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Survival disparities among racial/ethnic groups of women with ovarian cancer: An update on data from the Surveillance, Epidemiology and End Results (SEER) registry

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ABSTRACT

Objective: Update information on racial disparities in ovarian cancer survival from the Surveillance, Epidemiology, and End Results (SEER) Program.

Methods: Data on women with epithelial ovarian cancer from the SEER Program between 1995–2015 were collected including; patient ID, age at diagnosis, year of diagnosis, surgery, chemotherapy, radiation, insurance status, region of registry, tumor grade, tumor histology, tumor summary stage, survival months, race/ethnicity, and vital status. Multivariable analyses were performed to examine overall survival, differences in survival by age at diagnosis, by year of diagnosis, risk of not receiving surgery, and risk of 12-month death across racial/ethnic groups.

Results: Non-Hispanic black women (n = 4261) had an increased risk of overall mortality (HR = 1.28, CI: 1.23–1.33) when compared to non-Hispanic white women (n = 47,475), which appears more pronounced among women diagnosed under age 50. Hispanic women (n = 7052) had no difference in survival when compared to non-Hispanic white women (HR = 1.03, CI: 0.99–1.07). Non-Hispanic Asian/PI women (n = 5008) exhibited slightly reduced risk (HR = 0.95, CI: 0.91–0.99) when compared to non-Hispanic white women. Risk of not receiving surgical intervention remains high among non-Hispanic black women and Hispanic women, when compared to non-Hispanic white women. Non-Hispanic black women, non-Hispanic Asian/PI women, and Hispanic women were all at significantly greater risk of dying within the first 12 months of cancer diagnosis when compared to non-Hispanic white women.

Conclusion: Disparities in survival remain across various racial/ethnic groups, when compared to non-Hispanic white women with ovarian cancer. These disparities should continue to be examined in an effort to decrease such gaps.

1. Introduction

The Surveillance, Epidemiology, and End Results (SEER) Program is a United States cancer registry that collects clinical data on U.S. patients that may aide in understanding incidence and mortality with regard to cancer [1]. It is known that incidence of ovarian cancer is higher in white women, and that overall, the median age of diagnosis is 63 years among women in the U.S. [2]. While ovarian cancer is not among the top 10 cancers in terms of incidence in the U.S., it is the fifth leading cause of cancer-related death among U.S. women, and there remain racial disparities within survival outcomes for this disease [2,3].

In 2012, a study of ovarian cancer from the SEER database through 2008 demonstrated a 31% increase in all-cause mortality among non-Hispanic black women when compared to non-Hispanic white women in the U.S. [4]. Additionally, their results showed that 5-year survival for non-Hispanic black women with ovarian cancer has declined over time, despite advancements in treatment. Epidemiologic studies have shown that non-Hispanic black women tend to have more pregnancies, which is known to be associated with reduced risk of ovarian cancer [5,6]. However, non-Hispanic black women have been found to be less likely to obtain proper surgical and chemotherapeutic interventions with regard to ovarian cancer treatment, which may in part reflect lack of access to adequate medical care, or medical coverage [7–9]. An update on survival outcomes is necessary to understand where potential improvements and outcomes research is needed.

In addition, a recent publication reported on epithelial ovarian cancer mortality among Hispanic women from SEER data, years 1992–2013 [10]. This study compared subgroups of women reporting

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Hispanic ethnicity, but did not compare to non-Hispanic white women in the U.S. Thus, there is reason to examine the potential differences in outcomes related to race/ethnicity and survival.

Our study sought to answer the question of current racial and ethnic disparities in survival among non-Hispanic black women, non-Hispanic Asian/Pacific Islander (PI) women, Hispanic women, and non-Hispanic white women with epithelial ovarian cancer, identifying particular ages at risk of mortality and women at higher risk of dying within 12 months of ovarian cancer diagnosis. Highly fatal ovarian cancer was of particular interest in this study, as 12-month mortality risk may identify a high-risk subgroup of patients, by race and ethnicity, which should be further explored. With our interest in examining disparities within the United States, our study was restricted to U.S. data.

2. Methods

2.1. Data collection

Data were abstracted from the SEER registry. Restrictions for database selection were initially set as including only female cancer patients with tumors at the ovarian site. Variables abstracted included: patient ID, age at diagnosis, year of diagnosis, region of registry, tumor grade, tumor histology, tumor summary stage, ICD coding, tumor laterality, survival months, race/ethnicity, surgical intervention, chemotherapy, radiation, health insurance status, and vital status.

Due to missing information, particularly in disease staging which is a well-established prognostic factor, and inconsistencies in SEER data, years earlier than 1995 were excluded, and years 1995–2015 were retained for analysis. Additionally, with noted ICD clinical coding inconsistencies with metastatic tumors to the ovary of an alternative primary origin, study participants with missing tumor subtype histopathology data were excluded, leaving only patients with primary ovarian tumors in the final analyses. Because of inadequate sample sizes in 'Native Alaskan/Native Americans', and lack of informative data with 'non-Hispanic of unknown race', these groups were excluded from the study. Finally, due to the significant differences in disease outcomes, women with ICD coding of non-epithelial ovarian cancers were omitted from this study (Supplementary Fig. 1). The final number of participants, and characteristics across study participants, are shown in Table 1.

2.2. Statistical analysis

An ANOVA test was utilized to compare mean age (years) at diagnosis by race/ethnicity. Chi-square tests were performed on each categorical variable to identify any differences between the study groups. Overall survival was analyzed utilizing a multivariable Cox proportional hazard model and corresponding 95% confidence intervals (CIs), with survival months as the time scale. Age at diagnosis (continuous), stage (local, regional, or distant), grade (I, II, III, IV), tumor subtype (serous, endometrioid, mucinous, clear cell), tumor laterality (left, right, bilateral involvement), chemotherapy (any, none/unknown), radiation (any, none, unknown), surgical intervention (debulking details), and SEER registry region (East, Northern Plains, Pacific Coast, Southwest) were preselected for adjustments in the multivariable model, due to either established prognostic value, and/or significant differences across study groups. As non-Hispanic white women are more likely to be diagnosed with ovarian cancer and thus much of the literature is on this patient group, we sought to use them as a reference group to identify any disparities among other race/ethnicities in comparison to these women. Additional multivariable Cox proportional hazard models with corresponding 95% CIs were utilized to assess patients diagnosed under age 50, age 51–74, and 75 and older, in an effort to compare mortality rates among differing age groups of women from various racial/ethnic backgrounds. Risk of mortality between differing year-intervals of diagnosis was analyzed using multivariable Cox proportional hazard ratios with corresponding 95% CIs. After identifying increased risk of death during these different time intervals, we examined changes in survival between the two time intervals, by each race specifically, using multivariable Cox proportional hazard models with corresponding 95% CIs. Multivariable logistic regression with corresponding 95% CIs was used to assess risk of women not receiving surgery for their disease in the years 1995–2004, and in 2005–2015, adjusting for age at diagnosis, disease stage, chemotherapy, radiation, insurance status, tumor grade, and tumor subtype. Association between race/ethnicity and risk of highly fatal ovarian cancer (mortality within 12 months of diagnosis) was examined with multivariable logistic regression with corresponding 95% CIs to formulate odds ratios, adjusting for age at diagnosis, disease stage, tumor grade, tumor subtype, surgical status, chemotherapy, radiation, insurance status, and SEER registry region. Interaction testing was performed on significant prognostic variables of age category, chemotherapy, and disease staging. A significant interaction was identified for race/ethnicity and disease stage, as well as race/ethnicity and age category. In order to examine differences in survival outcomes by race/ethnicity with regard to summary stage at diagnosis, a stratified Cox proportional hazard model with corresponding 95% CIs was then used. Lastly, we used a Cox proportional hazard model with corresponding 95% CIs to identify differences in survival among only women who are treated with chemotherapy. Model fit and proportionality testing was assessed with Schoenfeld's residuals. All statistical analyses were performed using SAS version 9.4.

3. Results

Non-Hispanic Asian/PI women were diagnosed at the youngest age, followed by Hispanic women, then non-Hispanic black women, and non-Hispanic white women being diagnosed at the oldest age (Table 1). Non-Hispanic Asian/PI women, Hispanic women, and non-Hispanic black women had less accrual to the SEER registry before the year of 2005. More Non-Hispanic Asian/PI women, and Hispanic women, were registered in the Pacific Coast region of the U.S., whereas non-Hispanic black women had the highest frequency of SEER registration in the East region of the U.S. They presented at different tumor grades, with Hispanic women presenting with lower grade tumors. Non-Hispanic Asian/PI women and Hispanic women presented at earlier disease stages. Non-Hispanic black women had a lower frequency of surgical intervention. Hispanic women had the lowest frequency of any radiation, as well as any chemotherapy. Hispanic women had the highest frequency of being medically uninsured. All of the aforementioned differences in frequencies of characteristics were statistically significant, as seen in Table 1.

3.1. Overall survival

We first examined survival by racial/ethnic group among women diagnosed with ovarian cancer at any age. When compared to non-Hispanic white women, non-Hispanic black women were at 28% increased risk of mortality (HR = 1.28, CI:1.23–1.33) (Table 2, Fig. 1). By contrast, Hispanic women had no significant difference in survival (HR = 1.03, CI: 0.99–1.07), while non-Hispanic Asian/PI women had slightly reduced risk of mortality (HR = 0.95, CI: 0.91-0.99).

3.2. Survival among varying age groups

Among women diagnosed with ovarian cancer at age 50 or below, non-Hispanic black women remain at significantly greater risk of mortality (HR = 1.46, CI: 1.33–1.61) compared to non-Hispanic white women (Table 2, Supplementary Fig. 2). Non-Hispanic Asian/PI women, and Hispanic women, did not have significant differences in mortality risk in this age group (HR = 1.02, CI: 0.92–1.12 and HR = 1.04, CI: 0.96–1.12, respectively) (Table 2, Supplementary Fig. 2). Among women diagnosed at 51–74 years of age, non-Hispanic

Table 1
Distribution of characteristics among epithelial ovarian cancer patients from different racial backgrounds collected from SEER data between 1995 and 2015.

Characteristics	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Asian/PI	Hispanic Any Race	P- Value
N	47,475	4261	5008	7052	
Age at diagnosis:					
Mean (SD)	62.3 (13.5)	60.2 (13.6)	55.8 (13.5)	56.3 (14.1)	< .0001*
Year of diagnosis					
1995-2004	16,453 (34.7%)	1244 (29.2%)	1403 (28%)	1827 (25.9%)	
≥2005	31,022 (65.3%)	3017 (70.8%)	3605 (72%)	5225 (74.1%)	< .0001*
SEER registry region:					
East	18,466 (38.9%)	2494 (58.5%)	594 (11.9%)	956 (13.6%)	
Northern Plains	5,616 (11.8%)	534 (12.5%)	87 (1.7%)	120 (1.7%)	
Pacific Coast	20,946 (44.1%)	1209 (28.4%)	4285 (85.6%)	5379 (76.3%)	
Southwest	2,447 (5.2%)	24 (0.6%)	42 (0.8%)	597 (8.5%)	< .0001*
Tumor grade:					
Grade I	4,138 (8.7%)	329 (7.7%)	499 (10%)	766 (10.9%)	
Grade II	7,764 (16.4%)	614 (14.4%)	812 (16.2%)	1131 (16%)	
Grade III	16,772 (35.3%)	1404 (33%)	1662 (33.2%)	2383 (33.8%)	
Grade IV	7,981 (16.8%)	632 (14.8%)	897 (17.9%)	1038 (14.7%)	
Unknown	10,820 (22.8%)	1282 (30.1%)	1138 (22.7%)	1734 (24.6%)	< .0001*
Tumor subtype:					
Serous	33,263 (70.1%)	3117 (73.2%)	2677 (53.5%)	4590 (65.1%)	
Endometrioid	7,017 (14.8%)	478 (11.2%)	944 (18.9%)	1203 (17.1%)	
Mucinous	3,818 (8%)	469 (11%)	556 (11.1%)	764 (10.8%)	
Clear Cell	3,377 (7.1%)	197 (4.6%)	831 (16.6%)	495 (7%)	< .0001*
Stage:					
Localized	7,410 (15.6%)	551 (12.9%)	1039 (20.8%)	1309 (18.6%)	
Regional	9,773 (20.6%)	745 (17.5%)	1388 (27.7%)	1509 (21.4%)	
Distant	30,292 (63.8%)	2965 (69.6%)	2581 (51.5%)	4234 (60%)	< .0001*
Laterality (ovary involvement):					
Right ovary	12,028 (25.3%)	1072 (25.2%)	1547 (30.9%)	1848 (26.2%)	
Left ovary	11,950 (25.2%)	986 (23.1%)	1546 (30.9%)	1827 (25.9%)	
Bilateral	19,366 (40.8%)	1656 (38.9%)	1633 (32.6%)	2767 (39.2%)	
Unspecified/unknown	4,131 (8.7%)	547 (12.8%)	282 (5.6%)	610 (8.7%)	< .0001*
Surgical intervention:					
No surgery performed	4,474 (11.6%)	751 (17.6%)	325 (6.5%)	626 (8.9%)	
Total removal of tumor	352 (0.9%)	70 (1.6%)	52 (1%)	91 (1.3%)	
*USO**	1264 (3.3%)	141 (3.3%)	216 (4.3%)	326 (4.6%)	
*BSO***	6437 (13.6%)	546 (12.8%)	815 (16.3%)	1117 (15.8%)	
USO or BSO w/ omentectomy	14,874 (31.3%)	1124 (26.4%)	1824 (36.4%)	2273 (32.2%)	
Debulking surgery unspecified	18,998 (40%)	1567 (36.8%)	1668 (33.3%)	2429 (34.4%)	
Pelvic exenteration	1,048 (2.2%)	61 (1.4%)	107 (2.1%)	186 (2.6%)	
Unknown	28 (0.06%)	1 (0.02%)	1 (0.02%)	4 (0.06%)	< .0001*
Radiation:					
Any radiation	652 (1.4%)	82 (1.9%)	95 (1.9%)	94 (1.3%)	
None	46,729 (98.4%)	4169 (97.8%)	4906 (98%)	6933 (98.3%)	
Unknown	94 (0.2%)	10 (0.2%)	7 (0.1%)	25 (0.4%)	0.0004*
Chemotherapy:					
Any chemotherapy	33,670 (70.9%)	2967 (69.6%)	3578 (71.5%)	4865 (69%)	
None/Unknown	13,805 (29.1%)	1294 (30.4%)	1430 (28.6%)	2187 (31%)	0.002*
Insurance status:					
Uninsured	662 (1.4%)	165 (3.9%)	109 (2.2%)	309 (4.4%)	
Insured	24,716 (52.1%)	2362 (55.4%)	2969 (59.3%)	4156 (58.9%)	
Unknown	22,097 (46.5%)	1734 (40.7%)	1930 (38.5%)	2587 (36.7%)	< .0001*
Vital status:					
Alive	20,158 (42.5%)	1591 (37.3%)	2948 (58.9%)	3763 (53.4%)	
Dead	27,317 (57.5%)	2670 (62.7%)	2060 (41.1%)	3289 (46.6%)	< .0001*
Death within 12 months of diagnosis:					
Yes	10,334 (21.8%)	1322 (31%)	1080 (21.6%)	1720 (24.4%)	
No	37,141 (78.2%)	2939 (69%)	3928 (78.4%)	5332 (75.6%)	< .0001*

*Denotes statistically significant difference between groups.
* Unilateral salpingo-oophorectomy.
** Bilateral salpingo-oophorectomy.

black women were at a 30% increased risk of mortality (HR = 1.30, CI: 1.23–1.37), whereas Hispanic women again did not have a significant difference in mortality risk (HR = 1.01, CI: 0.96–1.06) (Table 2, Supplementary Fig. 3). However, non-Hispanic Asian/PI women had a reduced risk of mortality within this age group (HR = 0.90, CI: 0.85-0.95). Among women diagnosed at age 75 or above, we found no significant differences between any of the racial/ethnic patient groups with regard to risk in mortality (Table 2, and Supplementary Fig. 4). There was a significant interaction found for race/ethnicity and age category (p = 0.02).

Table 2
Association between race/ethnicity and all-cause mortality among women with ovarian cancer.

Overall survival:			
	Crude HR (95% CI)	[a]Adj. HR (95% CI)	P-value
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.35 (1.30-1.41)	1.28 (1.23-1.33)	< .0001*
Non-Hispanic Asian/PI women	0.69 (0.66-0.72)	0.95 (0.91-0.99)	0.02*
Hispanic women	0.86 (0.83-0.89)	1.03 (0.99-1.07)	0.15
Among women diagnosed with ovarian cancer at age 50 or below:			
	Crude HR (95% CI)	[b]Adj.HR (95% CI)	P-value
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.69 (1.54-1.85)	1.46 (1.33-1.61)	< .0001*
Non-Hispanic Asian/PI women	0.88 (0.80-0.96)	1.02 (0.92-1.12)	0.75
Hispanic women	1.05 (0.97-1.13)	1.04 (0.96-1.12)	0.37
Among women diagnosed with ovarian cancer at age 51 to 74:			
	Crude HR (95% CI)	[b]Adj.HR (95% CI)	P-value
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.51 (1.44-1.59)	1.30 (1.23-1.37)	< .0001*
Non-Hispanic Asian/PI women	0.79 (0.74-0.84)	0.90 (0.85-0.95)	0.001*
Hispanic women	1.01 (0.97-1.06)	1.01 (0.96-1.06)	0.85
Among women diagnosed with ovarian cancer at age 75 or above :			
	Crude HR (95% CI)	[b]Adj.HR (95% CI)	P-value
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.21 (1.11-1.32)	1.05 (0.96-1.15)	0.29
Non-Hispanic Asian/PI women	0.80 (0.71-0.89)	0.91 (0.81-1.02)	0.09
Hispanic women	0.98 (0.90-1.07)	0.95 (0.87-1.04)	0.27

* Denotes statistically significant value.
[a] Adjusted for age at diagnosis, stage, grade, subtype, surgical intervention, chemotherapy, radiation, laterality, insurance status, and SEER registry region.
[b] Adjusted for stage, grade, subtype, surgical intervention, chemotherapy, radiation, laterality, insurance status, and SEER registry region.

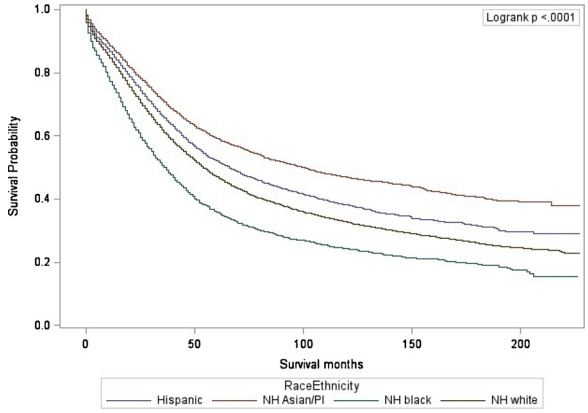

Fig. 1. Overall survival among women with epithelial ovarian cancers stratified by race/ethnicity, performed by unadjusted log rank test.

3.3. Survival across varying time intervals

Hazard ratios based on time intervals of diagnosis are seen in Table 3, Fig. 2. Between the diagnosis years of 1995–2004, non-Hispanic black women had a significant increased risk in mortality of 31% (HR = 1.31, CI: 1.23–1.40) when compared to non-Hispanic white women from the same time interval (Table 3, Fig. 2a). This increase in risk remained between the years of 2005–2015 (HR = 1.27, CI: 1.20–1.34) (Table 3, Fig. 2b). Non-Hispanic Asian/PI, as well as Hispanic women had no significant difference in risk of mortality across time intervals of diagnosis (Table 3, Fig. 2a, b). When looking at only non-Hispanic white women, we found that there was a 6% reduced risk of mortality (HR = 0.94, CI: 0.91-0.98) when diagnosed between the most recent time interval of 2005–2015 compared to the earlier time interval of 1995–2004 (Table 3). Among only non-Hispanic black women, there was no significant difference in risk of mortality between time intervals (HR = 0.90, CI: 0.80–1.02) (Table 3). Non-Hispanic Asian/PI women had a borderline significant reduction in risk of mortality (HR = 0.86, CI: 0.74-0.99) in the most recent time interval of diagnosis (Table 3). Finally, there was no significant difference in risk of mortality for Hispanic women (HR = 1.00, CI: 0.89–1.11) between year-intervals of diagnosis (Table 3).

3.4. Risk of not receiving tumor debulking surgery

Among women diagnosed between the years of 1995–2004, non-Hispanic black women were at a 2.32-fold (CI: 1.91–2.81) increased risk of not receiving surgical intervention for their disease when compared to non-Hispanic white women (Supplementary Table 1). Among women diagnosed between 2005–2015, non-Hispanic black women remained at an increased risk for not receiving surgical intervention, though now at a 2.12-fold risk (CI: 1.85–2.40). Non-Hispanic Asian/PI women did not differ in their risk of not receiving surgical intervention in either time interval (Supplementary Table 1). Hispanic women had a significant increased risk of not receiving surgical intervention (OR = 1.35, CI: 1.09–1.66) in the earlier time interval, that remained present in the most recent years of diagnosis (Supplementary Table 1).

3.5. Risk of highly fatal ovarian cancer by race/ethnicity

When analyzing the association between race/ethnicity and risk of

Table 3
Association between race/ethnicity and risk of mortality among women with epithelial ovarian cancer, stratified by year of diagnosis.

	Crude HR (95% CI)	Adj. HR (95% CI)	P-value
Diagnosed between 1995-2004:			
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.30 (1.22-1.39)	1.31 (1.23-1.40)	< .0001*
Non-Hispanic Asian/PI women	0.67 (0.62-0.72)	0.95 (0.88-1.02)	0.18
Hispanic women	0.89 (0.84-0.94)	1.04 (0.98-1.11)	0.20
Diagnosed between 2005-2015:			
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.40 (1.33-1.47)	1.27 (1.20-1.34)	< .0001*
Non-Hispanic Asian/PI women	0.71 (0.67-0.75)	0.96 (0.91-1.02)	0.21
Hispanic women	0.86 (0.82-0.90)	1.02 (0.98-1.07)	0.34
Non-Hispanic white women only, by year-interval of diagnosis:			
Diagnosed between 1995-2004	1.00 (ref.)	1.00 (ref.)	Ref.
Diagnosed between 2005-2015	0.91 (0.89-0.93)	0.94 (0.91-0.98)	0.002*
Non-Hispanic black women only, by year-interval of diagnosis:			
Diagnosed between 1995-2004	1.00 (ref.)	1.00 (ref.)	Ref.
Diagnosed between 2005-2015	0.92 (0.85-1.00)	0.90 (0.80-1.02)	0.10
Non-Hispanic Asian/PI women only, by year-interval of diagnosis:			
Diagnosed between 1995-2004	1.00 (ref.)	1.00 (ref.)	Ref.
Diagnosed between 2005-2015	0.95 (0.86-1.04)	0.86 (0.74-0.99)	0.03*
Hispanic women only, by year-interval of diagnosis:			
Diagnosed between 1995-2004	1.00 (ref.)	1.00 (ref.)	Ref.
Diagnosed between 2005-2015	0.88 (0.82-0.95)	1.00 (0.89-1.11)	0.94

Adjusted model includes: age at diagnosis, stage, grade, subtype, surgical intervention, chemotherapy, radiation, laterality, insurance status, and SEER registry region.

* Denotes statistically significant value.

highly fatal ovarian cancer (women who died within 12 months of ovarian cancer diagnosis), non-Hispanic black women, non-Hispanic Asian/PI women, and Hispanic women, all demonstrated higher risk relative to non-Hispanic white women. Non-Hispanic black women had a 1.41-fold (CI: 1.30–1.52) increased risk, non-Hispanic Asian/PI women had a 1.27-fold increased risk (CI: 1.17–1.37), while Hispanic women had a 1.39-fold increased risk (CI: 1.30–1.49) of highly fatal ovarian cancer (Table 4).

Table 4
Association between race/ethnicity and risk of dying within 12 months from diagnosis with ovarian cancer.

	Crude OR (95% CI)	Adj. OR (95% CI)	P-value
Non-Hispanic white women	1.00 (ref.)	1.00 (ref.)	Ref.
Non-Hispanic black women	1.62 (1.51–173)	1.41 (1.30–1.52)	< .0001*
Non-Hispanic Asian/PI women	0.99 (0.92–1.06)	1.27 (1.17–1.37)	< .0001*
Hispanic women	1.16 (1.09–1.23)	1.39 (1.30–1.49)	< .0001*

Adjusted model includes: age at diagnosis, stage, grade, subtype, surgical intervention, chemotherapy, radiation, laterality, insurance status, and SEER registry region.

* Denotes statistically significant value.

3.6. Risk of dying among various racial/ethnic groups stratified by stage of disease at diagnosis

When stratified by disease summary stage at diagnosis, non-Hispanic black women demonstrated a significant increased risk of mortality across all stages, when compared to non-Hispanic white women (Supplementary Table 2). This disparity was lowest among non-Hispanic black women presenting with distant metastasis at diagnosis, which is known to significantly increase risk of dying from ovarian

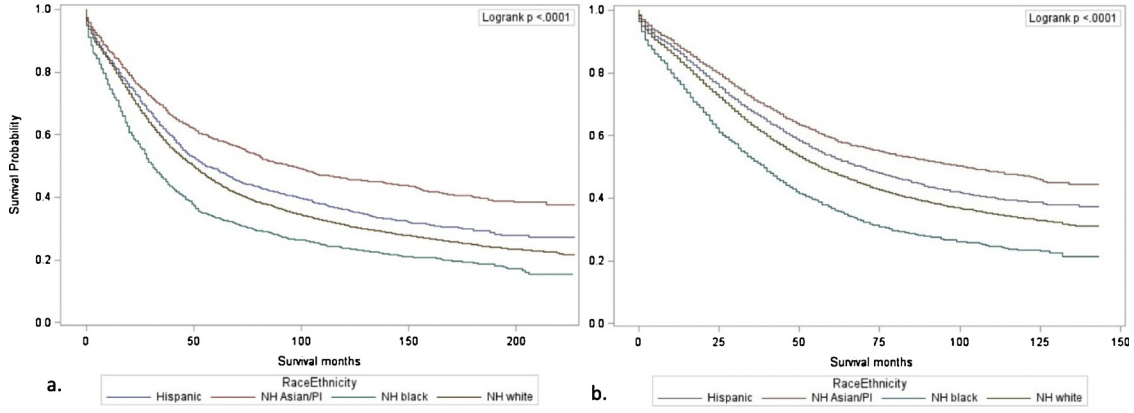

Fig. 2. (a) Association between race/ethnicity and all-cause mortality among women diagnosed with epithelial ovarian cancer between 1995–2004. **(b)** Association between race/ethnicity and all-cause mortality among women diagnosed with epithelial ovarian cancer between 2005–2015. Survival curves performed by unadjusted log rank test.

cancer for all women with this disease (HR = 1.21, CI: 1.15–1.26, Supplementary Table 2). [2] There were no significant differences in survival among non-Hispanic Asian/PI women, when stratified by stage. There was a significant interaction found for race/ethnicity and disease summary stage ($p < 0.0001$).

3.7. Disparities in survival among only women treated with chemotherapy

When examining only women who are treated with any chemotherapy, non-Hispanic black women remain at an increased risk of dying when compared to non-Hispanic white women (HR = 1.31, CI: 1.24–1.37, Supplementary Table 3), while non-Hispanic Asian/PI women have a reduced mortality risk (HR = 0.93, CI: 0.88-0.98, Supplementary Table 3). Hispanic women had no significant difference in risk.

4. Discussion

Consistent with past reports, our study demonstrated significant disparities in ovarian cancer survival by race/ethnicity. Among women diagnosed under the age of 50, non-Hispanic black women had highest risk of mortality. They remain at increased risk of mortality compared to non-Hispanic white women, among patients diagnosed between the ages of 51–74. Interestingly, we found no statistically-significant differences in survival by race/ethnicity among women diagnosed at ≥ 75 years of age. Hispanic women have no significant difference in survival when compared to non-Hispanic white women, either overall or by age at diagnosis, but still remain at substantially greater risk of highly fatal ovarian cancer. While Hispanic women were more likely to be diagnosed with earlier-stage disease, they were less likely to receive surgical intervention for their cancer, which is concerning. Non-Hispanic Asian/PI women demonstrate slightly reduced risk of mortality overall, but higher risk of highly fatal ovarian cancer, relative to non-Hispanic white women.

While dissimilarities in clinical care may explain a large extent to which disparities in cancer survival exist, there are alternative explanations that could be explored in ovarian cancer patient populations. Obesity has been linked to potential increased risk of certain subtypes of ovarian tumors (endometrioid, mucinous), as well as increased risk of mortality among ovarian cancer patients [11,12]. This could potentially arise from adipose tissue associations with pro-inflammatory mediators and overall chronic inflammatory processes involved in carcinogenesis and tumor progression [13]. Obesity has also been linked to increased levels of insulin, which has been associated with tumor etiology and progression. Hispanic women, as well as non-Hispanic Black women, have been identified as patient groups in which obesity is more prevalent, which may be due to disparities among socioeconomic factors [14–16]. While this may provide an additional explanation for the likely multifactorial racial disparity among non-Hispanic black women with regard to survival in ovarian cancer, mechanisms surrounding this should be further explored, particularly due to the potential complex socioeconomic confounders. A more extensive epidemiologic study that includes biomarkers, treatment details, and socioeconomic factors would provide a more conclusive association between risk factors among various racial/ethnic groups and ovarian cancer survival.

There are many strengths for this study. As ovarian cancer is a rare disease, using SEER data allows us to draw conclusions on large sample sizes of patients with this disease. The conclusions from these analyses provide a baseline understanding for moving forward with future research. One area in particular, is identifying the highest risk subgroups of women with this disease. For example, understanding that non-Hispanic black women diagnosed at a younger age have a higher risk of death identifies a subgroup of ovarian cancer patients to be further researched, to identify potential strategies to offset this disparity. Furthermore, analyzing the risk of highly fatal ovarian cancer, that is death within 12 months from diagnosis, may benefit future clinical studies to examine more aggressive approaches early on in treatments. Finally, identifying continued disparities in surgical interventions for patients in our study provides insight on the need for more research to identify explanations for this disparity.

There are also limitations to this study that should be noted. While using SEER data is beneficial in that it may better represent the cancer populations in the United States as a whole, diagnostic coding can be quite variable based on the individuals entering patient information, and therefore, are at risk of misclassification. We attempted to alleviate some of this potential bias through excluding patients with ambiguous tumor coding. Additionally, there appeared to be significantly less information collected by SEER in past decades, thus leading us to exclude missing staging and such years of SEER collections. By doing so, we are able to draw more accurate conclusions with regard to patient comparability. We were able to include variables for chemotherapy and radiation. However, treatment differences reflected by these variables need to be interpreted with caution, particularly the chemotherapeutic variable. This is due to the binary categorization in the SEER database of chemotherapy as 'any chemotherapy' and 'none/unknown'. As none and unknown are under the same category, there is risk of misclassification of chemotherapeutic intervention among these patients. However, these variables are still of value to further understand where disparities in survival may arise from. Surgical debulking had a large amount of patients under a largely unspecified debulking status, meaning that they were coded as having had debulking surgery, but without details to know to what extent. Likewise, there were a large portion of patients, within all race/ethnicity, who had unknown status for medical insurance. Due to sample sizes, Hispanic women were analyzed as one category in these analyses, though it is important to acknowledge that outcomes may vary among subgroups of Hispanic ethnicity. Lastly, SEER data does not include extensive epidemiological variables (i.e. smoking history, BMI, and reproductive variables that may be associated with ovarian cancer risks and outcomes), preventing us from identifying deeper relationships between exposures that could further explain the outcomes in these populations.

In the most recent report looking at racial and ethnic disparities among women with gynecologic malignancies, Rauh-Hain et al. performed a thorough and useful analysis looking at trends among racial/ethnic groups of women with ovarian, endometrial, cervical, and vulvar cancer [17]. These authors reported decreased receipt of chemotherapy among non-Hispanic black, non-Hispanic Asian, and Hispanic women when compared to non-Hispanic white women. Similar to our results, they found that non-Hispanic Asian women had highest rates of survival, compared to non-Hispanic white women. However, they identified Hispanic women also having higher rates of survival compared to non-Hispanic white women. Likewise, they found that non-Hispanic black women had the lowest rate of survival. However, they did not examine individual age groups to identify where the gap in survival lies among these women, and did not analyze highly fatal ovarian cancer. In light of these facts, we have expanded on the analyses to provide more detailed information on precisely where the disparities exist among different racial/ethnic groups of women with ovarian cancer.

Though our study focused on U.S. data from the SEER registry, our findings are also consistent with global concerns regarding racial disparities in ovarian cancer survival [18]. A recent review of literature in addition to GLOBOCAN data (global cancer data registry effort), reported the U.S. having among the highest incidences of ovarian cancer across all racial groups when compared to South America, Australia, Japan, Asia, Central America, and Africa. They noted highest incidence being in non-Hispanic white women. Similar to our findings, they identified non-Hispanic black women are at highest risk of dying. They report socioeconomic status and access to quality healthcare as the main obstacles in overcoming such disparities.

Our study differs from past reports in that it examines specific subgroups among varying racial/ethnic groups of women with ovarian

cancers, such as those defined by age at diagnosis, short survival duration, or non-receipt of surgical intervention, while updating trends over time. Overall, non-Hispanic black women continue to be at a disadvantage for survival from ovarian cancer when compared to non-Hispanic white women. While lack of adequate surgical and therapeutic interventions may explain some of this disparity, more research is needed to provide a well-rounded, conclusive understanding of potential lifestyle, socioeconomic, and biological differences as well. While non-Hispanic Asian/PI women, and Hispanic women, had comparable or even improved overall and age-specific survival relative to non-Hispanic white women, the increased risk of highly fatal ovarian cancer among non-Hispanic Asian/PI, and Hispanic women in addition to non-Hispanic black women, demonstrates a need to further research the subgroup of women who are dying within 12 months of ovarian cancer diagnosis.

Ethical statement

Our paper did not require an ethical board approval because this study utilized data from the de-identified SEER database, and is not a study that contains identifiable humans or animal trials.

Author contribution

This research paper was written by AES and KBM, with substantial input from MFB.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose, including no financial supports for the research, authorship, and/or publication of this article.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.101580.

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