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Social Exposome and Thyroid Cancer Outcomes in a Population-Based Study

Eman A. Toraih [1,2], Mohammad H. Hussein [3], Tessa Lavorgna [4], Isabel Riccio [5], Alexandra C. LaForteza [6], Baraah Abu Alsel [7], Safya E. Esmaeel [8] and Manal S. Fawzy [9,*]

1 College of Health Professions, Upstate Medical University, New York, NY 13210, USA; toraihe@upstate.edu
2 Genetics Unit, Department of Histology and Cell Biology, Faculty of Medicine, Suez Canal University, Ismailia 41522, Egypt
3 Ochsner Clinic Foundation, New Orleans, LA 70112, USA; mohamed.hussein@ochsner.org
4 Internal Medicine Residency Program, Department of Medicine, University of Miami, Jackson Memorial Hospital, Miami, FL 33136, USA; tlavorgn@tulane.edu
5 Department of Otolaryngology-Head and Neck Surgery, Loyola University Medical Center, Maywood, IL 60153, USA; isabel.riccio@luhs.org
6 School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA 70112, USA; alafo2@lsuhsc.edu
7 Medical Sciences & Preparatory Year Department, North Private College of Nursing, Arar 73244, Saudi Arabia; baraahsel@nec.edu.sa
8 Physiology Department, College of Medicine, Northern Border University, Arar 91431, Saudi Arabia; safya.ebraheem@nbu.edu.sa
9 Center for Health Research, Northern Border University, Arar 73213, Saudi Arabia
* Correspondence: manal.darwish@nbu.edu.sa

Abstract

Background/Objectives: Thyroid cancer incidence has risen in recent decades, with emerging evidence that social determinants of health and environmental exposures contribute to geographic and population-level disparities in risk and outcomes. This study applies a social exposome perspective to characterize how community-level social and environmental factors shape thyroid cancer patterns. This work aims to examine how geospatial social exposome factors and environmental exposures influence thyroid cancer incidence and outcomes in a population-based context. Methods: Surveillance, Epidemiology, and End Results (SEER) registry data were analyzed to estimate thyroid cancer incidence by demographic and pathological characteristics. Multivariate regression and decision tree models were used to assess associations between social and environmental risk factors and thyroid cancer rates. Results: The age-adjusted thyroid cancer incidence was 15.5 per 100,000, with higher rates among younger adults, females, and white populations. Incidence was elevated in metropolitan and higher-income communities ($p < 0.001$). American Indian/Alaska Native individuals had a lower overall incidence but were more likely to present with advanced disease, whereas Black individuals had the lowest incidence but the poorest survival. Socioeconomic disadvantage was positively associated with thyroid cancer burden, while smoking cessation, fruit consumption, and higher ultraviolet (UV) exposure were protective. Conclusions: Thyroid cancer incidence is highest in affluent, metropolitan, predominantly white communities, likely reflecting greater access to screening and diagnostic services. At the same time, socially and economically underserved groups experience more advanced disease at diagnosis and worse survival. These findings underscore the importance of community-level, targeted prevention and early detection strategies that address social exposome factors and structural inequities in thyroid cancer care and outcomes.

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1. Introduction

Cancer affects all population groups worldwide, but certain communities bear a disproportionate burden due to complex interactions among social, environmental, and economic factors [1]. The "social exposome" represents the cumulative integration of ecological exposures, socioeconomic status (SES), and molecular genomics in relation to health effects and outcomes [2]. This framework offers a more comprehensive lens for examining health disparities, extending beyond traditional socioeconomic markers to encompass the full spectrum of environmental exposures that may influence health outcomes [3].

The social exposome framework has demonstrated value in understanding various cancers [4,5]. For instance, analysis of urothelial carcinoma "hotspots" revealed significant associations with socioeconomic status, proximity to airports and heavy traffic, and industrial discharge [6]. Similarly, exposure to polycyclic aromatic hydrocarbons has been linked to both urothelial and thyroid carcinoma development [6,7]. In sub-Saharan Africa, the exposome approach identified biomass fuel use (including burned wood, charcoal, coal, and dung) as a contributing factor to esophageal squamous cell carcinoma development [8], adding to known risk factors such as alcohol consumption, tobacco use, hot beverages, and poor oral hygiene [9]. Together, these findings illustrate how the social exposome framework can reveal previously unrecognized environmental risk factors and their interactions with established disease causes.

In the present study, the social exposome was operationalized as a set of contextual, county-level indicators representing social and material conditions that may shape thyroid cancer detection, stage at presentation, and survival. The selected variables were chosen because they capture complementary pathways through which place-based conditions can influence cancer outcomes. Socioeconomic indicators, including household income, educational attainment, health insurance coverage, language isolation, and household crowding, reflect access to material resources, health literacy, healthcare navigation, and barriers to timely diagnostic evaluation [10–14]. Residential rurality and population mobility were included as structural and geographic indicators that may influence access to specialist care, diagnostic facilities, continuity of care, and social stability [11,15,16]. Lifestyle-related measures, including smoking, alcohol consumption, physical activity, dietary patterns, and body mass index, were considered behavioral and community-contextual correlates of health that may cluster with social disadvantage and differential access to health-promoting resources [17–20]. Ultraviolet radiation exposure was included as a physical-environmental indicator because environmental conditions may operate alongside social context to influence disease risk and health-related behaviors [21–23].

This variable set therefore spans socioeconomic, structural/psychosocial, behavioral, and physical-environmental domains of the social exposome. It does not represent the full exposome, which would ideally include individual-level residential histories, occupational exposures, air pollution, endocrine-disrupting chemicals, ionizing radiation, psychosocial stress, healthcare utilization, and molecular or biologic susceptibility markers measured longitudinally [24]. Such data were not consistently available in the SEER-linked county-level datasets used for this population-based analysis. Consequently, the selected indicators were intended to characterize contextual patterns of social and environmental disadvantage rather than to quantify individual exposure profiles.

Thyroid cancer warrants particular attention through this lens, as it is projected to surpass colorectal carcinoma as the fourth most common cancer in the United States by 2030 [25]. While mortality rates have remained relatively stable at 0.5 deaths per 100,000 people, the incidence increased from 4.9 to 14.3 per 100,000 individuals between 1975 and 2009 [25]. This increase shows marked demographic differences, with new thyroid cases in women increasing at a rate 4 times that observed in men [25]. However, debate persists as to whether this rising incidence represents a true disease increase or overdiagnosis of clinically silent tumors [26,27], given the stable mortality rate and lower autopsy prevalence than current statistics suggest [28].

Multiple risk factors have been associated with thyroid cancer, including family history, elevated body mass index, and prior radiotherapy exposure [29–31]. Socioeconomic markers also play a crucial role—individuals with educational attainment below the high school level exhibit higher rates of advanced thyroid cancers at initial presentation [32], a significant finding given that cancer stage at presentation strongly predicts survival outcomes for follicular, medullary, and anaplastic thyroid cancers [33]. Furthermore, low monthly income independently predicts advanced-stage presentation, with 10-year overall survival rates significantly decreased in the bottom income quartile [34,35].

Environmental exposures have also demonstrated significant impacts on thyroid cancer development [36]. The most notable example remains the 1986 Chornobyl nuclear power plant accident, where exposure to radioactive iodine-131 showed a clear dose–response relationship with subsequent thyroid cancer development, particularly in children under 15 years of age at the time of exposure [29]. More recent research has identified links between thyroid cancer and air pollution, specifically exposure to Nitrogen Dioxide (NO_2) and particulate matter [36].

Despite increasing attention to social disparities in health, no widely adopted framework exists to define and measure health disparities in thyroid cancer comprehensively. While associations between thyroid cancer risk and various socioeconomic or environmental factors have been studied independently, the interplay between these factors remains poorly understood. This fragmented approach may impede effective communication about cancer-related health disparities and hinder public health organizations' ability to monitor progress in cancer control and management. To our knowledge, this study represents the first comprehensive analysis of the social exposome of disproportionately affected communities to assess disparities in thyroid cancer incidence and risk.

2. Materials and Methods

2.1. Data Source

A retrospective cohort analysis was conducted using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. The SEER database includes population-based cancer registries that capture comprehensive information on cancer incidence, patient demographics, and tumor characteristics, covering approximately 34.6% of the United States population. To establish long-term trends in thyroid cancer incidence, we used SEER 9 (1975–2018) and SEER 13 (1992–2018) registries (https://seer.cancer.gov/statfacts/html/thyro.html) accessed on 6 February 2025.

2.2. Study Population

The study population comprised all patients diagnosed with thyroid cancer between 2000 and 2016. Cases were identified using tumor site and histology codes based on the World Health Organization criteria in the International Classification of Diseases for Oncology, Third Edition (ICD-O-3). Histologic codes included papillary carcinoma (8050, 8052, 8260, 8340–8341, 8343–8344, 8350), follicular carcinoma (8290, 8330–8332, 8335), medullary

carcinoma (8345–8346, 8510, 8520), and anaplastic carcinoma (8012, 8020–8021, 8030–8032). We included patients of all ages with histologically confirmed well-differentiated and undifferentiated/anaplastic thyroid tumors, regardless of clinical stage at diagnosis.

Race was categorized into four groups: Caucasian/White, African American/Black, American Indian/Alaska Native (AI/AN), and Asian/Pacific Islander, with additional stratification by Hispanic ethnicity. Patients with unknown race/ethnicity, thyroid cancer diagnosed in association with other primary malignancies, or unknown histology were excluded from the analytic cohort.

2.3. Study Variables

SEER census tract–level socioeconomic and environmental indicators were evaluated across multiple domains. Socioeconomic indicators included household income (categorized from <$35,000 to >$75,000), educational attainment (proportion with less than grade 9 education and high school completion), health insurance coverage, language barriers (proportion of non–English-speaking households), and household crowding (defined as >1 person per room).

Environmental factors included urban–rural residence (classified using Rural–Urban Continuum Codes), ultraviolet (UV) radiation exposure, and residential mobility (the percentage of the population moving to a different state or county within the past year). Lifestyle-related variables included smoking status, alcohol consumption, physical activity levels, dietary patterns, and body mass index. "Aerobic activity" denotes the county-level prevalence of adults meeting the aerobic component of the Physical Activity Guidelines for Americans, defined as at least 150 min per week of moderate-intensity activity, at least 75 min per week of vigorous-intensity activity, or an equivalent combination. This measure is distinct from "No physical activity," which denotes the prevalence of adults reporting no leisure-time physical activity [37]. All behavioral variables are county-level, self-reported prevalence estimates describing the general adult population of each county rather than patients with thyroid cancer, and they are not disaggregated by sex.

Variables were selected a priori to represent available county-level indicators across socioeconomic, structural/geographic, behavioral, and physical-environmental domains; because the data were ecological and registry-linked, these measures should be interpreted as contextual characteristics of communities rather than individual patient exposures.

2.4. Study Outcomes

Primary outcomes included: (1) age-adjusted thyroid cancer incidence rates, (2) stage-specific incidence rates, and (3) overall and cancer-specific survival. Age-adjusted incidence rates were calculated for demographic subgroups defined by gender, race/ethnicity, county of residence, household income strata, and tumor characteristics at diagnosis. All rates were standardized to the 2000 US standard population and expressed per 100,000 person-years to facilitate comparisons across populations with differing age structures. For state-specific racial/ethnic analyses, the numerator was the number of incident thyroid cancer cases within each racial/ethnic group in a given state, and the denominator was the corresponding state-specific racial/ethnic population. Thus, estimates represent age-adjusted incidence rates per 100,000 persons within each racial/ethnic population, rather than case counts or percentages of the total state population. For temporal analyses, we evaluated cases diagnosed between 2014 and 2018.

Stage-specific incidence rates were calculated to assess disease severity at presentation across population subgroups. Disease stage was classified according to SEER Summary Stage criteria as localized (confined to the thyroid), regional (direct extension beyond the thyroid or involvement of regional lymph nodes), or distant (metastasis to remote organs

or non-regional lymph nodes). These categories enabled examination of diagnostic patterns and potential disparities in healthcare access across sociodemographic groups.

Incidence-based mortality from thyroid cancer was also evaluated. Age-adjusted survival was calculated as the ratio of observed survival among thyroid cancer patients to expected survival derived from matched population life tables. Survival analyses were stratified by race/ethnicity, socioeconomic status, and disease stage to identify disparities in treatment outcomes.

For survival analyses, relative survival estimates were obtained from SEERStat and were based on follow-up and vital-status information ascertained by SEER registries through their standardized data-collection and linkage procedures. Relative survival was used to estimate survival among patients with thyroid cancer relative to the expected survival of comparable individuals in the general population. Because the present study used de-identified, publicly available registry-derived estimates, the investigators did not independently ascertain follow-up completeness or update vital status. Stage at diagnosis, tumor characteristics, and cause-specific outcomes were based on registry-coded variables. Although standardized SEER coding procedures enhance comparability across registries, some misclassification of stage, cause of death, demographic characteristics, or diagnosis-related variables remains possible.

2.5. Statistical Analysis

Statistical analyses were conducted using a multi-stage approach. First, all incidence rates were age-adjusted to the 2000 US standard population using direct standardization and expressed per 100,000 person-years with 95% confidence intervals (CIs) calculated using the modified Tiwari method. Temporal trends in incidence were examined using Joinpoint regression to identify significant changes in slope over time and to estimate annual percent change (APC) and average annual percent change (AAPC). The Joinpoint Regression Program (version 4.8.0.1; National Cancer Institute, Bethesda, MA, USA) was used, with statistical significance set at $p < 0.05$. Incidence-based mortality rates were calculated using SEER*Stat software (version 8.3.8; National Cancer Institute), and mortality was compared by sex and race/ethnicity; rate ratios with 95% CIs quantified the magnitude of disparities.

Socioeconomic analyses employed several complementary methods. Pearson correlation coefficients were calculated to assess relationships between county-level social determinants and thyroid cancer outcomes. Two-factor analysis of variance (ANOVA) followed by Bonferroni post hoc tests was used to compare incidence rates across income and racial/ethnic groups. For rural–urban comparisons, Student's t tests evaluated differences in incidence between metropolitan and non-metropolitan counties. Geographic analyses assessed state-level variation in thyroid cancer patterns; trends were classified as rising when the 95% CI for AAPC was entirely above 0, stable when the CI included 0, and falling when it was entirely below 0. To ensure statistical reliability and protect confidentiality, state-specific data were suppressed when <16 cases were reported for a given area–sex–race category.

Potential confounding was addressed using complementary approaches appropriate to each analysis. Incidence and mortality rates were age-adjusted to the 2000 US standard population. Analyses were stratified by sex, race/ethnicity, stage, histologic subtype, income category, and rural-urban residence where data were available. Multivariable regression models and propensity score matching were used to account for measured covariates and to reduce imbalance between comparison groups, as applicable. However, adjustment was limited to variables available in the linked registry and area-level datasets; therefore, residual confounding from unmeasured individual-level factors, including co-

morbidity, healthcare utilization, treatment characteristics, occupational and residential exposures, and molecular tumor features, cannot be excluded.

All statistical tests were two-sided, with significance set at $p < 0.05$. Analyses were conducted using Python 3.8, with NumPy (1.21.0), Pandas (1.3.0), and SciPy (1.7.0) for data management and statistical computations. Data visualization was performed using Matplotlib (version 3.4.2) and Seaborn (version 0.11.1), and geospatial mapping was conducted using ArcGIS Pro 2.8 (Esri, Redlands, CA, USA).

3. Results

3.1. Thyroid Cancer Incidence Patterns

3.1.1. Overall Age-Adjusted Incidence Rates

The age-adjusted incidence rate of thyroid cancer was 15.5 per 100,000 (95% CI: 15.4–15.6) for all ages combined, with systematic differences across demographic groups (Supplementary Table S1). The highest rates were observed among adults aged 50–64 years (27.3 per 100,000, 95% CI: 27.0–27.6), females (22.8 per 100,000, 95% CI: 22.6–22.9), and non-Hispanic White individuals (16.9 per 100,000, 95% CI: 16.7–17.0). In contrast, lower rates were documented among males (8.0 per 100,000, 95% CI: 7.9–8.1), American Indian/Alaska Native (AI/AN) populations (9.6 per 100,000, 95% CI: 8.7–10.6), and Black individuals (9.4 per 100,000, 95% CI: 9.2–9.6). Papillary carcinoma was the predominant histologic subtype (13.9 per 100,000, 95% CI: 13.8–14.0), and most cancers were diagnosed at a localized stage (9.3 per 100,000, 95% CI: 9.2–9.3).

3.1.2. Race/Ethnicity-Specific Analysis

Stratification by race/ethnicity revealed distinct incidence patterns across subgroups (Supplementary Table S2). Non-Hispanic White populations exhibited elevated rates across multiple categories, including both sexes (female: 24.5 per 100,000, 95% CI: 24.2–24.7; male: 9.3 per 100,000, 95% CI: 9.1–9.4) and localized disease at diagnosis (10.2 per 100,000, 95% CI: 10.1–10.3). Asian/Pacific Islander populations demonstrated particularly high rates in the 50–64-year age group (29.3 per 100,000, 95% CI: 28.3–30.3) and higher rates of regional-stage disease (5.5 per 100,000, 95% CI: 5.3–5.7). For histologic subtypes, non-Hispanic White individuals had the highest rates of both papillary (15.2 per 100,000, 95% CI: 15.0–15.3) and follicular carcinoma (1.0 per 100,000, 95% CI: 1.0–1.0).

3.1.3. Temporal Trends

Temporal trend analysis identified significant shifts in incidence over time (Supplementary Table S3, Figure S1A). Overall thyroid cancer incidence increased by an average of 3.18% per year from 1975 to 2013. The most rapid growth occurred between 2000 and 2009, with an annual increase of 7.4% (95% CI: 6.9–7.9), followed by a slower rise of 2.4% (95% CI: 1.1–3.7) from 2009 to 2014. From 2014 to 2018, incidence declined significantly by 2.5% per year (95% CI: −3.7 to −1.3; $p < 0.01$). This decline was most pronounced among Black populations (−5.5% per year, 95% CI: −9.3 to −1.6), whereas AI/AN (3.9%, 95% CI: 1.9–5.9) and Asian/Pacific Islander (1.7%, 95% CI: 0.8–2.6) groups continued to show increasing incidence from 2009 to 2018 (Figure S1B,C).

3.2. State-Level Geographic Distribution

Geographic analysis demonstrated substantial regional variation in thyroid cancer incidence (Supplementary Table S4, Figure S1D). Utah, New York, New Jersey, Pennsylvania, and West Virginia had the highest overall incidence rates. Despite the general decline from 2014 to 2018, seven states continued to increase, led by Nebraska (APC 5.7, 95% CI: 2.9–8.6) and Delaware (APC 3.6, 95% CI: 2.3–4.9). Among Black populations,

Louisiana had the highest age-adjusted thyroid cancer incidence rate per 100,000 Black residents (5.6, 95% CI: 4.1–7.1), followed by Wisconsin (5.5, 95% CI: 1.9–9.1). Among Hispanic populations, Arkansas had the highest age-adjusted thyroid cancer incidence rate per 100,000 Hispanic residents (5.8, 95% CI: 0.7–11.3), followed by North Carolina (5.4, 95% CI: 3.3–7.5) and Louisiana (5.2, 95% CI: 2.3–8.1). These state-specific estimates, particularly those with wide confidence intervals, should be interpreted cautiously because of limited case counts in some racial/ethnic strata.

Stage-Specific Distribution

Most thyroid cancers were diagnosed at early stages: 67.2% were localized and 26.6% presented with regional disease (Figure 1A). However, clear demographic disparities were evident. Females were more likely to be diagnosed with localized disease (69.9% of cases) than males (57.6%), whereas males had a higher proportion of distant-stage disease at diagnosis (5.6% vs. 2.4% among females) (Figure 1B).

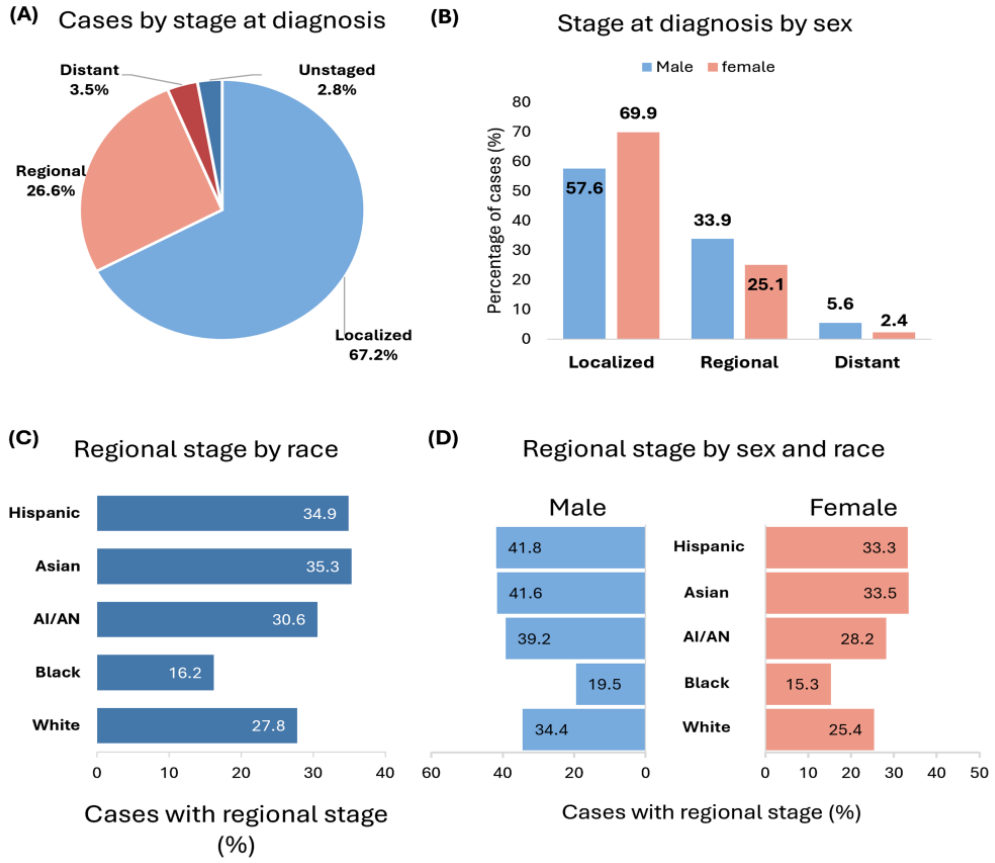

Figure 1. Stage distribution of thyroid cancer cases by demographic characteristics, 2014–2018. Stage distribution of thyroid cancer cases among different demographic groups. (**A**) The overall distribution of thyroid cancer cases by stage at diagnosis. (**B**) Sex-specific distribution of disease stage, showing differences between males and females in localized, regional, and distant disease. (**C**) Racial and ethnic differences in stage at diagnosis reveal disparities in the presentation of advanced-stage disease. (**D**) Combined analysis of stage distribution by race/ethnicity and sex, highlighting specific patterns within subgroups. Localized cancer is confined to the primary site; regional cancer has spread directly beyond the primary site (regional extension) or to regional lymph nodes; distant cancer has spread to other organs (distant extension) or remote lymph nodes. All *p*-values for racial/ethnic comparisons were calculated using the White population as the reference group ($p < 0.001$). Data source: US Cancer Statistics Working Group, US Cancer Statistics Data Visualizations Tool, based on 2020 submission data (1999–2018) [38]. Counts and percentages were suppressed if fewer than 16 cases were reported in any specific category.

Marked racial and ethnic disparities in stage at presentation were also observed (Figure 1C,D). Although AI/AN populations had a lower overall incidence (9.6 per 100,000), they had a higher proportion of advanced disease (30.6%) than White populations (27.8%). They were the only group with an increasing trend in advanced-stage disease (APC 1.7%, 2014–2018). An advanced-stage presentation was similarly more frequent among Hispanic (34.9%) and Asian (35.3%) populations than among White populations (27.8%; $p < 0.001$ for all comparisons). Stage distribution also varied by combined race and sex (Figure 1D). Black populations had the lowest proportion of regional disease (16.2% overall; 15.3% for females and 19.5% for males), whereas Hispanic males had the highest proportion (41.8%) among male subgroups, and Asian females had the highest proportion (33.5%) among female subgroups.

3.3. Socioeconomic Determinants

3.3.1. Income and Incidence

The median US family income was $77,263, and the median household income was $62,843. Thyroid cancer rates varied across median household income categories, ranging from <$35,000 to >$75,000 (Figure 2A). Populations with annual household incomes of $35,000–$49,999 had significantly lower age-adjusted incidence compared with those earning <$35,000, whereas individuals with incomes ≥ $75,000 had a 10.9% higher rate ratio than those in the lowest income category (Figure 2B).

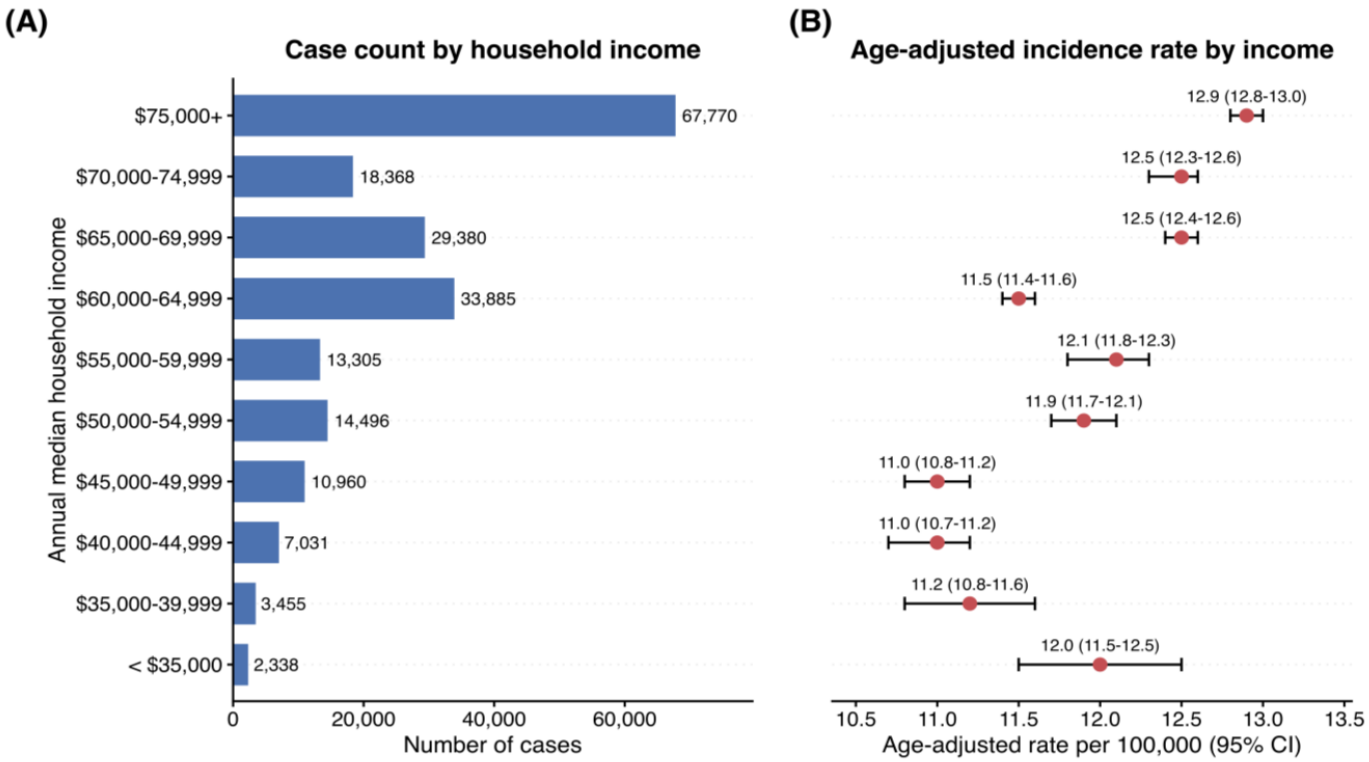

Figure 2. Thyroid cancer incidence rate by annual median household income (SEER 18 registry, 2000–2018). (**A**) Count by annual median household income. (**B**) Rate by median yearly household income. Data source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER Research Data, 18 Registries, Nov 2020 Sub (2000–2018)—Linked to County Attributes—Time-Dependent (1990–2018) Income/Rurality, 1969–2019 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2021, based on the November 2020 submission.

Race/ethnicity-stratified analyses revealed additional disparities (Supplementary Table S5). Non-Hispanic Black (rate ratio 1.40) and Hispanic populations (rate ratio 1.48) with median annual incomes of $50,000–$54999 had higher rate ratios than those in the lowest income tier, suggesting that higher income does not uniformly confer reduced thyroid cancer risk in these groups. To explore whether healthcare access could contribute to these patterns, we evaluated the county-level prevalence of residents without health insurance. Higher county-level uninsurance was inversely correlated with age-adjusted thyroid cancer incidence ($r = -0.48$, $p < 0.001$), consistent with the possibility that limited insurance coverage and reduced access to diagnostic services contribute to lower observed case ascertainment.

3.3.2. Residential Patterns

Among 67,138 patients (61,075 urban and 6063 rural), substantial urban–rural disparities in incidence were observed (Supplementary Table S6). Metropolitan counties had higher age-adjusted incidence rates (14.5 per 100,000, 95% CI: 14.4–14.7) than non-metropolitan areas (13.6 per 100,000, 95% CI: 13.3–14.0; $p = 0.005$), with the highest rates in mid-sized metropolitan areas (250,000–1,000,000 population; 15.3 per 100,000, 95% CI: 15.0–15.5).

Race/ethnicity-stratified analyses showed consistent urban–rural gradients across all groups (Supplementary Table S7). Non-Hispanic White populations had the highest incidence in both metropolitan (16.3 per 100,000, 95% CI: 16.1–16.5) and non-metropolitan settings (15.0 per 100,000, 95% CI: 14.6–15.4). Urban–rural contrasts were most pronounced among AI/AN populations, with metropolitan rates of 12.5 per 100,000 (95% CI: 11.0–14.1) compared with 9.3 per 100,000 (95% CI: 7.2–11.7) in non-metropolitan areas ($p = 0.019$). Similar significant disparities were seen among Asian/Pacific Islander ($p = 0.011$), non-Hispanic Black ($p < 0.001$), and Hispanic populations ($p < 0.001$).

3.3.3. Socioeconomic, Lifestyle, and Environmental Factors

SEER census tract–level prevalence of social determinants was compared with age-adjusted thyroid cancer incidence and annual case counts. As shown in Figure 3, annual thyroid cancer counts were positively correlated with language barriers ($r = 0.67$, $p < 0.001$), low educational attainment (<9th grade; $r = 0.65$, $p < 0.001$), household crowding (>1 person per room; $r = 0.37$, $p = 0.007$), and lack of residential mobility in the past year ($r = 0.34$, $p = 0.015$). In contrast, case counts decreased in counties with higher rates of interstate migration ($r = -0.53$, $p < 0.001$) and high school graduation ($r = -0.46$, $p = 0.001$). Incidence rates were inversely associated with recent county-level mobility ($r = -0.29$, $p = 0.038$), lack of health insurance ($r = -0.48$, $p < 0.001$), and higher poverty rates ($r = -0.33$, $p = 0.017$).

Lifestyle and environmental factors exhibited complex associations with thyroid cancer risk (Figure 4). Annual case counts were negatively correlated with ever smoking ($r = -0.32$, $p = 0.022$) but positively associated with vegetable consumption ($r = 0.29$, $p = 0.041$). Incidence rates were inversely related to fruit intake ($r = -0.36$, $p = 0.009$) and UV exposure ($r = -0.30$, $p = 0.027$). Aerobic activity was not significantly correlated with either the age-adjusted incidence rate or the average annual case count, and no coefficient is therefore displayed for these comparisons in Figure 4B. Aerobic activity was, however, inversely correlated with obesity ($r = -0.76$) and current smoking ($r = -0.61$), indicating that county-level behavioral indicators cluster with one another and with the broader socioeconomic profile of a community.

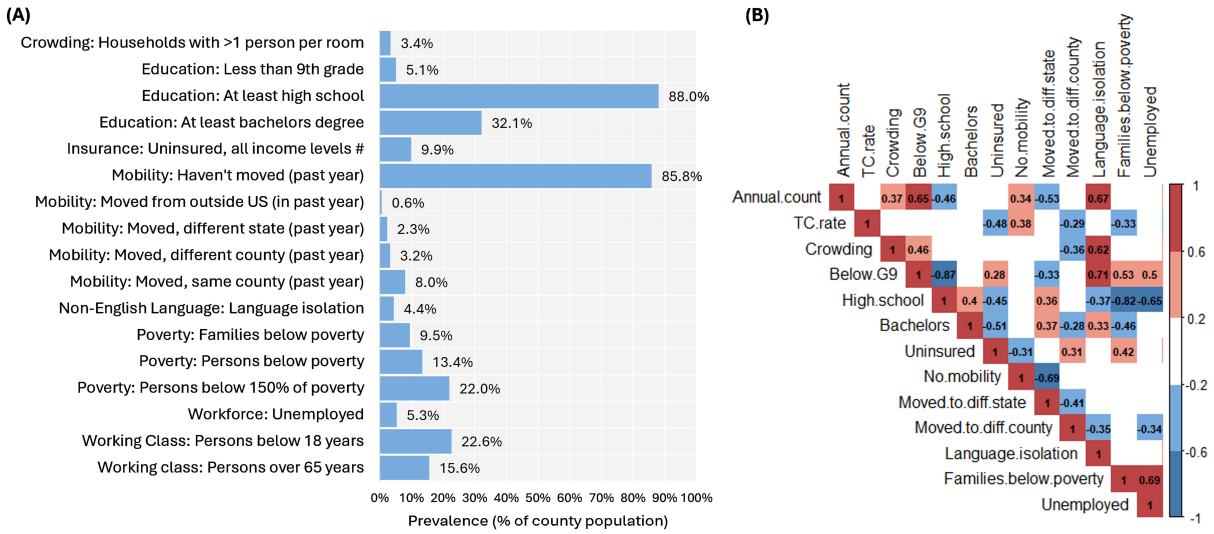

Figure 3. The Influence of Socioeconomic Status on Thyroid Cancer Risk. (**A**) Prevalence of socioeconomic parameters in the US. All races, both sexes, and all age groups were included. Data source: 2015–2019 American Community Survey 5-Year Data for all factors except insurance, which was retrieved from the 2019 Small Area Health Insurance Estimates Data for ages < 65 years [39]. (**B**) Correlation matrix showing the relationships between the prevalence of social factors in counties, age-adjusted incidence rates, and the average annual count. Pearson's correlation analysis was used. Only a significant correlation coefficient was shown. Counties of Puerto Rico were removed from the correlation matrix due to missing values for mobility, insurance, and language isolation.

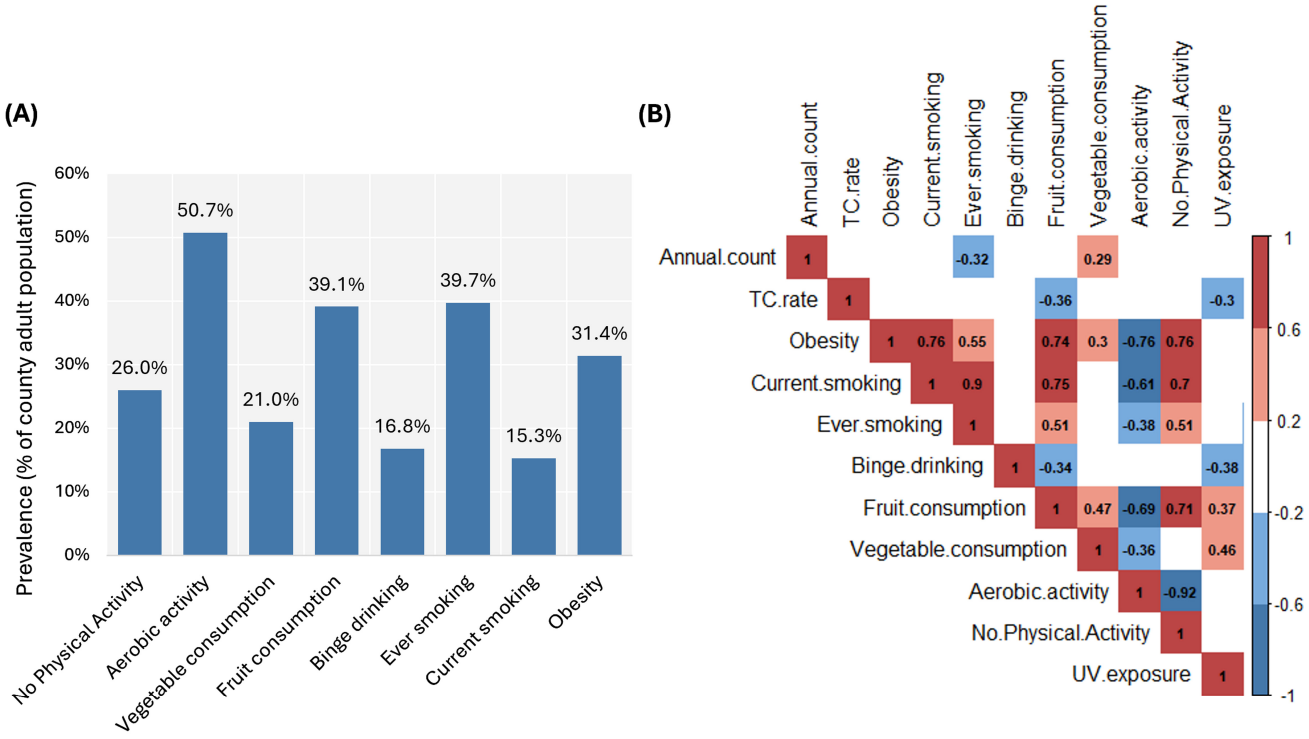

Figure 4. Association of environmental risk factors with thyroid cancer risk. (**A**) Prevalence of different lifestyle and environmental factors in the population. The *y*-axis shows the prevalence (%) of each factor in the adult population of the county, and the *x*-axis identifies the lifestyle or environmental factor. (**B**) Correlation matrix showing the relationships between the prevalence of social factors in counties, age-adjusted incidence rates, and the average annual count. The color scale denotes the Pearson correlation coefficient (r); only statistically significant coefficients ($p < 0.05$) are displayed, and blank cells denote non-significant correlations.

3.4. Survival Analysis

3.4.1. Overall and Stage-Specific Survival

Five-year relative survival for thyroid cancer varied markedly by stage at diagnosis. Localized disease was associated with excellent outcomes (99.9% five-year survival), whereas survival for distant-stage disease was substantially lower (52.5%) (Figure 5A). This stage gradient was consistent across demographic groups, although the magnitude of survival differed by race/ethnicity and sex (Figure 5B–D).

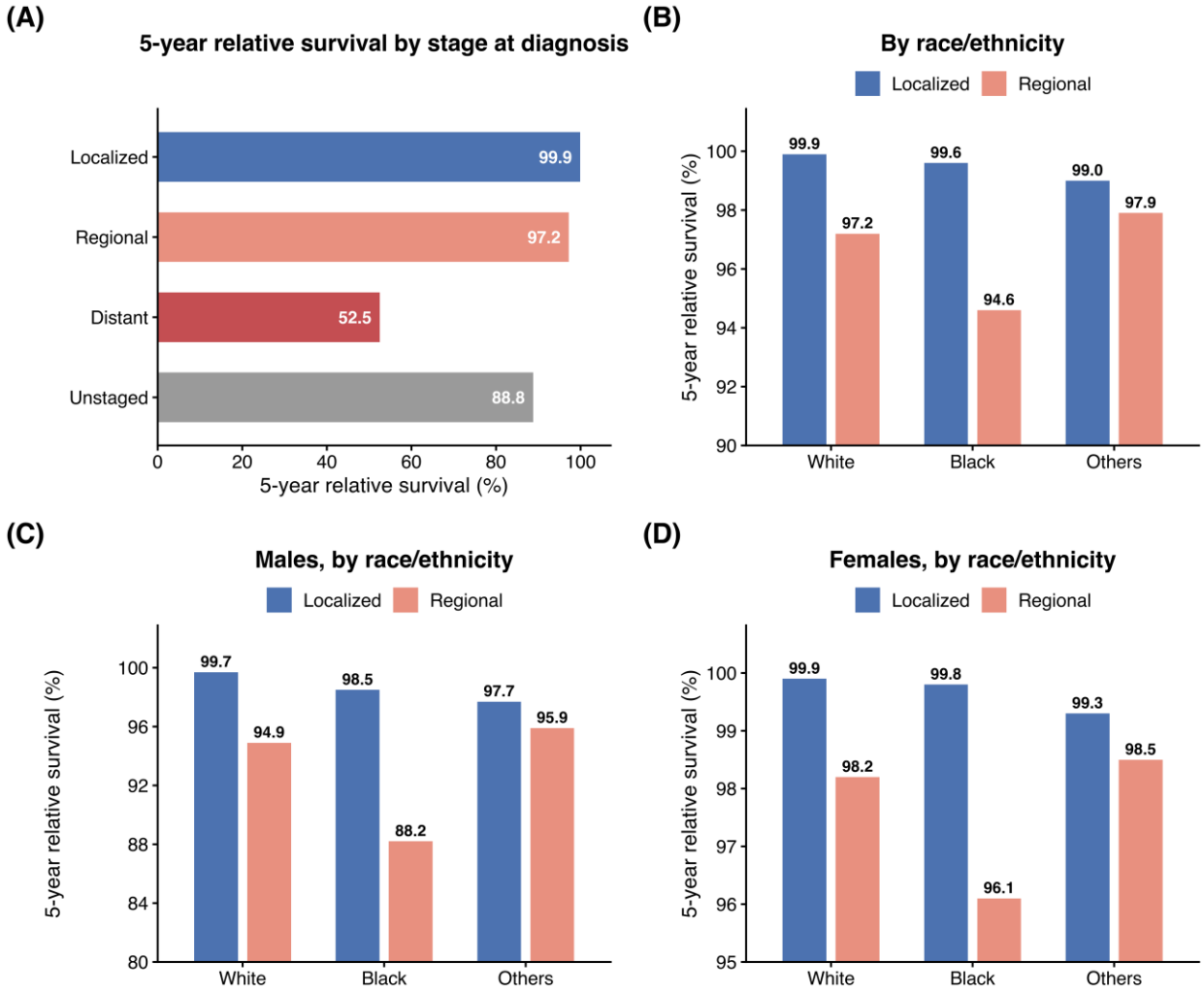

Figure 5. Relative survival rates by time since diagnosis. (**A**) Five-year relative survival by stage at diagnosis; (**B**) Stratified by race/ethnicity; (**C**) Stratified by race/ethnicity in males; and (**D**) Stratified by race/ethnicity in females for thyroid cancer patients with distant disease, 2004–2017.

3.4.2. Racial/Ethnic Survival Patterns

Long-term survival analysis demonstrated significant racial/ethnic disparities (Supplementary Table S8). Across 10 years of follow-up, Black individuals experienced consistently lower relative survival than other groups (Figure 6). Among Black populations, relative survival ranged from 63.1% (95% CI: 58.4–67.4) at year 1 to 38.9% (95% CI: 32.4–45.4) at year 10. In contrast, Asian/Pacific Islander populations maintained higher survival, from 72.9% (95% CI: 69.5–76.0) at year 1 to 41.0% (95% CI: 36.1–45.8) at year 10. Disparities were most pronounced for regional-stage disease, where Black populations had significantly lower five-year survival (94.6%) than other racial/ethnic groups.

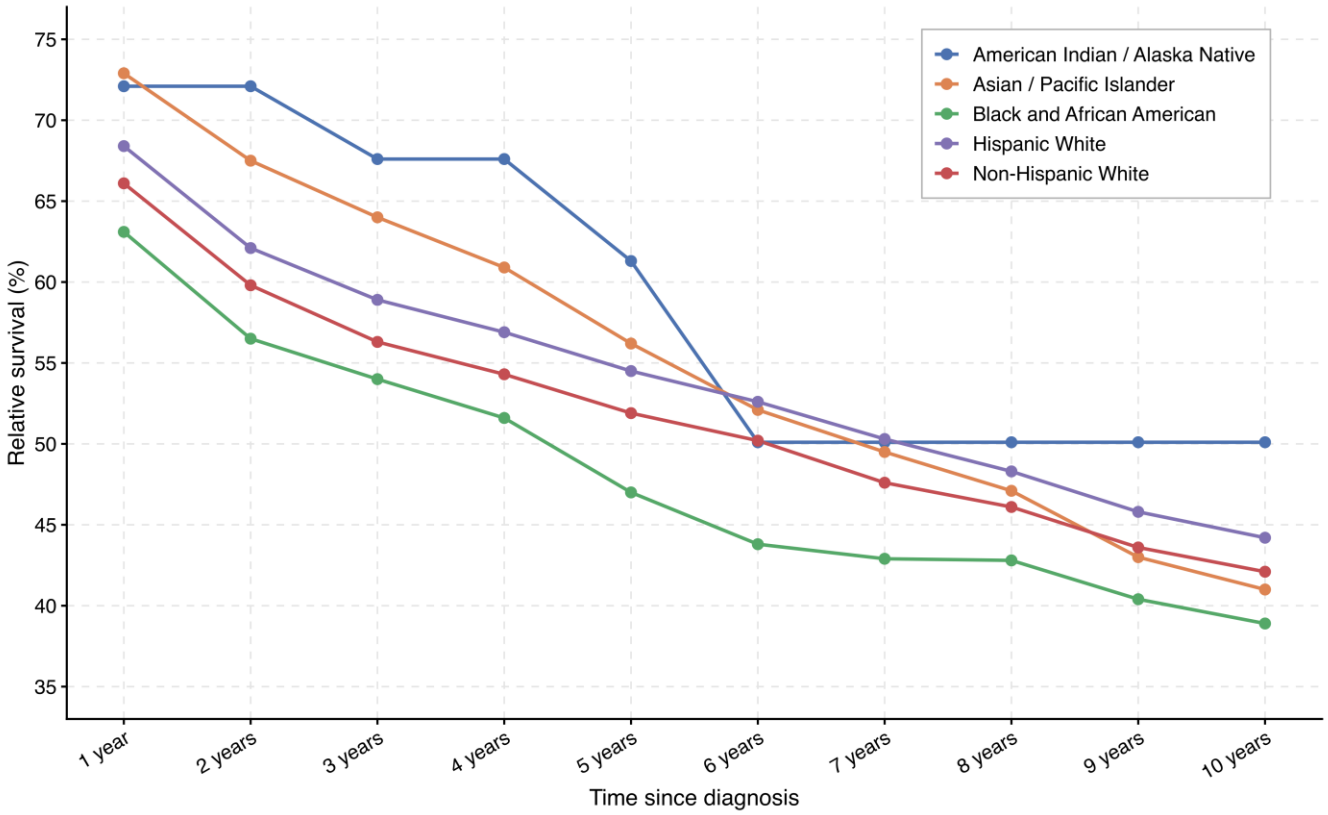

Figure 6. Relative survival rates by time since diagnosis stratified by race/ethnicity for thyroid cancer patients with distant disease, 2004–2017. Time trends in relative survival rates for distant-stage thyroid cancer showed distinct patterns across racial/ethnic groups. American Indian/Alaska Native populations maintained the highest long-term survival rates, stabilizing at approximately 50% after 6 years. In contrast, Black populations demonstrated consistently lower survival rates throughout follow-up, declining from about 65% at 1 year to approximately 40% at 10 years. Asian/Pacific Islander and White populations (both Hispanic and non-Hispanic) showed intermediate patterns, with survival rates converging around 40–45% by 10 years post-diagnosis.

4. Discussion

The study's findings reveal a complex interplay between socioeconomic status and thyroid cancer outcomes that extends beyond simple correlations. While higher-income populations, particularly those with annual household incomes exceeding $75,000, showed increased incidence rates, they concurrently demonstrated better survival outcomes. This apparent contradiction likely reflects enhanced access to preventive care and screening services rather than true biological differences in disease occurrence. This pattern is consistent with the established role of diagnostic intensity in the observed epidemiology of thyroid cancer, whereby greater access to primary care, thyroid ultrasonography, specialist consultation, and diagnostic work-up may increase the detection of small or indolent tumors [40]. Thus, the higher recorded incidence in affluent communities may partly reflect earlier and more complete case ascertainment rather than a higher underlying biological disease burden. The pattern aligns with Zevallos et al.'s findings that lower socioeconomic status correlates with more advanced disease at presentation, suggesting delayed diagnosis rather than lower disease burden [41]. Supporting this interpretation, counties with a higher prevalence of uninsured residents had lower recorded thyroid cancer incidence rates in our analysis. This finding is compatible with reduced access to primary care, diagnostic imaging, endocrinology consultation, and biopsy; however, it does not establish that insurance status caused the observed income-related differences because insurance coverage was measured at the county level and may reflect other correlated

socioeconomic and healthcare-system characteristics [42]. Furthermore, populations with higher socioeconomic status may be better equipped to navigate complex healthcare systems and maintain comprehensive insurance coverage, extending advantages from initial diagnosis through treatment adherence and long-term follow-up care. This interpretation is also consistent with previous evidence that socioeconomic conditions influence the use of adjuvant radioactive iodine therapy in papillary thyroid cancer [41].

The relationship between educational attainment and cancer outcomes provides additional insight into these disparities. The study's finding that education below 9th grade correlates with a higher cancer incidence rate and advanced disease presentation suggests that health literacy and proactive healthcare-seeking behaviors play crucial roles in early detection and treatment success. This observation is consistent with prior evidence linking low socioeconomic status to advanced-stage thyroid cancer at presentation [32]. Lower educational attainment may impair recognition of early symptoms, reduce engagement with preventive services, and limit patients' ability to advocate effectively within healthcare systems, thereby widening existing disparities [43,44]. However, because education was evaluated as an area-level measure, these findings should be interpreted as contextual associations and not as direct estimates of individual educational effects.

The observed disparities between metropolitan and rural communities underscore the need to consider structural inequities in healthcare delivery carefully. The concentration of specialist providers and advanced diagnostic facilities in urban areas creates a self-reinforcing cycle of enhanced detection and treatment capabilities, as documented by Blake et al. [45] in their analysis of barriers to rural healthcare access. Rural populations face unique challenges in accessing specialized care, including long travel distances and limited public transportation. These barriers may explain why rural communities show lower incidence rates of screen-detectable cancers, paralleling patterns observed by Moss et al. [46] in breast cancer studies. Accordingly, the lower incidence observed in non-metropolitan communities in our analysis should not be assumed to represent a lower underlying burden of thyroid cancer; it may partly reflect reduced access to thyroid imaging, specialist assessment, and timely diagnostic evaluation [47]. The lower population density in rural areas may also make it economically challenging to maintain specialized endocrine services, further entrenching systemic barriers to early detection, timely referral, and optimal treatment.

Our findings on racial disparities reveal troubling patterns that suggest deep-rooted systemic issues requiring urgent attention. The observation that Black and Native American populations experience lower incidence rates but worse survival outcomes suggests a critical delay in diagnosis, aligning with Harari et al.'s research showing an increased likelihood of metastatic disease at presentation among racial minorities [48]. This pattern is broadly consistent with previous population-based research showing racial and socioeconomic disparities in the presentation and outcomes of well-differentiated thyroid cancer [48–50]. Furthermore, Shah et al.'s findings regarding the under-treatment of minorities with radioactive iodine therapy suggest that disparities persist even after initial healthcare access is achieved [51]. These patterns suggest potential bias in treatment recommendations or in access to specialized care along the entire continuum of care, from diagnosis to definitive therapy and survivorship. Potential mechanisms include delayed diagnostic work-up, barriers to referral to high-volume specialty services, differences in insurance coverage, treatment access, and continuity of follow-up care. Although chronic psychosocial stress and cumulative social disadvantage may also affect healthcare engagement and biologic stress responses, these pathways could not be evaluated directly in this ecological analysis [52–55].

The success of "barbershop" health programs in Black communities, as documented in several studies [56–58], suggests that culturally competent, community-embedded healthcare delivery models could help address these disparities. Although these programs were not developed specifically for thyroid cancer, their community-based and culturally responsive approach may offer a useful model for improving health education, risk awareness, navigation to diagnostic services, and engagement with follow-up care in historically underserved populations. This approach could be particularly effective for thyroid cancer screening, given the disease's strong emphasis on early detection. Such programs could serve as a model for developing targeted interventions that address both cultural barriers and systemic inequities in healthcare delivery. Adapting these models to include thyroid health education, risk assessment, and navigation to appropriate diagnostic services may help bridge gaps for populations that are historically marginalized within conventional healthcare settings [59–61].

The study's examination of environmental factors reveals important mechanisms through which social conditions may influence thyroid cancer outcomes. The correlation between household crowding and increased thyroid cancer risk suggests that ecological stressors may disproportionately affect disadvantaged populations. This association should be interpreted cautiously because household crowding may also function as a contextual marker of material deprivation, residential instability, or limited access to healthcare and healthy resources, rather than a direct causal exposure. Additionally, the inverse correlation between fruit consumption and thyroid cancer risk, combined with the reality of food deserts in low-income areas [62,63], indicates that nutritional disparities may contribute to cancer risk. This interpretation is supported by Fong et al.'s research, which shows lower survival rates among cancer patients residing in food deserts [64]. Together, these patterns highlight how constrained access to healthy foods and chronic environmental stressors can interact with social disadvantage to shape cancer risk and prognosis. Nevertheless, dietary intake and other lifestyle variables were assessed at the area level; therefore, no causal inferences regarding individual dietary behaviors can be made. These behavioral indicators are strongly correlated with one another and with area-level socioeconomic position, and the individual coefficients should therefore not be interpreted as independent or causal effects. Notably, county-level aerobic activity was not associated with thyroid cancer incidence in this analysis, and its high prevalence reflects a characteristic of the underlying population rather than a determinant of risk.

The positive correlation between low educational attainment and thyroid cancer risk may reflect accumulated environmental and occupational exposures over time, suggesting that social determinants influence cancer risk through multiple pathways. Alternatively, this finding may reflect unmeasured contextual factors that co-occur with low educational attainment, including differential access to healthcare, occupational conditions, residential exposures, and health-related resources [17,65,66]. This finding underscores the importance of accounting for lifetime exposure patterns when evaluating cancer risk and developing preventive interventions [67]. Incorporating longitudinal, life-course perspectives into exposome research may therefore be essential to fully characterize how social position and environment jointly influence thyroid cancer outcomes.

The study's comprehensive approach to analyzing the social exposome offers several methodological advantages, while also acknowledging important limitations. The large, nationally representative sample enables robust stratification across multiple demographic and socioeconomic variables, providing reliable estimates of effect sizes. The county-level analysis captures community-level factors that may be overlooked in individual-level analyses, providing insights into systemic and structural determinants of health outcomes. However, this ecological design, while necessary for confidentiality and statistical stability,

may mask individual-level variations and causal relationships. As a result, the observed associations should be interpreted as indicators of population-level patterns rather than definitive evidence of individual-level risk.

These findings suggest several priority areas for future research and policy intervention. Healthcare access could be improved through targeted expansion of specialist services in rural and underserved areas, potentially leveraging telemedicine and mobile screening programs. The development and evaluation of culturally competent, community-based screening programs modeled on successful interventions in other cancer types could help address racial and ethnic disparities. Further investigation into the biological mechanisms linking social determinants to thyroid cancer outcomes, with a particular focus on modifiable environmental exposures, could inform more effective preventive strategies. Integrating geospatial, environmental, and molecular data may be particularly valuable for disentangling complex pathways that connect social context to tumor biology and clinical outcomes.

The development of comprehensive policies that address both healthcare access and broader social determinants of health remains crucial, recognizing the complex interplay between social conditions and cancer outcomes. Such policies should consider the multifaceted nature of healthcare disparities and work to address both immediate access issues and underlying social inequities that contribute to differential cancer outcomes. Partnerships between public health agencies, community organizations, and healthcare systems will be essential to the design and implementation of context-specific, sustainable, and responsive interventions that align with community priorities.

Limitations

The results of this study should be interpreted in light of several important limitations. First, as with all population-based observational studies, causal relationships between social exposome factors and thyroid cancer outcomes cannot be inferred. Second, reliance on SEER registry data imposes inherent constraints related to cancer registration procedures, including potential underreporting in underserved and rural areas, geographic variation in diagnostic practices, and incomplete follow-up for some population groups. The predominance of cancer registries in urban areas may also limit the characterization of thyroid cancer patterns in rural populations. In addition, outcome ascertainment depended on registry-coded information. Although SEER applies standardized procedures for case ascertainment, staging, follow-up, and vital-status determination, outcome misclassification remains possible, particularly for stage at diagnosis, cause-specific mortality, and variables that may be incompletely recorded or differentially captured across geographic areas and population groups. The study investigators could not independently verify follow-up completeness, vital status, or cause-of-death coding. Any incomplete follow-up or nondifferential outcome misclassification could have attenuated observed associations, whereas differential recording across communities could have contributed to apparent disparities.

Third, residual confounding may remain despite age adjustment and stratified analyses, because the analyses were limited to variables available in the SEER-linked area-level datasets. Important individual-level factors, including comorbidity, healthcare-seeking behavior, access to and quality of treatment, occupational and residential exposures, and tumor molecular characteristics, were not consistently available and therefore could not be fully accounted for. Although histologic subtype was included in the case definition and incidence analyses, survival analyses were not further stratified by histologic subtype. Accordingly, the contribution of differences in prognosis among papillary, follicular, medullary, and anaplastic thyroid carcinomas to the observed survival patterns could not be evaluated directly.

Fourth, our operationalization of the social exposome was necessarily incomplete and constrained by the availability of linked SEER and area-level data. Although the selected indicators captured multiple contextual domains, including socioeconomic conditions, healthcare-related barriers, residential characteristics, lifestyle-related factors, and ultraviolet radiation exposure, they could not encompass the full range of potentially relevant exposures. In particular, individual-level data on lifetime residential history, occupational exposures, air pollution, endocrine-disrupting chemicals, ionizing-radiation dose, psychosocial stress, healthcare utilization, treatment access, and tumor molecular characteristics were not consistently available. Moreover, finer-scale neighborhood characteristics and broader structural determinants, such as measures of residential segregation, local healthcare capacity, transportation infrastructure, and policy context, could not be comprehensively evaluated. Because the behavioral, environmental, and healthcare-related measures were aggregate county-level prevalences and were not linked to individual patients, they may not reflect heterogeneity in exposures or resources within counties or accurately represent individual patient circumstances. These features introduce the potential for ecological bias and exposure misclassification; thus, associations observed at the area level may not hold at the individual level. In particular, county-level estimates of health insurance coverage could not be linked to individual patients. Therefore, this study could not determine whether individual insurance status mediated the association between household income and thyroid cancer detection, stage at diagnosis, or survival. The inverse association between county-level uninsurance and recorded thyroid cancer incidence should be interpreted as consistent with possible differences in access to diagnostic services, rather than as evidence that lack of insurance directly caused lower incidence. In addition, because these measures were not disaggregated by sex in the source datasets and the corresponding incidence measures were calculated for both sexes combined, sex-stratified ecological correlation analyses were not possible.

The limited availability and geographic resolution of environmental data also constrained the evaluation of specific exposures. Future studies integrating individual-level, longitudinal exposure histories with fine-scale geospatial, clinical, treatment, and molecular data are needed to clarify the pathways linking social and environmental conditions to thyroid cancer outcomes. Finally, historical changes in screening practices, diagnostic criteria, and treatment approaches over the study period may have influenced observed incidence and survival trends. In addition, because this analysis was based on SEER registry data and area-level contextual measures, the findings may not be directly generalizable to populations with different healthcare systems, cancer-registration practices, environmental conditions, or sociodemographic profiles. Notwithstanding these limitations, the present findings provide insights into population-level patterns linking social and environmental context with disparities in thyroid cancer outcomes.

5. Conclusions

This population-based study demonstrates that the social exposome significantly impacts thyroid cancer outcomes. We found that affluent, metropolitan, mostly Caucasian populations have higher incidence rates, possibly due to better screening and early diagnosis rather than biological differences in disease prevalence. Underserved populations, such as Black and Native American communities, those with lower educational attainment, and rural residents, have a lower incidence but more advanced disease and worse survival outcomes, suggesting critical diagnosis and treatment delays.

Environmental exposures, access to dietary resources, health literacy, and structural inequalities in healthcare delivery contribute to the reported differences. These findings underscore the critical need for focused healthcare access and social determinant–

oriented interventions. Comprehensive nutritional and environmental policies, community-embedded, culturally competent screening programs, and the planned development of specialized services in underdeveloped areas might help reduce these disparities. Future studies should further elucidate the biological and contextual pathways linking social exposures to thyroid cancer outcomes and rigorously evaluate multilevel interventions designed to address the complexity of these inequities.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/endocrines7030056/s1, Figure S1: Incidence rate and trends of thyroid cancer. Population-based cancer registry data- Surveillance, Epidemiology, and End Results (SEER) and National Program of Cancer Registries data were used. (A) The age-adjusted incidence rate of thyroid cancer across years. Both SEER registries 9 and 13 showed similar trends. Data source: (https://seer.cancer.gov/statfacts/html/thyro.html). (B) The age-adjusted incidence rate of thyroid cancer is stratified by age, sex, and race (SEER registry 21). Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups—Census P25-1130). (C) Average Annual Percent Change (AAPC) Estimates stratified by age, sex, and race (SEER registry 21). (*) $p < 0.01$. The Annual Percent Change (APC) and Average Annual Percent Change (AAPC) estimates were calculated from the underlying rates using the Joinpoint Trend Analysis Software, Version 4.9, March 2021, National Cancer Institute. (D) US map of thyroid cancer incidence rates. Incidence rates (cases per 100,000 population per year) are adjusted to the 2000 US standard population (19 age groups: <1, 1–4, 5–9, ...80–84, 85+). Rates are calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by the National Cancer Institute. The 1969–2018 US population data file was used for SEER and NPCR incidence rates. Rates are calculated using cancers classified as malignant according to the ICD-O-3. Alaska, DC, Hawaii, and Puerto Rico are not drawn to scale; Table S1: The five-year age-adjusted incidence rate of thyroid cancer by sex, race, subtype, and stage of cancer at diagnosis (2014–2018); Table S2: The incidence rate of thyroid cancer is stratified by age, sex, tumor stage, and race (SEER registry 21); Table S3. Recent 5- and 10-year trends in SEER age-adjusted incidence rates of thyroid cancer by age, sex, race, and subtype of cancer, 2009–2018; Table S4: Trends in incidence rate report by State for all stages, all races (includes Hispanic), both sexes, all ages, 2014–2018; Table S5. Race/ethnic thyroid cancer incidence rate by annual household income (SEER 18 registry, 2000–2018); Table S6: Race/ethnic thyroid cancer incidence rate by rural-urban distribution (SEER 18 registry, 2000–2018); Table S7: Race/ethnic thyroid cancer incidence rates stratified by residential area (SEER 18 registry, 2000–2018); Table S8: Relative survival rates, percentage by time since diagnosis, by race/ethnicity, 2004–2017.

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Abbreviations

The following abbreviations are used in this manuscript:

SEER	Surveillance, Epidemiology, and End Results Program
SES	Socioeconomic status
AI/AN	American Indian/Alaska Native
UV	Ultraviolet (radiation)
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
NO_2	Nitrogen dioxide
BMI	Body mass index
APC	Annual percent change
AAPC	Average annual percent change
CI	Confidence interval
ANOVA	Analysis of variance
PRCDA	Purchased/Referred Care Delivery Area
NHIA	NAACCR Hispanic Latino Identification Algorithm

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