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Missing information in statewide and national cancer databases: Correlation with health risk factors, geographic disparities, and outcomes☆

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ABSTRACT

Objective. The objectives of this study were to analyze factors associated with outcomes and missing data in women with epithelial ovarian cancer using institutional, state and national databases.

Methods. Data were abstracted from the University of Virginia cancer registry, Virginia Department of Health (VDH) database, and Surveillance, Epidemiology, and End Results (SEER) Program and analyzed for correlations with demographics, cancer characteristics, and outcomes. Statewide spatial associations between health risk factors such as smoking, obesity, and missing grade/stage were evaluated using bivariate LiSA in Geoda.

Results. There were 524 institutional, 3544 VDH, and 44,464 SEER cases of epithelial ovarian cancer. Institutional cases were younger, most often of white race, had increased grade 1, and decreased unknown grade and stage (all $p < 0.001$). Significant predictors of unknown grade were non-white race, older age, no surgery, unknown stage/stage IV, and unknown histology/adenocarcinoma. Unknown grade correlated with a significant survival disadvantage. Missing stage and grade correlated with county-level obesity and smoking, as rural regions in Southwest and Southside Virginia had high rates of health risk factors and missing stage/grade compared to urban, affluent regions in Northern Virginia.

Conclusions. Over a third of nationally reported cases have an unknown grade and 10–20% have an unknown stage which correlates with the worst survival. Predictors of unknown grade include insurance, age, race, smoking status, obesity, and rural setting. Missing data may represent geographical differences or disparities in cancer care available as significantly fewer cases had an unknown grade/stage at a tertiary academic medical center compared to VDH and SEER.

1. Introduction

Ovarian cancer is the leading cause of gynecologic cancer death and the fifth-leading cause of cancer death overall for women in the United States [1]. In 2018 there will be an estimated 22,240 new cases of ovarian cancer with an expected 14,070 deaths from ovarian cancer [1]. Pathologic grade is known to be one of the strongest independent predictors of disease outcomes as low grade serous ovarian carcinomas occur in younger women and have better survival than their high grade serous counterparts [2–5]. Because of this, ovarian cancer is increasingly thought of as a two-tier binary system, with low and high grade serous ovarian carcinomas appearing to develop along distinct pathways [6–9]. This highlights the important prognostic role of histopathologic grade in patient outcomes which is likely secondary to the divergent molecular makeup of low and high grade serous carcinomas [9–13]. Low grade ovarian tumors represent up to 10% of all serous ovarian cancers and have higher rates of favorable histologies, with higher rates of endometrioid histology and lower rates of clear cell histology [14–16]. Low grade tumors are also more likely to have mucinous histology which is prognostically unfavorable, but current data suggest this is only relevant in late-stage disease [14–16]. Low grade ovarian carcinomas are often associated with somatic mutations in *BRAF* and *KRAS* with a higher expression of ER, PR, and E-cadherin, contrasting with high grade ovarian carcinomas which tend to be associated with more deleterious germline mutations (e.g. *BRCA1*, *BRCA2*) and different somatic mutations such as *p53*, *p16*, *BCL-2*, *HER-2/neu*, among others [17–25].

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Given the prognostic importance of histopathologic grade in ovarian carcinoma and its role in therapeutic decision-making, particular attention has been paid to grading systems over the past few decades. While individual classification systems have been debated, it is generally accepted that distinguishing between low grade and high grade ovarian epithelial carcinomas is essential for optimal treatment and counseling. However, national databases have alarmingly high rates of missing grade, as well as missing stage, reliable residual disease data, and other variables. This is problematic not only because of the therapeutic consequences of having a large proportion of cases go without histopathologic grading, but also because it potentially skews large-scale database analyses that rely on grade as a prognostic variable.

Virginia varies widely in socioeconomic makeup as the Southwest and Southside regions are rural and less affluent compared to Northern Virginia which is very urban and one of the most affluent regions in the country. Due to this variation, special emphasis was placed on evaluation of geographic correlation of missing stage/grade data with behavioral risk factors such as smoking and obesity throughout the Commonwealth of Virginia.

The objectives of this study were to assess ovarian cancer patients at multiple levels (institutional, state, and national) and to analyze differences in outcomes and patient characteristics based on grade. Secondary objectives were to compare the institutional, state, and national data and to evaluate for factors associated with a missing clinical stage and histopathologic grade.

2. Methods

Institutional review board approval was obtained before data (2006–2013) were abstracted from the University of Virginia's (UVA) cancer registry, the Virginia Department of Health (VDH) and the Surveillance, Epidemiology, and End Results Program (SEER). The UVA registry data were supplemented as necessary with chart review and these cases were also excluded out of the state registry data set. Cases were limited to epithelial ovarian cancer. For all three data sources, histologic type and behavior codes (ICD-O-3) were used to classify the cancer into histology groupings.

The association between predictors and data source was first statistically tested using non-parametric tests (Kruskal Wallis) for continuous predictors and Chi-square tests for categorical predictors. Then, association with missing grade (Y/N) was assessed by logistic regression. A comparison of trends between missing grade strata for overall survival/recurrence was next conducted by Cox Proportional Hazards. In addition, the association between overall survival and recurrence with grade category was examined by comparing Kaplan-Meier Survival Curve trends. Statistical difference in trends was tested using log-rank tests.

Random effects logistic regressions were next used to examine the association between obesity prevalence, smoking, and health risk factor score (definitions in next paragraph) with missing grade, stage, and grade I-II. The random intercept term was made to vary by county and made to assume exponential spatial covariance structure. No covariates were adjusted for, and Proc GLIMMIX in SAS was used. The models were fit using categorical indicators based on quartiles and also linear trend where the county rates standardized by interquartile rates was used instead of the original rates in order to enable effect comparison across measures.

Obesity prevalence at the county level was derived from estimates from the Behavioral Risk Factor Surveillance System (BRFSS) data set, a state surveillance survey on health outcomes conducted by the CDC [26]. Methods for estimating prevalence in Virginia are based on using adjusted BMI self-report to calculate individual obesity (BMI ≥ 30 kg/m^2) and then deriving areal estimates by fitting best predictive small area models [27]. The average obesity prevalence was calculated by taking the mean from 2006 to 2011. Female current smoking prevalence at the county level was calculated using the Institute for Health Metrics and Evaluation data from 2006 to 2012. Estimates were used from self-reported data in the BRFSS [28]. The average smoking rate was calculated by taking the mean from 2006 to 2012. A health risk factor score at the county level based on 2010 county health Virginia data available from the Robert Wood Johnson foundation was used. The health risk factor is based on a composite score weighted 30% on health behavior metrics (tobacco use, diet and exercise, alcohol and drug use, sexual activity), 20% clinical care (access to care, quality of care), 40% socioeconomic factors (education, employment, income, family and social support), and 10% physical environment (air and water quality, housing and transit).

The spatial association between smoothed missing stage, missing grade, and grade I, II vs female obesity and female smoking prevalence at a geographical level was furthermore investigated using bivariate Local Indicators of Spatial Associations (LiSA) [29]. This technique

Table 1
Clinicopathologic characteristics of ovarian cancer cases, stratified by data source.

Variable	UVA (n = 524)	VDH (n = 3544)	SEER (n = 44,464)	p value
Mean age in years (std dev.)	61.5 (13.4)	64.2 (14.8)	63.6 (14.8)	p < 0.001[a]
Race				p < 0.001[b]
White	472 (90.1)	2871 (81.0)	37,088 (83.4)	
Black	42 (8.0)	478 (13.5)	3524 (7.9)	
Other/NOS/unknown	10 (1.9)	195 (5.5)	3852 (8.7)	
Insurance				p < 0.001[b]
Medicare/private	478 (91.2)	2801 (79.0)	30,940 (69.6)	
Medicaid	19 (3.6)	86 (2.4)	4510 (10.1)	
Uninsured/self pay	23 (4.4)	155 (4.4)	1574 (3.5)	
Other/unknown	4 (0.8)	502 (14.2)	7440 (16.7)	
Histology				p < 0.001[b]
Adenocarcinoma	50 (9.5)	497 (14.0)	5480 (12.3)	
Carcinoma	18 (3.4)	239 (6.7)	3591 (8.1)	
Carcinosarcoma	14 (2.7)	78 (2.2)	1290 (2.9)	
Clear cell	41 (7.8)	190 (5.4)	2272 (5.1)	
Endometrioid	53 (10.1)	316 (8.9)	4161 (9.4)	
Mixed	24 (4.6)	130 (3.7)	2021 (4.6)	
Mucinous	25 (4.8)	184 (5.2)	2419 (5.4)	
Neuroendocrine	3 (0.6)	18 (0.5)	225 (0.5)	
Papillary serous	286 (54.6)	1561 (44.1)	19,855 (44.7)	
Squamous NOS	2 (0.4)	17 (0.5)	241 (0.5)	
Transitional/Brenner	5 (1.0)	18 (0.5)	205 (0.5)	
Unknown	3 (0.6)	296 (8.4)	2694 (6.1)	
Grade				p < 0.001[b]
1	54 (10.3)	273(7.7)	2803 (6.3)	
2	61 (11.6)	421 (11.9)	4695 (10.6)	
3/4	284 (54.2)	1625 (45.9)	21,124 (47.5)	
Unknown/missing	125 (23.9)	1225 (34.6)	15,842 (35.6)	
Stage				p < 0.001[b]
I	90 (17.2)	670 (18.9)	8668 (19.5)	
II	58 (11.1)	254 (7.2)	3303 (7.4)	
III	265 (50.6)	1144 (32.3)	14,882 (33.5)	
IV	85 (16.2)	797 (22.5)	11,803 (26.6)	
Unknown/missing	26 (5.0)	679 (19.2)	5808 (13.1)	
Residual disease				p < 0.001[b,c]
R = 0	76 (14.5)	503 (29.1)	7076 (32.1)	
R ≤ 1	37 (7.1)	102 (5.9)	1494 (6.8)	
R > 1	60 (11.5)	74 (4.3)	910 (4.1)	
No surgery	50 (9.5)	499 (28.9)	6673 (30.3)	
Size not known	0 (0)	208 (12.0)	1892 (8.6)	
Unknown	301 (57.4)	342(19.8)	4015 (18.2)	
Neoadjuvant chemotherapy[d]				p < 0.001[b]
Yes	35 (13.7)	112 (6.5)	1247 (5.7)	
No/unknown	220 (86.3)	1616 (93.5)	20,813 (94.4)	

[a] p-Values for Kruskal-Wallis test.
[b] p-Values for Chi-square tests.
[c] Evaluated only on non-missing values.
[d] 2010–2013 only.

calculates a measure of association between one variable and another variable's average values in neighboring geographical units (chosen as contiguous regions) determined by a weighting matrix. Output from the Geoda software includes a scatter plot showing the correlation between standardized values at a location of outcome (missing stage, missing grade, and grade I, II) vs the standardized exposure mean of the surrounding regions. Additional plots include cluster map showing presence of high outcome with high exposure, color coded as red, and equivalent hi-lo, lo-hi, and lo-lo, color coded as blue, which are selected according to individual tests of significance. $p < 0.01$ was used to indicate significance. The regression slope between local statistics at each county is equivalent to Moran's I spatial autocorrelation statistic. The smoothed values for missing stage, grade, and grade I, II was calculated by aggregating the latitude/longitude points by county and then using a spatial empirical Bayes technique (available in Geoda) which calculates smoothed values based not only on local and rates of surrounding neighbors.

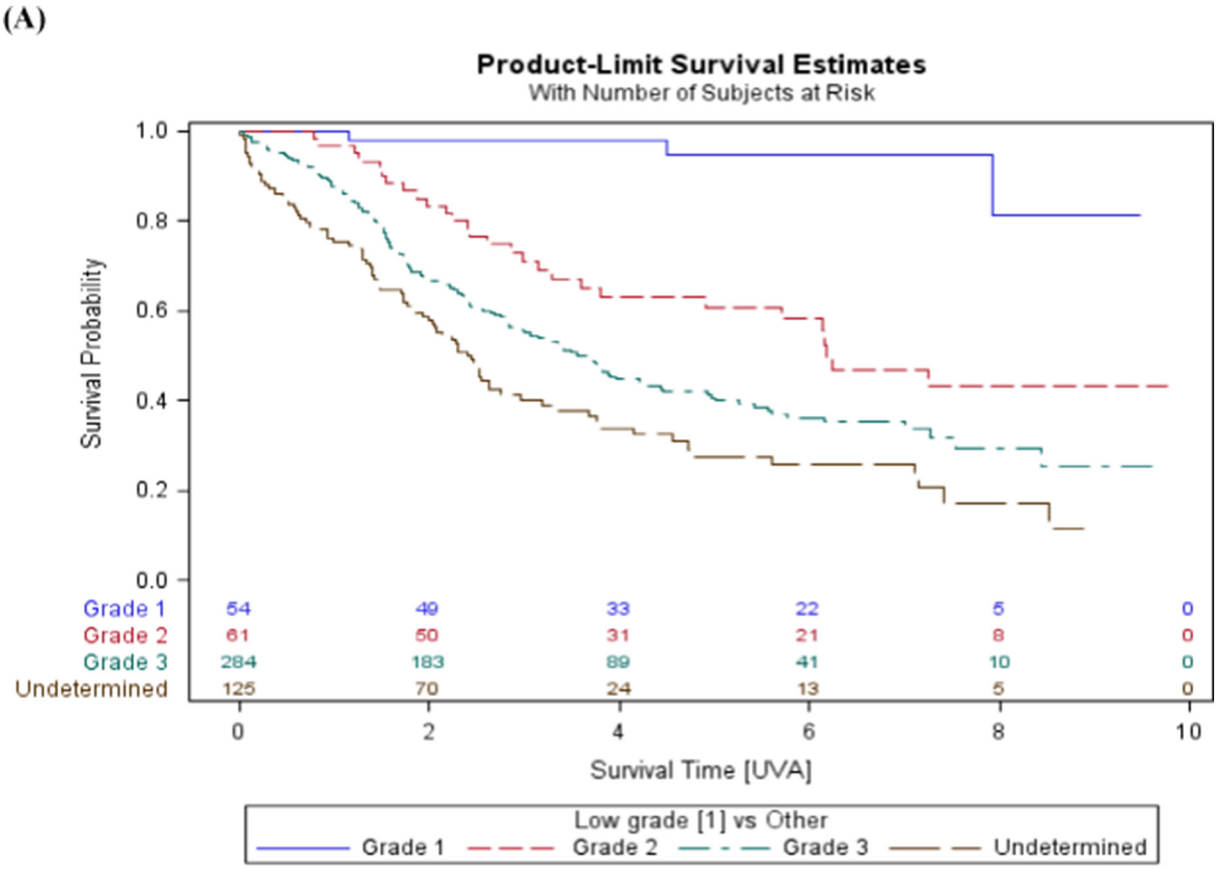
3. Results

There were 524 institutional cases, 3544 VDH cases, and 44,464 SEER cases of epithelial ovarian cancer. The institutional cases were younger, more often of white race, had increased grade 1, decreased unknown grade, and decreased unknown stage ($p < 0.001$, Table 1). Missing data are rampant across the three data sets. Pathologic grade was missing/unknown in 23.9, 34.6, 35.6% (UVA, VDH, SEER, respectively) of cases, stage was missing/unknown in 5.0, 19.2, 13.1% of cases, and residual disease was missing in 57.4, 19.8, 18.2% of cases. In all three data sets, women with grade 1 tumors were a decade younger (mean age UVA 51.6 vs 62.6, VDH 54.6 vs 65.0, SEER

Table 2
Odds ratio associations between clinicopathologic characteristics of ovarian cancer cases and missing grade, stratified by data source.

Outcome: Missing grade	UVA cases (N = 524)	VDH cases (N = 3544)	SEER cases (N = 44,464)
	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Age			
Q1 (9–51)	0.18 (0.09, 0.36)	0.22 (0.19, 0.28)	0.24 (0.23, 0.26)
Q2 (52–62)	0.30 (0.17, 0.53)	0.23 (0.19, 0.28)	0.25 (0.24, 0.26)
Q3 (63–73)	0.42 (0.25, 0.72)	0.36 (0.30, 0.43)	0.35 (0.33, 0.37)
Q4 (74+)	Ref	Ref	Ref
Linear trend (10 year increase)	1.59 (1.34, 1.90)	1.59 (1.51, 1.68)	1.51 (1.49, 1.53)
Race			
Black	3.00 (1.57, 5.72)	1.30 (1.07, 1.59)	1.73 (1.61, 1.85)
Other/NOS/unknown	2.42 (0.67, 8.73)	0.78 (0.57, 1.08)	0.80 (0.74, 0.86)
White	Ref	Ref	Ref
Insurance			
Medicaid	1.49 (0.55, 4.01)	1.15 (0.73, 1.82)	1.58 (1.48, 1.68)
Other/unknown	1.08 (0.11, 10.45)	4.58 (3.74, 5.60)	1.90 (1.81, 2.00)
Self-pay/uninsured	0.90 (0.33, 2.47)	0.83 (0.57, 1.20)	1.27 (1.15, 1.42)
Medicare/private	Ref	Ref	Ref
Histology			
Adenocarcinoma	4.04 (2.17, 7.52)	8.41 (6.71, 10.55)	9.41 (8.78, 10.08)
Endometrioid	0.29 (0.11, 0.80)	0.36 (0.24, 0.54)	0.42 (0.38, 0.47)
Mucinous	1.29 (0.52, 3.20)	1.22 (0.86, 1.74)	1.53 (1.40, 1.67)
Clear cell	N/A	N/A	N/A
Carcinosarcoma	N/A	N/A	N/A
Other	1.32 (0.68, 2.54)	2.53 (2.02, 3.18)	3.24 (3.05, 3.43)
Unknown	22 (0.72, 692)	428 (123, >999)	138 (107, 178)
Papillary serous	Ref	Ref	Ref
Stage			
Unknown	5.08 (1.93, 13.39)	11.83 (9.04, 15.47)	13.64 (12.55, 14.75)
IV	3.95 (1.90, 8.20)	6.59 (5.10, 8.53)	4.79 (4.49, 5.12)
III	1.77 (0.92, 3.41)	1.50 (1.16, 1.95)	1.40 (1.30, 1.49)
II	0.56 (0.19, 1.66)	0.80 (0.52, 1.24)	1.01 (0.91, 1.12)
I	Ref	Ref	Ref
Residual disease			
No residual tumor	0.08 (0.03, 0.19)	0.07 (0.05, 0.10)	0.09 (0.08, 0.10)
Residual tumor < 1 cm	0.12 (0.05, 0.34)	0.11 (0.07, 0.20)	0.09 (0.07, 0.10)
Residual tumor > 1 cm	0.12 (0.05, 0.28)	0.15 (0.08, 0.26)	0.11 (0.09, 0.13)
No surgery	Ref	Ref	Ref
Neo-adjuvant chemotherapy			
No/unknown	1.21 (0.52, 2.81)	1.25 (0.83, 1.90)	1.57 (1.38, 1.79)
Yes	Ref	Ref	Ref
Outcome: Survival	**UVA cases (N = 524)**	**VDH cases (N = 3544)**	**SEER cases (N = 44,464)**
	Hazard ratio (95% CI)	Hazard ratio	Hazard ratio (95% CI)
Time until recurrence			
Missing grade	2.05 (1.58, 2.66)	N/A	N/A
Non-missing grade	Ref		
Survival time			
Missing grade	1.94 (1.50, 2.50)	N/A	2.64 (2.57, 2.71)
Non-missing grade	Ref		Ref

Notes: 1. Residual disease: Analysis restricted to cases diagnosed in 2010 or later and excluding unknown and size not stated residual disease (UVA N = 222;VDH N = 1178; SEER N = 16,153). 2. Neo-adjuvant chemotherapy: Analysis restricted to cases diagnosed in 2010 or later (UVA N = 255; VDH N = 1728; SEER N = 22,060). 3. Time until recurrence: Cases with missing time until recurrence N = 80 (15.3% of total). 4. Survival time: Cases with missing survival time (VDH N = 38, 1.1% of total; SEER N = 649, 1.5% of total).



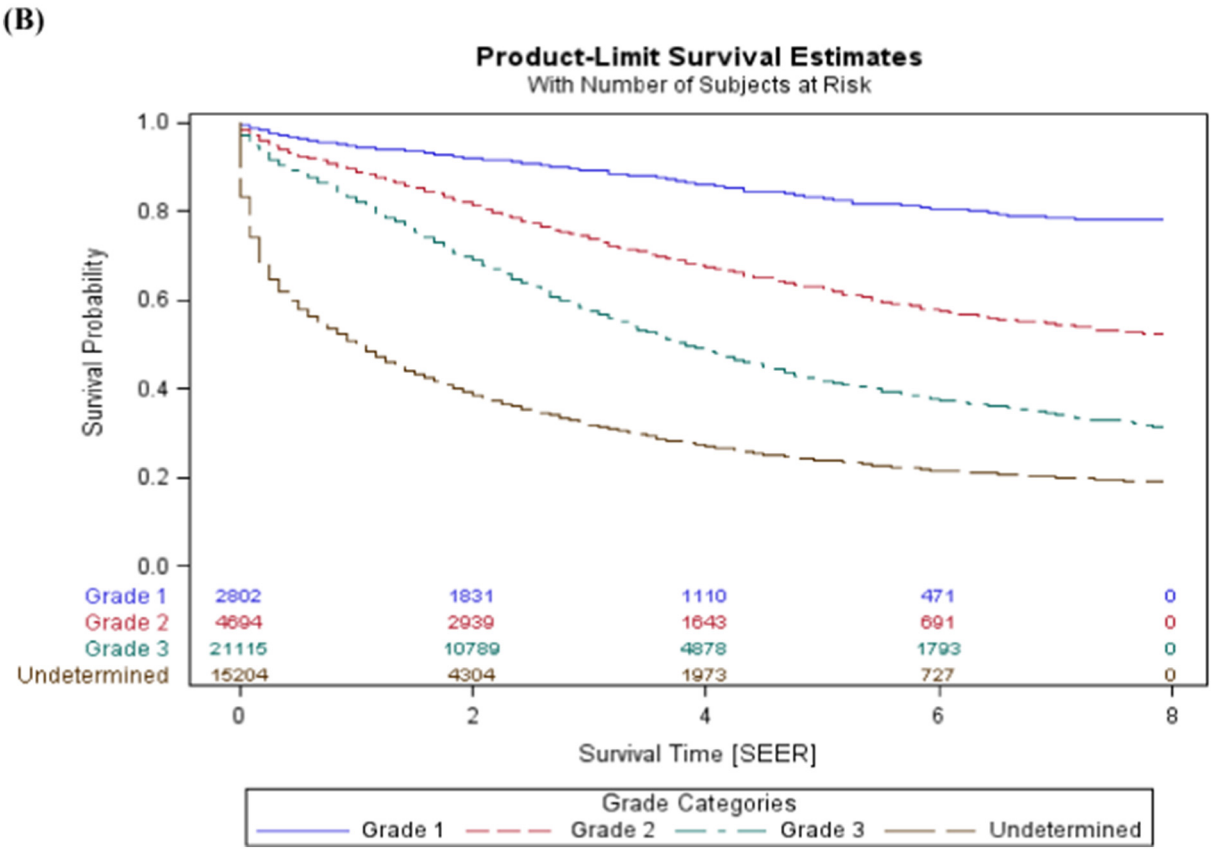


Fig. 1. Kaplan-Meier curves showing overall survival stratified by grade in the (A) UVA sample and (B) SEER sample.

Table 3
Logistic regression analysis of associations of obesity, smoking, and health risk factor score with missing grade and stage.

	Missing stage	Missing grade	Grade I, II vs III, IV
Obesity %			
Q1 (≤35%)	0.79 (0.56, 1.11)	0.58 (0.45, 0.75)	1.11 (0.82, 1.49)
Q2 (35% < −37.55%)	0.85 (0.59, 1.22)	0.72 (0.55, 0.95)	0.96 (0.69, 1.35)
Q3 (37.55% < −41.48%)	1.02 (0.72, 1.45)	0.71 (0.54, 0.93)	1.12 (0.80, 1.58)
Q4 (41.48%<)	Ref	Ref	Ref
Linear trend	1.22 (1.06, 1.40)	1.17 (1.05, 1.32)	1.06 (0.97, 1.16)
Current smoking %			
Q1 (≤19.48%)	0.66 (0.46, 0.94)	0.92 (0.69, 1.24)	1.03 (0.77, 1.39)
Q2 (19.49% < −22.28%)	0.62 (0.44, 0.88)	1.15 (0.86, 1.53)	0.95 (0.69, 1.31)
Q3 (22.28% < −24.26%)	0.68 (0.47, 0.97)	1.16 (0.86, 1.56)	0.88 (0.62, 1.26)
Q4 (24.26%<)	Ref	Ref	Ref
Linear trend	1.18 (1.03, 1.40)	1.08 (0.96, 1.21)	1.06 (0.98, 1.15)
Health factors score			
Q1 (≤ − 0.32) low risk	0.68 (0.52, 0.90)	0.68 (0.54, 0.85)	0.88 (0.69, 1.13)
Q2 (−0.32 < −0.02)	0.63 (0.44, 0.88)	0.67 (0.51, 0.89)	0.79 (0.58, 1.09)
Q3 (0.02 < −0.33)	0.79 (0.55, 1.12)	0.80 (0.60, 1.07)	0.81 (0.57, 1.16)
Q4 (0.33<) highest risk	Ref	Ref	Ref
Linear trend	1.22 (1.06, 1.41)	1.20 (1.06, 1.34)	1.11 (1.0, 1.24)

Notes: 1. Health factors: two entities omitted due to missing health factors ranking (Highland County and Lexington City), making N = 134 cities/counties.

54.0 vs 64.2; $p < 0.001$), most often early stage I (UVA 53.7%, VDH 61.2%, SEER 68.2%; $p < 0.001$), and most often had endometrioid histology as opposed to papillary serous compared to other grades (UVA 67.5% vs 8.7%, VDH 51.4% vs 13.1%, SEER 66.6% vs 13.3%; $p < 0.001$).

By assessing odds ratios significance based on 95% confidence intervals (Table 2), predictors of greater missing grade risk across all three datasets included black vs white (OR 1.30–3.00), having an unknown histology (OR 22–428) or adenocarcinoma (OR 4.04–9.41) vs papillary serous, and having an unknown stage (OR 5.08–13.64) or stage IV (OR 6.59–3.95) vs stage I. Conversely, younger age categories were less likely to have missing grade compared to older (74+, OR 0.18–0.42) across all three datasets. Compared to papillary serous (reference), endometrioid (OR 0.29–0.42) cases were less likely to have missing grade. Compared to no surgery, having no residual tumor or a residual tumor recorded was less likely to have missing grade (OR 0.08–0.15). Missing grade was a significant negative prognostic predictor in the cox PH model (HR = 2.05 UVA recurrence, HR = 1.94 UVA and HR = 2.64 SEER overall survival). When comparing between all grade categories, overall survival was worst in the missing grade group compared to other grade classifications (log rank test $p < 0.001$) (Fig. 1A and B).

County level obesity, current smoking, and health factors were found to associate with missing stage, with increasing prevalence and risk resulting in higher odds of missing stage. Obesity prevalence and health factors were associated with missing grade, with increasing obesity score associated with greater odds of having a missing grade, but not low grade (I, II) histology (Table 3).

Missing stage was found to correlate with obesity and smoking when overlaid with county-level population data in the Commonwealth of Virginia. There was a hotspot in the rural Southside region with high rates of obesity and missing stage (Supplemental Fig. 1A) and a region in Southwest Virginia with high rates of smoking and missing stage (Supplemental Fig. 1B). Northern Virginia, a very urban setting, had very low rates of missing stage and both obesity and smoking (Supplemental Fig. 1A–B). Missing grade followed a similar pattern, with high rates of obesity/smoking and missing grade in the rural Southside/Southwest regions and low rates of risk factors and missing grade in the urban areas of Northern Virginia (Fig. 2A–B). When plotting missing stage and grade rates across the state, Southwest Virginia was found to have high rates of both missing grade and stage, and Northern Virginia was found to have low rates of both missing grade and stage (Fig. 3A–B).

4. Discussion

Patients with low grade ovarian cancer are younger and have improved survival over patients with high grade ovarian cancer. Despite the independent effect of grade on prognosis, over a third of nationally reported epithelial ovarian cancer cases have an unknown grade. Cases with a missing grade have the worst survival of any other grade category, and predictors of missing grade status include insurance, age, race, smoking status, obesity, rural setting, and more recent year of diagnosis (possibly due to increases in neoadjuvant chemotherapy). When compared to a national database (SEER) and statewide database (VDH), a tertiary academic medical center (University of Virginia) had a lower percentage of cases with a missing grade.

This analysis highlights potential disparities in healthcare delivery within our subspecialty. At all levels, non-white patients were less likely to be fully staged or be assigned a histopathologic grade. Other studies have demonstrated racial disparities in outcomes in our subspecialty, consistently showing a significant survival disadvantage associated with black race, low socioeconomic status, and treatment by low-volume providers which is often associated with nonadherence to treatment guidelines [30–32]. The current analysis showed a disadvantage with respect to missing grade for these same factors. Across all data sets, black versus white race had increased missing grade. Within Virginia, poorer and more rural regions (i.e. Southwest Virginia and Southside) had higher rates of missing grade and stage when compared to affluent, highly-educated regions of the state (i.e. Northern Virginia). This geographic disparity potentially represents a distance-related disadvantage in access to tertiary care with respect to distance traveled, socioeconomic status, and lack of access to routine care in rural parts of the state. These geographic socioeconomic factors were compounded by obesity, smoking, and health risk factor score which were also found to be associated with missing grade and stage.

Tertiary care academic medical centers are most often found in urban areas and have a higher case volume, higher concentration of subspecialty-trained providers, and a higher likelihood of clinician/pathologist interaction for the continuum of care. Other studies have shown that tertiary care academic medical centers have improved outcomes due to increased availability of high volume providers who can achieve optimal tumor debulking, which is associated with a better prognosis in women with ovarian cancer [33–36]. Further, a recent analysis at another tertiary care center suggests that treatment at a high volume center remedies racial disparities in outcomes [37]. The current analysis also suggests that treating facility type influences reported results and possibly outcomes. For example, the percentage of cases with a missing histopathologic grade at a tertiary care academic medical center was significantly lower than both national and state-wide databases which could be due to a multitude of factors.

Access to pathologists who can render accurate and consistent grade classifications and histotypes may be one factor contributing to improved outcomes at tertiary care academic medical centers, as these are both prognostically significant. There are high ovarian cancer case volumes for both clinicians and pathologists at tertiary care academic medical centers, making their clinical judgment better informed, more practiced, and highly honed. Current College of American Pathologists guidelines recommend two- or three-tier grading systems for serous, mucinous, and endometrioid histologic subtypes and do not recommend grading clear cell carcinomas and carcinosarcomas as they are typically considered high grade by default.

As national and institutional databases of cancer cases have high rates of missing grade data, studies that rely on grade are thrown into question. It cannot be safely assumed that the cases with a missing grade are evenly distributed among the other grade classes, as missing

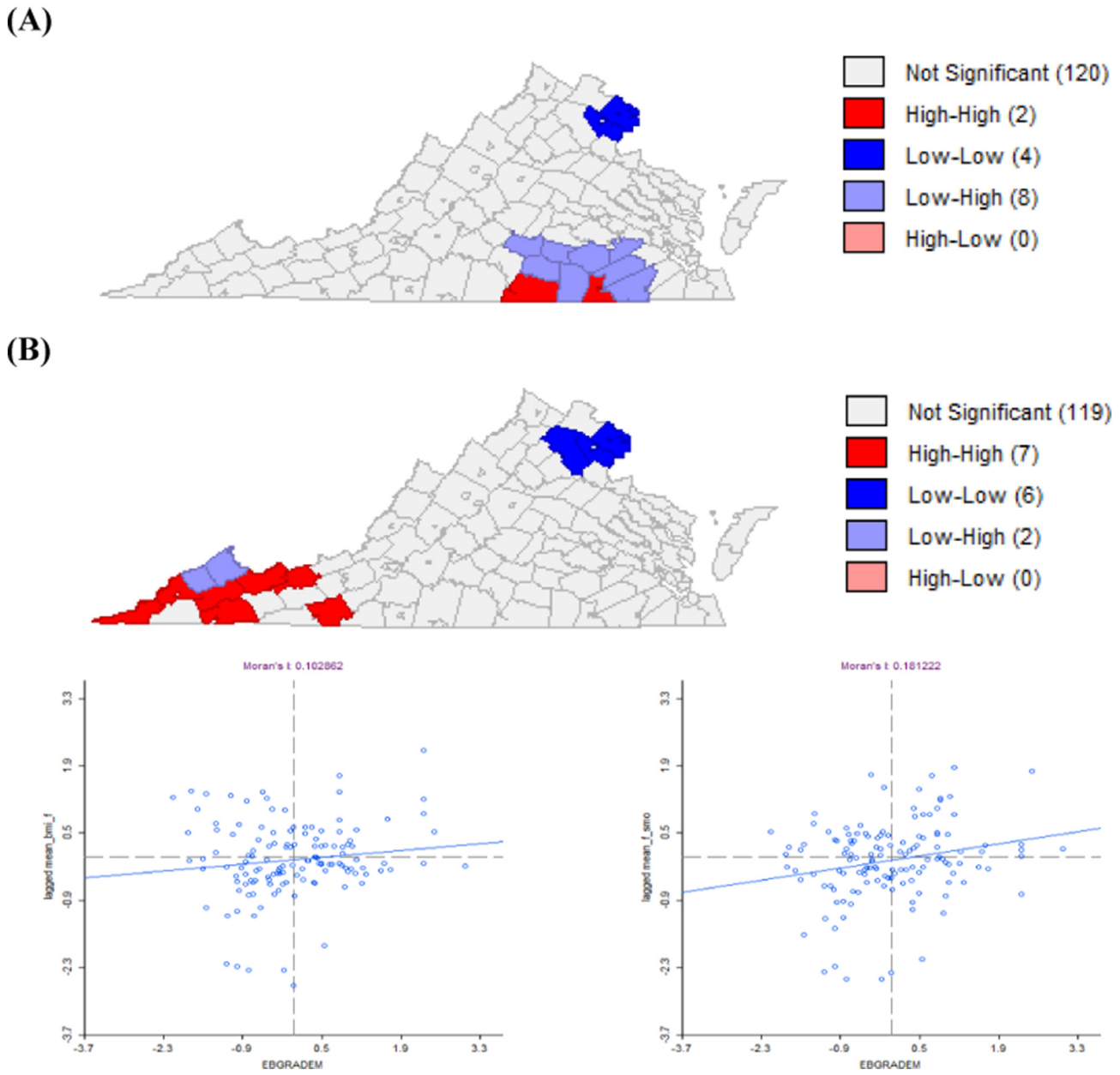


Fig. 2. Maps of Virginia showing missing grade correlated with (A) female obesity prevalence and (B) female smoking prevalence. Moran's plots are presented below. 2A: Moran's I: 0.103, p = 0.017. 2B: Moran's I: 0.181, p = 0.001.

grade was associated with the worst overall survival of any other grade category. Potentially these were women who never went to surgery or had extremely advanced disease at presentation, further highlighting why this missing data is highly problematic for large dataset studies. In the past, some have used algorithms that predict grade based on a variety of factors, but these are invariably imperfect and are not uniformly applied across the literature, leading to potentially conflicting information with respect to the role of histopathologic grade in ovarian cancer.

Taken together, the conclusions drawn from this work show that missing data are not randomly distributed. Rather, it is indicative of underlying disparities in the care provided to women in our subspecialty. This study demonstrates that health risk factors, geographic location, and race, among other things predict missing data in the care of women with ovarian cancer, and further, that these missing data are associated with poorer survival outcomes. It is important for investigators conducting database studies in the future to be mindful of missing data and report this information. It is important for us all to pay close attention to how many cases must be excluded due to missing data and question how this affects our conclusions.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.10.029.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Author contributions

Mackenzie W. Sullivan was the primary author of this work.

T. Fabian Camacho was the statistician and contributed written portions of the methods and results.

Anne Mills was consulted for advice regarding the pathologic content and direction of this work.

Susan C. Modesitt was the primary investigator of this work.

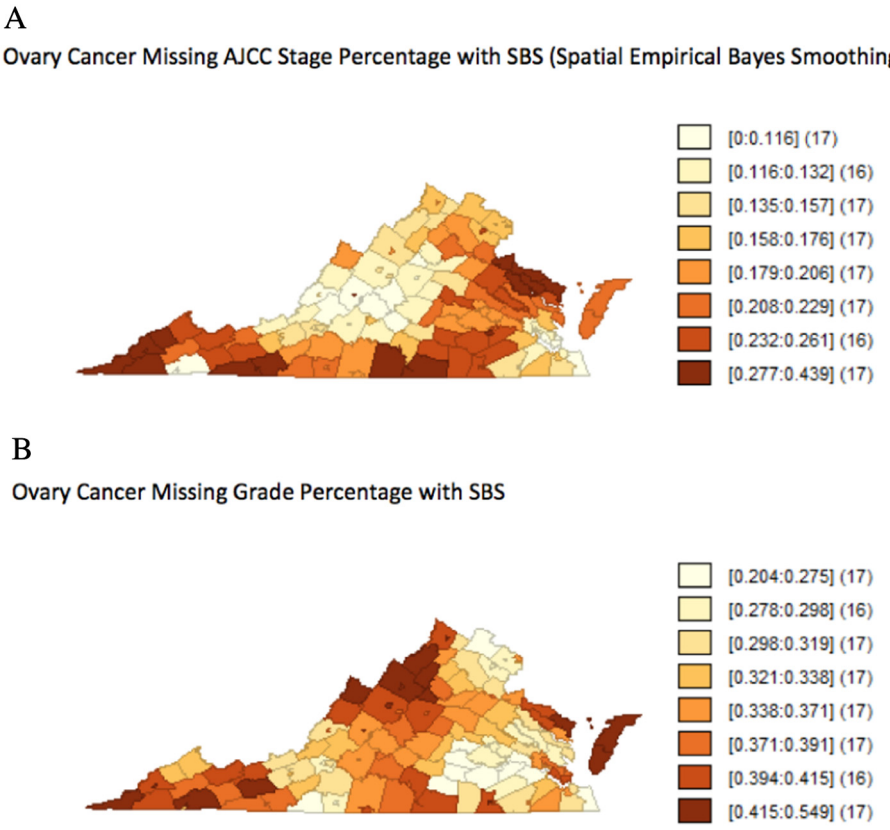


Fig. 3. Map of Virginia with (A) missing stage and (B) missing grade.

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