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Guideline-Adherent Treatment, Sociodemographic Disparities, and Cause-Specific Survival for Endometrial Carcinomas

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BACKGROUND: Adherence to National Comprehensive Cancer Network guidelines have been adopted as the standard of care for various cancers and have been cited to have survival benefits. Few studies have examined the association of adherent treatment and endometrial cancer survival among various racial/ethnic groups and socioeconomic statuses. **METHODS:** Between January 1, 2006 and December 31, 2015, 83,673 women diagnosed with endometrial carcinomas were identified from the Surveillance, Epidemiology, and End Results database. Descriptive statistics of demographic and clinical characteristics were performed. Cox-proportional hazards models were used to examine the effect on cause-specific survival for adherence to guidelines across racial/ethnic and socioeconomic groups. **RESULTS:** Within our sample, 59.5% were treated according to guidelines. Nonadherence to treatment guidelines was significantly associated with decreased survival compared with adherent care (adjusted hazard ratio [HR], 1.59; 95% CI, 1.52-1.67). Being of Black (adjusted HR, 1.41; 95% CI, 1.32-1.51) or Native Hawaiian/Pacific Islander (adjusted HR, 1.44; 95% CI, 1.19-1.73) race/ethnicity compared with White women was significantly associated with worse survival. Being of Asian race/ethnicity (adjusted HR, 0.86, 95% CI, 0.78-0.94) was significantly associated with improved survival compared with White women. Lower neighborhood socioeconomic status was associated with a negative effect on survival relative to women in the highest socioeconomic status category. **CONCLUSIONS:** Findings from this study suggest treatment adherence is an independent predictor of improved survival; however, improved survival was not observed equally among all racial/ethnic and socioeconomic status groups. *Cancer* 2021;0:1-9. © 2021 American Cancer Society.

LAY SUMMARY:

- The National Comprehensive Cancer Network (NCCN) has developed guidelines for physicians to follow in treating various cancers. Within this study of 83,673 women with endometrial cancer, 59.5% of women were treated according to the NCCN guidelines. The findings suggest following NCCN guidelines for treatment of endometrial cancer improves survival.
- Black or Native Hawaiian/Pacific Islander race and lower neighborhood socioeconomic status has worse survival rates compared with other groups, indicating the importance of exploring other factors that may shape treatment across racial/ethnic and socioeconomic status groups.

KEYWORDS: endometrial neoplasms, health care disparities, race, social class, survival analysis, treatment adherence.

INTRODUCTION

Uterine cancer is the most common gynecologic malignancy among women in the United States.¹⁻⁴ Endometrial carcinomas represent the most common form of uterine cancer and among those, over 80% are diagnosed at an early stage and low grade.^{1,5,6} Uterine cancer incidence in the United States has steadily risen over the last few decades,⁷ increasing 14.5% from 2006 to 2016.⁸ A recent report notes increases in uterine cancer for all racial/ethnic groups, with the lowest increases among White women.⁷ In addition, uterine cancer mortality rates are also rising.^{3,4,7} Disparities in mortality from uterine cancer are well documented. Black women experience the highest mortality rates, double those among White and Latina women; this pattern has remained consistent over time.^{8,9} The 5-year-survival rate for localized uterine cancer is 95%,⁸ the highest among all gynecologic cancers. However, disparities in survival are also apparent as the lowest survival is observed among Black women.⁸ Although there are known disparities for uterine cancer between White and Black women across the cancer continuum, population-based studies are needed to investigate treatment differences across various racial/ethnic groups.

The National Comprehensive Cancer Network (NCCN) has established evidenced-based and consensus-driven guidelines that have widely been adopted as the standard of care for various cancers.¹⁰⁻¹⁴ Adherence to NCCN guidelines has been cited in the literature to have a survival benefit for sites such as endometrial,¹⁵ ovarian,^{14,16} cervical,¹⁷

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pancreatic,¹¹ colorectal,¹⁸ melanoma,¹⁹ gastric,¹³ and head and neck cancers.²⁰ These guidelines have also been viewed as a measure of quality of care and have shown improved cost effectiveness.^{21,22} Despite these benefits, past research on NCCN guidelines has shown that rates of adherence remain low.^{10,11,16,17,22,23} Studies have shown that rates of adherence and standard treatment regimens are lower for Black women when compared with White women.^{4-6,11,16,21} Additionally, studies that examine neighborhood socioeconomic status (SES) as a predictor for adherence have found that rates of adherence are lowest for lower SES groups.^{3,16,17,21,22}

Despite the high endometrial cancer prevalence in the United States, there is limited data examining rates of adherence to NCCN-treatment guidelines among women with endometrial cancer. Although there are known disparities in treatment, mortality, and survival between Black and White women with endometrial cancer, there is a lack of research on the association of adherent treatment and endometrial cancer survival among other racial/ethnic groups in the United States. Furthermore, examination of treatment adherence to endometrial cancer guidelines across SESs is needed to see if there are similar disparities within lower SES groups as we have seen in other cancer sites. Therefore, the objectives of this study were to 1) evaluate adherence to NCCN guidelines among women with endometrial carcinomas and 2) quantify the impact of adherence to NCCN guidelines on cause-specific survival across racial/ethnic and socioeconomic groups.

MATERIALS AND METHODS

Data Source and Study Population

This study used data from the Surveillance, Epidemiology, and End Results (SEER) national cancer registry from between January 1, 2006 and December 31, 2015, and received approval from the institutional review board of the University of California, Irvine (UCI IRB HS# 2019-5081). The SEER database compiles population-based cancer registries throughout the United States and includes information on demographics, cancer characteristics, initial cancer treatment, and mortality. Cases were identified using the SEER primary site code for endometrial cancers (C54.1) and histologic types classified as endometrial carcinomas.^{7,24}

The study population included women aged 18 years and older who were diagnosed with their first or only endometrial cancer with carcinoma histology. Exclusion criteria included unknown or missing cause of death, unknown race/ethnicity, unknown census tract information,

unknown stage of diagnosis, missing or unknown clinical data (ie, surgical treatment, surgical staging, extent of disease, diagnostic confirmation), and cases or information obtained from autopsy or death certificates.^{21,22} After exclusions (Fig. 1), 83,673 women diagnosed with endometrial carcinomas were included in the analyses.

Measures

The main outcome variable was endometrial cancer-specific survival, defined as time since diagnosis to death caused by endometrial cancer. Predictors of survival included patient and clinical characteristics. Patient characteristics included race/ethnicity, neighborhood SES, age at diagnosis, and year of diagnosis. Race/ethnicity of the patient was classified into non-Latina White (henceforth White), non-Latina Black (henceforth Black), Latina, non-Latina Asian (henceforth Asian), non-Latina Native Hawaiian/Pacific Islander (henceforth NHPI), and non-Latina American Indian/Alaska Native (henceforth AI/AN). Neighborhood SES was classified into quintiles based on the Yost score.²⁵ The Yost score is a composite index of neighborhood SES using census tracts in combination with several indicators of education, income, and occupation.²⁵ Age at diagnosis was used as a categorical variable based on quartile distribution: <54 years, 54 to 61 years, 62 to 68 years, and ≥69 years. Year of diagnosis was a continuous variable. Clinical characteristics included adherence to NCCN-treatment guidelines, stage of diagnosis, histology, and grade of disease. Adherence to NCCN-treatment guidelines was limited to the first course of treatment, which accounts for changes in the guidelines that occurred during the study period,²⁶⁻²⁸ and was treated as a dichotomous variable (adherent vs nonadherent).^{11,12,14,16-18} Recommended guidelines were a combination of therapies dependent on histologic subtype (eg, endometrioid carcinomas or other carcinomas) and extent of disease (eg, diseases limited to uterus, suspected or gross cervical involvement, and suspected extrauterine disease).²⁶⁻²⁸ Adherence to NCCN-treatment guidelines are further described in Supporting Tables 1-3. Stage of diagnosis was categorized into stages I, II, III, and IV. Histology was classified by the *International Classification of Diseases for Oncology, third edition* (ICD-O-3) histology codes, which included endometrioid carcinomas (8380) and other carcinomas (8000-8379, 8381-8790, 8981, 9700-9701),⁷ and was coded as a binary variable. Grade was categorized into grade 1 well differentiated, grade 2 moderately differentiated, grade 3 poorly differentiated, grade 4 undifferentiated or anaplastic, and unknown.

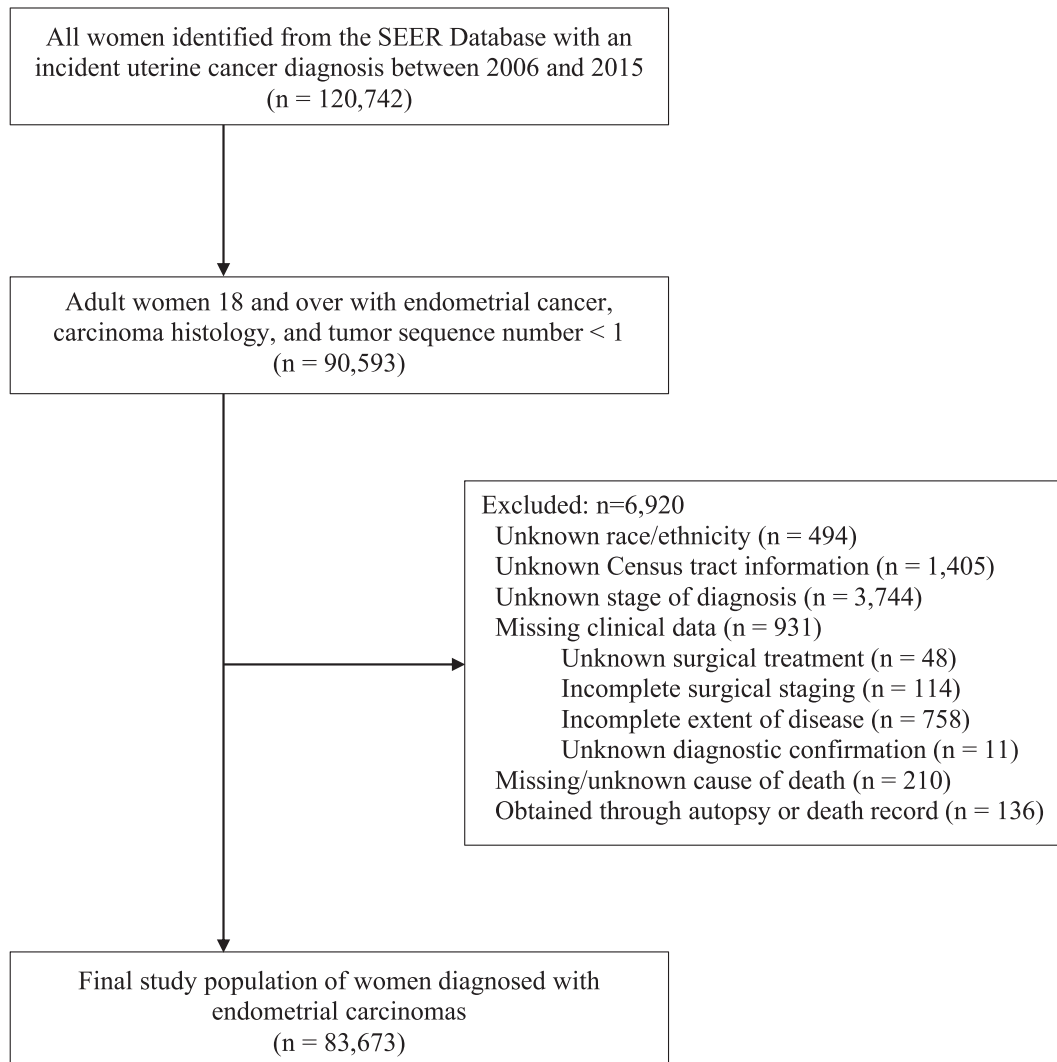


Figure 1. Study population exclusions. This diagram details how patients diagnosed between 2006 and 2015 were included in the study. SEER indicates surveillance, epidemiology, and end results.

Statistical Analysis

Descriptive statistics for demographic and clinical characteristics by patient's receipt of NCCN guideline adherence for first course of treatment were performed. Kaplan-Meier estimate of survival probability and log-rank tests were performed. Proportionality assumptions were tested and failed for year of diagnosis. Cox proportional hazards models were fitted to evaluate the independent effect on survival for each predictor with year of diagnosis included as strata.²⁹ Adjusted hazard ratios (HRs) and 95% CIs were generated. As a sensitivity analysis, we repeated our multivariable models with stratification by low versus high grade to address potential differences in tumor biology. Categorization of low versus high grade is further

described in Supporting Table 4. Analyses were performed using Stata 16 (Stata Corp).

RESULTS

Study Population Characteristics

A total of 83,673 women with endometrial carcinomas were included in this study. Sociodemographic and clinical characteristics are shown in Table 1. The majority of women had stage I disease (76.4%), endometrioid carcinoma histology (75.0%), and well-differentiated grade (37.9%). Most women were within the aged 54-61 years group, with the mean age of diagnosis being 61.3 years (range, 18-110 years; SD, 11.63). White women represented the majority of the sample (71.1%), followed

TABLE 1. Demographic and Cancer Characteristics of Endometrial Carcinoma Cases Between 2006 and 2015 in the Surveillance, Epidemiology, and End Results (SEER) Database (N = 83,673)

Characteristic	Total Sample (N = 83,673)		Adherent Treatment		Nonadherent Treatment		P ^a
	No.	%	No.	%	No.	%	
Adherence to NCCN guidelines			49,771	59.5	33,902	40.5	
Race/ethnicity							<.001
White	59,513	71.1	35,913	60.3	23,600	39.7	
Black	6,531	7.8	3,731	57.1	2,800	42.9	
Latina	10,036	12.0	5,466	54.5	4,570	45.5	
Asian	6,039	7.2	3,761	62.3	2,278	37.7	
Native Hawaiian/Pacific Islander	1,038	1.2	628	60.5	410	39.5	
American Indian/Alaska Native	516	0.6	272	52.7	244	47.3	
Neighborhood SES							<.001
Highest	19,379	23.2	12,240	63.2	7,139	36.8	
Higher middle	18,845	22.5	11,380	60.4	7,465	39.6	
Middle	17,238	20.6	10,141	58.8	7,097	41.2	
Lower middle	15,579	18.6	9,005	57.8	6,574	42.2	
Lowest	12,632	15.1	7,005	55.5	5,627	44.5	
Age at diagnosis							<.001
<54	18,921	22.6	9,759	51.6	9,162	48.4	
54-61	24,320	29.1	14,717	60.5	9,603	39.5	
62-68	19,455	23.3	12,321	63.3	7,134	36.7	
≥69	20,977	25.1	12,974	61.9	8,003	38.2	
Stage at diagnosis							<.001
I	63,907	76.4	36,378	56.9	27,529	43.1	
II	5,026	6.0	3,813	75.9	1,213	24.1	
III	10,225	12.2	7,966	77.9	2,259	22.1	
IV	4,515	5.4	1,614	35.8	2,901	64.3	
Histology							<.001
Endometrioid carcinomas	62,767	75.0	38,468	61.3	24,299	38.7	
Other carcinomas	20,906	25.0	11,303	54.1	9,603	45.9	
Grade							<.001
1	31,694	37.9	15,358	48.5	16,336	51.5	
2	19,831	23.7	14,128	71.2	5,703	28.8	
3	12,059	14.4	8,628	71.6	3,431	28.5	
4	3,875	4.6	2,550	65.8	1,325	34.2	
Unknown	16,214	19.4	9,107	56.2	7,107	43.8	

Abbreviations: NCCN, National Comprehensive Cancer Network; SES, socioeconomic status.
^aχ² test is for association between patient characteristics and NCCN-treatment adherence. All P values are 2-sided.

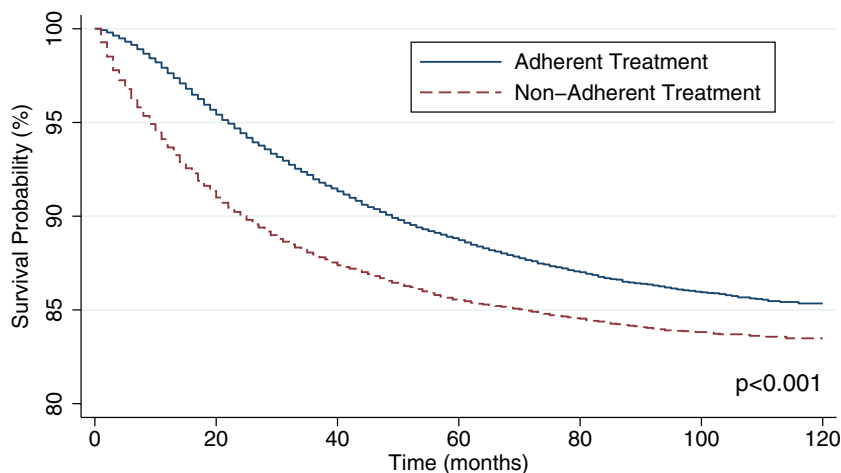


Figure 2. Kaplan-Meier survival estimates by adherence to National Comprehensive Cancer Network-treatment guidelines among endometrial carcinoma patients, SEER 2006-2015. SEER indicates surveillance, epidemiology, and end results.

by Latina (12.0%), Black (7.8%), Asian (7.2%), NHPI (1.1%), and AI/AN (0.6%). Overall, 59.5% of the sample received NCCN guideline-adherent care. Asian, White, and NHPI women received the highest percentages of adherent care (62.3%, 60.3%, and 60.5%, respectively). Whereas AI/AN, Latina, and Black women received the lowest percentages of adherent care (52.7%, 54.5%, and 57.1%, respectively). Adherence to treatment guidelines increased with neighborhood SES, ranging from 55.5% for the lowest SES group to 63.2% for the highest SES group. A lower proportion of women diagnosed before 54 years of age received adherent care (51.6%) compared with women in all other age groups (54-64 years, 60.5%; 62-68 years, 63.3%; and 69 years and older, 61.9%).

Endometrial Cancer-Specific Survival

Univariable survival analysis revealed a significant difference in endometrial cancer-specific survival between patients receiving NCCN adherent and nonadherent guideline treatment (Fig. 2). Univariable Cox proportional hazards models were performed to determine which sociodemographic and clinical characteristics were significantly associated with endometrial cancer-specific survival (Table 2). Nonadherence to NCCN-treatment guidelines, Black, Latina, and NHPI race/ethnicity, lower neighborhood SES, age at diagnosis, stage at diagnosis, histology, and grade of disease were all significantly associated with poorer survival. Asian race was significantly associated with improved survival. Covariates in the multivariate Cox proportional hazards model included adherence to NCCN-treatment guidelines, race/ethnicity, neighborhood SES, age at diagnosis, stage at diagnosis, histology, and grade. Additionally, the multivariate model adjusted for year of diagnosis as strata. After adjustment, nonadherence to NCCN-treatment guidelines was associated with a significant decrease in survival compared with adherent care (HR, 1.59; 95% CI, 1.52-1.67).

After adjusting for adherence to NCCN guidelines and other prognostic characteristics, we examined disparities in survival by race/ethnicity and neighborhood SES. Compared with White women, Black (HR, 1.41; 95% CI, 1.32-1.51) or NHPI (HR, 1.44; 95% CI, 1.19-1.73) women had significantly worse survival. Asian women (HR, 0.86; 95% CI, 0.78-0.94) had significantly better survival compared with White women. Results suggest a socioeconomic gradient in survival: lower neighborhood SES (lowest SES group HR, 1.27; 95% CI, 1.18-1.36; lower-middle SES group HR, 1.19; 95% CI, 1.11-1.27; middle SES group HR, 1.15; 95% CI, 1.07-1.23; and higher-middle SES group HR, 1.07;

TABLE 2. Univariate and Multivariate Cox Proportional Hazards Model for Endometrial Cancer-Specific Survival From 2006 to 2015 in the SEER National Cancer Registry (N = 83,673)

	Unadjusted HR			Adjusted HR		
	HR	95% CI	P	HR	95% CI	P
Adherence to NCCN guidelines						
Adherent treatment	1.00	—	—	1.00	—	—
Nonadherent treatment	1.40	1.34-1.46	**	1.59	1.52-1.67	**
Race/ethnicity						
White	1.00	—	—	1.00	—	—
Black	2.36	2.22-2.51	**	1.41	1.32-1.51	**
Latina	1.08	1.01-1.16	*	1.04	0.96-1.11	
Asian	0.91	0.83-0.99	*	0.86	0.78-0.94	*
Native Hawaiian/ Pacific Islander	1.27	1.05-1.52	*	1.44	1.19-1.73	**
American Indian/ Alaska Native	1.13	0.86-1.48		1.23	0.93-1.61	
Neighborhood SES						
Highest	1.00	—	—	1.00	—	—
Higher middle	1.11	1.04-1.19	*	1.07	1.00-1.15	*
Middle	1.21	1.14-1.30	**	1.15	1.07-1.23	**
Lower middle	1.37	1.29-1.47	**	1.19	1.11-1.27	**
Lowest	1.55	1.45-1.66	**	1.27	1.18-1.36	**
Age, y						
<54	1.00	—	—	1.00	—	—
54-61	1.45	1.34-1.56	**	1.32	1.22-1.43	**
62-68	2.09	1.94-2.26	**	1.65	1.52-1.78	**
≥69	2.63	3.39-3.90	**	2.45	2.28-2.63	**
Stage at diagnosis						
I	1.00	—	—	1.00	—	—
II	3.40	3.11-3.71	**	2.70	2.47-2.95	**
III	8.31	7.86-8.78	**	5.73	5.40-6.08	**
IV	35.36	33.45-37.38	**	16.58	15.58-17.65	**
Histology						
Endometrioid carcinomas	1.00	—	—	1.00	—	—
Other carcinomas	3.59	3.44-3.74	**	1.23	1.17-1.29	**
Grade						
1	1.00	—	—	1.00	—	—
2	3.24	2.97-3.52	**	2.23	2.04-2.43	**
3	13.41	12.42-14.49	**	4.27	3.92-4.65	**
4	18.87	17.27-20.63	**	4.46	4.04-4.93	**
Unknown	4.86	4.46-5.30	**	2.82	2.58-3.08	**

Abbreviations: HR, Hazard ratio; NCCN, National Comprehensive Cancer Network; SES, socioeconomic status. In the multivariate model, the year of diagnosis was included as strata. *P < .05, **P < .001.

95% CI, 1.00-1.15) was associated with a significant negative effect on survival relative to women in the highest SES category. Results also suggest a gradient in survival for age of diagnosis: Being older (≥69 years HR, 2.45; 95% CI, 2.28-2.63; 62-68 years HR, 1.65; 95% CI, 1.52-1.78; and 54-61 years HR, 1.32; 95% CI, 1.22-1.43) was associated with significant negative effect on survival relative to women in the youngest age

group. Results indicate a significant negative impact on survival for later stage at diagnosis as women with stage II (HR, 2.70; 95% CI, 2.47-2.95), stage III (HR, 5.73; 95% CI, 5.40-6.08), and stage IV (HR, 16.58; 95% CI, 15.58-17.65) had substantially worse survival when compared with women with stage I disease. Compared with endometrioid carcinomas, other carcinomas were significantly associated with worse survival (HR, 1.23; 95% CI, 1.17-1.29). Grade of disease also had a significant negative impact on survival as women with grade 2 (HR, 2.23; 95% CI, 2.04-2.43), grade 3 (HR, 4.27; 95% CI, 3.92-4.65), and grade 4 (HR, 4.46; 95% CI, 4.04-4.93) had worse survival compared with women with grade 1 disease. In sensitivity analyses of whether patterns differed by low versus high grade of disease, the overall significance and effect of adherent treatment, race/ethnicity, and neighborhood SES on survival across grade remained consistent with our multivariable model (Supporting Table 4).

DISCUSSION

Principal Findings

This study evaluated adherence to NCCN guidelines among women with endometrial carcinomas and the impact of treatment adherence on cause-specific survival across racial/ethnic and socioeconomic groups. There are 3 key findings from this study. First, we found that 59.5% of the sample received NCCN-adherent treatment. Second, our findings indicate racial/ethnic disparities in NCCN-adherent care and survival. Third, our results suggest socioeconomic disparities in NCCN-adherent care and survival.

Results and Research Implications

Other studies have found similar percentages of adherence to NCCN guidelines, with rates ranging from 37% to 49% for pancreatic,¹¹ cervical,¹⁷ ovarian,¹⁰ and gynecologic cancers.¹² One study of invasive endometrioid endometrial cancers found 75% adherence to NCCN guidelines,¹⁵ higher than we found in our sample. However, that study was consistent with our study in which women who received adherent treatment had better survival compared with those who received nonadherent treatment.¹⁵ Overall, our findings align with past research among other cancers, showing that adherence to NCCN guidelines have survival benefits for endometrial cancer.

We found that a lower percentage of Black, Latina, and AI/AN women received adherent treatment compared with NHPI, Asian, and White women. Additionally,

Black and NHPI women had worse survival compared with White women, whereas Asian women had improved survival compared with White women. The literature indicates that Black women are more likely to have an advanced stage at diagnosis and more aggressive tumors than other racial/ethnic groups, which could shape differences observed in overall survival.^{1,2,9,15,30,31,32,33} Although our review of the literature did not identify any studies specific to NHPI women, few noted Asian/Pacific Islander women having higher grade tumors and less favorable histologic types compared with White women.^{15,33,34} Our study found that racial/ethnic disparities in endometrial cancer survival persisted for Black and NHPI women relative to White women, despite controlling for receipt of adherent treatment, stage, histology, and grade. Our finding that Black women were less likely to receive adherent care and experienced decreased survival compared with White women is a common finding within various cancer sites.^{5,6,30} However, findings from a study that examined NCCN adherence among White, Black, Latina, and Asian/Pacific Islander women with nonendometrioid endometrial carcinomas did not find any racial/ethnic disparities in treatment.³¹ Another study on endometrial cancer found that racial disparities persisted between Black and White women even when they received similar chemotherapy intensity and dosage, indicating that other factors may influence these disparities.³² Although we observed that Black women in our study were more likely to have advanced stage and more aggressive grade of disease and histologic subtypes, the findings presented here point to the need for further research that unpacks how social, clinical, and epigenetic factors may shape persistent racial/ethnic disparities in survival. Although differences in tumor biology are an important clinical factor to consider, research also needs to explore the structural inequalities that exist for Black individuals (ie, experiences of racism, economic inequalities, and inadequate access to and quality of health care) and the influence these inequalities have on subsequent poorer health outcomes and decreased survival compared with Whites.^{1,2,9,30,32,35} Future research should also consider and explore structural inequalities in addition to clinical characteristics for other racial/ethnic minority groups. Past research has indicated that although Latina women are less likely to receive standard treatment, their survival is comparable with White women and may be mediated by country of origin.^{2,30} Similarly, we did not find a significant difference in survival for Latina women compared with White women after controlling for NCCN-adherent care and

covariates. Future research should continue to examine survival among Latina women and should also include country of origin as a covariate to examine which Latina subgroups are at a greater risk for poor survival. We did not find any significant differences in survival among AI/AN women relative to White women; however, AI/AN women experienced the lowest rates of treatment adherence in our study. These patterns should be further examined with larger samples of AI/AN women. Patterns for Asian women supported findings from other studies that have found similar or better survival for Asian women compared with White women.^{30,31,36} However, our study was the first that we are aware of to observe that NHPI women have a poorer survival rate compared with White women. Many studies group Asian and NHPI women into 1 racial/ethnic category, but our study shows that there are important differences in these 2 groups, and results should be disaggregated by subgroup to examine potential disparities.^{37,38} Our data present counterintuitive findings as NHPI women have among the highest rates of treatment adherence, yet show poorer survival compared with White women. Future research should explore social and clinical factors that may shape this pattern for NHPI women, and these patterns should be further examined with larger sample sizes of NHPI women.

Neighborhood SES was evaluated through an index that used census tracts and combines together several indicators of education, income, and occupation.²⁵ We observed that a lower proportion of women in lower SES groups, assessed at the census tract level, received treatment adherence compared with those with higher SES. Women of lower SES had worse survival compared with higher SES groups. However, adjusting for treatment did not fully improve survival for all groups. Our results indicate that standard treatment alone does not improve disparities in endometrial cancer survival for all racial/ethnic minorities and SES groups. Our findings support past studies that show lower SES status groups have lower rates of adherent treatment and worse survival,^{2,3,9,22} indicating that SES is an important predictor in survival outcomes and future investigations should explore survival among these vulnerable groups. Various studies have also used proxies for SES such as insurance status or insurance type as predictors for treatment adherence and survival, and findings have been mixed.^{18,39} However, future research should include insurance as a covariate to determine whether racial/ethnic and socioeconomic disparities are improved by accounting for insurance status and insurance type for endometrial cancer.

Strengths and Limitations

This study has several notable strengths. First, the SEER registry provided a large sample size, allowing for inclusion of multiple years in the study period in which treatment guidelines did not substantially change. Second, the registry allowed for inclusion of a diverse population of women from multiple racial/ethnic groups and neighborhood socioeconomic backgrounds. The inclusion of multiple racial/ethnic groups is especially important as the majority of research on disparities in endometrial cancer to date focuses on White versus Black women.^{17,30,39} As racial/ethnic minority groups in the United States continue growing, it is important to examine and account for disparities across racial/ethnic groups as we do in our study. Third, our study disaggregated Asian and NHPI women to view each of these racial/ethnic groups separately instead of together as they often are in the literature.^{37,38} Notably, this study identified important differences in NCCN-adherent care and survival for Asian and NHPI women. It is important to note that Asian race is comprised of many different subgroups; so future research should disaggregate Asians even further to examine whether survival rates differ among these groups.

Despite these strengths, our study has limitations that should be acknowledged. First, our sample of NHPI and AI/AN women is small; hence, our results should be interpreted with caution. However, these racial/ethnic groups are often excluded in the literature, so this is an important starting point in looking at the patterns of treatment adherence and survival among these populations. Nonetheless, it should be noted that patient demographics in the SEER database, including racial/ethnic classification, are ascertained by medical records or administrative information. Hence, they may not be accurate or aligned with the patients' self-reported race/ethnicity. Second, SEER treatment data are limited to the first course of treatment and do not include hormonal therapy or specific dose of radiation or chemotherapy. This additional treatment information and inclusion of adjuvant therapies would be helpful to examine the granularity of NCCN-treatment adherence for both first-course and adjuvant treatment. Future studies are warranted regarding additional treatment patterns. Third, the SEER database does not include information on medical comorbidities that may have influenced whether a patient was able to receive NCCN-guideline-adherent care and its impact on cause-specific survival. Future research should include comorbidities as a confounder for treatment adherence and survival. Fourth, the SEER database does not

include reasons for treatment nonadherence. However, research on other cancer sites has cited reasons for nonadherence to include providers' consideration of risk factors and judgment to provide other treatment, medical comorbidities, or disease progression, as well as patient refusal of recommended treatment.^{11,14,18,40} Future research should explore reasons for nonadherence to NCCN guidelines to determine how to improve adherence and subsequent outcomes and cancer survival. Fifth, the SEER registry lacks information on other potential confounders related to access to care and hospital/provider characteristics (ie, insurance provider, geographic location, facility type, surgeon specialty). Future research should include these unmeasured variables in models examining NCCN-treatment adherence and survival. Finally, we used neighborhood-level SES and may have not fully accounted for individual-level SES.²⁵ Future studies that disentangle the role of individual- and community-level SES are needed.

In summary, NCCN-treatment adherence is an important quality measure of improved cancer survival.^{11,17,18} However, our study suggests that although treatment adherence is an independent predictor of improved survival, this is not observed equally among all racial/ethnic and SES groups. Thus, it is important to explore social and clinical factors that shape the unique treatment adherence and survival patterns across racial/ethnic and socioeconomic groups. In addition, it is also essential to consider and address structural factors that could reduce these disparities and improve outcomes. For instance, we need to address barriers relating to delayed diagnoses; cost of, access to, and engagement of care; and improved communication and shared decision-making with patients that addresses potential provider bias and fully educates patients on types of treatment options available.^{2,4,9,41} If we are to reduce and eventually eliminate racial/ethnic and class inequalities, these findings suggest we cannot treat all groups the same. Thus, standard treatment is a starting point but not an exhaustive task. Considerations should also be made for factors before diagnosis and survivorship factors after treatment that may impact survival across racial/ethnic and SES groups.

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CONFLICT OF INTEREST

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Victoria E. Rodriguez: Conceptualization, formal analysis, data curation, writing—original draft, preparation, and funding acquisition. **Alana M. W. LeBrón:** Conceptualization, resources, writing—review and editing, and supervision. **Jenny Chang:** Formal analysis, validation, resources, and writing—review and editing. **Robert E. Bristow:** Conceptualization, resources, writing—review and editing, and supervision.

REFERENCES

- Feldman A, Chaugle S, Burmeister C, Munkarah A, Elshaiikh MA. A matched analysis on the prognostic impact of race on survival end-points of women with early-stage endometrial cancer. *Gynecol Obstet Invest.* 2019;84:283-289.
- Liu FW, Bristow RE, Tergas AI. Racial/ethnic disparities in gynecological cancer screening, treatment, and survival. In: Giordano A, Macaluso M, eds. *Gynecological Cancers.* Springer; 2016:151-166.
- Von Behren J, Abrahão R, Goldberg D, Gomez SL, Setiawan VW, Cheng I. The influence of neighborhood socioeconomic status and ethnic enclave on endometrial cancer mortality among Hispanics and Asian Americans/Pacific Islanders in California. *Cancer Causes Control.* 2018;29:875-881.
- Zahnd WE, Hyon KS, Diaz-Sylvester P, Izadi SR, Colditz GA, Brard L. Rural–urban differences in surgical treatment, regional lymph node examination, and survival in endometrial cancer patients. *Cancer Causes Control.* 2018;29:221-232.
- Foote JR, Gaillard S, Broadwater G, et al. Disparities in the surgical staging of high-grade endometrial cancer in the United States. *Gynecol Oncol Res Pract.* 2017;4:1.
- Rauh-Hain JA, Buskwofie A, Clemmer J, Boruta DM, Schorge JO, del Carmen MG. Racial disparities in treatment of high-grade endometrial cancer in the medicare population. *Obstet Gynecol.* 2015;125:843-851.
- Henley SJ, Miller JW, Dowling NE, Benard VB, Richardson LC. Uterine cancer incidence and mortality—United States, 1999-2016. *Morb Mortal Wkly Rep.* 2018;67:1333-1338.
- National Cancer Institute. Uterine cancer statistics. Cancer stat facts. 2019. Accessed March 11, 2020. <https://seer.cancer.gov/statfacts/html/corp.html>
- Chatterjee S, Gupta D, Caputo TA, Holcomb K. Disparities in gynecological malignancies. *Front Oncol.* 2016;6:1-7.
- Cliby WA, Powell MA, Al-Hammadi N, et al. Ovarian cancer in the United States: contemporary patterns of care associated with improved survival. *Gynecol Oncol.* 2015;136:11-17.
- Jaap K, Fluck M, Hunsinger M, et al. Analyzing the impact of compliance with national guidelines for pancreatic cancer care using the National Cancer Database. *J Gastrointest Surg.* 2018;22:1358-1364.
- Levinson KL, Riedel DJ, Ojalvo LS, et al. Gynecologic cancer in HIV infected women: treatment and outcomes in a multi-institutional cohort. *AIDS.* 2018;32:171-177.
- Worhunsky DJ, Ma Y, Zak Y, et al. Compliance with gastric cancer guidelines is associated with improved outcomes. *J Natl Compr Canc Netw.* 2015;13:319-325.
- Lee J-Y, Kim TH, Suh DH, et al. Impact of guideline adherence on patient outcomes in early-stage epithelial ovarian cancer. *Eur J Surg Oncol.* 2015;41:585-591.
- Kaspers M, Llamocca E, Quick A, Dholakia J, Salani R, Felix AS. Black and Hispanic women are less likely than White women to receive guideline-concordant endometrial cancer treatment. *Am J Obstet Gynecol.* 2020;223:398.e1-398.e18.
- Bristow RE, Chang J, Ziogas A, Campos B, Chavez LR, Anton-Culver H. Sociodemographic disparities in advanced ovarian cancer survival and adherence to treatment guidelines. *Obstet Gynecol.* 2015;125:833-842.
- Pfaendler KS, Chang J, Ziogas A, Bristow RE, Penner KR. Disparities in adherence to National Comprehensive Cancer Network Treatment guidelines and survival for stage IB-IIA cervical cancer in California. *Obstet Gynecol.* 2018;131:899-908.

18. Hines RB, Barrett A, Twumasi-Ankrah P, et al. Predictors of guideline treatment nonadherence and the impact on survival in patients with colorectal cancer. *J Natl Compr Canc Netw*. 2015;13:51-60.
19. Erickson Foster J, Velasco JM, Hieken TJ. Adverse outcomes associated with noncompliance with melanoma treatment guidelines. *Ann Surg Oncol*. 2008;15:2395-2402.
20. Lewis CM, Hessel AC, Roberts DB, et al. Prereferral head and neck cancer treatment: compliance with National Comprehensive Cancer Network treatment guidelines. *Arch Otolaryngol Neck Surg*. 2010;136:1205.
21. Bristow RE, Chang J, Ziogas A, Anton-Culver H, Vieira VM. Spatial analysis of adherence to treatment guidelines for advanced-stage ovarian cancer and the impact of race and socioeconomic status. *Gynecol Oncol*. 2014;134:60-67.
22. Hodeib M, Chang J, Liu F, et al. Socioeconomic status as a predictor of adherence to treatment guidelines for early-stage ovarian cancer. *Gynecol Oncol*. 2015;138:121-127.
23. Voss RK, Chiang Y-J, Torres KE, et al. Adherence to National Comprehensive Cancer Network guidelines is associated with improved survival for patients with stage 2A and stages 2B and 3 extremity and superficial trunk soft tissue sarcoma. *Ann Surg Oncol*. 2017;24:3271-3278.
24. National Cancer Institute. SEER ICD-O-3 coding materials. SEER. Accessed March 11, 2020. <https://seer.cancer.gov/icd-o-3/index.html>
25. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control*. 2001;12:703-711.
26. Greer BE, Koh WJ, Abu-Rustum N, et al. Uterine cancers: clinical practice guidelines in oncology™. *J Natl Compr Canc Netw*. 2006;4:438-462.
27. Greer BE, Koh W-J, Abu-Rustum N, et al. Uterine neoplasms. *J Natl Compr Canc Netw*. 2009;7:498-531.
28. Koh W-J, Greer BE, Abu-Rustum NR, et al. Uterine neoplasms, Version 1.2014. *J Natl Compr Canc Netw*. 2014;12:248-280.
29. Bradburn M, Clark T, Love S, Altman D. Survival analysis part II: multivariate data analysis—an introduction to concepts and methods. *Br J Cancer*. 2003;89:431-436.
30. Rauh-Hain JA, Melamed A, Schaps D, et al. Racial and ethnic disparities over time in the treatment and mortality of women with gynecological malignancies. *Gynecol Oncol*. 2018;149:4-11.
31. Dholakia J, Llamocca E, Quick A, Salani R, Felix AS. Guideline-concordant treatment is associated with improved survival among women with non-endometrioid endometrial cancer. *Gynecol Oncol*. 2020;157:716-722.
32. Farley JH, Tian C, Rose GS, et al. Chemotherapy intensity and toxicity among Black and White women with advanced and recurrent endometrial cancer: a Gynecologic Oncology Group study. *Cancer*. 2010;116:355-361.
33. Kost ER, Hall KL, Hines JF, et al. Asian-Pacific Islander race independently predicts poor outcome in patients with endometrial cancer. *Gynecol Oncol*. 2003;89:218-226.
34. Horne ZD, Teterichko SR, Glaser SM, et al. Race-driven survival differential in women diagnosed with endometrial cancers in the USA. *Int J Gynecol Cancer*. 2020;30:1893-1901.
35. Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. *The Lancet*. 2017;389:1453-1463.
36. Bandera EV, Lee VS, Rodriguez-Rodriguez L, Powell CB, Kushi LH. Racial/ethnic disparities in ovarian cancer treatment and survival. *Clin Cancer Res*. 2016;22:5909-5914.
37. Chen MS, Hawks BL. A debunking of the myth of healthy Asian Americans and Pacific Islanders. *Am J Health Promot*. 1995;9:261-268.
38. Srinivasan S, Guillermo T. Toward improved health: disaggregating Asian American and Native Hawaiian/Pacific Islander data. *Am J Public Health*. 2000;90:1731-1734.
39. Fader AN, Habermann EB, Hanson KT, Lin JF, Grendys EC, Dowdy SC. Disparities in treatment and survival for women with endometrial cancer: a contemporary national cancer database registry analysis. *Gynecol Oncol*. 2016;143:98-104.
40. Erickson BK, Martin JY, Shah MM, Straughn JM, Leath CA. Reasons for failure to deliver National Comprehensive Cancer Network (NCCN)-adherent care in the treatment of epithelial ovarian cancer at an NCCN cancer center. *Gynecol Oncol*. 2014;133:142-146.
41. Baskovic M, Lichtensztajn DY, Nguyen T, Karam A, English DP. Racial disparities in outcomes for high-grade uterine cancer: a California cancer registry study. *Cancer Med*. 2018;7:4485-4495.