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Cardiovascular Disease Mortality Among Asian American And Pacific Islander Breast Cancer Survivors In The United States By Socioeconomic Status And Rurality, 2000-2018

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ABSTRACT

Background: Known racial/ethnic disparities in cardiovascular disease (CVD) mortality among breast cancer survivors exist and it is well-documented that non-Hispanic Black (NHB) breast cancer survivors experience higher incidence of CVD mortality compared to NHW women. However, few studies have examined CVD mortality among Asian American, Native Hawaiian, and other Pacific Islanders (AANHPI) survivors, especially with respect to socioeconomic factors and rurality at the county-level. The aim of this study was to describe how county-level factors influence disparities in CVD mortality among AANHPI breast cancer survivors.

Methods: Using Surveillance, Epidemiology, and End Results 18 registries, we analyzed a retrospective cohort of 60,184 AANHPI women diagnosed with first primary, invasive breast cancer at ages 18-84 years between 2000-2017 who survived at least one year. We used Poisson regression models to calculate relative risks (RR) of CVD mortality, accounting for rates in the general population of AANHPI, according to county-level tertiles of SES (measured by the Yost Index), median income, and degree of rurality. We then assessed for trends in county-level SES and tested for heterogeneity by rurality. We additionally calculated 10-year cumulative CVD mortality estimates accounting for competing risks (non-CVD deaths).

Results: After adjusting for breast cancer stage, age, and year at diagnosis, AANHPI breast cancer survivors living in counties of the lowest SES had a 22% higher risk of CVD mortality (RR = 1.22; 95% CI [1.05, 1.41], p-trend <0.001) compared to those living in counties of the highest SES, a 12% higher risk (RR = 1.12; 95% CI [0.99,1.28], p-trend 0.080) for those living in the poorest relative to wealthiest counties, and 56% higher risk (RR = 1.56; 95% CI [1.25, 1.95], p-heterogeneity <0.001) for those living in the most rural relative to most urban counties. The poorest counties had a 10-year cumulative CVD mortality of 2.33% (95% CI 2.04%,2.65%) compared to the wealthiest counties of 2.19% (95% CI 1.99%, 2.40%). Estimates were amplified by rurality where the most rural counties had a 10-year cumulative CVD mortality of 4.38% (95% CI 3.34%, 5.64%) compared to the most urban counties at 1.84% (95% CI 1.68%, 2.01%).

Conclusion: County-level SES factors and rurality affect AANHPI breast cancer survivors' CVD mortality risk.

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INTRODUCTION

Background

Asian Americans, Native Hawaiian, and other Pacific Islanders (AANHPI) are the fastest growing group of racial/ethnic minority in the United States[1] , but breast cancer epidemiology in this group remains understudied due to a number of factors. First, aggregation of racial/ethnic data in this group overlooks the heterogeneity and diversity of ethnicities, cultures, and immigration histories of different racial/ethnic populations that are collectively and broadly categorized under the AANHPI label. This often complicates or may even limit the generalizability of epidemiological studies as different racial/ethnic groups may have health beliefs and practices which can influence health-seeking behavior such as cancer screening[2]. Second, the vast heterogeneity in different AANHPI groups also translate into heterogeneity across socioeconomic status (SES), where lower socioeconomic status is often a risk factor for poorer health outcomes and a determinant of disparities, especially among cancer survivors[3,4].

Although breast cancer rates have been decreasing overall, breast cancer incidence has increased most rapidly among AANHPI at about 1.5% per year from 2001 to 2016, yet this group experienced the lowest decrease in mortality (0.8% compared to 2.1% in Hispanics during 2013 to 2017)[5]. At first glance, AANHPI had the highest 5-year breast cancer survival rate for both localized and regional cancers in 2009 to 2015. However, when this data were analyzed by specific AANHPI ethnicities, researchers were able to identify the vast heterogeneity in survival rates for different groups. For instance, Solanki et al. demonstrated that in a retrospective cohort of AANHPI women diagnosed with breast cancer between 1991 and 2011, AANHPI women as an aggregated group experienced reduced breast-cancer specific, cardiovascular, and all-cause mortality compared to NHW women. When this data was disaggregated, Filipino women were actually found to have a breast cancer mortality risk similar to that of NHW women (HR 0.93, 95% CI 0.86-1.00) but that Pacific Islander women had a significantly higher risk of breast cancer mortality (HR 1.44, 95% CI 1.17-1.78)[2]. While disaggregating AANHPI data is a step in the right direction, prior work still needs to be done with describing health disparities in the larger AANHPI group compared to the non-Hispanic white (NHW) population in regards to breast cancer survivorship due to the relatively limited research focused on AANHPI in general.

Related to breast cancer treatment and survival is the risk of cardiovascular disease (CVD) mortality which is thought to be caused in part due to treatment effects[6]. Routine chemotherapy and radiation therapy have been documented to produce latent cardiotoxic effects during breast cancer treatment[7]. Chemotherapeutic agents such as anthracyclines have been demonstrated to be associated with atrial fibrillation and left ventricular dysfunction, and radiation leakage to the heart and lungs was also found to accelerate atherosclerosis[8,9]. Immunotherapies such as trastuzumab have also been documented as a cardiotoxin and its effects are magnified when also used in conjunction with anthracyclines[10,11]. Thus, women treated for breast cancer who received some combination of chemotherapy, immunotherapy, and/or radiation therapy may be at subsequent risk of CVD. Data regarding cardiovascular disease are limited for AANHPI breast cancer survivors.

However, treatment receipt is not the sole factor in determining CVD mortality risk among survivors. In addition to treatment effects and race/ethnicity, neighborhood-level SES factors may additionally influence mortality rates as social determinants such as income, education, and degree of rurality among other factors, can often determine an individual's ability to access and afford cancer treatment. These differences in access and quality of healthcare can modulate health disparities and health outcomes[12]. Examining the role of neighborhood-level SES factors on CVD mortality is then especially important for AANHPI breast cancer survivors as cancer and cardiovascular disease are the first and second leading causes of death for AANHP[13]. Furthermore, research has shown that the CVD proportionate mortality ratio (PMR) varies for several AANHPI ethnicities, but is already elevated in many groups compared to the CVD PMR in NHW individuals, independent of breast cancer treatment effects[14,15].

Purpose

The importance of examining the role of socioeconomic factors calls for understanding how determinants such as income, educational attainment, and rurality, among other factors, influence an individual or group's ability to access and afford cancer treatment at the neighborhood-level, thus modulating health outcomes and disparities. To our knowledge, the overall rates of CVD mortality, specifically among AANHPI breast cancer survivors has not yet been described, much less as a function of neighborhood-level, socioeconomic effects.

The primary aim of this study was to describe disparities in cardiovascular disease (CVD) mortality among AANHPI breast cancer survivors in the United States by county-level socioeconomic factors and rurality. We specifically 1) examined the risk of CVD mortality in AANHPI breast cancer survivors compared to the general population of AANHPI using Standardized Mortality Ratios by tertiles of county-level SES, income, and degree of rurality, 2) determined the relative risk of CVD mortality for survivors living in low SES or high rurality counties compared to high SES or more urban counties, and 3) explored potential trends in CVD mortality by SES and rurality among survivors based on treatment receipt including chemotherapy, radiation, chemotherapy plus radiation, or surgery only.

Our hypothesis is that AANHPI breast cancer survivors living in lower SES and more rural counties will have an increased risk of dying from CVD compared to those living in higher SES and more urban counties, while accounting for CVD mortality rates in the general population of AANHPI women in the United States. We hypothesize that survivors living in counties of lower SES status are expected to have a higher CVD mortality risk relative to those living in counties of higher SES. We predict the same pattern for rurality in which survivors living in more rural counties are also more likely to have a higher CVD mortality risk compared to those living in more urban counties.

METHODS

Study population

We utilized data from the Surveillance, Epidemiology, and End Results 18 Registries database (SEER 18) which includes population data that represents approximately 28% of the US population to conduct a retrospective study examining the incidence of CVD mortality among AANHPI breast cancer survivors. We limited our population to AANHPI women, who were identified as non-Hispanic Asian or Pacific Islander individuals, diagnosed with first primary, invasive localized, regional, or distant breast cancers, and received surgery as initial treatment. We further limited the cohort to only include women who were diagnosed between January 1, 2000 to December 31, 2017, diagnosed at age 18-84, and survived for 12 months or longer. Information on mortality was obtained through the US Mortality Database, which maintained by the National Center for Health Statistics and accessible through SEER*Stat.

Outcome

Our primary outcome of interest was CVD mortality defined using the International Classification of Diseases (ICD)-10 codes: I00-I13, I20-I51, I60-I78.

County-level socioeconomic attributes

To measure SES, we used macro-level county attributes that were ascertained from the US Census and American Community survey (ACS). We measured SES via the Yost Index, which is a composite SES score comprised of seven census variables: median household income, median house value, median rent, percent below 150% of poverty line, education index, percent working class, and percent unemployed[16]. These variables capture various metrics that can influence SES. As demonstrated in past literature, different AANHPI groups have vastly different income levels[1,17]. Although median income is a variable that is nested in the Yost Index, we further examined median household income (measured as household income from the past 12 months, inflation adjusted to 2019 US dollars) to understand whether median income has a specific effect on mortality risk. We classified both the Yost Index and median income into tertiles representing low, middle, and high SES or income which are based on the population distribution of AANHPI across counties. We then measured degree of rurality by categorizing the Rural-Urban Continuum codes determined by the US department of Agriculture into 3 groups from most rural to most urban (nonmetropolitan, metropolitan with a population <1 million, metropolitan with a population ≥ 1 million).

Statistical Analysis

We calculated Standardized Mortality Ratios (SMRs) from CVD (SMRs = observed number of CVD deaths among AANHPI breast cancer survivors/expected number of CVD deaths among the AANHPI general population) and their corresponding 95% confidence intervals (CIs), matched by age and calendar year using SEER*Stat 8.3.9.2. We did not report data for outcome events which contained less than 5 deaths.

We then conducted multivariable Poisson regression models to estimate the relative risk (RR) of CVD deaths, using log-transformed expected counts of CVD deaths as the offset. All models were adjusted for age at diagnosis (<65, 65+), stage at diagnosis (localized, regional, distant), and year of diagnosis (2000-2004, 2005-2009, 2010-2017). In doing so, we obtained the RR estimates by comparing the tertiles of county-level SES and median income using the highest SES and wealthiest tertile as the reference group. Similarly, we obtained RR estimates for rurality by comparing the rurality categories to the most urban counties as the reference group. We conducted p-trend analyses to assess for trends among the tertiles of county-level SES

and median income (continuous variables). We additionally conducted p-heterogeneity by rurality (categorical variable) using likelihood ratio tests. These analyses were conducted using RStudio (Version 1.4.1106).

We then stratified the CVD SMRs and RRS by stage at diagnosis (localized, regional, distant), age at breast cancer diagnosis (≤ 65, 65+), latency (time since diagnosis; 1-4, 5-9, and 10+ years), and by treatment receipt (chemotherapy only, radiation only, chemotherapy and radiation, surgery only).

To quantify the absolute risk of CVD mortality, we conducted a competing risk analysis using the stcompet package in STATA (version 17, StataCorp, College Station, TX) with any non-CVD death as the competing event of interest. All non-CVD related deaths, including breast cancer, were considered the competing event. We calculated and 10-year cumulative mortality estimates by tertiles of median income and categories of rurality to observe the absolute risk of CVD mortality between the poorest county and wealthiest county and similarly, most rural and most urban counties. We were unable to calculate cumulative mortality estimates with the Yost Index due to restrictions in SEER*STAT.

RESULTS

Characteristics of cohort: AANHPI breast cancer survivors

Of 60,184 AANHPI breast cancer survivors, 1,292 women died from cardiovascular disease (median follow-up = 7.86 years, range = 1 to 18.96 years) between 2001 and 2018 (**Table 1**). The majority of survivors were diagnosed in recent years between 2010-2017 (52.8%), and most were also younger than 65 years old at the time of diagnosis (73.4%). Most were diagnosed with localized stage (66.7%), estrogen receptor positive (78%), progesterone receptor positive (67.4%), and HER2 negative breast cancers (40.4%). In terms of initial treatment, more survivors received surgery only (28.1%) compared to those who received chemotherapy only (25.6%), radiation therapy only (19.6%), or chemotherapy and radiation (26.5%).

CVD RRs by SES, Income, and Rurality

Overall

Overall, AANHPI breast cancer survivors who lived in counties with the lowest SES profile had a 22% higher risk of CVD mortality (RR = 1.22; 95% CI [1.05, 1.41]) compared to individuals who lived in counties with the highest SES profile (**Table 2**). The risk for CVD mortality was attenuated for median income and rurality. Survivors who lived in the poorest counties had a 12% higher risk of CVD mortality (RR = 1.12; 95% CI

[0.99,1.28]) compared to those who lived in the wealthiest counties. We observed an inverse trend of increasing CVD mortality with worsening SES (p-trend<0.001), but this trend was not significant for median income (p-trend = 0.08). The magnitude of disparities was more pronounced for survivors who lived in the most rural counties as they had a 56% higher risk of CVD mortality compared to those who lived in the most urban counties (RR = 1.56; 95% CI [1.25, 1.95]). We also determined that the risk of mortality from CVD was different across rurality categories (p-heterogeneity <0.001).

By Stage at Diagnosis

We observed broadly similar patterns in disparities between the counties of the lowest SES compared to highest SES when stratified across stage of breast cancer diagnosis for localized (RR = 1.27; 95% CI [1.07, 1.52]), regional (RR = 1.15; 95% CI [0.88, 1.50]), and distant (RR = 1.22; 95% CI [0.31, 4.10]) cancers (**Table 3**). The results were similar in pattern, but smaller in magnitude for median income across all stages of diagnosis (18% for localized, 2% for regional, and 44% for distant). The most rural counties had the highest risk for CVD mortality compared to the most urban counties across all stages of diagnosis (63% for localized, 41% for regional). We found a statistically significant trend of increasing CVD mortality with decreasing SES for any of the stages of diagnosis for localized stage (p-trend = 0.009), but not for regional nor distant stage. Similarly, we only found a significant trend for increasing CVD mortality with decreasing median income for localized stage only (p-trend: 0.029). However, we did find significant differences in CVD mortality across degrees of rurality for localized (p-heterogeneity <0.001) and regional (p-heterogeneity <0.001) cancers but not for distant cancers (p-heterogeneity = 0.728).

By Age at Diagnosis

When stratified by age at diagnosis, survivors who were aged 65 or older showed similar patterns to our overall, unstratified analysis where those who lived in counties with the lowest SES had a higher risk for CVD mortality (RR = 1.29; 95% CI [1.10, 1.53]) compared to those who lived in counties with the highest SES (**Table 4**). Similarly, older survivors living in the poorest counties had a 24% higher risk compared to those who lived in the wealthiest counties. Those in the most rural counties also saw an elevated risk of CVD mortality compared to the most urban counties (RR = 1.36; 95% CI [1.05, 1.76]). We observed a significant trend of increasing CVD mortality with decreasing SES (p-trend = 0.002), as well as for decreasing median income (p-

trend = 0.006), but there were no significant differences in CVD mortality risk across degrees of rurality (p-heterogeneity = 0.064).

The pattern for CVD mortality was slightly different for survivors who were diagnosed when they were younger than 65 years old. We did not observe a significantly elevated risk for younger survivors who lived the lowest SES counties compared to counties of the highest SES (RR = 1.01; 95% CI [0.74, 1.36]), but counties of moderate SES did demonstrate an elevated risk relative to the highest SES counties (RR = 1.40; 95% CI [1.06,1.85]). This pattern is unlike that observed for the overall risk estimates and estimates observed stratified by stage or age at diagnosis, but is again seen for median income where younger survivors in the poorest counties did not see an elevated risk for CVD while middle income counties did have a non-significant increased risk for CVD mortality (RR = 1.09; 95% CI [0.81, 1.46]) compared to the wealthiest counties. This particular pattern for younger survivors was not observed for rurality as the most rural counties had a significantly magnified risk for CVD mortality (RR = 2.44; 95% CI [1.57, 3.77]) relative to the most urban counties. As a result, we did not observe a significant trend of increasing CVD mortality with decreasing SES (p-trend = 0.951) nor with decreasing median income (p-trend = 0.252), but we did see significant differences in CVD mortality across degrees of rurality (p-heterogeneity <0.001).

By Latency

Among all groups of latency, survivors who lived in the lowest SES counties saw an increased risk of CVD mortality (40% for 1-4 years, 13% for 5-9 years, and 16% for 10+ years) compared to the highest SES counties **(Table 5)**. We only observed significant increasing risk of CVD mortality with decreasing SES for survivors with 1-4 years latency (p-trend = 0.008), but not for 5-9 years or 10+ years of latency. Results were similar for median income as survivors with 1-4 years latency saw a 35% elevated risk for CVD mortality in the poorest relative to the wealthiest counties, but there was no significant increased risk beyond 5 years of latency. As follows, we observed significant trends of increasing CVD mortality with decreased wealth for survivors 1-4 years post-diagnosis (p-trend = 0.005), but not the other latency periods.

Disparities were greater in magnitude for rurality with increased risk of CVD mortality across all latency periods for survivors in the most rural compared to most urban counties (77% for 1-4 years, 76% for 5-9 years, and 77% for 10+ years). We only observed significant differences in CVD mortality risk across degrees of rurality

among survivors 1-4 years latency (p-heterogeneity = 0.002) and 5-9 years latency (p-heterogeneity = 0.011), but not for survivors with 10+ years latency.

By Treatment Receipt

Compared to the overall, unstratified analysis, the results for survivors who received only surgery as their initial treatment with no adjuvant and/or radiation therapy demonstrated a similar risk profile. Survivors who received only surgery without any other form of treatment saw statistically significantly increased risks for CVD mortality for all comparisons. Those living in the lowest SES counties saw a 35% increased risk of CVD mortality relative to the highest SES counties, 27% increased risk for the poorest relative to wealthiest counties, and 64% for the most rural relative to most urban counties.

For those who received chemotherapy only or radiation therapy only, living in the lowest SES counties relative to the highest SES counties did not confer an increase in CVD mortality risk. A 18% increased risk was however, observed for survivors who received radiation therapy only (RR = 1.18; 95% CI [0.89,1.58]). Results were more interesting for rurality as it was survivors who lived in the middle group of counties with moderate urbanity that saw an elevated risk for CVD mortality relative to the most urban counties among those who received only one type of treatment (chemotherapy only RR = 1.61; 95% CI [1.11,2.34], radiation therapy only RR = 1.24; 95% CI [1.00, 1.53]). Those who received both chemotherapy and radiation saw significant differences in CVD mortality risk (p-heterogeneity <0.001) with the most rural counties showing a 145% increased risk (RR = 2.45; 95% CI [1.46,4.11]) and moderately urban counties at 62% increased risk (RR = 1.62; 95% CI [1.20,2.19]), relative to the most urban counties.

We only observed a trend for increasing CVD mortality risk with decreasing SES and decreasing wealth among survivors who received surgery only (SES p-trend = 0.005, median income p-trend <0.001), but not among those who received chemotherapy or radiotherapy. We did, however, observe significant differences in CVD risk among the degrees of rurality for those who received surgery only (p-heterogeneity = 0.006) and chemotherapy plus radiation (p-heterogeneity <0.001), but not for those who only received chemotherapy alone or radiotherapy alone.

Cumulative Cardiovascular Disease Mortality – by Age at Diagnosis

The absolute risk of CVD mortality increased with age and was substantially larger among those who were diagnosed at 65 years or older compared to those diagnosed at less than 65 years (**Figure 2**). Disparities were more apparent when stratified by rurality in which older survivors in the most rural counties had a 10-year cumulative CVD mortality of 10.4% (95% CI 7.71-13.55) compared to the most urban counties at 6.12% (95% CI 5.54-6.74), constituting to an absolute risk difference of 4.28%. In comparison, younger survivors had a 10-year cumulative CVD mortality of only 1.25% (95% CI 0.64-2.24) in the most rural counties and 0.51% (95% CI 0.42-0.62) compared to most urban, equating to an absolute risk difference of 0.74%.

DISCUSSION

To our knowledge, this is the first study to describe disparities in CVD mortality at the county-level among AANHPI breast cancer survivors by SES, income, and rurality compared to the general population of AANHPI in the United States. We found significant trends demonstrating that in general, the risk of CVD mortality among survivors increases with worsening SES even when stratified by age, stage, latency, and treatment receipt. We additionally observed heterogeneity by rurality and that some of the largest disparities in CVD mortality existed in the most rural counties compared to more urban counties. Interestingly, younger survivors living in moderately urban counties had the highest risk for CVD mortality, even moreso than those living in the most rural counties, relative to the most urban counties. We theorize that the elevated CVD mortality risk among younger survivors may be due to potential underlying differences in health insurance coverage among individuals under 65 years old, who are ineligible for Medicare, as variations in insurance, types, coverage, and their related restrictions can affect treatment access or the quality of care received[18]. Highly rural areas require cancer patients and survivors to travel substantial differences to get to and from a healthcare facility. The negative effects of differences in access and quality of care can be compounded in these rural areas at multiple stages in the continuum of cancer screening, diagnosis, and survival outcomes as the relative difficulty of accessing healthcare means patients are more likely to be diagnosed at a more advanced cancer stage[19,20].

Interestingly, survivors who received surgery only had a significant trend of increasing CVD mortality risk as SES worsens as well as significant heterogeneity in risk as degree of rurality increases. This may be related to differential access in care wherein survivors who received surgery only may not have had the opportunity to be regularly seen and potentially screened for other diseases, routines that may happen during

follow-up appointments among survivors who received adjuvant therapy. As follows, counties of lower SES or higher rurality may contribute to access issues, lowering the frequency of contact with medical care, and deepen disparities. On the contrary, those who received both chemotherapy and radiation saw significant heterogeneity by rurality, with the highest risk for CVD mortality occurring among the most rural counties. Survivors living in these rural counties likely also experience issues of physical access, and therefore infrequent, healthcare access, which only serves to exacerbate CVD mortality risk and disparities as they may suffer from the compounded cardiotoxic effects of chemotherapy and radiation. Additional may be needed to better understand the barriers and characteristics of breast cancer survivorship care with specific respect to CVD outcomes and disparities.

Limitations and Further Research

One of the limitations of our study include the lack of individual-level SES factors, which may provide additional nuanced information on variations in SES, access to care, and health outcomes. Individual-level SES information could lend potential to better understanding the unique environments in which AANHPI groups tend to reside within ethnic enclaves, which can affect health outcomes by mechanisms of the community providing social or financial support[21]. Therefore, the findings of our study is limited to county-level socioeconomic determinants and additional work is needed to understand how these individual-level factors can modulate cancer and CVD risk, especially for AANHPI survivors living in more rural areas where as they may be relatively farther removed not only from structural inequalities such as access to care, but also from social networks or culturally competent care designed around caring for a specific AANHPI group[22]. Understanding the characteristics of ethnic enclaves can better inform interventions which involve targeting structural inequalities, healthcare access, and allocation of resources with respect to preventing or managing secondary chronic diseases such as CVD among breast cancer survivors.

SEER contains limited data on breast cancer treatment, lacking treatment-specific details such as the type of chemotherapeutic agents used, type of immunotherapy used, dose of radiation, or duration of therapy. Treatment variables including chemotherapy and radiation therapy are simply coded as “yes” or “no/unknown”, which introduces further consideration for potential misclassification or incomplete data in the variable[23]. As a result, SEER data regarding chemotherapy, radiation, and hormone therapy status across all cancer sites varies in sensitivity (68%, 80%, and 69%, respectively). Although, the positive predictive value (PPV) of SEER

correctly identifying female breast cancer individuals' who truly received treatment by treatment type is high (91.2% for chemotherapy, 97.5% for radiation therapy) compared to the PPV for all treatment types across all cancer sites (85%), SEER still cannot capture the treatment status for all who received treatment[24]. Because of this limitation in data specificity and the lack of ability to account for treatment-specific details, we used stage at diagnosis as a proxy for treatment in the adjustments for our Poisson models, assuming that stage is representative of the severity of disease, to which more aggressive treatment is required for more advanced disease stage.

Another limitation of the study is the grouping of multiple, diverse Asian ethnicities into the broader label of AANHPI. The use of aggregated data may fail to capture the nuanced diversity and experiences of different AANHPI groups, which diminishes the generalizability and applicability of our findings when studying a particular group and especially within the context of socioeconomic status and health disparities. There is considerable heterogeneity in SES among different AANHPI ethnicities. For example, as a collective, AANHPI were found to have a median household income of $73,000 compared to the US median household income of $53,000 in 2019. However, disaggregating this data reveals that Indian Americans in particular have a median household income of $100,000, which is greatly disparate to that of Burmese Americans at $36,000[17,25]. Aggregated racial/ethnic data can often neutralize socioeconomic differences, which then fails to capture the broad set of experiences among AANHPI and potentially mask health disparities related to socioeconomic status. Further investigations aiming for greater granularity by disaggregating the data into more detailed AANHPI ethnicity groups (either by individual categories such as Chinese, Vietnamese, Korean, etc. or broad, yet relatively more specific groupings such as East Asian, South Asian, or Southeast Asian) can reveal more nuanced information on how additional determinants such as immigration history[15,26], genetic ancestry, or cultural interactions with health and healthcare can affect CVD and breast cancer outcomes.

CONCLUSIONS

Overall, our study demonstrated that the county-level SES conditions where a AANHPI cancer survivor lives at the time of diagnosis can affect their CVD mortality outcomes. This study provided much needed, detailed data on disparities in CVD mortality among AANHPI breast cancer survivors by county-level SES and rurality. Further studies are needed to understand how CVD mortality may be affected by individual-level

socioeconomic factors and how CVD mortality in relation to breast cancer survivorship may differ among different AANHPI groups.

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APPENDIX

Table 1. Descriptive Characteristics of AAPI Breast Cancer Survivors (N=60,184)

			Cardiovascular Disease SMR			
	n	%	O	E	SMR	95% CI
Overall	60,184	100.0%	1,292.00	1,262.81	1.02	(0.97,1.08)
Age						
<65	44,198	73.4%	307	247.84	**1.24***	(1.10,1.39)
≥65	15,986	26.6%	985	1014.97	0.97	(0.91,1.03)
Stage						
Localized	40,126	66.7%	899	968	**0.93***	(0.87,0.99)
Regional	19,085	31.7%	376	286.72	**1.31***	(1.18,1.45)
Distant	973	1.6%	17	7.96	**2.13***	(1.24,3.42)
Calendar Year of Breast Cancer Diagnosis						
2000-2004	12,858	21.4%	406	423.89	0.96	(0.87,1.06)
2005-2009	15,529	25.8%	439	473.36	0.93	(0.84,1.02)
2010-2017	31,797	52.8%	447	365.56	**1.22***	(1.11,1.34)
Latency (Years since breast cancer diagnosis)						
1-4 years	60,184	100.0%	645	606.91	1.06	(0.98,1.15)
5-9 years	38,645	64.2%	434	420.11	1.03	(0.94,1.13)
10+ years	19,588	32.5%	213	235.78	0.90	(0.79,1.03)
Laterality						
Left	30,499	50.7%	675	644.74	1.05	(0.97,1.13)
Right	29,659	49.3%	616	617.73	1.00	(0.92,1.08)
Bilateral	8	0.0%	1	0.06	16.36	(0.41,91.14)
Unknown	18	0.0%	0	0.28	0.00	(0.00,13.3)
ER Status						
ER+	46,971	78.0%	998	977.8	1.02	(0.96,1.09)
ER-	10,319	17.1%	178	178.22	1.00	(0.86,1.16)
Unknown/Borderline ER	2,585	4.3%	116	104.13	1.11	(0.92,1.34)
Unavailable	309	0.5%	0	2.65	0.00	(0.00,1.39)
PR Status						
PR+	40,565	67.4%	839	815.09	1.03	(0.96,1.1)
PR-	15,984	26.6%	320	312.31	1.02	(0.92,1.14)
Unknown/Borderline PR	3,326	5.5%	133	132.75	1.00	(0.84,1.19)
Unavailable	309	0.5%	0	2.65	0.00	(0.00,1.39)
HER2 Status						
HER+[a]	5,616	9.3%	24	26.43	0.91	(0.58,1.35)
HER-[a]	24,308	40.4%	166	194.34	**0.85***	(0.73,0.99)
Unknown/Borderline HER2	1,712	2.8%	23	14.54	**1.58***	(1.00,2.37)
Unavailable	28,548	47.4%	1079	1027.5	1.05	(0.99,1.11)
Treatment Receipt						
Chemotherapy	15,426	25.6%	374	452	**0.83***	(0.75,0.92)
Radiation Therapy	11,785	19.6%	137	119	1.15	(0.96,1.36)
Chemotherapy and Radiation	16,032	26.6%	196	152	**1.29***	(1.12,1.48)
Surgery only	16,941	28.1%	585	540	1.08	(1.00,1.17)

Note. O=observed, E=expected, SMR=standardized mortality ratios, CI=confidence interval. [a]Restricted to women diagnosed in 2010+.

Table 2. SMRs and RR of cardiovascular disease mortality by county level quintiles

	O	E	SMR	95% CI	p	RR	95% CI
Yost Index							
-1.846-1.160 (Low SES)	430	390.51	1.10	(1.00,1.21)	<0.001	1.22	(1.05,1.41)
1.161-1.617	541	512	1.06	(0.97,1.15)		1.18	(1.03,1.36)
1.618-1.849 (High SES)	321	360	**0.89***	(0.80,0.99)		REF	
Median Income ($)							
≤ $64,999	364	326.4	**1.12***	(1,1.24)	0.080	1.12	(0.99,1.28)
$65,000 - $74,999	217	210	1.03	(0.9,1.18)		1.03	(0.89,1.21)
$75,000+	711	726	**0.98**	(0.91,1.05)		REF	
Education Index							
1004.5-1382.5	454	415.73	1.09	(0.99,1.20)	0.002	1.40	(1.17,1.66)
1382.6-1427.0	654	605	1.08	(1.00,1.17)		1.40	(1.19,1.66)
1427.1-1569.5	184	242	**0.76***	(0.66,0.88)		REF	
Rurality (people)							
Nonmetropolitan	87	61	**1.42***	(1.14,1.75)	<0.001	1.56	(1.25,1.95)
Metropolitan, < 1 million	420	363	**1.16***	(1.05,1.27)		1.28	(1.14,1.44)
Metropolitan, ≥ 1 million pop	785	838	0.94	(0.87,1.00)		REF	

Note. O=observed, E=expected, SMR=standardized mortality ratios, CI=confidence interval, RR=Relative risk, comparing SMR of quintile/category to the most privileged, high income, or most urban counties, adjusted for age at and year of breast cancer diagnosis and stage. P indicates p-trend for Yost Index and median income, and p-heterogeneity for rurality.

Table 3. SMRs and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by stage.

	N	%	O	E	SMR	95% CI	p-value	RR	95% CI
Localized (N=40,126)									
Yost Index									
-1.846-1.160 (Low SES)	12,917	32.19%	291	288.57	1.01	(0.90,1.13)	0.009	1.27	(1.07,1.52)
1.161-1.617	12,764	31.81%	388	401.7	0.97	(0.87,1.07)		1.22	(1.02,1.44)
1.618-1.849 (High SES)	14,445	36.00%	220	277.86	**0.79***	(0.69,0.90)		REF	
Median Income ($)									
≤ $64,999	10,133	25.25%	247	239.27	1.03	(0.91,1.17)	0.029	1.18	(1.01,1.38)
$65,000 - $74,999	7,413	18.47%	151	157.66	0.96	(0.81,1.12)		1.09	(0.91,1.31)
$75,000+	22,580	56.27%	501	571.2	**0.88***	(0.80,0.96)		REF	
Education Index									
1004.5-1382.5	12,225	30.47%	303	309.57	0.98	(0.87,1.10)	0.007	1.42	(1.15,1.75)
1382.6-1427.0	13,923	34.70%	467	471.96	0.99	(0.90,1.08)		1.43	(1.17,1.75)
1427.1-1569.5	13,978	34.84%	129	186.58	**0.69***	(0.58,0.82)		REF	
Rurality (people)									
Nonmetropolitan	1,374	3.42%	67	48.19	**1.39***	(1.08,1.77)	<0.001	1.63	(1.26,2.10)
Metropolitan, < 1 million	9,386	23.39%	293	291.01	1.01	(0.89,1.13)		1.18	(1.02,1.36)
Metropolitan, ≥ 1 million pop	29,366	73.18%	539	628.93	**0.86***	(0.79,0.93)		REF	
Regional (N=19,085)									
Yost Index									
-1.846-1.160 (Low SES)	6,482	33.96%	134	99.71	**1.34***	(1.13,1.59)	0.329	1.15	(0.88,1.50)
1.161-1.617	6,166	32.31%	147	107.43	**1.37***	(1.16,1.61)		1.14	(0.88,1.49)
1.618-1.849 (High SES)	6,437	33.73%	95	79.58	1.19	(0.97,1.46)		REF	
Median Income ($)									
≤ $64,999	5,176	27.12%	113	85.3	**1.32***	(1.09,1.59)	0.954	1.02	(0.81,1.29)
$65,000 - $74,999	3646	19.10%	61	50.9	**1.20**	(0.92,1.54)		0.90	(0.68,1.21)
$75,000+	10,263	53.78%	202	150.52	**1.34***	(1.16,1.54)		REF	
Education Index									
1004.5-1382.5	6,239	32.69%	144	103.51	**1.39***	(1.17,1.64)	0.120	1.35	(0.97,1.86)
1382.6-1427.0	6,707	35.14%	179	129.87	**1.38***	(1.18,1.60)		1.32	(0.96,1.81)
1427.1-1569.5	6,139	32.17%	53	53.34	0.99	(0.74,1.30)		REF	
Rurality (people)									
Nonmetropolitan	583	3.05%	20	12.95	1.54	(0.94,2.39)	<0.001	1.41	(0.89,2.23)
Metropolitan, < 1 million	4,045	21.19%	124	71.11	**1.74***	(1.45,2.08)		1.55	(1.24,1.93)
Metropolitan, ≥ 1 million pop	14,457	75.75%	232	202.66	**1.14***	(1.00,1.30)		REF	

Table 3. SMRs and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by stage. (Continued)

	Distant (N=973)								
Yost Index									
-1.846-1.160 (Low SES)	316	32.48%	5	2.24	2.23	(0.72,5.21)	0.870	1.22	(0.31,4.10)
1.161-1.617	319	32.79%	6	3.03	1.98	(0.73,4.31)		0.90	(0.27,3.05)
1.618-1.849 (High SES)	338	34.74%	6	2.69	2.23	(0.82,4.85)		REF	
Median Income ($)									
≤ $64,999	251	25.80%	4	1.84	2.17	(0.59,5.56)	0.431	1.44	(0.39,5.29)
$65,000 - $74,999	191	19.63%	5	1.67	2.99	(0.97,6.97)		1.96	(0.62,6.25)
$75,000+	531	54.57%	8	4.45	1.80	(0.78,3.54)		REF	
Education Index									
1004.5-1382.5	315	32.37%	7	2.64	**2.65***	(1.07,5.46)	0.273	2.46	(0.48,12.57)
1382.6-1427.0	356	36.59%	8	3.62	2.21	(0.96,4.36)		1.83	(0.38,8.89)
1427.1-1569.5	302	31.04%	2	1.71	1.17	(0.14,4.23)		REF	
Rurality (people)									
Nonmetropolitan	31	3.19%	0	0.13	0	(0.00,29.04)	0.728	0	(0.00, INF)
Metropolitan, < 1 million	225	23.12%	3	1.3	2.31	(0.48,6.75)		0.70	(0.15,3.19)
Metropolitan, ≥ 1 million pop	717	73.69%	14	6.54	**2.14***	(1.17,3.59)		REF	

Note. O=observed, E=expected, SMR=standardized mortality ratios, CI=confidence interval, RR=Relative risk, comparing SMR of quintile/category to the most privileged, high income, or most urban counties, adjusted for age at and year of breast cancer diagnosis and stage. P indicates p-trend for Yost Index and median income, and p-heterogeneity for rurality.

Table 4. SMR and RR of cardiovascular disease mortality by county level socioeconomic status and rurality, stratified by age at breast cancer diagnosis

Age at breast cancer diagnosis	<65 years (N=307)							65-84 years (N=985)						
	O	E	SMR	95% CI	p	RR	95% CI	O	E	SMR	95% CI	p	RR	95% CI
Yost Index														
-1.846-1.160 (Low SES)	87	80.71	1.08	(0.86,1.33)	0.951	1.01	(0.74,1.36)	343	309.8	1.11	(0.99,1.23)	0.002	1.29	(1.1,1.53)
1.161-1.617	140	93.26	**1.50***	(1.26,1.77)		1.40	(1.06,1.85)	401	418.9	0.96	(0.87,1.06)		1.12	(0.95,1.32)
1.618-1.849 (High SES)	80	73.86	1.08	(0.86,1.35)		REF		241	286.26	**0.84***	(0.74,0.96)		REF	
Median Income ($)														
< $35,000 - $69,999	71	68.43	1.04	(0.81,1.31)	0.252	0.83	(0.63,1.09)	293	257.97	**1.14***	(1.01,1.27)	0.006	1.24	(1.07,1.43)
$70,000 - $74,999	62	43.31	**1.43***	(1.10,1.84)		1.09	(0.81,1.46)	155	166.92	0.93	(0.79,1.09)		1.01	(0.84,1.21)
$75,000+	174	136.1	**1.28***	(1.10,1.48)		REF		537	590.08	**0.91***	(0.83,0.99)		REF	
Education Index														
1004.5-1382.5	97	88.72	1.09	(0.89,1.33)	0.962	1.21	(0.84,1.76)	357	327.01	1.09	(0.98,1.21)	<0.001	1.46	(1.2,1.78)
1382.6-1427.0	169	111.39	**1.52***	(1.30,1.76)		1.68	(1.19,2.39)	485	494.06	0.98	(0.90,1.07)		1.32	(1.09,1.61)
1427.1-1569.5	41	47.73	0.86	(0.62,1.17)		REF		143	193.9	**0.74***	(0.62,0.87)		REF	
Rurality (people)														
Nonmetropolitan	23	10.22	**2.25***	(1.43,3.38)	<0.001	2.44	(1.57,3.77)	64	51.04	1.25	(0.97,1.60)	0.064	1.36	(1.05,1.76)
Metropolitan, < 1 million	110	57.1	**1.93***	(1.58,2.32)		2.05	(1.62,2.61)	310	306.32	1.01	(0.90,1.13)		1.11	(0.96,1.27)
Metropolitan, ≥ 1 million pop	174	180.52	0.96	(0.83,1.12)		REF		611	657.6	0.93	(0.86,1.01)		REF	

Note. O=observed, E=expected, SMR=standardized mortality ratios, CI=confidence interval, RR=Relative risk, comparing SMR of quintile/category to the most privileged, high income, or most urban counties, adjusted for age at and year of breast cancer diagnosis and stage. P indicates p-trend for Yost Index and median income, and p-heterogeneity for rurality

Table 5. SMR and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by latency.

Years since diagnosis	**1-4 years post diagnosis**						
	O	E	SMR	95% CI	p	RR	95% CI
Yost Index							
-1.846-1.160 (Low SES)	153	136.69	1.12	(0.95,1.31)	0.008	1.40	(1.09,1.79)
1.161-1.617	146	151.17	0.97	(0.82,1.14)		1.20	(0.93,1.55)
1.618-1.849 (High SES)	107	136.02	**0.79***	(0.64,0.95)		REF	
Median Income ($)							
≤ $64,999	129	114.26	1.13	(0.94,1.34)	0.005	1.35	(1.08,1.69)
$65,000 - $74,999	80	71.22	1.12	(0.89,1.40)		1.33	(1.02,1.73)
$75,000+	197	238.41	**0.83***	(0.71,0.95)		REF	
Education Index							
1004.5-1382.5	153	134	1.14	(0.96,1.33)	<0.001	1.76	(1.32,2.35)
1382.6-1427.0	182	178	1.02	(0.88,1.18)		1.61	(1.21,2.14)
1427.1-1569.5	71	111.45	**0.64***	(0.50,0.80)		REF	
Rurality (people)							
Nonmetropolitan	28	19.27	1.45	(0.97,2.10)	0.002	1.77	(1.20,2.62)
Metropolitan, < 1 million	134	118.53	1.13	(0.95,1.34)		1.37	(1.11,1.70)
Metropolitan, ≥ 1 million pop	244	286.1	**0.85***	(0.75,0.97)		REF	

Table 5. SMR and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by latency. (Continued)

Years since diagnosis	5-9 years post diagnosis						
	O	E	SMR	95% CI		RR	95% CI
Yost Index							
-1.846-1.160 (Low SES)	139	145.73	0.95	(0.80,1.13)	0.362	1.13	(0.88,1.44)
1.161-1.617	178	186.77	0.95	(0.82,1.10)		1.16	(0.92,1.47)
1.618-1.849 (High SES)	122	140.86	0.87	(0.72,1.03)		REF	
Median Income ($)							
≤ $64,999	116	115.91	1.00	(0.83,1.20)	0.763	1.08	(0.86,1.35)
$65,000 - $74,999	69	86.06	0.80	(0.62,1.01)		0.81	(0.62,1.06)
$75,000+	254	271.39	0.94	(0.82,1.06)		REF	
Education Index							
1004.5-1382.5	141	153.93	0.92	(0.77,1.08)	0.674	1.1	(0.83,1.46)
1382.6-1427.0	223	232.59	0.96	(0.84,1.09)		1.17	(0.90,1.53)
1427.1-1569.5	75	86.85	0.86	(0.68,1.08)			
Rurality (people)							
Nonmetropolitan	32	23	1.41	(0.97,2.00)	0.011	1.76	(1.22,2.55)
Metropolitan, < 1 million	136	137	1.00	(0.84,1.18)		1.22	(1.00,1.51)
Metropolitan, ≥ 1 million pop	271	314	**0.86***	(0.76,0.97)		REF	

Table 5. SMR and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by latency. (Continued)

Years since diagnosis	10+ years post diagnosis						
	O	E	SMR	95% CI		RR	95% CI
Yost Index							
-1.846-1.160 (Low SES)	138	108.09	**1.28***	(1.07,1.51)	0.333	1.16	(0.89,1.51)
1.161-1.617	217	174.22	**1.25***	(1.09,1.42)		1.18	(0.92,1.51)
1.618-1.849 (High SES)	92	83.24	1.11	(0.89,1.36)		REF	
Median Income ($)							
≤ $64,999	119	96.24	**1.24***	(1.02,1.48)	0.952	1.00	(0.80,1.24)
$65,000 - $74,999	68	52.94	1.28	(1.00,1.63)		1.07	(0.81,1.40)
$75,000+	260	216.38	**1.20***	(1.06,1.36)		REF	
Education Index							
1004.5-1382.5	160	127.38	**1.26***	(1.07,1.47)	0.183	1.45	(1.02,2.07)
1382.6-1427.0	249	194.85	**1.28***	(1.12,1.45)		1.52	(1.08,2.14)
1427.1-1569.5	38	43.33	0.88	(0.62,1.20)		REF	
Rurality (people)							
Nonmetropolitan	27	19	1.39	(0.92,2.03)	0.099	1.77	(1.20,2.62)
Metropolitan, < 1 million	150	108	**1.38***	(1.17,1.62)		1.37	(1.11,1.70)
Metropolitan, ≥ 1 million pop	270	238	**1.14***	(1.00,1.28)		REF	

Note. O=observed, E=expected, SMR=standardized mortality ratios, CI=confidence interval, RR=Relative risk, comparing SMR of quintile/category to the most privileged, high income, or most urban counties, adjusted for age at and year of breast cancer diagnosis and stage.

Table 6. SMRs and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by Treatment Receipt.

	O	E	SMR	95% CI	p-value	RR	95% CI
Chemotherapy only (N=15,426)							
Yost Index							
-1.846-1.160 (Low SES)	43	43.86	0.98	(0.71,1.32)	0.576	0.89	(0.57,1.38)
1.161-1.617	56	42.31	1.32	(1.00,1.72)		1.12	(0.74,1.71)
1.618-1.849 (High SES)	38	33.13	1.15	(0.81,1.57)		REF	
Median Income ($)							
≤ $64,999	34	36.63	0.93	(0.64,1.30)	0.333	0.80	(0.53,1.21)
$65,000 - $74,999	29	22.14	1.31	(0.88,1.88)		1.04	(0.67,1.61)
$75,000+	74	60.54	1.22	(0.96,1.53)		REF	
Education Index							
1004.5-1382.5	49	45.4	1.08	(0.80,1.43)	0.721	1.00	(0.58,1.74)
1382.6-1427.0	70	53.87	**1.30***	(1.01,1.64)		1.19	(0.70,2.03)
1427.1-1569.5	18	20.04	0.90	(0.53,1.42)		REF	
Rurality (people)							
Nonmetropolitan	5	5.18	0.97	(0.31,2.25)	0.061	1.12	(0.45,2.78)
Metropolitan, < 1 million	42	26.37	**1.59***	(1.15,2.15)		1.61	(1.11,2.34)
Metropolitan, ≥ 1 million pop	90	87.77	1.03	(0.82,1.26)		REF	
Radiation Only (N=11,785)							
Yost Index							
-1.846-1.160 (Low SES)	92	104.09	0.88	(0.71,1.08)	0.247	1.18	(0.89,1.58)
1.161-1.617	183	208.69	0.88	(0.75,1.01)		1.14	(0.89,1.48)
1.618-1.849 (High SES)	99	138.87	**0.71***	(0.58,0.87)		REF	
Median Income ($)							
≤ $64,999	77	87.73	0.88	(0.69,1.10)	0.670	1.07	(0.82,1.38)
$65,000 - $74,999	53	65.3	0.81	(0.61,1.06)		0.99	(0.73,1.33)
$75,000+	244	298.62	**0.82***	(0.72,0.93)		REF	
Education Index							
1004.5-1382.5	101	111.21	0.91	(0.74,1.10)	0.574	1.41	(1.02,1.96)
1382.6-1427.0	212	239.13	0.89	(0.77,1.01)		1.37	(1.02,1.84)
1427.1-1569.5	61	101.32	**0.60***	(0.46,0.77)		REF	
Rurality (people)							
Nonmetropolitan	13	16.23	0.80	(0.43,1.37)	0.178	1.01	(0.57,1.76)
Metropolitan, < 1 million	148	157	0.94	(0.80,1.11)		1.24	(1.00,1.53)
Metropolitan, ≥ 1 million pop	213	278.42	**0.77***	(0.67,0.87)		REF	

Table 6. SMRs and RR of cardiovascular disease mortality by county level socio-economic status and rurality, stratified by Treatment Receipt. (Continued)

Chemotherapy and Radiation (N=16,032)							
Yost Index							
-1.846-1.160 (Low SES)	44	40.49	1.09	(0.79,1.46)	0.710	0.92	(0.61,1.38)
1.161-1.617	99	66.8	**1.48***	(1.20,1.80)		1.27	(0.90,1.80)
1.618-1.849 (High SES)	53	44.55	1.19	(0.89,1.56)		REF	
Median Income ($)							
≤ $64,999	38	33.33	1.14	(0.81,1.56)	0.390	0.85	(0.59,1.22)
$65,000 - $74,999	33	25.08	1.32	(0.91,1.85)		0.96	(0.65,1.42)
$75,000+	125	93.43	**1.34***	(1.11,1.59)		REF	
Education Index							
1004.5-1382.5	52	44.18	1.18	(0.88,1.54)	0.797	1.00	(0.64,1.57)
1382.6-1427.0	110	77.54	**1.42***	(1.17,1.71)		1.23	(0.82,1.84)
1427.1-1569.5	34	30.13	1.13	(0.78,1.58)		REF	
Rurality (people)							
Nonmetropolitan	17	6.98	**2.43***	(1.42,3.90)	<0.001	2.45	(1.46,4.11)
Metropolitan, < 1 million	80	51.18	**1.56***	(1.24,1.95)		1.62	(1.20,2.19)
Metropolitan, ≥ 1 million pop	99	93.68	1.06	(0.86,1.29)		REF	
Surgery only (N=16,941)							
Yost Index							
-1.846-1.160 (Low SES)	251	202.08	**1.24***	(1.09,1.41)	0.005	1.35	(1.09,1.67)
1.161-1.617	203	194.35	1.04	(0.91,1.20)		1.17	(0.94,1.47)
1.618-1.849 (High SES)	131	143.57	0.91	(0.76,1.08)		REF	
Median Income ($)							
≤ $64,999	215	168.71	**1.27***	(1.11,1.46)	0.011	1.27	(1.06,1.52)
$65,000 - $74,999	102	97.71	1.04	(0.85,1.27)		1.06	(0.84,1.33)
$75,000+	268	273.58	0.98	(0.87,1.10)		REF	
Education Index							
1004.5-1382.5	252	214.95	**1.17***	(1.03,1.33)	0.008	1.54	(1.17,2.01)
1382.6-1427.0	262	234.92	1.12	(0.98,1.26)		1.5	(1.15,1.96)
1427.1-1569.5	71	90.14	**0.79***	(0.62,0.99)		REF	
Rurality (people)							
Nonmetropolitan	52	32.87	**1.58***	(1.18,2.07)	0.006	1.64	(1.23,2.20)
Metropolitan, < 1 million	150	128.87	1.16	(0.99,1.37)		1.19	(0.98,1.44)
Metropolitan, ≥ 1 million pop	383	378.26	1.01	(0.91,1.12)		REF	

Note. O=observed, E=expected, SMR=standardized mortality ratios, CI=confidence interval, RR=Relative risk, comparing SMR of quintile/category to the most privileged, high income, or most urban counties, adjusted for age at and year of breast cancer diagnosis and stage. P indicates p-trend for Yost Index and median income, and p-heterogeneity for rurality.

Figure 1. 10-year cumulative mortality of CVD by rurality, overall

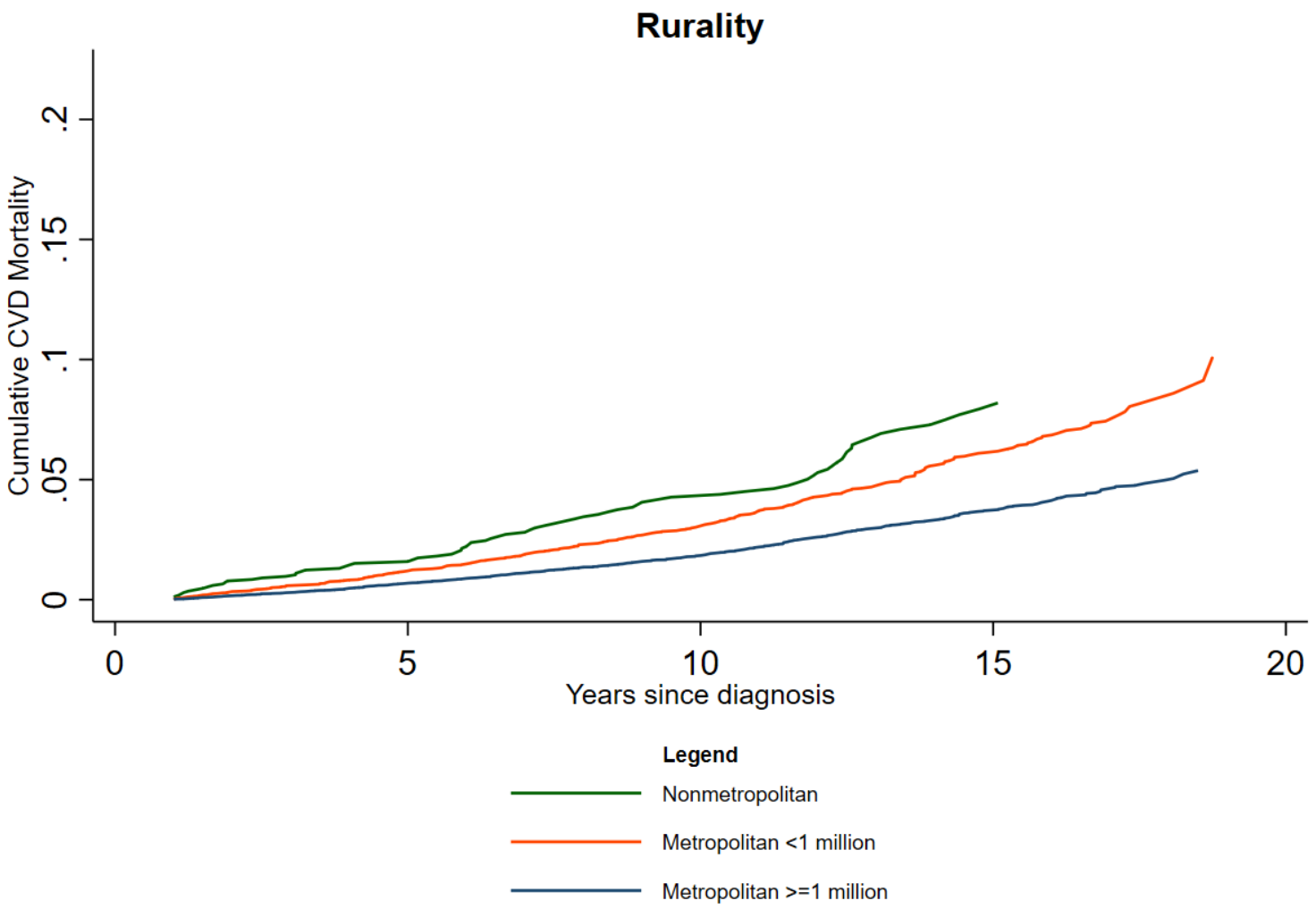
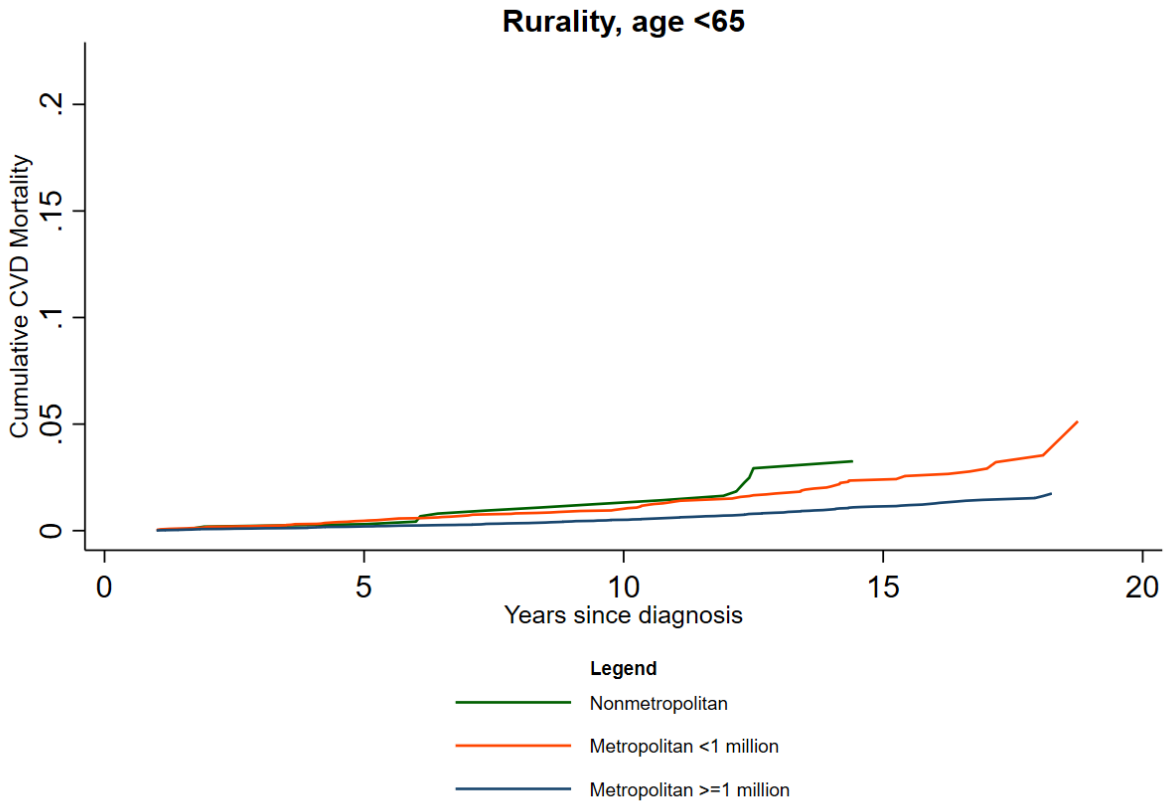
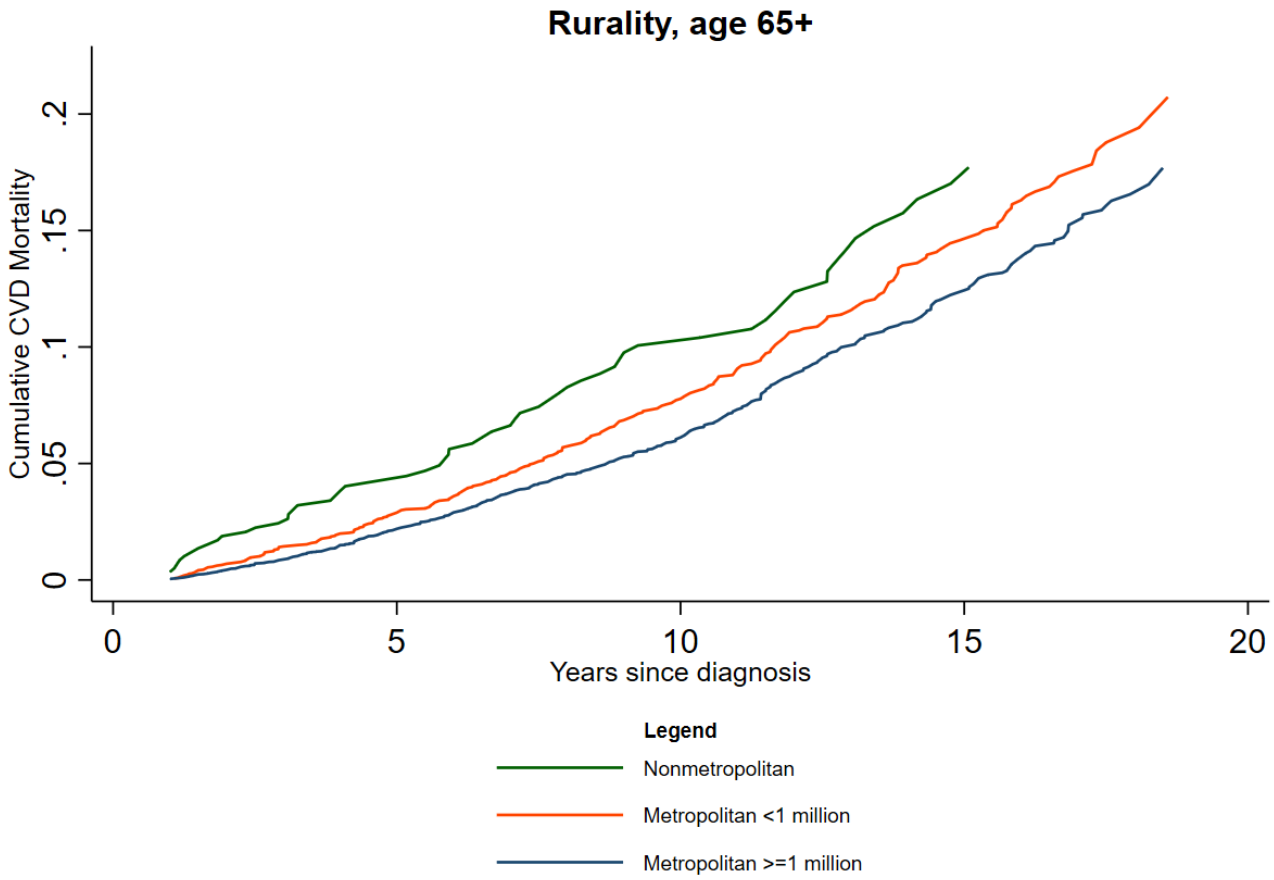


Figure 2. 10-year cumulative mortality of CVD by rurality, stratified by age at diagnosis




Rurality, age 65+
Cumulative CVD Mortality
0
.05
.1
.15
.2
0
5
10
15
20
Years since diagnosis
Legend
Nonmetropolitan
Metropolitan <1 million
Metropolitan >=1 million