Expanding opportunistic bilateral salpingectomy to laparoscopic cholecystectomy to prevent ovarian cancer: A feasibility and safety trial

Study Protocol

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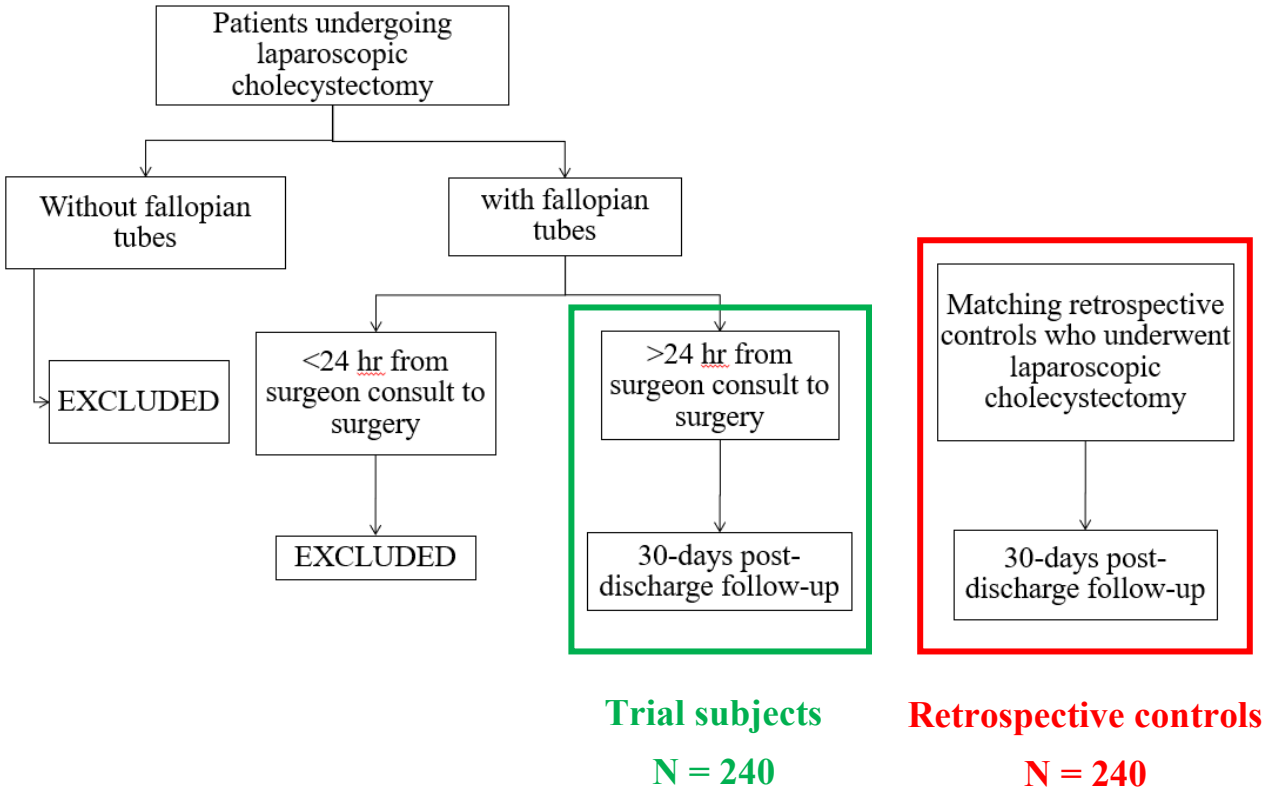
List of Abbreviations

BC	British Columbia
FoM	Faculty of Medicine
HGSC	High-grade serous cancer
ICER	Incremental cost-effectiveness ratio
IUD	Intra-uterine device
Lap Chole	Laparoscopic Cholecystectomy
OBS	Opportunistic bilateral salpingectomy
ON	Ontario
OR	Operating room
RC	Research Coordinator
REDCap	Research Electronic Data Capture
STICs	Serous tubal intraepithelial carcinoma lesions
UBC	University of British Columbia
VGH	Vancouver General Hospital

1. TREATMENT SCHEMA



1.1 Hypothesis

The investigators hypothesize that opportunistic bilateral salpingectomy (OBS) at the time of laparoscopic cholecystectomy (lap chole) is a feasible, safe and cost-effective primary prevention strategy for ovarian cancer.

The investigators hypothesize that the procedure will only take 10-20 minutes of additional OR time, and integrating the identified partners and knowledge users, as well as adding relevant knowledge users as the project progresses will affect the rapid mobilization of the findings.

1.2 Primary objective

To estimate the feasibility and safety of having general surgeons perform OBS during lap chole.

1.3 Secondary objectives

To understand any health services consequences of offering OBS during lap chole including how much overall and additional OR time is required when OBS is performed concurrently with the primary procedure, how many additional ports are placed, how many additional instruments are used, and whether the patient needed repositioning during the surgery.

2. INTRODUCTION AND RATIONALE

2.1 Background

Ovarian cancer remains a devastating diagnosis, with high-grade serous cancer (HGSC) being the subtype that accounts for ~70% of ovarian cancers[1] and 90% of deaths from ovarian cancer.[2] HGSC is primarily diagnosed at advanced stages, and most cases recur, contributing to the low 5-year survival rate of 34%.[3] There is no effective screening method for HGSC,[4] and treatment innovations have not resulted in meaningful improvement in survival rates,[5] making prevention our most powerful tool for reducing morbidity and mortality.

Although the ovary is frequently the site of the dominant tumor mass, the investigators now know that most HGSCs arise in the fallopian tube epithelium.[6,7] The evidence for the tubal origin of HGSC originated with the examination of fallopian tubes removed at risk-reducing salpingo-oophorectomy (RRSO) in *BRCA1/2* pathogenic variant carriers (people at high genetic risk for ovarian cancer). These specimens revealed the presence of preinvasive lesions in the distal end of the fallopian tubes (serous tubal intraepithelial carcinoma lesions; STICs),[8-12] but no ovarian lesions. Systematic analysis of fallopian tubes and ovaries has since shown that STICs and p53 signature lesions are found in individuals with *BRCA* pathogenic variants, and in sporadic and incidental HGSCs.[13] STICs are rarely found in people at average ovarian cancer risk undergoing salpingectomy for benign gynecologic conditions.[13,14] Genomic studies show hierarchical relationships between STICs and ovarian cancers, increasing our confidence that these lesions in the fallopian tubes are precursors to HGSC.[15]

Prevention of HGSC in the general population

While the general population's lifetime risk of ovarian cancer is 1.4%,[16] people with an inherited germline *BRCA1* or *BRCA2* mutation have an average cumulative risk of 59% and 17%, respectively.[17] In *BRCA 1/2* mutation carriers, bilateral salpingo-oophorectomy (removal of fallopian tubes and ovaries) is recommended because mortality from HGSC is so high in this population.[18] However, removal of the ovaries is not recommended for the general population, as it is associated with increased mortality, coronary heart disease, and osteoporosis.[19] Thus, a different preventive strategy is needed for people at average risk of ovarian cancer, who make up 80% of cases of HGSCs. In recognition of both the potential risk of removing ovaries and the evidence indicating that the fallopian tube was the tissue of origin for most HGSCs, opportunistic bilateral salpingectomy became the primary prevention approach for HGSC in the general population. Opportunistic bilateral salpingectomy (OBS) refers to the removal of the fallopian tubes during another pelvic surgery. To date, this has most commonly been hysterectomy or tubal sterilization.

Opportunistic bilateral salpingectomy for ovarian cancer prevention

In 2010, British Columbia (BC) became the first jurisdiction worldwide to implement OBS as an ovarian cancer prevention approach. BC's ovarian cancer research team launched a province-wide strategy asking general gynaecologists to discuss OBS with patients undergoing hysterectomy or seeking tubal sterilization. By 2020, 80% of hysterectomies with ovarian preservation included OBS and 82% of tubal sterilizations were converted to OBS in BC.[20]

Considerable amounts of observational research have illustrated that neither hysterectomy with OBS nor OBS for sterilization are associated with increased risk of perioperative adverse outcomes such as hospital readmission, blood transfusion, or a longer length of stay in hospital.[21-25] There is also evidence that OBS does not increase risk for minor complications.[25] Most recently, the first randomized controlled trial (run in Sweden and started back in 2019) comparing salpingectomy to tubal occlusion for sterilization reported that laparoscopic salpingectomy was non-inferior to tubal occlusion when examining any complication up to 8 weeks post-operatively.[26]

While the fallopian tubes do not produce hormones, there was some concern that their removal may affect blood flow to the ovary and thus subsequently affect hormone production. Many studies to date, including those examining ovarian sonographic parameters and hormonal assays with follow-up for up to five years post-surgery, have been reassuring.[27-32] Recent work in BC also reported no difference in time to initiation of HT or in time to first physician visit for a menopausal concern among any OBS groups (both at the time of hysterectomy or for tubal sterilization, compared with those undergoing hysterectomy alone or tubal ligation),[33] and a recent Cochrane systematic review reported finding no evidence of any difference in onset of menopause after hysterectomy with salpingectomy, suggesting that OBS is unlikely to reduce the age of onset of menopause.[34] Members of this research team have also shown that OBS at the time of gynecologic surgery is cost-effective.[35]

Most importantly, the investigators have been amassing data on the effectiveness of OBS in preventing HGSC. Recent data from BC examined the level of risk reduction afforded by OBS, and these data indicate that OBS reduces risk for HGSC by ~80% with a crude hazard ratio of 0.22 (95%CI 0.05, 0.95) compared to those who underwent hysterectomy alone or tubal ligation.[36] Given that safety data for OBS are good, and there appears to be a dramatic risk reduction for HGSC, the investigators now must consider how best to use OBS to reduce the incidence of ovarian cancer at the population level.

Reaching the highest preventive potential

Two recent studies have examined the preventive potential of offering OBS more widely in all elective abdominal surgeries. A published study examining medical records of those diagnosed with HGSC at Johns Hopkins or Memorial Sloan Kettering between June 1, 2015, and June 1, 2021, examined medical records to calculate the proportion of patients with missed opportunities for OBS. They found that 23.7% of patients had a missed opportunity (defined as a history of a surgical procedure resulting in permanent contraception at any age or another abdomino-pelvic surgery at 45 years or older), and that ~20% of these opportunities were laparoscopic cholecystectomies (herein referred to as lap choles). In fact, lap chole was the most common missed opportunity among women 45 years or older. A missed opportunity for OBS was identified in 23.2% of the patients who died of HGSC.[41]

A second study that used very similar methodology and a similar temporal period (HGSC patients diagnosed during calendar years 2014 to 2021) from Mayo Clinic found that 57% had a history of abdominal or pelvic surgery that met the criteria for an OBS. While gynecologists performed the largest proportion of these surgeries, 38% of the missed opportunities were performed by general surgeons, and 26% of these were elective lap choles.[37] The investigators also know that when counseled about OBS, between 80% and 95% will choose to undergo the risk-reducing procedure during their other pelvic surgery.[42] If OBS reduces risk for HGSC by 80%, as suggested by the BC data, then taken together, these studies suggest that offering patients OBS during general

surgeries as well as gynecological surgeries could save at least 20% of lives lost to ovarian cancer and potentially more. No new treatments have provided such a significant improvement in survival for ovarian cancer patients over the past 50 years.

Performing OBS during lap chole

There has been one multicentre study of patients ≥ 45 years of age who underwent elective lap chole with OBS with matched historical controls.[43] The procedure was successfully completed in 98 patients (93.3%) with adhesions preventing successful completion in the remaining 6.7%. The majority of these were performed by the general surgeon independently, but 19 were done by a gynaecologist and 7 were collaborative efforts. There were no reported intraoperative or postoperative complications reported. The median additional operating room (OR) time was 13 minutes (range of 4 to 45 mins).[43]

2.2 Rationale

The investigators have completed recruitment on a clinical trial of OBS during colorectal surgery and have found it is safe and feasible for general surgeons to remove fallopian tubes during colorectal surgery. Members of this research team have been working with the Shared Services Committee of Doctors of BC on a campaign to educate general surgeons about OBS, with a goal of increasing uptake of OBS during general surgery by 20% by 2027. This has involved a considerable amount of direct communication with general surgeons across BC and Canada. During that consultation, the investigators heard reluctance from general surgeons to begin performing OBS during lap chole outside of the context of a research study. While these surgeons were aware of the small Austrian study,[43] given the complexities of including OBS during lap chole compared to colorectal or similar pelvic surgeries (i.e., appendectomy), they felt that more evidence was needed. These complexities include potentially repositioning the patient, inserting any additional port(s) in the pelvis, and the use of different instruments to perform the salpingectomy than those commonly used for lap chole. Many surgeons use clips and monopolar cautery during lap chole rather than bipolar vessel sealing devices (e.g., Ligasure) or Endoloops (which are pieces of equipment that are sometimes preferred for salpingectomies). Surgeons will need to ensure they are comfortable working with the equipment they normally use for lap chole to also perform OBS, as it is not encouraged to open additional equipment from a cost and environmental sustainability perspective.

3. DETAILED OBJECTIVES

The investigators will address the following aims:

1. To understand the feasibility of OBS at the time of lap chole by measuring how many patients successfully undergo removal of both fallopian tubes at the time of their lap chole.
2. To understand the safety profile of OBS at the time of lap chole. The investigators will compare well-studied surgical complications and use the Clavien-Dindo classification of surgical complications to compare those undergoing OBS with a control group of patients undergoing lap chole without OBS.
3. To understand any health services consequences of offering OBS during lap chole, the investigators will measure how much overall and additional OR time is required when OBS is performed concurrently with the primary procedure, how many additional ports are placed, how many additional instruments are used, and whether the patient needed repositioning during the surgery.
4. To use the results from aims 1 to 3 to estimate the cost-effectiveness of OBS for HGSC prevention at the time of lap chole.

4. STUDY POPULATION

4.1 Inclusion Criteria

- Individuals with fallopian tubes who are undergoing lap chole and have more than 24 hours from surgeon consult to surgery, regardless of menopausal status
- Age of 35 years and older
- Patient must be able to give oral and written informed consent
- Premenopausal patients will be included but will be counseled regarding their fertility

4.2 Exclusion Criteria

- Less than 24 hours available from surgeon consult to surgery
- Individuals with a desire for a future pregnancy
- Previously had a salpingectomy or salpingo-oophorectomy

4.3 Sample Size Calculation

All power calculations are based on an alpha of 0.05 and a power of 0.90. The investigators set the percentage of patients that met the primary outcome definition based on the existing literature of these expected complication rates following lap chole and have used the higher end of the range to ensure they have an adequate sample size. The investigators assume the rate of complications in both the intervention and control groups will be equal, as is standard for sample size calculations for non-inferiority trials. Using the non-inferiority limit of 5%, the investigators found that they will have sufficient power with 476 patients, which corresponds to 238 in each group.

Outcome	**30-day readmission**	**Surgical infection**	**Blood transfusion or hemostatic agent required**	**Length of stay**
Expected rate in lap chole	2.8-3.7%[48-50]	0.3%-3.4%[51]	0.5-1.2%[52-54]	61.2 hours[55]
Allowable detectable difference	5%	5%	5%	7 hours
Sample size needed for 5% noninferiority limit	476 238 in each group	452 226 in each group	164 82 in each group	396 198 in each group

5. METHODS

5.1 General Study Design

The investigators will conduct a multi-center, open label, non-inferiority clinical trial with two sites in BC, Canada and one site in ON, Canada. Appendix I includes a Table of Assessments and Follow Up.

5.2 Study Duration

Recruitment will take place over 30 months from July 1, 2026 – January 31, 2029.

Participants will be followed from preoperative assessment until 30 days following discharge from their surgery.

5.3 Retrospective Controls

Given the considerable effectiveness of OBS, members of the study team do not feel it is ethical to deny any patient OBS. While it is not currently standard of practice to offer OBS during lap chole in ON, given the educational campaign in BC, there may be some general surgeons who begin to do so, and thus the investigators would not want to randomize patients to a control arm.

The investigators will choose the nearest neighbor match by age at the same site as the intervention patient. The research coordinators (RC) will run each potential eligible control patient by the surgeon running that site to ensure that they would have been eligible for the trial and their data will be obtained from their electronic medical record. All identifiable data will be removed and replaced with study IDs. Given that no control patients can be identified and nothing the investigators learn will have direct clinical relevance to the patient, a waiver of consent is deemed ethical.

5.4 Study Procedures

5.4.1 Enrollment

1. The RC at each site will have access to the electronic booking system at each site and screen eligible patients.
2. The surgeon will introduce that the patient is eligible for a study during their consult.
3. If the patient expresses interest in learning more about the study, the RC will approach patients and offer them the option to participate in a trial of OBS during their lap chole.
4. If the patient remains interested, they will be provided with an information leaflet which includes a link to an online video, developed for patients, explaining OBS during general surgery. They will be provided with the electronic consent documents by email or on a tablet managed by the research team. They can also be offered a paper version should they prefer that option. Should there be any instances where in-person consenting may not be possible or inconvenient, consenting will be done over the phone.

5.4.2 Intervention plan

The responsibility for the treatment of participants rests with individual investigators. The surgeon will determine if the patient is a good candidate for OBS during their lap chole. Once a patient has consented to participate in the trial, the surgeon will determine the appropriate method to perform OBS.

The RC will attend the OR and will collect data on the fallopian tube removal. In the rare instances where the RC is not present, an OR nurse or another person in the OR will perform those duties. The RC will record how long it takes for the surgeon to remove both fallopian tubes. If the patient has had a prior tubal ligation, the surgeon will report that to the RC.

Start time: RC will begin timing fallopian tube removal when the camera and instruments are positioned away from the abdomen and into the pelvis, with or without insertion of additional port sites. The surgeon will signal when fallopian tube removal begins.

End time: The fallopian tube removal will be considered finished when both tubes are separated from the ovaries and uterus. The surgeon will signal when both tubes are separated from the ovaries and uterus or when the attempt to remove both fallopian tubes was abandoned in cases where OBS was not feasible.

During and after the surgery, the RC will record the following:

1) Blood transfusion or use of hemostatic agents, as measured by any procedure in which whole blood or blood parts are put into a patient's bloodstream through a vein, or any hemostatic agent is used;
2) OR time required to remove fallopian tubes.
3) Total OR time.
4) Clips in place if prior tubal ligation.
5) Number of additional ports placed.
6) Instruments used.
7) Additional instruments that were opened solely for the salpingectomy.

5.4.3 30 Days Follow-up

At 30 days after the discharge, the RC would follow up on:

1) Length of hospital stay, as measured from admission time to discharge time;
2) 30-day hospital readmission rate, as indicated by any return to hospital with an inpatient stay in the 30 days following discharge from their surgery;
3) Surgical site infection, which includes any infection that develops at the site of the surgical incision within 30 days that requires further treatment.

These data are available in the patient's medical chart and are also available through chart review for the patients in the retrospective control group.

Perioperative complications will be graded according to the Clavien-Dindo classification of surgical complications. Any Grade 4 or 5 complications will be immediately reviewed by the study team to determine whether the study needs to be stopped.

5.4.4 Outcomes Measures

5.4.4.1 Feasibility

The feasibility of OBS during lap chole will be calculated as the percentage of patients who consented to OBS and went on to successfully have both fallopian tubes removed during their lap chole.

There are instances where both tubes are not easily accessible during surgery, and the investigators do not recommend altering the surgical approach to access the tubes. Surgeons are informed that this is a prophylactic procedure and that it should be abandoned if there is any reason to believe that it is not safe to perform on a patient. The most common safety concern is substantial adhesions in the pelvis.

5.4.4.2 Safety: Length of hospital stays

The investigators will examine the number of days hospitalized from admission time to discharge time, within 30 days after surgery.

5.4.4.3 Safety: 30-day hospital readmission rate

The investigators will evaluate the rate of readmission to the hospital indicated by any return to the hospital with an inpatient stay in the 30 days following discharge from the surgery.

5.4.4.4 Safety: Blood transfusion

The investigators will examine whether a blood transfusion was required or any other hemostatic agents were used, as measured by any procedure in which whole blood or blood parts are put into a patient's bloodstream through a vein

5.4.4.5 Safety: Surgical site infection.

The investigators will assess any infection that develops at the site of the surgical incision within 30 days that requires further treatment

5.4.4.6 Health Services Outcomes: Duration of Surgery

The following durations will be examined for this aim:

(1) OR time required to remove fallopian tubes;
(2) Total OR time

5.4.4.7 Health Services Outcomes: Instruments used during laparoscopic cholecystectomy

The investigators will assess the instruments used during the laparoscopic cholecystectomy compared to the salpingectomy, if different.

5.4.4.8 Health Services Outcomes: Number of additional ports placed

The investigators will examine the number of additional ports placed for salpingectomy.

RCs will report the overall surgical time in the operative report to compare the overall surgical time between intervention and retrospective controls. The investigators will calculate both the average additional number of minutes spent in the OR removing fallopian tubes during lap chole as well as the total operative time for the lap chole to ensure the investigators completely understand any changes to OR time.

The investigators will closely examine the operative reports of all historical controls and compare these with recruited intervention patients to examine the average number of additional ports that will need to be placed during a lap chole to also remove the fallopian tubes.

The investigators will compare the instrumentation used in OBS patients to the instrumentation used in the retrospective controls to examine whether including OBS has important cost and environmental considerations due to additional equipment use. The investigators encourage all surgeons to work with the equipment they will already be using and training includes videos illustrating multiple ways to conduct OBS with the equipment on hand.

5.4.5 Cost-effectiveness

To determine the cost-effectiveness of OBS at the time of lap chole, the investigators will use the data generated regarding additional OR time, and any additional health services considerations, as well as any additional complications in their modeling. Direct and indirect health care costs will be derived from previously existing sources, including previous publications, and the CIHI patient cost estimators that includes provincial cost estimates for lap chole surgeries by province. Lifetime risks of HGSC will be modeled from the Canadian Cancer Statistics. Competing mortality risks that are age and sex dependent will be derived from Canadian Life Tables. The investigators will use published costs for treatment of HGSC[56-59] and compare the direct HGSC-related costs (costs associated with either prevention or treatment of HGSC) across all groups.

Monte Carlo simulations will estimate the number of people who will be diagnosed with HGSC in the future after OBS compared to those not having this procedure, based on the effectiveness data generated from OBS at the time of hysterectomy and tubal sterilization (i.e., risk reduction of 78%). The time horizon will be 50 years. The investigators will allow for uncertainty around various parameters, including the effectiveness of OBS, the proportion of women who will undergo this procedure in the general population, and total health care costs by conducting extensive sensitivity analyses.

To incorporate measures of quality of life into the model, the investigators will estimate quality-adjusted life years based on utilities associated with various health states, including postoperative recovery and potential complications. The primary outcome measure will be the incremental cost-effectiveness ratio (ICER), and OBS at the time of lap chole surgery will be considered cost-effective if its ICER is less than $50,000 per year of life gained (chosen in accordance with willingness-to-pay research).[60]

5.5 Subject Withdrawal

A patient can withdraw their study participation at any point in time, without providing an explanation for withdrawal. Patients will have an option to request the destruction of all of their information collected during the study or to allow the investigators to keep the data already collected. Withdrawal of participation will have no negative effect on the patient's care.

Data will not be destroyed once information is already deidentified and has already been merged with other data.

5.6 Expected Loss to Follow-up

There is no loss to follow-up expected for this trial, given that there will be no contact with patients post-surgery and patients will only be followed up by the research team at 30 days post-discharge.

6. SAFETY REPORTING

6.1 Risks to Participants

There are no clinical risks for patients beyond the standard surgical management for lap chole. Patients will be carefully counselled on the risks, benefits, and alternatives to proceeding with their standard of care operation.

There is substantial evidence from studies conducted in British Columbia and in the United States indicating that opportunistic salpingectomy is safe when performed at the time of gynecologic surgeries. The addition of salpingectomy does increase time in the operating room (less than 15 minutes). But this has not meaningfully altered other surgical outcomes.

6.2 AEs and SAEs

6.2.1 Adverse events (AEs)

Adverse events (AEs) are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the trial intervention. All AEs reported spontaneously by the subject or observed by the investigator or their staff, will be recorded.

All symptoms that are to be expected according to the surgical procedure and healing process are not considered AEs. All AEs will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures, and/or may require referral to the general physician or a medical specialist.

Perioperative complications will be graded according to the Clavien-Dindo classification of surgical complications, which uses a grading approach. Any Grade 4 or 5 complications will be immediately reviewed by the study team to determine whether the study needs to be stopped.

6.2.2 Serious adverse events (SAEs)

A serious adverse event is any untoward medical occurrence or effect that:

- results in death
- is life threatening (at the time of the event)
- requires hospitalization or prolongation of existing inpatients' hospitalization

- results in persistent or significant disability or incapacity
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been, based upon appropriate judgment by the investigator.

7. STATISTICAL ANALYSIS

7.1 Proposed Analyses

The investigators will calculate:

1) The percentage of patients who consented to OBS and went on to successfully have both fallopian tubes removed during their lap chole.
2) Whether lap chole with OBS has an adverse event profile that is non-inferior to standard lap chole without OBS. A non-inferiority margin of 5% will be considered clinically meaningful. 95% confidence intervals will be used to describe treatment differences for the safety outcomes and to determine non-inferiority (lower confidence limit ≥5%). A non-inferiority p-value will be calculated using a Wald test to aid interpretation. Multiple comparison adjustments for the pairwise treatment comparisons will be made.
    a. The investigators will conduct a per-protocol analysis as the primary population for analysis, given that this is standard for non-inferiority trials;
    b. The investigators will also complete an intention to treat analysis as a secondary analysis.

7.2 Interim Analyses

Interim analysis will be conducted annually. Interim analyses will be conducted to evaluate safety and confirm study feasibility by assessing recruitment rates, protocol adherence, and assessing whether any new barriers to the trial are identified.

8. DATA MONITORING

8.1 Data Handling

A central Research Coordinator located at the Lead Site (VGH) will be responsible for data handling. All data will be monitored using the University of British Columbia Faculty of Medicine (UBC FoM) REDCap. Quarterly virtual meetings will be conducted with all site leads, RCs, and relevant study personnel. The Principal Investigator will have regular contact with each site lead to ensure enrollment, recruitment, and correct data entry.

8.2 Data Storage

All de-identified data are recorded and stored on the UBC FoM REDCap. Only the Lead Site research team will have the ability to see the entire dataset; each collaborating site will only be able to see the data they input from their own site.

A password-protected master list (Excel spreadsheet) that links study ID, participants' PHN and email address will be housed on a secure institutional share drive at each site. This master list is kept separate from the dataset and only the local site will have access to this list.

8.3 Privacy, Confidentiality and Security

Patients will be assigned a unique study ID and no identifiers will be retained for analysis. A master list linking patients' PHN and the study ID will be retained only during data collection to avoid duplication of data entry. The master list will be stored as a password-protected Excel spreadsheet on the institutional share drive (e.g., UBC Microsoft OneDrive). Only study personnel will have access to the spreadsheet. Once the collection is completed, this master list will be deleted and data will be completely de-identified.

All data analyses will be conducted on-site, so that no individual-level data leaves the site. All files will be retained for 5 years after publication.

The FoM REDCap servers are located at the UBC University Data Centre (UDC) and use SSD (Solid State Drives) for storage. UDC is monitored 24/7 from the IT Operations Centre and IT staff & Researchers will have 24-hour access to their equipment. Access to the network/storage rooms will be limited to UBC IT authorized personnel. The data transmission from client computer to data servers is encrypted.

FoM REDCap is a data management tool that uses a web server that employs Secure Socket Layer (SSL) technology for the secure transfer of data between a client computer and the server. The application and the database are housed on separate virtual networks providing enhanced security. The IT network is protected and governed by security mechanisms defined in the UBC Research IT security policies.

The FoM REDCap system itself has a built-in data integrity protection system whereby changes that need to be made to an instrument that is already in use are restricted, controlled and tracked. The Super Admin receives the request and can then verify and approve the proposed changes. An

audit trail is attached to this feature and retains old versions of all instruments. The collected data can only be viewed by granted personnel with specific rights.

8.4 Data Transportation

In order for another entity to collaborate on this study, they must sign a Data Transfer Agreement with the Lead Site. Once they obtain ethics approval from their own site and an agreement is established, they will be given access to UBC FoM REDCap. Any UBC researcher who wishes to contribute to the study will be added to the existing ethics application (H26-00688) as a co-Investigator.

9. LOGISTICS AND ADMINISTRATIVE ASPECTS

9.1 Ethical Considerations

This study will be conducted in accordance with the principles of the Declaration of Helsinki (Brazil, 2013), the guidelines of Good Clinical Practice (GCP) issued by ICH, and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2, 2022).

Each collaborating site is required to obtain ethics approval from its own institutional REB. Investigators must notify their Research Ethics Boards (REBs) of events which involve corrective action(s) to be taken as a result of any safety issues or otherwise that result in protocol and/or informed consent changes.

9.2 Knowledge Dissemination and Publication Policy

This study will be registered on clinicaltrials.gov. The study has obtained 4 years of funding from the Canadian Institutes of Health Research Project Grant: Fall 2025 and Spring 2026. Final trial results will be presented at national and international conferences and published in a peer-reviewed journal.

Following publication, trial data will be uncoded and securely stored on UBC Microsoft OneDrive and can be provided upon request.

9.3 Study Communication

Summarized study results will be disclosed to participants via email in plain language, along with a copy of the journal article in which this study is published.

10. REFERENCES

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11. APPENDIX

11.1 Appendix I: Table of Assessments and Follow Up

Assessment	Enrollment	Surgery	30-days post-discharge
Prospective trial patients			
Screen using inclusion criteria	X		
Obtain informed consent	X		
Surgical Intervention	Opportunistic bilateral salpingectomy at the time of laparoscopic cholecystectomy		
Data collection on prospective patients		X	X
Retrospective matching controls			
Find matching retrospective controls		X	
Data collection on retrospective patients		X	X