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Persistence with Mammography Screening and Stage at Breast Cancer Diagnosis among Elderly Appalachia-West Virginia Women

Ami Vyas, MBA, PhD, University of Rhode Island
Suresh Madhavan, MBA, PhD, West Virginia University
Usha Sambamoorthi, PhD, West Virginia University
**Corresponding Author: Ami Vyas, Department of Pharmacy Practice, College of Pharmacy, University of Rhode Island, 7 Greenhouse Road, Kingston, RI 02881
avyas@uri.edu

ABSTRACT

The objective of this study is to evaluate the association between persistence with mammography screening and stage at breast cancer diagnosis in elderly Appalachia-West Virginia women diagnosed with first incident breast cancer. The study utilized West Virginia Cancer Registry-Medicare linked database to identify women age 70 and above diagnosed with first incident breast cancer in 2007. Persistence to mammography screening was defined as having had at least three mammography screenings before breast cancer diagnosis. A multiple logistic regression was conducted to assess the association between persistence with mammography screening and stage at breast cancer diagnosis in these women. Of the 221 elderly Appalachia-West Virginia women included in the analysis, 113 women (51.1%) were persistent to mammography screening before their diagnosis with breast cancer. In a multiple logistic regression after adjusting for all the variables, as compared to elderly women who were not persistent with mammography screening, women who were persistent with mammography screening were significantly more likely to be diagnosed with early stage breast cancer (adjusted odds ratio=4.25, 95% confidence interval=1.96-9.19). Persistence with mammography screening is significantly associated with earlier stages of breast cancer in the rural and underserved Appalachia-West Virginia women. The study findings suggest targeting interventions to encourage regular mammography in these women for whom there are no clear guidelines.

Keywords: Persistence, Mammography Screening, West Virginia Cancer Registry, Medicare

INTRODUCTION

Breast Cancer and Mammography Screening in Appalachia-West Virginia

West Virginia (WV), the only state that lies entirely in Appalachia, is largely a rural and medically underserved region in the United States (US) characterized by high poverty rates, low level of education, aging population, high rates of chronic diseases, and poor health behaviors (Kaiser State Health Facts, 2008; Kaiser State Health Facts, 2009; United States Census Bureau, 2010; United States Census Bureau, 2010). WV is reported to have higher rates of advanced and unstaged breast cancer (BC) (United States Cancer Statistics, 2010; United States Cancer Statistics, 2012; Lengerich, Chase, Beiler, & Darnell, 2006; SEER State Cancer Profiles, 2010; Wingo, Tucker, & Jamison, 2007), which has been attributed to lower mammography screening rates in women in this state (Khanna, Bhanegaonkar, Colsher, Madhavan, & Halverson, 2009; Lengerich et al., 2006; SEER State Cancer Profiles, 2010). Also, in elderly WV women, BC accounted for 21.9% of all the incident cancer cases for year 2004 (United States Cancer Statistics, 2008) and 11.4% of all the cancer deaths for year 2007 (CDC National Center for Health Statistics, 2015). The authors of several studies and reports have argued that low mammography screening rates and less access to health services in these vulnerable WV women may be one of the significant factors contributing to this higher BC-related mortality (Hall, Uhler, Coughlin, & Miller, 2002; SEER State Cancer Profiles, 2010).

Persistence with Mammography Screening and Stage at Breast Cancer Diagnosis

Persistence with mammography screening defined as having had at least three mammography screenings in five years is associated with presentation of BC at earlier stages in elderly women (Vyas, Madhavan, & Sambamoorthi, 2014). In addition, regular use of mammography screening helps detect tumor when its size is small and potentially treatable and patients may have less aggressive treatments (Humphrey, Helfand, Chan, & Woolf, 2002). Previous studies which reported the beneficial effects of mammography screening on early stage of BC representation using SEER-Medicare data captured use of mammography screening in two years before diagnosis which may not necessarily take into account past screening behavior and intervals between recent and prior screenings (McCarthy et al., 2000; Randolph, Goodwin, Mahnken, & Freeman, 2002). These studies are also limited with the fact that they have either utilized data from fewer cancer registries (McCarthy et al., 2000; Randolph et al., 2002). Previous studies which analyzed persistent mammography screening behavior in five years prior to BC diagnosis in using SEER-Medicare data have been conducted among women age 80 and above (Badgwell et al., 2008) and could not be generalized to the rural elderly women in Appalachia-WV due to its distinct demographic and socio-economic characteristics. In addition, the SEER-Medicare data reflects a population more likely to be residing in urban setting (Warren, Klabunde, Schrag, Bach, & Riley, 2002), due to which no information is available about the beneficial effects of mammography screening on stage at BC diagnosis among elderly Medicare beneficiaries from rural and medically underserved regions, and from non-SEER Medicare states. Moreover, these previous published studies except the one by Vyas et al. (2014) did not utilize any model or technique to differentiate between screening and diagnostic mammograms which is one of the major issues with Medicare claims data. Nevertheless, the Vyas et al. (2014) study focused on the entire SEER population with no information on rural and medically underserved population (Vyas et al., 2014). A recently published study has recommended a three-step algorithm with high sensitivity of 99.7% and positive predictive value

of 97.4% to identify screening mammograms from the Medicare claims data (Fenton et al., 2014).

The purpose of the study is to determine the association between persistence with mammography screening and stage at BC diagnosis in Appalachia-WV Medicare fee-for-service (FFS) women beneficiaries diagnosed with a first incident BC utilizing a WV Cancer Registry-Medicare linked dataset built to study cancer disparities in the state.

METHODS

Data Source

West Virginia Cancer Registry-Medicare-Area Resource File linked dataset. Established by the WV Department of Health and Human Resources in 1993, the West Virginia Cancer Registry (WVCR) is a state-level cancer registry that provides information on cancer incidence and mortality in WV (West Virginia Department of Health and Human Resources, 2012). The registry collects and provides data on the primary site of cancer, tumor grade, date and stage of diagnosis, date and cause of mortality, and demographics such as age, gender, race, and also zip code information (for location of residence). The de-identified linked WVCR-Medicare dataset was established at West Virginia University (WVU) in full compliance with the WVU Institutional Review Board and HIPPA requirements (Nadpara & Madhavan, 2012). The details of the WVCR-Medicare linkage and dataset are described elsewhere (Nadpara & Madhavan, 2012). Through the state and county Federal Information Processing Standards codes for each beneficiary, the Area Resource File (ARF) was linked to the WVCR-Medicare dataset to identify the census level information on healthcare facilities and socioeconomic characteristics of the region's population.

Study Design and Study Cohort

This retrospective study comprised of women age 70 and older with the first primary incident BC diagnosed in 2007. As persistence with mammography screening during the period of five years before BC diagnosis was to be evaluated, women age 70 and above who were continuously enrolled in Medicare parts A and B for at least five years before BC diagnosis, and who were not enrolled in health maintenance organizations (HMOs) at any time during the study period were included in the study. Women with a previous cancer, unknown/missing stage, and who were diagnosed through death certificate or autopsy were excluded from the study. Out of a total of 661 women diagnosed with BC in 2007, the following women were excluded: 168 women who were younger than 70 years at diagnosis, 99 women with previous cancer, seven women who were diagnosed during death or autopsy, 56 women for whom BC stage information was unknown/missing, 32 women who were not continuously enrolled in Medicare parts A and B, and 72 women who had been members of a HMO in the five years prior to diagnosis. From the remaining 227 women, only 6 women (2.6%) belonged to 'other' race which resulted in very small cell-size for stage at diagnosis categories, and hence were removed from the analyses. Finally, a total of 221 non-Hispanic white Appalachia-WV women were included in the study.

Measures

Dependent Variable-Stage at diagnosis: The SEER summary staging system which is a combination of the most accurate clinical and pathological documentation of the extent of disease (Young, Roffers, Ries, Fritz, & Hurlbut, 2001) and which uses all the data in the medical record was utilized to define BC stage at diagnosis. It was categorized into 'early stage'

consisting of carcinoma in situ and localized cancers, and 'late stage' consisting of regional and distant cancers.

Key Independent Variable-Persistence with mammography screening: This study utilized a three-step algorithm with sensitivity of 99.7% and positive predictive value of 97.4% of a screening designation to identify screening mammograms from the Medicare claims files (Fenton et al., 2014). As per this algorithm, firstly all the mammograms, irrespective of whether they were for screening or diagnostic purpose, were identified from the Medicare claims files for each woman in five years before her BC diagnosis. If a woman had a mammogram within nine months of another mammogram then those mammograms were removed. If a woman did not have a mammogram within nine months then the Healthcare Common Procedure Coding System (HCPCS) code for those mammograms was determined. If the HCPCS code for a mammogram was for 'screening' purpose then those mammograms were considered to be screening mammograms. If the HCPCS code for a mammogram was for 'diagnostic' purpose then the BC-related symptom within 349 days prior to the diagnostic mammogram were identified. If a women had a BC-related symptom beyond 350 days or more prior to a diagnostic mammogram then those mammograms were considered to be screening mammograms. All the mammograms with HCPCS code for 'screening' purpose and those for which BC-related symptom was beyond 350 days or more were considered to be 'actual' screening mammograms and were utilized to determine persistence with mammography screening for each woman in the study.

As defined in a recently published study, a woman was considered persistent with mammography screening if she had at least three screening mammograms in the five years prior to her BC diagnosis (Vyas et al., 2014). Hence, based on total number of screening mammograms a woman had in the five years prior to her BC diagnosis, the study cohort was dichotomized into non-persistent users (with 0-2 screening mammograms) and persistent users (with three or more screening mammograms).

Other Independent Variables: The covariates consisted of age at BC diagnosis (70-74, 75-79, 80 and older); census tract median household income (<$30,000; ≥$30,000); and census tract percentage of people age ≥ 25 years with at least 4 years of college education (<15%, ≥15%); comorbidity scores (0 (no comorbidity), 1, ≥2); the number of primary care physicians (PCP) visits in the five years before BC diagnosis categorized into two groups (0-23, ≥24) based on its median value; location of residence (metro, urban, rural) and the number of hospitals offering BC screening/mammography services in the area of residence categorized into 0, 1, ≥2. Comorbidity scores were calculated from the co-occurring chronic conditions obtained from the Medicare files.

Statistical Analyses

To determine significant differences between persistence with mammography screening groups across all the independent variables, chi-square statistics were conducted. In addition, significant differences between early and late stage BC across all the independent variables were analyzed. The percentage of women by stage of disease according to persistence with mammography screening was also determined. Logistic regression was conducted to determine the association between persistence with mammography screening and an early BC stage, after controlling for all the independent variables. "Late stage breast cancer" was used as the reference group for the dependent variable. From the logistic regression, the parameter estimates were transformed into odds ratios and their corresponding 95% confidence intervals were

determined and the findings that were significant with p-values less than or equal to 0.05 levels are discussed. All analyses were conducted using statistical analysis systems software SAS 9.4 (SAS® version 9.4, SAS Institute Inc., Cary, NC, USA).

RESULTS

Description of the Study Cohort by Persistence with Mammography Screening

The left columns of Table 1 characterize the study cohort of 221 elderly Appalachia-WV women diagnosed with first primary incident BC in 2007. A majority of the study cohort was age 80 and above (40%), resided in metro areas (54%), had household income below $30,000 (51%), resided in areas with higher education (54%), had no comorbidity (48%) and had higher PCP visits in five years before BC diagnosis. The right side column of Table 1 describes the results from the chi-square statistics for differences in persistence with mammography screening across all the independent variables. A majority of elderly Appalachia-WV women (51%) were persistent to mammography screening while 49% of the women were not persistent to mammography screening. Among all women age 70-79 years, a majority of them were persistent with mammography screening, while older women age 80 and older were less likely to be persistent with mammography screening. All the other independent variables were not significant in the chi-square analyses at the $\leq$ 0.05% level.

To identify if persistence with mammography screening would differ between women with ‘known’ and ‘unknown’ stage BC, analyses was conducted after retaining women with ‘unknown’ BC stage. It was found that there was no significant differences in persistence with mammography screening in women with ‘known’ and ‘unknown’ stage BC (data not shown).

Table 1
West Virginia Medicare FFS Beneficiaries with Incident Breast Cancer
By Persistence with Mammography Screening
West Virginia Cancer Registry-Medicare 2007 Cases

Variables	l	%	Persistent Users§	%	Non-Persistent Users	%	Sig
	221		113	51.1	108	48.9	
Stage at Diagnosis							***
Early Stage	175	79.2	100	88.5	75	69.4	
Late Stage	46	20.8	13	11.5	33	30.6	
Age at Diagnosis							*
70-74	72	32.6	38	33.6	34	31.5	
75-79	61	27.6	38	33.6	23	21.3	
≥80	88	39.8	37	32.7	51	47.2	
Location of Residence							
Metro	120	54.3	55	48.7	65	60.2	
Urban	63	28.5	40	35.4	23	21.3	
Rural	38	17.2	18	15.9	20	18.5	
Census Tract Household Income							
<$30,000	113	51.1	60	53.1	53	49.1	
≥$30,000	108	48.9	53	46.9	55	50.9	
Census Tract Education							
<15%	101	45.7	57	50.4	44	40.7	
≥15%	120	54.3	56	49.6	64	59.3	
Comorbidity							
0	105	47.5	60	53.1	45	41.7	
1	63	28.5	30	26.5	33	30.6	
≥2	53	24.0	23	20.4	30	27.8	
PCP visits							
0-23	109	49.3	55	48.7	54	50.0	
≥24	112	50.7	58	51.3	54	50.0	
Total BC Screening Centers							
0	21	9.5	9	8.0	12	11.1	
1	102	46.2	53	46.9	49	45.4	
≥2	98	44.3	51	45.1	47	43.5	

Note: FFS, Fee For Service; PCP, Primary Care Physicians; BC, Breast Cancer; Sig, Significance.
§Persistent users of screening mammograms are those women who have had at least three screening mammograms in the five years prior to their breast cancer diagnosis.

Asterisks represent statistically significant group differences based on $\chi 2$ tests by persistence with mammography screening
***P<0.001; **001<=P<.01

Description of the Study Cohort by Stage at Breast Cancer Diagnosis

Table 2 describes the results from the chi-square statistics for differences in stage at BC diagnosis across all the independent variables. Among all the persistent users of mammography screening, a majority (89%) were diagnosed at an early stage BC. All the other independent variables were not significant in the chi-square analyses at the $\leq$ 0.05% level.

Table 2
West Virginia Medicare FFS Beneficiaries with Incident Breast Cancer
By Stage at Diagnosis
West Virginia Cancer Registry-Medicare 2007 Cases

Variables	Early Stage	%	Late Stage	%	Sig
	175	79.2	46	20.8	
Persistence with Mammography Screening					***
Persistent Users	100	57.1	13	28.3	
Non-Persistent Users	75	42.9	33	71.7	
Age at Diagnosis					
70-74	55	31.4	17	37.0	
75-79	46	26.3	15	32.6	
≥80	74	42.3	14	30.4	
Location of Residence					
Metro	96	54.9	24	52.2	
Urban	51	29.1	12	26.1	
Rural	28	16.0	10	21.7	
Census Tract Household Income					
<$30,000	88	50.3	25	54.3	
≥$30,000	87	49.7	21	19.4	
Census Tract Education					
<15%	75	74.3	26	25.7	
≥15%	100	88.3	20	47.8	
Comorbidity					
0	86	49.1	19	41.3	
1	47	26.9	16	34.8	
≥2	42	24.0	11	23.9	
PCP visits					
0-23	84	48.0	25	54.3	
≥24	91	52.0	21	45.7	
Total BC Screening Centers					
0	18	10.3	3	6.5	
1	74	42.3	28	60.9	
≥2	83	47.4	15	32.6	

Note: FFS, Fee For Service; PCP, Primary Care Physicians; BC, Breast Cancer; Sig, Significance.
Asterisks represent statistically significant group differences based on $\chi 2$ tests by stage at diagnosis
***P<0.001

Stage at Breast Cancer Diagnosis by Persistence with Mammography Screening

Figure 1 describes disease stage by persistence with mammography screening. Among women who were persistent with mammography screening, an overwhelming 89% of them were diagnosed with an early stage disease. Among women who were not persistent with mammography screening, 69% were diagnosed with an early stage disease.

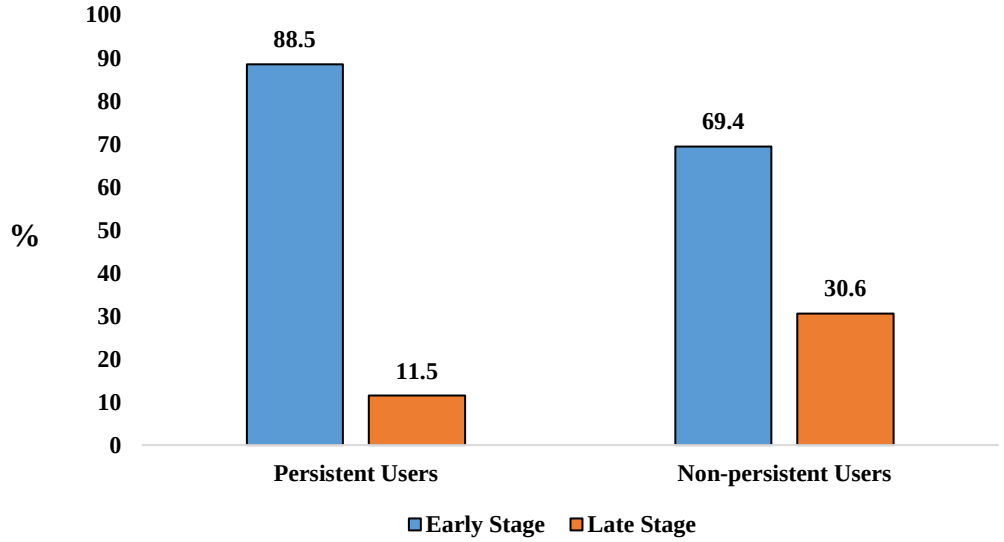

Figure 1: Stage at Breast Cancer Diagnosis by Persistence with Mammography Screening Among West Virginia Medicare Fee-for-Service Beneficiaries with Incident Breast Cancer – 2007 Cases

Association between Persistence with Mammography Screening and Stage at Breast Cancer Diagnosis

Table 3 describes the results from the multiple logistic regression. Appalachia-WV women who were persistent with mammography screening were four times more likely of being diagnosed at an early stage BC (Adjusted odds ratio (AOR) = 4.25, 95% confidence interval (CI) = 1.96-9.19) as compared to elderly women who were not persistent with mammography screening. No other factors significantly affected the probability of being diagnosed at an early stage except for persistence with mammography screening.

Table 3
Adjusted Odds Ratios and 95% Confidence Intervals from Logistic Regression
on Early Stage at Breast Cancer Diagnosis
For Persistence with Mammography Screening
West Virginia Cancer Registry-Medicare 2007 Cases

Variables	Early Breast Cancer Stage		
	AOR	95% CI	Sig
Persistence with Mammography Screening			
Persistent Users	4.25	[1.96 , 9.19]	***
Non-Persistent Users	**1**		
Age at Diagnosis			
70-74	**1**		
75-79	0.75	[0.31 , 1.80]	
80,+	1.69	[0.71 , 4.00]	
Location of Residence			
Metro	**1**		
Urban	1.36	[0.53 , 3.50]	
Rural	1.29	[0.37 , 4.53]	
Census Tract Household Income			
<$30,000	**1**		
≥$30,000	1.03	[0.40 , 2.65]	
Census Tract Education			
<15%	**1**		
≥15%	2.24	[0.87 , 5.76]	
Comorbidity			
0	**1**		
1	0.72	[0.31 , 1.69]	
≥2	1.01	[0.39 , 2.59]	
PCP visits			
0-23	**1**		
≥24	1.15	[0.54 , 2.45]	
Total BC Screening Centers			
0	**1**		
1	0.26	[0.06 , 1.11]	
≥2	0.48	[0.10 , 2.30]	

Note: PCP, Primary Care Physicians, BC, Breast Cancer; AOR, Adjusted Odds Ratio; CI. Confidence Interval. "Late stage at breast cancer diagnosis" is the reference group for the dependent variable. 1 represents the reference groups within each independent variable. Asterisks represent statistically significant group differences compared with the reference group

***P<0.001

DISCUSSION

To our knowledge, this is the first study which assessed the effect of persistence with mammography screening on stage at BC diagnosis in elderly women from a rural and medically underserved state such as WV, after accurately identifying screening mammograms from the Medicare claims data using a recently published algorithm. In the absence of data on persistence with mammography screening from a rural setting and from non-SEER-Medicare states, this study fills a significant literature gap related to the important issue of mammography screening among elderly, rural, and underserved women of Appalachia-WV.

Nearly half of elderly Appalachia-WV women diagnosed with BC were persistent with mammography screening in the five years prior to their BC diagnosis; the proportion which is higher than the proportion of elderly women who were regular users of mammography screening as reported in previous studies (Badgwell et al., 2008; McCarthy et al., 2000; Randolph et al., 2002; Vyas et al., 2014). Though the proportion of elderly WV women who were persistent with mammography screening is higher, the findings of the study should be interpreted with caution given the smaller sample size of the study cohort.

Among those who were persistent with mammography screening, an overwhelming 89% of elderly WV women were diagnosed at early stages of BC. In addition, elderly Appalachia-WV women who were persistent with mammography screening were four times more likely to be diagnosed at early stages of BC, thereby indicating the beneficial effects of mammography screening in this elderly group which is inherently at higher risk of advanced and unstaged BC. The AOR in this study representing the impact of persistence with mammography screening on early stage BC is consistent though higher than those reported in the previous studies (Badgwell et al., 2008; McCarthy et al., 2000; Vyas et al., 2014). This may be because of smaller sample size of the study which may have affected both AOR and wider confidence intervals.

Even though current BC screening guidelines from US Preventive Services Task Force reported insufficient evidence for mammography screening for women above 74 years (Siu, & U.S. Preventive Services Task Force, 2016), our study findings demonstrated a higher likelihood of diagnosing BC at early stages for these elderly women who were persistent with mammography screening. Our findings also suggest that among women age 80 and above, a higher proportion was not persistent with mammography screening, a finding consistent with a previous study (Badgwell et al., 2008). Hence, efforts towards increasing awareness about regular mammography screening should be highly encouraged in the elderly women age 70 and above for whom there are no clear guidelines. However, with increasing evidence of overdiagnosis of BC in these elderly women (van Ravesteyn et al., 2015), healthcare providers should also consider discussing the benefits and harms of mammography screening to make informed choices.

Even though a higher proportion of the elderly Appalachia-WV women included in the analysis had lower income and education levels, had at least one comorbidity and resided in areas with no or just one BC screening center, there were no significant differences between the persistent users and non-persistent users except for the variable age. In the multiple logistic regression model, only persistence with mammography screening was highly associated with early stages of BC thereby indicating that none of the included covariates had any negative

impact on persistence with mammography screening in the Appalachia-WV women diagnosed with BC. Thus, these women were diagnosed at earlier stages when the treatments are usually less aggressive, and survival is significantly better.

A major strength of this study is that the findings of this study help in understanding the benefits of persistence with mammography screening in elderly women age 70 and above in a rural setting such as WV, which has lower mammography screening rates than women in the age group 50-65 years of age (Khanna et al., 2009). Utilization of the recently published algorithm with very high sensitivity and high predictive value to identify the screening mammograms from the Medicare claims files (Fenton et al., 2014) must also be considered a major strength of the study. However, there are some limitations worth noting. As this study utilized a cancer registry-Medicare linked database, certain patient characteristics such as annual household income, education level, access to BC screening centers at the patient level are not available, and hence census tract information for these variables were utilized which may provide overestimation of these variables. However, census-tract information for these variables provide complimentary information on living circumstances and have been widely used in the epidemiological studies (Roux, Kiefe, Jacobs, Haan, & Jackson, 2001; Krieger, 1992). Women who belonged to HMOs were excluded from the analyses as the use of physician services cannot be determined in Medicare beneficiaries enrolled in HMO plans, and thus mammography screening in women enrolled in these plans cannot be assessed. Another limitation of the study is the smaller sample size which may affect the precision of the estimates. In addition, certain unmeasured confounders such as severity of comorbidities, functional limitations, body mass index and views and attitudes towards mammography screening which may affect screening behavior were not accounted for in the analyses. Overdiagnosis of breast cancer in these elderly women was not captured and accounted for in the study; however overdiagnosis can be precisely measured in a randomized controlled trial with a long follow-up period. Lastly, the findings of the study are generalizable only to elderly Appalachia-WV women age 70 and above, and to other rural areas having similar characteristics as that of WV.

CONCLUSION

More than half of the elderly Appalachia-WV women with BC were persistent with mammography screening before their diagnosis. Persistence with mammography screening is significantly associated with earlier stage at BC diagnosis in this rural and underserved population, which suggests targeting interventions to encourage regular mammography use in these women.

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FOOTNOTES

Conflicts of Interest: The authors report no conflicts of interests.

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