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Factors Predicting Use of Neoadjuvant Chemotherapy Compared With Primary Debulking Surgery in Advanced Stage Ovarian Cancer—A National Cancer Database Study

Gary S. Leiserowitz, MD, MS, Jeff F. Lin, MD,† Ana I. Tergas, MD,‡ William A. Cliby, MD,§ and Robert E. Bristow, MD, MBA||*

Objectives: We performed a patterns-of-care study to characterize the types of patients with epithelial ovarian cancer (EOC) who received neoadjuvant chemotherapy (NACT) versus primary debulking surgery (PDS) using the National Cancer Database (NCDB).
Methods: We identified patients with stages IIIC and IV EOC in the NCDB diagnosed from 2003 to 2011. Patients who received chemotherapy (CT) prior to surgery were classified as receiving NACT; if surgery preceded CT, then it was classified as PDS. Data collected from the NCDB included demographics, medical comorbidity index, cancer characteristics and treatment, and hospital characteristics. Univariate and multivariable analyses were performed using χ^2 test, logistic regression, log-rank test, and Cox proportional hazards modeling as indicated. Statistical significance was set at $P < 0.05$.
Results: A total of 62,727 patients with stages IIIC and IV EOC were identified. The sequence of surgery and CT was identified, of which 6922 (11%) had NACT and 31,280 (50%) had PDS. Neoadjuvant CT was more frequently done in stage IV than stage IIIC (13% vs 9%), and its use markedly increased over time. Variables associated with increased likelihood of NACT use were as follows: age older than 50 years and those with higher comorbidities, stage IV, and higher-grade EOC. Neoadjuvant CT use was also associated with hospitals that were adherent to the National Comprehensive Cancer Network guidelines, high-volume facilities, those in the Midwest and West, and academic centers.
Conclusions: Evidence suggests that patients with greater adverse risk factors are more likely to receive NACT instead of PDS. Use of NACT has significantly increased over the study period, especially in patients with stage IV ovarian cancer.

Key Words: Neoadjuvant chemotherapy, Ovarian cancer, Patterns of care

Received October 6, 2016, and in revised form December 7, 2016.
Accepted for publication December 8, 2016.

(*Int J Gynecol Cancer* 2017;27: 675–683)

*Department of Obstetrics and Gynecology, University of California Davis Medical Center, Sacramento, CA; †Magee-Women's Hospital of University of Pittsburgh Medical Center, Pittsburgh, PA; ‡New York-Presbyterian Hospital/Columbia University Medical Center, New York, NY; §Mayo Clinic, Rochester, MN; and ||University of California Irvine Medical Center, Orange, CA.

Address correspondence and reprint requests to: Gary S. Leiserowitz, MD, MS, Department of Obstetrics and Gynecology, 4860 Y St, Suite 2500, Sacramento, CA 95817.
E-mail: gsleiserowitz@ucdavis.edu.

ISSN: 1048-891X
DOI: 10.1097/IGC.0000000000000967

The authors declare no conflicts of interest.

Historically, primary management of advanced-stage epithelial ovarian cancer (EOC) included primary debulking surgery (PDS), followed by adjuvant chemotherapy (CT).[1] The primary goal of surgical therapy is to reduce the overall tumor burden in the abdomen and pelvis to minimal or no gross residual disease (optimal debulking) to maximize the effectiveness of adjuvant CT.[2,3] Numerous retrospective studies show clear survival advantages for patients who undergo optimal cytoreduction compared with those who are not optimally debulked.[2–4] A critical barrier to this goal is that many patients with stages III and IV EOC do not have optimal cytoreduction at the end of their primary operation.

Neoadjuvant CT (NACT), CT given prior to surgery, emerged as an alternative to primary surgery for advanced ovarian cancer in the 1990s.[5,6] Neoadjuvant CT addressed several challenges associated with primary surgery: inability to achieve optimal debulking in many patients, especially with stage IV disease, and many patients are medically unsuitable because of age, performance status, or other medical comorbidities.[7] The goals of NACT are to decrease tumor burden prior to interval debulking surgery to increase the likelihood of complete tumor resection at the time of surgery.[8] Multiple studies, including 2 recent randomized controlled clinical trials, support the selected use of NACT as an alternative to PDS.[9,10] The rate of optimal debulking (residual tumor <1 cm) was markedly improved in the NACT group compared with the PDS groups in the studies of both Vergote et al[10] (80.6% vs 41.6%) and Kehoe et al[9] (73% vs 41%), and overall survival was not compromised by use of NACT. Nonetheless, the sequence of NACT versus PDS remains highly contested among experts, who focus on whether NACT compromises the survival of patients with advanced-stage ovarian cancer.[11–13]

The National Cancer Database (NCDB) was developed to track outcomes from 1500 US American College of Surgeon's Commission on Cancer–accredited programs and captures approximately 80% of ovarian cancer cases.[14] This database contains broad information about patient demographics and EOC characteristics, treating institution, and types of treatments including surgery and CT. We sought to use the NCDB to evaluate patterns of care in the use of NACT versus primary surgery in the management of advanced-stage EOC. We examined if there was a trend in the use of NACT during the time period and if there were factors associated with its use during a period that predated the publication of the studies of Vergote et al[10] and Kehoe et al.[9]

METHODS

This study received exempt status from the institutional review board of Washington University and the University of Pittsburgh. Our methodology parallels that previously detailed with hospital data abstracted as described by Bristow et al.[15] Data were obtained using a public use file provided by the NCDB. The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The data used in this study are derived from a deidentified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are neither responsible for the analytic or statistical methodology used or the conclusions drawn from these data by the investigators.

The subjects and hospitals were deidentified for aggregate data analysis. Patients with invasive EOC diagnosed between January 1, 2003, and December 31, 2011, were identified using the NCDB by topography code C56.9. We limited our analysis to subjects from 2003 onward, because therapy sequence data began to be reliably recorded at that time. The year of diagnosis was divided into 3 periods: 2003 to 2004, 2005 to 2008, and 2009 to 2011. Histological types were identified according to the *International Classification of Diseases for Oncology, Third Revision* and included 8010 to 8569, 8940 to 8949, and 9000. Records were included if the tumor corresponded to 1 malignancy or the first of 2 or more independent malignant primary tumors and if either the pathological or clinical staging was known. Patients with borderline ovarian tumors were excluded from analysis. We limited our study population to include only patients with International Federation of Gynecology and Obstetrics and American Joint Committee on Cancer stages IIIC/IV disease. Grade was recorded as 1, 2, 3, undifferentiated, or missing. Histologies were recorded as serous or nonserous. The identified treatments for ovarian cancer included the following: PDS followed by adjuvant CT, NACT followed by surgery, surgery alone, CT alone, unknown sequence, or no surgery or CT. Surgical procedures included the following: local tumor destruction, total removal of a tumor, unilateral or bilateral oophorectomy, omentectomy, debulking/cytoreductive surgery, pelvic exenteration, or other oophorectomy/surgery type not otherwise specified. Chemotherapy was recorded as given if associated with initial treatment and was categorized as follows: (1) none, (2) unknown, (3) single agent, (4) multiagent, (5) no CT because of contraindications, (6) no CT because of patient death, (7) no CT because of unknown reasons, or (8) no CT because of patient/family refusal. The NCDB captures the first cycle of CT regardless of the location where it was administered. No information was available about the number of cycles, the specific type of CT agents given, or if CT was given for subsequent recurrences.

Patient demographic information included age, insurance status, education, ethnicity, and income. Insurance status was recorded as private insurance (which includes managed care), Medicare/Medicaid, other government insurance, not insured, and unknown. Education was identified as the percent of the population in the subject's zip code of residence at the time of diagnosis that did not have a high school diploma, after linking the NCDB to the US Census data, because education is not captured in the NCDB. Ethnicity included white, African American, Hispanic, Native American, Asian/Pacific Islander, or unknown. Income was the median household income in the subject's zip code of residence (using US Census data). The Charlson-Deyo Comorbidity Index was used as a measure of patient comorbid illnesses.

Information about the hospitals included the type of institution (community cancer program, comprehensive community cancer program, or academic/research comprehensive cancer program), location (Northeast, South, Midwest, and West), the number of ovarian cancer operations per year, and the distance that the patient lived from the hospital

of record. It was also noted if the ovarian cancer care was adherent with the National Comprehensive Cancer Network (NCCN) published guidelines, based on stage specific recommendations for surgical and CT treatment according to the time period of diagnosis.[14,16] Surgery was considered to be adherent if it included oophorectomy with omentectomy and debulking procedures including bowel resection, or exenteration. Chemotherapy was considered to be adherent if multiagent CT was administered.

Statistical Analysis

Descriptive statistics of cases and institutions were extracted from NCDB 2011 ovarian data set that was released and revised in the first quarter of 2014. We grouped continuous variables into quartiles for univariate and multivariable analyses. Univariate χ^2 analyses were performed to identify significant relationships between individual patient/facility/disease/treatment factors and undergoing NACT as opposed to PDS. Factors found to have significant relationships to a treatment sequence after Bonferroni-Holm correction were considered as potential covariates for subsequent multivariable modeling.

Linear trends for use of PDS and NACT were calculated over the periods of the study by plotting the rate of use of various therapeutic approaches over time and applying simple linear regression to estimate trend over time, then applying Wald runs test for randomness for each linear regression model to assess systematic deviation from linearity of the data. Each linear regression model was compared with others using analysis of covariance as detailed by Zar[17] to determine if use of various therapeutic approaches changed proportionately over time.

Multivariable logistic regression was used to analyze likelihood to receive NACT instead of PDS for patient demographics, tumor characteristics, comorbidity index, institutional characteristics, and adherence to NCCN guidelines, adjusted for age, ethnicity, stage, grade, payer status, and household income. Multivariable logistic regression models (1 for stage IIIC, 1 for stage IV, and 1 for both stages IIIC and IV) were constructed using backward, stepwise selection based on the maximum partial likelihood estimates. Odds ratios (ORs) with 95% confidence intervals were generated; OR greater than 1.0 indicated an increased likelihood of receiving NACT.

Point estimates with 95% confidence interval and levels of significance based on 2-tailed tests are reported as *P* values where appropriate. Threshold for significance was set at an α level of 0.05. All analyses were generated using either IBM SPSS version 19.0 (Armonk, NY) or GraphPad Prism version 6 (La Jolla, CA).

RESULTS

We identified 62,727 patients in the total cohort who met criteria for study inclusion, at stages IIIC-IV invasive EOC and older than 18 years. In the period 2003 to 2011, there were 31,280 patients (49.9% of total) who underwent PDS and 6922 patients (11.1%) who had NACT prior to surgery (Fig. 1). We also identified patients who had neither PDS nor NACT: 7479 (11.9%) with surgery alone, 8130 (13.0%) with CT alone, 5805 (9.3%) who had neither surgery nor CT, and 3111 (5.0%) with an unknown sequence. Among patients with stage IIIC ovarian cancer, 22,604 (63%) had PDS, whereas only 3332 (9%) had NACT. However, in stage IV patients, the treatment sequences were more heterogeneous, with far fewer patients who had PDS (8675; 32%), and 3590 (13%) had NACT, then CT alone in 6171 (23%), surgery alone in 2646 (10%), and no surgery or CT in 4816 (18%).

In the total cohort of stages IIIC and IV cancers, there were a decreasing number of patients who received PDS (decreasing from 3527 in 2003 to 3056 in 2011) and a doubling in the number who received NACT (from 500 in 2003 to 1131 in 2011; linear trend over time for NACT, $P < 0.001$). Figure 2

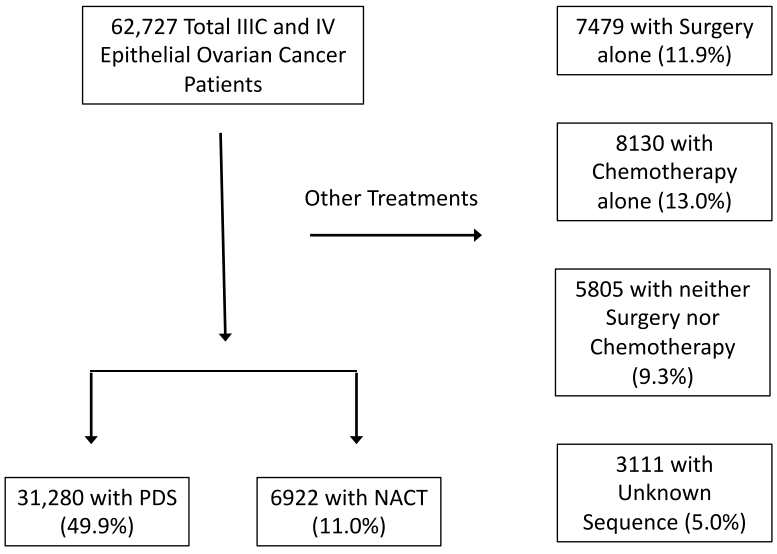

FIGURE 1. Flowchart of treatment categories for total stages IIIC and IV EOC patients, NCDB, 2003 to 2011.

shows the annual trends for all treatments for stage IIIC disease, showing that there was an increase in the number and proportion of NACT over the period. There was a decrease in the absolute number of PDS; however, the proportion varied but was largely unchanged during the period. Figure 3 shows the trends for all treatments for stage IV disease. There was a clear decrease in the number and proportion of PDS over the period, but the increased use of NACT was far greater compared with what was seen in stage IIIC disease.

Table 1 shows the characteristics of the cohort, limited to those patients who had PDS or NACT. Because the patient ages were non–normally distributed, we include the median and interquartile ranges. The patients who received NACT were significantly older than those who had PDS. The distribution of race/ethnicity was different among the patients who received the 2 treatments, with slightly more white women receiving PDS and slightly more African American receiving NACT. Comorbidity was higher in the patients who received NACT instead of PDS; if patients had no comorbidities, then NACT was 17.6%, but increased to 21.6% if they had 2 or more comorbid conditions. Neoadjuvant CT was more frequently done in the West, whereas PDS was more commonly done in the Northeast and South. The number of ovarian cancer operations per hospital varied between those who had NACT versus PDS, with NACT being done more frequently in high-volume hospitals. Neoadjuvant CT was more common if the patient was more than 27.7 miles from the primary hospital. Neoadjuvant CT was more commonly done in facilities that were adherent with NCCN guidelines (18.6%) compared with those in non–NCCN-adherent facilities (16.3%).

Cancer characteristics were different among the patients. Neoadjuvant CT was much more frequently provided to stage IV patients (29.3%) compared with stage IIIC patients (12.8%). Neoadjuvant CT was more frequently done with patients with grade 3 cancers compared with lower grades and nonserous versus serous histologies.

On logistic regression analysis to assess the likelihood of receiving NACT compared with PDS, several notable trends were observed (Table 2). Patients were almost twice as likely to receive NACT in the period 2009–2011 than in 2003–2004 (OR, 1.8). Patient characteristics associated with increased likelihood to receive NACT included increasing age older than 50 years, up to 1.69 for 71 years or older. African American women were more likely to receive NACT (OR, 1.35), but other ethnicity/race groups were the same. A Charlson-Deyo Comorbidity Index of 1 was modestly associated with use of NACT versus PDS (OR, 1.17), but not 0 or greater than 2. Patients who lived in neighborhoods where residents were more likely to have high school diplomas were more likely to have PDS instead of NACT. In contrast, patients who lived in more affluent neighborhoods were more likely to get NACT instead of PDS. Insurance status did not influence the choice of treatment sequence.

Among the tumor characteristics, patients with stage IV disease were far more likely to receive NACT compared with stage IIIC (OR, 2.86). If the patient had grade 3 disease, her

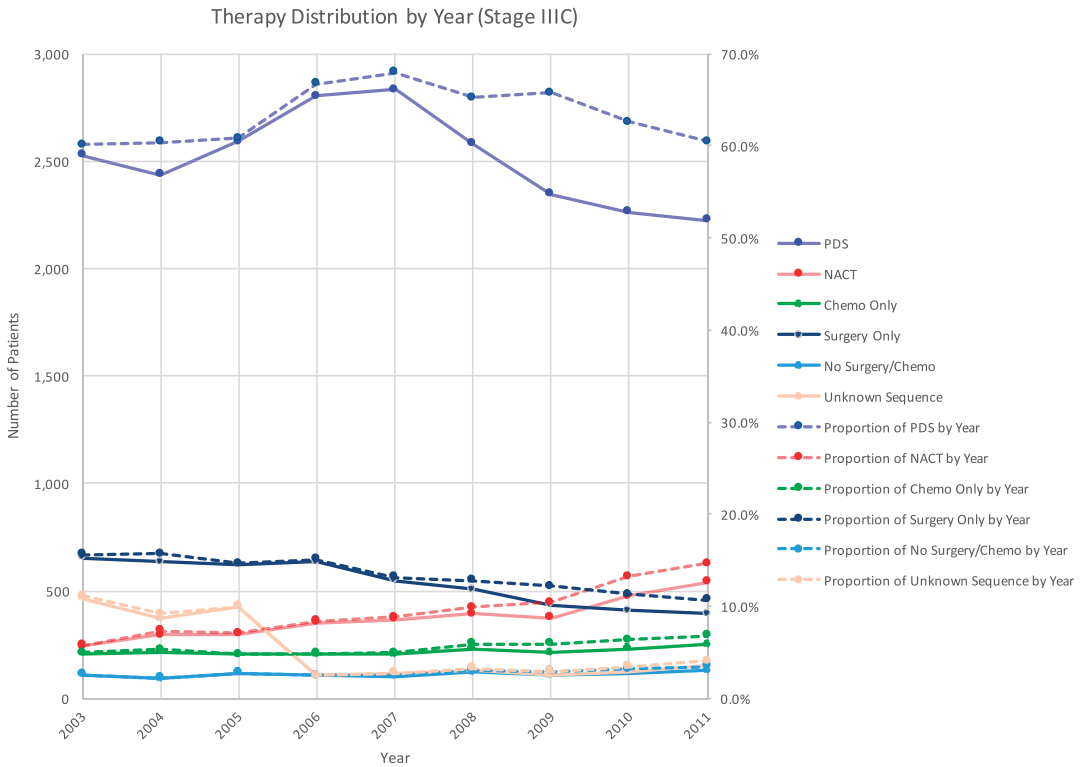

FIGURE 2. Trends in the use of different treatments for stage IIIC EOC, 2003 to 2011. Linear trend over time for NACT, $P < 0.001$.

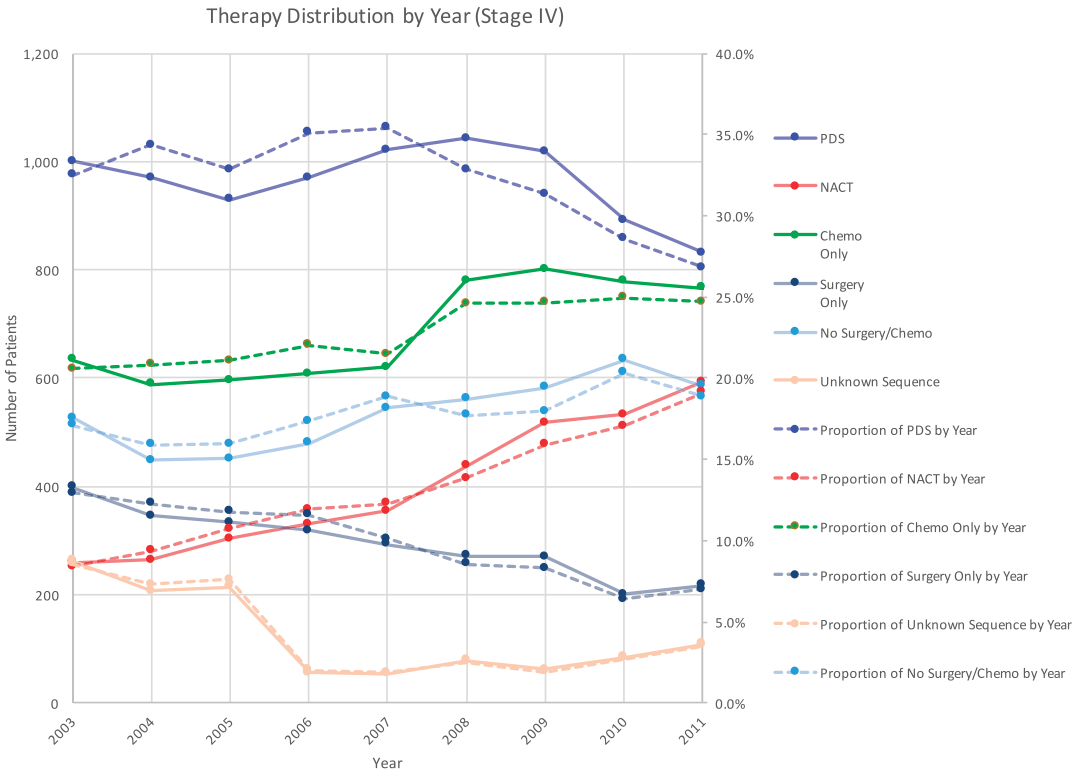

FIGURE 3. Trends in the use of different treatments for stage IV EOC, 2003 to 2011. Linear trend over time for NACT, $P < 0.001$.

likelihood of receiving NACT was much higher. If the patient received treatments at an institution that was adherent to NCCN ovarian cancer guidelines, she was more likely to receive NACT instead of PDS. There was no difference in NACT use based on serous versus nonserous histologies (different than the univariate analysis).

Several characteristics about the treating institutions also appeared to influence the likelihood of treatment sequence. Those programs that were located in a comprehensive community cancer or an academic medical center were more likely to use NACT compared with community cancer programs. Southern institutions had a higher propensity toward PDS compared with those in the Northeast, in contrast to those in the West and Midwest that were more likely to perform NACT. Hospitals that recorded the greatest volume of annual ovarian cancer cases (>27.7/year) were more likely to choose NACT compared with lower-volume facilities. Patients who lived more than 25 miles away from their primary treating hospital were more likely to get NACT compared with those who lived near their hospital.

DISCUSSION

In this patterns-of-care study over the study period 2003 to 2011, we found that primary surgery was provided far more commonly than NACT for advanced-stage ovarian cancer. Similarly, a Society of Gynecologic Oncology practice patterns survey (covering a similar period) reported that the majority of survey respondents (60%) said that they give NACT to less than 10% of their advanced-stage patients.[18] It is also consistent with a patterns-of-care population-based study by Thrall et al[19] using the SEER (Surveillance, Epidemiology and End Results) database linked to the Medicare claims database: 71% of Medicare beneficiary patients had primary surgery, 14% had NACT, and 15% had palliative CT alone. Nonetheless, we did find a decreasing trend in the use of PDS for both stages IIIC and IV patients and an increased rate of NACT, far greater with stage IV disease than stage IIIC, a pattern also noted by Meyer et al.[20] Similar to the study of Thrall et al,[19] we found that in stage IV disease alternatives to primary surgery were increasingly used: CT alone was provided more frequently than NACT, and a significant proportion of patients receive surgery alone or no treatment. Both of these latter nonstandard treatments have also increased over time, despite the more frequent use of NACT, which may reflect a palliative approach to treatment of some patients with poor-prognosis ovarian cancer.

We found several factors that distinguished the likelihood to receive NACT versus PDS. The greatest difference was seen between patients with stages IIIC and IV disease: NACT was done in 13% of stage IIIC, but increased to 29% in stage IV (OR, 2.86). The other factors associated with NACT use included older patients, African American women, and those with grade 3 disease. Less significant factors associated with increased use of NACT included living in a more affluent neighborhood and receiving care in comprehensive community cancer programs or academic centers, in a facility more likely to be adherent to NCCN ovarian cancer guidelines, and a Western

TABLE 1. Cohort characteristics and association of PDS versus NACT for stages IIIC and IV, NCDB, 2003–2011

Characteristics	All), n n = 62,727)*	PDS (n = 31,280)†	NACT (n = 6922)†	*P*‡
Age (median, interquartile range),§ y	64, 19	61, 18	64, 16	<0.0005
	n (%)	n (%)	n (%)	
Race				0.001
Non-Hispanic white	31,948	26,283 (82.3)	5665 (17.7)	
Non-Hispanic African American	2686	2139 (79.6)	547 (20.4)	
Hispanic	1891	1510 (79.9)	381 (20.1)	
Native American	122	101 (82.8)	21 (17.2)	
Asian/Pacific Islander	934	755 (80.8)	179 (19.2)	
Charlson/Deyo Comorbidity Index				<0.0005
0	31,578	26,034 (82.4)	5544 (17.6)	
1	5482	4350 (79.4)	1132 (20.6)	
≥2	1141	895 (78.4)	246 (21.6)	
Insurance				<0.0005
Uninsured	1546	1284 (83.1)	262 (16.9)	
Private insurance	18,986	16,102 (84.8)	2884 (15.2)	
Medicare/Medicaid	16,480	12,962 (78.7)	3518 (21.3)	
Governmental insurance	356	290 (81.5)	66 (18.5)	
Median neighborhood education				0.001
≥29% without high school diploma	5366	4323 (80.6)	1043 (19.4)	
20%–28.9%	7798	6343 (81.3)	1455 (18.7)	
14%–19.9%	8644	7149 (82.7)	1495 (17.3)	
<14%	13,943	11,515 (82.6)	2428 (17.4)	
Median neighborhood income				0.432
<$30,000	4265	3492 (81.9)	773 (18.1)	
$30,000–$34,999	6283	5115 (81.4)	1168 (18.6)	
$35,000–$45,999	10,012	8214 (82.0)	1798 (18.0)	
≥$46,000	15,194	12,512 (82.3)	2682 (17.7)	
Institution type				0.002
Community cancer	1866	1594 (85.4)	292 (15.6)	
Comprehensive community cancer	19,533	16,027 (82.1)	3506 (17.9)	
Academic	16,546	13,451 (81.3)	3095 (18.7)	
Geographic region				<0.0005
Northeast	7632	6337 (83.0)	1295 (17.0)	
South	11,128	9322 (83.8)	1806 (16.2)	
Midwest	12,885	10,529 (81.7)	2356 (18.3)	
West	6556	5091 (77.7)	1465 (22.3)	
No. of ovarian cancer cases per year				<0.0005
<7.1	6505	5356 (82.3)	1149 (17.7)	
7.1–16.4	9470	7826 (82.6)	1644 (17.4)	
16.5–27.7	10,898	9080 (83.3)	1818 (16.7)	
≥27.7	11,328	9017 (79.6)	2311 (20.4)	
Stage				<0.0005
IIIC	25,936	22,604 (87.2)	3332 (12.8)	
IV	12,265	8675 (70.7)	3590 (29.3)	

(Continued on next page)

TABLE 1. *(Continued)*

Characteristics	All), n n = 62,727)*	PDS (n = 31,280)†	NACT (n = 6922)†	*P*‡
Tumor grade				<0.0005
1	1015	930 (91.6)	85 (8.4)	
2	4443	3945 (88.8)	498 (11.2)	
3	26,214	21,872 (83.4)	4342 (16.6)	
Tumor histology				<0.0005
Nonserous	10,975	8778 (80.0)	2197 (20.0)	
Serous	27,226	22,501 (82.6)	4725 (17.3)	
NCCN adherence				<0.0005
Nonadherent	8578	7179 (83.7)	1399 (16.3)	
Adherent	29,623	24,100 (81.4)	5523 (18.6)	
Distance (facility to patient zip code), mi				<0.0005
0–5	8499	7038 (82.8)	1461 (17.2)	
5.01–10	7165	5941 (82.9)	1224 (17.1)	
10.01–25	9216	7620 (82.7)	1596 (17.3)	
>25.01	11,336	9122 (80.5)	2214 (19.5)	

*Total patients include stages IIIC and IV EOC patients, including treatments with PDS, NACT, CT alone, surgery alone, no treatment, and sequence unknown.

†Percentages of PDS and NACT were added, excluding other treatment modalities.

‡*P* values (all 2-sided) were obtained from χ^2 tests for categorical variables and Mann-Whitney *U* tests for non–normally ¢continuous variables.

§Age distribution is nonnormal by Kolmogorov-Smirnov testing against a normal distribution; therefore, median (interquartile range) (75th percentile to 25th percentile) is used rather than mean (SD).

institution (vs other regions). The interpretation of these trends suggests that the selection of NACT over PDS is probably not a reflection of adverse socioeconomic discrimination.

The increasing use of NACT for advanced-stage EOC likely reflects a change in the paradigm of care for this challenging, heterogeneous group of patients. We limited our cohort to patients with stage IIIC disease or worse, since NCCN guidelines clearly favor use of primary surgery for patients who have less than stage IIIC disease.[1] Our study showed a trend of increasing use of NACT occurred even before the publication of the first randomized controlled trial of NACT versus PDS (that of Vergote et al[10]). The recommendation to consider NACT in selected patients (bulky stage IIIC and stage IV and/or poor surgical candidates) was upgraded to category I in the 2012 version of the NCCN guidelines.[16] Facility factors that favored NACT use included participation by academic centers, centers adherent to NCCN guidelines, and facilities with a higher annual volume of ovarian cancer cases. This may suggest that familiarity with emerging literature and NCCN guidelines may have increased the likelihood to use NACT.

Our findings that NACT was more frequently given in patients with adverse disease characteristics and/or worse performance status are consistent with other studies.[19,21–23] Outcome comparisons of primary surgery compared with NACT are very difficult to validate, because choosing one modality over another requires multifaceted decision making that weighs multiple factors, including clinician experience. Wright et al[22] used a linked SEER and Medicare claims database to analyze outcomes in patients with stages II-IV disease and older than 65 years. They found that patients who were more likely to receive primary CT (NACT instead of primary surgery) were likely to be older, be diagnosed more recently, have serous cancers, and live in a metropolitan area. They also determined that there were substantial factor imbalances between the 2 treatment groups.

Limitations to this study are common to other population-based epidemiological studies. The most critical limitation is the lack of information about pretreatment tumor burden or tumor residual disease after surgery. Similarly, there is no documentation about the rationale behind the choice of PDS versus NACT in these patients with advanced-stage ovarian cancer. Clinician knowledge, skill, and experience are unknown. Similarly, the elements that influenced patient choices, such as social factors or family support, are missing. Use of the Charlson Comorbidity Index underestimates the severity of coexisting diseases because they must appear as secondary diagnoses on the hospital discharge record to be recorded. No central pathology review is available to confirm histological diagnoses. The strengths of this study are due to the large size of the cohort, the breadth and detail of data collected, and that the abstracted data were audited for validity.

This study was not intended as a justification for use of one modality over another. Nor is it an argument for a less aggressive surgical approach in ovarian cancer management. Rather, it suggests that clinicians do appear to exercise

TABLE 2. Logistic regression analysis of PDS versus NACT for stages IIIC and IV, NCDB 2003–2011*

	OR†	95% Lower	95% Upper	*P*
Year of diagnosis				
2003–2004	1			Reference
2005–2008	1.17	1.061	1.291	0.002
2009–2011	1.844	1.671	2.035	<0.001
Age, y				
18–50	1			Reference
51–60	1.324	1.185	1.478	<0.001
61–70	1.49	1.331	1.667	<0.001
≥71	1.694	1.493	1.922	<0.001
Race/ethnicity				
White	1			Reference
African American	1.345	1.18	1.533	<0.001
Hispanic	0.994	0.846	1.168	0.943
Native American	0.762	0.426	1.364	0.361
Asian/Pacific Islander	1.07	0.865	1.324	0.533
Charlson-Deyo Comorbidity Index				
0	1			Reference
1	1.166	1.063	1.278	0.001
≥2	1.045	0.866	1.261	0.646
Insurance status				
Uninsured	1			Reference
Private insurance	0.853	0.713	1.02	0.082
Medicare/Medicaid	1.079	0.897	1.299	0.420
Government insurance	1.267	0.887	1.81	0.193
Percent of population without high school diploma				
≥29%	1			Reference
20%–28.9%	0.978	0.867	1.104	0.722
14%–19.9%	0.811	0.71	0.927	0.002
<14%	0.804	0.699	0.924	0.002
Household income				
<$30,000	1			Reference
$30,000–$34,999	1.116	0.976	1.275	0.107
$35,000–$45,999	1.159	1.012	1.327	0.032
≥$46,000	1.285	1.107	1.492	0.001
Stage				
IIIC	1			Reference
IV	2.857	2.674	3.058	<0.001
Grade				
1	1			Reference
2	1.231	0.943	1.607	0.126
3	1.752	1.365	2.247	<0.001
Tumor Histology				
Nonserous	1			Reference
Serous	0.965	0.88	1.059	0.456
Adherent to NCCN guidelines				
Nonadherent	1			Reference
Adherent	1.293	1.185	1.41	<0.001
Institution type				
Community cancer	1			Reference
Comprehensive Community Cancer	1.32	1.08	1.612	0.007
Academic	1.408	1.141	1.736	<0.001
Region				
Northeast	1			Reference
South	0.894	0.804	0.994	0.039
Midwest	1.162	1.054	1.28	0.003
West	1.471	1.314	1.645	<0.001
No. of annual ovarian cases				
<7.1	1			Reference
7.1–16.4	1.063	0.94	1.202	0.330
16.5–27.7	1.015	0.896	1.15	0.809
≥27.7	1.345	1.188	1.524	<0.001
Distance from hospital, mi				
0–5	1			Reference
5.01–10	0.981	0.882	1.09	0.718
10.01–25	1.011	0.915	1.119	0.825
>25.01	1.186	1.074	1.309	<0.001

*The logistic regression modeling was adjusted for the above covariates.

†An OR of greater than 1.0 means greater likelihood to receive NACT compared with PDS.

judgment in their treatment selection based on multiple patient characteristics. It is somewhat reassuring that 2 factors that are associated with better ovarian cancer outcomes, treatment at high-volume centers[15] and adherence to NCCN guidelines,[14] are not proportionally lower in patients who receive NACT instead of PDS. Selection of primary surgery or

NACT requires knowledge, experience, and mature clinical judgment. Future studies will show if NACT trends increase for treatment of advanced-stage ovarian cancer, and if the selection criteria favoring use of NACT are liberalized over time.

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