

Category: Clinical Guidance Statement

C-Gyn 25 Managing the adnexa at the time of hysterectomy for benign gynaecological disease

This statement has been developed by the Endoscopic Surgery Advisory Committee (ESAC) and approved by the Women's Health Committee (WHC) and associated working groups, RANZCOG Council and Board.

WHC membership list is in Appendix A: Women's Health Committee Membership and ESAC membership is in Appendix B: RANZCOG Endoscopic Surgery Advisory Committee Membership.

Conflict of Interest disclosures have been received from all members of these committees. (<u>Appendix C</u>)

Disclaimer: This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances (<u>Appendix D</u>)

Objectives:	To provide advice on the removal of healthy ovaries and fallopian tubes at the time of hysterectomy for benign disease.	
Target audience:	t audience: This statement was developed primarily for use by gynaecologists and women considering hysterectomy. *See: RANZCOG's Interim statement on gendered language (below).	
Background:	This statement was first developed by the WHC in July 2009 and was reviewed in July 2017 and updated in 2022. The statement was most recently updated by the Endoscopic Surgery Advisory Committee, in association with AGES and RANZCOG's Women's Health Committee in February /2023.	
Funding:	The development and review of this statement was funded by RANZCOG.	

^{*} RANZCOG currently uses the term 'woman' in its documents to include all individuals needing obstetric and gynaecological healthcare, regardless of their gender identity. The College is firmly committed to inclusion of all individuals needing O&G care, as well as all its members providing care, regardless of their gender identity.



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1. Plain language summary

The **removal of ovaries** at the time of hysterectomy is often suggested in order to reduce the likelihood of developing ovarian cancer. This approach was common but it is now recognised that there may be health benefits associated with conserving the ovaries. Evidence from one systematic review and the ten studies summarised in this statement, suggest that while removal of the ovaries (oophorectomy) resulted in fewer diagnoses and deaths from ovarian cancer, there was no overall benefit in improving mortality from the removal of the ovaries at any age (low and very low-quality evidence). There was no age when removing the ovaries improved overall survival. Removing the ovaries of younger women (< 50 years old) was associated with increased mortality in later years, particularly if women did not use hormone therapy.

The **removal of fallopian tubes** at the time of hysterectomy is increasingly common as it has been reported that the majority of ovarian cancers arise in the fallopian tubes. Evidence from four systematic reviews and five studies were summarized. There was only one study on the removal of the fallopian tubes at the time of hysterectomy. In the other studies the removal of the tubes was performed for other reasons such as ectopic pregnancy, tubal infection and where other pathology was noted, which raises the possibility of verification bias. There was data suggesting reduced number of diagnoses of ovarian cancer but there was no data on reduced deaths from ovarian cancer. Studies of hysterectomy and bilateral salpingectomy did not report a difference in surgery related adverse related events compared to hysterectomy without salpingectomy.

2. Purpose and scope

In 2022, under the auspices of a joint AGES-RANZCOG Endoscopic Surgery Advisory Committee (ESAC), the existing C-Gyn 25 statement was updated. The Committee determined the purpose of this Clinical Guidance Statement would be to provide advice on the removal of healthy ovaries and fallopian tubes at the time of hysterectomy for benign gynaecological disease.

The methodology used to develop this Clinical Guidance Statement is detailed in Methods.

3. Executive summary

This statement has been updated. The following recommendations were made.

List of recommendations

Recommendation 1

Evidence based recommendation

Weak/Conditional

For women < 50 years who are considering oophorectomy at the time of a hysterectomy, it is suggested that the discussion include the benefits and harms of the procedure including increased mortality at an older age and reduced diagnoses of ovarian cancer and deaths from ovarian cancer. *Quality of evidence: Low for mortality, moderate for diagnosis of ovarian cancer.*

For women 50 years and older who are considering oophorectomy at the time of a hysterectomy, it is suggested that the discussion includes the reduced diagnoses of ovarian cancer and death from ovarian cancer and that there is no evidence of survival benefit when both ovaries are removed. *Quality of evidence: Low for mortality, moderate for diagnosis of ovarian cancer*

Recommendation 2

Evidence based recommendation

Weak/Conditional

It is suggested that women who are considering a hysterectomy, discuss the benefits and harms of bilateral salpingectomy, including that although reduced ovarian cancer diagnoses have been reported following

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salpingectomy, no studies reported ovarian cancer mortality or overall mortality data and additionally, that there was no increase in surgical adverse events with salpingectomy.

Quality of evidence: Very low

4. Introduction

Rationale

The removal of one or both ovaries at the time of hysterectomy (sometimes called opportunistic removal) is often suggested with the aim of reducing the likelihood of developing ovarian cancer. This approach used to be common, but it is now recognised that there may be benefits in later years in conserving the ovaries.¹

The majority of high-grade ovarian cancers (epithelial ovarian cancers Type II) arise in the fallopian tube.²⁻⁴ This information has led to the suggestion of removing both fallopian tubes at the time of hysterectomy.

The purpose of this statement is to consider the benefits and harms of removing the ovaries or fallopian tubes at the time of hysterectomy for benign gynaecological disease (non-cancerous pathology such as fibroids and endometriosis).

Background epidemiology

Ovarian cancer is an uncommon cancer with poor outcomes. In Australia it is the 9th most common cancer in women and the 6th most common cause of death in women, accounting for 4.6% of all cancer deaths in women.⁵ Half of the women diagnosed with ovarian cancer will die within five years. In 2022, the estimated lifetime risk of being diagnosed with ovarian cancer in Australia is 1.2% by the age of 85. The risk of dying from ovarian cancer by age 85 is 1 in 148 (or 0.68%).⁵

In Aotearoa New Zealand ovarian cancer is the 5th leading cause of death in wahine.⁶

90% of ovarian cancers come from cells on the outside of the ovary (epithelial ovarian cancer (EOC)) and more than two thirds are diagnosed at an advanced stage when treatments may be less effective.⁴

There are two subtypes of EOC:

- **Type 1** which are low grade serous carcinomas (LGSC), mucinous carcinomas, Brenner tumours, low grade endometroid, clear cell & seromucinous carcinomas.
- **Type 2** which are high grade serous carcinoma (HGSC), high-grade endometroid carcinoma, undifferentiated carcinoma and malignant mixed mesodermal tumours. Approximately 70% of EOC are Type 2, and 90% of the deaths from ovarian cancer are associated with Type 2. ^{3,5} The majority of Type 2 have been found to arise in the fallopian tube ²⁻⁴ leading to the suggestion that removal of the fallopian tubes may reduce the likelihood of later development of ovarian cancer.

5. Methods

The statement was developed according to approved RANZCOG processes, available in the <u>Manual</u> for Developing and Updating Clinical Guidance Statements.



Following these processes, the Research and Policy Team conducted an electronic search for studies of opportunistic salpingectomy and oophorectomy on 12th October 2022. The following databases were searched: Cochrane Library, MEDLINE, Embase and Epistemonikos. This search included 1346 studies, of which 60 potential studies were identified and their abstracts were screened. Full text articles were retrieved for 34 studies and 10 studies of oophorectomy (included one systematic review AMSTAR rating High), and nine studies of salpingectomy were included (included 4 systematic reviews (AMSTAR ratings all high) GRADE assessments were done. Studies of patients at high risk (BRCA) and those who had undergone tubal ligation were excluded.

Detailed evidence profiles for each clinical question including study results and absolute effect estimates and evidence to decision tables are in Appendix D- Evidence profiles.

6. Clinical questions and findings

Clinical Question 1

Does removal of the ovaries at the time of hysterectomy improve long term health?

P- Women at low risk of ovarian cancer (all age ranges).

I - hysterectomy and removal of both ovaries

C- hysterectomy with conservation of both ovaries

O- Overall mortality (any cause); diagnoses of cardiovascular disease, breast, and ovarian cancer; mortality from specific causes – cardiovascular disease and breast and ovarian cancer; surgical complications; timing of onset of menopausal symptoms.

Excluded: women with risk factors for ovarian cancer such as family history and BRCA, and studies with unilateral salpingo-oophorectomy.

Summary of evidence

One systematic review⁷ and eight studies were identified that study women with hysterectomy alone were compared to women with hysterectomy and bilateral salpingo-oophorectomy (BSO).⁸⁻¹⁷ Two studies that compared hysterectomy with bilateral oophorectomy with no hysterectomy/surgery, did not meet the criteria and were excluded.^{16,17} There was one study using a Markov model to study the impact of oophorectomy at the time of hysterectomy.¹⁸

Overall mortality: The quality of the four studies for the outcome of mortality was low to very low certainty. In all studies of women having hysterectomy and both ovaries removed compared with ovarian conservation there was no difference in the overall mortality.⁸⁻¹²

In younger premenopausal women (aged <50 years, 35-45 years) who had hysterectomy and both ovaries removed there was an increase in the overall mortality two to three decades following the surgery (two studies, low to very low certainty).^{8,12} In one of the studies, the mortality was only increased in those not using hormone therapy (low certainty).⁸ The percentages of women with an overall increase in mortality ranged from 0.5% to 16.9%. In older women having a hysterectomy and both ovaries removed compared with ovarian conservation there was no difference in the overall mortality.

There was no age group where removing both ovaries increased survival.^{8-17,2}

Diagnosis of ovarian cancer and death from ovarian cancer: The quality of the studies that reported ovarian cancer diagnoses and deaths from ovarian cancer was moderate to very low.



In those women who had both ovaries removed at the time of hysterectomy there was evidence of a decrease of ovarian cancer diagnoses and deaths from ovarian cancer in all studies (moderate to low certainty).⁸⁻¹⁸

The number needed to treat to prevent the occurrence of one additional ovarian cancer diagnosis at 20 years of follow up was 260 (all women). The number needed to treat for the same outcome for women aged \geq 50 years at the time of BSO was 161.¹³

Mortality from other causes: Three studies reported a decrease in the number of diagnoses of breast cancers following BSO.^{8,9,14} Two of the studies did not report mortality from breast cancer.^{9,14} The one study that reported deaths from breast cancer did not report a difference between ovarian conservation and BSO.⁸

Cardiovascular mortality was increased with women who had a hysterectomy and BSO compared to hysterectomy alone OR 1.41 (1.09, 1.83).⁸ Cardiovascular disease was more often reported in younger women <45 years of age who had both ovaries removed and not been treated with oestrogen.^{8,12} Two other studies reported no difference.^{9, 11}

Surgical morbidity: Women who had hysterectomy with ovarian conservation experienced slightly increased readmission rates at 30 days and 90 days respectively, compared to women who had a hysterectomy without ovarian conservation.¹⁴

Other concerns: An association between oophorectomy and reduced cognition in later decades has also been reported.¹⁹

Recommendation 1

Evidence based recommendation

Weak recommendation

For women < 50 years who are considering oophorectomy at the time of a hysterectomy, it is suggested that the benefits and harms of the procedure including increased mortality at an older age and decreased diagnoses of ovarian cancer and death from ovarian cancer.

Quality of evidence: Low for mortality, moderate for diagnosis of ovarian cancer.

For women 50 years and older who are considering oophorectomy at the time of a hysterectomy, it is suggested that the discussion includes the reduced diagnoses from ovarian cancer and death of ovarian cancer and that there is no evidence of survival benefit when both ovaries were removed. *Quality of evidence: Low for mortality, moderate for diagnosis of ovarian cancer*

Clinical Question 2

Does removal of the fallopian tubes at the time of hysterectomy reduce ovarian cancer?

P- Women at low risk of ovarian cancer

I - Hysterectomy and removal of both fallopian tubes

C- hysterectomy with retention of both fallopian tubes

O- Diagnoses of cardiovascular disease, breast, and ovarian cancer; mortality from any cause; mortality from specific causes – cardiovascular disease and breast and ovarian cancer; surgical complications; timing of onset of menopausal symptoms.

Excluded: Women with risk factors for ovarian cancer.

Evidence summary

Four systematic reviews¹⁸⁻²¹ and five additional studies met the inclusion criteria.^{15, 22-26}

Ovarian cancer or overall mortality: No studies reported ovarian mortality or overall mortality data for bilateral salpingectomy.

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Ovarian cancer diagnoses: Only one study considered removal of both fallopian tubes at the time of hysterectomy and compared these with women who had hysterectomy alone. The study reported reduced ovarian cancer diagnoses in women who had their tubes removed 9 years earlier (low quality).²⁷

A further three studies reported salpingectomy at the time of surgery (but not at the time of hysterectomy). For women who had both fallopian tubes removed at any surgery there was a decrease in ovarian cancer diagnoses. Verification bias is possible in these studies as surgeons may have removed tubes that looked abnormal at the time of surgery for other indications. (Very low – downgraded as most studies not at time of hysterectomy).

Surgical morbidity: There was no evidence of a difference reported in surgery related adverse events following surgery for salpingectomy and no salpingectomy (low to very low).^{19, 21}

Quality of life: There was no evidence of a difference reported in the quality-of-life measures following surgery for salpingectomy and no salpingectomy (low to very low).²¹

Postoperative hormonal status (AMH, FSH levels) and menopausal symptoms: One study reported an increased risk of menopausal symptoms one year after hysterectomy with bilateral salpingectomy²⁴ but studies of AMH and FSH levels have not reported a difference between salpingectomy and no salpingectomy (moderate quality).²²

Survey data: A survey of 77 patients in the Netherlands reported that 46% of patients were concerned about removing healthy organs.²⁸

• A survey of 204 health professionals reported that 66% were concerned about risks due to adhesions and the feasibility of women having a hysterectomy with bilateral salpingectomy using the vaginal approach.⁷

Weak/Conditional It is suggested that women considering a hysterectomy discuss the benefits and harms of bilateral salpingectomy including that although decreased ovarian cancer diagnoses have been reported following salpingectomy, no studies reported ovarian cancer mortality or overall mortality data and additionally, that there was no increase in surgical adverse events with salpingectomy. *Quality of evidence: Very low*

Evidence based recommendation

7. Legal and ethical implications

There are no legal or ethical implications. Consent for hysterectomy with and without oophorectomy or salpingectomy should follow the College guidance in (C-Gen 2a and C-Gen 2b).

8. Recommendations for future research

Three long term studies are underway.

Recommendation 2

- NCT03045965. Hysterectomy and OPPortunistic SAlpingectomy (HOPPSA) [Hysterectomy and Opportunistic Salpingectomy]. clinicaltrials.gov/ct2/show/NCT03045965 (first received 8 February 2017).
- NCT02086344. Ovarian Reserve Modification After Lps Hysterectomy With Bilateral Salpingectomy [The Effect in Term of Ovarian Reserve Modification of Adding Prophylactic Bilateral Salpingectomy (PBS) to TLH for Preventing Ovarian Cancer]. clinicaltrials.gov/ct2/show/NCT02086344 (first received 13 March 2014).



• NCT01628432. Effect of Salpingectomy During Conservative Hysterectomy (SALPINGOVA) [Effect of Total Salpingectomy During Conservative Hysterectomy for Benign Disease on Ovarian Function: Non-Inferiority Randomized Controlled Trial]. clinicaltrials.gov/ct2/show/NCT01628432 (first received 26 June 2012).

Quality of life: further research is needed on impacts on quality of life.

Further studies should report the ovarian and overall mortality of women who have bilateral salpingectomy at the time of hysterectomy.



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10. Links to relevant College Statements

• Evidence-based Medicine, Obstetrics and Gynaecology (C-Gen 15)

11. Links to relevant Consumer resources

• RANZCOG Patient Information Pamphlets can be accessed at: http://ranzcog.edu.au/resource-hub/?resource_audience=for-public

12. Links to relevant ATMs and learning modules

To be determined

13. Useful links/support groups

 <u>https://www.cancer.org.nz/cancer/types-of-cancer/ovarian-cancer/</u> <u>https://cureourovariancancer.org/nz/ovarian-cancer/</u>



Appendices

Appendix A: Women's Health Committee Membership

Name	Position on Committee
Dr Scott White	Chair
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Anna Clare	Deputy Chair, Obstetrics
Associate Professor Amanda Henry	Member and Councillor
Dr Samantha Scherman	Member and Councillor
Dr Marilla Druitt	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Dr Kasia Siwicki	Member and Councillor
Dr Jessica Caudwell-Hall	Member and Councillor
Dr Sue Belgrave	Member and Councillor
Dr Marilyn Clarke	Aboriginal and Torres Strait Islander Representative
Professor Kirsten Black	SRHSIG Chair
Dr Nisha Khot	Member and SIMG Representative
Dr Judith Gardiner	Diplomate Representative
Dr Angela Brown	Midwifery Representative, Australia
Ms Adrienne Priday	Midwifery Representative, Aotearoa New Zealand
Ms Leigh Toomey	Community Representative
Dr Rania Abdou	Trainee Representative
Dr Philip Suisted	Māori Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)
Dr Steve Resnick	Co-opted member

Appendix B: RANZCOG Endoscopic Surgery Advisory Committee Membership

Name	Position on Committee
Dr Marilla Druitt	Chair and RANZCOG Member
Dr Michael Wyn-Williams	Deputy Chair and AGES Member
Dr Helen Green	AGES Member
Dr Rachel Green	AGES Member
A/Professor George Condous	AGES Member
Dr Stephen Lyons	AGES Member
Dr Phil Suisted	RANZCOG Member
Dr Gary Swift	RANZCOG Member
Professor Yee Leung	RANZCOG Member
Research & Policy Team ²	Position
Professor Cindy Farquhar	Dean of Research & Policy
Ms Jinty Wilson	Head of Research & Policy

² RANZCOG wish to acknowledge the contribution of the technical support provided by the University of Auckland (Dr Karyn Anderson, Ms Marian Showell) who have supported the identification and appraisal of evidence.



Appendix C: Overview of the development and review process for this statement

i. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of RANZCOG Women's Health Committee or working groups. A declaration of interest form specific to guidelines and statements (approved by the RANZCOG Board in September 2012). All members of the Statement Development Panels, Statement and Guideline Advisory Group (SaGG) and Women's Health Committee were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

ii. Steps in developing and updating this statement

This statement was first developed in 2009 and updated in 2012 by the Women's Health Committee. It was reviewed by the ESAC, in association with AGES and the Women's Health Committee in 2021. It was most recently reviewed by the Women's Health Committee in March 2023. The following steps were undertaken by the Research and Policy Team and the ESAC/WHC in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the month/year meeting of the Women's Health Committee, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise, as set out in the Methodology section below.

RANZCOG statements are developed following the standards of the Australian National Health and Medical Research Council (NHMRC), which includes the use of GRADE methodology. The Evidence to Decision framework embedded within the MAGIC (Making GRADE the Irresistible Choice) digital platform (<u>https://magicevidence.org</u>) is used to publish the updated statement recommendations. The recommendations published by RANZCOG are approved by the RANZCOG Women's Health Committee, Council and Board respectively. The processes used to develop RANZCOG clinical guidance statements are described in detail at: <u>https://ranzcog.edu.au/wp-</u> content/uploads/2022/08/Manual-for-developing-and-updating-clinical-guidance-statements.pdf

iii. Developing recommendations using GRADE methodology

Phrasing for recommendations differs according to the strength of evidence. The relevant GRADE assessments for each recommendation are presented within the online platform used to structure the clinical guidance statement: MAGICapp; <u>https://magicevidence.org/magicapp/</u>.



Appendix D- Evidence profiles

Clinical Question 1

Does removal of ovaries at the time of hysterectomy improve long term health?

P- Women at low risk of ovarian cancer (all age ranges).

I- Hysterectomy and removal of both ovaries

C- Hysterectomy with conservation of both ovaries

O- Overall mortality (any cause); Diagnoses of cardiovascular disease, breast and ovarian cancer; mortality from specific causes – cardiovascular disease and breast and ovarian cancer; surgical complications; timing of onset of menopausal symptoms.

Excluded: women with risk factors for ovarian cancer such as family history and BRCA, and studies with unilateral salpingo-oophorectomy.

Evidence to decision

Benefits and harms

Important harms

Small benefits (reduced diagnosis and deaths from ovarian cancer) and moderate harm (increased overall mortality, especially if ovaries removed before 45 years old)8-15

In younger premenopausal women (<50, 35-45 yo) who had hysterectomy and both ovaries removed there was an increase in the overall mortality in 2 to 3 decades following the surgery. (2 studies, low to very low certainty).^{8,12} In one of the studies the mortality was only increased in those not using hormone therapy (low certainty)⁸. The percentages of women with the overall increase in mortality ranged from 0.5% to 16.8%. In older women having hysterectomy and both ovaries removed compared with ovarian conservation there was no difference in the overall mortality.

There was no age group where removing both ovaries increased survival.⁸ In those women who had both ovaries removed at the time of hysterectomy there was evidence of a decrease of ovarian cancer diagnoses and deaths from ovarian cancer in all studies (moderate to low certainty)

Cardiovascular mortality was increased with women who had hysterectomy and BSO compared to hysterectomy alone. OR 1.41 (1.09, 1.83)⁸. Cardiovascular disease was more often reported in younger women <45 who had both ovaries removed and not been treated with estrogen). ^{8,12} Other concerns about the association between oophorectomy and cognition in later decades have also been reported. (Rocca 2022)¹⁸

Domain	Summary of judgement	Comment
Certainty of evidence	Low to moderate	All the studies were observational studies. Low quality for the outcome of mortality, moderate quality for the diagnosis of ovarian cancer.
Values and preferences	Substantial variability is expected or uncertain	Women wish to avoid a diagnosis of ovarian cancer but the possibility of increasing their overall chance of dying from cardiovascular disease may influence that decision.
Resources	Not considered	Cost studies were out of scope but the removal of the ovaries at the time of a hysterectomy is not likely to increase the short term costs.



Equity	No important issues with recommended alternatives	There were no equity issues except that all women have the right to a discussion of the harms and benefits.
Acceptability	Important issues or potential issues not investigated	Most women would probably want to avoid a diagnosis of ovarian cancer but the possibility of increasing their overall chance of dying from cardiovascular disease may influence that decision.
Feasibility	No important issues with recommended alternatives	There are no concerns about feasibility of removing the ovaries at the time of hysterectomy except perhaps for the women having a vaginal hysterectomy.

Evidence profiles for oophorectomy

Population: Women at low risk for ovarian cancer Intervention: Hysterectomy Comparator: Hysterectomy with oophorectomy

Outcome Timeframe	Study results and measurements	Absolute effe	ect estimates Hysterectomy with oophorectomy	Certainty of the Evidence (Quality of evidence)	Plain language summary
		OVERALL N	IORTALITY		
Overall mortality (Parker 2013) ⁷ 28 yrs	Hazard ratio: 1.13 (Cl 95% 1.06 - 1.21) Based on data from 30117 participants Follow up 28		168 per 1000 more per 1000 re - 139 more)	Low Although large study and addressed confounding the patients were predominantly white (94%) and all nurses.	Hysterectomy with oophorectomy may worsen overall mortality
Overall mortality (Jacoby 2011) ⁸	Hazard ratio: 0.98 (CI 95% 0.87 - 1.1) Based on data from 25448 participants	59 per 1000	60 per 1000	Low	Hysterectomy with oophorectomy may have little or no difference on
8 yr 5	8 yrs Follow up 7 years		nore per 1000 ver - 6 more)		overall mortality
Overall mortality (Tuesley 2020) ¹⁰ 26 yrs	Hazard ratio: 1.04 (Cl 95% 0.97 - 1.11) Based on data from 1544150 participants Follow up 26	3.8 per 1000 Difference: 1 r (CI 95% 0 fev	4.8 per 1000 more per 1000 ver - 4 more)	Low	Hysterectomy with oophorectomy may have little or no difference on overall mortality



Overall mortality (Cusimano 2022) ¹¹ 14 years	Hazard ratio not provided Based on data from 195282 participants Follow up 16	66.0 per 1000 Difference: 14	80.0 per 1000 more per 1000	Very low, no HR in paper	We are uncertain whether hysterectomy with oophorectomy increases or decreases overall mortality
Overall mortality < 50 never used ET (Parker 2013) ⁷ 28 yrs f-up	Hazard ratio: 1.41 (Cl 95% 1.04 - 1.92) Based on data from 30117 participants Follow up 28 years		39 per 1000 more per 1000 pre - 26 more)	Low Although large study and addressed confounding the patients were predominantly white (94%) white and all nurses.	Hysterectomy with oophorectomy may worsen overall mortality < 50 never used menopausal hormone treatments
Overall mortality in women with hysterectomy aged 35 to 45 yrs (Mytton 2017) ¹² 3 to 13 years	Adj Hazard ratio: 1.56 (Cl 95% 1.37 – 1.82 Based on data from 113679 participants Follow up 3-13 years	6 per 1000 Difference: 4 mo (CI 95% 3 mo	10. per 1000 ore per 1000 ore – 5 more)	Low	Data included early deaths where diagnosis was made shortly after the surgery.
		INCIDENCE OF O	VARIAN CANCER		
Incidence of ovarian cancer in women with hysterectomy aged 35 to 45 yrs (Mytton 2017) ¹² 3 to 13 years	Hazard ratio: 3.85 (CI 95% 2.70 – 5.26) Based on data from 113679 participants Follow up 3-13 years		2.9 per 1000 . more per 1000 ore – 2.98 fewer)	Low	Data included early deaths where diagnosis was made shortly after the surgery. This resulted diagnoses in more ovarian cancers benign detected than expected.
Incidence of ovarian cancer only (Cusimano 2022) ¹¹	Hazard ratio: 0.23 (CI 95% 0.14 - 0.38) Based on data from 195282		0.23 per 1000 7 fewer per 1000 wer - 0.62 fewer)	Low Low numbers with cancer	Hysterectomy with oophorectomy may decrease

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16 yr (median)	participants in 1 studies Follow up 16 yrs				incidence of ovarian cancer
Incidence of ovarian cancer only (Falconer 2015) ¹³ 10+ years	No hazard ratios Based on data from 135374 participants in 1 studies Follow up 10+ yrs	2.8 per 1000 Difference: fe	0.2 per 1000 wer per 1000	Low	Hysterectomy with oophorectomy may improve incidence of ovarian cancer
Incidence of ovarian cancer only (Jacoby 2011) ⁸ 7.5 yrs	No Hazard ratios Based on data from 25448 participants Follow up 7.5 years	3.3 per 1000 Difference: 3.1	0.2 per 1000 fewer per 1000	Low	Hysterectomy with oophorectomy may decrease incidence of ovarian cancer
Diagnoses of ovarian cancer only (Chan 2013) ¹⁵	Hazard ratio: 8.33 (CI 95% 3.57 - 20 Based on data from 52716 participants Follow up 8 years	1.4 per 1000 Difference: 1.32 (CI 95% 1.42 fev	0.23 per 1000 fewer per 1000 ver - 1.08 fewer)	Low	Hysterectomy with oophorectomy may decrease incidence of ovarian cancer
		DEATH FROM OV	ARIAN CANCER		
Death from ovarian cancer only (Parker 2013) ⁸ 28 years	Hazard ratio: 0.06 (Cl 95% 0.02 - 0.17) Based on data from 30117 participants Follow up 28 years		3.3 per 1000 fewer per 1000 er - 0.17 fewer)	Very low only 48 women developed cancer over 28 years - 44 in no BSO arm and 4 in the BSO arm	We are uncertain whether hysterectomy with oophorectomy increases or decreases death from ovarian cancer
Death from ovarian cancer only (Gaudet 2014) ¹⁴ 14 years	Hazard ratio (Cl 95% -) Based on data from 52716 participants	8.9 per 1000 Difference: fe	0.8 per 1000 wer per 1000	Low 30	Hysterectomy with oophorectomy may decrease death from ovarian cancer
Death from ovarian cancer	Hazard ratio: 0.3 (Cl 95% 0.16 - 0.57)	1.0 per 1000	0.3 per 1000	Low	Hysterectomy with



only (Cusimano 2022) ¹¹ 14 yr (median)	Based on data from 195282 participants		7 fewer per 1000 wer - 0.43 fewer)		oophorectomy may decrease death from ovarian cancer
Death from ovarian cancer in women with hysterectomy	Hazard ratio: 4.76 (CI 95% 2.0 – 11.1) Based on data from 113679	0.1 per 1000	0.5 per 1000	Low	Hysterectomy with oophorectomy may decrease
aged 35 to 45 yrs (Mytton 2017)1 ²	participants Mean follow up 6 years	1	0.39 more per 000 ore – 1.01 more)		death from ovarian cancer

Clinical Question 2

Does removal of fallopian tubes at the time of hysterectomy reduce ovarian cancer?

P- Women at low risk of ovarian cancer

I- Hysterectomy and removal of both fallopian tubes

C- Hysterectomy with retention of both fallopian tubes

O- Diagnoses of cardiovascular disease, breast, and ovarian cancer; mortality from any cause; mortality from specific causes – cardiovascular disease and breast and ovarian cancer; surgical complications; timing of onset of menopausal symptoms. Excluded: Women with risk factors for ovarian cancer.

Evidence to Decision

Benefits and harms	Small net benefit, or little difference
	<u>between alternatives</u>

Small benefits and trivial harms

In women who have both fallopian tubes removed at any surgery there is a decrease of ovarian cancer diagnoses (very low – downgraded as most studies not at time of hysterectomy – discernment bias possible). There was no evidence of a difference reported in the surgery related adverse events following surgery for salpingectomy and no salpingectomy (low to very low). There was no evidence of a difference reported in the quality-of-life measures following surgery for salpingectomy and no salpingectomy and no salpingectomy and ro salpingectomy (low to very low). Studies of AMH and FSH levels have not reported a difference (moderate quality).

Domain	Summary of judgement	Comment
Certainty of evidence	Very low to moderate	All the studies were observational studies. Very low quality for the outcome of mortality from ovarian cancer and diagnosis of ovarian cancer. All the studies were downgraded for indirectness as they were not salpingectomies at the time of hysterectomy. Verification bias (see and treat at surgery if suspicious) is likely in these studies.



		Moderate quality evidence for AMH and hormone levels.
Values and preferences	Substantial variability is expected or uncertain	While most women would probably want to avoid a diagnosis of ovarian cancer almost half of the patients were concerned about the removal of health organs in a qualitative study. but the possibility of increasing their overall chance of dying from cardiovascular disease may influence that decision. ²⁶
Resources	Not considered	Cost studies were out of scope but the removal of the fallopian tubes at the time of a hysterectomy is not likely to increase costs.
Equity	No important issues with recommended alternatives	There were no equity issues except that all women have the right to a discussion of the harms and benefits of removing the fallopian tubes.
Acceptability	Important issues or potential issues not investigated	Probably acceptable. We note a study of patient perspectives reported concerns about removing health organs.26
Feasibility	No important issues with recommended alternatives	Probably feasible. We note a study of 204 health professionals reported that 66% were concerned about additional risks due to adhesions and using the vaginal approach. feasibility of removing the ovaries at the time of hysterectomy except perhaps for the women having a vaginal hysterectomy.

Evidence profiles for salpingectomy

		Absolute effect estimates				
Outcome Timeframe	Study results and measurements	No salpingectomy with and without hysterectomy	Salpingectomy with and without hysterectomy	Certainty of the Evidence (Quality of evidence)	Plain language summary	
	DIAGNOSIS OF OVARIAN CANCER					
Diagnosis of ovarian cancer - epithelial type I only (Darelius 2021) ¹⁹	Odds ratio: 1.16 (CI 95% 0.75 - 1.78)		137 per 1000 ' more per 1000 wer - 75 more)	Very low Due to serious indirectness	We are uncertain whether salpingectomy with and without hysterectomy increases or decreases diagnosis of ovarian cancer - epithelial type I only	
Diagnosis of ovarian cancer - epithelial type II only BILATERAL SALPINGECTOMY	Odds ratio: 0.1 (Cl 95% 0.01 - 0.71)		13 per 1000 7 fewer per 1000 ewer - 32 fewer)	Very low Due to serious indirectness	We are uncertain whether salpingectomy with and without hysterectomy	



and HYSTERECTOMY (Darelius 2021) ¹⁹					increases or decreases diagnosis o ovarian cancer – epithelial type ii only
Diagnosis of ovarian cancer - epithelial type II - only SALPINGECTOMY (Darelius 2021) ¹⁹	Odds ratio: 0.62 (CI 95% 0.45 - 0.85)		78 per 1000 fewer per 1000 wer - 16 fewer)	Very low Due to serious inconsistency, Due to serious indirectness	We are uncertain whether salpingectomy alone increases or decreases diagnosis of ovarian cancer - epithelial type ii only
Diagnosis of ovarian cancer - epithelial type II only HYSTERECTOMY ALONE as the intervention ¹⁹	Odds ratio: 0.81 (CI 95% 0.68 - 0.96)		99 per 1000 fewer per 1000 ewer - 4 fewer)	Very low Due to serious inconsistency, Due to serious indirectness	We are uncertain whether salpingectomy with and without hysterectomy increases or decreases diagnosis of ovarian cancer - epithelial type ii only hysterectomy alone as the intervention
Diagnosis of epithelial ovarian cancer (Masden 2015) ²³ 13 yrs	Odds ratio: 0.58 (CI 95% 0.36 - 0.95) Based on data from 207930 participants Follow up 13 years		73 per 1000 fewer per 1000 ewer - 5 fewer)	Very low Due to serious indirectness ¹³	We are uncertain whether salpingectomy with and without hysterectomy increases or decreases diagnosis of epithelial ovarian cancer
Diagnosis of ovarian cancer (Falconer 2015) ¹³	Hazard ratio: 0.65 (CI 95% 0.52 - 0.81) Based on data from 5483550 participants		80 per 1000 fewer per 1000 wer - 22 fewer)	Very low Due to serious indirectness	We are uncertain whether salpingectomy with and without hysterectomy increases or decreases diagnosis of ovarian cancer
Diagnosis of epithelial ovarian cancer (Hanley 2022) ²⁶	No hazard ratio provided. Based on data from 25889 who had hysterectomy	0.65 per 1000 Difference: 0.45	0.2 per 1000 fewer per 1000	Low Due to serious imprecision	We are uncertain whether salpingectomy with and without hysterectomy increases or



	and bilateral salpingectomy and 32080 who had hysterectomy				decreases diagnosis of ovarian cancer
		SURGICAL	OUTCOMES		
Surgery-related adverse events - Short-term postoperative complications (van Leishout 2019) ²²	Odds ratio: 0.13 (CI 95% 0.01 - 2.14) Based on data from 152 participants in 3 studies		3 per 1000 fewer per 1000 wer - 29 more)	Moderate Due to serious indirectness, Due to serious imprecision	We are uncertain whether salpingectomy with and without hysterectomy improves or worsen surgery-related adverse events - short-term postoperative complications
Surgery-related adverse events - Short-term postoperative complications (van Leishout 2019) ²²	Odds ratio: 0.66 (CI 95% 0.11 - 3.94) Based on data from 286 participants in 5 studies		13 per 1000 fewer per 1000 wer - 57 more)	Moderate down graded for imprecision	We are uncertain whether salpingectomy with and without hysterectomy increases or decreases surgery- related adverse events - intraoperative complications
Conversion rate to open surgery (van Leishout 2019) ²²	Odds ratio: 0.66 (CI 95% 0.11 - 3.94) Based on data from 172 participants in 2 studies ²²		23 per 1000 fewer per 1000 wer - 90 more)	Moderate Due to imprecision	We are uncertain whether salpingectomy with and without hysterectomy increases or decreases conversion rate to open surgery
Quality of life - Mental health (van Leishout 2019) ²²	Measured by: Scale: - High better Based on data from 54 participants		/ID 1.32 lower er - 2.36 higher)	Moderate Due to serious imprecision ²⁴	Salpingectomy with and without hysterectomy probably has little or no difference on quality of life - mental health



Quality of life - Physical health (van Leishout 2019) ²²	Measured by: Scale: - High better Based on data from 54 participants in 1 studies	Difference: MD 1.01 lower (Cl 95% 4.29 lower - 2.27 higher)	Moderate Due to serious imprecision	Salpingectomy with and without hysterectomy probably has little or no difference on quality of life - physical health
Total surgical time (van Leishout 2019) ²²	Measured by: Scale: - Lower better Based on data from 286 participants in 5 studies	Difference: MD 0.35 higher (CI 95% 6.64 lower - 7.33 higher)	Moderate Due to serious imprecision	Salpingectomy with and without hysterectomy probably has little or no difference on total surgical time
		IMPACT ON HORMONAL STATUS		
Postoperative hormonal status (AMH) (van Leishout 2019) ²²	Measured by: Scale: - High better Based on data from 283 participants in 5 studies	Difference: MD 0.94 lower (Cl 95% 1.89 lower - 0.01 higher)	Low Due to serious risk of bias, Due to serious inconsistency	Salpingectomy with and without hysterectomy may have little or no difference on postoperative hormones
Postoperative hormonal status (AMH) (Gelderbolm 2022) 21	Measured by: Scale: - High better Based on data from participants in 11 studies	Difference: MD 0.07 lower (Cl 95% 1.18 lower - 0.05 higher)	Low Due to serious risk of bias, Due to serious inconsistency ²⁹	Salpingectomy with and without hysterectomy may have little or no difference on postoperative hormones
Postoperative hormonal status (FSH) (Gelderbolm 2022) ²¹	Measured by: Scale: - High better Based on data from 6 studies	Difference: MD 0.33 lower (Cl 95% 0.15 lower - 0.81 higher)	Low Due to serious risk of bias, Due to serious inconsistency	Salpingectomy with and without hysterectomy may have little or no difference on post op hormones



Appendix E: Full Disclaimer

Purpose

This statement has been developed to guide registered health professionals about advice on the removal of healthy ovaries and fallopian tubes at the time of hysterectomy for benign gynaecological disease, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any person. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual person and the particular circumstances of each case.

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Version	Date of Version	Pages revised / Brief Explanation of Revision		
V4.0	Nov / 2022	Endoscopic Surgery Advisory Committee		
V4.0	Feb / 2023	RANZCOG Women's Health Committee		
Policy Ve	rsion:	Version 4.0		
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Review of Policy:		March / 2028		