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Ovarian cancer in the United States: Contemporary patterns of care associated with improved survival☆,„☆☆

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Abstract

Background—Ovarian cancer (OC) requires complex multidisciplinary care with wide variations in outcome. We sought to determine the impact of institutional and process of care factors on overall survival (OS) and delivery of guideline care nationally.

Methods—This was a retrospective cohort study of primary OC diagnosed from 1998 to 2007 using the National Cancer Data Base (NCDB) capturing 80% of all U.S. cases. Patient- (demographics, comorbidities, stage/grade), process of care (adherence to guidelines) and institutional- (facility type, case volume) factors were evaluated. Primary outcomes were OS and delivery of guideline therapy. Multivariable logistic regression and Cox proportional hazards models were used for analysis.

Results—We analyzed 96,802 consecutive cases. Five-year OS was 84%, 66.3%, 32% and 15.7% for stages I, II, III and IV, respectively. The annual mean facility case volumes varied by cancer center type (range: 5.7 to 26.7), with 25% of cases spread over 65% of centers — all treating fewer than 8 cases. Overall, 56% of cases received non-guideline care. Low facility case volume and higher comorbidity index independently predicted non-guideline care; high volume centers were less likely to deliver non-guideline care (OR: 0.44, 95% CI: 0.41–0.47). Delivery of non-guideline care (OR: 1.4, 95% CI: 1.36–1.44), and higher facility case volume (OR: 0.91, 95% CI: 0.86–0.96) were both independent predictors of OS.

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Conflict of interest

The authors have no conflict of interests to report.

Conclusions—Delivery of guideline care and facility case volume are important drivers of overall survival. Most cancer centers treat very few women with OC. National efforts should focus on improved access to centers with expertise in OC and ensuring delivery of guideline care.

Keywords

Ovarian cancer; Care patterns; Volume; Survival; United States; Cancer center

Introduction

Epithelial ovarian cancer (OC) is the 5th cause of cancer death in women [1]. Advances have improved survival rates including, development of subspecialty care; improved surgical staging and adjuvant chemotherapy; improved rates of cytoreduction and use of intraperitoneal chemotherapy [2].

National Comprehensive Cancer Network (NCCN) guidelines were established to establish stage-specific standards of care [3]. Applying these guidelines is a crucial cost-effective strategy to improve outcomes, but evidence suggests poor compliance with these standards. For example, using medicare data, only 30% of ovarian cancer cases received standard therapy for advanced stage OC (defined as receiving primary surgery and 6 cycles of adjuvant chemotherapy) [4]. The Health Care Cost and Utilization Project demonstrated that 50% of women received inadequate staging: rates of debulking procedures were dependent upon physician specialty and hospital volume [5]. Harlan et al. reported similar findings for early stage disease [6]. Hospital and surgeon volume have remained consistent predictors of oncologic surgical outcomes since the pivotal report by Begg et al. [7,8] including OC [9].

The National Cancer Database (NCDB) was developed by the American College of Surgeons' (ACoS) Commission on Cancer (CoC) and the American Cancer Society (ACS) [10] to track outcomes from more than 1500 U.S. CoC-accredited programs. In the US, nearly 80% of all OC cases are captured, allowing a broad analysis to examine current care and foster recommendations for improved access, delivery and quality of care.

We sought to evaluate the patterns of OC care in the US to specifically define the influence of patient and institutional factors on overall survival (OS) including the independent relationship between volume and outcomes. We limited this analysis to invasive epithelial OC to allow more focused conclusions.

Methods

Case ascertainment and definitions

This study received exempt status from the Institutional Review Board of Washington University. Invasive epithelial OC diagnosed between January 1, 1998 and December 31, 2008 was identified from the NCDB by topography code C56.9; subjects and facilities were de-identified in the public use file (PUF). Records were included if malignant, or the first of two or more independent malignant primary tumors, and if either pathological or clinical staging was known. Histology was classified as serous, mucinous, endometrioid, clear, mixed and undifferentiated: grade was dichotomized as well/moderately differentiated vs.

poorly/undifferentiated/anaplastic. Non-epithelial and borderline tumors were excluded. We constructed an overall tumor staging variable that equals pathological staging: if missing or improperly staged (e.g. not sub-staged into A, B, C) we used the clinical staging. Stages were classified according to the International Federation of the Gynecologists and Obstetricians (FIGO) system (1988) [11], briefly defined as: I — growth limited to the ovaries; II — growth with pelvic extension; III — peritoneal implants outside of the pelvis and/or metastatic retroperitoneal nodes; IV — distant metastasis.

The annual hospital OC volume was ranked into quartiles. Zip code of residence was matched against year 2000 US census and Department of Agriculture data to estimate median household income, percentage of residents with college degrees, and continuum of rural/urban residence. Payer status was consolidated into six categories. Private insurance included fee-for-service, health maintenance organization, or independent physician association. Managed care insurance, TRICARE, and other military insurance were considered Managed Care. Medicare included Medicare, including supplemental coverage. Medicaid, Public Health Service, and other Federal programs were consolidated into Medicaid. Patients without insurance were classified as not insured/self pay, and the remainder classified as Unknown.

Statistical analysis

Descriptive statistics and chi-square tests were used to describe cases and centers. Adherence to NCCN guidelines for OC was based upon stage specific recommendations for surgical and chemotherapy treatment according to the time period of diagnosis taking into account any changes in NCCN guidelines [3]. Surgery for advanced stage was considered adherent to guidelines if it included oophorectomy with omentectomy, debulking procedures including intestinal resection, or exenteration. Early stages (FIGO I–IIIB) required examination of lymph nodes for adherent care. Chemotherapy was considered adherent if NCCN-specified delivery of multi-agent chemotherapy occurred: the NCDB captures the first cycle of chemotherapy regardless of location given, but does not include number of cycles administered so this was not considered.

Independent predictors of adherence to NCCN guidelines for ovarian cancer care were identified using multivariable logistic regression analysis. Data for the Charlson/Dayo Comorbidity Index, a covariate in the logistic regression model, were available for patients with tumors diagnosed from 2003 to 2007. Survival data were only available for 1998–2002 cases. Descriptive analyses were separated by the 2 eras of cancer diagnosis to compare changes in the two time periods in the number of cases reported by facility types using Tukey adjusted multiple comparisons of proportions [12]. Case fatality ratios and 95% confidence intervals (CIs) based on facility type and hospital volume were reported.

a) For the survival analyses, we used life table methods and log-rank pairwise comparisons for 5-year survival probability based on adherence to NCCN guidelines, annual hospital OC volume and facility type (academic/research comprehensive cancer program (ACCP), comprehensive community cancer program (CCCP), or community cancer program (CCP)) [13]. Hazard ratios (HRs) and 95% CIs were estimated from multilevel Cox regression models [14]. Overall survival risk estimates were adjusted for age at diagnosis, diagnosis

era, and tumor characteristics including tumor stage, grade, and histology type. Multilevel Cox regression model allowed adjustment for correlation of subjects within the same facility.

Graphical methods were used to assure that the statistical assumptions for the multivariable survival and logistic regression models were reasonable [12]. When the assumption of proportional hazards being constant over time was questionable, a time dependent interaction of ln(time) was added to the model which then met the necessary assumptions. Statistical significance was set to $p < 0.05$ and all analyses were performed using SAS 9.2.

Results

We identified 144,449 eligible cases and a total of 96,802 cases met study inclusion criteria, with cases evenly distributed between the two intervals of analysis (n = 49,160, 1998–2002; n = 47,642, 2003–2007). (Supplemental Fig. 1)

Overall characteristics and trends are shown in Table 1. There were minimal changes observed in the mean age or income categories between time periods. We observed shifts in payer mix: most significantly privately insured patients decreased from 19.4% to 12.9%, while managed care increased from 28.4 to 35.5% ($p < 0.001$). We observed minor changes in stage distribution, with the largest increase in unknown classification (6.8% to 10.6%, $p < 0.001$). Additional details of non-key variables are shown in Supplemental Table 1.

One-quarter of all OC patients receive treatment in very low volume centers (1–7 cases annually, Table 1). There were differences between time periods, specifically, the number of patients treated in the lowest volume centers decreased from 27% to 23.3% ($p < 0.001$). Additionally, there were minor shifts away from community cancer care programs toward academic/research cancer programs. When comparing cancer centers, the majority would be considered very low OC volume centers. Specifically, 65% of centers (n = 636) treated 1–7 cases annually; 19% (n = 248) treated between 8 and 16 cases; 9.8% (n = 125) treated 17–28 cases; 5.5% (n = 70) treated more than 28 cases. Of note, cases from low volume centers had to be excluded more often due to missing or inconsistent stage and grade elements (18% vs. 11%, $p < 0.001$).

To characterize centers more completely, we investigated the relationship between facility type and case volume (Supplemental Table 2). While community cancer programs (CCP) represented 37.6% of all reporting hospitals, they cared for only 12.3% of evaluable cases. Conversely while less than 20% of programs were classified as academic/research comprehensive cancer programs (ACCP), they cared for 43.1% of cases. The remaining 42.5% of hospitals were comprehensive community cancer programs (CCCP), treating 44.64% of cases. There was a decrease in the percent of cases seen in CCP/CCCP and a corresponding increase in cases treated in ACCP. The mean case volumes were 5.7, 15.0, and 26.7 in CCP, CCCP and ACCP, respectively. In community of non-comprehensive cancer centers, 75% of programs treated fewer than 5 patients annually (Supplemental Fig. 2).

Patients differed little with regard to comorbid conditions based on facility type (Table 2). The Charlson/Deyo Comorbidity Index was not available within NCDB until the 2003–2007 time periods. The vast majority of cases in all 3 facility types were reported as having either zero or 1 comorbid conditions, with minor differences across facility type. Cases with a Charlson/Deyo Comorbidity Index of 3 represented less than 1% of patients in all centers. Given the minor changes in other demographic factors between the two eras, we made the assumption that changes in the distribution of comorbidities were also minimal. In contrast, the distribution by age groups (all years) seen in the 3 facility types differed significantly. A greater percentage of women at CCP (non-comprehensive) was >75 years old (25.38% vs. 21.36% CCCP vs. 15.23% ACCP, $p < 0.001$), and conversely women <60 years old were more often seen in academic centers (37.66% in CCP vs. 48.44% in ACCP, $p < 0.001$) (Table 2). The rates of receiving NCCN guideline adherent care across centers varied from 30.8% to 49.1% (CCP vs. ACCP, respectively). Regarding stage and grade distribution across centers, we identified a higher proportion of stage III cancers in academic centers (48% vs. 44% vs. 38%, academic, comprehensive community and community, respectively). However, when collectively considering stages III and IV together which may be more accurate given the limitations of the database, the percentage in the 3 center types is amazingly similar at 73%. Correspondingly then, the frequency of stage I/II cases collectively is not different. There was a minimal difference in grade distribution across center types.

Overall 5-year survival was available only for the 1998–2002 cohort and was 84%, 66.3%, 32% and 15.7% for stages I, II, III and IV, respectively. Case fatality ratios (CFR) were used to compare survival by facility characteristics (Table 3). Unadjusted survival was strongly associated with facility type overall, with significantly better CFR for ACCP. Adjusting for NCCN guideline adherent care, the differences in CFR were smaller, though CFR remained significantly better in ACCP. Overall, CFR were significantly worse for low volume centers (0.66 vs. 0.58 for centers in the lowest volume quartile vs. highest quartile, respectively) (Table 3c), and the association between CFR and volume was observed across all quartiles. Importantly, the relationship between better CFR and higher volume persisted even after adjusting for adherent care: specifically even when comparing only cases that received NCCN guideline therapy, CFR was better in highest volume centers (Table 3d).

Predictors of OS are shown in Table 4. Age was an important patient specific factor that independently correlated with improved survival (adjusted HR 1.28, 95% CI 1.24–1.33 for 60–75 years old and 2.09, 95% CI 2.0–2.20, for >75 years old). Not receiving NCCN care was associated with worse OS (HR 1.40, 95% CI 1.36–1.45) and OS was best in highest volume centers (HR 0.91, 95% CI 0.86–0.96). Five-year OS ranged from 34% to 42.1% for lowest to highest facility case volume ($p < 0.001$, log-rank, Supplemental Fig. 3A). Tumor specific factors independently associated with worse OS were increasing stage and grade. Other independent factors for survival included nonwhite race and payor type. In examining the fit of the multivariable survival model, we discovered that the effects were not constant over time. This was particularly true for the effects of not receiving NCCN care where the effect was most potent closer to treatment and was more muted over time (Supplemental Fig. 3B). This was not unexpected given that the expected impact from the initial treatments would be highest closest to those initial treatments. To model these changing hazard ratios

over time we fit a multivariable model with an interaction of a time dependent effect of ln(time) with each factor. This model is shown in Supplemental Table 3 which demonstrates that the impact is minimal for other factors.

We reasoned that adherence to guidelines is multifactorial, reflecting a center's rigor with regard to process, availability of subspecialty and multidisciplinary care, and inability/refusal of some patients to tolerate standard therapy. The 2003–2007 data included comorbidity index to examine predictors of adherent care (Table 5). Many of the same factors observed to be important in OS were important for type of care, including age (particularly >75 years old, adjusted HR 2.57, 95% CI 2.43–2.71) and non-white race. While Charlson/Deyo Comorbidity Index was an important predictor of guideline care, its influence was limited to just 3.7% of cases overall (e.g. those with index scores ≥2). However, we observed strong and progressive associations between increasing case volume and likelihood of receiving guideline care, independent of age and comorbidities. The highest volume centers had an adjusted HR of 0.44 (range: 0.41–0.47) for administering non-guideline care vs. lowest volume centers. These data demonstrate that both patient and center factors are critical for the delivery of guideline care in OC.

Discussion

The strengths of this study, one of the largest patterns of care study in OC, include the use of the most comprehensive dataset reporting long-term, stage-specific cancer outcomes available. Our findings identify several opportunities for improvements that can be used to inform policy makers, payors and health-care systems. Our data also provide important insights into the design of relevant and controllable quality measures that can be used by such groups to track quality.

First, survival has increased slightly for stage II and III disease when compared to prior analyses. These results mirror the more limited SEER data comparing 1973–1997 trends [2]. Second, only 43% of cases receive NCCN guideline care, and this was independently associated with worse survival. This low rate of adherence to guidelines has not changed appreciably since earlier reports [6]. Third, facility case volume is an important independent predictor for receiving guideline adherent care. Most centers treat fewer than 8 cases annually: non-comprehensive community programs represent 37.6% of all centers but care for only 12.3% of cases, and 50% of CCCP have annual case volumes of less than 12. While specialty of treating provider was unavailable, we presume that low case volumes reflect lack of gynecologic oncology subspecialty care. Finally, even after adjusting for receipt of guideline care, case volume independently predicts OS. These findings suggest important opportunities to improve access to, and delivery of, care nationally.

The present study of roughly 100,000 cases allows a detailed exploration of both patient and process of care factors. In contrast to earlier studies, [15] we included only invasive OC given their impact on mortality. Comparing national 5-year survival rates from the 1998–2002 cohort to the 1988 report shows improved survival for stage II (66.3% vs. 60.1%), and stage III cases (32% vs. 27.3%) but minimal changes in stage I and IV disease. The real differences are likely larger given the inclusion in the earlier report of lower risk subtypes.

The number of approved cancer centers increased from 754 to 1279, with a shift toward more comprehensive and academic cancer centers [15]. Thus, while fewer patients are now cared for in non-comprehensive cancer programs compared to 1993 (12.3% vs. 32.3%), there has been minimal change in median facility case volume. Two-thirds of all centers providing initial management of OC treat 1–7 cases annually. There was a progressive trend in median case volumes increasing from 5.7 to 26.7 dependent upon facility type. Given the associations between case volume, OS and delivery of guideline care, this is an important barrier to standards of care. Many challenges face patients and providers when deciding whether to remain in a low-volume center instead of traveling to a center with more experience. Not surprisingly, patients in community cancer programs tend to be older, although the reported incidence of comorbid conditions was comparable across facility type. Age often impacts decisions about type and aggressiveness of care. However case volume remained a strong predictor of receipt of guideline care, irrespective of age. This independent contribution of case volume suggests an important interaction between patient factors and facility experience in managing complex cancer therapy overall — particularly in elderly and sick patients. Multiple studies support the validity of concept that higher volume of care and specialty treatment results in superior outcomes [16,5,9,17–19].

Targeting where patients receive care and ensuring delivery of guideline care should be a high priority given their associations with outcomes. Low case volume was independently associated with both survival and delivery of guideline care (which itself is a significant correlate of survival). Currently less than half of all patients received guideline therapy. These statistics have not changed since an earlier SEER data comparing 1991 and 1996 OC outcomes [6]. These observations imply that case volume serves as a surrogate for lack of subspecialty expert care, a point illustrated in a recent systematic review [20]. The authors fairly addressed the complexities in determining the relative impact of hospital volume vs. subspecialty care. The sub-specialization of the treating physician was the strongest factor associated with superior outcomes, with institutional factors following a weaker but similar trend. This is supported by a recent study by Phippen et al. who demonstrated excellent care in a low volume gynecologic oncology unit [21]. The issues of facility type, case volume and specialty care are intermingled and inevitably correlated to some degree. Our study cannot assess the relative contributions of these factors.

The combination of rural demographics and rare disease makes specialized treatment locally problematic. Other health systems made significant improvements by centralizing OC care. Norway instituted a concerted effort toward centralization in 1995 and recently published their 10-year experience [22]. Rates of OC being delivered in academic specialty hospitals rose from an already impressive rate of 72% to 92% and demonstrated a stable increase after the initial 3-year transition phase. Concomitantly, rates of appropriate staging (i.e. guideline care) at centralized vs. non-centralized centers were 81% vs. 3%, respectively, and rates of residual disease less than 1 cm were 71% vs. 15%, respectively. These findings were echoed in the Netherlands where superior rates of staging and cytoreduction and improved OS were seen for patients treated in specialized centers and by higher volume surgeons [23]. Most recently Woo et al. summarized higher quality publications regarding centralization of care for gynecologic cancers in a Cochrane review [24]. The authors concluded that women receiving treatment at specialized centers, or centers with specialist care, had longer survival

times and that the evidence was strongest for OC. These examples validate the concept that adherence to care guidelines, quality, value and ultimately survival can be improved with conscious efforts to treat patients in centers with expertise in this complex disease.

There are important limitations to our study. First, though externally monitored for quality, there are inevitable reporting errors [25]. Second, a minority of OC cases are not treated in CoC-accredited cancer programs, which could introduce minor selection bias. Third, survival was available for 1998–2002, while data on comorbidity was available only for 2003–2007. While unlikely based on other demographic data, shifts in the percentage of women with multiple comorbid conditions could impact outcomes for a minority of cases. Fourth, residual disease cannot be assessed in this database. However, this would be reflected as quality of care in terms of OS. Additionally, we have adjusted for critical independent variables (stage, comorbidities and age). Also, the NCDB does not include factors that impact the decision for nonstandard care: we adjusted for the most common factors that might impact such decisions. Importantly, the limitations of complete data captured in such large databases undoubtedly inflate the percentage of cases assigned to non-adherent care, but these differences should apply similarly across centers. Finally, the NCDB does not provide detailed data on the method of chemotherapy administration or details on outpatient chemotherapy such as the number of cycles completed.

In summary, it is relevant to reflect on a recent editorial by Uziel Beller who wrote, “one of the most important aspects of health care delivery for cancer patients involves the need for centralization of treatment to high quality centers…It is indeed surprising that even patient advocates of various malignant diseases do not appreciate the importance of the improved quality of care administered through centralization” [26]. Our data suggest both need and opportunity to improve access to expert subspecialty care and to raise the standards of care nationally for OC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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HIGHLIGHTS

- In the United States, 56% of ovarian cancer cases do not receive NCCN guideline care.
- Delivery of non-guideline care for ovarian cancer is correlated with facility case volume and survival.
- 65% of U.S. cancer centers treat fewer than 8 cases of ovarian cancer annually.

Table 1

Descriptive statistics for NCDB invasive epithelial ovarian cancer cohort based on era of diagnosis (1998–2002, 2003–2007) (N = 111,956).

Risk factor	All		Era of diagnosis 1998–2002		Era of diagnosis 2003–2007		p-Value
	N	%	N	%	N	%	
Patient characteristics							
Age (mean, SD)	62.29	14.03	62.32	14.14	62.27	13.92	0.6059
<60 years	48,215	43.07	23,518	42.47	24,697	43.65	<.0001
60–75 years	41,013	36.63	20,636	37.26	20,377	36.02	
>75 years	22,728	20.30	11,226	20.27	11,502	20.33	
Race							<.0001
White	99,265	88.66	49,491	89.37	49,774	87.98	
African Americans	11,110	9.92	5214	9.41	5896	10.42	
Unknown	1581	1.41	675	1.22	906	1.60	
Median household income — 2000							<.0001
$46,000 +	43,341	38.71	21,145	38.18	22,196	39.23	
$35,000–$45,999	29,997	26.79	14,965	27.02	15,032	26.57	
<$35,000	32,163	28.73	16,337	29.50	15,826	27.97	
Missing	6455	5.77	2933	5.30	3522	6.23	
Primary payer at diagnosis							<.0001
Private insurance	18,059	16.13	10,738	19.39	7321	12.94	
Medicare/medicare supplements	44,727	39.95	22,109	39.92	22,618	39.98	
Managed care/TRICARE/military	35,813	31.99	15,718	28.38	20,095	35.52	
Medicaid/federal insurance programs/public health service	4991	4.46	2213	4.00	2778	4.91	
Not insured — self pay	4344	3.88	1984	3.58	2360	4.17	
Missing: insurance status unknown	4022	3.59	2618	4.73	1404	2.48	
Tumor characteristics							
Tumor stage							<.0001
Stage I	19,516	17.43	9995	18.05	9521	16.83	
Stage II	7941	7.09	4042	7.30	3899	6.89	
Stage III	43,918	39.23	21,888	39.52	22,030	38.94	
Stage IV	27,587	24.64	14,605	26.37	12,982	22.95	

Risk factor	All		Era of diagnosis 1998–2002		Era of diagnosis 2003–2007		p-Value
	N	%	N	%	N	%	
UNK	9756	8.71	3783	6.83	5973	10.56	
NA	53	0.05	16	0.03	37	0.07	
Improperly staged	3185	2.84	1051	1.90	2134	3.77	
Hospital ovarian cancer volume/year							<.0001
1–7 cases/year	28,122	25.12	14,961	27.02	13,161	23.26	
8–16 cases/year	27,946	24.96	13,764	24.85	14,182	25.07	
17–28 cases/year	27,839	24.87	13,216	23.86	14,623	25.85	
≥29 cases/year	28,049	25.05	13,439	24.27	14,610	25.82	
Facility type							<.0001
Community cancer program	13,777	12.31	7209	13.02	6568	11.61	
Comprehensive community cancer program	49,977	44.64	24,960	45.07	25,017	44.22	
Academic/research program (includes NCI-designated comprehensive cancer centers)	48,202	43.05	23,211	41.91	24,991	44.17	
Total	111,956	100.00	55,380	100.00	56,576	100.00	

Table 2

Comparisons of facility types treating EOC in terms of Charlson/Deyo Comorbidity Index (2003–2007), age and adherence to treatment status (1998–2007).

	Facility Type							
	Community cancer program		Comprehensive community cancer program		Academic/research program		Total	
	N	%	N	%	N	%	N	%
Charlson/Deyo Comorbidity Index								
0: no co-morbidities	4209	80.28	16,797	81.11	18,034	83.14	39,040	81.94
1	809	15.43	3074	14.84	2965	13.67	6848	14.37
2	178	3.40	670	3.24	559	2.58	1407	2.95
3	47	0.90	168	0.81	132	0.61	347	0.73
Total	5243	100.00	20,709	100.00	21,690	100.00	47,642	100.00
Age								
<60 years	4267	37.66	17,311	40.45	20,671	48.44	42,249	43.64
60–75 years	4187	36.96	16,344	38.19	15,508	36.34	36,039	37.23
>75 years	2875	25.38	9141	21.36	6498	15.23	18,514	19.13
Total	11,329	100.00	42,796	100.00	42,677	100.00	96,802	100.00
Overall adherence to NCCN guidelines of care								
Adherent	3491	30.81	17,416	40.70	20,956	49.10	41,863	43.25
Non-adherent	7838	69.19	25,380	59.30	21,721	50.90	54,939	56.75
Total	11,329	100.00	42,796	100.00	42,677	100.00	96,802	100.00
Tumor stage								
I	2021	17.84	7585	17.72	7750	18.16	17,356	17.93
II	931	8.22	3562	8.32	3448	8.08	7941	8.20
III	4345	38.35	18,916	44.20	20,657	48.40	43,918	45.37
IV	4032	35.59	12,733	29.75	10,822	25.36	27,587	28.50
Total	11,329	100.00	42,796	100.00	42,677	100.00	96,802	100.00
Tumor grade								
Well/moderately differentiated (ref)	2998	38.73	11,072	34.27	11,068	32.81	25,138	34.07
Poorly/undifferentiated/anaplastic	4743	61.27	21,236	65.73	22,662	67.19	48,641	65.93
Total	7741	100.00	32,308	100.00	33,730	100.00	73,779	100.00

Notes:

1. Charlson/Deyo Comorbidity Index:
   - **a.** 0: no co-morbidities.
   - **b.** 1: MI, CHF, peripheral vascular disease; cerebrovascular disease; dementia; CPD; RD; PUD; mild liver disease.
   - **c.** 2: diabetes; diabetes with chronic complications; hemiplegia or paraplegia; renal disease.
   - **d.** 3: moderate or severe liver disease.

Table 3

Case Fatality Ratio by facility type, adherence to guideline care recommendations, and hospital volume.

(a) Case fatality ratio by facility type (1998–2002)

Facility type	Dead	Total	CFR	95% CI	
				Lower	Upper
Community cancer program	3898	6086	0.6405	0.6283	0.6526
Comprehensive community cancer program	13,851	22,087	0.6271	0.6207	0.6335
Academic/research cancer program	12,338	20,987	0.5879	0.5812	0.5946

(b) Case Fatality ratio by facility type and adherence to Rx (1998–2002)

Facility type	Dead	Total	CFR	95% CI	
				Lower	Upper
Community cancer program	1140	1879	0.6067	0.5842	0.6289
Comprehensive community cancer program	5590	9017	0.6199	0.6098	0.6300
Academic/research cancer program	6049	10,390	0.5822	0.5726	0.5917

(c) Case fatality ratio by average hospital ovarian cancer case volume/year (1998–2002)

Average hospital ovarian cancer case volume/year 1998–2002	Dead	Total	CFR	95% CI	
				Lower	Upper
1–6 cases/year	8140	12,398	0.6566	0.6481	0.6649
7–14 cases/year	7451	12,200	0.6107	0.6020	0.6194
15–25 cases/year	7300	12,146	0.6010	0.5923	0.6098
≥26 cases/year	7196	12,416	0.5796	0.5708	0.5883

(d) Case fatality ratio by average hospital ovarian cancer case volume/year and adherence to Rx (1998–2002)

Average hospital ovarian cancer case volume/year 1998–2002	Dead	Total	CFR	95% CI	
				Lower	Upper
1–6 cases/year	2352	3752	0.6269	0.6112	0.6424
7–14 cases/year	2926	4847	0.6037	0.5897	0.6175
15–25 cases/year	3579	5935	0.6030	0.5905	0.6155
≥26 cases/year	3922	6752	0.5809	0.5690	0.5927

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Table 4

Predictors of overall survival for EOC within NCDB cohort (1998–2002).

Risk factor	N	%	Unadjusted HR	95% CI		Adjusted HR	95% CI	
				Lower	Upper		Lower	Upper
Patient characteristics								
Age (years)								
<60	21,087	42.89	Referent			Referent		
60–75	18,610	37.86	1.750	**1.704**	**1.796**	1.282	**1.240**	**1.325**
>75	9463	19.25	3.267	**3.155**	**3.383**	2.095	**1.999**	**2.195**
Race								
Whites	43,995	89.49	Referent			Referent		
Non-Whites	4568	9.29	1.232	**1.167**	**1.301**	1.204	**1.149**	**1.261**
Unknown	597	1.21	1.012	0.908	1.127	1.108	**1.001**	**1.227**
Payer information								
Private insurance	9680	19.69	Referent			Referent		
Medicare/medicare supplements	19,371	39.40	2.155	**2.082**	**2.230**	1.236	**1.186**	**1.289**
Managed care/TRICARE/military	14,221	28.93	1.026	0.988	1.065	1.019	0.982	1.058
Medicaid/federal insurance programs/public health service	1949	3.96	1.481	**1.385**	**1.584**	1.263	**1.177**	**1.355**
Not insured— self pay	1744	3.55	1.385	**1.281**	**1.498**	1.276	**1.171**	**1.391**
Insurance status unknown	2195	4.47	1.438	**1.323**	**1.562**	1.119	**1.001**	**1.252**
Adherence to NCCN guidelines for Rx								
Yes	21,286	43.30	Referent			Referent		
No	27,874	56.70	1.322	**1.284**	**1.361**	1.403	**1.362**	**1.446**
Tumor characteristics								
Tumor stage								
Stage I	8625	17.54	Referent			Referent		
Stage II	4042	8.22	2.402	**2.208**	**2.613**	2.131	**1.963**	**2.313**
Stage III	21,888	44.52	6.399	**6.010**	**6.812**	5.881	**5.516**	**6.270**
Stage IV	14,605	29.71	11.785	**11.074**	**12.542**	9.476	**8.893**	**10.098**
Tumor grade								
Well/moderately differentiated	13,244	26.94	Referent			Referent		

Risk factor	N	%	Unadjusted HR	95% CI		Adjusted HR	95% CI	
				Lower	Upper		Lower	Upper
Poorly/undifferentiated/anaplastic	25,538	51.95	1.786	**1.724**	**1.850**	1.200	**1.159**	**1.242**
Missing	10,378	21.11	3.114	**2.987**	**3.246**	1.472	**1.416**	**1.531**
Facility characteristics								
Facility type								
Academic/research cancer program	20,987	42.69	Referent			Referent		
Comprehensive community cancer program	22,087	44.93	1.124	**1.080**	**1.169**	1.020	0.980	1.061
Community cancer program	6086	12.38	1.256	**1.190**	**1.325**	1.054	0.996	1.114
Average hospital ovarian cancer case volume/year (1998–2002)								
1–6 cases/year	12,398	25.22	Referent			Referent		
7–14 cases/year	12,200	24.82	0.848	**0.813**	**0.885**	0.955	0.912	1.000
15–25 cases/year	12,146	24.71	0.785	**0.751**	**0.821**	0.920	**0.876**	**0.966**
≥26 cases/year	12,416	25.26	0.738	**0.702**	**0.775**	0.910	**0.858**	**0.964**
Total	49,160	100.00						

Hazard Ratios Bolded for $p < 0.05$.

Table 5

Predictors of nonadherence to NCCN guidelines for ovarian cancer care (2003–2007).

Risk factor	N	%	Unadjusted OR	95% CI		Adjusted OR	95% CI	
				Lower	Upper		Lower	Upper
Patient characteristics								
Age (years)								
<60	21,162	44.42	Referent			Referent		
60–75	17,429	36.58	1.120	**1.076**	**1.166**	1.075	**1.031**	**1.120**
>75	9051	19.00	2.825	**2.675**	**2.984**	2.566	**2.426**	**2.714**
Race								
Whites	42,017	88.19	Referent			Referent		
Non-Whites	4862	10.21	1.264	**1.189**	**1.344**	1.335	**1.253**	**1.421**
Unknown	763	1.60	1.121	0.969	1.297	1.355	**1.167**	**1.573**
Charlson/Dayo Comorbidity Index								
0	39,040	81.94	Referent			Referent		
1	6848	14.37	1.287	**1.221**	**1.356**	1.164	**1.102**	**1.230**
2	1407	2.95	1.754	**1.565**	**1.967**	1.426	**1.266**	**1.605**
3	347	0.73	3.134	**2.412**	**4.071**	2.558	**1.956**	**3.345**
Facility characteristics								
Facility type								
Academic/research cancer program	21,690	45.53	Referent			Referent		
Comprehensive community cancer program	20,709	43.47	1.392	**1.340**	**1.447**	1.071	**1.026**	**1.119**
Community cancer program	5243	11.00	2.139	**2.006**	**2.281**	1.197	**1.107**	**1.293**
Average hospital ovarian cancer case volume/year (1998–2002)								
1–7 cases/year	11,838	24.85	Referent			Referent		
8–16 cases/year	11,960	25.10	0.599	**0.568**	**0.632**	0.662	**0.624**	**0.703**
17–26 cases/year	12,005	25.20	0.458	**0.435**	**0.483**	0.515	**0.485**	**0.547**
≥27 cases/year	11,839	24.85	0.373	**0.354**	**0.394**	0.438	**0.411**	**0.467**
Total	47,642	100.00						

Hazard Ratios Bolded for $p < 0.05$.