OBSTETRICS

Cost-effectiveness of opportunistic salpingectomy vs tubal ligation at the time of cesarean delivery

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BACKGROUND: Removal of the fallopian tubes at the time of hysterectomy or interval sterilization has become routine practice to prevent ovarian cancer. While emerging as a strategy, uptake of this procedure at the time of cesarean delivery for pregnant women seeking permanent sterilization has not been widely adopted due to perceptions of increased morbidity and operative difficulty with a lack of available data in this setting.

OBJECTIVE: We sought to conduct a cost-effectiveness analysis comparing strategies for long-term sterilization and ovarian cancer risk reduction at the time of cesarean delivery, including bilateral tubal ligation, opportunistic salpingectomy, and long-acting reversible contraception.

STUDY DESIGN: A decision-analytic and cost-effectiveness model was constructed for pregnant women undergoing cesarean delivery who desired permanent sterilization in the US population, comparing 3 strategies: (1) bilateral tubal ligation, (2) bilateral opportunistic salpingectomy, and (3) postpartum long-acting reversible contraception. This theoretic cohort consisted of 110,000 pregnant women desiring permanent sterilization at the time of cesarean delivery and ovarian cancer prevention at an average of 35 years who were monitored for an additional 40 years based on an average US female life expectancy of 75 years. The primary outcome measure was the incremental cost-effectiveness ratio. Effectiveness was measured as quality-adjusted life years. Secondary outcomes included: the number of ovarian cancer cases and deaths, procedure-related complications, and unintended and ectopic pregnancies. The 1-, 2-, and 3-way and Monte Carlo probabilistic sensitivity analyses were performed. The willingness-to-pay threshold was set at $100,000.

RESULTS: Both bilateral tubal ligation and bilateral opportunistic salpingectomy with cesarean delivery have favorable cost-effectiveness ratios. In the base case analysis, salpingectomy was more cost-effective with an incremental cost-effectiveness ratio of $23,189 per quality-adjusted life year compared to tubal ligation. Long-acting reversible contraception after cesarean was not cost-effective (ie, dominated). Although salpingectomy and tubal ligation were both cost-effective over a wide range of cost and risk estimates, the incremental cost-effectiveness ratio analysis was highly sensitive to the uncertainty around the estimates of salpingectomy cancer risk reduction, risk of perioperative complications, and cost. Monte Carlo probabilistic sensitivity analysis estimated that tubal ligation had a 49% chance of being the preferred strategy over salpingectomy. If the true salpingectomy risk of perioperative complications is >2% higher than tubal ligation or if the cancer risk reduction of salpingectomy is <52%, then tubal ligation is the preferred, more cost-effective strategy.

CONCLUSION: Bilateral tubal ligation and bilateral opportunistic salpingectomy with cesarean delivery are both cost-effective strategies for permanent sterilization and ovarian cancer risk reduction. Although salpingectomy and tubal ligation are both reasonable strategies for cesarean patients seeking permanent sterilization and cancer risk reduction, threshold analyses indicate that the risks and benefits of salpingectomy with cesarean delivery need to be better defined before a preferred strategy can be determined.

Key words: cesarean delivery, cost-effectiveness, ovarian cancer, pregnancy, salpingectomy, sterilization, tubal ligation

Introduction

Close to 1 in 10 births in the United States is followed by bilateral tubal ligation (hereafter referred to as tubal ligation) for permanent sterilization, resulting in 340,000 tubal ligations per year.[1] Nearly a third of pregnant US women have a cesarean delivery.[2] Annually, >100,000 US women undergo permanent sterilization by tubal ligation with cesarean delivery. Opportunistic salpingectomy (hereafter, referred to as salpingectomy) with interval sterilization and hysterectomy is becoming a more common procedure due to emerging evidence as an ovarian cancer prevention strategy.[3–5] However, the risk-benefit tradeoff of salpingectomy with cesarean delivery is not well-characterized, and data on the safety and feasibility in this setting are limited.[6–9] Nonetheless, many obstetrician/gynecologists have adopted salpingectomy with cesarean delivery.[10]

Removal of the fallopian tubes may decrease the risk of ovarian cancer by as much as 70%, which is more than the risk reduction attributed to tubal ligation (26–34%).[11–14] Salpingectomy appears to be safe[15,16] and cost-effective[12,17] with hysterectomy or interval sterilization.[4,5] In a recent randomized controlled trial (RCT) of 80 women allocated to salpingectomy vs tubal ligation with cesarean delivery, only 67% of women had a successful salpingectomy compared to 95% of tubal ligations,[18] and using the RCT data, the investigators found salpingectomy to be cost-effective compared to tubal ligation (preliminary Society for Maternal-Fetal Medicine abstract data), but surgical complications were not modeled given the small sample size.[19] Another recent RCT conducted among 44 women undergoing salpingectomy vs tubal ligation with cesarean reported a high completion rate for salpingectomy (95%).[20] Before

Cite this article as: Venkatesh KK, Clark LH, Stamilio DM. Cost-effectiveness of opportunistic salpingectomy vs tubal ligation at the time of cesarean delivery. Am J Obstet Gynecol 2019;220:106.e1-10.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2018.08.032

Related editorials, pages 8 and 10.

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population-based data are available,[21] a decision-analytic model can estimate the risk-benefit tradeoffs, and identify influential factors to help select a preferred surgical strategy in the short term and to guide future research in the long term.

We conducted a cost-effectiveness analysis of salpingectomy vs tubal ligation for sterilization and ovarian cancer prevention among pregnant women in the United States desiring permanent sterilization with cesarean delivery.

Materials and Methods

We developed a decision-analytic model to compare salpingectomy vs tubal ligation among US pregnant women who undergo cesarean delivery and desire permanent sterilization and ovarian cancer risk reduction. A third strategy of no surgical sterilization intervention, but with postpartum placement of long-acting reversible contraception (LARC), was incorporated to represent a baseline reference strategy among women who desire long-term contraception without surgical sterilization. LARC was defined as a composite of the 3 most commonly used devices in the United States, namely copper intrauterine device (IUD), progestin implant, and progestin-containing IUD. This analysis was performed from the societal perspective, using relevant estimates for cost and clinical outcomes to estimate which strategy was the most cost-effective.[22] This study was exempt from research ethics board review.

We estimated that 110,000 pregnant women with mean age of 35 years would desire permanent sterilization following cesarean delivery in the United States per year.[1,2] We assumed the average maternal age for the cohort to be 35 years, given female sterilization was the most common contraception method in this age group.[15,23] The theoretic cohort size was based on the following: approximately 643,000 female sterilizations were performed annually, or 9% of all births in the United States, of which 340,000 (53%) were performed within 48 hours postpartum.[1,24,25] Given 32% of deliveries were by cesarean, we estimated that 108,800 women underwent sterilization with cesarean delivery.

The effectiveness of each strategy was assessed in terms of average years of life expectancy gained, measured as quality-adjusted life years (QALYs), and average lifetime relevant health costs incurred. Given the paucity of data available on salpingectomy with cesarean delivery, data on the risks and benefits were largely derived from salpingectomy with hysterectomy and permanent sterilization with a wide range of uncertainty for sensitivity analyses. To identify the best probability estimates, we performed a systematic review on PubMed, supplemented by bibliographic review, using the following search terms: "tubal ligation," "salpingectomy," and "permanent sterilization." We used the most rigorous available research for base case probability estimates in a hierarchical order: meta-analysis, RCT, cohort study, and case-control study. Case series and small studies ($N < 100$) were used to help inform sensitivity analysis ranges. Estimates of utilities were derived from published and validated valuations of health states. Costs were derived from published values or estimates from Medicaid reimbursement (ie, not charges).

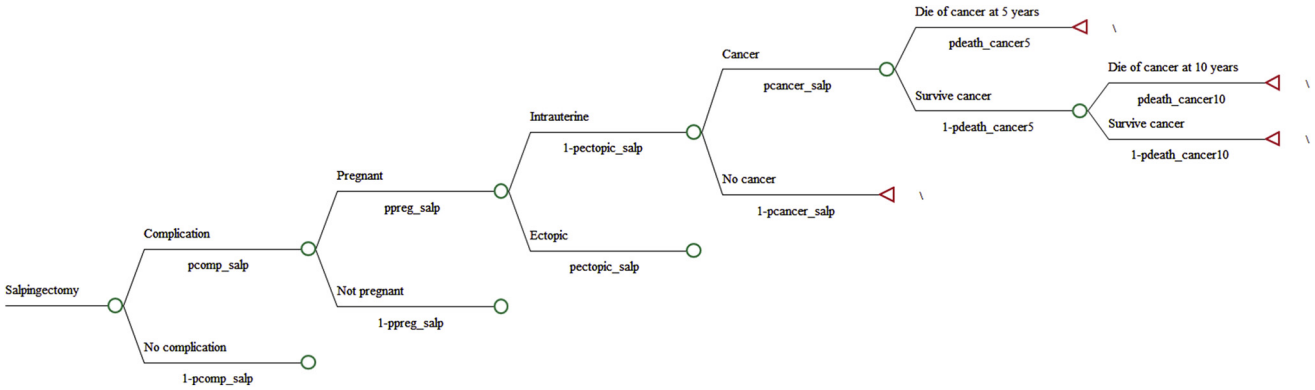
We performed a cost-utility analysis and reported cost-effectiveness ratios and incremental cost-effectiveness (ICE) ratios (ICER). Our primary outcome was the ICER, which was the differential cost of 1 additional QALY gained moving from one strategy to another. A strategy was "absolutely dominated" and rejected if it was costlier and less effective than another strategy. A strategy was cost-effective if it had an ICER of $<$\$100,000 per year of life gained relative to an alternative strategy (ie, willingness-to-pay [WTP] threshold).[26] We calculated total costs and QALYs to determine ICERs for each strategy. QALYs were calculated using utilities, which were predefined, validated values attributed to a year of life in a certain health state. Secondary outcomes included number of ovarian cancer cases, unintended pregnancies, ectopic pregnancies, and surgical complications for each strategy. We assumed that pregnant women were comparable across strategies with respect to other risk factors for ovarian cancer, such as obstetrical history, family history, body mass index, and oral contraceptive use history.

For the decision model, each patient in the theoretic cohort could follow 1 of 3 strategies: (1) cesarean with tubal ligation, (2) cesarean with salpingectomy, or (3) cesarean followed by LARC (Figure 1). For each strategy there was a procedure-specific complication risk, a risk of unintended pregnancy, including ectopic vs intrauterine, and a residual risk for ovarian cancer based on the procedure's estimated risk reduction from baseline cancer risk. Women diagnosed with ovarian cancer had a risk of cancer-related death at 5 and 10 years; those who survived for $\geq$10 years were assumed to have a low likelihood of recurrent disease, at which point they were subject to age-dependent mortality risks.[27] The average age of ovarian cancer diagnosis was 60 years.[28] Women who died of ovarian cancer had shorter life expectancies than average based on the modeled 5- and 10-year cancer survival rates and average age of cancer diagnosis. The average maternal age for sterilization at the time of cesarean delivery was 35 years as explained above, and these women were modeled to survive for an additional 40 years based on an average US female life expectancy of 75 years[29] or until death from cancer (eg, age 65 or 70 years).

With regard to baseline probabilities, ovarian cancer rates were calculated based on US surveillance lifetime population risk of 1.28%[30] (Table 1). In a separate high-risk model for sensitivity analyses, this baseline probability was also varied using estimates well above the population risk to reflect potential high-risk groups for which salpingectomy might represent an even more important strategy (eg, BRCA1/2 or Lynch syndrome). In these subgroup analyses, the baseline probability of ovarian cancer rate was estimated as 44% for BRCA1, 17% for BRCA2, and 8% for Lynch syndrome.[31,32]

Based on observational studies in which ovarian cancer cases were primarily high-grade serous carcinomas of

FIGURE 1
Abbreviated decision tree of pregnancy and cancer prevention strategies postcesarean



Decision tree branches for tubal ligation and LARC with cesarean delivery are structured same as decision tree above.

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tubal origin, we estimated that salpingectomy would decrease the risk of ovarian cancer by 64% (relative risk [RR], 0.36; 95% confidence interval [CI], 0.13−1.02) resulting in 0.46% residual absolute risk; and tubal ligation would decrease the risk of ovarian cancer by 34% (RR, 0.66; 95% CI, 0.60−0.73) resulting in 0.84% residual risk.[13,14,33] The risk of ovarian cancer with LARC was estimated to be a 25% reduction from baseline to 0.96%,[34,35] and in sensitivity analysis was modeled to be as much as 75% greater than baseline (maximum absolute risk 2.24%) based on older data before the use of hormone-releasing IUDs.[36] In the high-risk model subgroups, interventions would result in a 15.8% residual cancer risk for BRCA1 with salpingectomy vs 29.0% with tubal ligation; 6.1% vs 11.2% in BRCA2; and 2.9% vs 5.3% in Lynch syndrome. These estimates assume a similar procedure-related risk reduction within high-risk groups, which may not be a valid assumption.

The baseline perioperative complication risk for a cesarean delivery, such as bowel or bladder injury, blood transfusion, reoperation, wound complication, and endometritis, was estimated at 6.9%.[37−41] The limited observational data suggested that salpingectomy with cesarean appeared not to be associated with an increase in perioperative complications compared to tubal ligation;[6−8,18,20,42] however, these studies were restricted by small sample size (salpingectomy N = 16, 19, 23, 40, 99, and 206, respectively) and were not adequately powered to assess differences in the rate of complications. Applying data from general and gynecologic surgery that showed a linear direct relationship between increased operative time and the risk of perioperative complications[43−45] and data that demonstrated that salpingectomy required 10 more minutes than tubal ligation with cesarean and that tubal ligation required 10 more minutes than cesarean alone,[7,46] the perioperative complication rate (which included the background complication rate for cesarean) for salpingectomy was 8.3% and for tubal ligation was 7.6%.[6−9,47] We assumed that salpingectomy and tubal ligation could be performed in 100% of surgeries. However, it is unclear whether this is the case for salpingectomy with cesarean based on 2 recent small clinical trials with completion rates ranging from 67−95%.[18,20] The complication rate with postpartum LARC (eg, uterine perforation) was estimated as an additional 0.01% above the complication rate of a cesarean delivery.[48] The probability of an unintended pregnancy was 0.38% for salpingectomy (likely a conservatively high estimate), 0.45% for tubal ligation, and 1% for LARC based on excisional tubal ligation procedures,[49] and postpartum LARC.[50−52] Procedure-specific estimates for the likelihood of ectopic pregnancy among those with an unintended pregnancy were 10% for salpingectomy,[53] 20% for tubal ligation,[53] and 53% for postpartum LARC.[50−52] Once ovarian cancer was diagnosed, the risk of death from ovarian cancer was estimated to be 56% at 5 years and an additional 8% (64% total) at 10 years based on US national surveillance data.[28,30]

Baseline costs for hospital and physician fees were calculated using publicly available government payer data for each procedure *Current Procedural Terminology* code.[54,55] Ovarian cancer costs incorporated costs of initial diagnosis (initial year), yearly treatment (intervening years), and the final year of life (terminal year).[56] The cost of perioperative complications was derived from the cost of major and minor complications following general surgery procedures.[57,58] The cost of unintended and ectopic pregnancies was derived from observational data.[54,55,59−62] All costs were adjusted for 2017 US dollars using the Consumer Price Index.[63]

With regard to utilities, a year of life in perfect health was assigned a utility of 1, death a utility of 0, and other intermediate health states a value between 0 to 1 for up to 1 year of a woman's life based on

TABLE 1
Selected data for base case

Probabilities and costs	Probability[a]	Utility	Range for sensitivity analysis[b]	Source
Baseline probabilities				
Surgical complication[c]				
Cesarean delivery	0.069		0.03–0.28	37–41
After tubal ligation	0.076		0.03–0.28	6–9,47
After salpingectomy	0.083		0.03–0.28	6–9,47
After LARC	0.070		0.03–0.28	48
Unintended pregnancy				
After tubal ligation	0.0045		0.0006–0.0084	49
After salpingectomy	0.0038		0.00–0.0114	49
After LARC	0.01		0.002–0.042	50–52
Ectopic pregnancy among women with unintended pregnancy				
After tubal ligation	0.20		0.16–0.65	53
After salpingectomy	0.10		0.01–0.20	53
After LARC	0.53		0.49–0.57	50–52
Ovarian cancer risk				
Baseline	0.0128		0.0126–0.0130	30
After tubal ligation	0.0084		0.0077–0.0093	14,33
After salpingectomy	0.0046		0.001–0.010	33
After LARC[d]	0.0096		0.0095–0.0224	30,34–36
Death from ovarian cancer[e]				
At 5 y from diagnosis	0.56		0.55–0.56	28,30
At 10 y from diagnosis	0.64		0.63–0.65	
Cost and utility estimates[f]	Cost	Utility	Utility/cost, ranges	
Procedure[g]				
Cesarean delivery (*CPT* 59510)	$8551	0.95	0.93–0.99/$4275–12,826	54,55,62,69
Tubal ligation (*CPT* 58611)	$8629	0.95	0.93–0.99/$4314–12,944	54,55
Salpingectomy (*CPT* 58700)	$9348	0.95	0.93–0.99/$4674–14,022	54,55
LARC (*CPT* 58300 + 99214)	$9435	0.95	0.93–0.99/$4717–14,152	55,70
Surgical complication[h]	$20,891	0.77	0.38–0.99/$13,927–38,998	57,58,62
Unintended pregnancy	$13,143	0.74	0.48–0.99/$6571–19,715	59–61
Ectopic pregnancy (*CPT* 59150)	$8708	0.87	0.77–0.92/$4354–13,062	54,55,62
Ovarian cancer (5-y survival)				
Initial y	$68,655	0.62	0.24–0.94/$65,749–71,564	56,64
Years 2–4	$5183	0.72	0.32–0.99/$4709–5657	
Terminal y	$66,798	0.16	0.01–0.99/$64,469–69,126	

CPT, *Current Procedural Terminology* code; *LARC*, long-acting reversible contraception; *LNG-IUS*, levonorgestrel-releasing intrauterine system.

[a] All costs converted to 2017 dollars using Consumer Price Index inflation calculator; [b] All sensitivity analyses ranges were obtained from original cited source, unless stated otherwise; [c] Ovarian cancer risk with LARC was estimated to be 25% reduction from baseline based on recent data, and in sensitivity analysis was estimated to be 75% greater than baseline based on earlier historical data; [d] Surgical complication sensitivity ranges vary from minor to major complication across general surgery procedures; [e] In 1- and 2-way sensitivity analyses, wider range was also tested >95% confidence interval from original cited source; [f] Procedure, unintended pregnancy, and ectopic pregnancy cost sensitivity ranges vary from 50% below and 50% greater than point estimate; [g] Cost derivations: LARC device cost estimated as combined average cost for copper intrauterine device ($650), implant ($717), and LNG-IUS 20 μg/24 h ($765), at $710—for other cost inputs as follows: cesarean delivery: $2401 (physician fee) + $6150 (hospital fee) = $8551, tubal ligation: $8551 + $78.60 (physician fee) = $8,629.60, salpingectomy: $8551 + $797.45 (physician fee) = $9348.45, LARC: $8551 + $710 (LARC device) + $104 (insertion fee) + $70 (follow-up intrauterine device check) = $9435, ectopic pregnancy: $796 (physician fee) + 7912 (hospital fee) = $8708; [h] Utility for surgical complications sensitivity ranges vary from 50% below and 50% greater than point estimate.

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TABLE 2
Clinical outcomes in study population of pregnant women seeking permanent sterilization at time of cesarean delivery

Strategy	No. of ovarian cancer cases	No. of ovarian cancer deaths over 10 y	No. of surgery complications	No. of intrauterine pregnancies	No. of ectopic pregnancies
Cesarean delivery with salpingectomy	507	302	9130	376	42
Cesarean delivery with tubal ligation	929	554	8360	396	99
Cesarean delivery with LARC	1051	625	7700	517	583

Assuming study population of 110,000 pregnant women desiring permanent sterilization at time of cesarean delivery.

LARC, long-acting reversible contraception.

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health state valuation research.[60–62] The utilities of a perioperative complication and an ectopic pregnancy were modeled as disutilities for a duration of 1 year because they occurred concurrently with their respective baseline health states, cesarean or unintended pregnancy state, respectively. The utility of a diagnosis of ovarian cancer was estimated to be 0.62 for the initial year, 0.72 for each intervening year, and 0.16 for the terminal year.[64] Each patient gained a health state-specific utility for each year of life for a given life expectancy specific to a cancer or noncancer health state (eg, age 65, 70, or 75 years). All costs and utilities were discounted at a rate of 3% per year.[22]

We performed 1-, 2-, and 3-way sensitivity analyses, as well as Monte Carlo probabilistic sensitivity analysis to assess the robustness of the decision model and cost-effectiveness results (Table 1). Ranges of uncertainty around probability and utility point estimates were based on published 95% CI when available from a single study or meta-analysis or by a range found in the literature. The underlying distribution (ie, normal, triangular, beta, or uniform) for the range of uncertainty for each variable was selected based on the data source, the observed distribution, and data type (probability, cost, or utility). All computations were performed using commercially available decision-analysis software (Tree-Age Pro 2017; Tree Age Inc, Williamstown, MA).

Results

Among a theoretic cohort of 110,000 pregnant women desiring permanent sterilization at the time of cesarean delivery and ovarian cancer prevention, the base case analysis indicates that compared to the LARC strategy, performing tubal ligation would result in 122 fewer ovarian cancer diagnoses, 71 fewer ovarian cancer deaths over 10 years, 121 fewer unintended intrauterine pregnancies, and 484 fewer ectopic pregnancies. Compared to the tubal ligation strategy, the salpingectomy strategy would incrementally result in 422 fewer ovarian cancer diagnoses, 252 fewer ovarian cancer deaths, 20 fewer unintended intrauterine pregnancies, and 57 fewer ectopic pregnancies, but an additional 770 major perioperative complications (Table 2).

The average discounted cost, effectiveness as measured by QALYs, and ICERs for women undergoing cesarean delivery with tubal ligation, salpingectomy, or LARC are presented in Table 3. Tubal ligation with cesarean is cost-saving ($3588) compared to salpingectomy with cesarean ($3651) or LARC after cesarean ($6667). Salpingectomy is more effective compared with tubal ligation or LARC with cesarean delivery, with average gains of 12.2370, 12.2342, and 12.2305 QALYs, respectively. Both

TABLE 3
Cost-utility analysis of tubal ligation, salpingectomy, and long-acting reversible contraception at time of cesarean delivery

Strategy	Cost, $	Incremental cost, $	Effectiveness, QALY	Incremental effectiveness, QALY	Cost-effectiveness ratio, $/QALY	ICER, $/QALY gained[a]
Cesarean delivery with salpingectomy	3651.82	63.75	12.2370	0.0065	298.42	23,189.88
Cesarean delivery with tubal ligation	3588.06	—	12.2342	0.0038	293.28	—
Cesarean delivery with LARC	6667.72	3015.90	12.2305	—	545.17	Dominated[b]

ICER, incremental cost-effectiveness ratio; *LARC*, long-acting reversible contraception; *QALY*, quality-adjusted life year.

[a] Represents additional cost/QALY above what would be expended using tubal ligation; [b] Strategy is more costly and less effective.

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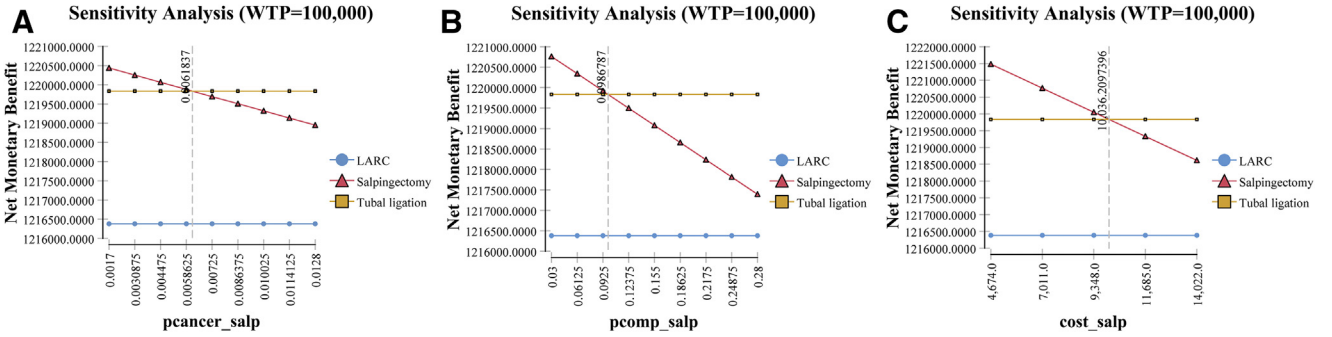
FIGURE 2
One-way sensitivity analysis of A, ovarian cancer risk reduction; B, perioperative complication rate; and C, cost comparing salpingectomy, tubal ligation, and long-acting reversible contraception (LARC) with cesarean delivery



Absolute risk of cancer threshold (0.0062; 0.62%) represents relative risk reduction of 52% (relative risk 0.48). Absolute risk of salpingectomy procedure complication threshold (0.0986; 9.9%) translates to absolute 2% increase over tubal ligation risk. Salpingectomy cost threshold ($10,036.21) translates to $688 increase over tubal ligation cost.

cost_salp, cost of salpingectomy; *pcancer_salp*, probability of ovarian cancer after salpingectomy; *pcomp_salp*, probability of complications from salpingectomy; *WTP*, willingness to pay.

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tubal ligation and salpingectomy with cesarean delivery have favorable cost-effectiveness ratios of $293.28 per QALY and $298.42 per QALY, respectively. In the base case analysis, the salpingectomy strategy was more cost-effective than the tubal ligation strategy with an ICER of $23,189.88 per QALY. The LARC strategy was costlier and less effective than the other 2 strategies (ie, dominated) (Appendix Figure A1).

Sensitivity analyses were performed to assess the robustness, or confidence, of the model base case results and to identify threshold effects of key variables using the CI or plausible range of uncertainty for each variable (Table 1). One-way sensitivities were first evaluated in a tornado plot to identify the most influential variables on the results of the base case scenario. The tornado plot indicated that the large majority (97%) of uncertainty, or sensitivity, was attributable to imprecise published estimates of the risk of perioperative complications, cancer risk reduction of salpingectomy, as well as the cost of salpingectomy and tubal ligation (Appendix Figure A2). One-way sensitivity analyses of the most influential variables, namely cancer risk reduction, complications, and cost, identified important thresholds at which the preferred strategy changed from salpingectomy to tubal ligation. The base case estimate of cancer risk reduction with salpingectomy was 64% (RR, 0.36) with a wide CI based on the available observational research. If the true risk reduction of salpingectomy was <52% (RR > 0.48), then tubal ligation became the preferred strategy (Figure 2, A). The base case estimate of the complication risk of cesarean with salpingectomy was 8% (ie, 1% higher than cesarean with tubal ligation). If the true complication risk of salpingectomy with cesarean was >9.9%, or >2% higher than tubal ligation, then the tubal ligation strategy was the optimal strategy (Figure 2, B). If the true cost of salpingectomy was >$688 more than the base case estimate, tubal ligation became the preferred strategy (Figure 2, C).

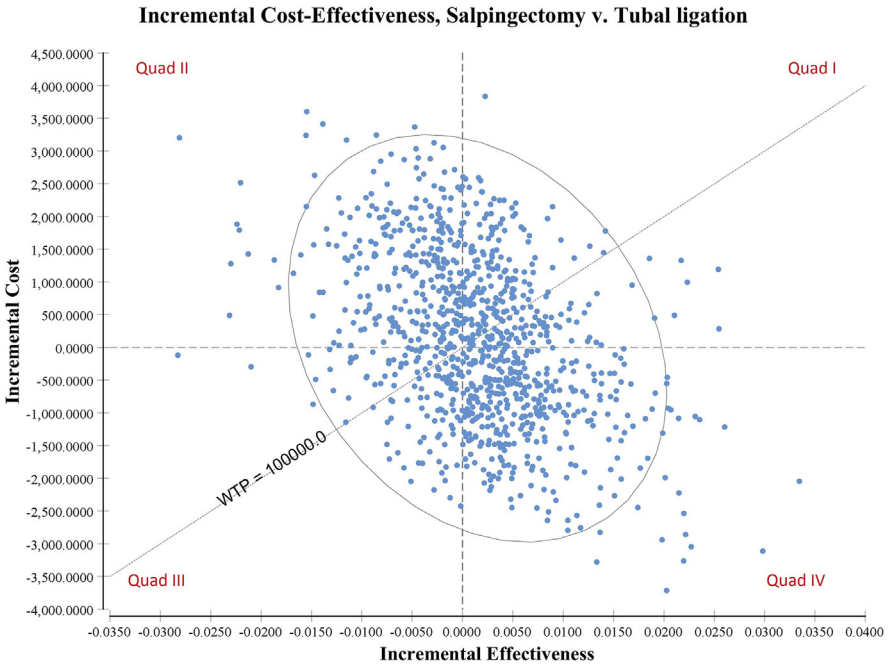
Monte Carlo simulation of 1000 trials were performed in which all model variables were randomly varied concurrently with a WTP threshold of $100,000 per QALY (Figure 3). The ellipse on the ICE scatter plot indicated the 95% CI for the ICE of salpingectomy compared to tubal ligation. The distribution of ICE point estimates across the 4 quadrants of the chart demonstrated a wide spectrum of variability and uncertainty with regard to the preferred strategy (Appendix Table A1). Based on the amount of uncertainty in the baseline estimates, salpingectomy and tubal ligation had a 50% and 49% chance of being the preferred strategies, respectively (Figure 4). If the WTP threshold was set more conservatively at $50,000, tubal ligation was the preferred strategy in the majority (50.4%) of simulation trials.

In the sensitivity analyses performed within the model of patients at high risk for cancer (eg, BRCA1/2, Lynch syndrome), the cesarean with salpingectomy strategy had a cost-effectiveness ratio of $541.12 per QALY, and dominated the other 2 strategies across the range of baseline cancer risk for high-risk patients (8–44%); in other words, tubal ligation and LARC were both more expensive and less effective. This result was stable in 2- and 3-way sensitivity analyses varying high-risk baseline lifetime cancer rate (8–44%), salpingectomy risk, and salpingectomy cancer risk reduction across the plausible ranges of uncertainty (Table 1).

Comment

Primary prevention of ovarian cancer through opportunistic salpingectomy is increasingly accepted as standard gynecologic practice at the time of hysterectomy or interval sterilization.[17] Given the high frequency of sterilization performed with cesarean delivery, there has been increasing debate about whether

FIGURE 3
Scatter plot of Monte Carlo simulation of incremental cost-effectiveness of salpingectomy vs tubal ligation with cesarean delivery



Data are available in tabular format with further explanations of each quadrant in online Appendix Table A1.

WTP, willingness to pay.

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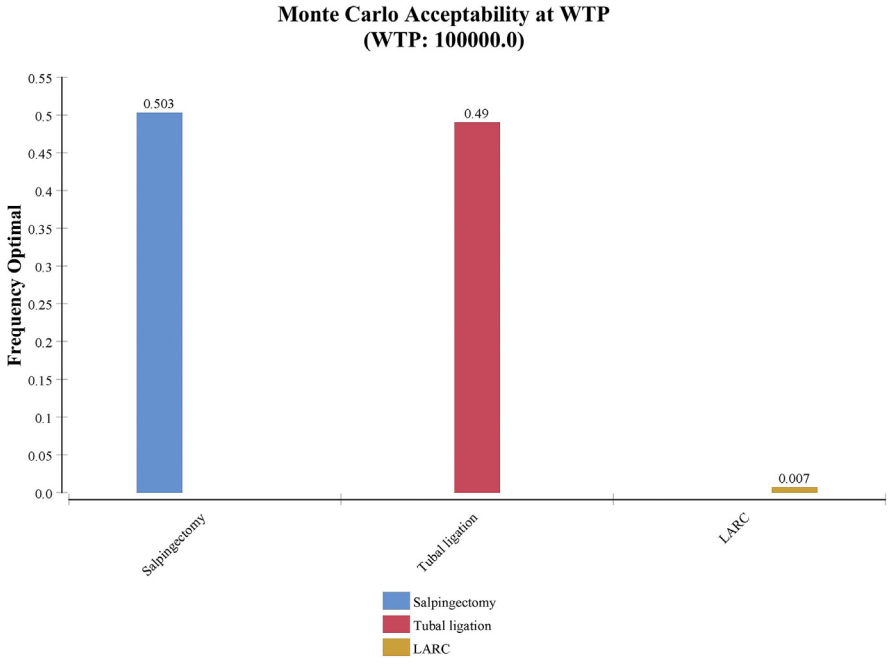
salpingectomy should be performed by obstetricians in lieu of tubal ligation[25] and in our region several providers have adopted salpingectomy with cesarean as an acceptable strategy. We found that salpingectomy and tubal ligation were both cost-effective strategies for pregnant women desiring both permanent sterilization and a cancer risk reduction intervention at the time of cesarean. Salpingectomy with cesarean was more cost-effective than tubal ligation with cesarean in base case analysis. However, uncertainty around the risk of perioperative complications and the incremental cancer risk reduction of salpingectomy compared to tubal ligation with cesarean had a significant impact on the results of this cost-effectiveness analysis.

This decision analysis suggests that the current care standard of tubal ligation, as well as salpingectomy, are both acceptable strategies for US pregnant women seeking permanent sterilization and ovarian cancer risk reduction at the time of cesarean delivery. However, the estimates of risks and benefits of salpingectomy are imprecise and must be better elucidated before one strategy can be preferred. It should be noted that this preliminary conclusion will likely evolve as newer data emerge. In the interim, other factors may also influence the preferred strategy, including patient-specific ovarian cancer risk factors, patient values and preferences, and surgeon skill set.

With regard to perioperative risks, we estimated that the salpingectomy perioperative risk was approximately 1% higher than tubal ligation with cesarean. Since peripartum salpingectomy outcome data are sparse,[6–8,18,20,42] the risk was estimated from the well-characterized risk of cesarean delivery plus additional risk from the increased operative time of salpingectomy and the association between operative time and complication rate.[43–45] The salpingectomy perioperative risk may be even higher given the vascular changes of pregnancy. Sensitivity analysis indicated that if the salpingectomy perioperative risk were >2% higher than tubal ligation, then tubal ligation was the preferred strategy. With regard to ovarian cancer risk reduction, salpingectomy was estimated to reduce the risk by 64% (RR, 0.36) with a wide CI that abutted 1.0.[13,14,33] If the true risk reduction of salpingectomy were <52% (RR > 0.48, resulting in absolute residual cancer risk >0.62%), then tubal ligation became the preferred strategy. Lastly, cost estimates for salpingectomy did not account for the increased operative time or possible use of specialized thermal ligation devices (eg, LigaSure; Medtronic, Minneapolis, MN, $450). Since the threshold at which tubal ligation became the most cost-effective strategy was about $690 above the base case estimate, it is possible that these costlier surgical approaches could make tubal ligation the preferred strategy when implemented widely by surgeons and facilities with variable experience and expertise.

Sensitivity analyses quantified the uncertainty around the base-case results but also identified thresholds of risk and benefit whereby the preferred strategy changed from salpingectomy to tubal ligation, including: detecting if salpingectomy has a perioperative complication rate that is >2% higher than tubal ligation and whether the ovarian cancer risk reduction of salpingectomy is at least 52% (RR, 0.48). Monte Carlo simulation (ie, multivariable sensitivity analysis) estimated that there is approximately a 50% chance that cesarean with tubal ligation is the preferred strategy over cesarean with salpingectomy. To date, the 6 largest studies comparing tubal ligation to salpingectomy with cesarean have included between 16–206 patients in the salpingectomy arm.[6–8,18,20,42] In comparison to the relatively well-characterized risk of perioperative complications, cancer risk reduction, and cost of tubal ligation with cesarean, salpingectomy with cesarean is a relatively new procedure with fewer available data. Thus, estimates of risks and benefits are

FIGURE 4
Bar graph of Monte Carlo simulation of acceptability



Bar graph of Monte Carlo simulation of acceptability of salpingectomy, tubal ligation, and long-acting reversible contraception (LARC) with cesarean delivery.

WTP, willingness to pay.

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less precise if not uncertain.[6–8,18,20,42] It is possible that certain populations at higher lifetime risk of ovarian cancer, such as Lynch syndrome (6–8% lifetime risk) and BRCA1 and 2 carriers (lifetime risk of ~40% and ~20%, respectively), may derive greater benefit from salpingectomy[31]; however, BRCA1/2 carriers who undergo salpingectomy without oophorectomy may not benefit from the same magnitude of reduction in cancer risk compared to those women who undergo salpingectomy with oophorectomy. For this reason, the National Comprehensive Cancer Network does not recommend salpingectomy-only for cancer risk reduction in these high-risk groups. Thus, our sensitivity analyses varying baseline cancer risk to reflect that of BRCA1/2 carriers or Lynch syndrome may grossly overestimate the risk reduction of the salpingectomy strategy, exaggerating its cost-effectiveness. We caution the reader that this high-risk portion of the analysis is exploratory and largely theoretical since it is unknown whether salpingectomy without oophorectomy provides risk reduction in these subpopulations genetically at high risk for cancer.

Our results provide clarity with regard to the risk-benefit tradeoff of salpingectomy relative to tubal ligation with cesarean during a time of emerging data and evolving practice. A recent cost-effective analysis compared salpingectomy vs tubal ligation with cesarean, and found salpingectomy to be the most cost-effective strategy[19]; however this analysis only utilized model inputs based on a recent trial of 80 women, and did not model the risk of procedure-specific complications given a low and apparently similar rate between groups. Studies from the gynecology literature support the cancer risk-reducing benefits and the cost-effectiveness of salpingectomy with hysterectomy (abdominal, laparoscopic, and vaginal) and interval laparoscopic sterilization.[3,17,65] The safety and efficacy of salpingectomy vs tubal ligation with cesarean delivery, including the frequency of increased operative time, blood loss, vascular injury, operative skill, and surgical equipment, will become evident over time as the optimal surgical technique becomes standardized and the procedure becomes more prevalent.[18,42]

The analysis is also limited by other assumptions. We did not account for the potential impact of peripartum salpingectomy on ovarian function and resulting morbidity, although recent data are reassuring.[47] These results were not stratified by histologic subtypes of ovarian cancer due to insufficient data. We did not model possible discontinuation rates of LARC, which are <20% among younger women and are likely lower among older women considering permanent sterilization.[66] We did not model the impact of oral contraceptives given the focus on permanent sterilization. However, oral contraceptive pills are roughly equivalent to LARC with regard to ovarian cancer risk reduction (25%),[67] which we modeled. We did not account for patient regret following sterilization, which is low (<5%) among women >35 years.[68] There are likely other noncancer benefits of salpingectomy compared to tubal ligation in addition to superior sterilization, including near elimination of future tubal pathology.[25] We did not use Markov modeling to represent annual cancer death rates because there were not adequate data to estimate annual transition probabilities among health states (ie, death, cured, or survived with disease). We assumed a 100% success rate for completing both types of sterilization procedures. Salpingectomy likely has a higher rate of being aborted than tubal ligation given the increased complexity of the procedure. This assumption likely overestimated the effectiveness of salpingectomy compared to tubal ligation. Some women who underwent tubal ligation may undergo a hysterectomy with salpingectomy in the future, which we did not model. This again likely overestimated the effectiveness of salpingectomy.

Salpingectomy and tubal ligation with cesarean delivery both appear to be

cost-effective strategies for concurrent pregnancy and ovarian cancer prevention. But, this modeling analysis suggests that salpingectomy with cesarean cannot be preferred or recommended over tubal ligation with cesarean as a strategy for US pregnant women seeking permanent sterilization and ovarian cancer risk reduction. This conclusion is made until the perioperative risks and ovarian cancer risk reduction of salpingectomy with cesarean delivery are more precisely known and are demonstrated to be more favorable than that of tubal ligation with cesarean delivery. Furthermore, we believe that if salpingectomy with cesarean is offered as a strategy, preoperative counseling should include a disclosure that the estimates of peripartum salpingectomy risks and benefits relative to tubal ligation are uncertain or imprecise. Importantly, our analysis makes the uncertain or missing information on safety and effectiveness unambiguous, and identifies important thresholds of safety and effectiveness to direct future research and policy development. Specifically, this analysis informs future research design (ie, sample size and outcome designation) since it identifies thresholds of operative complications and cancer RR reduction below which salpingectomy can be definitively identified as the preferred health care strategy and above which tubal ligation remains the preferred strategy. ■

References

1. Chan L, Westhoff CL. Tubal sterilization trends in the United States. Fertil Steril 2015;94:1–6.
2. Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Mathews TJ. Births: final data for 2015. Natl Vital Stat Rep 2017;66:1.
3. Dilley S, Straughn JM Jr, Leath CA III. The evolution of and evidence for opportunistic salpingectomy. Obstet Gynecol 2017;130:814–24.
4. Mikhail E, Salemi JL, Mogos MF, Hart S, Salihu HM, Imudia AN. National trends of adnexal surgeries at the time of hysterectomy for benign indication, United States, 1998-2011. Am J Obstet Gynecol 2015;213:e1–13.
5. Garcia C, Martin M, Tucker LY, et al. Experience with opportunistic salpingectomy in a large, community-based health system in the United States. Obstet Gynecol 2016;128:277–83.
6. Powell C, Alabaster A, Simmons S, et al. Salpingectomy for sterilization: change in practice in a large integrated health care system, 2011-2016. Obstet Gynecol 2017;130:961–7.
7. Danis R, Della Badia CR, Richard SD. Postpartum permanent sterilization: could bilateral salpingectomy replace bilateral tubal ligation? J Minim Invasive Gynecol 2016;23:928–32.
8. Shinar S, Blecher Y, Alpern S, et al. Total bilateral salpingectomy versus partial bilateral salpingectomy for permanent sterilization during cesarean delivery. Arch Gynecol Obstet 2017;295:1185–9.
9. Hsieh G, Antony K, Masand R, Anderson M. A prospective feasibility study of postpartum distal salpingectomy. Chicago, IL: American College of Obstetricians and Gynecologists; 2014.
10. Jones N, Schulkin J, Urban RR, et al. Physicians' perspectives and practice patterns toward opportunistic salpingectomy in high- and low-risk women. Cancer Invest 2017;35:51–61.
11. Rice M, Murphy MA, Tworoger SS. Tubal ligation, hysterectomy and ovarian cancer: a meta-analysis. J Ovarian Res 2012;5:13.
12. Dilley S, Havrilesky LJ, Bakkum-Gamez J, et al. Cost-effectiveness of opportunistic salpingectomy for ovarian cancer prevention. Gynecol Oncol 2017;146:373–9.
13. Falconer H, Yin L, Grönberg H, Altman D. Ovarian cancer risk after salpingectomy: a nationwide population-based study. J Natl Cancer Inst 2015;107.
14. Cibula D, Widschwendter M, Májek O, Dusek L. Tubal ligation and the risk of ovarian cancer: review and meta-analysis. Hum Reprod Update 2011;17:55–67.
15. McAlpine J, Hanley GE, Woo MM, et al. Ovarian cancer research program of British Columbia. Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention. Am J Obstet Gynecol 2014;210:e11.
16. Hanley G, McAlpine JN, Pearce CL, Miller D. The performance and safety of bilateral salpingectomy for ovarian cancer prevention in the United States. Am J Obstet Gynecol 2017;216:e1–270.
17. Kwon J, McAlpine JN, Hanley GE, et al. Costs and benefits of opportunistic salpingectomy as an ovarian cancer prevention strategy. Obstet Gynecol 2015;125:338–45.
18. Subramaniam A, Blanchard CT, Erickson BK, et al. Feasibility of complete salpingectomy compared with standard postpartum tubal ligation at cesarean delivery: a randomized controlled trial. Obstet Gynecol 2018;132:20–7.
19. Subramanian A BE, CK Blancahrd, BK Erickson, et al. The cost-effectiveness of salpingectomy versus standard tubal ligation at the time of cesarean delivery (abstract). Amer J Obstet Gynecol 2018;1:S380.
20. Garcia C, Moskowitz OM, Chisholm CA, et al. Salpingectomy compared with tubal ligation at cesarean delivery: a randomized controlled trial. Obstet Gynecol 2018;132:29–34.
21. Manchanda R, Menon U. Opportunistic bilateral salpingectomy (OBS) for the prevention of ovarian cancer should be offered in the context of a clinical trial: FOR: there is lack of clarity on a number of key issues. BJOG 2016;123:463.
22. Edejer TT, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans DB, Murray CJL, eds. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva, Switzerland: WHO Publications; 2003.
23. Jones J, Mosher W, Daniels K. Division of Vital Statistics. Current contraceptive use in the United States, 2006-2010, and changes in patterns of use since 1995. Natl Health Stat Report 2012;(60):1–25.
24. Westhoff C, Davis A. Tubal sterilization: focus on the US experience. Fertil Steril 2000;73:913–22.
25. Castellano T, Zerden M, Marsh L, Boggess K. Risks and benefits of salpingectomy at the time of sterilization. Obstet Gynecol Surv 2017;72:663–8.
26. King JJ, Tsevat J, Lave JR, Roberts MS. Willingness to pay for a quality-adjusted life year: implications for societal health care resource allocation. Med Decis Making 2005;25:667–77.
27. Cress R, Chen YS, Morris CR, Petersen M, Leiserowitz GS. Characteristics of long-term survivors of epithelial ovarian cancer. Obstet Gynecol 2015;126:491–7.
28. Baldwin L, Huang B, Miller RW, et al. Ten-year relative survival for epithelial ovarian cancer. Obstet Gynecol 2012;120:612–8.
29. National Center for Health Statistics. Life expectancy. Available at: https://www.cdc.gov/nchs/fastats/life-expectancy.htm. Accessed Jan. 3, 2018.
30. National Cancer Institute. SEER cancer statistics review, 1975-2013, based on November 2015 SEER data submission. Available at: https://seer.cancer.gov/csr/1975_2013/. Accessed Nov. 6, 2017.
31. Kuchenbaecker K, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. JAMA 2017;317:2402–16.
32. Bonadona V, Bonaïti B, Olschwang S, et al. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. JAMA 2011;305:2304–10.
33. Lessard-Anderson C, Handlogten KS, Molitor RJ, et al. Effect of tubal sterilization technique on risk of serous epithelial ovarian and primary peritoneal carcinoma. Gynecol Oncol 2014;135:423–7.
34. Ness R, Dodge RC, Edwards RP, Baker JA, Moysich KB. Contraception methods, beyond oral contraceptives and tubal ligation, and risk of ovarian cancer. Ann Epidemiol 2011;21:188–96.
35. Soini T, Hurskainen R, Grénman S, Mäenpää J, Paavonen J, Pukkala E. Impact of levonorgestrel-releasing intrauterine system use on the cancer risk of the ovary and fallopian tube. Acta Oncol 2016;55:1281–4.

36. Tworoger S, Fairfield KM, Colditz GA, Rosner BA, Hankinson SE. Association of oral contraceptive use, other contraceptive methods, and infertility with ovarian cancer risk. Am J Epidemiol 2007;166:894–901.
37. Burrows L, Meyn LA, Weber AM. Maternal morbidity associated with vaginal versus cesarean delivery. Obstet Gynecol 2004;103:907–12.
38. Allen V, O'Connell CM, Baskett TF. Maternal morbidity associated with cesarean delivery without labor compared with induction of labor at term. Obstet Gynecol 2006;108:286–94.
39. Allen V, O'Connell CM, Liston RM, Baskett TF. Maternal morbidity associated with cesarean delivery without labor compared with spontaneous onset of labor at term. Obstet Gynecol 2003;102:477–82.
40. Marshall N, Fu R, Guise JM. Impact of multiple cesarean deliveries on maternal morbidity: a systematic review. Am J Obstet Gynecol 2011;205:e1–8.
41. Temming L, Raghuraman N, Carter EB, et al. Impact of evidence-based interventions on wound complications after cesarean delivery. Am J Obstet Gynecol 2017;217:449.
42. Duncan J, Schenone MH, Mari G. Technique for bilateral salpingectomy at the time of cesarean delivery: a case series. Contraception 2017;95:509–11.
43. Cheng H, Chen BP, Soleas IM, Ferko NC, Cameron CG, Hinoul P. Prolonged operative duration increases risk of surgical site infections: a systematic review. Surg Infect 2017;18:722–35.
44. Procter L, Davenport DL, Bernard AC, Zwischenberger JB. General surgical operative duration is associated with increased risk-adjusted infectious complication rates and length of hospital stay. J Am Coll Surg 2010;210:60–5.
45. Mahdi H, Goodrich S, Lockhart D, DeBernardo R, Moslemi-Kebria M. Predictors of surgical site infection in women undergoing hysterectomy for benign gynecologic disease: a multicenter analysis using the national surgical quality improvement program data. J Minim Invasive Gynecol 2014;21:901–9.
46. Wilson S, Fecho K, Marshall J, Spielman F. Factors influencing cesarean delivery operative times: a prospective observational cohort study. Int J Obstet Anesth 2010;19:417–21.
47. Ganer Herman H, Gluck O, Keidar R, et al. Ovarian reserve following cesarean section with salpingectomy vs tubal ligation: a randomized trial. Am J Obstet Gynecol 2017;217:e1–6.
48. Heinemann K, Reed S, Moehner S, Minh TD. Risk of uterine perforation with levonorgestrel-releasing and copper intrauterine devices in the European active surveillance study on intrauterine devices. Contraception 2015;91:274–9.
49. Peterson H, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of pregnancy after tubal sterilization: findings from the US collaborative review of sterilization. Am J Obstet Gynecol 1996;174:1161–8.
50. Backman T, Rauramo I, Huhtala S, Koskenvuo M. Pregnancy during the use of levonorgestrel intrauterine system. Am J Obstet Gynecol 2004;190:50–4.
51. Mansour D, Inki P, Gemzell-Danielsson K. Efficacy of contraceptive methods: a review of the literature. Eur J Contracept Reprod Health Care 2010;15:4–16.
52. Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. N Engl J Med 2012;366:1998–2007.
53. Peterson H, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of ectopic pregnancy after tubal sterilization. US collaborative review of sterilization working group. N Engl J Med 1997;336:762–7.
54. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project. Available at: https://www.ahrq.gov/research/data/hcup/index.html. Accessed Nov. 12, 2017.
55. Centers for Medicaid and Medicare Services. Physician fee schedule look-up tool. Available at: https://www.cms.gov/apps/physician-fee-schedule/license-agreement.aspx. Accessed Nov. 12, 2017.
56. Yabroff K, Lamont EB, Mariotto A, et al. Cost of care for elderly cancer patients in the United States. J Natl Cancer Inst 2008;100:630–41.
57. Dimick J, Chen SL, Taheri PA, Henderson WG, Khuri SF, Campbell DA Jr. Hospital costs associated with surgical complications: a report from the private-sector national surgical quality improvement program. J Am Coll Surg 2004;199:531–7.
58. Boltz M, Hollenbeak CS, Julian KG, Ortenzi G, Dillon PW. Hospital costs associated with surgical site infections in general and vascular surgery patients. Surgery 2011;150:934–42.
59. Amaral G, Foster DG, Biggs MA, Jasik CB, Judd S, Brindis CD. Public savings from the prevention of unintended pregnancy: a cost analysis of family planning services in California. Health Serv Res 2007;42:1960–80.
60. Schwarz E, Smith R, Steinauer J, Reeves MF, Caughey AB. Measuring the effects of unintended pregnancy on women's quality of life. Contraception 2008;78:204–10.
61. Lundsberg L, Xu X, Schwarz EB, Gariepy AM. Measuring health utility in varying pregnancy contexts among a diverse cohort of pregnant women. Contraception 2017;96:411–9.
62. Teng T, Wallace A. One thousand health-related quality-of- life outcomes. Med Care 2000;38:583–637.
63. US Bureau of Labor Statistics. CPI inflation calculator. Available at: http://www.bls.gov/data/inflation_calculator.htm. Accessed Nov. 10, 2017.
64. Havrilesky L, Broadwater G, Davis DM, et al. Determination of quality of life-related utilities for health states relevant to ovarian cancer diagnosis and treatment. Gynecol Oncol 2009;113:216–20.
65. Cadish L, Shepherd JP, Barber EL, Ridgeway B. Risks and benefits of opportunistic salpingectomy during vaginal hysterectomy: a decision analysis. Am J Obstet Gynecol 2017;217:603.
66. Aoun J, Dines VA, Stovall DW, Mete M, Nelson CB, Gomez-Lobo V. Effects of age, parity, and device type on complications and discontinuation of intrauterine devices. Obstet Gynecol 2014;123:585–92.
67. Collaborative Group on Epidemiological Studies of Ovarian Cancer, Beral BV, Doll R, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet 2008;371:303–14.
68. Schmidt J, Hillis SD, Marchbanks PA, Jeng G, Peterson HB. Requesting information about and obtaining reversal after tubal sterilization: findings from the US collaborative review of sterilization. Fertil Steril 2000;74:892–8.
69. Wymer K, Shih YC, Plunkett BA. The cost-effectiveness of a trial of labor accrues with multiple subsequent vaginal deliveries. Am J Obstet Gynecol 2014;211:e12.
70. Wolters Kluwer Health. Medi-Span master drug database. Available at: http://www.medi-span.com/drug-pricing-analysis-pricerx.aspx. Accessed Nov. 17, 2017.

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Received May 9, 2018; revised Aug. 6, 2018; accepted Aug. 20, 2018.

The authors report no conflict of interest.

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