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# Hospital costs associated with adverse events in gynecological oncology

**Short title:** Cost of surgical complications: oncology

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**Abstract**

Background and objective: Treatment for gynaecological malignancies is complex and may cause unintended or accidental adverse events (AE). We evaluated the costs of hospitalization associated with those AEs among patients who had an abdominal or laparoscopic procedure for proven or suspected gynaecological cancer at a tertiary gynaecological cancer center in Australia.

Methods: Data on AEs were prospectively collected and matched with cost data (AU$ 2008) from the hospital's clinical costing unit and linked to demographical, clinical and histopathological data. Total costs were adjusted for various clinical factors and estimated using log-transformed ordinary least squared regression. Back-transformation was achieved using smearing factors. From epidemiological data, we also estimated the costs of AEs Australia-wide and undertook scenario and probabilistic sensitivity analyses to investigate the potential cost impact of reducing AEs.

Results: A total of 369 patients had surgical procedures of which 95 patients (26%) had at least one AE. Patients with AEs incurred an extra AU$ 12,780 on average, adjusted for age, co-morbidities, ovarian cancer, major or minor complications, surgical complexity, presence of malignancy and abdominal surgery. Mean adjusted costs (95% CI) for patients with intra-operative, minor post-operative and major post-operative AEs were AU$ 40,746 (11,582-71,859) AU$ 18,459 (17,270-19,713) and AU$ 67,656 (5,324-131,761), respectively. Up to an estimated AU$ 20.6 million/year could be saved if the AEs were reduced by 40%.

Conclusion: Adverse events are associated with significantly increased hospitalization costs and appropriate evidence-based interventions are justified to minimize AEs.

Keywords: cost, hospitalization, adverse events, complications, laparoscopy, laparotomy, quality of surgical care.

## Introduction

A landmark Australian study, the Quality of Australian Health Care Study (QAHCS), reviewed the quality of delivered health care and concluded that 16.6% of admissions were associated with adverse events (AEs) each year [1]. More than 50% of the AEs reported were associated with surgery and up to 48% of these AEs were considered preventable. The estimated costs associated with these AEs are exorbitant, at AU$ 1-2 billion dollars [2]. Recent studies based on 2003-2004 data have shown that the cost of AEs in Australia could exceed AU$ 2 billion per year [3].

In recent decades there has been a worldwide development towards reporting and analyzing the quality of delivered healthcare in specialized centers and, more specifically, in the field of surgery. This is arguably a direct consequence of ‘variations’ in outcomes noticed among different institutions for similar procedures. The shift in clinical attitudes towards greater transparency in performance regarding the quality of care to improve outcomes has led to a number of studies focusing on post-operative morbidity and mortality and the formation of adequate and validated models of risk assessment [4]. Such studies have had a positive influence on the quality of surgical practice and contributed to reduced AE rates[5].

The occurrences of AEs during or following a surgical procedure are not uncommon, especially in high-risk specialties such as surgical oncology. Surgeons in these sub-specialties utilize state-of-the-art procedures, innovative minimally-invasive techniques, combined with chemotherapy and or radiotherapy to improve patient outcomes. However, these procedures and management approaches are associated with serious risks of AEs, along with patient related and environmental factors, and are estimated to vary from 34% in head and neck cancers to as high as 69% in esophageal cancers [6]. The published incidence of AEs among

patients with gynaecological cancer varies from 26% to 54%[6, 7]. As there is potential scope for reducing AEs among these women, it is important to have a sound understanding of the current clinical outcomes as well as the economic costs so that future intervention studies can be adequately planned for and assessed for their effectiveness and cost-effectiveness. Therefore, the aim of our study was to quantify the nature and extent of AEs in the subspecialty of gynaecological oncology and estimate their associated hospital costs.

## Methods

All patients who underwent a laparoscopic procedure or laparotomy for suspected or proven gynaecological malignancies were enrolled from a major tertiary referral hospital in the state of Queensland, Australia. All the AEs were recorded prospectively between 1st January 2007 and 20th August 2008 by a dedicated patient safety officer. We reviewed all the medical records for potential risk factors for AEs. The methods have been previously reported [7] but briefly, all patients who underwent surgery between 1st January 2007 and 30th June 2008 were included. We reviewed electronic and paper-based medical records and extracted information related to: (1) patient-related risk factors (e.g., BMI, age); (2) clinical characteristics from pre-operative lab results (e.g., serum albumin and liver function tests); (3) surgical procedures (type and complexity of procedure, approach, duration of surgery, conversions, surgeon's experience (trainee/consultant)); (4) type of AEs classified as intra-operative or post-operative; and (5) other outcomes such as length of hospital stay and death within 30 days) [7]. Intra-operative AEs included injuries to the bladder, bowel, ureter, blood vessels, nerves and the need for intra-operative blood transfusions and post-operative AEs included wound infection, wound dehiscence, wound hematoma, secondary hematoma, pneumonia, pulmonary embolism, urinary tract infections, renal complication, stroke/cerebrovascular accidents, pelvic abscess, subphrenic abscess, other abscesses, septicemia, deep venous thrombosis,

gastric ileus, urinary fistula, gastro-intestinal fistula, cardiac complications and other post-operative events. These post-operative events were further classified into minor and major events based on the nature of the treatment used to manage these events.

To permit comparison of AE rates over time and across studies, post-operative AEs were classified using a standardized grading system [8]. This grading system is based on the interventions used to manage AEs. For example, grades I and II do not require surgical, endoscopic and radiological intervention whereas grade III does. Grade IV events are life-threatening requiring either intermediate care or intensive care unit management. Death of a patient is considered an AE of grade V. Patients in this study with grade III or above events were considered to have had a 'major' AE whereas those who had an AE below grade three were considered 'minor'.

AEs were prospectively collected and matched with cost data from the hospital's clinical costing and casemix unit and linked to demographical, clinical and histopathological data. Data linkage was achieved using a hospital identification number. The cost information was retrieved from the hospital's detailed costing system (Transition Systems Inc) which tracks all the resources used in caring for the patient. The total cost for the aggregated hospital resources used by each patient was provided to the research team and no further breakdown of the types of hospital resources were provided. As specific resource quantities were not separated from costs, here we used the aggregated cost figure and assumed that excess costs for the group of patients with AEs were fully attributed to the AEs.

**Statistical analyses**

Descriptive statistics were used to show baseline characteristics of patients. Multivariate modeling was used to quantify costs attributed to AEs adjusted for various clinical factors.

As health cost data is commonly skewed to reflect that some patients accrue very high costs, total patient costs ~~for patients~~ were log-transformed before using multivariate ordinary least squared regression. Re-transforming costs back to the raw cost scale were achieved with Duan's smearing factors [9]. We tested the model assumptions by examining the normality and heteroskedasticity of residuals while goodness-of-fit and model specification was assessed with the adjusted $R^2$, Pregibon's link test, Ramsey's reset test and the v-fold cross-validation Copas test for over-fitting [10]. Stratification by patients receiving a laparoscopy or laparotomy was also performed.

To extrapolate the costs of AEs attributed to gynecological oncology Australia-wide, we multiplied the cost figures to all new cases (ICD10, C51-C58) from the latest national incidence report [11] after inflating the number of cases to account for suspected cases of cancer later found to be benign (n=5736). One-way sensitivity analyses were performed to test if changing the probabilities of intra-operative, minor and major post-operative AEs by ±10% and ±20%, substantially varied the overall results. To account for multiple parameter uncertainty, probabilistic sensitivity analysis was performed where beta distributions were assigned to probabilities and gamma distributions to costs. Monte Carlo simulations were performed (5736 times) and total costs generated under different scenarios where the proportions of AEs were altered. STATA SE (version 11.0, StataCorp, Tx) and TreeAge Pro (2009) was used for statistical analyses. Costs are reported in 2008 (the year of data collection) Australian dollars.

**Results**

Overall the 369 women in the study ranged in age from 13 to 91 years with a mean (SD) age at the time of surgery of 56.3 (14.4) years with 63 patients (17.1%) aged≥ 70 years (Table 1).

The mean (SD) BMI was 30.3 (8.2) kg/m² with 44.7% of patients classified as obese (BMI ≥ 30).

The most common surgical procedures were hysterectomy and salpingo-oophorectomy followed by pelvic, para-aortic and groin lymph node dissection (Table 1). Nearly 73% of the patients underwent at least one procedure with a complexity grade 1. There was a significant difference in the distribution of surgical complexity (p=0.003) among AE categories with very complex procedures associated with major AEs. One hundred and forty five (39.4%) patients had a laparoscopic procedure. The proportions of patients who underwent laparoscopic procedures differed significantly between the AE categories (p=0.027) with lower rates of post-operative AEs noticed among patients who underwent a laparoscopic procedure. Nine patients (2.4%) required a conversion from a laparoscopic procedure to an abdominal procedure mostly due to dense adhesions and/or intra-operative complications. Two thirds (65%) of the patients required surgery for a malignant condition and 92% of the pathology was related to the ovaries or uterus.

Of the 369 patients, 95 (26%) developed at least one AE (Table 2) and 16 (4.3%) developed two or more AEs. Eighteen patients (4.9%) had at least one intra-operative AE without any post-operative AE. Sixty-three patients (17%) had at least one minor post-operative AE (either grade I or II). Fourteen patients (3.8%) had major AEs and included one patient who developed multi-organ dysfunction and died post-operatively (grade V). The most common intra-operative AE was injury to the bowel (2.7%) followed by injuries to the bladder and blood vessels (both 1.6%). Wound-related issues were the most common post-operative AEs with 33 (9%) women developing at least one wound infection and/or wound dehiscence and/or hematoma.

Hospital length of stay was 6.4 days (SD 11.1) on average for all women and ranged from 0.4 to 196 (Table 3). Women with major post-operative AEs had the longest average stay of 32.8 days (95% CI: 4.2 to 61.5) compared with those with minor AEs (8.0 days, 95% CI: 7.2 to 8.8), intra-operative AEs (18.1 days, 95% CI: 4.2 to 32.0) and no AEs (4.8 days, 95% CI: 4.5 to 5.1).

In the log-transformed regression model, the residuals were heteroskedastic with respect to presence of AEs and therefore costs were re-transformed to the raw cost scale with separate Duan's smearing estimators for patients with or without AEs (Table 3). Adjusted mean hospital costs were AU$12,872 for patients with no AEs compared with AU$25,652 for patients with AEs (Table 3). Patients with AEs incurred an extra AU$12,780 on average, adjusted for age, comorbidities, ovarian cancer, weighted activity unit (a measure of the relative value of care and resource utilization provided to patients), major or minor AEs, surgical complexity, presence of malignancy and abdominal surgery. Adjusted mean costs were significantly higher for patients with intra-operative AEs (AU$40,746), minor post-operative AEs (AU$18,459), major post-operative AEs (AU$67,656), those who received abdominal surgery (AU$17,644), complex surgery (AU$16,706), very complex surgery (AU$30,328) and patients with malignant tumors (AU$16,857) compared to patients with no AEs (AU$12,872). Overall, the log-transformed model exhibited good fit and performance as indicated by the adjusted $R^2$=0.63 (354 degrees of freedom), the link test (p=0.29), the Copas test ($\beta$=0.97, p= 0.46) but the model failed the Ramsey reset test (p=0.03).

Stratified analyses by patients receiving either laparoscopy (n=145) or laparotomy (n=224), indicated that the adjusted mean costs were higher, overall, for laparotomy AU$ 17,657 (95%

CI $16,187, $19,127) than laparoscopy AU$ 13,612 (95% CI $8,642, $18,582)(Table 4). Adjusted LOS was also higher overall for laparotomy 7.9 days (95% CI 7.2, 8.5 days) than laparoscopy 4.7 days (95% CI 1.2, 8.2 days). Adjusted mean costs were AU $4,000 to $5,000 higher for patients receiving laparotomy compared with laparoscopy when there were no complications or no major postoperative complications. When laparoscopy was used to treat patients with confirmed malignancy, adjusted costs were substantially lower, AU$ 12,300 (95%CI: $11,525, $13,075) versus laparotomy AU$19,168 (95%CI: 17,159, $21,176). For patients receiving either laparoscopic or laparotomy surgery, adjusted costs were higher for patients with ovarian cancer, compared with patients with other gynecological cancers but tumor site was not a strong predictor of patient costs (Table 4).

When our adjusted cost predictions for AEs were extrapolated to all gynecological cancers Australia wide, based on 4243 new cases of gynecological cancer in 2006[11], average hospitalization costs for patients with adverse events were an estimated AU$51.2 million annually. This comprises patients with intra-operative complications of AU$18.4 million (17%), minor post-operative complications of AU$18.1 million (17%) and major post-operative complications AU$14.7 million (14%). Sensitivity analyses indicated that when the proportion of intra-operative and minor or major post-operative complications varied by ± 10% or ±20%, relatively small changes to our base estimates occurred (Table 5). In multivariate sensitivity analyses, cost-savings per year could vary from AU$5.02 million (assuming 10% reduction in all AEs) to AU$20.62 million (assuming 40% reduction in all AEs) (Table 6). Reductions in minor post-operative AEs had the greatest potential for generating cost-efficiencies.

## Discussion

A quarter of all patients requiring surgery for proven or suspected gynaecological cancer develop at least one adverse event (AE) and incur higher hospitalization costs and longer hospital stays. This study highlights that even when relevant risk factors are controlled for, the costs remain significantly high in comparison with those who did not experience any AEs. Our findings also confirm that patients receiving laparoscopic surgery in this sub-specialty have shorter hospital stays and incur overall lower costs than those receiving more traditional open surgical techniques.

Most of the information currently available on the incidence of surgical AEs has been obtained from surgery for benign gynecological conditions. The incidence rates of bladder and ureteral injury are 1.6% and 0.5%, respectively, in this series which compares well with 3.6% and 1.7% in the current literature [12, 13]. The incidence of post-operative wound-related issues varies from 3% to 10% in the literature [14] whereas in our study it was 9%. Post-operative cardiac complications are also within expectations in our study (1.9%) compared to the published literature (3%) [15]. In general, the rates of AEs in our series are comparable to the rates published for patients treated for benign gynecological conditions. Sixty-five percent of patients in our series had a malignant condition and our study shows that AEs are more common among patients with a malignant condition (30%) compared to patients who underwent surgery for prophylaxis or a benign condition ($p=0.009$). However, our study also shows that AE rates associated with procedures performed by trainees were not significantly different to those of certified gynecologic oncologists ($p=0.522$).

A major strength of our study is that the AEs were collected prospectively on a consecutive real-world sample of gynecological patients with minimal missing data. This avoids the criticism of under-reporting associated with retrospective studies on selected patients.

Furthermore, surgeons and other staff were blinded to study participation and therefore were unlikely to bias patient selection and subsequent management or change their routine use of hospital resources. However, our patients were recruited from a single, high-volume tertiary referral center and therefore omit the potential variation in outcomes that may exist among patients across multiple health care facilities, and treated by a range of physicians. Patients treated in private health care facilities may have different AE rates and associated costs than those treated in public hospitals. However, we have addressed this uncertainty using probabilistic sensitivity analysis and found results ~~to be robust~~were stable to plausible variations in incidence of AEs. The regression modeling that we used may underestimate the actual costs associated with AEs, as our analyses were limited to events identified during the episode of care and up to a maximum of 30 days. Also, indirect costs such as patient and family travel and out-of-pocket expenses, time spent caring for the patient, and community health resources utilized, have not been taken into account. Therefore the true burden of AEs on patients and society will be higher.

We performed a sensitivity analysis with the incidence rates of intra-operative and post-operative AEs varying by ± 10% and ± 20% (Table 5). Evidence suggests that certain interventions may reduce the incidence of surgical complications [16]. Assuming a conservative 20% reduction across all complications, the savings Australia-wide will be at least AU$3.8 million from intra-op AEs, AU$3.6 million from minor AEs and another AU$2.9 million from major AEs. Our prior work on surgical risk prediction can help identify those who are at a higher risk for AEs and appropriate precautions can be taken to minimize such events [7]. This risk scoring system has attracted attention among specialists in the field of gynecologic oncology [17-19].

Innovative medical technologies, improvements in overall survival, greater emphasis on the quality of delivered care and increasing disease burden all contribute to escalating health care costs and straining health care budgets in most developed countries. Even though we used conservative estimates of 10% and 20% reduction in AE rates, some researchers estimate that 40% of AEs are preventable [20]. If reductions in AE of this magnitude can be achieved, it will significantly reduce patient suffering, enable a speedier recovery, improve their hospital experience and ultimately, reduce excess hospital costs.

In conclusion, AEs in gynaecological oncology may occur in 26% of patients with 4% considered to be of major severity. Hospital costs attributed to AEs are in the order of AU$12,780 per patient in our sample, on average, but are significantly higher for those with major complications and receiving laparotomies after accounting for baseline risk factors. There is considerable scope for hospital cost-savings if evidence-based mechanisms to reduce the incidence of adverse events are adopted.

**Conflict of interest statement:**

Prof. Andreas Obermair runs a subscription based website (www.surgicalperformance.com) which can be used as a tool by the surgeons to audit their performance.

All the other authors have declared that there are no conflicts of interest.

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**Table 1. Patient characteristics and surgical factors by broad type of adverse event**

| Characteristics | No AE (n=274) | Intra-op AE (n=18) | Minor post-op AE (n=63) | Major post-op AE (n=14) | Total (n=369) |
|---|---|---|---|---|---|
| *Demographics* | | | | | |
| Age, years, mean (SD) | 55.2 (14.5) | 57.2 (13.4) | 59.0 (14.1) | 65.1 (10.9) | 56.3 (14.4) |
| *Risk factors* | | | | | |
| Hypertension, n (%) | 88 (32.1) | 8 (44.4) | 23 (36.5) | 6 (42.9) | 125 (33.9) |
| Diabetes, n (%) | 25 (9.1) | 2 (11.1) | 10 (15.9) | 4 (28.6) | 41 (11.1) |
| Cardiac, n (%) | 24 (8.8) | 2 (11.1) | 5 (7.9) | 2 (14.3) | 33 (8.9) |
| Respiratory, n (%)[1] | 9 (3.3) | 3 (16.7) | 1 (1.6) | 3 (21.4) | 16 (4.3) |
| Neurologic, n (%) | 16 (5.8) | 1 (1 (5.6) | 3 (4.8) | 3 (21.4) | 23 (6.2) |
| Chronic kidney disease, n (%) | 5 (1.8) | 0 (0.0) | 0 (0.0) | 1 (7.1) | 6 (1.6) |
| Psychological, n (%) | 30 (11.0) | 4 (22.2) | 7 (11.1) | 2 (14.3) | 43 (11.7) |
| Prior surgery, n (%)[1] | 57 (20.8) | 8 (44.4) | 9 (14.3) | 5 (35.7) | 79 (21.4) |
| Disseminated cancer, n (%) | 21 (7.7) | 2 (11.1) | 6 (9.5) | 2 (14.3) | 31 (8.4) |
| *Clinical characteristics* | | | | | |
| Height (cm), mean (SD)[2] | 160.5 (6.6) | 158.6 (7.2) | 158.4 (6.8) | 158.3 (6.1) | 159.9 (6.7) |
| Weight (Kg), mean (SD) | 76.1 (20.9) | 83.5 (30.9) | 80.5 (18.9) | 77.2 (20.2) | 77.2 (21.2) |
| BMI (Kg/m$^2$), mean (SD)[2] | 29.6 (8.0) | 33.0 (11.5) | 32.1 (7.9) | 30.7 (7.2) | 30.3 (8.2) |
| Systolic BP (mmHg), mean (SD) | 122.7 (19.0) | 121.4 (14.1) | 127.1 (17.2) | 126.7 (28.0) | 123.6 (18.9) |
| Diastolic BP (mmHg), mean (SD)[1] | 71.6 (11.0) | 66.0 (9.2) | 73.3 (10.6) | 66.4 (14.4) | 71.4 (11.1) |
| *Surgical complexity*[1,3] | | | | | |
| Complex procedures, category 0 | 84 (30.7) | 3 (16.7) | 11 (17.5) | 2 (14.3) | 100 (27.1) |
| Complex procedures, category 1 | 174 (63.5) | 12 (66.7) | 48 (76.2) | 7 (50.0) | 241 (65.3) |
| Complex procedures, category 2 | 16 (5.8) | 3 (16.7) | 4 (6.4) | 5 (35.7) | 28 (7.6) |
| Laparoscopy[1] | 118 (43.1) | 8 (44.4) | 15 (23.8) | 4 (28.6) | 145 (39.3) |
| Surgical procedure by a trainee | 54 (19.7) | 6 (33.3) | 13 (20.6) | 3 (21.4) | 76 (20.6) |
| *Diagnosis* | | | | | |
| Benign | 95 (34.7) | 3 (16.7) | 14 (22.2) | 2 (14.3) | 114 (30.9) |
| Malignant | 167 (61.0) | 13 (72.2) | 47 (74.6) | 12 (85.7) | 239 (64.8) |
| Prophylactic | 12 (4.4) | 2 (11.1) | 2 (3.2) | 0 (0.0) | 16 (4.3) |
| *Primary pathology* | | | | | |
| Cervical | 15 (5.5) | 3 (16.7) | 6 (9.5) | 0 (0.0) | 24 (6.5) |
| Ovarian | 138 (50.4) | 10 (55.6) | 30 (47.6) | 8 (57.1) | 186 (50.4) |
| Uterine | 119 (43.4) | 4 (22.2) | 26 (41.3) | 5 (35.7) | 154 (41.7) |
| Vulval/vaginal | 2 (0.7) | 1 (5.6) | 1 (1.6) | 1 (7.1) | 5 (1.4) |

AE: Adverse Event; BMI: Body Mass Index; BP: Blood Pressure; SD: Standard Deviation;

1. Significant difference in the distribution ($P<0.05$);
2. Four patients had missing information
3. Complex procedures in category 1 include any of the following: Radical hysterectomy, pelvic lymphadenectomy, para-aortic lymphadenectomy, omentectomy, adhesiolysis and ureterolysis; Complex procedures in category 2 include any of the following: anterior rectal resection, colonic resection, small bowel resection, exenteration, urinary conduit, splenectomy, (sub) total peritonectomy and resection of the diaphragm. All other procedures were considered category 0.

392 **Table 2. Incidence of adverse events**
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| | *N* | *%* |
|---|---|---|
| Total number of patients operated | 369 | |
| Patients with at least one adverse event | 95 | 25.7 |
| Patients with 2 or more events | 16 | 4.3 |
| | | |
| *Intra-operative adverse events* | 29 | 7.9 |
| Bowel injury | 10 | 2.7 |
| Bladder injury | 6 | 1.6 |
| Vascular injury | 6 | 1.6 |
| Intra-operative blood transfusion | 6 | 1.6 |
| Nerve, ureteric and or other injuries | 4 | 1.1 |
| | | |
| *Post-operative adverse events* | 77 | 20.9 |
| Wound related | 33 | 8.9 |
| UTI | 8 | 2.2 |
| Renal | 5 | 1.4 |
| Gastric ileus | 7 | 1.9 |
| Pneumonia | 9 | 2.4 |
| Cardiac | 7 | 1.9 |
| Pelvic abscess/secondary hematoma | 4 | 1.1 |
| Septicemia | 2 | 0.5 |
| DVT | 3 | 0.8 |
| Lymphoedema | 3 | 0.8 |
| Other* | 13 | 3.5 |

UTI=Urinary tract infection, DVT= Deep vein thrombosis
*Other= multi organ failure, abscess, stroke, neuropathy, encephalopathy and psychological.

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**Table 3. Median and adjusted average hospital costs (2008 AUD) and length of stay**

| Hospital costs | N (%) | Total cost (AU$) | % of total cost | Median cost, AU$ (IQR) | Average cost per patient* | 95% CI* | | Excess cost |
|---|---|---|---|---|---|---|---|---|
| No AE | 274 (74.3) | $3,533,965 | 53% | $11,842 ($9,791-15,120) | $12,872 | $12,460 | $13,277 | Ref |
| Intra-op AE | 29 (7.9) | $1,093,510 | 16% | $18,069 ($12,131-33,259) | $40,746 | $11,582 | $71,859 | $27,874 |
| Minor post-op AE | 63 (17.1) | $1,192,691 | 18% | $15,903 ($12,196-21,355) | $18,459 | $17,270 | $19,713 | $5,587 |
| Major post-op AE | 14 (3.8) | $813,737 | 12% | $27,769 ($16,484-50,899) | $67,656 | $5,324 | $131,761 | $54,784 |
| | Total | $6,633,903 | | | | | | |

| Length of stay (LOS) | N (%) | Total LOS | % of total LOS | Median LOS, Days (IQR) | Average LOS* | 95% CI | | Excess LOS |
|---|---|---|---|---|---|---|---|---|
| No AE | 274 (74.3) | 1331.9 | 49% | 4.91 (2.2-6.2) | 4.8 | 4.5 | 5.1 | Ref |
| Intra-op AE | 29 (7.9) | 462.6 | 17% | 7.1 (5.3-13.0) | 18.1 | 4.2 | 32 | 13.3 |
| Minor post-op AE | 63 (17.1) | 526.9 | 20% | 7.0 (5.1-9.4) | 8 | 7.2 | 8.8 | 3.2 |
| Major post-op AE | 14 (3.8) | 372.9 | 14% | 11.5 (8.3-20.9) | 32.8 | 4.2 | 61.5 | 28 |
| | Total | 2694.3 | | | | | | |

*Log transformed regression with back-transformation on raw cost scale using smearing factors, costs are adjusted for types of AEs, weighted activity unit, age, presence of malignancy, surgical complexity, laparotomy, tumor type and multiple comorbidities;

Abbrevs: IQR: Inter Quartile Range; AE: Adverse Event; LOS: Length of Stay

**Table 4. Subgroups of adjusted mean costs stratified by laparoscopy versus laparotomy**

| | | Laparoscopy[2] | | | | Laparotomy[3] | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | n | mean | 95% CI | | n | mean | 95% CI | |
| Overall | | 145 | $ 13,612 | $ 8,642 | $ 18,582 | 224 | $ 17,657 | $ 16,187 | $ 19,127 |
| Any complications | yes | 27 | $ 28,780 | $ 1,450 | $ 56,109 | 68 | $ 23,796 | $ 19,367 | $ 28,225 |
| | no | 118 | $ 10,141 | $ 9,861 | $ 10,422 | 156 | $ 14,981 | $ 14,461 | $ 15,502 |
| Major postop complications | yes | 4 | $ 107,760 | -$ 174,385 | $ 389,906 | 10 | $ 47,422 | $ 19,073 | $ 75,772 |
| | no | 141 | $ 10,941 | $ 10,450 | $ 11,433 | 214 | $ 16,266 | $ 15,655 | $ 16,877 |
| Minor postop complications | yes | 15 | $ 16,701 | $ 14,050 | $ 19,352 | 48 | $ 18,930 | $ 17,789 | $ 20,072 |
| | no | 130 | $ 13,256 | $ 7,715 | $ 18,796 | 176 | $ 17,310 | $ 15,463 | $ 19,157 |
| Ovarian cancer | yes | 56 | $ 16,053 | $ 3,425 | $ 28,681 | 130 | $ 18,362 | $ 16,014 | $ 20,710 |
| | no | 89 | $ 11,972 | $ 11,235 | $ 12,709 | 94 | $ 16,660 | $ 15,393 | $ 17,927 |
| Complex surgery | yes | 66 | $ 17,728 | $ 6,751 | $ 28,705 | 175 | $ 16,186 | $ 15,581 | $ 16,792 |
| | no | 79 | $ 10,173 | $ 9,701 | $ 10,646 | 49 | $ 22,910 | $ 16,596 | $ 29,224 |
| Very complex surgery | yes | 0 | - | - | - | 28 | $ 29,967 | $ 19,574 | $ 40,360 |
| | no | 145 | - | - | - | 196 | $ 15,899 | $ 15,298 | $ 16,499 |
| Malignant tumor | yes | 80 | $ 12,300 | $ 11,525 | $ 13,075 | 159 | $ 19,168 | $ 17,159 | $ 21,176 |
| | no | 65 | $ 15,227 | $ 4,027 | $ 26,426 | 65 | $ 13,963 | $ 13,228 | $ 14,698 |

1. Adjusted for age, any complications, minor postop complications, major postop complications, weighted activity unit, malignant, ovarian cancer, complex surgery, very complex surgery.
2. Laparoscopy model performance: Adj R square=0.65, link test p=0.26, Ramsey reset test=0.54 and Copas test beta=0.72 p=0.09
3. Laparotomy model performance: Adj R square=0.49, link test p=0.52, Ramsey reset test=0.00(failed) and Copas test beta=0.84 p=0.05

Table 5. Summary of extrapolation to all Australian patients with suspected and confirmed gynecological cancers and one-way sensitivity analyses (n=5736*)

| | AU$ 2008 in million | % total costs |
|---|---|---|
| Total costs all cases | 105.99 | 100% |
| Total costs of cases with AE | 51.17 | 48% |
| Total costs of cases with intra-op AEs | 18.37 | 17% |
| Total costs of cases with minor post-op AEs | 18.08 | 17% |
| Total costs of cases with major post-op AEs | 14.72 | 14% |
| Baseline total costs | 105.99 | |
| | + 10% | -10% |
| Change in % no AEs | 100.51 | 111.47 |
| Change in % intra-operative cases | 107.84 | 104.17 |
| Change in % minor post-operative cases | 107.80 | 104.18 |
| Change in % major post-operative cases | 107.44 | 104.53 |
| | +20% | -20% |
| Change in % no AEs | 95.02 | 116.96 |
| Change in % intra-operative cases | 109.67 | 102.34 |
| Change in % minor post-operative cases | 106.61 | 102.37 |
| Change in % major post-operative cases | 108.93 | 103.04 |

*n=5736 calculated based on 4243 new cases of gynaecological cancer inflated to include benign and prophylactic cases (by factor 1.352).

Table 6. Estimated total hospital costs for all Australian gynecology oncology patients under different scenarios in the proportion of AEs (n=5736*)

| Scenario | Cost-savings (AU$ 2008) in million | Australia-wide (AU$ 2008) in million |
|---|---|---|
| Baseline case (no reduction) | - | 103.73** |
| Intra-operative AEs | | |
| 10% reduction | 1.75 | 101.98 |
| 20% reduction | 3.79 | 99.94 |
| 40% reduction | 7.38 | 96.35 |
| Minor post-operative AEs | | |
| 10% reduction | 1.81 | 101.92 |
| 20% reduction | 3.62 | 100.11 |
| 40% reduction | 7.25 | 96.48 |
| Major post-operative AEs | | |
| 10% reduction | 1.46 | 102.27 |
| 20% reduction | 2.86 | 100.87 |
| 40% reduction | 5.99 | 97.74 |

*Results based on 5736 simulations in probabilistic sensitivity analyses. N has been calculated based on 4243 new cases of gynaecological cancer inflated to include benign and prophylactic cases (by factor 1.352). AE: Adverse Event, AUD Australian Dollar

**This baseline estimate is slightly different than in Table 5 ($105.99) because it is based on probabilistic sensitivity results.