Research Square

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Racial disparities in survival among patients with pulmonary neuroendocrine tumors: a population–based cohort study

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Abstract

Introduction:

Pulmonary neuroendocrine neoplasms (PNENs) are rare malignancies with increasing incidence. While racial disparities in cancer outcomes are well-known, their patterns in PNENs remain poorly understood.

Materials and Methods:

This population-based cohort study analyzed data from the US SEER database (2000–2019) for patients with a first primary PNEN. Absolute and relative disparities in all-cause, cancer-specific, and non-cancer mortality were assessed. Sequential adjustment and mediation analyses evaluated contributions of demographic, socioeconomic, tumor, and treatment factors.

Results:

Among 125,932 patients, significant racial disparities were observed. Cancer-specific survival improved for all groups, with the greatest gains among Non-Hispanic Black patients. Conversely, disparities in non-cancer survival widened, with Black patients experiencing the largest disadvantage. Asian/Pacific Islander patients consistently showed survival advantages. Histology modified these disparities; Black patients had marked disadvantages in carcinoid tumors but improved survival in small cell carcinoma. Mediation analyses identified disparities in surgical access and marital status as key contributors to survival disadvantages among Black patients with carcinoids.

Conclusion:

Although cancer survival has improved, disparities in non-cancer mortality are widening. These inequities are largely driven by modifiable factors like surgical access. Interventions targeting equitable treatment and comorbidity management are urgently needed to reduce survival disparities in PNENs.

Introduction

Pulmonary Neuroendocrine Neoplasms (PNENs) are a heterogeneous group of lung malignancies that include typical carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma (LCNEC), and small cell lung cancer (SCLC)[1]. The incidence has increased in recent decades, and they now represent a significant proportion of neuroendocrine carcinomas of the lung [2]. Despite advances in molecular classification and treatment, clinical management of PNENs remains challenging due to their diverse biology and variable prognosis.

Racial and ethnic disparities have been documented across multiple cancer types, including gastrointestinal and pancreatic neuroendocrine tumors, where incidence and outcomes differ substantially between groups [3, 4]. For example, Black individuals have higher incidence across much of the gastrointestinal tract, while Asian/Pacific Islander populations demonstrate higher rates of rectal

NETs[5]. However, evidence on how race and ethnicity influence the epidemiology, treatment, and survival of PNENs is limited. Existing studies suggest that non–Hispanic White individuals have the highest PNEN incidence, whereas Asian/Pacific Islanders have the lowest. Yet, most analyses have been geographically restricted, limiting their generalizability [6].

A recent California–based study provided important insights into racial differences in PNEN outcomes, but broader, population–based analyses across racially diverse cohorts are lacking[7]. Furthermore, while disparities in cancer incidence and survival are recognized, little is known about their temporal trends or the underlying mechanisms—particularly whether differences in treatment access, socioeconomic context, or tumor biology drive observed inequalities.

Materials and Methods

Data Acquisition and Study Population

This study analyzed de–identified data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program (November 2024 Submission, SEER 22 Registries), for which data access was granted in January 2025. We included all patients diagnosed with a primary pulmonary neuroendocrine tumors between January 2000 and December 2019, identified by ICD-O-3 codes: typical carcinoid (8240), atypical carcinoid (8249), large cell neuroendocrine carcinoma (8013), and small cell carcinoma (8041). Cases were excluded for: (1) race/ethnicity classified as American Indian/Alaska Native_Non-Hispanic (statistical power concerns) or Unknown; (2) undefined Summary Stage; (3) unknown/missing values for median household income (inflation-adjusted to 2022) or Rural-Urban Continuum Code; (4) incomplete cause-of-death information (State DC not available or state DC available but no COD) or unknown survival months; and (5) diagnosis years 2020–2021 to mitigate survival truncation bias(**eFigure 1**). The reporting of this study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Covariates were classified into tumor-related, treatment-related, and sociodemographic domains to examine potential mechanisms underlying racial disparities (**eTable 1**) .

Ethical Considerations

The SEER database contains de-identified public-use data; thus, this study was deemed exempt from institutional review board approval per U.S. Department of Health and Human Services policy.

Mortality Disparity Analysis

Covariates included demographic, tumor-related, treatment-related, and socioeconomic factors. Demographic factors comprised sex, race/ethnicity, and age at diagnosis. Race/ethnicity was categorized as Non-Hispanic White, Non-Hispanic Black, Non-Hispanic API, Hispanic, or Non-Hispanic

AI/AN (the latter excluded due to limited sample size). Tumor characteristics included histology, stage, and grade. Treatment variables covered radiation, chemotherapy, and surgery. Socioeconomic factors included marital status, median household income, and rural-urban classification. Detailed variable definitions and processing steps can be found in the eMethods (**Supplement**).

Patients were followed from diagnosis until death, censoring, or the end of the study (December 31, 2019). Outcomes included all-cause mortality and cause-specific mortality (attributable to the primary cancer, other cancers, or non-cancer causes). Further classification criteria for cause-specific mortality can be found in the eMethods (**Supplement**).

We evaluated both absolute and relative temporal disparities in mortality. Cumulative incidence of death was estimated using the Fine and Gray subdistribution hazard model. Absolute disparities were quantified as differences in 5-year cumulative mortality between 2000–2004 and 2015–2019. Relative disparities were assessed using Accelerated Failure Time models to estimate time ratios (TRs) with 95% CIs, comparing racial/ethnic groups to non-Hispanic White patients. Temporal trends were evaluated via interaction terms between race and diagnostic period.

To examine contributing factors, we fitted sequential AFT models adjusting progressively for socioeconomic, tumor, and treatment variables. Causal mediation analyses were conducted to quantify the role of key mediators in observed disparities. All analyses were performed in R (v4.4.1), with false discovery rate controlled via Benjamini-Hochberg correction.

Detailed methods regarding model specifications, variable definitions, and additional sensitivity analyses are provided in the eMethods (**Supplement**).

Results

Study Cohort and Baseline Characteristics

A total of 125,712 patients with pulmonary neuroendocrine tumors diagnosed between 2000 and 2019 were identified from the SEER database. The racial/ethnic distribution was: non–Hispanic White (83.1%), Black (8.0%), Hispanic (5.2%), Asian/Pacific Islander (3.3%), and American Indian/Alaska Native (0.4%). Females accounted for 51.8% of the cohort, and 61.6% were aged ≥ 65 years.

Overall, small cell carcinoma was the predominant histological subtype (84.9%). Racial disparities in stage at diagnosis and treatment patterns were evident. Hispanic patients were most likely to undergo primary–site surgery (18.5% vs 11.7% for Whites), while American Indian/Alaska Native patients had the lowest surgical rates (9.7%) but the highest use of chemotherapy (64.4%) and radiotherapy (41.4%). Asian patients were disproportionately represented in high–income neighborhoods (71.9% with household income ≥$75,000).

Because of the limited sample size (0.4%), American Indian/Alaska Native patients were excluded from subsequent comparative and mediation analyses. Detailed demographic, clinical, and treatment characteristics are shown in Table 1.

Table 1
Demographic, Clinical, and Treatment Characteristics of Lung Cancer Patients Across Racial Groups in the SEER Database

Median follow-up (mo) (IQR)	**Overall**	**White**	**Black**	**Hispanic**	**API**	**AI/AN**
	85.0 (54.0, 135.0)	**87.0 (57.0, 137.0)**	**80.0 (50.0, 121.5)**	**78.0 (41.0, 128.0)**	**71.0 (34.0, 116.0)**	**89.5 (63.2, 134.2)**
Sex						
Female	65142 (51.8)	55036 (52.7)	4999 (49.7)	3340 (51.0)	1486 (35.8)	281 (55.9)
Male	60570 (48.2)	49414 (47.3)	5058 (50.3)	3212 (49.0)	2664 (64.2)	222 (44.1)
Age						
<55	15153 (12.1)	12022 (11.5)	1594 (15.8)	1093 (16.7)	380 (9.2)	64 (12.7)
55–64	33069 (26.3)	27323 (26.2)	3102 (30.8)	1546 (23.6)	925 (22.3)	173 (34.4)
65–74	44011 (35.0)	36904 (35.3)	3281 (32.6)	2181 (33.3)	1479 (35.6)	166 (33.0)
>75+	33479 (26.6)	28201 (27.0)	2080 (20.7)	1732 (26.4)	1366 (32.9)	100 (19.9)
Diagnosis period						
2000–2004	29478 (23.4)	25069 (24.0)	2171 (21.6)	1277 (19.5)	842 (20.3)	119 (23.7)
2005–2009	31266 (24.9)	26207 (25.1)	2384 (23.7)	1591 (24.3)	974 (23.5)	110 (21.9)
2010–2014	31867 (25.3)	26350 (25.2)	2663 (26.5)	1657 (25.3)	1084 (26.1)	113 (22.5)
2015–2019	33101 (26.3)	26824 (25.7)	2839 (28.2)	2027 (30.9)	1250 (30.1)	161 (32.0)
Vital status						
Alive	18956 (15.1)	15219 (14.6)	1407 (14.0)	1585 (24.2)	677 (16.3)	68 (13.5)
Dead (attributable to this cancer dx)	96481 (76.7)	80774 (77.3)	7678 (76.3)	4456 (68.0)	3168 (76.3)	405 (80.5)

Abbreviations: IQR, interquartile range; mo, months; API, Asian or Pacific Islander; AI/AN, American Indian or Alaska Native

Median follow-up (mo) (IQR)	Overall	White	Black	Hispanic	API	AI/AN
	85.0 (54.0, 135.0)	**87.0 (57.0, 137.0)**	**80.0 (50.0, 121.5)**	**78.0 (41.0, 128.0)**	**71.0 (34.0, 116.0)**	**89.5 (63.2, 134.2)**
Other cancer	2334 (1.9)	1908 (1.8)	220 (2.2)	135 (2.1)	64 (1.5)	7 (1.4)
Other non-cancer cause	7941 (6.3)	6549 (6.3)	752 (7.5)	376 (5.7)	241 (5.8)	23 (4.6)
Histology						
8013/3: Large cell neuroendocrine carcinoma	5446 (4.3)	4291 (4.1)	653 (6.5)	272 (4.2)	219 (5.3)	11 (2.2)
8041/3: Small cell carcinoma, NOS	106710 (84.9)	89246 (85.4)	8480 (84.3)	4978 (76.0)	3558 (85.7)	448 (89.1)
8240/3: Carcinoid tumor, NOS	12113 (9.6)	9768 (9.4)	808 (8.0)	1169 (17.8)	327 (7.9)	41 (8.2)
8249/3: Atypical carcinoid tumor	1443 (1.1)	1145 (1.1)	116 (1.2)	133 (2.0)	46 (1.1)	3 (0.6)
Lymph node surgery						
Lymph node_removed	24078 (19.2)	20352 (19.5)	1699 (16.9)	1297 (19.8)	644 (15.5)	86 (17.1)
No/Unknown	101634 (80.8)	84098 (80.5)	8358 (83.1)	5255 (80.2)	3506 (84.5)	417 (82.9)
Summary stage						
Distant	80719 (64.2)	67134 (64.3)	6539 (65.0)	3959 (60.4)	2750 (66.3)	337 (67.0)
Localized	15194 (12.1)	12529 (12.0)	1078 (10.7)	1101 (16.8)	436 (10.5)	50 (9.9)
Regional	26253 (20.9)	21897 (21.0)	2166 (21.5)	1253 (19.1)	837 (20.2)	100 (19.9)
Unknown/unstaged	3546 (2.8)	2890 (2.8)	274 (2.7)	239 (3.6)	127 (3.1)	16 (3.2)
Stage Group						
1	12760 (10.2)	10531 (10.1)	983 (9.8)	842 (12.9)	364 (8.8)	40 (8.0)

Abbreviations: IQR, interquartile range; mo, months; API, Asian or Pacific Islander; AI/AN, American Indian or Alaska Native

Median follow-up (mo) (IQR)	Overall	White	Black	Hispanic	API	AI/AN
	85.0 (54.0, 135.0)	**87.0 (57.0, 137.0)**	**80.0 (50.0, 121.5)**	**78.0 (41.0, 128.0)**	**71.0 (34.0, 116.0)**	**89.5 (63.2, 134.2)**
2	4174 (3.3)	3420 (3.3)	335 (3.3)	268 (4.1)	137 (3.3)	14 (2.8)
3	29867 (23.8)	24751 (23.7)	2579 (25.6)	1361 (20.8)	1056 (25.4)	120 (23.9)
4	69476 (55.3)	57994 (55.5)	5514 (54.8)	3389 (51.7)	2287 (55.1)	292 (58.1)
Not applicable	9435 (7.5)	7754 (7.4)	646 (6.4)	692 (10.6)	306 (7.4)	37 (7.4)
Primary site surgery						
Local procedure	14890 (11.8)	12202 (11.7)	1010 (10.0)	1209 (18.5)	424 (10.2)	45 (8.9)
None/Unknown	110637 (88.0)	92101 (88.2)	9030 (89.8)	5328 (81.3)	3721 (89.7)	457 (90.9)
Others	185 (0.1)	147 (0.1)	17 (0.2)	15 (0.2)	5 (0.1)	1 (0.2)
Radiation therapy						
No/Unknown	76676 (61.0)	63708 (61.0)	5758 (57.3)	4481 (68.4)	2434 (58.7)	295 (58.6)
Yes	49036 (39.0)	40742 (39.0)	4299 (42.7)	2071 (31.6)	1716 (41.3)	208 (41.4)
Chemotherapy						
No/Unknown	49898 (39.7)	41090 (39.3)	3834 (38.1)	3181 (48.6)	1614 (38.9)	179 (35.6)
Yes	75814 (60.3)	63360 (60.7)	6223 (61.9)	3371 (51.4)	2536 (61.1)	324 (64.4)
Recommendations for surgical resection						
No/Unknown	104939 (83.5)	87363 (83.6)	8632 (85.8)	4963 (75.7)	3550 (85.5)	431 (85.7)
Yes	20773 (16.5)	17087 (16.4)	1425 (14.2)	1589 (24.3)	600 (14.5)	72 (14.3)

Abbreviations: IQR, interquartile range; mo, months; API, Asian or Pacific Islander; AI/AN, American Indian or Alaska Native

Median follow-up (mo) (IQR)	Overall	White	Black	Hispanic	API	AI/AN
	85.0 (54.0, 135.0)	**87.0 (57.0, 137.0)**	**80.0 (50.0, 121.5)**	**78.0 (41.0, 128.0)**	**71.0 (34.0, 116.0)**	**89.5 (63.2, 134.2)**
Cancer directed surgery status						
No/Unknown	109772 (87.3)	91326 (87.4)	8982 (89.3)	5304 (81.0)	3706 (89.3)	454 (90.3)
Yes	15940 (12.7)	13124 (12.6)	1075 (10.7)	1248 (19.0)	444 (10.7)	49 (9.7)
Marital status						
Married	62925 (50.1)	53679 (51.4)	3267 (32.5)	3210 (49.0)	2561 (61.7)	208 (41.4)
Unknown	5335 (4.2)	4336 (4.2)	535 (5.3)	281 (4.3)	156 (3.8)	27 (5.4)
Unmarried	57452 (45.7)	46435 (44.5)	6255 (62.2)	3061 (46.7)	1433 (34.5)	268 (53.3)
Neighborhood income						
$75,000+	57562 (45.8)	47738 (45.7)	3494 (34.7)	3121 (47.6)	2982 (71.9)	227 (45.1)
<$75,000	68150 (54.2)	56712 (54.3)	6563 (65.3)	3431 (52.4)	1168 (28.1)	276 (54.9)
Urban-rural classification						
Rural	23788 (18.9)	21767 (20.8)	1220 (12.1)	417 (6.4)	260 (6.3)	124 (24.7)
Urban	101924 (81.1)	82683 (79.2)	8837 (87.9)	6135 (93.6)	3890 (93.7)	379 (75.3)

Abbreviations: IQR, interquartile range; mo, months; API, Asian or Pacific Islander; AI/AN, American Indian or Alaska Native

Racial Survival Trends

As shown in Fig. 1, **eTable 3** and **eTable 4**, significant racial disparities in mortality and distinct cause-specific patterns were observed among patients with pulmonary neuroendocrine neoplasms (PNENs). Cancer-specific death was the leading cause, with a 5-year cumulative incidence of 79.3%. Non-Hispanic White and Asian/Pacific Islander patients showed favorable cancer-specific survival, while Hispanic patients demonstrated the most favorable cancer-specific survival (5-year mortality rate: 71.8%). Despite non-Hispanic Black patients having a 10-year cancer-specific mortality (81.4%) that was not the highest, they still experienced the highest overall all-cause mortality (93.0%). This was entirely due to them

having the highest cumulative incidence of death from both other cancers and non-cancer causes, highlighting critical disparities in non-cancer health outcomes.

Analysis of survival outcomes revealed both improvements over time and persistent racial disparities, as detailed in Table 2. Cancer–specific survival (CSS) improved significantly for all racial groups between 2000 and 2019 (P for trend < 0.001). The most pronounced relative gain was observed among Black patients (time ratio [TR] 1.38, 95% CI 1.21–1.57). Asian/Pacific Islander patients consistently showed survival advantages across all metrics.

Table 2
Time Ratios (TR) for All-Cause and Cause-Specific Mortality Among PNENs Patients by Race/Ethnicity and Period, 2000–2019

Race	Period	All-causes	PNEN	Other cancer	Other non-cancer cause
White	2000–2019	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
White	2000–2004	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
White	2005–2009	1.05 (1.02–1.08)**	1.07 (1.04–1.11)***	0.74 (0.60–0.91)*	0.85 (0.74–0.96)*
White	2010–2014	1.03 (1.00-1.06).	1.07 (1.03–1.10)***	0.61 (0.50–0.75)***	0.73 (0.64–0.83)***
White	2015–2019	1.07 (1.04–1.11)***	1.13 (1.09–1.17)***	0.62 (0.50–0.76)***	0.65 (0.57–0.75)***
White	P for trend	< 0.001	< 0.001	0.423	0.006
Black	2000–2019	1.12 (1.08–1.16)***	1.16 (1.11–1.20)***	0.79 (0.64–0.98)	0.78 (0.68–0.90)**
Black	2000–2004	0.99 (0.87–1.13)	1.01 (0.88–1.16)	0.61 (0.26–1.39)	0.85 (0.48–1.48)
Black	2005–2009	1.14 (1.01–1.30)*	1.20 (1.05–1.37)***	0.54 (0.25–1.15)	0.74 (0.44–1.25)
Black	2010–2014	1.25 (1.11–1.42)***	1.33 (1.17–1.52)***	0.57 (0.28–1.17)	0.66 (0.41–1.06)
Black	2015–2019	1.23 (1.09–1.40)***	1.38 (1.21–1.57)***	0.55 (0.27–1.11)	0.42 (0.28–0.65)***
Black	P for trend	0.001	< 0.001	0.423	0.169
Hispanic	2000–2019	1.15 (1.10–1.21)***	1.15 (1.09–1.20)***	1.01 (0.77–1.31)	1.24 (1.03–1.50).
Hispanic	2000–2004	0.97 (0.81–1.15)	0.94 (0.78–1.12)	1.04 (0.30–3.58)	1.71 (0.70–4.21)
Hispanic	2005–2009	1.32 (1.12–1.55)***	1.36 (1.15–1.61)***	1.09 (0.39–3.10)	0.88 (0.47–1.67)
Hispanic	2010–2014	1.17 (1.00-1.37).	1.22 (1.03–1.44)**	0.51 (0.22–1.14)	0.86 (0.46–1.62)

Abbreviations: PNEN, pulmonary neuroendocrine neoplasms; API, Asian or Pacific Islander.
*P<0.05;**P<0.01;***P<0.001.

Race	Period	All-causes	PNEN	Other cancer	Other non-cancer cause
Hispanic	2015–2019	1.29 (1.11–1.51)***	1.35 (1.14–1.59)***	0.62 (0.28–1.40)	0.90 (0.50–1.62)
Hispanic	P for trend	0.001	< 0.001	0.423	0.113
API	2000–2019	1.26 (1.20–1.34)***	1.24 (1.17–1.32)***	1.58 (1.09–2.30).	1.43 (1.14–1.81)**
API	2000–2004	1.22 (0.99–1.51).	1.24 (1.00-1.55).	0.86 (0.22–3.31)	1.05 (0.43–2.56)
API	2010–2014	1.20 (1.00-1.44).	1.23 (1.02–1.49)*	0.91 (0.27–3.04)	0.87 (0.41–1.85)
API	2015–2019	1.46 (1.21–1.75)***	1.45 (1.20–1.76)***	1.42 (0.40–5.05)	1.43 (0.65–3.13)
API	2005–2009	1.35 (1.11–1.64)***	1.35 (1.10–1.65)***	1.50 (0.35–6.34)	1.27 (0.55–2.95)
API	P for trend	< 0.001	< 0.001	0.423	0.180

Abbreviations: PNEN, pulmonary neuroendocrine neoplasms; API, Asian or Pacific Islander.
*P<0.05;**P<0.01;***P<0.001.

In contrast, non–cancer survival (NCS) worsened over time, with disparities widening. Black patients experienced the greatest disadvantage (TR = 0.42, 0.30–0.60) and the largest absolute increase in non–cancer mortality, offsetting gains in cancer–specific outcomes. White patients also showed a decline in NCS (TR = 0.65). By comparison, Asian/Pacific Islander patients maintained favorable survival across all endpoints, with higher relative survival times and the lowest mortality rates.

These findings indicate a divergent pattern: while advances in cancer treatment benefited all groups, improvements in cancer–specific survival were counterbalanced by widening racial disparities in non–cancer mortality, particularly among Black patients.

Role of Adjusting Factors

Sequential adjustment models provided insights into the mechanisms underlying racial survival disparities (Fig. 2). In the fully adjusted model (Model 4, 2000–2019), Black patients had longer all–cause survival than White patients (TR = 1.12, 95% CI 1.08–1.16), driven primarily by improved cancer–specific survival (TR = 1.16, 1.11–1.20). However, a disadvantage persisted in non–cancer survival (TR = 0.78, 0.68–0.90). Both Hispanic (all–cause TR = 1.15, 1.10–1.21) and Asian patients (TR = 1.26, 1.20–1.34) demonstrated consistent advantages across most survival endpoints.

The impact of covariate adjustment varied across groups. For Black patients, all–cause survival was similar to Whites in the demographic–only model (TR = 0.96, 0.92–1.00). Their apparent survival advantage emerged only after sequential adjustment for socioeconomic, tumor, and treatment factors, suggesting that clinical and access–related factors may mask or reverse underlying disparities. By contrast, Hispanic patients' survival advantage was minimally affected by socioeconomic adjustment but attenuated after accounting for tumor characteristics (TR fell from 1.40 in Model 2 to 1.07 in Model 3), implying that more favorable tumor profiles contributed to their advantage. Asian patients maintained significant survival benefits across all models, suggesting the influence of unmeasured protective factors such as genetic background or health behaviors.

Overall, these findings indicate that access to care, tumor characteristics, and treatment patterns are key modifiers of racial survival disparities, with effects differing by racial and ethnic group.

Histology–Specific Disparities

Given the limited sample size, subgroup analyses were restricted to small cell lung cancer and carcinoid tumours, where the number of cases permitted a robust statistical examination. Subgroup analyses revealed that histology markedly influenced racial survival disparities. Among patients with carcinoid tumors (**eTable 5**), Black patients experienced a consistent and severe disadvantage compared with Whites, with all–cause survival reduced by 56% (TR = 0.44, 95% CI 0.35–0.55), cancer–specific survival by 64% (TR = 0.36, 0.25–0.52), and non–cancer survival also significantly shorter (TR = 0.43, 0.30–0.60). These disparities showed no evidence of improvement over time (P for trend ≥ 0.439). In contrast, survival outcomes for Hispanic and Asian patients with carcinoids were not significantly different from Whites. For small cell lung carcinoma (**eTable 6**), the pattern differed: Black patients demonstrated improved survival, with a 7% longer all–cause survival time (TR = 1.07, 1.03–1.12) and a 12% longer cancer–specific survival time (TR = 1.12, 1.07–1.17), although their non–cancer survival remained shorter (TR = 0.69, 0.58–0.82). Asian patients showed the most pronounced advantage, with 28% longer all–cause survival (TR = 1.28, 1.20–1.37) and 27% longer cancer–specific survival (TR = 1.27, 1.19–1.36), alongside a significant improving temporal trend (P for trend < 0.01). No significant survival differences were observed between Hispanic and White patients with small cell lung carcinoma. Overall, these findings identify histology as a key effect modifier of racial survival disparities: Black patients face substantial and persistent disadvantages in carcinoid tumors, whereas both Black and Asian patients derive notable benefits from advances in small cell lung carcinoma treatment, underscoring the importance of pathology–specific analyses in health equity research.

Mediation in Carcinoid Disparities

Given the marked survival disadvantage among Black patients with carcinoid tumors, mediation analysis was performed to identify contributing pathways(Table 3). Disparities in treatment access emerged as the primary mediators. Surgery–related factors—including surgery at the primary site (19.44%), cancer–directed surgery status (19.56%), regional lymph node surgery (17.11%), and recommendation for

resection (14.81%)—accounted for a substantial proportion of the survival gap, with consistent effects across all–cause, cancer–specific, and non–cancer mortality ($p < 0.05$). Marital status explained more than 15% of the disparity, while clinical stage and income contributed modestly (3–6%). Rural residence showed a small negative mediation effect (− 1.5% to − 2.7%), suggesting a minimal buffering effect for Black patients. Based on the key mediating variables that contributed to the survival disparities observed among Black patients, we further presented the distribution of these factors by race/ethnicity and diagnostic period (**eFigure 3**).

Table 3
Mediation Analysis of Racial Disparities in Survival Time Ratios (TR) among Patients with Carcinoid Tumors: Percentage Contribution of Clinicodemographic Mediators, 2000–2019

Mediator	Race	All-cause	Carcinoid	Other cancer	Other non-cancer cause
Lymph node surgery	Black	17.11 (11.33, 23.48)***	16.73 (11.17, 26.57)***	30.66 (-1630.60, 598.75)	13.96 (9.37, 23.81)***
Summary stage	Black	6.25 (3.29, 11.15)***	6.79 (3.32, 14.73)***	6.46 (-63.11, 89.81)	1.89 (0.62, 4.42)***
Stage Group	Black	3.71 (1.43, 6.42)***	3.20 (1.27, 6.50)***	4.44 (-57.04, 39.47)	0.92 (-0.16, 2.69).
Primary site surgery	Black	19.44 (13.63, 29.51)***	22.26 (13.30, 48.17)***	24.55 (-480.57, 426.46)	12.64 (7.66, 27.01)***
Radiation therapy	Black	2.84 (1.09, 5.23)***	2.90 (0.80, 6.27)***	1.12 (-26.73, 27.87)	1.09 (0.02, 2.77).
Chemotherapy	Black	3.58 (1.11, 6.57)***	3.85 (1.61, 7.59)***	4.46 (-70.52, 65.31)	-1.99 (-9.91, 0.25)
Recommendations for surgical resection	Black	14.81 (10.19, 24.13)***	17.47 (10.14, 42.71)***	23.26 (-379.77, 349.62)	9.90 (5.72, 19.61)***
Cancer directed surgery status	Black	19.56 (13.13, 32.15)***	21.95 (12.44, 57.60)*	27.93 (-894.54, 447.21)	11.82 (7.35, 23.37)***
Marital status	Black	15.05 (10.39, 21.35)***	14.63 (9.43, 22.72)***	18.56 (-64.31, 379.04)	14.36 (7.71, 24.54)***
Neighborhood income	Black	5.91 (3.25, 9.51)***	8.24 (3.62, 13.66)***	6.09 (-272.17, 94.70)	2.35 (-0.90, 7.70)
Urban-rural classification	Black	-1.52 (-3.26, -0.51)***	-2.68 (-4.85, -1.18)***	-0.33 (-20.88, 43.99)	0.64 (-1.19, 2.66)
Lymph node surgery	Hispanic	-9.73 (-90.49, 51.77)	-9.24 (-128.86, 57.05)	-6.04 (-83.38, 80.60)	-5.44 (-90.68, 179.12)
Summary stage	Hispanic	-5.66 (-48.67, 1.83)	-4.42 (-36.92, 15.16)	-2.12 (-71.92, 27.44)	-1.64 (-19.05, 25.14)
Stage Group	Hispanic	-3.17 (-22.28,	-3.00 (-57.34,	-1.35 (-20.62, 24.28)	-0.89 (-28.88,

Abbreviations: API, Asian or Pacific Islander. *P<0.05; ***P<0.001.

Mediator	Race	All-cause	Carcinoid	Other cancer	Other non-cancer cause
		17.16)	22.49)		12.60)
Primary site surgery	Hispanic	-11.04 (-106.82, -3.65)*	-10.35 (-99.99, 36.67).	-7.36 (-75.59, 218.03)	-9.09 (-92.06, 68.62)
Radiation therapy	Hispanic	0.25 (-13.83, 16.99)	0.27 (-11.86, 45.97)	-0.01 (-3.52, 2.77)	-0.04 (-13.96, 8.05)
Chemotherapy	Hispanic	-1.93 (-21.98, 20.04)	-1.54 (-24.50, 27.29)	-1.16 (-32.02, 15.73)	0.98 (-18.40, 12.88)
Recommendations for surgical resection	Hispanic	-9.82 (-46.70, -1.67)*	-8.46 (-44.76, 22.43).	-7.62 (-196.93, 28.58)	-8.13 (-76.18, 110.50)
Cancer directed surgery status	Hispanic	-11.92 (-74.72, -3.02)*	-9.82 (-88.33, 43.18).	-9.74 (-195.53, 65.53)	-8.51 (-81.69, 39.75)
Marital status	Hispanic	-16.09 (-76.50, 38.54)	-11.97 (-316.23, 306.86)	-4.61 (-91.38, 66.91)	-12.34 (-256.33, 256.23)
Neighborhood income	Hispanic	-8.24 (-97.10, 61.42)	-8.43 (-86.84, 136.12)	-2.89 (-59.83, 18.36)	-2.20 (-64.29, 17.85)
Urban-rural classification	Hispanic	9.17 (-49.81, 79.35)	15.77 (-182.28, 160.89)	0.24 (-53.08, 87.18)	-0.83 (-68.68, 76.88)
Lymph node surgery	API	-5.37 (-153.15, 425.46)	7.72 (-18.82, 65.59)	5.15 (-291.95, 67.83)	-3.52 (-13.82, 1.34)
Summary stage	API	-1.48 (-97.46, 195.20)	3.59 (-15.72, 27.37)	1.70 (-16.73, 43.40)	-0.55 (-3.22, 0.37)
Stage Group	API	-1.53 (-47.52, 125.13)	3.97 (-18.78, 29.82)	1.11 (-41.34, 49.30)	-0.46 (-2.55, 0.17)
Primary site surgery	API	-0.82 (-126.08, 170.09)	4.39 (-32.10, 36.97)	3.33 (-21.43, 71.55)	-1.33 (-5.58, 1.00)
Radiation therapy	API	0.18 (-27.90, 54.91)	0.74 (-7.69, 12.62)	0.09 (-6.87, 9.41)	-0.10 (-1.16, 0.47)

Abbreviations: API, Asian or Pacific Islander. *P<0.05; ***P<0.001.

Mediator	Race	All-cause	Carcinoid	Other cancer	Other non-cancer cause
Chemotherapy	API	-3.58 (-99.94, 176.44)	4.39 (-38.96, 41.62)	2.45 (-34.48, 35.54)	0.91 (-0.19, 5.17)
Recommendations for surgical resection	API	1.07 (-90.75, 106.41)	1.68 (-7.45, 20.49)	0.83 (-25.57, 23.96)	-0.46 (-4.49, 2.73)
Cancer directed surgery status	API	-2.64 (-85.54, 112.19)	5.02 (-11.94, 45.39)	3.21 (-51.04, 70.26)	-1.38 (-6.27, 2.08)
Marital status	API	6.90 (-99.01, 170.98)	-5.51 (-38.04, 2.23)	-1.57 (-50.12, 48.26)	2.17 (-0.21, 7.49).
Neighborhood income	API	9.54 (-250.31, 206.61)	-13.20 (-76.01, 93.47)	-4.33 (-270.41, 76.91)	1.94 (-0.72, 6.69)
Urban-rural classification	API	6.42 (-125.60, 130.02)	-8.99 (-48.62, 86.79).	-0.73 (-36.13, 37.18)	-1.09 (-5.66, 2.07)
Abbreviations: API, Asian or Pacific Islander. *P<0.05; ***P<0.001.					

In contrast, most clinical, treatment, and socioeconomic variables did not significantly mediate survival differences for Hispanic or Asian patients ($p > 0.05$). For Hispanics, surgery–related variables demonstrated negative mediation effects (– 9% to – 12%), but wide confidence intervals indicated unstable estimates. Overall, these findings suggest that reduced access to surgery and adverse social determinants—particularly marital status—are the key pathways driving the survival disadvantage of Black carcinoid patients, whereas these mechanisms appear less relevant for Hispanic and Asian patients, underscoring heterogeneity in the origins of racial disparities in carcinoid survival.

Discussion

Previous studies have documented persistent racial and ethnic disparities in lung cancer mortality in the United States [8–10], but the underlying mechanisms appear more complex than traditionally appreciated. Using SEER data, this study systematically revealed heterogeneity in survival disparities and their drivers among patients with pulmonary neuroendocrine neoplasms (PNENs), presenting a nuanced picture of concurrent advantages and disadvantages. Unlike earlier work suggesting minorities represent a uniformly disadvantaged group[9, 11, 12], we found that patterns varied by race and outcome. Black patients experienced significant temporal improvement in cancer–specific survival, suggesting a stronger benefit from advances in modern therapies. However, their persistent disadvantage in non–cancer mortality constrained overall survival, producing a paradoxical pattern of improvement in cancer outcomes but

worsening non–cancer health. Hispanic patients showed the strongest overall survival advantage and the largest decline in cancer mortality, indicating potential unmeasured protective factors. Asian patients also demonstrated favorable non–cancer survival, but these advantages were partly offset by later stage at diagnosis and increasing non–cancer mortality, suggesting erosion of traditional health benefits. This dynamic evolution of absolute and relative disparities underscores the diversity of racial health inequality mechanisms and the need for pathology–specific, mechanism–based approaches to health equity research.

Although cancer treatments have extended survival across all racial groups, our findings highlight that non–cancer mortality is an increasingly important and under–addressed equity issue. Cardiovascular disease (CVD) emerged as the leading cause of non–cancer death in PNEN patients (eTable 7), consistent with prior work[13]. Cancer and CVD share common risk factors and biological mechanisms [14–17], and lung cancer carries the highest burden of comorbid CVD among all malignancies[18]. CVD has been confirmed as an independent predictor of worse survival in stage I–III non–small cell lung cancer, regardless of timing relative to cancer diagnosis[19] .The significant decline in non–cancer survival among Whites, coupled with an even greater disadvantage for Blacks, demonstrates that the survival gains achieved through anti–cancer treatment are being undermined by disparities in comorbidity management. These findings argue for a shift from a cancer–centric model to one that integrates equitable management of cardiovascular and other chronic conditions, or else progress in cancer outcomes risks being offset by widening gaps in non–cancer mortality.

The survival advantage of Hispanics observed here reflects the well–known “Hispanic Paradox,” first described by Markides et al.[20]. Despite socioeconomic disadvantages comparable to Blacks, U.S. Hispanics—particularly of Mexican origin—often exhibit equal or better survival compared with Whites [21–23]. Proposed explanations include cultural support systems, the healthy immigrant effect, favorable dietary habits, Native American genetic ancestry, and lower smoking prevalence.

Asians also demonstrated a comprehensive survival advantage, though through potentially distinct mechanisms. While often treated as a homogeneous group, their observed benefits are likely multifactorial, including genetic, behavioral, and social influences. The healthy immigrant effect may contribute, but higher socioeconomic status—over 70% of Asians in our study resided in high–income neighborhoods—facilitates access to quality care, in contrast to Hispanics, whose advantages persist despite socioeconomic disadvantage. Additional protective factors may include dietary patterns, family support, low smoking rates, and greater adherence to treatment, all of which may reduce psychological stress and improve care utilization[24–26].The persistence of survival advantages after multivariable adjustment suggests that unmeasured genetic or biological factors may also contribute. Future studies should disaggregate Asian subgroups to better understand the heterogeneity and protective mechanisms underlying these advantages.

Our mediation analysis further highlighted the key role of treatment accessibility. Black patients were significantly less likely to undergo lung cancer surgery, consistent with prior reports[27]. Surgery at the

primary site, lymph node dissection, and related measures mediated a large share of their survival disadvantage, identifying surgical access as a critical structural barrier. Surgical resection is the standard of care for localized typical and atypical carcinoids and improves survival compared with watchful waiting[28, 29]. It is also recommended for selected early–stage small cell lung carcinoma and large cell neuroendocrine carcinoma [1]. The histology–specific analysis underscored this point: Black patients with carcinoid tumors had significantly higher mortality that persisted after adjustment, corroborating findings from smaller prior studies[7, 30]. In other histologies, such as small cell lung carcinoma, disparities followed different patterns, with Black and Asian patients showing relative advantages. These results indicate that the magnitude and direction of racial disparities vary across subtypes [31–33], necessitating attention to both biological and structural contributors.

The mediation results in carcinoids provide actionable targets. The disadvantage among Black patients was not attributable to inherent biological differences but rather to modifiable health system factors, particularly unequal access to surgery. High mediation effects from surgical measures pinpoint structural nodes where disparities arise. These findings translate the concept of racial disparity into practical reform opportunities, supporting interventions such as standardized treatment pathways, implicit bias training, and expanded insurance coverage to mitigate inequities.

This study has limitations. First, small sample size precluded inclusion of American Indian/Alaska Native populations and limited analysis of atypical carcinoids and large cell neuroendocrine carcinomas. Second, absence of geographic detail restricted assessment of regional effects. Third, lack of individual–level socioeconomic data (e.g., insurance, education, household income) constrained mechanistic interpretation. Finally, biological and lifestyle factors such as smoking, comorbidities, or genetic variation were unavailable, and residual confounding cannot be excluded.

In conclusion, this study demonstrates substantial racial disparities in PNEN survival, with patterns that are dynamic and histology–specific. While overall survival has improved across groups, inequities persist, particularly among Black patients with carcinoid tumors, largely mediated by modifiable structural barriers to surgery and comorbidity management. These results emphasize the need for equity–focused interventions that extend beyond cancer treatment alone. Future research should incorporate multi–omics data, detailed socioeconomic and geographic variables, and refined tumor biology to delineate mechanisms and guide targeted strategies to reduce disparities.

Conclusion

This study confirms significant racial disparities in PNEN survival, marked by improving cancer outcomes but widening non-cancer mortality gaps, especially among Black patients. Disparities were strongly mediated by unequal surgical access and socioeconomic factors. Interventions must simultaneously address cancer treatment equity and non-cancer health disparities to reduce racial inequities.

Abbreviations

Abbreviation	Full Term Definition
PNENs	Pulmonary Neuroendocrine Neoplasms
SEER	Surveillance, Epidemiology, and End Results
TR	Time Ratio
AFT	Accelerated Failure Time
CSS	Cancer-Specific Survival
NCS	Non-Cancer Survival
HR	Hazard Ratio
CI	Confidence Interval
DAG	Directed Acyclic Graph
BH	Benjamini-Hochberg
CVD	Cardiovascular Disease
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
RUCC	Rural-Urban Continuum Code

Declarations

Data sharing statement

The data supporting this study are available from the publicly accessible SEER database but cannot be redistributed by the authors due to data use restrictions. Access to the original data requires approval through the official SEER application process: https://seer.cancer.gov/data-software/.

Patient and Public Involvement

Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Declaration of Interest statement

We declare no competing interests.

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Author Contribution

Access and verification of the underlying study data, YMC, QZH, XG; Conceptualization, YMC, XXY, YZ; Data curation, QZH, ZY; Formal analysis,YMC, XXY; Funding acquisition, CC, XG, ZY; Investigation, YMC, XXY, YYP; Methodology, QZH, XG, QL; Project administration, YZ, ZY; Resources, YMC, QZH, XG; Software, GLL; Supervision, CC, ZY, GBX; Validation, JTD, RJH; Visualization, XXY, XYL; Writing – original draft, YMC, XXY, QZH; Writing – review & editing, All authors. All authors gave final approval to the submitted manuscript.

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Figures

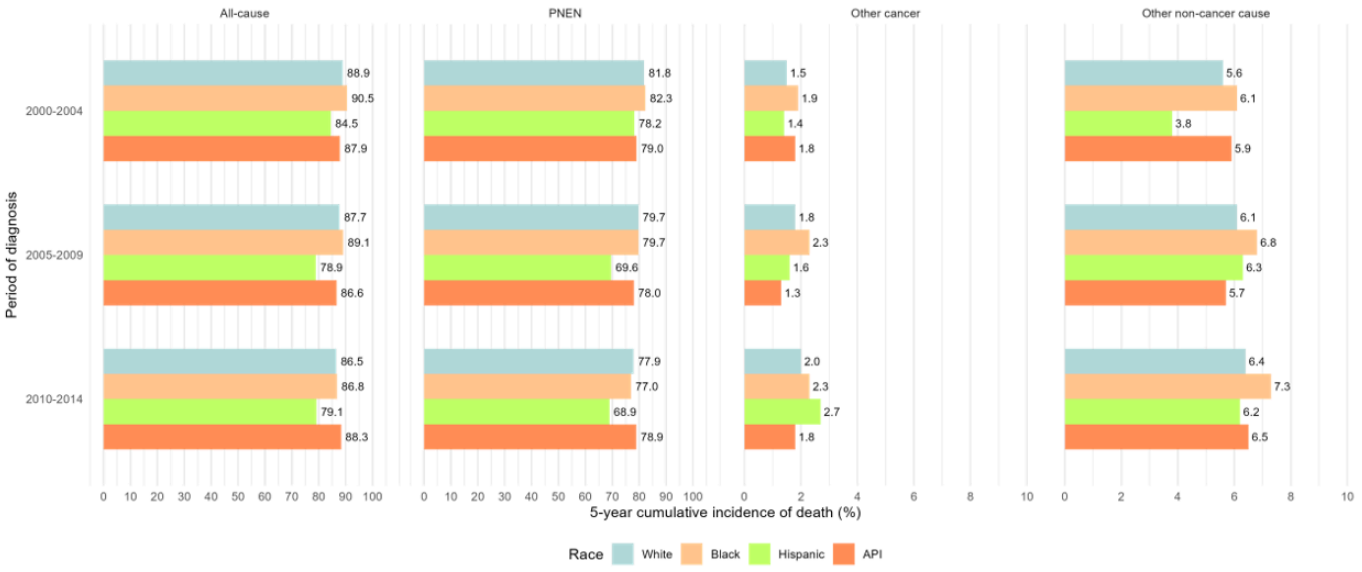


Figure 1

5-year cumulative incidence of four mortality outcomes (all-cause , cause-specific, other cancer, non-cancer) in patients with PNENs by race.

Abbreviations: PNEN, pulmonary neuroendocrine neoplasms; API, Asian or Pacific Islander.

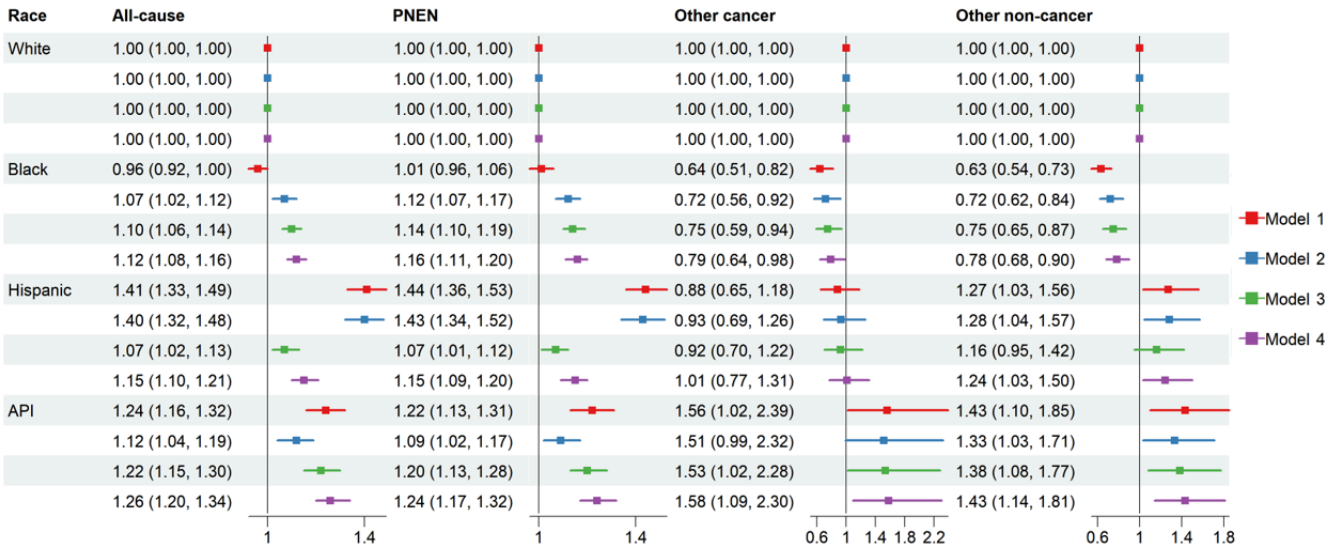


Figure 2

Time Ratios from the Accelerated Failure Time (AFT) Model for All-Cause and Cancer-Specific Mortality by Race/Ethnicity

Abbreviations: PNEN, pulmonary neuroendocrine neoplasms; API, Asian or Pacific Islander.

Supplementary Files

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