Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

Research Article

Cancer Epidemiology, Biomarkers & Prevention

The Growing Burden of Endometrial Cancer: A Major Racial Disparity Affecting Black Women

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Abstract

Background: In contrast with the decreasing incidence seen for most cancers, endometrial cancer has been increasing in the United States. We examined whether the increasing incidence and mortality from endometrial cancer are equally distributed by race/ethnicity and tumor histologic subtype.

Methods: Surveillance, Epidemiology, and End Results (SEER) endometrial cancer incidence and mortality data were obtained from 2000 to 2011. Age-adjusted incidence and incidence-based mortality rates, 95% confidence intervals, and annual percent changes (APC) were calculated. Rate ratios were calculated to compare racial/ethnic groups. Five-year relative survival rates were presented to explore survival by stage at diagnosis.

Results: Incidence rates for endometrial cancers are rising across all racial/ethnic groups, with the greatest APC seen among non-Hispanic black (NHB) and Asian women (APC, 2.5 for both). NHB women have significantly higher incidence rates of aggressive endometrial cancers (clear cell, serous, high-grade endometrioid, and malignant mixed Mullerian tumors) compared with non-Hispanic white (NHW) women. Hispanic and Asian women have incidence rates equal to or lower than NHW women for all tumor subtypes. For nearly every stage and subtype, the 5-year relative survival for NHB women is significantly less than NHW women, whereas Hispanic and Asian women have the same or better survival.

Conclusions: Endometrial cancer incidence is increasing for all women, particularly the aggressive subtypes. The disparity associated with excess incidence for these aggressive histologic subtypes and poorer survival is limited to NHB women.

Impact: Increasing rates of aggressive endometrial cancers may widen the survival disparity between NHW and NHB women. *Cancer Epidemiol Biomarkers Prev; 24(9); 1407–15. ©2015 AACR.*

Introduction

Endometrial cancer is the fourth most commonly diagnosed cancer among women, with nearly 50,000 cases diagnosed in the United States in 2013 (1). Overall, cancer incidence rates have been declining in the United States, but incidence rates for endometrial cancer have continued to climb over the last decade and are projected to continue to increase (2, 3). The rising incidence of endometrial cancer has been attributed to various factors, including the obesity epidemic (4), although it has been suggested that obesity alone is unlikely to explain the increase seen over the past decade (2). Limited evidence suggests that other factors may play a role, including the widespread decrease in the use of menopausal hormone therapy, including progestins, changes in reproductive behaviors, and the increasing prevalence of diabetes (2, 4–6).

Incidence of endometrial cancer has been shown to vary by race and ethnicity, with the highest rates among non-Hispanic White (NHW) women, and the lowest rates among Asian women (7). Although, once racial differences in hysterectomy prevalence have been considered, adjusted estimates show that non-Hispanic black (NHB) women actually have higher incidence rates of endometrial cancer than NHW women (8). In addition, it has been well established that NHB women are diagnosed more frequently with aggressive histologic subtypes, such as serous carcinomas, clear-cell carcinomas, and malignant mixed Mullerian tumors (MMMT, also referred to as carcinosarcomas) compared with other racial/ethnic groups (9). Women diagnosed with these tumors have dramatically worse outcomes compared with low-grade endometrioid tumors, the most commonly diagnosed histologic subtype.

Differences in histologic subtypes of endometrial cancer and related clinical parameters may partially explain the large survival disadvantage among NHB women (10). The number of deaths from endometrial cancer among NHB women exceed the number of deaths due to ovarian cancer in this population (n = 1,500 and n = 1,330 per year, respectively; ref. 11). The racial disparity in survival after a breast cancer diagnosis is broadly recognized, with NHB women experiencing a 41% higher mortality rate and a 12% difference in 5-year survival rates compared with NHW women (11). The racial disparity in survival after an endometrial cancer diagnosis is more striking, with NHB women experiencing an 80% higher mortality rate after an endometrial cancer diagnosis compared with NHW women, one of the greatest seen among common cancers (11, 12). The racial disparity is highlighted by the gap in 5-year survival rates, with 64% of NHB women surviving

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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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doi: 10.1158/1055-9965.EPI-15-0316

Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

compared with 86% of NHW women—a 22% difference (13). The limited reports currently available examining endometrial cancer mortality rates in Asian and Hispanic women suggest that rates are similar to or better than those of NHW women (14–16); however, most published cancer statistics do not jointly consider histologic subtype, tumor grade, and stage at diagnosis with respect to racial/ethnic disparities. A comprehensive analysis of these factors needs to be performed to better understand the basis for the racial/ethnic inequities that have thus far been incompletely described for the most common gynecologic cancer in the United States.

To address this need, the aim of this study was to use population-based cancer registry data to examine recent incidence and mortality rates of endometrial cancer. A detailed analysis of these data, including joint stratification by histologic subtypes, grade, and stage at diagnosis, is presented. Finally, estimates are provided for Asian and Hispanic women in addition to NHW and NHB women, to better represent the growing diversity of the U.S. population.

Materials and Methods

Study population

Endometrial cancer (corpus uteri and uterus, NOS) incidence and mortality data were obtained from the Surveillance, Epidemiology, End Results (SEER) database (17). The SEER program of the National Cancer Institute was established in 1973 and has expanded to 18 population-based registries that cover approximately 28% of the U.S. population. We included cases diagnosed from 2000 to 2011 to analyze the most current data available and to utilize all registry sites. SEER registries utilize active surveillance to collect data on patient demographics, tumor site, histology, grade, stage at diagnosis, first course of treatment, and annual follow-up for vital status (18). This research was considered exempt from Institutional Review Board approval as all data are deidentified and coded for public use.

Data coding in SEER

Tumor site, histology, and grade are coded as described by the International Classification of Diseases for Oncology, Third Edition (ICD-O-3; ref. 19). For this analysis, the following primary site codes were used to identify uterine cancers: C54.0–C54.3, C54.8–C54.9, C55.9, and all were classified as malignant tumors (behavior code, 3). Tumor histologic subtype was categorized as follows: clear cell (8310), endometrioid (8050, 8140, 8143, 8210–8211, 8260–8263, 8340, 8380–8384, 8560, 8570), mixed (8255, 8323), malignant Mullerian mixed tumors (MMMT) or carcinosarcoma (8950–8951, 8980–8981), and serous (8441, 8460–8461). Endometrioid tumors were further classified by grade (low grade: well-differentiated or moderately differentiated versus high grade: poorly differentiated, undifferentiated, or anaplastic; ref. 20). Other histologic subtypes such as neuroendocrine (8013, 8041, 8045–8046, 8574), undifferentiated (8020), endometrioid with unknown grade, and general histologic descriptions [carcinoma, nos (8010), neoplasm, malignant (8000), etc.] were included in the other category. Sarcomas of the corpus uterus and gestational trophoblastic tumors were excluded from this analysis. Stage of disease followed the classifications established by the Federation Internationale de Gynecologie et d'Obstetrique (FIGO; ref. 21). The SEER Summary Stage variable collapsed the FIGO staging into four categories: localized, FIGO IA, IB, IC, and FIGO stage I not further specified; regional, FIGO stage IIA, IIB, or FIGO stage II, not otherwise specified, FIGO stage IIIA, IIIB, and IIIC; and distant, FIGO stage IVA, IVB, and unknown. Months of survival were calculated from the date of diagnosis to the date of death.

Statistical analysis

Age-adjusted incidence and incidence-based mortality rates, along with 95% confidence intervals and annual percent changes (APC), for women diagnosed between 2000 and 2011, were calculated by race/ethnicity and histologic subtype. Unlike traditional cancer mortality rates that are based on death certificate information, incidence-based mortality rates are based on follow-up information from incidence data and allow for the calculation of mortality rates by disease features. Rates were age adjusted to the 2000 United States Standard Population. APC were calculated using a weighted least squares regression line with a two-sided P value to assess if the APC was not equal to 0. Rate ratios and 95% confidence intervals were calculated for each rate with NHW women as the referent. All confidence interval estimates for rates were calculated using the method described by Tiwari and colleagues (22). Five-year relative survival rates were calculated for women diagnosed from 2000 to 2007 by race/ethnicity, histologic subtype, and SEER summary stage. A relative survival rate is the ratio of observed survival to the expected survival seen in the general U.S. population taking into account age, race, sex, and year. Observed survival was calculated using the actuarial method, expected survival was calculated using the Ederer II methods, and a Z test was used to compare survival rates with NHW women (23). Percent change [(rate1−rate2)/rate1] to describe differences in rates was also calculated. P values <0.05 were considered to be statistically significant. All analyses were completed using SEER*-Stat software (24).

Results

Table 1 describes the age, histologic type, grade, and stage at diagnosis of 120,513 women diagnosed with endometrial cancer from 2000 to 2011 who were included in this analysis. The majority of women were NHW (n = 90,621), followed by Hispanics (any race, n = 11,386), NHB (n = 10,365), and Asians (n = 8,141). Due to insufficient sample size, once data were stratified by histologic subtype, 662 American Indian/Native American women and 782 women with unknown race were excluded from the analysis. Table 2 shows the age-adjusted incidence rates by histologic subtype and race/ethnic group, including incidence rate ratios (iRR) using NHW women as the reference category. NHB women have significantly lower incidence rates for all types combined and for the low-grade endometrioid subtype, but higher incidence rates of all high grade, aggressive endometrial cancers compared with NHW women. For example, NHB women were 1.9 times more likely to be diagnosed with clear cell tumors compared with NHW women (iRR, 1.90; 95% CI, 1.66–2.18), were 2.48 times more likely to be diagnosed with MMMT tumors (iRR, 2.48; 95% CI, 2.32–2.64) and 2.19 times more likely to be diagnosed with serous tumors (iRR, 2.19; 95% CI, 2.05–2.33). The disparity associated with excess incidence of endometrial cancer for these aggressive histologic subtypes is only seen among NHB women. Compared with NHW women, both Hispanic and Asian women had equal or lower incidence rate ratios for all histologic subtypes.

Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

Table 1. Distribution of clinical features of endometrial cancers by race and ethnicity, SEER, 2000–2011

	NHW *N* (%)	NHB *N* (%)	Hispanic *N* (%)	Asian *N* (%)
Total	90,621	10,365	11,386	8,141
Age at diagnosis				
<50	9,882 (11%)	1,196 (12%)	2,974 (26%)	2,021 (25%)
50–59	24,592 (27%)	2,338 (23%)	3,284 (29%)	2,780 (34%)
60–69	26,380 (29%)	3,584 (35%)	2,825 (25%)	1,924 (24%)
70–79	18,125 (20%)	2,281 (22%)	1,648 (14%)	1,009 (12%)
80+	11,642 (13%)	957 (9%)	655 (6%)	407 (5%)
Histology				
Endometrioid	73,531 (81%)	6,414 (62%)	9,009 (79%)	6,515 (80%)
Serous	4,230 (5%)	1,222 (12%)	613 (5%)	409 (5%)
Mixed	4,182 (5%)	522 (5%)	524 (5%)	403 (5%)
MMMT	4,019 (4%)	1,307 (13%)	554 (5%)	361 (4%)
Clear cell	1,103 (1%)	268 (3%)	151 (1%)	125 (2%)
Other	3,556 (4%)	623 (6%)	535 (5%)	328 (4%)
Grade				
Low (well to moderately differentiated)	58,578 (65%)	4,458 (43%)	7,390 (65%)	5,307 (65%)
High (poor to undifferentiated)	19,192 (21%)	3,776 (36%)	2,422 (21%)	1,914 (24%)
Unknown	12,851 (14%)	2,122 (20%)	1,574 (14%)	920 (11%)
SEER summary stage				
Local	63,316 (70%)	5,504 (53%)	7,512 (66%)	5,490 (67%)
Regional	16,173 (18%)	2,453 (24%)	2,189 (19%)	1,584 (19%)
Distant	7,458 (8%)	1,698 (16%)	1,175 (10%)	820 (10%)
Unknown	3,674 (4%)	701 (7%)	510 (4%)	247 (3%)

Over the 12-year study period, age-adjusted incidence rates for endometrial cancer have increased significantly for total endometrial cancers, among all racial and ethnic groups (Fig. 1A). Variations in the annual percentage change do vary by racial/ethnic group and histologic subtype. In Fig. 1A, the age-adjusted incidence rates for all types has increased the most for NHB and Asian women (APC, 2.5 for both). Rates of endometrioid endometrial cancers, both low- and high-grade, are decreasing for NHW women (APC, −0.8 and −2.5, respectively, Fig. 1B and C). This is the only histologic subtype where significant decreases in incidence are reported among at least one racial/ethnic population. For NHB women, low-grade endometrioid endometrial cancer increased (APC, 1.0, Fig. 1B), and rates were stable for Hispanic and Asian women. High-grade endometrioid endometrial cancers had nonsignificant decreases in incidence rates for all racial/ethnic groups, but remained highest for NHB (Fig. 1C). Significant increases in rates of serous endometrial cancer were seen across all racial/ethnic subgroups (Fig. 1D). Incidence rates for mixed tumors increased for all women but an APC could not be calculated for minority groups due to the limited number of cases per year (Fig. 1E). Incidence rates of MMMT have significantly increased over the study period for NHW, NHB, and Asian women (APC, 1.9, 3.4, and 3.3, respectively, Fig. 1F). Rates of clear-cell endometrial cancer are highest for NHB women, but the incidence rates for all race/ethnic groups have remained steady over the study period (Fig. 1G). Significantly increased incidence rates for "other" endometrial cancers were seen across all racial/ethnic groups (Fig. 1H). Corresponding 95% confidence intervals for the APC estimates can be found in Supplementary Table S1.

Incidence-based mortality rates by histologic subtype and racial/ethnic group were also examined. Compared with NHW women, NHB women have significantly higher mortality rates for all subtypes examined, with the exception of low-grade endometrioid tumors (Table 3). The highest mortality rate ratios (mRR) are for serous, MMMT, and clear-cell tumors, with NHB women having at least two times greater mortality than their NHW counterparts (mRR, 2.6, 2.9, and 2.4, respectively). Hispanic women and Asian women have either similar or lower mRR than their NHW counterparts.

Figure 2 shows 5-year relative survival rates overall, and by histologic subtype, racial/ethnic group, and stage at diagnosis. NHB women have poorer survival at every stage of diagnosis, regardless of histologic subtype, compared with NHW women. The percentage differences between NHB and NHW women with the same histologic subtype and diagnosed at the same stage have a wide range, with a 6% risk difference in survival for local stage, low-grade endometrioid cancers, to 59% lower survival for distant-stage clear-cell cancers. The percentage of Hispanic women and Asian women surviving 5 years after diagnosis is similar to the 5-year survival for NHW women across most stage/histologic subtype categories. These data are shown in detail in Supplementary Table S2.

Discussion

We report the most recent population-based data available for endometrial cancer incidence and mortality in the United States by subtype, and include estimates for both Hispanic and Asian women in addition to NHB and NHW women. Overall, endometrial cancer has increased in incidence over the past decade for all racial/ethnic subgroups included in this analysis. The number of endometrial cancer cases diagnosed annually is expected to increase dramatically in the next two decades in the United States. Rahib and colleagues (25) estimated that the approximately 50,000 cases seen in 2010 will increase to 82,000 cases annually in 2020, and more than double by 2030, with 122,000 cases expected to occur. Mortality is also expected to rise, with a 43% increase in the number of deaths due to endometrial cancer from 2010 to 2030 (25). Estimates were not presented by race/ethnicity, and do not account for histologic subtype, which suggests that

Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

Table 2. Age-adjusted incidence rates of endometrial cancer by histologic subtype, race, and ethnicity, SEER, 2000–2011

	N	Rate	Rate 95% CI		Rate ratio	Rate ratio 95% CI		*P*
All types								
NHW	90,621	24.38	24.22	24.54	1.00			
NHB	10,356	19.83	19.44	20.22	0.81	0.80	0.83	<0.0001
Hispanic	11,386	17.76	17.43	18.11	0.73	0.71	0.74	<0.0001
Asian	8,141	17.05	16.68	17.43	0.70	0.68	0.72	<0.0001
Endometrioid-low grade								
NHW	55,170	15.02	14.89	15.15	1.00			
NHB	4,067	7.48	7.25	7.71	0.50	0.48	0.51	<0.0001
Hispanic	6,908	10.23	9.98	10.48	0.68	0.66	0.70	<0.0001
Asian	4,959	10.24	9.95	10.53	0.68	0.66	0.70	<0.0001
Endometrioid-high grade								
NHW	10,789	2.86	2.80	2.91	1.00			
NHB	1,613	3.16	3.00	3.32	1.11	1.05	1.17	0.0003
Hispanic	1,287	2.12	2.00	2.25	0.74	0.70	0.79	<0.0001
Asian	1,016	2.15	2.02	2.29	0.75	0.70	0.80	<0.0001
Serous								
NHW	4,230	1.10	1.07	1.14	1.00			
NHB	1,222	2.41	2.28	2.56	2.19	2.05	2.33	<0.0001
Hispanic	613	1.12	1.03	1.22	1.02	0.93	1.11	0.7126
Asian	409	0.90	0.81	0.99	0.81	0.73	0.90	<0.0001
Mixed								
NHW	4,182	1.12	1.08	1.15	1.00			
NHB	522	1.00	0.92	1.09	0.90	0.82	0.99	0.0237
Hispanic	524	0.84	0.77	0.92	0.76	0.69	0.83	<0.0001
Asian	403	0.85	0.76	0.93	0.76	0.68	0.84	<0.0001
MMMT								
NHW	4,019	1.05	1.01	1.08	1.00			
NHB	1,307	2.59	2.45	2.74	2.48	2.32	2.64	<0.0001
Hispanic	554	0.99	0.91	1.08	0.95	0.86	1.04	0.2503
Asian	361	0.80	0.72	0.89	0.76	0.68	0.85	<0.0001
Clear cell								
NHW	1,103	0.29	0.27	0.31	1.00			
NHB	268	0.55	0.48	0.62	1.90	1.66	2.18	<0.0001
Hispanic	151	0.28	0.23	0.32	0.96	0.80	1.14	0.6550
Asian	125	0.28	0.23	0.33	0.96	0.79	1.16	0.7512
Other								
NHW	11,128	2.95	2.89	3.00	1.00			
NHB	1,357	2.64	2.50	2.78	0.90	0.84	0.95	0.0001
Hispanic	1,349	2.18	2.06	2.30	0.74	0.70	0.78	<0.0001
Asian	868	1.84	1.72	1.97	0.63	0.58	0.67	<0.0001

NOTE: Rates are per 100,000 and age-adjusted to the 2000 U.S. Standard Population (19 age groups—Census P25-1130) standard; confidence intervals (Tiwari mod) are 95% for rates and ratios.

the mortality rates presented may underestimate the actual increase for certain race and ethnic groups.

Our analysis provides strong evidence that the burden of endometrial cancer is not equally distributed across racial/ethnic groups. As previously noted, overall rates are generally lowest for Asian women, and then for Hispanic women, with highest rates seen in NHB and NHW women (26, 27). Analysis by subtype is critical to recognize the potential morbidity and mortality differences, as histologic type strongly influences prognosis and differs by race/ethnicity. The excess incidence of endometrial cancer for aggressive tumor subtypes (clear cell, serous, MMMT and high-grade endometrioid) is only seen among NHB women; however, the dramatic increases in APC for certain subgroups (e.g., APC, 9.0 for Asian women with serous cancer) warrants continued surveillance for all populations. Little is known about the risk factors associated with aggressive tumor subtypes, with one pooled analysis using data from 24 studies suggesting that most endometrial cancers share common etiologic factors, and those associations that differed were hampered by small sample sizes (28). A second analysis from the National Institute of Health–AARP Diet and Health study suggested that body mass index, menopausal hormone therapy use, and family history of breast cancer were differentially associated with endometrial cancer depending on tumor subtype (29). Both studies grouped tumors into broad type I and type II categories, as was suggested by Bokhman more than three decades ago (30). A third study from the Gynecologic Oncology Group had the advantage of pathologic review of all cases, and grouped endometrial cancers into type I and type II for most analyses, and further classified endometrioid tumors by grade. They report different risk associations by type II and low-grade endometrioid endometrial cancers for obesity, parity, and smoking (31). We chose to analyze the most homogenous groups possible, and thus did not combine into type I/type II groupings. Findings from The Cancer Genome Atlas suggest that at least four subtypes will eventually be used to refine classification and to potentially guide therapy (32). Including significant numbers of women with endometrial cancer from other racial/ethnic groups, besides NHW, in the development of classification schemes will be critical to understand the potential molecular differences that might be associated with race and ethnicity.

In addition to excess incidence of most nonendometrioid endometrial cancers, NHB women have significantly higher

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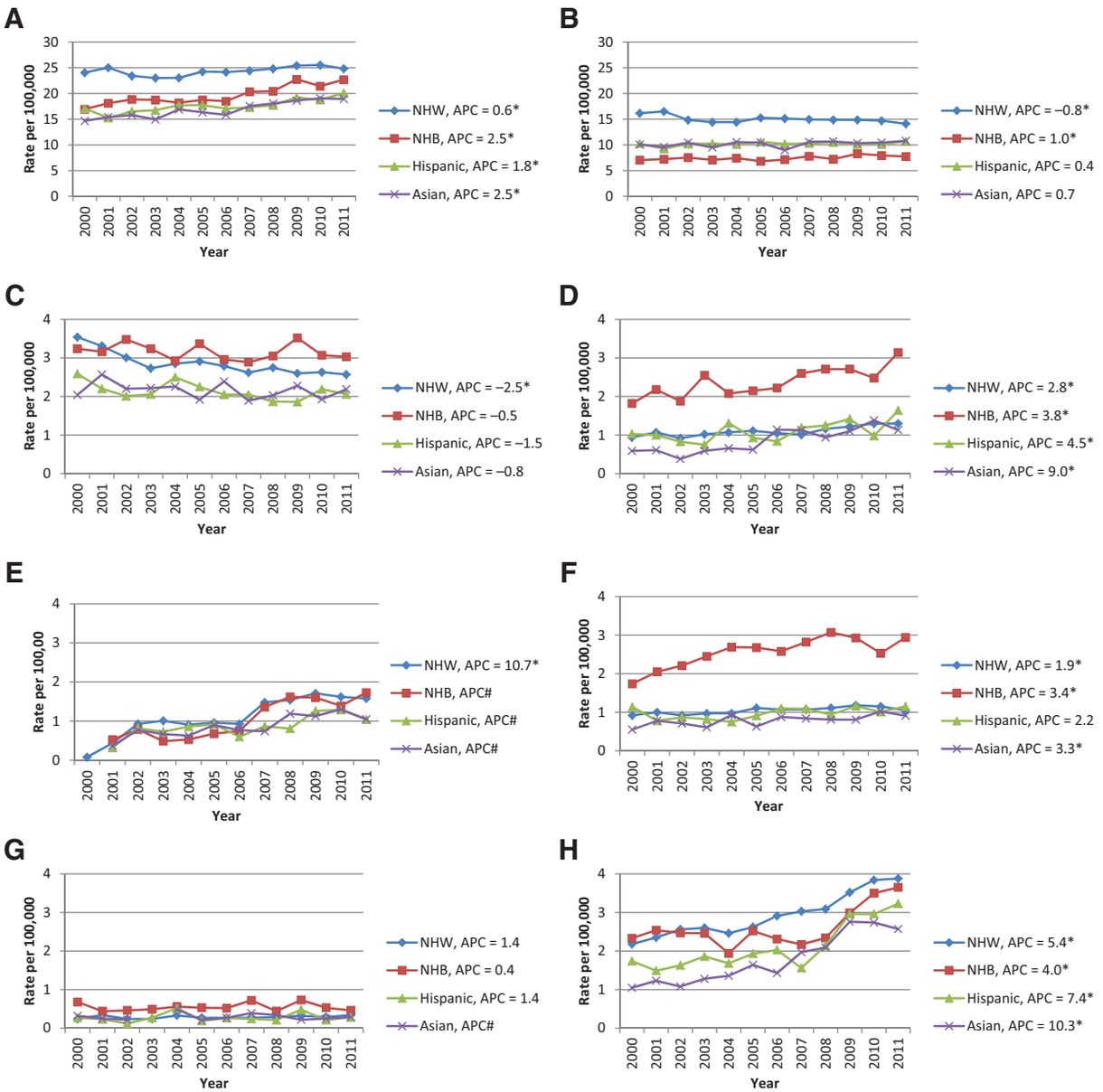

Figure 1.
Age-adjusted incidence rates for endometrial cancer by histologic subtype, race, and ethnicity, SEER, 2000–2011. A, all types; B, endometrioid-low grade; C, endometrioid-high grade; D, serous; E, mixed; F, MMMT; G, clear cell; H, other. * = statistically significant; # = value could not be calculated.

mortality rates for all histologic subtypes of cancer compared with NHW women, with the exception of low-grade endometrioid endometrial cancers. Mortality rates for Hispanics and Asians were the same or lower compared with NHW women, as has been reported previously across all subtypes (14, 15, 26, 33). It is somewhat surprising that Hispanic women do not suffer the same excess burden from endometrial cancer, given that rates of obesity and diabetes are similar to NHB women (34). These conditions have been associated with endometrial cancer etiology and, in some studies, with survival, with potential differences by race/ethnicity and histologic subtype, highlighting the complex underlying biologic pathways involved in carcinogenesis (35–39).

It is possible that the well-documented increases in obesity over the last several decades could be responsible for some of the increase in incidence rates, particularly for NHB and Hispanic populations that have the highest prevalence of obesity in the United States. A recent meta-analysis by Setiawan and colleagues suggested that the association between obesity and type II tumors (defined as serous and clear-cell cancers) was weaker (but still significant) than the association between obesity and type I (endometrioid) cancers (28). Our analysis demonstrates that nonendometrioid endometrial cancer rates have shown the greatest incidence rate increases over the last decade, supporting Wartko and colleagues in their conclusion that obesity is

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Table 3. Age-adjusted incidence-based mortality rates of endometrial cancer by histologic subtype, race, and ethnicity, SEER, 2000–2011

	N	Rate	Rate 95% CI		Rate ratio	Rate ratio 95% CI		*P*
All types								
NHW	22,037	5.70	5.62	5.78	1.00			
NHB	3,673	8.85	8.56	9.14	1.55	1.50	1.61	<0.0001
Hispanic	2,344	4.55	4.36	4.74	0.80	0.76	0.83	<0.0001
Asian	1,456	3.32	3.15	3.50	0.58	0.55	0.62	<0.0001
Endometrioid-low grade								
NHW	8,301	2.12	2.08	2.17	1.00			
NHB	701	1.68	1.56	1.81	0.79	0.73	0.86	<0.0001
Hispanic	714	1.36	1.26	1.47	0.64	0.59	0.69	<0.0001
Asian	412	0.94	0.85	1.03	0.44	0.40	0.49	<0.0001
Endometrioid-high grade								
NHW	4,228	1.11	1.08	1.14	1.00			
NHB	703	1.69	1.56	1.82	1.52	1.40	1.65	<0.0001
Hispanic	459	0.87	0.79	0.95	0.78	0.71	0.86	<0.0001
Asian	303	0.68	0.60	0.76	0.61	0.54	0.69	<0.0001
Serous								
NHW	2,061	0.55	0.52	0.57	1.00			
NHB	596	1.44	1.32	1.56	2.63	2.39	2.88	<0.0001
Hispanic	282	0.56	0.50	0.63	1.03	0.90	1.16	0.7168
Asian	171	0.39	0.34	0.46	0.72	0.61	0.84	<0.0001
Mixed								
NHW	1,017	0.27	0.25	0.28	1.00			
NHB	156	0.38	0.32	0.44	1.41	1.18	1.67	0.0002
Hispanic	123	0.23	0.19	0.28	0.88	0.72	1.06	0.1770
Asian	87	0.20	0.16	0.24	0.74	0.58	0.92	0.0055
MMMT								
NHW	2,319	0.62	0.59	0.64	1.00			
NHB	747	1.79	1.66	1.92	2.90	2.67	3.16	<0.0001
Hispanic	289	0.56	0.50	0.63	0.91	0.80	1.03	0.1557
Asian	209	0.47	0.41	0.54	0.77	0.66	0.89	0.0002
Clear cell								
NHW	496	0.13	0.12	0.14	1.00			
NHB	121	0.30	0.25	0.36	2.38	1.93	2.91	<0.0001
Hispanic	55	0.11	0.08	0.14	0.86	0.64	1.14	0.3209
Asian	46	0.11	0.08	0.15	0.86	0.62	1.17	0.3811
Other								
NHW	3,615	0.91	0.88	0.94	1.00			
NHB	649	1.57	1.45	1.70	1.72	1.58	1.87	<0.0001
Hispanic	422	0.85	0.77	0.94	0.93	0.84	1.03	0.1909
Asian	228	0.53	0.47	0.61	0.59	0.51	0.67	<0.0001

NOTE: Rates are per 100,000 and age-adjusted to the 2000 U.S. Standard Population (19 age groups—Census P25-1130) standard; confidence intervals (Tiwari mod) are 95% for rates and ratios.

contributing to, but not solely responsible for, the rising incidence rates of endometrial cancer (2). In addition, it is possible that obesity is associated with an earlier age of onset, particularly for endometrioid cancers (40). Continued surveillance of this issue, also considering morbidity and mortality, is warranted.

There are limitations of our study that should be considered. First, we were unable to perform a pathologic review of the cases included in the study. As described by Gilks and colleagues, the diagnosis of high-grade subtypes of endometrial cancer has particularly poor interobserver reproducibility, with consensus reached in only 62.5% of the cases presented in their study (41). There are also potential differences in pathologic classification that may influence incidence rates, particularly the "mixed" cancers, so these should be interpreted with caution. Thus, there is some degree of misclassification of histologic subtype, but it is unlikely to be associated with race/ethnicity. In addition, we did not adjust our findings to reflect the prevalence of hysterectomy in the overall population. Thus, these data presented here are underestimates of the rates of endometrial cancer among at-risk women (i.e., those with an intact uterus; ref. 8). Also, while SEER has the advantage of a large sample that is representative of the U.S. population, we did not have an adequate number of cases to examine American Indian/Native American women given the small numbers once these data were stratified by histologic subtype and stage. Additionally, we recognize that our broad race/ethnicity groupings represent many subpopulations that may differ in ancestral origin, cultural beliefs, and practices. These minority subgroups may also suffer a disproportionate burden from endometrial cancer. Finally, SEER does not collect information on other factors that may be associated with incidence and survival, thus we cannot further examine potential causes for the disparities identified in this analysis. It does provide an ample sample size, so that there is sufficient power to examine rates by histologic subtypes that might otherwise be grouped together, to better understand the burden of disease on the population.

The lower survival rates among NHB women persist at nearly every stage and histologic subtype examined. Various factors, including socioeconomic status (SES), access to care, and treatment decisions all affect this disparity to some extent [reviewed by Long and colleagues (9)], yet Hispanic women

Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

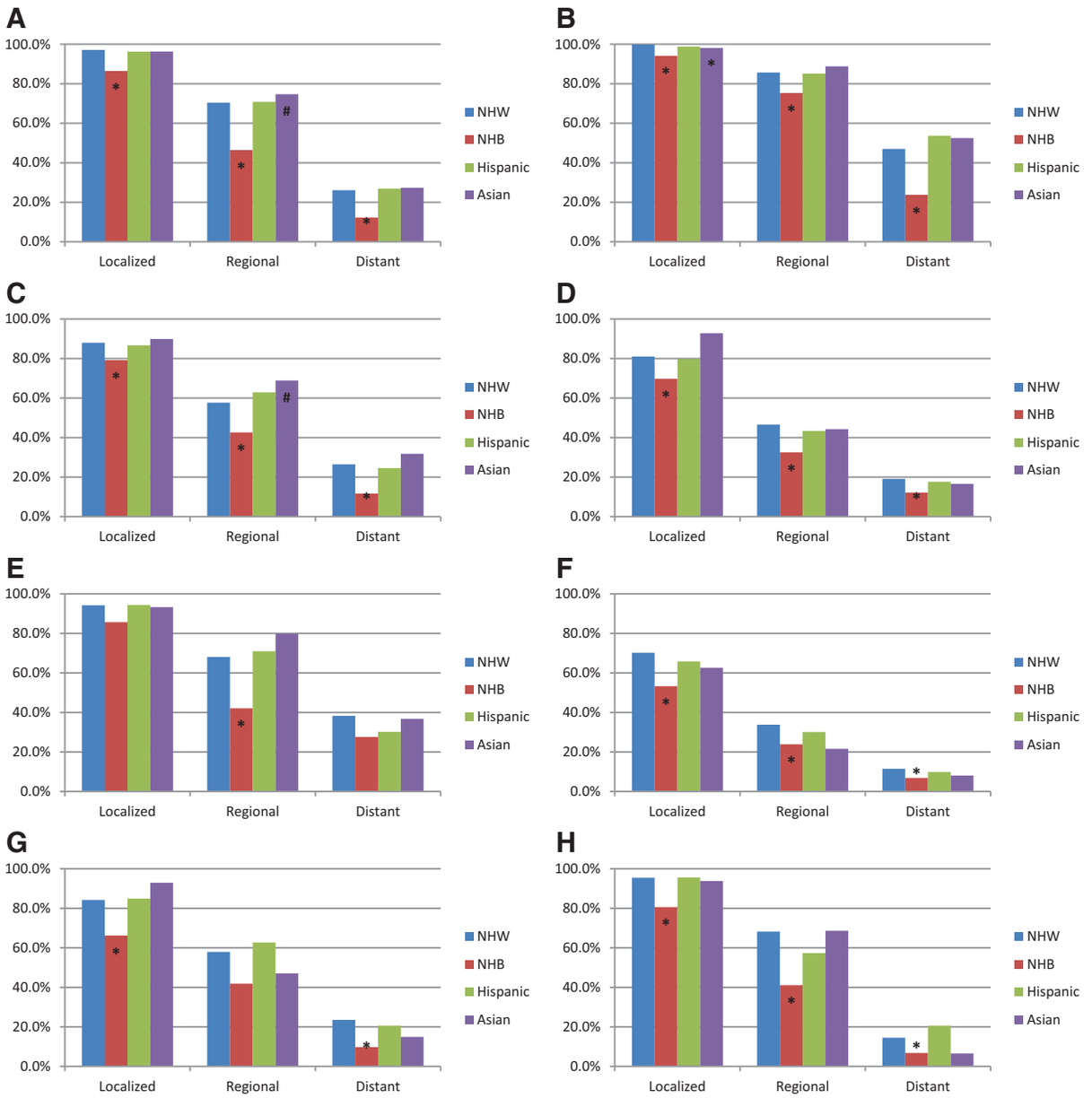

Figure 2.
Five-year relative survival by subtype, race, and ethnicity, and stage for endometrial cancers diagnosed 2000–2007, SEER. A, all types; B, endometrioid-low grade; C, endometrioid-high grade; D, serous; E, mixed; F, MMMT; G, clear cell; H, other. * = statistically significant; # = value could not be calculated.

who have many of the same challenges (42) are at lower risk of occurrence and have outcomes similar to their NHW counterparts after diagnosis (14, 43). Additionally, the most aggressive histologic subtypes of endometrial cancer are also more common among NHB women, and are among the endometrial cancer subtypes with increasing incidence rates. We have yet to fully account for these disparities seen primarily in NHB women and, without further investigation and intervention, they are likely to persist and potentially widen as endometrial cancer emerges as a significant cause of morbidity and mortality in the upcoming decades.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: M.L. Cote, J.J. Ruterbusch, K. Lu, R. Ali-Fehmi
Development of methodology: M.L. Cote
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): M.L. Cote
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): M.L. Cote, J.J. Ruterbusch, S.H. Olson, K. Lu
Writing, review, and/or revision of the manuscript: M.L. Cote, J.J. Ruterbusch, S.H. Olson, K. Lu, R. Ali-Fehmi

Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): M.L. Cote, J.J. Ruterbusch
Study supervision: M.L. Cote

Grant Support

This work was supported, in part, by the Epidemiology Core and NIH Center Grant P30 CA022453 to the Karmanos Cancer Institute at Wayne State University.

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Received March 26, 2015; revised June 19, 2015; accepted June 22, 2015; published OnlineFirst August 19, 2015.

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Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

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Published OnlineFirst August 19, 2015; DOI: 10.1158/1055-9965.EPI-15-0316

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Cancer Epidemiol Biomarkers Prev 2015;24:1407-1415. Published OnlineFirst August 19, 2015.