

## GYNECOLOGY

# Assessing endometrial cancer risk among US women: long-term trends using hysterectomy-adjusted analysis



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**BACKGROUND:** Commonly reported incidence rates for endometrial cancer fail to take into account both the large number of hysterectomies performed each year and the dynamic change in hysterectomy rate over the past decade. Large racial differences in premenopausal hysterectomy rates between Black and White women in the United States likely affect calculation of race-based risk.

**OBJECTIVES:** The objectives of the study were to determine how the long-term trends in Black-White differences in endometrial cancer incidence and histology type have changed over time for women at risk.

**STUDY DESIGN:** Using longitudinal Surveillance, Epidemiology, and End Results data from 1997 to 2014 and state-level hysterectomy prevalence from the Behavioral Risk Factor Surveillance System, we calculated hysterectomy-adjusted incidence rates of endometrial cancer and the proportion of high vs low-risk endometrial cancer, by race, over time.

**RESULTS:** In women older than 50 years who have not had a hysterectomy, endometrial cancer incidence is 87 per 100,000 from 1997 to 2014. Among White women endometrial cancer incidence changed from 102 (1997–2001) to 86 (2012–2014) cases per 100,000, with a nonsignificant decreasing linear trend (adjusted risk ratio, 0.95; 95% confidence interval, 0.91–1.00;  $p=0.05$ ). In contrast, incidence for Black

women was 88 (1997–2001), 101 (2002–2006), 100 (2007–2011), and 102 (2012–2014) cases per 100,000 with no decreasing trend (adjusted risk ratio, 1.02; 95% confidence interval, 0.96–1.10,  $P = .449$ ). High-risk histology increased among both groups (White: adjusted risk ratio, 1.06; 95% confidence interval, 1.01–1.11;  $P = .015$ ; Black: adjusted risk ratio, 1.06; 95% confidence interval, 1.02–1.10,  $P = .007$ ). Racial difference in the proportion of high-risk disease remained stable.

**CONCLUSION:** Updated hysterectomy-adjusted incidence demonstrates that endometrial cancer is the second most common cancer among women older than 50 years with a uterus and that endometrial cancer has been more common among Black women compared with White women in the United States since 2002. A clinical approach of proactive communication and routine screening for early symptoms in the perimenopausal and menopausal years, especially among Black women, is warranted. These findings can also inform equitable distribution of research funding for endometrial cancer and serve to promote public awareness of this common cancer.

**Key words:** African-Americans, endometrial neoplasms, epidemiology, health status disparities, hysterectomy

Endometrial cancer (EC) is the most common gynecological malignancy with more than 60,000 new cases and more than 10,000 deaths each year.<sup>1</sup> The absolute number of endometrial cancer cases is rising each year, reflecting the aging population, the falling rate of hysterectomy,<sup>2</sup> and population-level increases in the risk factors of diabetes and obesity.<sup>3</sup> The absolute number of cases however, is different from the incidence rate, or the number of new cases per the size of the population per year. In EC, current national incidence rates are reported based on all US women and not restricted to women who have not had a hysterectomy.<sup>4,5</sup>

Prior work has demonstrated that hysterectomy prevalence has an impact on population-level EC incidence.<sup>6,7</sup> When considering only women at risk (ie, women who have not had a hysterectomy), the population EC incidence rate nearly doubles from unadjusted estimates.<sup>7</sup>

In addition, hysterectomy rates vary by race, most pronounced in the premenopausal years, in which Black women have nearly double the hysterectomy rate compared with White women.<sup>8</sup> Earlier work by Jamison et al<sup>8</sup> reported a significant increase in nonendometrioid histology among Black women but not White women from 2004 to 2008.<sup>7</sup> Prior epidemiological research has not identified traditional risk factors that would explain racial differences in histology type among women who get EC.<sup>9,10</sup> Therefore, potential changes in racial patterns over time are important to follow to continue hypothesis generation.

The goal of this study was to update EC incidence rates by race with the most recently available national estimates of both EC cases and hysterectomy prevalence. In addition, we sought to evaluate time trends in the relative burden of low-risk compared with high-risk EC in the United States, with special respect to Black-White racial differences over time. We investigated whether the incidence of EC among Black women at risk has surpassed that of White women at risk and to determine whether earlier-noted trends in histology subtype have continued or are stabilizing.

## Materials and Methods

### Sample

To achieve a stable population to analyze over the long term, we used the Surveillance, Epidemiology, and End Results (SEER) -18 registry cohorts that included the entire state in the sample, which included Connecticut, California, Iowa, Kentucky, Louisiana, New Jersey, Utah, New Mexico, Utah, and the Alaska

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## AJOG at a Glance

**Why was this study conducted?**

Because large racial differences in the premenopausal hysterectomy rate between Black and White women in the United States likely affect the calculation of race-based risk, this study aimed to determine how long-term trends in Black-White differences in endometrial cancer (EC) incidence and histology type have changed over time.

**Key findings**

With hysterectomy adjustment, endometrial cancer is the second most common cancer among US women older than 50 years. Black women are at greater risk of developing EC than White women, and the relative proportion of all women diagnosed with high-risk endometrial cancer is increasing over time.

**What does this add to what is known?**

Both the risk of EC and the distribution of EC histology types are not static, and their prevalence has changed over time.

Native Tumor Registry. Endometrial cancer cases were captured from 1992 to 2014 because SEER coding practices for endometrial cancer were consistent starting in 1992 (site code C54.9 was used prior to 1992 and site code C54.1 after 1992).<sup>11</sup>

The cohorts were limited to cases with race coded as non-Hispanic White or non-Hispanic Black (heretofore referred to as White and Black), given the focus of this study. To ensure consistency in the base population over time, only SEER registries that reported cases for the entire state for any given year were included.

We excluded women younger than 50 years because of the small numbers producing unstable estimates. The Institutional Review Board, under the Human Subjects Division of the University of Washington determined that obtaining and using the SEER data does not constitute human subject research and so exempted the study from review.

**Histology**

Tumor grade was abstracted from registry data as grade 1, 2, or 3. Grade 4 cases (undifferentiated) were grouped with grade 3, given their similar treatment and prognosis from a clinical perspective. We defined the histology types of endometrioid, serous, carcinosarcoma, clear cell, and mixed from *International Classification of Disease for Oncology*

(ICD-O) codes (see [Supplemental Table 1](#)). Documentation of consistency for these morphology descriptions from ICD-O-2 (before 2001) and ICD-O-3 (after 2001) was confirmed.<sup>12</sup>

Criteria for the pathological classification of the nonendometrioid histology types, often referred to as type 2 classifications, were well established based on published gynecological pathology literature by 1982.<sup>13–15</sup> We used histological coding classification consistent with prior literature<sup>16,17</sup> to define high- and low-risk histology for the risk-specific calculations, with the exception of 8050 (in situ), which was excluded from the entire cohort because the description implies noninvasive disease.

In addition, codes for mixed histology and otherwise miscellaneous were excluded from the subset of risk-based calculations because of their vague descriptions, which do not allow for accurate risk stratification (for code list see [Supplemental Table 1](#)). Our final histology was grouped according to the ICD-O-3 code in the following manner: endometrioid (8260, 8262, 8384, 8140, 8210, 8380, 8381, 8382, 8383, 8440, 8480, 8481, 8482, 8560, 8570), serous (8450, 8441, 8460, 8461), carcinosarcoma (8950, 8951, 8980, 8981), clear cell (8313, 8310), and mixed/other (see [Supplemental Table 1](#)).

Cases were dichotomized into high risk and low risk by histology and grade,

mirroring clinically meaningful groupings in treatment guidelines<sup>18</sup> and national clinical trials.<sup>19</sup> Endometrioid grades 1 and 2 were grouped as low risk. Endometrioid grade 3, serous, clear cell, and carcinosarcoma were grouped as high risk.

**Hysterectomy**

Baseline hysterectomy rates were estimated from the Behavioral Risk Factor Surveillance System (BRFSS) data produced by the Centers for Disease Control and Prevention, as previously reported in the literature.<sup>7,20</sup> The estimation technique was as follows: for each year and age group (50–54, 55–59, 60–64, 65–69, 70–75, 75–79, 80 years or older), we calculated the proportion of women within each state, by race, that had a hysterectomy.

However, the BRFSS collected information about hysterectomies only biannually, so we performed the following modeling to predict rate of hysterectomy for years when the BRFSS did not collect this information: we ran modified Poisson models for each race and state, adjusting for a cubic function of age interacted with a cubic function of year. We then used the predicted value from these models to estimate the hysterectomy prevalence in nonreported years. Therefore, for each year we were able to generate the cumulative number of women in each age range, for each geographic region, that had already had a hysterectomy at anytime prior.

**Endometrial cancer incidence**

The EC incidence rate is the number of cases per population per year, and hysterectomy adjustment requires removing women who had already had a hysterectomy from the base population because they are no longer at risk. To do this, we summed the overall size of the female population from each statewide registry and the number of EC cases of each histology type by year and age group.

We then calculated the at-risk population by multiplying the population size by 1 minus the proportion of women having a hysterectomy, which generated the size of the female population that

**TABLE**  
**Endometrial cancer incidence rate per 100,000 US women, 1997–2014, adjusted for prior hysterectomy, by race**

Variables	Race	Overall: 1997–2014	1997–2001	2002–2006	2007–2011	2012–2014
Total	White	88.42 (86.1, 90.8)	101.79 (96.1, 107.4)	86.30 (82.5, 90.1)	86.34 (82.3, 90.4)	85.57 (79.7, 91.4)
	Black	99.20 (92.8, 105.6)	87.51 (74.0, 101.0)	100.82 (87.9, 113.8)	100.10 (90.3, 109.9)	101.75 (85.8, 117.1)
	<i>P</i> value <sup>a</sup>	.005	.15	.031	.028	.082
Low risk	White	55.96 (54.4, 57.5)	78.71 (73.24, 84.18)	71.74 (67.73, 75.74)	56.69 (54.16, 59.22)	53.86 (51.26, 56.47)
	Black	39.08 (36.3, 41.8)	52.32 (20.91, 83.73)	38.07 (31.39, 44.75)	41.51 (36.36, 46.67)	39.09 (34.59, 43.60)
	<i>P</i> value	< .001	.221	< .001	< .001	< .001
High risk	White	26.71 (25.8, 27.6)	31.44 (27.99, 34.88)	27.83 (25.58, 30.07)	24.71 (23.08, 26.35)	25.40 (23.84, 26.95)
	Black	51.34 (47.3, 55.4)	55.51 (34.70, 76.33)	45.36 (36.79, 53.93)	52.32 (44.02, 60.61)	50.35 (44.23, 56.46)
	<i>P</i> value	< .001	.079	< .001	< .001	< .001
Serous	White	4.58 (4.3, 4.9)	4.59 (3.77, 5.40)	4.79 (4.16, 5.42)	4.01 (3.56, 4.47)	4.24 (3.78, 4.70)
	Black	14.04 (12.3, 15.8)	13.87 (1.71, 26.02)	10.78 (6.85, 14.71)	12.82 (9.03, 16.61)	14.2 (11.97, 16.43)
	<i>P</i> value	< .001	.02	< .001	< .001	< .001
Carcinosarcoma	White	3.51 (3.3, 3.7)	4.21 (3.36, 5.05)	3.49 (3.00, 3.97)	3.53 (3.18, 3.89)	3.48 (3.11, 3.85)
	Black	11.90 (10.5, 13.3)	9.89 (0.48, 19.3)	10.03 (6.15, 13.92)	12.65 (10.03, 15.27)	12.60 (10.51, 14.69)
	<i>P</i> value	< .001	.128	< .001	< .001	< .001
Endometrial G3	White	17.54 (16.9, 18.1)	21.12 (18.57, 23.68)	18.20 (16.69, 19.71)	16.14 (15.12, 17.16)	16.57 (15.63, 17.52)
	Black	22.67 (20.7, 24.7)	28.8 (18.11, 39.49)	21.26 (16.71, 25.8)	24.07 (19.81, 28.33)	20.68 (17.83, 23.53)
	<i>P</i> value	< .001	.436	.27	< .001	.009
Other and mixed	White	5.75 (5.4, 6.1)	0.96 (0.64, 1.28)	2.23 (1.89, 2.56)	4.90 (4.48, 5.32)	7.08 (6.50, 7.66)
	Black	8.77 (7.5, 10.1)	3.49 (-6.13, 13.1)	4.08 (2.29, 5.87)	6.99 (5.28, 8.70)	10.66 (8.69, 12.63)
	<i>P</i> value	< .001	.276	.014	.009	< .001

<sup>a</sup> *P* value indicates hypothesis testing of whether incidence rate was significantly different between White and Black women for the given time frame within each category.

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**FIGURE 1**  
**Model-generated incidence rate per 100,000 for EC, 1997–2014 by race**

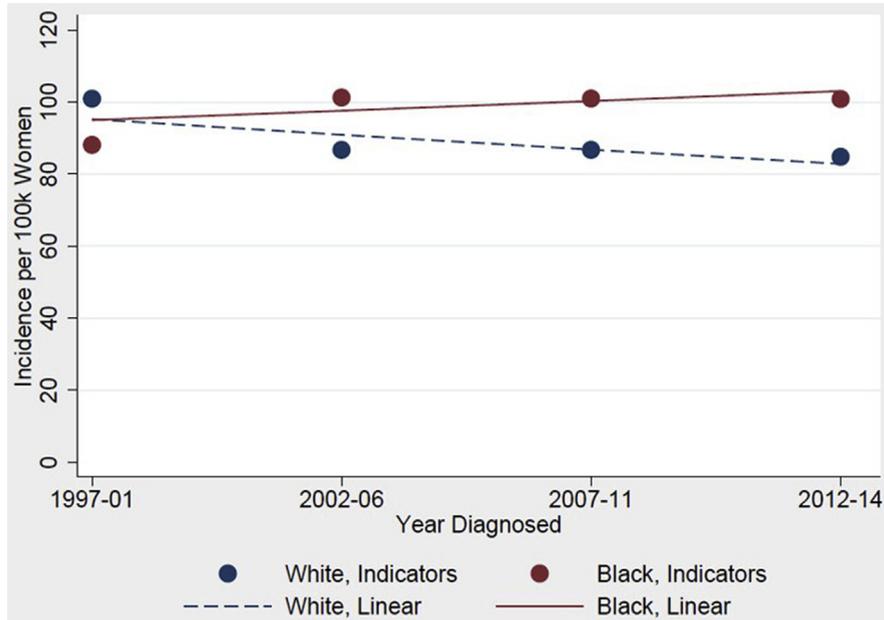


Figure plots the predicted hysterectomy-adjusted endometrial cancer incidence rates for White and Black women from 1997 to 2014. A generalized linear model with a log link and Poisson distribution was used to generate the incidence rates. All models were stratified by race and adjusted for age and age squared with SEs clustered at the state level. Based on this analysis, we then generated the predicted value using marginal standardization method.<sup>32</sup>

EC, endometrial cancer.

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had not had a hysterectomy. We then calculated the incidence rate by dividing the number of cases by this population and multiplied this number by 100,000 for standard reporting.

This method is consistent with previous work.<sup>6,7</sup> In addition to annual incidence rates, we also summarized incidence rates at roughly 5 year intervals (1997–2001, 2002–2006, 2007–2011, 2012–2014). We calculated incidence rates for having any endometrial cancer, high- or low-risk endometrial cancer, and the specific histologic subtypes of high-risk endometrial cancer (serous, carcinosarcoma, and high-grade endometrioid).

### Probability of high-risk disease

To examine trends in the probability of women having high-risk disease, we used patient-level data from SEER. The probability of an individual having high-risk disease, among women who were

diagnosed with endometrial cancer, was calculated with simple frequency to examine whether the relative risk of high- vs low-risk disease has changed in recent years.

### Statistical analysis

First, we examined how hysterectomy adjusted incidence rates vary over time using the 5 year intervals in graphic form for any endometrial cancer and each histological subtype of endometrial cancer using analytic weights. Next, we used a generalized linear model with a log link and Poisson distribution with analytic weights to generate the incidence rates with 95% confidence intervals and adjusted risk ratios. All models were stratified by race and adjusted for age and age squared with standard errors clustered at the state level. We generated the predicted values and 95% confidence intervals of the predicted values using marginal standardization method.<sup>21</sup>

### Sensitivity analyses

We created additional models that included a series of indicator variables for each year to relax any assumptions of linearity of the influence of time and to allow for maximum transparency for the reader in disentangling the relationship between time and incidence rates. In addition, instead of generating the predicted hysterectomy in years during which the BRFSS did not collect such information, we reran the analyses examining only the years during which hysterectomy information was collected.

### Results

The overall annual incidence rate of EC among women older than 50 years with a uterus for the entire study period was 88 cases per 100,000 for White women and 99 cases per 100,000 for Black women ( $P = .005$ , Table). In this population, the EC incidence changed from 101 (95% confidence interval [CI], 95–105) cases per 100,000 in 1997–2001 to 87 (95% CI, 82–92) cases per 100,000 in 2012–2014. For White women the incidence changed from 102 (1997–2001) to 86 (2012–2014) per 100,000 cases.

In contrast, the rates for Black women changed from 88 in 1997–2001 to 102 in 2012–2014 (Table). When we modeled the linear trends adjusted for age, the adjusted risk ratio [aRR] for White women was 0.95 (95% CI, 0.91–1.00;  $P = .050$ ) and for Black women was 1.02 (95% CI, 0.96–1.10;  $P = .449$ ). Figure 1 plots the predicted hysterectomy-adjusted incidence rates for White and Black women from 1997 to 2014. Since 2002, among the population of women who had not had a hysterectomy, Black women have had a statistically significant higher incidence of endometrial cancer than White women (Table and Figure 1).

With regard to high- and low-risk disease, Figure 2 depicts the trend in modeled incidence rate, by race, for the study period. Overall, the population-level incidence rate of low-risk endometrial cancer declined for both Black and White women (Figure 2). In our adjusted models, this decline was significant among White women (aRR, 0.88; 95% CI, 0.82–0.95;  $P = .001$ ) but

**FIGURE 2**  
**Model-generated incidence, histologic subtypes of high-risk EC by race, 1997–2014**

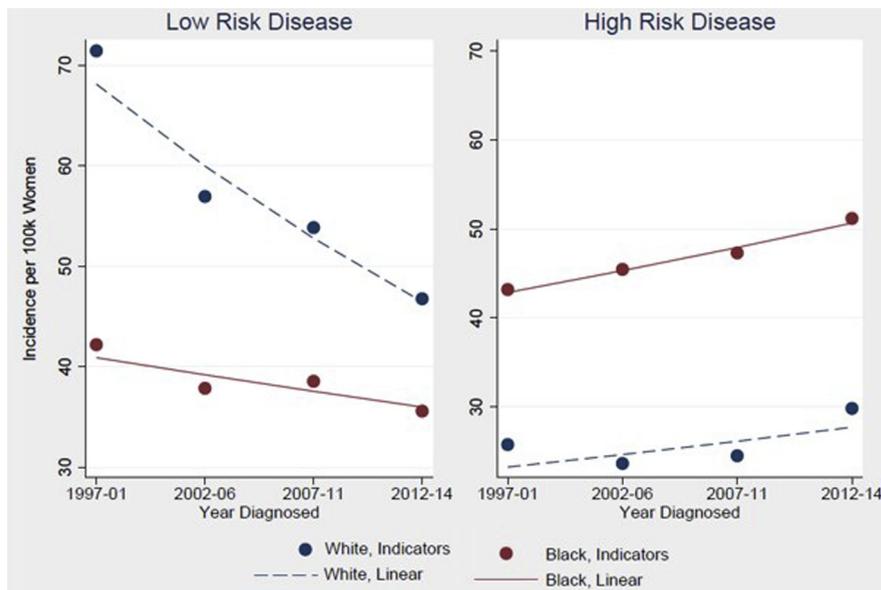


Figure depicts the trend in endometrial cancer incidence rate of low- and high-risk disease for White and Black women from 1997 to 2014. A generalized linear model with a log link and Poisson distribution was used to generate the incidence rates. All models were stratified by race and adjusted for age and age squared with SEs clustered at the state level. Based on this analysis, we then generated the predicted value using marginal standardization method.<sup>30</sup>

EC, endometrial cancer.

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not Black women (aRR, 0.96; 95% CI, 0.87–1.06;  $P = .393$ ). Comparatively, high-risk disease increased (Black women, aRR, 1.06; 95% CI, 1.02–1.10;  $P = .007$ ; White women, aRR, 1.06; 95% CI, 1.01–1.11;  $P = .015$ ).

Within high-risk disease, Figure 3 plots the trends in modeled hysterectomy-adjusted incidence of carcinosarcoma, serous, and grade 3 endometrioid histology separately. Among all types, the incidence rate of serous cancer increased in a linear fashion among both the White (aRR, 1.10; 95% CI, 1.05–1.16;  $P < .001$ ) and Black (aRR, 1.17; 95% CI, 1.07–1.28;  $P = .001$ ) women.

Overall, the probability of high-risk disease for a given woman who was diagnosed with endometrial cancer, for the entire study period, was 33% for White women and 55% for Black women. When examining this trend over time, high-risk disease, relative to low-risk disease, became more common in

both White women (aRR, 1.03; 95% CI, 1.03–1.03;  $P < .001$ ) and Black women (aRR, 1.01; 95% CI, 1.01–1.02;  $P < .001$ ) (Figure 4). The Black-White difference in probability of high-risk disease changed by 2.5%, which was not significant over time.

For the sensitivity analysis (Supplemental Table 2), when including only the years during which hysterectomy information was collected in the BRFSS data, the adjusted risk ratios were consistent with those in the primary analysis.

### Comment

Population-level statistics are necessary to assess the overall burden of disease and allocate resources appropriately at the national level. Thus, the total number of endometrial cancer cases and even the incidence rate for all women, regardless of surgical history, can help to inform the equitable distribution of research funding and advocate for

comprehensive coverage. However, from a clinical standpoint, it is also important to understand the risk for a particular population in a given disease.

In the case of this analysis, there are 3 important clinical statistics. First, the incidence rate of endometrial cancer for a US woman older than 50 years who still has a uterus is 87 cases per 100,000 women. Compared with statistics for breast cancer (126 cases per 100,000 women), lung cancer (53 cases per 100,000 women), and colon cancer (35 cases per 100,000 women),<sup>22</sup> this makes endometrial cancer the second most common in this population and supports a clinical approach of active and routine screening for early symptoms.

Second, the classical teaching that EC is more common among White women<sup>23</sup> is an artifact of the markedly higher premenopausal hysterectomy rate among Black women. The incidence of EC has been higher among Black women at risk compared with White women at risk since approximately 2002. In the era of personalized medicine and risk-based care, this means Black women older than 50 years in the United States are both most likely to develop and most likely to die from endometrial cancer than any other group.<sup>24</sup> It is reasonable in the perimenopausal and menopausal years to proactively communicate with women, especially Black women, about the endometrial cancer risk, early symptoms, and the importance of prompt diagnosis.

Finally, within the population of women diagnosed with endometrial cancer, the relative proportion of low- and high-risk histology has not been static over time. When considering endometrioid, serous, and carcinosarcomas, the overall proportion of low-risk disease is on the decline, while high-risk, aggressive disease is becoming more common among both Black and white women. There was a slight increase in the Black-White gap in the proportion of high-risk disease diagnosed among women with EC was not statistically significant.

Follow-up studies should continue to assess this trend because underlying racial trends in the alternative treatments that have replaced hysterectomy may be

FIGURE 3

Model-generated incidence of histologic subtypes, high-risk EC, by race, 1997–2014

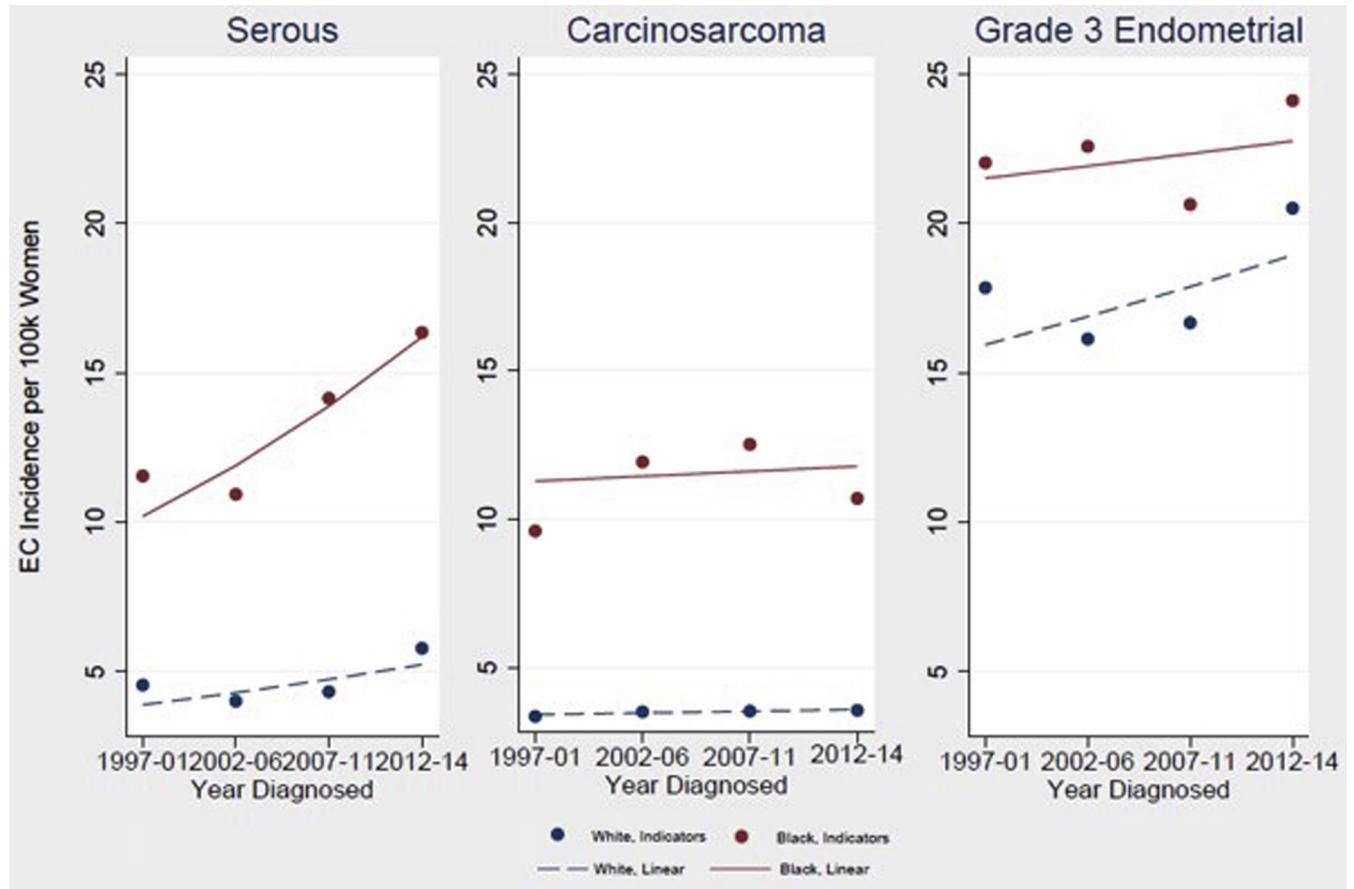


Figure plots the trends in hysterectomy-adjusted incidence of high-risk endometrial cancer (serous, carcinosarcoma, and grade 3 endometrioid histology) for White and Black women from 1997 to 2014. A generalized linear model with a log link and Poisson distribution was used to generate the incidence rates. All models were stratified by race and adjusted for age and age squared with SEs clustered at the state level. Based on this analysis, we then generated the predicted value using the marginal standardization method.<sup>30</sup>

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exerting a protective influence on the risk of developing low-risk disease. Specifically, the use of combination estrogen-progesterone oral therapy and progesterone-containing intrauterine devices reduce the effect of unexposed estrogen on the uterus, and these therapies are less commonly used by Black women in the United States.<sup>25–27</sup> These factors, combined with the increasing risk of serous cancer with older age, may be acting in concert to shift the distribution of high-risk compared with low-risk histology in White women.

Jamison et al<sup>7</sup> previously reported hysterectomy-adjusted EC incidence rates from 1992 to 2008 as 136 cases per

100,000 White women and 116 cases per 100,000 Black women, reporting that incidence was decreasing among White women but increasing among Black women in later years (2006–2008).

Our analysis differs from this previous one in a few ways. We used updated cancer registry and BRFSS data to generate more contemporary estimates. We also used a stricter definition of endometrial cancer cases. The higher adjusted rates in the previous study may be due to the choice to include all uterine cancers (codes C54 and C55) and not limit specifically to endometrial cancer codes (C54.1).

In addition, the inclusion of non-endometrial cancers by Jamison et al<sup>7</sup> would disproportionately increase cases among Black women who have a higher prevalence of other uterine cancers, like leiomyosarcoma.<sup>28,29</sup>

Finally, we chose to use clinically relevant risk groupings that more accurately stratify patients into groups, one including patients with high survival rates and low use of adjuvant therapy (grades 1–2 endometrioid) and another including those with markedly lower survival and a nearly universal need for adjuvant therapy (grade 3 endometrioid, serous, and carcinosarcoma).<sup>30</sup>

**FIGURE 4**  
**High- and low-risk histology among EC cases, US women >50**

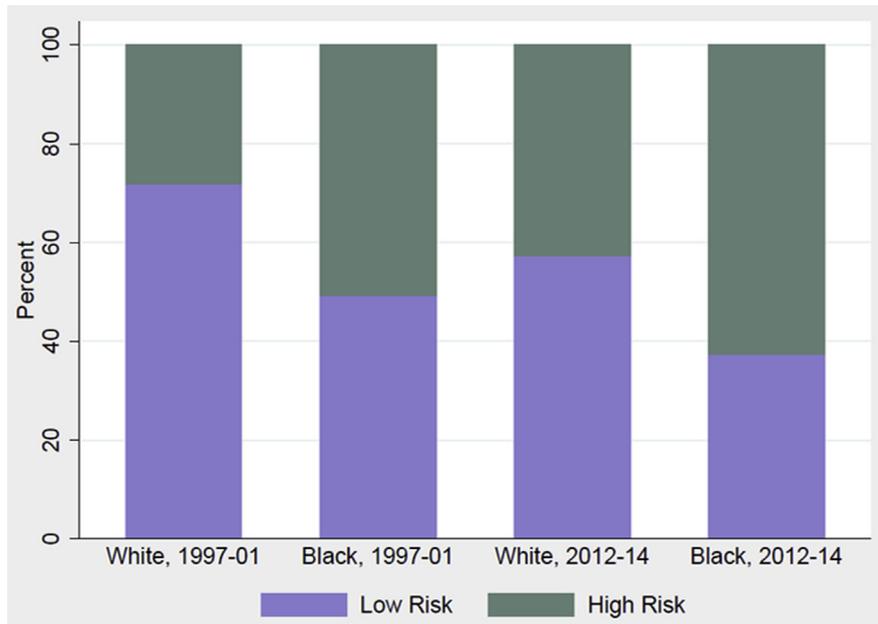


Figure shows distribution of high- and low-risk histology among EC cases, US women older than 50 years.

EC, endometrial cancer.

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This study has important limitations to consider. The SEER registry is nationally representative because of purposively sampling to create a racially, economically, and geographically diverse data set,<sup>31</sup> but SEER-18 captures just 28% of the total population. Thus, the incidence estimates may change with inclusion of larger samples.

There is also no central pathological review of histology classification within SEER. Although the coding uses the same structure used by pathologists in clinical care settings to classify tumor types and drive treatment decisions, there is no way to account for potential error at the assessment, recording, or abstraction of this information.

Finally, the publication of the American Joint Committee on Cancer, seventh edition, in June 2010, which altered staging for uterine sarcomas (not endometrial cancers), may have resulted in more scrutiny of histology and detection of the less common, high-risk types. We used strict definitions of endometrial cancer cases and histological

classifications to avoid the problem of inclusion of nonrelevant cancer types, which may have resulted in some underestimation of actual incidence.

A limitation of the BRFSS hysterectomy prevalence data is that it relies on self-report and cannot be verified in a health record. In addition, we chose to include only data in which both SEER registry data and BRFSS data were available for the entire geographic area. This limited the sample size for individual histology types in earlier years, resulting in wider confidence intervals and less precision, especially for Black women, in instances in which linear trends would suggest a significant effect.

We are strengthened by the longevity and rigor of the SEER data source, which purposely collects cases independent of site of care, insurance, and age and provides a stable base population cohort without which these trend analyses are not possible.<sup>11,31</sup>

Endometrial cancer among women older than 50 years with a uterus is common. In this population, Black

women have the highest incidence rate of endometrial cancer in the United States, marking them as a high-risk group for which clinical and research efforts should be prioritized. For both Black and White women, the proportion of high-risk histology types is increasing over time, which supports continued research into improved adjuvant therapy to decrease mortality from these aggressive subtypes and continued efforts to raise public awareness about endometrial cancer. ■

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## SUPPLEMENTAL TABLE 1

## Definitions of type of endometrial cancer used in analysis

EC type	ICD-O-3 codes
Endometrioid	8260, 8262, 8384, 8140, 8210, 8380, 8381, 8382, 8383, 8440, 8480, 8481, 8482, 8560, 8570
Serous	8450, 8441, 8460, 8461
Carcinosarcoma	8950, 8951, 8980, 8981
Clear cell	8313, 8310
Mixed	8255, 8323
Other	8000, 8001, 8012, 8013, 8014, 8015, 8020, 8021, 8022, 8032, 8033, 8045, 8046, 8051, 8072, 8120, 8130, 8141, 8143, 8230, 8261, 8263, 8211, 8246, 8320, 8340, 8490, 8574, 8575, 8576, 8933, 9080, 8041, 8070, 8071, 8076

EC, endometrial cancer; ICD-O-3, International Classification of Disease for Oncology (after 2001).

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## SUPPLEMENTAL TABLE 2

## Linear trends of endometrial cancer risk ratio among US women, adjusted to exclude women with prior hysterectomy, comparison between primary and sensitivity analyses

Subgroup	Primary analysis		Sensitivity analysis	
	aRR (95% CI)	Pvalue	aRR (95% CI)	Pvalue
Any endometrial cancer, White	0.95 (0.91–1.00)	.050	0.95 (0.91–0.99)	.024
Any endometrial cancer, Black	1.02 (0.96–1.10)	.449	1.03 (0.97–1.10)	.347
High-risk, White	1.06 (1.01–1.11)	.015	1.07 (1.01–1.13)	.014
High-risk, Black	1.06 (1.02–1.10)	.007	1.08 (1.05–1.11)	< .001
Low-risk, White	0.88 (0.82–0.95)	.001	0.87 (0.82–0.94)	< .001
Low-risk, Black	0.96 (0.87–1.06)	.393	1.00 (0.96–1.04)	.960
Serous, White	1.10 (1.05–1.16)	< .001	1.10 (1.05–1.17)	< .001
Serous, Black	1.17 (1.07–1.28)	.001	1.19 (1.10–1.30)	< .001
Carcinosarcoma, White	1.02 (0.98–1.05)	.340	1.04 (0.99–1.09)	.131
Carcinosarcoma, Black	1.01 (0.96–1.07)	.610	1.00 (0.92–1.09)	.978
High grade, White	1.06 (0.99–1.13)	.104	1.07 (0.99–1.15)	.101
High grade, Black	1.02 (0.97–1.07)	.480	1.06 (1.00–1.13)	.049

aRR, adjusted risk ratio; CI, confidence interval.

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