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Breast Cancer Mortality in Appalachia: Reversing Patterns of Disparity over Time

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Abstract

Breast cancer death rates in the U.S. have decreased in recent decades, however areas such as Appalachia with fewer cancer care resources may not have experienced comparable mortality declines. This study examines trends in breast cancer mortality rate disparities in Appalachian states and the continental U.S. using data from SEER mortality files 1969–2007 and the Area Resource File. Overall breast cancer mortality rates decreased significantly, with a smaller decline in Appalachian counties (17.5%) compared with non-Appalachian counties in Appalachian states (30.5%), and compared with non-Appalachia U.S. counties (28.3%). After accounting for poverty, rural/urban status, education, health care resources, and proportion White in the population, residence in Appalachian counties except for those in the Northern subregion was significantly associated with smaller reduction in breast cancer mortality rates. Lower levels of education, physician density, and percent White in the population were also associated with smaller reductions in breast cancer mortality.

Keywords

Breast cancer; mortality; Appalachia; disparity

Breast cancer is the most commonly diagnosed non-skin cancer and the second leading cause of cancer deaths among U.S. women.¹ Breast cancer death rates have decreased since 1990, declining from 33 per 100,000 in 1990 to 23 per 100,000 in 2006.¹ This decline has been attributed to increased early detection through mammography, as well as to improvements in breast cancer treatment.^{1–3} Geographic areas that are medically underserved with fewer mammography facilities and more limited options for cancer treatment,^{4,5} however, may not have experienced comparable declines in breast cancer mortality.

Appalachia is a geographic region that has long been characterized by poverty and reduced health care access.^{6–9} Based upon disparities in cancer incidence and outcomes, residents of the Appalachian region have been designated as a special population of interest by the National Cancer Institute.¹⁰ Women in Appalachia report fewer mammograms and being less likely than others to receive recommended treatment for breast cancer.^{6,11} Despite these barriers, researchers reported that during 1976–1996 breast cancer mortality rate was lower among Appalachian White women than among White women in other geographic regions.¹² It was the case, however, that this difference decreased over time.¹²

This study examines trends in breast cancer mortality rate disparities and rate reductions in Appalachian states and the continental U.S. The objectives of this research were: (I) to examine disparities and trends associated with breast cancer mortality rate in Appalachian states and the continental U.S., using updated data through 2007; (II) to examine the spatial distribution of reductions in breast cancer mortality; and (III) to examine the relationship between reduction of breast cancer mortality and Appalachian location, taking contextual factors including poverty and educational level into account.

Methods

Annual, population-based data from 1969 to 2007 regarding breast cancer deaths among White women in the continental U.S. and the District of Columbia were analyzed. These data, originally collected by the National Center for Health Statistics, were accessed through the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute.¹³ To account for changes in the International Classification of Disease (ICD) system over time, we used recoded cause of death data in SEER which allow comparison of breast cancer deaths originally coded according to ICD versions 8, 9, and 10. Breast cancer mortality data have been found to be reliable and valid across time and location in previous studies.^{14–17} We restricted the analysis to White women because the Appalachian population contains few non-White women, especially at the earlier time points of interest. This study also uses county-level data on poverty, rural/urban status, education, healthcare resources, and percent White in the population extracted from the Area Resource File in regression analyses.

We used SEER*Stat statistical software from the SEER Program¹⁸ to calculate breast cancer mortality rates (expressed as deaths per 100,000 individuals per year) and trends. We used SEER's multiple-year aggregate rates which improved the stability of the estimates; for 1969–1998, we calculated three-year aggregate rates, with four-year aggregate rates for 1999–2002 and five-year aggregate rates for 2003–2007 (<http://seer.cancer.gov/mortality/index.html>). The rates were age-adjusted by the direct method using 5-year age groups, with the 2000 U.S. standard population as the reference.

We calculated breast cancer mortality rates for Appalachian counties (n=420), non-Appalachian counties in the 13 Appalachian states (n=640) (note that all West Virginia counties are Appalachian), and non-Appalachian counties in the continental U.S. as a whole (n=2,756). We also calculated rates by age (younger than 65 years of age and 65 years and older) and for rural and urban counties, with those with Rural Urban Continuum Codes (RUCC) of 6–9 and 0–5 classified as rural and urban, respectively.¹⁹ We used the 2003 urban-rural continuum scheme to designate county rural status during the period 1999–2007, the 1993 scheme for the period 1990–1998, the 1983 scheme for the period 1981–1989, and the 1974 scheme for the period 1969–1980. Consequently, the number of counties designated as rural or urban changed over time; for example, in 1974, 670 counties were designated rural while in 2003, 494 were designated rural.

We tested the significance ($p < .05$) of linear trends of Appalachia/non-Appalachia rate ratios and calculated the annual percentage change by fitting a least squares regression line to the natural logarithm of the rates. We also conducted exploratory spatial data analysis to examine the spatial distribution of the reduction in county-specific mortality rates. The reduction was calculated as the absolute difference between nine-year aggregate rates for 1969–1977 and 1999–2007. The reduction in rates is presented as a choropleth map constructed with shapefiles from the Geography Division of U.S. Census Bureau.²⁰ Rates for counties with fewer than four deaths are not displayed.

The final stage of analysis included weighted multivariate regression to examine factors associated with reduction in breast cancer mortality rates, using SEER mortality data merged with county data from the Area Resource File. Two different regression models were estimated. The independent variables in the first model included Appalachian location, rural/urban status, White poverty rate, percent of Whites with a high school diploma, percent White in the population, and physicians per 1,000 residents during 1995–2000. These covariates were inspected and found to be relatively stable across years. The second model included the variables in the first model, substituting regional dummy variables to represent the five Appalachian sub-regions defined by the Appalachian Regional Commission in place of the overall Appalachian variable. The dependent variable in both models is the difference in aggregate county-level breast cancer mortality rates between 1969–1977 and 1999–2007.

Results

From 1969 to 2007, 1,197,281 breast cancer deaths occurred among U.S. White women, with 125,006 (10.4%) occurring in Appalachia. Over this period, the overall breast cancer mortality rate among White women decreased significantly, with a smaller decline in Appalachian counties (17.5%) than in non-Appalachian counties in Appalachian states (30.5%) and non-Appalachian counties in the U.S. as a whole (28.3%). The annual percentage change values are -0.42 , -0.88 , and -0.83 respectively in Appalachian counties, non-Appalachian counties in Appalachian states, and non-Appalachian counties in the U.S. The mortality rate in Appalachia during 2003–2007 (24.1 per 100,000 people, 95% CI: 23.8~24.5) is significantly higher than non-Appalachian counties in the U.S. (23.3 per 100,000 people, 95% CI: 23.2~23.4, p -value $<.001$). Figure 1 depicts changes in breast cancer mortality rates over time for U.S. counties, with the smallest declines indicated in black. Counties in central Appalachia, especially those in West Virginia, Kentucky, and Virginia, had among the smallest rate decreases.

Comparisons of Appalachian counties with non-Appalachian counties throughout the U.S

Figure 2 displays breast cancer mortality rates for Appalachian counties compared with non-Appalachian counties, stratified by age. As expected, women 65 years and older consistently had higher breast cancer mortality rates compared with younger women. Among older women, the breast cancer mortality rates increased over the early years, peaking in 1990–92 and declined thereafter in both Appalachian and non-Appalachian areas. From 1969–71 through 1996–98, rates in non-Appalachian women in this age group were significantly higher than rates for those living in Appalachia; however, by 1999–2002 and continuing through 2003–07, the rates in the two areas converged. For women under 65 years of age, rates declined throughout the study period in both Appalachia and non-Appalachia. Rates were significantly higher in non-Appalachia areas until the rates converged in 1981–83. By 2003–07, the disparity had reversed direction and the breast cancer mortality rate in Appalachia was significantly higher than the rate in non-Appalachian counties ($p<.001$).

Comparisons in Appalachian and non-Appalachian counties within Appalachian states

In addition to overall comparisons, Appalachian counties were compared to neighboring non-Appalachian counties within the same states. Table 1 displays Appalachian county/non-Appalachian county breast cancer mortality ratios for the 12 Appalachian states that include both county types. In 2003–07, the Appalachia/non-Appalachia mortality rate ratio was significantly greater than 1.0 in South Carolina (1.1031; $p<.05$) and Virginia (1.1508; $p<.01$). The trend in the Appalachia/non-Appalachia mortality rate ratio increased over time in Kentucky ($p<.001$), Ohio ($p=.019$), South Carolina ($p=.025$), Tennessee ($p=.045$) and Virginia ($p=.001$).

In addition to descriptive comparisons, we conducted analytic regression analyses to examine whether residence in Appalachian counties as opposed to neighboring non-Appalachian counties was associated with reduced breast cancer mortality after taking potentially confounding factors into account. As shown in Table 2, we ran separate models depending on the specification of the Appalachian variable. Looking first at Model 1, a negative and significant association was found between the Appalachia dummy variable and reduction in breast cancer mortality rate when controlling for other covariates in the model. In Model 2, residence in the North Central, Central, South Central, and Southern Appalachia regions was associated with smaller reductions in breast cancer mortality rates compared with non-Appalachian areas, while the North region was not significantly different. Education, *per capita* physician supply, and percent White in the population were positively associated with reduction of breast cancer mortality. Rural/urban status and poverty rate were not significantly associated with mortality rate reduction. The adjusted R^2 for the regression models ranged from 0.28 to 0.29.

Discussion

Although the overall breast cancer mortality rate has decreased since the early 1990s, the mortality advantage that was present for White women in Appalachia from 1969 until the early 1990s has disappeared. Women under 65 years of age in Appalachia now have a higher breast cancer mortality rate than women in the non-Appalachian counties of Appalachian states (5.2% greater) and for women in non-Appalachian counties in the U.S. (7.1% greater).

In interpreting the transformation in breast cancer mortality risk among White Appalachian women from comparatively low to significantly elevated, it is helpful to consider factors that have been previously suggested as being potentially protective, and changes in status that may have taken place in recent years. Hall and colleagues discussed several influences that may have contributed to lower risk breast cancer mortality risk in earlier decades:¹²

Lower underlying incidence of breast cancer secondary to lower risk factor prevalence among Appalachian women

The risk of developing breast cancer is increased by modifiable factors such as not breastfeeding, older age at first birth, oral contraceptive use, post-menopausal hormone therapy, overweight/obesity, physical inactivity, and drinking more than one alcoholic beverage daily.²¹ If the female Appalachian population had comparatively lower exposure to risk factors in the past and in recent decades has progressively become more exposed, underlying breast cancer incidence rates could be trending upward. For example, the prevalence of obesity is much higher in Appalachia than in the rest of the U.S. Eighty-one percent of counties in the Appalachian region have among the highest rates of obesity,²² and obesity rates in the region have risen substantially in recent years.²³ However, while data on long-term trends in breast cancer incidence in Appalachia as a whole are not available,¹² comparison of incidence rates in Appalachian areas of Kentucky, Pennsylvania, and West Virginia from 1994–1998 to 2002–2006 show no increase and in fact rates in these areas have declined in recent years.^{21,24}

Recent compositional changes in the Appalachian population through migration could also conceivably have led to a greater prevalence of women with genetic markers that predispose them to breast cancer. Because nearly half of recent population growth in Appalachia is attributable to an influx of non-White people,²⁵ however, the fact that the present study is limited to White women makes this possibility somewhat less salient.

Differences in the prevalence of breast cancer screening

Researchers noted that the lower breast cancer mortality rate observed previously in Appalachia could be due to more frequent detection of the disease at earlier stages through mammography screening.¹² Although information about past trends in screening prevalence in this region is incomplete, the traditionally low socioeconomic status characterizing the Appalachian region suggests that screening uptake patterns are not likely to have been optimal. Current data confirm that Appalachian women are less likely than others in the U.S. to receive mammography screening.²¹

Differential access to breast cancer treatment

Similarly, it may be the case that recommended breast cancer treatment is not currently reaching women in Appalachia at the same rate that it reaches other women in the U.S., leading to elevated mortality rates. In view of long-standing shortages of health care personnel and facilities as well as widespread economic disadvantage as discussed above,⁹ however, it seems unlikely that access to treatment was comparatively more optimal in previous decades. Clearly more research is needed to understand the mechanisms underlying the observed trends in breast cancer disparities.

The study findings suggest that heterogeneity exists in breast cancer mortality among states within the Appalachian region. Mortality rates for women from West Virginia and Appalachian Kentucky and Virginia have not decreased as fast as rates for women in non-Appalachian areas during 1990–2006. The geographic differences in trends in breast cancer mortality reduction may be a result of differential prevalence of risk factors for breast cancer incidence and mortality that may be amenable to policy intervention. One such spatially clustered risk factor is mountaintop coal mining and the subsequent environmental contamination of local air and water, which has been correlated with increased breast cancer mortality.²⁶

This study was limited by several factors. First, it applied county-level designation of urban/rural status to cases and the population. This may have introduced ecological bias; however, this method has been used previously.^{7,27} Second, the urban/rural designation changed over time. The rural-urban continuum coding scheme originated in 1974, and was updated in 1983, 1993, and 2003. While it is possible that the method of determining metro adjacency was not consistent across schemes, we used a consistent urban-rural cutoff point for all time periods.

The study also has several strengths. First, it is population-based and stratifies results by age and urban/rural status. Second, the study compares breast cancer mortality in Appalachia with neighboring non-Appalachian regions in the same states, thus controlling for statewide effects such as insurance coverage or implementation of public health programs like the Breast and Cervical Cancer Early Detection Program. In addition, the analyses go beyond previous descriptive research (e.g., Hall et al.¹²) in taking potentially confounding factors into account in multivariate analyses.

In conclusion, this is the first study to report trends in breast cancer mortality among White women in Appalachia with data through 2007, and to compare those trends to those in non-Appalachian areas. Comparative trend studies, particularly those that are stratified by important determinants, such as age and urban/rural residence, provide data to inform strategies to address emerging health disparities. Public health interventions could include enhanced breast cancer surveillance in Appalachia to monitor trends, testing and dissemination of community-based methods to increase screening among low-income women and women with limited access to health care, development of policies and regulations that reduce barriers to breast cancer screening and treatment, and provision of

services, such as patient navigation, that support guideline-concordant treatment of breast cancer.²⁸ More broadly, interventions are needed that address key mechanisms underlying breast cancer incidence and mortality, such as structural and behavioral programs focused on obesity prevention, and social policies that improve education and increase access to high-quality health care in Appalachia.

Notes

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Figure 1.

Reduction in age-adjusted White female breast cancer death rates by county, 48 continental states.

^aThe rate reduction is the absolute difference between age-adjusted death rates during 1969–1977 and rates during 1999–2007.

^bThe rates reduction could not be calculated for some counties due to fewer than 4 deaths in one or two 9-year time periods.

^cThe projected coordinate system of this map is USA Contiguous Lambert Conformal Conic.

^dData Sources: U.S. Mortality Data, 1969 to 2007. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Mortality—All COD, Aggregated With County, Total U.S. (1969–2007) <Katrina/Rita Population Adjustment>—Linked To County Attributes—Total U.S., 1969–2007 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released June 2010. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

Figure 2.

Comparison of Appalachian counties to non-Appalachian counties throughout the U.S., stratified by age group: three-year age-adjusted White female breast cancer death rates, 1969 to 2007.

^aSignificant difference (p-value <.001) between “women ≥65 in App counties” and “women ≥65 in non-App U.S.”

^bSignificant difference (p-value <.001) between “women <65 in App counties” and “women <65 in non-App U.S.”

^cThe last study period 2003–2007 is 5-years, and the period 1999–2002 is 4-years.

^dRates are age adjusted to the 2000 U.S. standard population (Census P25-1130).

^eSources: U.S. Mortality Data, 1969 to 2007. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Mortality—All COD, Aggregated With County, Total U.S. (1969–2007) <Katrina/Rita Population Adjustment>—Linked To County Attributes—Total U.S., 1969–2007 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released June 2010. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

COD = Classification of disease

DCCPS = Division of Cancer Control and Population Sciences

Table 1

APPALACHIAN/NON-APPALACHIAN RATIO OF 3-YEAR AGE-ADJUSTED FEMALE BREAST CANCER DEATH RATES BY STATE: WHITES ONLY, 12 APPALACHIAN STATES, 1969–2007^a

	Appalachian/Non-Appalachian Ratio of 3-year Age-Adjusted Female Breast Cancer Death Rates											
	Alabama	Georgia	Kentucky	Maryland	Mississippi	New York	North Carolina	Ohio	Pennsylvania	South Carolina	Tennessee	Virginia
1969–1971	.9733	.9414	.7947**	.8348	.8634	.8180***	.9634	.8721**	.9702	1.1644	.9375	.6653***
1972–1974	1.1887*	.9729	.7463***	.9632	.9578	.8654**	.909	.8876**	.9621	1.1556	.9222	.7166***
1975–1977	1.0436	.9692	.7003***	.9647	.9878	.8878**	.932	.9281	.9302**	1.0194	.9022	.8625*
1978–1980	1.0026	.9625	.7616***	.8808	.8896	.9302	.9341	.9695	.9075***	1.1422	.9923	.8335*
1981–1983	1.2010**	.9283	.8806*	.9898	.8946	.9100*	.9735	.9667	.9143***	1.1252	.913	.7583***
1984–1986	1.0188	1.0193	.8317**	.8496	.9314	.9271	.8952*	.9484	.9771	1.1313	.9729	.9066
1987–1989	1.0543	.9262	.9017	.8357	1.0569	.8408**	.92	.9022*	.9228**	1.1088	.9325	.8818*
1990–1992	.9923	.9783	.9013	.9438	.9895	.8896**	.9583	.8917**	.9688	.9944	.9662	.9435
1993–1995	.8851*	1.0521	1.0141	.7960*	1.1407	.9401	.9735	.9854	.958	.9247	.9745	1.0157
1996–1998	.9061	1.0213	.9801	.8365	.8726	.8584**	.9293	1.0184	.9547	1.0866	.9628	1.0447
1999–2002	.9724	.9594	1.0383	1.0592	.8642	.9508	.9234*	1.0075	.9605	.9719	1.0025	.9101
2003–2007	1.0142	1.0059	1.0839	1.1014	1.0312	.9751	1.0069	.9484	1.0159	1.1031*	.9907	1.1508**
p-value of the linear trend	.088	.197	<.0001	.932	.629	.168	.998	.019	.622	.025	.045	.001

* p-value <.05

** p-value <.01

*** p-value <.001

^aThe last study period 2003–2007 is 5-years, and the period 1999–2002 is 4-years. Rates are age adjusted to the 2000 U.S. standard population (Census P25-1130). Values are rate ratios; U.S. Mortality Data, 1969 to 2007. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov). SEER Stat Database: Mortality—All COD, Aggregated With County, Total U.S. (1969–2007) <Katrina/Rita Population Adjustment>—Linked To County Attributes—Total U.S., 1969–2007 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released June 201. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

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Table 2

RESULTS FROM MULTIVARIATE REGRESSION ANALYSES MODELING REDUCTION IN AGE-ADJUSTED WHITE FEMALE BREAST CANCER DEATH RATES,^a 1969–2007

	Model 1	Model 2
Number of counties included ^b	1008	1008
Intercept	−23.67 *	−18.99 **
Appalachian	−.65 **	
Sub-regions		
Northern Appalachia		.30
North Central Appalachia		−2.55 *
Central Appalachia		−3.63 *
South Central Appalachia		−3.88 ***
Southern Appalachia		−1.56 *
Rural status	.60	.56
% White Poverty	−.12	−.12
% White 25+ HS graduate or more	.28 ***	.23 ***
% Percent White in the Population	.06 ***	.06 ***
Number of physicians per 1,000 residents	.94 ***	.99 ***
R ²	.2859	.3016
Adjusted R ²	.2816	.2946
F statistics	66.79 ***	43.05 ***

*
p<.05

**
p<.01

p<.001

^a Mortality rates are expressed as deaths per 100,000 individuals per year, and the dependent variable is the difference in aggregate county-level mortality rates between 1969–1977 and 1999–2007.

^b The N of 1008 represents the number of counties in the 13 Appalachian states with complete data for all variables in the model.