

Trends in Uterine Cancer Mortality in the United States

A 50-Year Population-Based Analysis

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OBJECTIVE: To analyze mortality trends in uterine cancer in the United States over 50 years with an emphasis on age and race and ethnicity.

METHODS: Data on uterine cancer deaths from 1969 to 2018 were obtained from the National Center for Health Statistics. Trends were examined by age and race and ethnicity after adjustment for the hysterectomy rate and pregnancy.

RESULTS: Uterine cancer mortality decreased between 1969 and 1997 (from 6.03 to 4.00/100,000) but increased between 1997 and 2018 (from 4.00 to 5.02/100,000). From 2001 to 2018, mortality rates increased by 1.25-fold across

all age groups. In 2018, the mortality rate from uterine cancer for patients aged 70 years or older and 60–69 years was sixfold and threefold higher, respectively, than in younger patients (aged 50–59 years) (54.87/100,000 vs 27.80/100,000 vs 8.70/100,000). The mortality rate for non-Hispanic Black women was 2.2-fold higher than for non-Hispanic White, Hispanic, and non-Hispanic Asian or Pacific Islander women (17.6/100,000 vs 7.82/100,000, 6.54/100,000, and 4.24/100,000, respectively). On an intersection analysis of age and race, non-Hispanic Black women aged older than 60 years had a threefold higher mortality rate than non-Hispanic White women (72/100,000 vs 24/100,000). A notable finding was that young non-Hispanic Black and Hispanic women (30–39 years) had the highest annual increases in mortality at 3.3% and 3.8% per year compared with 2.2% in non-Hispanic White women.

CONCLUSION: Since 2001, the uterine cancer mortality rate has increased across all four racial and ethnic groups examined, with the highest increase seen among non-Hispanic Black women. The largest increase in mortality was observed among younger non-Hispanic Black and Hispanic women.

(*Obstet Gynecol* 2023;142:978–86)

DOI: 10.1097/AOG.0000000000005321

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Each author has confirmed compliance with the journal's requirements for authorship.

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Financial Disclosure

John Chan reports receiving funding from AstraZeneca, Glaxosmithkline, Immunogen, and Myriad for his efforts in this study. He also reports receiving direct payments from AstraZeneca, Eisai, Glaxosmithkline, Genmab/Seagen, Agenus, Immunogen, Merck, Mersana, MITI, Myriad, and Roche. He has also received research funding from the Denis Cobb Hale Chair, the Angela Wang Johnson Fund, and the Fisher Family Funds. The authors did not report any potential conflicts of interest.

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ISSN: 0029-7844/23

Uterine cancer is the fourth most common cancer and the sixth most common cause of death among women in the United States.^{1,2} It is the most frequent gynecologic cancer in the United States, with an estimated 66,200 new cases and 13,030 deaths in 2023.² Despite advances in cancer research, uterine cancer incidence in the United States continues to rise. Uterine cancer is currently one of the only cancers with increasing incidence and mortality in the United States.¹ Although it affects predominantly postmenopausal women, this rise in incidence has been reported across all age groups.³

Significant racial disparities also exist regarding uterine cancer. From 2010 to 2019, the mortality rate

for uterine cancer increased by 1.9% per year among non-Hispanic Black women compared with 1.6% per year among White women.⁴ In 2019, the mortality rate in non-Hispanic Black women was nearly double that in White women (9.0/100,000 vs 4.6/100,000), reflecting the largest Black–White disparity in 5-year relative survival of all cancers (63% vs 84%).⁴ Obesity is a significant risk factor for uterine cancer; it is suggested that the uptrend in uterine cancer incidence can be attributed to increasing rates of obesity and decreasing rates of hysterectomy for benign pathology.^{3,5} Although this may explain the increasing incidence of uterine cancer, the factors behind the rise in uterine cancer mortality rates are likely multifactorial and poorly understood.⁶

From 1999 to 2016, the Centers for Disease Control and Prevention (CDC) observed an average annual increase of 1.1% in the uterine cancer mortality rate.⁷ In addition, stark racial disparities in uterine cancer mortality rates were reported, consistent with prior literature.^{4,7,8} Between 1999 and 2016, the annual increase in mortality rates among non-Hispanic Black, Hispanic, and non-Hispanic Asian or Pacific Islander women was higher than in non-Hispanic White women (1.5%, 1.7%, and 2.5%, respectively, vs 1.0%).⁷ Moreover, non-Hispanic Black women experience uterine cancer mortality at a twofold greater rate compared with any other racial or ethnic group.⁸

Although uterine cancer mortality rates by race and ethnicity are well documented, the effect of the intersection of race and ethnicity and age on uterine cancer mortality remains unclear. These prior studies are also limited by a lack of analysis of trends over an extended period. In this report, we analyzed data over a 50-year period to explore the disparities in uterine cancer mortality in the United States with an emphasis on the intersection of age and race and ethnicity.

METHODS

Data on mortality attributable to uterine cancer from 1969 to 2018 were obtained from the National Center for Health Statistics (NCHS). The NCHS, part of the CDC, is a U.S. federal statistical agency that creates a publicly accessible database containing an extensive array of deidentified health data and statistical information. The NCHS collects data from birth certificates, death certificates, patient medical records, health care facilities, standardized physicals, laboratory tests, and patient interviews. These data collected over 50 years allow the examination of variations in trends over time. Without this extensive time period, it would not be possible to evaluate the extensive

positive and negative trends over time. The cohort was divided by six mutually exclusive age groups and four mutually exclusive racial and ethnic groups. Age groups were 0–29 years, 30–39, 40–49, 50–59, 60–69, and 70 or older. Age and race data were self-reported. Racial and ethnic groups were non-Hispanic Black, non-Hispanic White, Hispanic, and non-Hispanic Asian Pacific Islander. Race and age are included because we wanted to be comprehensive regarding the demographic variables that were included in the National Cancer Database and BRFSS (Behavioral Risk Factor Surveillance System) data sets.

BRFSS data from 2001 to 2018 were used to estimate hysterectomy and pregnancy prevalence within the cohort.⁹ We incorporated the pregnancy prevalence into our analysis to be comprehensive and to allow our data to accurately reflect clinical trial enrollment criteria and data. BRFSS is a publicly accessible national database sponsored primarily by the CDC that contains self-reported health data ranging from chronic conditions to risk behaviors and preventive service utilization. BRFSS collects data through random digit dialing telephone surveys and completes more than 400,000 interviews annually. The hysterectomy rate was assumed to be zero for women aged younger than 18 years. Pregnancy corrections were done only among women aged 20–45 years because BRFSS records pregnancy data only among that age group. Data from the National Cancer Database were additionally used to account for uterine cancer treatment–related hysterectomies by year and race and ethnicity. The National Cancer Database is a nationwide clinical oncology database supervised jointly by the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The National Cancer Database collects oncology hospital registry data from more than 1,500 facilities accredited by the Commission on Cancer. These estimates were used to adjust 2001–2018 mortality rates by hysterectomy and pregnancy, thereby correcting the specific population at risk. Because all data used in this study were deidentified, this study was exempt from IRB approval.

Overall uterine cancer mortality trends were determined with data from 1969 to 2018. Uterine cancer mortality trends by age and race were determined with data from 2001 to 2018 because data before 2001 did not report information on age or ethnicity. Average annual percent changes were used to quantify changes in mortality rates from 1969 to 2018 and were calculated with Joinpoint regression (Joinpoint 4.9.0.0), which allowed different slopes for four periods (1969–1989, 1989–1997, 1997–2008, and

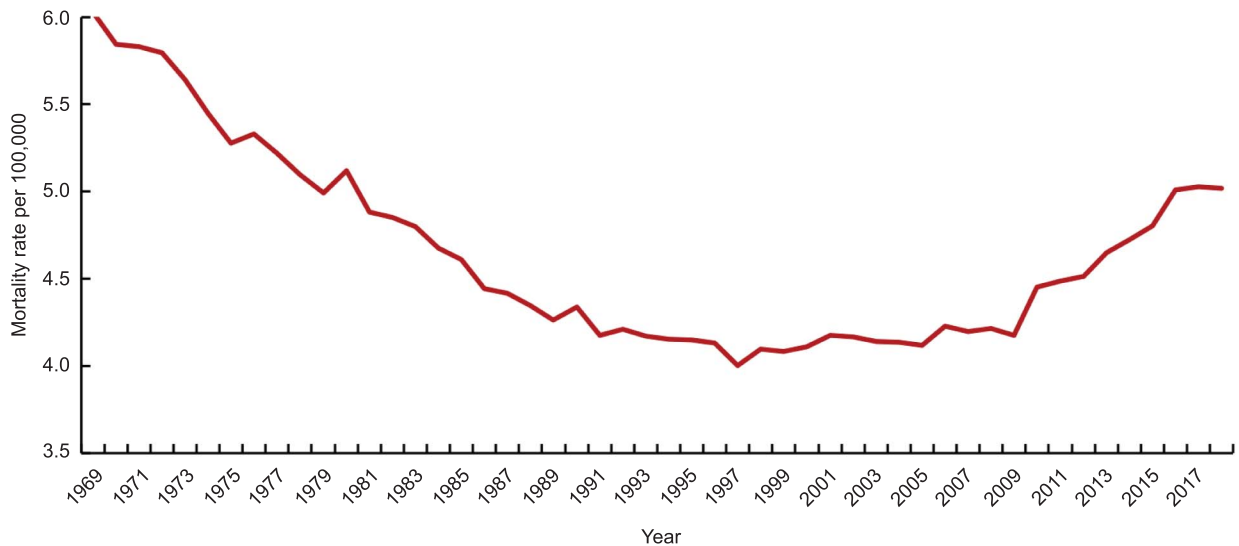


Fig. 1. Uterine cancer mortality trend over time, 1969–2018.

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2008–2018). To determine whether the average annual percent change was statistically significant, we used a two-sided *t* test for zero Joinpoints and a two-sided *z* test for one or more Joinpoints. Annual mortality rates per 100,000 women were age-adjusted to the 2000 U.S. standard population. Changes in uterine cancer mortality rates were considered increased if the average annual percent change was greater than 0 and decreased if the average annual percent change was less than 0. $P < .05$ was considered statistically significant using R 4.2.1.

RESULTS

From 1969 to 1997, the mortality rate from uterine cancer decreased by 1.5-fold (6.03–4.00/100,000). The largest average annual decrease was seen between 1969 and 1989 at 1.66% ($P < .001$). However, the mortality rate subsequently increased by 1.25-fold from 1997 to 2018 (4.00–5.02/100,000). The highest increase rate began in 2008, with an average annual increase of 1.94% ($P < .001$) from 2008 to 2018 (Fig. 1).

From 2001 to 2018, data on race and ethnicity and age were available for 843,118 women (Table 1). The mortality rate was directly proportional to age, with older women having higher rates of uterine cancer mortality than younger women. Compared with women aged 50–59 years, those aged 60–69 years and 70 years or older had threefold and sixfold higher mortality rates in 2018, respectively (8.7/100,000 vs 27.8/100,000 vs 54.87/100,000). Women aged 50–59 years, 60–69, and 70 or older demonstrated annual increases in mortality of 0.65% ($P = .136$), 1.07% ($P < .001$), and 0.94% ($P < .001$), respectively. The uter-

ine cancer mortality rate rose from 2001 to 2018 across all age groups after adjustment for hysterectomy and pregnancy. However, the highest average annual percent increase in mortality was seen among women aged younger than 50 years. Women aged 0–29 years, 30–39, and 40–49 had annual increases in mortality of 2.27% ($P = .255$), 2.87% ($P < .001$), and 2.20% ($P < .001$), respectively (Table 2).

From 2001 to 2018, uterine cancer mortality rates increased across all four racial and ethnic groups. Compared with non-Hispanic White, Hispanic, and non-Hispanic Asian or Pacific Islander women, non-Hispanic Black women had twofold, threefold, and

Table 1. Demographic Characteristics, 2001–2018, National Center for Health Statistics

Characteristic	n (%)
Total	843,118 (100)
Age (y)	
0–29	4,380 (0.5)
30–39	25,425 (3.0)
40–49	78,139 (9.3)
50–59	221,715 (26.3)
60–69	269,224 (31.9)
70 or older	244,235 (29.0)
Race and ethnicity	
Hispanic	67,534 (8.0)
NHAPI	28,204 (3.3)
NHB	87,400 (10.4)
NHW	649,144 (77.0)
None of the above or unknown	10,836 (1.3)

NHAPI, non-Hispanic Asian or Pacific Islander; NHB, non-Hispanic Black; NHW, non-Hispanic White.

Table 2. Uterine Cancer Mortality Rate in 2018 and Average Annual Percent Change by Age and Race from 2001 to 2018

	Mortality Rate (per 100,000) in 2018	AAPC % (95% CI) 2001–2018	AAPC <i>P</i>
Age (y)			
0–29	0.01	2.27 (–1.77 to 6.48)	.255
30–39	0.56	2.87 (1.76–3.99)	<.001
40–49	2.00	2.20 (1.48–2.93)	<.001
50–59	8.70	0.65 (–0.20 to 1.50)	.136
60–69	27.80	1.07 (0.76–1.38)	<.001
70 or older	54.87	0.94 (0.76–1.13)	<.001
Race and ethnicity			
Hispanic	6.54	1.85 (1.35–2.36)	<.001
NHAPI	4.24	2.11 (1.40–2.82)	<.001
NHB	17.59	1.87 (1.61–2.12)	<.001
NHW	7.82	0.84 (0.64–1.05)	<.001
None of the above or unknown	7.91	–0.61 (–2.33 to 1.14)	.465
Intersection of age and race and ethnicity			
30–39 y			
Hispanic	0.53	3.84 (1.09–6.66)	.009
NHAPI	0.51	1.87 (–1.95 to 5.84)	.319
NHB	0.76	3.27 (0.69–5.91)	.016
NHW	0.51	2.17 (1.04–3.31)	.001
40–49 y			
Hispanic	1.96	1.66 (0.55–2.79)	.006
NHAPI	1.73	2.21 (–0.033 to 4.80)	.084
NHB	2.99	2.80 (1.88–3.73)	<.001
NHW	1.81	1.89 (1.03–2.75)	<.001
50–59 y			
Hispanic	8.11	1.67(0.55,2.80)	<.001
NHAPI	6.57	2.27 (0.68,3.88)	.008
NHB	16.09	1.57 (0.87–2.27)	<.001
NHW	7.72	0.28 (–0.79 to 1.35)	.610
60–69 y			
Hispanic	21.58	1.50 (0.81–2.20)	<.001
NHAPI	14.29	0.29 (–1.79 to 2.41)	.789
NHB	71.96	1.71 (1.39–2.03)	<.001
NHW	23.74	0.82 (0.46–1.18)	<.001
70 y or older			
Hispanic	39.88	1.96 (1.25–2.68)	<.001
NHAPI	22.86	2.26 (1.02–3.53)	.001
NHB	108.18	1.97 (1.57–2.36)	<.001
NHW	52.90	0.83 (0.62–1.04)	<.001

AAPC, average annual percent change; NHAPI, non-Hispanic Asian or Pacific Islander; NHB, non-Hispanic Black; NHW, non-Hispanic White.

fourfold higher mortality rates, respectively (7.82/100,000 vs 6.54/100,000 vs 4.24/100,000 vs 17.59/100,000) (Fig. 2). Although uterine cancer mortality rates were lowest among non-Hispanic Asian or Pacific Islander women in 2018, this group had the highest average annual percent increase from 2001 to 2018. Specifically, non-Hispanic Asian or Pacific Islander women had an annual increase of 2.11% ($P<.001$) from 2001 to 2008 compared with 1.85% ($P<.001$), 1.87% ($P<.001$), and 0.84% ($P<.001$) for Hispanic, non-Hispanic Black, and non-Hispanic White women, respectively (Table 2).

In an intersectionality analysis by age and race and ethnicity, uterine cancer mortality was highest in older non-Hispanic Black women (Fig. 3). In 2018, the highest mortality rate was observed in non-Hispanic Black women aged 70 years or older (108.18/100,000), twofold that of non-Hispanic White women (52.90/100,000) of that age. The second-highest mortality rate was observed in non-Hispanic Black women aged 60–69 years, who had a threefold higher mortality rate than non-Hispanic White women of the same age (71.96/100,000 vs 23.74/100,000) (Table 2). Although overall uterine cancer mortality rates were

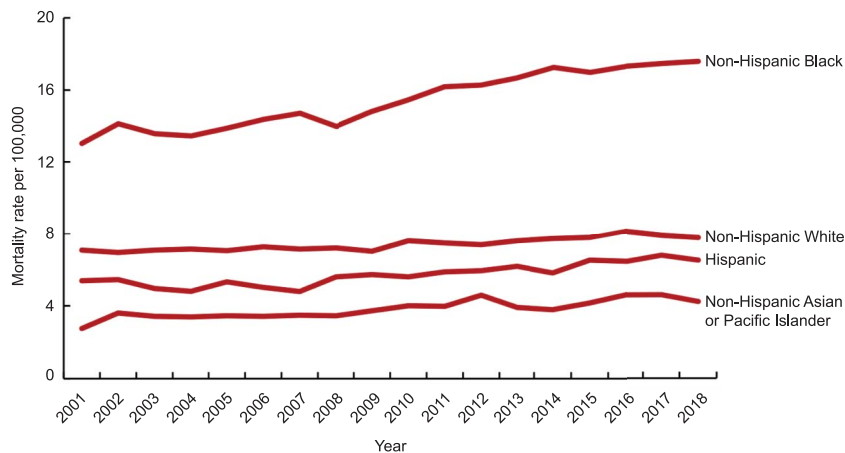


Fig. 2. Uterine cancer mortality rate by race and ethnicity, 2001–2018.

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lower among women aged younger than 50 years, non-Hispanic Black and Hispanic women aged 30–39 years had greater increases in uterine cancer mortality compared with non-Hispanic White women. From 2001 to 2018, 30–39-year-old non-Hispanic Black and Hispanic women had annual increases of 3.27% ($P=.016$) and 3.84% ($P=.009$) compared with 2.17% ($P=.001$) among non-Hispanic White women (Fig. 4).

DISCUSSION

In this analysis, we found that uterine cancer mortality rates increased from 1997 to 2018, with mortality rates being highest among older non-Hispanic Black women aged 70 years or older. In addition, mortality rates are increasing most rapidly among younger racial and ethnic minority groups, specifically non-Hispanic Black and Hispanic women, compared with non-Hispanic White women. Although previous data have shown an average annual percent change of 1.1% for uterine cancer mortality among non-Hispanic Black, our analysis over a longer period shows a greater average annual percent change of 1.87%.⁷ This rise in uterine cancer mortality and the racial disparities enmeshed in it have been similarly documented in other studies.^{3–5,8} These trends are in direct contrast to the decreases in mortality rates that have been observed in many other cancer types, including lung cancer and colorectal cancers.¹

Uterine cancer mortality is higher in older women compared with younger women. Several reasons contribute to this. First, older women are more likely to present with more aggressive pathologic features compared with younger women. Specifically, older women (70 years or older) are about two times more likely to present with advanced disease compared with younger patients (39% vs

19%).¹⁰ Older women are also less likely to receive comprehensive surgical care for their cancer and are more likely have treatment-related complications. Physician bias is also thought to contribute to lower rates of surgical care among older patients.¹¹

Women aged younger than 50 years had the highest average annual percent increase in mortality. Several studies have found a similar increase in the incidence of early-onset uterine cancer, particularly among non-Hispanic Black and Hispanic women.^{12–15} Guo et al¹⁵ reported a notable annual percent increase in uterine cancer in younger age groups between 2001 and 2017: 3.6% among 20–29-year-olds and 3% among 30–39-year-olds. This increase in early-onset uterine cancer is also seen in other obesity-related cancers, including colorectal, multiple myeloma, gallbladder, kidney, and pancreatic cancers.¹⁶ This points to a possible association between these trends and the rapid increase in the prevalence of obesity in younger age groups. In 2017–2018, the highest obesity rates in the country were seen among patients aged 40–59 years (11.5%), followed by those aged 20–39 years (9.1%) and then those aged 60 years or older (5.8%).¹⁷

The racial disparities in uterine cancer mortality that we found in our analysis have been similarly documented in the Surveillance, Epidemiology, and End Results database.⁹ One analysis showed overall significantly lower survival rates among non-Hispanic Black women compared with non-Hispanic White, Hispanic, and non-Hispanic Asian or Pacific Islander women, regardless of histology and stage (5-year relative survival 63.2% vs 86.1%, 81.4%, and 83.7%, respectively). Proposed factors that contribute to such disproportionately elevated mortality rates in racial and ethnic minority groups (particularly non-Hispanic Black women) fall into systemic, practitioner, and patient

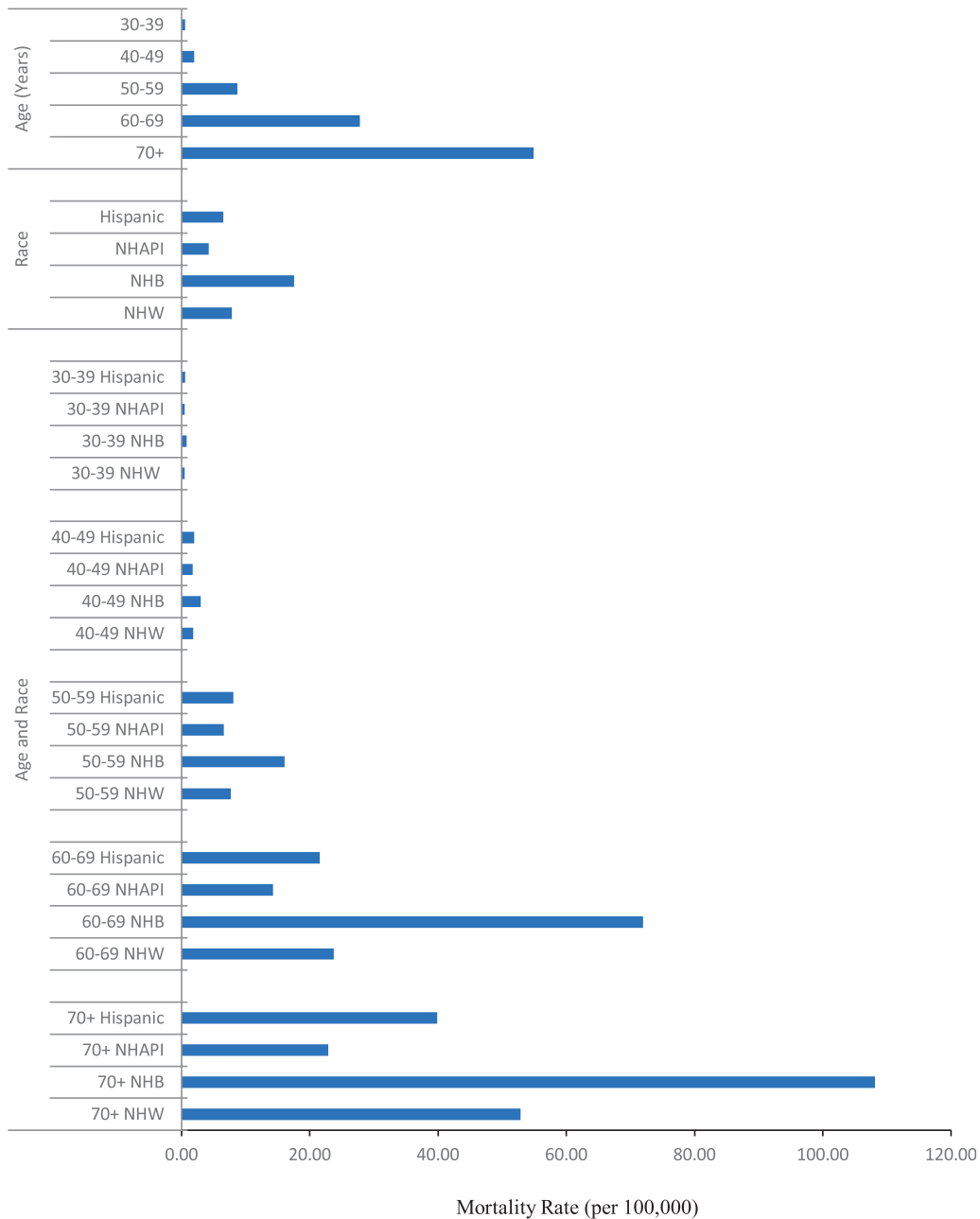


Fig. 3. Uterine cancer mortality rate by age and race and ethnicity, 2018. NHAPI, non-Hispanic Asian or Pacific Islander; NHB, non-Hispanic Black; NHW, non-Hispanic White.

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categories.⁸ Systemic factors relating to structural racism create differences in racialized individuals' ability to receive quality health care services. Practitioner-level factors involve issues with interpersonal communication, bias, and discrimination that can affect clinical decision making and reduce the likelihood of receiving guideline-concordant care.⁸ Those barriers to optimal care are thought to contribute to the well-documented differ-

ences in endometrial cancer treatment that non-Hispanic Black and Hispanic women receive. Several studies have documented non-Hispanic Black and Hispanic women's reduced likelihood of receiving definitive surgical treatment, optimal surgical procedures, sufficient lymph node sampling, and lymphadenectomy in the setting of their uterine cancer.¹⁸⁻²⁰ In addition, even though non-Hispanic Black women are more likely than

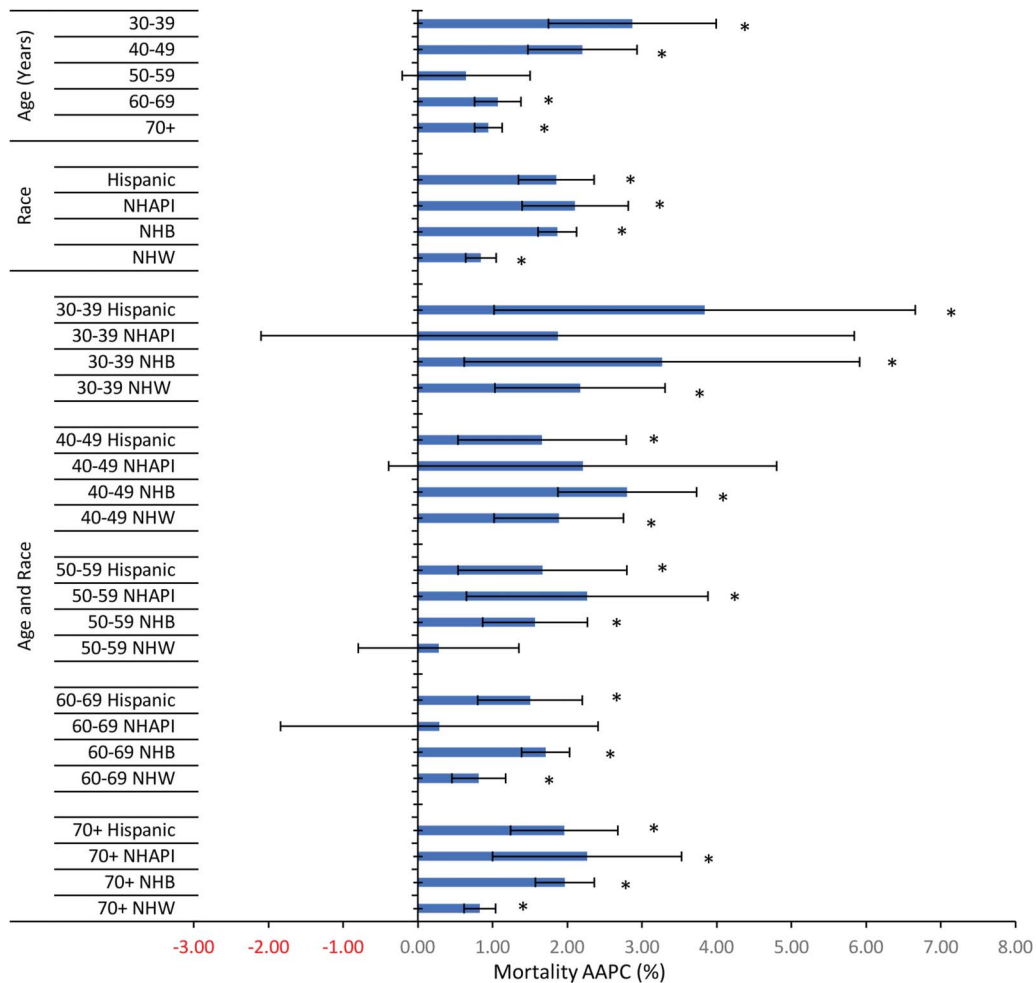


Fig. 4. Uterine cancer average annual percent change (AAPC) by age and race and ethnicity, 2001–2018. * $P < .001$. NHAPI, non-Hispanic Asian or Pacific Islander; NHB, non-Hispanic Black; NHW, non-Hispanic White.

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non-Hispanic White women to receive care at high-volume surgical centers, they continue to experience worse outcomes than White women in those facilities.²¹

Among several considerations, patient-level factors including molecular or genetic, cultural, educational, and socioeconomic differences. Her2/neu expression and p53 mutations are found more frequently in non-Hispanic Black patients with endometrial cancer and are associated with poor prognosis. Moreover, somatic mutations in DNA mismatch repair genes are reported more frequently in non-Hispanic Asian or Pacific Islander women.²² In addition, socioeconomic deprivation and having no or publicly funded insurance, both of which are more prevalent in racial and ethnic minority groups, are associated with worse survival from uterine cancer.⁸ Non-Hispanic Black women also have higher exposure to toxic chemicals found in hair-straightening products.

The highest mortality rate seen among older non-Hispanic Black patients sheds light on the complex interplay between different social systems that exaggerate inequities and health disparities. For example, an older non-Hispanic Black patient's age and race put her at higher risk of not receiving definitive surgical treatment for uterine cancer. The actual combined effect of the interactions between race and ethnicity and age-associated risk factors described previously remain poorly understood. In addition, part of the cause of higher uterine cancer mortality rates among older non-Hispanic Black women and younger minority women could be attributed in part to the higher rates of obesity in these populations.^{12–15,23} In 2017–2018, 39.8% of non-Hispanic White women, 43.7% of Hispanic women, 56.9% of non-Hispanic Black women, and 17.2% of non-Hispanic Asian or Pacific Islander women had obesity.²⁴ The

higher levels of obesity seen among racial and ethnic minorities have been attributed to a wide variety of social and structural factors.²⁵ Those include an increased likelihood of being surrounded by food deserts and higher levels of food insecurity, poor neighborhood walkability scores, and high crime rates, as well as elevated chronic stress levels.²⁵

The increase in uterine cancer mortality rates following a preceding period of declining rates from 1969 to 1997 might be attributed to the lower use of estrogen plus progesterone hormonal therapy, the decrease in the rates of hysterectomies, and the rise in obesity levels.^{26–28} In addition, alternative treatments of common benign gynecologic conditions that have previously been treated with hysterectomy led to a decline in the hysterectomy rate that started in the 1980s.²⁷ Moreover, endometrial cancers make up most uterine cancers, and as previously mentioned, the main risk factor for endometrial cancers is elevated body weight.²³ Women who have overweight or obesity are two to four times as likely to develop endometrial cancer as women with lower body mass index.²⁸ Data from the National Cancer Institute and CDC attributed 60.3% of corpus uteri tumors to obesity, further supporting uterine cancer being one of the cancers most strongly associated with obesity.^{28,29}

In addition, given the strong association between obesity and uterine cancer, interventions aimed at weight reduction are critical. Several studies point to a reduction in cancer risk and mortality associated with weight loss.^{28–31} For example, bariatric surgery has been shown to significantly decrease the risk of uterine cancer (odds ratio 0.43, 95% CI 0.26–0.71, $P=.010$).^{30,31} Equitable implementation of programs aimed at risk reduction through physical activity and access to healthy foods is essential and warrants national attention. Public policy efforts aimed at regulating access to processed foods and sugar-sweetened beverages can also help address the obesity epidemic.³² Such interventions, specifically when implemented among the target populations identified in this analysis, can result in reducing the disparities among uterine cancer mortality by age and race and ethnicity.

This is a large, nationally representative cohort study that evaluated uterine cancer trends by age and race and ethnicity, as well as the intersection of both age and race and ethnicity over a 50-year period. Despite our large sample size and correction for hysterectomy and pregnancy, there are important limitations to our analysis to consider. Reporting of race and ethnicity in the NCHS is based on data from medical records and death certificates, which may

not be fully accurate. In addition, all histologic tumor types were grouped into a broad category, which can mask varying trends by tumor type because it is known that certain uterine cancers, such as sarcomas, are far more aggressive and associated with a worse prognosis than others, such as endometrioid adenocarcinomas. In our analysis, we did not adjust for potential changes in rates of hysterectomy and pregnancy during the study period because these changes were minor and we did not speculate that the results would significantly change. Finally, our data did not have information on age and race before 2001. Given this limitation of our database, we elected to use the Census data from 2000, which is roughly the median time point in our study, as a standard for comparison.

In conclusion, uterine cancer mortality has increased across all racial and ethnic and age groups from 2001 to 2018. This increase, however, has disproportionately affected non-Hispanic Black women across age groups. Here, we explored some of the complex systemic, social, environmental, and molecular factors that might be contributing to these disparities. However, additional studies are needed to further explore the complex interplay of the multifactorial reasons behind these widening gaps to inform targeted prevention efforts.

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PEER REVIEW HISTORY

Received February 19, 2023. Received in revised form April 14, 2023. Accepted April 20, 2023. Peer reviews and author correspondence are available at <http://links.lww.com/AOG/D350>.