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The Association of Rurality and Breast Cancer Stage at Diagnosis: A National Study of the SEER Cancer Registry

KEY FINDINGS

- A greater proportion of rural patients received an initial breast cancer diagnosis at a late stage compared with urban patients (14.7% compared to 13.2%, respectively).
- Patients living in remote small rural counties had the highest rate of late-stage breast cancer at diagnosis (15.5% in remote small rural counties vs. 13.2% in metro counties).
- Black patients were more likely to be initially diagnosed with breast cancer at a late stage than non-Black patients (odds ratio 1.27).
- Uninsured patients were more than twice as likely as patients with health insurance other than Medicaid to have a late-stage breast cancer at diagnosis.
- Patients with Medicaid were more than one and a half times as likely to be initially diagnosed at late stage compared to those with private health insurance.
- These patterns have persisted over time, suggesting opportunities for policy changes in areas that address racial, socioeconomic and geographic health disparities.

BACKGROUND

Breast cancer screening is effective in early disease detection. Diagnosis of disease at an early state (stage 0, 1, 2) results in higher cure rates and less need for aggressive treatments. The success of screening is associated with the marked decrease in breast cancer mortality over the last 40 years.[1,2] Rural residents face more difficulty getting recommended breast cancer screening than their urban counterparts.[3,4] Local availability of screening, disparities in access by socioeconomic status, particularly for rural residents, and race/ethnicity all play a role.[3,5] Accordingly, breast cancer screening rates are significantly lower in rural populations than in urban populations,[6-10] with urban residents being 21% more likely to have received a recent mammogram.[6] This gap is greater between women in more remote rural locations and urban women.[9]

In addition to lower screening rates, rural patients experience poorer cancer outcomes and higher mortality despite overall lower incidence of cancers compared to urban populations.[11,12] Cancer deaths in rural areas from 2011 to 2015 were 180.4 per 100,000 individuals, compared with 157.8 per 100,000 individuals in large metropolitan areas.[11] Residents of rural communities face many barriers when trying to receive cancer care including limited availability of cancer treatments and cancer support providers, transportation barriers, financial issues, and limited access to clinical trials.[3,13,14]

Low rates of screening and poorer outcomes are associated with advanced cancer stage at diagnosis.[1,15] It is reasonable to hypothesize that rural breast cancer patients are initially diagnosed at later disease stages than their urban counterparts. However, existing literature on breast cancer stage at diagnosis is contradictory.[16-18] One large meta-analysis reports higher rates of late-stage diagnosis of breast cancer in rural residents, but many studies are from outside the U.S., minimizing generalizability for U.S. policy makers.[17] Unlike past studies, this investigation is national in scope, specific to U.S. populations, and reflects current disease staging protocols. We examine the extent to which U.S. rural residents are diagnosed at more advanced stages (stage 3 and 4) of disease for breast cancer compared to non-rural residents.

METHODS

Data sources: This cross-sectional study used the 2017 Surveillance Epidemiology and End Results (SEER) cancer registry data (the most recent version at the time of data acquisition) from 352 rural and 235 urban counties in 10 states (California, Connecticut, Georgia, Hawaii, Iowa, Kentucky, Louisiana, New Mexico, Utah, Washington) representing all four U.S. Census Regions.[19] We used the 2015 U.S. Department of Agriculture Economic Research Service (USDA ERS) County Typology data to categorize patient geography and for county-level measures.[20]

We categorized patients by their Federal Information Processing Standard (FIPS) county codes into one of five (one urban and four levels of rural) residence categories based on the size of the county's largest town and adjacency to urban areas using Urban Influence Codes (UICs): (1) *metro or urban*, (2) *adjacent rural,* (3) *nonadjacent micropolitan,* (4) *small rural,* and (5) *remote small rural*.[21] Detailed definitions of each of these categories can be found in the technical appendix.

Study population: The study population included 306,726 rural and urban female breast cancer patients who were diagnosed in 2010-2014 inclusive.

Outcome variables: Clinical stage at diagnosis was the study's primary outcome of interest. We classified patients with stage 1 or 2 disease at diagnosis as 'early-stage' and those with stage 3 or 4 disease as 'late-stage.' We treated stage 0 cases (ductal carcinoma in situ) as a separate category. Stages 0, 1 and 2 have higher cure rates and often require less aggressive therapies. A late-stage diagnosis indicates advanced disease often requiring more aggressive treatments and carrying poorer prognosis.

Independent variables of interest: The independent variable of interest was the geographic residence status of patients, comparing urban and rural patients and the intra-rural categories listed above.

Statistical analysis: We calculated rates of late-stage breast cancer diagnosis among patients living in urban and different types of rural counties. We used logistic regression analysis to adjust for patient, cancer, and environmental characteristics available in the SEER cancer registry data or the 2015 USDA ERS County Typology data. We included variables that either improved the fit of the regression model, were significant predictors of late-stage diagnosis or were the independent variable of interest. We used SAS version 9.4 and SUDAAN version 11.0.3 software for analysis.

Additional details about the methods can be found in the technical appendix.

RESULTS

Table 1 shows the demographic characteristics of breast cancer patients by the rurality of their residence. Overall, the average age of breast cancer patients was 61.2 years and those living in rural counties were slightly older than those from

metro counties (63.1 vs. 61.0 respectively). Two-thirds (68.4%) of the study population were White non-Hispanic, but a larger percentage of breast cancer patients in rural counties were White non-Hispanic than their urban counterparts (85.0% vs. 66.2%). More than half (58.3%) of patients were married or partnered, 27.5% were single, separated, or divorced, and 14.2% were widowed. More urban patients were single, separated, or divorced (28.2% vs. 22.3% respectively) and more rural patients than urban were widowed (18.0% vs. 13.7% respectively). Almost all patients had some type of medical insurance (97.2%), and 11.7% were covered by Medicaid. Nearly a quarter of patients (23.5%) could not be classified by breast cancer subtype.

Table 1. Characteristics of Breast Cancer Patients from the U.S. SEER Registry Incidence Dataset (2010-2014)

Characteristic	Metropolitan	Non-Metropolitan	Adjacent Micropolitan	Nonadjacent Micropolitan	Small Rural	Remote Small Rural	Overall	P value[a]
n (%)[b]	271,887 (88.6%)	34,839 (11.4%)	20,335 (6.6%)	8,422 (2.8%)	3,321 (1.1%)	2,761 (0.9%)	306,726 (100%)	
Age, years								<.0001
Average	61.0	63.1	63.0	63.2	63.3	62.6	61.2	<.0001
<50	21.1%	15.8%	15.8%	15.4%	15.5%	17.5%	20.5%	
50-59	25.0%	23.0%	22.9%	23.3%	22.9%	22.8%	24.8%	
60-69	27.1%	29.4%	29.9%	28.8%	28.5%	28.5%	27.4%	
70-79	17.4%	20.9%	20.7%	21.1%	21.7%	21.3%	17.8%	
80+	9.4%	10.9%	10.8%	11.5%	11.4%	10.0%	9.6%	
Race/Ethnicity								<.0001
White Non-Hispanic	66.2%	85.0%	84.8%	80.2%	90.7%	93.3%	68.4%	
Black Non-Hispanic	10.4%	8.0%	10.3%	5.0%	6.6%	2.5%	10.2%	
AI/AN Non-Hispanic	0.4%	1.0%	0.7%	2.0%	0.2%	0.7%	0.5%	
Asian Non-Hispanic	10.4%	2.3%	0.7%	7.6%	0.2%	0.4%	9.5%	
Hispanic/Latino	12.5%	3.8%	3.5%	5.3%	2.3%	3.1%	11.5%	
Marital Status								<.0001
Married/Partnered	58.1%	59.7%	60.0%	57.6%	60.6%	62.9%	58.3%	
Single/Separated/Divorced	28.2%	22.3%	22.6%	23.8%	19.7%	19.3%	27.5%	
Widowed	13.7%	18.0%	17.5%	18.6%	19.7%	17.8%	14.2%	
Health Insurance Status								
Insured (not Medicaid)	87.2%	84.2%	84.9%	83.8%	80.9%	84.2%	86.8%	
Any Medicaid	11.4%	13.9%	13.2%	14.7%	16.7%	14.0%	11.7%	
Uninsured	1.4%	1.9%	1.9%	1.6%	2.4%	1.9%	1.5%	
Breast Cancer Stage								<.0001
Stage 0	20.4%	17.4%	17.9%	17.7%	15.5%	15.3%	20.1%	
Stage 1	38.9%	39.7%	40.0%	39.3%	39.5%	39.5%	39.0%	
Stage 2	27.6%	28.2%	27.8%	28.5%	29.8%	28.8%	27.7%	
Stage 3	7.3%	7.5%	7.3%	7.4%	7.9%	9.3%	7.3%	
Stage 4	5.8%	7.2%	7.2%	7.1%	7.4%	7.1%	6.0%	

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Table 1. Continued

Characteristic	Metropolitan	Non-Metropolitan	Adjacent Micropolitan	Nonadjacent Micropolitan	Small Rural	Remote Small Rural	Overall	P value[a]
Breast Cancer Subtype								<.0001
HER2-/HR+	56.1%	56.5%	55.9%	57.6%	56.5%	57.7%	56.2%	
HER2+	11.7%	12.1%	11.8%	12.2%	12.9%	12.7%	11.7%	
HR-/HER2-	8.5%	9.6%	9.7%	9.0%	10.4%	9.6%	8.6%	
State								<.0001
California	53.2%	10.8%	14.0%	8.0%	0.0%	8.8%	48.4%	
Connecticut	7.0%	2.9%	5.0%	0.0%	0.0%	0.0%	6.5%	
Georgia	12.3%	21.0%	26.3%	12.8%	17.5%	11.0%	13.3%	
Hawaii	2.0%	3.0%	0.0%	12.6%	0.0%	0.0%	2.2%	
Iowa	2.8%	17.3%	15.0%	17.4%	29.8%	19.7%	4.4%	
Kentucky	4.3%	22.4%	15.1%	27.3%	40.6%	39.7%	6.3%	
Louisiana	5.9%	8.2%	11.9%	2.2%	4.1%	4.1%	6.2%	
New Mexico	2.0%	6.0%	4.0%	11.9%	4.6%	4.9%	2.5%	
Utah	2.7%	2.6%	2.1%	1.6%	3.4%	7.5%	2.7%	
Washington	7.9%	5.7%	6.7%	6.2%	0.0%	4.5%	7.7%	
Persistent Poverty	1.8%	22.3%	19.8%	18.4%	36.7%	35.6%	4.1%	<.0001
Low Education	26.3%	23.0%	20.9%	16.2%	31.3%	48.4%	25.9%	<.0001
Low Employment	4.7%	48.6%	50.4%	38.7%	52.9%	60.1%	9.7%	<.0001
Population Loss	0.9%	13.9%	7.0%	13.8%	34.5%	40.5%	2.4%	<.0001

[a]Overall 5-category chi-squared or t-test
[b]Percentages in this row sum to 100%, other percentages sum by column to 100%
AI/AN = American Indian/Alaska Native
HER2-/HR+ = Breast cancer sub-type without human epidermal growth factor 2 receptors and with progesterone or estrogen receptors
HER2+ = Breast Cancer subtype with human epidermal growth factor 2 receptors
HR-/HER2- = Breast cancer subtype without progesterone or estrogen receptors and without human epidermal growth factor 2 receptors

Patients from California made up almost half of the overall sample (48.4%) but only 10.8% of rural patients. Georgia had the largest number of rural patients and made up one-fifth (21.0%) of the rural sample. Rural patients were more likely to reside in counties designated as persistent poverty, low education, low employment, and/or population loss counties. A greater proportion of rural patients received a breast cancer diagnosis at a late stage compared with urban patients (14.7% vs. 13.2%).

The adjusted percentages of patients diagnosed with late-stage breast cancer by geographic category were as follows: metro 13.2%, adjacent micropolitan 13.9%, nonadjacent micropolitan 14.1%, small rural 14.0%, and remote small rural 15.3% (Table 2). In the multivariate adjusted analysis (Table 3), patients living in remote small rural, adjacent micropolitan and nonadjacent micropolitan counties were significantly more likely to be initially diagnosed with late-stage breast cancer than patients living in metro counties (remote small rural vs. metro: odds ratio 1.20; adjacent micropolitan vs. metro: odds ratio 1.06; nonadjacent micropolitan vs. metro: odds ratio 1.08).

The percentage of patients diagnosed at late stage also differed across other patient demographic categories (Table 2). Women ages 50-79 were less likely than those younger than 50 or those 80 or older to have late-stage breast cancer at diagnosis (Table 2). The rate of late-stage diagnosis was highest in Black non-Hispanics (15.7%) and lowest in non-Hispanic Asians (11.7%). Hispanic women had a higher rate of late-stage diagnosis (14.1%) than White non-Hispanics (13.0%). Both of

Table 2. Adjusted Rates of Stage 0, Early-Stage (1-2), and Late-Stage (3-4) Breast Cancer Disease at Diagnosis by Patient Residence Location and Individual Characteristics, 2010-2014

	Stage 0 Breast Cancer at Diagnosis (95% CI)	Early-Stage (1-2) Breast Cancer at Diagnosis (95% CI)	Late-Stage (3-4) Breast Cancer at Diagnosis (95% CI)
Residence Location			
Metro	20.1% (19.9 - 20.2)	66.7% (66.6 - 66.9)	13.2% (13.1 - 13.3)
Adjacent Micropolitan	18.3% (17.9 - 18.8)	67.8% (67.2 - 68.5)	13.9% (13.3 - 14.4)
Nonadjacent Micropolitan	19.1% (18.4 - 19.8)	66.8% (65.9 - 67.7)	14.1% (13.4 - 14.9)
Small Rural	17.1% (16.0 - 18.2)	68.6% (67.1 - 70.1)	14.0% (12.8 - 15.3)
Remote Small Rural	17.6% (16.5 - 18.7)	66.8% (65.2 - 68.4)	15.3% (14.0 - 16.7)
Age, years			
< 50	20.7% (20.5 - 20.9)	63.8% (63.5 - 64.1)	15.4% (15.1 - 15.7)
50 – 59	20.9% (20.7 - 21.1)	65.7% (65.4 - 66.0)	13.3% (13.1 - 13.6)
60 – 69	20.3% (20.1 - 20.5)	67.7% (67.4 - 68.0)	12.0% (11.8 - 12.3)
70 – 79	19.2% (18.9 - 19.4)	69.2% (68.9 - 69.6)	11.7% (11.4 - 11.9)
80+	14.6% (14.2 - 15.0)	69.8% (69.3 - 70.3)	15.2% (14.7 - 15.6)
Race/Ethnicity			
White Non-Hispanic	19.6% (19.5 - 19.8)	67.4% (67.2 - 67.6)	13.0% (12.8 - 13.1)
Black Non-Hispanic	20.5% (20.2 - 20.8)	63.7% (63.2 - 64.2)	15.7% (15.3 - 16.2)
AI/AN Non-Hispanic	19.7% (18.4 - 21.1)	67.0% (64.9 - 69.0)	13.2% (11.7 - 14.9)
Asian Non-Hispanic	20.9% (20.6 - 21.2)	67.3% (66.9 - 67.8)	11.7% (11.3 - 12.1)
Hispanic	19.9% (19.6 - 20.2)	66.0% (65.6 - 66.5)	14.1% (13.7 - 14.4)
Marital Status			
Married/Partnered	20.4% (20.2 - 20.5)	67.5% (67.2 - 67.7)	12.1% (11.9 - 12.3)
Single/Separated/Divorced	19.2% (19.0 - 19.5)	65.9% (65.6 - 66.2)	14.8% (14.6 - 15.1)
Widowed	19.2% (18.9 - 19.6)	65.9% (65.5 - 66.4)	14.8% (14.4 - 15.1)
Health Insurance Status			
Insured (not Medicaid)	20.2% (20.1 - 20.4)	67.6% (67.5 - 67.8)	12.1% (12.0 - 12.3)
Any Medicaid	17.5% (17.2 - 17.8)	62.2% (61.8 - 62.7)	19.6% (19.2 - 20.0)
Uninsured	15.8% (15.0 - 16.6)	59.5% (58.2 - 60.7)	24.0% (22.8 - 25.2)
Breast Cancer Subtype			
HER2-/HR+	2.5% (2.5 - 2.6)	83.9% (83.7 - 84.1)	13.5% (13.4 - 13.7)
HER2+	6.0% (5.7 - 6.2)	71.6% (71.2 - 72.1)	22.5% (22.0 - 22.9)
HR-/HER2-	1.6% (1.5 - 1.8)	78.7% (78.3 - 79.2)	19.4% (19.0 - 19.9)

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these groups were more likely than White non-Hispanic women to have a late-stage diagnosis (odds ratios 1.27 and 1.10, respectively), while Asian women were less likely (odds ratio 0.88). Single and widowed patients were more likely than married patients to have a late-stage diagnosis (Table 3, odds ratios 1.28 and 1.27, respectively).

The rate of late-stage breast cancer at diagnosis varied notably by patient health insurance status. Uninsured patients were more than twice as likely than patients with insurance other than Medicaid to have a late-stage breast cancer at

Table 2. Continued

	Stage 0 Breast Cancer at Diagnosis (95% CI)	Early-Stage (1-2) Breast Cancer at Diagnosis (95% CI)	Late-Stage (3-4) Breast Cancer at Diagnosis (95% CI)
State			
California	19.0% (18.8 - 19.2)	67.6% (67.4 - 67.9)	13.4% (13.2 - 13.6)
Connecticut	22.6% (22.2 - 23.0)	65.7% (65.1 - 66.2)	11.5% (11.1 - 12.0)
Georgia	20.4% (20.1 - 20.7)	66.4% (66.0 - 66.8)	13.2% (12.8 - 13.5)
Hawaii	21.9% (21.3 - 22.5)	65.6% (64.6 - 66.6)	12.6% (11.8 - 13.5)
Iowa	23.8% (23.3 - 24.4)	64.0% (63.2 - 64.7)	12.6% (12.1 - 13.3)
Kentucky	20.3% (19.9 - 20.7)	66.3% (65.6 - 66.8)	13.6% (13.1 - 14.1)
Louisiana	20.0% (19.6 - 20.4)	65.9% (65.3 - 66.5)	14.1% (13.6 - 14.6)
New Mexico	15.9% (15.3 - 16.6)	70.6% (69.7 - 71.6)	13.7% (12.9 - 14.5)
Utah	18.9% (18.4 - 19.5)	66.1% (65.2 - 66.9)	15.0% (14.2 - 15.8)
Washington	21.0% (20.7 - 21.3)	65.7% (65.2 - 66.2)	13.1% (12.7 - 13.6)
Low Employment			
No	19.9% (19.8 - 20.1)	66.9% (66.7 - 67.1)	13.2% (13.1 - 13.3)
Yes	19.4% (19.0 - 19.8)	66.3% (65.8 - 66.9)	14.2% (13.7 - 14.7)
Low Education			
No	20.0% (19.8 - 20.1)	66.9% (66.7 - 67.1)	13.1% (13.0 - 13.3)
Yes	19.5% (19.3 - 19.7)	66.8% (66.4 - 67.1)	13.7% (13.5 - 14.0)

AI/AN = American Indian/Alaska Native
CI = Confidence interval
HER2-/HR+ = Breast cancer sub-type without human epidermal growth factor 2 receptors and with progesterone or estrogen receptors
HER2+ = Breast Cancer subtype with human epidermal growth factor 2 receptors
HR-/HER2- = Breast cancer subtype without progesterone or estrogen receptors and without human epidermal growth factor 2 receptors

Table 3. Impact of Patient Characteristics on the Adjusted Odds of Late-Stage Breast Cancer Disease at Diagnosis, 2010-2014

Characteristic	Odds Ratio (95% Confidence Interval)
Residence Location	
Metro	Ref
Adjacent Micropolitan	**1.06 (1.01 - 1.11)**
Nonadjacent Micropolitan	**1.08 (1.01 - 1.16)**
Small Rural	1.07 (0.95 - 1.22)
Remote Small Rural	**1.20 (1.07 - 1.34)**
Age, years	
< 50	Ref
50 – 59	**0.84 (0.81 - 0.86)**
60 – 69	**0.74 (0.72 - 0.77)**
70 – 79	**0.72 (0.69 - 0.74)**
80+	0.98 (0.94 - 1.03)

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diagnosis (odds ratio 2.36) and those with Medicaid were more than one and a half times as likely (odds ratio 1.81). Uninsured patients had a higher rate of late-stage diagnosis (24.0%) compared to patients with Medicaid (19.6%) and other insured patients (12.1%).

Patients with more aggressive tumor subtypes, like HER2+ and HR- (see the Control Variables section in the Technical Appendix for tumor subtype definitions), were more likely to be diagnosed at late stage. Patients with HER2+ tumors were almost twice as likely to be diagnosed at late stage compared to HR+/HER2- patients (odds ratio 1.88). HR-/HER2- patients were about one and a half times as likely to be diagnosed in late stage.

Differences among states in the rate of late-stage breast cancer at diagnosis ranged from 11.5% in Connecticut to 15.0% in Utah (Table 2).

Table 3. Continued

Characteristic	Odds Ratio (95% Confidence Interval)
Race/Ethnicity	
White Non-Hispanic	Ref
Black Non-Hispanic	**1.27 (1.22 - 1.31)**
AI/AN Non-Hispanic	1.02 (0.88 - 1.19)
Asian Non-Hispanic	**0.88 (0.85 - 0.92)**
Hispanic	**1.10 (1.07 - 1.14)**
Marital Status	
Married/Partnered	Ref
Single/Separated/Divorced	**1.28 (1.25 - 1.31)**
Widowed	**1.27 (1.22 - 1.32)**
Health Insurance Status	
Insured (not Medicaid)	Ref
Any Medicaid	**1.81 (1.75 - 1.86)**
Uninsured	**2.36 (2.20 - 2.54)**
Breast Cancer Subtype	
HER2-/HR+	Ref
HER2+	**1.88 (1.82 - 1.93)**
HR-/HER2-	**1.56 (1.50 - 1.61)**
State	
Connecticut	Ref
California	**1.20 (1.14 - 1.26)**
Georgia	**1.17 (1.11 - 1.24)**
Hawaii	**1.11 (1.01 - 1.24)**
Iowa	**1.12 (1.04 - 1.20)**
Kentucky	**1.22 (1.14 - 1.30)**
Louisiana	**1.27 (1.19 - 1.35)**
New Mexico	**1.23 (1.13 - 1.34)**
Utah	**1.37 (1.27 - 1.49)**
Washington	**1.17 (1.10 - 1.24)**
Low Employment	
No	Ref
Yes	**1.09 (1.05 - 1.14)**
Low Education	
No	Ref
Yes	**1.05 (1.02 - 1.08)**

Statistically significant findings are bolded.
AI/AN = American Indian/Alaska Native
HER2-/HR+ = Breast cancer sub-type without human epidermal growth factor 2 receptors and with progesterone or estrogen receptors
HER2+ = Breast Cancer subtype with human epidermal growth factor 2 receptors
HR-/HER2- = Breast cancer subtype without progesterone or estrogen receptors and without human epidermal growth factor 2 receptors

DISCUSSION

Rural breast cancer patients are more likely to be diagnosed at late-stage breast cancer than their urban counterparts. This study clarifies a conflicting body of literature that includes studies that are older, insufficiently powered, or study non-U.S. populations.[16-18] Our findings are consistent with an older meta-analysis of 21 U.S. studies that found that patients residing in rural areas were more likely to be diagnosed with more advanced breast cancer.[17]

Late stage at diagnosis is associated with poorer breast cancer outcomes.[22] Rural patients have poorer breast cancer survival rates when compared to urban patients.[23,24] Healthy People 2020 has placed a focus on geographical variation and specifically called out goals to reduce cancer mortality in cancers that can be detected through screening methods.[25] One explanation for the higher rate of late stage breast cancer at diagnosis seen in patients from remote small counties may be decreased utilization of breast cancer screening[6-10] in the most rural areas. Barriers to effective screening may be many, including low health literacy, physician referral patterns, availability of services, travel times, poorer quality screening, and other factors.[26-28]

This study found that sociodemographic factors in addition to rural versus urban location, including patient characteristics, health insurance status, and state of residence, play a large role in the stage of cancer at the time of diagnosis. Individual patient characteristics found to be significantly associated with late-stage diagnosis were Black race, Hispanic ethnicity, single or widowed status, and older age. Data more than a decade old support our findings, suggesting little progress towards ameliorating these disparities.[29]

The strongest predictor of late-stage diagnosis in our study is being uninsured. Research spanning the last twenty years supports the relationship between no health insurance and late-stage cancer diagnosis and poorer outcomes.[29-33] Prohibitively expensive costs of care, lack of transportation, lack of availability of specialty care, and low health literacy—all more common barriers among patients with lack of insurance—may all play a role in these findings. It is notable that uninsured patients had a similar (higher) likelihood of being initially diagnosed with late-stage disease as those with the most aggressive tumor types. Patients with Medicaid were more likely to be diagnosed with late-stage disease than non-Medicaid patients but less likely than those with no insurance, suggesting that this safety net program provides important access to care. With the implementation of the Patient Protection and Affordable Care Act, a trend towards diagnosis of early-stage cancers in Medicaid expansion states has been noted.[30]

Regional variation has been seen in studies of cancer treatment and the availability of a variety of medical services.[34-36] Our study found that the adjusted rate of patients from Connecticut diagnosed at a late clinical stage at diagnosis was substantially lower than patients in the Southern and Rocky Mountain states included in this study. These geographic differences have been attributed to differences in medical culture and supply of medical resources.

Study limitations include that SEER data on patient residence are only available at the county level. Assigning a patient's urban/rural status at the county level leads to some inappropriate classification (e.g., a person living in a small isolated place in a county with a large population center could be classified as an urban patient). Additionally, the data used in this study include registry data from patients in just 10 states, though all Census Regions are represented, and study cases represent about one third of all cancer patients nationally. The extent to which these patients differ from those not included (e.g., access to medical care, lifestyle differences, non-included geography, etc.) could affect the generalizability of the findings.

CONCLUSIONS AND POLICY IMPLICATIONS

We found that rural location is associated with initial diagnosis of breast cancer at a late-stage. Additionally, Black race and insurance status are associated with late-stage breast cancer at diagnosis, suggesting that racial and economic barriers to care play important roles. Breast cancer survival is known to be worse for rural patients compared to urban, and late stage at diagnosis may be a contributing factor. These disparities are longstanding and suggest areas for further research, advocacy, policy changes, and patient education. Further study is needed to identify appropriate screening availability in rural areas and the burdens that travel presents for patients where screening is not available. Similar outreach to high-risk populations is warranted.

States that had higher rates of late-stage breast cancer at diagnosis can utilize these findings to explore the individual patient and health care system factors that may contribute to these higher rates. Health systems, governmental agencies, advocacy groups, and others can use this study's results to identify needed services and plan educational outreach efforts to address the identified disparities.

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TECHNICAL APPENDIX

This appendix contains detailed technical notes regarding the methods used in this study.

Design and Data Sources

This cross-sectional study used 2017 Surveillance Epidemiology and End Results (SEER) cancer registry data from 352 rural and 235 urban counties in 10 states (California, Connecticut, Georgia, Hawaii, Iowa, Kentucky, Louisiana, New Mexico, Utah, Washington) representing all four U.S. Census Regions.

We used the 2015 U.S. Department of Agriculture Economic Research Service (USDA ERS) County Typology data to categorize patient geography and for county-level measures. County-level economic indicators from the USDA ERS County Typology codes included dichotomous variables indicating persistent poverty, low employment, low education, and population loss. Persistent poverty indicates that 20% or more residents of a county were poor as measured by the 1980, 1990, and 2000 Census and the American Community Survey (ACS) 5-year average from 2007 to 2011. Low employment indicates that less than 65% of county residents ages 25-64 were employed based on the ACS 5-year average from 2008 to 2012. Low education indicates that 20% or more of county residents had neither a high school diploma nor GED based on the ACS 5-year average from 2008 to 2012. Counties designated with population loss had a decline in the number of county residents both between the 1990 and the 2000 Census and between the 2000 and 2010 Census.[37]

We categorized patients by their Federal Information Processing Standard (FIPS) county codes into one of five (one urban and four levels of rural) residence categories based on the size of the county's largest town and adjacency to urban areas using Urban Influence Codes (UICs): (1) metro or urban: the county has a town/urban cluster with a population of at least 50,000 (UIC 1,2); (2) adjacent rural: counties that are geographically adjacent to a metropolitan area (UICs 3-7); (3) nonadjacent micropolitan: counties that are not adjacent to a metropolitan area and whose largest town/urban cluster has 10,000 to 49,999 residents (UIC 8); (4) small rural: counties that are adjacent to a micropolitan area and whose largest town has less than 10,000 residents (UIC 9, 10); and (5) remote small rural: counties that are not adjacent to a micropolitan area and whose largest town has less than 10,000 residents (UIC 11, 12).

Sample

We identified all patient cases in the SEER breast data files with a diagnosis in 2010-2014 inclusive. Data from registries in 10 states (CA, CT, GA, HI, IA, KY, LA, NM, UT, WA) with both urban and rural counties were included in the study population. Registries from two states (MI, NJ) with only urban counties were excluded. The Alaska registry was also excluded because the county of residence could not be determined for any patients.

Overall, patients lived in 587 different counties, (352 rural and 235 urban). We classified patients into the categories previously described based on the UIC of their county of residence. We excluded patients whose residence county could not be classified due to missing county data (n=45). The resulting study population included 306,726 breast cancer patients.

Outcome Variables

Clinical stage at diagnosis was the study's primary outcome of interest. We classified patients with stage 3 or stage 4 disease at diagnosis as 'late-stage' and those whose clinical stage at diagnosis was stage 0, 1 or 2 as 'early-stage'. In our analyses calculating adjusted rates, we treated stage 0 cases (ductal carcinoma in situ) as a separate category. A late-stage diagnosis indicates advanced disease often requiring more aggressive treatments and carrying poorer prognosis. Stages 0, 1 and 2 have higher cure rates and often require less aggressive therapies. We excluded patients with missing information about clinical stage at diagnosis (n=11,841, 3.7%).

Control Variables

Available patient-level control variables in the SEER data included age, sex, race/ethnicity, marital status, and health insurance status. We defined breast cancer that was either estrogen receptor or progesterone receptor positive as HR+. We defined a breast cancer subtype with human epidermal growth factor 2 receptors as HER2+. We included combined human epidermal growth factor receptor 2 (HER2) status with hormone receptor (HR) status. The triple negative subtype is defined as HR-/HER2-. HER2+ and HR- tumors sub-types tend to be more aggressive, be more difficult to treat and have higher mortality rates. To account for regional practice variation, we included the patients' residence state.

Statistical Analysis

We calculated patient demographic characteristics by geographic category and the unadjusted percent of patients classified as late-stage presenters. We used logistic regression to investigate the relationship between late-stage disease at diagnosis and patient characteristics as well as county-level characteristics including level of rurality, persistent poverty, low education, and low employment. Final logistic regression models included patient level and environmental variables that were either significant predictors of late-stage diagnosis, improved the fit of the model, or were the independent variables of interest. The two county-level variables measuring persistent poverty and population loss were removed from the model because they did not meet any of these criteria. We used general estimating equation methods to account for patient clustering by county in all logistic regression models. From the logistic regression models, we calculated rates of late-stage diagnosis adjusted for urban and each rural residence category, environmental factors, as well as for all patient demographic characteristics. Since the state of patient residence was highly associated with late-stage disease at diagnosis and because rural patients primarily came from only a few states in this study, we only present adjusted results. We conducted analyses using SAS version 9.4 and SUDAAN version 11.0.3 software.

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