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Disparities in endometrial cancer outcomes between non-Hispanic White and Hispanic women

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HIGHLIGHTS

- We compare non-Hispanic White and Hispanic women with endometrial cancer for differences in demographics, tumor characteristics, and treatment.
- Hispanic women have higher cancer-specific mortality and cancer characteristics (stage and lymph node involvement) mediate most disparity.
- More Hispanic women in 2006–2010 than in 2000–2005 were diagnosed at later stages.

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ABSTRACT

Objective. To compare demographics, tumor characteristics, the first course of treatment, and cancer-specific survival of non-Hispanic White and Hispanic women with endometrial cancer.

Methods. We used public-use data from the Surveillance, Epidemiology, and End Results (SEER) Program. The study included 69,764 non-Hispanic White and Hispanic women diagnosed with endometrial cancer between 2000 and 2010. Using Cox proportional hazards models, demographics, tumor characteristics, and treatment were assessed as potential explanatory variables for the survival disparity between non-Hispanic Whites and Hispanics.

Results. Kaplan–Meier estimation with Bonferroni correction showed statistically different cancer-specific survival for U.S.-born and foreign-born Hispanics compared to non-Hispanic Whites, but no difference between birthplace-unknown Hispanics and non-Hispanic Whites. In 2000–2005, U.S.-born and foreign-born Hispanics had a higher risk of endometrial cancer death compared to non-Hispanic Whites after full adjustment (hazard rate (HR) = 1.61, 95% Confidence Interval (CI):1.44–1.79 and 1.27, 95% CI:1.13–1.43). In 2006–2010, the risk of endometrial death was not statistically significant for U.S.-born Hispanics (HR = 1.16, 95% CI:0.99–1.36), but increased for foreign-born Hispanics (HR = 1.31, 95% CI:1.12–1.52). Most of the survival disparity between Hispanic and non-Hispanic White women was mediated by cancer characteristics, specifically, stage and node involvement.

Conclusions. Hispanic women have higher cancer-specific mortality compared to non-Hispanic Whites. Compared to 2000–2005, more Hispanics were diagnosed at later stages and fewer received combination therapy in 2006–2010. Early detection is vital to improving endometrial cancer survival as most of the disparity was mediated by stage. Increased efforts are needed to improve education and access to care for Hispanic women.

Introduction

Endometrial cancer is the most common malignancy of the female reproductive organs, with an estimated 49,560 new cases and 8190 deaths reported in 2013 [1]. While the incidence is higher in non-Hispanic White (NHW) women, minority patients tend to be diagnosed with more aggressive cancer [2]. Although known risk factors (i.e., socioeconomic status, obesity, reproductive history, and use of exogenous estrogens) are associated with racial/ethnic variation in endometrial cancer, the basis for racial/ethnic survival differences is not clearly defined [3,4].

To date, most research has focused on the comparisons of White and Black women with endometrial cancer [3–7]. Disparities in incidence and survival between Blacks and NHWs are well documented [3,5,8]. Black women are diagnosed at later stage, higher grade and with

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more lethal histologic types than NHWs. They also have less favorable survival for each stage, grade, and histologic type [3–5]. However, limited research examined the age distribution, disease presentation, and endometrial cancer outcomes among minority women, especially Hispanic women [2,4,9–14].

Hispanics are one of the largest and fastest growing demographic groups in the United States (U.S.) [15]. In 2010, Hispanics made up 50.5 million of the 310 million U.S. residents (16.3%) [16]. Hispanics differ from non-Hispanics in age, socioeconomic status, and immigration history [15]. Hispanics tend to be younger than the general U.S. population, with a median age of 27 years compared to 37 years [17]. One in ten Hispanics are 55 years and older, the age group when most cancers (77%) are diagnosed [15]. Compared to NHWs, Hispanics are more likely to be in poverty (26.6% versus 9.9%) and uninsured (30.7% versus 11.7%) [18]. More Hispanics are foreign-born compared to NHWs (~37% versus 3.9%) [15].

The Hispanic population has substantial heterogeneity. For example, the socioeconomic profile of Cuban Americans is more similar to NHWs than to Mexican Americans. More than one-third (34.7%) of foreign-born Hispanics have resided in the U.S. for <10 years [15]. Research has shown that birthplace influences breast cancer diagnosis and treatment in Hispanic women [19]. There has been one study looking at endometrial cancer outcomes among U.S.-born and foreign-born Hispanics [20]. However, they limited their comparison to NHWs and Hispanic Whites with serous, clear cell or grade 3 endometrioid EC (type II) or aggressive endometrial cancer [20]. Therefore, the objective of this study is to determine whether demographic factors, tumor characteristics, and treatment influence the endometrial cancer-specific survival of all Hispanic women compared with NHW women using Surveillance, Epidemiology, and End Results (SEER) Program data.

Materials and methods

Data source

This study used public-use data from the National Cancer Institute's SEER Program (1992–2010), including 18 population-based cancer registries covering approximately 28% of the U.S. population. The SEER Registries routinely collect data on demographics, primary tumor site, morphology, stage at diagnosis, treatment, and follow-up for vital status. Since the public-use SEER dataset contains only aggregated de-identified data, Institutional Review Board approval was not required.

Study cohort

NHW and Hispanic patients with a diagnosis of primary, invasive endometrial cancer (ICD-O-3) sites C54.0–C54.9 and C55.9 between 2000 and 2010 were included. The analysis was limited to cases diagnosed after 2000 to not bias our sample temporally since the number of registries varied. Additionally, including 1992–1999 data would only add 718 Hispanics. The exclusion criteria included other racial/ethnic groups, patients with unknown age, unknown first course of treatment, unknown lymphadenectomy or lymph node status, and a diagnosis by autopsy or death certificate. Migrant status may influence cancer differences [20,21]. Often, Hispanic SEER registry birthplace data is missing or unknown [22]. Since birthplace was unrecorded for 52% of 6548 Hispanic cases, this group was not excluded. Instead, Hispanics were divided into U.S.-born, foreign-born and birthplace-unknown. All endometrial cancer cases were included in order to compare the cancer-specific survival of Hispanics of any race and NHWs diagnosed with endometrial cancer.

Study variables

Data was extracted from the SEER database to compare the year of diagnosis, age at diagnosis, marital status, histology-based risk, grade, stage, and the first course treatment offered for endometrial cancer among U.S.-born Hispanic, foreign-born Hispanic, birthplace-unknown Hispanic and NHW women with endometrial cancer. The SEER variable for Hispanic origin uses the North American Association of Central Cancer Registries Hispanic Identification Algorithm (NHIA) for cases diagnosed since 1992. The NHIA variable is an algorithm that indirectly identifies Hispanic ethnicity based on birthplace, maiden or Spanish/Hispanic surname or Spanish origin, race and county of residence [19,23]. The NHIA variable was cross-referenced with the SEER race variable [23].

Hispanics included in this study were of any race (White, Black, etc.) Since birthplace was unknown for 52% of the Hispanic cohort, unknown birthplace was not excluded but instead included as a separate group. Using the methods described by Kouri et al.[19] and Clegg et al. [24], U.S.-born Hispanic women were classified as women born in one of the 50 states or the District of Columbia; foreign-born if their birthplace was outside of the 50 states or the District of Columbia or if the birthplace was unknown but not in the U.S.; and birthplace-unknown if the birthplace was not recorded. Previous research shows that cancer registry cases with missing birthplace data are more likely to be U.S.-born [22,24–27]. U.S.-born Hispanic women may be more assimilated and have characteristics similar to NHWs.

Year of diagnosis was categorized into 2000–2005 (Time Period 1) and 2006–2010 (Time Period 2). Age at diagnosis was used as both a continuous and a categorical variable (≤30, 31–40, 41–50, 51–60, 61–70 and ≥70 years). Marital status was categorized into single, married, other (separated, divorced, widowed, or living with an unmarried partner), and unknown.

As established by the National Cancer Institute [28] and Mahdi et al. [21], stage was determined using SEER information. SEER provides information on the stage of disease based on clinical, intra-operative and pathological findings. Based on the International Federation of Gynecology and Obstetrics (FIGO) 2009 recommendations, Stages III and IV represent the actual FIGO stage. Stages I and II contain a combination of actual FIGO stage (I and II) and "clinically apparent stage" (I and II) cases. Unknown stage was classified as cases where detailed information on the extent of disease was unavailable. Histology-based risk was categorized as low, high, and other [2]. Low histology-based risk included endometrioid and mucinous histology. High histology-based risk included serous or clear cell histology. Other histology-based risk included other adenocarcinomas not mentioned above and other histology.

Endometrial cancer is graded as low, high or unknown based on how much the cancer forms glands similar to those found in normal, healthy endometrium [29]. In lower-grade cancers, more of the cancerous tumors form glands while more of the cancer cells are arranged in a haphazard or disorganized way or do not form glands in higher-grade cancers. Low grade included Grade I (well differentiated; differentiated, not otherwise specified (NOS)) and Grade II (moderately differentiated; intermediate differentiation). High grade included Grade III (poorly differentiated; differentiated) and Grade IV (undifferentiated; anaplastic).

Patients were categorized into three groups based on the lymph nodes reported (0 nodes, <10 nodes, and ≥10 nodes). The 10 lymph node cutoff was chosen based on the Gynecologic Oncology Group criteria for adequate lymphadenectomy [3]. For those who received a lymphadenectomy, the number of positive nodes was broken into 1, 2–5, and ≥5 positive nodes. First course of treatment (radiation, surgery, combination or no treatment) was determined by combining two SEER variables (radiatn and no_surg). Radiation is receipt of any radiation: beam radiation, radioactive implants, radioisotopes, combination of 1 with 2 or 3, radiation, NOS or other radiation. Surgery is receipt of any surgery as part of their first course of treatment. Combination treatment is receipt of both radiation and surgery. No treatment is defined as not receiving any radiation or surgery.

Statistical analysis

Frequency distributions for age, marital status, nativity, clinical presentation (i.e., histology, stage, grade, extent of lymphadenectomy and number of positive nodes), treatment, vital status, and cause of death were tabulated for NHW and Hispanic women. Associations between categorical covariates were assessed using chi-square tests while *t*-test was used to assess group differences for continuous covariates. A two-sided p-value of ≤0.05 was considered statistically significant. Survival curves were estimated using the Kaplan–Meier (KM) method with the log-rank statistic reported. Comparisons between the racial/ethnic groups were made using Bonferroni correction. Deaths due to causes other than endometrial cancer as well as those patients who were alive as of 12/31/2010 were censored. Two additional survival curves by time period were constructed to determine whether the disparity changed over time. Cox proportional hazards regression was used to identify independent predictors of cancer-specific survival. To understand the impact of diagnosis and treatment on cancer-specific survival, factors were added into the model in a three-step fashion: demographics, tumor characteristics, and treatment. Differences in cancer characteristics and treatment were compared among racial/ethnic groups between the time periods. To determine if early detection (stage and lymph node) or disease severity (grade and histology) mediated the effect of race/ethnicity on survival time, we assessed the degree to which each additional factor added to the models for each Hispanic subgroup in comparison to NHWs. This is estimated by the relative change in the odds ratio (OR) between the base model and subsequent model by using the formula, $[(OR_1 - OR_2) / (OR_1 - 1)]$ [30]. For example, to calculate the proportion of disparity explained when early diagnosis is added to the model, OR_1 is the OR of risk-adjusted mortality for a U.S.-born Hispanic patient and OR_2 is the OR for a U.S.-born Hispanic after early diagnosis differences. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

Results

Demographics, clinical and tumor characteristics

A total of 69,764 women with endometrial cancer met the inclusion criteria. Table 1A displays the demographic, clinical and pathological characteristics of the study population. Most patients were NHW (90.6%), >51 years (84.2%), and married (53.2%). Among Hispanics, 24.0% were U.S.-born, 23.8% were foreign-born, and 52.2% had unknown birthplace. A total of 16,441 patients died (23.6%), of whom 47.2% died of endometrial cancer (n = 7756).

Hispanics were younger at presentation than NHWs. The mean age for U.S.-born Hispanics was 58.0 ± 13.9 years, 59.7 ± 13.5 years for foreign-born Hispanics, 56.5 ± 13.2 years for birthplace-unknown Hispanics, and 63.4 ± 12.6 years for NHWs. Whereas 30.1% of the Hispanic cases presented at <50 years, only 14.3% NHW women were diagnosed in this age group.

Regardless of race/ethnicity, most women presented with early stage endometrial cancer (69.7%). More Hispanic women presented with late stage disease compared to NHWs (29.7% versus 25.7%, p = <0.0001). The proportion of patients with high-risk histology was slightly higher in U.S.-born and foreign-born Hispanics than in NHWs (4.8% and 5.9% versus 3.9%, p < 0.0001).

More than half (36,398/69,764, 52.2%) underwent a lymphadenectomy during the initial surgery. More NHWs underwent a lymphadenectomy than U.S.-born, foreign-born and birthplace-unknown Hispanic women (52.5% versus 47.9%, 49.8%, and 49.5%). The proportion of lymphadenectomy patients who had positive lymph nodes was significantly higher among U.S-born, foreign-born, and birthplace-unknown Hispanics than among NHWs (8.0%, 7.6%, and 6.8% versus 6.6%, p < 0.0001).

Most patients received surgery (70.0%) or a combination of radiation and surgery (22.4%) as the first course of treatment (Table 1A). Treatment varied among the groups. Hispanics had a higher proportion of patients who received no treatment than NHWs (7.2% versus 5.3%). Compared to NHWs, more U.S.-born and foreign-born Hispanics received radiation, but less surgery. Table 1B shows the treatment breakdown by radiation and surgery type. Of those who received radiation treatment, beam radiation was the most common type (12.1%). A total hysterectomy with removal of tubes and ovaries was the most common surgery type (77.6%).

Fig. 1 shows the KM cancer-specific survival curves for the different groups. Birthplace-unknown Hispanic women had significantly better survival (p < 0.0001) than NHW, U.S.-born Hispanic or foreign-born Hispanic women. Results show a median survival of 47 months with the poorest survival in foreign-born Hispanics. At five years (60 months), 91.6% birthplace-unknown Hispanics, 86.6% NHW, 79.6% U.S.-born Hispanics, and 78.4% foreign-born Hispanics had survived endometrial cancer (Fig. 1A). This trend continued at ten years with the survival rate slightly higher among birthplace-unknown Hispanics compared to NHWs.

To analyze the effect of diagnosis year on survival, KM survival curves were created separately for each time period. The results showed that birthplace-unknown Hispanics had better cancer-specific survival than the other groups (p < 0.0001) (Fig. 1B and C). For Time Period 1, the five-year cancer-specific survival rate was 90.9% for birthplace-unknown Hispanics, 86.5% for NHWs, 80.3% for U.S.-born Hispanics, and 80.0% for foreign-born Hispanics (Fig. 1B). The five-year cancer-specific survival rate for Time Period 2 was 92.3% for birthplace-unknown Hispanics, 87.4% for NHWs, 78.8% for U.S.-born Hispanics, and 76.9% for foreign-born Hispanics (Fig. 1C). The five-year cancer-specific survival rates increased over time for birthplace-unknown Hispanics and NHWs. Rates decreased for U.S.-born and foreign-born Hispanics. The Bonferroni correction for multiple-comparison adjustments (results not shown) showed a significant difference in disease-free survivor functions between the U.S.-born and NHWs (x^2 = 14.848, p-value = 0.0007). The difference between foreign-born Hispanics and NHWs was also statistically different (x^2 = 17.195, p-value = 0.0002), but the disease-free survivor functions for birthplace-unknown Hispanics and NHWs were not significantly different (x^2 = 6.060, p-value = 0.0830).

Table 2 provides the variation in cancer characteristics and treatment between Hispanics and NHWs over time. Overall, there was a significant difference in stage, histology and nodal metastasis among the different groups. Regardless of race/ethnicity, a higher percentage of patients were diagnosed at later stages in Time Period 2 than in Time Period 1. The same pattern was seen in histology with more patients diagnosed with low-risk endometrial tumors. The mean number of positive nodes increased for all groups in 2006–2010, with the greatest increase among foreign-born Hispanics. In terms of treatment, more patients received combination therapy in Time Period 1 than in Time Period 2. In 2006–2010, a higher percentage of patients received surgery even as more women were diagnosed at later stages. A higher percentage of U.S.-born Hispanics and birthplace-unknown Hispanics received no treatment for endometrial cancer in Time Period 2 than in Time Period 1.

The results of the Cox proportional hazards model for 2000–2010 showed that cancer-specific survival varied by race/ethnicity, year, age, marital status, SEER region, tumor characteristics, and treatment (results not shown). Because of significant interaction between race/ethnicity and year, the Cox proportional hazards models were stratified by time period. Table 3 shows the results of the Cox proportional hazards analysis to assess the effect of race/ethnicity and time period on survival after controlling for patient demographics (Model 1), cancer characteristics (Model 2) and treatment (Model 3). For Time Period 1 after controlling for demographics, U.S.-born and foreign-born Hispanics were more likely to die than NHWs (U.S.-born Hispanics hazard ratio (HR) = 1.92, 95% confidence interval (CI) = 1.72–2.14;

Table 1A
Demographic and clinico-pathologic characteristics of the study population, SEER 2000–2010 (n = 69,764).

Characteristics	Total n = 69,764		Non-Hispanic White n = 63,216		U.S.-born Hispanics[a] n = 1572		p-Value[b]	Foreign-born Hispanics[a] n = 1561		p-Value[c]	Hispanics with unknown birthplace[a] n = 3415		p-Value[c]
	n	%	n	%	n	%		n	%		n	%	
Year of diagnosis							0.0679			0.0128			<.0001
2000–2005	35,233	50.5%	32,266	51.0%	839	53.4%		747	47.9%		1381	40.4%	
2006–2010	34,531	49.5%	30,950	49.0%	733	46.6%		814	52.1%		2034	59.6%	
Region							<.0001			<.0001			<.0001
Northeast	13,469	19.3%	12,409	19.6%	123	7.8%		389	24.9%		548	16.0%	
South	15,198	21.8%	14,896	23.6%	76	4.8%		64	4.1%		162	4.7%	
Central	5438	7.8%	5393	8.5%	7	0.4%		4	0.3%		34	1.0%	
West	35,659	51.1%	30,518	48.3%	1366	86.9%		1104	70.7%		2671	78.2%	
Age at diagnosis							<.0001			<.0001			<.0001
Mean (SD)	62.9	(12.8)	63.4	(12.6)	58.0	(13.9)		59.7	(13.5)		56.5	(13.2)	
Median (IQR)	62.0	(54.0–72.0)	63.0	(55.0–72.0)	58.0	(48.0–68.0)		60.0	(50.0–70.0)		56.0	(47.0–65.0)	
≤30	404	0.6%	266	11.1%	32	2.0%		24	1.5%		82	2.4%	
31–40	2298	3.3%	1726	29.2%	144	9.2%		114	7.3%		314	9.2%	
41–50	8287	11.9%	7026	27.2%	285	18.1%		260	16.7%		716	21.0%	
51–60	20,368	29.2%	18,465	29.4%	447	28.4%		405	25.9%		1051	30.8%	
61–70	18,700	26.8%	17,179	27.2%	358	22.8%		400	25.6%		763	22.3%	
≥71	19,707	28.2%	18,554	29.4%	306	19.5%		358	22.9%		489	14.3%	
Marital status							<.0001			<.0001			<.0001
Single	9986	14.3%	8681	13.7%	278	17.7%		291	18.6%		736	21.6%	
Married	37,085	53.2%	33,734	53.4%	828	52.7%		760	48.7%		1763	51.6%	
Other[d]	19,866	28.5%	18,257	28.9%	418	26.6%		459	29.4%		732	21.4%	
Unknown marital status	2827	4.1%	2544	4.0%	48	3.1%		51	3.3%		184	5.4%	
Treatment							0.0004			<.0001			<.0001
Radiation	1494	2.1%	1346	2.1%	47	3.0%		52	3.3%		49	1.4%	
Surgery	48,852	70.0%	44,343	70.1%	1046	66.5%		968	62.0%		2495	73.1%	
Radiation and surgery	15,622	22.4%	14,200	22.5%	368	23.4%		402	25.8%		652	19.1%	
No radiation or surgery	3796	5.4%	3327	5.3%	111	7.1%		139	8.9%		219	6.4%	
Number of nodes examined[e]							0.0002			0.0207			<.0001
Mean (SD)	7.7	(11.1)	7.7	(11.0)	7.7	(11.8)		8.1	(12.6)		7.6	(11.0)	
Median (IQR)	2.0	(0.0–13.0)	2.0	(0.0–13.0)	0.0	(0.0–12.0)		0.0	(0.0–13.0)		0.0	(0.0–13.0)	
No nodes examined	33,366	47.8%	30,035	47.5%	824	52.4%		784	50.2%		1723	50.5%	
<10 nodes examined	14,249	20.4%	13,089	20.7%	276	17.7%		281	18.0%		603	17.7%	
≥10 nodes examined	22,149	31.7%	20,095	31.8%	472	30.2%		496	31.8%		1089	31.9%	
Number of positive nodes[f]							0.0091			0.0264			0.2351
Mean (SD)	3.4	(4.9)	3.3	(4.8)	3.4	(4.1)		4.1	(8.6)		3.1	(3.1)	
Median (IQR)	2.0	(1.0–4.0)	2.0	(1.0–4.0)	2.0	(1.0–3.0)		2.0	(1.0–4.0)		2.0	(1.0–4.0)	
1 positive node	1914	2.7%	1718	2.7%	53	3.4%		43	2.8%		100	2.9%	
2–5 positive nodes	1869	2.7%	1685	2.7%	48	3.1%		52	3.3%		84	2.5%	
≥5 positive nodes	868	1.2%	768	1.2%	24	1.5%		23	1.5%		49	1.4%	
Histology-based risk							0.0006			<.0001			0.4388
Low-risk (endometriod/mucinous)	43,571	62.5%	39,662	62.7%	914	58.6%		858	55.0%		2137	62.6%	
High-risk (serous/clear cell)	2720	3.9%	2435	3.9%	75	4.8%		92	5.9%		118	3.5%	
Others (adenocarcinoma/others)	23,473	33.6%	21,119	33.4%	583	37.3%		611	39.1%		1160	34.0%	
Grade							0.0266			<.0001			<.0001
Low grade	44,993	64.5%	40,836	64.6%	975	62.5%		856	54.8%		2326	68.1%	
High grade	15,018	21.5%	13,585	21.5%	382	24.5%		443	28.4%		608	17.8%	
Unknown grade	9753	14.0%	8795	13.9%	215	13.8%		262	16.8%		481	14.1%	
FIGO stage							<.0001			<.0001			0.5759
In situ (Stage 0)	975	1.4%	885	1.4%	23	1.5%		18	1.2%		49	1.4%	
Early stage (Stages I–II)	48,621	69.7%	44,295	70.1%	976	62.5%		906	58.0%		2444	71.6%	
Late stage (Stages III–IV)	18,193	26.1%	16,251	25.7%	533	34.1%		578	37.0%		831	24.3%	
Unknown stage	1975	2.8%	1785	2.8%	40	2.6%		59	3.8%		91	2.7%	
Vital status							<.0001			<.0001			<.0001
Alive	53,323	76.4%	48,150	76.2%	1063	68.1%		1095	70.1%		3015	88.3%	
Dead	16,441	23.6%	15,066	23.8%	509	32.6%		466	29.9%		400	11.7%	
Cause of death							<.0001			<.0001			<.0001
Endometrial cancer	7756	11.1%	7026	11.1%	259	16.6%		250	16.0%		221	6.5%	

[a] Hispanic ethnicity can be of any race.
[b] Comparison of non-Hispanic White vs US-born Hispanic.
[c] Comparison of non-Hispanic White vs foreign-born Hispanic.
[d] Other marital status includes separated, divorced, widowed or living with unmarried partner.
[e] Based on all who had a node exam with known number of nodes.
[f] Based on all who had a node exam with known number of positive nodes.

foreign-born Hispanics HR = 1.69, 95% CI = 1.50–1.90). Birthplace-unknown Hispanics were less likely to survive than NHWs (HR = 0.75, 95% CI = 0.66–0.86). For Time Period 2, HRs significantly increased for all Hispanics.

HR for survival for U.S.-born and foreign-born Hispanics in Time Period 1 decreased considerably after cancer characteristics were added (U.S.-born Hispanics HR = 1.61, 95% CI = 1.44–1.79; foreign-born Hispanics HR = 1.35, 95% CI = 1.20–1.52). The survival for birthplace-

Table 1B
Type of radiation or surgery as first course of treatment by race/ethnicity, SEER 2000–2010 (n = 69,764).

Characteristics	Total n = 69,764		Non-Hispanic White n = 63,216		U.S.-born Hispanics[a] n = 1572		Foreign-born Hispanics[a] n = 1561		Hispanics with unknown birthplace[a] n = 3415	
	n	%	n	%	n	%	n	%	n	%
Radiation type										
Beam radiation	8447	12.1%	7558	12.0%	231	14.7%	277	17.7%	381	11.2%
Radioactive implants	4167	6.0%	3903	6.2%	55	3.5%	59	3.8%	150	4.4%
Radioisotopes	107	0.2%	97	0.2%	1	0.1%	4	0.3%	5	0.1%
Combination of beam radiation with radioactive implants and radioisotopes	4162	6.0%	3777	6.0%	121	7.7%	108	6.9%	156	4.6%
Radiation, NOS[b]	233	0.3%	211	0.3%	7	0.4%	6	0.4%	9	0.3%
Unknown if radiation administered	51,550	73.9%	46,644	73.8%	1134	72.1%	1089	69.8%	2683	78.6%
No/refused radiation	1098	1.6%	1026	1.6%	23	1.5%	18	1.2%	31	0.9%
Surgery type										
No surgery	5331	7.6%	4704	7.4%	161	10.2%	194	12.4%	272	8.0%
Local tumor destruction or excision, NOS[b]	622	0.9%	521	0.8%	26	1.7%	26	1.7%	49	1.4%
Subtotal hysterectomy/supracervical hysterectomy/fundectomy	939	1.3%	822	1.3%	22	1.4%	28	1.8%	67	2.0%
Total hysterectomy without removal of tubes and ovaries	2316	3.3%	2018	3.2%	71	4.5%	56	3.6%	171	5.0%
Total hysterectomy with removal of tubes and ovaries	54,135	77.6%	49,401	78.1%	1136	72.3%	1082	69.3%	2516	73.7%
Modified radical or extended hysterectomy	3297	4.7%	2960	4.7%	74	4.7%	100	6.4%	163	4.8%
Hysterectomy, NOS[b]	2755	3.9%	2450	3.9%	74	4.7%	69	4.4%	162	4.7%
Exenteration	189	0.3%	173	0.3%	4	0.3%	3	0.2%	9	0.3%
Surgery, NOS[b]	157	0.2%	144	0.2%	4	0.3%	3	0.2%	6	0.2%
Unknown if surgery performed	23	0.0%	23	0.0%	0	0.0%	0	0.0%	0	0.0%

[a] Hispanic ethnicity can be of any race.
[b] NOS, not otherwise specified.

unknown Hispanics did not change considerably (HR = 0.71, 95% CI = 0.62–0.81). After adding treatment, the HR decreased for all groups except U.S.-born Hispanics. The HR reduced for foreign-born Hispanics (1.35 to 1.27) and birthplace-unknown Hispanics (0.71 to 0.69). The HR for U.S.-born and foreign-born Hispanics in Time Period 2 decreased substantially when cancer characteristics were added (U.S.-born Hispanics HR = 1.41, 95% CI = 1.20–1.65; foreign-born Hispanics HR = 1.35, 95% CI = 1.16–1.57). However, the HR for birthplace-unknown Hispanics did not change. In the final model when treatment was controlled, being U.S.-born Hispanic was no longer significant.

Additional analyses were conducted to determine if early detection (stage and lymph node involvement) or disease severity (grade and histology) mediated the effect of race/ethnicity on survival time (Table 4). This was estimated by the relative change in the odds ratio between the base model and subsequent models. Most of the mortality disparity between either U.S.-born or foreign-born Hispanics and NHWs in Time Period 2 were explained by cancer characteristics (62% and 67%, respectively). Stage and lymph node explained 48% and 44% of the disparity, respectively. After controlling for cancer characteristics, treatment explained an additional 21% of the disparity between U.S.-born Hispanics and NHWs and 44% of the disparity between foreign-born Hispanics and NHWs.

Discussion

Racial/ethnic disparities in endometrial cancer outcomes between NHW and Black women have been extensively investigated in epidemiologic studies. However, the focus on other minorities has been limited. In our analysis, U.S.-born, foreign-born, and birthplace-unknown Hispanics presented the disease at a younger age (<50 years) compared to NHWs. Birthplace-unknown Hispanics presented at younger than U.S.-born Hispanics. This is consistent with previous research [10]. Older age is predictive of poor prognosis in endometrial cancer [11]. The younger age at which Hispanic women present the disease may explain their improved survival.

Although many patients had early stage disease and low-risk histology, the data suggests that a higher percentage of Hispanic women had late stage disease (III or IV) and more aggressive histologic subtypes (serous or clear cell) compared to NHWs. This was evident in Time Period 2 when most of the disparity was mediated by cancer characteristics. Foreign-born Hispanic women had a higher prevalence of late stage disease and aggressive histologic subtypes (serous or clear cell) than other Hispanic women. Aggressive histologic subtypes account for a disproportionately high proportion of mortality in endometrial cancer patients. These findings are in accordance with those of Kost et al. [12], who found no difference in stage at presentation despite the fact that a higher proportion of minority women presented with high grade lesions and aggressive histologic subtypes than NHW women [12].

Although not addressed in this study, evidence indicates that cancer risk increases with duration of residence in the U.S. [15]. Acculturation or assimilation is the process by which immigrants adopt the attitudes, values, customs, beliefs, and behaviors of their new culture. The effects of acculturation are complex and can be associated with both positive and negative influences on health [31]. Assimilation may result in improved access to health care and preventive services. It may also result in adopting unhealthy behaviors (e.g., smoking, alcohol consumption) and decreased dietary quality and physical activity. The immense diversity within the Hispanic community in origin and degree of acculturation provides both challenges and opportunities for cancer control and etiologic study. The higher prevalence of diabetes, hypertension, and obesity among Hispanics varies depending on nativity and acculturation [32,33]. Obesity, diabetes, and hypertension are associated with elevated endometrial cancer risk [9,13,14,21,32].

Differences in access to care and the first course of treatment can potentially affect the outcome and contribute to the racial/ethnic disparity [2]. In this study, the proportion of NHW women who underwent lymphadenectomy was significantly higher than Hispanic women. However, the proportion of Hispanic patients with positive lymph nodes was significantly higher than NHWs. The prognostic impact of lymphadenectomy in endometrial cancer is controversial [2]. Given the absence of definitive lymphadenectomy guidelines and the potential for practice differences across U.S. regions, the observed differences may be secondary to practice location and physician decisions rather than race/ethnicity. This difference brings into question why Hispanics are not undergoing lymphadenectomy at a rate similar to NHWs.

Our results show that the first course of treatment is important to cancer-specific survival. The majority of patients received surgery as their first course of treatment (70.0%), and 22.4% received a combination of radiation and surgery. The proportion of patients who received

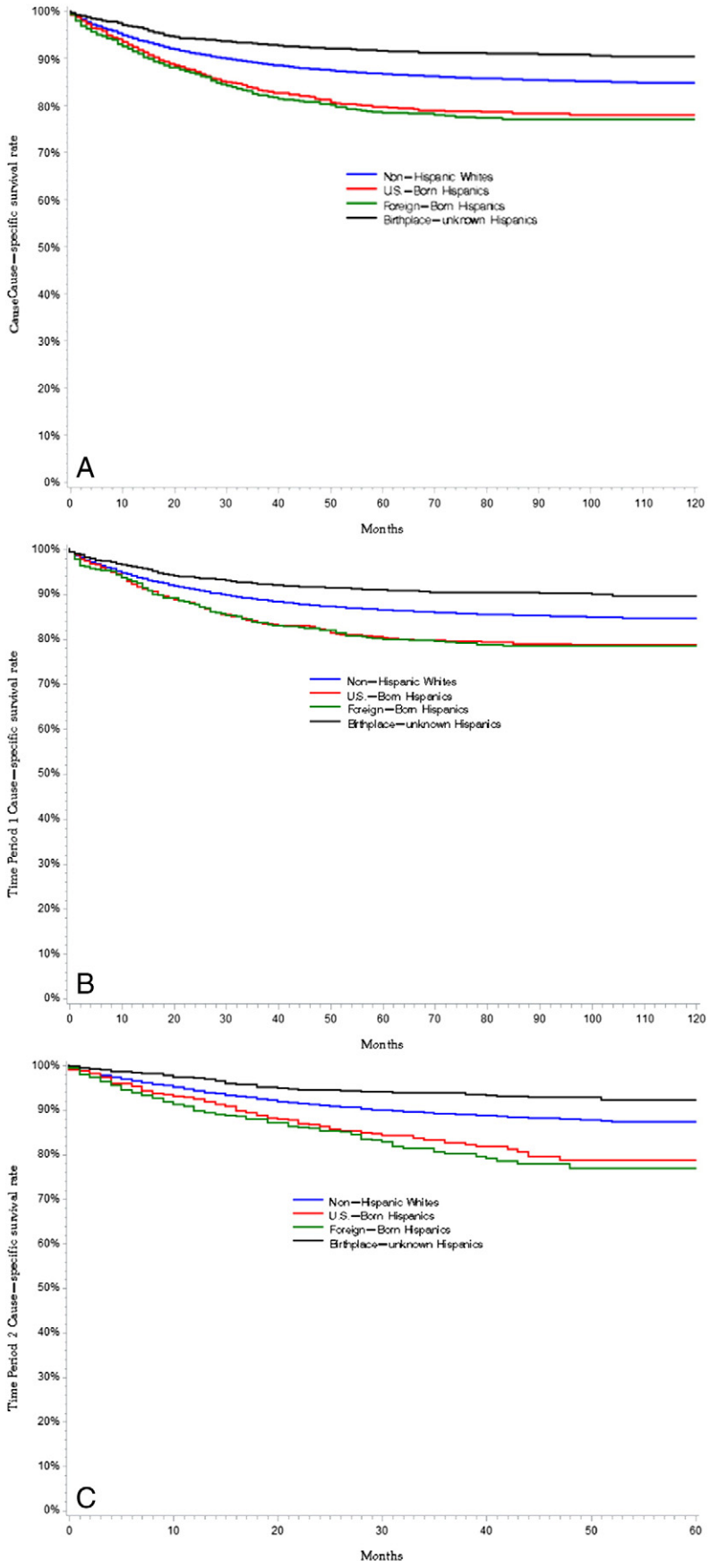

Fig. 1. Kaplan–Meier survival curves by racial/ethnic group. Results show that the median survival is 47 months with worst survival among foreign-born Hispanics (log-rank p value < 0.0001). A. Cancer-specific survival curves by race/ethnicity for patients with endometrial cancer between 2000 and 2010. B. Cancer-specific survival curves by race/ethnicity for patients with endometrial cancer in Time Period 1 (2000–2005). C. Cancer-specific survival curves by race/ethnicity for patients with endometrial cancer in Time Period 2 (2006–2010).

Table 2
Cancer characteristics and treatment by era and race/ethnicity, SEER 2000–2010 (n = 69,764).

Characteristics	Era 1 (2000–2005) n = 35,233				Era 2 (2006–2010) n = 34,531			
	Non-Hispanic Whites n = 32,266	U.S.-born Hispanics[a] n = 839	Foreign-Born Hispanics[a] n = 747	Birthplace-unknown Hispanics[a] n = 1381	Non-Hispanic Whites n = 30,950	U.S.-born Hispanics[a] n = 733	Foreign-born Hispanics[a] n = 814	Birthplace-unknown Hispanics[a] n = 2034
FIGO stage								
In situ (Stage 0)	543 (1.7%)	11 (1.3%)	9 (1.2%)	22 (1.6%)	342 (1.1%)	12 (1.6%)	9 (1.1%)	27 (1.3%)
Early stage (Stages I–II)	22,688 (70.3%)	527 (62.8%)	435 (58.2%)	999 (88.6%)	21,607 (69.8%)	449 (61.3%)	471 (57.9%)	1445 (71.0%)
Late stage (Stages III–IV)	7982 (24.7%)	284 (33.9%)	268 (35.9%)	320 (23.2%)	8269 (26.7%)	249 (34.0%)	310 (38.1%)	511 (25.1%)
Unknown stage	1053 (3.3%)	17 (2.0%)	35 (4.7%)	40 (2.9%)	732 (2.4%)	23 (3.1%)	24 (3.0%)	51 (2.5%)
Histology-based risk								
Low-risk (endometriod/mucinous)	18,595 (57.6%)	477 (56.9%)	396 (53.0%)	796 (57.6%)	21,067 (68.1%)	437 (59.6%)	462 (56.8%)	1341 (65.9%)
High-risk (serous/clear cell)	1297 (4.0%)	39 (4.7%)	47 (6.3%)	56 (4.1%)	1138 (3.7%)	36 (4.9%)	45 (5.5%)	62 (3.1%)
Others (adenocarcinoma/others)	12,374 (38.4%)	323 (38.5%)	304 (40.7%)	529 (38.3%)	8745 (28.3%)	260 (35.5%)	307 (37.7%)	631 (31.0%)
Grade								
Low grade	21,508 (66.7%)	540 (64.4%)	433 (58.0%)	985 (71.3%)	19,328 (62.5%)	435 (59.4%)	423 (52.0%)	1341 (65.9%)
High grade	6939 (21.5%)	204 (24.3%)	212 (28.4%)	240 (17.4%)	6646 (21.5%)	178 (24.3%)	231 (28.4%)	368 (18.1%)
Unknown grade	3819 (11.8%)	95 (11.3%)	102 (13.7%)	156 (11.3%)	4976 (16.1%)	120 (16.4%)	160 (19.7%)	325 (16.0%)
Number of nodes examined[b]								
Mean (SD)	0.7 (0.9)	0.7 (0.9)	0.8 (0.9)	0.7 (0.9)	1.0 (0.9)	0.9 (0.9)	0.9 (0.9)	0.9 (0.9)
Median (IQR)	0.0 (0.0–2.0)	0.0 (0.0–2.0)	0.0 (0.0–2.0)	0.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)
No nodes examined	17,344 (53.8%)	464 (55.3%)	386 (51.7%)	764 (55.3%)	12,961 (41.0%)	360 (49.1%)	398 (48.9%)	959 (47.2%)
<10 nodes examined	6645 (20.6%)	154 (18.4%)	149 (20.0%)	255 (18.5%)	6444 (20.8%)	122 (16.6%)	132 (16.2%)	348 (17.1%)
≥10 nodes examined	8277 (25.7%)	221 (26.3%)	212 (28.4%)	362 (26.2%)	11,815 (38.2%)	251 (34.2%)	284 (34.9%)	727 (35.7%)
Number of positive nodes[c]								
Mean (SD)	3.2 (4.2)	3.3 (4.2)	3.3 (3.9)	3.5 (3.5)	3.5 (5.3)	3.4 (4.1)	4.6 (10.6)	2.9 (2.8)
Median (IQR)	2.0 (1.0–3.0)	2.0 (1.0–4.0)	2.0 (1.0–4.0)	2.0 (1.0–5.0)	2.0 (1.0–4.0)	2.0 (1.0–3.0)	2.0 (1.0–4.0)	2.0 (1.0–4.0)
1 positive node	811 (2.5%)	27 (3.2%)	20 (2.7%)	34 (2.5%)	907 (2.9%)	26 (3.5%)	23 (2.8%)	66 (3.2%)
2–5 positive nodes	801 (2.5%)	21 (2.5%)	17 (2.3%)	23 (1.7%)	884 (2.9%)	27 (3.7%)	35 (4.3%)	61 (3.0%)
≥5 positive nodes	332 (1.0%)	10 (1.2%)	12 (1.6%)	21 (1.5%)	436 (1.4%)	14 (2.4%)	15 (1.8%)	28 (1.4%)
Treatment								
Radiation	686 (2.1%)	19 (2.3%)	23 (3.1%)	21 (1.5%)	660 (2.1%)	28 (3.8%)	29 (3.6%)	28 (1.4%)
Surgery	22,464 (69.6%)	537 (64.0%)	449 (60.1%)	1003 (72.6%)	21,879 (70.7%)	509 (69.4%)	519 (63.8%)	1492 (73.4%)
Radiation and surgery	7346 (22.8%)	230 (27.4%)	208 (27.8%)	274 (19.8%)	6854 (22.2%)	138 (18.8%)	194 (23.8%)	378 (18.6%)
No radiation or surgery	1770 (5.5%)	53 (6.3%)	67 (9.0%)	83 (6.0%)	1557 (5.0%)	58 (7.9%)	72 (8.9%)	136 (6.7%)

[a] Hispanic ethnicity can be of any race.
[b] Based on all who had a node exam with known number of nodes.
[c] Based on all who had a node exam with known number of positive nodes.

no treatment was significantly higher among Hispanics than NHWs. In recent years, more patients are being diagnosed at later stages. The percentage of patients receiving surgery increased while combination treatment decreased.

The survival curves showed that having Hispanic ethnicity, specifically, U.S.-born and foreign-born, is associated with less favorable outcomes than being NHW. This study revealed a difference in cancer-specific survival between U.S.-born, foreign-born and birthplace-unknown Hispanic and NHW women, even after adjusting for patient demographics. This is in accordance with Cook et al. [9] where Hispanic Whites have shown poorer cancer-specific survival than NHWs. However, Cook et al. [9] found that the cancer-specific survival was no longer significant when controlling for tumor characteristics, treatment and comorbid conditions. This study contrasts with Mahdi et al. [21], where there was no difference between Hispanic and NHWs.

In our study, the disparity in cancer-specific survival did not improve between time periods. Based on the KM estimates, cancer-specific survival in U.S.-born Hispanics did not improve between the time periods. For Time Period 2, the final model shows that the OR for U.S. Hispanics was 1.16 (95% CI = 0.99–1.36) (Table 3). This result is not statistically significant even after adjustment indicating that their survival is only comparable if they were diagnosed at similar stages and receiving similar treatments as NHWs.

Since Hispanic ethnicity in SEER is based on an algorithm using birthplace, maiden or Spanish/Hispanic surname or Spanish origin, race, and county of residence and research has shown that U.S. birthplace-unknown subjects are likely to be U.S.-born [25–27], this group may consist mainly of Hispanic Whites. These Hispanic Whites may have been in the U.S. for multiple generations. This factor may account for the ways in which this cohort is different from U.S.-born and foreign-born Hispanics. It may also explain why the cancer-specific survival rates of these subjects are similar to those of NHWs, due to acculturation and better access to care.

Data analysis was limited by the available information. The dataset lacked information on physician subspecialty, central pathologic review, adjuvant chemotherapy, disease recurrence, treatment of recurrent disease, socioeconomic status, and the presence of other comorbidities. To avoid selection bias, birthplace-unknown Hispanics were included as a separate group. However, the strengths of this study include the fact that this is the largest study evaluating endometrial cancer outcomes in U.S.-born and foreign-born Hispanics compared to NHWs. The results from this population-based study can be generalized to the entire U.S. population. The SEER registries are compiled from representative regions throughout the country, including large and small hospitals and small community practices. Consequently, the risk of referral or access to care bias is reduced in this study.

Foreign-born Hispanic women with endometrial cancer exhibited significantly poorer cancer-specific survival compared to NHW women, even after controlling for demographics, cancer characteristics and the first course of treatment. This difference in survival cannot be explained by the difference in age, SEER region, stage, histology-based risk, grade, extent of lymphadenectomy or the first course of treatment. Other potential comorbidities, environmental, and lifestyle differences not captured by our study may contribute to this observed difference.

Table 3
Multivariate analysis of factors associated with cancer-specific survival in non-Hispanic White and Hispanic women with endometrial cancer by era.

Variable		2000–2005						2006–2010					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
Race/ethnicity	Non-Hispanic White	1.00		1.00		1.00		1.00		1.00		1.00	
	U.S.-born Hispanics	1.92	1.72–2.14	1.61	1.44–1.79	1.61	1.44–1.79	2.09	1.78–2.45	1.41	1.20–1.65	1.16	0.99–1.36
	Foreign-born Hispanics	1.69	1.50–1.90	1.35	1.20–1.52	1.27	1.13–1.43	2.05	1.76–2.38	1.35	1.16–1.57	1.31	1.12–1.52
	Birthplace-unknown Hispanics	0.75	0.66–0.86	0.71	0.62–0.81	0.69	0.60–0.78	0.83	0.70–0.97	0.75	0.64–0.88	0.75	0.64–0.88
Age at diagnosis	Continuous	1.06	1.06–1.06	1.05	1.05–1.06	1.05	1.05–1.05	1.06	1.05–1.06	1.04	1.04–1.04	1.03	1.03–1.04
Marital status	Single	1.00		1.00		1.00		1.00		1.00		1.00	
	Married	1.40	1.32–1.49	1.30	1.22–1.39	1.27	1.19–1.35	1.58	1.46–1.72	1.35	1.24–1.47	1.23	1.13–1.34
	Other	1.28	1.23–1.34	1.20	1.15–1.25	1.18	1.13–1.23	1.40	1.31–1.49	1.23	1.16–1.32	1.18	1.10–1.26
	Unknown	1.30	1.19–1.43	1.16	1.06–1.25	1.05	0.96–1.16	1.51	1.32–1.73	1.12	0.98–1.29	0.98	0.86–1.13
SEER region	Northeast	1.00		1.00		1.00		1.00		1.00		1.00	
	South	1.02	0.96–1.08	1.02	0.96–1.08	1.06	1.00–1.12	1.13	1.04–1.23	1.08	0.99–1.18	1.09	1.00-1.19
	Central	0.96	0.89–1.04	1.00	0.92–1.07	1.04	0.96–1.12	1.11	0.99–1.24	1.00	0.89–1.12	0.99	0.88–1.11
	West	0.90	0.86–0.94	0.94	0.90–0.99	0.95	0.91–1.00	0.91	0.84–0.98	0.89	0.83–0.96	0.90	0.84–0.97
Stage	In situ (Stage 0)			1.00		1.00				1.00		1.00	
	Early stage (Stages I–II)			2.03	1.62–2.54	1.94	1.55–2.44			2.76	1.73–4.39	2.45	1.53–3.90
	Late stage (III–IV)			6.71	5.34–8.42	6.26	4.98–7.86			11.28	7.08–17.97	9.51	5.96–15.15
	Unknown stage			4.81	3.80–6.10	2.41	1.90–3.07			10.33	6.43–16.59	4.32	2.68–6.97
Histology-based risk	Low risk			1.00		1.00				1.00		1.00	
	High risk			1.28	1.19–1.37	1.31	1.22–1.41			1.23	1.10–1.37	1.12	1.00–1.26
	Others			1.34	1.29–1.40	1.28	1.23–1.33			1.76	1.65–1.88	1.64	1.54–1.75
Grade	Low grade			1.00		1.00				1.00		1.00	
	High grade			2.29	2.19–2.40	2.32	2.22–2.43			2.82	2.61–3.04	3.03	2.81–3.27
	Unknown grade			2.10	1.99–2.22	1.90	1.79–2.01			2.63	2.18–2.57	2.05	1.89–2.23
Lymphadenectomy	No nodes			1.00		1.00				1.00		1.00	
	<10 nodes			0.68	0.65–0.71	0.82	0.78–0.86			0.50	0.47–0.54	0.73	0.67–0.79
	≥10 nodes			0.53	0.51–0.56	0.65	0.61–0.68			0.36	0.33–0.38	0.52	0.48–0.57
Treatment	No surgery/radiation					1.00						0.64	0.57–0.72
	Radiation					0.77	0.70–0.85					1.00	
	Surgery					0.34	0.32–0.37					0.26	0.23-–0.28
	Radiation and surgery					0.28	0.26-–0.30					0.18	0.16–0.20

Though not addressed, future studies should include how a specific type of treatment or sequence of treatment affects cancer-specific survival. In both time periods, the majority of the disparity for U.S.-born Hispanics and foreign-born Hispanics was explained by cancer characteristics (stage and lymph node) and treatment. Since more patients are being diagnosed at later stages in more recent years, treatment is crucial in determining endometrial cancer survival. Treatment explained an additional 21% of the mortality in Time Period 2 between U.S.-born

Table 4
Factor affecting mortality differences stratified by race/ethnicity and time period.

Adjustments	Odds ratio (95% CI)				Proportion of disparity explained (%)		
	Non-Hispanic Whites	U.S.-born Hispanics	Foreign-born Hispanics	Birthplace-unknown Hispanics	U.S.-born Hispanics	Foreign-born Hispanics	Birthplace-unknown Hispanics
(A) Time Period 1: 2000–2005							
Demographics	1.00 [Reference]	1.92 (1.72–2.14)	1.69 (1.50–1.90)	0.75 (0.66–0.86)	***	***	***
Adjustments							
Early diagnosis	1.00 [Reference]	1.63 (1.47–1.82)	1.44 (1.28–1.62)	0.73 (0.64–0.83)	32	36	−8
Disease severity	1.00 [Reference]	1.83 (1.64–2.04)	1.48 (1.31–1.67)	0.74 (0.65–0.84)	10	30	−4
All cancer characteristics	1.00 [Reference]	1.61 (1.44–1.79)	1.35 (1.20–1.52)	0.71 (0.62–0.81)	34	49	−16
Treatment including all other factors	1.00 [Reference]	1.61 (1.44–1.79)	1.27 (1.13–1.43)	0.69 (0.60–0.78)	34	61	−24
Treatment only	1.00 [Reference]	1.83 (1.64–2.04)	1.50 (1.33–1.69)	0.71 (0.62–0.81)	−24	−22	0
(B) Time Period 2: 2006–2010							
Demographics	1.00 [Reference]	2.09 (1.78–2.45)	2.05 (1.76–2.38)	0.83 (0.70–0.97)	***	***	***
Adjustments							
Early diagnosis	1.00 [Reference]	1.57 (1.34–1.84)	1.59 (1.37–1.85)	0.79 (0.67–0.92)	48	44	−24
Disease severity	1.00 [Reference]	1.72 (1.47–2.02)	1.61 (1.38–1.87)	0.81 (0.69–0.94)	34	42	−12
All cancer characteristics	1.00 [Reference]	1.41 (1.20–1.65)	1.35 (1.16–1.57)	0.75 (0.64–0.88)	62	67	−47
Treatment including all other factors	1.00 [Reference]	1.16 (0.99–1.36)	1.31 (1.12–1.52)	0.75 (0.64–0.88)	85	70	−47
Treatment only	1.00 [Reference]	1.64 (1.40–1.93)	1.81 (1.56–2.11)	0.74 (0.64–0.87)	−21	−44	−6
(C) All years: 2000–2010							
Demographics	1.00 [Reference]	1.97 (1.80–2.15)	1.81 (1.65–1.99)	0.78 (0.71–0.86)	***	***	***
Adjustments							
Early diagnosis	1.00 [Reference]	1.63 (1.49–1.78)	1.51 (1.38–1.66)	0.76 (0.68–0.83)	35	37	−9
Disease severity	1.00 [Reference]	1.81 (1.65–1.98)	1.54 (1.41–1.69)	0.77 (0.69–0.85)	16	33	−5
All cancer characteristics	1.00 [Reference]	1.57 (1.43–1.71)	1.37 (1.25–1.50)	0.74 (0.67–0.82)	41	54	−18
Treatment including all other factors	1.00 [Reference]	1.54 (1.40–1.68)	1.32 (1.20–1.45)	0.73 (0.66–0.81)	44	60	−23
Treatment only	1.00 [Reference]	1.80 (1.64–1.97)	1.61 (1.46–1.76)	0.73 (0.66–0.81)	−24	−30	−5

*NS, not statistically significant.
Run in case STAGE makes a difference.

Hispanics and NHWs. For foreign-born Hispanics, treatment explained 44% of the mortality disparity.

Differences in screening and treatment may partly contribute to the survival differences between the time periods. Regardless of race/ethnicity, a higher percentage of patients were diagnosed at later stage in Time Period 2. This might be explained by their limited access to health care, which may delay diagnosis and treatment of endometrial cancer in Hispanics [8]. As more women are being diagnosed at later stages with low-risk histology, they are receiving surgery instead of radiation and surgery. Regardless of the time period, the first course of treatment was important, with improved survival for patients who received combination treatment. For this reason, early detection is vital to improving cancer-specific survival. Future research should aim to implement new interventions for Hispanic women to improve endometrial cancer education and increase access to early care.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

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