Long-term Patterns of Excess Mortality among Endometrial Cancer Survivors

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ABSTRACT

Background: We investigated excess mortality after endometrial cancer using conditional relative survival estimates and standardized mortality ratios (SMR).

Methods: Women diagnosed with endometrial cancer during 2000–2017 (N = 183,153) were identified in the Surveillance Epidemiology and End Results database. SMRs were calculated as observed deaths among endometrial cancer survivors over expected deaths among demographically similar women in the general U.S. population. Five-year relative survival was estimated at diagnosis and each additional year survived up to 12 years post-diagnosis, conditional on survival up to that year.

Results: For the full cohort, 5-year relative survival was 87.7%, 96.2%, and 97.1% at 1, 5, and 10 years post-diagnosis, respectively. Conditional 5-year relative survival first exceeded 95%, reflecting minimal excess mortality compared with the general population, at 4 years post-diagnosis overall. However, in subgroup analyses, conditional relative survival remained lower for Black women (vs. White) and for those with regional/distant stage disease (vs. localized) throughout the study period. The overall SMR for all-cause mortality decreased from 5.90 [95% confidence interval (CI), 5.81–5.99] in the first year after diagnosis to 1.16 (95% CI, 1.13–1.19) at 10+ years; SMRs were consistently higher for non-White women and for those with higher stage or grade disease.

Conclusions: Overall, endometrial cancer survivors had only a small survival deficit beyond 4 years post-diagnosis. However, excess mortality was greater in magnitude and persisted longer into survivorship for Black women and for those with more advanced disease.

Impact: Strategies to mitigate disparities in mortality after endometrial cancer will be needed as the number of survivors continues to increase.

Introduction

Endometrial cancer is the fourth most commonly diagnosed cancer among women in the United States, with more than 65,000 new cases estimated in the year 2020 (1). Fortunately, 5-year survival is high for patients with endometrial cancer overall, at more than 80% for all stages combined (1), and recent data project that the number of endometrial cancer survivors in the United States will grow from approximately 800,000 in 2019 to just more than 1 million by 2030 (2). With continued growth in the survivor population, there is a corresponding need for additional survivorship research to guide the long-term care of women with an endometrial cancer history.

Using standard survival curves, estimates of 5-year survival reflect a patient's probability of surviving for 5 years beyond the date of a cancer diagnosis. While useful for recently diagnosed patients, these estimates are clearly less relevant for patients who have already lived for several years after diagnosis because prognosis is generally expected to improve with each additional year survived. Thus, for mid- to long-term survivors, estimates of conditional survival, which account for the length of time already survived, are more useful measures, and provide indicators of prognosis relevant to specific stages of survivorship (3, 4). Examining conditional survival among cancer survivors relative to expected survival among similar groups in the general population (i.e., conditional relative survival) can reveal excess mortality remaining among survivors within specific time windows after diagnosis. Likewise, standardized mortality ratios (SMR), or ratios of observed mortality in a cancer cohort to expected mortality in the general population, are another measure that can be used to quantify excess mortality, from all causes, as well as from specific causes, among cancer survivors. A comprehensive examination of excess mortality according to time since an endometrial cancer diagnosis, using SMRs and conditional relative survival estimates, could inform planning for surveillance and follow-up care in the years after initial treatment, but to our knowledge, this has not been reported for U.S. endometrial cancer survivors.

The objective of this study was to estimate 5-year relative survival among U.S. women with endometrial cancer at the time of diagnosis and at each additional year survived (conditional relative survival) up to 12 years after diagnosis. We also estimated SMRs for all-cause and cause-specific mortality according to time since diagnosis to characterize how long-term patterns of mortality among endometrial cancer survivors compare with those among demographically similar women in general U.S. population. Analyses were performed overall and according to demographic and tumor characteristics.

Materials and Methods

Data source and study population

Women with an endometrial cancer diagnosis were identified using data from the Surveillance Epidemiology and End Results (SEER) program (5, 6), a system of population-based cancer registries which collects and reports data on cancer incidence and survival and covers approximately 35% of the U.S. population (7).

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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Information available in the SEER research database includes patient demographics, primary tumor site and morphology, stage, and vital status. For deceased patients, SEER recodes International Classification of Diseases (ICD) codes from the death certificate and reports cause of death in major groupings (8). Mortality data for the general U.S. population are accessible through the SEER database and come from the National Center for Health Statistics. This study was considered exempt by the University of North Carolina (Chapel Hill, NC) Institutional Review Board.

From the SEER 18 registries, we identified women with a first malignant primary endometrial cancer (sites C54.0–C54.9 and C55.9; ref. 9) between 2000 and 2017. We excluded death certificate or autopsy-only cases, those who were younger than 15 years at diagnosis, and those with missing information on race. In analyses of conditional 5-year relative survival, we also excluded those diagnosed after 2012, to allow a minimum of 5 years survival data through the end of follow-up for vital status on December 31, 2017. We used the following ICD-O-3 codes to define histologic subtypes as endometrioid: 8140, 8210, 8260, 8262, 8380–8384, 8440, 8480–8482, 8560, and 8570; serous: 8441, 8450, and 8460–8461; carcinosarcoma: 8950–8951 and 8980–8981; clear cell: 8310 and 8313; and mixed: 8255 and 8323 (10). All other codes were categorized together as other histologies.

Statistical analysis

We estimated 5-year relative survival among women with endometrial cancer at diagnosis and at each additional year survived up to 12 years after diagnosis, conditional on being alive at the beginning of that year. Relative survival was calculated as the ratio of observed survival among women with endometrial cancer to expected survival among women in the general U.S. population with a similar distribution of age, race, and calendar year. Survival was calculated using the actuarial method. Expected survival tables for the general population were generated using the Ederer II method. We considered the years at which conditional relative survival exceeded 90% and 95% to reflect little and minimal excess mortality, respectively, among endometrial cancer survivors compared with the general population (3, 4).

SMRs were estimated as the number of observed deaths among women with endometrial cancer divided by the number of expected deaths in the general population. The number of expected deaths was calculated as the product of the person-time at risk in the endometrial cancer cohort and the mortality rate for women in the general population with the same distribution of age, race (White, Black, and other), and calendar year. Confidence intervals (CI) for all SMRs were produced using exact methods. SMRs were estimated for all-cause mortality and for cause-specific mortality from endometrial cancer, other cancers, cardiovascular diseases (CVD: diseases of the heart; hypertension without heart disease; cerebrovascular diseases; atherosclerosis; aortic aneurysm and dissection; and other diseases of arteries, arterioles, and capillaries), and other causes (8). We also report absolute excess risks (AER), calculated as the difference between observed and expected deaths divided by the total person-years of observation, and expressed per 10,000 person-years. SMRs and AERs were estimated for the total study period and within the following time intervals: diagnosis–<1 year, 1–<5 years, 5–<10 years, and 10+ years post-diagnosis. Subgroup analyses were performed according to race, age at diagnosis, disease stage, histology, and grade. All analyses were performed using SEER*Stat, version 8.3.6.1.

Results

A total of 121,273 women, diagnosed with endometrial cancer during 2000–2012, contributed to analyses of conditional relative survival. Overall, 5-year conditional relative survival was 81.6% (95% CI, 81.4–81.9) at diagnosis and increased consistently to 87.7% (95% CI, 87.7–88.0), 96.2% (95% CI, 95.9–96.5), and 97.1% (95% CI, 96.5–97.6), respectively, at 1, 5, and 10 years post-diagnosis (**Table 1**; **Fig. 1**). Conditional relative survival first exceeded 95%, reflecting minimal excess mortality compared with the general population, at 4 years after diagnosis.

The year at which minimal excess mortality was reached varied considerably according to patient demographic and cancer-related characteristics. Among White women, relative survival was >95% by 4 years after diagnosis, compared with 8 years among Black women and 6 years among women of other races. Survival estimates were consistently somewhat higher for women who were younger at diagnosis, exceeding 95% at 4 years among those ages 15–64 years, and 5 years among those ages 65 years and older. While women with localized stage disease had minimal excess mortality at diagnosis and consistently thereafter, those with more advanced-stage disease did not surpass 95% relative survival by 12 years post-diagnosis; at 10 years, estimates were 91.3% (95% CI, 89.7–92.8) and 87.3% (95% CI, 81.6–91.3) among those with regional and distant stage disease, respectively. Likewise, throughout follow-up, relative survival remained consistently higher, and >95% was achieved earlier, for those with lower grade disease.

Patterns of conditional relative survival also varied according to histology; minimal excess mortality was observed as early as year 3 for those with endometrioid histology, but was observed much later or not within the study period for those with serous, carcinosarcoma, clear cell, mixed, or other histologies (**Table 1**). In analyses according to race stratified by stage, histology, and grade, Black women tended to reach little or minimal excess mortality later than White or other race women with similar disease characteristics (Supplementary Table S1). For example, among women with localized stage disease, 95% relative survival was first exceeded at diagnosis and 2 years for White women and women of other races, respectively, but not until 6 years for Black women.

SMR and AER analyses included a total of 183,153 women diagnosed with endometrial cancer between 2000 and 2017. Overall, the SMR for all-cause mortality decreased over time, from 5.90 (95% CI, 5.81–5.99) in the first year after diagnosis to 2.76 (95% CI, 2.72–2.79) and 1.30 (95% CI, 1.28–1.33) at 1–<5 years and 5–<10 years, respectively, but remained significantly elevated at 10+ years post-diagnosis (SMR, 1.16; 95% CI, 1.13–1.19; **Table 2**). In general, SMRs declined over time within all subgroups, but tended to be higher for those who were Black or other race, younger at diagnosis, had higher stage disease, and had nonendometrioid histologies. However, even at 10+ years, those with localized stage disease, grade 1 disease, and endometrioid histology had a small, but significant increase in all-cause mortality compared with the general population. AERs followed similar patterns for cancer-related characteristics, but for demographic characteristics, AERs were higher for older women, rather than younger, and were much higher for Black women than either White women or those of other races. Patterns according to race observed in overall analyses, with higher SMRs for all-cause mortality among Black and other race women and the highest AERs among Black women, were also generally apparent within subgroups defined by stage, histology, and grade (**Table 3**).

Table 1. Conditional relative survival among women with endometrial cancer, SEER 18, 2000–2012.

	At diagnosis		At 1 year		At 5 years		At 10 years			
	N at diagnosis	5-year relative survival (95% CI)	*N* survived to 1 year	5-year relative survival (95% CI)	*N* survived to 5 years	5-year relative survival (95% CI)	*N* survived to 10 years	5-year relative survival (95% CI)	>90% from year	>95% from year
All	121,273	81.6 (81.4–81.9)	108,990	87.7 (87.5–88.0)	88,536	96.2 (95.9–96.5)	42,325	97.1 (96.5–97.6)	2	4
Race										
White	100,182	83.9 (83.6–84.2)	91,104	89.2 (88.9–89.5)	74,976	96.6 (96.3–97.0)	36,424	97.3 (96.7–97.8)	2	4
Black	11,532	61.2 (60.2–62.2)	9,182	73.1 (72.0–74.2)	6,293	91.9 (90.5–93.1)	2,609	95.7 (92.7–97.5)	5	8
Other[a]	9,559	82.4 (81.6–83.2)	8,704	87.6 (86.8–88.4)	7,267	94.8 (94.0–95.6)	3,292	95.8 (94.1–97.0)	2	6
Age at diagnosis										
15–39	4,964	90.2 (89.3–91.0)	4,710	92.6 (91.8–93.4)	4,160	96.8 (96.1–97.4)	2,208	96.4 (95.0–97.4)	0	3
40–64	68,053	86.1 (85.8–86.4)	63,536	90.1 (89.8–90.4)	55,128	96.3 (96.0–96.6)	27,922	97.6 (97.1–98.0)	1	4
65+	48,256	74.2 (73.6–74.7)	40,744	83.2 (82.7–83.8)	29,248	95.9 (95.0–96.6)	12,195	95.8 (93.9–97.2)	3	5
Summary stage										
Localized	82,052	95.3 (95.0–95.5)	79,452	95.8 (95.6–96.1)	70,196	98.3 (98.0–98.6)	34,598	98.3 (97.6–98.8)	0	0
Regional	24,452	67.8 (67.1–68.5)	21,421	73.2 (72.5–73.9)	14,744	89.2 (88.3–90.0)	6,209	91.3 (89.7–92.8)	6	—
Distant	10,102	16.9 (16.1–17.7)	4,852	31.0 (29.7–32.4)	1,525	77.0 (74.0–79.8)	586	87.3 (81.6–91.3)	11	—
Unknown	4,667	52.6 (51.0–54.2)	3,265	68.6 (66.7–70.4)	2,071	85.4 (83.0–87.6)	932	93.3 (89.9–95.6)	9	—
Histology										
Endometrioid	93,738	90.0 (89.7–90.2)	88,120	92.8 (92.6–93.1)	75,650	97.2 (96.9–97.5)	37,172	97.5 (96.9–98.0)	1	3
Serous	5,830	48.4 (47.0–49.9)	4,796	54.4 (52.8–56.0)	2,458	86.2 (83.5–88.4)	844	92.2 (85.0–96.0)	7	—
Carcinosarcoma	5,437	38.8 (37.4–40.3)	3,577	55.7 (53.8–57.6)	1,833	88.7 (85.7–91.0)	719	91.1 (84.3–95.1)	7[b]	—
Clear cell	1,467	58.3 (55.3–61.2)	1,173	68.2 (64.9–71.3)	734	90.5 (85.4–93.8)	313	93.1 (80.8–97.6)	5	—
Mixed	5,453	77.6 (76.2–78.9)	4,953	82.3 (80.9–83.6)	3,774	94.5 (92.6–95.9)	1,288	96.0 (90.7–98.3)	3	6
Other	9,348	48.8 (47.7–49.9)	6,371	67.2 (65.9–68.5)	4,087	88.3 (86.7–89.6)	1,989	94.0 (91.5–95.7)	7	—
Grade										
1	43,704	97.9 (97.6–98.2)	42,608	98.2 (97.9–98.5)	38,755	98.8 (98.3–99.1)	19,736	98.2 (97.3–98.8)	0	0
2	31,171	89.7 (89.2–90.1)	29,549	91.4 (90.9–91.8)	25,015	96.3 (95.7–96.8)	12,752	97.3 (96.2–98.1)	1	4
3	20,868	59.3 (58.5–60.1)	16,846	69.4 (68.6–70.2)	10,855	91.2 (90.2–92.2)	4,909	95.1 (93.1–96.6)	5	10
Undifferentiated	6,553	44.8 (43.5–46.1)	4,772	58.1 (56.5–59.7)	2,595	88.4 (85.9–90.4)	961	92.7 (87.3–95.9)	6	—
Other/unknown	18,977	67.7 (67.0–68.5)	15,215	80.4 (79.6–81.2)	11,316	92.6 (91.6–93.5)	3,967	94.2 (92.1–95.8)	4	—

[a]Asian/Pacific Islander and American Indian/Alaska Native.
[b]Exceeded 90% at indicated year, but decreased to <90% before 12 years after diagnosis.

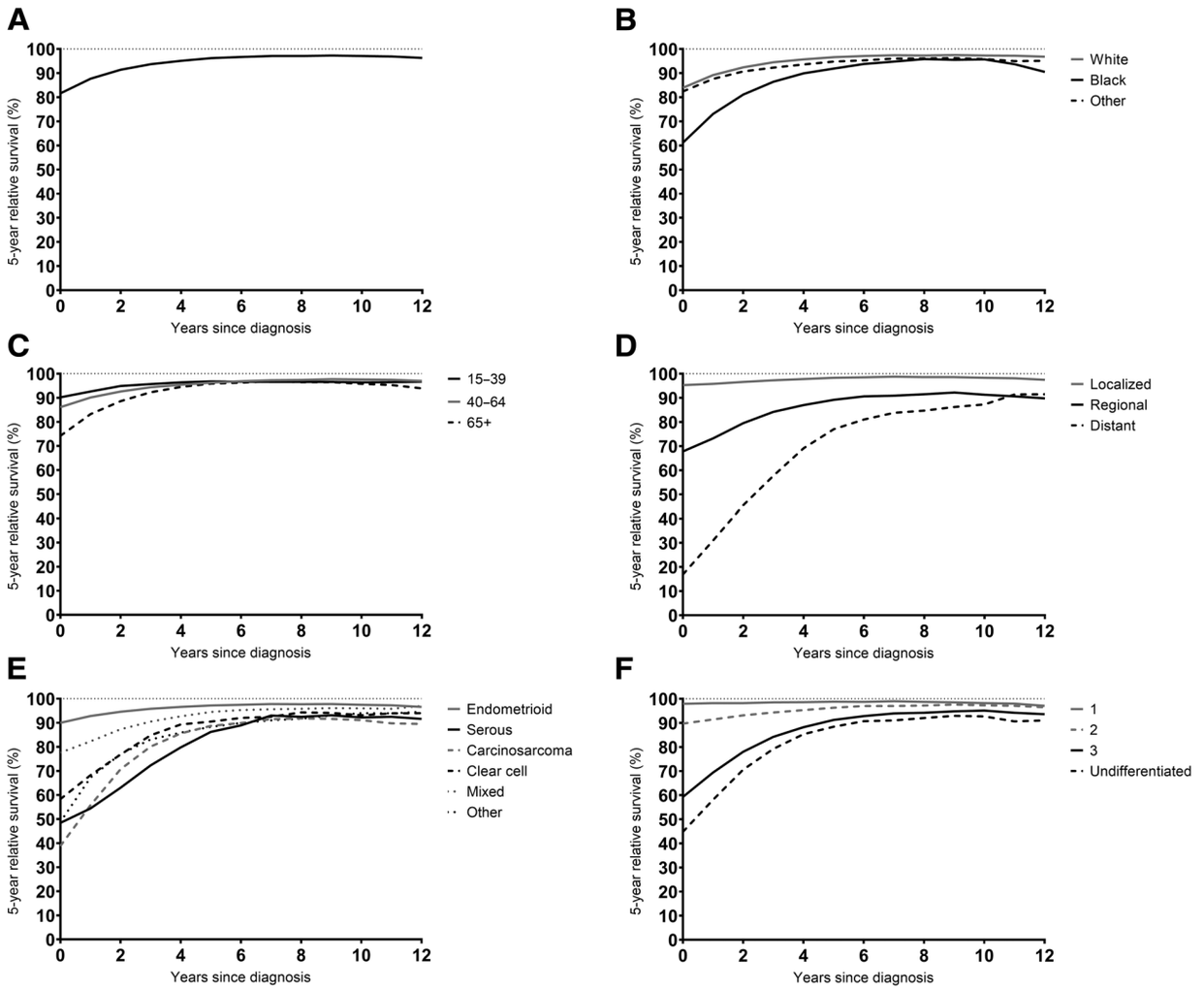

Figure 1.
Conditional relative survival among women with endometrial cancer: overall (**A**), by race (**B**), by age at diagnosis (**C**), by disease stage (**D**), by histology (**E**), and by grade (**F**).

Findings for cause-specific mortality, overall and according to race, are shown in **Table 4**. Overall, the SMR for endometrial cancer–specific mortality declined over time, but was still significantly elevated at 10+ years post-diagnosis (SMR, 10.37; 95% CI, 9.24–11.59; **Table 4**). SMRs for mortality from other cancers also declined consistently over time, from 3.93 (95% CI, 3.78–4.08) between diagnosis and <1 year, to 1.06 (95% CI, 1.00–1.13) at 10+ years. In contrast, mortality from CVDs and other causes (noncancer and non-CVD) was most elevated during the year after diagnosis, slightly elevated at 10+ years, and either significantly lower than or similar to the general population between 1 and <10 years. Although the number of deaths from CVDs and other causes exceeded the number of deaths from endometrial cancer at 5–<10 years and 10+ years, the AER for the full cohort was highest for endometrial cancer–related deaths within all time periods. In analyses according to race, SMRs for endometrial cancer were highest for women of other races during all time periods, but AERs were generally highest for Black women. For other cancers, CVDs, and other causes, SMRs were consistently higher for Black women and women of other races than White women, and AERs were nearly always highest for Black women. SMRs and AERs for cause-specific mortality according to age at diagnosis, stage, histology, and grade are shown in Supplementary Tables S2–S5. Although patterns varied somewhat according to cause of death and time since diagnosis, SMRs and AERs tended to be higher for women with more advanced-stage or higher grade disease and for those with nonendometrioid histologies.

Discussion

In this registry-based study, we estimated conditional 5-year relative survival up to 12 years after an endometrial cancer diagnosis and examined long-term patterns of excess mortality among endometrial cancer survivors according to demographic and cancer-related characteristics. As expected, relative survival increased with each additional year survived, and overall, exceeded 95% by 4 years after diagnosis. However, among the full cohort and within all subgroups, relative survival was still significantly below 100%, indicating some remaining elevation in mortality compared with the general population, at 10 years post-diagnosis. SMR and AER analyses further demonstrated

Table 2. SMRs for all-cause mortality among women with endometrial cancer, SEER 18, 2000–2017.

		Diagnosis–<1 year			1–<5 years			5–<10 years			10+ years			Total		
	N women	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER
All	183,153	16,055	5.90 (5.81–5.99)	806	22,641	2.76 (2.72–2.79)	311	9,317	1.30 (1.28–1.33)	68	5,122	1.16 (1.13–1.19)	47	53,135	2.36 (2.34–2.38)	279
Race																
White	148,936	11,667	5.00 (4.91–5.09)	688	17,566	2.43 (2.39–2.46)	265	7,992	1.24 (1.21–1.27)	57	4,555	1.13 (1.10–1.16)	41	41,780	2.09 (2.07–2.11)	235
Black	18,586	3,320	11.06 (10.68–11.44)	1,917	3,607	5.11 (4.95–5.28)	792	855	1.75 (1.63–1.87)	172	344	1.34 (1.20–1.49)	100	8,126	4.64 (4.54–4.74)	774
Other[a]	15,631	1,068	11.92 (11.21–12.66)	696	1,468	5.48 (5.21–5.77)	310	470	2.05 (1.87–2.25)	95	223	1.62 (1.41–1.84)	76	3,229	4.46 (4.31–4.62)	280
Age at diagnosis																
15–39	7,425	235	36.89 (32.32–41.92)	333	395	16.89 (15.26–18.64)	179	122	4.90 (4.07–5.85)	62	75	3.63 (2.85–4.55)	67	827	10.97 (10.24–11.75)	146
40–64	102,227	5,768	11.26 (10.97–11.56)	558	8,674	4.81 (4.71–4.91)	246	3,285	1.83 (1.76–1.89)	73	1,746	1.29 (1.23–1.35)	39	19,473	3.56 (3.51–3.61)	207
65+	73,501	10,052	4.56 (4.47–4.65)	1,219	13,572	2.13 (2.09–2.16)	437	5,910	1.11 (1.08–1.14)	58	3,301	1.08 (1.05–1.12)	64	32,835	1.93 (1.91–1.96)	432
Summary stage																
Localized	124,020	2,767	1.57 (1.52–1.63)	87	9,086	1.48 (1.45–1.51)	82	6,323	1.09 (1.06–1.12)	21	3,982	1.07 (1.04–1.11)	22	22,158	1.27 (1.26–1.29)	56
Regional	36,506	3,859	6.32 (6.13–6.53)	978	7,793	4.93 (4.82–5.04)	737	2,254	2.00 (1.92–2.09)	226	908	1.60 (1.50–1.71)	167	14,814	3.82 (3.75–3.88)	582
Distant	15,892	7,596	40.70 (39.79–41.62)	7,148	4,390	20.85 (20.23–21.47)	3,302	363	4.14 (3.72–4.59)	581	101	1.92 (1.57–2.34)	257	12,450	23.16 (22.76–23.57)	4,018
Unknown	6,735	1,833	10.88 (10.39–11.39)	3,255	1372	5.11 (4.84–5.39)	946	377	2.54 (2.29–2.81)	319	131	1.49 (1.25–1.77)	120	3,713	5.52 (5.34–5.70)	1,103
Histology																
Endometrioid	139,258	6,631	3.32 (3.24–3.40)	359	12,688	1.91 (1.87–1.94)	156	7,387	1.20 (1.17–1.23)	45	4,458	1.13 (1.10–1.17)	40	31,164	1.66 (1.64–1.68)	135
Serous	10,478	1,539	7.27 (6.91–7.64)	1,464	3,042	6.76 (6.52–7.00)	1,453	482	1.99 (1.81–2.17)	319	147	1.23 (1.04–1.45)	104	5,210	5.09 (4.95–5.23)	1,130
Carcinosarcoma	8,465	2,528	16.27 (15.64–16.91)	3,553	2,277	8.10 (7.77–8.44)	1,685	325	1.76 (1.58–1.97)	234	131	1.46 (1.22–1.73)	175	5,261	7.40 (7.20–7.60)	1,692
Clear cell	2,256	408	8.11 (7.34–8.94)	1,840	533	4.61 (4.22–5.01)	964	125	1.59 (1.33–1.90)	186	48	1.24 (0.91–1.64)	90	1,114	3.93 (3.71–4.17)	847
Mixed	9,084	722	5.01 (4.65–5.39)	697	1,433	3.51 (3.33–3.70)	474	401	1.42 (1.28–1.57)	98	125	1.16 (0.97–1.38)	48	2,681	2.84 (2.74–2.95)	381
Other	13,612	4,227	25.87 (25.09–26.66)	3,963	2,668	8.82 (8.49–9.16)	1,038	597	2.70 (2.49–2,93)	256	213	1.64 (1.43–1.87)	115	7,705	9.43 (9.22–9.64)	1,254
Grade																
1	61,484	1,050	1.38 (1.30–1.46)	49	3,335	1.17 (1.13–1.21)	25	3,043	1.05 (1.02–1.09)	11	2,090	1.08 (1.04–1.13)	23	9,518	1.13 (1.11–1.15)	23
2	41,228	1,689	2.55 (2.43–2.68)	263	4,612	1.99 (1.93–2.04)	185	2,815	1.27 (1.22–1.31)	63	1,647	1.15 (1.09–1.20)	46	10,763	1.62 (1.59–1.65)	137
3	29,325	5,129	9.24 (8.99–9.50)	1,796	7,000	4.99 (4.87–5.11)	916	1,748	1.66 (1.58–1.74)	183	757	1.28 (1.19–1.38)	99	14,634	4.06 (4.00–4.13)	781
Undifferentiated	11,508	2,702	14.66 (14.11–15.22)	2,687	2,906	7.74 (7.46–8.03)	1,438	423	1.86 (1.68–2.04)	235	145	1.41 (1.19–1.66)	133	6,176	6.93 (6.76–7.11)	1,375
Other/unknown	39,608	5,485	9.82 (9.56–10.08)	1,484	4,788	3.82 (3.71–3.93)	480	1,288	1.68 (1.59–1.78)	148	483	1.33 (1.21–1.45)	94	12,044	4.09 (4.02–4.17)	588

[a]Asian/Pacific Islander and American Indian/Alaska Native.

Table 3. SMRs for all-cause mortality among women with endometrial cancer, stratified by race according to cancer characteristics, SEER 18, 2000–2017.

	Diagnosis–<1 year			1–<5 years			5–<10 years			10+ years			Total		
	N deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER
Stage															
Localized															
White	2,123	1.38 (1.32–1.44)	60	7,367	1.34 (1.31–1.37)	62	5,496	1.05 (1.02–1.08)	11	3,558	1.05 (1.01–1.08)	15	18,544	1.18 (1.17–1.20)	40
Black	512	3.24 (2.97–3.53)	383	1,198	2.55 (2.41–2.70)	285	531	1.45 (1.33–1.58)	102	252	1.25 (1.10–1.42)	74	2,493	2.09 (2.00–2.17)	224
Other[a]	132	2.26 (1.89–2.69)	76	521	2.64 (2.42–2.88)	112	296	1.64 (1.45–1.83)	58	172	1.53 (1.31–1.78)	66	1,121	2.04 (1.93–2.17)	85
Regional															
White	2,809	5.55 (5.35–5.76)	877	5,907	4.37 (4.26–4.48)	665	1,897	1.93 (1.85–2.02)	220	794	1.59 (1.48–1.71)	173	11,407	3.42 (3.35–3.48)	526
Black	790	9.40 (8.75–10.07)	1,789	1,380	7.92 (7.51–8.35)	1,497	234	2.31 (2.03–2.63)	344	70	1.57 (1.23–1.99)	182	2,474	6.13 (5.89–6.37)	1,199
Other[a]	260	13.00 (11.47–14.68)	802	506	9.28 (8.49–10.13)	584	123	2.95 (2.45–3.52)	178	44	1.85 (1.35–2.49)	106	933	6.67 (6.25–7.11)	461
Distant															
White	5,303	36.58 (35.60–37.58)	6,776	3,244	18.70 (18.06–19.36)	3,124	285	3.69 (3.28–4.15)	535	89	1.87 (1.50–2.30)	260	8,921	20.13 (19.71–20.55)	3,700
Black	1,705	49.25 (46.94–51.65)	9,253	787	28.05 (26.12–30.08)	4,719	47	6.40 (4.70–8.51)	926	8	2.36 (1.02–4.66)	307	2,547	34.70 (33.36–36.07)	6,197
Other[a]	588	83.29 (76.69–90.30)	6,125	359	39.63 (35.63–43.95)	2,867	31	9.52 (6.47–13.51)	655	4	2.76 (0.75–7.08)	172	982	47.16 (44.26–50.21)	3,506
Histology															
Endometrioid															
White	5,204	2.94 (2.86–3.02)	315	10,464	1.75 (1.72–1.78)	136	6,471	1.16 (1.13–1.19)	37	4,001	1.11 (1.07–1.14)	34	26,140	1.54 (1.52–1.56)	116
Black	1,005	6.12 (5.75–6.51)	908	1,475	3.18 (3.02–3.34)	405	562	1.56 (1.43–1.69)	128	262	1.32 (1.17–1.49)	94	3,304	2.78 (2.69–2.88)	373
Other[a]	422	6.64 (6.02–7.30)	326	749	3.55 (3.30–3.81)	168	354	1.85 (1.66–2.05)	74	195	1.59 (1.38–1.83)	73	1,720	2.92 (2.79–3.06)	151
Serous															
White	963	6.08 (5.70–6.48)	1,268	2,157	6.19 (5.93–6.45)	1,403	358	1.82 (1.63–2.01)	281	121	1.19 (0.99–1.43)	91	3,599	4.47 (4.32–4.62)	1,029
Black	474	10.38 (9.47–11.36)	2,150	679	8.04 (7.45–8.67)	1,685	98	2.69 (2.19–3.28)	514	19	1.29 (0.78–2.02)	127	1,270	7.01 (6.63–7.41)	1,543
Other[a]	102	13.28 (10.83–16.12)	1,295	206	12.06 (10.47–13.83)	1,339	26	2.83 (1.85–4.14)	294	7	2.15 (0.86–4.42)	249	341	9.16 (8.22–10.19)	1,062
Carcinosarcoma															
White	1,673	14.71 (14.01–15.43)	3,366	1,527	6.91 (6.57–7.26)	1,483	256	1.72 (1.52–1.94)	229	106	1.46 (1.20–1.77)	182	3,562	6.41 (6.20–6.62)	1,506
Black	697	19.01 (17.63–20.48)	4,194	617	12.06 (11.13–13.05)	2,518	58	1.88 (1.43–2.43)	267	22	1.40 (0.88–2.12)	170	1,394	10.37 (9.83–10.93)	2,419
Other[a]	158	31.66 (26.92–37.00)	3,245	133	14.97 (12.53–17.74)	1,567	11	2.34 (1.17–4.19)	195	3	1.60 (0.33–4.67)	86	305	14.92 (13.29–16.69)	1,656
Clear cell															
White	285	7.27 (6.45–8.16)	1,724	379	4.23 (3.82–4.68)	895	100	1.59 (1.29–1.93)	191	41	1.30 (0.93–1.76)	117	805	3.60 (3.36–3.86)	785
Black	98	10.60 (8.61–12.92)	2,659	109	5.25 (4.31–6.33)	1,334	18	1.55 (0.92–2.45)	199	5	0.91 (0.29–2.11)	−47	230	4.88 (4.27–5.55)	1,280
Other[a]	25	13.54 (8.76–19.99)	1,259	45	8.35 (6.09–11.18)	914	7	1.81 (0.73–3.74)	131	2	1.20 (0.15–4.33)	29	79	6.19 (4.90–7.72)	683
Mixed															
White	529	4.35 (3.99–4.74)	607	1,109	3.11 (2.93–3.30)	421	336	1.35 (1.21–1.50)	84	113	1.16 (0.96–1.40)	51	2,087	2.53 (2.42–2.64)	333
Black	137	7.79 (6.54–9.20)	1,368	223	5.71 (4.98–6.51)	962	36	1.62 (1.14–2.24)	157	8	1.36 (0.59–2.68)	93	404	4.77 (4.31–5.25)	820
Other[a]	56	11.26 (8.51–14.63)	717	101	7.72 (6.29–9.38)	486	29	2.78 (1.86–3.99)	185	4	0.89 (0.24–2.27)	−16	190	5.76 (4.97–6.64)	408
Other															
White	3,013	23.18 (22.36–24.03)	3,812	1,930	7.88 (7.53–8.24)	976	471	2.57 (2.34–2.81)	254	173	1.57 (1.35–1.83)	111	5,587	8.36 (8.14–8.58)	1,176
Black	909	33.76 (31.60–36.03)	5,120	504	11.05 (10.11–12.06)	1,368	83	2.94 (2.34–3.65)	270	28	1.77 (1.17–2.55)	127	1,524	13.07 (12.42–13.74)	1,746
Other[a]	305	46.76 (41.66–52.32)	3,083	234	19.53 (17.11–22.20)	1,018	43	4.56 (3.30–6.14)	250	12	2.86 (1.48–5.00)	138	594	18.49 (17.03–20.03)	1,111

(Continued on the following page)

Table 3. SMRs for all-cause mortality among women with endometrial cancer, stratified by race according to cancer characteristics, SEER 18, 2000–2017. (Cont'd)

	Diagnosis–<1 year			1–<5 years			5–<10 years			10+ years			Total		
	N deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER
Grade															
1, 2															
White	2,248	1.76 (1.69–1.83)	117	6,663	1.42 (1.39–1.46)	74	5,135	1.10 (1.07–1.13)	22	3,372	1.09 (1.05–1.12)	27	17,418	1.27 (1.25–1.29)	56
Black	350	3.46 (3.11–3.85)	394	839	2.55 (2.38–2.73)	269	423	1.54 (1.39–1.69)	112	203	1.29 (1.12–1.48)	79	1,815	2.11 (2.01–2.21)	215
Other[a]	141	3.13 (2.64–3.69)	115	445	2.72 (2.48–2.99)	107	300	1.89 (1.68–2.12)	74	162	1.55 (1.32–1.81)	64	1,048	2.22 (2.09–2.36)	92
3, undifferentiated															
White	5,468	9.29 (9.04–9.54)	1,854	7,294	4.96 (4.84–5.07)	943	1,775	1.64 (1.56–1.71)	185	767	1.28 (1.19–1.37)	102	15,304	4.09 (4.02–4.15)	815
Black	1,762	14.23 (13.58–14.91)	2,996	1,866	7.78 (7.43–8.14)	1,608	280	1.93 (1.71–2.17)	271	88	1.29 (1.04–1.59)	106	3,996	6.92 (6.71–7.14)	1,524
Other[a]	601	22.49 (20.73–24.36)	1,887	746	11.25 (10.46–12.09)	993	116	2.32 (1.92–2.78)	168	47	1.78 (1.31–2.36)	122	1,510	8.91 (8.47–9.37)	864

[a]Asian/Pacific Islander and American Indian/Alaska Native.

that excess mortality, from all causes and from specific causes, compared with demographically similar women in the general U.S. population, tended to be greater among non-White women and those with less favorable disease characteristics, even at 10+ years after endometrial cancer diagnosis.

Conditional survival estimates provide valuable information for cancer survivors who are well beyond their initial diagnosis and treatment period, but remained concerned about the impact of their cancer history on their future mortality risk. Our analyses suggested that >95% relative survival, which we considered to reflect minimal excess mortality, was achieved relatively quickly by endometrial cancer survivors overall, at 4 years after diagnosis. However, this was largely driven by women with more favorable disease characteristics, namely those with localized and grade 1 disease, whose relative survival exceeded 95% at diagnosis and consistently thereafter. In contrast, among women with regional or distant stage disease, undifferentiated disease, and nonendometrioid histologies, relative survival increased over time since diagnosis, but did not reach 95% within the study period of up to 12 years post-diagnosis. Understanding which subgroups of survivors, defined by demographic and cancer-related characteristics, continue to have lower than expected survival for many years after cancer treatment can help in predicting the type and intensity of care that will be needed across various phases of survivorship.

In addition to estimating conditional relative survival, we also used SMRs and AERs to quantify excess deaths from all causes and specific causes among women with endometrial cancer within specified post-diagnosis time windows. Our findings suggested that even at 5–<10 and 10+ years post-diagnosis, the greatest contributor to excess mortality relative to the general population was still death from endometrial cancer. However, it was notable that certain subgroups, particularly Black women and those with more advanced-stage or higher grade disease, had excess deaths attributable to other cancers, CVDs, and other causes within certain post-diagnosis time periods. These findings underscore the importance of long-term follow-up and monitoring of women with an endometrial cancer history, particularly for Black women and those whose initial prognosis was less favorable.

Associations between obesity and endometrial cancer incidence (11) suggest that endometrial cancer survivors may have elevated rates of CVD incidence and mortality relative to the general population. Women with more advanced-stage disease, although they comprise a minority of all patients with endometrial cancer, may also be treated with certain chemotherapeutic agents that may have cardiotoxic effects and could also contribute to future risk of adverse cardiovascular outcomes (12, 13). A previous study using SEER data reported that women diagnosed with endometrial cancer between 1988 and 2012 were 8.8 (95% CI, 8.7–9.0) times more likely to die from CVDs than women in the general population (14). Our analyses suggested a smaller, although still significant increase in CVD mortality, which was most apparent among endometrial cancer survivors who were non-White, younger, or had more advanced-stage disease. We also found that the magnitude of the SMR was not consistent across time periods, with greater elevations in CVD mortality within the first year after endometrial cancer diagnosis and at 10+ years post-diagnosis. It is unclear the extent to which excess mortality from CVDs within the year after diagnosis reflects a direct impact of endometrial cancer diagnosis and treatment on CVD-related deaths, or misattribution of cancer-related death to CVDs. Nevertheless, these results suggest the importance of monitoring cardiovascular health during the initial cancer

Table 4. SMRs for cause-specific mortality among women with endometrial cancer, overall and stratified by race, SEER 18, 2000–2017.

	Diagnosis–<1 year			1–<5 years			5–<10 years			10+ years			Total		
	N deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER	*N* deaths	SMR (95% CI)	AER
Endometrial cancer mortality															
All	10,517	472.67 (463.68–481.79)	634	12,769	192.85 (189.52–196.22)	274	2,041	38.32 (36.68–40.02)	62	308	10.37 (9.24–11.59)	19	25,635	149.54 (147.72–151.38)	232
White	7,628	443.27 (433.38–453.34)	561	9,648	180.72 (177.13–184.36)	247	1,644	37.02 (35.25–38.85)	59	267	10.51 (9.29–11.85)	19	19,187	136.65 (134.72–138.60)	206
Black	2,123	515.09 (493.41–537.47)	1,345	2,189	217.16 (208.16–226.45)	594	247	37.03 (32.55–41.94)	113	20	6.44 (3.93–9.94)	19	4,579	190.95 (185.46–196.57)	553
Other[a]	766	832.46 (774.55–893.56)	544	932	339.29 (317.85–361.79)	240	150	68.80 (58.23–80.73)	58	21	17.65 (10.93–26.99)	18	1,869	265.60 (253.69–277.92)	208
Other cancer mortality															
All	2,594	3.93 (3.78–4.08)	117	4,206	2.14 (2.08–2.21)	48	1,970	1.26 (1.21–1.32)	13	913	1.06 (1.00–1.13)	4	9,683	1.92 (1.88–1.96)	42
White	1,834	3.25 (3.10–3.40)	94	3,206	1.86 (1.80–1.93)	38	1,657	1.19 (1.13–1.25)	10	814	1.05 (0.98–1.12)	3	7,511	1.69 (1.65–1.72)	33
Black	597	8.44 (7.78–9.15)	334	738	4.42 (4.10–4.75)	156	199	1.84 (1.59–2.11)	43	56	1.11 (0.84–1.44)	6	1,590	4.01 (3.82–4.21)	145
Other[a]	163	6.42 (5.47–7.49)	98	262	3.50 (3.09–3.95)	48	114	1.92 (1.58–2.31)	21	43	1.34 (0.97–1.80)	10	582	3.03 (2.79–3.29)	44
CVD mortality															
All	1,387	1.53 (1.45–1.61)	29	2,554	0.95 (0.91–0.99)	−3	2,355	1.01 (0.97–1.05)	1	1,687	1.16 (1.10–1.22)	16	7,983	1.08 (1.06–1.10)	5
White	1,045	1.36 (1.28–1.44)	20	2,121	0.90 (0.86–0.94)	−6	2,071	0.99 (0.95–1.04)	−1	1,490	1.13 (1.07–1.19)	14	6,727	1.03 (1.01–1.06)	2
Black	282	2.57 (2.27–2.88)	109	306	1.21 (1.08–1.35)	14	192	1.10 (0.95–1.26)	8	130	1.41 (1.18–1.67)	43	910	1.44 (1.35–1.54)	34
Other[a]	60	2.12 (1.62–2.74)	23	127	1.51 (1.26–1.79)	11	92	1.25 (1.01–1.53)	7	67	1.47 (1.14–1.87)	19	346	1.49 (1.34–1.66)	13
Other cause mortality															
All	1,557	1.38 (1.31–1.45)	26	3,112	0.89 (0.86–0.92)	−8	2,951	0.92 (0.89–0.95)	−8	2,214	1.06 (1.02–1.11)	9	9,834	0.99 (0.97–1.01)	−1
White	1,160	1.18 (1.12–1.25)	13	2,591	0.83 (0.80–0.86)	−13	2,620	0.90 (0.87–0.93)	−11	1,984	1.04 (0.99–1.09)	6	8,355	0.94 (0.92–0.96)	−6
Black	318	2.75 (2.46–3.07)	129	374	1.36 (1.23–1.51)	27	217	1.09 (0.95–1.24)	8	138	1.25 (1.05–1.48)	32	1,047	1.50 (1.41–1.59)	42
Other[a]	79	2.25 (1.78–2.81)	31	147	1.39 (1.17–1.63)	11	114	1.22 (1.00–1.46)	8	92	1.56 (1.26–1.91)	29	432	1.47 (1.34–1.62)	15

[a]Asian/Pacific Islander and American Indian/Alaska Native.

diagnosis and treatment period. Excess CVD mortality among longer term endometrial cancer survivors in our study also suggests that CVD prevention efforts should begin early in follow-up care. Neither the earlier SEER report nor ours was able to account for CVD risk factors, such as obesity and diabetes, or specific cancer treatments, because this information is not available in SEER. Future studies may be warranted to investigate the impact of these factors on CVD outcomes among endometrial cancer survivors, and why risk relative to the general population may vary according to time since endometrial cancer diagnosis.

Prior reports have documented pronounced racial disparities in endometrial cancer outcomes, with lower 5-year survival among Black women than White women that is not fully explained by different distributions of stage, grade, or histologic subtype by race (15–17). Our findings add information on the extent to which these disparities persist among longer term survivors. Overall and in every subgroup defined by disease characteristics, conditional relative survival among Black women increased steadily over time since diagnosis, but remained slightly lower than that of White women at 12 years, and >95% relative survival was reached later among Black women than White women. Likewise, in all post-diagnosis time windows up to 10+ years, both SMRs and AERs for all-cause mortality were consistently higher for Black women than for White women, even among those with localized stage or lower grade disease, and they tended to be higher for cause-specific mortality as well. Calculation of relative survival and SMRs accounts for race and, when stratified by race, estimates, therefore, reflect excess mortality among endometrial cancer survivors compared with women of the same race in the general population. Persistently lower conditional relative survival and higher SMRs long after diagnosis suggest a greater and more lasting impact of an endometrial cancer diagnosis on mortality among Black women, relative to their cancer-free peers, than among White women, and the need for efforts to reduce disparities not just among recently diagnosed patients, but also among long-term survivors.

Our study has several strengths and limitations. Use of the SEER database allowed for a large sample size and examination of long-term patterns of mortality according to basic demographic and disease-related characteristics. However, SEER data lack information on cancer recurrence, and information on first course of cancer treatment is thought to be fairly incomplete (18), so we were unable to consider these factors in our analyses. For some cancer characteristics, such as grade, a relatively high proportion of patients had missing information. We also did not have information on factors such as comorbidities, income, or obesity, all of which may be associated with patterns of mortality after endometrial cancer diagnosis. In addition, because all of our analyses involved comparisons with the general U.S. population, we were limited in our stratified analyses to only those factors accounted for by the U.S. population mortality statistics (e.g., age, sex, and race) used in this study. Cause-specific mortality analyses are also subject to potential misclassification due to inaccurate coding of cause of death on death certificates. Finally, race information in the SEER registries comes from patient medical records, and misclassification could occur if the race indicated in the medical record does not match the woman's identity or experience. Our analyses by race also do not account for diversity within racial categories. Nevertheless, our findings provide insight into how excess mortality among endometrial cancer survivors varies according to patient characteristics and time since cancer diagnosis, and may inform planning for follow-up care throughout survivorship.

Results of this study suggest that overall, endometrial cancer survivors have only a small, although significant, survival deficit beyond 4 years post-diagnosis. However, excess mortality was greater in magnitude and persisted longer into survivorship for Black women and those with more advanced-stage or higher grade disease. Strategies to mitigate disparities in mortality after endometrial cancer will be needed as the number of endometrial cancer survivors in the United States continues to increase.

Authors' Disclosures

No disclosures were reported.

Authors' Contributions

C. Anderson: Formal analysis, writing–original draft, writing–review and editing. **V.L. Bae-Jump:** Writing–review and editing. **R.R. Broaddus:** Writing–review and editing. **A.F. Olshan:** Writing–review and editing. **H.B. Nichols:** Writing–review and editing.

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