

## RESEARCH ARTICLE

## Trends in extent of surgical cytoreduction for patients with ovarian cancer

Deanna H. Wong<sup>1</sup>, Alexandra L. Mardock<sup>1</sup>, Erica N. Manriquez<sup>2</sup>, Tiffany S. Lai<sup>2</sup>, Yas Sanaiha<sup>3</sup>, Abdulrahman K. Sinno<sup>4</sup>, Peyman Benharash<sup>3</sup>, Joshua G. Cohen<sup>2\*</sup>

**1** David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, United States of America, **2** Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of California, Los Angeles, Los Angeles, California, United States of America, **3** Division of Cardiac Surgery, Cardiovascular Outcomes Research Laboratories (CORELAB), David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, United States of America, **4** Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Miami, Florida, United States of America

\* JGCohen@mednet.ucla.edu



## OPEN ACCESS

**Citation:** Wong DH, Mardock AL, Manriquez EN, Lai TS, Sanaiha Y, Sinno AK, et al. (2021) Trends in extent of surgical cytoreduction for patients with ovarian cancer. PLoS ONE 16(12): e0260255. <https://doi.org/10.1371/journal.pone.0260255>

**Editor:** Xiaodong Cheng, Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, China, CHINA

**Received:** January 11, 2021

**Accepted:** November 6, 2021

**Published:** December 8, 2021

**Peer Review History:** PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0260255>

**Copyright:** © 2021 Wong et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Data Availability Statement:** All relevant data are within the manuscript and its [Supporting information](#) files.

## Abstract

## Purpose

To identify patient and hospital characteristics associated with extended surgical cytoreduction in the treatment of ovarian cancer.

## Methods

A retrospective analysis using the National Inpatient Sample (NIS) database identified women hospitalized for surgery to remove an ovarian malignancy between 2013 and 2017. Extended cytoreduction (ECR) was defined as surgery involving the bowel, liver, diaphragm, bladder, stomach, or spleen. Chi-square and logistic regression were used to analyze patient and hospital demographics related to ECR, and trends were assessed using the Cochran-Armitage test.

## Results

Of the estimated 79,400 patients undergoing ovarian cancer surgery, 22% received ECR. Decreased adjusted odds of ECR were found in patients with lower Elixhauser Comorbidity Index (ECI) scores (OR 0.61,  $p < 0.001$  for ECI 2, versus  $ECI \geq 3$ ) or residence outside the top income quartile (OR 0.71,  $p < 0.001$  for Q1, versus Q4), and increased odds were seen at hospitals with high ovarian cancer surgical volume (OR 1.25,  $p < 0.001$ , versus low volume). From 2013 to 2017, there was a decrease in the proportion of cases with extended procedures (19% to 15%,  $p < 0.001$ ). There were significant decreases in the proportion of cases with small bowel, colon, and rectosigmoid resections ( $p < 0.001$ ). Patients who underwent ECR were more likely treated at a high surgical volume hospital (37% vs 31%,  $p < 0.001$ ) over the study period. For their hospital admission, patients who underwent ECR had increased mortality (1.6% vs. 0.5%,  $p < 0.001$ ), length of stay (9.6 days vs. 5.2 days,  $p < 0.001$ ), and mean cost (\$32,132 vs. \$17,363,  $p < 0.001$ ).

**Funding:** DHW received funding by the Dean's Leadership in Health and Science Scholarship at the David Geffen School of Medicine. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing interests:** The authors have declared that no competing interests exist.

## Conclusions

Likelihood of ECR was associated with increased medical comorbidity complexity, higher income, and undergoing the procedure at high surgical volume hospitals. The proportion of ovarian cancer cases with ECR has decreased from 2013–17, with more cases performed at high surgical volume hospitals.

## Introduction

Approximately 22,000 women in the United States each year are diagnosed with ovarian cancer, which continues to be the fifth most common cause of cancer-related death among women [1, 2]. Five-year survival across all women diagnosed with ovarian cancer is 48% [1], but each patient's prognosis is influenced by multiple variables including stage, social determinants of health, and volume of residual disease after surgical cytoreduction [3].

Due to screening and diagnostic limitations, 80% of patients are diagnosed with stage III or IV cancer [3]. At these advanced stages, survival is significantly decreased and treatment is more challenging due to spread of disease beyond the ovary. One important predictor of progression-free and overall survival is complete cytoreduction to no gross residual disease [4, 5], which is a practice recommended by the National Comprehensive Cancer Center (NCCN) [6] and is an important modifiable prognostic factor for ovarian cancer. Extended cytoreduction (ECR) is often required to achieve this state and involves surgical procedures beyond the standard hysterectomy and bilateral salpingo-oophorectomy. These additional procedures include tumor resection involving the bowel, diaphragm, liver, spleen, bladder, or stomach.

Receiving ECR and reaching complete cytoreduction have been shown to correlate with surgeon case volume [7, 8]. Studies show that ovarian cancer patients treated in the United States have improved surgical outcomes and survival when treated in higher volume hospitals and by gynecologic oncologists [7, 8]. However, not all patients have equal access to these resources. Age, race, income, and geography may limit a patient from being treated at higher volume hospitals, by gynecologic oncologists, and in accordance with NCCN guidelines [3, 9–13].

The objective of this study was to identify patient and hospital characteristics associated with ECR and to identify trends in extended procedures over the study time period. We hypothesized that patients with higher income or private insurance, those seen at hospitals with higher procedural volume, and those with greater disease burden would have increased likelihood of receiving ECR. Additionally, we postulated that ECR would be associated with higher risk of perioperative mortality and longer, more costly hospitalization.

## Methods

### Study design and data source

We performed a retrospective analysis of patient hospitalizations between January 1, 2013 and December 31, 2017 as identified by the National Inpatient Sample (NIS). The NIS is the largest publicly available all-payer inpatient database in the United States and is part of the Agency for Healthcare Research and Quality's (AHRQ) Healthcare Cost and Utilization Project. The database contains data from more than 7 million annual hospital discharges in 48 states and, through inherent survey weights, estimates over 35 million hospitalizations annually [14]. This

study was granted exemption from the Institutional Review Board at the University of California, Los Angeles given its use of deidentified data.

### Population and surgical procedures

The study cohort consisted of female patients aged 18 years or older who underwent any surgery involving oophorectomy and carried a diagnosis of ovarian, fallopian tube, or primary peritoneal cancer, as indicated by the *International Classification of Disease–Ninth and Tenth Revisions–Clinical Modification* (ICD-9 and ICD-10). Secondary procedure codes were used to identify patients who had undergone ECR, which was defined as any additional surgical procedure involving ileostomy/colostomy placement, splenectomy, bladder resection or resection of the colon, small intestine, liver, diaphragm, or stomach (Supplement 1) [15]. Given the national transition from ICD-9 to ICD-10 coding in October 2015, accurate conversion of procedure codes was confirmed using chi-square tests comparing the third and fourth quarters of 2015. This was performed for the proportion of each unique procedure that was studied in trend analysis—total extended procedures, small bowel resection, colon resection, rectosigmoid resection, and colostomy formation—and no significant change was found in the proportions identified by ICD-9 versus ICD-10 codes.

### Baseline patient and hospital characteristics

Patient demographics, clinicopathologic information, and treatment outcomes were obtained from the database, as were baseline characteristics of all treating institutions. Variables included patient age, race, primary payer, and income quartile by residential ZIP code. Comorbidities were identified and summarized using the Elixhauser Comorbidity Index (ECI), a validated tool based on 30 comorbidities identified using ICD-9 and ICD-10 codes [16].

Hospital characteristics included bed size, teaching status, geographic region, and ovarian cancer surgical volume. Hospital surgical volume was categorized as low, medium, or high based on ovarian cancer cytoreduction volume per institution per year, divided into tertiles. This was accomplished using the unique hospital identification numbers assigned each year within the NIS. Mortality was defined as death during the hospital admission.

### Statistical analysis

The primary outcome of this study was utilization of ECR across the study period. Secondary outcomes included factors independently associated with ECR, trends of extended procedure including hospital surgical volume over time, inpatient mortality, hospitalization cost, and length of stay in relation to ECR.

All numerical observations listed in this study were generated using survey weights included in the NIS database to provide nationally-representative estimates. Patient demographics among those undergoing extended versus non-extended procedures were compared using chi-square univariate analysis for categorical variables and adjusted Wald tests for continuous variables.

Multivariable logistic regression models were used to estimate the impact of the primary predictors (age, race, insurance status, income quartile by ZIP code, hospital geographic region, and hospital surgical volume) on the likelihood of receiving extended cytoreduction. The reference group was set as the majority group within each category. Trend analysis across the study period was conducted using the Cochran-Armitage test for trend of proportions. All analysis was performed using Stata Version 15.1 (Stata Corporation, College Station, TX), with statistical significance set at  $p < 0.05$ .

## Results

We identified 79,400 women who were admitted and underwent surgery for ovarian, fallopian tube or primary peritoneal cancer between January 1, 2013 and December 31, 2017. Of these patients, 22% underwent ECR. Patients who underwent extended cytoreductive procedures were primarily aged 60–69, more likely to have an ECI  $\geq 3$  (77% vs 59%,  $p < 0.001$ ), insured through Medicare (46% vs. 38%,  $p < 0.001$ ), residing in ZIP codes with the highest median income (31% vs. 27%,  $p < 0.001$ ), and were more likely treated at a high surgical volume hospital (37% vs 31%,  $p < 0.001$ ). For their hospitalization, these patients had an increased mortality (1.6% vs. 0.5%,  $p < 0.001$ ), length of stay (9.6 days vs. 5.2 days,  $p < 0.001$ ), and mean cost (\$32,132 vs. \$17,363,  $p < 0.001$ ). Demographics are listed in [Table 1](#).

To determine whether surgical volume was associated with ECR, multivariate logistic regression was performed adjusting for age, race, insurance status, and income quartile. Surgical volume was an independent predictor of receiving ECR. Decreased odds of receiving ECR were found in patients with ECI of  $< 3$  (OR 0.21 [0.18–0.26] and OR 0.61 [0.55–0.67] for ECI 1 and 2, respectively) and those residing in ZIP codes outside the top income quartile (OR 0.71 [0.63–0.81],  $p < 0.001$  for Q1, versus Q4). Detailed results are listed in [Table 2](#).

To further characterize the types of extended procedures performed, the annual percentages of each component of extended procedure were calculated. On average, rectosigmoid resection was performed in 10.8%, colon resection in 10.5%, small bowel resection in 3.7%, splenectomy in 3.0%, diaphragm resection in 2.7%, colostomy in 2.0%, ileostomy in 1.8%, bladder resection in 1.1%, hepatic resection in 1.0%, and gastrectomy in 0.9% of all cytoreduction cases.

In assessing the trends of ECR over the study period, the annual proportion of ECR performed each year decreased significantly from 19% to 15% over the study period ([Fig 1](#)). There was a significant decrease in the annual proportion of ECR procedures including rectosigmoid resections ( $p < 0.001$ ), colon resections ( $p < 0.001$ ), small bowel resections ( $p = 0.001$ ), and colostomies ( $p < 0.001$ ). The trends over time per procedure are shown in [Fig 2](#).

The proportion of extended procedures performed at low, medium, and high-volume hospitals changed over time significantly. By the end of the five-year study period, there was an increase in the proportion of cases at high-volume hospitals from 38.4% to 42.9%, ( $p = 0.001$ ) and a decrease in the proportion at medium-volume hospitals from 24.7% to 19.1% ( $p = 0.011$ ) ([Fig 3](#)).

Compared with the rest of the study population, patients undergoing ECR had higher post-operative mortality during their hospital admission (1.6% vs. 0.5%,  $p < 0.001$ ), longer length of index hospitalization (9.6 vs. 5.2 days,  $p < 0.001$ ), and a higher total mean cost of care (\$32,132 vs. \$17,363,  $p < 0.001$ ) for this hospitalization.

## Discussion

Standard ovarian cancer treatment typically requires a multimodal approach including both surgery and chemotherapy. Improved survival outcomes are associated with optimal surgical cytoreduction to no gross residual disease [4, 5]. In order to achieve this, extended cytoreductive procedures involving the bladder, spleen, bowel, or other abdominal organs are sometimes necessary. Our data suggest an association between ECR, hospital surgical volume, and certain patient demographic factors. While ECR has decreased over the study period, patients undergoing ECR experience a higher rate of perioperative mortality with longer hospitalization and cost of care compared to other ovarian cancer patients.

Our data indicate that ECR in ovarian cancer surgery is associated with certain patient demographics. Women with more comorbidities as identified with an ECI of 3 or more were more likely to undergo ECR. This may be attributed to late presentation to care or other factors

**Table 1. Population demographics stratified by occurrence of extended cytoreductive procedure.**

	Not extended (N = 61,850, 77.9%)	Extended (N = 17,550, 22.1%)	P-value
<b>Age</b>			
<40 years	4570 (7.4%)	635 (3.6%)	<0.001
40–49 years	8145 (13.2%)	1585 (9.0%)	<0.001
50–59 years	15720 (25.4%)	4000 (22.8%)	0.0013
60–69 years	17680 (28.6%)	5730 (32.6%)	<0.001
70–79 years	11730 (19.0%)	4345 (24.8%)	<0.001
80+ years	4005 (6.5%)	1255 (7.2%)	0.1579
<b>Year</b>			
2013	12220 (19.8%)	3935 (22.4%)	0.0062
2014	11955 (19.3%)	3825 (21.8%)	0.0104
2015	12150 (19.6%)	3625 (20.7%)	0.2973
2016	12805 (20.7%)	3070 (17.5%)	0.0019
2017	12720 (20.6%)	3095 (17.6%)	0.0018
<b>Race</b>			
White	43690 (70.6%)	12845 (73.2%)	0.0053
Black	4685 (7.6%)	1260 (7.2%)	0.4454
Hispanic	5115 (8.3%)	1185 (6.8%)	0.003
API	2605 (4.2%)	705 (4.0%)	0.6175
Other / Unknown	5755 (9.3%)	1555 (8.9%)	0.466
<b>Payer</b>			
Private	28150 (45.5%)	7340 (41.8%)	0.0002
Medicaid	6105 (9.9%)	1320 (7.5%)	<0.001
Medicare	23760 (38.4%)	8050 (45.9%)	<0.001
Other or unknown	3835 (6.2%)	840 (4.8%)	0.0018
<b>Median Income by ZIP Code</b>			
Q1 (lowest)	13415 (21.7%)	3420 (19.5%)	0.0088
Q2	15335 (24.8%)	3910 (22.3%)	0.0028
Q3	16110 (26.0%)	4385 (25.0%)	0.2041
Q4	15870 (25.7%)	5450 (31.1%)	<0.001
<b>Elixhauser comorbidity sum</b>			
1	10055 (16.3%)	730 (4.2%)	<0.001
2	15070 (24.4%)	3245 (18.5%)	<0.001
3+	36725 (59.4%)	13575 (77.4%)	<0.001
<b>Hospital Bed Size</b>			
Small	5240 (8.5%)	1505 (8.6%)	0.8771
Medium	14355 (23.2%)	3530 (20.1%)	0.001
Large	42255 (68.3%)	12515 (71.3%)	0.0054
<b>Hospital Teaching Status</b>			
Nonteaching	8225 (13.3%)	2335 (13.3%)	0.9927
Teaching	53625 (86.7%)	15215 (86.7%)	0.9927
<b>Hospital Region</b>			
Northeast	12645 (20.4%)	3360 (19.1%)	0.231
Midwest	13845 (22.4%)	4085 (23.3%)	0.3573
South	21045 (34.0%)	5915 (33.7%)	0.7761
West	14315 (23.1%)	4190 (23.9%)	0.4494
<b>Hospital Ovarian Cancer Surgical Volume</b>			
Low	26095 (42.2%)	6545 (37.3%)	<0.001

*(Continued)*

Table 1. (Continued)

	Not extended (N = 61,850, 77.9%)	Extended (N = 17,550, 22.1%)	P-value
Medium	16340 (26.4%)	4475 (25.5%)	0.367
High	19415 (31.4%)	6530 (37.2%)	<0.001
Mortality and Resource Utilization			
Mortality	295 (0.5%)	285 (1.6%)	<0.001
Mean Length of Stay (days) [95% CI]	5.2 [5.1–5.3]	9.6 [9.3–9.9]	<0.001
Mean cost (USD) [95% CI]	17,363 [17,053–17,673]	32132 [30,940–33,325]	<0.001

Values reported as N (%) or mean [95% CI].

API, Asian/Pacific Islander; CI, confidence interval; USD, United States dollars.

<https://doi.org/10.1371/journal.pone.0260255.t001>

contributing to disease burden. Balancing the survival benefits of lower residual disease to the higher postoperative morbidity and mortality associated with ECR, risk stratification should be used for optimal treatment planning [17, 18]. Emphasis on preoperative medical optimization and focus on shared decision making with patients may allow for improved perioperative outcomes in patients with numerous medical co-morbidities.

Socioeconomic factors and insurance status have been associated with access and type of surgical treatment. We found that residing in the highest income ZIP codes was an independent predictor of ECR ( $p < 0.001$ ), which is consistent with findings from previous studies [19]. Other studies have found that having private insurance was associated with better health-related quality of life; however, our findings suggest that private insurance does not influence odds of extended cytoreductive surgery in ovarian cancer [11, 20, 21]. High quality care, including surgical management, should be the goal for every patient. Further understanding of the impact social determinants of health have in the care of women with ovarian, fallopian tube, or primary peritoneal cancer will allow for improved perioperative management strategies and equal access to care.

In this report, the proportion of cases with extended procedures decreased from 2013–2017. This finding goes beyond the years studied by Jones et al., who demonstrated that from 1998 to 2013, ECR had increased from 1998 to 2010, declined in 2011, then rose again from 2012 to 2013 [15]. The use of neoadjuvant chemotherapy has been associated with increased likelihood of complete cytoreduction. With the increased use of neoadjuvant chemotherapy from 30% in 2010 to 39% in 2016, it is likely there is a decreased need for extended procedures during cytoreduction [22–25].

Cases were found to be increasingly performed at high volume centers, which may indicate patients are being referred to tertiary centers for specialized care. As shown in this study, patients undergoing primary debulking surgery at high volume centers have also been previously shown to be an independent predictor of ECR [26]. In addition, high volume centers have been associated with a higher likelihood of achieving complete gross resection compared to lower volume centers [27]. Surgical care of women with ovarian cancer has been trending towards centralized care, concentrating on the number of surgeons and hospitals, which has been associated with decreased perioperative mortality [28].

The decrease in the proportion of patients undergoing bowel resections seen over the study period is likely of multifactorial cause. One potential contributing cause is the increasing use of neoadjuvant chemotherapy, which may decrease tumor burden and reduce the need for extended procedures. This highlights the importance for standardization of care, with

**Table 2. Independent predictors of receiving ECR.**

	Odds Ratio	[95% CI]	P-value
<b>Age</b>			
<40	0.60	[0.48–0.74]	<0.001
40–49	0.71	[0.62–0.83]	<0.001
50–59	0.84	[0.75–0.94]	0.003
60–69	[REF]		
70–79	1.09	[0.97–1.22]	0.151
80+	0.90	[0.76–1.07]	0.243
<b>Elixhauser Comorbidity Index</b>			
1	0.21	[0.18–0.26]	<0.001
2	0.61	[0.55–0.67]	<0.001
3+	[REF]		
<b>Race</b>			
White	[REF]		
Black	0.98	[0.84–1.15]	0.844
Hispanic	0.95	[0.81–1.11]	0.504
API	1.03	[0.84–1.26]	0.787
Other or unknown	0.94	[0.81–1.09]	0.413
<b>Payer</b>			
Private	[REF]		
Medicaid	0.88	[0.76–1.03]	0.119
Medicare	0.92	[0.81–1.03]	0.137
Other or unknown	0.90	[0.75–1.09]	0.294
<b>Income Quartile of Residential ZIP Code</b>			
<25th percentile	0.71	[0.63–0.81]	<0.001
25th–50th percentile	0.72	[0.64–0.81]	<0.001
50th–75th percentile	0.78	[0.70–0.87]	<0.001
>75th percentile	[REF]		
<b>Hospital Region</b>			
Northeast	0.83	[0.72–0.96]	0.013
Midwest	0.99	[0.87–1.12]	0.847
South	[REF]		
West	1.02	[0.90–1.16]	0.785
<b>Hospital Volume</b>			
Low	[REF]		
Medium	1.04	[0.93–1.17]	<0.001
High	1.25	[1.12–1.40]	<0.001

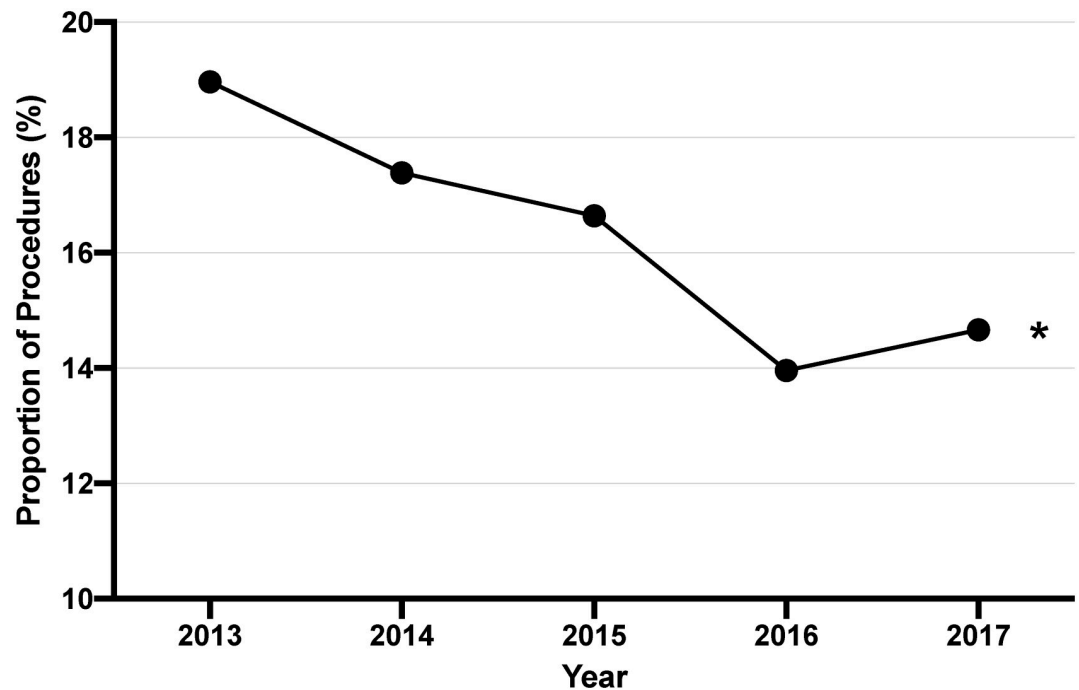
API, Asian/Pacific Islander; CI, confidence interval; REF, reference group.

<https://doi.org/10.1371/journal.pone.0260255.t002>

prospective data collection of outcomes. With the increasing use of neoadjuvant chemotherapy and trend in decreased ECR, measured surgical quality metrics will allow for gynecologic oncologists to maintain consistent levels of cytoreductive care whether patients are undergoing upfront or interval cytoreductive surgery.

Patients receiving ECR were associated with increased perioperative mortality, which likely reflects the greater disease burden requiring extended debulking procedures, as well as medical co-morbidities and the complexities of surgery. ECR is associated with a postoperative mortality of approximately 1.8%, which corresponds with our findings [29, 30]. Similarly, the





**Fig 1. The proportion of extended procedures across all hospitals each year.** \*Significance at  $P < 0.05$ .

<https://doi.org/10.1371/journal.pone.0260255.g001>

increased length of stay and corresponding higher cost of hospitalization for patients with ECR has been associated with the dissemination of disease, extent of surgery, and presence of comorbidities, consistent with our findings [31]. Gynecologic oncologists and stakeholders in the management of women with ovarian cancer must work to establish guidelines that require adherence and quality metrics that are measured in a national database similar to the National Surgical Quality Improvement Project (NSQIP). NSQIP has been used to improve the care of patients with colon and rectal cancer in a similar fashion [32]. Prospective data collection will allow for a better understanding of the role of surgical volume and patient demographics associated with ovarian cancer outcomes. This will be more important now than in the past as ECR procedures become less common with the use of neoadjuvant chemotherapy and current trainees may not have as much experience with radical tumor debulking prior to entering practice.

Strengths of this study include its use of a nationally-representative database with a large sample size and detailed information regarding age and socioeconomic status. Limitations include the retrospective study design and the dataset used. The identification of patients undergoing ECR within the NIS database was dependent upon billing codes, the accuracy of which may vary between institutions including the completeness of the coding. The database also does not allow for tracking of patients across multiple hospitalizations, so we are unable to determine the number of new ovarian cancer cases per year as it relates to our trend analysis. In addition, these codes do not report surgeon-specific data on cytoreduction, nor do they differentiate whether surgery was in the setting of upfront or neoadjuvant therapy. Nevertheless, timing of surgery should not impact the findings of this study which was to determine patient and hospital factors associated with undergoing ECR. Although the NIS includes information on a variety of health conditions, it lacks granular information specific to ovarian cancer, such as disease stage and histologic subtype. Finally, the database does not include information on



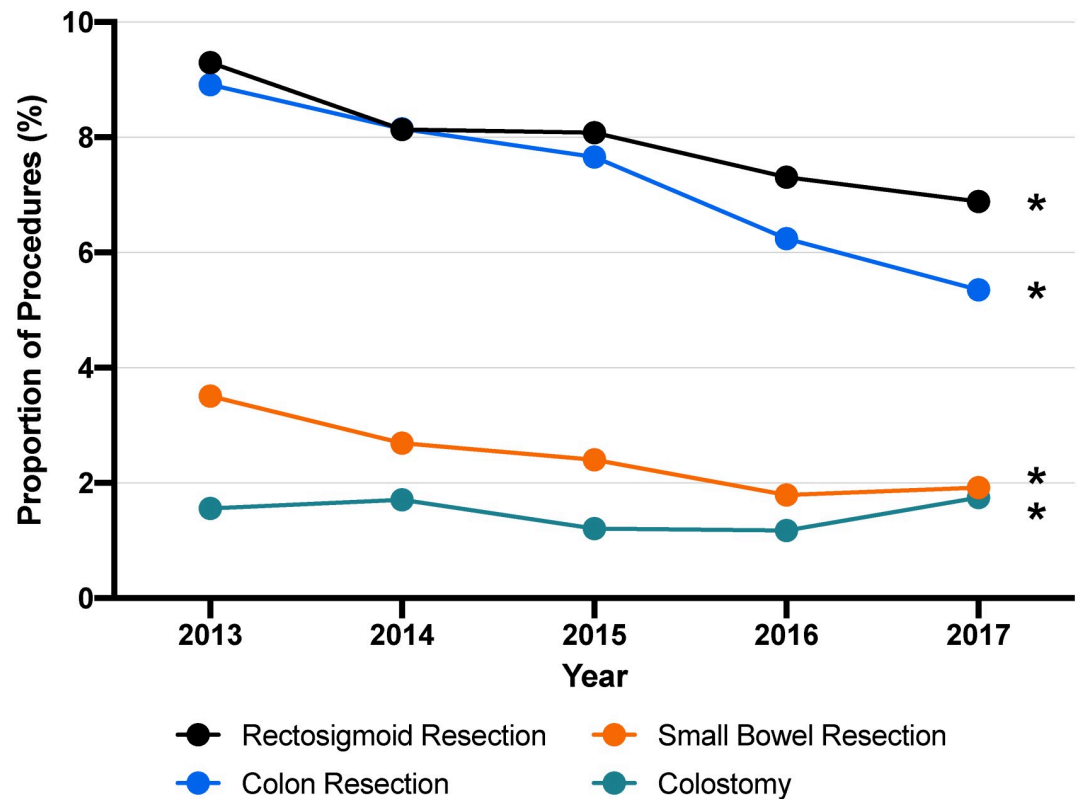


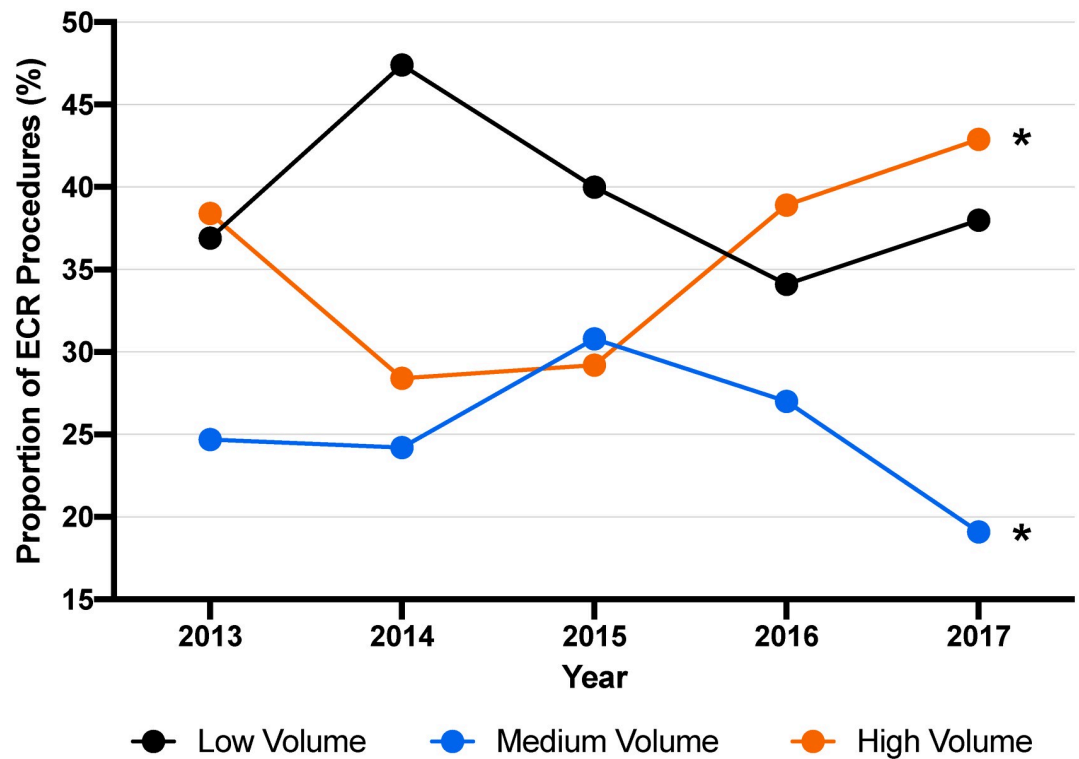
Fig 2. The proportion of all cytoreduction procedures involving the gastrointestinal tract each year. \*Significance at  $P < 0.05$ .

<https://doi.org/10.1371/journal.pone.0260255.g002>

the amount of residual disease after surgery. While lack of this data may be limiting, physicians frequently underestimate the rate of optimal cytoreduction, with one study reporting 40% of cases were inaccurately described as optimal [33]. Thus, since previous studies have shown that ECR increases the odds of reducing to minimal residual disease [34, 35], we focused on rates of ECR as a proxy for improved odds of optimal cytoreduction.

Our data highlights the current trends in ECR for patients with ovarian cancer. There is a decreasing trend in ECR, however these procedures continued to be associated with increased perioperative mortality, length of stay, and cost. ECR is a mainstay in the management of ovarian cancer and should remain a priority in gynecologic oncology training. A large-scale effort by stakeholders in the treatment of women with ovarian cancer must take place to ensure adequate care for these patients irrespective of socioeconomic status and hospital volume. Similar to what has been done in other fields such as rectal cancer, an ongoing database with metric outcomes is likely warranted. Future studies would benefit from use of institutional or ovarian cancer-specific databases that may better characterize the quality of ECR and its relation to patient centered outcomes.

In conclusion, our findings highlight an association between undergoing extended surgical cytoreduction, socioeconomic factors, and surgical volume of the treating institution. Over time, the proportion of cases with ECR has been decreasing, and more of these cases are being performed at high volume centers. Extended procedures performed are decreasing proportionally each year, which has important implications for the quality of care provided to ovarian cancer patients.



**Fig 3.** The proportion of extended procedures performed at high, medium, and low volume hospitals each year.  
\*Significance at  $P < 0.05$ .

<https://doi.org/10.1371/journal.pone.0260255.g003>

## Supporting information

**S1 Table. International classification of diseases (ICD) codes used for patient identification and characterization.**  
(DOCX)

## Author Contributions

**Conceptualization:** Deanna H. Wong, Joshua G. Cohen.

**Formal analysis:** Alexandra L. Mardock, Yas Sanaiha.

**Methodology:** Deanna H. Wong, Alexandra L. Mardock.

**Resources:** Peyman Benharash.

**Software:** Alexandra L. Mardock, Yas Sanaiha.

**Supervision:** Abdulrahman K. Sinno, Peyman Benharash, Joshua G. Cohen.

**Writing – original draft:** Deanna H. Wong.

**Writing – review & editing:** Deanna H. Wong, Alexandra L. Mardock, Erica N. Manriquez, Tiffany S. Lai, Peyman Benharash, Joshua G. Cohen.

## References

1. SEER Cancer Stat Facts: Ovarian Cancer Bethesda, MD: National Cancer Institute; 2019 <https://seer.cancer.gov/statfacts/html/ovary.html>.

2. Howlader N, Noone A, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review, 1975–2016 Bethesda, MD: National Cancer Institute; 2019 [https://seer.cancer.gov/csr/1975\\_2016/](https://seer.cancer.gov/csr/1975_2016/).
3. Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, et al. Ovarian cancer statistics, 2018. *CA Cancer J Clin*. 2018; 68(4):284–96. <https://doi.org/10.3322/caac.21456> PMID: 29809280
4. Chang SJ, Bristow RE. Evolution of surgical treatment paradigms for advanced-stage ovarian cancer: redefining 'optimal' residual disease. *Gynecol Oncol*. 2012; 125(2):483–92. <https://doi.org/10.1016/j.ygyno.2012.02.024> PMID: 22366151
5. Wallace S, Kumar A, Mc Gree M, Weaver A, Mariani A, Langstraat C, et al. Efforts at maximal cytoreduction improve survival in ovarian cancer patients, even when complete gross resection is not feasible. *Gynecol Oncol*. 2017; 145(1):21–6. <https://doi.org/10.1016/j.ygyno.2017.01.029> PMID: 28159407
6. Armstrong DK, Alvarez RD, Bakkum-Gamez JN, Barroilhet L, Behbakht K, Berchuck A, et al. NCCN Guidelines Insights: Ovarian Cancer, Version 1.2019. *J Natl Compr Canc Netw*. 2019; 17(8):896–909. <https://doi.org/10.6004/jnccn.2019.0039> PMID: 31390583
7. Wright JD, Chen L, Hou JY, Burke WM, Tergas AI, Ananth CV, et al. Association of Hospital Volume and Quality of Care With Survival for Ovarian Cancer. *Obstet Gynecol*. 2017; 130(3):545–53. <https://doi.org/10.1097/AOG.0000000000002164> PMID: 28796677
8. Bristow RE, Palis BE, Chi DS, Cliby WA. The National Cancer Database report on advanced-stage epithelial ovarian cancer: impact of hospital surgical case volume on overall survival and surgical treatment paradigm. *Gynecol Oncol*. 2010; 118(3):262–7. <https://doi.org/10.1016/j.ygyno.2010.05.025> PMID: 20573392
9. Bristow RE, Chang J, Ziogas A, Campos B, Chavez LR, Anton-Culver H. Sociodemographic disparities in advanced ovarian cancer survival and adherence to treatment guidelines. *Obstet Gynecol*. 2015; 125(4):833–42. <https://doi.org/10.1097/AOG.0000000000000643> PMID: 25751200
10. Ross J, Braswell KV, Madeira da Silva L, Mujica F, Stutsman S, Finan MA, et al. Unraveling the etiology of ovarian cancer racial disparity in the deep south: Is it nature or nurture? *Gynecol Oncol*. 2017; 145(2):329–33. <https://doi.org/10.1016/j.ygyno.2017.02.025> PMID: 28215839
11. Sinno AK, Li X, Thompson RE, Tanner EJ 3rd, Levinson KL, Stone RL, et al. Trends and factors associated with radical cytoreductive surgery in the United States: A case for centralized care. *Gynecol Oncol*. 2017; 145(3):493–9. <https://doi.org/10.1016/j.ygyno.2017.03.020> PMID: 28366546
12. Stewart SL, Harewood R, Matz M, Rim SH, Sabatino SA, Ward KC, et al. Disparities in ovarian cancer survival in the United States (2001–2009): Findings from the CONCORD-2 study. *Cancer*. 2017; 123 Suppl 24:5138–59. <https://doi.org/10.1002/cncr.31027> PMID: 29205312
13. Chan JK, Zhang M, Hu JM, Shin JY, Osann K, Kapp DS. Racial disparities in surgical treatment and survival of epithelial ovarian cancer in United States. *J Surg Oncol*. 2008; 97(2):103–7. <https://doi.org/10.1002/jso.20932> PMID: 17979133
14. Barrett M CR, Houchens R, Heslin K, Moles E, Coenen N. Methods Applying AHRQ Quality Indicators to Healthcare Cost and Utilization Project (HCUP) Data for the 2016 National Healthcare Quality and Disparities Report (QDR) 2017 <http://www.hcup-us.ahrq.gov/reports/methods/methods.jsp>.
15. Jones NL, Chen L, Chatterjee S, Tergas AI, Burke WM, Hou JY, et al. National Trends in Extended Procedures for Ovarian Cancer Debulking Surgery. *Int J Gynecol Cancer*. 2018; 28(1):19–25. <https://doi.org/10.1097/IGC.0000000000001132> PMID: 28953134
16. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998; 36(1):8–27. <https://doi.org/10.1097/00005650-199801000-00004> PMID: 9431328
17. Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Relationship among surgical complexity, short-term morbidity, and overall survival in primary surgery for advanced ovarian cancer. *Am J Obstet Gynecol*. 2007; 197(6):676 e1–7.
18. Gunakan E, Tohma YA, Tunc M, Akilli H, Sahin H, Ayhan A. Factors associated with surgical morbidity of primary debulking in epithelial ovarian cancer. *Obstet Gynecol Sci*. 2020; 63(1):64–71. PMID: 31970129
19. Bristow RE, Chang J, Ziogas A, Randall LM, Anton-Culver H. High-volume ovarian cancer care: survival impact and disparities in access for advanced-stage disease. *Gynecol Oncol*. 2014; 132(2):403–10. <https://doi.org/10.1016/j.ygyno.2013.12.017> PMID: 24361578
20. Boyd LR, Novetsky AP, Curtin JP. Ovarian cancer care for the underserved: are surgical patterns of care different in a public hospital setting? *Cancer*. 2011; 117(4):777–83. <https://doi.org/10.1002/cncr.25490> PMID: 20922804
21. Moss JL, Murphy J, Filiaci VL, Wenzel LB, Minasian L, Temkin SM. Disparities in health-related quality of life in women undergoing treatment for advanced ovarian cancer: the role of individual-level and contextual social determinants. *Support Care Cancer*. 2019; 27(2):531–8. <https://doi.org/10.1007/s00520-018-4340-9> PMID: 30003341

22. Kehoe S, Hook J, Nankivell M, Jayson GC, Kitchener H, Lopes T, et al. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *Lancet*. 2015; 386(9990):249–57. [https://doi.org/10.1016/S0140-6736\(14\)62223-6](https://doi.org/10.1016/S0140-6736(14)62223-6) PMID: 26002111
23. Morrison J, Haldar K, Kehoe S, Lawrie TA. Chemotherapy versus surgery for initial treatment in advanced ovarian epithelial cancer. *Cochrane Database Syst Rev*. 2012(8):CD005343. <https://doi.org/10.1002/14651858.CD005343.pub3> PMID: 22895947
24. Vergote I, Trope CG, Amant F, Kristensen GB, Ehlen T, Johnson N, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med*. 2010; 363(10):943–53. <https://doi.org/10.1056/NEJMoa0908806> PMID: 20818904
25. Matsuo K, Matsuzaki S, Nusbaum DJ, Maoz A, Oda K, Klar M, et al. Possible candidate population for neoadjuvant chemotherapy in women with advanced ovarian cancer. *Gynecol Oncol*. 2021; 160(1): 32–9. <https://doi.org/10.1016/j.ygyno.2020.10.027> PMID: 33196436
26. Bristow RE, Zahurak ML, Diaz-Montes TP, Giuntoli RL, Armstrong DK. Impact of surgeon and hospital ovarian cancer surgical case volume on in-hospital mortality and related short-term outcomes. *Gynecol Oncol*. 2009; 115(3):334–8. <https://doi.org/10.1016/j.ygyno.2009.08.025> PMID: 19766295
27. Nasioudis D, Kahn R, Chapman-Davis E, Frey MK, Caputo TA, Witkin SS, et al. Impact of hospital surgical volume on complete gross resection (CGR) rates following primary debulking surgery for advanced stage epithelial ovarian carcinoma. *Gynecol Oncol*. 2019; 154(2):401–4. <https://doi.org/10.1016/j.ygyno.2019.05.016> PMID: 31160074
28. Wright JD, Chen L, Buskwofie A, Tergas AI, St Clair CM, Hou JY, et al. Regionalization of care for women with ovarian cancer. *Gynecol Oncol*. 2019; 154(2):394–400. <https://doi.org/10.1016/j.ygyno.2019.05.025> PMID: 31171408
29. Bartels HC, Rogers AC, McSharry V, McVey R, Walsh T, O'Brien D, et al. A meta-analysis of morbidity and mortality in primary cytoreductive surgery compared to neoadjuvant chemotherapy in advanced ovarian malignancy. *Gynecol Oncol*. 2019; 154(3):622–30. <https://doi.org/10.1016/j.ygyno.2019.07.011> PMID: 31349996
30. Elattar A, Bryant A, Winter-Roach BA, Hatem M, Naik R. Optimal primary surgical treatment for advanced epithelial ovarian cancer. *Cochrane Database Syst Rev*. 2011(8):CD007565. <https://doi.org/10.1002/14651858.CD007565.pub2> PMID: 21833960
31. Smith CG, Davenport DL, Gorski J, McDowell A, Burgess BT, Fredericks TI, et al. Clinical Factors Associated with Longer Hospital Stay Following Ovarian Cancer Surgery. *Healthcare (Basel)*. 2019; 7(3). <https://doi.org/10.3390/healthcare7030085> PMID: 31277282
32. Eisenstein S, Stringfield S, Holubar SD. Using the National Surgical Quality Improvement Project (NSQIP) to Perform Clinical Research in Colon and Rectal Surgery. *Clin Colon Rectal Surg*. 2019; 32(1):41–53. <https://doi.org/10.1055/s-0038-1673353> PMID: 30647545
33. Eskander RN, Kauderer J, Tewari KS, Mannel RS, Bristow RE, O'Malley DM, et al. Correlation between Surgeon's assessment and radiographic evaluation of residual disease in women with advanced stage ovarian cancer reported to have undergone optimal surgical cytoreduction: An NRG Oncology/Gynecologic Oncology Group study. *Gynecol Oncol*. 2018; 149(3):525–30. <https://doi.org/10.1016/j.ygyno.2018.03.043> PMID: 29550184
34. Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Surgical treatment of diaphragm disease correlates with improved survival in optimally debulked advanced stage ovarian cancer. *Gynecol Oncol*. 2006; 100(2):283–7. <https://doi.org/10.1016/j.ygyno.2005.08.027> PMID: 16182350
35. Eisenhauer EL, Abu-Rustum NR, Sonoda Y, Levine DA, Poyner EA, Aghajanian C, et al. The addition of extensive upper abdominal surgery to achieve optimal cytoreduction improves survival in patients with stages IIIC-IV epithelial ovarian cancer. *Gynecol Oncol*. 2006; 103(3):1083–90. <https://doi.org/10.1016/j.ygyno.2006.06.028> PMID: 16890277