Comparing Female Permanent Contraception Options in High Resource Countries: A Systematic Review

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Research

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Abstract

Background: Multiple options for permanent or long-acting contraception are available, each with adverse effects and non-contraceptive benefits. A comprehensive comparison of methods to support decision-making for people seeking to end their fertility and their healthcare providers is needed.

We aimed to understand what is known from high quality studies about the comparability of options for permanent contraception. We sought studies comparing these methods of permanent or long-acting contraception: laparoscopic tubal ligation, hysteroscopic tubal occlusion, bilateral salpingectomy, and levonorgestrel-releasing intrauterine contraception (LNG-IUC), for effectiveness, adverse events, tolerability, patient recovery, non-contraceptive benefits and healthcare system costs among females in high resource countries seeking to permanently avoid conception.

Methods: We followed PRISMA guidelines, searched EMBASE, Pubmed (Medline), Web of Science, and screened retrieved articles to identify additional relevant studies. We extracted data on population, interventions, outcomes, follow-up, health system costs, and study funding source. We assessed risk of bias using the Newcastle-Ottawa Scale, excluding studies with high risk of bias. Due to considerable heterogeneity, we performed a narrative synthesis.

Results: Our search identified 6,612 articles. We reviewed the full text of 154 studies, yielding 35 studies which met inclusion criteria. We excluded 10 studies with high risk of bias, retaining 25 at low or medium risk for bias in our synthesis. Most studies assessed hysteroscopic tubal occlusion and/or laparoscopic tubal ligation. Most comparisons reported on effectiveness and adverse events, with fewer reporting tolerability, patient recovery, non-contraceptive benefits, and healthcare system costs. No comparisons reported accessibility, eligibility, or follow-ups required.

We found inconclusive evidence comparing the effectiveness of hysteroscopic tubal occlusion to laparoscopic tubal ligation. All studies reported adverse events. All forms of tubal interruption reported a protective effect against cancers. Tolerability appeared greater among tubal ligation patients compared to hysteroscopic tubal occlusion patients. No medium or high-quality studies compared LNG-IUC to other methods.

Conclusions: High-quality studies comparing outcomes relevant for those seeking female permanent contraception are needed to support informed decision-making. Research is needed to directly compare surgical forms of permanent contraception, such as tubal ligation or removal, with alternative options, such as intrauterine contraception.

Systematic review registration: PROSPERO [CRD42016038254].

Plain Language Summary

There are multiple options available to help people end their fertility, if desired. Each option will have accompanying benefits and risks. A comprehensive comparison of the benefits and risks of available options is important to support informed decision-making. We aimed to understand the comparability of laparoscopic tubal ligation, hysteroscopic tubal occlusion, bilateral salpingectomy, and the levonorgestrel-releasing intrauterine contraception (LNG-IUC) among females seeking permanent contraception in high resource countries.

We followed PRISMA guidelines for conducting systematic reviews. We assessed for risk of bias using the Newcastle-Ottawa scale, to ensure that we were including high-quality studies. As we found high heterogeneity among the included articles, we performed a narrative synthesis.

We identified 6,612 articles and reviewed the full text of 154, of which 35 met our inclusion criteria. We further excluded 10 studies due to high risk of bias. We included 25 articles in our synthesis. Most compared hysteroscopic tubal occlusion and/or laparoscopic tubal ligation. No included studies compared LNG-IUC to other methods. Most comparisons reported effectiveness and adverse events, with fewer reporting tolerability, patient recovery time, non-contraceptive benefits, and costs to the healthcare system. We found inconclusive evidence comparing the effectiveness of hysteroscopic tubal occlusion to laparoscopic tubal ligation. All options reported adverse events, and all forms of tubal interruption reported a protective effect against cancers.

There is insufficient research directly comparing surgical forms of permanent contraception, such as tubal ligation or removal, with alternative options, such as intrauterine contraception. High-quality studies are needed to support informed decision-making.

Introduction

Permanent contraception is the most common method of fertility control worldwide.^{1,2} Globally, nearly one in four females in high income countries use either intrauterine contraception or female sterilization.³ Female permanent contraceptive methods are the fourth most commonly relied upon method for preventing pregnancy among people in Canada,⁴ and the second most common method in the United States.⁵ Permanent contraception is traditionally achieved using laparoscopic tubal ligation, with the clipping, coagulation, or other blocking of the fallopian tubes to prevent sperm from travelling to an ovulated oocyte.² However, in the last two decades, other methods to achieve permanent contraception have emerged including bilateral salpingectomy and the levonorgestrel-releasing intrauterine contraceptive (LNG-IUC), while Essure,™ micro inserts used in hysteroscopic tubal occlusion, has been taken off the market in select countries.^{6–8}

Bilateral salpingectomy is increasingly being considered as an alternative option to laparoscopic tubal ligation. In the Canadian province of British Columbia, after an educational campaign led by the Ovarian Cancer Research Team highlighting emerging evidence that ovarian cancer originates in the fallopian tubes⁹, the province saw an increased trend in salpingectomy from 0.4% of female sterilization procedures in 2008 to 33.0% in 2011.¹⁰ Similar increases were seen in Texas and New York, ranging from 4.8 to 77.5% over a similar time period.¹¹ In June 2017, the Society of Obstetricians and Gynaecologists of Canada released a committee opinion that physicians should discuss the protective benefit of tubal ligation and the “fact that the complete removal of the fallopian tube may provide additional benefit.”¹² The additional benefit is primarily the anticipated greater protective effect against ovarian cancer with no additional

side-effects over those with laparoscopic tubal ligation.^{9,13} Two Markov simulation models, creating theoretical cohorts of patients using previously published data, suggested that bilateral salpingectomy could theoretically reduce ovarian cancer risk, diagnoses,¹⁴ and death.¹⁵ Bilateral salpingectomy was theorized to contribute to additional quality years of life when compared to laparoscopic tubal ligation, with a mean incremental cost of \$152 per person.¹⁴ Additional decades of follow up after salpingectomy are still needed to understand how closely reality will compare to this simulation.

Although a reversible contraceptive method, insertion of the LNG-IUC has efficacy and effectiveness rates similar to tubal ligation.^{1-3,5} Although the LNG-IUC requires re-purchase and re-insertion every 5 or more years,¹⁶ this option may be attractive due to the avoidance of surgery and of the faster recovery time compared to that required for other methods.¹⁷ For this reason, we have included LNG-IUC as a permanent contraception alternative for the purpose of this analysis.

Despite the many options available, we were unable to find a guide for clinicians or for people seeking female permanent contraception that systematically compares available methods according to important outcomes, nor any that include comparable long-acting reversible contraception. Permanent contraception decision-making can be complex. It is important that the realities and options are outlined so that people can make an informed choice that is aligned with their reproductive goals. Ultimately, the choice of which contraceptive method to utilize should be based on an informed understanding of not only the effectiveness, but also the potential risks, additional benefits, and accessibility in terms of associated costs and recovery time for the patient.

Objectives

We aimed to understand what is known from high quality studies about the comparability of permanent methods of contraception. In particular we included laparoscopic tubal ligation, hysteroscopic tubal occlusion, bilateral salpingectomy, and insertion of the LNG-IUC among people seeking permanent female contraception in high resource countries. Outcomes included effectiveness at preventing pregnancy, adverse events, tolerability, patient recovery, and non-contraceptive benefits. Secondary outcomes included the length of procedure, costs to the healthcare system, eligibility, accessibility, and follow-ups required to ensure completion or for safety monitoring. Thorough definitions of study objectives are explained in the systematic review protocol.¹⁸

Methods

We followed PRISMA guidelines¹⁹ for this analysis in accordance with the accompanying explanation and elaboration paper.²⁰ The PRISMA checklist is available in Additional file 1.

Protocol registration

We pre-specified and previously published¹⁸ objectives and analyses in a protocol registered on PROSPERO (CRD42016038254).

Eligibility criteria

We included studies that met the following criteria:

- Population comprised of females of reproductive age (15–49), without major comorbidities;
- Prospective and retrospective cohort, case-control, or randomized control trial methodology;
- The paper was published in a peer reviewed journal in English;
- The analysis took place in high resource countries as defined by the World Bank Country and Lending groups;²¹
- The interventions included comparisons of any two or more of: laparoscopic tubal ligation, hysteroscopic tubal occlusion, bilateral salpingectomy, or insertion of the LNG-IUC performed as permanent contraception, and/or controls;
- The outcomes assessed included at least one of the following: effectiveness, adverse events, tolerability, non-contraceptive benefits, patient recovery, accessibility, length of the procedure, follow-ups required, eligibility, or costs to the healthcare system.

We excluded studies with these characteristics:

- A case study or case series design;
- Conducted outside of high resource countries;
- Interventions included concomitant procedures.

Information Sources

We searched EMBASE, Pubmed (Medline), and Web of Science using a combination of MeSH terms and key words related to hysteroscopic tubal occlusion, laparoscopic tubal ligation, the LNG-IUC, and bilateral salpingectomy. We also reviewed the references of relevant articles as secondary screening. We did not set date restrictions, and performed the last search on January 30th, 2019.

Search strategy

We downloaded selected articles in Mendeley Desktop 1.19.3 software (Elsevier, 2008) for further assessment and handling. We consulted librarians to create our search strategy, which is available online:

[Http://med-fom-cart-grac.sites.olt.ubc.ca/files/2016/05/Search-Strategies-Librarian-edit.docx](http://med-fom-cart-grac.sites.olt.ubc.ca/files/2016/05/Search-Strategies-Librarian-edit.docx) .

Study selection

Three authors (RG, BC, BV) independently reviewed titles and abstracts of initial articles based on relevance. RG reviewed all identified articles, and BC and BV each reviewed a subset of articles and together reviewed all articles. After comparison of articles for relevance based on titles and abstracts, RG reviewed full text articles for inclusion or exclusion, noting reasons for exclusion.

Data collection process

RG created the data extraction form and initially pilot-tested the form on a randomly selected subset of studies to determine comprehensiveness. We extracted data from each study that met the inclusion criteria including: population, intervention, comparisons, outcomes, and study design (PICOS); follow-up period; and funding source for the study, where available.

RG extracted data from all relevant articles, and BV independently extracted data from a sample of articles. We compared the data extraction forms for accuracy. Any discrepancies were adjudicated by the senior author (WVN).

Data items

We defined all data items, including definitions of the variables sought, in detail in our protocol.¹⁸

Risk of bias in individual studies and across studies

We used the Newcastle Ottawa Scale (NOS) to determine risk of bias for cohort and case-control studies.²² We assessed risk of bias for each included study, and presented the results in a table stratified by study design. Any articles assessed to be at high risk of bias (NOS score < 7) were excluded from the narrative analysis.

We assessed the cumulative risk of bias based on the risk of bias found in individual studies, along with careful consideration of any outcome reporting bias, incomplete study data, or overall quality of the evidence presented and synthesized.

Synthesis of results

We aimed to perform a network meta-analysis, but heterogeneity was assessed as substantial ($I^2 \geq 80\%$), with wide variability in outcome reporting that precluded a valid pooling of results. Therefore, we undertook a narrative synthesis in accordance with the guidelines of the Cochrane Consumers and Communication Review Group.²³ We organized the narrative synthesis by outcome, describing the similarities, differences, and patterns of results.

Results

Study Selection

Figure 1 details our study selection process, including reasons for exclusion, following PRISMA guidelines.¹⁹ Our database search of EMBASE, Pubmed (Medline), and Web of Science revealed 6,826 documents, and we identified an additional 25 documents through secondary screening. After we excluded duplicates (239), RG, BC, BV reviewed titles and abstracts based on relevance. RG reviewed all 6,612, and BC and BV independently reviewed 1,647 and 5,088 studies respectively. Of these, we excluded 6,458 because they did not meet the inclusion criteria. RG reviewed the full text of the remaining 154 studies. BV reviewed 30 full text studies, and compared them with the relevant articles assessed by RG to check for accuracy. As discussed in the protocol, we did not include unpublished studies in this review. We extracted data and assessed risk of bias for 35 studies. We found medium to high risk of bias in 10 studies, leaving a total of 25 studies included in the narrative review synthesis.

Study Characteristics

The characteristics and results of all included studies can be found in Table 1. Of the studies included for the narrative synthesis, six compared effectiveness;^{24–29} sixteen assessed adverse effects;^{11, 24, 25, 28–40} three compared patient recovery;^{25, 35, 36} five compared non-contraceptive benefits, primarily the reduction of cancer risk;^{34, 41–44} six compared tolerability;^{24, 25, 27–29, 44} four compared costs to the healthcare system;^{28, 45–47} and six compared length of procedures.^{11, 28, 35, 36, 40, 47} No included studies compared accessibility, eligibility, or follow-up required. The majority of studies (n = 23) were observational cohorts, and the rest were case-control studies (n = 2). The studies were conducted in the United States (n = 14), Canada (n = 2), the UK (n = 2), France (n = 2), Denmark (n = 1), Spain (n = 1), Sweden (n = 1), Finland (n = 1), and Australia (n = 1). All included studies were published between 2003–2019. Enrolment of females of reproductive age (15–49) occurred between 1966–2016, with significant variations in follow-up ranging from two weeks to forty-four years.

People who had severe comorbidities were excluded. All studies were pairwise comparisons of females of reproductive age, who underwent an interval contraceptive procedure including either laparoscopic tubal ligation, hysteroscopic tubal occlusion, bilateral salpingectomy, or insertion of the LNG-IUC, or were selected as a control comparison.

Studies we included in the narrative analysis compared laparoscopic tubal ligation vs. control (n = 3), hysteroscopic tubal occlusion vs. laparoscopic tubal ligation (n = 12), laparoscopic tubal ligation vs. bilateral salpingectomy (n = 6), laparoscopic tubal ligation vs. bilateral salpingectomy vs. control (n = 3),

hysteroscopic tubal occlusion vs. bilateral salpingectomy vs. laparoscopic tubal ligation (n = 1). Our search revealed only one study which included outcomes with the LNG-IUC, however it was excluded from narrative synthesis due to risk of bias.

Risk of bias within studies

We excluded studies where risk of bias was determined to be medium to high (NOS 0–6) in at least one domain of assessment of risk, largely due to the observational study designs, non-random allocation of interventions, and differences in baseline characteristics between comparator groups. Our assessment of risk of bias for each study can be found in Additional File 2.

Results of individual studies

Results of individual studies can be found in Table 1.

Narrative synthesis of results

Effectiveness

Six studies reported the rate of pregnancy, all of which were cohort studies comparing hysteroscopic tubal occlusion and laparoscopic tubal ligation.^{24–29} Among the included studies, there was a wide range of follow-up time to assess effectiveness (from one year to a maximum of ten years)²⁴ and significant variance in directionality and strength of the outcome; this likely explains the considerable heterogeneity observed.

Three analyses found no significant difference in the risk or reported number of unintended pregnancies between laparoscopic tubal ligation and hysteroscopic tubal occlusion.^{24, 27, 28} A retrospective cohort in the United States found that the cumulative rate of pregnancy was 1.02 pregnancies per 100 person years for hysteroscopic tubal occlusion and 0.88 pregnancies per 100 person years for laparoscopic tubal ligation (p = 0.003). Patients who underwent hysteroscopic tubal occlusion were at 1.2 times higher risk of becoming pregnant compared to those who underwent laparoscopic tubal ligation [aHR = 1.20 (95% confidence interval = 1.09–1.33)].²⁹

Two studies, both conducted in France, found a higher risk of pregnancy among laparoscopic tubal ligation than hysteroscopic tubal occlusion;^{25, 26} however for one study, this difference was only significant at one year [aHR = 0.70 (0.53–0.92)], but not at three years [aHR = 1.04 (0.83–1.30)].²⁵

Adverse Effects

Sixteen studies assessed adverse effects using prospective/retrospective cohort designs. Results are organized by intervention: six compared hysteroscopic tubal occlusion and laparoscopic tubal ligation,^{24, 25, 28–31} three compared laparoscopic tubal ligation and a control,^{32–34} five compared laparoscopic tubal ligation and bilateral salpingectomy,^{11, 35–37, 40} one compared hysteroscopic tubal occlusion, laparoscopic tubal ligation with controls, and bilateral salpingectomy with controls,³⁸ and one compared bilateral salpingectomy with laparoscopic tubal ligation and with matched controls.³⁹

Hysteroscopic tubal occlusion vs. Laparoscopic tubal ligation Two studies^{24, 30} found no statistically significant difference in rates of adverse effects including abnormal uterine bleeding, pelvic pain, or opioid managed pain between the two interventions. One study found no difference between chronic pelvic pain, risk of hysterectomy, or abnormal uterine bleeding at 6 or 12 months post-procedure among women who underwent hysteroscopic tubal occlusion compared to laparoscopic tubal ligation, finding only a significantly lower risk of chronic pelvic pain and risk of hysterectomy among women undergoing hysteroscopic tubal occlusion at 24 months post-procedure.³¹

Hysteroscopic tubal occlusion was associated with a lower risk of surgical complications than laparoscopic tubal ligation [aOR = 0.18 (0.14–0.23)]²⁵ and a lower risk of iatrogenic complications after surgery [OR = 0.35 (0.20, 0.61)].²⁸ Two analyses found higher rates of gynecological complications with hysteroscopic tubal occlusion compared to laparoscopic tubal ligation,^{25, 29} with one analysis finding that menstrual dysfunction was significantly higher for people undergoing hysteroscopic tubal occlusion [aHR = 1.23 (1.20–1.27)].²⁹ However, pelvic pain incidence was found to be significantly lower in hysteroscopic tubal occlusion patients compared to laparoscopic tubal ligation patients [21.0% compared with 25.6% at 2 years, aHR = 0.83 (0.80–0.85)].²⁹

Laparoscopic tubal ligation vs. Comparison

Compared to controls, included studies did not find a statistically significant change in menstrual cycle after undergoing laparoscopic tubal ligation³² nor any differences in blood LH and E2 levels, ovarian volume, or number of antral follicles on third day of cycle.³³

One study found an increase in risk for anal cancer among those who underwent laparoscopic tubal ligation compared to those who did not [RR = 1.34 (1.11–1.63)]; however, no associations between laparoscopic tubal ligation and risk of endometrium, breast, cervix, or colorectal cancers, nor all cancers combined, were significant.³⁴

Laparoscopic tubal ligation vs. Bilateral salpingectomy

Three studies found that there was no significant difference when comparing risk of readmission, blood transfusion, or intraoperative complications between laparoscopic tubal ligation and bilateral salpingectomy,^{11, 35, 36} nor any difference in post-procedure physician visits for surgical infection or complication.³⁷ No significant differences in complications were found when assessing both immediate (2.9% vs. 2.5%, p = 1.0) and short-term (within 30 days) adverse events (14.7% vs. bilateral salpingectomy: 4.9%, p = 0.51) among people undergoing laparoscopic tubal ligation and bilateral salpingectomy, respectively.⁴⁰ However, there was a higher risk among people who underwent bilateral salpingectomy who required prescription analgesic use after surgery compared to those who underwent laparoscopic tubal ligation [(aOR = 1.21 (1.14–1.29))].³⁷

Hysteroscopic tubal occlusion vs. Laparoscopic tubal ligation vs. Bilateral salpingectomy vs. controls One study performed a retrospective cohort study using administrative data to assess risk of ectopic pregnancy among people who underwent surgical sterilizations including bilateral salpingectomy, laparoscopy with Filshie clip, minilaparotomy, laparotomy, and hysteroscopic tubal occlusion using Essure™ compared to an unspecified destruction or occlusion of fallopian tubes.³⁸ Hazard ratios for ectopic pregnancy did not remain significant for laparoscopy with Filshie clip, minilaparotomy, and laparotomy, and there were no ectopic pregnancies reported for bilateral salpingectomy nor hysteroscopic tubal occlusion with Essure™.³⁸

Bilateral salpingectomy vs. Tubal ligation vs. Historical Controls

When comparing bilateral salpingectomy and laparoscopic tubal ligation to historical controls, there was no significant difference when comparing estimated median blood loss between bilateral salpingectomy (5 ml) with laparoscopic tubal ligation current (7 ml, $p = 0.18$) or historical (10 ml, $p = 0.31$) controls.³⁹

Patient Recovery

Two studies comparing laparoscopic tubal ligation and bilateral salpingectomy found no significant difference in terms of length of hospital stay, although there was a wide variance in reported length between the two studies (median of 1.8 hours³⁶ to 1.31 days³⁵).

One study found that women who underwent hysteroscopic tubal occlusion required fewer sick days compared to women who underwent laparoscopic tubal ligation at one-year (.590 days vs. 6.50 days, $p < 0.001$) and at three years (28.3 vs. 32.3, $p < 0.001$).²⁵

Non-contraceptive benefits

Five studies measured non-contraceptive benefits, primarily assessing preventative benefits in reducing the risk of developing various cancers. Three compared bilateral salpingectomy or laparoscopic tubal ligation against controls,^{41–43} one compared laparoscopic tubal ligation against controls,³⁴ and the last compared hysteroscopic tubal occlusion and laparoscopic tubal ligation directly.⁴⁴ Two were a case-control studies^{42, 43} while the rest were cohorts using large administrative databases.^{34, 41, 44}

When looking exclusively at laparoscopic tubal ligation vs. a matched control, there was a reduction in ovarian cancer risk [RR = 0.80 (0.76–0.85)], peritoneal cancers [RR = 0.81 (0.66–0.98)], and cancers of the fallopian tube [RR = 0.60 (0.37–0.96)].³⁴

Both laparoscopic tubal ligation and bilateral salpingectomy had protective effects against cancers when compared to a matched control. In Falconer et al.'s Swedish population cohort, both laparoscopic tubal ligation [aHR = 0.72 (0.64, 0.81)] and salpingectomy [aHR = 0.65 (0.52, 0.81)] had protective effects against ovarian or tubal cancer compared to females who did not have any surgical intervention after an average 23.1 year follow-up.⁴¹ A sub-analysis found that bilateral salpingectomy had a greater reduction in risk than unilateral salpingectomy [aHR = 0.35 (0.17, 0.73) vs. aHR = 0.71 (0.56, 0.91) respectively], although data distinguishing laterality was only available up to 1996.⁴¹ Similarly, people in Denmark who underwent laparoscopic tubal ligation or bilateral salpingectomy had reduced odds of developing epithelial ovarian cancer ([OR = 0.87 (0.78, 0.98)] and [OR = 0.58 (0.36, 0.95)], respectively) compared to matched controls.⁴²

An age-matched case-control study in one state in the United States found that when adjusted, a history of any tubal sterilization proved to have a statistically non-significant odds ratio of reducing the risk of developing epithelial ovarian cancer [OR = 0.59 (0.29, 1.17)] compared to matched controls.⁴³ Further analyses comparing the effect of bilateral salpingectomy against matched controls, non-excisional techniques, and partial salpingectomy also remained statistically insignificant [OR = 0.22 (0.03, 1.87)].⁴³ Similarly, using data from the New York State Department of Health, Mao et al. found no difference in the incidences of gynecologic cancer [(0.1% vs. 0.1%, HR = 2.63, (0.70–9.91)] or other cancers [(1.2% vs. 1.3%, HR = 1.03 (0.78–1.36)] after initial hysteroscopic tubal occlusion compared with laparoscopic tubal ligation.⁴⁴

Tolerability

Nine studies assessed the ability to perform the intended method without requiring other procedures to either fix the procedure due to an unsuccessful first attempt, or a secondary procedure to remove hardware (micro inserts). All studies compared the tolerability of hysteroscopic tubal occlusion vs. laparoscopic tubal ligation with a wide variation in follow-up time, from an average of thirty days²⁴ to seven years.⁴⁴

Six studies found that there was a significantly higher risk of re-operation among those who underwent hysteroscopic tubal occlusion compared to laparoscopic tubal ligation,^{24, 25, 27–29, 44} with studies reporting an increased adjusted hazard ratio from 2.05,²⁹ to 3.26 (1 year post-procedure),²⁵ and reporting odds of re-operation as high as 10-fold the odds at one year post-procedure.²⁸ At three years follow up, one study found that the increased risk of re-operation remained (aHR = 1.62, 1.51–1.73).²⁵

Accessibility

We did not find an eligible study that systematically measured or compared the out-of-pocket costs for the procedure, wait times, or the locations where the procedure can be performed.

Secondary objectives

Eligibility

We did not find an eligible study that systematically measured or compared eligibility for the procedures.

Follow-up required

We did not find an eligible study that compared the number of follow-up visits needed, or required, to ensure that the method was completed or for safety monitoring.

Costs to the healthcare system

Four studies measured costs to the healthcare system by index cost. All studies compared total costs between hysteroscopic tubal occlusion and laparoscopic tubal ligation, either reporting the mean or the median index costs per patient when undergoing each procedure. Three studies found that hysteroscopic tubal occlusion was less costly to perform than laparoscopic tubal ligation,⁴⁵⁻⁴⁷ with costs for hysteroscopic tubal occlusion ranging between \$1374⁴⁶ and \$3964.⁴⁵ Costs for laparoscopic tubal ligation ranging between \$2264⁴⁷ and \$5163.⁴⁵ One study found that total medical and prescription costs (\$7093 vs. \$7568, $p < 0.0001$) and procedure-related costs (\$4971 vs. \$5407, $p < 0.0001$) were lower among women who underwent hysteroscopic tubal occlusion compared to tubal ligation.⁴⁵ However, costs related to complications or failures were higher with hysteroscopic tubal occlusion compared to laparoscopic tubal ligation (\$272 vs. \$176).⁴⁶ One study found higher total charges for hysteroscopic tubal occlusion compared to laparoscopic tubal ligation (median \$7832 vs. \$5068, $P < 0.01$).²⁸

Length of the Procedure

Six studies compared the length of the procedure, with four comparing bilateral salpingectomy and laparoscopic tubal ligation, and two comparing laparoscopic tubal ligation and hysteroscopic tubal occlusion.

Table 1: Characteristics of All Studies, Including Risk of Bias, included in the Comparing Female Permanent Contraception Options in High Resource Countries: A Systematic Review (n=35)

First author, year	Study period	N	Country	Population	Intervention	Comparison	Outcomes Reported	Study Design	Follo perio
Abbhul, 1997	1990-1991	24=LTL 182=Control	US	Mean 30.8 vs. 24.1	LTL	No sterilization	Adverse events, frequency of pelvic inflammatory disease	Retrospective cohort study	Not r
Antoun, 2017	2005-2015	1085=HTO 2412=LTL	UK	Mean age 36.1 Vs. 35.6	HTO	LTL	Effectiveness, adjusted hazard ratio Adverse events, intraoperative and post-operative complications Tolerability	Observational Cohort	Effec 1-10 (date steril proce Medi years Adve event days
Bouillon, 2018	2010-2015	71303=HTO 34054=LTL	France	Mean age 41.5 vs. 40.8	HTO	LTL	Effectiveness: adjusted hazard ratio Adverse events, in hospital surgical and medical complications Tolerability: adjusted hazard ratio Sick days	Cohort, nation-wide database	1-3 y
Carmona, 2003	1994	31=LTL 31=Control	Spain	36.4 vs. 36.1	LTL	No sterilization	Adverse events, abnormal menstrual changes	Case-control	5 yea
Carney, 2017	2010-2012	12031=HTO 7286=LTL	US	Mean age 37.0 vs. 35.8	HTO	LTL	Costs to Healthcare: mean index costs, and total all-cause medical and prescription costs per woman	Retrospective Cohort	6 mo
Conover, 2015	2005-2012	26927=HTO 44948=LTL	US	Mean age 37.8 vs. 36.6	HTO	LTL	Adverse events: Opioid managed pelvic pain	Prospective Cohort (administrative claims)	Mean days 283 l
Duffy, 2005	Not reported	59=HTO 24=LTL	UK	Mean age 35.1 vs. 36.1	HTO	LTL	Effectiveness (frequency) Adverse	Cohort controlled comparative trial	3 mo

							Pain during and post-procedure			
							Patient satisfaction immediately after and at 3 month follow up			
							Tolerability			
							Length of Procedure			
Falconer, 2015	1973-2009	34433=BS 81658=LTL 5449119=Unexposed	Sweden	35.7 37.9 35.9	LTL BS	Unexposed	Non-contraceptive benefits: adjusted hazard ratio for ovarian/tubal cancer of exposed vs. unexposed	Population based cohort study	18 vs. 20	
Fernandez, 2014	2006-2010	39169=HTO 70108=LTL	France	Median 41 vs. 40yrs	HTO	LTL	Effectiveness, hazard ratio	Retrospective cohort (hospital discharge)	1-4 y	
Franchini, 2009	2005-2007	24=LTL 25=HTO	Italy	Not reported	HTO	LTL	Days missed from work Cost to the healthcare system Length of procedure	Activity based cost management	Not r	
Gaitskell, 2016	1996-2001	294724=LTL 984059=Control	UK	Mean age 55.4 vs. 56.3	LTL	No sterilization	Adverse events (risk of cancer) Non-contraceptive benefits: prevention of cancer risk	Prospective cohort study	13.8	
Greisman, 1991	1981-1987	22=Ectopic with LTL 268=Ectopic no LTL	Canada	Mean age 33.5	LTL	No sterilization	Frequency of ectopic pregnancies	Case control	4.6 y average	
Hanley, 2018	2008-2014	19424=LTL 5839=BS	Canada (BC)	Mean age 35.3 vs. 36.4	LTL	BS	Adverse events Prescription analgesic medication, surgical infections,	Retrospective cohort study	2 weeks	

							surgical complications		
Hopkins, 2007	2003-2004	43=HTO 44=LTL	US	Mean age 37.2 vs. 37.3	HTO (operating room)	LTL	Cost to the healthcare system; Median hospital and physician costs Length of procedure	Retrospective cohort study	Not r
Jokinen, 2017	2009-2014	5631=HTO 4425=LTL	Finland	38.0 vs. 35.5, 37.8	HTO	LTL	Effectiveness, risk ratio Tolerability	National Register, study linkage	Not r
Kelekci, 2004	2002-2005	74=LTL 74=Controls	US	Mean age 34.2 vs. 35.1	LTL	Control	Adverse events Blood LH and E2 levels, ovarian volume, number of antral follicle on third day of cycle.	Controlled prospective study	12 m
Kjer, 1990	1978-1981	10104=LTL 847012=Control	Denmark	NA	LTL	No sterilization	Effectiveness, incidence of pregnancy Risk of hysterectomy	Case control	4-7 y
Kim, 2019	2013-2016	180=BS 242=LTL	US	33.1 vs. 32.3	LTL	BS	Adverse events Length of procedure	Retrospective cohort study	Not r
Lessard-Anderson, 2014	1966-2009	194=Cases 388=Controls	US	61.4 vs. 61.4	BS LTL	Matched control	Non-contraceptive benefits	Nested case-control	44 ye
Levie, 2005	Unspecified	Unspecified	US	Unspecified	HTO (office setting)	LTL (surgical)	Institutional cost comparison (including pre and post-operation costs)	Cost comparison analysis	Not r
Madsen, 2015	1982-2011	13241=Cases (ovarian cancer) 194689=Controls (ovarian cancer) 3605=Cases (ovarian tumour) 53322=Controls (ovarian tumour)	Denmark	Each case (30-84, no previous cancer) matched with 15 randomly selected matched on date of birth from Civil Registration	BS, LTL	Control	Non-contraceptive benefits (risk of cancers)	Case-control (register-based)	Not r
Malacova,	1990-2010	278=HTO	Australia	18-44,	HTO, BS,	Unspecified	Adverse	Retrospective	Up to

2014		20429=LTL 553=BS 22295=unspecified		history of EP excluded	LTL	destruction of tubes	events: Ectopic pregnancy	cohort study	
Mao, 2019	2005-2016	10143=HTO 53206=LTL	US (NY state)	34.9 vs. 35.0	HTO	LTL	Tolerability Non-contraceptive benefits	Observational cohort	Medi
Mao, 2015	2005-2013	8048=HTO	New York	Majority were between 30-39 in both arms	HTO	LTL	Effectiveness (odds ratio) Adverse events Tolerability Length of procedures Costs to healthcare system	Observational, Population based cohort study	1 yr
McAlpine, 2014	2008-2011	1569=BS 13719=LTL	Canada	36.0 (BS) vs. 34.8 (LTL)	BS	LTL	Length of hospital stay Adverse events: Blood loss or transfusion Length of procedure	Retrospective cohort study	Not r
Kathy, 2014	2008-2011	60=HTO 25=LTL	UK	Mean age 36.5 vs. 35.1	HTO	LTL	Effectiveness Tolerability Adverse events: antibiotics, analgesia readmission, wound infections Patient satisfaction: Postoperative pain Return to work	Retrospective chart review	6-50 Mear
Perkins, 2016	2007-2013	27724=HTO 42391=LTL	US	Mean 37.4 vs. 36.7	HTO	LTL	Effectiveness, adjusted hazard ratio	Retrospective cohort study	Medi vs. 2.

							Adverse events		
							Menstrual dysfunction		
							Pelvic pain		
							Tolerability		
Powell, 2017	2011-2016	1515=BS 2236=LTL	US (Northern California)	36 vs 36	BS	LTL	Adverse events: Median blood loss, Hospital readmission within 30 days Length of procedure	Retrospective cohort study	5 years
Rulin, 1993	Not reported	500=LTL 466=Comparison	US (3 hospitals: Pittsburgh, Atlanta, NY)	28 (LTL) vs. 27	LTL	Comparison	Abnormal menstrual cycle, prolonged bleeding, heavy bleeding, bleeding between periods, severe dysmenorrhea, bad menstrual cramps, Severe non-cycle pelvic pain	Cohort	3-4.5
Steward, 2017	2009-2012	3929=HTO 10875=LTL	US	Mean age 31.8 vs. 30.4 Insured	HTO	LTL	Adverse events 6 month outcomes: Hysterectomy Chronic pelvic pain Abnormal uterine bleeding 12 month outcomes: Hysterectomy Chronic pelvic pain Abnormal uterine bleeding 24 month outcomes: Hysterectomy Chronic pelvic pain Abnormal uterine bleeding	Retrospective cohort study	24 months

Syed, 2007	2003-2004	20=LTL 20=HTO	US – Staten Island Uni	42.5 vs. 38	HTO	LTL	Pain immediate, 1 week, 4 weeks postprocedure Length of hospital stay Pt satisfaction Length of procedure	Cohort study	6 not r
Theil, 2008	HTO=2005-2006 LTL=2001-2004	108=HTO 104=LTL	Regina, Canada	36.8 vs. 33.4	HTO	LTL	Tolerability Length of procedure Cost per index case	Retrospective cohort study	Not r
Trussel, 1995	1991-1993	20,000 public payments from commercial insurers	United States	Not reported	LTL	LNG-IUC	Cumulative costs to the healthcare system	Cohort	Not r
Westberg, 2017	2011-2015	81=BS 68=LTL	US (UC Davis Medical Center)	35.6 (BS) vs. 36.2 (LTL)	BS	LTL	Adverse events: Short term complication Length of procedure (surgical time)	Retrospective cohort study (chart review)	30 d
Zerden, 2018	2014-2015	13=BS 5=Current LTL 22=Historical LTL	US	35.0 vs. 34.6 vs. 34.9	BS	LTL (current and historical)	Adverse events: Blood loss (median)	Cohort study	Not r

Four studies found that the bilateral salpingectomy procedure took significantly longer than laparoscopic tubal ligation to complete (3–11 minutes longer).^{11, 35, 36, 40} Median/mean procedure times for bilateral salpingectomy ranged between 44⁴⁰ – 66³⁶ minutes, and for laparoscopic tubal ligation between 38⁴⁰ – 64³⁶ minutes.

Two studies comparing laparoscopic tubal ligation and hysteroscopic tubal occlusion found that the laparoscopic tubal ligation procedure took significantly longer (means and medians ranging between 27–52 minutes) than hysteroscopic tubal occlusion (means and medians ranging between 18–36 minutes).^{28, 47}

Risk of bias across studies

Overall, the cumulative evidence presented remains at low to medium risk of bias due to the observational study design used in all cases. Due to the observational study designs used, we found that there were significant sociodemographic differences between comparator groups that were not able to be adjusted for. Some studies did not fully report their patient demographic, leading to questions about comparability. With high heterogeneity found, our interpretation of evidence must be balanced and cautious. Our conclusions focus on comparisons between laparoscopic tubal ligation and hysteroscopic tubal occlusion, and we described tentative conclusions with other comparisons.

Additional Analysis

We did not conduct any additional analyses.

Discussion

Summary of Evidence

There is insufficient data to compare available options for people seeking female permanent contraception, especially comparing to the LNG-IUC. The majority of studies eligible for our review compared laparoscopic tubal ligation to hysteroscopic tubal occlusion using Essure™ micro inserts. The latter method is currently no longer available for use in some jurisdictions.^{6–8} As trends for alternatives to laparoscopic tubal ligation continue to increase, more research is needed to compare the options available so that people seeking female permanent contraception and their healthcare providers are able to make an informed decision.

While our review found that the majority of studies comparing hysteroscopic tubal occlusion and laparoscopic tubal ligation did not find a significant difference in effectiveness, it is important to note that for hysteroscopic tubal occlusion, success of effectiveness relied on participants using another form of contraception, or abstinence, before tubal occlusion could be confirmed with a hysterosalpingogram and correct bilateral placements of the micro inserts. Other options, including laparoscopic tubal ligation, bilateral salpingectomy, and insertion of the LNG-IUC are successful at preventing pregnancy immediately. Although studies that assessed the effectiveness of the LNG-IUC were not included, other reviews have demonstrated the high efficacy of this method, with a cumulative pregnancy rate of 0.5 per 100 users,⁴⁸ which appears comparable to laparoscopic tubal ligation.⁴⁹

Non-contraceptive benefits primarily looked at protective effects against various types of cancers. While the magnitude of the protective effect differed between methods of permanent contraception, it appears that undergoing some form of tubal interruption – whether it be occlusion, ligation, or removal – has a protective effect against several types of gynecologic cancers. In separate reviews, the LNG-IUC is also suggested to have protective effects against gynecological cancers,⁵⁰ as well as menorrhagia, endometriosis, adenomyosis, and fibroids.⁴⁸ Longer term cohort studies will be required to effectively compare these protective effects among all available options for female permanent or long acting contraception.

All options for female permanent contraception included in our review had risks of adverse effects; however, we did not find significant differences in opioid managed pain, pelvic pain, menstrual dysfunction, or intraoperative complications when comparing surgical methods and/or controls. Notably no studies comparing pain included patients selecting the LNG-IUC. One study found that hysteroscopic tubal occlusion patients had a lower risk of post-procedure hysterectomy 24-months post-procedure,³¹ but the strength of the evidence is diminished with potential bias in funding from Bayer, the company that created the Essure™ device. Multiple studies have found an association between an increased risk of anal cancer and a history of laparoscopic tubal ligation.^{34, 51} Although we did not find articles assessing adverse events of the LNG-IUC to include in our review, previous studies found minimal adverse effects, with some attributed to the device itself such as dysmenorrhea or irregular bleeding or to the levonorgestrel such as weight gain,⁴⁸ although there is conflicting evidence with weight gain due to levonorgestrel.⁵² The more serious complications, such as uterine perforation, are found to occur rarely (estimated 2.6 per 1000 insertions).⁵³

Patient recovery was only assessed by length of hospital stay between salpingectomy and tubal ligation, where no significant difference was found. Considerations including patient satisfaction, time to return to work, and other factors need to be explored further. Separate reviews have found that those who undergo the insertion of the LNG-IUC have high patient satisfaction and an almost immediate recovery time.^{54–56}

Lastly, we considered costs to the healthcare system. While three out of four studies assessing hysteroscopic tubal occlusion and laparoscopic tubal ligation found that hysteroscopic tubal occlusion was significantly less costly to perform than laparoscopic tubal ligation,^{45–47} costs related to complications or failures were higher after hysteroscopic tubal ligation.⁴⁶ Costs to the healthcare system also should balance preventative costs, such as savings per life-year gained with prevention of cancer cases. No studies calculated preventative cost-savings accompanying non-contraceptive benefits in each method, despite evidence that laparoscopic tubal ligation^{34, 41–44} and the LNG-IUC⁵⁷ provide potential cancer risk reduction. Three Markov models predicted a theoretically significant cost-effectiveness when bilateral salpingectomy is employed in place of laparoscopic tubal ligation in terms of ovarian cancer prevention and life-years gained.^{14, 15, 58} Actual patient cohort studies will be needed to determine if this savings is realized in practice.

Limitations

We found significant heterogeneity between the included articles. This high heterogeneity is likely driven by their methodological diversity and observational study designs, which did not allow for randomized allocation of participants. Therefore, significant differences in study population likely existed between the different intervention types, such as age, socioeconomic status, or underlying health conditions that were not excluded as a major comorbidity. Additionally, we found that follow-up times varied widely between the included studies, with some only allotting minimal weeks for follow-up time, which biases individual studies by not allowing for an accurate assessment of possible outcomes. Additionally, outcomes may thus be attributable to baseline differences and although associated with the interventions, may not necessarily be causally linked to the interventions.

Secondly, due to high heterogeneity, we were not able to complete a network meta-analysis and instead performed a narrative synthesis of results. Limitations to narrative synthesis include the potential biasing of results by overemphasizing the outcomes of particular studies, and the inability to objectively compare the different options available.

Thirdly, results primarily focused on findings comparing laparoscopic tubal ligation and/or hysteroscopic tubal occlusion, with 10 out of 25 studies assessing bilateral salpingectomy and no articles assessing the LNG-IUC. Therefore, for bilateral salpingectomy results of studies may be overemphasized as our outcomes are based on less available evidence.

Conclusions

Previous meta-analyses have compared outcomes between hysteroscopic tubal occlusion and laparoscopic tubal ligation, yet few have considered other options available for permanent contraception. Several studies illustrate an increasing trend of using bilateral salpingectomy for permanent contraception, and there are many calls to consider LNG-IUC as a permanent contraception alternative, as it offers similar effectiveness rates with fewer adverse effects. High quality studies that compare traditional forms of permanent contraception, such as the laparoscopic tubal ligation, with new and alternative methods, are urgently needed to provide evidence on the implications for all options available to people seeking permanent female contraception.

Abbreviations

MeSH
Medical Subject Heading
LNG-IUC
levonorgestrel-releasing intrauterine contraceptive
NOS
Newcastle Ottawa Scale

Declarations

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Availability of data and materials

The datasets we used and/or analysed during our review are available from the corresponding author upon reasonable request. Copies of the search strategies can be found at <http://med-fom-cart-grac.sites.olt.ubc.ca/files/2016/05/Search-Strategies-Librarian-edit.docx>.

Author's contributions

RG and WVN devised the project objectives and design, and RG wrote the initial draft. BV, BC, and WVN contributed to revisions of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

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Figures

PRISMA 2009 Flow Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7): e1000097. doi:10.1371/journal.pmed.1000097

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Figure 1

Details our study selection process, including reasons for exclusion, following PRISMA guideline

PRISMA 2009 Flow Diagram

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