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Ethnic Disparities in Cervical Cancer Survival Among Texas Women

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Abstract

Objective: The aim of this work was to determine whether minority women are more likely to die of cervical cancer. A population-based cohort study was performed using Texas Cancer Registry (TCR) data from 1998 to 2002.

Methods: A total of 5,166 women with cervical cancer were identified during 1998–2002 through the TCR. Measures of socioeconomic status (SES) and urbanization were created using census block group-level data. Multilevel logistic regression was used to calculate the odds of dying from cervical cancer by race, and Cox proportional hazards modeling was used for cervical cancer-specific survival analysis.

Results: After adjusting for age, SES, urbanization, stage, cell type, and treatment, Hispanic women were significantly less likely than non-Hispanic White women to die from cervical cancer (adjusted hazard ratio [aHR]=0.69; 95% CI [confidence interval]=0.59–0.80), whereas Black women were more likely to die (aHR=1.26; 95% CI=1.06–1.50). Black and Hispanic women were more likely to be diagnosed at a later stage than White women. Black women were significantly less likely to receive surgery among those diagnosed with localized disease ($p=0.001$) relative to both White and Hispanic women.

Conclusions: Relative to non-Hispanic White women, Black women were more likely to die of cervical cancer while Hispanic women were less likely to die; these survival differences were not explained by SES, urbanization, age, cell type, stage at diagnosis, or treatment.

Introduction

REASONS FOR RACIAL/ETHNIC DISPARITIES in cervical survival have yet to be determined. Factors, including socioeconomic status (SES), urbanization, stage at diagnosis, and treatment received, may explain decreased survival among Black women. Of studies addressing SES and cervical cancer survival,^{1–10} approximately one-third found that the association between low SES and poorer survival persisted after controlling for race/ethnicity.^{3,7,11} In our prior analysis, we observed that women living in neighborhoods of lower SES were less likely to survive from cervical cancer, yet Hispanic women had a pronounced survival advantage.² We hypothesized that differences in treatment received may influence these observed survival differences.

This report expands on the earlier study² using newly available treatment data obtained from the Texas Cancer Registry (TCR), as well as more precise census block group-

level data to define SES. The purpose of this population-based cohort study was to determine whether women of minority race remained at greater risk of dying from cervical cancer after considering demographic attributes, treatment received, cell type, and stage at diagnosis.

Methods

Cervical cancer cases were obtained from the TCR, a population-based registry of all cancer cases diagnosed in Texas. These data met Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) and North American Association of Central Cancer Registries (NAACCR) national cancer incidence data standards, and had a case completeness proportion of 99%.¹² Institutional Review Boards from the Texas Department of State Health Services and the University of Texas Health Science Center at Houston approved the study protocol. All data were analyzed

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using the statistical software package Intercooled Stata version 9.2. Incident cases from 1998–2002 were linked with the Texas Department of State Health Services mortality data through December 31, 2003 to identify vital status, date of death, and underlying causes of death. The study population included women 18 years or older diagnosed with an invasive primary cervical cancer (ICD-0-3 codes C53.0, C53.1, C53.8, and C53.9; excluding the following histology codes: 9590–9989, 9050–9055, and 9140).

Socioeconomic status, urbanization, and race

Individual data to characterize SES is not collected by the TCR; thus, block group-level data (U.S. Census from 2000) was used to create a composite variable for SES based on an accepted measure of community-level SES.^{13–15} Briefly, individual items from the census included in this measure were: median household income, proportion below poverty, proportion with a college education, proportion with a management/professional occupation, and median home value. Principal factor analysis with varimax rotation was utilized to retain one factor representing a composite SES. Analysis of the individual components of the composite variable showed good internal consistency (Cronbach's alpha = 0.87). SES was then categorized into quintiles based on the distribution among Texas residents. Data was geocoded by batch method using Atlas, version 4.0. Addresses that did not match were manually geocoded by relaxing attributes such as zip code and street (13% of all cases); by relaxing the requirement of matching all attributes, the probability of finding a match is improved. These addresses were not assigned to the center of the zip code, but used the remaining attributes of the address to code the data. Remaining cases were assigned to the block group of a randomly matched case identical to their zip code, race, age, and sex (16.5% of all cases).

Urbanization was defined using Rural Urban Commuting Area Codes (RUCA) available at the census tract level.¹⁶ The following categories were used: urban, large town, small town, and isolated town.

Race/ethnicity was abstracted from medical records by cancer registrars and categorized as non-Hispanic White, hereafter White (referent group); non-Hispanic Black, hereafter Black; and Hispanic. We did not have data to define race within the Hispanic grouping; however, in Texas, the overwhelming majority of Hispanic women are White and from Mexico or Central America.

Cancer stage

Data characterizing stage at diagnoses were obtained from the TCR and reported using the Surveillance, Epidemiology and End Results (SEER) summary staging guide.

Treatment

First course of treatment received was available from the TCR. Receipt of any treatment was first defined as a dichotomous variable: received any type of treatment or received no treatment. Treatments were then classified by the combination of all types received: surgery alone; surgery and chemotherapy or radiation; and chemotherapy or radiation alone. The type of surgery was also available and was categorized as follows: (1) loop, laser, or cone, (2) radical hyster-

ectomy, (3) total abdominal or vaginal hysterectomy, (4) exenteration, and (5) surgery of unknown type. For the purposes of this model, we assumed that those missing for the treatment did not receive the treatment.

Cervical cancer survival

Survival was measured in months from date of diagnosis to date of follow-up; 5,454 women were reported to the TCR with cervical cancer during 1998–2002. Vital status was determined through 2003 to allow for at least 1 year of follow-up (range, 1–6 years). Women were excluded from analyses for the following reasons: (1) unknown race/ethnicity ($n = 169$), (2) diagnosed by death certificate only ($n = 111$), and (3) no corresponding census data ($n = 8$). A total of 5,166 were available for final analysis. Additionally, women who died from causes other than cervical cancer ($n = 436$) were excluded from cause-specific survival analysis. The racial/ethnic distribution of women excluded from survival analysis did not differ from the full sample. Potential confounders included age, stage, and cancer cell type (grouped as squamous and non-squamous). The majority of cervical cancer is squamous cell in origin. Non-squamous cervical cancer is primarily adenocarcinoma and may have a lower survival rate than squamous cell cancer of the cervix.¹⁷

Statistical analysis

Using Stata version 9.2, the Generalized Linear Latent and Mixed Models (GLLAMM) program, was used to perform multilevel analyses to determine correlates of (1) being diagnosed beyond localized disease and (2) dying from cervical cancer. This hierarchical regression model was used to account for block group (community)-level measures of SES and urbanization combined with individual-level data, including race/ethnicity, age, cancer stage, cell type, vital status, and treatment. Multinomial logistic regression, calculating odds ratios (Ors), was used to investigate treatment differences across race/ethnicity while adjusting for SES, urbanization, age, cancer stage, and cell type.

A standard Kaplan-Meier approach was used in this survival analysis; survival curves are presented in Figure 1 by the three race/ethnicity groups. Differences in the following list of risk factors were investigated by race/ethnicity using multivariate modeling: SES, urbanization, age, stage, cell type, stage, and treatment received (Table 1). Multivariate Cox proportional hazards modeling was used to estimate the relative risk of dying from cervical cancer by race/ethnicity while adjusting for the covariates listed above, dying from other causes were censored (Table 2). Lastly, to examine the effect of stage on the association between race/ethnicity and survival, a parallel set of the Cox proportional hazard analyses to that presented in Table 1 were replicated by stage with cervical cancer-specific survival as the outcome (Table 3).

Results

Race/ethnic differences by covariates

When compared with White women, both Black and Hispanic women were more likely to live in lower SES neighborhoods and urban areas (Table 1). Black women were significantly more likely to be diagnosed at a later age compared with White or Hispanic women. Black and Hispanic

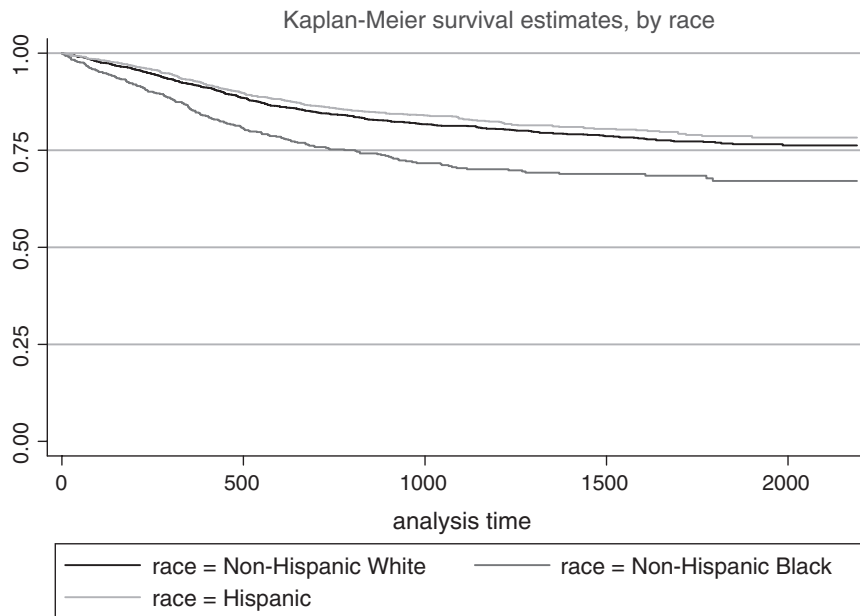


FIG. 1. Kaplan-Meier curves for cervical cancer-specific survival by race.

TABLE 1. MULTILEVEL ANALYSIS OF STAGE AT DIAGNOSIS BY SOCIODEMOGRAPHIC CHARACTERISTICS OF 5,166 CERVICAL CANCER CASES REPORTED TO THE TEXAS CANCER REGISTRY 1998–2002[†]

	<i>Non-Hispanic White</i>	<i>Non-Hispanic Black</i>	<i>Hispanic</i>
All	2698	711	1757
SES			
Highest SES	40.7%	16.5%	14.8%
Middle SES	34.6%	27.3%	26.4%
Lowest SES	24.7%	56.2%	58.8%
<i>p</i> for trend	REF	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Urbanization			
Urban	80.6%	86.9%	87.0%
Large town	10.4%	8.0%	9.0%
Small town/rural	9.0%	5.1%	4.0%
<i>p</i> for trend	REF	(<i>p</i> < 0.0001)	<i>p</i> < 0.0001
Age at diagnosis (mean)	49.71 (REF)	52.71 (<i>p</i> < 0.0001)	49.01 (<i>p</i> = 0.15)
Cell type			
Squamous	74.1%	83.0%	81.4%
Non-squamous	25.9%	17.0% (<i>p</i> < 0.0001)	18.6% (<i>p</i> < 0.0001)
Stage of diagnosis			
Localized	52.8%	43.2%	47.2%
Regional	25.0%	32.5%	30.3%
Distant	7.7%	9.1%	8.4%
Trend (excludes unknown stage)	REF	(<i>p</i> = 0.009)	(<i>p</i> = 0.04)
Unknown	14.5%	15.2%	14.1%
Treatment			
No treatment documented	10.86%	12.13% (0.44)	13.36% (0.48)
Missing treatment data	28.27%	29.96% (0.92)	29.16% (0.84)
Type of treatment			
Surgery alone	40.57%	26.86% (0.003)	31.15% (0.004)
Surgery + chemo/radiation	19.19%	17.58% (0.32)	20.56% (0.43)
Chemo/radiation	29.38%	42.19% (0.002)	36.16% (0.11)
Among those with localized disease	<i>n</i> = 1426	<i>n</i> = 307	<i>n</i> = 827
Surgery	77.98%	62.54% (0.001)	72.29% (0.21)
Among those diagnosed at regional/late stage at diagnosis	<i>n</i> = 882	<i>n</i> = 296	<i>n</i> = 681
Surgery + chemo/radiation; or chemo/radiation	78.68%	81.08% (0.57)	80.03% (0.92)

[†] Adjusting for all variables in the table.
 SES, socioeconomic status; REF, referent group.

TABLE 2. MULTIVARIATE PREDICTORS OF CERVICAL CANCER-SPECIFIC SURVIVAL FOR WOMEN DIAGNOSED AND REPORTED TO THE TEXAS CANCER REGISTRY DURING 1998–2002 WITH TREATMENT DATA

	N*	CxCa mortality rate [†]	Adjusted HR (95% CI) [‡]
All	4730	5.42	
Race/ethnicity			
Non-Hispanic White	2,458	5.16	1.00 (REF)
Non-Hispanic Black	636	8.44	1.26 (1.06–1.50)
Hispanic	1,636	4.70	0.69 (0.59–0.80)
SES			
High SES	1,365	4.42	1.00 (REF)
Mid SES	1,462	5.65	1.11 (0.93–1.32)
Low SES	1,903	5.97	1.27 (1.07–1.51)
<i>p</i> for trend			0.005
Urbanization			
Urban	3,971	5.28	1.00 (REF)
Large town	449	5.29	1.10 (0.88–1.37)
Small town/rural	310	7.11	1.27 (1.01–1.61)
<i>p</i> for trend			0.04
Age [continuous]	4,730	5.42	1.02 (1.01–1.02)
Cell type			
Squamous	3,710	5.50	1.00 (REF)
Non-squamous	1020	5.11	0.99 (0.84–1.16)
Treatment			
No treatment	508	10.08	1.59 (1.32–1.92)
Any treatment	4,222	4.95	1.00 (REF)
Type of treatment			
Surgery	1,749	1.02	0.20 (0.13–0.30)
Surgery + chemo/radiation	926	6.02	0.63 (0.44–0.89)
Chemo/radiation	1548	10.63	0.85 (0.70–1.04)
Surgery by type	2675		
Leep, laser, cone	536	4.08	0.75 (0.60–0.94)
Radical hysterectomy	798	1.77	0.39 (0.29–0.52)
Total abdominal or vaginal hysterectomy	1044	1.79	0.39 (0.30–0.50)
Exenteration	20	9.20	0.87 (0.41–1.84)
Surgery unknown type	256	4.19	0.51 (0.37–0.69)
Stage of diagnosis			
Localized	2,560	1.87	1.00 (REF)
Regional	1,441	8.95	4.30 (3.62–5.12)
Distant	418	30.32	12.99 (10.65–15.85)
Trend (excludes unknown stage)			<i>p</i> < 0.001
Unknown	747	6.03	2.53 (2.02–3.17)

*Women dying from causes other than cervical cancer ($n = 436$) were excluded from analysis.

[†]Mortality rate calculated per 1000 woman months.

[‡]Adjusted for age (continuous), race, stage, cell type, SES, urbanization, and treatment.

CxCa, cervical cancer; HR, hazard ratio; CI, confidence interval; SES, socioeconomic status; REF, referent group.

women were more likely than Whites to be diagnosed with squamous cell cervical cancer. Black (56.8%) and Hispanic women (52.9%) were more likely to be diagnosed with advanced disease (regional or distant stages) relative to White women (47.2%). The adjusted odds ratio (aOR) for this association for Black relative to White women was 1.27 (95% confidence interval [CI] = 1.06–1.52) and 1.16 (95% CI = 1.02–1.33) for Hispanic relative to White women. ORs were adjusted for age, race/ethnicity, SES, urbanization, and cell type. No statistically significant differences in the proportion of women who did not receive treatment or the completeness of medical records were noted across race/ethnicity. However, Black (26.9%) and Hispanic women (31.2%) were less likely to have received surgery alone compared with Whites (40.6%); the corresponding aOR for Black women was 0.61 (95% CI = 0.54–0.70) and 0.82 (95% CI = 0.76–0.88) for Hispanic women. Black women were more likely to have received

radiation or chemotherapy yet no surgery when compared with Whites (aOR = 1.55; 95% CI = 1.36–1.76). When restricted to localized disease, where surgery is the optimal treatment, Black women were significantly less likely to receive surgery compared to White women (aOR = 0.55; 95% CI = 0.45–0.67).

Kaplan-Meier survival curves by race/ethnicity

As can be observed in Figure 1, the survival curve for Black women is considerably lower than that for White or Hispanic women. This figure does not adjust for covariates. For these analyses, we turn to multivariate Cox.

Multivariate Cox analysis and multilevel GLLAMM

Black women were more likely to die of cervical cancer (HR: 1.26; 95% CI = 1.06–1.50), while Hispanic women were

TABLE 3. MULTIVARIATE PREDICTORS OF SURVIVAL FOR WOMEN DIAGNOSED WITH CERVICAL CANCER AND REPORTED TO THE TEXAS CANCER REGISTRY DURING 1998–2002 WITH TREATMENT DATA BY STAGE FOR CERVICAL CANCER-SPECIFIC MORTALITY

Attribute	Localized stage, adjusted HR (95% CI) [†]	Regional/distant stage, adjusted HR (95% CI) [†]	Unknown stage, adjusted HR (95% CI) [†]
<i>n</i> = 4370*	<i>n</i> = 2,441	<i>n</i> = 1,620	<i>n</i> = 669
Non-Hispanic White	1.00 (REF)	1.00 (REF)	1.00 (REF)
Non-Hispanic Black	1.19 (0.79–1.79)	1.16 (0.93–1.44)	1.83 (1.19–2.82)
Hispanic	0.83 (0.58–1.17)	0.66 (0.54–0.80)	0.95 (0.64–1.42)
Neighborhood SES			
High SES	1.00 (REF)	1.00 (REF)	1.00 (REF)
Mid SES	1.52 (1.03–2.24)	0.99 (0.80–1.23)	1.13 (0.72–1.79)
Low SES	1.43 (0.96–2.13)	1.15 (0.93–1.42)	1.11 (0.72–1.73)
<i>p</i> for trend	0.10	0.15	0.67
Urbanization			
Urban	1.00 (REF)	1.00 (REF)	1.00 (REF)
Large town	0.95 (0.59–1.54)	1.07 (0.81–1.41)	1.06 (0.64–1.75)
Small town/rural	1.00 (0.59–1.69)	1.31 (0.97–1.76)	1.59 (0.92–2.73)
<i>p</i> for trend	0.93	0.09	0.13
Age [continuous]	1.03 (1.02–1.04)	1.01 (1.00–1.02)	1.03 (1.02–1.04)
Cell type			
Squamous	1.00 (REF)	1.00 (REF)	1.00 (REF)
Non-squamous	1.06 (0.76–1.48)	1.13 (0.93–1.37)	0.93 (0.60–1.44)
Treatment			
Any treatment	1.00 (REF)	1.00 (REF)	1.00 (REF)
No treatment	4.56 (3.10–6.76)	1.94 (1.51–2.52)	1.17 (0.84–1.61)
Type of treatment			
Surgery	0.07 (0.04–0.12)	0.24 (0.16–0.37)	0.22 (0.11–0.44)
Surgery + chemo/radiation	0.27 (0.16–0.43)	0.44 (0.33–0.59)	1.12 (0.68–1.86)
Chemo/radiation	0.56 (0.37–0.85)	0.60 (0.46–0.78)	1.28 (0.90–1.82)
Surgery by type			
Leep, laser, cone	0.40 (0.24–0.64)	1.03 (0.78–1.36)	0.51 (0.28–0.94)
Radical hysterectomy	0.21 (0.12–0.37)	0.39 (0.27–0.54)	0.29 (0.09–0.90)
Total abdominal or vaginal hysterectomy	0.20 (0.12–0.31)	0.46 (0.33–0.62)	0.50 (0.24–1.04)
Exenteration	1.04 (0.14–7.65)	0.74 (0.28–2.00)	2.05 (0.46–9.14)
Surgery unknown type	0.30 (0.12–0.76)	0.60 (0.42–0.85)	0.42 (0.17–1.04)

*Women dying from causes other than cervical cancer (*n* = 436) were excluded from analysis.

[†]Adjusted for age (continuous), race, stage, cell type, SES, urbanization, and treatment.

SES, socioeconomic status; HR, hazard ratio; CI, confidence interval; REF, referent group.

less likely to die of cervical cancer (HR: 0.69; 95% CI = 0.59–0.80) when compared with White women and adjusting for confounders (Table 3). A similar pattern was also observed for the multilevel logistic analysis for cervical cancer-specific mortality as well as all cause survival (data not presented).

Other demographic factors associated with shorter cervical cancer-specific survival included lower SES, more rural residence, and increased age (Table 2). Not receiving treatment was associated with a 59% increased risk of dying from cervical cancer. Receipt of surgery alone was associated with a significant increase in survival (HR: 0.20; 95% CI = 0.13–0.30; Table 2). Similarly, receipt of surgery in combination with chemotherapy and/or radiation increased survival by 37%. As anticipated, advanced stage at diagnosis was associated with reduced survival. With the exception of the association with urbanization, all findings from survival analysis (Table 2) were supported in the multilevel logistic regression analysis (data not presented). Multivariate Cox analysis for cervical cancer-specific survival by stage (localized, regional/distant, and unknown stage; Table 3)

Analysis conducted by stage revealed that Black women with an unknown stage at diagnosis were almost twice as likely to die of cervical cancer (*p* < 0.0001) relative to Whites.

A reduced risk of dying of cervical cancer for Hispanic women relative to White women was observed, yet only among those diagnosed at regional or distant stage (Table 3).

Not receiving treatment was strongly associated with reduced survival for those diagnosed with localized and regional/distant disease. Receipt of surgery was associated with increased survival at all stages, while chemotherapy and radiation were associated with reduced survival for those diagnosed with localized and regional/distant disease (Table 3).

Discussion

The persistent survival advantage observed for Hispanic women corroborates our earlier analysis which did not have data to characterize treatment.² However, treatment did not explain survival differences between Hispanic and White women.

It is puzzling that Hispanic women have better survival than White women despite their lower SES. Reasons for this “Hispanic paradox”^{18–20} may include differences in comorbid conditions, social support, religion/faith, or other cultural influences.

While Hispanic women appear to have a cervical cancer survival advantage relative to White women, Black women were more likely to die of cervical cancer particularly if stage at diagnosis was unknown. Among those diagnosed with localized disease, Black women were significantly less likely to have surgery, while Hispanic women were similar to Whites in their receipt of surgery. These data suggest that Black women may receive less optimal treatment and are more likely to die of cervical cancer even among those who receive treatment. Explanations for this disparity in cervical cancer treatment and survival may include residual confounding by individual SES. However, Hispanic women reside in similar if not lower SES neighborhoods than do Black women yet Hispanic women have a survival advantage. Hispanic women do have treatment rates that are comparable to White women. Perhaps Hispanic women have social networks that support their receipt of health care at rates greater than that of White or Black women.

Strengths and weaknesses of the study

The use of a population-based cancer registry that meets national data quality standards and a high case completeness rate (99%) is a strength for this study.¹²

The use of census block group-level data to characterize SES is a strength as was the addition of treatment data. Missing data is always a limitation of analyses based on existing records. Older women ($p = 0.001$), those living in areas of very low SES ($p = 0.01$), those with no record of treatment ($p < 0.001$), and women with squamous cell cervical cancer ($p = 0.001$) were more likely to be missing stage information. In these data, missing data to characterize stage at diagnosis is likely not missing at random, and may be due to poor health status of the patient due to comorbidities. Women with missing treatment information were more likely to live in areas of very low SES ($p = 0.008$), large towns ($p = 0.007$), and be diagnosed in late stage ($p < 0.001$) or be missing stage ($p < 0.001$). We do not have information on comorbid conditions or other important risk factors for cervical cancer including cigarette smoking or education. However, neighborhood SES is highly correlated with individual education and smoking status.

We did not have information on insurance status for this analysis. An estimated 43% of Texans under the age of 65 had no health insurance for all or part of 2002–2003, and minority women are overrepresented among the uninsured.²¹ Insurance status may explain some of the observed differences in Black relative to White women, but not between Hispanic and Black women. Other investigators²² have posited that strong family and community ties, and willingness to pool resources may explain better outcomes for Hispanic women relative to White and Black women. While we did evaluate rural residence as a proxy for transportation barriers, we could not measure other social or cultural barriers to care.

Suggested future research directions with surveillance data include obtaining data at the individual level to better characterize SES, perhaps through health insurance coverage. Obtaining information on comorbid conditions as well as smoking status would also be an important contribution to

better understanding the effect of race/ethnicity on cervical cancer survival.

Further efforts are needed to better understand why Black women in particular have lower survival from cervical cancer and lower rates of treatment. Possible avenues to explore may include communication barriers between patients and providers, limited insurance coverage, claims denials, competing obligations such as caring for parents, children, and/or grandchildren, and limited social support to negotiate health care systems. Both qualitative and quantitative research may be beneficial in understanding why Black women are more likely than White women to die of cervical cancer.

Disclosure Statement

No competing financial interests exist.

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