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Racial Disparities in Young Women with Endometrial Cancer

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Abstract

Objective—Although racial disparities in treatment and outcome for endometrial cancer are well recognized, little work has explored disparities in young women. We performed a population-based analysis to compare survival between black and white women with endometrial cancer at <50 years of age.

Methods—We used the National Cancer Data Base to identify women <50 years of age with endometrial cancer from 1998–2012. Clinical and demographic characteristics were compared between black and white women and survival by race analyzed using Kaplan-Meier curves and multivariable Cox proportional hazards models.

Results—We identified a total of 35,850 women <50 years of age including 31,947 (89.1%) white and 3,903 (10.9%) black patients. Black women were more likely to have advanced stage, poorly differentiated, and non-endometrioid histology neoplasms (P<0.05 for all). In a multivariable model, survival was 19% worse for black patients than white patients (HR=1.19; 95%CI, 1.08–1.32). A similar effect was seen when limited to women with early-stage tumors (HR=1.24; 95%CI, 1.04–1.49), while among patients with advanced stage tumors, no association between race and survival was seen (HR=1.12; 95%CI, 0.89–1.41). Five-year survival rates were 90.6% (95%CI, 88.6–92.3%) for white and 81.5% (95%CI, 73.0–87.5%) for black women with stage IB tumors, and 75.1% (95%CI, 72.5–77.5%) and 63.3% (95%CI, 54.1–71.2%) for white and black women with stage III tumors, respectively.

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Conclusions—Young black women are more likely to present with pathologically aggressive, advanced stage tumors. Even after adjusting for these pathologic differences, young black women with endometrial cancer have higher mortality than white women.

Keywords

Endometrial cancer; uterine cancer; disparities; outcomes; hysterectomy

Introduction

There are significant racial disparities in the incidence, treatment and outcomes for women with endometrial cancer.[1] While endometrial cancer is more common in white women, black women often present with more advanced stage tumors and often harbor more aggressive histologic subtypes.[2–6] Black women are also more likely to die from endometrial cancer; compared to white women, black patients have an 80% higher mortality rate, one of the greatest disparities seen among common solid tumors.[7,8]

Patients under the age of 45 years account for 5–30% of all endometrial carcinoma cases.[9–11] There have been conflicting reports regarding the prognosis of endometrial cancer in younger patients, with some studies reporting favorable outcomes[9,10,12] and others reporting no difference when compared to older women.[13,14] Endometrial cancer in young women often derives from favorable histologic subtypes and is more commonly diagnosed at earlier stages.[10,12,15,16] Hence, young onset endometrial cancer is sufficiently different to be potentially considered as a unique subgroup within endometrial cancer as a whole and merits further study.

Although racial disparities in treatment and outcome for endometrial cancer are well recognized, little work has explored disparities in outcomes for young women with endometrial cancer. We performed a population-based analysis to compare survival between black and white women diagnosed with endometrial cancer at <50 years of age.

Methods

Data was derived from the National Cancer Data Base (NCDB), a clinical oncology database sourced from hospital registries of more than 1,500 Commission on Cancer (CoC)-accredited facilities.[17] NCDB data is used to analyze and track patients with malignant neoplastic diseases, their treatments, and outcomes. NCDB includes more than 70% of newly diagnosed cancer cases nationwide and more than 34 million records. The NCDB includes data on clinical and demographic characteristics, pathology, treatment, and survival.

We selected women <50 years of age with endometrial cancer who underwent hysterectomy from 1998–2012. Women who underwent preoperative radiotherapy and those without histologic confirmation were excluded. The cohort was limited to non-Hispanic white and black women.

Age was stratified as <35, 35–39, 40–44, and 45–49 years. Insurance status (private, Medicare, Medicaid, uninsured, and other) and median household income of each patient's

zip code (<$30,000, $30,000–$35,999, $36,000–$45,999, ≥$46,000, unknown) was recorded. Each patient's area of residence was categorized as urban, rural, or metropolitan. The Deyo classification of the Charlson comorbidity score was used to estimate a patient's comorbidity (0, 1, ≥2).[18,19] The American College of Surgeons Commission on Cancer Accreditation program classification schema was used to classify each reporting facility as a community cancer program, comprehensive community cancer program, academic/research program, or other program.[20] Each facility was further classified as academic and non-academic. The geographic region of the treating facility was coded as eastern, southern, midwestern, or western. Tumor characteristics included histology (endometrioid, serous, clear cell, sarcoma and other), grade (well, moderately, poorly differentiated, unknown), and stage based on American Joint Committee on Cancer criteria (IA, IB, I NOS, II, III, IV, and unknown). Therapeutic variables included use of chemotherapy (yes, no, unknown), and what type of radiation (none, external beam, vaginal brachytherapy) was utilized.

The primary outcome of the analysis was survival. The survival time was estimated as the number of months from diagnosis until the date of death from any cause. Survival is reported as all-cause mortality and includes death from cancer as well as other causes.[20]

Differences in categorical variables between black and white women were compared using χ^2 tests with p-values. Kaplan-Meier curves were developed to examine survival by race and compared using the log-rank test and reported with p-values. For each group, estimates of five-year survival with 95% confidence intervals are reported. Marginal multivariable Cox proportional hazards models were developed to determine the association between race and survival while adjusting for the other clinical, demographic and pathologic characteristics of the cohort while accounting for hospital-level clustering. Results from Cox proportional hazards models are reported as hazard ratios (HR) with 95% confidence intervals. A model for all patients and separate models for early-stage (stage I and II) and advanced stage (stage III and IV) are reported. Scaled Schoenfeld residuals for each variable in the Cox model were plotted to visually examine the assumption of proportionality.[21,22]

To determine whether disparities in survival had changed over time, separate marginal multivariable Cox proportional hazards models were developed for three distinct time periods: 1998–2002, 2003–2007, and 2008–2012. All hypothesis tests were two-sided. A P-value of <0.05 was considered statistically significant. All analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

Results

A total of 35,850 women <50 years of age were identified (Figure I). The cohort consisted of 31,947 (89.1%) white and 3,903 (10.9%) black patients (Table 1). Among white women, 7.8% were <35 years of age and 13.6% were 35–39 years of age compared to 13.6% and 15.6% of black women, respectively (P<0.001). Among white women, 79.9% were privately insured compared to 64.9% of black patients (P<0.001). Black women were more likely to have advanced stage, poorly differentiated, and non-endometrioid histology neoplasms. Stage IA tumors were noted in 49.3% of white women versus 39.9% of black women (P<0.01). Likewise, endometrioid neoplasms accounted for 68.7% of the cancers in white

women compared to 54.9% in black women (P<0.001), while grade 1 malignancies were seen in 51.8% and 40.0% (P<0.001) of the groups, respectively.

Mean 5-year overall survival rates were lower among black patients (Table 2). For women with stage IA neoplasms, 5-year survival was 97.2% (95% CI, 96.9–97.5%) among white women compared to 94.5% (95% CI, 93.0–95.8%) among black patients. Corresponding 5-year survival rates were 90.6% (95% CI, 88.6–92.3%) and 81.5% (95% CI, 73.0–87.5%), respectively, for those with stage IB neoplasms. The results were similar for advanced stage tumors. Among women with stage III cancers, 5-year survival was 75.1% (95% CI, 72.5–77.5%) in white women versus 63.3% (95% CI, 54.1–71.2%) in black patients. Figure 2 displays Kaplan-Meier survival curves stratified by stage, for each stage, survival was lower for black compared to white women (P<0.05 for all).

In a multivariable model (Table 3), black women were 19% more likely to die than white women (HR=1.19; 95% CI, 1.08–1.32). Older age, an increased number of comorbidities, advanced stage, non-endometrioid histology, and higher grade were associated with increased mortality (P<0.05 for all). In contrast, private insurance coverage, higher zip code income, and use of chemotherapy were associated with decreased mortality. In a model limited to women with early stage tumors, black women were 24% more likely to die than white women (HR=1.24; 95% CI, 1.04–1.49). Among patients with advanced stage tumors, there was no statistically significant association between race and survival (HR=1.12; 95% CI, 0.89–1.41).

When stratified by year of diagnosis, black women were 34% more likely to die than white women when diagnosed between 1998–2002 (HR=1.34; 95%CI, 1.14–1.58) (Table 4). Between 2003 and 2007, there was 22% increased risk of death for black compared to white women. (HR=1.22; 95%CI, 1.04–1.43) In contrast, there was no increased risk of mortality for black women diagnosed between 2008–2012 (HR=0.96; 95% CI 0.77–1.19) but it did not reach statistical significance.

Discussion

We noted that young black women are more likely to present with pathologically aggressive, advanced stage tumors than their white counterparts. Even after adjusting for these pathologic differences, young black women with endometrial cancer are 19% more likely to die than white women. The survival disparity is most pronounced in women with early-stage neoplasms.

Although, endometrial cancer is predominantly a disease of postmenopausal women, 5–10% of tumors occur in women less than 40 years of age.[23] The overall probability of developing endometrial cancer from birth to 39 years of age is approximately 0.05%.[24] Importantly, the incidence of endometrial cancer in young women has been rising steadily since the 1990's.[25] Endometrial cancer in young women is often associated with obesity and nulliparity and is typically associated with a more favorable prognosis than in older women.[26,27]

Black women are disproportionately affected by pathologically aggressive uterine tumors. Prior studies have consistently demonstrated that black women more frequently present with

non-endometrioid, aggressive histologic subtypes, have higher grade tumors, and more commonly have more advanced stage disease.[2,3,5,7,28–31] One population-based study noted that black women were 50% more likely to have uterine sarcomas, 85% more likely to have serous and clear cell tumors, and over twice as likely to have carcinosarcomas as their white counterparts.[2] We noted similar findings among young women with endometrial cancer; 69% of the tumors in white women were endometrioid histologies compared to only 55% in black patients. Likewise, 49% of white patients had stage IA tumors compared to 40% of black women.

Black women with endometrial cancer are significantly more likely to die from their tumors than white women.[2,5,30,32,33] An analysis of over 80,000 women found that even after adjusting for prognostic factors, black women were 60% more likely to die from their tumors than white women.[30] We identified similar disparate outcomes in young women with endometrial cancer. After adjustment for clinical and demographic factors, black women were 19% more likely to die than white women. The survival disadvantage was most pronounced for women with early-stage tumors.

While the survival difference between black and white women with endometrial cancer is well described, the factors that underlie the survival disparity have been harder to define. Decreased access to care and less aggressive treatment may explain a portion of the disparity in outcomes.[3–5,34,35] A previous study of the National Cancer Data Base found that black women were treated less often than white women at every stage. Among women who were treated, black women were less likely to undergo hysterectomy and less likely to receive adjuvant radiation therapy than white women.[3] In addition to access to care and treatment, a number of studies have suggested that biologic differences also account for a portion of the differences in outcomes between black and white women.[29] Mutations in the PTEN tumor suppressor gene, an abnormality associated with a favorable prognosis, are less common in tumors in black women.[36] In contrast, p53 mutations, often associated with aggressive tumors, occur more frequently in black women.[37–39]

While our study benefits from the inclusion of a large number of young women with endometrial cancer, we recognize a number of important limitations. First, NCDB lacks data on cause of death and we are only able to examine overall survival. Second, we lack detailed data on some important clinical details such as body mass index, follow-up care, as well as treatment of recurrent disease. Disparities in downstream care may have contributed to some of the differences in outcomes we noted. Third, given that there is no central pathology review, there may have been misclassification of a small number of women. Lastly, as with any study of observational data, we cannot account for individual patient and physician preferences that likely influenced treatment and outcomes.

Despite these limitations, our study suggests that there are pronounced differences in outcomes based on race for young women with endometrial cancer. Even after adjusting for the presence of more pathologically aggressive and advanced stage tumors in black women, we found that black women are nearly 20% more likely to die than their white counterparts. Given the rising incidence of endometrial cancer in young women, further studies to

examine the individual contributions of barriers to access to care, differential treatment, and biologic differences between young black and white women are needed.

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Research Highlights

- Young black women are more likely to present with aggressive, advanced stage tumors.
- Young black women with endometrial cancer have higher mortality than white women.
- Disparities in outcomes are most pronounced for early-stage disease.

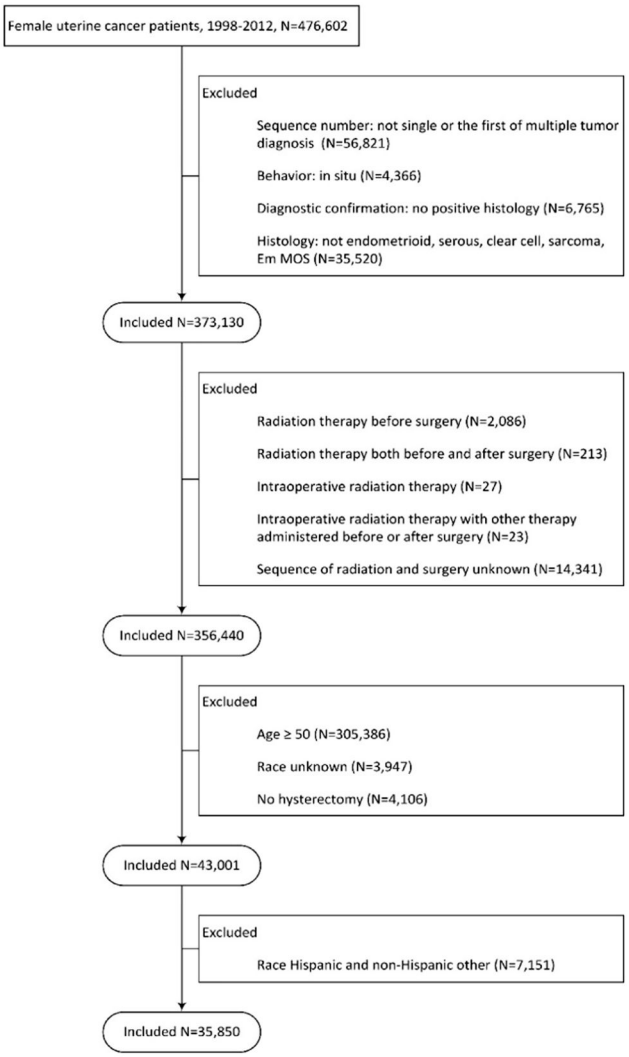

Figure 1.
Flowchart of cohort selection.

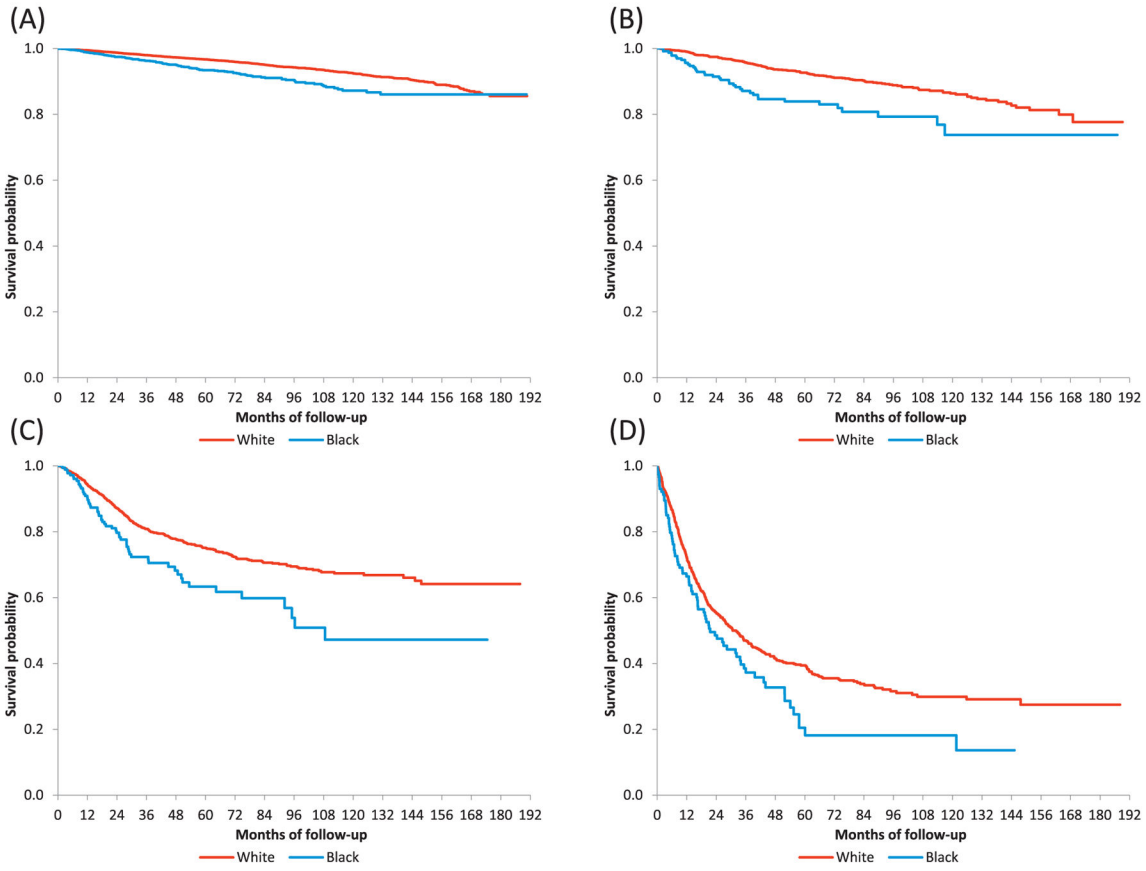

Figure 2.

Kaplan-Meier curves by race, stratified by stage. (A) stage I, *p*-value < 0.001; (B) stage II, *p*-value < 0.001; (C) stage III, *p*-value < 0.001; (D) stage IV, *p*-value = 0.02. Patients with missing follow-up time or vital status were excluded, including 1,691 stage I, 130 stage II, 218 stage III, and 87 stage IV patients. *P*-values were from log-rank tests.

Table 1

Demographical and clinical characteristics of the cohort.

	White		Black		
	N	**%**	**N**	**%**	***P*-value**
All	31,947	(89.1)	3,903	(10.9)	
Age					<0.001
<35	2,497	(7.8)	531	(13.6)	
35–39	4,330	(13.6)	609	(15.6)	
40–44	8,865	(27.7)	1,125	(28.8)	
45–49	16,255	(50.9)	1,638	(42.0)	
Year of diagnosis					<0.001
1998	1,750	(5.5)	150	(3.8)	
1999	1,781	(5.6)	142	(3.6)	
2000	1,839	(5.8)	173	(4.4)	
2001	2,001	(6.3)	229	(5.9)	
2002	1,977	(6.2)	234	(6.0)	
2003	2,139	(6.7)	238	(6.1)	
2004	2,120	(6.6)	253	(6.5)	
2005	2,253	(7.1)	262	(6.7)	
2006	2,314	(7.2)	266	(6.8)	
2007	2,181	(6.8)	257	(6.6)	
2008	2,240	(7.0)	310	(7.9)	
2009	2,330	(7.3)	346	(8.9)	
2010	2,384	(7.5)	324	(8.3)	
2011	2,315	(7.2)	375	(9.6)	
2012	2,323	(7.3)	344	(8.8)	
Insurance status					<0.001
Private	25,527	(79.9)	2,534	(64.9)	
Medicare	1,508	(4.7)	255	(6.5)	
Medicaid	2,199	(6.9)	549	(14.1)	
Other government/unknown	1,042	(3.3)	144	(3.7)	

	White		Black		*P*-value
	N	%	N	%	
Uninsured	1,671	(5.2)	421	(10.8)	
Income					<0.001
<$38,000	4,543	(14.2)	1,566	(40.1)	
$38,000–$47,999	7,640	(23.9)	860	(22.0)	
$48,000–$62,999	8,928	(27.9)	789	(20.2)	
$63,000+	10,106	(31.6)	571	(14.6)	
Unknown	730	(2.3)	117	(3.0)	
Location					<0.001
Metropolitan	25,162	(78.8)	3,405	(87.2)	
Urban	4,890	(15.3)	292	(7.5)	
Rural	522	(1.6)	46	(1.2)	
Unknown	1,373	(4.3)	160	(4.1)	
Charlson/Deyo comorbidity score					<0.001
0	18,127	(56.7)	2,314	(59.3)	
1	3,801	(11.9)	539	(13.8)	
≥2	671	(2.1)	122	(3.1)	
Unknown	9,348	(29.3)	928	(23.8)	
Facility type					<0.001
Community cancer	2,689	(8.4)	272	(7.0)	
Comprehensive community cancer	16,872	(52.8)	1,652	(42.3)	
Academic/research	12,358	(38.7)	1,974	(50.6)	
Other	28	(0.1)	5	(0.1)	
Facility region					<0.001
Eastern	6,845	(21.4)	660	(16.9)	
Midwest	11,740	(36.7)	1,234	(31.6)	
South	8,402	(26.3)	1,787	(45.8)	
West	4,960	(15.5)	222	(5.7)	
Stage					<0.001
IA	15,764	(49.3)	1,559	(39.9)	
IB	1,418	(4.4)	203	(5.2)	

	White		Black		*P*-value
	N	%	N	%	
INOS	1,470	(4.6)	156	(4.0)	
II	1,788	(5.6)	267	(6.8)	
III	1,639	(5.1)	208	(5.3)	
IV	747	(2.3)	141	(3.6)	
Unknown	9,121	(28.6)	1,369	(35.1)	
Histology					<0.001
Endometrioid	21,934	(68.7)	2,143	(54.9)	
Serous	374	(1.2)	55	(1.4)	
Clear Cell	198	(0.6)	26	(0.7)	
Sarcoma	3,593	(11.2)	1,082	(27.7)	
Other/not otherwise specified	5,848	(18.3)	597	(15.3)	
Grade					<0.001
Well	16,542	(51.8)	1,562	(40.0)	
Moderate	7,928	(24.8)	919	(23.5)	
Poorly	3,903	(12.2)	731	(18.7)	
Unknown	3,574	(11.2)	691	(17.7)	
Regional nodes examined					0.99
No	14,444	(45.2)	1,767	(45.3)	
Yes	17,068	(53.4)	2,082	(53.3)	
Unknown	435	(1.4)	54	(1.4)	
Radiation					<0.001
None	26,122	(81.8)	3,112	(79.7)	
External beam	3,698	(11.6)	551	(14.1)	
Brachytherapy	2,030	(6.4)	234	(6.0)	
Unknown	97	(0.3)	6	(0.2)	
Chemotherapy					<0.001
Yes	3,865	(12.1)	657	(16.8)	
No	27,523	(86.2)	3,157	(80.9)	
Unknown	559	(1.7)	89	(2.3)	

P-values were from Chi-square tests.

Table 2

Five-year survival rates by race.

	White (95% CI)	Black (95% CI)
Stage		
IA	97.2 (96.9–97.5)	94.5 (93.0–95.8)
IB	90.6 (88.6–92.3)	81.5 (73.0–87.5)
INOS	96.8 (95.5–97.8)	93.8 (80.1–98.2)
II	92.7 (91.2–93.9)	83.9 (77.9–88.4)
III	75.1 (72.5–77.5)	63.3 (54.1–71.2)
IV	39.4 (35.5–43.3)	20.4 (11.7–30.9)
Unknown	85.0 (84.2–85.8)	71.8 (69.1–74.3)

2,669 patients were not included because of missing follow-up time or vital status.

NOS: not otherwise specified.

Table 3

Multivariable model for predictors of mortality.

	All aHR (95% CI)	Early Stage aHR (95% CI)	Advanced Stage aHR (95% CI)
Race			
White	Referent	Referent	Referent
Black	1.19 (1.08–1.32) *	1.24 (1.04–1.49) *	1.12 (0.89–1.41)
Age			
<35	Referent	Referent	Referent
35–39	1.07 (0.91–1.26)	1.01 (0.74–1.37)	1.12 (0.80–1.55)
40–44	1.18 (1.02–1.37) *	1.25 (0.96–1.62)	1.02 (0.76–1.39)
45–49	1.34 (1.16–1.54) *	1.44 (1.13–1.84) *	1.18 (0.89–1.58)
Year of diagnosis	0.98 (0.96–0.99) *	0.99 (0.96–1.02)	1.00 (0.97–1.03)
Insurance status			
Private	Referent	Referent	Referent
Medicare	2.34 (2.05–2.68) *	2.68 (2.17–3.31) *	1.67 (1.27–2.19) *
Medicaid	1.59 (1.42–1.77) *	2.09 (1.74–2.51) *	1.15 (0.95–1.40)
Other government/unknown	1.08 (0.88–1.32)	1.32 (0.98–1.78)	0.87 (0.57–1.33)
Uninsured	1.53 (1.35–1.73) *	1.55 (1.21–1.98) *	1.17 (0.89–1.54)
Income			
<$38,000	Referent	Referent	Referent
$38,000–$47,999	0.87 (0.78–0.96) *	0.87 (0.73–1.03)	0.92 (0.75–1.13)
$48,000–$62,999	0.80 (0.72–0.90) *	0.71 (0.60–0.86) *	0.78 (0.62–0.97) *
$63,000+	0.67 (0.60–0.76) *	0.61 (0.49–0.75) *	0.66 (0.53–0.83) *
Unknown	1.30 (0.99–1.70)	1.38 (0.87–2.19)	1.26 (0.52–3.04)
Location			
Metropolitan	Referent	Referent	Referent
Urban	0.96 (0.86–1.06)	0.93 (0.77–1.12)	0.97 (0.79–1.20)
Rural	1.10 (0.86–1.42)	1.50 (1.07–2.10) *	0.90 (0.55–1.49)
Unknown	1.02 (0.79–1.31)	1.13 (0.80–1.59)	0.97 (0.42–2.21)
Charlson/Deyo comorbidity score			
0	Referent	Referent	Referent
1	1.30 (1.15–1.47) *	1.20 (0.95–1.51)	1.13 (0.90–1.42)
≥2	1.91 (1.52–2.39) *	2.86 (2.13–3.83) *	1.33 (0.82–2.16)
Unknown	1.04 (0.92–1.19)	1.04 (0.83–1.30)	0.99 (0.75–1.30)
Facility type			
Academic/research	Referent	Referent	Referent
Community cancer	1.02 (0.89–1.16)	0.93 (0.74–1.17)	1.10 (0.85–1.44)
Comprehensive community cancer	0.99 (0.92–1.07)	0.97 (0.84–1.12)	1.04 (0.90–1.21)
Other	0.94 (0.85–1.04)	1.74 (1.45–2.08) *	0.70 (0.53–0.92) *

	All aHR (95% CI)	Early Stage aHR (95% CI)	Advanced Stage aHR (95% CI)
Facility region			
Eastern	Referent	Referent	Referent
Midwest	1.00 (0.90–1.11)	1.16 (0.98–1.38)	0.88 (0.71–1.08)
South	1.10 (0.996–1.22)	1.29 (1.06–1.56) *	0.89 (0.72–1.09)
West	0.93 (0.82–1.05)	1.19 (0.94–1.50)	0.79 (0.62–1.01)
Stage			
IA	Referent	Referent	—
IB	1.71 (1.43–2.04) *	2.02 (1.65–2.48) *	—
INOS	0.84 (0.62–1.14)	0.90 (0.66–1.21)	—
II	1.54 (1.30–1.83) *	1.76 (1.44–2.14) *	—
III	2.60 (2.22–3.04) *	—	Referent
IV	6.94 (5.93–8.13) *	—	2.74 (2.34–3.21) *
Unknown	1.91 (1.72–2.11) *	—	—
Histology			
Endometrioid	Referent	Referent	Referent
Serous	1.11 (0.92–1.35)	0.62 (0.32–1.21)	1.30 (1.04–1.63) *
Clear Cell	1.14 (0.85–1.52)	1.12 (0.63–2.00)	1.24 (0.84–1.83)
Sarcoma	2.67 (2.41–2.95) *	2.63 (2.00–3.47) *	1.93 (1.53–2.44) *
Other/not otherwise specified	1.13 (1.02–1.24) *	1.00 (0.86–1.17)	1.26 (1.04–1.52) *
Grade			
Well	Referent	Referent	Referent
Moderate	1.73 (1.56–1.93) *	1.44 (1.26–1.66) *	1.52 (1.12–2.08) *
Poorly	4.01 (3.60–4.46) *	2.37 (1.96–2.87) *	3.04 (2.25–4.11) *
Unknown	2.19 (1.95–2.46) *	1.83 (1.43–2.34) *	2.46 (1.73–3.49) *
Radiation			
None	Referent	Referent	Referent
Brachytherapy	0.74 (0.62–0.88) *	0.87 (0.67–1.13)	0.53 (0.38–0.74) *
External beam	1.02 (0.93–1.12)	1.18 (0.96–1.45)	0.74 (0.64–0.86) *
Unknown	0.78 (0.48–1.27)	0.58 (0.20–1.67)	0.77 (0.32–1.89)
Chemotherapy			
Yes	Referent	—	Referent
No	0.53 (0.48–0.59) *	—	1.23 (1.05–1.45) *
Unknown	0.45 (0.35–0.59) *	—	0.72 (0.45–1.15)

Marginal Cox proportional hazard model included race, age, year of diagnosis, insurance status, income, location, comorbidity, facility type, region, stage, histology, grade and radiation in early stage patients (stage IA, IB, INOS and II) accounting for facility-level clustering. Chemotherapy was also adjusted for in the models for advanced stage (stage III and IV) and for all patients. In the model for all patients, 2,669 patients were excluded because of missing follow-up time or vital status, including 1,821 being excluded in the model for early stage, and 305 for advanced stage.

NOS: not otherwise specified. aHR: adjusted hazard ratio. CI: confidence interval.

* *P*-value < 0.05.

Table 4

Multivariable model for predictors of mortality stratified by year of diagnosis.

	1998–2002	2003–2007	2008–2012
	aHR (95% CI)	**aHR (95% CI)**	**aHR (95% CI)**
Race			
White	Referent	Referent	Referent
Black	1.34 (1.14–1.58) *	1.22 (1.04–1.43) *	0.96 (0.77–1.19)
Age			
<35	Referent	Referent	Referent
35–39	1.16 (0.90–1.50)	0.92 (0.70–1.21)	1.19 (0.85–1.66)
40–44	1.38 (1.09–1.75) *	1.08 (0.85–1.37)	0.98 (0.72–1.33)
45–49	1.55 (1.23–1.96) *	1.19 (0.96–1.49)	1.17 (0.87–1.56)
Year of diagnosis	1.00 (0.97–1.04)	0.99 (0.95–1.03)	0.99 (0.92–1.07)
Insurance status			
Private	Referent	Referent	Referent
Medicare	2.56 (2.03–3.22) *	2.27 (1.84–2.80) *	2.07 (1.51–2.82) *
Medicaid	1.58 (1.30–1.92) *	1.67 (1.40–1.99) *	1.52 (1.22–1.90) *
Other government/unknown	1.09 (0.85–1.40)	0.89 (0.61–1.30)	1.65 (1.08–2.54) *
Uninsured	1.50 (1.21–1.85) *	1.61 (1.32–1.96) *	1.46 (1.08–1.98) *
Income			
<$38,000	Referent	Referent	Referent
$38,000–$47,999	0.83 (0.71–0.97) *	0.83 (0.71–0.98) *	1.03 (0.81–1.30)
$48,000–$62,999	0.75 (0.63–0.88) *	0.84 (0.71–0.997) *	0.84 (0.66–1.07)
$63,000+	0.67 (0.56–0.79) *	0.63 (0.53–0.75) *	0.78 (0.60–1.003)
Unknown	1.09 (0.75–1.59)	1.44 (0.95–2.17)	1.70 (0.87–3.33)
Location			
Metropolitan	Referent	Referent	Referent
Urban	0.98 (0.82–1.16)	0.90 (0.75–1.07)	1.02 (0.83–1.26)
Rural	1.03 (0.68–1.57)	1.24 (0.85–1.83)	1.00 (0.56–1.79)
Unknown	1.00 (0.71–1.40)	0.94 (0.65–1.35)	1.33 (0.77–2.31)
Charlson/Deyo comorbidity score			
0	–	Referent	Referent
1	–	1.24 (1.06–1.45) *	1.48 (1.20–1.83) *
≥2	–	2.34 (1.78–3.08) *	1.56 (1.06–2.28) *
Facility type			
Academic/research	Referent	Referent	Referent
Community cancer	1.01 (0.83–1.23)	1.00 (0.81–1.24)	1.05 (0.79–1.40)
Comprehensive community cancer	1.01 (0.89–1.14)	0.93 (0.83–1.04)	1.06 (0.91–1.24)
Other	2.20 (1.79–2.72) *	–‡	–‡

	1998–2002	2003–2007	2008–2012
	aHR (95% CI)	**aHR (95% CI)**	**aHR (95% CI)**
Facility region			
Eastern	Referent	Referent	Referent
Midwest	1.06 (0.91–1.24)	0.94 (0.81–1.10)	0.97 (0.78–1.21)
South	1.13 (0.96–1.33)	1.06 (0.91–1.24)	1.06 (0.85–1.33)
West	0.80 (0.65–0.97) *	1.06 (0.88–1.28)	0.93 (0.72–1.21)
Stage			
IA	Referent	Referent	Referent
IB	1.67 (1.29–2.17) *	1.60 (1.18–2.19) *	2.39 (1.63–3.52) *
INOS	0.80 (0.45–1.42)	0.99 (0.65–1.51)	0.95 (0.49–1.86)
II	1.31 (1.02–1.68) *	1.67 (1.27–2.20) *	2.00 (1.32–3.04) *
III	1.97 (1.51–2.56) *	2.98 (2.31–3.83) *	3.87 (2.75–5.44) *
IV	5.36 (4.03–7.14) *	7.75 (6.13–9.80) *	11.03 (7.75–15.69) *
Unknown	1.68 (1.44–1.96) *	1.91 (1.62–2.26) *	2.88 (2.18–3.82) *
Histology			
Endometrioid	Referent	Referent	Referent
Serous	0.77 (0.54–1.09)	1.31 (0.99–1.74)	1.54 (1.08–2.21) *
Clear Cell	1.02 (0.66–1.58)	1.07 (0.63–1.84)	1.57 (0.83–2.98)
Sarcoma	2.28 (1.91–2.72) *	3.00 (2.55–3.54) *	2.90 (2.38–3.52) *
Other/not otherwise specified	0.97 (0.85–1.11)	1.25 (1.06–1.48) *	1.44 (1.06–1.94) *
Grade			
Well	Referent	Referent	Referent
Moderate	1.64 (1.41–1.90) *	1.81 (1.51–2.17) *	1.93 (1.46–2.54) *
Poorly	3.63 (3.07–4.29) *	3.84 (3.23–4.56) *	5.64 (4.27–7.44) *
Unknown	2.23 (1.88–2.65) *	2.06 (1.70–2.50) *	2.66 (2.02–3.52) *
Radiation			
None	Referent	Referent	Referent
Brahytherapy	0.84 (0.61–1.16)	0.73 (0.55–0.95) *	0.66 (0.49–0.88) *
External beam	1.22 (1.06–1.40) *	0.90 (0.77–1.04)	0.91 (0.73–1.13)
Unknown	_‡	0.95 (0.55–1.64)	0.63 (0.10–4.02)
Chemotherapy			
Yes	Referent	Referent	Referent
No	0.47 (0.40–0.56) *	0.56 (0.48–0.65) *	0.60 (0.48–0.75) *
Unknown	0.39 (0.26–0.59) *	0.45 (0.31–0.65) *	0.53 (0.27–1.02)

Marginal Cox proportional hazard models included race, age, year of diagnosis, insurance status, income, location, comorbidity, facility type, region, stage, histology, grade, radiation and chemotherapy accounting for facility-level clustering. In the stratum of 1998–2002, comorbidity was not adjusted for because all patients were unknown. In the stratum of 2008–2012, 2 patients in 2009 and 2,667 patients in 2012 were excluded because of missing follow-up time or vital status.

NOS: not otherwise specified. aHR: adjusted hazard ratio. CI: confidence interval.

[*] *P*-value < 0.05.

[≠] Non-estimable.