The cost-effectiveness of opportunistic salpingectomy versus standard tubal ligation at the time of cesarean delivery for ovarian cancer risk reduction☆,☆☆,☆☆☆

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HIGHLIGHTS

- In a population of 10,000 women, salpingectomy versus BTL would result in 17 fewer OvCa diagnoses and 13 fewer OvCa deaths
- Salpingectomy compared to BTL is cost-effective in >75% of simulated scenarios
- Salpingectomy was cost-saving when OvCa risk reduction with salpingectomy was >82%
- Salpingectomy was also cost-saving if its additional cost versus BTL was <$538.80 or procedural success of BTL was <81%

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ABSTRACT

Objectives. Opportunistic salpingectomy is a cost-effective strategy recommended for ovarian cancer (OvCa) risk reduction at the time of gynecologic surgery in women who have completed childbearing. We aimed to evaluate the cost-effectiveness of opportunistic salpingectomy compared to standard tubal ligation (TL) during cesarean delivery.

Study design. A cost-effectiveness analysis using decision modeling to compare opportunistic salpingectomy to TL at the time of cesarean using probabilities of procedure completion derived from a trial. Probability and cost inputs were derived from local data and the literature. The primary outcome was the incremental cost-effectiveness ratio (ICER) in 2017 U.S. dollars per quality-adjusted life year (QALY) at a cost-effectiveness threshold of $100,000/QALY. One- and two-way sensitivity analyses were performed for all variables. A probabilistic sensitivity analysis determined the proportion of simulations in which each strategy would be cost-effective.

Results. Opportunistic salpingectomy was cost-effective compared to TL with an ICER of $26,616 per QALY. In 10,000 women desiring sterilization with cesarean, opportunistic salpingectomy would result in 17 fewer OvCa diagnoses, 13 fewer OvCa deaths, and 25 fewer unintended pregnancies compared to TL – with an associated cost increase of $4.7 million. The model was sensitive only to OvCa risk reduction from salpingectomy and TL. Opportunistic salpingectomy was not cost-effective if its cost was >$3163.74 more than TL, if the risk-reduction of salpingectomy was <41%, or if the risk-reduction of TL was >46%. In probabilistic sensitivity analysis opportunistic salpingectomy was cost effective in 75% of simulations.

Conclusions. In women undergoing cesarean with sterilization, opportunistic salpingectomy is likely cost-effective and may be cost-saving in comparison to TL for OvCa risk reduction.

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1. Introduction

Ovarian cancer is the most lethal gynecologic malignancy with almost 22,000 cases diagnosed in the United States annually, and over 14,000 deaths from disease [1]. Given the lack of effective screening strategies and limited therapeutic options following recurrence, the recent focus of reducing ovarian cancer morbidity and mortality has been primary prevention [2]. With (more recent) studies suggesting that the majority of ovarian cancers (up to 70%) originate in the distal fallopian tube, opportunistic salpingectomy at the time of benign gynecologic surgery after completion of child-bearing has become a widespread practice for ovarian cancer risk reduction endorsed by both the American College of Obstetricians and Gynecologists and the Society of Gynecologic Oncology [3–9]. In addition, this practice has been repeatedly shown to be cost-effective [10,11].

In the United States, over 1.2 million cesarean deliveries are performed annually with nearly 10% (120,000) accompanied by a surgical sterilization with BTL [12,13]. In the Salpingectomy at Cesarean for Ovarian Cancer Reduction (SCORE) trial (NCT02374827), we demonstrated that in women desiring permanent sterilization, opportunistic salpingectomy in lieu of standard bilateral tubal ligation (BTL) at the time of cesarean delivery for the added benefit of ovarian cancer risk reduction is feasible (in nearly 70% of women); however, extends operative times by 15 min [14]. While this provides evidence supporting the use of this practice at the time of cesarean delivery, questions remain regarding the potential cost-effectiveness of such a strategy. As such, our objective was to evaluate the cost-effectiveness of opportunistic salpingectomy compared to BTL during cesarean delivery as an ovarian cancer risk reducing strategy.

2. Materials and methods

We designed a decision analytic model to compare the costs and effects of two strategies: [1] opportunistic salpingectomy and [2] standard bilateral tubal ligation (BTL) at the time of cesarean from a societal perspective. Specifically, we focused on unintended pregnancy and ovarian cancer. The study population included a theoretical cohort of women seeking permanent sterilization at the time of cesarean delivery. The time horizon for this cost-effectiveness analysis was over the lifetime of women starting from the time of cesarean until the time of death. We assumed the average age for women seeking sterilization was 33 years, equal to that observed in the primary trial (SCORE trial, NCT02374827), and the age at death for patients not experiencing ovarian cancer was 78, equal to the average American life expectancy in 2017 [14,15].

2.1. Model structure

The decision tree structure (Supplementary Figure) accounted for differences in operational success, subsequent risk of unintended pregnancy and ectopic pregnancy, subsequent risk of ovarian cancer, and the likelihood of early death from ovarian cancer. Patients in the model could experience a successful salpingectomy or unsuccessful salpingectomy. If unsuccessful with salpingectomy, we assumed surgeons would attempt BTL. After surgery, patients could go on to experience an unintended pregnancy, the risk of which differed depending on the type of sterilization procedure performed. Ectopic pregnancy was more common in patients who became pregnant after a successful sterilization procedure compared to those who became pregnant without a completed sterilization procedure [16,17]. Ovarian cancer risk in each patient was determined by calculation of age-adjusted ovarian cancer risk in patients without sterilization and adjusted according to published estimates of risk reduction in women having completed a salpingectomy or BTL [18–23]. This model did not account for whether women would have had genetic testing or would subsequently seek out risk-reducing bilateral salpingo-oophorectomy, but assumed that

these factors are accounted for in a population-based risk for developing ovarian cancer. As we used these population-based estimates, both low and high-risk (i.e. BRCA positive) were included in our model, but we did not specifically aim to identify the high-risk women in whom different risk-reducing strategies are appropriate. Similarly, this model did not account for patient regret and consider reversal of salpingectomy or BTL as these procedure as considered permanent.

Probabilities, utilities, and cost estimates were derived from two sources: the published literature and the trial data (Tables 1 and 2) [16–36]. We conducted a thorough PubMed search of keywords and Medical Subject Headings (MeSH) terms related to each probability, cost, and utility input. Abstracts were reviewed for relevance by two authors (AS and BDE). Studies published in the United States in the last 10 years were prioritized and weighted more heavily, but we included earlier data when large good-quality studies were available before this time. Trial data were used whenever available, specifically for procedural outcomes. When multiple estimates were available in the literature and from trial data, we calculated pooled weighted averages for model inputs. Low and high estimates in the literature were included in sensitivity analyses.

2.2. Costs

The additional procedural costs attributable to salpingectomy were estimated from local charge data at the University of Alabama Birmingham (UAB). The difference in procedural charges between the two strategies is explained primarily by operating room time-based charges which accrue at 30-minute intervals. In the trial, the average total operating room time (including cesarean) was 75 min in the salpingectomy group and 60 min in the BTL group ($p = 0.004$) [14]. Costs of unintended pregnancy and ovarian cancer treatment, survival, and death were derived from studies in the literature. We did not include the cost of lost productivity for the patient after receiving a diagnosis of unintended pregnancy or ovarian cancer. In addition, we did not include pathology costs as only in high-risk women is serial sectioning and pathologic evaluation recommended. All costs were adjusted to

Table 1

Probability and utility inputs for the base case model and sensitivity analyses.

	Base case estimate	Low range	High range	Ref
Probabilities				
Successful completion of sterilization procedure				
Salpingectomy	67.5%	50%	95%	Trial data [12],
Tubal ligation	95%	80%	99%	low and high range
Tubal ligation if failed salpingectomy	84.5%	50%	99%	intentionally wide
Unintended pregnancy				
After salpingectomy	0.38%	0.19%	0.57%	[a]
After tubal ligation	0.75%	0.38%	1.14%	16,17
Ovarian cancer risk				
No sterilization	1.26%	1.24%	1.40%	_SEER_ [18]
After salpingectomy (risk reduction)	54%	27%	83%	19,20
After tubal ligation (risk reduction)	34%	10%	58%	19–23
Risk of dying from ovarian cancer if diagnosed	75.4%	54.0%	78.1%	18
Utilities				
Unintended pregnancy	0.88	0.7	0.99	24–26
Ectopic pregnancy	0.75	0.55	0.92	25–27
Cancer in treatment	0.61	0.16	0.81	28
Cancer in remission	0.78	0.18	1.0	28
Death	0	0	0	Assumed
Healthy	1	1	1	Assumed

[a] We assumed that the unintended pregnancy rate after salpingectomy was half that after bilateral tubal ligation.

Table 2
Costs of the base case and ranges for sensitivity analyses in 2017 US dollars.

	Base case cost	Low cost	High cost	Ref
Surgery				
Tubal ligation at cesarean	0	0	0	
Salpingectomy at cesarean	1236	0	2472	Patient-level data
Unintended pregnancy				
Intrauterine pregnancy	12,903	5547	27,585	[29,30]
Ectopic pregnancy	8843	1241	27,871	[31–34]
Ovarian cancer (per year)				
First year of treatment	93,321	63,618	143,062	[35,36]
Treatment cost per year	9176	4684	13,764	[36]
Treatment cost last year	110,294	64,122	165,441	[36]

All costs in 2017 US dollars ($).

2017 U.S. dollars ($) using the health care component of the U.S. price index for personal consumption expenditures [37].

2.3. Analysis

The primary outcome for the base-case analysis was the incremental cost effectiveness ratio (ICER) which was calculated as cost divided by quality-adjusted life years (QALYs). An ICER willingness-to-pay of $100,000 per QALY was defined as the a priori threshold for determining cost-effectiveness [38]. For the sake of illustration, we performed a cost-benefit analysis of the base-case to demonstrate the tradeoff between costs and outcomes under each strategy in a population of 10,000 women undergoing sterilization. Future costs and utilities were discounted at a standard 3% yearly rate.

The robustness of the analysis was tested in one-way and two-way sensitivity analyses for each model input, across a wide range of variable assumptions (Tables 1 and 2). Sensitivity analyses were performed using low and high estimates reported in the literature (except as otherwise noted). Threshold analyses were performed on all variables to determine the circumstances under which each strategy was cost-effective or cost-saving. A probabilistic sensitivity analysis accounting for plausible parametric variation was performed with second order Monte Carlo simulation in a series of 10,000 iterations to determine the proportion of simulations in which BTL or salpingectomy would be cost-effective. Beta and gamma distributions were calculated for probabilities, costs, and utilities, and parametrized using trial data and published estimates for use in probabilistic sensitivity analyses.

To ensure generalizability to hospital settings with strikingly different cost structures for sterilization at the time of cesarean, we intentionally expanded the difference in cost between salpingectomy and BTL from no difference to 200% of the base-case estimate. In doing so, we could use sensitivity analyses to explore even extreme cost differences between the two procedures.

For modeling and analysis, we used TreeAge Pro 2016 (TreeAge Software, Williamstown, MA). The study was approved by the University of Alabama Birmingham Institutional Review Board as within the scope of the primary trial (SCORE) IRB approval.

2.4. Assumptions

Our model relies on several assumptions in addition to those already mentioned. First, we assumed the procedure-related complication rate was equal between salpingectomy and BTL groups, based on the SCORE trial data and a PUBMED search yielding no conclusive evidence that complication rates (including diminished long-term ovarian reserve) differ between salpingectomy and BTL [7,14,39–41]. Second, we assumed that patients not experiencing unintended pregnancy or ovarian cancer would have perfect health between the time of cesarean and onset of diagnosis. This assumption stands on the understanding that life should not be appreciably different for a given woman after one procedure compared to the other procedure. For patients experiencing an

unintended pregnancy, the detriment to their health state was calculated over a single year, at which time the health state utility would return to baseline. Third, we assumed that the utility for death was 0. Lastly, we assumed that a perfect health state utility was equal to 1. This assumption is built the understanding that non-cancer disutility over time (age-related health changes) will be equally distributed between branches in the healthy proportion of our modeled population. But assuming a perfect health state over the decades of additional life span in this patient population might lead to overestimating the benefit of ovarian cancer risk reduction [42]. We viewed this assumption as necessary since most estimates of cancer-related disutility in the literature (and thus, in our model) are compared to a perfect health state, not an age-related health state. To account for the possibility that the original model overestimated the benefit of ovarian cancer risk reduction, we performed post-hoc sensitivity analyses to explore declining non-cancer health states using three age-related disutility principles based on United State index population norms by age group [43].

3. Results

3.1. Base-case analysis

The results of the base case analysis are seen in Table 3. Opportunistic salpingectomy at the time of cesarean for patients desiring sterilization was cost-effective with an ICER of $26,616 per QALY based on an incremental cost of $471.96 for 0.0018 additional QALYs. In a population of 10,000 women undergoing sterilization at the time of cesarean, a salpingectomy strategy resulted in 17 fewer ovarian cancer cases, 13 fewer ovarian cancer deaths, and 25 fewer unintended pregnancies compared to a strategy of BTL (204 fewer cases, 156 fewer deaths, and 300 fewer unintended pregnancies annually in a population of 120,000) (Table 4). This reduction was associated with a cost increase of $4.7 million, which is the total of $8.3 million additional in procedure costs at the time of cesarean minus the cost savings attributable to reduced cancer incidence ($3.3 million) and decreased unintended pregnancy ($0.3 million). If adopting a strategy of opportunistic salpingectomy instead of BTL, the cost per prevented case of ovarian cancer, cost per prevented ovarian cancer death, and cost per prevented unintended pregnancy would be $277,624, $363,046, and $188,784, respectively.

3.2. Sensitivity analyses

One-way sensitivity analyses of all variables demonstrated that the results of the model were sensitive to changes in ovarian cancer risk reduction estimates for both BTL (risk reduction 10% to 58%) and salpingectomy (risk reduction 27% to 83%). Varying all other model inputs across their plausible ranges did not result in a change in the base-case conclusion that salpingectomy is cost effective at a willingness-to-pay threshold of $100,000 per QALY. Notably, the conclusion that salpingectomy is cost-effective was true across the entire range of cost differences between salpingectomy and BTL up to the pre-defined high estimate of $2472 (200% of the base-case estimate). Only in a post-hoc threshold analysis, ranging the incremental cost of salpingectomy up past our pre-defined threshold, did we find that the cost of salpingectomy would have to be >$3163.74 greater than BTL to be considered not cost-effective. Similarly, procedural success as low as 50% did not change the conclusion that salpingectomy is cost-effective.

In our primary model, assuming no age-related utility decrement, the ICER for SPG versus BTL was $26,616.56 per QALY. In the first alternative model accounting for age-related utility decrements, and assuming the minimal value between cancer-related and age-related norms for a given health state, the ICER for SPG versus BTL was $32,831.03 per QALY. In the second alternative model accounting for age-related utility decrements, assuming the multiplicative value of cancer-related

Table 3
Base case incremental cost-effectiveness.

Strategy	Cost ($)	Incremental cost ($)	Effectiveness (QALY)	Incremental effectiveness (QALY)	Incremental cost effectiveness ($/QALY)
BTL	1904.92	–	45.909	–	–
Salpingectomy	2376.88	471.96	45.927	0.0177	26,616.56

Costs in 2017 US dollars ($).

utility and age-related utility, the ICER for SPG versus BTL was $29,473.97.

Threshold analyses of variables to which the model was sensitive showed that salpingectomy was no longer cost-effective when the ovarian cancer risk reduction from salpingectomy dropped below 41% or when ovarian cancer risk reduction from BTL was >46.2% (compared to base-case estimates of 54% for salpingectomy and 34% for BTL). To account for broad variation in ovarian cancer risk reduction estimates, a two-way sensitivity analysis of these variables was performed (Fig. 1). A strategy of salpingectomy was no longer cost-effective when, in combination, ovarian cancer risk reduction from salpingectomy was considerably lower and ovarian cancer risk reduction from BTL was higher than the base-case estimate. In contrast, at higher estimates of risk reduction from salpingectomy and lower estimates of risk reduction from BTL, a strategy of salpingectomy was cost-saving.

A strategy of salpingectomy was cost-saving under several conditions: [1] when ovarian cancer risk reduction with salpingectomy was >81.6%, [2] when the additional cost associated with salpingectomy versus BTL was <$538.80, or [3] when the procedural success of BTL was <80.7% (compared to a base-case estimate of 95% success for BTL and in comparison to the observed 67.5% procedural success of salpingectomy) [14].

In probabilistic sensitivity analyses (Fig. 2), salpingectomy was cost-effective at a willingness-to-pay of $100,000 per QALY in 75.5% of Monte Carlo simulations. At a more restrictive willingness-to-pay threshold of $50,000 per QALY, salpingectomy was cost-effective in 64.4% of simulations. Additionally, salpingectomy was cost-saving in 18.7% of simulations.

4. Comment

Our model shows that opportunistic salpingectomy as compared to BTL at the time of cesarean delivery is almost always the most cost-effective strategy for ovarian cancer risk reduction when considering a wide range of assumptions, variables, and willing-to-pay thresholds. Furthermore, a policy of opportunistic salpingectomy at the time of cesarean delivery would decrease the number of ovarian cancer cases, ovarian cancer deaths, and decrease unintended pregnancies. As long as the additional cost of salpingectomy compared to BTL was < $3163.74 (much higher than probable), or if the ovarian cancer risk reduction of salpingectomy is >41% (relative to base case BTL risk reduction of 34%), or if ovarian cancer reduction with BTL is <46% (relative to base case risk reduction of 54% for salpingectomy), salpingectomy remains cost-effective. Even when the procedural success rate of salpingectomy is as low as 50%, it still remains cost-effective. In addition, under multiple plausible assumptions, salpingectomy is actually cost-saving.

This study, one of the first to evaluate salpingectomy at cesarean delivery, supports prior work evaluating the cost-effectiveness of salpingectomy, albeit at the time of routine benign gynecologic surgery [10,11]. In a 2015 cost-effectiveness analysis based on Canadian health systems data, Kwon et al. demonstrated that opportunistic salpingectomy at the time of hysterectomy was cost-saving, while salpingectomy at the time of permanent sterilization was cost-effective based on the degree of ovarian cancer risk-reduction [10]. Using data from the United States, Dilley et al. similarly demonstrated that salpingectomy at hysterectomy was cost-savings (23.9 million health care dollars saved), while salpingectomy at the time of permanent sterilization (laparoscopic) was cost effective with an ICER of $31,423/QALY compared to BTL [11]. Furthermore, Dilley et al. noted that salpingectomy at permanent sterilization remained cost-effective as long as its associated ovarian cancer risk reduction was at least 54%, and in probabilistic sensitivity analyses, was cost-effective in 55% of Monte Carlo trials [11]. Our model provides stronger evidence of the cost-effectiveness of salpingectomy compared to BTL at the time of cesarean delivery, with an ICER of $26,616/QALY, cost-effectiveness persisting as long as the associated risk-reduction of salpingectomy is >41%, and in 75% of simulations demonstrating cost-effectiveness.

As with all decision models, the validity of the results is directly related to the validity of the inputs. Sensitivity analyses are used to account for the uncertainty in these variables, and help to assess the validity and robustness of the model. Specifically, the true ovarian cancer risk reduction associated with salpingectomy and BTL, particularly at the time of cesarean is not known and is estimated from large population-based epidemiologic literature. This is due in part to the fact that ovarian cancer often develops decades after the average age of sterilization. Our model used sensitivity analysis to account for the intentionally-wide ranges of reported reductions in ovarian cancer risk after salpingectomy and BTL (Fig. 1). We have shown, across wide plausible ranges of ovarian cancer risk reduction, that salpingectomy is likely cost-effective or even cost-saving; however, we do acknowledge that are results are limited by the lack of knowledge regarding the absolute risk-reductions of these procedures.

There is also limited available information regarding the absolute procedural risks/operative complications (transfusion, re-operation, drop in hemoglobin) associated with salpingectomy and BTL. Our randomized trial, though small in size, showed no difference in procedural risks/operative complications (composite complication rate 20% vs. 12.5%, $p = 0.36$) between the salpingectomy and BTL groups [14]. This is supported by data from other studies, as Shinar, Ganer Herman, Powell, Danis, and Garcia et al., have all independently demonstrated no increased risk of short-term complications including postoperative complications, estimated blood loss, or changes in ovarian reserve between salpingectomy and BTL performed at cesarean delivery [39–41,44,45]. Likewise, in larger studies of opportunistic salpingectomy at the time of abdominal and laparoscopic hysterectomy, there appears to be no clear safety concern in performing salpingectomy or concerns about long-term ovarian reserve [7,40,46]. While we also

Table 4
Cost-benefit analysis in a population of 10,000.

Strategy	Cancer cases[a]	Cancer deaths[a]	Unintended pregnancies[a]	Procedure costs	Cancer costs	Pregnancy costs	Total costs
BTL	86	65	171	$0	$16,905,556	$2,143,664	$19,049,220
Salpingectomy	69	52	146	$8,343,000	$13,588,210	$1,837,610	$23,768,820

Costs in 2017 US dollars ($).
[a] Population of 10,000 (given a potential for 120,000 sterilizations yearly, real-life yearly rates would be multiplied by 12).
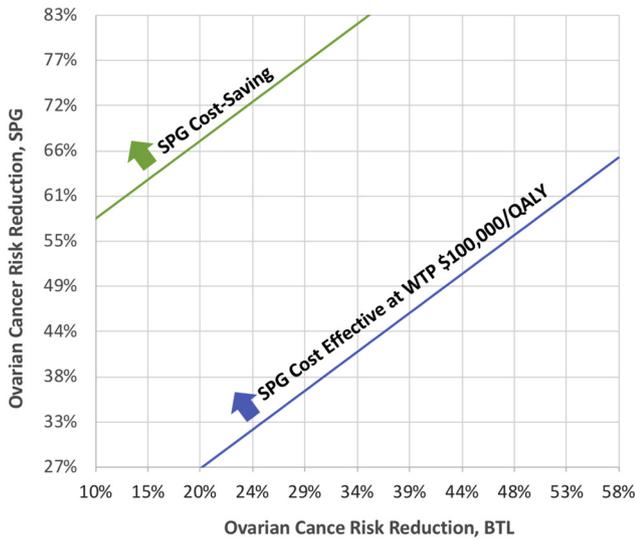
Fig. 1. Two-way sensitivity analysis of ovarian cancer risk reduction estimates for salpingectomy and bilateral tubal ligation. Legend: Blue line signifies the threshold of cost-effectiveness at a willingness-to-pay of $100,000 per QALY. Combinations of input variables below and to the right of the blue line denote circumstances in which salpingectomy is not cost-effective. Green line signifies the threshold of cost-savings. Combinations of input variables above and to the left of the green line denote circumstances in which salpingectomy is cost-saving. Between the blue and green line, salpingectomy is cost-effective.

acknowledge the potential long-term impacts of salpingectomy compared to tubal ligation (e.g. heart disease risk, other cancers, bone health) are unknown and not considered in our modeling, concerns about immediate procedural complications of salpingectomy or ovarian reserve do not appear to be supported by data. Therefore, we feel confident in our assumption that complications would not greatly differ between the opportunistic salpingectomy strategy and the bilateral tubal ligation strategy.

Another limitation for our study is that modeling cannot possibly capture the complexity of real world situations (such as rare ovarian cancer histotypes). Despite this, our conclusions are supported by a robust series of sensitivity analyses in which our assumptions,
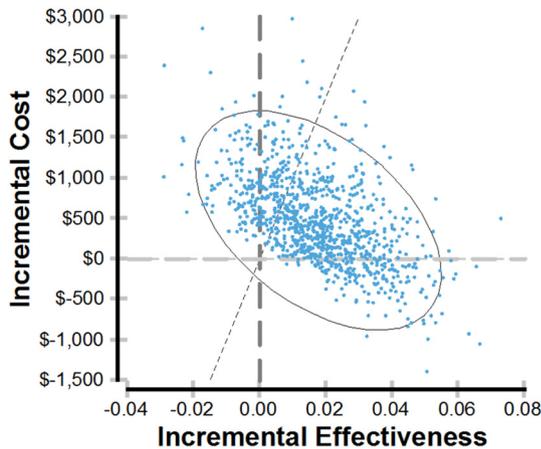
probabilities, and costs could be explored over wide variable ranges. Thus, we were able to evaluate a scenario in our large tertiary care institution and apply findings to a variety of scenarios utilizing sensitivity analysis modeling.

One additional limitation is the imprecise estimated cost difference between salpingectomy and BTL (>$1200). This additional cost of salpingectomy is likely exaggerated for any real estimate of cost as it reflects billing data for an additional block of time in the operating room as opposed to true minute-by-minute cost data. Operative room costs are difficult to measure on a minute-by-minute scale, and the downstream consequences of prolonged cases on the overall flow and cost of running a labor and delivery unit are difficult to predict [47]. As such, we intentionally used higher-than-likely estimates of cost differences between salpingectomy and BTL to explore whether the cost increase associated with the salpingectomy procedure would, over the course of thousands of procedures overwhelm the cost-savings of preventing unintended pregnancies and preventing ovarian cancer. Our modeling demonstrates that, despite a large cost associated with the procedure itself, a strategy of salpingectomy is still cost-effective. While future studies could be developed to study this true cost, even in this extreme condition of salpingectomy cost, salpingectomy remains cost-effective under most assumptions and in most circumstances. Moreover, our model suggests that if the additional cost of salpingectomy is, very plausibly, less than $538 the strategy is likely to save costs to the health care system in comparison to BTL.

In conclusion, we have previously shown that salpingectomy in lieu of BTL at the time of cesarean delivery is feasible, and this practice is on the rise both in the United States and globally [41,48]. Thus, evaluating the cost-effectiveness of this strategy is necessary. In women undergoing cesarean with permanent sterilization, opportunistic salpingectomy is almost always cost-effective, and can even be cost-saving, in comparison to BTL for ovarian cancer risk reduction. To refine the true health care costs benefits of opportunistic salpingectomy, future studies should be aimed at evaluating the true risk reduction of both of these sterilization procedures, the absolute costs of salpingectomy and BTL, as well as other techniques such as electrothermal devices that may shorten operative time and costs of the opportunistic salpingectomy procedure. However, based on our model, opportunistic salpingectomy can be considered as a cost-effective primary method for surgical sterilization during cesarean delivery in women with undesired fertility.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.11.009.

Conflict of interest

The authors have no conflicts of interest to disclose.

Author contribution

Akila Subramaniam was involved in design and execution of the primary trial as well as design and conduct of this secondary analysis. Involved in all aspects of the study protocol and performance.

Brett Einerson was the primary analyst for the cost analysis. Involved in all aspects of this cost analysis conduct.

Christina Blanchard was involved in trial design and statistical analysis of primary trial as well as design and conduct of this secondary analysis. Involved in all statistical aspects of the study protocol and performance.

Britt Erickson was involved in design and execution of the primary trial as well as design and conduct of this secondary analysis. Involved in all aspects of the study protocol and performance.

Jeff Szychowski was involved in trial design and statistical analysis of primary trial as well as design and conduct of this secondary analysis. Involved in all statistical aspects of the study protocol and performance.

Fig. 2. Results of the probabilistic sensitivity analysis. Legend: Each blue dot is plotted as the result of a single simulation among 10,000 simulations in probabilistic sensitivity analysis. The black dashed diagonal line is the threshold for cost-effectiveness at a willingness-to-pay of $100,000 per QALY. Dots below and to the right of the diagonal line signify simulations in which salpingectomy was cost-effective. The solid black line forming a circle is the 95% confidence ellipse in which 95% of simulations are expected to result.

CRediT authorship contribution statement

Akila Subramaniam: Conceptualization, Data curation, Formal analysis, Project administration, Supervision, Writing - original draft, Writing - review & editing. **Brett D. Einerson:** Data curation, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Christina T. Blanchard:** Data curation, Methodology, Project administration, Software, Validation. **Britt K. Erickson:** Conceptualization, Investigation, Methodology. **Jeff Szychowski:** Data curation, Methodology, Project administration, Software, Validation. **Charles A. Leath:** IIIConceptualization, Data curation, Formal analysis, Project administration, Supervision, Writing - original draft, Writing - review & editing. **Joseph R. Biggio:** Conceptualization, Data curation, Formal analysis, Project administration, Supervision, Writing - original draft, Writing - review & editing. **Warner K. Huh:** Conceptualization, Data curation, Formal analysis, Project administration, Supervision, Writing - original draft, Writing - review & editing.

References

[1] American Cancer Society, Ovarian cancer, Available at: http://www.cancer.org/cancer/ovariancancer/detailedguide/ovarian-cancer-key-statistics, Accessed date: 25 September 2017.

[2] K.A. Lowe, V.M. Chia, A. Taylor, C. O'Malley, et al., An international assessment of ovarian cancer incidence and mortality, Gynecol. Oncol. 130 (2013) 107–114.

[3] R.J. Kurman, I. Shih, The origin and pathogenesis of epithelial ovarian cancer: a proposed unifying theory, Am. J. Surg. Pathol. 34 (2010) 433–443.

[4] B.K. Erickson, M.G. Conner, C.N. Landen Jr., The role of the fallopian tube in the origin of ovarian cancer, Am. J. Obstet. Gynecol. 209 (2013) 409–414.

[5] C.P. Crum, Intercepting pelvic cancer in the distal fallopian tube: theories and realities, Mol. Oncol. 3 (2009) 165–170.

[6] D.W. Kindelberger, Y. Lee, A. Miron, M.S. Hirsch, et al., Intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: evidence for a causal relationship, Am. J. Surg. Pathol. 31 (2007) 161–169.

[7] S.E. Dilley, J.M. Straughn Jr., C.A. Leath III, The evolution of and evidence for opportunistic salpingectomy, Obstet. Gynecol. 130 (2017) 814–824.

[8] J.L. Walker, C.B. Powell, L. Chen, J. Carter, et al., Society of Gynecology Oncology recommendations for the prevention of ovarian cancer, Cancer 121 (2015) 2108–2120.

[9] Committee on Gynecologic Practice, Committee opinion no. 620: salpingectomy for ovarian cancer prevention, Obstet. Gynecol. 125 (1) (2015) 279–281.

[10] J.S. Kwon, J.N. McAlpine, G.E. Hanley, S.J. Finlayson, et al., Costs and benefits of opportunistic salpingectomy as an ovarian cancer prevention strategy, Obstet. Gynecol. 125 (2015) 338–345.

[11] S.E. Dilley, L.J. Havrilesky, J. Bakkum-Gamez, D. Cohn, et al., Cost-effectiveness of opportunistic salpingectomy for ovarian cancer prevention, Gynecol. Oncol. 146 (2) (2017) 373–379.

[12] B.E. Hamilton, J.A. Martin, M.J. Osterman, Births: preliminary data for 2015, Natl. Vital Stat. Rep. 65 (3) (2016) 1–14.

[13] L.M. Chan, Westhoff Cl, Tubal sterilization trends in the United States, Fertil. Steril. 94 (2010) 1–6.

[14] A. Subramaniam, C.T. Blanchard, B.K. Erickson, J. Szychowski, et al., Feasibility of complete salpingectomy compared with standard postpartum tubal ligation at cesarean delivery: a randomized controlled trial, Obstet. Gynecol. 132 (1) (2018) 20–27.

[15] K.D. Kochanek, S.L. Murphy, J.Q. Xu, E. Arias, Mortality in the United States, NCHS Data Brief, no 293, , National Center for Health Statistics, Hyattsville MD, 2016 2017.

[16] H.B. Peterson, Z. Xia, J.M. Hughes, L.S. Wilcox, L.R. Tylor, J. Trussell, The risk of pregnancy after tubal sterilization: findings from the U.S. collaborative review of sterilization, Am. J. Obstet. Gynecol. 174 (4) (1996) 1161–1168.

[17] M.D. Creinin, N. Zite, Female Tubal Sterilization, Obstet. Gynecol. 124 (3) (2014) 596–599.

[18] SEER stat fact sheets: ovary cancer, Available at: http://seer.cancer.gov/statfacts/html/ovary.html, Accessed date: 30 July 2017.

[19] H. Falconer, L. Yin, H. Grönberg, D. Altman, Ovarian cancer risk after salpingectomy: a nationwide population-based study, J. Natl. Cancer Inst. 107 (2) (2015) dju410.

[20] C. Madsen, L. Baandrup, C. Dehlendorff, S.K. Kjaer, Tubal ligation and salpingectomy and the risk of epithelial ovarian cancer and borderline ovarian tumors: a nationwide case-control study, Acta Obstet. Gynecol. Scand. 94 (1) (2014) 86–94.

[21] D. Cibula, M. Widschwendter, O. Majek, L. Dusek, Tubal ligation and the risk of ovarian cancer: review and meta-analysis, Hum. Reprod. Update 17 (1) (2010) 55–67.

[22] M.S. Rice, M.A. Murphy, A.F. Vitonis, et al., Tubal ligation, hysterectomy and epithelial ovarian cancer in the New England case-control study, Int. J. Cancer 133 (10) (2013) 2415–2421.

[23] M.S. Rice, S.E. Hankinson, S.S. Tworoger, Tubal ligation, hysterectomy, unilateral oophorectomy, and risk of ovarian cancer in the nurses' health studies, Fertil. Steril. 102 (1) (2014) 192–193.

[24] E.B. Schwarz, R. Smith, J. Steinauer, M.F. Reeves, A.B. Caughey, Measuring the effects of unintended pregnancy on women's quality of life, Contraception 78 (3) (2008) 204–210.

[25] F.A. Sonnenberg, R.T. Burkman, C.G. Hagerty, L. Speroff, T. Speroff, Costs and net health effects of contraceptive methods, Contraception 69 (6) (2004) 447–459.

[26] A. Gariepy, E.B. Schwarz, L. Lundsberg, Quantifying the effects of unintended pregnancy on quality of life, Contraception 94 (4) (2016) 433.

[27] K.J. Smith, J. Tsevat, R.B. Ness, H.C. Wiesenfeld, M.S. Roberts, Quality of life utilities for pelvic inflammatory disease health states, Sex. Transm. Dis. 35 (3) (2008) 307–311.

[28] L.J. Havrilesky, G. Broadwater, D.M. Davis, et al., Determination of quality of life-related utilities for health states relevant to ovarian cancer diagnosis and treatment, Gynecol. Oncol. 113 (2) (2009) 216–220.

[29] A. Sonfield, K. Kost, R.B. Gold, L.B. Finer, The public costs of births resulting from unintended pregnancies: national and state-level estimates, Perspect. Sex. Reprod. Health 43 (2) (2011) 94–102.

[30] G. Amaral, D.G. Foster, M.A. Biggs, C.B. Jasik, S. Judd, C.D. Brindis, Public savings from the prevention of unintended pregnancy: a cost analysis of family planning services in California, Health Serv. Res. 42 (5) (2007) 1960–1980.

[31] F. Lecuru, F. Robin, S. Chasset, F. Leonard, S. Guitti, R. Taurelle, Direct cost of single dose methotrexate for unruptured ectopic pregnancy. Prospective comparison with laparoscopy, Eur. J. Obstet. Gynecol. Reprod. Biol. 88 (1) (2000) 1–6.

[32] B.W. Mol, P.J. Hajenius, S. Engelsbel, et al., Treatment of tubal pregnancy in the Netherlands: an economic comparison of systemic methotrexate administration and laparoscopic salpingostomy, Am. J. Obstet. Gynecol. 181 (4) (1999) 945–951.

[33] M.C. Sowter, C.M. Farquhar, G. Gudex, An economic evaluation of single dose systemic methotrexate and laparoscopic surgery for the treatment of unruptured ectopic pregnancy, BJOG 108 (2) (2001) 204–212.

[34] M.D. Creinin, A.E. Washington, Cost of ectopic pregnancy management: surgery versus methotrexate, Fertil. Steril. 60 (6) (1993) 963–969.

[35] A.S. Bercow, L. Chen, S. Chatterjee, et al., Cost of care for the initial management of ovarian cancer, Obstet. Gynecol. 130 (6) (2017) 1269–1275.

[36] A.B. Mariotto, K. Robin Yabroff, Y. Shao, E.J. Feuer, M.L. Brown, Projections of the cost of cancer care in the United States: 2010-2020, J. Natl. Cancer Inst. 103 (2) (2011) 117–128.

[37] A. Dunn, S.D. Grosse, S.H. Zuvekas, Adjusting health expenditures for inflation: a review of measures for health services research in the United States, Health Serv. Res. 30 (3) (2016) 568.

[38] P.J. Neumann, J.T. Cohen, M.C. Weinstein, Updating cost-effectiveness–the curious resilience of the $50,000-per-QALY threshold, N. Engl. J. Med. 371 (9) (2014) 796–797.

[39] S. Shinar, Y. Blecher, S. Alpern, A. Many, et al., Total bilateral salpingectomy versus partial bilateral salpingectomy for permanent sterilization during cesarean delivery, Arch. Gynecol. Obstet. 295 (5) (2017 May) 1185–1189.

[40] H. Ganer Herman, O. Gluck, R. Keidar, R. Kerner, et al., Ovarian reserve following cesarean section with salpingectomy vs. tubal ligation: a randomized trial, Am. J. Obstet. Gynecol. 217 (4) (Oct 2017) 472.e1–472.e6.

[41] C.B. Powell, A. Alabaster, S. Simmons, C. Garcia, et al., Salpingectomy for sterilization: change in practice in a large integrated health care system, 2011–2016, Obstet. Gynecol. 130 (5) (2017 Nov) 961–967.

[42] R. Ara, J.E. Brazier, Using health state utility values from the general population to approximate baselines in decision analytic models when condition-specific data are not available, Value Health 14 (4) (2011) 539–545.

[43] A. Szende, B. Janssen, J. Cabasés, Self-reported Population Health: An International Perspective Based on EQ-5D, Springer, Netherlands, 2014.

[44] R.B. Danis, C.R. Della Badia, S.D. Richard, Postpartum permanent sterilization: could bilateral salpingectomy replace bilateral tubal ligation? J. Minim. Invasive Gynecol. 23 (6) (2016 Sep-Oct) 928–932.

[45] C. Garcia, O.M. Moskowitz, C.A. Chisholm, L.R. Duska, et al., Salpingectomy compared with tubal ligation at cesarean delivery: a randomized controlled trial, Gynecol. 132 (1) (2018) 29–34.

[46] A. Darelius, M. Lycke, J.M. Kindblom, B. Kristjansdottir, et al., Efficacy of salpingectomy at hysterectomy to reduce the risk of epithelial ovarian cancer: a systematic review, BJOG 124 (6) (2017 May) 880–889.

[47] A. Macario, What does one minute of operating room time cost? J. Clin. Anesth. 22 (4) (2010 Jun) 233–236.

[48] F.L. Potz, G. Tomasch, S. Polterauer, R. Laky, et al., Incidental (prophylactic) salpingectomy at benign gynecologic surgery and cesarean section: a survey of practice in Austria, Geburtshilfe Frauenheilkd. 76 (12) (2016 Dec) 1325–1329.