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Ovarian Cancer in California: Guideline Adherence, Survival, and the Impact of Geographic Location, 1996-2014

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Abstract

Background: Evidence suggests that geographic location may independently contribute to ovarian cancer survival. We aimed to investigate how the association between residential location and ovarian cancer-specific survival in California varies by race/ethnicity and socioeconomic status.

Methods: Additive Cox proportional hazard models were used to predict hazard ratios (HRs) and 95% confidence intervals (CI) for the association between geographic location throughout California and survival among 29,844 women diagnosed with epithelial ovarian cancer between 1996 and 2014. We conducted permutation tests to determine a global p-value for significance of location. Adjusted analyses considered distance traveled for care, distance to closest high-quality-of-care hospital, and receipt of National Comprehensive Cancer Network guideline care. Models were also stratified by stage, race/ethnicity, and socioeconomic status.

Results: Location was significant in unadjusted models (P=0.009 among all stages) but not in adjusted models (P=0.20). HRs ranged from 0.81 (95% CI: 0.70, 0.93) in Southern Central Valley

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to 1.41 (95% CI: 1.15, 1.73) in Northern California but were attenuated after adjustment (maximum HR = 1.17, 95% CI: 1.08, 1.27). Better survival was generally observed for patients traveling longer distances for care. Associations between survival and proximity to closest high-quality-of-care hospitals were null except for women of lowest socioeconomic status living furthest away (HR = 1.22, 95% CI: 1.03, 1.43).

Conclusions: Overall, geographic variations observed in ovarian cancer-specific survival were due to important predictors such as receiving guideline-adherent care. Improving access to expert care and ensuring receipt of guideline-adherent treatment should be priorities in optimizing ovarian cancer survival.

Keywords

geographic disparities; spatial location; ovarian cancer; survival

1. INTRODUCTION

In the United States, ovarian cancer (OC) continues to be the deadliest gynecologic malignancy (1). Nationally, approximately 21,750 women are estimated to be given an OC diagnosis in 2020 (2). While the number of deaths attributed to this disease have decreased, the proportion of women overall surviving five years post-diagnosis is 48.6% (3). Furthermore, disparities in survival by race and socioeconomic status (SES) have become prominent, with women of Non-Hispanic Black (NHB) race and lower SES backgrounds disproportionally experiencing worse prognosis (4–12). Efforts to better understand the outcome differences observed by sociodemographic factors have focused on identifying sources of inequity and factors influencing OC outcomes.

It is well documented that receiving guideline-adherent treatment for OC is associated with improved survival (4, 7). The National Comprehensive Cancer Network (NCCN) has established stage-specific guidelines for the treatment of OC (13) and adherence to them has been recognized as a significant predictor of prognosis (14). Aside from age and cancer characteristics, determinants of receiving guideline care and OC survival are multifactorial and include race, insurance (4, 5, 10, 15–19), individual and area-level SES (4, 9, 18–21), proximity to services (18, 19, 22), and characteristics of the treating hospital and physician (21–31). All of these factors are known to vary geographically.

Geographic location can impact OC outcomes in multiple ways. Researchers have examined spatial variations in adherence to appropriate treatment for OC (18, 19, 32–35), geographic access to care (18, 19, 36), service availability (37), and OC mortality (5, 33, 38, 39). Recently, significant geographic disparities in the receipt of NCCN guideline-adherent care at the geocoded address-level in California were identified (18). Little is known about whether residential location at this geographic resolution also influences survival. The goal of this analysis was to investigate the relationship between geographic location and OC-specific survival, both as an independent predictor and after accounting for sociodemographic factors, disease and treatment characteristics, receipt of NCCN guideline care, and distance to receive care. We also examined the influence of geographic factors by

race/ethnicity and SES to determine if spatial accessibility contributes to survival differences.

2. METHODS

2.1. Study population

We employed a retrospective population-based cohort study design to investigate the association between geographic location and OC-specific survival. Cases at least 18 years of age were obtained from the California Cancer Registry (CCR) for women who had been first diagnosed with invasive epithelial OC between 1996 and 2014, with follow-up available through 2016. Cases were identified from the CCR using the International Classification of Disease Codes for Oncology (ICD-O-3 C56.9). Data from the CCR, whose case reporting within 6 months is nearly 99% and follow up approximately 95% (40, 41), was then linked to California's Office of Statewide Health Planning and Development (OSHPD) patient discharge data. We considered all OC stages (International Federation of Gynecology and Obstetrics (FIGO) - Stage I-IV) in this analysis. Exclusions are presented in Supplemental Table S1. This study received approval from the Institutional Review Board of the University of California, Irvine (UCI 14-66/HS# 2014-1476).

2.2. Study covariates

The main variable of interest was women's geographic location, represented by the geocoded residential address at time of diagnosis. We examined the independent effect of geographic location on ovarian cancer-specific survival as well as determined whether the presence of any unadjusted spatial patterns were due to confounding variables. Two additional variables were included to assess geographic factors that may impact access to care: the distance women traveled from their residential address to their reporting hospital (the hospital women received their initial treatment) and the distance from their residential address to the closest high quality hospital at the time of the woman's diagnosis. The closest high-quality-of-care (high-QOC) hospital was the nearest hospital providing high quality OC services, which could vary by year based on the observed-to-expected (O/E) ratio of adherence to the NCCN treatment guidelines, as determined by Galvan-Turner et al. (24). Briefly, this ratio is calculated by taking the number of cases at a given hospital that adhered to the NCCN guidelines at the time of patient's diagnosis and dividing it by the number expected to receive adherent care based on that hospital's patient demographics (24). High-QOC hospitals had greater adherence than expected and at least 5 cases a year. While treatment guidelines vary by stage, they generally recommend surgery followed by chemotherapy. Treatment adherence and hospital quality were updated over time as guidelines changed. Both distance variables were calculated using the Streetmap Premium HERE street data in ArcGIS Network Analyst (ArcGIS version 10.4.1, ESRI; Redlands, CA). Each distance variable was grouped into quintiles based on the distribution of the respective variable.

Demographic variables examined were age at diagnosis, race/ethnicity, SES, insurance status, and marriage status. Race/ethnicity was grouped as non-Hispanic white (NHW), non-Hispanic black (NHB), Hispanic, Asian and Pacific Islander (API), and other (includes

American Indian, other, and unknown race/ethnicity). Two indexes were used to assign patients into SES quintiles (Lowest, Lower-Middle, Middle, Higher-Middle, Highest). For patients with a diagnosis before 2006, the Yost score was used (42), while the Yang index was used for those diagnosed after 2006 (43). Insurance status was grouped into six categories: managed care (including privately insured), Medicare, Medicaid, other insurance, not insured, and unknown insurance status. We also controlled for cancer characteristics traditionally known to affect survival, including histology type, tumor grade, tumor size, and stage at diagnosis (Stages I-IV).

Other clinical predictors considered were comorbidity status, quality of care received, and quality of hospital where initial treatment was received. OSHPD hospital discharge data was used to extract patient's comorbid conditions 12 months before ovarian cancer diagnosis. Comorbidity status was measured using the Deyo-adapted Charlson Comorbidity Score and classified into the subsequent categories: no comorbidities, one comorbidity, two or more comorbidities, and unknown (44, 45). The quality of care was determined by whether the initial treatment received was adherent to the stage-specific NCCN guidelines for OC (18, 24, 46–52). Both surgical and chemotherapy guidelines had to be adherent in order to be considered having received quality care. Lastly, the O/E ratio metric was used to assign the hospital quality where women were treated, grouped as low-QOC (lowest quartile of O/E ratio or <5 cases/year), intermediate-QOC (middle two quartiles of O/E ratio), and high-QOC (highest quartile of O/E ratio and > 5 cases) (24).

2.3. Statistical analyses

Spatial patterns were assessed using Cox proportional additive hazards model, an extension of the Cox proportional hazards model that includes a loess smooth term for latitude and longitude as a predictor (5, 53–55). Loess, a locally-weighted smoother, is often used in spatial analyses because it adapts to population density (53). Without the smoother for location, the models are reduced to the more common Cox proportional hazards model. A prediction grid of 7,579 points was created across the extent of the study area. Log hazards and 95% confidence intervals (CI) were calculated for locations across California, using the average hazards as a referent for calculating the hazards ratio (HR) and keeping covariate values constant. The amount of smoothing selected was based on minimizing the Akaike's Information Criterion (53, 54). We did not compute the hazards for areas with low data density (56).

We examined the relationship between location and OC-specific survival for all stages combined and stage-stratified (early vs. late stages) in unadjusted and adjusted models. In order to determine whether location was an independent predictor, unadjusted models were fit using the smoother of women's geocoded address at diagnosis with no other covariates. We then adjusted the model for all covariates, including sociodemographic variables, cancer characteristics, and treatment and access to care factors. Permutations were run for each model to determine their respective global p-value for the significance of geographic location (54). Maps were created to visualize the distribution of HRs across California with contour lines denoting significant areas of higher and lower hazards of survival. All analyses and mapping were conducted using the MapGam package in R (Version 3.4.4).

Aspatial multivariable weighted cox regression models without location were used to examine the association between sociodemographic, clinical, and distance variables with OC-specific survival. These models were chosen because the cox proportional hazards assumptions were found to be violated for several variables when plotting the cumulative log hazards as well as examining the scaled Schoenfeld residuals (57, 58). These weighted models report the hazards averaged over the time period, while minimizing the influence of outlying survival times and using robust variance (59, 60). Survival time was calculated in months. OC-specific deaths were considered events, while women were censored if they were alive at the end of the follow-up period, had a death due to other causes, or were lost to follow up. The variables included in the adjusted models were age, race/ethnicity, insurance status, tumor size, grade, histology, diagnosis stage, marriage status, comorbidity status, and treatment adherence. We also ran the models stratified by race/ethnicity and SES to evaluate differences in associations with geographic access to care variables.

3. RESULTS

3.1. Patient characteristics

Between 1996 and 2014, 29,844 women were diagnosed with invasive epithelial OC in California, with the median age at the time of diagnosis being 60 years (Table 1). The majority of women were diagnosed in late stages (67.4%) and more than half were NHW (63.4%). Only 38.3% of all women received NCCN guideline-adherent care. The median survival time for all women was 34.5 months, but this varied by stage, race/ethnicity, and SES (Table 2). The highest median survival was among API women (38.6 months) and those with the highest SES (40.4 months), while the lowest was among NHB women (23.0 months) and those with the lowest SES (28.2 months).

The distribution of OC cases and 426 treating hospitals are displayed in Figure 1. Thirty hospitals were considered to be high-QOC. Distance traveled to receive care ranged from 0.01 km to 1,088 km with a median of 12.7 km (Table 2). Women treated at a high-QOC hospital traveled further for care than those treated at low-QOC hospitals (median of 17.3 km versus 8.8 km, respectively). The median distance between residential location and the nearest high-QOC hospital was 19.3 km. Women of API background and those of highest SES lived closest to a high-QOC hospital.

3.2. Spatial analyses of OC-specific survival

Cox additive models revealed significant spatial patterns in the unadjusted models for all stages combined (P=0.009; Figure 2A). HRs for location ranged from 0.81 (95% CI: 0.70, 0.93) to 1.41 (95% CI: 1.15, 1.73). Areas of increased hazards of mortality included northern and southernmost regions of California. A decreased risk of mortality was observed in the southern part of the San Francisco Bay Area, south Central Valley, and greater Los Angeles county. Geographic location was also significant in the late stages unadjusted model (HR range for location: 0.72 (95% CI: 0.63, 0.82) to 1.27 (95% CI: 1.10, 1.46), P=0.002; Figure 3A). Once the models were adjusted for covariates, patterns were no longer significant [Figures 2B (P=0.20) and 3B (P=0.33)]. Location was not associated with early-

stage survival in either the unadjusted or adjusted models [Figures 3C (P=0.41) and 3D (P=0.98)].

3.3. Determinants of OC-specific survival

Table 1 reports the HRs for the fully-adjusted aspatial model of all stages combined. Overall, increasing age was associated with worst outcomes (HR = 1.03, 95% CI: 1.02, 1.03). Race/ethnicity, SES, and insurance were also significantly associated with survival. Compared to NHW women, NHB women had 19% increased hazards (P <0.001). An inverse association existed between SES and hazards of mortality, with lower SES categories being correlated with greater hazards. Women in higher-middle, middle, lower-middle, and the lowest SES groups had 11%, 9%, 19%, and 18% increased hazards of mortality compared to the highest SES group, respectively. Having Medicaid insurance (HR = 1.10, 95% CI: 1.01, 1.19) and not being insured (HR = 1.26, 95% CI: 1.11, 1.45) were also associated with increased risk of death whereas being married was protective, with a 12% decreased risk of mortality (P<0.001).

Several cancer and treatment characteristics were associated with survival. Using Stage 1 as the referent, each advancing stage of diagnosis resulted in significantly worse survival, with a Stage IV diagnosis being most detrimental (HR = 10.84, 95% CI: 9.44, 12.45). Receiving non guideline-adherent care was also associated with poorer outcomes (HR = 1.29, 95% CI: 1.23, 1.35), as was having a comorbidity score of 1 (HR = 1.13, 95% CI: 1.07, 1.20). Longer distances traveled to receive care were associated with better outcomes. Women who traveled between 10-16 km, 17-32 km, and >32 km had an 11%, 14%, and 13% decrease in hazards. Hazards associated with being treated at a high-QOC hospital versus a low- (HR = 1.07, 95% CI: 0.97, 1.18) or intermediate-QOC hospital (HR = 1.00, 95% CI: 0.95, 1.06) and distance to the closest high-QOC hospital (HRs for each increasing distance category = 1.02, 1.07, 0.99, 0.96, all P>0.05), however, were null when modeled with receiving non guideline-adherent care and distance traveled to receive care.

3.4. Stratified results

The hazards associated with geographic distance variables stratified by SES and race/ethnicity are presented in Tables 3 and 4, respectively. The influence of geographic access to care varied by SES category. Distance traveled to receive care had no significant impact on hazards for women in the highest SES, but all other SES categories were found to be significantly protective. Traveling >32 km for initial treatment improved chances of survival for women of lower-middle SES (HR = 0.78, 95% CI: 0.68, 0.89) and middle SES (HR = 0.86, 95% CI: 0.76, 0.98). While traveling between 10 and 32 km for care was associated with better survival for women in the lowest SES group, living >48 km from a high-QOC hospital significantly increased hazards of mortality by 22%.

Longer distances traveled to receive care were associated with a decreased risk of mortality, but only among NHW, Hispanic, and API women (Table 4). NHW women traveling >32 km for care had a 12% decreased hazards of dying compared to those who were <6 km away. For Hispanic women, every increasing category of distance traveled up to 32 km had significant protective effects on survival. Living further away from high-QOC hospitals had

a negative impact on survival among women of Other race (HR = 4.12, 95% CI: 1.34, 12.67), although interpretation should be made with caution due to small sample sizes. Furthermore, for NHB women, greater distances from a high-QOC hospital was protective for those who lived between 15-24 km (HR = 0.72, 95% CI: 0.57, 0.92) and 25-48 km away (HR = 0.70, 95% CI: 0.54, 0.91).

4. DISCUSSION

We examined the impact of women's geocoded residential address on OC-specific survival in California. We found no evidence of a spatial relationship with OC survival for those with early-staged disease. Geographic location was no longer significantly associated with survival for women diagnosed in late stages and in models with all stages combined after adjusting for sociodemographic factors, cancer and treatment characteristics, and geographic access variables. Consistent with existing literature, several sociodemographic factors in our analyses were correlated with worse prognosis, including being of NHB race, lower SES, and Medicaid insurance status or having no insurance (5–10, 19). Unlike other studies (22–24), we did not find that treatment at a high-QOC hospital improved OC-specific survival overall; this is likely because we also controlled for receipt of NCCN-adherent care. Overall, our findings indicate that much of the unadjusted spatial variation was explained by patient and treatment variables, and location was not an important predictor after controlling for receipt of NCCN-adherent care.

In British Columbia, differences in OC survival were observed by five Health Authority Regions (35). The respective authors determined the geographic differences were due to variations in receipt of appropriate treatment and tumor characteristics (35). A study of OC mortality by Hospital Referral Region found significant geographic patterns among a Medicare population that did not persist after controlling for receipt of cancer-directed therapy (33). In contrast, a previous spatial analysis in California using CCR data from 1996-2006 showed that geographic location at the census tract-level was associated with survival among women with late-staged disease, even after adjusting for treatment (5). A study in Spain looked at smoothed relative risk of OC mortality by municipality and found evidence of differences in the distribution of deaths but did not consider treatment (38). In the United States, an age-adjusted county-level spatial analysis of OC mortality from 2000-2014 identified several significant clusters nationwide including one in the Pacific Northwest and northern CA, which was also elevated in our unadjusted models (39).

We assessed two access-to-care variables. Our results indicate that distance traveled to receive care for OC was associated with survival and was a better predictor than the distance between residential address and the closest high-QOC hospital. Women traveling longer distances to their initial treatment location generally had a survival advantage over those traveling the shortest distances. While not well understood, this relationship has been observed frequently in the broader cancer literature, including among pancreatic (61, 62), liver, colon (62), breast, lung (63), and OC patients (5). Proximity did appear to impact women in several subgroups, however. Living furthest from a high-QOC hospital was associated with worse survival among women in the lowest SES category and those of Other

race, but better survival among NHB women. More research is needed to better understand the association between race/ethnicity and geographic access variables.

Traveling further to receive care has been associated with superior cancer outcomes, yet proximity to specialized care, such as high volume hospitals, cancer centers, and gynecologic oncologists, has been correlated with better survival (5, 22, 36, 37). Over one-third of women nationwide live >50 miles from a gynecologic oncologist (36). In a national analysis of proximity to gynecologic oncologists and OC death rates, increasing distance from these specialized doctors increased the odds of dying from OC by almost 60% (37). In our study population, high-QOC hospitals were unevenly distributed across California, and living closer to a high-QOC hospital did not significantly improve OC-specific survival.

Factors influencing patients' ability and willingness to travel are multifactorial. Some have suggested that SES, insurance status, race, and age are predictors of patient's likelihood to travel (64). While we were unable to identify why traveling longer distances was advantageous to survival, one probable explanation is that women who are able to travel farther have more financial resources to do so (62). A survey of cancer patients identified costs of travel to/from treatment as a major factor considered in treatment decisions (65). Furthermore, in a cross-sectional analysis of barriers to treatment among cancer patients, Hispanics and blacks were more likely than whites to report transportation as an obstacle to treatment (66). Access to a vehicle, distance of the treating facility, and finding somebody to drive patients to care were all cited as reasons to forgo care (66). Women who are already more healthcare-oriented may be more likely to travel to access expert care (62). They may also be more cognizant of available resources within treatment centers, such as social workers who may help connect them to needed services (64, 65).

This is the first study to our knowledge examining spatial variations in OC survival at a geocoded address-level resolution. Prior work linking location and OC mortality have used larger units of analysis (5, 39). One possibility for the lack of association found is that individual-level data avoids the issue of induced clustering that may result from census level geocoding. Another possibility is that we may not accurately be capturing temporal variability in spatial patterns as the impact of location on survival was averaged over a long period of time. Future studies should examine whether there were any trends in the relationship between geographic location, geographic access to services, and OC survival over time, as this time period coincides with many important changes in government administrations that may impact health care access.

This work has several strengths including the large cohort size and number of years examined, which provided considerable follow-up time to examine spatial patterns in OC mortality. Furthermore, we were able to adjust for changes over time in treatment adherence and hospital quality. In addition, the availability of geocoded location of patient's residence allowed us to examine its influence at a finer resolution than previous work, which have typically used larger units of analysis such as zip code and census block. We were also able to use a novel statistical method to test the significance of geographic location while simultaneously controlling for covariates. With the use of ArcGIS Network analyst, the distances between location and hospitals are more precise than the calculation of the

Euclidian or “straight-line” distance between two points. Lastly, we were able to adjust for the impact of comorbidities on survival, a noted gap in previous work (5).

Our analyses were, however, limited by the data available. This is a retrospective study that uses registry data, which introduces the possibility of unmeasured confounders. We were unable to account for the use of public transportation or preferences in travel routes. This may result in bias due to exposure misclassification, the direction of which is unclear if misclassification is differential by location. We were also limited by the lack of information on physician type and specialty, as this information is not included in the CCR. We were unable to determine the extent of residual disease, which has been shown to affect mortality. The amount of data excluded due to missing stage information varied over time and may bias results if missingness was not random by location. Furthermore, the reporting hospital may not be the main facility where care was received, and it’s possible that some satellite clinics report under one hospital. These situations are considered rare and are not likely to affect our results. The CCR only collects address at time of diagnosis and we therefore could not account for patient mobility. With distances calculated based on the patient’s address at baseline and with the inability to account for relocation, some misclassification may occur.

4.1. Conclusion

While geographic location was an independent predictor of OC mortality in CA for women overall and those diagnosed in late stages, no significant association was found between location and survival in models adjusted for sociodemographic, treatment, and geographic access variables. Greater distance traveled was generally associated with better survival, while proximity to high-QOC was only a determinant for select subgroups. Ensuring resources are in place so that all women have access to treatment that meets the stage-specific NCCN guidelines is crucial for optimizing outcomes among all women. Possible strategies for doing so may include provision of transportation to hospitals and increasing satellite clinics in underserved areas. Improving access to expert care facilities is necessary to making sure women of all race/ethnicities receive guideline-adherent care, particularly among women who are socioeconomically disadvantaged.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights:

- Traveling farther distances for care was associated with better survival
- Location not a significant predictor after adjusting for patient characteristics
- Socioeconomically disadvantaged women disproportionately receive inferior care
- Ensuring adequate access to care may optimize ovarian cancer survival for all women

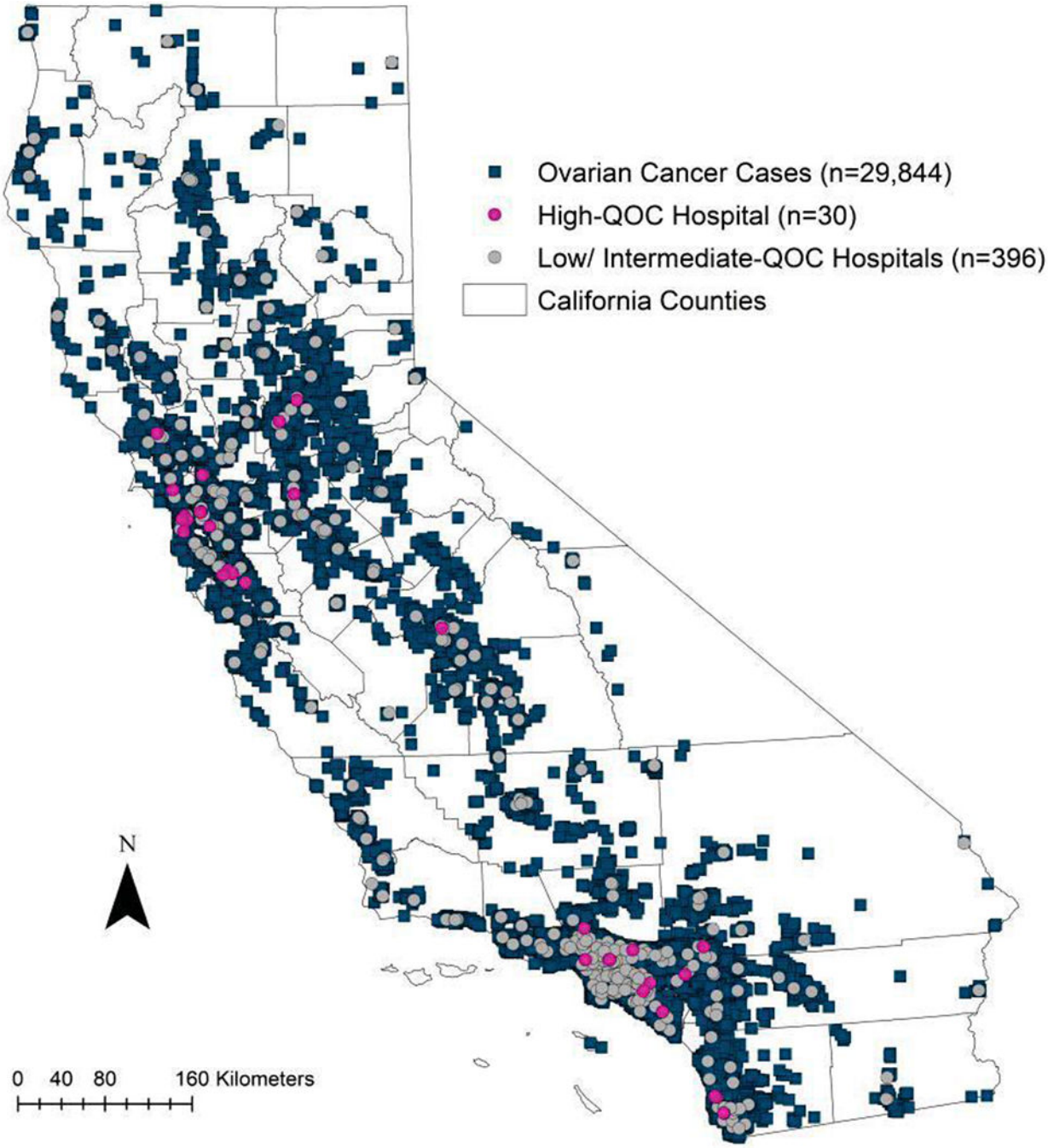

Figure 1: >Distribution of Hospitals and Cases of Epithelial Ovarian Cancer Cases between 1996-2014

Figure 1 shows the distribution of epithelial ovarian cancer cases diagnosed between 1996 and 2014 in California. Hospitals treating cases during those years are displayed by category of quality of care delivered.

Abbreviations: *QOC*, Quality of care

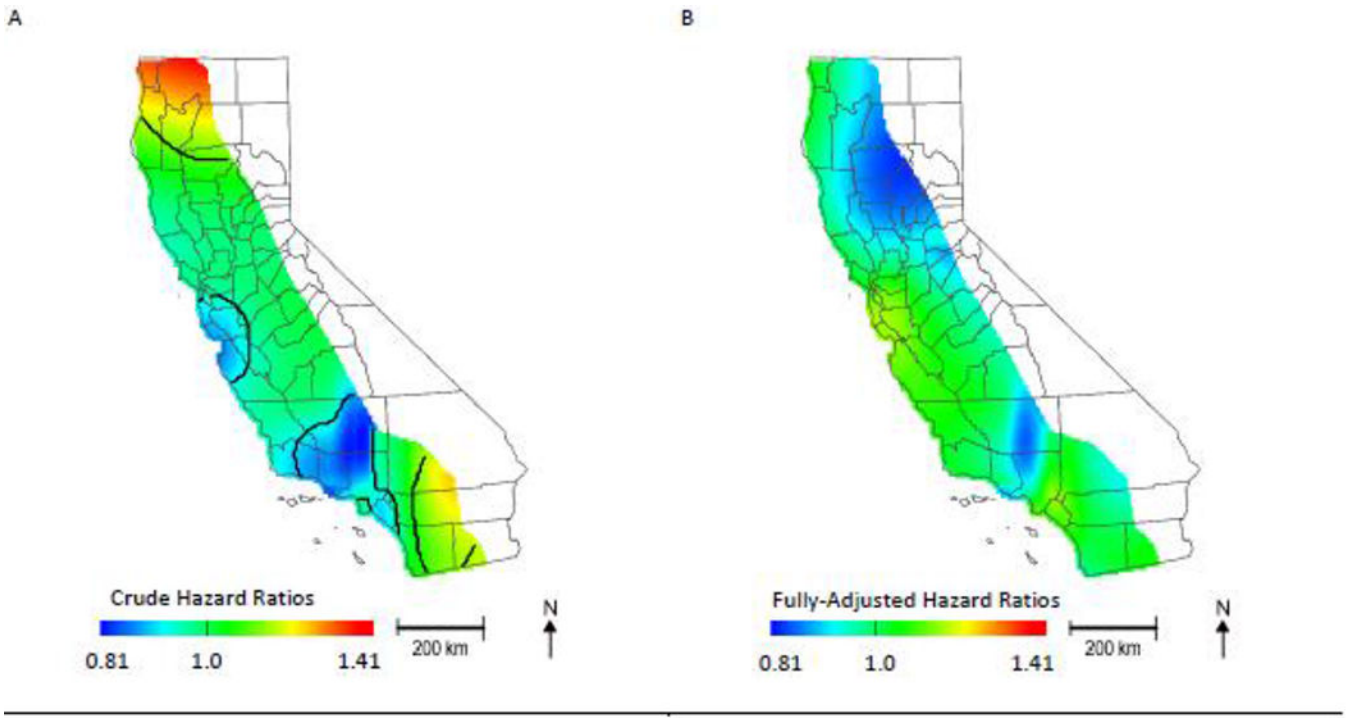

Figure 2. Geographic location and ovarian cancer-specific survival in California among Stages I-IV

(A) The crude and (B) fully-adjusted effect of geographic location on ovarian cancer-specific survival for all stages combined (Stages I-IV). The fully-adjusted map displays the hazard ratios for location after controlling for age, cancer stage, tumor histology, tumor grade, tumor size, race, socioeconomic status, insurance, marital status, comorbidity status, treatment adherence, hospital quality, distance traveled for care, distance of closest high quality-of-care hospital. Areas delineated by contour lines represent statistically significant geographic areas.

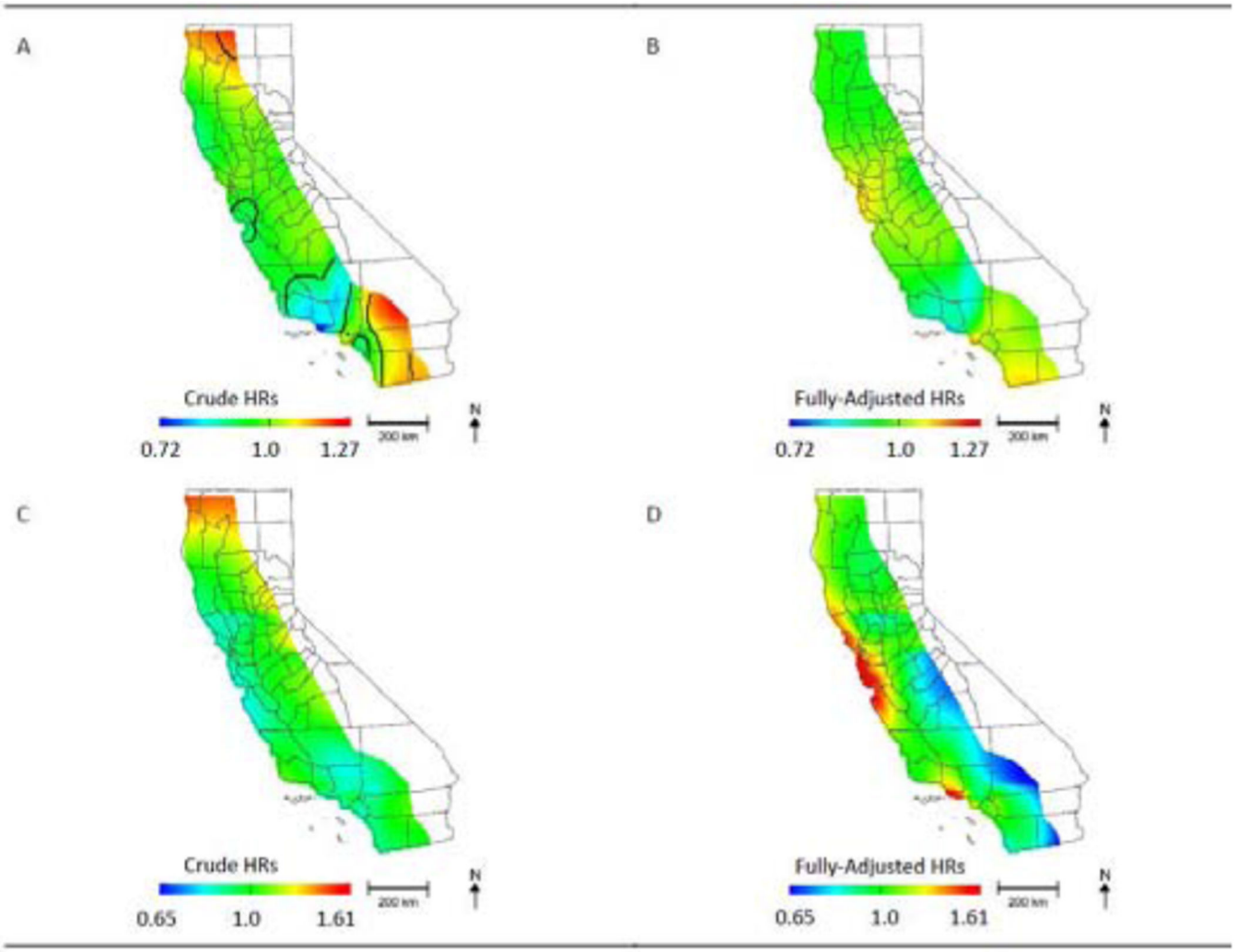

Figure 3: Geographic location and ovarian cancer-specific survival in California among early (I&II) and late (III&IV) stages

(A) The crude and (B) fully-adjusted effect of geographic location on ovarian cancer-specific survival for late stages (Stages III & IV). (C) The crude and (D) fully-adjusted effect of geographic location on ovarian cancer-specific survival for early stages (Stages I & II). The fully-adjusted maps display the hazard ratios for location after controlling for age, cancer stage, tumor histology, tumor grade, tumor size, race, socioeconomic status, insurance, marital status, comorbidity status, treatment adherence, hospital quality, distance traveled for care, distance of closest high quality-of-care hospital. Areas delineated by contour lines represent statistically significant geographic areas.

Abbreviations: *HR*, Hazard Ratios

Table 1.

Patient Characteristics and Fully-Adjusted Hazard Ratios for All Stages Combined of Ovarian Cancer among California Women, 1996-2014 (n=29,844)

Characteristic	N (%)	HR	95% CI	*P* Value
Age (years)				
Median (SD)	60 (14.9)	1.03	1.02, 1.03	<0.001
Race/Ethnicity				
Non-Hispanic White	18,920 (63.4)	1.00	Ref	
Non-Hispanic Black	1416 (4.7)	1.19	1.08, 1.30	<0.001
Hispanic	5,749 (19.3)	0.96	0.90, 1.02	0.197
Asian / Pacific Islander	3,564 (11.9)	0.96	0.89, 1.04	0.351
Other	195 (0.7)	0.87	0.68, 1.10	0.243
Socioeconomic Status (SES)				
Lowest SES	4,037 (13.5)	1.18	1.10, 1.27	<0.001
Lower-Middle SES	5,435 (18.2)	1.19	1.12, 1.26	<0.001
Middle SES	6,324 (21.2)	1.09	1.03, 1.16	0.004
Higher-Middle SES	6,860 (23.0)	1.11	1.01, 1.21	0.024
Highest SES	7,188 (24.1)		Ref	
Insurance Type				
Managed Care	14150 (47.4)	1.00	Ref	
Medicare	7653 (25.6)	0.97	0.92, 1.01	0.151
Medicaid	2725 (9.1)	1.10	1.01, 1.19	0.021
Other Insurance	3825 (12.8)	0.94	0.88, 1.01	0.096
Not insured	889 (3.0)	1.26	1.11, 1.45	<0.001
Unknown	602 (2.0)	1.19	0.76, 1.87	0.435
Tumor Size, mm				
<50	3734 (12.5)	1.00	Ref	
50-99	5885 (19.7)	1.07	0.96, 1.18	0.216
≥100	9336 (31.3)	0.98	0.92, 1.05	0.572
Unknown	10889 (36.5)	1.18	1.10, 1.26	<0.001
Tumor Grade				
1	2374 (8.0)	1.00	Ref	
2	4359 (14.6)	1.10	0.72, 1.67	0.668
3	10051 (33.7)	1.19	0.79, 1.79	0.398
4	4192 (14.0)	1.22	0.82, 1.81	0.329
Unknown	8868 (29.7)	1.46	0.97, 2.20	0.067
Histology				
Serous	12857 (43.1)	1.00	Ref	
Mucinous	1900 (6.4)	1.26	1.06, 1.50	0.007
Endometrioid	3318 (11.1)	0.79	0.68, 0.91	0.001
Clear cell	1829 (6.1)	1.26	1.14, 1.40	<0.001
Adenocarcinoma, NOS	3178 (10.6)	1.39	1.31, 1.48	<0.001

Characteristic	N (%)	HR	95% CI	*P* Value
Others	6762 (22.7)	1.21	1.13, 1.31	<0.001
Stage				
Stage 1	7238 (24.3)	1.00	Ref	
Stage 2	2496 (8.4)	2.94	2.04, 4.23	<0.001
Stage 3	11263 (37.7)	6.61	5.85, 7.48	<0.001
Stage 4	8847 (29.6)	10.84	9.44, 12.45	<0.001
Marital Status				
Single	14688 (49.2)	1.00	Ref	
Marrried	15156 (50.8)	0.88	0.83, 0.93	<0.001
Treatment Adherence				
Adherent	11419 (38.3)	1.00	Ref	
Non-Adherent	18425 (61.7)	1.29	1.23, 1.35	<0.001
CCS				
0	14219 (47. 6)	1.00	Ref	
1	6807 (22.8)	1.13	1.07, 1.20	<0.001
2+	6726 (22.5)	1.03	0.97, 1.09	0.289
Unknown	2092 (7.0)	1.00	0.92, 1.10	0.917
Year Category				
1996 – 2002	9557 (32.0)	1.00	Ref	
2003 – 2006	8053 (27.0)	0.98	0.93, 1.02	0.301
2007 – 2014	12234 (41.0)	0.97	0.93, 1.02	0.241
Hospital Quality-of-Care				
Low	6990 (23.4)	1.00	Ref	
Intermediate	17275 (57.9)	1.07	0.97, 1.18	0.178
High	5579 (18.7)	1.00	0.95, 1.06	0.921
Distance traveled to care				
<6 km	5969 (20.0)	1.00	Ref	
6-9 km	5969 (20.0)	0.93	0.84, 1.02	0.127
10-16 km	5968 (20.0)	0.89	0.80, 0.98	0.025
17-32 km	5969 (20.0)	0.86	0.78, 0.95	0.003
>32 km	5969 (20.0)	0.87	0.79, 0.96	0.006
Closest High-QOC Hospital				
<9 km	5969 (20.0)	1.00	Ref	
9-14 km	5969 (20.0)	1.02	0.96, 1.09	0.554
15-24 km	5968 (20.0)	1.07	0.95, 1.20	0.259
25-48 km	5969 (20.0)	0.99	0.92, 1.05	0.676
>48 km	5969 (20.0)	0.96	0.89, 1.04	0.300

Abbreviations: *CI,* Confidence Interval; *CCS,* Charlson Comorbidity Score; *HR,* Hazard Ratios; *km,* kilometers; *NCCN,* National Comprehensive Cancer Network; *NOS,*Not Otherwise Specified; *QOC,* Quality-of-Care; *SES,* Socioeconomic Status; *SD,* Standard Deviation

Table 2:

Select Patient Characteristics by Geographic Access Variables Among California Women Diagnosed with Ovarian Cancer, 1996-2014

	Median Survival (months)	Distance Traveled to Care (km)			Closest High-QOC hospital (km)		
		Mean	Median	Range	Mean	Median	Range
Total	34.5	28.3	12.7	(0.01 - 1087.98)	37.4	19.3	(0.20 - 500.95)
Stage							
Early	73.7	28.5	13.6	(0.14 - 847.24)	35.5	18.5	(0.20 - 500.95)
Late	24.6	28.2	12.3	(0.01 - 1087.98)	38.3	19.7	(0.27 - 489.50)
Race/Ethnicity							
Non-Hispanic White	35.3	30.7	12.8	(0.17 - 1087.98)	42.6	21.6	(0.20 - 500.95)
Non-Hispanic Black	23.0	19.5	12.0	(0.01 - 583.07)	22.9	16.2	(0.61 - 282.32)
Hispanic	32.2	24.6	12.5	(0.18 - 792.78)	33.6	18.1	(0.38 - 484.07)
Asian / Pacific Islander	38.6	22.1	12.2	(0.14 - 819.64)	20.3	13.0	(0.27 - 480.84)
Other	37.1	40.8	15.2	(1.00 - 685.90)	57.7	20.9	(0.66 - 467.50)
Socioeconomic Status							
Lowest SES	28.2	28.0	11.5	(0.23 - 791.77)	43.2	17.8	(0.38 - 497.99)
Lower-Middle SES	30.1	31.4	12.9	(0.14 - 1087.98)	48.1	22.3	(0.39 - 484.07)
Middle SES	33.5	32.6	13.4	(0.01 - 808.23)	44.0	21.1	(0.20 - 500.95)
Higher-Middle SES	36.2	28.2	12.9	(0.26 - 847.24)	33.5	19.2	(0.26 - 483.74)
Highest SES	40.4	22.4	12.3	(0.23 - 955.27)	23.9	16.7	(0.23 - 258.17)

Abbreviations: *km,* kilometers; *QOC,* Quality-of-Care; *SES,* Socioeconomic Status

Table 3.

Stratified Analysis: Hazard Ratios for Geographic Access Variables by Socioeconomic Status in California Women Diagnosed with Ovarian Cancer, 1996-2014 (n=29,844)

	Lower SES			Lower-Middle SES			Middle SES			Upper-Middle SES			Upper SES		
	N(%)	HR	95% CI	N(%)	HR	95% CI	N(%)	HR	95% CI	N(%)	HR	95% CI	N(%)	HR	95% CI
Distance Traveled															
<6 km	924(22.9)	1.00	Ref	1127(20.7)	1.00	Ref	1239(19.6)	1.00	Ref	1357(19.8)	1.00	Ref	1322(18.4)	1.00	Ref
6-9 km	828(20.5)	0.96	0.83, 1.11	1027(18.9)	0.93	0.82, 1.07	1212(19.2)	1.01	0.89, 1.15	1303(19.0)	0.88	0.77, 1.01	1599(22.2)	1.03	0.92, 1.16
10-16 km	858(21.3)	0.86	0.74, 0.99	1070(19.7)	0.95	0.83, 1.08	1178(18.6)	0.91	0.80, 1.03	1382(20.1)	0.86	0.74, 1.00	1480(20.6)	0.99	0.87, 1.11
17-32 km	672(16.6)	0.77	0.65, 0.91	1039(19.1)	0.84	0.74, 0.96	1257(19.9)	0.90	0.79, 1.02	1420(20.7)	0.88	0.76, 1.01	1581(22.0)	0.99	0.88, 1.12
>32 km	755(18.7)	0.87	0.74, 1.03	1172(21.6)	0.78	0.68, 0.89	1438(22.7)	0.86	0.76, 0.98	1398(20.4)	0.83	0.68, 1.02	1206(16.8)	1.05	0.92, 1.20
Closest High-QOC Hospital															
<9 km	814(20.2)	1.00	Ref	851(15.7)	1.00	Ref	1165(18.4)	1.00	Ref	1433(20.9)	1.00	Ref	1706(23.7)	1.00	Ref
9-14 km	902(22.3)	1.13	0.98, 1.32	1094(20.1)	0.94	0.82, 1.08	1163(18.4)	1.01	0.89, 1.15	1264(18.4)	1.01	0.89, 1.15	1546(21.5)	1.00	0.89, 1.13
15-24 km	691(17.1)	1.12	0.94, 1.32	1006(18.5)	1.05	0.91, 1.21	1196(18.9)	1.03	0.91, 1.18	1480(21.6)	1.13	0.97, 1.33	1595(22.2)	0.90	0.80, 1.02
25-48 km	553(13.7)	1.08	0.90, 1.30	955(17.6)	1.04	0.90, 1.19	1185(18.7)	1.05	0.93, 1.20	1529(22.3)	0.93	0.81, 1.08	1747(24.3)	0.92	0.82, 1.04
>48 km	1077(26.7)	1.22	1.03, 1.43	1529(28.1)	0.97	0.84, 1.11	1615(25.5)	0.95	0.83, 1.08	1154(16.8)	1.01	0.87, 1.16	594(8.3)	0.84	0.72, 0.99

Abbreviations: *CI,* confidence interval; *HR,* hazard ratio; *km,* kilometers; *QOC,* quality-of-care, *SES,* socioeconomic status

Note: Models were adjusted for age, cancer stage, tumor histology, tumor grade, tumor size, race, socioeconomic status, insurance, marital status, comorbidity status, treatment adherence, hospital quality, distance traveled for care, distance of closest high quality-of-care hospital.

Table 4:

Stratified Analysis: Hazard Ratios for Geographic Access Variables by Race/Ethnicity in California Women Diagnosed with Ovarian Cancer, 1996-2014 (n=29,844)

	Non-Hispanic White			Non-Hispanic Black			Hispanic			Asian/Pacific Islander			Other		
	N(%)	HR	95% CI	N(%)	HR	95% CI	N(%)	HR	95% CI	N(%)	HR	95% CI	N(%)	HR	95% CI
Distance Traveled															
<6 km	3831(20.2)	1.00	Ref	291(20.6)	1.00	Ref	1099(19.1)	1.00	Ref	715(20.1)	1.00	Ref	33(16.9)	1.00	Ref
6-9 km	3716(19.6)	0.97	0.88, 1.07	293(20.7)	0.91	0.71, 1.16	1205(21.0)	0.86	0.75, 0.99	718(20.1)	0.92	0.76, 1.11	37(19.0)	0.83	0.25, 2.73
10-16 km	3545(18.7)	0.91	0.81, 1.02	345(24.4)	1.01	0.80, 1.27	1241(21.6)	0.86	0.74, 0.98	804(22.6)	0.90	0.75, 1.09	33(16.9)	0.96	0.39, 2.33
17-32 km	3657(19.3)	0.91	0.82, 1.01	300(21.2)	0.94	0.73, 1.20	1226(21.3)	0.81	0.70, 0.93	750(21.0)	0.75	0.61, 0.92	36(18.5)	1.14	0.42, 3.14
>32 km	4171(22.0)	0.88	0.79, 0.97	187(13.2)	0.85	0.64, 1.12	978(17.0)	0.92	0.77, 1.10	577(16.2)	0.89	0.70, 1.12	56(28.7)	0.27	0.07, 1.09
Closest High-QOC Hospital															
<9 km	3418(18.1)	1.00	Ref	308(21.8)	1.00	Ref	1121(19.5)	1.00	Ref	1083(30.4)	1.00	Ref	39(20.0)	1.00	Ref
9-14 km	3399(18.0)	1.03	0.95, 1.12	319(22.5)	0.90	0.71, 1.13	1275(22.2)	1.10	0.95, 1.26	939(26.3)	0.88	0.73, 1.05	37(19.0)	0.68	0.22, 2.13
15-24 km	3547(18.7)	1.09	0.96, 1.24	436(30.8)	0.72	0.57, 0.92	1267(22.0)	1.14	0.98, 1.31	692(19.4)	0.94	0.77, 1.13	26(13.3)	1.75	0.49, 6.33
25-48 km	4034(21.3)	0.99	0.92, 1.06	234(16.5)	0.70	0.54, 0.91	1050(18.3)	1.14	0.92, 1.40	619(17.4)	0.92	0.75, 1.14	32(16.4)	4.12	1.34, 12.67
>48 km	4522(23.9)	0.97	0.90, 1.05	119(8.4)	0.87	0.64, 1.20	1036(18.0)	1.06	0.91, 1.24	231(6.5)	0.96	0.74, 1.25	61(31.3)	1.29	0.42, 3.94

Abbreviations: *CI,* confidence interval; *HR,* hazard ratio; *km,* kilometers; *QOC,* quality-of-care

Note: Models were adjusted for age, cancer stage, tumor histology, tumor grade, tumor size, race, socioeconomic status, insurance, marital status, comorbidity status, treatment adherence, hospital quality, distance traveled for care, distance of closest high quality-of-care hospital.