

# Hysterectomy-Corrected Uterine Corpus Cancer Incidence Trends and Differences in Relative Survival Reveal Racial Disparities and Rising Rates of Nonendometrioid Cancers

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**PURPOSE** Uterine corpus cancer incidence rates have been projected to increase, a prediction often attributed to the obesity epidemic. However, correct estimation of these rates requires accounting for hysterectomy prevalence, which varies by race, ethnicity, and region. Here, we evaluated recent trends in hysterectomy-corrected rates by race and ethnicity and histologic subtype and estimated differences in relative survival by race and ethnicity, subtype, and stage.

**METHODS** We estimated hysterectomy prevalence from the Behavioral Risk Factor Surveillance System. Hysterectomy-corrected age-standardized uterine corpus cancer incidence rates from 2000 to 2015 were calculated from the SEER 18 registries. Incidence rates and trends were estimated separately by race and ethnicity, region, and histologic subtype. Five-year relative survival rates were estimated by race and ethnicity, histologic subtype, and stage.

**RESULTS** Hysterectomy-corrected incidence rates of uterine corpus cancer were similar among non-Hispanic whites and blacks and lower among Hispanics and Asians/Pacific Islanders. Endometrioid carcinoma rates were highest in non-Hispanic whites, whereas nonendometrioid carcinoma and sarcoma rates were highest in non-Hispanic blacks. Hysterectomy-corrected uterine corpus cancer incidence increased among non-Hispanic whites from 2003 to 2015 and among non-Hispanic blacks, Hispanics, and Asians/Pacific Islanders from 2000 to 2015. Overall incidence rates among non-Hispanic blacks surpassed those of non-Hispanic whites in 2007. Endometrioid carcinoma rates rose among non-Hispanic blacks, Hispanics, and Asians/Pacific Islanders but were stable among non-Hispanic whites; however, nonendometrioid carcinoma rates rose significantly among all women. Non-Hispanic blacks had the lowest survival rates, irrespective of stage at diagnosis or histologic subtype.

**CONCLUSION** Among all women, rates of nonendometrioid subtypes have been rising rapidly. Our analysis shows profound racial differences and disparities indicated by higher rates of nonendometrioid subtypes and poorer survival among non-Hispanic black women.

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## ASSOCIATED CONTENT

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## Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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## INTRODUCTION

Uterine corpus cancer is the most common and second deadliest gynecologic cancer diagnosed in the United States, with approximately 63,230 new cases and 11,350 deaths occurring in 2018.<sup>1</sup> Unlike in most cancers, uterine corpus (hereafter referred to as uterine) cancer incidence rates have been increasing over the past two decades<sup>2</sup> and have been projected to rise substantially.<sup>3,4</sup> These trends and predictions have been largely attributed to increasing obesity rates, population aging, and decreased use of combined menopausal hormone therapy.<sup>5</sup> Uterine carcinomas with endometrioid histology are the most common, have good prognosis, and are strongly associated with obesity and other estrogen-related risk factors.

Uterine carcinomas with nonendometrioid histology (eg, serous and clear cell carcinomas) are more aggressive and are suggested to be less hormone dependent, with worse outcomes and survival.<sup>6,7</sup> Sarcomas generally arise in the myometrium, are less common, and have not been well studied.

Despite having historically lower uterine cancer incidence rates, black women have been more likely to be diagnosed with aggressive nonendometrioid subtypes and have been twice as likely to die as a result of uterine cancer compared with white women, making this one of the largest racial disparities observed for any cancer type.<sup>8,9</sup> Recent studies using population-based registry data have suggested that nonendometrioid cancer incidence rates have been disproportionately

increasing among black women.<sup>8,10-12</sup> However, these studies did not correct for hysterectomy prevalence, which varies widely by age, race, ethnicity, geographic region, and calendar time. Women who have had a hysterectomy are no longer at risk for developing uterine cancer, and failure to remove them from the population at risk may result in biased comparisons.<sup>13-16</sup> Few studies of racial and ethnic differences in uterine cancer incidence have accounted for hysterectomy prevalence, with the most recent evaluating trends through 2008.<sup>13,16</sup>

With the availability of several additional years of data and larger population coverage in the recent release of the SEER 18 database, we sought to evaluate the extent of racial and ethnic differences in uterine cancer incidence and patient survival. We evaluated trends in rates overall and by histologic subtype, accounting for racial, ethnic, and geographic differences in hysterectomy prevalence. Furthermore, we present uterine cancer survival estimates by race and ethnicity according to histologic subtype and stage at diagnosis.<sup>17</sup>

## METHODS

### SEER Database

We obtained incidence data on microscopically confirmed cases of invasive corpus uteri and uterine corpus not otherwise specified (NOS; excluding uterine cervical) cancers from the SEER database in 18 population-based registries representing approximately 28% of the US population (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose–Monterey, Los Angeles, Alaska Native Registry, rural Georgia, California [excluding San Francisco, San Jose–Monterey, and Los Angeles], Kentucky, Louisiana, New Jersey, and Georgia [excluding Atlanta and rural Georgia]), diagnosed between 2000 and 2015.<sup>18</sup> In SEER, race and ethnicity data are abstracted from medical records and grouped into race and origin categories using standardized algorithms.<sup>19</sup> We included women of Hispanic and non-Hispanic origin/ethnicity and, among non-Hispanics, white, black, and Asian/Pacific Islander race (hereafter referred to as whites, blacks, and Asians, respectively); non-Hispanic American Indian/Alaska Native and unknown races were excluded because of the small number of cases. We excluded the few cases diagnosed in women younger than age 30 years and those age 80 years or older because age-specific hysterectomy data were not available. Cases from the Alaska Native SEER registry were excluded because this registry does not provide information on ethnicity (ie, Hispanic *v* non-Hispanic). Cases were classified by histologic subtypes defined by the third edition of the International Classification of Diseases for Oncology histology codes and included endometrioid and non-endometrioid carcinomas and sarcomas (Appendix Table A1, online only). Cases coded as adenocarcinoma NOS (*n* = 8,140) decreased from 32% of all cases in 2000 to only 4.1% in 2015. For the incidence analyses, we reclassified

them according to the observed distribution of endometrioid and nonendometrioid cases by year, age, race, ethnicity, and region. For example, of the 10 adenocarcinoma NOS cases diagnosed during 2000 among whites in the Northeast age 35 to 39 years, nine and one were reclassified according to the observed proportions of endometrioid (90%) and nonendometrioid (10%) cases, respectively. All other malignant uterine cancers combined (ie, other) were included in analyses of overall incidence rates (Appendix Table A1). We classified stage at diagnosis using SEER Summary Stage 2000 as localized, regional, distant, or unstaged/unknown.

### Behavioral Risk Factor Surveillance System

The Behavioral Risk Factor Surveillance System (BRFSS) is a nationally representative cross-sectional telephone survey that collects data on health-related risk behaviors, chronic health conditions, and use of preventive services in the noninstitutionalized adult civilian US population.<sup>20</sup> BRFSS uses a dual-frame sample design, conducting both landline and cell phone (as of 2011) surveys using random-digit dialing. Survey-weighted estimates of hysterectomy prevalence were calculated for women age 30 to 79 years. Because BRFSS only obtains information on hysterectomy in even-numbered years, hysterectomy prevalence was estimated for the odd-numbered years by calculating a population-weighted average of the neighboring years. To ensure stable estimates of hysterectomy prevalence, we used data from women residing in all 50 states and defined regions according to US Census Bureau designation (Northeast, Midwest, South, and West).

### Statistical Analysis

Age-adjusted incidence rates, uncorrected for hysterectomy prevalence, were calculated using SEER\*Stat software (version 8.3.5) for uterine cancer overall and by histologic subtype, stratified by 5-year age groups (ie, 30 to 34, 35 to 39, and continuing to 75 to 79), year of diagnosis (2000 to 2015), region (Northeast [Connecticut and New Jersey], Midwest [Michigan and Iowa], South [Georgia, Kentucky, and Louisiana], and West [California, Hawaii, New Mexico, Washington, and Utah]), and race and ethnicity (white, black, Hispanic, and Asian). Rates were age adjusted to the 2000 US standard population and expressed per 100,000 woman-years.

We estimated smoothed survey-weighted hysterectomy prevalence using logistic regression with coefficients for 5-year age group, year, an interaction term for age group and year, race and ethnicity, and geographic region using data from BRFSS. Adjusted prevalence estimates were predicted from the model, within strata of race and ethnicity, age group, year, and region. These estimates were used to correct the corresponding populations at risk by removing the proportion of women with a hysterectomy from the denominator. To account for the fact that women with uterine cancer undergo hysterectomy for treatment, we added cases back into the corrected denominator.

**TABLE 1.** Age-Adjusted Incidence Rates of Microscopically Confirmed Uterine Corpus Cancer Overall and by Histology and Race and Ethnicity, Uncorrected and Corrected for Hysterectomy Prevalence, Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015)

Category	No. of Cases	Uncorrected		Corrected		Increase in Rate With Correction for Hysterectomy Prevalence (%)
		Age-Adjusted Incidence (95% CI)	IRR (95% CI)	Age-Adjusted Incidence (95% CI)	IRR (95% CI)	
Total	161,260	40.0 (39.8 to 40.2)	—	63.7 (63.4 to 64.0)	—	59.3
Histologic subtype						
Endometrioid	121,095	30.0 (29.4 to 30.2)	—	47.3 (47.0 to 47.6)	—	57.7
Nonendometrioid	29,537	7.3 (7.2 to 7.4)	—	12.4 (12.2 to 12.6)	—	69.9
Sarcomas	7,579	1.9 (1.9 to 2.0)	—	2.8 (2.7 to 2.9)	—	47.4
Other	3,049	0.8 (0.7 to 0.8)	—	1.2 (1.1 to 1.2)	—	50.0
Race and ethnicity						
Non-Hispanic white	115,480	42.7 (42.4 to 42.9)	Ref	67.6 (67.1 to 67.9)	Ref	58.3
Non-Hispanic black	15,643	37.3 (37.0 to 38.0)	0.87 (0.86 to 0.88)	67.6 (67.0 to 68.8)	1.00 (0.99 to 1.01)	81.2
Hispanic	17,591	32.7 (32.3 to 33.2)	0.77 (0.76 to 0.78)	47.5 (46.9 to 48.2)	0.70 (0.70 to 0.71)	45.3
Non-Hispanic Asian/Pacific Islander	12,546	32.6 (32.1 to 33.2)	0.76 (0.76 to 0.77)	40.0 (39.4 to 40.7)	0.59 (0.58 to 0.60)	22.7
Histologic subtype × race and ethnicity						
Endometrioid						
Non-Hispanic white	90,476	33.4 (33.2 to 33.7)	Ref	52.6 (52.3 to 52.9)	Ref	57.5
Non-Hispanic black	8,295	19.5 (19.1 to 20.0)	0.58 (0.57 to 0.59)	34.5 (33.7 to 35.2)	0.65 (0.65 to 0.66)	76.9
Hispanic	12,883	23.5 (23.1 to 24.0)	0.70 (0.69 to 0.71)	33.7 (33.1 to 34.4)	0.64 (0.63 to 0.65)	43.4
Non-Hispanic Asian/Pacific Islander	9,441	24.4 (23.9 to 24.9)	0.73 (0.72 to 0.74)	29.6 (29.0 to 30.2)	0.56 (0.56 to 0.57)	21.3
Nonendometrioid						
Non-Hispanic white	18,747	6.8 (6.7 to 6.9)	Ref	11.4 (11.2 to 11.6)	Ref	67.6
Non-Hispanic black	5,462	13.4 (13.0 to 13.7)	1.98 (1.93 to 2.03)	25.9 (25.0 to 26.5)	2.27 (2.23 to 2.31)	93.3
Hispanic	3,120	6.5 (6.3 to 6.7)	0.96 (0.93 to 0.98)	10.1 (9.7 to 10.3)	0.89 (0.87 to 0.91)	55.4
Non-Hispanic Asian/Pacific Islander	2,208	5.9 (5.6 to 6.1)	0.86 (0.84 to 0.89)	7.5 (7.1 to 7.8)	0.66 (0.64 to 0.68)	27.1
Sarcomas						
Non-Hispanic white	4,396	1.7 (1.7 to 1.8)	Ref	2.5 (2.5 to 2.6)	Ref	47.1
Non-Hispanic black	1,405	3.2 (3.1 to 3.4)	1.86 (1.77 to 1.95)	5.2 (5.0 to 5.5)	2.07 (1.99 to 2.15)	62.5
Hispanic	1,149	2.0 (1.8 to 2.1)	1.12 (1.06 to 1.18)	2.6 (2.4 to 2.8)	1.03 (0.99 to 1.08)	33.3
Non-Hispanic Asian/Pacific Islander	629	1.6 (1.5 to 1.8)	0.94 (0.89 to 0.99)	1.9 (1.8 to 2.1)	0.77 (0.73 to 0.81)	18.8

(continued on following page)

**TABLE 1.** Age-Adjusted Incidence Rates of Microscopically Confirmed Uterine Corpus Cancer Overall and by Histology and Race and Ethnicity, Uncorrected and Corrected for Hysterectomy Prevalence, Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015) (continued)

Category	No. of Cases	Uncorrected		Corrected		Increase in Rate With Correction for Hysterectomy Prevalence (%)
		Age-Adjusted Incidence (95% CI)	IRR (95% CI)	Age-Adjusted Incidence (95% CI)	IRR (95% CI)	
Other						
Non-Hispanic white	1,861	0.7 (0.7 to 0.7)	Ref	1.1 (1.1 to 1.1)	Ref	57.1
Non-Hispanic black	481	1.2 (1.1 to 1.3)	1.63 (1.51 to 1.76)	2.1 (2.0 to 2.4)	1.85 (1.74 to 1.96)	75.0
Hispanic	439	0.8 (0.8 to 0.9)	1.17 (1.08 to 1.28)	1.3 (1.3 to 1.5)	1.10 (1.03 to 1.17)	62.5
Non-Hispanic Asian/Pacific Islander	268	0.7 (0.6 to 0.8)	0.99 (0.91 to 1.08)	0.9 (0.8 to 1.0)	0.78 (0.73 to 0.84)	28.6

Abbreviations: IRR, incidence rate ratio; Ref, reference.

**TABLE 2.** Age-Adjusted Incidence Rates of Microscopically Confirmed Uterine Corpus Cancer Overall and by Region, Uncorrected and Corrected for Hysterectomy Prevalence, Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015)

Category	No. of Cases	Uncorrected		Corrected		Increase in Rate With Correction for Hysterectomy Prevalence (%)
		Age-Adjusted Incidence (95% CI)	IRR (95% CI)	Age-Adjusted Incidence (95% CI)	IRR (95% CI)	
Region						
Northeast	31,574	48.7 (48.1 to 49.2)	Ref	67.6 (66.8 to 68.3)	Ref	38.8
Midwest	17,098	47.7 (46.9 to 48.4)	0.98 (0.97 to 0.99)	74.6 (73.3 to 75.7)	1.10 (1.09 to 1.11)	56.4
South	29,866	34.1 (33.7 to 34.4)	0.70 (0.69 to 0.71)	59.6 (58.9 to 60.1)	0.88 (0.87 to 0.89)	74.8
West	82,722	38.5 (38.2 to 38.8)	0.79 (0.78 to 0.80)	60.9 (60.4 to 61.4)	0.90 (0.89 to 0.91)	58.2
Histologic subtype × region						
Endometrial						
Northeast	23,891	36.8 (36.3 to 37.3)	Ref	50.7 (50.0 to 51.4)	Ref	37.8
Midwest	12,879	35.9 (35.3 to 36.6)	0.98 (0.96 to 0.99)	55.7 (54.8 to 56.8)	1.10 (1.09 to 1.11)	55.2
South	22,076	25.1 (24.7 to 25.4)	0.68 (0.67 to 0.69)	43.3 (42.7 to 43.9)	0.85 (0.85 to 0.86)	72.5
West	62,268	28.9 (28.6 to 29.1)	0.79 (0.78 to 0.80)	45.3 (44.8 to 45.6)	0.89 (0.88 to 0.90)	56.7
Non-Endometrial						
Northeast	5,768	8.9 (8.6 to 9.1)	Ref	12.9 (12.4 to 13.2)	Ref	44.9
Midwest	3,228	8.9 (8.6 to 9.2)	1.00 (0.97 to 1.00)	14.7 (14.2 to 15.2)	1.14 (1.12 to 1.16)	65.2
South	5,658	6.4 (6.2 to 6.5)	0.73 (0.71 to 0.74)	12.2 (11.8 to 12.4)	0.95 (0.93 to 0.97)	90.6
West	14,864	7.0 (6.9 to 7.1)	0.78 (0.76 to 0.80)	11.7 (11.5 to 11.9)	0.91 (0.89 to 0.93)	67.1
Sarcomas						
Northeast	1,389	2.2 (2.1 to 2.3)	Ref	2.9 (2.8 to 3.0)	Ref	31.8
Midwest	703	2.1 (1.9 to 2.3)	0.95 (0.90 to 1.00)	3.0 (2.7 to 3.3)	1.03 (0.99 to 1.08)	42.9
South	1,524	1.8 (1.7 to 1.9)	0.82 (0.78 to 0.86)	2.8 (2.6 to 3.0)	0.99 (0.95 to 1.03)	55.6
West	3,963	1.9 (1.8 to 2.0)	0.86 (0.82 to 0.90)	2.7 (2.6 to 2.8)	0.96 (0.92 to 1.00)	42.1
Other						
Northeast	526	0.8 (0.7 to 0.8)	Ref	1.2 (1.0 to 1.2)	Ref	50.0
Midwest	288	0.8 (0.7 to 0.8)	1.02 (0.94 to 1.10)	1.3 (1.1 to 1.3)	1.12 (1.05 to 1.20)	62.5
South	608	0.7 (0.6 to 0.8)	0.85 (0.78 to 0.92)	1.2 (1.0 to 1.4)	1.06 (0.99 to 1.13)	71.4
West	1,627	0.8 (0.7 to 0.8)	0.93 (0.86 to 1.01)	1.2 (1.1 to 1.2)	1.07 (1.00 to 1.04)	50.0

Abbreviations: IRR, incidence rate ratio; Ref, reference.

Hysterectomy-corrected rates were age standardized to the 2000 US population. We estimated incidence rate ratios and 95% CIs to compare incidence rates between groups and calculated the percentage change between uncorrected and corrected rates.

Trends in uterine cancer incidence were estimated using the National Cancer Institute Joinpoint regression software (version 4.6),<sup>21</sup> which calculates annual percentage changes (APCs) and 95% CIs and uses *t* tests to determine whether APCs are statistically significantly different from zero. The program selects the best-fitting log-linear regression model to identify years when APCs significantly changed, providing a minimum number of joinpoints necessary to fit the data. In most cases, a single segment best fit the data (single APC), with the exception of overall uterine cancer rates in all women and among whites. If more than one APC was estimated, trends were summarized by the average APC (AAPC). Trends were plotted using a semilogarithmic scale.<sup>22</sup>

We estimated 5-year relative survival rates for patients diagnosed with uterine cancer during 2000 to 2014 by race and ethnicity, stratified by histology and stage at diagnosis. Cases diagnosed by autopsy or death certificate and those missing follow-up information were excluded. Expected survival was estimated with the Ederer II method.<sup>23</sup> Individuals in the survival cohort were matched to the socioeconomic, geographic, and race annual life tables by age, sex, race and ethnicity, calendar year, and county of

residence at the time of cancer diagnosis, and relative survival was estimated as the ratio of the observed to the expected survival rate of matched patients using the actuarial method.<sup>17</sup> All statistical tests were two sided, and statistical significance was assessed at an  $\alpha$  level of  $P < .05$ .

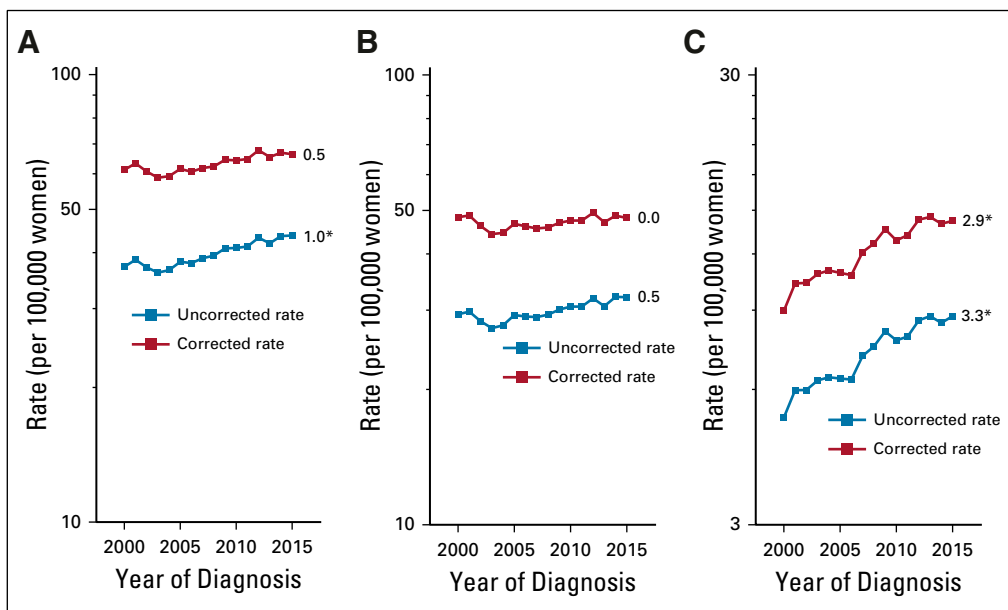
## RESULTS

### Prevalence of Hysterectomy Among US Women

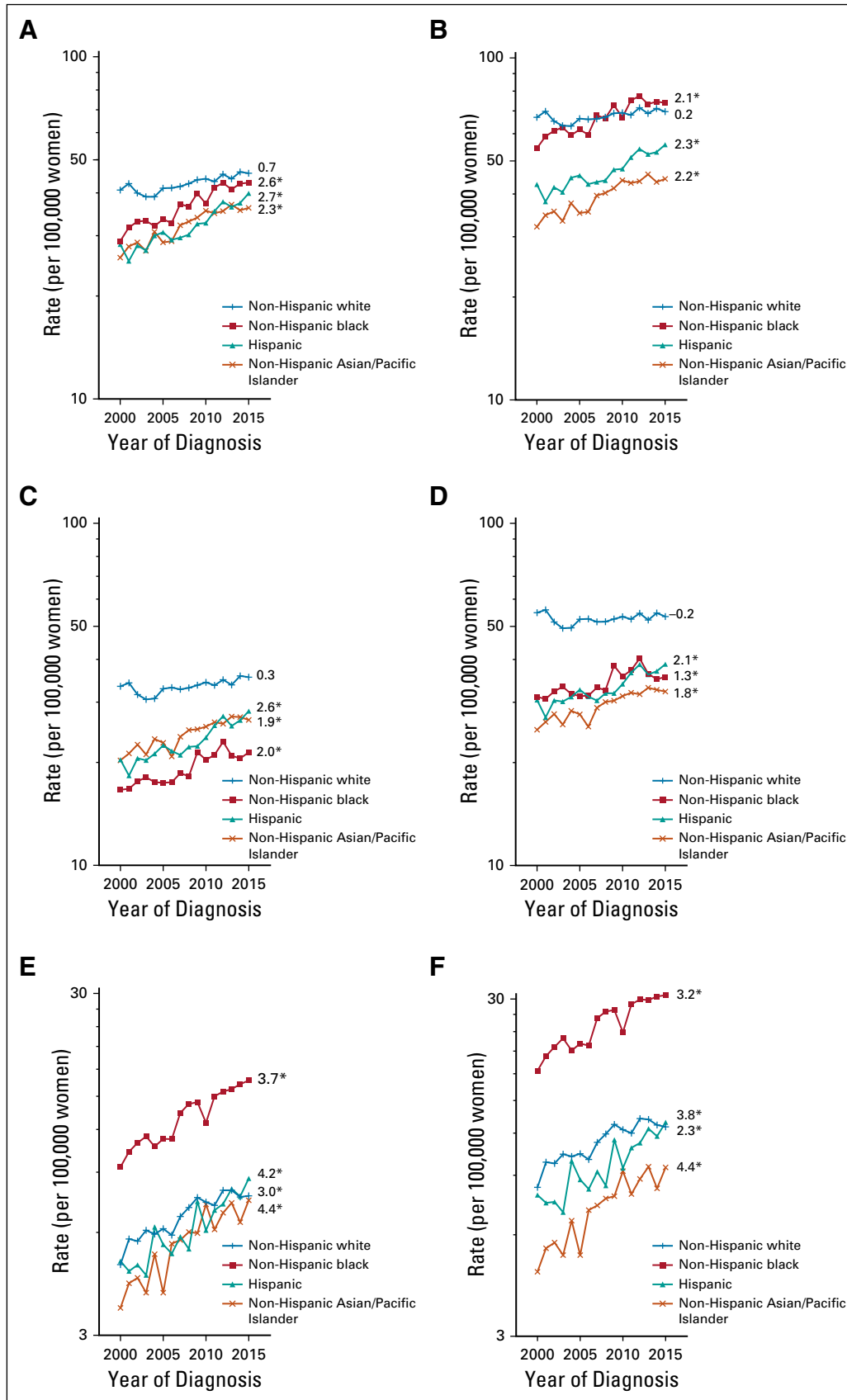
The prevalence of hysterectomy declined from 27.3% in 2000 to 23.9% in 2015, with an overall prevalence of 25.2% during 2000 to 2015. Hysterectomy prevalence varied by race and ethnicity, with the highest rate in blacks (29.0%; declining from 31.4% to 27.6%), followed by whites (25.5%; from 27.7% to 24.2%), Hispanics (22.7%; from 24.8% to 21.5%), and Asians (16.0%; from 16.7% to 15.3%). Prevalence estimates also varied by region, with the highest observed in the South (29.5%), followed by the Midwest (24.3%), West (25.0%), and Northeast (18.1%). The rates of decline were similar across regions.

### Uncorrected and Corrected Age-Adjusted Uterine Cancer Incidence Rates, 2000 to 2015

Overall, the hysterectomy-corrected incidence rate of 63.7 per 100,000 woman-years was 59% higher than the corresponding uncorrected rate (40.0; Table 1). Hysterectomy-corrected incidence varied widely by histologic subtype, being the highest for endometrioid carcinomas (47.3), followed by nonendometrioid carcinomas



**FIG 1.** Trends in age-adjusted incidence rates of microscopically confirmed uterine corpus cancer (A) overall and by (B) endometrioid and (C) nonendometrioid subtypes, uncorrected and corrected for hysterectomy prevalence, among US women age 30 to 79 years according to SEER 18 (2000 to 2015). All trends are summarized by a single annual percentage change estimate, with the exception of uncorrected and corrected overall rates, which are summarized by the average annual percentage change; trends for nonendometrioid carcinomas are plotted on a different scale. (\*) Significantly different than zero at  $P < .05$ .



**FIG 2.** Trends in age-adjusted incidence rates of microscopically confirmed uterine corpus cancer by race and ethnicity: (A, B) overall and by (C, D) endometrioid and (E, F) nonendometrioid subtypes, (A, C, E) (continued on following page)

(12.4), sarcomas (2.8), and other malignancies (1.2). Hysterectomy correction increased rates by 81.2 among blacks, 58.3 among whites, 45.3 among Hispanics, and 22.7 among Asians. Hysterectomy-corrected rates for uterine cancer overall were similar for whites and blacks (67.6, respectively) but significantly lower among Hispanics (47.5) and Asians (40.0). Corrected endometrioid carcinoma rates were significantly higher among whites (52.6) compared with blacks (34.5), Hispanics (33.7), and Asians (29.6). In contrast, corrected nonendometrioid carcinoma rates were significantly higher among blacks (25.9) compared with whites (11.4), Hispanics (10.1), and Asians (7.5). Rates for sarcomas and for other malignancies were also highest among blacks (5.2 and 2.1, respectively).

Uterine cancer rates overall and by subtype varied regionally (Table 2), with corrected rates highest in the Midwest. Overall, hysterectomy correction had the largest impact on rates in the South, particularly among blacks (Appendix Table A2, online only).

### Trends in Age-Adjusted Uterine Cancer Incidence Rates Overall and by Histologic Subtype

Hysterectomy correction had an important impact on uterine cancer trends. Among all women, uncorrected rates increased at approximately 1.0% (95% CI, 0.4% to 1.5%) per year during 2000 to 2015. After correction, the AAPC was reduced to 0.5% (95% CI, -0.1% to 1.1%) for the whole interval (Fig 1); however, corrected rates rose significantly between 2003 and 2015 (APC, 1.1%; 95% CI, 0.7% to 1.4%). Both uncorrected and corrected endometrioid cancer trends were stable, at 0.5% (95% CI, -0.1% to 1.2%) and 0.0% (95% CI, -0.7% to 0.6%), respectively. In contrast, uncorrected nonendometrioid cancer rates rose significantly, at 3.3% (95% CI, 2.8% to 3.7%) per year and similarly at 2.9% per year (95% CI, 2.4% to 3.4%) after correction. Both uncorrected and corrected sarcoma rates were stable (Appendix Fig A1, online only).

Hysterectomy-corrected trends for uterine cancer between 2000 and 2015 among whites were stable, with an AAPC of 0.2% (95% CI, -0.5% to 0.9%; Fig 2); however, rates rose significantly between 2003 and 2015 (APC, 0.8%; 95% CI, 0.4% to 1.2%). Corrected rates increased rapidly among blacks (APC, 2.1%; 95% CI, 1.5% to 2.6%), Hispanics (APC, 2.3%; 95% CI, 1.8% to 2.8%), and Asians (APC, 2.2%; 95% CI, 1.7% to 2.7%). Of note, corrected uterine cancer rates among blacks surpassed those among whites

in 2007 and were consistently higher from 2011 through 2015 (Fig 2).

For endometrioid carcinomas, corrected rates were stable among whites (APC, -0.2%; 95% CI, -0.9% to 0.5%). Corrected rates increased among blacks (APC, 1.3%; 95% CI, 0.7% to 2.0%), Hispanics (APC, 2.1%; 95% CI, 1.5% to 2.6%), and Asians (APC, 1.8%; 95% CI, 1.4% to 2.3%). Nonendometrioid carcinoma rates rose significantly among women in all racial/ethnic groups: 2.3% (95% CI, 1.0% to 3.7%) among whites, 3.2% (95% CI, 2.5% to 4.0%) among blacks, 3.8% (95% CI, 2.8% to 4.9%) among Hispanics, and 4.4% (95% CI, 3.1% to 5.6%) among Asians. Corrected sarcoma rates were stable in all groups (Appendix Fig A1).

### Five-Year Relative Survival Overall, by Race and Ethnicity, Histologic Subtype, and Stage

The overall 5-year relative survival rate among patients with uterine cancer was 83.3% and ranged from 95.4% among those with localized-stage to 69.9% among those with regional-stage and to 18.1% in those with distant-stage disease (Table 3). The 5-year relative survival rate was 91.8% in patients with endometrioid carcinomas (excluding adenocarcinoma NOS) and was significantly lower among those with nonendometrioid carcinomas or sarcomas (57.5% and 52.8%, respectively). Blacks had the lowest survival rates, irrespective of stage at diagnosis or histologic subtype (Table 3; Fig 3; Appendix Fig A2, online only). There were no apparent differences in survival among regions after stratifying by stage and histology (Appendix Table A3, online only).

## DISCUSSION

Our analysis shows that hysterectomy-corrected uterine cancer incidence rates have been significantly increasing by approximately 1% per year from 2003 to 2015, with the most rapid increases occurring in Hispanic, Asian, and black women, respectively. Among all women, we observed a concerning trend of increasing incidence of aggressive nonendometrioid subtypes, with particularly high rates in black women. Building on a previous observation,<sup>13</sup> we show that hysterectomy-corrected uterine cancer rates in blacks have consistently exceeded those of whites since approximately 2007. In addition to higher incidence of nonendometrioid cancers, black women had substantially lower 5-year relative survival, irrespective of stage at diagnosis or histologic subtype, supporting previous observations and demonstrating strong racial differences and

**FIG 2.** (Continued). uncorrected and (B, D, F) corrected for hysterectomy prevalence, among US women age 30 to 79 years according to SEER 18 (2000 to 2015). Uncorrected and corrected rates are shown separately among non-Hispanic whites (+), non-Hispanic blacks (solid square), Hispanics (solid triangle), and non-Hispanic Asians/Pacific Islanders (×). All trends are summarized by a single annual percentage change estimate, with the exception of uncorrected and corrected overall rates among non-Hispanic whites, which are summarized by the average annual percentage change; trends for nonendometrioid carcinomas are plotted on a different scale. (\*) Significantly different than zero at  $P < .05$ .



**TABLE 3.** Five-Year Relative Survival for Patients With Microscopically Confirmed Uterine Corpus Cancer Age 30 to 79 Years by Race and Ethnicity Overall and by Stage and Histologic Type According to SEER 18 (2000 to 2014)

Category	Total		Non-Hispanic White		Non-Hispanic Black		Hispanic		Non-Hispanic Asian/Pacific Islander	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Overall	129,473	83.3 (83.0 to 83.5)	92,528	86.1 (85.8 to 86.4)	12,555	63.2 (62.2 to 64.2)	14,258	81.4 (80.6 to 82.2)	10,132	83.7 (82.8 to 84.5)
Stage at diagnosis										
Localized	89,532	95.4 (95.2 to 95.6)	66,235	96.5 (96.2 to 96.8)	6,909	86.4 (85.2 to 87.4)	9,574	93.9 (93.2 to 94.6)	6,814	95.1 (94.4 to 95.8)
Regional	26,030	69.9 (69.2 to 70.6)	17,726	73.1 (72.3 to 73.8)	3,134	48.7 (46.6 to 50.8)	2,952	70.0 (68.0 to 71.9)	2,218	74.0 (71.9 to 76.1)
Distant	10,473	18.1 (17.3 to 18.9)	6,337	20.0 (18.9 to 21.1)	1,970	9.7 (8.3 to 11.3)	1,288	19.6 (17.2 to 22.1)	878	20.4 (17.3 to 23.6)
Unknown/unstaged	3,438	65.5 (63.6 to 67.3)	2,230	68.4 (66.1 to 70.5)	542	48.3 (43.3 to 53.1)	444	68.3 (62.8 to 73.2)	222	70.6 (63.0 to 76.9)
Histologic subtype										
Endometroid*	101,113	90.8 (90.6 to 91.1)	75,112	92.1 (91.8 to 92.4)	7,256	78.7 (77.5 to 79.9)	10,850	89.5 (88.8 to 90.3)	7,895	91.0 (90.2 to 91.7)
Endometroid without NOS	87,404	91.8 (91.5 to 92.1)	64,997	92.9 (92.6 to 93.2)	6,019	81.7 (80.4 to 83.0)	9,419	90.5 (89.6 to 91.2)	6,969	91.8 (91.0 to 92.6)
Adenocarcinoma NOS	13,709	84.7 (84.0 to 85.4)	10,115	87.3 (86.5 to 88.1)	1,237	64.1 (61.0 to 67.1)	1,431	83.6 (81.3 to 85.7)	926	84.6 (81.8 to 87.0)
Nonendometroid	19,651	57.5 (56.7 to 58.3)	12,332	61.8 (60.8 to 62.8)	3,739	41.8 (39.8 to 43.7)	2,085	57.5 (54.9 to 60.0)	1,495	59.7 (56.8 to 62.5)
Sarcoma	6,333	52.8 (51.4 to 54.1)	3,633	55.9 (54.1 to 57.6)	1,187	42.0 (38.8 to 45.0)	977	53.3 (49.7 to 56.7)	536	54.5 (49.7 to 59.0)
Histologic subtype × stage										
Endometroid*										
Localized	77,163	97.5 (97.3 to 97.7)	58,268	98.1 (97.9 to 98.4)	4,960	92.3 (91.0 to 93.4)	8,096	96.5 (95.8 to 97.1)	5,839	97.1 (96.4 to 97.7)
Regional	17,623	79.0 (78.3 to 79.7)	12,588	80.5 (79.6 to 81.4)	1,461	62.6 (59.6 to 65.5)	1,994	79.2 (77.0 to 81.3)	1,580	81.8 (79.4 to 84.0)
Distant	3,997	24.4 (22.9 to 25.9)	2,660	26.6 (24.8 to 28.5)	544	11.4 (8.5 to 14.8)	472	23.5 (19.2 to 28.0)	321	28.0 (22.6 to 33.6)
Unknown/unstaged	2,330	71.7 (69.5 to 73.8)	1,596	73.2 (70.5 to 75.6)	291	55.3 (48.2 to 61.7)	288	75.1 (68.4 to 80.6)	155	80.7 (71.9 to 87.0)
Endometroid without NOS										
Localized	67,161	97.6 (97.4 to 97.9)	50,667	98.2 (97.9 to 98.4)	4,266	92.9 (91.5 to 94.0)	7,055	96.7 (95.9 to 97.3)	5,173	97.3 (96.5 to 97.9)
Regional	15,663	80.5 (79.7 to 81.3)	11,210	81.7 (80.8 to 82.6)	1,218	65.6 (62.3 to 68.8)	1,796	80.9 (78.6 to 83.0)	1,439	82.8 (80.3 to 85.0)
Distant	2,944	29.1 (27.3 to 30.9)	1,987	31.5 (29.2 to 33.8)	351	14.9 (10.8 to 19.6)	362	26.2 (21.1 to 31.5)	244	32.9 (26.4 to 39.6)
Unknown/unstaged	1,636	73.8 (71.1 to 76.3)	1,133	74.5 (71.3 to 77.4)	184	59.6 (50.5 to 67.6)	206	77.9 (69.8 to 84.0)	113	82.4 (72.1 to 89.1)
Adenocarcinoma NOS										
Localized	10,002	96.7 (96.1 to 97.3)	7,601	97.7 (97.0 to 98.3)	694	88.5 (84.9 to 91.3)	1,041	95.1 (93.0 to 96.6)	666	95.7 (93.2 to 97.3)
Regional	1,960	67.7 (65.3 to 70.0)	1,378	71.1 (68.2 to 73.7)	243	47.5 (40.3 to 54.3)	198	64.5 (56.5 to 71.3)	141	72.1 (63.1 to 79.3)
Distant	1,053	11.3 (9.3 to 13.5)	673	12.3 (9.7 to 15.1)	193	5.3 (2.6 to 9.5)	110	14.4 (8.1 to 22.5)	77	13.9 (6.8 to 23.4)
Unknown/unstaged	694	66.9 (62.8 to 70.7)	463	69.7 (64.7 to 74.1)	107	47.0 (36.1 to 57.1)	82	69.2 (56.0 to 79.2)	42	77.5 (58.3 to 88.7)

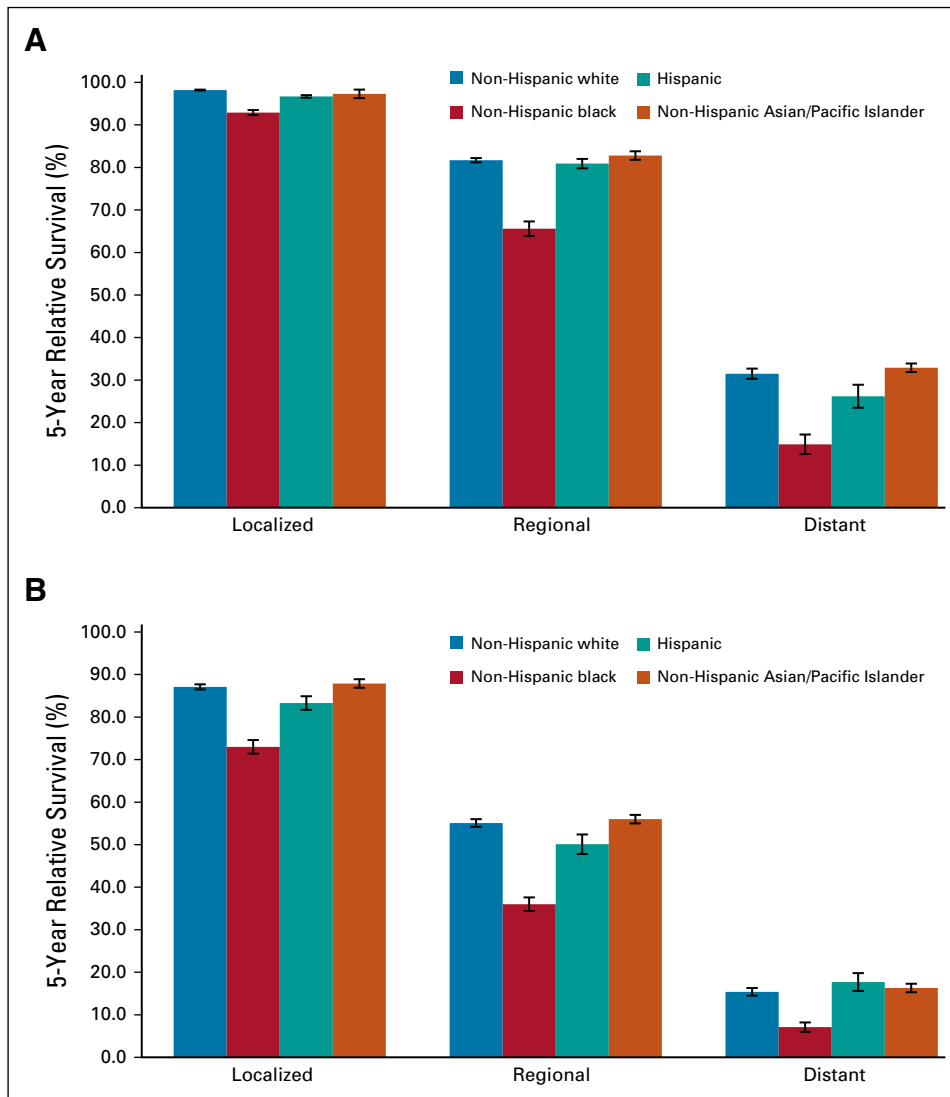
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**TABLE 3.** Five-Year Relative Survival for Patients With Microscopically Confirmed Uterine Corpus Cancer Age 30 to 79 Years by Race and Ethnicity Overall and by Stage and Histologic Type According to SEER 18 (2000 to 2014) (continued)

Category	Total		Non-Hispanic White		Non-Hispanic Black		Hispanic		Non-Hispanic Asian/Pacific Islander	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Nonendometrioid										
Localized	8,391	84.6 (83.6 to 85.6)	5,548	87.1 (85.8 to 88.3)	1,340	73.0 (69.8 to 76.0)	892	83.3 (79.9 to 86.2)	611	87.9 (84.2 to 90.7)
Regional	6,909	50.8 (48.3 to 52.2)	4,260	55.1 (53.3 to 56.8)	1,414	36.0 (33.0 to 39.0)	725	50.1 (45.5 to 54.4)	510	56.0 (50.9 to 60.8)
Distant	3,943	13.9 (12.6 to 15.2)	2,296	15.4 (13.7 to 17.1)	868	7.1 (5.2 to 9.3)	427	17.7 (13.7 to 22.0)	352	16.3 (11.8 to 21.4)
Unknown/unstaged	408	40.0 (34.5 to 45.5)	228	46.9 (39.3 to 54.2)	117	24.5 (15.9 to 34.1)	41	46.1 (27.8 to 62.6)	22	27.8 (9.5 to 49.9)
Sarcoma										
Localized	3,216	73.6 (71.7 to 75.4)	1,918	75.5 (73.2 to 77.7)	506	66.0 (61.1 to 70.4)	502	73.6 (68.9 to 77.8)	290	74.3 (68.0 to 79.5)
Regional	1,019	47.2 (43.6 to 50.7)	597	50.6 (46.1 to 54.9)	192	35.5 (27.9 to 43.2)	149	47.8 (38.7 to 56.4)	81	51.5 (39.6 to 62.2)
Distant	1,794	16.1 (14.2 to 18.1)	941	17.0 (14.4 to 19.7)	432	13.6 (10.2 to 17.4)	272	17.1 (12.4 to 22.4)	149	13.7 (8.1 to 20.7)
Unknown/unstaged	304	65.0 (58.5 to 70.8)	177	66.9 (58.7 to 73.8)	57	60.3 (44.6 to 72.9)	54	61.4 (43.9 to 75.0)	16	82.0 (51.0 to 94.3)

Abbreviation: NOS, not otherwise specified.

\*Includes adenocarcinoma NOS.



**FIG 3.** Five-year relative survival for patients with microscopically confirmed uterine corpus cancer age 30 to 79 years by stage at diagnosis and race and ethnicity for (A) endometrioid and (B) non-endometrioid subtypes. Expected survival for patients diagnosed between 2000 and 2014 was estimated with the Ederer II method, and relative survival was calculated by estimating the observed to the expected survival rate using the actuarial method. Error bars indicate standard error.

disparities related to both biologic and care-related factors among black women.<sup>24-27</sup>

Previous studies of uterine cancer incidence trends by race and ethnicity and histology have been mixed. A study evaluating trends in hysterectomy-corrected rates in women age 50 years or older suggested increasing rates of both endometrioid and nonendometrioid cancers in blacks but a significant decrease in the rate of endometrioid and nonstatistically significant increase in the rate of nonendometrioid cancers among whites.<sup>13</sup> A study of women younger than 50 years of age suggested stable trends of hysterectomy-corrected rates of endometrioid carcinomas among whites and blacks but a significantly increasing trend among Hispanics.<sup>15</sup> A recent study reported increasing rates of endometrioid carcinoma rates from 1999 to 2015 among all women, with decreases observed for all other histologic types; however, these rates were not corrected for hysterectomy prevalence.<sup>11</sup> Moreover, in that analysis, cases with adenocarcinoma NOS histology

were incorrectly grouped with nonendometrioid types, resulting in likely misattribution of many endometrioid carcinomas as nonendometrioid types, particularly in the earlier years.<sup>11</sup>

Our analysis of hysterectomy-corrected uterine cancer incidence rates among women age 30 to 79 years shows that rising rates are largely a result of the rapid increase of nonendometrioid subtypes among all racial and ethnic groups. Our data are in line with a recent study of hysterectomy-corrected uterine cancer incidence in Denmark, which showed increasing rates of nonendometrioid but not endometrioid carcinomas.<sup>28</sup> Endometrioid carcinomas are more likely to be diagnosed at an early stage, with good overall survival; they are described as estrogen dependent and are more strongly associated with obesity.<sup>29</sup> In contrast, patients with nonendometrioid carcinomas have worse survival, and risk has been less strongly associated with estrogen-related risk factors and obesity.<sup>29</sup> Thus, the observed increases in nonendometrioid cancer

incidence, combined with more stable rates of endometrioid cancers, challenge the prevailing hypothesis that the obesity epidemic and changing prevalence of hormonal risk factors are major contributors to rising uterine cancer incidence. Identifying risk factors and exposures more specifically associated with nonendometrioid cancers is needed to better understand the strong increases in this subtype and potentially address racial disparities.

To our knowledge, our study is the first to describe hysterectomy-corrected trends by histologic subtype among Hispanics and Asians. Despite lower uterine cancer incidence in these groups, rates have risen most rapidly among Hispanics and Asians, particularly nonendometrioid carcinomas. Risk factors such as obesity, diabetes, and metabolic syndrome are highly prevalent among Hispanic women<sup>30-32</sup> and have been increasing among Asian American populations.<sup>33,34</sup> However, it is unlikely that these risk factors cannot fully explain the pronounced increases in nonendometrioid cancer rates among these women. With respect to survival, we found that Asians had 5-year relative survival similar to those of whites, whereas survival was poorer among Hispanics, in line with some<sup>35,36</sup> but not all studies.<sup>37-39</sup> It is possible that these differences result from variation in cohort selection, data sources, and the ability to account for differences in treatment and comorbidities.

Another unique aspect of this study was the assessment of uterine cancer incidence and survival by geographic region. Hysterectomy prevalence varied widely by region, with the highest rates in the South and lowest in the Northeast. Hysterectomy correction decreased regional differences observed using uncorrected rates, suggesting these differences largely reflect regional variation in hysterectomy prevalence rather than true differences in cancer incidence. Our analysis underscores the importance of using hysterectomy-corrected rates to understand variation in the regional burden of uterine cancer in the United States.<sup>16</sup> Importantly, after stratifying by race and ethnicity, histology, and stage at diagnosis, we did not observe strong regional differences in the survival rates of patients with uterine cancer.

Our analysis provides nationally representative hysterectomy-corrected estimates of uterine cancer incidence and trends, overall and by histologic subtype, using the most

recent data from SEER 18 registries. In addition, we used a new approach to better account for unclassified adenocarcinomas compared with previous studies. The proportion of adenocarcinomas NOS has decreased substantially over time, and incorrect attribution of these poorly classified cases can affect subtype-specific rates.<sup>11</sup> Our proportional allocation of adenocarcinomas NOS to the two main subtypes provides incidence estimates that are closer to the true underlying incidence. Some limitations are worth noting. First, although BRFSS is the only nationally representative database with state-level hysterectomy prevalence estimates, response rates have been lower compared with other surveys, which may affect data representativeness.<sup>40</sup> Moreover, it is possible that the region-specific hysterectomy prevalence estimates do not completely overlap with SEER catchment areas. Finally, although SEER registries use standardized codes and procedures for classifying race and ethnicity data, initial collection of this information is carried out by health care facilities and practitioners, and misclassification is possible.<sup>41</sup>

To our knowledge, this study represents the most comprehensive analysis of hysterectomy-corrected uterine cancer incidence trends and survival conducted to date. Our findings show profound racial differences and disparities with respect to subtype-specific incidence and survival, indicated by the higher burden of nonendometrioid subtypes and poorer survival irrespective of stage or histology among black women, suggesting a combination of biologic and care-related factors. We confirm that uterine cancer incidence rates among black women have surpassed those of white women since 2007 and have remained consistently higher through 2015. A striking finding from our study is that recent increases have been primarily driven by rising rates of aggressive nonendometrioid histologic subtypes among all racial and ethnic subgroups. Contrary to prior assumptions, it is unlikely that the rising prevalence of obesity and changes in hormonal risk factors can fully explain the increasing uterine cancer incidence trends, because these factors are equally or more strongly associated with endometrioid cancers, the rates for which remained more stable over time in our study. Future studies are needed to clarify the factors underlying the remarkable rise in nonendometrioid carcinoma incidence.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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## AUTHOR CONTRIBUTIONS

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**Data analysis and interpretation:** All authors

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

**Accountable for all aspects of the work:** All authors

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**Hysterectomy-Corrected Uterine Corpus Cancer Incidence Trends and Differences in Relative Survival Reveal Racial Disparities and Rising Rates of Nonendometrioid Cancers**

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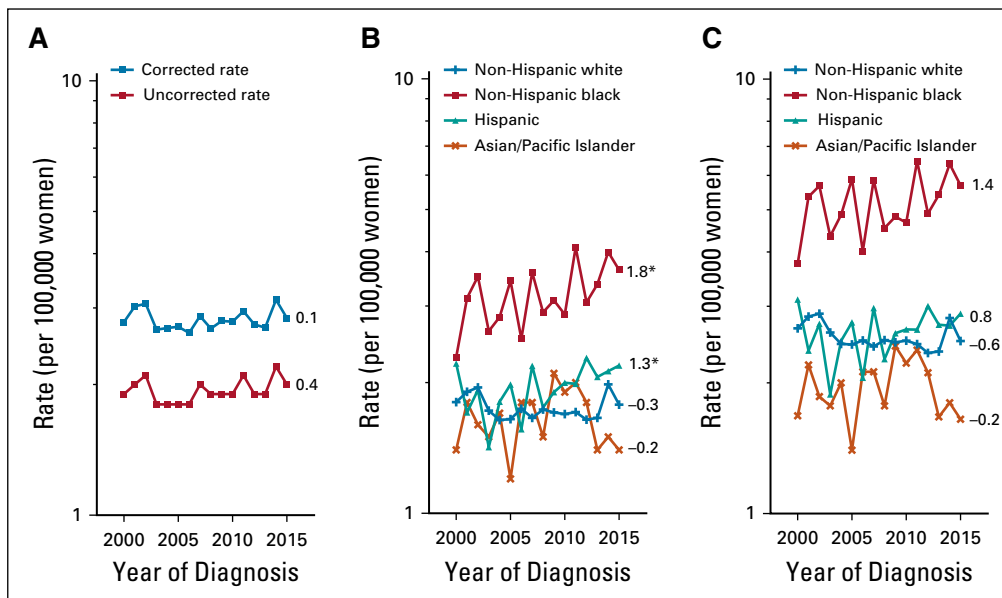
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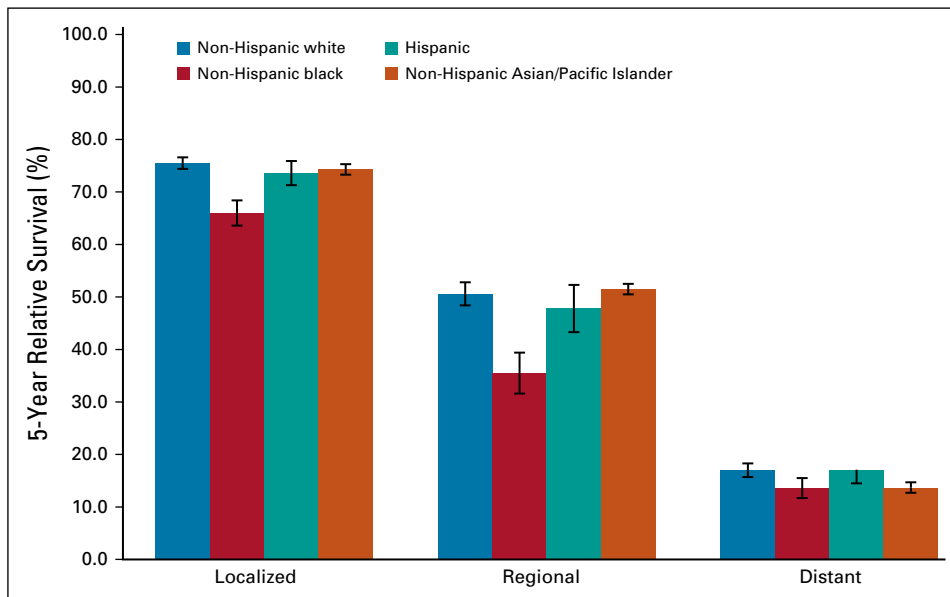
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APPENDIX



**FIG A1.** Trends in age-adjusted incidence rates of microscopically confirmed uterine corpus sarcomas overall and by race and ethnicity, uncorrected and corrected for hysterectomy prevalence, among US women age 30 to 79 years according to SEER 18 (2000 to 2015). (A) Uncorrected and corrected rates for sarcomas among all women. (B) Uncorrected and (C) corrected rates for non-Hispanic whites (+), non-Hispanic blacks (solid square), Hispanics (solid triangle), and non-Hispanic Asians/Pacific Islanders (x). Annual percentage change estimates are shown next to each respective curve. (\*) Significantly different than zero at  $P < .05$ .



**FIG A2.** Five-year relative survival for patients with microscopically confirmed uterine corpus sarcoma age 30 to 79 years by stage at diagnosis and race and ethnicity. Expected survival for patients diagnosed between 2000 and 2014 was estimated with the Ederer II method, and relative survival was calculated by estimating the observed to the expected survival rate using the actuarial method. Error bars indicate standard error.



**TABLE A1.** Number of Cases by ICD-O-3 Histology Codes by Histologic Subtype Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015)

<b>Histology</b>	<b>No. of Cases</b>
<b>Endometrioid</b>	
8050/3: Papillary carcinoma, NOS	85
8141/3: Scirrhus adenocarcinoma	4
8210/3: Adenocarcinoma in adenomatous polyp	770
8211/3: Tubular adenocarcinoma	1
8260/3: Papillary adenocarcinoma, NOS	433
8261/3: Adenocarcinoma in villous adenoma	4
8262/3: Villous adenocarcinoma	69
8263/3: Adenocarcinoma in tubulovillous adenoma	104
8380/3: Endometrioid carcinoma	101,779
8381/3: Endometrioid adenofibroma, malignant	30
8382/3: Endometrioid adenocarcinoma, secretory variant	254
8383/3: Endometrioid adenocarcinoma, ciliated cell variant	89
8440/3: Cystadenocarcinoma, NOS	13
8470/3: Mucinous cystadenocarcinoma, NOS	2
8471/3: Papillary mucinous cystadenocarcinoma	3
8480/3: Mucinous adenocarcinoma	1,257
8481/3: Mucin-producing adenocarcinoma	90
8490/3: Signet ring cell carcinoma	9
8560/3: Adenosquamous carcinoma	1,393
8570/3: Adenocarcinoma with squamous metaplasia	1,584
8571/3: Adenocarcinoma with cartilaginous and osseous metaplasia	1
8140/3: Adenocarcinoma, NOS*	16,053
<b>Nonendometrioid</b>	
8255/3: Adenocarcinoma with mixed subtypes	609
8310/3: Clear cell adenocarcinoma, NOS	1,924
8323/3: Mixed cell adenocarcinoma	7,419
8441/3: Serous cystadenocarcinoma, NOS	4,256
8460/3: Papillary serous cystadenocarcinoma	4,280
8461/3: Serous surface papillary carcinoma	507
8950/3: Mullerian mixed tumor	2,972
8951/3: Mesodermal mixed tumor	307
8980/3: Carcinosarcoma, NOS	4,325
8981/3: Carcinosarcoma, embryonal	6
<b>Sarcomas</b>	
8800/3: Sarcoma, NOS	367
8801/3: Spindle cell sarcoma	41
8802/3: Giant cell sarcoma	23
8803/3: Small cell sarcoma	2
8804/3: Epithelioid sarcoma	14
8805/3: Undifferentiated sarcoma	105
8810/3: Fibrosarcoma, NOS	2
8811/3: Fibromyxosarcoma	2

(continued on following page)

**TABLE A1.** Number of Cases by ICD-O-3 Histology Codes by Histologic Subtype Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015) (continued)

Histology	No. of Cases
8814/3: Infantile fibrosarcoma	1
8840/3: Myxosarcoma	2
8850/3: Liposarcoma, NOS	1
8853/3: Round cell liposarcoma	1
8855/3: Mixed liposarcoma	1
8858/3: Dedifferentiated liposarcoma	1
8860/3: Angiomyoliposarcoma	1
8890/3: Leiomyosarcoma, NOS	3,575
8891/3: Epithelioid leiomyosarcoma	210
8895/3: Myosarcoma	2
8896/3: Myxoid leiomyosarcoma	141
8900/3: Rhabdomyosarcoma, NOS	70
8901/3: Pleomorphic rhabdomyosarcoma, adult type	17
8902/3: Mixed-type rhabdomyosarcoma	7
8910/3: Embryonal rhabdomyosarcoma, NOS	15
8912/3: Spindle cell rhabdomyosarcoma	2
8920/3: Alveolar rhabdomyosarcoma	5
8930/3: Endometrial stromal sarcoma, NOS	1,107
8931/3: Endometrial stromal sarcoma, low grade	877
8933/3: Adenosarcoma	779
8935/3: Stromal sarcoma, NOS	193
8936/3: GI stromal sarcoma	3
9120/3: Hemangiosarcoma	4
9180/3: Osteosarcoma, NOS	2
9220/3: Chondrosarcoma, NOS	2
9240/3: Mesenchymal chondrosarcoma	1
9260/3: Ewing sarcoma	3
Other	
8000/3: Neoplasm, malignant	285
8001/3: Tumor cells, malignant	2
8004/3: Malignant tumor, spindle cell type	6
8005/3: Malignant tumor, clear cell type	10
8010/3: Carcinoma, NOS	1,234
8011/3: Epithelioma, malignant	1
8012/3: Large-cell carcinoma, NOS	6
8013/3: Large-cell neuroendocrine carcinoma	29
8014/3: Large-cell carcinoma with rhabdoid phenotype	1
8015/3: Glassy cell carcinoma	4
8020/3: Carcinoma, undifferentiated, NOS	248
8021/3: Carcinoma, anaplastic, NOS	14
8022/3: Pleomorphic carcinoma	8
8030/3: Giant cell and spindle cell carcinoma	2
8031/3: Giant cell carcinoma	6

(continued on following page)

**TABLE A1.** Number of Cases by ICD-O-3 Histology Codes by Histologic Subtype Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015) (continued)

<b>Histology</b>	<b>No. of Cases</b>
8032/3: Spindle cell carcinoma, NOS	18
8033/3: Pseudosarcomatous carcinoma	18
8040/3: Tumorlet, malignant	1
8041/3: Small-cell carcinoma, NOS	95
8045/3: Combined small-cell carcinoma	6
8046/3: Non-small-cell carcinoma	30
8051/3: Verrucous carcinoma, NOS	3
8052/3: Papillary squamous cell carcinoma	6
8070/3: Squamous cell carcinoma, NOS	458
8071/3: Squamous cell carcinoma, keratinizing, NOS	45
8072/3: Squamous cell carcinoma, large cell, nonkeratinizing, NOS	42
8073/3: Squamous cell carcinoma, small cell, nonkeratinizing	1
8074/3: Squamous cell carcinoma, spindle cell	1
8076/3: Squamous cell carcinoma, microinvasive	4
8082/3: Lymphoepithelial carcinoma	2
8083/3: Basaloid squamous cell carcinoma	4
8084/3: Squamous cell carcinoma, clear cell type	1
8098/3: Adenoid basal cell carcinoma	3
8120/3: Transitional cell carcinoma, NOS	8
8130/3: Papillary transitional cell carcinoma	7
8144/3: Adenocarcinoma, intestinal type	2
8200/3: Adenoid cystic carcinoma	1
8201/3: Cribriform carcinoma, NOS	2
8220/3: Adenocarcinoma in adenomatous polyposis coli	1
8221/3: Adenocarcinoma in multiple adenomatous polyps	1
8230/3: Solid carcinoma, NOS	4
8244/3: Mixed adenoneuroendocrine carcinoma (ICD-O-3 update)	2
8246/3: Neuroendocrine carcinoma, NOS	106
8249/3: Atypical carcinoid tumor	1
8290/3: Oxyphilic adenocarcinoma	1
8313/3: Clear cell adenocarcinofibroma	3
8320/3: Granular cell carcinoma	2
8370/3: Adrenal cortical carcinoma	1
8384/3: Adenocarcinoma, endocervical type	10
8410/3: Sebaceous adenocarcinoma	1
8450/3: Papillary cystadenocarcinoma, NOS	9
8482/3: Mucinous adenocarcinoma, endocervical type	41
8507/3: Ductal carcinoma, micropapillary	1
8510/3: Medullary carcinoma, NOS	1
8562/3: Epithelial-myoeithelial carcinoma	2
8574/3: Adenocarcinoma with neuroendocrine differentiation	28
8575/3: Metaplastic carcinoma, NOS	7
8576/3: Hepatoid adenocarcinoma	1

(continued on following page)

**TABLE A1.** Number of Cases by ICD-O-3 Histology Codes by Histologic Subtype Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015) (continued)

<b>Histology</b>	<b>No. of Cases</b>
8580/3: Thymoma, malignant, NOS	1
8590/3: Sex cord–gonadal stromal tumor, malignant, NOS	4
8620/3: Granulosa cell tumor, malignant	1
8806/3: Desmoplastic small round cell tumor	1
8825/3: Myofibroblastoma, malignant	2
8830/3: Malignant fibrous histiocytoma	4
8897/3: Malignant tumor of smooth muscle	1
8934/3: Carcinofibroma	2
8940/3: Mixed tumor, malignant, NOS	7
8960/3: Nephroblastoma, NOS	1
8963/3: Malignant rhabdoid tumor	9
8990/3: Mesenchymoma, malignant	5
9014/3: Serous adenocarcinofibroma	4
9015/3: Mucinous adenocarcinofibroma	1
9065/3: Germ cell tumor, nonseminomatous	1
9071/3: Yolk sac tumor	7
9080/3: Teratoma, malignant, NOS	2
9085/3: Mixed germ cell tumor	1
9100/3: Choriocarcinoma, NOS	99
9101/3: Choriocarcinoma combined with other germ cell elements	3
9104/3: Malignant placental site trophoblastic tumor	1
9105/3: Trophoblastic tumor, epithelioid	17
9110/3: Mesonephroma, malignant	12
9130/3: Hemangioendothelioma, malignant	1
9150/3: Hemangiopericytoma, malignant	1
9251/3: Malignant giant cell tumor of soft parts	1
9364/3: Peripheral neuroectodermal tumor	9
9380/3: Glioma, malignant	1
9473/3: Primitive neuroectodermal tumor	8
9508/3: Atypical teratoid/rhabdoid tumor	1
9581/3: Alveolar soft part sarcoma	4

Abbreviations: ICD-O-3, International Classification of Diseases for Oncology (third edition); NOS, not otherwise specified.

\*Cases of adenocarcinoma NOS were proportionally reclassified according to the observed distribution of endometrioid and nonendometrioid cases by year, age, race, ethnicity, and region.

**TABLE A2.** Age-Adjusted Incidence Rates of Microscopically Confirmed Uterine Corpus Cancer Overall and by Race and Ethnicity and Region, Uncorrected and Corrected for Hysterectomy Prevalence, Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015)

Variable	No. of Cases	Uncorrected		Corrected		Increase in Rate With Correction for Hysterectomy Prevalence (%)
		Age-Adjusted Incidence (95% CI)	IRR (95% CI)	Age-Adjusted Incidence (95% CI)	IRR (95% CI)	
Race and ethnicity × region						
Non-Hispanic white						
Northeast	25,229	52.2 (51.6 to 52.9)	Ref	72.4 (71.6 to 73.4)	Ref	38.7
Midwest	14,584	49.5 (48.7 to 50.3)	0.95 (0.94 to 0.96)	77.5 (76.1 to 78.6)	1.07 (1.06 to 1.08)	56.6
South	22,577	35.1 (34.6 to 35.5)	0.67 (0.66 to 0.68)	60.7 (60.0 to 61.6)	0.84 (0.83 to 0.85)	72.9
West	53,090	41.4 (41.0 to 42.7)	0.79 (0.78 to 0.80)	66.4 (65.8 to 68.5)	0.92 (0.91 to 0.92)	60.4
Non-Hispanic black						
Northeast	2,978	42.6 (41.0 to 44.1)	Ref	64.2 (61.8 to 66.5)	Ref	50.7
Midwest	2,054	41.3 (39.5 to 43.1)	0.97 (0.96 to 0.98)	71.6 (68.5 to 74.7)	1.12 (1.11 to 1.13)	73.4
South	6,384	34.2 (33.3 to 35.0)	0.80 (0.79 to 0.81)	68.9 (67.1 to 70.5)	1.07 (1.06 to 1.08)	101.5
West	4,227	37.4 (36.3 to 38.6)	0.88 (0.87 to 0.89)	67.0 (65.0 to 69.1)	1.04 (1.04 to 1.05)	79.1
Hispanic						
Northeast	2,428	39.1 (37.5 to 40.8)	Ref	51.5 (49.4 to 53.7)	Ref	31.7
Midwest	290	43.1 (38.1 to 48.6)	1.10 (1.09 to 1.11)	62.1 (54.9 to 70.0)	1.21 (1.20 to 1.22)	44.1
South	583	28.0 (25.6 to 30.6)	0.72 (0.71 to 0.72)	45.8 (41.9 to 50.1)	0.89 (0.88 to 0.90)	63.6
West	14,290	31.9 (31.4 to 32.5)	0.82 (0.81 to 0.83)	46.8 (46.1 to 47.7)	0.91 (0.90 to 0.92)	46.7
Asian/Pacific Islander						
Northeast	939	26.3 (24.6 to 28.1)	Ref	30.0 (28.1 to 32.1)	Ref	14.1
Midwest	170	23.4 (19.9 to 27.4)	0.89 (0.88 to 0.90)	29.0 (24.7 to 34.0)	0.97 (0.95 to 0.98)	23.9
South	322	19.2 (17.1 to 21.5)	0.73 (0.72 to 0.74)	24.9 (22.2 to 27.9)	0.83 (0.82 to 0.84)	29.7
West	11,115	34.3 (33.7 to 35.0)	1.31 (1.29 to 1.32)	41.5 (40.8 to 42.3)	1.38 (1.36 to 1.40)	21.0
Subtype × race and ethnicity × region*						
Endometrioid						
Non-Hispanic white						
Northeast	19,810	41.0 (40.4 to 41.6)	Ref	56.5 (55.7 to 57.3)	Ref	37.8
Midwest	11,473	38.9 (38.2 to 39.6)	0.95 (0.94 to 0.96)	60.5 (59.4 to 61.6)	1.07 (1.06 to 1.08)	55.5
South	17,963	27.9 (27.5 to 28.3)	0.68 (0.67 to 0.69)	47.8 (47.1 to 48.5)	0.85 (0.84 to 0.85)	71.3
West	41,231	32.1 (31.8 to 32.4)	0.78 (0.77 to 0.79)	51.1 (50.6 to 51.6)	0.90 (0.89 to 0.91)	59.2
Non-Hispanic black						
Northeast	1,584	22.4 (21.4 to 23.5)	Ref	33.3 (31.8 to 35.0)	Ref	48.7
Midwest	1,074	21.2 (20.0 to 22.5)	0.94 (0.93 to 0.96)	35.8 (33.7 to 38.1)	1.08 (1.06 to 1.09)	68.9
South	3,451	18.1 (17.5 to 18.7)	0.81 (0.79 to 0.82)	35.3 (34.0 to 36.4)	1.06 (1.05 to 1.07)	95.0
West	2,186	19.1 (18.3 to 19.9)	0.85 (0.84 to 0.87)	30.9 (29.7 to 32.3)	0.93 (0.92 to 0.94)	61.8
Hispanic						
Northeast	1,788	28.2 (26.8 to 29.6)	Ref	36.6 (34.8 to 38.4)	Ref	29.8
Midwest	216	33.0 (28.7 to 37.8)	1.10 (1.09 to 1.12)	43.9 (38.2 to 50.3)	1.20 (1.19 to 1.21)	41.2
South	419	19.7 (17.7 to 21.8)	0.70 (0.69 to 0.71)	31.9 (28.7 to 35.2)	0.87 (0.86 to 0.88)	61.9
West	10,460	22.9 (22.4 to 23.4)	0.81 (0.80 to 0.82)	33.1 (32.4 to 33.8)	0.90 (0.89 to 0.91)	44.5

(continued on following page)

**TABLE A2.** Age-Adjusted Incidence Rates of Microscopically Confirmed Uterine Corpus Cancer Overall and by Race and Ethnicity and Region, Uncorrected and Corrected for Hysterectomy Prevalence, Among US Women Age 30 to 79 Years According to SEER 18 (2000 to 2015) (continued)

Variable	No. of Cases	Uncorrected		Corrected		Increase in Rate With Correction for Hysterectomy Prevalence (%)
		Age-Adjusted Incidence (95% CI)	IRR (95% CI)	Age-Adjusted Incidence (95% CI)	IRR (95% CI)	
Nonendometrioid						
Non-Hispanic white						
Northeast	4,143	8.4 (8.2 to 8.7)	Ref	12.2 (11.9 to 12.7)	Ref	45.2
Midwest	2,416	7.7 (7.4 to 8.0)	0.92 (0.90 to 0.94)	13.2 (12.7 to 13.7)	1.09 (1.07 to 1.11)	41.7
South	3,344	4.8 (4.6 to 5.0)	0.57 (0.56 to 0.59)	9.5 (9.1 to 9.9)	0.78 (0.77 to 0.80)	97.9
West	8,844	6.4 (6.3 to 6.5)	0.77 (0.75 to 0.79)	11.5 (11.3 to 11.7)	0.95 (0.93 to 0.97)	79.7
Non-Hispanic black						
Northeast	1,050	15.3 (14.3 to 16.3)	Ref	23.9 (22.3 to 25.5)	Ref	56.2
Midwest	717	13.9 (12.9 to 15.0)	0.91 (0.89 to 0.93)	27.3 (25.3 to 29.5)	1.14 (1.12 to 1.16)	96.4
South	2,152	11.1 (10.6 to 11.6)	0.73 (0.71 to 0.74)	26.3 (25.1 to 27.5)	1.10 (1.08 to 1.11)	137.0
West	1,543	13.1 (12.5 to 13.8)	0.86 (0.84 to 0.88)	26.3 (25.1 to 27.7)	1.10 (1.08 to 1.11)	100.0
Hispanic						
Northeast	413	7.5 (6.7 to 8.4)	Ref	10.4 (9.3 to 11.6)	Ref	38.7
Midwest	56	9.8 (7.1 to 13.3)	1.31 (1.28 to 1.34)	15.3 (11.0 to 20.7)	1.47 (1.44 to 1.50)	56.1
South	110	6.2 (4.8 to 7.7)	0.83 (0.80 to 0.85)	10.9 (8.5 to 13.5)	1.04 (1.02 to 1.07)	75.0
West	2,541	6.3 (6.0 to 6.5)	0.84 (0.81 to 0.86)	9.9 (9.4 to 10.2)	0.95 (0.93 to 0.97)	57.1

Abbreviations: IRR, incidence rate ratio; Ref, reference.

\*Rates by subtype and region not calculated for non-Hispanic Asians/Pacific Islanders because of low numbers.

**TABLE A3.** Five-Year Relative Survival of Patients With Microscopically Confirmed Uterine Corpus Cancer Age 30 to 79 Years by Race and Ethnicity, Stage, Histologic Type, and Region According to SEER 18 (2000 to 2014)

Variable	Non-Hispanic White		Non-Hispanic Black		Hispanic	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Endometrioid without NOS						
Northeast						
Localized	10,971	98.3 (97.6 to 98.7)	813	91.3 (87.9 to 93.8)	956	95.7 (93.2 to 97.3)
Regional	2,528	82.1 (80.1 to 83.1)	244	68.4 (60.8 to 74.8)	245	74.0 (66.5 to 80.0)
Distant	404	28.5 (23.7 to 33.5)	57	14.6 (5.2 to 28.5)	44	14.1 (4.9 to 27.9)
Unknown/unstaged	340	79.7 (73.7 to 84.4)	60	64.9 (48.1 to 77.5)	51	90.5 (71.9 to 97.1)
Midwest						
Localized	6,635	97.9 (97.0 to 98.5)	566	91.0 (86.7 to 93.9)	121	94.8 (86.2 to 98.1)
Regional	1,349	82.2 (79.6 to 84.6)	162	69.6 (60.1 to 77.2)	46	68.0 (44.3 to 83.3)
Distant	252	33.8 (27.6 to 40.1)	44	12.0 (3.9 to 24.9)	2	—
Unknown/unstaged	127	63.9 (53.4 to 72.6)	24	—	4	—
South						
Localized	9,849	97.3 (96.6 to 97.9)	1,718	93.1 (90.8 to 94.8)	219	93.5 (86.9 to 96.9)
Regional	2,098	79.3 (77.0 to 81.5)	488	62.3 (56.6 to 67.4)	65	76.7 (61.2 to 86.7)
Distant	422	28.2 (23.4 to 33.1)	140	14.1 (8.3 to 21.4)	9	—
Unknown/unstaged	333	80.2 (74.3 to 84.8)	54	65.8 (48.9 to 78.3)	3	—
West						
Localized	23,212	98.6 (98.1 to 98.9)	1,169	94.5 (91.7 to 96.4)	5,759	97.0 (96.1 to 97.6)
Regional	5,305	82.4 (81.0 to 83.6)	324	65.6 (58.9 to 71.5)	1,440	82.5 (80.0 to 84.8)
Distant	909	33.5 (30.1 to 36.9)	110	16.3 (9.0 to 25.6)	307	28.3 (22.6 to 34.2)
Unknown/unstaged	333	66.9 (60.7 to 72.4)	46	49.4 (30.6 to 65.7)	148	73.3 (63.4 to 81.0)
Nonendometrioid						
Northeast						
Localized	1,268	88.3 (85.5 to 90.5)	231	72.8 (64.7 to 79.3)	106	82.8 (71.4 to 90.0)
Regional	897	58.7 (54.8 to 62.4)	262	35.2 (28.1 to 42.2)	106	48.1 (36.3 to 58.9)
Distant	468	16.8 (13.1 to 20.9)	178	5.2 (2.1 to 10.4)	43	26.8 (12.3 to 43.7)
Unknown/unstaged	86	50.3 (37.6 to 61.6)	34	23.0 (10.1 to 39.1)	11	—
Midwest						
Localized	736	86.3 (82.5 to 89.3)	193	78.4 (69.6 to 84.9)	12	—
Regional	554	57.7 (52.6 to 62.4)	221	33.2 (25.9 to 40.7)	9	—
Distant	301	13.2 (9.2 to 18.0)	92	7.3 (2.5 to 15.4)	3	—
Unknown/unstaged	28	49.3 (28.2 to 67.4)	12	—	1	—
South						
Localized	973	84.4 (81.0 to 87.3)	491	64.8 (58.8 to 70.1)	28	70.5 (38.9 to 87.9)
Regional	776	50.5 (46.1 to 54.8)	557	36.7 (31.9 to 41.6)	25	54.1 (29.9 to 73.1)
Distant	424	15.0 (11.2 to 19.3)	346	5.9 (3.4 to 9.4)	8	—
Unknown/unstaged	60	52.0 (36.4 to 65.6)	47	24.4 (11.4 to 40.0)	2	—
West						
Localized	2,571	87.6 (85.7 to 89.3)	425	79.3 (73.5 to 83.9)	746	84.1 (80.3 to 87.2)
Regional	2,033	54.3 (51.7 to 56.9)	374	37.2 (31.3 to 43.1)	585	50.3 (45.2 to 55.1)
Distant	1,103	15.4 (13.1 to 18.0)	252	9.7 (5.9 to 14.4)	373	16.9 (12.9 to 21.4)
Unknown/unstaged	54	34.1 (20.1 to 48.6)	24	—	27	40.1 (19.6 to 59.9)

NOTE. Survival not calculated for non-Hispanic Asians/Pacific Islanders because of low numbers. Dash indicates statistic could not be calculated because there were fewer than 25 cases during the time period.

Abbreviation: NOS, not otherwise specified.