

Health Evidence Review Commission (HERC)

Coverage Guidance:

Opportunistic Salpingectomy for Ovarian Cancer Prevention

Approved 11/9/2017

HERC Coverage Guidance

Opportunistic salpingectomy during gynecological procedures is recommended for coverage, without an increased payment (i.e., using a form of reference-based pricing) (*weak recommendation*).

Note: Definitions for strength of recommendation are in Appendix A. *GRADE Informed Framework Element Description*.

Table of Contents

HERC Coverage Guidance	1
Rationale for development of coverage guidances and multisector intervention reports	3
GRADE-Informed Framework	4
Should opportunistic salpingectomy be recommended for coverage for ovarian cancer risk reduction?	4
Clinical Background	7
Indications.....	7
Technology Description	7
Evidence Review	8
Darelius et al., 2017	8
Kho et al., 2017	9
Madsen et al., 2015	9
Lessard-Anderson et al., 2014	10
Falconer et al., 2015.....	10
Song, Lee, Kim, Heo, & Kim, 2016.....	11
Evidence Summary.....	11
Policy Landscape	11
Payer Coverage Policies	11
Professional Society Guidelines	12
Quality Measures	12
References	12
Evidence Sources	12
Other Citations.....	13
Appendix A. GRADE-Informed Framework Element Descriptions.....	15
Appendix B. GRADE Evidence Profile.....	17
Appendix C. Methods.....	18
Scope Statement.....	18
Search Strategy	18
Appendix D. Applicable Codes	20

Rationale for development of coverage guidances and multisector intervention reports

Coverage guidances are developed to inform coverage recommendations for public and private health plans in Oregon as plan administrators seek to improve patient experience of care, population health, and the cost-effectiveness of health care. In the era of public and private sector health system transformation, reaching these goals requires a focus on maximizing the benefits and minimizing the harms and costs of health interventions. Multisector intervention reports will be developed to address these population-based health interventions or other types of interventions that occur outside of the typical clinical setting.

HERC uses the following principles in selecting topics for its reports to guide public and private payers:

- Represents a significant burden of disease or health problem
- Represents important uncertainty with regard to effectiveness or harms
- Represents important variation or controversy in implementation or practice
- Represents high costs or significant economic impact
- Topic is of high public interest

HERC bases its reports on a review of the best available research applicable to the intervention(s) in question. For coverage guidances, which focus on clinical interventions and modes of care, evidence is evaluated using an adaptation of the GRADE methodology. For more information on coverage guidance methodology, see Appendix A.

Multisector interventions can be effective ways to prevent, treat, or manage disease at a population level. In some cases, HERC has reviewed evidence and identified effective interventions, but has not made formal coverage recommendations when these policies are implemented in settings other than traditional health care delivery systems because effectiveness may be dependent on the environment in which the intervention is implemented.

GRADE-Informed Framework

HERC develops recommendations by using the concepts of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for performing the steps involved in developing recommendations. The table below lists the elements that determine the strength of a recommendation. HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Estimates of effect are derived from the evidence presented in this document. The level of confidence in the estimate is determined by HERC based on the assessment of two independent reviewers from the Center for Evidence-based Policy. In some cases, no systematic reviews or meta-analyses encompass the most current literature. In those cases HERC may describe the additional evidence or alter the assessments of confidence in light of all available information. Such assessments are informed by clinical epidemiologists from the Center for Evidence-based Policy. Unless otherwise noted, estimated resource allocation, values and preferences, and other considerations are assessments of HERC.

Should opportunistic salpingectomy be recommended for coverage for ovarian cancer risk reduction?

Outcomes	Estimate of Effect for Outcome/ <i>Confidence in Estimate</i>	Resource Allocation	Values and Preferences	Other Considerations
Ovarian cancer incidence, morbidity, and mortality <i>(Critical outcome)</i>	Salpingectomy for any indication vs. no surgery Incidence rate of ovarian cancer 13.0 vs. 24.4 per 100,000 person-years AHR 0.65 (95% CI 0.52 to 0.81, p = .05) Bilateral salpingectomy is associated with reduced odds of epithelial ovarian cancer vs. no surgery aOR 0.58 (95% CI 0.36 to 0.95) Unilateral salpingectomy is not associated with a statistically significant reduction in the risk of epithelial ovarian cancer vs. no surgery aOR 0.90 (95% CI 0.72 to 1.12) Excisional tubal sterilization is not associated with a statistically significant reduction in the risk of ovarian cancer aOR (0.36, 95% CI 0.13 to 1.02)	Opportunistic salpingectomy would add a small to moderate cost to the overall surgical cost. However, gynecological surgeries that would be eligible for opportunistic salpingectomy are extremely common, and ovarian cancer is relatively uncommon. The cost-effectiveness of opportunistic salpingectomy is unknown given the	Women would likely strongly prefer strategies that would result in a lower risk of ovarian cancer. There would likely be low variability in this preference if there is no harm associated with the intervention.	Currently, obstetricians and gynecologists are sometimes offering salpingectomy for tubal sterilization for the potential benefits of ovarian cancer prevention. However, the entire billed claim for the sterilization procedure is often being denied in these cases, because the salpingectomy is not

Should opportunistic salpingectomy be recommended for coverage for ovarian cancer risk reduction?

Outcomes	Estimate of Effect for Outcome/ Confidence in Estimate	Resource Allocation	Values and Preferences	Other Considerations
	●○○○ (Low confidence, based on 1 retrospective cohort study and 2 case-control studies)	limited evidence demonstrating decreased ovarian cancer as well as variability in the point estimates. The prevalence of gynecological procedures compared to the infrequency of ovarian cancer would decrease the potential cost-effectiveness.		an add-on code, but rather the primary technique that is being used for the sterilization.
Ovarian function (Critical outcome)	No differences in surrogate measures of ovarian function at 3 to 6 months ●○○○ (Low confidence, based on 2 RCTs and 1 cohort study)			
Operative time (Important outcome)	No difference in operative time between hysterectomy alone and hysterectomy with salpingectomy MD 2.4 minutes (95% CI -12.5 to 17.3 minutes) ●○○○ (Low confidence, based on 4 cohort studies)			
Length of hospital stay (Important outcome)	Shorter length of stay when hysterectomy with salpingectomy is compared to hysterectomy alone MD -0.18 days (95% CI -0.27 to -0.10 days) ●○○○ (Low confidence, based on 4 cohort studies)			
Harms (Important outcome)	No differences in surgical complication rates, blood loss, reoperation, or readmission when hysterectomy with salpingectomy is compared to hysterectomy alone ●○○○ (Low confidence, based on 9 studies with mixed designs)			

Balance of benefits and harms: There is low confidence from a limited number of indirect studies that salpingectomy may result in reduced rates of epithelial ovarian cancer. There appears to be a dose-response effect: bilateral salpingectomy appears to be associated with greater cancer risk reduction benefit than unilateral salpingectomy. The evidence demonstrates no significant perioperative or short-term harms of opportunistic salpingectomy, although there is low confidence in this outcome. Long-term harms are unknown. The evidence shows a balance in favor of opportunistic salpingectomy, but it is limited by indirectness and concerns about indication and detection bias.

Should opportunistic salpingectomy be recommended for coverage for ovarian cancer risk reduction?

Outcomes	Estimate of Effect for Outcome/ <i>Confidence in Estimate</i>	Resource Allocation	Values and Preferences	Other Considerations
<p>Rationale: There is limited indirect evidence to suggest that opportunistic salpingectomy may substantially decrease the rate of ovarian cancer without short-term harms. Although promising, there is no information available about potential long-term harms, and there would be a significant cost given the prevalence of gynecological procedures. Patient preferences also drive the balance in favor of opportunistic salpingectomy. Therefore, the balance of benefits, harms, and patient preferences weigh in favor of opportunistic salpingectomy, but the evidence is too weak to support an increased reimbursement rate. Noncoverage is resulting in denials of some surgeries (i.e., tubal sterilization).</p>				
<p>Recommendation: Opportunistic salpingectomy during gynecological procedures is recommended for coverage, without an increased payment (i.e., using a form of reference-based pricing) (<i>weak recommendation</i>).</p>				

Note: GRADE-informed framework elements are described in Appendix A. A GRADE Evidence Profile is in Appendix B.

Clinical Background

Approximately 1.3% of women will be diagnosed with ovarian cancer at some point during their lifetime (National Cancer Institute [NCI], n.d.). Ovarian cancer is the fifth leading cause of cancer death among women, and 14,276 women in the United States died from ovarian cancer in 2013 (Centers for Disease Control and Prevention [CDC], 2017). The five-year survival rate for ovarian cancer is 46.5%, according to data from 2007 to 2013 (NCI, n.d.). Factors that increase the risk of ovarian cancer include being aged 40 or older, having a family history of ovarian cancer or BRCA1 or BRCA2 gene mutations; being of Eastern European or Ashkenazi Jewish ancestry; and being nulliparous (CDC, 2017). Currently, there is no effective screening test for ovarian cancer (CDC, 2017).

The most common type of ovarian cancer is epithelial ovarian cancer (EOC). The cellular origin and pathogenesis of EOC, particularly of the high-grade serous type, is the subject of ongoing research. One hypothesis posits that most high-grade serous EOCs arise from precancerous lesions of the distal fallopian tubes known as serous tubal intraepithelial carcinoma (STIC) that is associated with mutations in the p53 tumor suppressor gene (Li, Fadare, Kong, & Zheng, 2012).

Opportunistic salpingectomy is the removal of the fallopian tubes during pelvic surgery for another indication to reduce the risk of epithelial carcinoma of the fallopian tube, ovary, or peritoneum. Opportunistic salpingectomy is a relatively new strategy to prevent ovarian cancer. The traditional understanding of ovarian carcinogenesis is that the ovarian surface epithelium undergoes metaplastic changes, leading to the different histologic types of EOC. A more recent understanding of epithelial ovarian carcinogenesis is that serous, endometrioid, and clear cell carcinomas are derived from the fallopian tube and the endometrium, not directly from the ovary (American College of Obstetricians and Gynecologists, 2015).

Indications

An opportunistic salpingectomy is performed for women at average risk for ovarian cancer to reduce their ovarian cancer risk and to conserve the ovaries. The procedure is most commonly performed on women undergoing a hysterectomy for benign indications, and the procedure is also used in place of tubal ligation for women desiring sterilization. Women at high risk of ovarian cancer are typically advised to undergo salpingo-oophorectomy after completion of childbearing to reduce their risk of ovarian cancer.

Salpingectomy is an option for women who desire surgical sterilization. Compared with other tubal sterilization procedures, postpartum partial salpingectomy is among the most effective techniques for preventing unintended pregnancy (Peterson, Xia, Hughes, Wilcox, Ratliff Tylor, & Trussell, 1996).

Technology Description

Opportunistic salpingectomy involves removal of the distal one-third (fimbria and infundibulum, portion of ampulla) of both fallopian tubes, however, the entire tube can also be removed. The surgery can be completed through open, laparoscopic, robotic, or vaginal surgery.

Evidence Review

Darelius et al., 2017

This is a fair-quality systematic review of salpingectomy to reduce the risk of EOC. The review used an adapted GRADE methodology to rate the confidence in the estimates of effect. The quality of the systematic review was downgraded because the search strategy missed a small case-control study that reported on the effects of salpingectomy, thus raising a question as to the completeness of the search.

Although the initial scope of the systematic review was focused on salpingectomy at the time of hysterectomy for benign indications, because the authors identified no direct studies of opportunistic salpingectomy, they opted to include studies examining the effects of indicated salpingectomy (common indications include ectopic tubal pregnancy, hydrosalpinx, endometriosis, and pelvic inflammatory disease) on EOC risk reduction. Thus, the authors stated that the results should be interpreted as describing the effects of salpingectomy per se, as opposed to opportunistic salpingectomy at the time of gynecological or pelvic surgery for benign causes.

The review summarized the results of two large observational studies that compared the effects of indicated salpingectomy to no surgery on the risk of ovarian cancer. The authors of the systematic review assessed both studies as having a high risk of bias because of indication and detection bias, and thus rated the quality of evidence for ovarian cancer risk reduction as very low. These studies (Madsen et al., 2014; Falconer et al., 2015) and the small case-control study that was not included in the systematic review (Lessard-Anderson et al., 2014) are discussed separately below.

Three studies included in the systematic reviews (two RCTs and one cohort study) reported on measures of postoperative ovarian endocrine function after hysterectomy with opportunistic salpingectomy. Two of the studies found no statistically significant difference in anti-Müllerian hormone levels at three months after surgery. The third study compared the effects of total bilateral salpingectomy to partial bilateral salpingectomy on several hormonal and imaging-based indicators of ovarian function and found no statistically significant differences in any of the outcomes at six months. Because of concerns about small samples, short follow-up periods, and the reliance on biochemical and imaging markers of ovarian function, the systematic review authors rated the quality of evidence for ovarian function as low.

Five studies included in the systematic review (four cohort studies and one case series) reported on surgical complications for opportunistic or indicated salpingectomy. None of the included studies found statistically significant differences in the surgical complication rate, but the authors rated the quality of evidence as very low because of the use of historical controls as comparators in three of the four studies.

Six studies included in the systematic review (one RCT and five cohort studies) compared the effects on operative time of hysterectomy with or without salpingectomy. Two studies did not report the surgical approach, and the remaining three studies used different laparoscopic techniques. The single small RCT (n = 30) found no statistically significant difference in operative time (115.2 minutes for hysterectomy alone compared to 115.7 minutes for hysterectomy with salpingectomy, p = .97). In a meta-analysis of four of the five cohort studies (a fifth was excluded because of an “extreme, skewed distribution”), salpingectomy resulted in a mean difference of 2.4 minutes of added operative time (95% CI -12.5 to 17.3 minutes). The level of heterogeneity was high, and the authors rated the quality of evidence as low.

Five studies included in the systematic review (all cohort studies) compared the effects on length of stay of hysterectomy with or without salpingectomy. In a meta-analysis of four of the five cohort studies (a fifth was again excluded because of an “extreme, skewed distribution”), the mean difference in the length of stay was 0.18 days shorter when salpingectomy was added to hysterectomy (95% CI -0.27 to -0.10 days), but the authors stated that these estimates were at high risk of bias because of the use of historical controls. The authors rated the quality of evidence as very low.

Overall, the systematic review authors concluded that there is insufficient evidence on the effects of opportunistic salpingectomy on ovarian cancer risk reduction and uncertainty about the potential complications.

Kho et al., 2017

This is a good-quality systematic review of 10 studies (eight retrospective cohort studies and two RCTs) examining operative outcomes for benign hysterectomy with or without opportunistic salpingectomy. Four of the cohort studies were rated good quality, three were fair quality, and one was poor quality; one of the RCTs was rated poor quality and one was rated good quality. Some of the included studies were also included in the review by Darelius et al. (2017).

Nine of the included studies reported on operative time; seven found no differences between the groups. One study found a median increase in operative time of 16.3 minutes, and another study found a mean decrease in operative time of five minutes, but only when salpingectomy was added to total laparoscopic hysterectomy (not in conjunction with vaginal or total abdominal hysterectomy).

Nine of the included studies reported on estimated blood loss; eight found no difference in blood loss between the groups. The remaining study found less estimated blood loss in the opportunistic salpingectomy group (median of 100 mL vs. 150 mL, $p < .01$). Studies that reported on the incidence of blood transfusion or change in hemoglobin found no differences.

Nine of the included studies reported on hospital length of stay. Four of the cohort studies found shorter lengths of stay with opportunistic salpingectomy (mean reductions ranging from 0.3 to 0.43 days). The remaining studies found no statistically significant differences in the length of stay.

Surgical complications were reported in nine of the included studies. The complications included infection, fever, need for reoperation, emergency visits, readmission, and intraoperative complications. None of the included studies found these complications to be more likely when opportunistic salpingectomy was performed compared to hysterectomy alone.

Overall, the systematic review authors concluded that the addition of opportunistic salpingectomy to benign hysterectomy did not increase operative time, operative blood loss, or the rate of operative complications.

Madsen et al., 2015

This is a good-quality population registry-based case-control study assessing the effects of tubal ligation or indicated salpingectomy on the risk of ovarian cancer in women in Denmark. The study used several comprehensive population-based registries. Cases were defined as a first diagnosis of histologically verified EOC in women between the ages of 30 and 84 with no previous cancer diagnosis. Exposures were ascertained from the National Patient Register, which contains information on nearly all surgical procedures performed since 1977. For each case, 15 randomly selected, date-of-birth-matched

concurrent controls were selected. Tubal ligation was associated with reduced odds of any EOC after adjustment for age, parity, infertility, endometriosis, pelvic inflammatory disease, and hysterectomy (adjusted odds ratio [aOR] 0.87, 95% CI 0.78 to 0.98). Bilateral salpingectomy was also associated with a reduction in any EOC after adjustment for age, parity, and tubal ligation (aOR 0.58, 95% CI 0.36 to 0.95). Unilateral salpingectomy was not associated with a statistically significant reduction in the odds of any EOC after adjustment (aOR 0.90, 95% CI 0.72 to 1.12). The main limitations of this study were the low numbers of tubal ligations and salpingectomies and indication bias.

Lessard-Anderson et al., 2014

This is a fair-quality nested case-control study assessing the effect of a tubal sterilization technique on the risk of EOC in women in the Rochester Epidemiology Project. Cases were defined as women with a new diagnosis of serous EOC or primary peritoneal cancer (PPC) diagnosed between 1966 and 2009 while residing in Olmstead County. Cases were age-matched to two controls from the general population of women living in Olmstead County. Exposures were ascertained through review of operative and pathology reports; complete salpingectomy, partial salpingectomy, and distal fimbriectomy were all classified as excisional tubal sterilization. In the analysis, adjustments were made for previous hysterectomy or salpingo-oophorectomy, contraceptive use, endometriosis, infertility, and parity. There were 194 cases and 388 matched controls; 14 of the cases (7.2%) and 46 (11.9%) of the controls had undergone any tubal sterilization, and five of the cases (2.6%) and 25 of the controls (6.4%) had undergone excisional tubal sterilization. Excisional tubal sterilization reduced the adjusted odds of EOC or PPC by 64%, but the result was not statistically significant (aOR 0.36, 95% CI 0.13 to 1.02). When sensitivity analyses were performed by excluding serous borderline tumors, excluding partial salpingectomy, or both, the results remained non-statistically significant. Limitations of the study included the small sample size, changing patterns of oral contraceptive use during the studied period, and lack of information about familial cancer history.

Falconer et al., 2015

This is a good-quality population-based retrospective cohort study that assessed the effects of indicated salpingectomy on ovarian cancer risk in women in Sweden. The study relied on comprehensive nationwide registries to identify women who had undergone one of four procedures (hysterectomy, hysterectomy with bilateral salpingo-oophorectomy (BSO), salpingectomy, or tubal sterilization) and women with incident ovarian or tubal cancer (borderline tumors were excluded). Information on parity and educational attainment was also obtained from national registries. In the overall analysis with full adjustment for age, parity, and educational attainment, salpingectomy was associated with a reduced risk of ovarian cancer (adjusted hazard ratio [AHR] 0.65, 95% CI 0.52 to 0.81). By comparison, hysterectomy (AHR 0.79, 95% CI 0.70 to 0.88) and tubal sterilization (AHR 0.72, 95% CI 0.64 to 0.81) showed slightly lower risk reduction, and hysterectomy with BSO showed the greatest risk reduction (AHR 0.06, 95% CI 0.03 to 0.12). Bilateral salpingectomy (AHR 0.35, 95% CI 0.17 to 0.73) was associated with a greater risk reduction than unilateral salpingectomy (AHR 0.71, 95% CI 0.56 to 0.91), which could be interpreted as evidence of a dose-response effect. The incidence rate of ovarian cancer was 25.2 per 100,000 person-years in the unexposed group, compared to 13.0 per 100,000 person-years in the salpingectomy group. The main limitation of this study is confounding by indication; the most common reasons for salpingectomy were ectopic pregnancy (which may confer protection against ovarian cancer)

or conditions involving tubal inflammation (infection, endometriosis, and hydrosalpinx), which are thought to confer greater risk of ovarian cancer.

Song, Lee, Kim, Heo, & Kim, 2016

This is a fair-quality retrospective cohort study comparing the effects of laparoscopic myomectomy with or without opportunistic salpingectomy on operative outcomes and ovarian reserve. Overall, 45 patients had laparoscopic myomectomy with opportunistic salpingectomy and 65 patients had laparoscopic myomectomy without salpingectomy. The two groups were similar with respect to baseline characteristics. For all outcomes, including ovarian reserve (as assessed by rate of decline of anti-Müllerian hormone levels at three months), operative time, conversion to laparotomy, estimated blood loss, need for transfusion, and operative complications, there were no statistically significant differences between the two groups. The authors concluded that the addition of opportunistic salpingectomy to laparoscopic myomectomy does not result in decreased ovarian reserve or increased operative complications. The major limitations of this study stem from the small sample size, the “relatively advanced reproductive age” of most participants (average age was approximately 43 years old in both groups), and questions of generalizability because all of the procedures were performed by attending surgeons at four institutions.

Evidence Summary

There is no direct evidence that opportunistic salpingectomy at the time of gynecological or pelvic procedures for benign indications or sterilization reduces the risk of EOC. Indirect evidence from case-control and cohort studies suggests an association between salpingectomy per se and a reduced risk of EOC, but these studies are subject to indication and detection bias. However, the large effect size and the apparent dose-response relationship allow increased confidence in the estimate of effect. Most studies that have compared the addition of opportunistic salpingectomy to a gynecological or pelvic procedure without salpingectomy have not found significant differences in ovarian endocrine function, surgical complications, operative time, or length of stay.

Policy Landscape

Payer Coverage Policies

Medicaid

No coverage policy for opportunistic salpingectomy was identified for Washington’s Medicaid program. In addition, [Washington Medicaid](#) does not cover salpingectomy when performed solely for the purpose of sterilization.

Medicare

No Medicare National Coverage Determinations or Local Coverage Determinations were identified for salpingectomy.

Private Payers

Coverage policies for opportunistic salpingectomy were assessed for Aetna, Cigna, Moda, and Regence. [Aetna](#) considers opportunistic salpingectomy in low-risk women to be experimental and investigational because of insufficient evidence of its effectiveness. No coverage policy on opportunistic salpingectomy was identified for Cigna, Moda, or Regence.

Professional Society Guidelines

The American College of Obstetricians and Gynecologists (2015) guideline on *Salpingectomy for Ovarian Cancer Prevention* includes these recommendations:

- The surgeon and patient should discuss the potential benefits of removal of the fallopian tubes during a hysterectomy in women at population risk of ovarian cancer who are not having an oophorectomy.
- When counseling women about laparoscopic sterilization methods, clinicians can communicate that bilateral salpingectomy can be considered a method that provides effective contraception.

The American College of Obstetricians and Gynecologists guideline states that prophylactic salpingectomy may provide an opportunity to prevent ovarian cancer, but that randomized controlled trials are needed to support the validity of this approach.

A European Menopause and Andropause Society position statement (Perez-Lopez et al., 2017) states that opportunistic bilateral salpingectomy may prevent ovarian cancer, and the procedure should be recommended in cases of hysterectomy for benign conditions. In addition, bilateral salpingectomy should be preferred to tubal ligation for women seeking sterilization.

The *Clinical Practice Statement: Salpingectomy for Ovarian Cancer Prevention* from the Society of Gynecologic Oncology (2013) states, “For women at population risk (average) for ovarian cancer, salpingectomy should be considered (after completion of childbearing) at the time of hysterectomy, in lieu of tubal ligation, and also at the time of other pelvic surgery.”

The guidelines from the Scottish Intercollegiate Guidelines Network (2013) on *Management of Epithelial Ovarian Cancer* do not mention opportunistic salpingectomy for average-risk women.

Quality Measures

No quality measures related to salpingectomy were identified when searching the [National Quality Measures Clearinghouse](#).

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The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

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Appendix A. GRADE-Informed Framework Element Descriptions

Element	Description
Balance of benefits and harms	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. An estimate that is not statistically significant or has a confidence interval crossing a predetermined clinical decision threshold will be downgraded.
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed in the absence of likely cost offsets—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Other considerations	Other considerations include issues about the implementation and operationalization of the technology or intervention in health systems and practices within Oregon.

Strong recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the balance of benefits and harms, resource allocation, values and preferences and other factors.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the balance of benefits and harms, resource allocation, values and preferences and other factors.

Weak recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the balance of benefits and harms, resource allocation, values and preferences and other factors., but further research or additional information could lead to a different conclusion.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the balance of benefits and harms, cost and resource allocation, and values and preferences, but further research or additional information could lead to a different conclusion.

Confidence in estimate rating across studies for the intervention/outcome

Assessment of confidence in estimate includes factors such as risk of bias, precision, directness, consistency and publication bias.

High: The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.

Moderate: The subcommittee is moderately confident in the estimate of effect: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

Low: The subcommittee's confidence in the estimate of effect is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.

Very low: The subcommittee has very little confidence in the estimate of effect: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

Appendix B. GRADE Evidence Profile

Quality Assessment (Confidence in Estimate of Effect)							
No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Ovarian Cancer Incidence, Morbidity, and Mortality							
2	Observational	Moderate	Not Serious	Serious	Serious	Large effect size and apparent dose-response effect	Low ●●○○
Ovarian Function							
3	Mixed	Moderate	Serious	Not serious	Not serious		Low ●●○○
Operative Time							
4	Observational	Moderate	Not serious	Not serious	Not serious		Low ●●○○
Length of Stay							
4	Observational	Moderate	Not serious	Not serious	Not serious		Low ●●○○
Harms							
9	Mixed	Moderate	Not serious	Not serious	Not estimable		Low ●●○○

Appendix C. Methods

Scope Statement

Populations

Women at average risk of ovarian cancer who are undergoing pelvic surgery

Population scoping notes: None

Interventions

Opportunistic salpingectomy

Intervention exclusions: None

Comparators

No intervention, oral contraceptive pills

Outcomes

Critical: Ovarian cancer incidence, mortality and morbidity, ovarian function (e.g., premature menopause)

Important: Operative time and length of hospital stay, harms

Considered but not selected for the GRADE table: None

Key Questions

KQ1: What is the comparative effectiveness of an opportunistic salpingectomy for the prevention of ovarian cancer?

KQ2: How does the comparative effectiveness of opportunistic salpingectomy vary by:

- a) Age
- b) Race or ethnicity
- c) Patient history, including previous pelvic surgeries
- d) Baseline risk within an average-risk screening population (as ascertained by risk assessment tools)
- e) Type of and indication for pelvic surgery
- f) Laparoscopic versus open approach
- g) Total versus partial salpingectomy

KQ3: What are the harms of an opportunistic salpingectomy?

Search Strategy

A full search of the core sources was conducted to identify systematic reviews, meta-analyses, and technology assessments meeting the criteria for the scope described above. Searches of core sources were limited to citations published after 2012. The following core sources were searched:

Agency for Healthcare Research and Quality (AHRQ)
Blue Cross/Blue Shield Center for Clinical Effectiveness
Canadian Agency for Drugs and Technologies in Health (CADTH)
Cochrane Library (Wiley Online Library)

Institute for Clinical and Economic Review (ICER)
Medicaid Evidence-based Decisions Project (MED)
National Institute for Health and Care Excellence (NICE)
Tufts Cost-effectiveness Analysis Registry
Veterans Administration Evidence-based Synthesis Program (ESP)
Washington State Health Technology Assessment Program

A MEDLINE search was also conducted to identify systematic reviews, meta-analyses, and technology assessments, using the search term salpingectomy. The search was limited to publications in English published since 2012. In addition, a MEDLINE search was conducted for studies published after the search dates of the Darelius et al. systematic review (2017). The search was limited to publications in English published after September 2015 (the end search date for the Darelius et al. systematic review, which was judged to be the most comprehensive review on this topic).

Searches for clinical practice guidelines were limited to those published since 2012. A search for relevant clinical practice guidelines was also conducted using MEDLINE and the following sources:

Australian Government National Health and Medical Research Council (NHMRC)
Canadian Agency for Drugs and Technologies in Health (CADTH)
Centers for Disease Control and Prevention (CDC) – Community Preventive Services
National Guidelines Clearinghouse
National Institute for Health and Care Excellence (NICE)
Scottish Intercollegiate Guidelines Network (SIGN)
United States Preventive Services Task Force (USPSTF)
Veterans Administration/Department of Defense (VA/DOD) Clinical Practice Guidelines

Inclusion/Exclusion Criteria

Studies were excluded if they were not published in English, did not address the scope statement, or were study designs other than systematic reviews, meta-analyses, technology assessments, randomized controlled trials, observational studies, or clinical practice guidelines.

Appendix D. Applicable Codes

CODES	DESCRIPTION
CPT Codes	
58150	Total abdominal hysterectomy (corpus and cervix), with or without removal of tube(s), with or without removal of ovary(s);
58180	Supracervical abdominal hysterectomy (subtotal hysterectomy), with or without removal of tube(s), with or without removal of ovary(s)
58260	Vaginal hysterectomy, for uterus 250 g or less;
58262	Vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s), and/or ovary(s)
58290	Vaginal hysterectomy, for uterus greater than 250 g;
58291	Vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58541	Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less;
58542	Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58543	Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g;
58544	Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58544	Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58550	Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less;
58552	Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58553	Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g;
58661	Laparoscopy, surgical; with removal of adnexal structures (partial or total oophorectomy and/or salpingectomy)
58570	Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less;
58571	Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58572	Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g;
58573	Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58600	Ligation or transection of fallopian tube(s), abdominal or vaginal approach, unilateral or bilateral
58661	Laparoscopy, surgical; with removal of adnexal structures (partial or total oophorectomy and/or salpingectomy)
58670	Laparoscopy, surgical; with fulguration of oviducts (with or without transection)
58671	Laparoscopy, surgical; with occlusion of oviducts by device (e.g., band, clip, or Falope ring)
58700	Salpingectomy, complete or partial, unilateral or bilateral (separate procedure)
58720	Salpingo-oophorectomy, complete or partial, unilateral or bilateral (separate procedure)
58940	Oophorectomy, partial or total, unilateral or bilateral;

Note: Inclusion on this list does not guarantee coverage.