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Costs of treatment for elderly women with advanced ovarian cancer in a Medicare population

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HIGHLIGHTS

- NACT and PDS are comparable in cost for women with stage IIIC EOC.
- PDS is 12% more expensive for women with stage IV EOC.
- Increasing Charlson score was associated with an increase in 7-month cost of care in both stages.

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ABSTRACT

Objective. To analyze the cost of treating women with advanced stage epithelial ovarian cancer (EOC) undergoing primary debulking surgery (PDS) or neo-adjuvant chemotherapy (NACT).

Methods. The Surveillance, Epidemiology, and End Results (SEER) — Medicare database (1992 to 2009) was used to evaluate the 7-month cost of care following PDS and NACT for advanced EOC. Multivariate analyses were used to evaluate differences between women treated by PDS and NACT on cost and survival.

Results. Of the 4506 women eligible for analysis, 82.4% underwent PDS and 17.6% received NACT. Eighty-five percent with stage IIIC and 78.5% with stage IV EOC underwent PDS ($p < 0.0001$). No significant difference in the median cost of care between PDS and NACT existed in women with stage IIIC EOC ($59,801 vs. $59,905). There was a 12% increase in adjusted cost of care for stage IV patients ($63,131 vs. $55,302) who received PDS ($p < 0.0001$). Increasing Charlson score was associated with an increase in 7-month cost of care in both stages. NACT was associated with a decreased 5-year overall survival in women with stage IIIC EOC (HR = 1.27, 95% CI: 1.10–1.47) and stage IV EOC (HR = 1.19, 95% CI: 1.03–1.37) compared to PDS.

Conclusion. NACT and PDS are comparable in cost for women with stage IIIC EOC, and PDS is minimally more expensive for women with stage IV EOC. PDS was associated with an increase 5-year overall survival. Future investigations should include cost-effectiveness analyses where additional measures such as quality adjusted life years and propensity scored survival are included.

1. Introduction

In 2014 the incidence of ovarian cancer in the United States is expected to exceed 21,000 and over 14,000 women are projected to succumb to this disease [1]. Currently, primary debulking surgery (PDS) followed by doublet chemotherapy with a platinum based agent and a taxane is the first line therapy and offers the greatest survival advantage for women with advanced stage epithelial ovarian cancer (EOC) [2]. PDS is intended to remove as much tumor as possible because the quantity of residual tumor is inversely proportional to improvement in 5-year progression free survival and 5-year overall survival (OS) [3–11]. In contrast, the results of a European Organization for Research and Treatment of Cancer (EORTC) trial demonstrate that PDS without optimal tumor resection is not associated with a survival advantage [12]. In patients with significant comorbidities where optimal PDS may be unachievable or carry an unacceptable high morbidity, neo-adjuvant chemotherapy (NACT) is an alternative approach that is extensively described in the literature [3–12]. The results of the CHORUS trial also demonstrated a survival advantage in women undergoing PDS [13]. However, one of the main criticisms of both CHORUS and EORTC are the reported optimal debulking rates of 15% and 41%, respectively, which is much lower than what is published elsewhere. This is significant given the clear survival advantage conveyed following optimal tumor resection compared to sub-optimal resection. Wright et al. recently published a survival analysis encompassing a period from 1990 to 2007 for women with stage II to IV EOC using SEER-Medicare data.

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They concluded that survival for PDS and NACT was equivalent. This data is limited in that it encompasses a time period with significant changes in practice standards including the incorporation of taxanes into first-line therapy and the introduction of intra-peritoneal chemotherapy. In summary, the data does not reflect current practice standards [14].

Prior studies have not considered differences in the treatment costs for women undergoing PDS and NACT. A cost analysis may provide additional insights into this highly debated topic and help guide clinical decision-making. An important concept in healthcare delivery is that of value, which is defined as measured outcomes obtained per the cost of care. One of the benefits of using value to compare treatment options is that it allows for a more accurate comparison of treatment modalities. In particular, the cost benefits of PDS and NACT should be characterized to ensure that patients are not undergoing more costly procedures that do not significantly improve their overall survival or the quality of their remaining years of life. The purpose of this investigation is to compare 7-month cost of care in women with advanced epithelial ovarian cancer who underwent PDS or NACT using SEER-Medicare data.

2. Methods

The study design was a retrospective population based study using the linked Surveillance, Epidemiology, and End Results (SEER) — Medicare database. IRB approval was obtained (HS # 2012-9076). The SEER program of the National Cancer Institute (NCI) contains approximately 97% of all incident cancer cases from tumor registries that covered 14% of U.S. population in 1995 to 28% currently [15,17]. The SEER Program registries collect data on patient demographics, primary tumor site, tumor morphology and stage, first course of treatment, and follow-up for vital status. Among patients older than 65 years old in SEER data, 93% were identified in the Medicare enrollment file and their records were successfully matched to SEER cases in the linkage process performed by NCI and Center for Medicare and Medicaid Services [16,17]. Medicare claims database includes all inpatient hospitalizations, outpatient, physician/supplier data, durable medical equipment, hospice and home health care. All claims are longitudinal from the time of a person's Medicare eligibility until death. Our analysis data include SEER cases from 1992 to 2009 and their Medicare claims from 1991 to 2010.

2.1. Study population

A total of 38,792 patients diagnosed between January 1, 1992 and December 31, 2009 with invasive ovarian cancer (SEER primary site code C569) as their only tumor or first primary tumor and second tumor was at least two years after the first ovarian cancer were identified in SEER data. We sequentially removed 287 cases with missing tumor histology information, 117 with germ cell or sex cord tumor, 820 with autopsy or death certificate only, 10,468 with age at diagnosis less than 66 years old, 3337 with missing tumor stage information, 8731 with early stage (stage IIIB and below), 36 with missing diagnosis month, 12 with missing median income in census tract and 4696 without continuous enrollment of Medicare Part A and Part B or ever enrolled in a HMO from the 12 month prior to diagnosis. Out of 10,300 cases that were identified from SEER data, 10,097 patients who were Medicare beneficiaries and had claims in the Medicare database were identified. Using International Classification of Disease 9th Revision, Clinical Modification (ICD-9-CM) procedure and diagnosis code in claims data (Supplemental Table 1. Procedure and diagnosis codes), 4714 patients were identified having both ovarian cancer surgery and chemotherapy. In order to account for survival bias, patients observed for less than 5 months after the cancer diagnosis were excluded, which resulted in excluding 196 patients, and the final study population consists of 4506 stage IIIC or IV ovarian cancer patients that received both surgery and chemotherapy. By limiting the study to those who had at least 5 months of data we attempted to capture the entire primary treatment duration whether PDS preceded chemotherapy or chemotherapy preceded interval-debulking surgery.

2.2. Outcomes

Cost of care was calculated as the sum of the amount that Medicare reimbursed for all inpatient, outpatient, physician/supplier, durable medical equipment, home health care and hospice claims during 7 month period after diagnosis of ovarian cancer. A 7-month time horizon was selected to represent costs associated with the initial treatment by PDS or NACT and to exclude downstream costs related to second-line treatment, palliation or end of life care. Costs were inflation adjusted and presented in 2010 dollars using consumer price index for medical care services from the Bureau of Labor Statistics [18]. Another outcome, survival time was defined as the time between diagnosis and death or last follow-up date.

2.3. Treatment groups

Surgery date was estimated by admission date of inpatient stay for the surgery. Starting date of chemotherapy was estimated by the date of first chemotherapy claim after cancer diagnosis. Patients who had an earlier surgery date or the same surgery and chemotherapy dates were placed in the PDS arm and patients with earlier chemotherapy start dates were placed in the NACT arm. Patients who started chemotherapy during the hospital stay for the surgery were identified as belonging to the PDS arm.

2.4. Covariates

Other covariates used in cost and survival comparisons included patient, tumor, and clinical characteristics. Patient characteristics were race/ethnicity (White or Non-white), age at diagnosis (66–69, 70–74, 75–79, 80+ years old), year of diagnosis (1992–1995, 1996–2000, 2001–2005, 2006–2010), quartile of median household income in census tract, residence area (metropolitan, non-metropolitan), and marital status (married/ unmarried or unknown). Patient's comorbidity was measured by Deyo adaptation of the Charlson Comorbidity Index. Comorbidity score was calculated by using all ICD-9 diagnosis codes, procedure codes, and HCPCS procedure codes included in the inpatient, outpatient and physician claims in 12 months before the cancer diagnosis [19,20]. To prevent over-estimation of the comorbidity when using physician or outpatient claims a patient's diagnoses must appear on at least two different claims that were more than 30 days apart. Conditions that did not appear on two different claims were not counted as comorbid conditions [21]. Tumor characteristic included tumor stage (stage IIIC or IV), tumor grade (grade I or II, III, IV or not stated), tumor histology (serous or non-serous), and tumor size ($\leq$5 cm, 5–10 cm, $\geq$10 cm or unknown size).

2.5. Statistical analysis

Frequency distributions of patients' demographic, clinical characteristic were analyzed with the χ^2 test or Fisher's exact test for categorical variables in bivariate analysis. Descriptive summary statistics of 7-month cost of care was presented and analyzed with Kruskal–Wallis test for each subcategory in each stage. After checking the distribution of the cost, natural log transformation of the cost was used as the outcome in multivariate linear regression model. Stepwise selection was used for final model. Estimates of the regression model were transformed back for interpretation. Patient's survival time was defined as the time between diagnosis and death or last follow-up. Five-year survival curves and log rank tests were performed using Kaplan–Meier estimates of survival probability for each stage. After verifying proportionality assumptions, proportional hazards model was fitted to evaluate the effect of treatment on survival after controlling for patient demographic and tumor characteristics. In multivariate survival analysis,

non-significant factors were removed from the final model using stepwise selection. All p values are two sided. Statistical analysis was performed on SAS 9.2.

3. Results

3.1. Cohort characteristics

Of the 4506 women deemed eligible for this analysis, 82.4% underwent PDS and 17.6% received NACT (Table 1). Women with stage IV EOC were more likely to receive NACT than those with stage IIIC EOC ($p < 0.0001$). No significant difference in age distribution in two treatment group with 32% of patients in 70–74 age group. Of women with stage IIIC and IV EOC, 85.4% and 78.5% received PDS, respectively. Serous histology was the most common (66%). There were significant differences in tumor histology, grade tumor size and Charlson scores in women who received PDS and NACT. The trend towards NACT increased from 6.9% to 23.7% from the year range 1992–1995, to 2006–2009, respectively ($p < 0.0001$) and with increasing Charlson score.

3.2. Stage IIIC EOC

For stage IIIC EOC there was a significant difference in cost of care between age groupings (Tables 2 and 3). Median treatment costs for patients' age 80+ was 8% less than for patients 66–69 years of age ($58,179 vs. $63,370). Compared to serous histology, other histology

Table 1
Patient and tumor characteristics by treatment arm in study population.

Characteristics	Stage IIIC							Stage IV						
	All		PDS		NACT		Chi square or Fisher exact test p-value	All		PDS		NACT		Chi square or Fisher exact test p-value
	n	%	n	%	n	%		n	%	n	%	n	%	
Total	2531	100	2162	85.4	369	14.6		1987	100.0	1560	78.5	427	21.5	
Age at diagnosis							0.319							0.734
1 = 65–69	676	26.7	588	87.0	88	13.0		556	28.0	441	79.3	115	20.7	
2 = 70–74	775	30.6	661	85.3	114	14.7		646	32.5	498	77.1	148	22.9	
3 = 75–79	694	27.4	583	84.0	111	16.0		520	26.2	414	79.6	106	20.4	
4 = 80–84	317	12.5	275	86.8	42	13.2		195	9.8	150	76.9	45	23.1	
5 = 85+	69	2.7	55	79.7	14	20.3		70	3.5	57	81.4	13	18.6	
Stage														
1 = IIIC	2531	100.0	2162	85.4	369	14.6		1987	100.0	1560	78.5	427	21.5	
2 = IV														
Histology							<0.0001							<0.0001
Serous	1769	69.9	1510	85.4	259	14.6		1238	62.3	1013	81.8	225	18.2	
Mucinous	36	1.4	36	100.0	0	0.0		38	1.9	36	94.7	2	5.3	
Endometrioid	157	6.2	149	94.9	8	5.1		83	4.2	77	92.8	6	7.2	
Clear cell	37	1.5	33	89.2	4	10.8		38	1.9	31	81.6	7	18.4	
Adenocarcinoma	184	7.3	130	70.7	54	29.3		256	12.9	146	57.0	110	43.0	
Other	348	13.7	304	87.4	44	12.6		334	16.8	257	76.9	77	23.1	
Grade							<0.0001							<0.0001
Grade I or II	412	16.3	366	88.8	46	11.2		269	13.5	235	87.4	34	12.6	
Grade III	1320	52.2	1148	87.0	172	13.0		983	49.5	806	82.0	177	18.0	
Grade IV	399	15.8	344	86.2	55	13.8		250	12.6	208	83.2	42	16.8	
Unknown grade	400	15.8	304	76.0	96	24.0		485	24.4	311	64.1	174	35.9	
Tumor size							<0.0001							<0.0001
<5 cm	408	16.1	357	87.5	51	12.5		280	14.1	228	81.4	52	18.6	
5–10 cm	471	18.6	418	88.7	53	11.3		273	13.7	235	86.1	38	13.9	
≥10 cm	483	19.1	444	91.9	39	8.1		245	12.3	214	87.3	31	12.7	
Size unknown	1169	46.2	943	80.7	226	19.3		1189	59.8	883	74.3	306	25.7	
Charlson score							0.283							0.004
0	1709	67.5	1473	86.2	236	13.8		1351	68.0	1084	80.2	267	19.8	
1	542	21.4	455	83.9	87	16.1		434	21.8	334	77.0	100	23.0	
≥2	280	11.1	234	83.6	46	16.4		202	10.2	142	70.3	60	29.7	
Year of DX							<0.0001							<0.0001
1992–1995	273	10.8	260	95.2	13	4.8		485	24.4	446	92.0	39	8.0	
1996–2000	511	20.2	457	89.4	54	10.6		383	19.3	302	78.9	81	21.1	
2001–2005	987	39.0	821	83.2	166	16.8		623	31.4	478	76.7	145	23.3	
2006–2009	760	30.0	624	82.1	136	17.9		496	25.0	334	67.3	162	32.7	
Race							0.668							0.539
White	2289	90.4	1962	85.7	327	14.3		1802	90.7	1413	78.4	389	21.6	
African American	114	4.5	95	83.3	19	16.7		98	4.9	81	82.7	17	17.3	
Asian	57	2.3	48	84.2	9	15.8		44	2.2	32	72.7	12	27.3	
Hispanic	29	1.1	24	82.8	5	17.2		11	0.6	10	90.9	1	9.1	
Other/unknown	42	1.7	33	78.6	9	21.4		32	1.6	24	75.0	8	25.0	
Quartile of median household income in census tract[a]							0.857							0.326
Lowest quartile	607	24.0	521	85.8	86	14.2		508	25.6	412	81.1	96	18.9	
Second quartile	643	25.4	554	86.2	89	13.8		496	25.0	385	77.6	111	22.4	
Third quartile	636	25.1	538	84.6	98	15.4		492	24.8	387	78.7	105	21.3	
Highest quartile	644	25.4	548	85.1	96	14.9		480	24.2	367	76.5	113	23.5	
Residential area							0.4695							0.614
Metropolitan	2171	85.8	1850	85.2	321	14.8		1664	83.7	1303	78.3	361	21.7	
Nonmetropolitan	360	14.2	312	86.7	48	13.3		323	16.3	257	79.6	66	20.4	
Marital status							0.2157							0.592
Married	1299	51.3	1110	85.5	189	14.5		1003	50.5	780	77.8	223	22.2	
Unmarried	1155	45.6	981	84.9	174	15.1		939	47.3	746	79.4	193	20.6	
Unknown	77	3.0	71	92.2	6	7.8		45	2.3	34	75.6	11	24.4	

[a] n = 12 had missing information.

was associated with a 6% increase in cost of care, respectively. A Charlson scores ≥2 was associated with a 13% higher cost of care when compared to patients with Charlson scores equal to zero. Year of diagnosis groupings 1996–2000 and 2001–2005 were associated with a statistically significant increase in adjusted cost of care compared to the referent 1992–1995 group, 11% and 19%, respectively. The adjusted cost of care was 3% lower during 2006–2009 compared to the referent, which may be an artifact of the 2006 to 2009 recession. For stage IIIC EOC the adjusted median cost of care was $59,801 for PDS and $59,905 for NACT (p = 0.9462). NACT was associated with a decreased survival in women with stage IIIC EOC (HR = 1.27, 95% CI: 1.10–1.47).

3.3. Stage IV EOC

For patients with stage IV EOC there was a significant difference in cost of care between age groupings (Tables 2 and 3). Patients age 75–79 and 80+ incurred a 6% and 4% lower median cost of care than patients 66–69 years of age respectively ($61,264 and $62,782 vs.

Table 2
Summary statistics of 7 month treatment cost in study population.

Characteristics	Stage IIIC						Kruskal–Wallis test p-value	Stage IV						Kruskal–Wallis test p-value
	7 month total cost of care (in 2010$)[a]							7 month total cost of care (in 2010$)[a]						
	n	Median	Mean	Minimum	Maximum	Std dev		n	Median	Mean	Minimum	Maximum	Std dev	
Total	2531	60,154	68,673	4463	583,672	40,069		1987	62,677	70,216	3237	740,258	39,870	
Age at Dx							0.0247							0.2828
1 = 65–69	676	63,370	69,943	14,566	354,014	36,869		556	65,408	73,245	7869	428,232	43,035	
2 = 70–74	775	59,207	68,824	14,960	469,260	42,524		646	62,686	69,706	3237	303,881	35,598	
3 = 75–79	694	60,176	69,603	4463	583,672	43,765		520	60,883	68,167	4494	740,258	43,383	
4 = 80–84	317	58,887	65,150	11,201	275,671	31,351		195	65,079	69,498	11,842	234,089	32,941	
5 = 85+	69	50,595	61,382	14,670	276,482	37,861		70	57,015	68,079	19,641	282,635	41,096	
Histology							<0.0001							0.6781
Serous	1769	58,883	67,243	11,201	583,672	38,913		1238	62,287	70,893	6946	740,258	43,304	
Mucinous	36	66,277	74,569	23,786	156,159	38,250		38	67,366	72,672	30,808	167,170	30,909	
Endometrioid	157	57,889	65,268	17,238	211,638	31,793		83	61,245	68,888	4494	217,257	33,865	
Clear cell	37	47,661	53,648	24,672	142,241	24,932		38	67,459	73,233	26,366	147,321	28,537	
Adenocarcinoma	184	67,112	76,144	4463	469,260	48,177		256	61,797	69,130	7869	292,037	33,965	
Other	348	65,144	74,521	17,478	503,575	44,644		334	63,340	68,245	3237	248,186	33,812	
Grade							0.0584							0.1333
Grade I or II	412	60,612	67,181	17,238	275,671	32,737		269	64,080	73,530	3237	740,258	55,284	
Grade III	1320	59,554	68,265	11,201	583,672	39,791		983	64,450	70,474	6946	363,778	34,697	
Grade IV	399	59,844	66,721	14,960	416,996	39,938		250	58,180	70,034	17,021	303,881	42,467	
Unknown grade	400	62,859	73,506	4463	503,575	47,129		485	61,468	67,948	4494	428,232	38,059	
Tumor size							0.0019							0.5033
<5 cm	408	58,847	67,188	14,960	288,797	37,515		280	61,977	69,520	6946	210,319	33,918	
5–10 cm	471	57,428	65,253	20,096	354,014	34,966		273	65,077	76,016	18,590	740,258	60,322	
≥10 cm	483	58,161	66,572	14,670	583,672	40,033		245	60,442	69,973	10,495	217,257	35,338	
Size unknown	1169	62,527	71,438	4463	503,575	42,649		1189	62,388	69,098	3237	314,716	35,895	
Charlson score							0.0001							0.0045
0	1709	59,200	66,688	4463	583,672	39,212		1351	60,194	69,350	3237	740,258	42,060	
1	542	60,993	71,546	14,566	416,996	41,826		434	65,819	71,407	4494	212,262	33,667	
≥2	280	63,149	75,234	23,744	354,014	40,871		202	70,401	73,444	14,708	282,635	36,931	
Race							0.0271							0.0101
White	2289	59,646	68,003	4463	583,672	39,811		1802	61,459	69,365	3237	740,258	39,829	
African American	114	64,421	75,259	20,400	255,668	43,009		98	71,419	80,030	18,975	217,257	39,715	
Asian	57	63,518	68,697	20,718	156,159	31,380		44	69,585	72,412	25,265	142,105	28,028	
Hispanic	29	66,300	84,217	28,256	217,014	42,401		11	76,823	84,575	10,495	196,238	48,842	
Other/unknown	42	63,188	76,590	22,523	276,482	50,748		32	63,192	80,145	32,102	279,719	48,493	
Year of DX							<0.0001							<0.0001
1992–1995	273	55,431	66,572	4463	272,768	41,000		485	56,316	65,975	4494	363,778	38,654	
1996–2000	511	60,642	71,273	14,670	469,260	42,915		383	62,288	67,894	3237	282,635	34,503	
2001–2005	987	65,080	73,666	14,566	583,672	42,112		623	71,092	78,432	14,708	740,258	45,076	
2006–2009	760	53,063	61,197	11,201	288,797	33,368		496	56,507	65,837	6946	303,881	36,317	
Quartile of median household income in census tract[b]							0.0723							0.0803
Lowest quartile	607	58,315	66,513	15,073	503,575	39,448		508	60,970	67,579	6946	428,232	37,957	
Second quartile	643	59,351	68,425	14,566	416,996	39,201		496	61,940	67,978	3237	292,037	32,723	
Third quartile	636	61,274	69,062	17,478	583,672	39,992		492	62,561	71,998	10,495	363,778	39,450	
Highest quartile	644	61,457	70,540	4463	469,260	41,568		480	64,887	73,584	8086	740,258	47,932	
Residential area							<0.0001							<0.0001
Metropolitan	2171	61,177	69,832	4463	583,672	40,907		1664	64,455	71,999	3237	740,258	41,529	
Non-metropolitan	360	54,000	61,684	14,566	392,283	33,801		323	55,833	61,029	6946	180,186	28,212	
Marital status							0.095							0.0297
Married	1299	58,976	67,647	14,960	392,283	36,960		1003	60,657	68,851	3237	428,232	37,499	
Unmarried	1155	61,657	69,824	4463	583,672	41,751		939	65,011	72,146	4494	740,258	42,688	
Unknown	77	56,622	68,738	25,616	469,260	60,073		45	57,913	60,368	19,700	135,538	25,632	
Treatment arm							0.2367							0.0299
PDS	2162	59,805	68,811	14,566	583,672	41,383		1560	63,067	71,695	8086	740,258	41,880	
NAC	369	62,565	67,867	4463	252,528	31,313		427	60,442	64,813	3237	200,885	30,898	

[a] 7 month total cost = Medicare payments for inpatient, outpatient, physician claims, durable medical equipment, home health, hospice claims within 7 month after DX and adjusted for inflation.
[b] n = 12 had missing information.

Table 3
Results from multivariate regression model on cost.[a]

Factors	Stage IIIC				Stage IV			
		p-Value	Unadjusted median cost ($)	Adjusted median cost ($)		p-Value	Unadjusted median cost ($)	Adjusted median cost ($)
Age at Dx								
1 = 65–69	Reference		63,370		Reference		65,408	
2 = 70–74	4% less than ref	0.0733	59,207	60,726	3% less than ref	0.2201	62,686	63,245
3 = 75–79	3% less than ref	0.1716	60,176	61,284	6% less than ref	0.0255	60,883	61,303
4 = 80–84	8% less than ref	0.0107	58,887	58,571	3% less than ref	0.5044	65,079	63,708
5 = 85+	15% less than ref	0.006	50,595	54,156	8% less than ref	0.1695	57,015	60,220
Histology								
Serous	Reference		58,883		Reference		62,287	
Mucinous	4% more than ref	0.5873	66,277	61,365	6% more than ref	0.4755	67,366	65,859
Endometrioid	2% less than ref	0.5628	57,889	57,609	0.4% less than ref	0.9468	61,245	62,062
Clear cell	16% less than ref	0.0216	47,661	49,550	7% more than ref	0.3604	67,459	66,886
Adenocarcinoma	10% more than ref	0.0048	67,112	65,050	3% more than ref	0.4464	61,797	63,886
Other	10% more than ref	0.0002	65,144	64,973	1% less than ref	0.787	63,340	61,792
Charlson score								
0	Reference		59,200		Reference		60,194	
1	6% more than ref	0.0084	60,993	62,794	5% more than ref	0.0875	65,819	62,955
≥2	12% more than ref	<.0001	63,149	66,572	8% more than ref	0.0418	70,401	64,784
Year of DX								
1992–1995	Reference		55,431		Reference		56,316	
1996–2000	10% more than ref	0.0040	60,642	61,143	7% more than ref	0.0422	62,288	60,197
2001-2005	18% more than ref	<.0001	65,080	65,531	27% more than ref	<.0001	71,092	71,495
2006-2009	3% less than ref	0.3026	53,063	53,604	4% more than ref	0.2101	56,507	58,583
Race								
White	Reference		59,646		Reference		61,459	
African American	7% more than ref	0.1137	64,421	63,885	12% more than ref	0.0204	71,419	68,912
Asian	1% more than ref	0.912	63,518	60,047	4% more than ref	0.6293	69,585	63,643
Hispanic	21% more than ref	0.0264	66,300	71,930	10% more than ref	0.5158	76,823	67,458
Other/Unknown	7% more than ref	0.3118	63,188	64,035	12% more than ref	0.182	63,192	68,785
Residential area								
Metropolitan	Reference		61,177		Reference		64,455	
Non-metropolitan	12% less than ref	<.0001	54,000	54,114	15% less than ref	<.0001	55,833	54,617
Treatment arm								
PDS	Reference		59,805		Reference		63,067	
NACT	0.5% less than ref	0.8483	62,565	59,510	13% less than ref	<.0001	60,442	55,182

[a] 7 month total cost = Medicare payments for inpatient, outpatient, physician claims, durable medical equipment, home health, hospice claims within 7 month after DX and adjusted for inflation.

$65,374). There were no significant differences in cost of care based on tumor histology. Patients with Charlson scores ≥2 had an 8% higher cost of care than patients with Charlson scores of zero. Cases diagnosed in 1996–2000 and 2001–2005 were associated with a statistically significant increase in adjusted cost of care when compared to the referent 1992–1995 grouping. For stage IV EOC the adjusted median cost of care was $63,131 for PDS and $55,302 for NACT ($p < 0.0001$). NACT was associated with a decreased survival in women with stage IV EOC (HR 1.19, 95% CI: 1.03–1.37).

4. Discussion

Removal of gross disease greater than 1 cm is associated with an increase in survival [3,4]. Among the hypotheses that attempt to explain the molecular mechanisms of improved survival following optimal tumor debulking two are related to the role of removing drug resistant clones and removing poorly perfused areas of tumor by surgical resection. Another explanation is the fractional kill hypothesis. This hypothesis states that a fixed percentage of malignant cells are killed with chemotherapy and that surgery decreases the overall tumor burden while increasing the benefits of chemotherapy. In addition to the biochemical factors, practice patterns may play a role in the survival in patients with EOC. Provider bias may be related to their clinical training and the practice patterns within their local community.

The results of the only two prospective trials to date failed to show a survival benefit and demonstrated that morbidity was increased in patients who underwent PDS [12,13]. The first, the European Organization for Research and Treatment of Cancer (EORTC) compared optimal debulking rates, operative times, post-operative complications, length of hospital stay, progression free survival (PFS), and 5-year survival differences between patients who underwent PDS and received NACT and found that NACT was associated with a lower mortality, morbidity and equivalent PFS and overall survival than PDS [12]. These results are met with criticism. Chi et al., conducted an analysis on patients at Memorial Sloan Kettering Cancer Center (MSKCC) treated during the same time period as the EORTC trial and demonstrated a higher PFS and OS than reported in the EORTC trial. They proposed the following confounders regarding these findings; 1) the improved outcomes in the PDS arm may be related to selection biasing sicker patients to the trial arm and 2) substandard surgical technique [8]. Though the disposition of patients to NACT who are thought to be poor surgical candidates makes sense, it also significantly limits the ability to compare certain aspects of these treatment options. We attempted to account for this in our study by controlling for Charlson score and other patient characteristics.

The second, the CHORUS trial, was conducted in the UK and compared upfront surgery to chemotherapy in patients newly diagnosed with clinical stage III and IV ovarian cancer. They concluded that PDS and NACT groups experienced a similar OS, and that NACT was associated with decreased mortality and increased optimal debulking rates [13]. One of the main criticisms is that the optimal debulking rate from PDS in the CHORUS trial was 15%, which is several times lower than rates typically reported in the US.

In the current study, patient demographics are consistent with that of other analyses comparing PDS to NACT for Stage IIIC and IV EOC. Whites comprised more than 90% of the total study population and the average age of our population was between 70 and 74 years of age. Our OS results are in agreement with other retrospective analyses

comparing PDS to NACT. We found that PDS was associated with an increased 5-year OS in women with stage IIIC and IV EOC, however, we acknowledge that the survival advantage observed in retrospective analyses is highly confounded.

PDS was also associated with a comparable 7-month cost of care across the entire population. A sub-analysis revealed that no significant cost differences exist between PDS and NACT for stage IIIC EOC. In patients with stage IV EOC there is a statistical difference between the costs of care favoring NACT. In patients with both stage IIIC EOC and IV EOC, age, histology, Charlson score and year of diagnosis were all associated with differences in 7-month cost of care.

Even after excluding patients from the original pool for age <65, early stage disease and lack of continuous enrollment in Medicare A and B, one of the strengths of this investigation is the large sample size and that SEER database is known for its accuracy and completeness. One of the limitations of this study is that it is retrospective and based on information extracted from claims data in a fee-for-service population. In addition, our analysis was performed on women ≥65 years of age and may not accurately predict costs of care or survival in younger women. Also death due to other causes may be underreported. Furthermore, patients treated with NACT may represent a more complex baseline disease that is difficult to capture. Other limitations include the possibility for staging differences favoring more accurate staging in women undergoing PDS over NACT and an inability to accurately determine if sicker patients were biased to NACT. The difficulty in identifying patients treated by providers with substandard surgical technique or accurately quantify the amount of residual disease is also one of the limitations. Despite these limitations, the survival advantage associated with PDS in our investigation is consistent with what has been shown in other retrospective analyses.

5. Conclusion

In conclusion, there was no cost savings associated with NACT for stage IIIC. Patients with stage IV EOC treated with PDS had an incremental cost increase over NACT. These data can inform the discussion about appropriate management for patients with advanced ovarian cancer by bringing cost discussions into the equation. Future studies should investigate the cost effectiveness of PDS when compared to NACT and include quality of life measures.

Conflict of interest statement

The authors have no disclaimers.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ygyno.2015.03.050.

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