GYNECOLOGY

The rapid adoption of opportunistic salpingectomy at the time of hysterectomy for benign gynecologic disease in the United States

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BACKGROUND: Mounting evidence for the role of distal fallopian tubes in the pathogenesis of epithelial ovarian cancer has led to opportunistic salpingectomy being increasingly performed at the time of benign gynecologic surgery. Opportunistic salpingectomy has now been recommended as best practice in the United States to reduce future risk of ovarian cancer even in low-risk women. Preliminary analyses have suggested that performance of opportunistic salpingectomy is increasing.

OBJECTIVE: To examine trends in opportunistic salpingectomy in women undergoing benign hysterectomy and to determine how the publication of the tubal hypothesis in 2010 may have contributed to these trends.

STUDY DESIGN: This is a population-based, retrospective, observational study examining the National Inpatient Sample between January 2001 and September 2015. Women younger than 50 years who underwent inpatient hysterectomy for benign gynecologic disease were grouped as hysterectomy alone vs hysterectomy with opportunistic salpingectomy. All women had ovarian conservation, and those with adnexal pathology were excluded. Linear segmented regression with log transformation was used to assess temporal trends. An interrupted time-series analysis was then used to assess the impact of the 2010 publication of the tubal hypothesis on opportunistic salpingectomy trends. A regression-tree model was constructed to examine patterns in the use of opportunistic salpingectomy. A binary logistic regression model was then fitted to identify independent characteristics associated with opportunistic salpingectomy. Sensitivity analysis was performed in women aged 50–65 years to further assess surgical trends in a wider age group.

RESULTS: There were 98,061 (9.0%) women who underwent hysterectomy with opportunistic salpingectomy and 997,237 (91.0%) women who underwent hysterectomy alone without opportunistic salpingectomy. The rate at which opportunistic salpingectomy was being performed gradually increased from 2.4% to 5.7% between 2001 and 2010 (2.4-fold increase; $P<.001$), predicting a 7.0% rate of opportunistic salpingectomy in 2015. However, in 2010, the rate of opportunistic salpingectomy began to increase substantially and reached 58.4% by 2015 (10.2-fold increase; $P<.001$). In multivariable analysis, the largest change in the performance of opportunistic salpingectomy occurred after 2010 (adjusted odds ratio, 5.42; 95% confidence interval, 5.34–5.51; $P<.001$). In a regression-tree model, women who had a hysterectomy at urban teaching hospitals in the Midwest after 2013 had the highest chance of undergoing opportunistic salpingectomy during benign hysterectomy (76.4%). In the sensitivity analysis of women aged 50–65 years, a similar exponential increase in opportunistic salpingectomy was observed from 5.8% in 2010 to 55.8% in 2015 (9.8-fold increase; $P<.001$).

CONCLUSION: Our study suggests that clinicians in the United States rapidly adopted opportunistic salpingectomy at the time of benign hysterectomy following the publication of data implicating the distal fallopian tubes in ovarian cancer pathogenesis in 2010. By 2015, nearly 60% of women had undergone opportunistic salpingectomy at benign hysterectomy.

Key words: hysterectomy, ovarian cancer pathophysiology, ovarian cancer prevention, salpingectomy, United States epidemiology

Ovarian cancer has the highest mortality rate of all gynecologic malignancies. In the United States, 13,940 deaths due to ovarian cancer are estimated for 2020.[1] High-grade serous ovarian cancer (HGSOC) is the most common histologic type of ovarian cancer, and given that there are no effective means of screening, it typically presents at advanced stage with poor survival.[2] Ovarian cancer prevention strategies, particularly through risk-reducing surgery, are therefore of great interest.[3]

The emergence of *BRCA* and other high-risk germline mutations, for which risk-reducing salpingo-oophorectomy is recommended in the fourth to fifth decade of life, has led to key discoveries in tumor pathogenesis. Specifically, serous tubal intraepithelial carcinoma (STIC) lesions were initially described in 2001 in tubal specimens from *BRCA* carriers.[4] Over the following decade, pathologic evidence for the role of STIC lesions in HGSOC solidified, and epidemiologic data suggested the protective effect of tubal ligation on ovarian cancer risk (Figure 1).[5–10] This culminated in a landmark publication by Kurman and Shih in 2010 detailing a unifying theory of ovarian cancer pathogenesis beginning with the distal fallopian tube (ie, the tubal hypothesis), which has since been widely cited.[11]

Since 2010, several retrospective studies have demonstrated impressive reductions in ovarian cancer risk ranging from 24% to 65% after salpingectomy or tubal ligation.[12–16] Publication of improved protocols for histopathologic sectioning and examination of tubal

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AJOG at a Glance

Why was this study conducted?

Opportunistic salpingectomy is now recommended in the United Sates at the time of benign gynecologic surgery to prevent high-grade serous ovarian cancer. However, utilization and national practice patterns of opportunistic salpingectomy remain unknown.

Key findings

Since the publication of the tubal hypothesis in 2010, performance of opportunistic salpingectomy at the time of benign hysterectomy increased substantially. By 2015, opportunistic salpingectomy rates had increased 10-fold such that nearly 60% of women had undergone opportunistic salpingectomy. Opportunistic salpingectomy varies based on patient demographics, surgical approach, and hospital characteristics.

What does this add to what is known?

Since 2010, clinicians in the United States have rapidly adopted opportunistic salpingectomy at the time of benign hysterectomy.

specimens in high-risk women and those with ovarian cancer, such as the sectioning and extensively examining the fimbriated end (SEE-FIM) protocol, has improved the detection and our understanding of STIC lesions.[8,9,17] Molecular markers and gene expression profiles, specifically with regard to *TP53* mutation lineage, have also substantiated the role of STIC lesions in ovarian cancer pathogenesis.[18,19] This evidence has informed a Committee Opinion by the American College of Obstetricians and Gynecologists (ACOG) and a Practice Statement by the Society of Gynecologic Oncology (SGO) in support of opportunistic salpingectomy at the time of benign gynecologic surgery even in low-risk women (Figure 1).[3,12]

Preliminary studies have suggested that rates of opportunistic salpingectomy are increasing[20]; however, recent national practice patterns are unknown in the United States. Given that approximately a half million hysterectomies are performed per year in the United States,[21] practice changes with regard to the performance of opportunistic salpingectomy have the potential to affect a very large number of women and therefore deserve further study. This study aimed to examine trends in the performance of opportunistic salpingectomy in women undergoing benign hysterectomy in the United States and to hypothesize how publication of the aforementioned evidence implicating the distal fallopian tubes in ovarian cancer pathogenesis may have contributed to these trends.

Materials and Methods

Data source

The National Inpatient Sample (NIS) is a publicly available and deidentified population-based database distributed as part of the Healthcare Cost and Utilization Project by the Agency for Healthcare Research and Quality.[22] The NIS database includes hospital discharge data for >90% of the United States population when weighted and provides patient demographic and resource use information, such as diagnosis and intervention types, length of stay and hospital charges, and hospital-specific data, including location, bed capacity, and teaching status. The University of Southern California Institutional Review Board deemed the study exempt owing to the use of publicly available deidentified data.

Study eligibility

This population-based, retrospective, cross-sectional observational study examined the NIS between January 2001 and September 2015. Women younger than 50 years who underwent inpatient hysterectomy for benign gynecologic disease were grouped as hysterectomy alone without opportunistic salpingectomy and hysterectomy with opportunistic salpingectomy. All women had ovarian conservation at hysterectomy, and those with adnexal pathology were excluded.

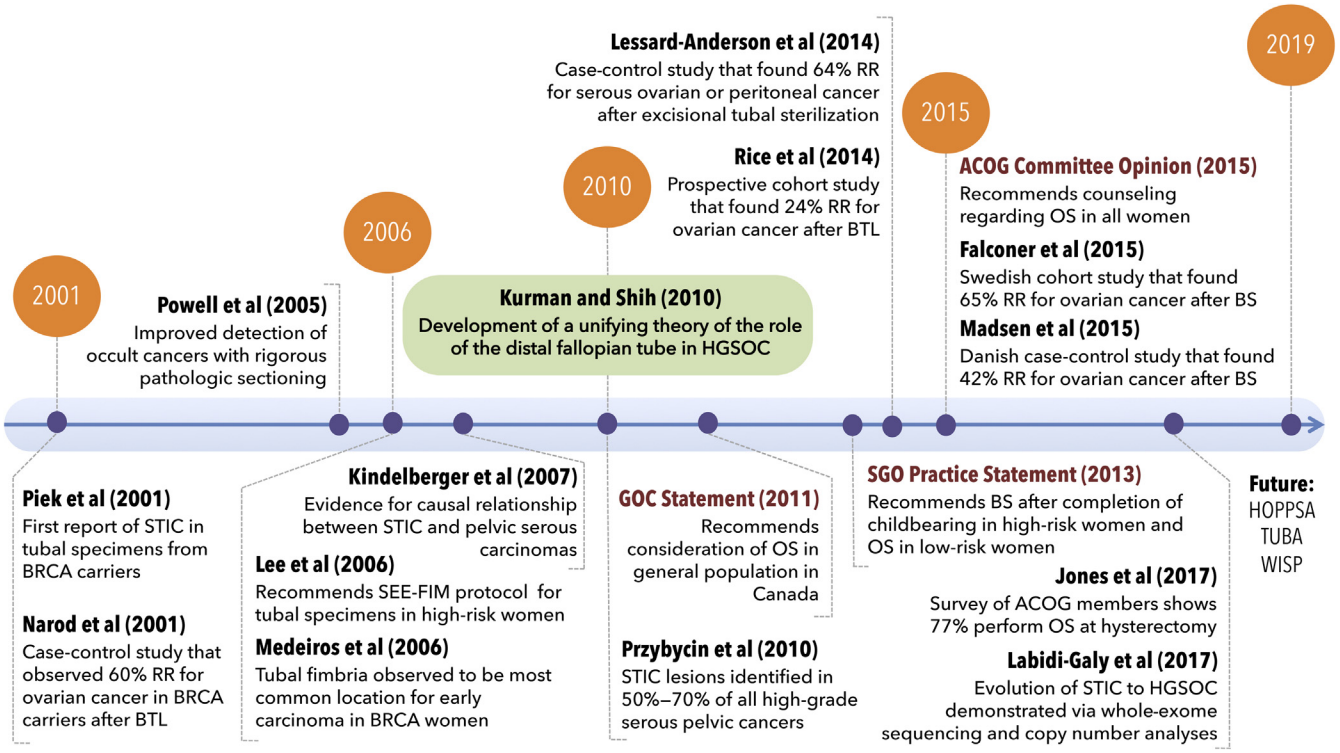
The study population was limited to women younger than 50 years to minimize potential for confounding variables for 2 reasons: (1) ovarian conservation rates at benign hysterectomy are highest before the age of 50 years (52.3%−64.7%) and decrease by nearly 50% thereafter,[20,23] and (2) older women have a higher likelihood of prior adnexal surgery (either tubal ligation or salpingo-oophorectomy). Ovarian conservation was determined by the absence of oophorectomy *International Classification of Disease, Ninth Revision* (ICD-9) codes (Supplemental Table 1). Performance of opportunistic salpingectomy was recorded by the presence or absence of ICD-9 codes that detailed salpingectomy (66.4, 66.5, and 66.6), and the ICD-9 codes remained the same during the study period.

Clinical information

Among cases eligible for analysis, the following information was abstracted from the NIS database: patient demographics, diagnoses and procedures performed during the index hospitalization, gynecologic pathologic information, and hospital information. Patient demographics included age (<30, 30−39, and 40−49 years), calendar year of hysterectomy (2001−2003, 2004−2006, 2007−2009, 2010−2012, and 2013−2015), race/ethnicity (white, black, Hispanic, Asian, Native American, and others), medical comorbidities, obesity (nonobese, class I−II, and class III), primary expected payer (Medicare, Medicaid, private insurance, self-pay, no charge, and others), and median household income (<$39,000, $39,000−$47,999, $48,000−$62,999, and ≥$63,000). Obesity was defined by ICD-9 codes and grouped into class I−II obesity (body mass index, 30−39.9 kg/m^2) and class III obesity (≥40 kg/m^2) per the Centers for Disease Control and Prevention classification.[24]

For medical comorbidities, the Charlson Comorbidity Index (0, 1, 2,

FIGURE 1
Evolution of opportunistic salpingectomy from 2001 to 2019



Key studies on opportunistic salpingectomy from 2001 to 2019 are listed by the first author and year of publication with brief explanation of important findings. Published practice recommendations or guidelines are shown in red. Selected publications are listed. Figure is not drawn to scale and is not intended to be comprehensive.

BS, bilateral salpingectomy; *BTL*, bilateral tubal ligation; *GOC*, The Society of Gynecologic Oncology of Canada; *HGSOC*, high-grade serous ovarian cancer; *HOPPSA*, Hysterectomy and Opportunistic Salpingectomy randomized clinical trial on opportunistic salpingectomy at the time of hysterectomy; *OS*, opportunistic salpingectomy; *RR*, risk reduction; *SEE-FIM*, sectioning and extensively examining the fimbriated end; *SGO*, Society of Gynecologic Oncology; *STIC*, serous tubal intraepithelial lesion; *TUBA*, Tubectomy in BRCA mutation carriers; *WISP*, Women Choosing Surgical Prevention.

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and ≥3) was calculated for each patient based on ICD-9 codes for the specified medical conditions in each category and weighted appropriately to calculate a final score as described previously (Supplemental Table 1).[23,25,26] Gynecologic factors abstracted from the database included the presence of uterine myomas, adenomyosis or endometriosis, abnormal uterine bleeding, pelvic infection, uterine polyps, and/or adnexal pathology. As previously discussed, those with any adnexal pathology were excluded to only capture women for whom salpingectomy was not indicated based on adnexal pathology and thus was truly opportunistic.

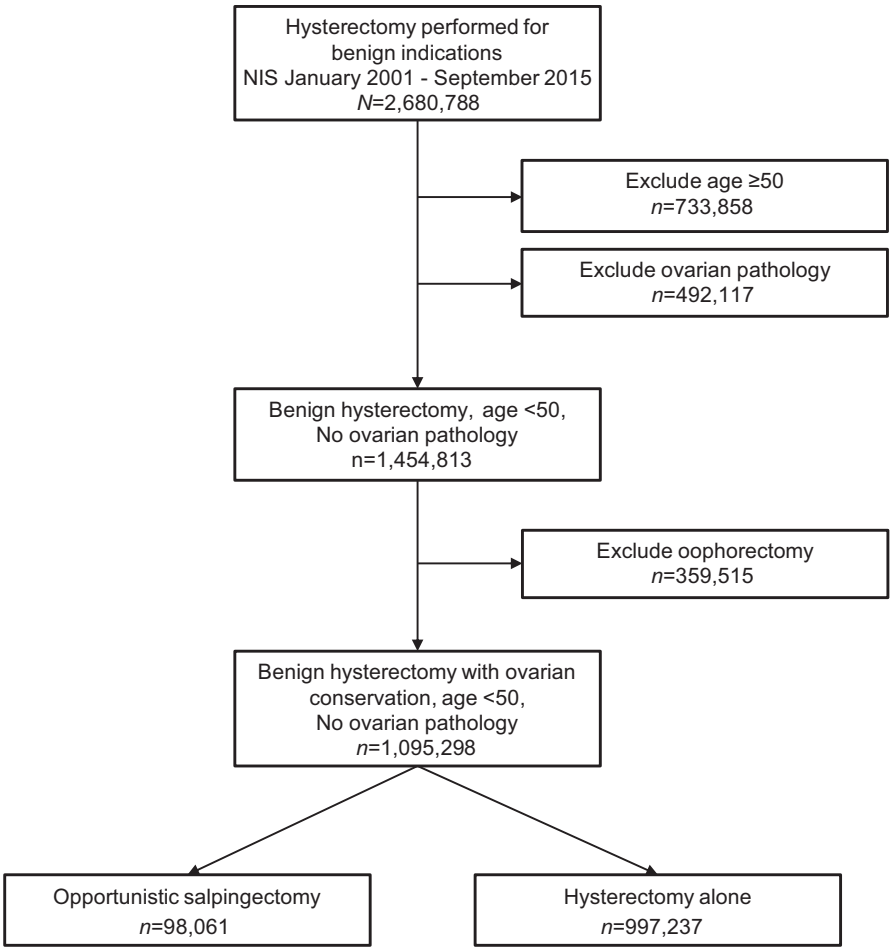
Surgical approach was divided into the following groups: total abdominal hysterectomy (TAH), total laparoscopic hysterectomy (TLH), abdominal supracervical hysterectomy (Abd-SCH), laparoscopic supracervical hysterectomy (LSC-SCH), total vaginal hysterectomy (TVH), and laparoscopy-assisted vaginal hysterectomy (LAVH). Laparoscopic approaches included robotic-assisted surgery. Hospital data included hospital bed capacity (small, medium, and large), teaching status (rural, urban nonteaching, and urban teaching), and hospital region (Northeast, Midwest, South, and West). Hospital bed size was defined by hospital geographic region, urban-rural designation, and teaching status per the program.[27]

Statistical considerations

To test the main hypothesis that opportunistic salpingectomy may have increased after the landmark publication of the role of distal fallopian tubes in the pathogenesis of ovarian cancer, various analytical approaches were undertaken. First, an interrupted time-series analysis, a quasi-experimental statistical method, was used to evaluate for a potential cause-and-effect relationship between the publication and an increase in opportunistic salpingectomy performance.[28] In this analysis, the study period was divided into the time period before and after 2010 in line with the Kurman and Shih publication,[11] and the temporal trend of opportunistic salpingectomy was assessed at each study time point.

Linear segmented regression with log transformation was used to assess temporal trends of the utilization of opportunistic salpingectomy by calendar year

FIGURE 2
Consolidated Standards of Reporting Trials diagram for study schema



NIS, National Inpatient Sample.

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using the National Cancer Institute's Joinpoint Regression Program.[29] The magnitude of statistical significance on each identified segment was expressed with annual percent change (APC) and 95% confidence interval (CI). The theoretical difference in the utilization of opportunistic salpingectomy was also calculated as the difference between the observed 2015 rate of opportunistic salpingectomy and the expected 2015 rate of opportunistic salpingectomy based on the estimated modeled values between 2001 and 2010.

A multivariable model was also used to establish if an independent publication effect existed. A binary logistic regression model was fitted (opportunistic salpingectomy, yes vs no), and the association between opportunistic salpingectomy use and the calendar year was adjusted for all baseline factors (patient demographics, hospital information, surgical type, gynecologic pathology) in the final model. Variance inflation factor was assessed among the covariates, and factors exhibiting multicollinearity were not entered into the model. The statistical estimate was expressed as adjusted odds ratio (aOR) and 95% CI.

A recursive partitioning analysis was then performed to construct a regression-tree model for opportunistic salpingectomy utilization patterns.[30] All baseline characteristics were entered into the analysis, and chi-square automatic interaction detector method was used to determine the nodes with a stopping rule at levels of 3. Age and calendar year were entered as continuous variables, and other variables were grouped as described previously.

Various sensitivity analyses were undertaken to test the strength of the study results. First, we examined women aged between 50 and 65 years, as these women were excluded from the primary analysis but are known to still benefit from ovarian conservation until the age of 65 years.[31,32] Second, a sensitivity analysis was performed on only those without any evidence of pelvic infection because salpingectomy is frequently performed if there is any evidence of current or prior infection or in the setting of tubo-ovarian abscess.

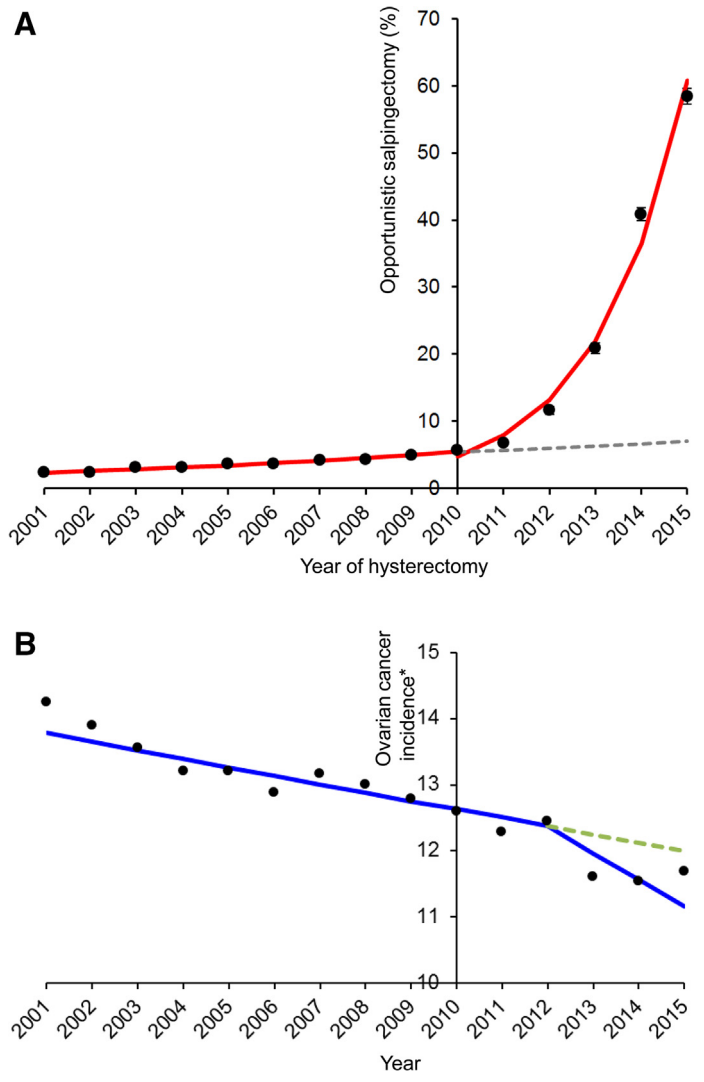
All the analyses were based on the weighted values provided by the NIS program. Two-tailed hypotheses were applied for all statistical analyses, and $P<.05$ was considered statistically significant. SPSS version 24.0 (IBM Corp, Armonk, NY) was used for all analyses. The STROBE guidelines were used in the design of this observational study.[33]

Results

Among 2,680,788 women who underwent benign hysterectomy during the study period, 1,095,298 women were younger than 50 years and had ovarian conservation without adnexal pathology (Figure 2). Among those, 98,061 (9.0%) women underwent hysterectomy with opportunistic salpingectomy, and the remaining 997,237 (91.0%) women underwent hysterectomy alone without opportunistic salpingectomy.

Temporal trends in the utilization of opportunistic salpingectomy were examined before and after the 2010 publication of the tubal hypothesis (Figure 3A). Performance of opportunistic salpingectomy gradually increased from 2.4% in 2001 to 5.7% in 2010 (2.4-fold increase; APC, 9.9; 95% CI, 8.2−11.6; $P<.001$). This was followed by a larger increase from 5.7% in 2010 to 58.4% in 2015 (10.2-fold increase; APC, 66.5; 95% CI, 51.9−82.6; $P<.001$). The projected trend in opportunistic salpingectomy based on the pre-2010 opportunistic salpingectomy trend was

FIGURE 3
Temporal trends of opportunistic salpingectomy and ovarian cancer incidence between 2001 and 2015



A, The red line shows the modeled trend of opportunistic salpingectomy from 2001 to 2015. An interrupted time-series analysis was performed to reflect the change in the performance of opportunistic salpingectomy over time, indicating a significant change in 2010, the year of the landmark publication by Kurman and Shih implicating the fallopian tubes in the pathogenesis of serous epithelial ovarian cancer.[11] The gray dashed line after 2010 represents the expected modeled trend of opportunistic salpingectomy based on the pre-2010 trend without intervention, whereas the red line after 2010 represents the modeled observed trend in opportunistic salpingectomy. Dots and bars represent the actual observed values with 95% confidence intervals. **B,** The modeled trend in ovarian cancer incidence in the United States between 2001 and 2015 is shown with the blue line. These results are adopted and modified from the SEER 13 data. The asterisk symbol represents the number of women diagnosed with ovarian cancer per 100,000 persons.[48] A temporal trend analysis was again performed for ovarian cancer incidence, indicating a significant change in 2012. The green dashed line after 2012 represents the modeled expected trend in ovarian cancer incidence, while the blue line the modeled observed trend. The y-axis is truncated to 10%—15%. Dots represent actual observed values.

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computed (dashed line in Figure 3A) to determine the effect difference of the 2010 publication. In the absence of this post-2010 increase, the expected rate of opportunistic salpingectomy in 2015 was 7.0%, which is 51.5% lower than the actual observed rate in 2015 (58.4%).

On univariable analysis, compared with women who underwent hysterectomy alone, women who underwent opportunistic salpingectomy were more likely to be older, of nonwhite race, obese, and in the lowest quartile for median household income and have a higher comorbidity index, more recent year of surgery, and Medicaid insurance (all, $P<.001$; Table 1). Hospitals at which opportunistic salpingectomy was performed were more likely to have small/medium bed capacity and urban teaching designation and be located in the Northeast region of the United States (all, $P<.001$). Women in the opportunistic salpingectomy group were more likely to have uterine myomas and/or pelvic infection but had a lower rate of adenomyosis, abnormal uterine bleeding, and uterine polyps compared with the nonopportunistic salpingectomy group (all, $P<.001$).

On multivariable analysis (Table 2), year >2010 remained an independent factor for opportunistic salpingectomy performance after controlling for patient demographics, hospital information, surgical type, and gynecologic pathology (aOR, 5.42; 95% CI, 5.34—5.51; $P<.001$). Of note, the effect size of year >2010 for performance of opportunistic salpingectomy was disproportionally larger compared with all other significant factors (aOR, 5.42 vs 1.03—1.87) (Table 2).

A regression-tree model was constructed to examine patterns in opportunistic salpingectomy during the study period (Supplemental Table 2). There were 73 patterns identified, and calendar year was the strongest discriminatory factor associated with opportunistic salpingectomy. Women who underwent TLH after 2013 in the Midwest had the highest rates of opportunistic salpingectomy among the identified patterns (opportunistic salpingectomy rate,

TABLE 1
Patient demographics

Characteristic	Hysterectomy with OS	Hysterectomy alone	*P* value
Number	98,061	997,237	
Age, y	42.1 (±4.9)	41.3 (±5.1)	<.001
<30	1625 (1.7)	25,675 (2.6)	
30–39	24,439 (24.9)	296,362 (29.7)	
40–49	71,968 (73.4)	674,231 (67.6)	
Missing	29 (<0.1)	969 (0.1)	
Year			<.001
2001–2003	3656 (3.7)	137,482 (13.8)	
2004–2006	911 (9.3)	248,538 (24.9)	
2007–2009	14,273 (14.6)	305,583 (30.6)	
2010–2012	18,356 (18.7)	218,019 (21.9)	
2013–2015	52,665 (53.7)	87,615 (8.8)	
Race/ethnicity			<.001
White	38,080 (38.3)	432,320 (43.4)	
Black	27,894 (28.4)	202,206 (20.3)	
Hispanic	15,556 (15.9)	114,114 (11.4)	
Asian or Pacific Islander	3087 (3.1)	21,307 (2.1)	
Native American	329 (0.3)	3532 (0.4)	
Other	3643 (3.7)	26,508 (2.7)	
Missing	9473 (9.7)	197,249 (19.8)	
Obesity			<.001
Nonobese	85,946 (87.6)	914,175 (91.7)	
Class I–II	8280 (8.4)	58,897 (5.9)	
Class III	3835 (3.9)	24,165 (2.4)	
Charlson Comorbidity Index			<.001
0	81,797 (83.4)	857,354 (86.0)	
1	13,039 (13.3)	117,703 (11.8)	
2	2187 (2.2)	16,290 (1.6)	
≥3	1040 (1.1)	5892 (0.6)	
Median household income			<.001
<$39,000	25,754 (26.3)	226,754 (22.7)	
$39,000–$47,999	22,440 (22.9)	235,390 (23.6)	
$48,000–$62,999	24,031 (24.5)	252,753 (25.3)	
≥$63,000	23,916 (24.4)	262,604 (26.3)	
Missing	1920 (2.0)	19,736 (2.0)	

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76.4%), followed by women who had TLH after 2013 in the Northeast and West (opportunistic salpingectomy rate, 70.3%).

Trends of opportunistic salpingectomy were examined in women aged 50–65 years. Among 163,065 women who had ovarian conservation at hysterectomy, 15,575 (9.6%) women had opportunistic salpingectomy. Performance of opportunistic salpingectomy steadily increased from 3.9% in 2003 to 5.8% in 2010 (1.5-fold increase; APC, 6.0; 95% CI, 1.7–10.6; *P*=.016). This was followed by a striking increase from 5.8% in 2010 to 55.8% in 2015 (9.8-fold increase; APC, 64.8; 95% CI, 48.6–82.9; *P*<.001) (Supplemental Figure 1). On multivariable analysis, year >2010 remained the strongest predictor for opportunistic salpingectomy use (aOR, 4.55; 95% CI, 4.37–4.74; *P*<.001).

Moreover, when the study population was restricted to those without pelvic infection (n=967,530), 78,732 (8.1%) women had opportunistic salpingectomy. Similar to the whole cohort, there was a surge in rate of opportunistic salpingectomy from 5.0% to 58.4% from 2010 to 2015 (11.6-fold increase; APC, 71.5; 95% CI, 54.1–90.8; *P*<.001) compared with the pre-2010 period (1.9%–5.0%; 2.6-fold increase; APC, 11.0; 95% CI, 8.4–13.6; *P*<.001). In this population subset limited to those without pelvic infection, on multivariable analysis, year >2010 still remained the strongest predictor for opportunistic salpingectomy use (aOR, 6.73; 95% CI, 6.61–6.84; *P*<.001).

Comments

Principal findings

Our study suggests that clinicians in the United States rapidly adopted opportunistic salpingectomy at the time of benign hysterectomy following the publication of evidence implicating the distal fallopian tubes in the pathogenesis of HGSOC in 2010. By 2015, nearly 60% of women had undergone opportunistic salpingectomy at benign hysterectomy; however, practice patterns varied by patient demographics, surgical approach, and hospital characteristics.

Results and clinical implications

Based on our results, we hypothesize that the 2010 publication of the tubal hypothesis fueled a paradigm shift that resulted in a substantial increase in the performance of opportunistic salpingectomy. In addition, after

TABLE 1
Patient demographics *(continued)*

Characteristic	Hysterectomy with OS	Hysterectomy alone	*P* value
Primary expected payer			<.001
Medicare	2606 (2.7)	22,924 (2.3)	
Medicaid	16,026 (16.3)	117,653 (11.8)	
Private including HMO	70,090 (71.5)	773,620 (77.6)	
Self-pay	4217 (4.3)	32,560 (3.3)	
No charge	1076 (1.1)	6368 (0.6)	
Other	3877 (4.0)	41,821 (4.2)	
Missing	169 (0.2)	2291 (0.2)	
Hospital bed size			<.001
Small	13,943 (14.2)	128,845 (12.9)	
Medium	28,412 (29.0)	276,709 (27.7)	
Large	55,557 (56.7)	587,200 (58.9)	
Missing	150 (0.2)	4483 (0.4)	
Hospital teaching status			<.001
Rural	7641 (7.8)	116,972 (11.7)	
Urban nonteaching	33,187 (33.8)	439,377 (44.1)	
Urban teaching	57,083 (58.2)	436,406 (43.8)	
Missing	150 (0.2)	4483 (0.4)	
Hospital region			<0.001
Northeast	21,852 (22.3)	172,173 (17.3)	
Midwest	18,370 (18.7)	207,662 (20.8)	
South	35,057 (35.8)	385,605 (38.7)	
West	22,782 (23.2)	231,797 (23.2)	
Surgical approach			<.001
TAH	45,097 (46.0)	325,343 (32.6)	
Abd-SCH	12,827 (13.1)	120,268 (12.1)	
TLH	11,639 (11.9)	37,552 (3.8)	
LSC-SCH	5704 (5.8)	66,843 (6.7)	
TVH	9920 (10.1)	288,743 (29.0)	
LAVH	11,660 (11.9)	153,018 (15.3)	
RH	987 (1.0)	3561 (0.4)	
Missing	227 (0.2)	1910 (0.2)	
Uterine myoma			<.001
No	11,239 (11.5)	164,432 (16.5)	
Yes	86,822 (88.5)	832,805 (83.5)	
Adenomyosis/endometriosis			<.001
No	77,634 (79.2)	704,644 (70.7)	
Yes	20,427 (20.8)	292,592 (29.3)	

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publication of the tubal hypothesis, several retrospective studies and meta-analyses validated the theory, providing further support for opportunistic salpingectomy (Figure 1).[13,14,34] The reason for the small gradual increase in opportunistic salpingectomy before 2010 may be related to early studies from the late 1990s and early 2000s that started to identify but did not yet confirm the role of distal fallopian tubes in HGSOC. Other factors that may have contributed to the increasing rates of salpingectomy may include improvements in minimally invasive surgical technology making the procedure technically easier to perform, a decrease in vaginal route of hysterectomy at which salpingectomy is often difficult because of visualization, and national trends of increased surgery for sterilization.[21,35,36]

Other studies have similarly reported increasing rates of opportunistic salpingectomy. A large 5-year study using the same dataset also highlighted a 371% increase in the uptake of hysterectomy with opportunistic salpingectomy between 2008 and 2013, which was highest in large teaching hospitals.[20] However, this study terminated the analysis in 2013, when the rate of opportunistic salpingectomy among those undergoing hysterectomy with ovarian conservation was only 15.8%. Since that time, the rate of opportunistic salpingectomy has increased nearly 4-fold. Trends of opportunistic salpingectomy have also dramatically increased in Canada.[37,38]

Studies that are in support of performing opportunistic salpingectomy have reported no increase in operative time, perioperative complications, requirement for transfusion, infection, or fever perioperatively and that opportunistic salpingectomy at the time of hysterectomy is potentially cost-effective for ovarian cancer prevention.[20,37,39–41] Evidence on the impact of salpingectomy on ovarian function and ovarian reserve has been conflicting, much of which stems from the literature on salpingectomy in the setting of assisted reproductive technology.[42,43] Further study is warranted to address ovarian function after

TABLE 1
Patient demographics *(continued)*

Characteristic	Hysterectomy with OS	Hysterectomy alone	*P* value
Abnormal uterine bleeding			<.001
No	46,166 (47.1)	459,903 (46.1)	
Yes	51,894 (52.9)	537,334 (53.9)	
Pelvic infection			<.001
No	78,732 (80.3)	888,798 (89.1)	
Yes	19,329 (19.7)	108,439 (10.9)	
Uterine polyp			<.001
No	95,718 (97.6)	961,517 (96.4)	
Yes	2343 (2.4)	35,720 (3.6)	

Data are expressed as mean (±SD) or n (%). Chi-square test or Student *t*-test was used for *P* values. Total number may not be 1,095,298 because of weighted values.

Abd-SCH, abdominal supracervical hysterectomy; *LAVH*, laparoscopy-assisted vaginal hysterectomy; *LSC-SCH*, laparoscopic supracervical hysterectomy; *OS*, opportunistic salpingectomy; *TAH*, total abdominal hysterectomy; *TLH*, total laparoscopic hysterectomy; *TVH*, total vaginal hysterectomy; *RH*, radical hysterectomy.

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opportunistic salpingectomy and how it may affect menopausal symptoms or age of menopause.

Both SGO and ACOG have now recommended that opportunistic salpingectomy be incorporated into routine gynecologic practice.[3,12] In fact, in a survey of ACOG members in 2017, 77% of respondents reported that they routinely performed opportunistic salpingectomy at the time of hysterectomy, which paralleled our findings.[44] Such rapid adoption of this evidence is reassuring because it represents clinical practice based on recommended guidelines. The generally held belief is that the risks of opportunistic salpingectomy are few. Slight increases in operative risk and surgical time are not considered to be major risks, and the effect, if any, on ovarian function would likely be small and outweighed by ovarian cancer risk reduction.

Although opportunistic salpingectomy is thought to be generally a positive practice change, the rapid adoption into surgical practice may have been slightly premature given the lack of prospective evidence indicating a reduction in ovarian cancer. For the sake of comparison, oral contraceptives are associated with a 40%−50% reduction in lifetime risk of ovarian cancer,[45−47] yet they are rarely prescribed for this purpose alone, albeit other adverse effects and risk profiles are associated with hormonal contraception. Gynecologists should, of course, discuss the benefits and risks of opportunistic salpingectomy with patients so that they may make an informed decision.

TABLE 2
Multivariable analysis for opportunistic salpingectomy

Characteristics	aOR (95% CI)	*P* value
Year		
2001−2010	1	
2011−2015	5.42 (5.34−5.51)	<.001
Age, y		<.001*
<30	1	
30−39	1.09 (1.03−1.15)	.003
40−49	1.22 (1.16−1.29)	<.001
Race/ethnicity		<.001*
White	1	
Black	1.04 (1.02−1.06)	<.001
Hispanic	1.11 (1.09−1.14)	<.001
Asian/Pacific islander	1.20 (1.05−1.14)	<.001
Native American	0.93 (0.82−1.05)	.231
Others	1.08 (1.04−1.12)	<.001
Missing	0.86 (0.83−0.88)	<.001
Obesity		<.001*
No	1	
Class I−II	1.04 (1.01−1.07)	.005
Class III	1.09 (1.05−1.13)	<.001

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Research implications

In a post hoc analysis, the temporal trend in ovarian cancer incidence was examined as ascertained from the Surveillance, Epidemiology, and End Results 13 data between 2001 and 2015 (Figure 3B).[48] Ovarian cancer incidence decreased over the study period from 14.3 new cases per 100,000 persons in 2001 to 11.7 in 2015. An accelerated decrease in ovarian cancer incidence was observed in 2012, such that by 2015, observed ovarian cancer incidence was 6.9% lower than expected: the projected ovarian cancer incidence based on the 2001−2012 trend model was 11.99 vs 11.16 per 100,000 for the 2012−2016 model.[48]

Given the concomitant rise in the performance of opportunistic

TABLE 2
Multivariable analysis for opportunistic salpingectomy *(continued)*

Characteristics	aOR (95% CI)	*P* value
Charlson index		<.001*
0	1	
1	0.98 (0.95–0.99)	.016
2	1.03 (0.99–1.09)	.182
≥3	1.13 (1.05–1.22)	.001
Primary expected payer		<.001*
Medicare	1	
Medicaid	1.10 (1.05–1.15)	<.001
Private including HMO	1.01 (0.97–1.06)	.609
Self-pay	1.11 (1.05–1.18)	<.001
No charge	1.38 (1.27–1.49)	<.001
Others	0.92 (0.87–0.97)	.003
Missing	0.79 (0.67–0.94)	.007
Median household income		.004*
<$39,000	1	
$39,000–$47,999	1.00 (0.98–1.02)	.742
$48,000–$62,999	0.97 (0.95–0.99)	.003
≥$63,000	1.00 (0.98–1.02)	.855
Missing	0.99 (0.94–1.05)	.805
Hospital region		<.001*
Northeast	1.13 (1.11–1.16)	<.001
Midwest	1	
South	0.87 (0.85–0.88)	<.001
West	1.06 (1.03–1.08)	<.001
Hospital bed size		<.001*
Small	1.05 (1.03–1.08)	<.001
Medium	1.03 (1.01–1.04)	.001
Large	1	
Hospital teaching status		<.001*
Rural	1	
Urban nonteaching	1.05 (1.02–1.08)	<.001
Urban teaching	1.47 (1.43–1.51)	<.001

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salpingectomy, it is plausible that increases in opportunistic salpingectomy use have possibly contributed at least in part to the accelerated decrease in ovarian cancer incidence. Women in the age group of 50–65 years who underwent opportunistic salpingectomy closer to the average age of ovarian cancer diagnosis may be driving this initial decrease.[48] However, recent evolutionary data estimate that the time to progress from STIC to ovarian cancer is 6–7 years; thus, a lead time of 2 years is likely too short to see a resulting decrease in ovarian cancer incidence.[18] Other factors such as risk-reducing salpingo-oophorectomy for women with hereditary familial ovarian cancer syndromes or use of oral contraceptives also likely contributed largely to the decrease in ovarian cancer incidence.

As stated above, prospective data are needed to fully understand if opportunistic salpingectomy may have a prophylactic effect on ovarian cancer development. Unfortunately, a prospective randomized trial would now be difficult to conduct in the United States given that opportunistic salpingectomy has already been largely adopted into routine practice. However, the Hysterectomy and Opportunistic Salpingectomy (HOPPSA) trial, a randomized controlled trial in Sweden where no national guidelines have been issued yet, is now underway and will help elucidate both short- and long-term outcomes.[49] Outcomes planned for their analysis include complication rates, incidence of and time to ovarian cancer, menopausal symptoms, and change in antimüllerian hormone levels. In addition, 2 phase II studies in *BRCA* carriers, the Tubectomy in BRCA mutation carriers (TUBA) and Women Choosing Surgical Prevention (WISP) trials, are investigating the impact of stepwise early risk-reducing salpingectomy followed by delayed oophorectomy between the ages of 35–40 years for *BRCA1* and 40–45 years for *BRCA2*, which has great implication for the treatment of high-risk women with regard to premature menopause and cancer risk reduction.[50,51]

Strengths and limitations

The large sample size of this population-based analysis is a major strength of this study. The quasi-experimental study design and multiple approaches to the analysis improved statistical rigor. Various sensitivity analyses also enhanced the strength of the study findings, particularly for women older than 50 years. There are, however, several limitations to a study of this nature. The first most profound limitation is that this study is solely driven by hypothesis, and we are unable to prove causality. The true reasons for the striking rise in opportunistic salpingectomy and the decrease in ovarian cancer incidence can never be

TABLE 2
Multivariable analysis for opportunistic salpingectomy *(continued)*

Characteristics	aOR (95% CI)	*P* value
Surgical approach		<.001*
TAH	1	
Abd-SCH	0.84 (0.82–0.86)	<.001
TLH	1.58 (1.54–1.62)	<.001
LSC-SCH	0.79 (0.76–0.81)	<.001
TVH	0.51 (0.50–0.52)	<.001
LAVH	0.86 (0.84–0.88)	<.001
RH	1.62 (1.50–1.74)	<.001
Missing	1.12 (0.97–1.29)	.132
Uterine myoma		
No	1	
Yes	0.92 (0.89–0.94)	<.001
Adenomyosis/endometriosis		
No	1	
Yes	0.87 (0.85–0.89)	<.001
Abnormal uterine bleeding		
No	1	
Yes	0.94 (0.93–0.95)	<.001
Pelvic infection		
No	1	
Yes	1.87 (1.84–1.91)	<.001
Uterine polyp		
No	1	
Yes	0.86 (0.82–0.90)	<.001

A binary logistic regression model was used for analysis. All listed variables were entered in the final model. **P* value for interaction.

Abd-SCH, abdominal supracervical hysterectomy; *aOR*, adjusted odds ratio; *CI*, confidence interval; *HMO*, health maintenance organization; *LAVH*, laparoscopy-assisted vaginal hysterectomy; *LSC-SCH*, laparoscopic supracervical hysterectomy; *RH*, radical hysterectomy; *TAH*, total abdominal hysterectomy; *TLH*, total laparoscopic hysterectomy; *TVH*, total vaginal hysterectomy.

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fully known. There is also the potential for unmeasured bias owing to variables missing from the NIS program, including those involved in the surgical decision-making process to perform opportunistic salpingectomy, long-term follow-up data, and prior surgical history of tubal ligation, salpingectomy, or adnexal surgery. This database also only includes inpatient hysterectomies; thus, any procedures performed as an outpatient or in an ambulatory surgery center are not captured and may lead to selection bias. Utilization of opportunistic salpingectomy was also ascertained by ICD-9 coding, and although the ICD-9 codes were unchanged throughout the study period, they are subject to human error and misclassification. Furthermore, this study was conducted in the United States alone, and thus, generalizability to opportunistic salpingectomy trends in different countries or populations may not be possible.

Conclusion

Publication of the tubal hypothesis for the pathogenesis of HGSOC led to a rapid adoption of opportunistic salpingectomy in the United States, such that by 2015, nearly 60% of women had undergone opportunistic salpingectomy at the time of benign hysterectomy. Although this study team speculates that this increase in opportunistic salpingectomy may be in part contributing to an accelerated decrease in ovarian cancer incidence, it also reflects a dramatic practice paradigm shift in the absence of prospective evidence. Prospective data are needed to confirm a prophylactic effect of opportunistic salpingectomy on ovarian cancer. ■

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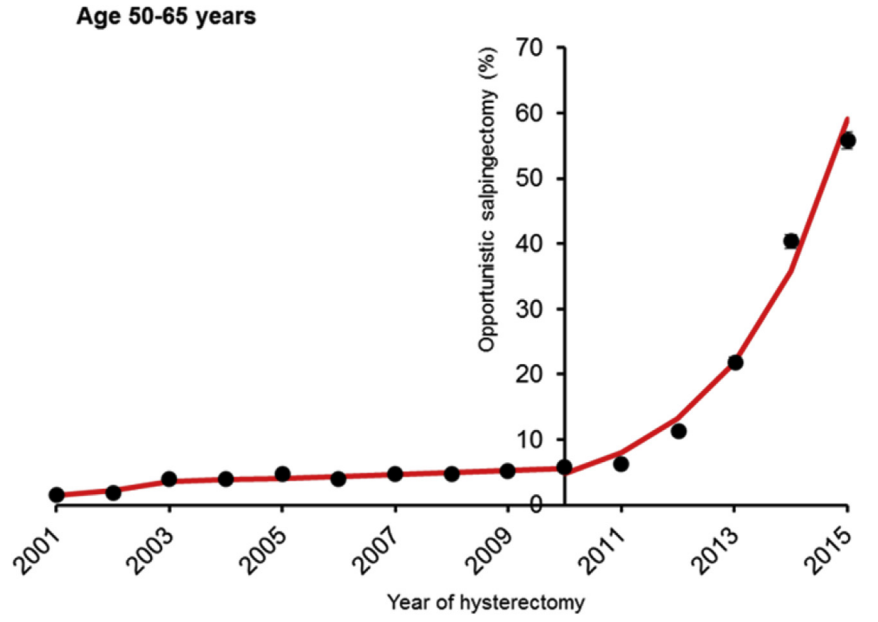
SUPPLEMENTAL FIGURE 1
Results of the sensitivity analysis



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SUPPLEMENTAL TABLE 1
ICD-9 Diagnosis and Procedure Codes

ICD-9 Procedure Codes	
Hysterectomy	
Total Abdominal Hysterectomy	6849
Abdominal Supracervical Hysterectomy	6839
Total Laparoscopic Hysterectomy	6841
Laparoscopic Supracervical Hysterectomy	6831
Total Vaginal Hysterectomy	6859
Laparoscopic-Assisted Vaginal Hysterectomy	6851
Radical Hysterectomy	6861, 6869, 6871, 6879
Salpingectomy	664, 665, 666
Oophorectomy or Salpingo-oophorectomy	653, 654, 655, 656
ICD-9 Diagnosis Codes	
Benign Indications for Hysterectomy	
Leiomyoma	218, 219
Uterine Polyp	6210
Endometriosis/Adenomyosis	617
Abnormal uterine bleeding	626, 6270
Adnexal pathology	
Endometriosis	617
Benign ovarian or tubal mass	620, 220, 221
Malignancy	V1043, 1830, 1986, 2362
Ectopic pregnancy	633
Pelvic Inflammatory Disease or Pelvic Infection	614,615
Obesity	27800, 27801
Charlson Comorbidity Index	
CC1: Myocardial Infarction	410, 411, 412
CC2: Congestive Heart Failure	39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493, 4254, 4255, 4357, 4258, 4259, 428
CC3: Peripheral Vascular Disease	0930, 4373, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 451, 452, 453, 454, 455, 456
CC4: Cerebrovascular Disease	3623, 430, 431, 432, 433, 434, 435, 436, 437, 438
CC5: Dementia	290, 294, 331
CC6: Chronic Pulmonary Disease	415, 416, 490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 506, 507, 508, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519
CC7: Connective Tissue Disease	710, 711, 712, 713, 714, 715, 716
CC8: Peptic Ulcer Disease	531, 532, 533, 534, 535
CC9: Mild Liver Disease	0701, 0703, 0705, 07070, 0709, 5710, 5713, 5714, 5716, 5718, 5719, 5731, 5732, 5733, 5738, 5739
CC10: Diabetes without complications	2490, 2500

(continued)

SUPPLEMENTAL TABLE 1
ICD-9 Diagnosis and Procedure Codes *(continued)*

CC11: Diabetes with complications	2491, 2492, 2493, 2494, 2495, 2496, 2497, 2498, 2499, 2501, 2502, 2503, 2504, 2505, 2506, 2507, 2508, 2509
CC12: Paraplegia and hemiplegia	3341, 342, 343, 344
CC13: Renal disease	403, 404, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593
CC14: Cancer	140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 170, 171, 172, 173, 174, 175, 176, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209
CC15: Moderate or Severe Liver Disease	4560, 4561, 4562, 570, 5711, 5712, 5715, 572, 5730, 5734, 5735, V427, 99682
CC16: Metastatic Carcinoma	196, 197, 198, 199
CC17: HIV/AIDS	042, 07953, 79571, V08

SUPPLEMENTAL TABLE 2

Results of regression-tree model for opportunistic salpingectomy patterns

Node	Year	Hyst	Region	Teaching	Obesity	Income	PID	Payer	Age	Number	%	OS rate, %
103	>2013	TLH	MW							1565	0.1%	76.4%
101	>2013	TLH	NE, W							3925	0.4%	70.3%
96	>2013	RH			C3, nonobese					860	0.1%	64.0%
102	>2013	TLH	S							2790	0.3%	59.7%
93	>2013	LSC-SCH, LAVH	W							2660	0.2%	57.3%
94	>2013	LSC-SCH, LAVH	NE, MW							3105	0.3%	52.7%
100	>2013	TAH, Abd-SCH		Teaching						39,710	3.6%	51.5%
95	>2013	LSC-SCH, LAVH	S							2635	0.2%	43.3%
99	>2013	TAH, Abd-SCH		Urban nonteaching						17,000	1.5%	41.3%
92	>2013	TVH				4QT				1090	0.1%	34.4%
98	>2013	TAH, Abd-SCH		Rural						5525	0.5%	33.8%
87	2011–2013	TLH	NE, W							7065	0.6%	31.0%
86	2011–2013	LSC-SCH, RH					Yes			1200	0.1%	30.8%
74	2010–2011						Yes	Self		409	0.0%	26.7%
82	2011–2013	LAVH					Yes			1315	0.1%	25.9%
56	2006–2008						Yes	No charge		171	0.0%	25.7%
91	>2013	TVH				3QT				1465	0.1%	25.3%
89	2011–2013	TLH	MW							3040	0.3%	22.5%
90	>2013	TVH				1–2QT				3350	0.3%	21.6%
85	2011–2013	LSC-SCH, RH					No			8265	0.8%	21.1%
88	2011–2013	TLH	S							4895	0.4%	18.8%
73	2010–2011						Yes	Medicare, other		802	0.1%	18.5%
84	2011–2013	TAH, Abd-SCH					Yes			11,040	1.0%	18.3%
81	2011–2013	LAVH					No			11,705	1.1%	16.7%
63	2008–2010	TLH, TVH					Yes			2303	0.2%	15.5%
40	2000–2004	LSC-SCH					Yes			832	0.1%	14.7%
55	2006–2008						Yes	Other		1269	0.1%	14.5%
71	2010–2011						Yes	Private		7813	0.7%	14.1%
83	2011–2013	TAH, Abd-SCH					No			60,370	5.5%	13.3%

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(continued)

SUPPLEMENTAL TABLE 2

Results of regression-tree model for opportunistic salpingectomy patterns *(continued)*

Node	Year	Hyst	Region	Teaching	Obesity	Income	PID	Payer	Age	Number	%	OS rate, %
65	2008–2010	LSC-SCH					Yes			1967	0.2%	13.1%
34	≤2002		NE, MW				Yes			1756	0.2%	13.0%
70	2010–2011	RH					No			552	0.1%	12.1%
46	2004–2006		NW, MW				Yes			9061	0.8%	11.9%
38	200–2004	TVH					Yes			2256	0.2%	11.8%
54	2006–2008						Yes	Medicare, Medicaid		4067	0.4%	11.3%
72	2010–2011						Yes	Medicaid, no charge		1553	0.1%	10.5%
97	>2013	RH			C1–2					**	0.0%	**
47	2004–2006		S				Yes			8467	0.8%	10.0%
64	2008–2010	TAH, Abd-SCH					Yes			20,237	1.8%	9.9%
79	2011–2013	TVH							43–46	2495	0.2%	9.4%
53	2006–2008						Yes	Private, self		23,180	2.1%	9.2%
52	2006–2008	RH					No			824	0.1%	9.0%
62	2008–2010	TLH, RH					No			10858	1.0%	8.2%
69	2010–2011	TLH					No			6674	0.6%	8.1%
76	2011–2013	TVH							34–39	2390	0.2%	7.9%
39	200–2004	Abd-SCH, LAVH					Yes			6163	0.6%	7.9%
80	2011–2013	TVH							>46	2745	0.2%	7.5%
33	≤2002		S, W				Yes			4152	0.4%	7.1%
77	2011–2013	TVH							39–42	2695	0.2%	5.9%
51	2006–2008	TLH					No			5395	0.5%	5.9%
45	2004–2006		W				Yes			4970	0.5%	5.7%
67	2010–2011	TAH, LSC-SCH, LAVH					No			46,384	4.2%	5.7%
59	2008–2010	LAVH					No			20,689	1.9%	5.1%
68	2010–2011	Abd-SCH					No			7095	0.6%	4.7%
61	2008–2010	TAH					No			74,672	6.8%	4.6%
60	2008–2010	Abd-SCH, LSC-SCH					No			29,756	2.7%	4.0%
44	2004–2006	TAH, TLH, RH					No			26,056	2.4%	3.8%
50	2006–2008	Abd-SCH					No			19,466	1.8%	3.8%

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SUPPLEMENTAL TABLE 2
Results of regression-tree model for opportunistic salpingectomy patterns *(continued)*

Node	Year	Hyst	Region	Teaching	Obesity	Income	PID	Payer	Age	Number	%	OS rate, %
75	2011–2013	TVH							≤34	1205	0.1%	3.7%
43	2004–2006	Abd-SCH					No			30,264	2.7%	3.5%
49	2006–2008	TAH, LAVH					No			117,083	10.6%	3.4%
37	200–2004						No		>46	14,246	1.3%	3.4%
66	2010–2011	TVH					No			10,579	1.0%	3.4%
36	200–2004						No		44–46	11,352	1.0%	2.9%
58	2008–2010	TVH					No			27,092	2.5%	2.9%
48	2006–2008	LSC-SCH, TVH					No			52,011	4.7%	2.9%
42	2004–2006	LSC-SCH, LAVH					No			48,673	4.4%	2.9%
35	200–2004						No		≤44	71,797	6.5%	2.3%
41	2004–2006	TVH					No			72,891	6.6%	2.2%
31	≤2002			Rural, teaching			No			47,440	4.3%	2.2%
78	2011–2013	TVH							42–43	860	0.1%	1.7%
32	≤2002			Urban nonteaching			No			41,209	3.7%	1.5%
57	2006–2008						Yes	unk		**	0.0%	**

Abd-SCH, abdominal supracervical hysterectomy; *C*, class; *C3*, class III, *Hyst*, hysterectomy; *LAVH*, laparoscopy-assisted vaginal hysterectomy; *LSC-SCH*, laparoscopic supracervical hysterectomy; *MW*, Midwest; *NE*, Northeast; *OS*, opportunistic salpingectomy; *PID*, pelvic inflammatory disease; *TAH*, total abdominal hysterectomy; *TLH*, total laparoscopic hysterectomy; *TVH*, total vaginal hysterectomy; *QT*, quartile; *RH*, radical hysterectomy; *S*, South; *unk*, unknown; *W*, West.

** Numbers suppressed per Healthcare Cost and Utilization Project instruction.

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