Exploring the Intersection Between Persistent Poverty and Rurality Status for Advanced Stage Diagnosis of Breast Cancer using the Surveillance, Epidemiology, and End Results (SEER) Program

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Abstract

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Persistent poverty has been associated with disparities in cancer outcomes. Prior studies have described these disparities as most important for rural areas. This study seeks to provide insight into the roles of persistent poverty and rurality status, on receiving an advanced stage breast cancer diagnosis (stage II, III, and IV) relative to stage I. This cross-sectional study utilized the SEER database, including female individuals diagnosed from 2010 to 2020. Persistent poverty was defined as an area that has consistently maintained a poverty rate of 20% or more for a period of at least 30 years. Urban rural status was defined based on the percentage of people living in a non-urban area. Adjusted multinomial logistic regression models were used to estimate the likelihood of receiving an advanced stage diagnosis associated with persistent

poverty and urban-rural status. Stratified analysis and a likelihood ratio test comparing models with and without interaction terms were used to assess effect modification by urban-rural status. A total of 492,050 female individuals were included in this study of which 6.9% lived in persistent poverty areas. Individuals residing in persistent poverty areas had higher risks of presenting with a more advanced stage at diagnosis. The risks were also higher for individuals residing in mostly rural and all rural areas. Stratified analysis by urban-rural classification revealed that the effect of persistent poverty was greater among all urban and mostly urban areas. Effect modification was found by urban-rural classification ($p=0.002$). This study found that persistent poverty and urban-rural status is associated with advanced breast cancer stage at diagnosis. Additionally, we found that the effect of persistent poverty is modified by urban-rural classifications.

Introduction

Persistent poverty is an extreme form of poverty that is defined as an area where 20% or more of the population has consistently lived in poverty for over 30 years[1]. Residents in persistent poverty areas face poor health outcomes due to inadequate medical infrastructure and limited access to healthcare[2,3]. Structural inequality, in the form of residential segregation and a lack of investment in public health infrastructure, further marginalizes communities into areas of economic and environmental degradation[2,3]. A study examining the impact of poverty duration on cancer outcomes found that patients in persistent poverty areas are more likely to present with advanced stage breast and lung cancer, and have a lower likelihood of surgical resection for localized disease compared to those not residing in a persistent poverty area[4].

The issues associated with persistent poverty are exacerbated within the context of rurality. Persistent poverty counties are typically located in rural geographical areas that already face unique place-based structural barriers[5]. Rurality-associated disparities have been well documented, including lower rates of cancer screening and advanced stage at diagnosis[6]. Aggregating challenges faced by rural populations in persistent poverty areas can exacerbate health disparities.

Very few studies have examined the intersection between poverty and rurality. One study found that African American/Black individuals residing in rural areas with persistent poverty had the highest cancer-specific mortality rates compared to White individuals in the same areas[5]. When looking at early-onset colorectal survival, patients living in both rural and persistent poverty areas had a greater risk of colorectal cancer death compared to patients not living in a persistent poverty and rural area[7]. While these studies provide valuable information on the disparities in cancer mortality, they have overlooked the joint impact of persistent poverty and

rurality on stage at diagnosis. This study expands on the overall knowledge of the joint effect of persistent poverty and rurality on stage at diagnosis for screen-detected cancers.

The primary aim of this study was to examine how persistent poverty is associated with the odds of being diagnosed with more advanced stage breast cancer (stage II, III, and IV) relative to stage I breast cancer. We hypothesized that individuals who reside in census tracts with persistent poverty will more likely be diagnosed at later stages compared to individuals not living in persistent poverty areas.

Our secondary aim was to examine how urban-rural status is associated with the odds of being diagnosed with advanced stage breast cancer relative to stage I. We hypothesized that residents in census tracts with a rural status (mostly urban, mostly rural, all rural) will be more likely to be diagnosed at advanced stages compared to residents in all-urban areas.

Our final aim was to examine whether urban-rural classifications modify the association between persistent poverty and advanced stage at diagnosis. We hypothesize that the association between persistent poverty and stage at diagnosis will differ with urban-rural classification. Understanding this joint effect is important in creating effective interventions, as it will provide insight into the role of contextual factors and their influence on cancer outcomes.

Methods

Study Design

This cross-sectional study utilized the SEER specialized incidence data and census tract attributes database[8]. This database includes patient-level data from 17 registries (San Francisco-Oakland, Connecticut, Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Atlanta, San Jose-Monterey, Los Angeles, Rural Georgia, California excluding SF/SJM/LA, Kentucky,

Louisiana, New Jersey, and Greater Georgia) covering approximately 26.5% of the U.S. population. Patient-level data included cases diagnosed from 2010 to 2020.

The first exposure of interest was persistent poverty. The SEER census-tract database provides one variable with two categories: residing in a persistent poverty area and not residing in a persistent poverty area. Tracts classified as persistent poverty were considered the exposure group for both our primary and tertiary aims. A persistent poverty tract is defined as an area that has consistently maintained a *high poverty* status (poverty rate of 20% or more) for a period of 30 years or more[8,9]. This threshold is based on research suggesting that areas with long-term poverty concentrations of 20% or more may experience greater systemic disparities, such as reduced healthcare access, compared to areas with lower concentrations of poverty[10]. Individuals not residing in a persistent poverty area are those that live in an area that has not met the definition of persistent poverty. Data sources used for identifying persistent poverty areas are based on the 1990, 2000 decennial censuses and the American Community survey 5-year estimates from 2007-11 and 2015-19[8].

The second exposure of interest was urban-rural status. This study used a census tract-level variable provided by SEER known as the Urban Rural Indicator Code (URIC). This variable is based on the 2010 Census Bureau's percentage of people living in a non-urban area and has the following four categories: all urban (100% urban), mostly urban (≥ 50% but <100% urban), mostly rural (>0% but <50% urban), and all rural (100% rural)[8]. An urbanized area is defined by the Census Bureau as an area of 50,000 people or more[11]. Our reference group was the "all urban" category. Motivated by literature, this categorical variable was thought to better reflect the immediate rural environment of a patient's residence.

The primary outcome of interest was stage at diagnosis based on the American Joint Committee on Cancer (AJCC). Data on AJCC staging is available in SEER for different diagnosis years. A categorical variable with stages I, II, III, and IV, was created by regrouping stages from the following three variables: 8th edition Derived EOD 2018 Stage Group (2018+), AJCC 7th edition Derived SEER Combined Stage Group (2016-2017), and 7th edition Derived AJCC Stage Group (2010-2015). Stage I was the reference group to which other stages were compared.

Confounders for all aims were considered a priori based on previous studies examining similar relationships between persistent poverty, rurality, and cancer outcome[7,12]. These covariates include marital status at diagnosis (single, married, separated, divorced, widowed, unmarried/domestic partner, unknown, blank), race and origin (Non-Hispanic (NH) White, NH Black, NH American Indian/Alaska Native, NH Asian Pacific Islander, Hispanic), age at diagnosis, and year of diagnosis.

Study Setting

Data were sourced from the Surveillance, Epidemiology, and End Results (SEER) program. This program is composed of multiple cancer registries across the United States that receive and collect data about cancer patients. Each of the 50 states have different laws regarding reporting of newly diagnosed cancers to registries. Identification of cancer cases can occur in settings such as hospitals, outpatient clinics, laboratories, or any setting that is involved in diagnosing or providing cancer care. Registries are required to collect cancer data according to the North American Association of Central Cancer Registries' (NAACCR) Data Standards[13]. This includes data such as patient demographics, tumor characteristics, treatment, and outcomes. Confidentiality measures are implemented through policies, laws and regulations that strictly

guide data management to protect the privacy and confidentiality of patients, physicians, and other healthcare entities. This ensures that all data are de-identified to prevent identification of individuals and also make the data exempt from IRB review.

Study Subjects

We analyzed de-identified data of female patients aged 18 and older diagnosed with breast cancer during the years 2010-2020 (Figure 1). Male individuals and patients for whom breast cancer is not their first or only cancer diagnosis were excluded from this study. Additional exclusions included patients whose cancer diagnosis was stage 0, NOS, or unknown. Based on results from the missing data analysis described below, a complete case analysis was determined to be most appropriate, and we excluded patients with missing values for any variable in our study.

Data Collection

The SEER program collects cancer data from various cancer registries across the United States. The data includes patient demographics, primary tumor site, stage at diagnosis, first course treatment, and follow-up for vital status. The US census defines census tract as small, permanent statistical subdivisions of a county[14]. The SEER data we used is composed of 17 registries from the United States, all of which were included in this study.

Analysis

We first examined the degree of missingness within the dataset by summarizing the proportion of missingness within each variable. The proportion of missingness within each variable was less than 10%, therefore we determined that a complete case analysis was appropriate for this study. Descriptive statistics were conducted and stratified by persistent

poverty and rurality to gain a better understanding on the distribution of demographics for patients.

For our first and second aim, two multinomial logistic regression models were fit to determine associations between stage at diagnosis and the predictors, persistent poverty, and urban-rural status, adjusted for covariates. A Wald test with a significance level of 0.05, was used to assess any significant associations between the predictors and stage at diagnosis. For the tertiary aim, a separate multinomial logistic regression model, adjusted for covariates, was fit with three interaction terms (Mostly Urban*PP, Mostly Rural*PP, and All Rural*PP) to assess if the association between stage at diagnosis and persistent poverty is modified by urban-rural classification. We used the "All urban" category as our reference group for the effect of persistent poverty. A likelihood ratio test (LRT) was used to test if the effect of persistent poverty significantly differs by urban-rural classification. The LRT compared the model with an interaction term between persistent poverty and urban-rural status, to a reduced model that excluded this interaction term. Effect modification was concluded to be present at a significance level of 0.05 for the LRT p value associated with this comparison.

Additionally, we conducted a stratified analysis by urban-rural status to further evaluate effect modification by assessing differences in measures of association. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were the measure of association for all aims. Statistical analysis and data management was conducted using R studio.

Results

Demographic Statistics

A total of 492,050 female individuals with a breast cancer diagnosis were included in this study (Table 1). There were 33,961 (6.9%) individuals living in a persistent poverty tract of

whom 22,057 (64.9%) lived in an all-urban area, 6,359 (18.7%) lived in a mostly urban area, 2,088 lived in a mostly rural area (6.1%), and 3,457 (10.2%) lived in an all-rural area (Table 1). Most patients in the study were between the ages of 60-69 (27.3%), NH White (66.1%), and married (58.0%). Similar distributions of stage I and stage II diagnoses were seen for patients residing in persistent poverty areas and across all urban-rural classifications. When stratified by race and ethnicity, areas with persistent poverty were seen to have higher percentages of NH Black (32.0%) and Hispanic (22.2%) individuals compared to areas with no persistent poverty.

Persistent Poverty

After adjusting for covariates, we found that compared to individuals not residing in a persistent poverty area, those residing in persistent poverty areas had 1.16 (95%CI: 1.13,1.20), 1.29 (95%CI: 1.25, 1.35), and 1.37 (95%CI: 1.31,1.43) higher odds of being diagnosed with stage II, stage III, and stage IV breast cancer, respectively.

Urban-Rural Status

After adjusting for covariates, no significant associations were found between individuals residing in a mostly urban area compared to an all-urban area for stage II ($p=0.54$), stage III ($p=0.53$), and stage IV diagnoses ($p=0.38$) (Table 2). However, significant associations were found between individuals residing in mostly rural areas and all stage at diagnosis when compared to living in all-urban areas (stage II $p<0.001$; stage III $p<0.001$; and Stage IV $p<0.001$). Compared to individuals living in all-urban areas, those residing in mostly rural areas had higher odds of presenting with a more advanced stage at diagnosis as opposed to stage I (stage II aOR: 1.05 (95%CI: 1.02, 1.08); stage III aOR: 1.13 (95%CI: 1.08, 1.17); stage IV aOR: 1.10 (95%CI: 1.05, 1.16)). Significant associations were found across all stages for individuals residing in an all-rural area (stage II $p<0.001$; stage III $p<0.001$; stage IV $p<0.001$). The odds of

presenting with a stage II, III, and IV diagnosis were greater for all-rural areas than individuals residing in an all-urban area (stage II aOR: 1.11 (95%CI: 1.08, 1.14); stage III aOR: 1.20 (95%CI:1.15, 1.25); stage IV aOR: 1.20 (95%CI: 1.14, 1.27)).

Intersection of Persistent Poverty and Urban-Rural Status

The likelihood ratio test yielded a p-value of 0.002, indicating that there is sufficient evidence of effect modification by urban-rural status in the association between persistent poverty and stage at diagnosis (Table 3). Among individuals in a persistent poverty area, the odds of stage II diagnosis compared to stage I was higher for individuals residing in an all urban (aOR: 1.18 95%CI: 1.14, 1.22), mostly urban (aOR: 1.13 95% CI: 1.06, 1.20), mostly rural (aOR: 1.07 95%CI: 0.96, 1.19), and all rural area (aOR: 1.13 95%CI: 1.04, 1.24) compared to individuals not living in a persistent poverty area. Similarly, the odds of receiving a stage III diagnosis for individuals residing in a persistent poverty area compared to not living in a persistent poverty area, was higher among those also residing in an all urban (aOR: 1.33 95%CI: 1.27, 1.39), mostly urban (aOR: 1.30 95%CI: 1.20, 1.41), and all rural area (aOR: 1.16 95%CI: 1.02, 1.30). Finally, the odds of receiving a stage IV diagnosis were higher among individuals residing in both a persistent poverty area and either an all urban area (aOR: 1.42 95%CI: 1.35, 1.50), mostly urban (aOR: 1.33 95%CI: 1.20, 1.47), mostly rural (aOR: 1.08 95%: 0.90, 1.30) and all rural classification (OR: 1.14 95%: 0.99, 1.32). Significant associations were found across all stages, in the relationship between persistent poverty and stage at diagnosis, among individuals residing in an urban and mostly urban area. No significant associations were found among individuals residing in a mostly rural area across all stages. Significant associations were found among individuals residing in an all-rural area for stages II and III, but not stage IV.

Discussion

This study sought to examine the roles of persistent poverty and rural urban status on receiving a later stage at diagnosis. Overall, persistent poverty was significantly associated with receiving a later breast cancer stage diagnosis relative to stage I. We observed increased odds of stage II, III, and IV breast cancer diagnosis among individuals residing in a persistent poverty area when compared to individuals not residing in a persistent poverty area. Additionally, persistent poverty was seen to have an increasing gradient effect with later stage diagnosis. For example, the odds of receiving a stage II breast cancer diagnosis as opposed to stage I, was 1.16 times greater for individuals residing in a persistent poverty area. This is consistent with existing literature examining the association between persistent poverty and the odds of advanced stage diagnosis. A study by Papageorge et al. 2023 examined the impact of the duration of poverty on receiving an advanced stage diagnosis[4]. In that study, receiving an advanced diagnosis was defined as a combination of stages III and IV. They found significant associations between persistent poverty areas and higher odds of receiving an advanced stage for breast and non-small cell lung cancer, compared to areas with low poverty. Our study expands on Papageorge et al.'s study, by further stratifying to examine the effect of persistent poverty on each cancer stage.

When looking at the impact of urban-rural classification, significant associations were found for mostly rural and all rural classifications across all stages. Overall, individuals living in a mostly rural area had higher odds of receiving a later stage diagnosis compared to those living in an all-urban area. However, the odds were even greater for individuals living in an all-rural area when compared to an all-urban area. No associations were found between mostly urban areas and receiving a later stage diagnosis. Estimates from this analysis provide valuable contextual information on urban-rural spectrum and its role on cancer outcomes. Past studies

examining the effect of rurality on advanced stage diagnosis have found significant associations. Most studies however, explored the association using a binary urban-rural variable. Our study was able to add to this knowledge by exploring the effect of the immediate urban-rural environment of an individual by using a variable with more categories. This allowed us to examine the effect on stage at diagnosis across a wider urban-rural spectrum.

We observed a significant joint effect of persistent poverty and urban-rural status. This supports our hypothesis, that the effect of persistent poverty on the odds of receiving a later stage diagnosis is modified by urban-rural classifications. Overall, we observed that individuals living in a persistent poverty area had increased odds of having a later stage diagnosis in most urban-rural classifications. Interestingly, compared to individuals not living in a persistent poverty area, the odds of receiving a later stage at diagnosis for individuals residing in a persistent poverty area was higher among all urban and mostly urban classifications. This could indicate that living in an area with persistent poverty might have a greater effect in increasing the chances of receiving a later stage at diagnosis in all urban and mostly urban areas. This is an unexpected finding given that areas that are both rural, and experiencing persistent poverty, face a disproportionate burden of disinvestment resulting in reduced healthcare access, and poor medical infrastructure[3]. Therefore, it would be expected that the effect of persistent poverty would have a higher magnitude in risk among all rural residents. However, we did not observe this in our findings. More information is needed as to the mechanisms driving the effect of persistent poverty among all urban and mostly urban areas.

Our study has several strengths, including that the SEER database was able to provide a large population sample size which allowed us to use a more granular urban-rural classification variable as opposed to using a binary urban-rural variable.

A major limitation to this study was that we were unable to adjust for individual level covariates such as insurance, education, smoking, screening history, and other health behaviors or risk factors that may influence the relationship stage at diagnosis and our predictors, persistent poverty and urban-rural status. Additionally, we were unable to account for factors such as in- and out- migration which could impact the duration of an individual's time in a rural setting. A limitation of using the persistent poverty variable is that some census tracts may have over-inflated variables[8]. This may be due to some tracks having unique communities with high student populations or areas with prisons that tend to report low incomes.

In conclusion, women living in areas where persistent poverty is present are more likely to be diagnosed with advanced stage breast cancer. Our study also found women living in mostly rural and all rural areas had higher risks of late stage breast cancer compared to those living in an all-urban area. This study also found evidence that urban-rural classification modifies the association between persistent poverty and stage at diagnosis. Compared to individuals not living in a persistent poverty area, those that did live in a persistent poverty area had higher odds of receiving a later stage diagnosis across most urban rural classifications. Our study emphasizes the importance of understanding contextual factors that disproportionally affect impoverished and rural communities. Findings from this study can help inform public health by identifying burdened communities for targeted primary and secondary prevention interventions such as improving access to mammography screening.

Appendix

Figure 1. Flow diagram displaying inclusion/exclusion criteria for our final analytic sample.

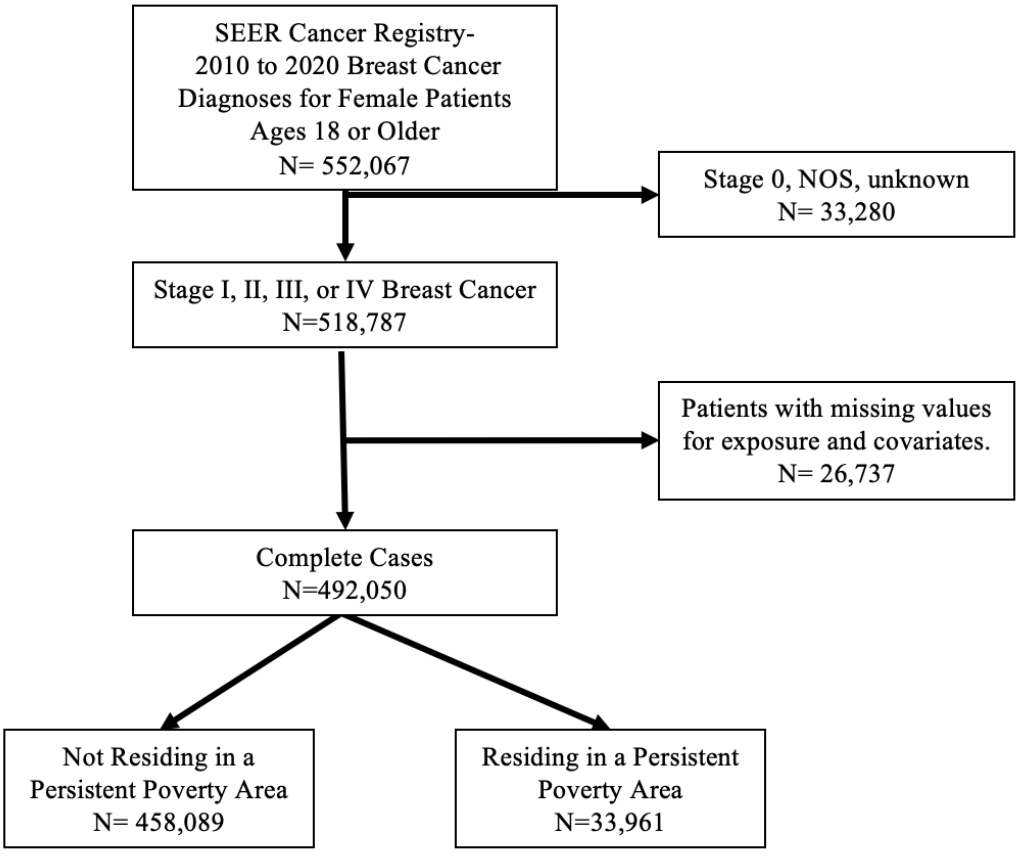

Table 1. Demographic characteristics of female individuals diagnosed with breast cancer between years 2010 to 2020 by residence in a persistent poverty area: Surveillance, Epidemiology, and End Results (SEER) 17 Registries.

		Residence in a Persistent Poverty Area	
	Overall N = 492,050[1]	**No** N = 458,089[1]	**Yes** N = 33,961[1]
Urban-Rural Status			
All Urban	328,152 (66.7%)	306,095 (66.8%)	22,057 (64.9%)
Mostly Urban	103,854 (21.1%)	97,495 (21.3%)	6,359 (18.7%)
Mostly Rural	32,314 (6.6%)	30,226 (6.6%)	2,088 (6.1%)
All Rural	27,730 (5.6%)	24,273 (5.3%)	3,457 (10.2%)
Stage at Diagnosis			
Stage I	271,519 (55.2%)	255,624 (55.8%)	15,895 (46.8%)
Stage II	140,289 (28.5%)	129,651 (28.3%)	10,638 (31.3%)
Stage III	50,384 (10.2%)	45,833 (10.0%)	4,551 (13.4%)
Stage IV	29,858 (6.1%)	26,981 (5.9%)	2,877 (8.5%)
Age (years)			
< 40	27,329 (5.6%)	25,151 (5.5%)	2,178 (6.4%)
40-49	81,379 (16.5%)	75,939 (16.6%)	5,440 (16.0%)
50-59	120,062 (24.4%)	111,604 (24.4%)	8,458 (24.9%)
60-69	134,484 (27.3%)	125,171 (27.3%)	9,313 (27.4%)
70-79	87,205 (17.7%)	81,397 (17.8%)	5,808 (17.1%)
80+	41,591 (8.5%)	38,827 (8.5%)	2,764 (8.1%)
Race and Ethnicity			
NH White	325,278 (66.1%)	311,758 (68.1%)	13,520 (39.8%)
NH Black	52,331 (10.6%)	41,463 (9.1%)	10,868 (32.0%)
NH AI/AN	2,350 (0.5%)	2,019 (0.4%)	331 (1.0%)
NH Asian/Pacific Islander	48,586 (9.9%)	46,876 (10.2%)	1,710 (5.0%)
Hispanic (All Races)	63,505 (12.9%)	55,973 (12.2%)	7,532 (22.2%)
Marriage Status			
Single (Never Married)	80,081 (16.3%)	71,142 (15.5%)	8,939 (26.3%)
Married	285,371 (58.0%)	271,165 (59.2%)	14,206 (41.8%)
Separated	5,792 (1.2%)	4,990 (1.1%)	802 (2.4%)
Divorced	54,805 (11.1%)	50,306 (11.0%)	4,499 (13.2%)
Widowed	63,660 (12.9%)	58,285 (12.7%)	5,375 (15.8%)
Unmarried or Domestic Partner	2,341 (0.5%)	2,201 (0.5%)	140 (0.4%)

[1] n (%)

Table 2. Multinomial logistic regression odds ratio estimates of stage at diagnosis for persistent poverty and urban-rural status: Surveillance, Epidemiology, and End Results (SEER) 2010-2022.

	aOR[1, 2]	95% CI
Stage II vs. Stage I		
Residence in a Persistent Poverty Area		
No	1.00	(ref)
Yes	1.16*	1.13, 1.20
Urban-Rural Status		
All Urban	1.00	(ref)
Mostly Urban	0.99	0.98, 1.01
Mostly Rural	1.05*	1.02, 1.08
All Rural	1.11*	1.08, 1.14
Stage III vs. Stage I		
Persistent Poverty		
No	1.00	(ref)
Yes	1.29*	1.25, 1.35
Urban-Rural Status		
All Urban	1.00	(ref)
Mostly Urban	1.01	0.98, 1.03
Mostly Rural	1.13*	1.08, 1.17
All Rural	1.20*	1.15, 1.25
Stage IV vs Stage I		
Persistent Poverty		
No	1.00	(ref)
Yes	1.37*	1.31, 1.43
Urban-Rural Status		
All Urban	1.00	(ref)
Mostly Urban	0.99	0.96, 1.02
Mostly Rural	1.10*	1.05, 1.16
All Rural	1.20*	1.14, 1.27
No. Obs.	492,050	

[1]* $p<0.001$

Abbreviations: CI = Confidence Interval, aOR = Adjusted Odds Ratio

[2] Estimates adjusted for age, year at diagnosis, race/ethnicity, and marital status.

Table 3. Adjusted odds ratio estimates of stage at diagnosis comparing residence in a persistent poverty area to not residing in a persistent poverty area within each urban rural classification: Surveillance, Epidemiology, and End Results (SEER) 2010-2022.

	Residence in a Persistent Poverty Area vs. Not Residing in a Persistent Poverty Area aOR[1,2]	**95% CI**
Stage II vs Stage I		
Urban Rural Classification		
All Urban	1.18***	1.14, 1.22
Mostly Urban	1.13***	1.06, 1.20
Mostly Rural	1.07	0.96, 1.19
All Rural	1.13**	1.04, 1.24
Stage III vs Stage I		
Urban Rural Classification		
All Urban	1.33***	1.27, 1.39
Mostly Urban	1.30***	1.20, 1.41
Mostly Rural	1.02	0.87, 1.19
All Rural	1.16*	1.02, 1.30
Stage IV vs Stage I		
Urban Rural Classification		
All Urban	1.42***	1.35, 1.50
Mostly Urban	1.33***	1.20, 1.47
Mostly Rural	1.08	0.90, 1.30
All Rural	1.14	0.99, 1.32
		P-value for interaction = 0.002
No. Obs.	492,050	

[1] *p<0.05; **p<0.01; ***p<0.001

Abbreviations: CI = Confidence Interval, aOR = Adjusted Odds Ratio

[2] Estimates adjusted for age, year at diagnosis, race/ethnicity, and marital status.

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