Region Västra Götaland, HTA-centrum
Regional activity-based HTA [Verksamhetsbaserad HTA]
Health Technology Assessment
HTA-report 2016:86

Does salpingectomy reduce the risk of ovarian cancer?

Darelius A, Freadrich K, Kristjansdottir B, Lycke M, Persson J, Strandell A, Sundfeldt K, Svanberg T, Kindblom JM

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Does salpingectomy reduce the risk of ovarian cancer? [Minskar salpingektomi risken för ovarialcancer?]

Darelius A[1*], Freadrich K[3], Kristjansdottir B[1], Lycke M[1], Persson J[2], Strandell A[2], Sundfeldt K[1], Svanberg T[3], Kindblom JM[2],

[1]Department of Gynecology and Obstetrics, Sahlgrenska University Hospital, Gothenburg, Sweden
[2]HTA-centrum of Region Västra Götaland, Sweden.
[3]Medical Library, Sahlgrenska University Hospital, Göteborg, Sweden

[*]Corresponding author

Published March 2016
2016:86
Suggested citation: Darelius A, Freadrich K, Kristjansdottir B, Lycke M, Persson J, Strandell A, Sundfeldt K, Svanberg T, Kindblom JM. Does salpingectomy reduce the risk of ovarian cancer? [Minskar salpingektomi risken för ovarialcancer?]. Göteborg: Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-centrum; 2016. Regional activity-based HTA 2016:86

Table of contents

1. Abstract

Background
Recent findings indicate that the Fallopian tubes are central for the development of epithelial ovarian cancer (EOC), and that the ovary is involved secondarily. This has changed the understanding of the origin of EOC. For premenopausal women at average risk of ovarian cancer, the benefits with an opportunistic oophorectomy (removal of the ovaries) at the time of hysterectomy do not outweigh the risks. However, based on the new theory of EOC origin, it has been argued that removal of the Fallopian tubes would reduce the risk of EOC.

Objective
This report evaluates if opportunistic salpingectomy in women undergoing benign hysterectomy or other abdominal gynaecological surgical procedures, reduces the incidence of ovarian cancer, affects survival, health related quality of life (HRQoL), ovarian function, duration of surgery or hospital stay.

Methods
A systematic literature search was conducted in PubMed, Embase, the Cochrane Library, and a number of HTA-databases. At least two authors independently screened titles, abstracts and full-text articles for inclusion and extracted data. The certainty of evidence was appraised according to GRADE.

Main results
Two randomised controlled studies, seven cohort studies, one case control study, one case series and one cost-effectiveness study met the inclusion criteria. No study evaluated survival or HRQoL.

Ovarian cancer: No study evaluated the risk of ovarian cancer after *opportunistic* salpingectomy. The question concerning opportunistic salpingectomy could thus not be evaluated. Two observational studies reported a reduced risk for ovarian cancer after *indicated* salpingectomy (due to tubal pathology). Both studies were hampered by serious indirectness, some study limitations and uncertain precision due to few cases of EOC. For indicated salpingectomy, it is uncertain whether there is any differences in risk of developing ovarian cancer after salpingectomy compared with no salpingectomy.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Endocrine function: Early onset of menopausal symptoms were not evaluated in any study. The evaluation of different surrogate outcomes for endocrine function did not reveal any significant difference in two small RCTs and one cohort study. There may be little or no difference in ovarian function after salpingectomy compared with no salpingectomy.
Low certainty of evidence (GRADE ⊕⊕◯◯).

Complications: Complications were reported in five studies, four cohort studies and one case series. The cohort studies had serious study limitations due to historical controls in three of four studies. It is uncertain whether there is any difference in risk of complications after salpingectomy.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Duration of surgery: One small RCT demonstrated no difference in duration of surgery, while one very large register study demonstrated 16 minutes longer duration of surgery if salpingectomy is added to hysterectomy. The addition of salpingectomy may slightly increase the duration of surgery for women who undergo hysterectomy.
Low certainty of evidence (GRADE ⊕⊕◯◯).

Hospital stay: Five cohort studies reported length of hospital stay, with historical controls as a major study limitation for three of them. It is uncertain whether there is any difference in length of hospital stay for women who undergo concomitant salpingectomy compared with only hysterectomy.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Conclusion

Opportunistic salpingectomy at the time of hysterectomy for a benign indication has not been evaluated for risk reduction of ovarian cancer. Salpingectomy by indication has been compared only with no surgery. Importantly, the risk for complications, particularly procedure-induced menopause, is insufficiently evaluated. Thus, despite a biological rationale for removal of the Fallopian tubes, benefits with the procedure have not been confirmed, and the risk of complications or adverse effects of the procedure is not yet fully elucidated. Adding salpingectomy to a hysterectomy may slightly increase the duration of surgery and the cost correspondingly.

2. Svensk sammanfattning – Swedish summary

Bakgrund
Epitelial äggstockscancer (EOC) står för 3 % av cancerincidensen bland kvinnor i västvärlden och är den gynekologiska malignitet som orsakar flest dödsfall. Sjukdomen upptäcks ofta i ett sent skede och har då dålig prognos. Nya rön gör gällande att äggledarna spelar en central roll för uppkomsten av epitelial äggstockscancer. För den mest aggressiva typen av EOC kan förstadium uppstå i själva äggledaren, medan andra typer härrör från livmoderns slemhinna, endometriet, och via äggledarna involverar äggstocken sekundärt. Kvinnor med ärftlighet och därmed hög risk för äggstockscancer genomgår ofta borttagande av äggstockarna och livmodern när de inte har önskan om bevarad fertilitet. För kvinnor med medelhög risk för äggstockscancer överväger inte fördelarna med att ta bort äggstockarna nackdelarna. Baserat på teorin om cancerns ursprung i äggledarna, har det föreslagits att borttagande av äggledarna (salpingektomi) i samband med att livmodern opereras bort (hysterektomi) skulle kunna minska risken för framtida äggstockscancer.

Frågeställning
Hos vuxna kvinnor som genomgår hysterektomi eller annat abdominellt gynekologiskt ingrepp, kan samtidig salpingektomi minska risken för äggstockscancer (inklusive borderline, tubar- och peritonealcancer), påverka överlevnad, hälsorelaterad livskvalitet, ovariefunktion, operationstid eller sjukhusvistelsens längd?

Metod
Systematisk litteratursökning gjordes i PubMed, Embase, Cochrane Library och ett antal HTA-databaser (september 2015). Minst två av författarna läste oberoende av varandra artikeltitlar, abstrakt och fulltextartiklar för inklusion av studier och för dataextraktion.

Resultat
Litteratursökningen identifierade tolv artiklar: två randomiserade kontrollerade studier (RCT), sju kohortstudier, en fall-kontrollstudie, en fallserie och en studie av kostnadseffektivitet. Ingen studie utvärderade effekten av salpingektomi för mortalitet eller livskvalitet.

Äggstockscancer: Ingen studie utvärderade opportunistisk salpingektomi (borttagande av friska äggledare) för risken för äggstockscancer. Två observationsstudier (en kohortstudie och en fall-kontrollstudie) visade reducerad risk för äggstockscancer efter indicerad salpingektomi (på grund av sjukdomstillstånd i äggledarna). Studierna hade betydande brister avseende överförbarhet och vissa brister avseende studiekvalitet och precision.
Slutsats: Det är osäkert huruvida indicerad salpingektomi resulterar i någon skillnad i risk för äggstockscancer jämfört med ingen salpingektomi.
Otillräckligt vetenskapligt underlag (GRADE ⊕◯◯◯).

Endokrin funktion: Klimakteriesymtom eller för tidigt klimakterium utvärderades inte i någon studie. Analys av olika surrogatmarkörer för äggstocksfunktion avslöjade inga signifikanta skillnader mellan grupperna i två små RCT och en liten kohortstudie.
Slutsats: Salpingektomi i samband med hysterektomi kan leda till ingen eller liten skillnad i äggstocksfunktion jämfört med enbart hysterektomi.
Begränsat vetenskapligt underlag (GRADE ⊕⊕◯◯)

Komplikationer: Fem studier rapporterade komplikationer, fyra kohortstudier och en fallserie. En begränsning i tre av fyra studier var historiska kontroller.
Slutsats: Det är osäkert om salpingektomi i samband med hysterektomi resulterar i någon skillnad avseende risk för komplikationer jämfört med enbart hysterektomi.
Otillräckligt vetenskapligt underlag (GRADE ⊕◯◯◯).

Operationstid: En liten RCT påvisade ingen skillnad i operationstid, medan en mycket stor registerstudie påvisade en ökning av operationstiden på 16 minuter när salpingektomi utfördes tillsammans med hysterektomi.
Slutsats: Salpingektomi i samband med hysterektomi kan öka operationstiden något, jämfört med enbart hysterektomi.
Begränsat vetenskapligt underlag (GRADE ⊕⊕◯◯)

Sjukhusvistelse: Fem kohortstudier rapporterade sjukhusvistelsens längd. En allvarlig brist var att historiska kontroller användes i tre av de fem studierna
Slutsats: Det är osäkert om salpingektomi i samband med hysterektomi resulterar i någon skillnad avseende längden på sjukhusvistelsen jämfört med enbart hysterektomi.
Otillräckligt vetenskapligt underlag (GRADE ⊕◯◯◯).

Sammanfattande slutsats
Ingen studie utvärderade opportunistisk salpingektomi (borttagande av friska äggledare) för risken för äggstockscancer. Två observationsstudier antyder ett samband mellan indicerad salpingektomi (borttagande av patologiska äggledare) och minskad risk för framtida äggstockscancer, men resultaten är inkonklusiva eftersom kontrollgrupperna är inadekvat valda. Komplikationsrisken vid borttagande av äggledarna, och framför allt risken för att ingreppet kan tidigarelägga klimakteriet, har inte studerats tillräckligt. Trots att det finns studier som pekar ut äggledarna som ursprung till ovarialcancer har alltså fördelar med opportunistisk salpingektomi inte kunnat slås fast, och nackdelarna är ofullständigt kartlagda. När salpingektomi utförs i tillägg till hysterektomi kan operationstiden öka något och därmed kostnaden.

The above summaries were written by representatives from the HTA-centrum. The HTA-report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The Swedish summary is a brief summary of the systematic review intended for decision makers, and is ended with a concluding summary.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 2016-02-23

Christina Bergh	Anders Larsson	Henrik Sjövall
MD, Professor	MD, PhD	MD, Professor
Elisabeth Hansson-Olofsson	Olle Nelzén	Petteri Sjögren
PhD, Senior lecturer	MD, Associate professor	DDS, PhD
Magnus Hakeberg	Christian Rylander	Maria Skogby
OD, Professor	MD, PhD	RN, PhD
Lennart Jivegård	Ola Samuelsson	Annika Strandell
MD, Senior university lecturer	MD, Associate professor	MD, Associate professor
Jenny Kindblom	Ninni Sernert	Therese Svanberg
MD, Associate professor	Associate professor	HTA-librarian

3. Summary of Findings (SoF-table)

Outcomes	Study design Number of studies	Relative effect (95%CI)	Absolute effect Mean (SD) unless otherwise stated	Certainty of evidence GRADE
Ovarian cancer	1 register cohort study 1 register case control study	aHR$_{(salpingectomy\ vs.\ no\ surgery)}$ = 0.65 (0.52-0.81) aOR $_{(salpingectomy\ vs\ no\ salpingectomy)}$ = 0.52 (0.36.0.95)	Not presented	⊕◯◯◯ Very low[1]
Endocrine function	2 RCT 1 cohort	Not presented	ΔAMH (0-3 m) intervention vs control: 1 RCT: 0.07 (0.90) vs -0.08 (1.45) 1 cohort: -0.06 (0.1) vs -0.08 (0.1)	⊕⊕◯◯ Low[2]
Complications	4 cohort studies (n= 145-43,931) 1 case series (n= 425)	Not presented	No significant difference in blood transfusion, intra-and postoperative complications, readmissions.	⊕◯◯◯ Very low[3]
Duration of surgery	1 RCT (n=30) 5 cohort studies (n=50-43,931)	Not presented	RCT no difference Range in minutes (median and mean): Intervention: 71-143 Control: 90-140 Difference between groups in the two largest studies: 13-16 min longer in salpingectomy group	⊕⊕◯◯ Low[4]
Hospital stay	5 cohort studies	Not presented	Range in days (median and mean): Intervention: 1-4.9 Control: 2-5.1	⊕◯◯◯ Very low[5]

aHR = adjusted hazard ratio, aOR= adjusted odds ratio, ΔAMH = difference in anti-müllerian hormone, RCT= randomized controlled trial

[1] Serious indirectness due to detection bias (salpingectomy compared with no surgery), some study limitations due to baseline differences between the groups, and uncertain precision due to few cases. Intervention is not opportunistic but indicated salpingectomy.

[2] The RCTs were limited by serious indirectness (young study population, small sample sizes), some study limitations (short follow up and outcome measured as surrogate markers) and uncertain precision (small sample sizes). The cohort study had serious study limitations due to historical controls.

[3] Serious study limitations, retrospective controls in 3/4 studies.

[4] RCT: Serious study limitations, baseline difference in BMI. Indirectness; young population. Very serious imprecision; no power calculation.

[5] Serious study limitations; historical controls in 3/5 studies.

Certainty of evidence

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

4. Abbreviations

AFC =	Antral Follicle Count
AMH=	Anti Müllerian Hormone
BSE=	Bilateral Salpingectomy
BSO=	Bilateral Salpingectomy Oophorectomy
EOC=	Epithelial Ovarian Cancer
E2=	Estradiol
FSH=	Follicle Stimulating Hormone
HGSC=	High Grade Serous Cancer
Hyst=	Hysterectomy
LASH=	Laparoscopic Supra Cervical Hysterectomy
LAVH=	Laparoscopic Assisted Vaginal Hysterectomy
LGSC=	Low Grade Serous Cancer
LH=	Luteinizing Hormone
STIC=	Serous Tubal Intraepithelial Carcinoma
TLH=	Total Laparoscopic Hysterectomy

5. Background

Epithelian ovarian cancer

Epithelial ovarian cancer (EOC) accounts for three percent of cancers in women in the Western World and is the gynecologic malignancy with the highest mortality. Approximately 240 000 new cases are diagnosed globally each year, and 152 000 die in the disease (Torre et al., 2015). In Sweden, 674 new cases and 538 deaths were registered during 2013 (Socialstyrelsen, 2013). Early stage EOC is highly curable, but the majority of patients are diagnosed in late stages with a poor prognosis. The current screening modalities for early detection, serum markers and transvaginal ultrasound, are associated with poor specificity and leads to unnecessary surgery (Jacobs et al., 2011, Menon et al., 2015). Despite more advanced surgery and chemotherapy the overall survival rate for women with EOC has improved only marginally in the past 50 years (5-year survival less than 50%) (Torre et al., 2015).

Change in the understanding of the pathogenesis

During the past 15 years a change in the understanding of the etiology of ovarian cancer has been suggested. EOC is not one disease but a group name of extremely heterogeneous carcinomas. EOC is at least five distinct diseases (high grade serous (HGSC), low grade serous (LGSC), endometrioid, clear cell and mucinous cancer), all with differences regarding morphology, molecular biology, intrinsic gene expression and diversity in biologic behavior (Prat, 2012). A dualistic genetic based model has been proposed to classify these neoplasms (Kurman et al 2010); Type I carcinomas (LGSC, low grade endometrioid, clear cell and mucinous carcinomas) are genetically stable, commonly exhibit different mutations (KRAS, BRAF, CTNNB1, PIK3CA, PTEN, ARID1A or PPP2RIA) from those in Type II carcinomas, are slow growing, develop from well-established precursor lesions in stepwise manner (benign-borderline-low grade cancer), and are frequently diagnosed at an early stage. In contrast, Type II carcinomas (HGSC, HG-endometrioid) are highly aggressive, with chaotic genome which almost always harbor TP53 mutations, and are usually diagnosed in a late stage. These tumors have no defined preclinical lesions in the ovaries. However, precursor lesions, called serous tubal intra epithelial carcinoma (STIC), and an early alteration in TP53 gene function happening before STIC, have been found in the epithelium of the distal fimbria of the Fallopian tube, first detected in patients with mutations in the breast cancer genes BRCA 1 or 2 (Piek et al., 2003). STIC from the tubal fimbria is supposed to implant onto the ovarian and/or peritoneal surfaces, and after an occult period will develop into fast growing HGSC. Immuno-histochemical, morphologic and molecular genetic analyses propose that EOCs are metastases (Crum et al. 2007, Karst et al. 2011, Kurman et al., 2011). Recent findings indicate that the Fallopian tube is the site of origin for most of the aggressive HGSC, and that endometrioid and clear cells carcinomas develop from the endometrium and endometriosis due to retrograde menstruation and involve the ovary secondarily (Kindelberger et al., 2007, Kurman et al., 2010, Kurman et al., 2011).

Prevention and risk factors

Development of EOC has been related to ovulation and its inflammatory process, increased age and heredity in 10-15% (BRCA1/2) (Fathalla, 1971, Ness et al., 1999). Oral contraceptive use is associated with a 40-50% lifetime risk reduction of EOC in the general population (Havrilesky et al., 2013, Beral et al., 2008). Multiparity and long lactation periods have also been considered protective against ovarian cancer (Adami et al., 1994, Jordan et al. 2012). Chronic inflammation, in pelvic inflammatory disease or endometriosis for example, contributes to the progression of ovarian cancer (Maccio, 2012, Pavone, 2015) and inflammatory diseases like salpingitis (Lin, 2011) has been shown to associate with an increased risk of EOC. Bilateral salpingo-oophorectomy (BSO) is a preventive strategy for risk reduction of ovarian cancer in women with a family history of ovarian cancer (BRCA1 or BRCA2 mutation carriers) after childbearing is completed. This procedure dramatically decreases both the incidence of, and the mortality in, EOC (Finch et al., 2014). However, oophorectomy in premenopausal women will also result in premature menopause, which confers increased risk of cardiovascular morbidity, osteoporosis (fractures), and symptoms of reduced estradiol (hot flashes, changes in sexual function). Thus, for premenopausal women without family history of ovarian cancer, the benefits do not outweigh the risks with an opportunistic oophorectomy at the time of hysterectomy for benign indication (Parker et al., 2009) and it is therefore not recommended.

Opportunistic Salpingectomy

The highly aggressive HGSC represent 75 % of all cases of ovarian cancer and is responsible for 90% of deaths in ovarian cancer (Kurman et al., 2010).Since a majority of carcinomas have precursor lesions in the Fallopian tube, salpingectomy has been hypothesized to reduce the incidence of EOS. The Fallopian tubes have no known function after the fertile period. Salpingectomy without any tubal pathology will be referred to as *opportunistic salpingectomy* throughout the present report, and salpingectomy when tubal pathology is present will be referred to as *indicated salpingectomy*.

6. Health Technology

Salpingectomy added to hysterectomy or other abdominal gynecological procedure for a benign indication

Hysterectomy is performed due to uterine pathology. Opportunistic salpingectomy at the time of hysterectomy for a benign indication is a matter of controversy and it has been argued that it should be introduced in routine health care. Salpingectomy is already well established in the routine clinical praxis in the management of other gynaecological conditions such as ectopic pregnancies and chronically or acutely affected Fallopian tubes. The procedure is simple to perform in most cases. There is a concern that salpingectomy may impair the vascular and nervous supply to the ovary, resulting in an impaired ovarian function. Special care in the surgical technique minimises this risk (Leblanc 2011).

7. Objective

Does opportunistic salpingectomy reduce the incidence of ovarian cancer (including borderline, tubal and peritoneal cancer), affect survival, health related quality of life, endocrine function, duration of surgery or hospital stay in adult women who undergo hysterectomy or any other abdominal gynecological procedure?

PICO
P= Patients, I= Intervention, C= Comparison, O=Outcome

P	Adult women
I	Salpingectomy at the time of hysterectomy or another abdominal gynecological benign surgical intervention.
C	No salpingectomy
O	Critical outcomes (for decision making) Ovarian cancer including borderline tumor, malignancy of the Fallopian tubes, peritoneal cancer Survival Important outcomes (for decision making) Endocrine function (ovarian function during fertile age and induced menopausal symptoms) after bilateral salpingectomy Complications Health related quality of life Less important outcomes (for decision making) Duration of surgery Hospital stay

8. Methods

Systematic literature search (Appendix 1)

During September 2015 two authors (TS, KF) performed systematic searches in PubMed, Embase and the Cochrane Library. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all the participants of the project group. All authors read the articles independently and decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence

The included studies, their design and patient characteristics are presented in Appendix 2. Studies evaluating salpingectomy by indication, as opposed to opportunistic salpingectomy, were included in the assessment. Appendix 2 includes information on type of salpingectomy (opportunistic or indicated) in the studies. The excluded studies and the reasons for exclusion are presented in Appendix 3. The included studies have been critically appraised using checklists modified from SBU (Swedish Council on Health Technology Assessment and Assessment of Social Services), and a checklist for assessment of case series, modified from Guo et al (2013) by HTA-centrum. However the cost-effectiveness study by Kwon et al using mathematical modelling in a hypothetical cohort, has not been appraised but is instead commented upon under Economic aspects (page 15). The results and the assessed quality of each article have been summarised per outcome in Appendix 4. A summary result per outcome and the associated certainty of evidence are presented in a Summary-of-findings table (page 9). The certainty of evidence was defined according to the GRADE system (Atkins et al, 2004; GRADE Working group).

Ongoing research

A search in Clinicaltrials.gov (2015-10-15) using variations of the words *salpingectomy, tubectomy and fallopian tube removal* identified 91 trials. Fourteen were potentially relevant for our question (page 18).

9. Results

Literature search

The literature search identified 844 articles after removal of duplicates. After reading the abstracts 815 articles were excluded. Another six articles were excluded after reading the articles in full text. The remaining 23 articles were sent to all participants of the project group, and 12 articles (two RCTs, seven cohort studies, one case-control study and one case series) and one cost-effectiveness study were finally included in the assessment (Appendix 2).

Critical outcomes

Survival

No study reported the outcome survival.

Ovarian cancer (Appendix 4.1)

No study evaluated the risk of ovarian cancer after opportunistic salpingectomy. Further, no study compared hysterectomy with and without salpingectomy. The question concerning opportunistic salpingectomy could thus not be evaluated.

Two observational studies reported a reduced risk for ovarian cancer after indicated salpingectomy (no concomitant hysterectomy). One cohort study (Falconer et al, 2015) demonstrated an adjusted hazard ratio (aHR) for EOC of 0.65 (95% CI 0.52 to 0.81) after indicated salpingectomy, compared with no surgery at all. For hysterectomy alone, compared with no surgery the aHR was 0.79 (95% CI 0.70-0.88). One case-control study (Madsen et al, 2015) compared indicated bilateral salpingectomy with no surgery. It showed an adjusted odds ratio (aOR) for EOC of 0.58 (95% CI 0.36 to 0.95). Both studies were hampered by serious indirectness (not the target population), some study

limitations due to serious detection bias (salpingectomy compared with no surgery) and baseline differences between the groups, and uncertain precision due to few cases of EOC.
Conclusion: No study evaluated opportunistic salpingectomy. The question concerning opportunistic salpingectomy could thus not be evaluated. For indicated salpingectomy, it is uncertain whether there is any difference in risk of developing ovarian cancer after salpingectomy compared with no salpingectomy. Very low certainty of evidence (GRADE ⊕◯◯◯).

Important outcomes

Endocrine function (Appendix 4.2)
Procedure-induced menopausal symptoms were not evaluated in any study. Three studies reported ovarian function as an outcome after opportunistic salpingectomy; two small RCTs (n=24 and n=30, respectively) and one cohort study. Ovarian function was evaluated by surrogate outcomes. No consistent differences were seen between the study groups. The RCTs were limited by serious indirectness due to a young study population, uncertain precision due to small sample sizes, and some study limitations such as short follow up and that endocrine function was measured as surrogate markers. The cohort study had serious study limitations due to historical controls.
Conclusion: Induced menopausal symptoms were not evaluated in any study. There may be little or no difference in endocrine function after salpingectomy compared with no salpingectomy. Low certainty of evidence (GRADE ⊕⊕◯◯).

Complications (Appendix 4:3)
Five studies reported complications as an outcome after opportunistic or indicated salpingectomy, four cohort studies and one case series. The studies had serious study limitations due to retrospective controls in three of four studies. Complication rates varied from 0 to 19% and there were no differences when the groups were compared.
Conclusion: It is uncertain whether there is any difference in risk of complications after salpingectomy. Very low certainty of evidence (GRADE ⊕◯◯◯).

Health related quality of life
No study reported HRQoL.

Less important outcomes

Hospital stay (Appendix 4.4)
Five cohort studies reported length of hospital stay after opportunistic or indicated salpingectomy. A major study limitation for three of the studies was the use of historical controls. Generally, controls without salpingectomy had longer hospital stay than patients with a concomitant salpingectomy, possibly explained by the use of historical controls.
Conclusion: It is uncertain whether there is any difference in length of hospital stay for women who undergo concomitant salpingectomy compared with only hysterectomy.
Very low certainty of evidence (GRADE ⊕◯◯◯).

Duration of surgery (Appendix 4.5)
Six studies reported duration of surgery as an outcome after opportunistic and indicated salpingectomy; one small RCT and five cohort studies.
The RCT (n=30) reported no significant difference in duration of surgery. A large cohort study (n=36 224) reported a prolonged duration of surgery by 16 minutes if concomitant salpingectomy

was performed in addition to hysterectomy. The four other cohort studies (n=50 to 540) showed no significant differences in duration of surgery between the two groups.
Conclusion: The addition of salpingectomy may slightly increase the duration of surgery for women who undergo hysterectomy.
Low certainty of evidence (GRADE ⊕⊕◯◯).

10. Ethical consequences

Opportunistic salpingectomy at hysterectomy means an extended, but not new, surgical procedure. The added procedure is the removal of the Fallopian tubes, which would otherwise be left in place. In this HTA we have examined the current evidence for opportunistic salpingectomy for risk reduction of epithelial ovarian cancer (EOC).
Research findings during the last decade indicate that the Fallopian tubes are the origin of the most aggressive type of EOC. It has also been argued that the Fallopian tubes have no known function after the childbearing period. These two statements are the rationale behind the suggestion of opportunistic salpingectomy. Opportunistic salpingectomy, ie the removal of *healthy* tubes, has not been evaluated for the prevention of EOC, although salpingectomy for *pathological* tubes compared with no surgery has indicated an associated risk reduction. Thus, there is no adequate study evaluating the effect of salpingectomy on EOC.
The risk for surgical complications associated with opportunistic salpingectomy is believed to be low, but has been insufficiently investigated. The potential risk of ovarian failure, in terms of menopausal symptoms, has not been evaluated.

The ethical problem includes the following questions:
Is the biological evidence sufficient to advocate opportunistic salpingectomy? Is the added procedure of salpingectomy harmless? As of today, the biological evidence is convincing but there is insufficient knowledge about both benefits and risks after salpingectomy. With insufficient data on risks and patient benefits associated with opportunistic salpingectomy, it is essential to recognise the need for further research. It is also important that opportunistic salpingectomy is limited to the research setting and performed only within the framework of research studies, in order to evaluate the risk-benefit balance, and to act according to new knowledge.

Considering the four medical-ethical principles *do good*, *not harm*, *autonomy*, and *fairness*, the present HTA report demonstrates that both the “do good” and “not harm” currently are impossible to evaluate due to the scarcity of evidence. The patient has a right to receive judicious and balanced information reflecting the current understanding of the evidence in order to assess the risk-benefit for herself. When the principles do good, and not harm are unknown for medical professionals, it is even more difficult for the patient to make informed decisions, and thus to practice autonomy. The principle of fairness is presently not relevant to discuss since the method needs further research. It is important to be aware that if the method is used despite insufficient evidence it could imply a possible waste of resources. Hence, there is a need for further research.

11. Organisation

Time frame for the putative introduction of opportunistic salpingectomy

Opportunistic salpingectomy would, if implemented, primarily involve women that are enrolled for hysterectomy on benign indication. Salpingectomy is already in use for gynaecological indications such as ectopic pregnancies and tubal pathologies. It is a well-established surgical method all over the world. There is no need for new equipment or additional training of the staff. Opportunistic salpingectomy has already been implemented in routine health care in a number of surgical centers in different parts of the world.

Present use in other hospitals in Region Västra Götaland

To our knowledge no hospital or surgical department in the Region Västra Götaland has implemented opportunistic salpingectomy for women who undergo hysterectomy or abdominal benign gynaecological surgery. However, in Sweden the university hospitals in Stockholm and many of the smaller hospitals near Stockholm have implemented the procedure.

Consequences for personnel

Gynaecological surgeons are already familiar with the procedure. The staff in the operating room is well acquainted with the equipment and the procedure. Hence, there is no need for any further staff training.

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland

The department of pathology would be affected if opportunistic salpingectomy was implemented, since the amount of tissue samples that would be examined after surgery would be slightly increased with two Fallopian tubes for histopathological examination. However, the analysis of the Fallopian tubes is a common, well known procedure and does not require any extra equipment for the pathology departments.

12. Economic aspects

Present cost of hysterectomy

During 2015, 256 hysterectomies were performed at the Sahlgrenska University Hospital with an estimated average cost per patient of 104,000 SEK. The annual cost was estimated to 26.6 million SEK.

Expected costs of adding salpingectomy to a hysterectomy

The estimated extra time if a salpingectomy is added to a hysterectomy is approximately 16 minutes, resulting in an extra cost of 4,800 SEK per patient. Hence, the average cost per patient for hysterectomy combined with salpingectomy was estimated to 109,000 SEK. Under the assumption that the 256 performed hysterectomies also could be combined with salpingectomy, the annual cost during 2015 could be estimated to 27.9 million SEK.

Total change of cost

The total additional cost of hysterectomy combined with salpingectomy was estimated to 4,800 SEK per patient and 1.3 million SEK per year. This is a relative increase of 5 %. The calculation of the average cost per patient includes operating theatre and material costs, surgeon, nurses, anesthesia, physician and nurse managing the anesthesia. We assumed that there would be no difference in costs between hysterectomy versus hysterectomy and salpingectomy neither regarding the post-operative care, nor for complications, and therefore these costs have not been included in the analysis.

According to Kwon et al., 2015, combining hysterectomy with salpingectomy compared with hysterectomy alone, results in a decrease of cases diagnosed with ovarian cancer with 37 per 10,000. Under the assumption that the 256 performed hysterectomies at the Sahlgrenska University Hospital also could be combined with salpingectomy, one case of ovarian cancer could be avoided each year. Except for the risk of mortality, and avoidance of pain and suffering for the patient, the Sahlgrenska University hospital could also save approximately 400,000 SEK by avoiding one case of ovarian cancer. Hence, 83 salpingectomies could be funded by avoidance of one case of ovarian cancer.

Can the new technology be adopted and used within the present budget (clinic budget/hospital budget)?

The addition of an opportunistic salpingectomy for all women who undergo a benign hysterectomy is possible within the present clinical and hospital budget, provided that the operation methods are not changed due to the added salpingectomy. Presently, approximately 30% of hysterectomies are performed via a vaginal approach, through which it is not always possible to perform a salpingectomy. If implementation of opportunistic salpingectomy would necessitate a change in operative approach to increase the possibility to remove the Fallopian tubes, the associated costs would not fit within the present budget.

Available analyses of health economy or cost advantages or disadvantages

Kwon et al., 2015, used a mathematic simulation model to estimate the costs and expected life years of opportunistic salpingectomy compared to hysterectomy alone. Salpingectomy with hysterectomy was less costly and more effective ($11,044 and 21.12 life years) compared to hysterectomy alone ($11,207 and 21.10 life years). The ovarian cancer risk reduction was estimated at 50%, which is much higher than what has been indicated by the Scandinavian register studies. The study did not include quality adjusted life years (QALY) as an outcome measure, hence even though life years were gained there was no information about the quality of life in those gained years of life.

13. Discussion

Ovarian cancer is a rare malignant disease and studies on the prevention of ovarian cancer are faced with several challenges; the need for large population samples and long follow up being some of them. The aim of the present systematic review was to analyse whether or not opportunistic salpingectomy reduces the risk of ovarian cancer and other associated outcomes.

Seventy-five percent of EOC are diagnosed at an advanced stage with poor prognosis, partly due to a long asymptomatic phase and no effective screening. In contrast, early detection of EOC, with tumour growth limited to the ovaries, is associated with a better prognosis. Despite a low lifetime risk of EOC any screening, prevention or early diagnose would probably increase survival. Since the majority of EOC are thought to have precursor lesions in the Fallopian tube, salpingectomy at the time of hysterectomy on benign indication has been suggested to reduce the risk of ovarian cancer.

This HTA-report demonstrates that there is currently no evidence that opportunistic salpingectomy reduces the risk of ovarian cancer later in life. Both observational studies, reporting an associated reduced risk of EOC after salpingectomy, compared indicated salpingectomy with no surgery. The results may therefore be confounded by detection bias. Furthermore, conditions with chronic tubal inflammation (infection, sactosalpinx, endometriosis) constitute both an indication for salpingectomy and a risk factor for EOC, and may also confound the results. There is an increasing amount of biological data indicating that the Fallopian tubes are the origin of aggressive EOC, and the Fallopian tubes probably are of no use to the woman if the uterus is removed. It is believed that a hysterectomy can lead to procedure-induced menopause (Moorman et al., 2011) and a concern that the addition of salpingectomy, due to the anatomical proximity to the ovaries, could further increase the risk of ovarian failure. So far, only short term surrogate markers for ovarian function have been investigated and no increased short term risk has been reported after salpingectomy.

Thus, despite a rationale for removal of the Fallopian tubes, benefits with the procedure have not been confirmed, and the risk of complications or adverse effects of the procedure is not yet fully elucidated. To be able to assess the risk- benefit with opportunistic salpingectomy, the risks need to be addressed and thoroughly investigated. Even a very small reduction of ovarian cancer incidence would be of benefit, due to the severity and the high mortality of the disease, if opportunistic salpingectomy in future studies is shown not to carry an increased risk of complications.

14. Future perspective

Scientific knowledge gaps

The systematic literature search did not identify any studies that have investigated opportunistic bilateral salpingectomy and the risk for ovarian cancer. Thus, opportunistic salpingectomy has not been evaluated for the prevention of ovarian cancer and therefore, this represents a major knowledge gap that needs to be addressed in further studies. Another scientific knowledge gap is whether or not opportunistic salpingectomy carries the risk to induce menopause.

Ongoing research

A search in Clinicaltrials.gov (2015-10-15) identified 91 trials, fourteen of which were potentially relevant for our question at issue (Table 1): Four RCT’s evaluated the effect of salpingectomy on Anti Müllerian Hormone (AMH) levels and two RCT’s compared salpingectomy and tubal ligation and their effect on AMH levels. Two cohort studies evaluated the effect of salpingectomy on AMH levels and one of the cohort studies evaluated whether women choose risk reducing bilateral salpingectomy or standard tubal ligation when they are enrolled for sterilisation. None of the RCTs evaluated risk reduction for ovarian cancer as a primary outcome.

Interest at the clinic/research group/organization to start studies/trials within the research field at issue

At this time point there is an interest to initiate studies for further research in the field. Two national RCT’s are planned from the Sahlgrenska University Hospital:

1. Opportunistic salpingectomy at the time of hysterectomy for a benign indication. Primary outcomes are safety aspects, defined as complication related to salpingectomy and subsequent ovarian failure, measured as menopausal symptoms and need of hormone replacement therapy. Long term outcome is ovarian cancer.
2. Salpingectomy vs tubal ligation for sterilisation. Primary outcome is ovarian function, measured both as AMH, menopausal symptoms and need of hormone replacement therapy.

Table 1 Ongoing studies relevant for our question at issue.

NCT nr	Country	Study design	Number (n)	Intervention	Primary outcome	Planned completion date
NCT02374827	USA	RCT	100	Procedure: Standard postpartum tubal ligation|Procedure:	Time to complete sterilization procedure, Total operative	2016-05-01
NCT02281487	Netherlands	RCT	100	Procedure: Hysterectomy plus Tubectomy|Procedure: Hysterectomy|Device: light microscopy	Change in Anti mullerian hormone (AMH) pre- and post operatively	2016-09-01
NCT02284711	France	RCT	80	Device: Bipolar electric energy|Device: ultrasound energy	Change in AMH levels pre- and post operatively	2017-06-01
NCT01578759	USA	RCT	30	Procedure: Salpingectomy	Change in ovarian function measured by AMH	2013-10-01
NCT01893086	Korea	RCT	68	Procedure: LH alone|Procedure: LH with opportunistic salpingectomy	Change in ovarian reserve measured by AMH	2015-12-01
NCT01888159	Sweden	RCT	100	Procedure: Bilateral Salpingectomy|Procedure: Tubal sterilization with bipolar energy	Change in AMH and follicle stimulation hormone (FSH) levels pre- and post operatively	Unknown
NCT02377128	Israel	RCT	45	Procedure: Bilateral salpingectomy|Procedure: Tubal ligation	Change in AMH levels	2016-03-01
NCT01628432	France	RCT	350	Procedure: conservative hysterectomy I|Procedure: Conservative hysterectomy II	Change in AMH levelsone year postoperatively	2017-10-01
NCT02086370	Greece	RCT	177	Procedure: Standard PBS|Procedure: Radical PBS	Ovarian reserve change measured by AMH, FSH, estradiol antral follicle count, volume and power doppler of the ovary	2015-04-01
NCT01929148	Greece	Intervention, cohort study	154	Procedure: Prophylactic bilateral salpingectomy|Procedure: Laparoscopic myomectomy without PBS	Ovarian reserve change measured by AMH, FSH, estradiol antral follicle count, volume and power doppler of the ovary	2015-11-01
NCT02165709	USA	Intervention, cohort study	50	Procedure: Salpingectomy|Procedure: Traditional sterilization	Percentage of women accepting risk reducing salpingectomy (RRS) vs standard tubal ligation	2015-09-01
NCT01782807	Israel	Intervention, cohort study	60	Procedure: Salpingectomy or Fimbriectomy	Ovarian function measured by AMH, FSH, follicle count and ultrasound	2011-10-01
NCT02086344	Greece	Intervention, cohort study	167	Procedure: PBS|Procedure: TLH _adnexal preservation	Ovarian reserve modification measured by AMH, FSH, estradiol antral follicle count, volume and power doppler of the ovary	2015-12-01
NCT01544049	USA	Observational, cohort study, descriptive study	25	Queistionare and phone interviews of women who had fallopian tubes removed as a method of ovarian cancer prevention, yearly follow up	Describe subject experience in undergoing salpingectomy as a means of risk reduction	2014-08-01

(Clinicaltrials.gov)

15. Participants in the project

The question was nominated by

Corinne Pedroletti, MD, PhD, Department of Gynecology and Obstetrics, Sahlgrenska University Hospital (SU)

Participants from the clinical departments

Anna Darelius, MD, Gynecology and Obstetrics, SU
Maria Lycke, MD, Gynecology and Obstetrics, SU
Karin Sundfeldt, MD, PhD, Professor, Gynaecology and Obstetrics, SU
Björg Kristjansdottir, MD, PhD, Gynaecology and Obstetrics, SU

Participants from the HTA-centrum

Jenny Kindblom, MD, PhD, Associate professor, HTA-centrum and Clinical Pharmacology, SU
Annika Strandell, MD, PhD, Associate professor, HTA-centrum and Gynaecology and Obstetrics, SU
Therese Svanberg, HTA librarian, HTA-centrum, Region Västra Götaland
Kirsten Freadrich, librarian, Medical library, SU, Region Västra Götaland
Josefine Persson, MSc, Health economist, HTA-centrum, Region Västra Götaland

External reviewers

Ylva Carlsson, MD, PhD, Gynecology and Obstetrics, SU
Eva Angenete, MD, PhD, Associate professor, Surgery, SU

Conflicts of interest

None declared.

Project time

HTA was accomplished during the period of 2015-08-31 – 2016-02-23
Literature searches were made in September 2015

Appendix 1, Search strategy, study selection and references

Question(s) at issue:
Does opportunistic salpingectomy reduce the incidence of ovarian cancer (including borderline, tubal and peritoneal cancer), affect survival, health related quality of life, endocrine function, duration of surgery or hospital stay in adult women who undergo hysterectomy or any other abdominal gynecological procedure?

PICO
P= Patients, I= Intervention, C= Comparison, O=Outcome

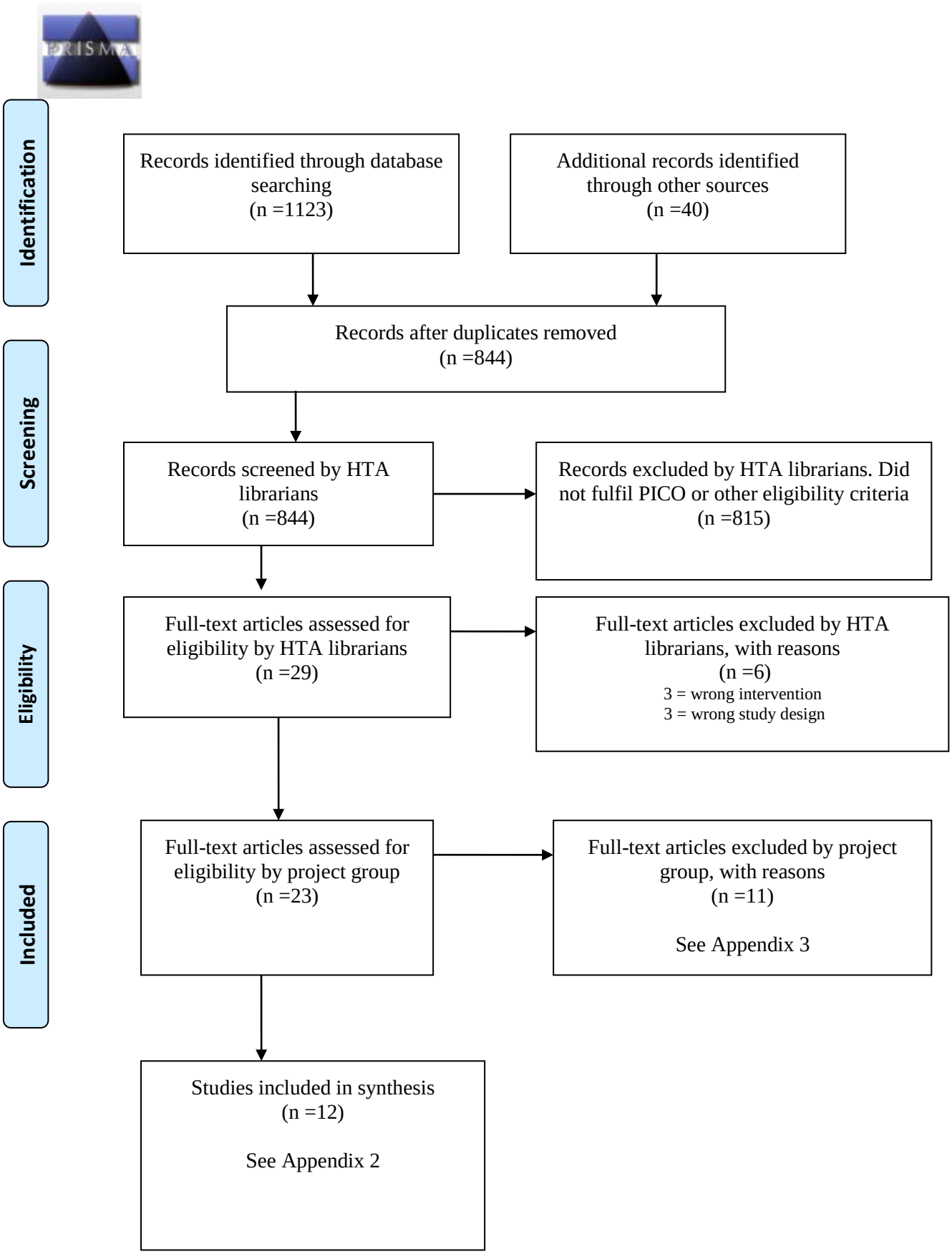
P	Adult women
I	Salpingectomy at the time of hysterectomy or another abdominal gynecological benign surgical intervention.
C	No salpingectomy
O	Critical outcomes (for decision making) Ovarian cancer including borderline tumor, malignancy of the Fallopian tubes, peritoneal cancer Survival Important outcomes (for decision making) Endocrine function (ovarian function during fertile age and induced menopausal symptoms) after bilateral salpingectomy Complications Health related quality of life Less important outcomes (for decision making) Duration of surgery Hospital stay

Eligibility criteria

Study design:
Systematic reviews
Randomized controlled trials
Non-randomized controlled studies
Case series for complications, including premature menopause. Studies regarding ovarian function together with in vitro fertilisation are not included.
No case reports or review articles

Language:
English, Swedish, Norwegian, Danish

Selection process – flow diagram



Search strategies

Database: PubMed
Date: 2015-09-03
No of results: 564

Search	Most Recent Queries	Result
#20	**Search #13 NOT #16 Filters: Danish; English; Norwegian; Swedish**	**564**
#17	Search #13 NOT #16	639
#16	Search #14 OR #15	5405283
#15	Search (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])	1422676
#14	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	4037581
#13	Search #8 AND #12	681
#12	Search #10 OR #11	4297858
#11	Search prophylactic*[tiab] OR risk[tiab] OR risks[tiab] OR reduc*[tiab] OR prevent*[tiab] OR opportunistic*[tiab]	4297850
#10	Search "Prophylactic Surgical Procedures"[Mesh]	39
#8	Search #1 OR #2 OR #7	2327
#7	Search #5 AND #6	414
#6	Search removal[tiab] OR remove[tiab]	301991
#5	Search "Fallopian Tubes"[Mesh] OR (fallopian[tiab] AND (tube[tiab] OR tubes[tiab]))	16207
#2	Search tubectom*	178
#1	Search salpingectomy[mesh] OR salpingectom*	1801

Database: EMBASE (OVID SP)
Date: 2015-09-03
No of results: 527

#	Searches	Results
1	exp salpingectomy/	2666
2	(salpingectom$ or tubectom$).ti,ab.	2048
3	(fallopian adj5 (tube or tubes)).ti,ab.	9170
4	exp uterine tube/	11704
5	(removal or remove).ti,ab.	352120
6	3 or 4	16254
7	5 and 6	433
8	1 or 2 or 7	3611
9	exp prophylactic surgical procedure/	77
10	(prophylactic$ or risk or risks or reduc$ or prevent$ or opportunistic$).ti,ab.	5290372
11	9 or 10	5290391

12	8 and 11	977
13	(animal not (animal and human)).sh.	1261620
14	12 not 13	969
15	**limit 14 to (embase and (danish or english or norwegian or swedish) and (article or conference paper or note or "review"))**	**527**

Database: The Cochrane Library
Date: 2015-09-03
No of results: 32
Cochrane reviews 10
Other reviews 0
Technology assessments 0
Economic evaluations 1
Clinical trials 21

ID	Search	Hits
#1	salpingectomy or salpingectomies:ti,ab,kw (Word variations have been searched)	84
#2	tubectomy or tubectomies:ti,ab,kw (Word variations have been searched)	3
#3	fallopian tube or fallopian tubes:ti,ab,kw (Word variations have been searched)	545
#4	removal or remove:ti,ab,kw (Word variations have been searched)	14632
#5	#3 and #4	25
#6	#1 or #2 or #5	105
#7	prophylactic* or risk or risks or reduce* or prevent* or opportunistic*:ti,ab,kw (Word variations have been searched)	259009
#8	**#6 and #7**	**32**

Reference lists
A comprehensive review of reference lists brought 40 new records

---

Reference lists

Included studies:

Berlit S, Tuschy B, Kehl S, Brade J, Sutterlin M, Hornemann A. Laparoscopic supracervical hysterectomy with concomitant bilateral salpingectomy--why not? Anticancer Res. 2013;33(6):2771-4.

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

Findley AD, Siedhoff MT, Hobbs KA, Steege JF, Carey ET, McCall CA, et al. Short-term effects of salpingectomy during laparoscopic hysterectomy on ovarian reserve: a pilot randomized controlled trial. Fertil Steril. 2013;100(6):1704-8.

Ghezzi F, Cromi A, Siesto G, Bergamini V, Zefiro F, Bolis P. Infectious morbidity after total laparoscopic hysterectomy: does concomitant salpingectomy make a difference? BJOG.

2009;116(4):589-93.

Madsen C, Baandrup L, Dehlendorff C, Kjaer SK. Tubal ligation and salpingectomy and the risk of epithelial ovarian cancer and borderline ovarian tumors: a nationwide case-control study. Acta Obstet Gynecol Scand. 2015;94(1):86-94.

McAlpine JN, Hanley GE, Woo MM, Tone AA, Rozenberg N, Swenerton KD, et al. Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention. Am J Obstet Gynecol. 2014;210(5):471.e1-11.

Minig L, Chuang L, Patrono MG, Cardenas-Rebollo JM, Garcia-Donas J. Surgical outcomes and complications of prophylactic salpingectomy at the time of benign hysterectomy in premenopausal women. J Minim Invasive Gynecol. 2015;22(4):653-7.

Morelli M, Venturella R, Mocciaro R, Di Cello A, Rania E, Lico D, et al. Prophylactic salpingectomy in premenopausal low-risk women for ovarian cancer: primum non nocere. Gynecol Oncol. 2013;129(3):448-51.

Robert M, Cenaiko D, Sepandj J, Iwanicki S. Success and Complications of Salpingectomy at the Time of Vaginal Hysterectomy. J Minim Invasive Gynecol. 2015;22(5):864-9.

Sezik M, Ozkaya O, Demir F, Sezik HT, Kaya H. Total salpingectomy during abdominal hysterectomy: effects on ovarian reserve and ovarian stromal blood flow. J Obstet Gynaecol Res. 2007;33(6):863-9.

Vorwergk J, Radosa MP, Nicolaus K, Baus N, Jimenez Cruz J, Rengsberger M, et al. Prophylactic bilateral salpingectomy (PBS) to reduce ovarian cancer risk incorporated in standard premenopausal hysterectomy: complications and re-operation rate. J Cancer Res Clin Oncol. 2014;140(5):859-65.

Cost-effectiveness analysis, no appraisal done, only commented on:

Kwon JS, McAlpine JN, Hanley GE, Finlayson SJ, Cohen T, Miller DM, et al. Costs and benefits of opportunistic salpingectomy as an ovarian cancer prevention strategy. Obstet Gynecol. 2015;125(2):338-45.

Excluded studies:

Batista CS, Osako T, Clemente EM, Batista FC, Osako MT. Observational evaluation of preoperative, intraoperative, and postoperative characteristics in 117 Brazilian women without uterine prolapse undergoing vaginal hysterectomy. Int J Womens Health. 2012;4:505-10.

Beck DH, McQuillan PJ. Fatal carbon dioxide embolism and severe haemorrhage during laparoscopic salpingectomy. Br J Anaesth. 1994;72(2):243-5.
Chan CC, Ng EH, Li CF, Ho PC. Impaired ovarian blood flow and reduced antral follicle count following laparoscopic salpingectomy for ectopic pregnancy. Hum Reprod. 2003;18(10):2175-80.

Guldberg R, Wehberg S, Skovlund CW, Mogensen O, Lidegaard O. Salpingectomy as standard at hysterectomy? A Danish cohort study, 1977-2010. BMJ Open. 2013;3(6).

Kreiger N, Sloan M, Cotterchio M, Kirsh V. The risk of breast cancer following reproductive surgery. Eur J Cancer. 1999;35(1):97-101.

Mohamed H, Maiti S, Phillips G. Laparoscopic management of ectopic pregnancy: a 5-year experience. J Obstet Gynaecol. 2002;22(4):411-4.

Nandakumar A, Anantha N, Dhar M, Ahuja V, Kumar R, Reddy S, et al. A case-control investigation on cancer of the ovary in Bangalore, India. Int J Cancer. 1995;63(3):361-5.

Oelsner G, Goldenberg M, Admon D, Pansky M, Tur-Kaspa I, Rabinovitch O, et al. Salpingectomy by operative laparoscopy and subsequent reproductive performance. Hum Reprod. 1994;9(1):83-6.

Rabban JT, Garg K, Crawford B, Chen LM, Zaloudek CJ. Early detection of high-grade tubal serous carcinoma in women at low risk for hereditary breast and ovarian cancer syndrome by systematic examination of fallopian tubes incidentally removed during benign surgery. Am J Surg Pathol. 2014;38(6):729-42.

Repasy I, Lendvai V, Koppan A, Bodis J, Koppan M. Effect of the removal of the Fallopian tube during hysterectomy on ovarian survival: the orphan ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2009;144(1):64-7.

Ross JA, Davison AZ, Sana Y, Appiah A, Johns J, Lee CT. Ovum transmigration after salpingectomy for ectopic pregnancy. Hum Reprod. 2013;28(4):937-41.

Other references:

Adami HO, Lambe M, Persson I, Ekbom A, Hsieh CC, Trichopoulos D, Leon D, Janson PO. Parity, age at first childbirth, and risk of ovarian cancer. Lancet. 1994 Nov 5;344(8932):1250-4.

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004 Jun 19;328(7454):1490-4.

Beral, V., et al., 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(9609):303-14.

Cancerincidens i Sverige 2013 - Nya diagnosticerade cancerfall år 2013 [Elektronisk resurs]. Socialstyrelsen; 2014. Hämtad från http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19613/2014-12-10.pdf

Cass I, Walts A, Karlan BY. Does risk-reducing bilateral salpingo-oophorectomy leave behind residual tube? Gynecol Oncol. 2010 Apr 30;117(1):27-31.

[Checklist from SBU regarding cohort studies. Version 2010:1]. [Internet]. [cited 2016 February 01] Available from: http://www.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/B03_Granskningsmall%20f%c3%b6r%20kohortstudier%20med%20kontrollgrupper.doc

[Checklist regarding case series modified from Guo]. [Internet]. [cited 2016 February 01] Available from: https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/Granskningsmall%20f%c3%b6r%20fallserier%202015-03-25.docx

Crum, C.P., et al. The distal fallopian tube: a new model for pelvic serous carcinogenesis. Curr Opin Obstet Gynecol. 2007. 19(1):3-9.

Fathalla, M.F. Incessant ovulation--a factor in ovarian neoplasia? Lancet. 1971. 2(7716):163.

Finch AP, Lubinski J, Møller P, Singer CF, Karlan B, Senter L, Rosen B, Maehle L, Ghadirian P, Cybulski C, Huzarski T. Impact of oophorectomy on cancer incidence and mortality in women with a BRCA1 or BRCA2 mutation. J Clin Oncol. 2014 May 20;32(15):1547-53.

GRADE Working Group. List of GRADE working group publications and grants [Internet]. [Place unknown]: GRADE Working Group, c2005-2009 [cited 2012 Mar 8]. Available from: http://www.gradeworkinggroup.org/publications/index.htm

Havrilesky LJ, Moorman PG, Lowery WJ, Gierisch JM, Coeytaux RR, Urrutia RP, Dinan M, McBroom AJ, Hasselblad V, Sanders GD, Myers ER. Oral contraceptive pills as primary prevention for ovarian cancer: a systematic review and meta-analysis. Obstet Gynecol. 2013 Jul 1;122(1):139-47.

Jacobs I, Menon U. Can ovarian cancer screening save lives? The question remains unanswered. Obstet Gynecol. 2011 Dec 1;118(6):1209-11.

Jordan SJ, Siskind V, Green AC, Whiteman DC, Webb PM. Breastfeeding and risk of epithelial ovarian cancer. Cancer Causes & Control. 2010 Jan 1;21(1):109-16.

Karst, A.M. and R. Drapkin. The new face of ovarian cancer modeling: better prospects for detection and treatment. F1000 Med Rep. 2011. 3: 22.

Kindelberger DW, Lee Y, Miron A, Hirsch MS, Feltmate C, Medeiros F, Callahan MJ, Garner EO, Gordon RW, Birch C, Berkowitz RS. Intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: evidence for a causal relationship. Am J Surg Pathol. 2007 Feb 1;31(2):161-9.

Kurman RJ, Shih IM. The Origin and pathogenesis of epithelial ovarian cancer-a proposed unifying theory. Am J Surg Pathol. 2010 Mar;34(3):433-43.

Kurman RJ, Shih IM. Molecular pathogenesis and extraovarian origin of epithelial ovarian cancer—shifting the paradigm. Hum Pathol. 2011 Jul 31;42(7):918-31.

Leblanc E, Narducci F, Farre I, Peyrat JP, Taieb S, Adenis C, Vennin P. Radical fimbriectomy: a reasonable temporary risk-reducing surgery for selected women with a germ line mutation of BRCA 1 or 2 genes? Rationale and preliminary development. Gynecol Oncol. 2011 Jun 1;121(3):472-6.

Lin, W.W. and M. Karin. A cytokine-mediated link between innate immunity, inflammation, and cancer. J Clin Invest. 2007. 117(5):1175-83

Menon U, Ryan A, Kalsi J, Gentry-Maharaj A, Dawnay A, Habib M, Apostolidou S, Singh N, Benjamin E, Burnell M, Davies S. Risk algorithm using serial biomarker measurements doubles the number of screen-detected cancers compared with a single-threshold rule in the United Kingdom Collaborative Trial of Ovarian Cancer Screening. J Clin Oncol. 2015 May 11:JCO-2014.

Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21;6(7):e1000097.

Moorman PG, Myers ER, Schildkraut JM, Iversen ES, Wang F, Warren N. Effect of hysterectomy with ovarian preservation on ovarian function. Obstet Gynecol. 2011 Dec;118(6):1271-9.

Morse AN, Schroeder CB, Magrina JF, Webb MJ, Wollan PC, Yawn BP. The risk of hydrosalpinx formation and adnexectomy following tubal ligation and subsequent hysterectomy: a historical cohort study. Am J Obstet Gynecol. 2006 May 31;194(5):1273-6.

Ness, R.B. and C. Cottreau. Possible role of ovarian epithelial inflammation in ovarian cancer. J Natl Cancer Inst. 1999. 91(17):1459-67

[Nyren, Olle. Karolinska institutet. Checklist original articles not RCT]

Maccio, A. and C. Madeddu. Inflammation and ovarian cancer. Cytokine. 2012. 58(2):133-47

Pavone ME, Lyttle BM. Endometriosis and ovarian cancer: links, risks, and challenges faced. Int J Womens Health. 2015(7):663.

Parker WH, Broder MS, Chang E, Feskanich D, Farquhar C, Liu Z, Shoupe D, Berek JS, Hankinson S, Manson JE. Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study. Obstet Gynecol. 2009 May;113(5):1027.

Piek, J.M., et al. Histopathological characteristics of BRCA1- and BRCA2-associated intraperitoneal cancer: a clinic-based study. Fam Cancer. 2003. 2(2):73-8.

Prat J. New insights into ovarian cancer pathology. Ann Oncol. 2012 Sep 1;23(suppl 10):x111-7.

Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015 Mar 1;65(2):87-108.

Salpingectomy
Appendix 2 – Characteristics of included studies

Author, Year, Country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n)	Mean age (years)	Outcome variables
Berlit 2013 Germany	Cohort[2] (historical controls)	Aug 2010 - Oct 2012	LASH alone vs LASH with BSE	Exp: 25 Unexp: 25	Exp: 49.8 Unexp: 47.6	Hospital stay Duration of surgery
Falconer 2015 Sweden	Cohort[1] Register study	1973-2009	Hyst, hyst+BSO, BSE, tubal ligation vs unexposed for any surgery	Exp: 251,465 Unexp: 5,449,119	Hyst alone: 51.2 Hyst+BSO: 63.1 BSE: 35.7 Tubal ligation: 37.9 Unexp: 35.9	Ovarian cancer
Findley 2013 USA	RCT[2]	04-09 2012	TLH vs TLH with BSE	Exp: 15 Unexp: 15	Exp: 36.6 Unexp: 37.8 All: 37.2	Duration of surgery Endocrine function/AMH
Ghezzi 2009 Italy	Cohort[2]	Mar 2005 – May 2008	TLH vs TLH with BSE	Exp: 137 Unexp: 145	Exp: 44 Unexp: 44	Complications (postoperative infections) Hospital stay Duration of surgery
Kwon 2015 Canada	Cohort Monte Carlo mathematical model					ICER
Madsen 2015 Denmark	Case-Control[1] Register study	1982-2011	Cases (ovarian cancer) , Tubal ligation and BSE vs unexposed	Exp: 16846 Unexp: 248011	not reported	Ovarian cancer
McAlpine 2014 Canada	Cohort[1,2]	2008-2011	Hyst alone vs Hyst with BSO or BSE AND BSE vs tubal ligation	Exp 1(Hyst+BSE or BSO): 12574 Exp 2 (BSE): 1569 Unexp 1 (Hyst only) : 8362 Unexp 2(Tubal ligation): 13719	All: 44.7	Complications Duration of surgery Hospital stay
Minig 2015 Spain	Cohort[2]	Oct 2010 – Jul 2014	Hyst with and without BSE	Exp: 97 Unexp: 71	Exp: 45.4 Unexp: 45.1	Hospital stay Duration of surgery Complications
Morelli 2013 Italy	Cohort[2]	Sep 2008 - Sep 2012	TLH alone vs TLH with BSE	Exp: 79 Unexp: 79	Exp: 45.8 Unexp: 46.5	Endocrine function (AMH, FSH, AFC, mean ovarian diameters)

Salpingectomy
Appendix 2 – Characteristics of included studies

Author, Year, Country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n)	Mean age (years)	Outcome variables
Robert 2015 Canada	Case series[2]	Oct 2011 – Jan 2014	Hyst (Vaginal, LAVH and abdominal) comparing successful vs unsuccessful salpingectomy	Exp: 372 Unexp: 53	Exp: 46.2 Unexp: 50.9	Complications
Sezik 2007 Turkey	RCT[2]	During 2 years, each woman followed for 6 m	Hyst with BSE vs hyst with partial BSE (leaving fimbrie)	Exp: 12 Unexp: 12	Exp: 41.6 Unexp: 41.1	Endocrine function (FSH, LH, ovarian volume, oestrogen, PI)
Vorwergk 2014 Germany	Cohort[2]	2001-2010	LAVH vs LAVH+BSE	Exp: 127 Unexp: 413	Exp: 46.42 Unexp: 46.23	Complications Duration of surgery Hospital stay

[1] Indicated salpingectomy (removal of Fallopian tubes due to tubal pathology)

[2] Opportunistic salpingectomy (removal of Fallopian tubes without tubal pathology)

Hyst= Hysterectomy
BSO= Bilateral Salpingo-Oophorectomy
BSE= Bilateral Salpingectomy
LAVH= Laparoscopic Assisted Vaginal Hysterectomy
LASH= Laparoscopic Supracervical Hysterectomy
TLH= Total Laparoscopic Hysterectomy
ICER= Incremental Cost-Effectiveness Ratio
FSH= Follicle-Stimulating Hormone
LH= Luteinizing Hormone
PI= Pulsatility Index
Exp= exposed for the intervention
Unexp: not exposed for the intervention (controls)

Appendix 3. Excluded articles

Study (author, publication year)	Reason for exclusion
Batista et al, 2012	Not correct PICO. (Complications not presented for salpingectomy separately.)
Beck et al, 1994	Not correct PICO. Case report on fatal outcome of laparoscopic salpingectomy. The complication (carbon dioxide embolism) is a known complication of the laparoscopic technique and not associated with salpingectomy.
Chan et al, 2003	Not correct PICO. (Wrong intervention)
Guldberg et al, 2013	Not correct PICO. (Salpingectomy studied as outcome)
Kreiger et al, 1999	Not correct PICO. (Wrong outcome)
Mohamed et al, 2002	Not correct PICO. (Wrong intervention and comparison)
Nandakumar et al, 1995	Not correct PICO. (Wrong intervention)
Oelsner et al, 1994	Not correct PICO. (Wrong intervention and comparison)
Rabban et al, 2014	Not correct PICO. (Case series, no complication data presented)
Repasy et al, 2009	Not correct PICO. (Wrong population)
Ross et al, 2013	Not correct PICO. (Case series, no complication data presented)

Project: Salpingectomy
Appendix 4.1
Outcome variable: Ovarian cancer

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Falconer 2015 Sweden	Cohort register study	5,483,552	n.a.	Salpingectomy aHR: 0.65 (95% CI 0.52-0.81) Hysterectomy aHR: 0.79 (0.70-0.88)	No surgery No surgery	81 cases of ovarian cancer in the salpingectomy group Women with hysterectomy and concomitant salpingectomy excluded (n=2646)	-	?	?
Madsen 2014 Denmark	Case-control register study	13,135 cases 192,896 Controls	n.a.	Bilateral salpingectomy aOR: 0.58 (0.36-0.95)	No salpingectomy	Among cases very few bilateral salpingectomies (n=17) Adjusted for age, parity and tubal ligation.	?	?	?

aHR= adjusted Hazard Ratio, aOR= adjusted Odds Ratio, n.a.= not applicable

Project: Salpingectomy
Appendix 4.2
Outcome variable: Endocrine function

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts I= Intervention, C= Controls	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Findley 2013 USA	RCT	30	**6 weeks** I: 3, C:4 **3 months** I: 2, C:1	n=15 Mean±SD **AMH baseline** (ng/ml) TLH+BSE: 2.26±2.72 **AMH 4-6 weeks** TLH+BSE: 1.03±1.04 **AMH 3 month** TLH+BSE: 1.86±1.99 **ΔAMH (baseline-3months)** TLH+BSE: . 0.07±0.90	n=15 TLH:2.25±2.57 p=0.99 TLH:1.25±2.09 p=0.76 TLH: 1.82±3.12 p=0.97 TLH:-0.08±1.45 p=0.98		?	?	-
Seziq 2007 Turkey	RCT	24	-	Total BSE Change from baseline **ΔFSH** (IU/L) 1 month: -0.6±0.2 6 months: -0.4±0.7 **ΔLH** **(**IU/L) 1 month: 0.1±0.3 6 months: 0.3±0.1 **ΔE2** (pg/mL) 1 month: 1.1±3.3 6 months: -0.5±3.2 **ΔMean ovarian volume** (cm^3) 1 month: 0.1±0.4 6 months: 0.1±0.2 **ΔPulsatility Index** 1 month: -0.15±0.18 6 months: -0.3±0.27 **ΔResistance Index** 1 month: -0.09±0.04 6 months: -0.11±0.09 **ΔS/D ratio** 1 month: -0.24±0.10 6 months: 0.13±0.3	Partial BSE -0.7±0.1 NS -0.4±0.4 NS -0.2±0.1 NS 0.2±0.1 NS -0.3±1.3 NS -3.9±2.1 NS -0.7±0.1 NS 0.3±0.1 NS -0.40±0.07 0.02 -0.68±0.03 NS -0.10±0.04 NS -0.22±0.11 NS -0.5±0.30 NS -1.10±0.40 0.07	p-values not reported	-	?	-

Project: Salpingectomy
Appendix 4.2
Outcome variable: Endocrine function

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts I= Intervention, C= Controls	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Morelli 2013 Italy	Cohort	158	-	**ΔAMH** (ng/mL) Mean ±SD TLH+BSE: -0.06±0.1 **ΔFSH** (mIU/mL) TLH+BSE: 1.3±1.1 **ΔAFC** (n) TLH+BSE: -0.27±0.6 **ΔMean ovarian diameter** (mm) TLH+BSE: -0.25±0.8	TLH: -0.08±0.1 p=0.35 TLH:1.0±0.8 p=0.15 TLH:-0.14±0.3 p=0.09 TLH:-0.19±0.6 p=0.57		+	?	+

TLH= Total Laparoscopic Hysterectomy
BSE= Bilateral Salpingectomy
AFC= Antral Follicle Count
FSH= Follicle Stimulating Hormone
LH= Luteinizing Hormone
E2= Estradiol
AMH= Anti Müllerian Hormone

Project: Salpingectomy
Appendix 4.3
Outcome variable: Complications

* + No or minor problems
? Some problems
- Major problems

Author, year Country	Study design	Number of patients n=	With drawals - dropouts	Type of complication	Results		Comment	* Directness	* Study limitations	* Precision
					Intervention	Control				
Ghezzi 2008 Italy	Cohort	282	-	Intra-op complications: Non-infectious post-op complications:	n (%) TLH+BSE: 0 TLH +BSE: 0	 TLH: 1 (0.7) p=0.49 TLH: 1 (0.7 p=0.49		+	?	+
McAlpine 2014 Canada	Cohort	43.931	Not applicable (register)	Readmission: Blood transfusion:	aOR (95%CI): Hyst+BSE: 0.91 (0.75-1.10) BSE: 0.83(0.56-1.23) Hyst+BSE: 0.86 (0.67-1.10) BSE: 0.77 (0.56-1.23)	 Hyst: p=0.347 Tubal ligation p=0.547 Hyst p=0.183 Tubal ligation p=0.36		+	?	+
Minig 2014 Spain	Cohort	168	100% follow-up	**Intraoperative:** Blood loss, mean (SD) Blood transfusion, n (%) Conversion to laparotomy, n (%) Bladder damage, n (%) **Postoperative:** Urinary tract infection, blood transfusion, scar infection, intraabdominal infection, vesico vaginal fistula, vaginal cuff dehiscence Emergency visit	 Hyst+BSE: 126.2 (100.2) Hyst+BSE: 1 (1.4) Hyst +BSE: 1 (1.4) Hyst+BSE: 2 (2.8) Hyst+BSE: 12 (12.4) Hyst+BSE: 13 (13.4)	 Hyst: 143.2(83.5) p=0.095 Hyst: 1 (1.0) p=1 Hyst: 1 (1.0) p=1 Hyst: 2 (2.1) p=1 Hyst: 8 (11.3) p=0.827 Hyst: 9 (12.7) p=0.890		+	-	-

Project: Salpingectomy
Appendix 4.3
Outcome variable: Complications

* + No or minor problems
? Some problems
- Major problems

Author, year Country	Study design	Number of patients n=	With drawals - dropouts	Type of complication	Results		Comment	* Directness	* Study limitations	* Precision
					Intervention	Control				
Robert 2015 Canada	Case series	425 (Hyst+ BSE n=372 Hyst n=53)	At 6 week follow-up: Dropouts,n(%) 39(9).		Intraoperative 4 (0.9) Emergency room visit 20 (4.7) Readmission 24 (5.6) Reoperation 13 (3.1) 15% overall complication rate, 3.8% attributable to salpingectomy		Only vaginal hyst	?	?	+
Vorwergk 2014 Germany	Cohort	540	-	Surgical complications: n (%) Urinary tract lesions, pelvic abscess, post op hemorrhage, vaginal vault dehiscence, increased wound pain, urinary tract infection, abdominal bloating	LAVH+BSE 24 (18.9%)	LAVH 73 (17.7%) p=0.79		?	-	?

Hyst= Hysterectomy
BSO= Bilateral Salpingo-Oophorectomy
BSE= Bilateral Salpingectomy
LAVH= Laparoscopic Assisted Vaginal Hysterectomy
TLH= Total Laparoscopic Hysterectomy
aOR= adjusted Odds Ratio

Project: Salpingectomy
Appendix 4.4
Outcome variable: Hospital stay

* + No or minor problems
? Some problems
- Major problems

Author year Country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Berlit 2013 Germany	Cohort (historical controls)	50	Not applicable	Mean (SD) days: LASH+BSE: 3.16 (0.37)	LASH: 3.44 (0.65) p= 0.091		-	-	?
Ghezzi 2009 Italy	Cohort (historical controls)	282	Not applicable	Median (range) days: TLH+BSE: 1 (1-6)	TLH: 2 (1-10) p=0.002		+	?	+
McAlpine 2014 Canada	Retrospective cohort	36224	Not applicable	Mean (SD) days: Hyst+BSE: 2.37 (1.9)	Hyst: 2.52 (3.0) p=0.01		+	?	+
Minig 2015 Spain	Cohort (historical controls)	168	Not applicable	Mean (SD) hours: Hyst+ BSE: 43.7 (22.4)	Hyst: 53.9 (26.5) p=0.008		+	-	-
Vorwergk 2014 Germany	Retrospective cohort	540	Not applicable	Mean (SD) days: LAVH+BSE: 4.93 (1.51)	LAVH: 5.11(1.82) p=0.31		?	-	?

Hyst= Hysterectomy
LASH= Laparoscopic Supracervical Hysterectomy
BSE= Bilateral Salpingectomy
LAVH= Laparoscopic Assisted Vaginal Hysterectomy
TLH= Total Laparoscopic Hysterectomy
BSO= Bilateral Salpingo-Oophorectomy

Project: Salpingectomy
Appendix 4.5
Outcome variable: Duration of Surgery

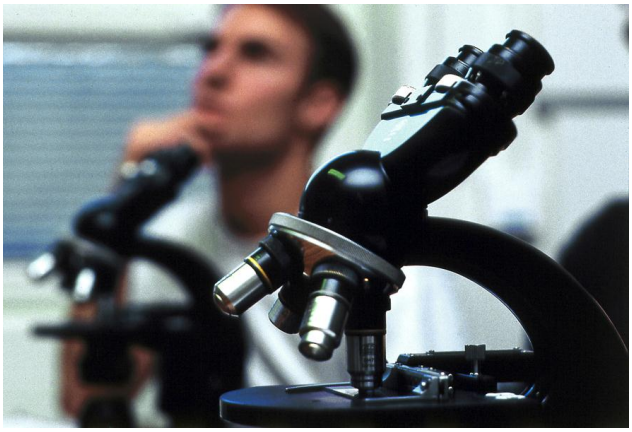
* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention	Control				
Findley 2013 USA	RCT	30	Not applicable	Mean (SD) min Hyst+BSE: 115.7 (33)	Hyst:115.2 (44) p=0.97		?	?	-
Berlit 2013 Germany	Cohort	50	Not applicable	Mean (SD) min: LASH+BSE:106.3 (46.4)	LASH: 115.3 (43.41) p= 0.233		-	-	?
Ghezzi 2009 Italy	Cohort	282	Not applicable	Median (range) min: TLH+BSE: 80 (30-245)	TLH: 90 (30-300) p=0.35		+	?	+
McAlpine 2014 Canada	Cohort	36224	Not applicable	Mean (SD) min: Hyst+BSE: 133.6 (50.1)	Hyst: 117.3 (47.7) p=<0.001	Historical controls	+	?	+
Minig 2015 Spain	Cohort	168	Not applicable	Mean (SD) min: Hyst+BSE: 87.1 (26.2)	Hyst: 94.0 (31.1) p=0.119		+/?	-	?
Vorwergk 2014 Germany	Cohort	540	Not applicable	Mean (SD) min LAVH+BSE: 143.0 (63.3)	LAVH: 139.7 (49.3) p=0.55	Historical controls	?	-	?

Hyst= Hysterectomy
BSE= Bilateral Salpingectomy
BSO= Bilateral Salpingo-Oophorectomy
LASH= Laparoscopic Supra-cervical Hysterectomy
LAVH= Laparoscopic Vaginal Hysterectomy
TLH= Total Laparoscopic Hysterectomy

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

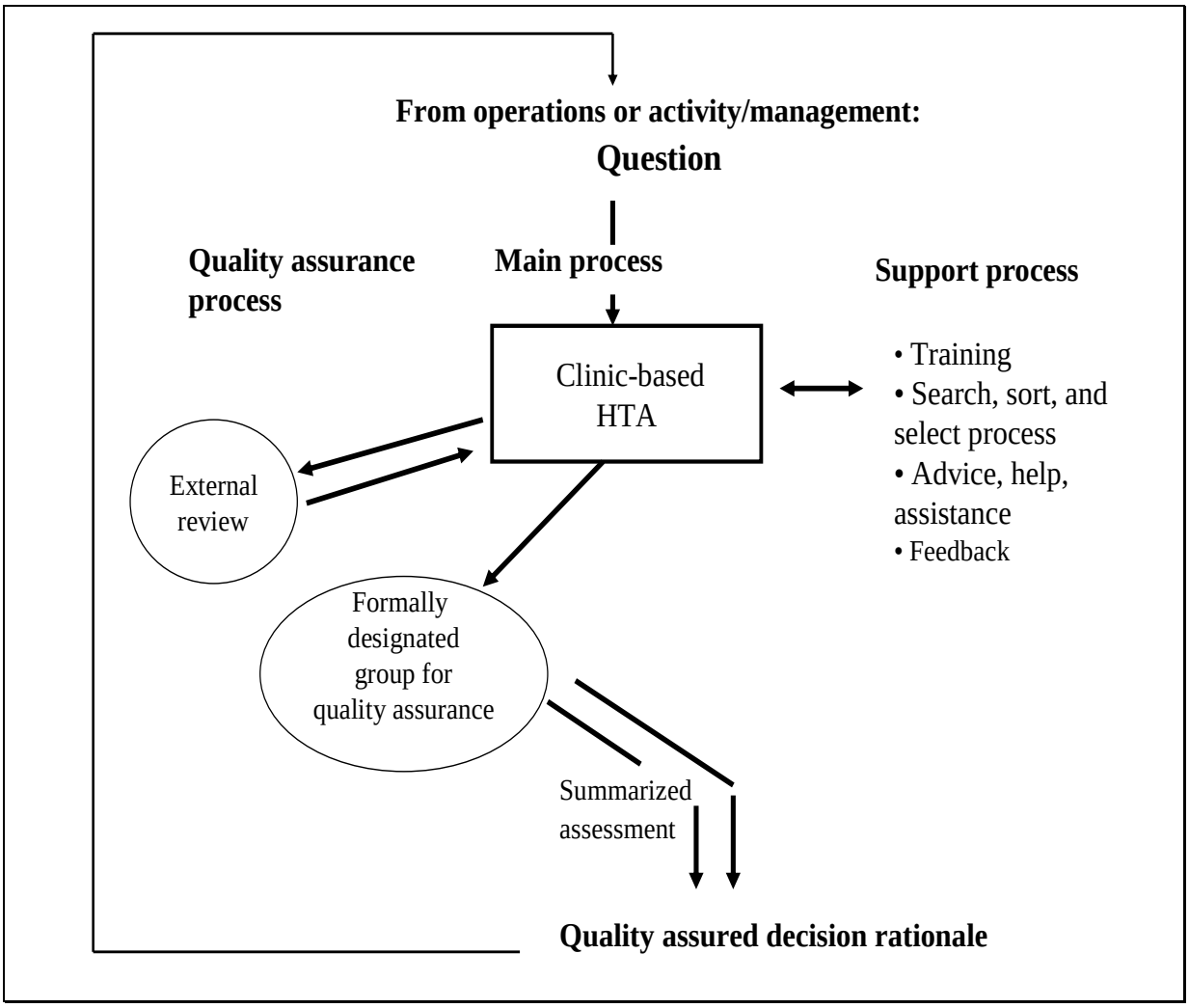
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/hta-centrum