

## RESEARCH ARTICLE

# Pharmaceuticals Account for the Majority of Actual Cost of Care from Diagnosis to Death in the Treatment of Ovarian Cancer

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## Abstract

**Objective:** To analyze the actual detailed direct cost of treating women with ovarian cancer who die to their disease.

**Background:** While ovarian cancer is not the most common gynecologic malignancy, it is the most deadly, and presumably most costly. The high cost of ovarian cancer is multi-factorial.

**Methods:** We used cost data from our hospitals centers as well as physicians fees to gather every cost associated with taking care of a patient with ovarian cancer from diagnosis to death. This included blood, pharmacy, labs, surgery, physician fees, nursing, radiology, pathology. We did not evaluate charges nor reimbursement, purely direct cost to the study hospital and physicians for the care of these patients. We analyzed the last 10 patients who died of ovarian cancer at our institution.

**Results:** Of the included 10 patients, the majority was advanced stage (80%) and of serous histology (70%), the overall survival was 21 months. We found the direct cost to the institution to be \$1,132,773 for 10 patients, ranging from \$30,611 to \$263,514 per patient. The majority of cost (43%) was from pharmacy and the highest single expense was for Bevacizumab, which composed 51% of the total direct cost of pharmaceuticals, and 22% of the cost of all expenses. The remaining cost came from physician services (16%), inpatient nursing unit costs (14%), and the cost related to infusion related services (6%), respectively.

**Conclusions:** We found that cost varies significantly between patients and not unexpectedly, increases with increased survival time. Pharmacy costs ie (chemotherapy) significantly outweighs any other cost, and a significant proportion of cost accrued during the last 30 days of life. The actual direct cost to an institution to take care of a patient with ovarian cancer is approximately \$113,277, based on a small sample size. The majority of this cost is for pharmacy and specifically for Bevacizumab. This aspect of evaluating cost should be further analyzed.

**Keywords:** Ovarian Cancer; Chemotherapy; Cost

## Introduction

Ovarian cancer is the most deadly gynecologic malignancy, and presumed most costly [1]. The lifetime risk of invasive ovarian cancer in the US is 1 in 75 (based on 2011-2013 data) and the 5-year survival rate is 47.4% (based on 2008-2014) [1]. In women aged 40-59 and 60-79 years, ovarian cancer is the fourth and fifth leading cause of cancer-related death, respectively [1]. In 2018, there were estimated to be more than 22,240 new cases of ovarian cancer and of those with the diagnosis, over 14,070 will die from their disease [1]. Over the last 40 years, despite advances in surgical technique for primary debulking surgery, changes in chemotherapy (i.e. the use of platinum-based combination therapy, dose dense regimens, or intra-peritoneal delivery), and introduction of targeted therapies, the 5-year survival rate have only marginally increased [1]. In 1975, the 5-year survival rate was 33.6%; based on 2008-2014 data, the 5-year survival rate is now 47.4%. This change is by prolonging the life expectancy of women with recurrent ovarian cancer, not by increasing the cure rate of the disease.

Screening methods to detect ovarian cancer are not reliable and therefore most women present with advanced disease (stage III-IV) [2-5]. The standard of care for advanced stage ovarian cancer includes cytoreductive surgery and combination platinum/taxane chemotherapy, as outlined in the National Comprehensive Cancer Network (NCCN) treatment guidelines [2,3]. Despite advances in chemotherapy and biologic agents, there is no standard of therapy for recurrent ovarian cancer [2,3]. Any treatment approach for recurrence is almost never curative, is associated with increased morbidity and adds significant cost. The inability to increase the number of women who are cured from ovarian cancer in large part stems from the lack of adequate screening and surveillance strategies.

The costs associated with cancer treatment impact both the affected individual and the health care system. Health care costs in general have risen dramatically, now exceeding 17.5% of GDP (2014 data) [6,7]. This unsustainable cost trajectory has led to the development of renewed attention on health care value, defined as achieving high-quality outcomes with efficiency and lowest cost. Ovarian cancer in particular is susceptible to rising costs due to influx of novel chemotherapeutics, biologic agents and genetic tumor profiling. All of which are substantially more costly than established front-line therapies but have limited proven benefit [8,9].

The high cost of ovarian cancer is multi-factorial based on the chronic nature of the disease, high recurrence rates, complex surgeries, prolonged hospital stays, chemotherapy regimens, and late referrals to hospice. Studies have shown that costs associated with the care of an ovarian cancer patient are highest during the first year of diagnosis where major surgery is performed and chemotherapy is given, and the last year of life where patients often spend a substantial amount of time in the hospital [8-10].

The definition of cost in health care is not easily defined. There are many aspects of cost—from charges by facilities, reimbursement from insurance, and the actual cost of providing a specific service. The direct cost of ovarian cancer is largely unknown. As quality and cost are actively being scrutinized, we wanted to look at the direct detailed cost of care for a patient suffering from ovarian cancer. In order to achieve a finite study period, we evaluated the cost associated with the last 10 consecutive ovarian cancer patients who died from their disease. We examined every aspect of cost associated with their treatment from diagnosis to death. Our objective is to shed light on the components and drivers of costs for the treatment of ovarian cancer from the perspective of the hospital and physician.

## Patients and Methods

Approval was obtained from Rush University Medical Center (RUMC) Internal Review Board. We analyzed the total detailed cost of 10 consecutive patients that died from ovarian cancer and received care from 2008 until 2014. We excluded patients who received any portion of care outside the study hospital. We chose to include only patients who died of their disease to give a distinct end point. Clinical data was obtained from the medical center's electronic medical records. Financial data was obtained using Alliance Decision Support Software, MedAssets™ Inc., Atlanta, GA, and the hospitals cost accounting system. This analysis

Cost Category	Definition
Blood	Any service provided by the blood bank including ABO typing, serological cross-matching, procurement and screening of all blood products.
ER	Any service provided in the emergency department such as IV injections, pulse oximetry, or glucose monitoring, and includes an adjustment for intensity of service (Levels I-V) as well as time spent in the observation area.
Infusion Related Services	Any service involving the infusion of antineoplastic agents in the outpatient environment.
Inpatient Radiology	Any radiologic procedure, excluding cardiac testing or electroencephalography services, for patients during their hospital stay, includes diagnostic services, interventional radiology and positron emission tomography.
Lab	Any inpatient or outpatient lab service that was provided including general chemistry, pathology and microbiology.
Nursing Unit	Includes the direct costs related to time spent on a non-ICU nursing unit measured in days in private room, or hours as an outpatient in a bed or in observation.
Nursing Unit (ICU)	Includes the direct costs related to time spent on an ICU nursing unit, measured in days.
Other	Any service provided by the cardiac testing department, the endoscopy suite, evoked potentials, peripherally inserted central catheter line placement, services from clinical psychology, and pulmonary function testing.
Outpatient Radiology	All professional and facility charges bundled into a single value for outpatient CT or MRI. To estimate the direct cost for services, the charges have been multiplied times the study hospitals cost to charge ratio (0.17).
Pharmacy	Includes the direct costs for all medications. Does not include the cost of any medication distributed by the patient for use at home.
Physicians Services	Includes the professional and facility portion of services provided in both either inpatient and outpatient settings including any physician providing services as a member of the medical staff at the study hospital.
PT/OT/ Speech	Includes the direct costs for all services provided by a physical, speech or occupational therapist in both inpatient and outpatient settings.
Surgical Services	Includes direct costs incurred in the pre-operative area, operating suites and recovery areas. Costs are determined based on time increments in each area, as well as anesthesia method, equipment and supplies utilized.

Table 1: Cost Category Definition

included hospital, outpatient costs and physician professional fees. The hospital and outpatient costs are representative of the direct costs to the organization using a methodology where each cost for a unit of service (e.g., staff, time, supplies, pharmacy and non-capital equipment) required for patient care was charged directly to a cost center. This study did not include the costs related to graduate medical education or indirect cost (fixed hospital costs required to keep the hospital in operation, such as electricity, major pieces of equipment, land and buildings). The direct cost for both inpatient and outpatient physician professional services were included. For physicians that are not employed at the study hospital (anesthesiology, pathology, and inpatient radiology), charges were obtained and multiplied by the study hospital’s cost to charge ratio (0.17), to estimate the direct cost for services provided by these specialties. Detailed explanation for each of the cost categories can be seen in Table 1. These data were not adjusted to reflect inflation, which cumulatively has reached 10.5% from 2008 to 2014.

## Results

### Clinical

The median age at diagnosis was 62. The median overall survival for our population was 21.1 months. The majority of patients (80%) were diagnosed with Stage IIIc/IV disease, and with serous histology (70%). Most patients (90%) had upfront surgery, of which 50% were optimally debulked (<1cm). All patients received intravenous chemotherapy; none received intraperitoneal chemotherapy. The median number of chemotherapy cycles was 17. Half (50%), received bevacizumab at some point during their treatment. Only 50% enrolled in hospice. Detailed characteristics of each patient can be seen in Table 2.

Patient	Age	Stage	Histology	Chemo regimens	Cycles of bevacizumab	Survival time (months)	Cost	Hospice enrollment
1	70	IV	Serous	22	9	23.3	\$127,137	yes
2	76	IIIC	Carinosarcoma	4	0	1.4	\$30,611	no
3	53	IIIC	Clear cell	13	2	11.5	\$57,363	yes
4	62	IIIC	Serous	32	9	54.3	\$164,582	no
5	45	IIIC	Serous	35	17	43.9	\$148,174	yes
6	62	IV	Serous	20	0	40.7	\$91,077	no
7	50	IC	Serous	54	21	49.7	\$263,514	yes
8	27	IC	Mucinous	8	0	18.9	\$85,186	yes
9	78	IV	Serous	13	0	14.8	\$90,929	no
10	75	IV	Serous	14	0	16.0	\$74,200	no

Table 2: Clinical characteristics

### Cost

The median cost of a patient who dies from their ovarian cancer out our institution is \$91,003, with a range from \$30,611 to

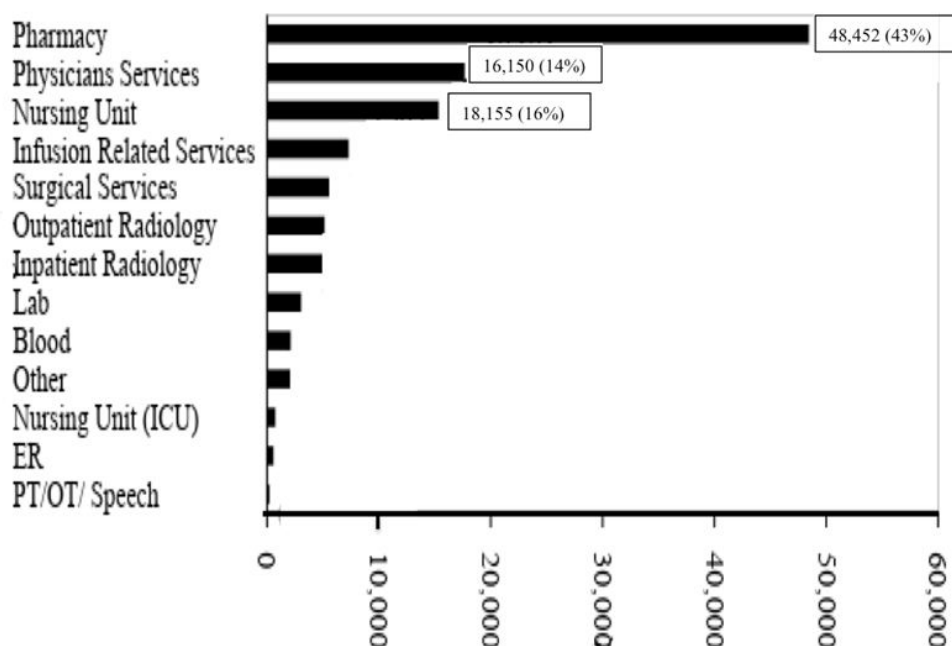


Figure 1: Average Cost by Category

\$263,514. The majority of cost comes from pharmacy (43%), followed by physician services (16%), and nursing (14%), as seen in Figure 1.

A closer examination of pharmacy costs showed that in this population, bevacizumab, which was used in only 50% of our population's care, accounted for 22% of total cost on average, and 51% of all pharmacy costs (Figure 2). Evaluation of physician cost by specialty revealed: gynecologic oncology accounted for the majority of the cost, followed by internal medicine, and radiology, as seen in Figure 3. The average cost of labs per patient was \$3,044, with an average of 457 labs tested per patient. Each patient had an average of 21 CT scans, with all imaging (not including physician professional services) accounting for 4% of total costs. Patients had an average of 23.8 (range 12-44) physician visits during this time period. The average numbers of admissions was 4.6 ranging from 3 to 6 admissions, and an average length of stay per patient was 6.5 days. We found that cost was associated with the total length of treatment, as seen in Figure 4.

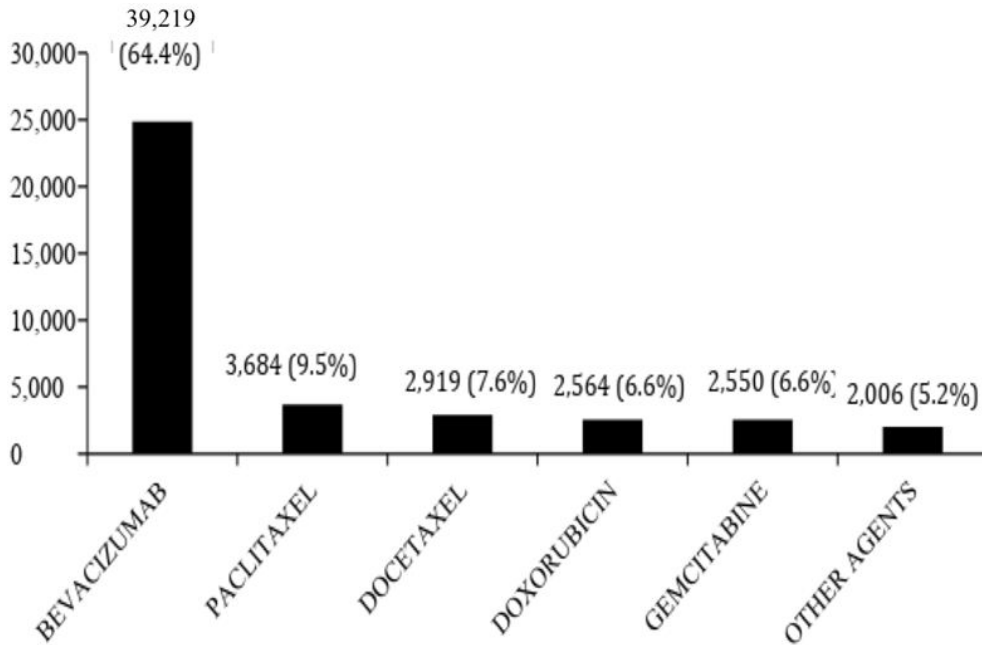


Figure 2: Average cost Anti neoplastic Agents

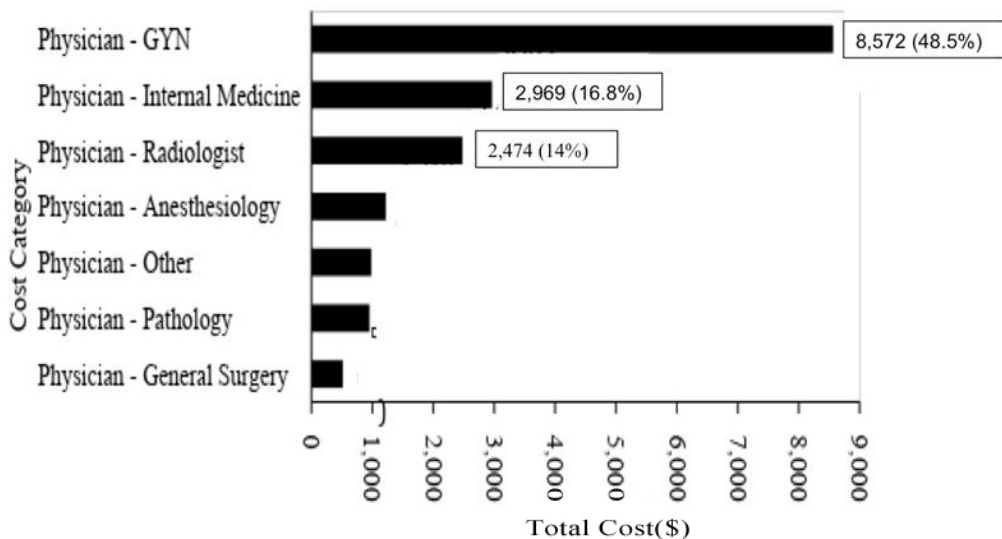


Figure 3: Average Cost by Physician Services

### Last 30 days of Life

Half (50%) of the patients spent at least some time in the hospital during their last 30 days of life, averaging from 3 to 17 days. The percent of cost during these last 30 days of life ranged from 6% to 21% of their total treatment cost.

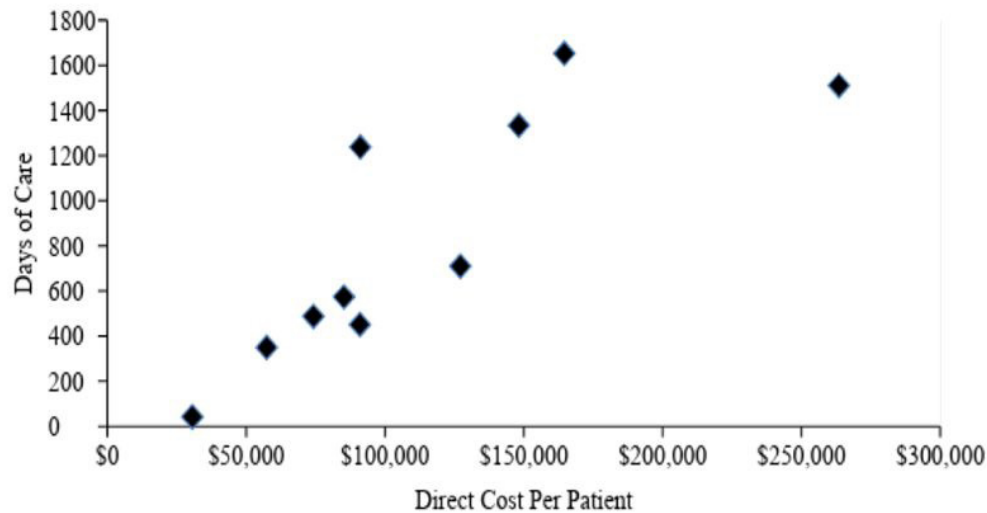


Figure 4: Total Cost and Treatment Length

## Discussion

With ovarian cancer being the most deadly of all gynecologic cancers, and presumably the most costly, we wanted to explore the actual direct costs from diagnosis to death for ovarian cancer [1]. Our objective was to shed light on the components and drivers of costs for ovarian cancer from the perspective of the hospital and physician. We found that many cost utility and/or cost analysis studies obtain cost amounts from Medicare reimbursement or modeling based on reimbursement. Cost varies significantly between patients and not unexpectedly, increases with increased survival time. Pharmacy costs i.e. (chemotherapy) significantly outweigh any other cost category. Additionally, a substantial proportion of cost is accrued during the last 30 days of life.

In our patient population, the median age of diagnosis was 62, and median overall survival was 21.1 months. Most (80%) were diagnosed with Stage IIIC/IV disease, and with serous histology (70%). Our population largely fits within national averages of age of diagnosis, overall survival, stage at diagnosis and histology [1-3].

In our study, almost all patients received the standard of care- 90% had upfront surgery, of which 50% were optimally debulked (<1cm), followed by chemotherapy [2,3]. The median number of chemotherapy cycles was 17. Several studies have questioned whether neoadjuvant chemotherapy, prior to surgery, should be considered as standard therapy in certain circumstances. A cost effectiveness analysis of primary debulking surgery (PDS) compared to neoadjuvant chemotherapy (NACT) was done using Surveillance, Epidemiology, and End Results data linked to Medicare claims (SEER-Medicare) [9]. Using a Markov model, authors modeled cost and survival inputs between 1992 and 2009 [9]. In their model, women with stage IIIC disease had a higher mean adjusted treatment cost for PDS when compared to NACT (\$31,945 v \$30,016) but yielded greater quality-adjusted life-years (QALYs) (1.79 v 1.69) [9]. Women with stage IV disease again had a higher mean adjusted treatment cost following PDS when compared to NACT (\$31,869 v \$27,338) but yielded greater QALYs (1.69 v 1.66) [9]. Authors concluded that PDS was far more cost effective given the QALYs for stage IIIC disease, again validating this approach [9]. For stage IV disease, PDS was still slightly more cost-effective [9].

Half (50%) of our patients received bevacizumab at some point during their treatment. Though some survival benefits were found with bevacizumab, cost-effective analyses have shown that a price reduction between 46-67% would be required for the product to be cost effective in the high-risk subgroup [12]. This percentage is based on the National Institute for Health and Care Excellence's threshold, and recent decision to not recommend bevacizumab for advanced ovarian cancer [12,13].

Only 50% of our patient population enrolled in hospice for end of life care. Studies have shown that end-of-life (EOL) medical consumes 10-12% of national health care expenditures and 27% of Medicare dollars annually [14]. Additionally, studies suggest that hospice services decrease EOL expenditures by 25-40% [14]. A study by Lewin, *et al.* compared the total cost of hospital-based resources utilized in ovarian cancer patients during their final 60 days of life for those enrolled in hospice versus those not enrolled [14]. Demographic, histologic and staging characteristics as well as platinum sensitivity and mean number of chemotherapy cycles were similar between the two groups before the last 60 days of life [14]. However, during the study period, the mean total cost per patient in the non-hospice group was \$59,319 versus \$15,164 in the hospice group ( $P = 0.0001$ ) [14]. A significant difference in cost was noted for mean inpatient days (\$6,584 vs. \$1,629,  $P = 0.0007$ ), radiology (\$6,063 vs. \$2,343,  $P = 0.003$ ), laboratory (\$2,281 vs. \$2,026,  $P = 0.0004$ ), and pharmacy charges (\$13,650 vs. \$4,465,  $P = 0.0017$ ) as well as for treating physician per patient (\$112,707 vs. \$34,677,  $P = 0.04$ ) [14]. Overall survival for the two groups was the same [14]. Authors concluded that there is a significant cost difference with no appreciable improvement in survival between ovarian cancer patients treated aggressively versus those enrolled in hospice at the EOL [14]. These data suggest that earlier hospice enrollment is beneficial.

A major strength of our article is that we were able to examine the direct actual cost to 10 of our patients who died from their disease. The total cost was evaluated from diagnosis through death. Again, we found that pharmacy costs i.e. (chemotherapy) significantly outweigh any other cost, and a significant proportion of cost was accrued during the last 30 days of life. To our knowledge this is one of the first studies evaluating actual cost of care for patients with ovarian cancer, looking at the cost to a facility and/or cost center. Weaknesses to our approach include lack of associated costs accrued outside the hospital, break down of cost for patients with platinum-sensitive v platinum-resistant ovarian cancer, as well as the cost of hospice care in our population. These areas in particular would have been interesting to include and serve as areas for future studies.

To reiterate what Sfakianos, *et al.* stated in their article, “while decisions surrounding the diagnosis and treatment of cancer are difficult and cost is not usually the most pressing concern of decision makers, the increasing burden of the rising cost of health care demands attention. As newer, higher-cost therapies become available, formal evaluation of the costs and benefits of these new treatments in comparison to existing and established strategies should be a high priority” [8]. Our patients deserve dedication to delivering the highest quality care that is proven cost-effective. Our study highlights several areas that serve as starting point for future studies on cost-effectiveness.

## Conflict of interest statement

The authors have no disclaimers.

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