Title

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# Ovarian Cancer Rates After Hysterectomy With and Without Salpingo-oophorectomy

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## Abstract

**Objective—**To estimate ovarian and peritoneal cancer rates after hysterectomy with and without salpingo-oophorectomy for benign conditions.

**Methods—**All patients after hysterectomy for benign disease from 1988–2006 in Kaiser Permanente Northern California, an integrated health organization. Incidence rates per 100,000 person-years were calculated.

**Results—**Of 56,692 patients, the majority (54%) underwent hysterectomy with bilateral salpingo-oophorectomy (BSO); 7% had hysterectomy with unilateral salpingo-oophorectomy, and 39% had hysterectomy alone. There were 40 ovarian and eight peritoneal cancers diagnosed during follow-up. Median age at ovarian and peritoneal cancer diagnosis was 50 and 64 years, respectively. Age-standardized rates (per 100,000 person-years) of ovarian or peritoneal cancer were 26.7 (95%CI=16–37.5) for those with hysterectomy alone, 22.8 (95%CI=0.0–46.8) for hysterectomy and unilateral salpingo-oophorectomy, and 3.9 (95%CI=1.5–6.4) for hysterectomy and BSO. Rates of ovarian cancer were 26.2 (95%CI=15.5–37) for those with hysterectomy alone, 17.5 (95%CI=0.0–39.1) for hysterectomy and unilateral salpingo-oophorectomy, and 1.7 (95%CI=0.4–3) for those with hysterectomy and BSO. Compared to women undergoing hysterectomy alone, those also receiving an unilateral salpingo-oophorectomy had a hazard ratio

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(HR) for ovarian cancer of 0.58 (95%CI=0.18–1.9); those undergoing BSO had a HR of 0.12 (95%CI=0.05–0.28).

**Conclusions—**The removal of both ovaries decreases incidence of ovarian and peritoneal cancers. Removal of one ovary might also decrease the incidence of ovarian cancer but warrants further investigation.

## INTRODUCTION

Advances are needed in the prevention of epithelial ovarian cancer, the most lethal gynecologic cancer. (1, 2) Prophylactic salpingo-oophorectomy after completion of childbearing in women with BRCA1/2 mutations can significantly decrease the risk of ovarian cancer. (3) However, the benefit associated with removing one or both ovaries in low-risk populations remain unclear.(4, 5)

Of women aged 50–54 years who underwent a hysterectomy, 78% also had a synchronous bilateral salpingo-oophorectomy (BSO). (6, 7) The risk of developing ovarian cancer in retained ovaries contrasted by other health-related conditions associated with removing ovaries warrant further study. The decision for women to elect to undergo a BSO during a hysterectomy is particularly difficult in light of the data from the Women's Health Initiative randomized trials demonstrating more harm than benefit associated with postmenopausal hormone therapy. (8) Since women are more averse to taking hormone replacement (9, 10), the decision to undergo an elective BSO during hysterectomy is even more challenging.

The benefits of removing one or both ovaries in women at low risk for ovarian cancer have not been extensively studied. A prospective cohort study showed that although BSO at the time of hysterectomy for benign disease is associated with a decreased risk of ovarian cancer, there was an increased risk of all-cause mortality associated with other health conditions such as coronary heart disease. (11) The results suggested that ovarian conservation until at least age 65 benefits long-term survival for women at average risk of ovarian cancer. (11, 12) This study adopted published age-specific risk analyses from a hypothetical and homogenous cohort of patients. On the other hand, Jacoby *et al* showed that BSO may not have such harmful effects on total mortality when compared with hysterectomy and ovarian preservation. (5)

We performed a large retrospective cohort study of women at average risk for ovarian cancer to determine the incidence of ovarian and peritoneal carcinoma after elective removal of one or both ovaries at the time of hysterectomy for benign disease.

## METHODS

We conducted a retrospective cohort study utilizing data from Kaiser Permanente of Northern California (KPNC). The study was approved by the Kaiser Permanente Northern California Institutional Review Board. KPNC is a prepaid, integrated managed care health plan that provides comprehensive medical services to over 3 million current members, approximately 30% of the Northern California population. The membership is

demographically representative of the population in its catchment area, although it slightly under-represents the extremes of income and education. (13, 14)

Female KPNC members between the age of 18–84 years undergoing a hysterectomy for a benign condition between January 1, 1988 and December 31, 2006 were identified using the KPNC automated hospitalization database. This database records information on the primary discharge diagnosis and up to 15 secondary discharge diagnoses as well as the primary procedure and up to 7 secondary procedures using the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM).

We categorized patients into three surgery groups: hysterectomy alone, hysterectomy with unilateral salpingo-oophorectomy, and hysterectomy with bilateral salpingo-oophorectomy (BSO).Type of surgical procedure was based on ICD-9-CM procedure codes and included: hysterectomy—subtotal (68.3, 68.31, 68.39), hysterectomy—abdominal (68.4, 68.41, 68.49), hysterectomy—vaginal (68.5, 68.51, 68.59), and hysterectomy NOS (68.9), unilateral oophorectomy (65.3, 65.31, 65.39), unilateral salpingo-oophorectomy (65.4, 65.41, 65.49), bilateral oophorectomy (65.5, 65.51, 65.52, 65.53, 65.54), bilateral salpingo-oophorectomy (65.6, 65.61, 65.62, 65.63, 65.64). Patients who had a radical hysterectomy (68.6, 68.61, 68.69, 68.7, 68.71, 67.79) for benign conditions (n=86) were included in the hysterectomy with synchronous BSO group. If one remaining ovary was removed during the hysterectomy hospitalization (65.52, 65.54, 65.62, 65.64), the patient was categorized as having had a hysterectomy with synchronous BSO.

Patients were excluded if their hysterectomy hospitalization: 1) had an ICD-9-CM discharge diagnosis of any malignancy including cervical cancer (180, 180.1, 180.8, 180.9), uterine cancer (182, 182.1, 182.8), ovarian cancer (183, 183.2, 183.3, 183.4, 183.5, 183.8, 183.9), or other malignant neoplasms (140–209, 230–239) except for non-melanoma skin cancer (173); 2) had an ICD-9-CM discharge diagnosis of pre-malignant lesions including disorders of uterus NOS (621), endometrial hyperplasia with or without atypia (621.3, 621.30, 621.31, 621.32, 621.33), non-inflammatory disorders of cervix (622), dysplasia of cervix (622.1, 622.10, 622.11, 622.12), abnormal Papanicolaou smear (795.0), and 3) had an ICD-9-CM procedure code indicating a cesarean section (74.0, 74.1, 74.2, 74.3, 74.4, 74.9). Other reasons for exclusion were: 1) diagnosis prior to the hysterectomy of an ovarian or peritoneal cancer in the KPNC tumor registry, 2) diagnosis within 90 days after their hysterectomy of an ovarian or peritoneal cancer in the KPNC tumor registry (n=16), and 3) follow-up of less than 90 days after their hysterectomy.

The KPNC tumor registry, a contributor to the Surveillance, Epidemiology, and End Results program of cancer registries, was used to identify new primary ovarian and peritoneal cancers. Information obtained from the registry included diagnosis date, type of cancer, stage, and histology. Primary analyses were conducted with invasive and borderline cancers as outcomes; secondary analyses were restricted to invasive cases only. Follow-up began at hysterectomy and ended at diagnosis of ovarian or peritoneal cancer, death, end of health plan membership, or end of study period, whichever came first. A total of 19,085 (33.7%) patients left the health plan during the study period; their median follow-up time was 3.0 years. The attrition rates were similar across the three surgical groups.

Age-specific and age-standardized (standardized to the 2000 US Census population) cancer rates per 100,000 person-years were calculated. Cox regression modeling was used to estimate the hazard ratios (HR) of ovarian or peritoneal cancer associated with different types of surgical procedures, adjusting for patient age at surgery and race. The type of surgical procedure was treated as time-varying. For example, a patient who had a hysterectomy alone and then subsequently had a BSO had their follow-up time from entry until the date of their BSO attributed to hysterectomy alone, and then once they had the BSO their subsequent follow-up time was attributed to hysterectomy plus non-synchronous BSO. However, since there were so few women who had a hysterectomy and then a later, non-synchronous BSO (n=725 patients, 0 cancers) or non-synchronous unilateral salpingo-oophorectomy (n=201 patients, 0 cancers), we did not present separate results for these surgical categories. Likewise, since there were few patients who received a hysterectomy and salpingectomies with ovarian preservation, the data were not presented.

## RESULTS

We identified 56,692 patients who underwent hysterectomy for benign conditions. The median age at hysterectomy was 45 years (range: 19–92). Approximately 59% were White, 12% were Black, 11% Hispanic, 7% were Asian, 2% other race, and 9% unknown race/ethnicity. (Table 1) The majority (54%) of patients undergoing hysterectomy had a bilateral salpingo-oophorectomy (BSO), whereas 7% had a hysterectomy with unilateral salpingo-oophorectomy and 39% underwent hysterectomy alone. The median age in the hysterectomy with BSO group was 47 years (range: 19–92) compared to 43 years (range: 21–85) for hysterectomy with unilateral salpingo-oophorectomy and 42 years (range: 19–92) for hysterectomy alone. The years of surveillance were similar in these three groups. There were 40 ovarian cancers and eight peritoneal cancers identified during a median follow-up of 5.1 years. Six of the 40 ovarian cancers were borderline cancers (see the Appendix, available online at http://links.lww.com/xxx). The median age at the diagnosis of ovarian or peritoneal cancer was 50 (range: 32–85) and 64 years (range: 49–75), respectively. The median time from hysterectomy for benign disease to ovarian cancer was 7.9 years while the median time from hysterectomy to peritoneal cancer was 4.2 years.

The age-specific rates of ovarian and peritoneal cancer stratified by age and type of surgery are shown in Table 2. The age-standardized rates of ovarian or peritoneal cancer per 100,000 person years were 26.7 (95% confidence interval [CI] 16–37.5) for those with a hysterectomy alone, 22.8 (95% CI=0.0–46.8) for hysterectomy and unilateral salpingo-oophorectomy, and 3.9 (95% CI=1.5–6.4) for those with hysterectomy and BSO (Figure 1a). The rates of ovarian cancer alone were 26.2 (95% CI=15.5–37) for those with a hysterectomy, 17.5 (95% CI=0.0–39.1) for hysterectomy and unilateral salpingo-oophorectomy, and 1.7 (95% CI=0.4–3) for those with hysterectomy and BSO (Figure 1b).

Compared to women aged 18–39 years at the time of hysterectomy, those patients 50–59 years (HR=3.36; 95% CI=1.07–10.59), 60–69 years (HR=5.82; 95% CI=1.94–17.49), and ≥70 years (HR=9.50; 95% CI=3.14–28.69) had significantly higher rates of ovarian or peritoneal cancers. The age and race-adjusted HR for ovarian or peritoneal cancer associated with hysterectomy and BSO was 0.22 (95% CI=0.11–0.44) when compared to hysterectomy

alone. The adjusted HR for unilateral salpingo-oophorectomy was 0.76 with 95% CI=0.27–2.16; however, this was not statistically significant. (Table 3) Although the overall number of cancers decreased, the greater risk reduction was seen in ovarian cancer alone. The adjusted HR for patients undergoing hysterectomy with BSO was 0.12 (95% CI=0.05–0.28), whereas the adjusted HR for hysterectomy with unilateral salpingo-oophorectomy was 0.58 (95% CI=0.18–1.90) compared to hysterectomy alone. Results did not significantly change after restricting outcomes to invasive cancer cases (Table 4).

## DISCUSSION

The rates of ovarian cancer were lowest among those who underwent a synchronous bilateral salpingo-oophorectomy during hysterectomy in our study cohort. However, our data also suggested that those who had one ovary removed had lower rates of ovarian cancer compared to women who had both ovaries preserved. Prophylactic oophorectomy was found to decrease the risk of ovarian and breast cancer at the cost of an increased risk in all-cause mortality due to other serious medical conditions. (5, 11, 12) However, these initial studies were limited to risk-based analyses from prior publications without an actual study cohort. As such, we proposed to study a large cohort of community-based patients of low-risk and with equal access to care to determine the incidence of ovarian or peritoneal carcinoma after the removal of one or two ovaries during hysterectomy for benign disease. It was interesting that the risk reduction of hysterectomy with unilateral salpingo-oophorectomy was greater for ovarian cancer rather than for the combined ovarian/peritoneal cancer group. These findings may be a result of the small numbers of peritoneal cancers within the cohort.

The option of removing one ovary at the time hysterectomy to decrease the risk of ovarian cancer while preserving the other ovary for hormonal function in younger women at low risk for ovarian cancer is provocative. Our analysis suggested a decreased incidence of ovarian cancer after hysterectomy with unilateral salpingo-oophorectomy, though our numbers were small and the finding was not statistically significant. In addition, we did not have data proving that all women who underwent hysterectomy with unilateral salpingo-oophorectomy were left with a remaining ovary which may lead to an overestimate of the reduction in risk. The practice of removing one ovary to reduce cancer risk, while preserving hormonal function, requires investigation. Further, if this practice is validated, the laterality of ovarian cancer also warrants consideration.(15)

Although the exact mechanism of protection has yet to be proven, it is possible that various gynecologic surgeries including hysterectomy, unilateral oophorectomy, tubal ligation, or unilateral oophorectomy and tubal ligation decrease ovarian cancer risk by reducing the number of ovulatory cycles. (16–21) Recent studies have also suggested that high grade serous ovarian, fallopian tube, and primary peritoneal carcinomas are comprised of cells that resemble fallopian tube epithelium. As such, primary fallopian tubal carcinoma may account for a significant proportion of extra-uterine pelvic serous carcinomas. (22–25) Given these findings, some have suggested that salpingectomies during hysterectomy for benign conditions may decrease serous ovarian and peritoneal cancer incidence. (26) In order to validate this recent practice, it would require a large cohort of patients with extended follow-up. Even though this is one of the larger series with long follow-up, the numbers of patients

who underwent hysterectomy with salpingectomy for benign conditions was low. Nevertheless, the effect of this surgery on cancer prevention and quality of life needs to be studied prospectively.

Although our study population is large, the incidence of ovarian cancer is relatively low. Therefore, our rate estimates, especially our age-specific estimates, of ovarian cancer and particularly primary peritoneal cancer may be imprecise. As such, we performed a subset analysis to estimate the rate of ovarian cancer alone. It is also important to note that the median age at diagnosis of ovarian cancer was lower than expected. This finding may be partially explained the duration of follow-up after surgery. Although we were able to follow these women up to 19 years after surgery with the high retention rate within the Kaiser system, we are unable to follow all patients into their older ages which likely resulted in a younger median age at ovarian cancer diagnosis and lower lifetime risk than expected. Nonetheless, this is one of the larger cohorts of patients undergoing hysterectomy for benign conditions in the United States.

Other limitations of this study include our inability to account for several potential confounding factors, such as family history of breast or ovarian cancer, BRCA status, oral contraceptive use, history of endometriosis and prior gynecologic surgery resulting in oophorectomy. We also could not account for reproductive history, which was recently utilized by Vitonis *et al* in conducting a risk score for patients at the time of hysterectomy. (27) Moreover, another limitation of our study was the lack of comprehensive information to evaluate the benefits of oophorectomy balanced against potential harms which may include risks of cardiovascular disease and osteoporosis. These additional analyses are beyond the scope of this current study aims but warrant investigation. Clearly, the difficult decision for women to remove normal ovaries during a hysterectomy for benign conditions needs to be individualized to each patient after considering the potential harm and benefits.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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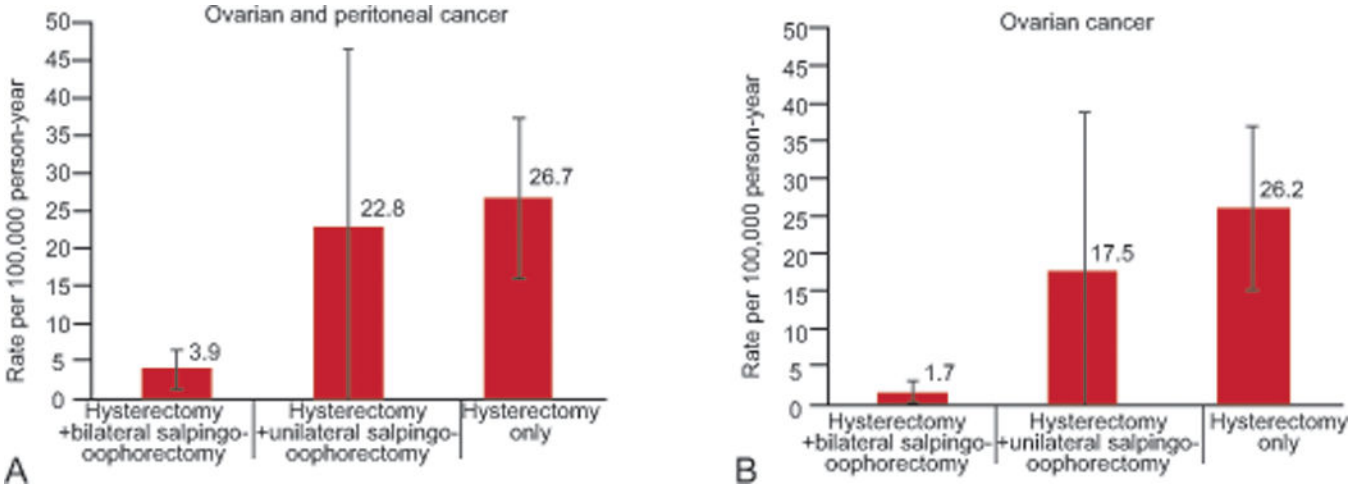


**Figure 1.**

Incidence Rates (per 100,000 person-years) of Ovarian or Peritoneal Cancer Cancer by Type of Surgery (n=56,692) Age-adjusted to United States year 2000 female population. In age-adjusted poisson regression analyses, differences between the hysterectomy+bilateral salpingo-oophorectomy (BSO) and the hysterectomy alone groups were statistically significant (p less than 0.0001 for ovarian or peritoneal cancer; p less than 0.0001 for ovarian cancer). Differences between the hysterectomy+ unilateral salpingo-oophorectomy (USO) and the hysterectomy alone groups were not statistically significant (p= 0.60 for ovarian or peritoneal cancer; p= 0.37 for ovarian cancer only).

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**Table 1**

Year of Surgery, Patient Demographics, Ovarian and Peritoneal Cancer Counts by Type of Surgery (n=56,692)

| | Hysterectomy Alone (n=22,051) | | Hysterectomy + USO (n=3,976) | | Hysterectomy + BSO (n=30,665) | | Total |
|---|---|---|---|---|---|---|---|
| Calendar year, n (%) | | | | | | | |
| 1988–1990 | 2,791 | (37.5%) | 593 | (8.0%) | 4,052 | (54.5%) | 7,436 |
| 1991–1993 | 2,947 | (33.9%) | 594 | (6.8%) | 5,162 | (59.3%) | 8,703 |
| 1994–1996 | 3,348 | (36.3%) | 596 | (6.5%) | 5,279 | (57.2%) | 9,223 |
| 1997–1999 | 3,492 | (38.6%) | 600 | (6.6%) | 4,951 | (54.7%) | 9,043 |
| 2000–2002 | 3,540 | (36.9%) | 646 | (6.7%) | 5,415 | (56.4%) | 9,601 |
| 2003–2006 | 5,933 | (46.8%) | 947 | (7.4%) | 5,806 | (45.8%) | 12,686 |
| Age at hysterectomy, median (range) | | 42 (19–92) | | 43 (21–85) | | 47 (19–92) | 45 (19–92) |
| Age at hysterectomy, n (%) | | | | | | | |
| 18–29 | 460 | (51.3%) | 100 | (11.1%) | 337 | (37.6%) | 897 |
| 30–39 | 6658 | (58.3%) | 1,126 | (9.9%) | 3,634 | (31.8%) | 11,418 |
| 40–49 | 11,132 | (37.8%) | 2,017 | (6.8%) | 16,334 | (55.4%) | 29,483 |
| 50–59 | 1.677 | (18.0%) | 402 | (4.3%) | 7,265 | (77.7%) | 9,344 |
| 60–69 | 1,165 | (33.5%) | 214 | (6.2%) | 2,096 | (60.3%) | 3,475 |
| 70–79 | 827 | (45.4%) | 105 | (5.8%) | 890 | (48.8%) | 1,822 |
| >=80 | 132 | (52.2%) | 12 | (4.7%) | 109 | (43.1%) | 253 |
| Follow-up (years), median (range) | | 4.5 (0.25 – 19) | | 4.6 (0.25 – 18.9) | | 5.9 (0.25 – 19) | 5.3 (0.25–19) |
| Race or ethnicity | | | | | | | |
| Asian | 1,574 | (36.9%) | 260 | (6.1%) | 2,431 | (57.0%) | 4,265 |
| Black | 3,432 | (49.3%) | 641 | (9.2%) | 2,882 | (41.4%) | 6,955 |
| Hispanic | 2,739 | (45.7%) | 410 | (6.8%) | 2,839 | (47.4%) | 5,988 |
| White | 11,727 | (35.3%) | 2,233 | (6.7%) | 19,288 | (58.0%) | 33,248 |
| Other | 400 | (38.5%) | 87 | (8.4%) | 553 | (53.2%) | 1,040 |
| Unknown | 2,179 | (41.9%) | 345 | (6.6%) | 2,672 | (51.4%) | 5,196 |
| Cancer | | | | | | | |
| Ovarian – invasive | 25 | (77.5%) | 2 | (7.5%) | 7 | (15.0%) | 34 |
| Ovarian – borderline | 5 | (83.3%) | 1 | (16.7%) | 0 | (0.0%) | 6 |

| | Hysterectomy Alone (n=22,051) | | Hysterectomy + USO (n=3,976) | | Hysterectomy + BSO (n=30,665) | | Total |
|---|---|---|---|---|---|---|---|
| Peritoneal - invasive | 1 | (12.5%) | 1 | (12.5%) | 6 | (75.0%) | 8 |
| All | 31 | (64.6%) | 4 | (8.3%) | 13 | (27.1%) | 48 |

USO, unilateral salpingo-oophorectomy; BSO = bilateral salpingo-oophorectomy.

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**Table 2**

Age-Specific Incidence (per 100,000 Person-Years) of Ovarian or Peritoneal Cancer by Type of Surgery (n=56,692)

| | Hysterectomy Alone (n=22,051) | | | | Hysterectomy + USO (n=3,976) | | | | Hysterectomy + BSO (n=30,665) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age Group* | Person-Years | No. of Cancer Cases† | Rate‡ | 95% CI | Person-Years | No. of Cancer Cases† | Rate‡ | 95% CI | Person-Years | No. of cancer Cases† | Rate‡ | 95% CI |
| 18–29 | 670 | 0 | 0 | - | 153 | 0 | 0 | - | 497 | 0 | 0 | - |
| 30–39 | 16,915 | 2 | 11.8 | 0 – 28 | 3,032 | 0 | 0 | - | 9,779 | 0 | 0 | - |
| 40–49 | 62,779 | 5 | 8.0 | 1.0 –15 | 11,024 | 0 | 0 | - | 67,417 | 1 | 1.5 | 0 – 4 |
| 50–59 | 31,710 | 11 | 34.7 | 14.2 – 55 | 7,057 | 1 | 14.2 | 0 – 42 | 92,884 | 5 | 5.4 | 0.7 – 10 |
| 60–69 | 9,249 | 3 | 32.4 | 0 – 69 | 1,947 | 1 | 51.4 | 0 – 152 | 30,848 | 6 | 19.4 | 3.9 – 35 |
| 70–79 | 8,487 | 4 | 47.1 | 0.9 – 93 | 1,171 | 2 | 170.8 | 0 – 407 | 11,293 | 1 | 8.8 | 0 – 26 |
| ≥80 | 3,622 | 6 | 165.7 | 33.1 – 298 | 284 | 0 | 0 | - | 3,097 | 0 | 0 | - |

*Age at follow-up (time-varying).

†There was 1 peritoneal cancer in the hysterectomy alone (age 50–59), 1 peritoneal cancer in the hysterectomy + USO (age 60–69), and 6 peritoneal cancers in the hysterectomy+ BSO surgical groups.

‡Rate per 100,000 person-years

USO, unilateral salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy; CI, confidence interval.

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**Table 3**

Hazard Ratios for Ovarian or Peritoneal Cancer and for Ovarian Cancer Alone Associated With Age, Race, and Type of Surgery (n=56,692)

| | | Ovarian or Peritoneal Cancer | | | Ovarian Cancer | | |
|---|---|---|---|---|---|---|---|
| | Total Patients | No. of Cases (Column %) | Hazard Ratio* | 95% CI | No. of Cases (Column %) | Hazard Ratio* | 95% CI |
| **Age at hysterectomy (years)** | | | | | | | |
| 18–39 | 12,315 | 5 (10%) | 1.00 | Reference | 5 (12%) | 1.00 | Reference |
| 40–49 | 29,483 | 17 (35%) | 1.80 | 0.66 – 4.91 | 14 (35%) | 1.61 | 0.58 – 4.50 |
| 50–59 | 9,344 | 8 (17%) | 3.36 | 1.07 – 10.59 | 7 (17%) | 3.65 | 1.12 – 11.82 |
| 60–69 | 3,475 | 9 (19%) | 5.82 | 1.94 – 17.49 | 6 (15%) | 4.15 | 1.26 – 13.70 |
| ≥70 | 2,075 | 9 (19%) | 9.50 | 3.14 – 28.69 | 8 (20%) | 8.75 | 2.82 – 27.15 |
| **Race** | | | | | | | |
| White | 33,248 | 36 (75%) | 1.00 | Reference | 29 (72%) | 1.00 | Reference |
| Non-white | 18,248 | 6 (12%) | 0.43 | 0.18 – 1.03 | 6 (15%) | 0.52 | 0.21 – 1.28 |
| Unknown | 5,196 | 6 (12%) | 0.60 | 0.23 – 1.61 | 5 (12%) | 0.67 | 0.24 – 1.89 |
| **Type of surgery** | | | | | | | |
| Hysterectomy alone | 22,051 | 31 (66%) | 1.00 | Reference | 30 (75%) | 1.00 | Reference |
| Hysterectomy + USO | 3,976 | 4 (8%) | 0.76 | 0.27 – 2.16 | 3 (7%) | 0.58 | 0.18 – 1.90 |
| Hysterectomy + BSO | 30,665 | 13 (27%) | 0.22 | 0.11 – 0.44 | 7 (17%) | 0.12 | 0.05 – 0.28 |

CI, confidence interval; USO, unilateral salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy.

*Hazard ratios adjusted for all variables in the table.

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**Table 4**

Hazard Ratios for Invasive Ovarian or Peritoneal Cancer and for Invasive Ovarian Cancer Alone Associated With Age, Race, and Type of Surgery (n=56,692)

| | | Invasive Ovarian or Peritoneal Cancer | | | Invasive Ovarian Cancer | | |
|---|---|---|---|---|---|---|---|
| | Total Patients | No. of Cases* | Hazard Ratio† | 95% CI | No. of Cases* | Hazard Ratio† | 95% CI |
| **Age at hysterectomy (years)** | | | | | | | |
| **18–39** | 12,315 | 2 | 1.00 | Reference | 2 | 1.00 | Reference |
| 40–49 | 29,483 | 15 | 3.86 | 0.88 – 16.95 | 12 | 3.37 | 0.75 – 15.12 |
| 50–59 | 9,344 | 8 | 8.06 | 1.67 – 38.93 | 7 | 8.95 | 1.81 – 44.24 |
| 60–69 | 3,475 | 9 | 14.59 | 3.13 – 68.01 | 6 | 10.57 | 2.11 – 52.85 |
| ≥70 | 2,075 | 8 | 21.25 | 4.46 – 101.19 | 7 | 19.53 | 3.99 – 95.44 |
| **Race** | | | | | | | |
| White | 33,248 | 32 | 1.00 | Reference | 25 | 1.00 | Reference |
| Non-white | 18,248 | 6 | 0.51 | 0.21 – 1.25 | 6 | 0.65 | 0.26 – 1.63 |
| Unknown | 5,196 | 4 | 0.40 | 0.12 – 1.37 | 3 | 0.42 | 0.10 – 1.66 |
| **Type of surgery** | | | | | | | |
| Hysterectomy alone | 22,051 | 26 | 1.00 | Reference | 25 | 1.00 | Reference |
| Hysterectomy + USO | 3,976 | 3 | 0.68 | 0.20 – 2.24 | 2 | 0.46 | 0.11 – 1.94 |
| Hysterectomy + BSO | 30,665 | 13 | 0.25 | 0.13 – 0.50 | 7 | 0.13 | 0.06 – 0.32 |

CI, confidence interval; USO, unilateral salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy.

*Restricted to invasive cancers; borderline cancers (n=6 ovarian cases) were censored at diagnosis

†Hazard ratios adjusted for all variables in the table.