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Hysteroscopic Tubal Sterilization: An Evidence-Based Analysis

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Abstract

Background

Hysteroscopic tubal sterilization is a minimally invasive alternative to laparoscopic tubal ligation for women who want permanent contraception. The procedures involves non-surgical placement of permanent microinserts into both fallopian tubes. Patients must use alternative contraception for at least 3 months postprocedure until tubal occlusion is confirmed. Compared to tubal ligation, potential advantages of the hysteroscopic procedure are that it can be performed in 10 minutes in an office setting without the use of general or even local anesthesia.

Objective

The objective of this analysis was to determine the effectiveness and safety of hysteroscopic tubal sterilization compared with tubal ligation for permanent female sterilization.

Data Sources

A standard systematic literature search was conducted for studies published from January 1, 2008, until December 11, 2012.

Review Methods

Observational studies, randomized controlled trials (RCTs), systematic reviews and meta-analyses with 1 month or more of follow-up were examined. Outcomes included failure/pregnancy rates, adverse events, and patient satisfaction.

Results

No RCTs were identified. Two systematic reviews covered 22 observational studies of hysteroscopic sterilization. Only 1 (N = 93) of these 22 studies compared hysteroscopic sterilization to laparoscopic tubal ligation. Two other noncomparative case series not included in the systematic reviews were also identified. In the absence of comparative studies, data on tubal ligation were derived for this analysis from the CREST study, a large, multicentre, prospective, noncomparative observational study in the United States (GRADE low). Overall, hysteroscopic sterilization is associated with lower pregnancy rates and lower complication rates compared to tubal ligation. No deaths have been reported for hysteroscopic sterilization.

Limitations

A lack of long-term follow-up for hysteroscopic sterilization and a paucity of studies that directly compare the two procedures limit this assessment. In addition, optimal placement of the microinsert at the time of hysteroscopy varied among studies.

Conclusions

Hysteroscopic sterilization is associated with:

- lower pregnancy rates compared to tubal ligation (GRADE very low)
- lower complication rates compared to tubal ligation (GRADE very low)
- no significant improvement in patient satisfaction compared to tubal ligation (GRADE very low)

Plain Language Summary

Hysteroscopic tubal sterilization is a minimally invasive alternative to conventional tubal ligation for women who want a permanent method of contraception. Both approaches involve closing off the fallopian tubes, preventing the egg from moving down the tube and the sperm from reaching the egg.

Tubal ligation is a surgical procedure to tie or seal the fallopian tubes, and it usually requires general anesthesia. In contrast, hysteroscopic tubal sterilization can be performed in 10 minutes in an office setting without general or even local anesthesia. A tiny device called a microinsert is inserted into each fallopian tube through the vagina, cervix, and uterus without surgery. An instrument called a hysteroscope allows the doctor to see inside the body for the procedure. Once the microinserts are in place, scar tissue forms around them and blocks the fallopian tubes.

Health Quality Ontario conducted a review of the effectiveness and safety of hysteroscopic tubal sterilization compared to tubal ligation.

This review indicates that hysteroscopic tubal sterilization is associated with:

- lower pregnancy rates compared to tubal ligation
- lower complication rates compared to tubal ligation
- no significant improvement in patient satisfaction compared to tubal ligation

However, we found a number of limitations to the studies available on hysteroscopic tubal sterilization. Among other concerns, most studies did not include long-term follow-up and only 1 study directly compared hysteroscopic tubal sterilization to tubal ligation.

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List of Abbreviations

CI	Confidence interval
CREST	Collaborative Review of Sterilization study
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HQO	Health Quality Ontario
HSG	Hysterosalpingogram
RCT	Randomized controlled trial

Background

Objective of Analysis

The objective of this analysis was to determine the effectiveness and safety of hysteroscopic tubal sterilization compared with tubal ligation for permanent female sterilization.

Clinical Need and Target Population

Tubal Sterilization

Tubal sterilization is a permanent type of contraception for women. The procedure aims to prevent fertilization by blocking the passage of sperm cells through the fallopian tubes. The conventional approach, laparoscopic tubal ligation, closes the fallopian tubes by the use of rings, clips, electrocoagulation, or excision. (1) Laparoscopic tubal ligation can be done as day surgery under general or local anesthesia and requires gas insufflation to distend the peritoneal cavity to enhance visualization of the abdominal and pelvic organs. (1)

Data on the long-term follow-up of women who have undergone laparoscopic tubal ligation have been derived from the Collaborative Review of Sterilization (CREST) in the United States. (2) This study was a multicentre, prospective, noncomparative cohort study that examined 10,685 women who received laparoscopic tubal sterilizations and were followed for 8 to 14 years. When all procedures were considered in aggregate, the 10-year cumulative life-table probability of failure (meaning pregnancy) was 18.5 per 1,000 procedures (95% confidence interval [CI], 15.1–21.8). (2) Minor complications from bilateral tubal ligation include infection (1%), bleeding (0.6%) or uterine perforation (0.6%). (3) Major complications include ectopic pregnancy (0.1%), bleeding (1%), injury to adjacent organs (0.6%), anesthesia-related events (1–2%) or death (0.004%). (3) Hendrix et al (3) did not define or differentiate bleeding for “minor” versus “major” complications.

Technology

Hysteroscopic Tubal Sterilization

Hysteroscopic tubal sterilization is a minimally invasive alternative to laparoscopic tubal ligation. A hysteroscope, which allows direct visualization into the uterus, is used to place permanent microinserts into both fallopian tubes. (4) The microinserts consist of an inner coil composed of stainless steel/polyethylene terephthalate fibres and an outer coil of nitinol, a nickel-titanium alloy. (4) The nitinol coil expands to anchor into the fallopian tube while the polyethylene terephthalate fibres induce ingrowth and fibrosis of local tissue, blocking the fallopian tube. (4)

Product labeling stipulates that patients must use alternative contraception for 3 months postprocedure until correct placement of the microinserts is confirmed by pelvic x-ray, transvaginal ultrasound, or hysterosalpingogram (HSG). (5-7) Pelvic x-ray and transvaginal ultrasound are first-line confirmation tests. HSG is recommended when there is: (7)

- difficulty or uncertainty during the placement of microinserts
- procedure time greater than 15 minutes
- zero or more than 7 coil loops of a microinsert visible in the uterus (indicating the device is not correctly placed inside the fallopian tube)
- unusual postoperative pain without any other identifiable cause

Hysterosalpingogram is also recommended if x-ray or transvaginal ultrasound results are unsatisfactory or equivocal. (7)

Microinserts should be implanted in the early proliferative phase of the menstrual cycle to avoid placement during an early undiagnosed pregnancy and a thickened endometrium, which may compromise the visual field. (8)

Contraindications to the procedure include: (6)

- patient uncertainty about desire to end fertility
- known abnormality of the uterine cavity or fallopian tubes that makes visualization of the tubal ostia and/or cannulation of the proximal fallopian tube difficult or impossible
- pregnancy or suspected pregnancy
- delivery or termination of a pregnancy less than 6 weeks before microinsert placement
- active or recent upper or lower pelvic infection
- known allergy to contrast media
- known hypersensitivity to nickel confirmed by skin test

According to Cooper et al, (8) approximately 10% of women may not be able to undergo bilateral microinsertion due to tubal spasm, tubal occlusion, or anatomic variation.

Potential advantages to hysteroscopic tubal sterilization are that it can be performed within approximately 10 minutes in an office setting without the use of general or even local anesthesia. (9)

Regulatory Status

The Essure Permanent Birth Control System (Conceptus, Inc.; Mountain View, CA) is licensed by Health Canada (Device Class III, License Number 34212) for bilateral occlusion of the fallopian tubes.

Ontario Context

In fiscal year 2008/2009**,** an estimated 8,923 women in Ontario underwent tubal occlusion procedures, including tubal ligation and hysteroscopic sterilization (Source: Ministry of Health and Long-Term Care). Ontario has no specific fee code for hysteroscopic sterilization. Any such procedures are likely claimed under the general code S741 (tubal occlusion / interruption / removal by any method or approach for the purpose of sterilization). The fee associated with this code is $155.70 (Cdn). (10)

According to the device manufacturer:

- Ten gynecologists in Ontario perform hysteroscopic sterilization.
- Fewer than 200 procedures were performed in Ontario in 2012.
- Approximately 1,300 procedures were performed in Canada in 2012.

(Personal communication, William Bisson, March 13, 2013)

Evidence-Based Analysis

Research Questions

What is the effectiveness and safety of hysteroscopic tubal sterilization compared with tubal ligation for permanent female sterilization?

Research Methods

Literature Search

Search Strategy

A literature search was performed on December 11, 2012, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database for studies published from January 1, 2008, until December 11, 2012. (Appendix 1 provides details of the search strategy.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-text publications
- published between January 1, 2008, and December 11, 2012
- observational studies, randomized controlled trials (RCTs), systematic reviews, and meta-analyses
- enrolled adult patients who underwent hysteroscopic tubal sterilization for permanent female sterilization
- ≥ 1 month follow-up

Exclusion Criteria

- studies where discrete results cannot be extracted

Outcomes of Interest

- failure/pregnancy rates
- adverse events
- patient satisfaction

Quality of Evidence

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (11) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (11) For more detailed information, please refer to the latest series of GRADE articles. (11)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Evidence-Based Analysis

The database search yielded 324 citations published between January 1, 2008, and December 11, 2012 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded in the analysis.

Four studies (2 systematic reviews and 2 observational studies) met the inclusion criteria.

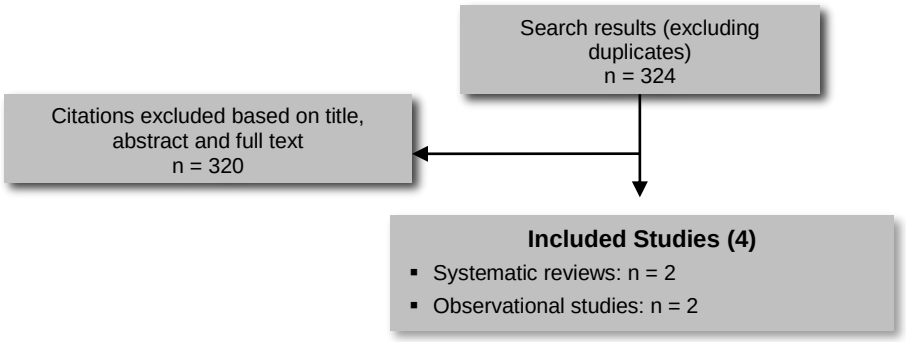

Figure 1: Citation Flow Chart

For each included study, the study design was identified. These are summarized in Table 1, which is a modified version of a hierarchy of study design by Goodman. (12)

Table 1: Body of Evidence Examined According to Study Design

Study Design	Number of Eligible Studies
RCT Studies	
Systematic review of RCTs	
Large RCT	
Small RCT	
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with non-contemporaneous controls	
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	
Database, registry, or cross-sectional study	2*
Case series	
Retrospective review, modelling	2
Studies presented at an international conference	
Expert opinion	
Total	4

Abbreviation: RCT, randomized controlled trial
*Systematic reviews of noncomparative case series

Systematic Reviews

Two systematic reviews were identified. (5;13)

Cleary et al (5) systematically reviewed pregnancy rates following hysteroscopic sterilization, with a literature search cut-off date of March 2012. The authors identified 22 noncomparative case series studies (12 prospective and 10 retrospective). Details of the 22 studies (N= 66,773 women) are shown in Appendix 2, Table A1. Sample sizes in the studies ranged from 36 to 50,000 patients. Device placement was confirmed by HSG, x-ray, or ultrasound in the studies. The quality of evidence, determined by the U.S. Preventive Services Task Force grading system, (14) was "fair" and subject to a number of limitations. Fair evidence is defined as "sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes." (14)

Four case series (15-18) followed a total of 1,070 women for up to 3 months—before the microinsert is considered reliable for contraception. The combined pregnancy rate for these 4 studies was 3/1,070 (0.3%). Reasons for the pregnancies included 1 patient who did not use an alternate form of contraception, 1 patient who was pregnant at the time of microinsert placement, and 1 patient who did not undergo follow-up imaging at 3 months when an x-ray at the time of placement showed that the device was suspiciously located.

Eighteen case series (N = 65,703 patients) reported results for women who received a microinsert and were followed beyond the initial 3 months postprocedure (range, 3 months to 7 years). (19-36) Details of the studies are described in Appendix 2, Table A1. In total, there were 99 pregnancies (0.2%). For 7 of the 18 studies (26;29;31-35), follow-up times were not specified and were assumed to be beyond 3 months.

Most pregnancies occurred when usage deviated from manufacturer's directions, such as failure to ensure placement in the first early proliferative phase of the menstrual cycle to avoid early undiagnosed

pregnancies, failure to image at 3 months to document proper placement, and failure to use alternative contraception until occlusion of the fallopian tubes is confirmed.

Limitations to the case series include:

- Most studies had less than 5 years of follow-up. One study reported 7 years of follow-up. (36)
    - Patient loss to follow-up was high in some studies. (19;21;30;32;36)
    - 7 studies did not report follow-up duration. (26;29;31-35)
- 10 studies were retrospective. (23;26;27;29;31-36)
- 4 studies reported ≤ 3 months follow-up. (15-18)
- Optimal placement of the microinserts at the time of hysteroscopy varied among studies (e.g., visibility in uterine cavity was reported as: 3 to 12 loops; 3 to 10 coils; 3 to 8 mm of the device; 5 to10 mm of insert; 4 to 8 coils; black stop ring reached fallopian tube; positioning based on 3-dimensional ultrasound; 1 to 8 coils; or not reported).
- Kerin et al (19;21) stated:
    - Early versions of the device were occasionally expelled, and changing the design of the device allowed more distal and successful placement in the tube.
    - All instances of perforation were associated with use of an additional support catheter, which was discontinued.
- Few studies reported the timing of pregnancies during follow-up. With varied reporting of follow-up times, it is not possible to calculate cumulative failure rates.

Hurskainen et al (13) systematically reviewed the efficacy and safety of the Essure system, with a literature search cut-off date of April 2008. All the studies in the report were included in the more recent systematic review by Cleary et al. (5) Overall, Hurskainen et al concluded the following:

- In general, the studies suggest that the Essure method is safe, well tolerated, and effective in the short term. However, some uncertainty comes from relatively low follow-up rates and a lack of long-term data on effectiveness and safety.
- The device has been improved since it was introduced, and this has to be taken into consideration when comparing results from the different time points.

Table 2: Summary of Systematic Reviews

Author, Year, Country	Purpose	Inclusion Criteria	Conclusion
Cleary et al (5) 2012 United States Literature search up to March 2012	To assess when and how often pregnancies occur following hysteroscopic sterilization	Primary research articles that reported whether or not pregnancies occurred among women who underwent Essure placement	Fair-quality evidence suggests that among women who were followed beyond 3 months after hysteroscopic sterilization, pregnancies were rare and generally occurred among women who had no imaging follow-up or had inadequate confirmation of placement or occlusion. Few pregnancies occurred in women with bilateral tubal occlusion documented by HSG.
Hurskainen et al (13) 2010 Finland Literature search up to April 2008	To examine the efficacy and safety of the Essure system	Updated a June 2006 systematic review by the Alberta Heritage Foundation for Medical Research	Essure system appears to be safe, permanent, irreversible, and a less invasive method of contraception compared with laparoscopic sterilization.

Abbreviations: HSG, hysterosalpingogram.

Comparative Study of Hysteroscopic Sterilization Versus Tubal Ligation

One comparative study (16) was identified in the systematic review by Cleary et al. (5) However, for the purposes of their review, Cleary et al only looked at the group of patients who received hysteroscopic sterilization. The full comparative study is described below.

Duffy et al (16) compared 59 patients who received hysteroscopic sterilization to 24 patients who underwent laparoscopic sterilization. For hysteroscopic sterilization, 48/59 patients had bilateral placement of the devices, and 34/59 patients completed their 3-month follow-up and had tubal occlusion documented by HSG.

The primary end point of the study was patient satisfaction as determined by questionnaires on days 7 and 90 following the procedure, and the difference in satisfaction rates between the 2 groups did not reach statistical significance. Results are shown in Table 3.

Table 3: Results for Comparative Study by Duffy et al (16)

End point	Hysteroscopic Sterilization (n = 59)	Laparoscopic Sterilization (n = 24)	*P* Value
Anesthesia	30% received local anesthesia	All under general anesthesia	NA
Patient satisfaction at day 90 postprocedure (% "very satisfied" or "somewhat satisfied")	94 (n = 34 at 3 months)	81 (n = 24 at 3 months)	NS
Procedure time (minutes, mean)	13.2 (SD, 7.73)	9.7 (SD, 4.3)	0.05
Overall time in hospital (minutes, mean)	188.7 (SD, 181.2)	369.1 (SD, 141.1)	< 0.005
Patient tolerance of procedure (% "good" or "excellent")	82	41	0.0002
Postprocedure pain in recovery room (% "moderate" or "severe')	31	63	0.008
Pregnancy (n)	1 (patient did not undergo HSG)	0	NR
Adverse events in recovery room (number of patients)	2 vasovagal reaction 2 postoperative pain 1 cervical bleeding 1 suspected tubal perforation	3 cervical tear 1 nausea and vomiting 1 postoperative pain 1 uterine fundal perforation	NS (*P* value not reported)
Adverse events reported 1 week postprocedure (number of patients)	1 pain/infection in perineum/bleeding/thrush/mood swings 1 headache 1 vaginal spotting	1 inflammation of umbilicus/retention of urine 1 backache and cramp 1 constipation/hemorrhoids/wound infection 1 headache/dizziness/abdominal pain	NS (*P* value not reported)
Adverse events reported 3 months postprocedure (number of patients)	2 right-sided abdominal pain 1 mild pain on left side of abdomen 1 bilateral pelvic pain 1 musculoskeletal pain in right lower quadrant 1 possible salpingitis	2 wound infections 1 lower abdominal pain 1 inflammation of umbilicus 1 weeping wound 1 headaches and reflux esophagitis	NS (*P* value not reported)

Abbreviations: HSG, hysterosalpingogram; NA, not applicable; NR, not reported; NS, not significant; SD, standard deviation.

Limitations to the study by Duffy et al (16) include:

- lack of detail about how patients were recruited or assigned to study groups
- no sample size calculation reported for the primary end point (therefore the lack of statistical significance may be due to a type 2 error)
- no statistical tests reported to assess the primary end point of the study
- follow-up limited to 3 months (period in which patient cannot rely on microinsert and must use other contraception)
- high loss to follow-up: at 3 months, 29/59 hysteroscopic sterilization patients and 12/24 patients from the laparoscopic sterilization group had provided information regarding adverse events.

Recent Studies not Included in Systematic Reviews

Two recent studies were not included in the systematic reviews. (37;38) Both were noncomparative case series, and their results are summarized in Table 4.

Levie et al (37) assessed pain and patient satisfaction in patients who underwent hysteroscopic sterilization and found patients' average pain during the procedure was significantly lower than their average menstrual pain ($P = 0.001$). However, the authors did not report data on pregnancies or adverse events and may have used part of the patient population from a 2006 publication. (17)

Zurawin et al (38) reviewed adverse events associated with suspected nickel hypersensitivity in patients who received microinserts. The reported incidence of adverse events suspected to be related to nickel hypersensitivity was very small (0.01%) and consistent with data from other nickel-containing devices such as cardiac implants. (38)

Table 4: Summary of Recent Studies not Included in Systematic Reviews

Author, Year, Country	Design	Objective	Results	Limitations
Levie et al (37) 2010 United States	Noncomparative case series of 209 patients who received hysteroscopic sterilization	Assess pain during the procedure and patient satisfaction at 13 weeks to 1 year after the procedure	Standardized pain scores showed 149 (70%) of patients experienced average pain that was less than or equal to pain experienced from their last menses. Average pain for procedure significantly lower than average menses pain ($P < 0.001$). Most patients reported that they were extremely satisfied with the procedure. Average satisfaction score was 4.7 (SD, 0.71) using satisfaction scale 1 ("not satisfied") to 5 ("very satisfied").	Follow-up data were collected from 176 patients (84%) who were enrolled in the study. Patient population may be duplicated from 2006 publication by same authors. (17) A provider involved with the procedure took part in the pain survey, which may have affected patients' responses. No data on pregnancies or adverse events were reported.
Zurawin et al (38) 2011 United States	Noncomparative case series	Review of adverse events associated with suspected nickel hypersensitivity in patients who received Essure implants from 2001 to 2010	63 reports of suspected nickel hypersensitivity were identified. Of 20 patients who underwent patch testing, 13 tested positive and 7 tested negative. "Of 436,937 Essure kits sold since its commercial release there have been 63 reported cases in which nickel hypersensitivity was suspected or 0.014%." "Incidence of reported nickel-related reactions or complications from Essure microinsert remains below the range of 18% to 24% in women with contact nickel allergy."	Adverse events may be underreported. Lack of detailed follow-up for some of the patients makes it difficult to determine the relationship between reported symptoms and true allergy.

Abbreviations: SD, standard deviation.

Effectiveness and Safety of Hysteroscopic Sterilization Compared to Other Forms of Sterilization

Table 5 summarizes the comparative effectiveness data of different types of sterilization. Data for vasectomy and all tubal ligation methods came from the CREST study, a large, multicentre, prospective noncomparative cohort study. (2;39) Data for hysteroscopic sterilization were from the most recent prospective noncomparative study, in which confirmatory imaging was performed at 3 months in 1,612/1,615 patients, (30) and from the largest and most recent retrospective study to date, in which 4,108/4,282 patients underwent confirmatory 3-month follow-up imaging. (36)

Overall, hysteroscopic sterilization was associated with lower pregnancy rates compared to tubal ligation or vasectomy. However, lack of long-term follow-up, lack of comparable durations of follow-up, and a paucity of studies that directly compare interventions are limitations to this assessment of comparative effectiveness.

Table 5: Comparative Effectiveness of Different Types of Sterilization

Intervention	Pregnancies per 1,000 women at 5 years	Pregnancies per 1,000 women at 10 years
Vasectomy (CREST study) (39)	11.3	NA
Tubal ligation, all methods (CREST study) (2)	13	7.5–36
Hysteroscopic sterilization		
Arjona et al (30)	3/1,615[a]	NA
Povedano et al (36)	7/4,108[b]	NA

[a]Life table analysis of pregnancy rates accumulated over 42 months.
[b] Followup 3 months to 7 years.
Abbreviations: NA, not available.

Table 6 shows the safety profile for tubal ligation methods from the CREST study (40;41) compared to hysteroscopic sterilization. Data for hysteroscopic sterilization were from the two noncomparative studies discussed above with regard to effectiveness.(30;36) Overall, hysteroscopic sterilization was associated with lower complication rates compared to tubal ligation. No deaths linked to hysteroscopic sterilization have been reported.

Table 6: Comparative Safety of Different Types of Sterilization

Tubal Ligation, All Methods CREST Study (40;41)	Hysteroscopic Sterilization Arjona et al (30)		Hysteroscopic Sterilization Povedano et al (36)	
Complications	**Complication**	**Number (%) of patients**	**Complication**	**Number (%) of patients**
Overall: 0.9–1.6 per 100 procedures	Vasovagal syncope	16 (1)	Vasovagal syncope	85 (1.9)
Mortality: 1–2 per 100,000 procedures	Expulsion of 1 microinsert	12 (0.73)	Expulsions:	19 (0.4)
	Migration to abdominal cavity	3 (0.18)	• Device erroneously placed in myometrium	3 (0.06)
	Intramyometrial placement of device	2 (0.12)	• Asymptomatic migration into abdominal cavity	2 (0.04)
	Nickel allergy	1 (0.6)	Allergy to nickel	2 (0.04)
	Uterus perforation	0 (0)	Persistent abdominal pain	1 (0.02)
	Pelvic inflammatory disease	0 (0)	Tubal perforation	1 (0.02)

Kerin et al (19;21) stated that early versions of the device were occasionally expelled and that changing the design of the device allowed more distal and successful placement in the tube. Instances of perforation were associated with use of an additional support catheter, which was discontinued.

As with our analysis of the evidence on effectiveness, limitations to the comparative safety analysis include lack of long-term follow-up for hysteroscopic sterilization and a paucity of studies that directly compare hysteroscopic sterilization and tubal ligation.

Limitations

In summary:

- No randomized controlled trials were identified.
- Most studies had less than 5 years of follow-up. One study reported 7 years of follow-up.
- 10 studies were retrospective.
- 7 studies did not report follow-up duration.
- 4 studies reported only 3 months or less of follow-up.
- Optimal placement of the microinsert at the time of hysteroscopy varied among studies.
- Results for tubal ligation were derived from the CREST trial, a large, multicentre, prospective, noncomparative observational study (GRADE low).

Conclusions

Hysteroscopic sterilization was associated with:

- lower pregnancy rates compared to tubal ligation (GRADE very low)
- lower complication rates compared to tubal ligation (GRADE very low)
- no significant improvement in patient satisfaction compared to tubal ligation (GRADE very low)

Appendix 3 shows details about the GRADE profile on quality of evidence for each outcome.

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Appendices

Appendix 1: Literature Search Strategies

Search date: December 11, 2012
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase; Cochrane Library; Centre for Reviews and Dissemination (CRD)
Limits: 2008-current; English
Filters: None
Database: Ovid MEDLINE(R) <1946 to November Week 3 2012>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <December 6, 2012>, Embase <1980 to 2012 Week 49>

Search Strategy:

1	exp *Sterilization, Reproductive/ use mesz	8746
2	exp *female sterilization/ use emez	9984
3	exp Hysteroscopy/	10103
4	exp Hysteroscope/ use emez	385
5	1 or 2	18730
6	3 or 4	10256
7	5 and 6	338
8	(essure or microinsert* or transcervical tubal occlusion).ti,ab.	571
9	(hysteroscop* adj2 sterili?ation).ti,ab.	413
10	7 or 8 or 9	815
11	limit 10 to English language	710
12	limit 11 to yr="2008 -Current"	431
13	remove duplicates from 12	318

Cochrane

ID	Search	Hits
#1	MeSH descriptor: [Sterilization, Reproductive] explode all trees	315
#2	MeSH descriptor: [Hysteroscopy] explode all trees	280
#3	#1 and #2	8
#4	(essure or microinsert* or transcervical tubal occlusion*):ti,ab,kw (Word variations have been searched)	11
#5	(hysteroscop* near/2 sterili?ation*):ti,ab,kw (Word variations have been searched)	9
#6	#3 or #4 or #5 from 2008 to 2012	5

CRD

Line	Search	Hits
1	MeSH DESCRIPTOR sterilization, reproductive EXPLODE ALL TREES	43
2	MeSH DESCRIPTOR Hysteroscopy EXPLODE ALL TREES	42
3	#1 AND #2	7
5	(essure or microinsert* or transcervical tubal occlusion*)	6
6	(hysteroscop* adj2 sterili?ation*)	7
7	#3 OR #4 OR #5	10
8	(#6) FROM 2008 TO 2012	1

Appendix 2: Results

Appendix 2: Results

Table A1: Studies Included in the Systematic Review by Cleary et al (5)

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
Follow-Up for 3 Months							
Ubeda et al (15) 2004 Spain	Prospective noncomparative	85	3 months	78/85 on first attempt 79/85 by second attempt	X-ray performed at 3 months follow-up in 75 patients HSG requested when no, unilateral or incorrect placement	0/79	Loss to follow-up for imaging. Optimal placement defined as 3 to 12 loops remaining visible at time of procedure. Follow-up interval was during time when other contraception must be used. Oral naproxen and diazepam given to patients 2 hours before procedure. No short- or long-term complications were observed in the patients. 61 patients scheduled in the proliferative phase of the menstrual cycle.
Duffy et al (16) 2005 United Kingdom	Prospective noncomparative (for purpose of review by Cleary et al)	59	3 months	45/59 on first attempt 48/59 by second attempt	HSG performed at 3 months in 35 patients	1/48 X-ray at time of placement showed 1 device suspiciously located; patient did not follow-up for HSG	Loss to follow-up for imaging. Definition of successful placement at time of procedure not reported. Follow-up interval was during time when other contraception must be used. 30% of patients underwent local anesthesia. One week postprocedure: 1 patient reported pain, infection in perineum, prolonged bleeding, thrush, mood swings. 1 patient reported headache. 1 patient reported vaginal spotting.
Levie et al (17) 2006 United States	Prospective noncomparative	102	3 months	97/102 on first attempt 98/102 by second attempt	HSG performed at 3 months in 92 patients	1/98 Patient pregnant within first cycle after procedure and not using other contraception; coil was free in uterine cavity at HSG	Follow-up interval was during time when other contraception must be used. Definition of successful placement at time of procedure not reported. Loss to follow-up for imaging. All patients received ketorolac 30 minutes before the procedure as well as local anesthetic during the procedure.
Mino et al (18) 2007 Spain	Prospective noncomparative	857	3 months	827/857 on first attempt 845/857 by second attempt	X-ray performed in 857 patients HSG performed in 77 women	1/845 Patient pregnant at time of placement	Follow-up interval was during time when other contraception must be used. Optimal placement defined as 3 to 10 coils remaining visible in the uterine cavity during hysteroscopic insertion. Patients received ibuprofen and diazepam 1 hour prior to procedure; 50% of patients received local anesthetic. HSG performed if > 10 or < 3 coils remained visible during hysteroscopic insertion, if insertion was not possible in both tubes, or when the plain radiological imaging was inconclusive.

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
							As study progressed, inconclusive x-rays were followed up with ultrasound. Overall patient satisfaction 3 months after the procedure was rated as "very high" by 94% of women (n = 806) and "high" by 6% (n = 51). None of the women were dissatisfied.
Follow-Up for Greater than 3 Months							
Kerin et al (19) 2001 Australia	Prospective noncomparative	130	3, 6, 12 and 18 months	111/130 (first or second attempt not explicitly reported)	HSG performed at 3 months in 111 women with bilateral or unilateral placement	0/108 patients with bilateral occlusion	Optimal position of insert occurred when 3 to 8 mm of the proximal device was visible at the ostium. Large loss to follow-up (and variability in reporting): 3 months (n = 109), 6 months (n = 106), 12 months (n = 78), 18 months (n = 25). Patients received indomethacin and local anesthetic. Included unilateral placement. **Adverse events (experienced by 9/130 women):** **Adverse event** — **Number of patients** Distal ball of device detached in fallopian tube — 1 Device perforation — 2 Device placed too far in fallopian tube — 3 Breakage of device at detachment step of placement — 3 *Early versions of the device were occasionally expelled. Changing device design allowed more distal and successful placement in the tube.* *All instances of perforation were associated with use of an additional support catheter; the use of which was discontinued.* Patient diary at 3 months: 102/114 patients experienced "no pain or unusual symptoms." 12 patients reported pain during intercourse. Patient diary "after 3 months": 6/114 reported pain/bleeding (1 undiagnosed pain during period; 1 right ovarian cyst; 1 urinary tract infection; 1 change in menstrual frequency; 2 with occasional spotting).
Cooper et al (20) 2003 Australia, Europe, United States ("Phase 3 Trial")	Prospective noncomparative	507	mean 21.4 months; 9,620 "woman-months"	446/507 on first attempt 464/507 by second attempt X-ray performed within 24 hours after placement to "serve as a baseline evaluation of device location"	HSG performed at 3 months in 456/464 patients who had bilateral placement	0/449 patients with bilateral occlusion	Optimal position of the insert occurs when 5 to 10 mm of the proximal end of the insert is visible at the ostium. Nonsteroidal anti-inflammatory drug given before and local anesthetic during the procedure. Specific follow-up times not reported. 14 instances of expulsion (proximal placement in 13 cases and placement into endometrial tissue in 1 case) and 4 cases of perforation (2 cases each of pre-existing tubal occlusion and poorly identified ostium). None of these adverse events occurred in women with properly placed microinserts.

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
							Trial protocol did not allow removal of misplaced microinserts at time of procedure, which increased number of expulsions. "During study, FDA approval provided product labelling that allowed removal of microinserts that have 18 or more coils trailing in the uterine cavity which should reduce risk of expulsions in routine clinical setting." Postoperative recovery uneventful in 316 patients (58%). In 228 procedures, women reported cramping (30%), pain (13%), and nausea (9%). Of those with symptoms, complete resolution before discharge was attained in 56%. Symptoms not resolved by time of discharge involved cramping or bleeding. "In general, symptoms during recovery were similar to those typically seen after a diagnostic hysteroscopic procedure, namely mild uterine cramping and light bleeding."
Kerin et al (21) 2003 Australia, Europe, United States ("Phase 2 trial")	Prospective noncomparative	227	21–45 months; 6.015 "woman-months"	196/227 on first attempt 200/227 by second attempt	HSG performed at 3 months in 200/200 patients who had bilateral placement	0/198 patients with bilateral occlusion followed for 1 year 0/181 patients with bilateral occlusion followed for at least 2 years 0/34 patients with bilateral occlusion followed for at least 3 years	Optimal position of the insert occurred when 3 to 8 mm of the proximal end was visible at the ostium. Nonsteroidal anti-inflammatory drug given before procedure. Local anesthesia given in some cases. General anesthetic used in 10 patients (4%). Specific follow-up times not reported. **Side effects:**

Side effect	Number (%) of patients
Pain postprocedure:	156/206 (76%)
No analgesia required	52/156 (33%)
Analgesia required (48% given ibruprofen, 50% given codeine-containing drug)	104/156 (67%)
Bleeding postprocedure (resolved within 1 day in 27% of cases; 3 days in 64%; 7 days in 96%; 15 days in 100%)	171/206 (83%)
Dyspareunia (first 3 months based on diaries; resolved in all cases)	18/206 (9%)
Pain during menses (first 3 months based on diaries)	27/206 (13%)

Adverse events (occurred in 15/227 women [7%]):

Adverse event	Number (%) of patients
Vasovagal response (treated with atropine)	2/227(1%)
Device proximal band detachment* (no clinical sequelae)	3/227 (1%)
Unsatisfactory device location (1 expulsion; 6 perforations; 2 unsatisfactorily placed devices)	9/227 (4%)
4 perforations thought to be due to use of support catheter which was subsequently discontinued	
Broken device tip* (occurred during intraprocedural hysteroscopic device removal/no clinical sequelae)	1 (< 1%)

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
							**Problems addressed by subsequent design/manufacturing improvements*
Kerin et al (22) 2004 Australia	Prospective noncomparative	102	559 "patient-months"	100/102 (only 1 attempt reported)	X-ray performed after procedure and before discharge to assess microinsert position HSG performed at 3 months in 94/100 patients who had bilateral placement	0/93 patients with bilateral occlusion	Definition of placement success at time of procedure not reported. Specific follow-up times and number of women followed not reported. Nonsteroidal anti-inflammatory administered 1 hour prior to procedure, and paracervical block used in 80% of patients. Postprocedure recovery reported as "uneventful" by 99 (97%) of patients, and 3 (3%) experienced some nausea and vomiting on the day of procedure. Light vaginal bleeding was experienced by 56/98 women (57%) for up to 1 week postprocedure. 30 patients (31%) experienced some pain during first week. During HSG at 3 months postprocedure, 1 perforation was identified ("probable tubal perforation at time of device placement").
Chern et al (23) 2005 Thailand	Retrospective noncomparative	80	1,218 cumulative months	72/80 on first attempt 77/80 by second attempt	HSG performed at 3 months in 63/77 patients who had bilateral placement X-ray performed in 4 patients at 3 months	0/67 patients with bilateral occlusion	**Retrospective.** Optimal placement indicated by visualizing 4 to 8 coils of the device at the ostia. Nonsteroidal anti-inflammatory drugs administered before procedure (except the first 30 patients; reason not stated). Local anesthetic only administered if cervical dilatation required. No device-related or procedural-related adverse events were observed. No adverse events (e.g., perforation, pain) were observed. Specific follow-up times not reported.
Litta et al (24) 2005 Italy	Prospective noncomparative	36	mean 11.5 months	31/36 on first attempt 32/36 by second attempt	HSG performed at 3 months in 32 women who had successful placement	0/32 women with bilateral occlusion	Optimal placement determined when black stop ring of device wire reached the level of the ostia. Patients received diazepam prior to procedure. "No short- or long-term severe complications." Range of follow-up times not reported.
Gibon et al (25) 2006 France	Prospective noncomparative	50	1 year; 670 "woman-months"	6 placement failures (unclear if included in the 50 patients followed for 1 year)	HSG performed at 3 months (number of patients not reported)	0/50	Placement success not defined at time of procedure. Number of patients who underwent HSG not reported. Patients received local anesthetic.
Nichols et al (26) 2006 United States	Retrospective noncomparative	320	Not reported	91% success in office and 88% success in operating room	Patients told to undergo HSG but number not reported in results	0/320	**Retrospective.** Optimal placement defined as 3 to 8 coils visible in the uterine cavity at conclusion of the placement procedure. 13.4% of patients received general anesthesia. 9.7% of patients received local anesthetic only. 33% of patients received local anesthetic and intravenous sedation. No major complications observed. Minor adverse events included 2 device expulsions (the first was successful after the second placement, and the second was successful after the third placement).

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
							Follow-up time not reported.
Famuyide et al (27) 2008 United States	Retrospective noncomparative	175	mean 20 months (range 7–34 months)	167/175 (first or second attempt not explicitly reported)	HSG performed at 3 months in 149 women	0/159 patients who had "follow-up care after sterilization"	**Retrospective.** Placement success not defined at time of procedure. Patients received conscious sedation (midazolam). No major intraoperative complications were observed (e.g., perforation). Variation in the number of patients followed up and reported on.
Andersson et al (28) 2009 Sweden	Prospective noncomparative	61	mean 23 months (range 7–67 months)	52/61 on first attempt 58/61 by second attempt	Ultrasound or x-ray performed in 58 women who had successful placement	0/50 patients who completed outcome questionnaires	Device optimally positioned when 3 to 8 coils visible at the tubal ostia. Nonsteroidal anti-inflammatory drug given prior to procedure. Local anesthetic given during procedure to 44/61 patients. Reasons for failed placement: material defects, 2 (3.2%); tubular spasm, 4 (6.5%); obstructed view, 2 (3.2%); failure to pass cervix, 1 (1.6%). Via outcome questionnaires, no expulsions or perforations were reported; 9 women (14%) reported heavier periods while 8 women reported lighter periods. Unclear if follow-up was only in women with confirmed placement.
Levy et al (29) 2007 Multicentre International	Retrospective noncomparative	50,000 (estimated)	Not reported	Not reported	HSG or x-ray at 3 months	64/ 50,000 (estimated) placements	**Retrospective.** Placement success not reported. "Most common manifestation of noncompliance was patient failure to return for 3 months follow-up HSG (n = 14) or return for follow-up visit after expulsion, perforation or unilateral placement (n = 6). Among patients failing to return for follow-up, there was 1 unsatisfactory device location, 3 perforations, 7 expulsions, 3 unilateral placements, and 6 of unknown cause. Other issues included failure to use alternate birth control after the procedure or after detection of patency at HSG (n = 4)." "6 pregnancies associated with physician noncompliance. In 2 cases, patients were instructed that there was no need to return for a follow-up appointment at 3 months. In 4 cases the physicians instructed patients to rely on only 1 microinsert for contraception, contrary to the manufacturer's instructions for use. In 2 cases, only 1 microinsert was placed, there was 1 case of unilateral expulsion and 1 case of unilateral perforation." Study reported on worldwide procedures. Pregnancies reported to device manufacturer only. Timing of pregnancies not reported. **Reasons for pregnancies:** Reason: Patient or physician noncompliance — 30 Misread x-ray or HSG — 18 Pregnant at time of placement — 8 Old device design — 1

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
							"Other" 7
Arjona et al.(30) 2008 Spain	Prospective noncomparative	1,630	15–42 months	1,615/1,630	X-ray performed at 3 months in 1,612 patients Ultrasound or HSG if placement not satisfactory (> 10 or < 3 coils visible by hysteroscopy, insertion only in 1 tube, unclear radiologic results)	3/1,615 patients with successful placement: 2 in first 90 days in women using oral contraception 1 in first 90 days in woman not using other contraception after procedure	Optimal placement defined as 3 to 8 coils remaining visible in the uterine cavity. Patients pretreated with ibuprofen and benzodiazepine. "15 women dropped out because of failure in the procedure." Number of confirmed placements not reported. Large loss to follow-up (177 women followed for 42 months). No pregnancies were diagnosed among the 1,419 women with ≥ 18 months of follow-up (excluding 3 pregnancies diagnosed in the first 90 days after procedure). **Complications during the procedure and follow-up up to 42 months** (several patients presented more than 1 complication; details not reported by authors) **Complication / Number / %** Uterus perforation 0 0 Pelvic inflammatory disease 0 0 Vasovagal syncope 16 1.0 Migration to abdominal cavity 3 0.18 Expulsion of 1 microinsert 12 0.73 Intramyometrial placement of device 2 0.12 Nickel allergy 1 0.6 Pregnancy 3 0.18 **Total 33 2.45** Procedure well tolerated as "excellent or very good" in 1,398/1,615 (86.5%) women; 166 (10.2%) felt pain similar to normal menstruation as "good"; and 3.1% felt more pain than with menstruation as "fair or poor." Of 1,612 women (99.8%) who completed the 3-month follow-up, 722 were surveyed with questionnaires on satisfaction. 91% of women (n = 658) gave a satisfaction score of 10 and the lowest rating was 8 (out of 10, with 10 being "highly satisfied").
Grosdemouge et al (31) 2009 France	Prospective and retrospective noncomparative	1051	Not reported	952/1,051 on first attempt 1,015/1,051 by second attempt	X-ray (ultrasound or HSG if placement in doubt) at 3 months; number not reported	2/1,015 patients with successful placement: 1 pregnant at time of placement 1 improper implant placement	**Retrospective.** Optimal placement was 3 to 8 coils visible in the uterus. Number of women undergoing imaging not reported. Placement success rates include some with unilateral placement. Follow-up duration not reported.
Savage et al (32) 2009 United States	Retrospective noncomparative	884	Not reported	850/884 on first attempt	HSG performed in 739 patients (confirmed bilateral occlusion)	8/850 patients: 1 never returned for HSG 4 had HSG showing at least 1 patent tube	**Retrospective.** Definition of optimal placement success not reported. Unclear if HSG was performed at 3 months. 13% loss to follow-up before HSG could be obtained. Timing of pregnancies not reported.

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
						3 had HSG interpreted as bilaterally occluded	Adverse effects not reported.
Shavell et al (33) 2009 United States	Retrospective noncomparative	316	Not reported	294/316 on first attempt 296/316 by second attempt Tubal ostia too large for device (n = 1)	Not reported (HSG results not documented for any of the patients)	3/296 (0.95%) patients with successful placement (occurred at 4, 5, and 13 months after procedure; all with unilateral absence of device on follow-up ultrasound)	**Retrospective.** Definition of optimal placement success not reported. Follow-up time and imaging not reported. 172 (54.4%) cases performed under general anesthesia. 132 (41.8%) under "sedation." 12 (3.8%) under local anesthesia. **Reason for placement failures:** **Reason** / **Number of patients** Difficulty visualizing tubal ostia: 11 Device malfunction: 3 Uterine perforation by device: 2 Uterine perforation by hysteroscope: 1 Tubal perforation: 1
Veersema et al (34) 2010 Netherlands	Retrospective noncomparative	6,000 (estimated)	Not reported	Not reported	HSG at 3 months for part of study period; ultrasound for remainder of study period	10/ 6,000 (estimated) placements (0–24 months after procedure	**Retrospective.** Definition of optimal placement success not reported. Exact number of women undergoing procedure or with confirmed occlusion unknown. Timing of pregnancies not reported. **Device failures:** **Cause of failure** / **Conclusion** Perforation: Misread Expulsion: Patient noncompliance Unilateral placement: Nonadherence to protocol Expulsion: Misread Unknown: Unknown Perforation: Nonadherence to protocol Partial expulsion: Patient noncompliance Unilateral placement: Nonadherence to protocol Unilateral placement: Nonadherence to protocol Luteal pregnancy: Nonadherence to protocol and patient noncompliance
Legendre et al (35) 2011 France	Retrospective noncomparative	311	Not reported	293/311 (first or second attempt not explicitly reported)	3-dimensional ultrasound, x-ray or HSG performed at 3 months in 276/293 women	2/293 (0.7%) patients with successful placement: 4 and 6 months after procedure (both patients did not follow-up for 3-month imaging)	**Retrospective.** Optimal position determined by positioning based on 3-dimensional ultrasound. Included unilateral implantations (history of salpingectomy) in analysis. Nonsteroidal anti-inflammatory administered prior to procedure Follow-up time not reported.

Author, Year, Country	Design	Number of Women Receiving Device	Follow-up Duration	Success in Placing Microinserts	Follow-up Imaging	Pregnancy Rate	Limitations/Comments
							General anesthesia used in 175 (57.4%) patients; local anesthesia 31(10.2%); none 38 (12.5%). HSG performed in 64/276 (23.2%) patients. **Complications:** Early (not defined by authors) expulsion: 5 (1.7%) Late (defined as occurring at 18 months postprocedure) expulsion: 1 (0.3%) Tubal perforation: 1 (0.3%) Nickel allergy: 0 (0%)
Povedano et al (36) 2012 Spain	Retrospective noncomparative	4,306	3 months to 7 years	4,075/4,306 on first attempt 4,242/4,306 by second attempt	X-ray, ultrasound or HSG performed at 3 months in 4,108/4,242 patients (HSG performed if x-ray and ultrasound provided unclear results)	7/4,108 patients with imaging follow-up: 3 occurred at < 3 months follow-up 4 occurred at > 3 months follow-up	**Retrospective.** Optimal placement defined as 1 to 8 coils remaining visible in uterine cavity. Large loss to follow-up by 7 years (921 patients at 7 years). All patients received ibruprofen and diazepam prior to the procedure. 472 patients received local anesthesia. **Complications:** Vasovagal syncope: 85 (1.9%) Expulsions: 19 (0.4%) Device erroneously placed in myometrium: 3 (0.06%) Asymptomatic migration into abdominal cavity: 2 (0.04%) Allergy to nickel: 2 (0.04%) Persistent abdominal pain: 1 (0.02%) Tubal perforation: 1 (0.02%) **Perioperative pain:** Non-existent/mild: 3,568 (82.8%) Moderate: 513 (11.9%) Severe: 155 (3.5%)

Abbreviations: HSG, hysterosalpingogram

Appendix 3: Evidence Quality Assessment

Table A2: GRADE Evidence Profile for Comparison of Hysteroscopic Sterilization and Tubal Ligation

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Pregnancy							
21 noncomparative case series (15;17-36) 1 comparative observational study (16)	Very serious limitations (-2)[a]	Some serious limitations (-1)[b]	No serious limitations	Serious limitations (-1)[e]	Undetected	None	⊕ Very Low
Adverse Events							
17 noncomparative case series (15;19-24;26-30;33-36;38) 1 comparative observational study (16)	Some serious limitations (-1)[a, c]	Some serious limitations (-1)[b]	No serious limitations	Serious limitations (-1)	Undetected	None	⊕ Very Low
Patient Satisfaction							
3 noncomparative case series (18;30;37) 1 comparative observational study (16)	Very serious limitations (-2)[a, d]	No serious limitations	No serious limitations	Serious limitations (-1)	Undetected	None	⊕ Very Low

[a] All observational studies; therefore, GRADE starts at low quality. 10 case series were retrospective; most studies had less than 5 years of follow-up; 6 studies did not report follow-up duration; definition of optimal placement of the microinsert at the time of hysteroscopy varied among studies; most pregnancies occurred when use deviated from manufacturer's directions including failure to ensure placement in the first/early proliferative phase of the menstrual cycle to avoid early undiagnosed pregnancies, failure to image at 3 months to confirm proper placement and occlusion of fallopian tubes, and failure to use of alternative contraception until documented occlusion of the fallopian tubes; and change in device design and disuse of a support catheter appeared to be associated with more successful placement in fallopian tube and reduced perforation. Comparative observational study did not provide details as to how patients were recruited or assigned to study groups; no sample size calculation was reported; follow-up was during time when other contraception must be used by the patient (within first 3 months); and there was a high loss to follow-up.

[b] Change in device design and disuse of a support catheter appeared to be associated with more successful placement in fallopian tube and reduced perforation. Variability in response among studies.

[c] Long-term studies lacking. Most studies had less than 5 years of follow-up with patient loss to follow-up. Definition of optimal placement of the microinsert at the time of hysteroscopy varied among studies.

[d] Satisfaction scales not referenced or validated. The lack of significance in the comparative observational study may be due to a type 2 error.

[e] Level of imprecision among studies unclear. Confidence intervals not reported.

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