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Spatial analysis of adherence to treatment guidelines for advanced-stage ovarian cancer and the impact of race and socioeconomic status ☆

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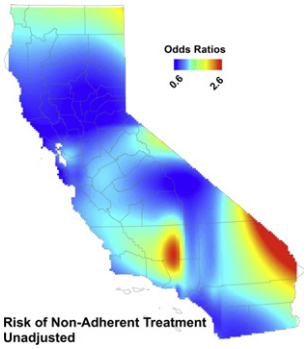
HIGHLIGHTS

- Geographic proximity to a high-volume hospital and travel distance are associated with treatment guideline adherence for advanced-stage ovarian cancer.
- Geographic barriers to standard ovarian cancer treatment disproportionately affect racial minorities and women of low-SES.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective. To determine the impact of geographic location on advanced-stage ovarian cancer care adherence to the National Comprehensive Cancer Network (NCCN) guidelines in relation to race and socioeconomic status (SES).

Methods. Patients diagnosed with stage IIIC/IV epithelial ovarian cancer (1/1/96–12/31/06) were identified from the California Cancer Registry. Generalized additive models were created to assess the effect of spatial distributions of geographic location, proximity to a high-volume hospital (≥20 cases/year), distance traveled to receive care, race, and SES on adherence to NCCN guidelines, with simultaneous smoothing of geographic location and adjustment for confounding variables. Disparities in geographic predictors of treatment adherence were analyzed with the x^2 test for equality of proportions.

Results. Of the 11,770 patients identified, 45.4% were treated according to NCCN guidelines. Black race (OR = 1.49, 95%CI = 1.21–1.83), low-SES (OR = 1.46, 95%CI = 1.24–1.72), and geographic location ≥80 km/50 mi from a high-volume hospital (OR = 1.88, 95%CI = 1.61–2.19) were independently associated with an increased risk of non-adherent care, while high-volume hospital treatment (OR = 0.59, 95%CI = 0.53–0.66) and travel distance to receive care ≥32 km/20 mi (OR = 0.80, 95%CI = 0.69–0.92) were independently protective. SES was inversely associated with location ≥80 km/50 mi from a high-volume hospital, ranging from 6.3% (high-SES) to 33.0% (low-SES) ($p < 0.0001$). White patients were significantly more likely to travel ≥32 km/20 mi to receive care (21.8%) compared to Blacks (14.4%), Hispanics (15.9%), and Asian/Pacific Islanders (15.5%) ($p < 0.0001$).

Conclusion. Geographic proximity to a high-volume hospital and travel distance to receive treatment are independently associated with NCCN guideline adherent care for advanced-stage ovarian cancer. Geographic barriers to standard ovarian cancer treatment disproportionately affect racial minorities and women of low-SES.

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Introduction

In the United States, more than 22,000 new cases of ovarian cancer are diagnosed annually, with over 14,000 disease-related deaths [1]. Recently, adherence to the National Comprehensive Cancer Network (NCCN) treatment guidelines for ovarian cancer has been validated as correlating with improved disease-specific survival and suggested as a viable process measure of quality cancer care [2]. Improving adherence to evidence-based processes that improve survival has been championed as a key requirement for improving the quality of ovarian cancer care [3]. Race, poverty level, and insurance status have been identified as independent predictors of both an increased likelihood of non-standard treatment and worse survival [4–9].

The U.S. Department of Health and Human Services has targeted disparities in access to health care as the centerpiece of the Healthy People 2020 campaign [10]. For ovarian cancer, perhaps more so than any other gynecologic malignancy, improving survival outcomes for all segments of the population hinges upon universal access to expert care and the administration of effective contemporary treatment programs [11–15]. While racial minorities and the socioeconomically disadvantaged are confronted with multiple barriers to appropriate care, the potential contribution of geography to disparities in ovarian cancer treatment has not been widely explored. The objective of the current study was to determine the impact of geographic location on adherence to NCCN treatment guidelines for advanced-stage ovarian cancer care in relation to race and socioeconomic status (SES).

Methods

The study design was a retrospective population-based analysis of the effect of geographic variation on adherence to NCCN guidelines for the treatment of advanced-stage invasive epithelial ovarian cancer reported to the California Cancer Registry using generalized additive models (GAMs), with simultaneous smoothing of location and adjustment for known confounders [16,17]. The study received exempt status by the Institutional Review Board of the University of California, Irvine (HS#2011-8317). Registry case reporting is estimated to be 99% for the entire state of California, with follow-up completion rates exceeding 95% [18]. The International Classification of Disease Codes for Oncology based on the World Health Organization's criteria was used for tumor location and histology. Cases were identified using ovarian Surveillance, Epidemiology, and End Results (SEER) primary site code (C569).

The initial study population included women who were age ≥ 18 years at diagnosis of a first or only invasive epithelial ovarian cancer. A total of 21,044 incident cases were identified during the time period 1/1/96–12/31/06. We sequentially excluded: 101 borderline tumors, 165 of non-epithelial histology, 246 cases that had missing ICD-O-2 morphology code, 742 cases prepared from autopsy or death certificate only, 1410 with incomplete clinical information, 78 with incomplete hospital information or location outside of California, and 98 with missing census tract information. Among the remaining 18,204 cases of all stages, 11,770 patients diagnosed with the International Federation of Gynecology and Obstetrics (FIGO) stage IIIC/IV disease were selected as the study population and represent a subset of a prior analysis investigating predictors of access to high-volume providers [11].

The primary analysis was the effect of geographic variation on adherence to NCCN treatment guidelines for stage IIIC/IV epithelial ovarian cancer based on recommendations for surgery and chemotherapy according to the time period of diagnosis [19–23]. A minimum of oophorectomy (with or without hysterectomy) and omentectomy was considered adherent surgical care, and either initial surgery or chemotherapy was characterized as appropriate. Administration of multiagent chemotherapy was characterized as adherent care. Dichotomous variables, adherence or non-adherence, were created for the overall treatment program.

The GAM estimates the log odds of NCCN guideline treatment adherence throughout California by applying a bivariate smooth of the latitude and longitude of participants' location, represented by the centroid of the address census block. A locally weighted regression smoother (loess) was used in the analyses. The loess smoother predicts the log odds by fitting a regression to data points closest to the prediction point and weighting the data points with a tri-cube function of their distance from the prediction point [24]. The number of data points used for smoothing was determined by minimizing Akaike's Information Criterion. An evenly spaced grid of prediction points approximately 5 km apart that extended across the latitude and longitude coordinates of participants' locations throughout California was generated, resulting in a grid of over 13,000 prediction points. At each point on the grid the log odds and odds ratios were calculated, with the study area serving as the referent group; the log odds at each point was divided by the log odds from a reduced model which did not include the smooth of latitude and longitude [16,17].

GAMs provide a useful framework for hypothesis testing [25]. We used permutation tests to test the null hypothesis that the odds of adherence to NCCN guidelines was not dependent on the geographic location of subjects. Residential locations were permuted 999 times while preserving participants' outcome status and covariates. For each permutation, the GAM was refit and a global deviance statistic was computed. If the global statistic indicated that residential location was a significant predictor of the outcome ($p < 0.05$), point-wise departures from the null hypothesis using the same set of permutations were evaluated. Areas of significantly increased or decreased odds were defined as points ranking in the extreme 2.5% of the distribution of permuted odds ratios at each point. Spatial analyses were conducted in the R Package (version 2.12.02; Vienna, Austria) using the GAM and MapGam packages. Odds ratios were mapped in ArcMap (version 10.0, ESRI; Redlands, CA) using a continuous color scheme (dark red to dark blue) and a constant scale range. Areas of significantly elevated or lowered odds were mapped using black contour bands.

Without the bivariate smooth term, the GAM reduces to an ordinary logistic regression. The model included age at diagnosis as a continuous variable, tumor characteristics (FIGO stage, grade, histology and tumor size), insurance type, race, and SES. Insurance type was grouped into 6 categories: Managed Care (managed care, HMO, PPO, other private insurance), Medicare, Medicaid, Other Insurance (military, county-funded), Not Insured (self-pay), and Unknown. SES was classified according to increasing quintile of Yost score: lowest (SES-1), low-middle (SES-2), middle (SES-3), high-middle (SES-4) and highest (SES-5) [18]. The Yost score is an index of SES level based on a principal components analysis of variables at the census block-level and includes education, household income, proportion below 200% poverty level, house value, rent, percent employed, and percent with blue-collar employment [26]. In addition, the model included a variable to indicate if the hospital for each subject was a high-volume hospital (HVH) or a low-volume hospital (LVH). Hospital volume was calculated based on the average annual number of all ovarian cancer cases (stages I–IV) that were admitted in that hospital. Hospitals with ≥20 cases per year were classified as HVH, and hospitals with <20 cases per year were considered low-volume [12–15]. Lastly, the model included variables for distance between each subject and the treating hospital, as well as distance to the closest HVH. Distances were calculated using ArcMap (version 10.0, ESRI; Redlands, CA) and categorized by quintiles: distance to care (<5 km/3 mi; 5–9 km/3–5 mi; 10–16 km/6–9 mi; 17–31 km/10–19 mi; ≥32 km/20 mi) and distance to closest HVH (<9 km/5 mi; 9–17 km/5–10 mi; 18–33 km/11–20 mi; 34–79 km/21–49 mi; ≥80 km/50 mi).

Secondary analyses investigated disparities across racial and SES classifications associated with geographic characteristics