Urban versus Rural Residence and Outcomes in Older Patients with Breast Cancer
Kelly M. Kenzik, Gabrielle B. Rocque, Wendy Landier, and Smita Bhatia

ABSTRACT

Background: A total of 20% of the U.S. population resides in rural areas, yet is served by 3% of oncologists, and 7% of nononcology specialists. Access to care issues can be compounded by lower socioeconomic status (SES) in rural areas, yet this issue is unexplored among older patients with breast cancer.

Methods: Using Surveillance Epidemiology and End Results-Medicare, 109,608 patients diagnosed at ≥65 years with breast cancer between 2000 and 2011 were identified. Residence status was combined with Federal Poverty levels: urban (high, medium, and low poverty) and rural (high, medium, and low poverty). Five-year overall survival (OS) and healthcare utilization [HCU: visits to primary care provider (PCP), oncologist, nononcology specialist, and emergency department (ED)] were examined using urban/low poverty as reference. The residence, HCU, and mortality association was examined using mediation and moderation analyses.

Results: Median age was 76 years; 12.5% were rural, 15.6% high poverty. Five-year OS was 69.8% for rural and 70.9% for urban. Both urban- and rural/high-poverty patients had a 1.2-fold increased mortality hazard. Rural/high-poverty patients had a higher rate of PCP [year 1 (Y1): incidence rate ratio (IRR) = 1.23; year 2 (Y2)–year 5 (Y5): IRR = 1.19] and ED visits (Y1: IRR = 1.82; Y2–Y5: IRR = 1.43), but lower nononcology specialist visit rates (Y1: IRR = 0.74; Y2–Y5: IRR = 0.71). Paucity of nononcology specialist visits mediated 23%–57% of excess mortality risk. The interaction between residence/SES and paucity of nononcology specialist visits accounted for 49%–92% of excess mortality risk experienced by rural/high-poverty patients versus urban/low poverty.

Conclusions: Urban–rural residence mortality differences among older patients with breast cancer are highly predicated by poverty level.

Impact: Rural/high-poverty patients demonstrate less use of nononcology specialists compared with urban/low poverty, with disparities moderated by specialist use.

Introduction
Overall, individuals living in rural counties experience higher annual age-adjusted cancer-related mortality rates when compared with those residing in urban areas (180 vs. 158 deaths/100,000/year; ref. 1). In contrast to lung, prostate, and colon cancer, the impact of rurality on age-adjusted mortality rates for patients with breast cancer varies based on the level of metro or rural classification (1, 2). Current evidence suggests that the gap in cancer-related mortality rates associated with urban and rural residence is widening over time (1, 3). The outcome disparity may be in part explained by lack of access to healthcare resources in the rural areas (4). While 20% of the U.S. population resides in rural areas, only 3% of medical oncologists have rural practices (5, 6). Similarly, nononcology specialists tend to practice in urban areas (134 vs. 40 specialists/10,000; ref. 6). These workforce issues suggest that rural patients with cancer are likely to face challenges in accessing adequate cancer care, and this could explain the differences in outcome by rurality (7). Low socioeconomic status (SES) can further compound these outcome disparities (3). Differences in economic and demographic characteristics between rural and urban counties largely explain the disparity in age-adjusted mortality in the general population (3). However, there has been no previous systematic attempt to understand the impact of rural residence and SES on overall survival (OS) in older patients with breast cancer. Furthermore, the impact of healthcare utilization (HCU) in mediating the disparities in outcome due to residence (rural vs. urban) or SES is not known. We address this knowledge gap in a population-based sample of patients with breast cancer diagnosed over the age of 65, using Surveillance Epidemiology and End Results (SEER) data linked to Medicare administrative claims data.

Materials and Methods

Data source
SEER is comprised of 20 geographically diverse cancer registries, designed to represent U.S. cancer incidence and mortality. SEER data were linked to Medicare administrative claims, providing billing information for diagnosis codes from inpatient, outpatient, and noninstitutional settings (8). This study was deemed exempt by University of Alabama at Birmingham’s Institutional Review Board (Birmingham, AL).

Population
Females ≥65 years of age and enrolled in Medicare with incident breast cancer diagnosed between January 1, 2000 and December 31, 2011 were included. Medicare claims were captured 1 year prior to diagnosis to establish preexisting comorbidities and up to December 31, 2013 or death, whichever occurred first. We excluded those diagnosed with no information regarding stage of disease. Individuals enrolled in Medicare Advantage or those lacking Medicare coverage

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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for inpatient care or doctors’ services or outpatient care at any point during the eligible period were excluded because health services could not be captured in their entirety for such patients (n = 109,608; Supplementary Fig. S1).

Outcomes

OS was examined from the end of primary breast cancer treatment (not including hormone therapy) to death, 5 years, or end of study (December 31, 2013). End of treatment was used as a starting point to mitigate immortal time bias introduced from patients who survived long enough to receive treatment. Healthcare visits to primary care physicians (PCP; internal medicine, family medicine, geriatrician, and primary care), oncologists (hematology/oncology, radiation oncology, and surgical oncology), and nononcology specialists, as well as hospitalizations and emergency department (ED) visits were captured from end of treatment to 1 month prior to death or end of study. Physician specialties were identified using unique physician identification number and the national provider identifier codes linked to the American Medical Association Masterfile (9). HCU was described for two time periods. The first time period captured from end of treatment to end of year 1, 1 month prior to death, or end of study. The second time period captured from the beginning of year 2 to the end of year 5, 1 month prior to death, or end of study. We hypothesize that the first-year time frame may have increased HCU due to proximity to diagnosis and treatment and year 2 to year 5 may be more representative of long-term utilization trends.

Independent variables

Rural versus urban residence was defined using the Rural/Urban Continuum Codes (10). “Urban” included all metropolitan counties with ≥250,000 people and urban counties (≥20,000) adjacent to metropolitan counties. “Rural” included urban counties not adjacent to metropolitan counties, completely rural counties, or urban counties with <2,500 people. SES was defined using the proportion of population in the census tract below Federal Poverty Level (FPL) based on residence at diagnosis (11). The cohort was categorized into low-poverty (0%–10% below FPL), medium-poverty (10%–20%), and high-poverty (20%–100%) groups (12, 13). A composite measure of rural/urban residence and SES was also created, where patients were categorized as urban/low poverty, urban/medium poverty, urban/high poverty, rural/low poverty, rural/medium poverty, and rural/high poverty.

Covariates

Age at diagnosis was categorized as 66–70 years, 71–75 years, 76–80 years, and 80+ years. Stage at diagnosis was determined using the SEER summary stage and the 6th American Joint Committee on Cancer staging. Race/ethnicity was categorized as non-Hispanic white (NHW), Hispanic, non-Hispanic black (NHB), and Asian American/Pacific Islander. Comorbidity was measured using the Elixhauser Comorbidity index (14) in the 12 months prior to breast cancer diagnosis. Chemotherapy and radiation details were drawn from outpatient claims, physician carrier claims, inpatient claims, durable medical equipment Medicare claims, and from Part D data (chemotherapy only for 2007–2013; Supplementary Table S1). Patients were categorized as having received chemotherapy (yes/no) and having received radiation (yes/no). Surgical intervention was identified from inpatient claims and SEER file. Patients were categorized as having received no surgery, partial mastectomy, and total mastectomy.

Statistical analysis

OS was examined using Kaplan–Meier method and proportional subdistribution hazards model for multivariate analysis. OS was examined by urban versus rural residence, by SES categories (high, medium, and low poverty), and by the combined rural–urban/SES variable.

The relative rate of healthcare visits per person-time [incidence rate ratios (IRR)] was examined for PCP visits, oncology visits, nononcology specialist visits, hospitalizations, and ED visits. IRRs were modeled for visits during year 1 and years 2–5. Covariates included age at breast cancer diagnosis, race/ethnicity, preexisting comorbidities, stage at diagnosis, surgery, chemotherapy, and radiation. For each model, count-based models (Poisson, negative binomial, and zero-inflated negative binomial) were examined to determine the best fitting model [overdispersion factors, Akaike information criterion (AIC), and Bayesian information criterion (BIC)]. Analyses were repeated including any subsequent malignant neoplasms (SMN) diagnosed during years 2–5 as a competing event.

We hypothesized that physician visits, as a proxy for access to healthcare, may either act as a mediator or effect modifier of the association between the residence/SES status and OS. To evaluate this, we estimated mediation and interaction simultaneously using effect decomposition (15, 16). “Exposure” was defined as the residence/SES combined measure; we made a specific two-category comparison: urban/low poverty versus rural/high poverty. A priori, the mediator and/or moderators of interest were healthcare visits for the three physician visit types (PCP, nononcology specialist, and oncology specialist), creating dichotomous variables that indicated whether the patient had at least one visit per year versus no visit. We examined HCU spanning from end of treatment to 1 month prior to death to avoid survival bias due to treatment and capturing end of life visits. We stratified the analyses by Elixhauser comorbidity score (0, 1, and ≥2) and by stage of breast cancer (stages 0–III and stage IV), adjusting for age at diagnosis, race/ethnicity, and treatment. We hypothesized that ≥1 visit/year with a nononcology specialist would mediate and/or moderate the association between residence/SES and mortality in the strata with 0 and 1 comorbidities. Furthermore, ≥2 visits/year with a nononcology specialist would mediate and/or moderate the association between residence/SES and mortality in the strata with ≥2 comorbidities. Final model selections were informed by the iterative process of constructing the model for each mediation (i.e., associations between residence/SES and healthcare visits, and associations between healthcare visits and mortality). We specified an accelerated failure time model with Weibull distribution since the event is nonrare by the end of follow-up. Results from this analysis allowed us to examine excess relative risk of mortality attributed to HCU. Supplementary Data S1 describes the decomposition of excess risk into controlled direct effects, interaction only effects, mediation only effects, and mediated interaction effects.

Results

Population characteristics

Table 1 describes patient characteristics overall, and by the residence/SES combined measure. Of the 109,608 patients with breast cancer included in this cohort, 12.5% were rural dwellers, 15.6% resided in high-poverty areas, 86% were NHW, and 7% were NHB. The median age at diagnosis of breast cancer was 76 years (66–106) and the majority (56%) were diagnosed with stage I–II disease. Supplementary Table S1 describes patient characteristics by rural/urban status and SES separately.
Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Overall N = 109,608</th>
<th>Urban/low poverty n = 59,654</th>
<th>Urban/medium poverty n = 23,303</th>
<th>Urban/high poverty n = 12,908</th>
<th>Rural/low poverty n = 3,681</th>
<th>Rural/medium poverty n = 5,843</th>
<th>Rural/high poverty n = 4,219</th>
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<tr>
<td><strong>Stage at diagnosis</strong></td>
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<tr>
<td>Stage 0</td>
<td>16,819 (15%)</td>
<td>9,742 (16%)</td>
<td>3,414 (15%)</td>
<td>1,787 (14%)</td>
<td>752 (14%)</td>
<td>1,376 (23%)</td>
<td>1,105 (26%)</td>
</tr>
<tr>
<td>Stage I</td>
<td>45,651 (42%)</td>
<td>24,870 (42%)</td>
<td>9,734 (42%)</td>
<td>5,344 (41%)</td>
<td>1,526 (41%)</td>
<td>2,412 (41%)</td>
<td>1,765 (42%)</td>
</tr>
<tr>
<td>Stage II</td>
<td>23,270 (21%)</td>
<td>11,464 (19%)</td>
<td>5,319 (23%)</td>
<td>3,618 (28%)</td>
<td>623 (14%)</td>
<td>1,177 (20%)</td>
<td>1,069 (25%)</td>
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<tr>
<td>Stage III</td>
<td>6,156 (6%)</td>
<td>3,081 (5%)</td>
<td>1,343 (6%)</td>
<td>701 (5%)</td>
<td>110 (2%)</td>
<td>143 (2%)</td>
<td>131 (3%)</td>
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<tr>
<td><strong>Surgery</strong></td>
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<tr>
<td>No surgery identified</td>
<td>40,687 (37%)</td>
<td>23,320 (39%)</td>
<td>8,250 (35%)</td>
<td>3,946 (31%)</td>
<td>1,532 (42%)</td>
<td>2,254 (39%)</td>
<td>1,385 (33%)</td>
</tr>
<tr>
<td>Partial mastectomy</td>
<td>16,819 (15%)</td>
<td>9,742 (16%)</td>
<td>3,414 (15%)</td>
<td>1,787 (14%)</td>
<td>752 (14%)</td>
<td>1,376 (23%)</td>
<td>1,105 (26%)</td>
</tr>
<tr>
<td>Total mastectomy</td>
<td>45,651 (42%)</td>
<td>24,870 (42%)</td>
<td>9,734 (42%)</td>
<td>5,344 (41%)</td>
<td>1,526 (41%)</td>
<td>2,412 (41%)</td>
<td>1,765 (42%)</td>
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<td><strong>Chemotherapy</strong></td>
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<tr>
<td>Any chemotherapy</td>
<td>50,523 (46%)</td>
<td>26,349 (44%)</td>
<td>10,864 (47%)</td>
<td>6,307 (49%)</td>
<td>1,585 (43%)</td>
<td>2,862 (49%)</td>
<td>2,286 (54%)</td>
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<tr>
<td><strong>Radiation</strong></td>
<td>29,255 (27.2%)</td>
<td>16,336 (27.9%)</td>
<td>6,201 (27%)</td>
<td>3,370 (26.5%)</td>
<td>804 (22.4%)</td>
<td>1,466 (25.6%)</td>
<td>1,078 (26%)</td>
</tr>
</tbody>
</table>

There was an overrepresentation of rural dwellers in the high-poverty group (30.7% vs. 13.5%; P < 0.001) and among NHW (91.4% vs. 85.3%; P < 0.001) patients. Rural dwellers were less likely to have stage 0 disease (13.7% vs. 15.6%; P < 0.001); all other stages were comparable. Rural dwellers were also more likely to undergo total mastectomy (47.6% vs. 34.1%; P < 0.001) and to receive chemotherapy (49% vs. 45.4%; P < 0.001).

High-poverty group patients were more likely to be diagnosed with stage III (26.1% vs. 21.7%; P < 0.001) or stage IV (7.3% vs. 5.2%; P < 0.001) disease. High-poverty group patients were also more likely to receive chemotherapy (50.2% vs. 44.1%; P < 0.001) and more likely to undergo total mastectomy (42.9% vs. 32.3%; P < 0.001). Furthermore, the high-poverty group patients were also more likely to have multiple (2+) comorbidities (27.4% vs. 19.1%; P < 0.001; Supplementary Table S1).

Rural/high-poverty patients were more likely to be diagnosed at younger ages (66–70 years: 29% vs. 25–27%; P < 0.001), receive total mastectomies (50% vs. 31–47%; P < 0.001), and receive chemotherapy (54.3% vs. 43.1–49.2%; P < 0.001) compared with all other groups. Urban/high-poverty patients were more likely to be NHB (27% vs. 1–10%; P < 0.001) and to have two or more comorbidities (28% vs. 17–25%; P < 0.001) compared with all other groups (Table 1).

OS

Five-year OS (5 y OS) was 71% for the urban dwellers versus 69% for the rural dwellers (P < 0.001). The 5 y OS was 73% for low-poverty, 69% for the medium-poverty, and 63% for the high-poverty group (P < 0.001; Supplementary Table S2; Supplementary Fig. S2A and S2B).

The 5 y OS was lowest for the urban/high poverty (73.5%) and rural/low-poverty (73.4%) patients, P = 0.9 (Fig. 1). Furthermore, the 5 y OS was lowest for the urban/high poverty (62.5%), and was significantly lower than that for the rural/high-poverty (65.9%) patients (Fig. 1; P < 0.001). Similar patterns were observed when including SMNs as competing events (Supplementary Table S2; Supplementary Figs. S2C and S2D and S3).

Adjusting for age at diagnosis, race/ethnicity, stage of breast cancer at diagnosis, treatment, and preexisting comorbidity, the urban/high-poverty patients were at a 1.22-fold increased hazard [95% confidence interval (CI), 1.15–1.29; P < 0.001] and among NHW (91.4% vs. 85.3%; P < 0.001) disease. High-poverty group patients were also more likely to undergo total mastectomy (47.6% vs. 34.1%; P < 0.001) and to receive chemotherapy (49% vs. 45.4%; P < 0.001). Furthermore, the 5 y OS was lowest for the urban/high poverty (62.5%), and was significantly lower than that for the rural/high-poverty (65.9%) patients (P < 0.001). Similar patterns were observed when including SMNs as competing events (Supplementary Table S2; Supplementary Figs. S2C and S2D and S3).

HCU Year 1 by residence

Rural dwellers had a higher rate of PCP visits (IRR, 1.25; 95% CI, 1.23–1.27) and ED visits (IRR, 1.62; 95% CI, 1.51–1.74), and a lower rate of nononcology specialist visits (IRR, 0.75; 95% CI, 0.74–0.76).
when compared with urban dwellers, after adjusting for age, stage at diagnosis, race/ethnicity, comorbidity, and treatment (Table 2).

Year 1 by SES
High-poverty patients had a higher rate of PCP visits (IRR, 1.07; 95% CI, 1.05–1.08), oncology visits (IRR, 1.06; 95% CI, 1.04–1.09), ED visits (IRR, 1.40; 95% CI, 1.30–1.51), and hospitalizations (IRR, 1.07; 95% CI, 1.04–1.10), but a lower rate of nononcology specialist visits (IRR, 0.87; 95% CI, 0.85–0.88) compared with the low-poverty patients, after adjusting for covariates listed in the previous model (Table 2).

Year 1 by combined residence/SES measure
Table 3 shows that rural patients had a higher rate of PCP visits across all SES categories (rural/low poverty: IRR, 1.33; rural/medium poverty: IRR, 1.27; and rural/high poverty: IRR, 1.23; P < 0.001). They also had a higher rate of ED visits (rural/low poverty: IRR, 1.66; rural/medium poverty: IRR, 1.68; and rural/high poverty: IRR, 1.82; P < 0.001), but significantly lower rates of nononcology specialist visits (rural/low poverty: IRR, 0.69; rural/medium poverty: IRR, 0.74; and rural/high poverty: IRR, 0.74; P < 0.001) compared with the urban/low-poverty group. There was no significant difference in hospitalization rates. Urban/high-poverty patients had higher rates of PCP visits (IRR, 1.08; P < 0.001), hospitalizations (IRR, 1.07; P < 0.001), and ED visits (IRR, 1.31; P < 0.001), but lower rates of nononcology specialist visits (IRR, 0.89; P < 0.001) compared with urban/low-poverty patients.

Years 2–5 by residence
Table 2 shows that rural dwellers had a higher rate of PCP visits (IRR, 1.17; 95% CI, 1.15–1.19) and ED visits (IRR, 1.34; 95% CI, 1.29–1.41), but a lower rate of nononcology specialist visits (IRR, 0.71; 95% CI, 0.69–0.72) compared with urban dwellers, after adjusting for age, stage at diagnosis, race/ethnicity, preexisting comorbidities, and treatment (surgery, receipt of chemotherapy, and/or radiation).

Years 2–5 by SES
High-poverty patients had a higher rate of PCP visits (IRR, 1.08; 95% CI, 1.07–1.10), hospitalizations (IRR, 1.14; 95% CI, 1.11–1.17), and ED visits (IRR, 1.21; 95% CI, 1.15–1.27), but a lower rate of nononcology specialist visits (IRR, 0.84; 95% CI, 0.83–0.86) compared with low-poverty patients after adjusting for covariates (Table 2).

Years 2–5 by combined residence/SES measure
Table 3 shows that rural patients had a higher rate of PCP visits across all SES categories (rural/low poverty: IRR, 1.21; rural/medium income: IRR, 1.17; and rural/high poverty: IRR, 1.19; P < 0.001) and ED visits (rural/low poverty: IRR, 1.30; rural/medium poverty: IRR, 1.42; and rural/high poverty: IRR, 1.43; P < 0.001), but lower rates of nononcology specialist visits (rural/low poverty: IRR, 0.63; rural/medium poverty: IRR, 0.69; and rural/high poverty: IRR, 0.71; all P < 0.001) compared with the urban/low-poverty patients. Rural/high-poverty patients had significantly higher rates of hospitalization compared with urban/low-poverty patients (IRR, 1.11; P < 0.001). Urban/high-poverty patients had higher rates of PCP visits (IRR, 1.08; P < 0.001), hospitalizations (IRR, 1.13; P < 0.001), and ED visits (IRR, 1.15; P < 0.001), but significantly lower rates of nononcology specialist visits (IRR, 0.85; P < 0.001) compared with urban/low-poverty patients. Supplementary Table S5 provides results including SMN as an endpoint.

Mediation and interaction analyses
Given the significantly higher rates of PCP visits and lower rates of nononcology specialist visits by the rural/high-poverty patients when...
compared with the urban/low-poverty patients, we explored the
mediating/moderating effects of nononcology specialist visits on the
association between residence/SES and mortality. Nononcology special-

ist visits are likely correlated with the presence of comorbidities and
are also likely to be different for patients with stage IV disease when
compared with stages 0–III disease.

As shown in Table 4, rural/high-poverty patients experienced a total excess mortality risk of 26%–57% when compared with urban/low-
poverty patients across the various strata. Paucity of nononcology specialist visits mediated 23%–47% of the total excess mortality risk,
while the interaction between residence/SES and paucity of nononcology specialist visits accounted for 49%–92% of the total excess mort-
ality risk experienced by the rural/high-poverty patients. Supplementary Data S2 provide further interpretation of results for all strata.

Discussion

The impact of rurality on OS in a population of older Medicare
beneficiaries diagnosed with breast cancer was largely predicated on
SES. Overall, the high-poverty patient populations of both urban and
rural residence demonstrated the lowest 5-year survival rates from end
of treatment (63% and 66%, respectively) compared with the 74%
5-year survival rates seen in both urban and rural low-poverty patients.
Differences in HCU were most apparent when taking SES into
consideration. Rural/high-poverty patients had higher rates of PCP
and ED visits, but lower rates of nononcology specialist visits com-
pared with their urban counterparts—both patients in low and high
poverty. Furthermore, patients with breast cancer living in urban/high-
poverty areas at diagnosis had up to 40% excess risk of mortality
compared with those living in urban/low-poverty areas, and this excess
risk was largely attributed to the interaction between residence/SES
status and paucity of nononcology specialist visits (5, 6).

Previous studies have examined the impact of rural residence or SES
cancer-related mortality or on healthcare access in isolation (17).
We find that urban and rural high-poverty older patients with breast
cancer were more likely to be diagnosed with stage III disease (26%)
compared with their low-poverty counterparts (22%). This contrasts
with studies reporting that rural residence is associated with delays in

Table 2. Association of urban/rural residence and SES on relative rate of health care utilization.

<table>
<thead>
<tr>
<th>Year 1 from end of treatment</th>
<th>PCP IRR (95% CI)</th>
<th>Oncology IRR (95% CI)</th>
<th>Nononcology IRR (95% CI)</th>
<th>Hospitalization IRR (95% CI)</th>
<th>ED IRR (95% CI)</th>
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<tr>
<td>Overall</td>
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<tr>
<td>Urban vs. rural (ref = urban)</td>
<td>1.25 (1.23–1.27)</td>
<td>1.06 (1.04–1.09)</td>
<td>0.75 (0.74–0.76)</td>
<td>0.97 (0.95–1.00)</td>
<td>1.62 (1.15–1.74)</td>
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<td>SES (ref = low poverty)</td>
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<tr>
<td>Medium poverty</td>
<td>1.07 (1.05–1.08)</td>
<td>1.06 (1.04–1.08)</td>
<td>0.90 (0.89–0.91)</td>
<td>1.02 (0.99–1.04)</td>
<td>1.15 (1.08–1.22)</td>
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<tr>
<td>High poverty</td>
<td>1.10 (1.08–1.11)</td>
<td>1.06 (1.04–1.09)</td>
<td>0.87 (0.85–0.88)</td>
<td>1.07 (1.04–1.10)</td>
<td>1.40 (1.30–1.51)</td>
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<table>
<thead>
<tr>
<th>Years 2–5 from end of treatment</th>
<th>PCP IRR (95% CI)</th>
<th>Oncology IRR (95% CI)</th>
<th>Nononcology IRR (95% CI)</th>
<th>Hospitalization IRR (95% CI)</th>
<th>ED IRR (95% CI)</th>
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<tr>
<td>Overall</td>
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<tr>
<td>Urban vs. rural (ref = urban)</td>
<td>1.17 (1.15–1.19)</td>
<td>1.01 (0.98–1.05)</td>
<td>0.71 (0.69–0.72)</td>
<td>0.92 (0.89–0.95)</td>
<td>1.34 (1.29–1.41)</td>
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<tr>
<td>SES (ref = low poverty)</td>
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<tr>
<td>Medium poverty</td>
<td>1.05 (1.04–1.06)</td>
<td>1.03 (1.00–1.06)</td>
<td>0.88 (0.87–0.89)</td>
<td>1.05 (1.02–1.07)</td>
<td>1.11 (1.07–1.16)</td>
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<tr>
<td>High poverty</td>
<td>1.08 (1.07–1.10)</td>
<td>1.03 (0.99–1.06)</td>
<td>0.83 (0.82–0.84)</td>
<td>1.14 (1.11–1.17)</td>
<td>1.21 (1.15–1.27)</td>
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</table>

Note: All models adjusted for age at diagnosis, stage at diagnosis, race/ethnicity, Elixhauser comorbidity index, surgery received, chemotherapy, and radiation.
Comparing rural high-poverty to urban low-poverty patients, stratiﬁcation of the total effect is decomposed into the ERR due to the controlled direct effect, the ERR due to reference interaction, the ERR due to mediated interaction, and the ERR due to indirect effect. The controlled direct effect is estimated at a probability of seeing a nononcology specialist and how that effect is reﬁned on the mortality for the individual.

### Table 4. ERRs of 5-year mortality and OPA to number of annual visits to nononcology specialist as the mediator and moderator, comparing rural high-poverty to urban low-poverty patients, stratified by number of comorbidities.

<table>
<thead>
<tr>
<th>Elizhauser index = 0</th>
<th>ERR 95% CI</th>
<th>P</th>
<th>OPA&lt;sub&gt;med&lt;/sub&gt; 95% CI</th>
<th>Mediation effect</th>
<th>P</th>
<th>OPA&lt;sub&gt;int&lt;/sub&gt; 95% CI</th>
<th>Interaction effect</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;: Stage 0–III: urban/low poverty vs. rural/high poverty</td>
<td>CDE</td>
<td>0.01 (−0.05 to 0.07)</td>
<td>0.720</td>
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<tr>
<td></td>
<td>INTref</td>
<td>0.17 (−0.01 to 0.35)</td>
<td>0.067</td>
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<tr>
<td></td>
<td>INTmed</td>
<td>0.02 (−0.002 to 0.04)</td>
<td>0.077</td>
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<tr>
<td></td>
<td>PIE</td>
<td>0.07 (0.05–0.09)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>Total excess risk&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.27 (0.07–0.46)</td>
<td>0.001</td>
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<tr>
<td>Model 2&lt;sup&gt;a&lt;/sup&gt;: Stage IV: urban/low poverty vs. rural/high poverty</td>
<td>CDE</td>
<td>−0.03 (−0.14 to 0.01)</td>
<td>0.520</td>
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<tr>
<td></td>
<td>INTref</td>
<td>0.16 (0.14–0.25)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>INTmed</td>
<td>0.04 (0.01–0.07)</td>
<td>0.005</td>
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<tr>
<td></td>
<td>PIE</td>
<td>0.08 (0.05–0.12)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>Total excess risk&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.26 (0.13–0.38)</td>
<td>0.001</td>
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<tr>
<td>Elizhauser index = 1</td>
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<tr>
<td>Model 3&lt;sup&gt;a&lt;/sup&gt;: Stage 0–III: urban/low poverty vs. rural/high poverty</td>
<td>CDE</td>
<td>0.06 (−0.009 to 0.13)</td>
<td>0.093</td>
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<td></td>
<td>INTref</td>
<td>0.23 (0.03–0.42)</td>
<td>0.022</td>
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<tr>
<td></td>
<td>INTmed</td>
<td>0.02 (0.002–0.08)</td>
<td>0.034</td>
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<tr>
<td></td>
<td>PIE</td>
<td>0.06 (0.04–0.08)</td>
<td>0.001</td>
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<td></td>
<td>Total excess risk&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.37 (0.16–0.58)</td>
<td>0.001</td>
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<tr>
<td>Model 4&lt;sup&gt;a&lt;/sup&gt;: Stage IV: urban/low poverty vs. rural/high poverty</td>
<td>CDE</td>
<td>0.08 (−0.02 to 0.18)</td>
<td>0.102</td>
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<td></td>
<td>INTref</td>
<td>0.17 (0.03–0.32)</td>
<td>0.016</td>
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<td></td>
<td>INTmed</td>
<td>0.06 (0.007–0.10)</td>
<td>0.026</td>
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<td></td>
<td>PIE</td>
<td>0.16 (0.10–0.21)</td>
<td>0.001</td>
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<td></td>
<td>Total excess risk&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.47 (0.27–0.67)</td>
<td>0.001</td>
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<tr>
<td>Elizhauser index ≥ 2</td>
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<tr>
<td>Model 5&lt;sup&gt;a&lt;/sup&gt;: Stage 0–III: urban/low poverty vs. rural/high poverty</td>
<td>CDE</td>
<td>−0.03 (−0.07 to 0.01)</td>
<td>0.123</td>
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<td></td>
<td>INTref</td>
<td>0.33 (0.22–0.45)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>INTmed</td>
<td>0.03 (0.02–0.05)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>PIE</td>
<td>0.06 (0.05–0.07)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.40 (0.28–0.52)</td>
<td>0.001</td>
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<tr>
<td>Model 6&lt;sup&gt;a&lt;/sup&gt;: Stage IV: urban/low poverty vs. rural/high poverty</td>
<td>CDE</td>
<td>−0.04 (−0.10 to 0.01)</td>
<td>0.117</td>
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<tr>
<td></td>
<td>INTref</td>
<td>0.25 (0.17–0.33)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>INTmed</td>
<td>0.08 (0.05–0.10)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>PIE</td>
<td>0.13 (0.10–0.18)</td>
<td>0.001</td>
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<tr>
<td></td>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.41 (0.31–0.52)</td>
<td>0.001</td>
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</tbody>
</table>

Note: CDE: The controlled direct effect is excess relative risk of mortality for an individual that is rural/high poverty and who does not visit a nononcology specialist ≥1/year, compared with those individuals with urban/high income and who visit a nononcology specialist ≥1/year. INTref: The reference interaction is the ERR of mortality for an individual due to the interacting effect of being rural/high poverty and not having visited nononcology specialists ≥1/year. INTmed: The mediated interaction component is interpreted as the ERR of mortality for an individual due to both the interacting effect between being rural/high poverty and not seeing a nononcology specialist, but also due to the effect that being rural/high poverty has on the individual’s likelihood of visiting a nononcology specialist ≥1/year and how that affects the mortality. PIE: Pure indirect effect is interpreted as the ERR of mortality for an individual that results from the effect that being rural/high poverty has on the individual’s probability of seeing a nononcology specialist and how that effect is reﬂected on the mortality for the individual. Abbreviations: ERR, excess relative risk; OPA, overall proportion attributable.

<sup>a</sup>All models: effects are based on the average characteristics of the stage-speciﬁc population (age at diagnosis, race/ethnicity, and treatment).

<sup>b</sup>The total effect is decomposed into the ERR due to the controlled direct effect, the ERR due to reference interaction, the ERR due to mediated interaction, and the ERR due to indirect effect. The controlled direct effect is estimated at a ﬁxed level of the mediator.

Diagnosis resulting in later stage at diagnosis (18). Urban/high-poverty patients were more likely to be NHB and to have more comorbidities than all other groups. Previous evidence demonstrates that NHB women with early-stage breast cancer are less likely to receive treatment, more likely to discontinue therapy, and have worse survival than NHW women (19). Taking stage at diagnosis into account, rural/low-poverty patients in our study were more likely to have total mastectomies and receive chemotherapy compared with both their urban/low-poverty and urban/high-poverty counterparts. Treatment-related differences are important to consider to understand the observed mortality disparity among patients with breast cancer from rural areas or with high poverty, compared with their urban and low-poverty counterparts (20–23). There was no signiﬁcant difference in visits to oncologists between these two groups, which is in contrast to prior literature suggesting that rural patients may receive less cancer-related care, including radiation (20) and oncology services (21). This may be partially attributable to the fact that this patient population is consistently insured under Medicare and is nationally representative, while the prior studies are largely regionally focused and include a variety of insurance coverage.

Another important characteristic to consider in an older patient population is the high rate of comorbid conditions, which contribute to a need for access to nononcology specialists (7). High-poverty patients with breast cancer, both urban and rural, had the highest prevalence of...
comorbidities, yet had a lower rate of nononcology specialist visits. However, through the first year after diagnosis, rural patients had higher rates of PCP visits, irrespective of SES, when compared with their urban/low-poverty counterparts. This generally supports the estimates that while there are fewer PCPs in rural areas, there are even fewer medical specialists in the rural setting.

A large proportion of excess mortality risk in rural/high-poverty patients was attributable to the interacting effect of nononcology specialist visits across all levels of comorbidity, and disease stage, suggesting that this population has complex medical needs. However, the proportion of excess risk attributable to the mediating effect of nononcology specialists was lower, suggesting that visits to nononcology specialists were likely not the only explanatory factor in the pathway from residence/SES to mortality, and that other unmeasured mechanisms likely played a role. Visits to a nononcology specialist may be a proxy for other healthcare-seeking behavior, which is an inter-

esting finding in light of the fact that this population is technically an insured population and, theoretically, should have access to receiving care.

Recent studies have asked the question whether providing insurance to patients with cancer actually mitigates negative health effects of living in disadvantaged communities (defined by low median household income, percent of population below FPL, and education achieve-

ment in the area; ref. 24). Abdelsattar and colleagues found that when examining uninsured, insured, and Medicaid patients diagnosed with cancer between the ages of 18 to 64 years, health insurance did appear to somewhat mitigate the relationship between a community's SES and cancer care and outcomes, but it did not completely resolve the disparities (24). This is echoed in our study where all patients assessed had continuous health care coverage, yet outcomes varied distinctively across poverty level. The relationship between patient-level and community-level characteristics and the health care policies and resources available in that area are highly complex, warranting a greater examination of the factors that should be targeted to facilitate greater healthcare parity.

This study needs to be examined in the context of its limitations. The urban/rural status and SES of the patient is anchored to when they were diagnosed with breast cancer; the study did not update either the residence or SES through the 5 years of follow-up. Cancer-tract poverty information does not capture patient-level measures of eco-

nomic hardship, potentially introducing ecologic bias. Administrative claims are designed for billing purposes and present inherent limitations. In addition, our results only apply to patients with breast cancer, and future studies may examine the differences in the effect of residence/SES on HCU and mortality in other cancer types. Finally, it is possible that not all relevant confounders were captured in these analyses.

This population-based study of older patients with breast cancer finds that rural/urban disparities in survival were modest, but that the underlying SES largely accounts for the patterns of HCU, potentially explaining some of these disparities in outcomes.

Disclosure of Potential Conflicts of Interest

G.B. Rocque is a consultant for Pfizer and Genentech and reports receiving commercial research grants from Pfizer, Genentech, and Carevive. No potential conflicts of interest were disclosed by the other authors.

Authors’ Contributions

Conception and design: K.M. Kenzik, G.B. Rocque, S. Bhatia

Development of methodology: K.M. Kenzik

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): K.M. Kenzik

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): K.M. Kenzik, G.B. Rocque, W. Landier, S. Bhatia

Writing, review, and/or revision of the manuscript: K.M. Kenzik, G.B. Rocque, W. Landier, S. Bhatia

Study supervision: S. Bhatia

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1319

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Kelly M. Kenzik, Gabrielle B. Rocque, Wendy Landier, et al.


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