1.0 (.914,1.13), .792	0.68 (.620,.741), <.0001
Uninsured	1.2 (.751,1.81), .497	1.0 (.869,1.20), .813
Race (vs. White, non-Hispanic)	Overall p=.549	Overall p=.953
White, Hispanic	0.92 (.816,1.05), .207	0.89 (.786,1.00), .058
Black, Non-Hispanic	0.89 (.776,1.01), .077	1.1 (.971,1.20), .156
Male gender (vs. female)	1.2 (1.08,1.24), <.0001	1.1 (1.05,1.21), .001
Age (HR multiplies for each year increase)	1.1 (1.041,1.053), <.0001	1.02 (1.013,1.021), <.0001
Year of diagnosis (HR multiplies per year)	1.0 (.985,1.01), .739	1.0 (.984,1.01), .648
Income (vs. <$38K/year)	Overall p<.0001	Overall p=.0001
$38,000-$47,999	0.93 (.835,1.05), .241	0.98 (.875,1.10), .730
$48,000-$62,999	0.89 (.797,.999), .049	0.95 (.849,1.07), .384
$63,000+	0.80 (.718,.902), .0002	0.86 (.767,.968), .012
Miles from hospital (HR multiplies by per 10-mile increment)	0.99 (.991,.998), .006	0.99 (.994,.999), .015
Region (vs. West)	Overall p=.018	Overall p=.001
East	1.1 (1.01,1.26), .033	1.2 (1.05,1.32), .006
New England	1.0 (.918,1.12), .764	1.1 (.950,1.17), .321
Pacific/mountain	1.1 (.968,1.24), .150	1.1 (.967,1.24), .150
Population area (vs. Rural)	Overall p=.240	Overall p=.749
Metro	1.1 (.845,1.40), .515	1.1 (.803,1.38), .705
Metro adjacent	1.2 (.899,1.53), .241	1.1 (.844,1.49), .425
Not metro adjacent	0.95 (.701,1.28), .730	1.1 (.766,1.44), .754
Charlson/Deyo score (HR multiplies by per unit increase)	1.2 (1.15,1.26), <.0001	1.1 (1.03,1.15), .002
Disease site (vs. Other)	Overall p<.0001	Overall p<.0001
C250	1.6 (1.32,1.89), <.0001	1.3 (1.09,1.53), .003
C251	1.3 (1.07,1.59), .008	1.1 (.896,1.31), .412
C252	1.2 (.969,1.40), .105	1.0 (.853,1.20), .887
C258	1.2 (.985,1.53), .067	1.1 (.859,1.29), .627
C259	1.6 (1.32,1.92), <.0001	1.2 (1.00,1.43), .046
Tumor type (vs. carcinoid)	Overall p<.0001	Overall p<.0001
Non-secretory	1.2 (.884,1.48), .304	1.3 (1.02,1.68), .037
Secretory	1.3 (1.17,1.45), <.0001	1.6 (1.38,1.79), <.0001
Tumor grade (vs. well-differentiated)	Overall p<.0001	Overall p<.0001
Poor/Undifferentiated	3.3 (2.88,3.68), <.0001	4.5 (3.97,5.03), <.0001
Moderately differentiated	1.4 (1.21,1.60), <.0001	1.4 (1.18,1.58), <.0001
Undetermined	1.6 (1.49,1.79), <.0001	1.9 (1.69,2.03), <.0001

Factor	Model 1: HR (95% CI), p-value	Model 2: HR (95% CI), p-value
Tumor size ≤39mm (HR multiplies per mm increase)	1.01 (1.002,1.015), .016	1.01 (1.006,1.021), .0007
Tumor >39mm	1.4 (1.15,1.73), .001	1.6 (1.28,1.96), <.0001
T stage (vs. 0/1)	Overall p<.0001	Overall p<.0001
T2	1.0 (.787,1.25), .956	1.1 (.806,1.37), .719
T3	1.1 (.893,1.41), .322	1.3 (1.03,1.71), .031
T4/X	1.7 (1.34,2.03), <.0001	2.1 (1.66,2.64), <.0001
Metastasis	2.6 (2.41,2.85), <.0001	3.2 (2.93,3.48), <.0001

[a]Model 1= patients 65 and older (pooled adjusted R2=0.33, pooled AUC=0.76)

[b]Model 2= patients <65 (pooled adjusted R2=0.30, pooled AUC=0.80)