Alberta STE Report

Hysteroscopic tubal sterilization

September 2014

IHE
INSTITUTE OF HEALTH ECONOMICS
ALBERTA CANADA

INSTITUTE OF HEALTH ECONOMICS

The Institute of Health Economics (IHE) is an independent, not-for-profit organization that performs research in health economics and synthesizes evidence in health technology assessment to assist health policy making and best medical practices.

IHE BOARD OF DIRECTORS

INSTITUTE OF HEALTH ECONOMICS
ALBERTA CANADA

Alberta STE Report

Hysteroscopic tubal sterilization

Alberta STE Report: Policy-driven Health Technology Assessment reports that include an analysis of the social and system demographics, technological effectiveness and economic implications of a health technology. The reports are written under contract with the Alberta Health Technologies Decision Process and contextualized for use in Alberta.

Acknowledgements

The Institute of Health Economics is grateful to the Expert Advisory Committee for the provision of information and comments on the draft report. The authors would like to thank Wendy McIndoo (IHE) for her support with checking references and formatting/editing the document.

We would also like to thank the following individuals for their assistance and provision of contextual information for the Background and Context section of the report:

- Albert Rosengarten, Rockyview General Hospital, Department of Obstetrics & Gynecology, Calgary, Alberta
- Sheila Watson, Rockyview General Hospital, Department of Obstetrics & Gynecology, Calgary, Alberta
- Amber Burridge, Rockyview General Hospital, Department of Obstetrics & Gynecology, Calgary, Alberta
- John Thiel, Women's Health Clinic, Regina General Hospital, Regina, Saskatchewan

We also thank Sebastiaan Veersema, St. Antonius Hospital, Department of Obstetrics & Gynecology, Nieuwegein, the Netherlands for providing clarification on populations included in two published studies for the Technology Effectiveness/Efficacy section of the report.

We also thank the CRM and Data Access group at Alberta Health for providing administrative data and the Health Technology Assessment and Innovation group at Alberta Health Services for providing operational, financial and contextual data.

The views expressed in the final report are those of the Institute of Health Economics.

Corresponding Author

Please direct any inquiries about this report to:
Dr. Anderson Chuck
Director of Economic Evaluation and Analytics, Institute of Health Economics
achuck@ihe.ca
780-448-4881

Funding

This report was supported by a financial contribution from Alberta Health (AH) through the Alberta Health Technologies Decision Process, The Alberta model for health technology assessment and policy analysis. The completed report was submitted to AH in April, 2014.

The views expressed herein do not necessarily represent the official policy of Alberta Health.

Declared Competing Interest of Authors

Competing interest is considered to be financial interest of non-financial interest, either direct or indirect, that would affect the research contained in this report or create a situation in which a person's judgement could be unduly influenced by a secondary interest such as personal advancement.

The authors of this publication claim no competing interest.

Suggested Citation (ICMJE or Vancouver Style)

Institute of Health Economics. *Hysteroscopic tubal sterilization*. Edmonton AB: Institute of Health Economics. 2014.

Web Address

This publication is available for free download from the IHE website at http://www.ihe.ca.

Executive Summary

Technology Effects and Effectiveness

Background and context

Permanent fertility control by bilateral occlusion of the fallopian tubes is achieved by various methods. The choice of the most appropriate method of sterilization depends upon a mix of factors such as an individual's or couple's preferences, provider's training, the woman's medical history, anatomy and medical assessment of risk, access to services, and timing of intervention (interval, postpartum, or post-abortion). The fallopian tubes are reached for occlusion either by the abdominal (laparoscopic or laparotomic) or transcervical (hysteroscopic) routes. Hysteroscopic tubal sterilization (HTS) using the Essure® system was investigated and found to be a less invasive, potentially safe, and effective method of permanent sterilization.

Technology

The Essure® system is manufactured by Conceptus Inc., Mountain View, California (CA), United States of America (USA), and in Canada, was granted a Medical Device License Class III by Health Canada in November 2001. The System is comprised of the Essure® micro-insert, a disposable delivery device, and a disposable split introducer. The mode of action is a combination of mechanical insertion of the implant, and tissue in-growth for device retention and obstruction of the fallopian tubes. After the HTS procedure, women need to use alternative methods of birth control for a three month period until the occlusion of the fallopian tubes becomes effective. Hysterosalpingography (HSG) at three months after HTS is a minimally invasive procedure recommended by the manufacturer of the Essure® system for the determination of tubal occlusion and device location. Other follow-up procedures such as pelvic radiography and transabdominal or transvaginal ultrasound have been used as alternative tests to HSG to check the position and alignment of the micro-inserts. The Essure® method is completely irreversible. Physicians need special training in the handling and insertion techniques of the Essure® micro-inserts under supervision of a Conceptus Inc.-designated preceptor or trainer until achieving competency in performing the HTS. The duration of professional training for gynecologists is about two days. The learning curve for those who are comfortable with hysteroscopy is between five and seven cases.

Project context

A local feasibility pilot study on HTS was conducted in Calgary at the Rockyview General Hospital between 2007 and 2010. In Alberta, a total of 72 HTS procedures (range 14 to 24 each year) were performed between 31 March 2008 and 31 March 2012, with the majority of the procedures done in the pilot study. Presently, in Alberta, there is much interest and increased demand by the public and by private providers in offering HTS using the Essure® system as an alternative to laparoscopic tubal sterilization (LTS). Although the demand for HTS grows, only a handful of clinicians have been involved in conducting this procedure, in Calgary. Presently, gynecologists at Rockyview Hospital are offering HTS using the Essure® system to women who have a contraindication for LTS and who meet certain medical criteria. Alberta Health Services (AHS) covers the costs of HTS for medically indicated cases. If the HTS is merely an option and not medically required, AHS pays for the procedure while women pay for the device. The cost of the device is presently considered a limitation in implementing the HTS procedure.

Technology Efficacy and Safety

Objective

The objective of the Technology Effects and Effectiveness section of this report was to perform a structured review and critical appraisal of the published research on the safety and efficacy/effectiveness of hysteroscopic tubal sterilization for permanent birth control.

Results

A search of electronic databases for articles published between 2006 and February 2012 identified eight case series studies, with a combined sample size of 2566 women. The studies were conducted in the USA, the UK, Spain, the Netherlands, and Sweden, and the majority of studies had a prospective design. The reporting of characteristics of women and risk of bias varied across studies. The studies included women ranging in age from 22 to 49 years (mean ages between 35 and 39.6 years in six studies). Two studies included women with comorbidities (that is, diabetes mellitus, obesity and previous abdominal or pelvic surgeries) that were contraindications for laparoscopic tubal sterilization (LTS).

The reported rate of bilateral placement of the Essure® micro-inserts was between 71 and 96% on first attempt and 87 and 98% after the initial and second attempts. These rates are in line with previously reported rates by the manufacturer and in other publications. Failure of the HTS procedures was due to anatomic reasons (for example, stenotic or previously occluded tubes, unsuspected tubal or uterine abnormalities, or tubal spasm) or the expertise level of the provider.

Successful occlusion of the fallopian tubes was reported in the majority of cases investigated at the three-month follow-up. Follow-up investigations were usually conducted by pelvic radiography and transvaginal ultrasound; HSG was used only in cases of suspected unsatisfactory placement of the micro-inserts. A total of 24 women who failed the procedure underwent LTS.

Follow-up periods were short and evidence was lacking about the long-term nature of the tissue response to the Essure® micro-inserts and the maintenance of the effectiveness of the HTS in avoiding pregnancies. Six unintended pregnancies were reported in three studies having follow-ups from three to 24 months, mainly due to non-adherence to the manufacture's protocol.

Major adverse events were reported in a small number of cases, and consisted of expulsion of micro-inserts (14 cases in two studies), perforation of the fallopian tubes (nine cases in three studies), and migration of the device to the abdominal cavity (three cases in one study). Vasovagal reactions were reported in 24 cases from three studies. A total of 454 women, representing 13 to 75% of participants in each study, experienced pain during the insertion of the device, and 231 women reported pain, usually mild, within the first 48 hours. The most prevalent adverse events experienced on short- and medium-terms included pain, vaginal bleeding or discharge, and changes in menstrual patterns.

For women using an IUD for contraception, results from one study with a small sample size indicated that providers may consider placing the Essure® device while leaving the IUD in situ for contraceptive reasons until occlusion of the fallopian tubes is demonstrated at the three-month follow-up. Some limitations that affect the ability to complete the procedure in IUD users were related to undiagnosed anatomic tubal defects such as stenosis or occlusion or blockage of tubal

ostia by the IUD device, and the need, in some cases, to remove the IUD device prior to HTS with Essure®.

In most studies, the technique was considered fast, with a reported mean procedure time in five studies of between 6.8 and 14 minutes.

Conclusions

Based on current evidence, HTS using the Essure® system can be an alternative to LTS in women with visualization of both tubal ostia and the anatomical possibility to place the micro-inserts. At relatively short follow-up periods the intervention seems to be adequate in terms of safety and effectiveness, with few reported failures or cases of major adverse events. One important disadvantage of the intervention is its irreversibility and the potential of regret downstream in younger women. The intervention prevents pregnancies at at least the same level as do the traditional methods available for female sterilization. However, the nature of the tissue, the cellular and fibrotic response, and the ability of the tissue to maintain occlusion of the fallopian tubes are not known for longer periods of time. This is more important if the Essure® system is provided to younger women who need to rely on permanent fertility control throughout their reproductive years.

Good communication and compliance with the protocol by professionals and women are important factors that impact the success of the intervention. The Essure® system has the advantages of avoiding surgical incisions and general anesthesia, and of promising a faster recovery time. The hysteroscopic approach could probably be a clear indication in women with a relative contraindication to laparoscopy due to morbid obesity, intra-abdominal adhesions, or cardiopulmonary diseases, or those with contraindications for general anesthesia. Several sterilization options are available to couples and these options need to be compared, over the longer term, to the Essure® system, using a risk/benefit approach. Appropriate education and counseling are key, due to the irreversibility of the Essure® system.

Economics Analysis

Objective

The objectives of the Economic Analysis section of this report were to determine the cost-effectiveness of hysteroscopic tubal sterilization (HTS) compared to laparoscopic tubal sterilization (LTS) and to determine the budget impact of HTS.

Methods

Cost-effectiveness was addressed through a systematic review of economic studies and an economic evaluation using a decision analytic model. The decision analytic model compared the health benefits and resource expenditures associated with three alternative protocols:

- the Calgary HTS protocol (HTS – Calg.)
- the Saskatchewan HTS protocol (HTS – Sask.)
- LTS currently conducted in Alberta

The analysis adopted a payer perspective and considered direct medical service costs to the Alberta health system, including physician, hospital, and confirmative diagnosis costs. The time horizon for the analysis considered costs from initial surgery to follow-up diagnosis and up to six months post-surgery.

Clinical and epidemiological data came from a review of literature (see T-section) and expert opinions. Costs pertaining to HTS were primarily obtained from the Calgary pilot study, supplemented by data obtained from the Alberta schedule of medical benefits. Hospital facility costs were obtained from the literature. Cost data for LTS were obtained from three provincial administrative databases.

The cost impact of replacing eligible LTS procedures with HTS was addressed through a budget impact analysis. Patients undergoing LTS accompanying another surgical procedure (for example, Cesarean section) were not considered eligible for HTS. Data estimating the number of eligible LTS patients for HTS were extracted from provincial administrative databases.

Results

HTS does not dominate LTS by being both less costly and more effective (not unequivocally cost-effective), but rather there is a trade-off regarding whether the additional effectiveness is worth the additional cost. The cost per additional successful sterilization ranged between $3,588 and $20,322 for HTS – Sask. and between $4,789 and $26,249 for HTS – Calg.

The budget impact, if the policy were to fund all women or only those contraindicated for LTS, is approximately $2,033,783 or $1,130,600 respectively. The cost savings if the limited number of HTS procedures were to cease is approximately $46,842.

Conclusion

In Alberta, HTS is more costly and more effective than LTS. It is important to identify the services that would be displaced, expanded, or contracted in the health system to obtain the resources needed to adopt HTS and to examine the associated foregone health benefits of such action, because the value for money associated with HTS is dependent upon determining whether its associated health benefits are worth the additional cost.

Abbreviations

All abbreviations that have been used in this report are listed here unless the abbreviation is well known, has been used only once, or has been used only in tables or appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

ACCS	Ambulatory Care Classification System
AE	adverse event
AH	Alberta Health
AHS	Alberta Health Services
AHFMR	Alberta Heritage Foundation for Medical Research
ACCS	Ambulatory Care Classification System
BIA	budget impact analysis
BMI	body mass index
CCI	Canadian Classification of Health Interventions
CCS	Canadian Conception Study
CI	confidence interval
CMG	case mix group
CEA	cost-effectiveness analysis
CV	cardiovascular
DAD	Discharge Abstract Database
EAG	Expert Advisory Group
FDA	Food and Drug Administration
GoA	Government of Alberta
HSG	hysterosalpingogram
HTA	health technology assessment
HTS	hysteroscopic tubal sterilization
ICER	incremental cost-effectiveness ratio
IQR	interquartile range
IUD	intrauterine device
LTS	laparoscopic tubal sterilization
MAUDE	manufacturer and user facility device experience
Me	median
mm	millimeter

mo	month
N, n	number
n/a	not applicable
NICE	National Institute for Health and Clinical Excellence
nr	not reported
NSAID	non-steroidal anti-inflammatory drug
OR	operation room
QHES	quality of health economic studies
PID	pelvic inflammatory disease
PMA	premarket approval
SD	standard deviation
SOMB	Schedule of Medical Benefits
SPS	standardized pain score
STD	sexually transmitted disease
TOA	tub-ovarian abscess
TVU	transvaginal ultrasound
US	ultrasound
VAS	visual analogue scale

Glossary

The glossary terms listed below were obtained and adapted from the following sources:

Taber's Cyclopedic Medical Dictionary, 21st ed., F.A. Davis Company, (Philadelphia, Pennsylvania); 2009, Editor Venes D

Medical Dictionary Online (*www.online-medical-dictionary.org*)

Food and Drug Administration and manufacturer documents

Bicornuate uterus (uterus bicornis)	A uterus in which the fundus is divided into two parts.
Delivery catheter	A long tube-like device that helps the doctor place the *Essure* micro-inserts in the fallopian tubes.
Dysmenorrhea	Pain in association with menstruation.
Dyspareunia	Pain in the labia, vagina, or pelvis during or after sexual intercourse.
Elective therapy	A treatment or surgical procedure not requiring immediate attention and therefore planned for the patient's or provider's convenience.
Endometrial ablation	Procedures used for the targeted destruction of the mucous membrane lining of the uterine cavity.
Endometrium	The mucous membrane that lines the uterus.
Essure® system	A method of permanent birth control (sterilization) for women. In this system, small metal coils are placed in a woman's fallopian tubes. Unlike other sterilization procedures for women, this system does not require incisions or general anesthesia. Instead, a doctor implants the coils by threading them through the vaginal opening.
Fallopian tubes	The hollow, cylindrical structure that extends laterally from the lateral angle of the fundal end of the uterus and terminates near the ovary. It conveys the ovum from the ovary to the uterus and spermatozoa from the uterus toward the ovary. Each lies in the superior border of the broad ligament of the uterus. Tubes through which an egg travels from the ovary to the uterus.
Hydrosalpinx	Distention of the fallopian tube by clear fluid.
Hypervolemia	An abnormal increase in the volume of circulating blood.
Hysterectomy	Surgical removal of the uterus.
Hysterosalpingography	Radiography of the uterus and oviducts after injection of a contrast medium.
Hysteroscope	An instrument for examining the uterine cavity.
Hysteroscopy	Inspection of the uterus by use of a special endoscope.

Intrauterine device (IUD)	Contraceptive device that diminish the likelihood of or prevent conception, placed high in the uterine fundus.
Laparoscopic sterilization	Sterilization by use of a laparoscope to gain access to the fallopian tubes so they can be banded, clipped, or electrocoagulated.
Laparoscopy	A procedure in which a Laparoscope (Laparoscopes) is inserted through a small incision near the navel to examine the abdominal and pelvic organs in the Peritoneal Cavity. Abdominal exploration with an endoscope.
Laparotomy	The surgical opening of the abdomen.
Ligation (tubal)	The application of a rubber band or ligature around a superficial bit of tissue.
Malposition	Faulty or abnormal position or placement.
Micro-insert	A small, flexible, coil-type device that is put into a fallopian tube for permanent pregnancy prevention.
Myometrium	The smooth muscle layer of the uterine wall, forming the main mass of the uterus.
Nulliparous	Never having borne a child.
Occlusion	The acquired or congenital closure, or state of being closed, of a passage.
Outpatient	A patient treated in a hospital and released the same day.
Parity	The number of live children a woman has delivered.
Pelvis	The bony compartment comprising the innominate bones, the sacrum, and the coccyx, joined at the symphysis pubis, sacroiliac, and sacrococcygeal articulations by a network of cartilage and ligaments.
Salpingectomy	The surgical removal of a fallopian tube.
Salpingography	Radiography of the fallopian tubes after the introduction of a radiopaque contrast medium; used in testing for patency of the tubes.
Sterilization	A permanent method of birth control.
Transcervical (route)	Done through the cervical opening of the uterus.
Transvaginal (routes)	Through the vagina. The term is used to describe surgical and ultrasonic imaging procedures.
Patency (tubal)	The state of being freely open.
Tubal sterilization	Procedures that render the female sterile by interrupting the flow in the Fallopian tube. These procedures generally are surgical, and may also use chemicals or physical means.

Tuboplasty	Plastic repair of a fallopian tube or tubes in an attempt to restore patency so that fertilization of the ovum may occur.
Ultrasonography	The use of ultrasound to produce an image or photograph of an organ or tissue. Ultrasonic echoes are recorded as they return from reflecting or refracting tissues of different densities.
Uterus	A reproductive organ for containing and nourishing the embryo and fetus from the time the fertilized egg is implanted to the time the fetus is born.
Vasovagal reactions	General discomfort or loss of consciousness due to a reduction in blood pressure that is associated with an increase in vagal tone and peripheral vasodilation.

Table of Contents

SECTION ONE: Background and Context

Carmen Moga MD, MSc; Christa Harstall, MLS, MHSA

The Background and Context section of this report provides a summary of the information on the health- and policy-related issues that motivated the request, the population (women seeking permanent tubal sterilization), the intervention (permanent method of contraception for women by hysteroscopic tubal sterilization [HTS]), the technology under consideration (Essure® system, currently licensed by Health Canada), and the current state regarding the use of the intervention and health service capacity in Alberta.

Research questions

The background and context section of the report attempts to briefly address the following questions:

Background

- What are the options for the interruption of tubal patency for female sterilization?
- How does HTS work? What different HTS procedures are available?
- Are other interventions required to ensure the success of HTS?
- What HTS technologies are licensed by Health Canada?
- For which population is HTS indicated?
- Do any issues exist related to acceptability of HTS, and adherence to or compliance with HTS follow-up (including the use of an alternative form of contraception during the first three months)?
- How does HTS compare to other options—particularly tubal ligation—for female sterilization?
- Are any quality of life, social, ethical, and/or legal issues associated with the provision of HTS?
- Do any issues exist related to physician's training?
- Are clinical practice guidelines and policies in place, in Alberta, Canada, or internationally, for elective permanent female sterilization?

Context

- What is the prevalence of elective permanent female sterilization in Canada and Alberta?
- What is the standard practice for elective permanent female sterilization in Alberta and other Canadian provinces?
- Is HTS currently being delivered in Alberta? If so, is the provision public, private, or both? How is the service provided? What do the healthcare professionals who perform HTS think of it in terms of its clinical utility?
- What resources are needed for provision of HTS in Alberta?

Background

Female sterilization by tubal occlusion or ligation is the most common permanent method for contraception used globally by married or in-union women aged 15 to 49 years.[1] Female sterilization prevents pregnancy by occluding or disrupting the fallopian tube patency, impeding sperm transport to the ampulla of the tube where fertilization of the ovum occurs.[1]

Female sterilization methods

A number of female sterilization methods are available and the choice of the most appropriate method depends upon a mix of factors such as individual preference, medical history, need for other gynecological procedures, assessment of acute risk and anatomy, provider's training, expertise and experience, availability of suppliers, and access to services.[2,3] It also depends on whether the sterilization is performed remote from a pregnancy (interval sterilization, any time during the menstrual cycle but preferably between the sixth and 13th day of the menstrual cycle), postpartum (ideally carried out within two days or six weeks after delivery), or after an abortion (during the first week, provided there is no suspicion of pelvic infection).[2]

The fallopian tubes are reached for occlusion either via the abdominal or the transcervical (hysteroscopic) route (see Table 1).

Table 1: Methods of female sterilization

Approach	Surgical procedure & timing	Occlusion techniques	Advantages	Disadvantages/Limitations
Abdominal	Laparoscopy (*standard procedure*) • interval only, contraindicated postpartum	Electrocoagulation (unipolar, bipolar) Mechanical devices (clips, rings)	• Preferred over mini-laparotomy for interval sterilization • Can be done as day case; hospitalization is not required • Effective immediately • Mechanical devices: clips are less destructive to the fallopian tube, might increase reversibility; rings are simple, inexpensive	• Requires special equipment (operating room) and experience • Requires general anesthesia • Not recommended in women with morbid obesity, chronic heart disease, or prior abdominal or pelvic surgeries • Necessitates one or two small incisions • Postoperative pain (greater with mechanical devices); requires two to seven days of recovery • Electrocoagulation: higher failure rate and potential for serious complications secondary to inadvertent tubal perforation, or to heat transfer resulting in burns to the adjacent bowel
	Mini-laparotomy • postpartum, post-abortion, or interval	Ligation and excision Mechanical devices (clips, rings)	• Less invasive, reduced recovery time, better cosmetic result than laparotomy • Ideal for thin women with no pelvic disease or adhesions • In thin, small women can be performed with instruments less costly than those required for laparoscopy • Effective immediately	• Performed in operating room • Difficult to perform in obese women or in women who have had inflammatory disease of the fallopian tubes • Longer and painful recovery time compared with laparoscopy
	Laparotomy • in conjunction with other elective surgery (e.g., Cesarean section, salpingectomy, ovarian cystectomy)	Ligation and excision Mechanical devices (clips, rings)	• Conducted concurrent with elective surgery • Effective immediately	

Transcervical	Hysteroscopy • interval only	Physical occlusion using micro-inserts (Essure® system)	• Minimally invasive • No incisions, less discomfort • Fast recovery, same day in most cases • Indicated in all women, including those with comorbidities which contraindicate general anesthesia • Can be performed as outpatient procedure • Local rather than general anesthesia	• Women must use another method of birth control until their fallopian tubes are completely blocked (at three months) • Relatively new; potential long-term risks are unknown • Irreversible
		Mechanical, formed-in-place silicone plug (Ovabloc)	• Non-surgical; high success rate • Silicon conforms to shape of tube • Plug position can be confirmed by x-ray at three months after the procedure	• Tubal spasm may require repeat applications in up to 20% of women • Fracture of the silicone plug with migration may occur • Expensive delivery equipment • Reports exist of extravasation of the silicone into paratubal or myometrial tissue
		Chemical agents (quinacrine)	• Simple • Non-surgical • High success rate with two applications • Low cost	• Often requires several applications; sterilization can take up to three months • Failure rates depend on dosage and number of insertions • Inability of a method to confirm the occlusion such as X-ray, HSG, or solography; performing an HSG may increase the failure rate • Shown to be mutagenic in in vitro studies, raising safety concerns; unconfirmed in large studies
		Thermal electrocoagulation	• Ease of access • Moderate success rates	• Significant complications, including tubal and uterine perforation, bowel damage, and peritonitis

HSG – hysterosalpingography

Adapted from: [2,4-10]

Abdominal approach to tube

Fallopian tubes may be surgically cut or ligated with or without a section of the tube being removed, they may be mechanically blocked using clips or rings, or they may be electrically coagulated.[1]

Interval sterilization is most commonly performed via laparoscopy using mechanical methods such as the Hulka-Clemens spring clip, the Filshie hinged clip, or the Falope or Yoon silastic ring or band, or using electrosurgical methods consisting of unipolar or bipolar electrocoagulation of a portion of the fallopian tube.[3] The intervention may also be performed postpartum and as interval sterilization via a "mini" laparotomy incision. This involves the same techniques as used for occlusion or, more commonly, an excision of a segment of the tube and ligation of the ends (the Pomeroy method which is the most common method, the Irving technique, the Pritchard (Parkland) method, or the Uchida method), fimbriectomy, and salpingectomy.[3]

Tubal ligation, the standard procedure for female sterilization is reported to be 99.5% effective as a form of contraception at one year of follow-up and it is immediately effective post-procedure (see Table 2).[11] In the long term, one multicentre prospective study by Peterson et al. (Collaborative Review of Sterilization (CREST) study) published in 1996, conducted in the USA, reported a 10-year failure rate of 1.85% for all methods of tubal ligation (uni- and bipolar tubal coagulation, silicone ring, spring clip (Hulka), interval, and postpartum partial salpingectomy) (see Table 3).[11]

Table 2: Effectiveness of sterilization methods: Failure rates after procedure

Method	Rate (%)
Vaginal tubal ligation	4.8*
Tubal ligation	0.5†
• Filshie clip application	1.2*
• Falope ring	1.4*
• Hulka clip (spring clip)	3.4*

*Birdsall's et al. 1994 review (as cited in[11]); †World Health Organization 2001 (as cited in[11])

Table 3: Effectiveness of sterilization methods: 10-year failure rates

Method	Rate (%, range) (unless otherwise stated)
All methods	1.85 (1.51 to 2.18)*; 0.5†
Bipolar tubal coagulation	2.48 (1.63 to 3.33)*
Unipolar tubal coagulation	0.75 (0.11 to 1.39)*
Silicone ring	1.77 (1.01 to 2.53)*
Hulka clip (spring clip)	3.65 (2.53 to 4.77)*
Filshie clip	0.2 to 0.3%‡
Interval partial salpingectomy	2.01 (0.47 to 3.56)*
Postpartum partial salpingectomy	0.75 (0.27 to 1.23)*

*Peterson et al. (CREST study) 1996 (as cited in[11]); †Reported lifetime risk of failure, in general, source: Royal College of Obstetricians & Gynaecologists Guideline, UK;[12]; ‡Royal College of Obstetricians & Gynaecologists Guideline, UK[12]

Although the various techniques of laparoscopic procedure are associated with high effectiveness rates they are not without risks. Reported potential risks and complications include CO_2 embolism, injuries to the gastrointestinal tract (bowel), bladder, urinary tract or blood vessels, or extraperitoneal insufflations.[6,13] Potential adverse events and risks associated with mechanical sterilization methods are: postoperative pain, bleeding (0.6 to 1% of total cases), infection (1%), anesthesia-related events (1 to 2%), post-surgical complications (women's regret), and ectopic (tubal) pregnancy.[3] Electrocoagulation technique has potential serious complications secondary to inadvertent heat transfer resulting in burns to the adjacent bowel.[10] The recovery time after laparoscopic tubal sterilization is around two to seven days (average three to four days) (EAG member, email, 21 August 2012). Women who have underlying medical conditions such as diabetes, morbid obesity, a history of previous multiple abdominal or pelvic surgeries, or chronic heart disease with or without a severe pulmonary component such as pulmonary artery hypertension,[14] or those who receive general anesthesia, are at higher risk for surgical complications by undergoing laparoscopic tubal sterilization.[3,12]

Transcervical routes

Less invasive methods of tubal occlusion have been investigated as potentially safe and effective alternative methods of sterilization. These include hysteroscopic insertion through the vagina into the fallopian tubes of micro-inserts (Essure® system)[15,16] or substances such as liquid siloxane (Ovabloc) or quinacrine pellets, or application of an electrosurgical technique (see Table 1).[6,9-11] The presence of the micro-inserts or chemicals induces a fibrotic reaction and subsequently results in blockage of the fallopian tubes.[1] Long-term technical failures of the Ovabloc method, including implant expulsion, are reported in approximately 6% of cases, while the cumulative pregnancy rate after three years was 0.99% in one small study.[2] The effectiveness rates of quinacrine pellets vary, with two-year failure rates ranging between 0 and 1.2%[10] and pregnancy rates reported from 1 to 12% at one and 10 years, respectively.[9] Blocking the tubes by heat generated electrically (electrocoagulation) was associated with a high rate of failure, up to 35%, and with potentially serious complications secondary to inadvertent tubal perforation or heat transfer resulting in injury to the adjacent bowel.[2] The cryocoagulation method has the potential for sterilization through the use of cryoprobe, causing necrosis of the endometrium and subsequent fibrosis of the corneal area, however data concerning its efficacy are lacking.[2] The use of macrolide antibiotics (erythromycin tablets) for female sterilization was studied in few studies and showed a high failure rate of 35.8%.[10] A gel formulation of erythromycin is currently being investigated.[10] Other methods under investigation are the Intratubal Ligation Device (manufactured by BioMedical Engineering Solutions) and a Reversible Tubal Occlusion Device (manufactured by Berkeley Applied Science and Engineering).[10]

The focus of this report is on hysteroscopic tubal sterilization using the Essure® system, the only HTS device licensed and available for clinical use in Canada.

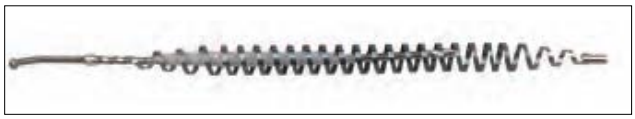
Technology

The Essure® system, manufactured by Conceptus Inc., Mountain View, CA, USA, is indicated for women who desire permanent fertility control by bilateral occlusion of the fallopian tubes.[4,17,18] It may also be used in women who desire sterilization and who have comorbidities that are contraindications for laparoscopic tubal sterilization due to a higher surgical risk.

The System is comprised of the Essure® micro-insert, a disposable delivery device, and a disposable split introducer.[4,17,19]

The Essure® micro-insert is a spring-like device 40 millimeter (mm) in length and 0.8 mm in diameter that consists of a stainless steel inner coil, a nickel-titanium (Nitinol) expanding outer coil, and polyethelene terephthalate (PET) fibers (see Figure 1). The PET fibers are wound in and around the inner coil. The device is placed into the fallopian tube, spanning the utero-tubal junction, using a standard 5-mm hysteroscope.[17] The disposable delivery system consists of a single-handed ergonomic handle which contains a delivery wire, a release catheter, and a delivery catheter.[17] Since its initial introduction, the manufacturer has reported improvements in the design of the device, such as the development of a new coil catheter delivery system designed to carry the micro-insert past the areas of tubal resistance. [4,19,19] During the procedure, physiologic saline at an infusion pressure of 100 to 120 mm Hg is used for uterine distension, facilitating the insertion of the devices into the fallopian tubes. When released from the delivery system, the outer coil expands to a diameter of 1.5 to 2.0 mm, to anchor the micro-insert in the fallopian tube. The optimal placement of the coils is to position the micro-insert with three to eight coils into the uterus to prevent expulsion.[17] The effectiveness of the Essure® system in preventing pregnancy is believed to be a result of a combination of the space-filling design of the device and a local, occlusive, benign tissue in-growth resulting from a chronic inflammatory and fibrotic response to the terephthalate device fibers.[6] The procedure is usually done under local anesthesia, with or without intravenous sedation.[6,9]

Figure 1: Expanded outer coil with white PET fibers on inner coil



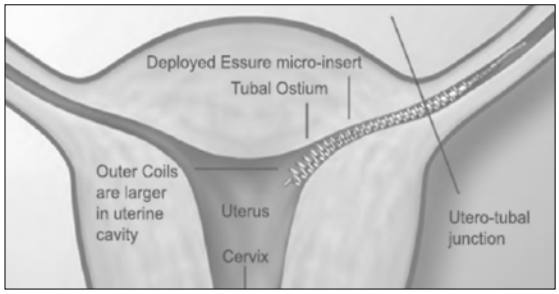
Source: Essure® physician training manual[17]

After the HTS procedure, women need to use alternative methods of birth control for a three-month period.[4,17,19] Over the three months the PET fibers are eliciting benign tissue in-growth into the coils of the Essure® micro-insert and around the PET fibers themselves.[4,4,17-19,19-21]

Bilateral placement of the Essure® system

About 85 to 99% of women undergoing the HTS with the Essure® system obtain successful placement (see Figure 2), and one in seven women may fail to achieve bilateral placement of the device. At the three-month follow-up, approximately 4% of the women who did receive placement of micro-inserts in both tubes were found to have them in the incorrect position.[6,18] Factors impeding bilateral placement appear to be related to pre-existing comorbidity or pathology (such as endometrial polyps or obesity), anatomic abnormalities (uterine anomalies such as adhesions or bicornuate uterus, endometrium blocking view of the ostia, cervical stenosis, laterally placed fallopian tubes, stenotic tubes, proximal tubal occlusion, or tortuosity), or procedure related difficulties (such as poor visualization or tubal spasm).[6,17,22]

Figure 2: Ideal Essure® micro-insert placement



Source: Essure® physician training manual[17]

Confirmation of fallopian tubal occlusion

Hysterosalpingography (HSG) at three months after HTS is a minimally invasive procedure considered the gold standard and recommended by the manufacturer of the Essure® system for determination of tubal occlusion and device location.[23,24] HSG consists of a radiography examination (fluoroscopy), after the injection of radio-opaque water-soluble contrast material, to monitor closure of the fallopian tubes.[25,26] The manufacturer indicates that a minimum of six still radiographs must be taken to assess the location and tubal occlusion of the device.[24] Satisfactory placement requires that the distal end of the inner coil is within the tube, with less than 50% of the length of the inner coil trailing into the uterine cavity, or the proximal end of the inner coil must appear to be up to 30 mm into the tube from where contrast material fills the uterine cornu.[24] If unilateral or bilateral patency of the fallopian tubes is evident, HSG is repeated after an additional three months.[27] Potential risks and side effects of HSG include: infection or pelvic inflammatory disease, vasovagal reaction, intravasation of radio-opaque dye, allergic reactions to the material used, uterine perforation, spotting or light bleeding, uterine cramps, and irreparable damage to the fallopian tubes during the test.[25] There are reports of women's intolerance and low compliance with the three-month HSG.[5,26-29] Follow-up rates of HSG at three months vary widely, from 13 to 94%, with the highest follow-up rates reported in the original HTS clinical trials performed by the manufacturer.[9] Poor adherence to HSG may be due to inappropriate counseling, inconvenience, system barriers, the burden of an additional visit, or change in insurance status.[29,30]

Because of the potential risks, higher cost, and discomfort associated with HSG, pelvic radiography is used as alternative to check the position and alignment of the micro-inserts.[5,10,26,31] Conventional plain film pelvic radiography can identify coil retention, but it provides limited information about the soft tissue structures that envelop it and it is impossible to determine whether the coils are within the fallopian tube or whether they have perforated the tube and become adherent to the posterior uterine fundus.[10] Both HSG and pelvic radiography expose the woman to minimal radiation.[5,25]

Ultrasound (transabdominal and transvaginal) technique is often used as an alternative for assessing placement of the Essure® micro-inserts. Ultrasound seems to have the ability to locate the proximity of the device to the uterotubal junction and visualize its relationship with the surrounding tissue, but the imaging makes no assessment of tubal occlusion or of whether the device was placed in an intratubal position.[26,29,32] The visualization of the device on a single plane seems to be difficult due to its curved configuration after placement, and the same difficulty is encountered for the ends of the micro-inserts due to bowel gas.[26] Due to these noted limitations, ultrasound has been used in practice as a method of checking the fallopian tube occlusion after an uncomplicated procedure

which is considered by clinicians to have an extremely low chance of incorrect placement of the Essure® system.[23]

Other reported techniques used to confirm the occlusion of the fallopian tubes are hysterosonography, hysterosalpingo-contrast-sonography and three- and four-dimensional ultrasound.[5,10,23,32-35]

Most of the studies and protocols that used non-HSG procedures were based in Europe and Australia.[26] In these studies, HSG was reserved only for women with incorrect insertion or remaining uncertainty of correct placement following a plain radiography or ultrasound. Other criteria used to indicate the need for an HSG reported in these studies were: duration of the HTS procedure of more than 15 minutes, less than three or more than eight coils visible, the need for more than two devices for a single attempt, tubal ostia not directly visible, high resistance experienced during the procedure, experience of higher than average pain, or when the physician just felt uncomfortable with the insertion device during the procedure.[23]

In the USA, the HSG is a mandatory procedure as part of the Food and Drug Administration (FDA) approval of the Essure® system.[10,26,27,31] With the introduction of new follow-up methods, new potential pitfalls might appear along with them and future research needs to confirm their reliability.[23]

Permanency of tubal occlusion and sterilization

The long-term nature of the tissue, cellular, and fibrotic response and the ability of the tissue response and the Essure® micro-insert to maintain occlusion of the fallopian tubes, is not well known beyond five years follow-up in the published studies.[17] The estimated crude pregnancy rate in the clinical setting after Essure® is 0.2%.[29] Sixty-four pregnancies out of an estimated 50,000 procedures were reported to the device manufacturer between 1997 and December 2005.[36] Most pregnancy cases were reported in women without appropriate follow-up due to woman or physician noncompliance (30 cases), misread HSG or x-ray tests (18 cases), and undetected pre-procedure pregnancies (eight cases). The pregnancy risk following the HTS procedure may be reduced by improving women's education and counseling prior to the procedure, by proper timing of the procedure during the early proliferative phase of the woman cycle, by ensuring that patients use effective contraceptive before and after the placement, by following the instructions for use, and by increasing the adherence to the Essure® HSG protocol.[29,36] It is expected that more data will become available as participants in the clinical trials of safety and effectiveness continue to be followed.

The Essure® method is completely irreversible and any attempt at surgical reversal will require micro-insert removal by laparotomy and utero-tubal reimplantation.[17] No data are available about the safety or effectiveness of surgery to reverse the Essure® procedure.[17]

Safety issues

The approval of the Essure® system by the FDA was based on outcomes reported from two multicentre case series (the Phase II Study[37] and the Pivotal [Phase III] Study.[38]) The main adverse events reported in these studies are summarized in Appendix A.

An analysis of the reports associated with the Essure® HTS by reviewing the Food and Drug Administration's Manufacturer and User Facility Device Experience (MAUDE) database from November 2002 to February 2011 identified 365 adverse events.[39] Pain was the most prevalent reported symptom (151 events). Abnormal bleeding was reported in 29 cases. The adverse events

that prevented reliance on Essure® for contraception were: device malfunction (102 events), perforation (69 events) and micro-insert malpositioning (25 events). Fifty post-sterilization pregnancies (26 of which were ectopic pregnancies) were reported. The evaluation and management of these events resulted in an additional 179 surgical procedures, of which 31 were hysterectomies.

Other potential adverse events mentioned by the manufacturer[17] include: breakage of the Essure® micro-insert, fluid over-absorption, and the potential for pelvic inflammatory disease (adnexal infection and salpingitis).

Hypersensitivity to nickel was initially included in the manufacturer's list of contraindications for the Essure® procedure and women with known hypersensitivity to nickel were required to undergo a skin test to assess hypersensitivity prior to undergoing the procedure.[17] A review[21] of the adverse events due to suspected nickel hypersensitivity associated with the Essure® implants collected from 2001 through 2010 from the Conceptus Inc., de-identified data obtained from the MAUDE database, and from reports to the manufacturer directly, as well as from the results reported by 650 women from two multicentre case series[37,38] which showed that of the 436,937 Essure® kits sold since its commercial release, nickel hypersensitivity was suspected in only 63 reported cases, representing 0.014% of the total procedures. Presently, based on these findings, testing for nickel sensitivity is not part of the protocol nor recommended prior to undergoing of the HTS procedure (EAG meeting minutes, 19 June 2012). The FDA approved this change to the procedure instructions in 2011, and nickel sensitivity is no longer listed as a contraindication in the instructions for use of the Essure® micro-insert (communication, EAG member, emails, 3 July, 2012 and 19 November 2012).

Removal of the Essure® micro-inserts due to adverse effects such as recurrent or persistent pelvic pain requires surgery, including an abdominal incision and general anesthesia and possible hysterectomy.[17] According to manufacturers, women who choose the Essure® method of sterilization are requested to notify the manufacturer if they undergo surgery (such as hysterectomy) that will result in removal of the micro-inserts. Long-term sterilization failures are also continually recorded.[17]

The safety and effectiveness of the Essure® procedure is unknown in women younger than 21 years of age or older than 45 years of age, nulliparous, nor in women who delivered a baby or terminated a pregnancy in less than six weeks before Essure® micro-insert placement.[17]

Contraindications for use of the Essure® system listed by manufacturer are:[6,17,40]

- uncertainty about the desire to end fertility
- prior tubal ligation, pregnancy or suspected pregnancy, delivery or termination of a pregnancy less than six weeks before device placement or during menstruation
- unwillingness to use another method of contraception for at least three months after the Essure® placement procedure
- allergy to contrast media
- history of tubal surgery (for example, tubal ligation, ectopic pregnancy, tuboplasty)
- uterine structural abnormalities that might impede placement of the Essure® micro-inserts (for example, bicornuate uterus)
- women in whom only one micro-insert can be placed (for example, unicornuate uterus)

- hydrosalpinx
- active or recent pelvic infection
- current immunosuppressive therapy (for example, systemic corticosteroids, chemotherapy)

Comparison between sterilization with Essure® system and other methods of sterilization

A comparison of the advantages and limitations of HTS with Essure® system with other methods of female sterilization, particularly the traditional method of sterilization by laparoscopic tubal ligation, is presented in Table 1 and Table 4.

Table 4: Advantages and limitations: Essure® system & laparoscopic tubal ligation

Hysteroscopic tubal sterilization	Laparoscopic tubal ligation
⊕ Minimally invasive; avoids entry into the peritoneal cavity	⊖ Invasive
⊕ Non-incisional (the lack of a visible scar is appealing to women, likely for both cosmetic and privacy reasons)	⊖ One or two small incisions
⊕ Less discomfort, including pain during and post-intervention	⊖ Pain post-intervention
⊕ Fast recovery, return to work same day in most cases	⊖ Recovery and return to normal activities in four to seven days
⊕ Indicated for women seeking permanent contraception, including those with higher surgical risk of complications for laparoscopic tubal ligation, e.g., cardiopulmonary diseases, obesity, diabetes mellitus, previous abdominal or pelvic surgery	⊖ Not recommended in the following high-risk groups: women with cardiopulmonary disease, morbid obesity, intra-abdominal adhesions, hemorrhagic diathesis
⊖ Not recommended in women in whom only one micro-insert can be placed, including women with apparent contralateral proximal tubal occlusion and women with suspected unicornuate uterus; gynecological comorbidities such as active or recent upper or lower pelvic infection, cervicitis, undiagnosed vaginal bleeding, submucous leiomyoma, suspected or known gynecological malignancy; known allergy to contrast media	
⊕ Can be performed as an outpatient procedure	⊖ Performed in an operation room
⊕ Local rather than general anesthesia	⊖ Most women receive general anesthesia
⊖ Adverse events: perforation (1.8%), expulsion (2.2%), vaso-vagal reactions	⊖ Adverse events (fewer than 1%): injury to bowel, bladder, major vessels or other adjacent organs, regardless of the method used
⊖ Risks: pregnancy, ectopic pregnancy; estimated crude pregnancy rate in the clinical setting 0.2%; pregnancy rates of less than 1% may be achieved by adhering to a follow-up protocol confirming successful placement	⊖ Risks: pregnancy, ectopic pregnancy; failure rate 0.5% in first 12 months of use; 1.85% at 10 years of cumulative use

⊖ Women must use another method of birth control until their fallopian tubes are completely blocked (after at least three months)	⊕ Effective immediately
⊖ Irreversible	⊕ Reversible when using mechanical devices (clips and rings)
⊖ Because is relatively new, it is not known whether long-term risks exist	⊕ Standard practice for elective, permanent sterilization

Adapted from:[1,2,4,6,8,9,11,14,17,22,29,40] and communications with EAG members, by email, teleconference, and meeting, between June and August 2012

Physician training

Physicians need special training in the handling and insertion techniques in order to ensure a successful placement of the Essure® micro-inserts.[11] The Essure® physician's training manual,[17] issued by the manufacturer, indicates that a physician should be a knowledgeable hysteroscopist prior to taking Essure® training, needs to complete a simulator and an instructional training, and needs to conduct approximately five procedures under the supervision of a Conceptus Inc. designated preceptor or trainer in order to achieve competency in performing the HTS. The duration of professional training for gynecologists to perform HTS is about two days. The learning curve for someone who is comfortable with hysteroscopy is between five and seven cases. Most residents can perform this procedure in a similar time (EAG meeting minutes, 19 June 2012; communication, EAG member, emails 3 July 2012 and 2 August 2012).

The results of a post-approval FDA-mandated multicentre cross-sectional study initiated in 2007 and funded by Conceptus Inc., with the aim of comparing the successful bilateral placement of the Essure® model ESS305 by newly trained and experienced physicians, indicated that the HTS procedure can be performed with high bilateral placement rates regardless of physician experience. The reported success rate was 98% for experienced physicians versus 96% for novice physicians. Experienced physicians were defined as doctors who had performed more than 25 Essure® micro-inserts placements using an early model of the device ESS205. Newly trained physicians were those who had never used the ESS205 model, had recently completed training, and had performed only three to five proctored cases. Based on interim results, the FDA granted early termination of the study in 2009.[18,41]

Ethical and legal aspects

Sterilization is a voluntary act, with the request coming from the person who wishes to be rendered infertile, and is irrespective of age or marital status. Due to its irreversibility, the procedure involves both ethical and legal aspects that must be considered for obtaining informed consent before the intervention. The aspect of informing couples about the consequences of transcervical sterilization was stressed in the Canadian Contraceptive Consensus document published by the Society of Obstetricians and Gynaecologists of Canada[11] and by guidelines issued in the United Kingdom.[12,42]

The counseling process should include discussions about alternative contraceptive methods, an explanation of benefits, risks, and available options, and the determination of whether the person is competent to understand the information. The decision about sterilization should be made by individuals with respect of their autonomy, without pressure or coercion from anyone else.[11] When the person has a mental disability, it is even more difficult for the physician to determine their

capacity to provide informed consent.[11] In Canada, the non-therapeutic sterilization of any individual who is not competent to give informed consent is considered illegal.[43]

Regret after female sterilization is not infrequent and is likely to be associated with factors such as young age at the time of sterilization, having small children at the time of sterilization, low parity, sterilization performed soon after vaginal delivery or Cesarean section, induced abortion, the loss of a child, non-white race, change in partner and or marital status, and financial crisis.[3,11,12,28] Reported rates of women's regret following the procedure range from 0.9 to 30%.[3,28] Findings from the Collaborative Review of Sterilization (CREST) study on poststerilization regret within 14 years after tubal sterilization showed that 20.3% of women aged 30 or younger at the time of sterilization and 5.9% of those 30 years of age or older at the time of sterilization expressed regret[2]. Women having uterine or tubal disease who are ambivalent about sterilization or who feel uncomfortable about having a device or materials inserted into their fallopian tubes should not be offered this intervention.[11]

Regulation status (Health Canada and US FDA) and diffusion within the Health System

In Canada, the Essure® permanent birth control system manufactured by Conceptus, Inc., Mountain View, CA, was granted a Medical Device License (license no. 34212) by Health Canada, as a Class III device, in November 2001.[44] The Essure® system is indicated for female sterilization by bilateral occlusion of the fallopian tubes. Since the initial approval, Health Canada has approved new models of the Essure® system. The third generation of the Essure® device, the ESS305 model, was approved in 2006 and includes design modifications made to the delivery system, which reduces the number of steps a physician is required to perform during a placement procedure, and also offers improvements of the hysteroscopic visualization of the implant and placement markers.[45]

Health Canada's approval process for marketing a Class III device relies upon information submitted mainly by the manufacturer: background and device-specific information, a summary of the safety and efficacy studies, conclusions drawn from these studies by the manufacturer, and compliance with quality systems requirements (CAN/CSA-ISO 13485:03).[46]

No formal accreditation or certification is required for practicing the HTS procedure.

The device is distributed in Canada by Provincial Medical Supplies Ltd., Mississauga, ON (unpublished report[47]).

In the USA, the Center for Devices and Radiological Health (CDRH) of the FDA issued Premarket Approval (PMA) P020014 (Class III) for the Essure® system in November 2002.[19,20] The approval was based on outcomes of the Essure® system reported from two multicentre case series (that is, the Phase II Study[37] and the Pivotal [Phase III] Study[38]), which included 745 women. The main adverse events reported in the case series studies that prevented licensure beyond PMA for the Essure® system included: perforation, expulsion, unsatisfactory micro-insert location, and initial tubal patency (see Appendix A).

The PMA status requires the manufacturer to continuously provide reports on long-term follow-up of the participants in the two case series studies, such as the number of pregnancies, adverse events, and histological explant data following any extirpative surgeries. Also, the FDA requested results from a post-approval study that evaluated the rates of successful bilateral placement and identification of factors predictive of failure to achieve bilateral placement of the system on first

attempt by newly trained physicians.[19,19,20] The manufacturer is also requested to continually update the information on the professional and patient labeling[48] if new data is obtained during the long-term follow-up period.[19,20]

Clinical practice guidelines and policies

The Society of Obstetricians and Gynaecologists of Canada, Canadian Contraception Consensus Committee published guidelines in April 2004 for healthcare providers on the use of contraceptive methods to prevent pregnancy and sexually transmitted diseases.[11] The guidelines were based on a scientific search of databases, publications, and position papers published between 1988 and March 2003, and include expert opinion. The published scientific evidence was considered by the experts to be of weak methodological design. Transcervical sterilization was considered an effective, safe, and less invasive technique but virtually impossible to reverse. The only device available for clinical use in Canada for transcervical sterilization is the Essure® system. The recommendations made by the consensus group were that couples should be informed about the risks and benefits of different sterilization procedures before a procedure choice is made. New techniques of female and male sterilization should be available to all Canadians.

The Royal College of Obstetricians and Gynecologists in the United Kingdom (UK) issued guidelines in January 2004 for male and female sterilization, based on a database search of the literature up to December 2002.[12] Information was available from studies of weak methodological design, and included expert committee reports or opinions. The Essure method (Essure®, Conceptus Europe) is licensed for use in the UK. Hysteroscopic methods for tubal occlusion were considered still under evaluation and the HTS should only be used within the present guidance system for new surgical interventions. The guidelines suggested that women must be fully informed about the irreversibility of the method and of the procedure's risks and uncertain efficacy, and that this should be fully documented in the woman's notes.

The National Institute for Health and Clinical Excellence (NICE) in the UK published an updated guidance in September 2009 for hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants.[42] The guidance is based on scientific evidence published until March 2009, and on the opinions of specialist advisors.[49] The scientific evidence was mainly from case series studies published between 2003 and 2008. They state that "*current evidence on the safety and efficacy of hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance and audit.*" Clinicians wishing to undertake HTS should ensure that women understand that additional contraception is needed until appropriate imaging confirms satisfactory placement of the micro-inserts. Regarding the imaging they state that *"… may be by X-ray or ultrasound scanning initially, followed by HSG in selected patients or by HSG as a routine test to ensure that the fallopian tubes have been occluded.*"

The American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice, published their opinion in June 2010 on the use of HSG after HTS.[27] They state that "… *according to the US device labeling, the HSG is the only method to be used for confirmation of tubal occlusion. … patients considering hysteroscopic sterilization need careful counseling regarding the need for interim contraception and the need to return for postoperative HSG. … If bilateral tubal occlusion is not confirmed on the HSG performed at 3 months, patients must be counseled to use interim contraception and have a repeat HSG 3 months later. If bilateral occlusion is still not confirmed on the repeat study, patients must be counseled not to rely on the HTS and to use alternative contraception.*"

Project context

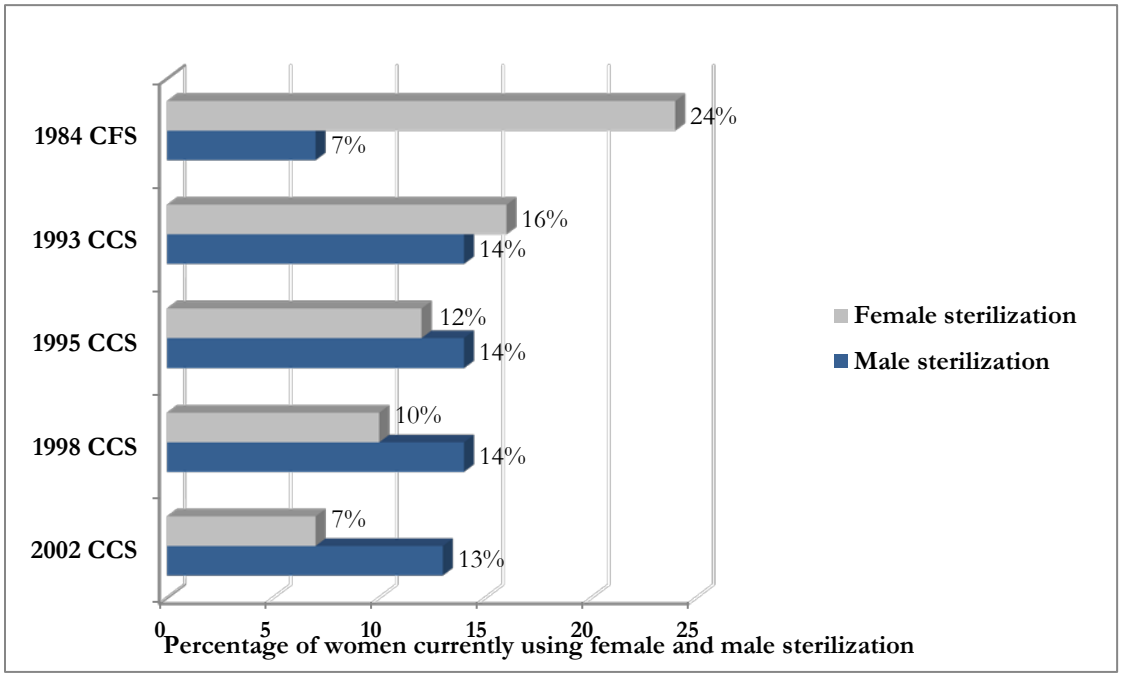
The section on project context briefly describes the standard practice for elective permanent sterilization in Canada and Alberta, the status of diffusion of the Essure® technology in Alberta and other Canadian provinces, and the resources needed and funding of HTS with the Essure® system in Alberta.

Standard practice

A report published by the United Nations Population Division in 2009 estimates that the female sterilization prevalence rate among women aged 15 to 49 years is 20.1% in North America, (11% in Canada and 21.2% in the USA, respectively).[50]

Over two decades in Canada, a comparison of the results from previous Canadian Fertility Survey (CFS) conducted in 1984 and Canadian Contraception Studies (CCSs) conducted in 1993, 1995, 1998, and 2002 on national representative samples of women aged 15 to 44 years shows a linear decline of reliance on female sterilization, while rates of male sterilization (vasectomy) have stabilized at 14% and 13% (see Figure 3).[51-54] Female sterilization was the most popular single method of contraception employed by Canadians in 1984, used by 24% of all women. This method has declined in prevalence and was used by just 7% of the women in the 2002 CCS study, while 13% of women relied on male sterilization.[51-53]

Figure 3: Rates of use of female and male sterilization, percentage of all respondents (women aged 15 to 44 years who had and who never had intercourse) (surveys 1984–2002)



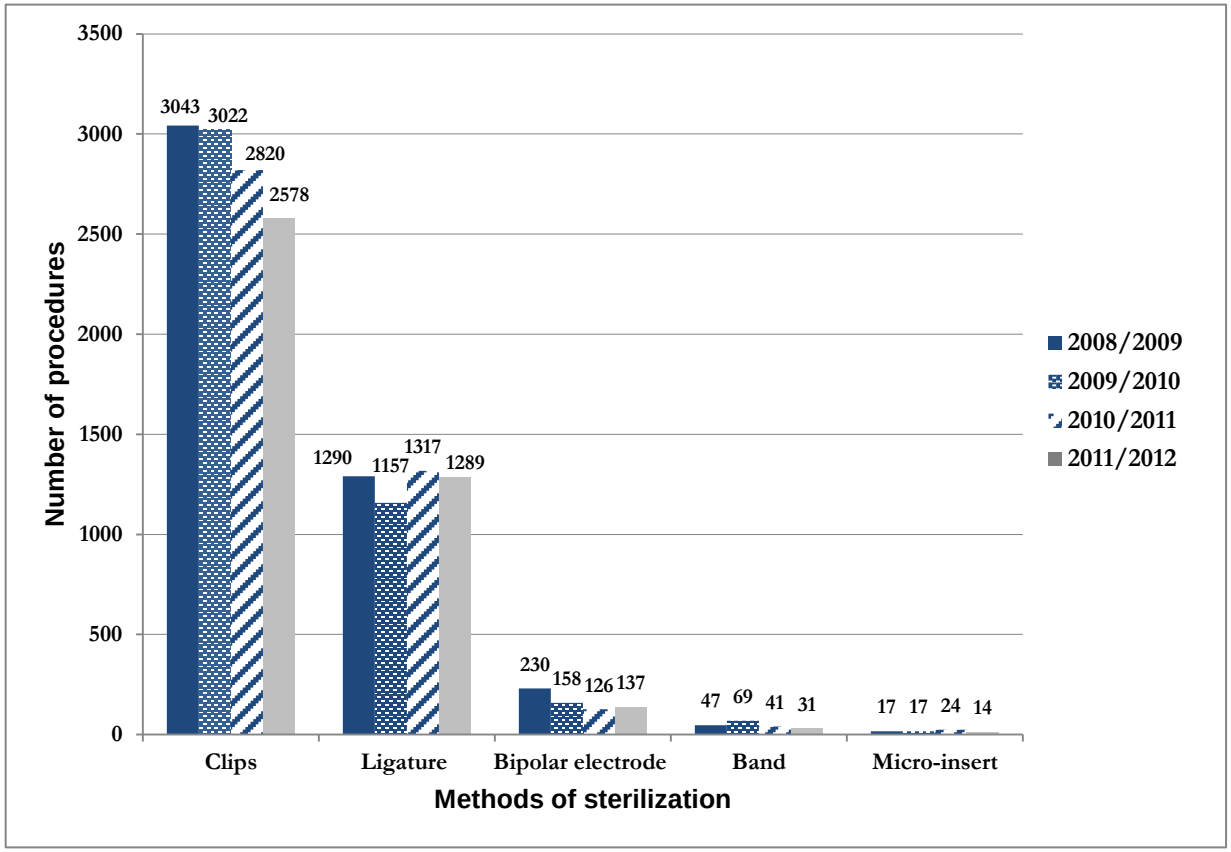
CCS – Canadian Contraception Study; CFS – Canadian Fertility Survey
Source: Fisher et al.[51,53] and Canadian Federation for Sexual Health[54]

The standard practice for elective permanent sterilization in Alberta is laparoscopic tubal ligation. However, this intervention requires the use of general anesthesia, which increases the risk of the

procedure (EAG meeting minutes, 19 June 2012). The data available from two Alberta administrative databases, the Discharge Abstract Database (DAD) and the Ambulatory Care Classification System (ACCS) (see Appendix B, Table B.1), indicate that the majority of inpatient tubal sterilizations interventions performed between 31 March 2008 and 31 March 2012 were tubal ligations performed at the same time with Cesarean section delivery interventions (range 1708 to 1765 procedures annually), while tubal ligation as a unique intervention was the most prevalent procedure in , outpatient settings (range 1577 to 2077 procedures annually). Less prevalent was tubal sterilization performed in both inpatient and outpatient settings together with other interventions for diseases of the genitourinary, digestive, and renal system, and neoplasia of uterus or ovary, and also in association with procedures related to pregnancy with abortive outcome, maternal disorders predominantly related to pregnancy or complications of labour and delivery. In terms of the methods of tubal ligation, in inpatient settings the most prevalent method involved open laparotomy with ligature and transection or resection of the fallopian tube (range 1059 to 1208 procedures annually), followed by open laparotomy and tubal ligation using clips (range 560 to 732 procedures annually) (see Appendix B, Table B.2). In outpatient settings, the most common procedure was laparoscopy (range 1939 to 2287 procedures annually). In both inpatient and outpatient settings, a slightly constant decrease was seen of the total number of fallopian tubal ligation procedures mainly by using clips, performed each year from 2008 to 2012 (see Figure 4).

In Alberta, 72 hysteroscopic tubal sterilizations were performed between 31 March 2008 and 31 March 2012 (annual range 14 to 24) (see Figure 4 and Appendix B, Table B.2).

Figure 4: Women's sterilizations performed in Alberta, by method, between 31 March 2008 and 31 March 2012 (annual number of procedures)



The Calgary experience with HTS

A local feasibility pilot study on HTS interventions was conducted in Calgary at the Rockyview General Hospital from March 2007 into 2010 (EAG meeting minutes, 19 June 2012; communications EAG members, emails, and teleconferences between June and August 2012; unpublished report [47]). Unpublished results of the first 58 Essure® cases indicated that the most common reason for undergoing the Essure® HTS procedure was woman's choice (37 women). Sixteen women who received the Essure® micro-inserts had a contraindication to laparoscopy (a high BMI (seven women) or a history of multiple laparotomies and pelvic adhesions (10 women)), while 10 women had severe underlying conditions that contraindicated general anesthesia, including thrombophilias or severe cardiac conditions. The HTS interventions were performed with local anesthesia in 54 women, sedation was administered to 45 women, and two women received general anesthesia. The cases with special medical conditions received the intervention in the operation room. The reported mean procedure time was 16.25 minutes (range seven to 40 minutes) and the total mean time in the operating room was 33 minutes (range 14 to 50 minutes). Successful bilateral placement of the Essure® micro-inserts was achieved in 53 women (91%), while in five cases the procedure failed due to tubal spasm, small fallopian tubes, or inability to visualize the tubal ostia. No adverse events or complications were reported except for two cases of pain encountered intra-operatory and post-intervention. Forty-three women showed bilateral tubal occlusion at the three-month follow-up and two women at the six-month follow-up. Thirteen women did not complete

the follow-up procedure to confirm the occlusion of fallopian tubes and rely on sterilization. The successful occlusion of the fallopian tubes at the three-month follow-up was confirmed by HSG in most cases. The HSG was considered a reasonable and non-painful test and the compliance of women at the three-month follow-up HSG test was reported acceptable. The pelvic radiography test at the three-month follow-up was considered almost as good as HSG by Calgary professionals, and was used only occasionally in the Calgary pilot, for example, in women allergic to HSG dye (communication, EAG member, email, 17 July 2012). It was noted that experienced professionals could identify at the time of the Essure® procedure, in most of the cases, whether the micro-implants were positioned satisfactorily or not. Based on the Calgary experience, approximately 5% of cases need an extended follow-up at six months after the HTS procedure to confirm fallopian tube occlusion.

For safety reasons, early in the learning curve most of the HTS interventions were performed in the operating room with only a few performed remotely in the outpatient unit (EAG meeting minutes, 19 June 2012). Presently, 66% of the procedures are performed in an outpatient setting; the degree of comfort of physicians increases with the cumulated experience.

Service provision in Alberta and other Canadian provinces

After finalization of the pilot project, Rockyview General Hospital gynecologists continued to offer HTS using the Essure® system to women who had a contraindication for laparoscopic tubal sterilization and met certain medical criteria (EAG meeting minutes, 19 June 2012). Seventy cases were performed in Calgary until August 2012, of which only five necessitated a second attempt for bilateral placement of the Essure® micro-inserts and one underwent laparoscopic tubal sterilization after failure the HTS procedure (communication, EAG members, teleconference, 31 July 2012).

Almost every gynecologist in Saskatchewan offers the Essure® HTS procedure or refers women for this intervention and the procedure is available in every centre where gynecologists are practicing (communication, EAG member, email, 2 August 2012). The experience with the HTS intervention has a high impact on the rate of success of bilateral placement of the Essure® micro-inserts at first attempt. In many cases, at the origin of the failure of the bilateral placement of micro-inserts is tubal spasm, which may be related to the practitioner's experience, number of procedures performed, and time necessary to insert the coils. In Saskatchewan, the three-month follow-up for confirmation of normal placement of the Essure® micro-inserts and the potential misplaced and perforation events is conducted by tri-dimensional ultrasound.[34,35] HSG is used only for unsatisfactory results obtained at the ultrasound test. The compliance of women with the ultrasound test was much higher than with HSG.

Starting in September 2012, the Women's Health Centre at the British Columbia Women's Hospital offered a pilot project of HTS using the Essure® system for women requesting permanent sterilization in an outpatient setting.[55]

The HTS with the Essure® system is also performed in small numbers, without a specific program, by gynecologists from other Canadian Provinces including Québec (Montreal) and Ontario (Ottawa) (communication, EAG member, emails, November 2012).

Resources needed and funding of service in Alberta

Presently, in Edmonton and Calgary, public and private providers are showing much interest in providing HTS using the Essure® system (EAG meeting minutes, 19 June 2012). Although the

demand for HTS has been growing, only a handful of clinicians have been involved in conducting this procedure in Calgary, Alberta. Clinicians consider that the HTS intervention has a short learning curve for professionals with expertise in hysteroscopy (between five and seven proctored cases), it is easy to offer, it is safer (with minimal risk of complications) than other traditional methods of sterilization (for example, laparoscopic tubal ligation), and it is ideal at least for cases where traditional approaches are not optimal. The procedure has a high success rate and is appropriate for all women, including those with morbid obesity, thin women, and women with contraindications for laparoscopy and general anesthesia, such as those with cardiovascular and pulmonary conditions. In the Calgary feasibility trial it was estimated that 20 to 30% of women may have a contraindication for laparoscopic tubal sterilization and may choose the HTS with Essure® if the procedure is available (unpublished report[47]). The HTS procedure could be introduced and provided initially to those cases. In future, HTS has the potential to displace laparoscopic tubal sterilization by tubal ligation based on the clinical benefits for most women, and could become the standard procedure for female sterilization, while laparoscopic tubal ligation could be used in combination with another surgical procedure, such as for ovarian cyst removal or during a Cesarean section delivery intervention (EAG meeting minutes, 19 June 2012).

Alberta Health Services (AHS) fully covers the costs of HTS with Essure® system for medically indicated cases in Calgary. If HTS is merely an option, AHS pays for the procedure while the woman pays for the cost of the device. The cost of the device is presently considered a limitation in implementing the HTS procedure (EAG meeting minutes, 19 June 2012).

A minor HTS intervention conducted in an operation room at the Rockyview Hospital in Calgary requires the attendance of two physicians and two nurses, while a major intervention performed in the operating room employs two physicians and the equivalent of 2.5 nurses for staff coverage and anesthetic support shared between two surgical suites. Similar equipment is required to perform both minor and major interventions. General anesthesia is required for major interventions while minor HTS interventions are conducted under local anesthesia.

In Saskatchewan, the personnel considered adequate to perform the HTS procedure in an outpatient setting consists of one trained physician/obstetrician and a support nurse for the women, with no need for a scrub nurse or another assistant for the procedure, as the device can be loaded by the physician performing the Essure® insertion (communication, EAG member, email, 3 July 2012).

Appendix A: Adverse Events

Table A.1: Adverse events reported in two multicentre case series studies

Event	Phase II Study*[37] (N = 227) No. (%)	Pivotal Study†[38] (N = 518) No. (%)
Adverse events that prevented reliance on Essure® for contraception		
Perforation	7/206 (3.4)[a]	5/476 (1.1)
Expulsion	1/206 (0.5)	14/476 (2.9)[c]
Other unsatisfactory micro-insert location	1/206 (0.5)	3/476 (0.6)
Initial tubal patency	7/200 (3.5)[b]	16/456 (3.5)[d]
Adverse events per procedures, reported on day of placement procedure		
Band detachment	3/233 (1.3)	2/544 (0.4)
Vaso-vagal response/fainting	2/233 (0.9)	7/544 (1.3)
Pain	2/233 (0.9)	70/544 (12.9)
Cramping	n/a	161/544 (29.6)
Nausea/vomiting	n/a	59/544 (10.8)
Dizziness/light headed	n/a	48/544 (8.8)
Post-procedural bleeding	n/a	37/544 (6.8)
Vaginal spotting		
Hypervolemia	n/a	2/544 (0.4)
Other[e]	n/a	16/544 (2.9)
Adverse events by body systems, first year of reliance[f]		
Abdominal		
Pain/cramps	n/a	18/476 (3.8)
Gas/bloating	n/a	6/476 (1.3)
Musculo-skeletal		
Back-pain/low back pain	n/a	43/476 (9.0)
Arm/leg pain	n/a	4/476 (0.8)
Nervous/psychiatric		
Headache	n/a	12/476 (2.5)
Premenstrual syndrome	n/a	4/476 (0.8)
Genitourinary		
Dysmenorrhea/menstrual cramps (severe)	n/a	14/476 (2.9)
Pelvic/lower abdominal pain (severe)	n/a	12/476 (2.5)
Persistent increase in menstrual flow	n/a	9/476 (1.9)[g]
Vaginal discharge/vaginal infection	n/a	7/476 (1.5)
Abnormal bleeding – timing not specified (severe)	n/a	9/476 (1.9)

Menorrhagia/prolonged menses (severe)	n/a	5/476 (1.1)
Dyspareunia	n/a	17/476 (3.6)
Pain/discomfort – uncharacterized	n/a	14/476 (2.9)

*Phase II Study[37] – prospective, multicentre, single-arm, non-randomized international study

†Pivotal (Phase III) Study[38] – prospective, multicentre, single-arm, non-randomized international study

N, n – number of women; n/a – not applicable

[a] One woman relied on Essure® micro-inserts for contraception for 31 months prior to laparotomy and corneal resection, due to monthly pain associated with presence of the device. The other six women never relied on Essure® micro-inserts for contraception.

[b] Tubal patency was demonstrated in seven women at the three-month hysterosalpingography (HSG), but all seven women were shown to have tubal occlusion at a repeat HSG performed six months after Essure® placement.

[c] Fourteen women experienced an expulsion, however nine chose to undergo second placements, which were successful.

[d] Tubal patency was demonstrated in 16 women at the three-month HSG, but all women were shown to have tubal occlusion at a repeated HSG performed at six to seven months after Essure® placement.

[e] Includes (no.): ache (3), hot/hot flashes (2), shakiness (2), uncomfortable (1), weak (1), profuse perspiration (1), bowel pain (1), sleepiness (1), skin itching (1), loss of appetite (1), bloating (1), allergic reaction to saline used for distension (1).

[f] Only events occurring in ≥ 0.5% are reported.

[g] Eight women reported persistent decrease in menstrual flow.

Adapted from: [20,56]

Appendix B: Alberta Data

Table B.1: Alberta data* – Sterilization by fallopian tubal ligation, 31 March 2008 to 31 March 2012 (number of procedures)

	Inpatient (source DAD)				Outpatient (source ACCS)			
Procedures	**2008/2009**	**2009/2010**	**2010/2011**	**2011/2012**	**2008/2009**	**2009/2010**	**2010/2011**	**2011/2012**
1. Tubal ligation only	14	27	25	12	2077	1873	1789	1577
2. Tubal ligation plus C-section	1765	1734	1729	1708	0	0	0	0
3. Tubal ligation plus procedures related to neoplasms of uterus or ovary	9	14	12	4	41	35	37	31
4. Tubal ligation for overweight	2	2	2	1	2	2	1	3
5. Tubal ligation plus procedures related to diseases of the digestive and renal systems	8	9	9	5	51	46	35	48
6. Tubal ligation plus procedures related to diseases of the genitourinary system	30	31	27	29	329	358	377	369
7. Tubal ligation plus procedures related to pregnancy with abortive outcome, maternal disorders predominantly related to pregnancy or complications of labour and delivery	61	64	53	38	37	41	20	35
Total	1889	1881	1857	1797	2537	2355	2259	2063

*Based on diagnosis (ICD-10: the International Statistical Classification of Diseases and Related Health Problems, 10th Revision) and procedure (CCI: the Canadian Classification of Health Interventions) codes

ACCS – the Ambulatory Care Classification System; DAD – Discharge Abstract Database

Table B.2: Methods – Fallopian tubal ligation,* 31 March 2008 to 31 March 2012 (number of procedures)

Year	Approach Method	Inpatient (source: DAD)			Outpatient (source: ACCS)			Total
		Laparoscopic	Culdoscopy & HTS	Open	Laparoscopic	Culdoscopy & HTS	Open	
2008/ 2009	Using band (ring)	—	—	—	46	1	—	47
	Using bipolar electrode	12	—	7	207	3	1	230
	Using clips (e.g., plastic)	56	3	642	2287	29	26	3043
	Using ligature (and transection or resection)	19	1	1155	88	—	27	1290
	Using coil (micro-insert)†	—	—	—	—	17	—	17
2009/ 2010	Using band (ring)	2	—	—	64	3	—	69
	Using bipolar electrode	7	—	5	134	10	2	158
	Using clips (e.g., plastic)	65	1	732	2179	27	18	3022
	Using ligature (and transection or resection)	21	1	1059	64	—	12	1157
	Using coil (micro-insert)†	—	—	—	—	17	—	17
2010/ 2011	Using band (ring)	1	—	1	34	4	1	41
	Using bipolar electrode	2	—	2	120	2	—	126
	Using clips (e.g., plastic)	54	2	585	2147	15	17	2820
	Using ligature (and transection or resection)	12	1	1208	79	3	14	1317
	Using coil (micro-insert)†	—	—	—	—	24	—	24

2011/ 2012	Using band (ring)	—	—	—	29	1	1	31
	Using bipolar electrode	4	—	3	129	—	1	137
	Using clips (e.g., plastic)	44	2	560	1939	15	18	2578
	Using ligature (and transection or resection)	7	4	1181	70	—	27	1289
	Using coil (micro-insert)†	—	—	—	—	14	—	14

* Based on the Canadian Classification of Health Interventions (CCI) code, unless otherwise specified

† Hysteroscopic sterilization procedure recorded in any procedure position. (CCI code: 1RF51FJ%). AHS Financial Report Date, 19 April 2012.

ACCS – the Ambulatory Care Classification System; DAD – Discharge Abstract Database; HTS – hysteroscopic tubal sterilization

References

1. Lawrie TA, Nardin JM, Kulier R, Boulvain M. Techniques for the interruption of tubal patency for female sterilisation. *SO: Cochrane Database of Systematic Reviews* 2011;(2). Available from: *www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003034/frame.html*.
2. Beerthuizen R. State-of-the-art of non-hormonal methods of contraception: V. Female sterilisation. *European Journal of Contraception & Reproductive Health Care* 2010;15(2):124-135.
3. Bartz D, Greenberg JA. Sterilization in the United States. *Reviews in Obstetrics & Gynecology* 2008;1(1):23-32.
4. Abbott J. Transcervical sterilization. *Current Opinion on Obstetrics & Gynecology* 2007;19(4):325-330.
5. Shavell VI, Al-Safi Z, Billis-Gergics LC, Kmak DC, Diamond MP, Berman JM. Reasons for poststerilization hysterosalpingography noncompliance in a clinic population. *Journal of Reproduction Medicine* 2010;55(11-12):459-463.
6. Theroux R. The hysteroscopic approach to sterilization. *Journal of Obstetric, Gynecologic, & Neonatal Nursing* 2008;37(3):356-360.
7. Thurkow AL. Hysteroscopic sterilization: away with the laparoscope? *Gynaecology, Obstetrics, and Reproductive Medicine in Daily Practice* 2005;1279:184-188.
8. Greenberg JA. Hysteroscopic sterilization: history and current methods. *Revue Obstetricale et Gynecologique* 2008;1(3):113-121.
9. Castano PM, Adekunle L. Transcervical sterilization. *Seminars in Reproductive Medicine* 2010;28(2):103-109.
10. Chapman L, Magos A. Female sterilization. *Expert Review of Medical Devices* 2008;5(4):525-537.
11. Fortin CA, Guilbert E. Canadian contraception consensus [Part 3], Society of Obstetricians and Gynaecologists of Canada. Chapter 10: Sterilization. *Journal of Obstetrics & Gynaecology* 262004:347-387.
12. Royal College of Obstetricians and Gynaecologists. Male and female sterilisation. Evidence-based Clinical Guideline Number 4, 2004. Available from: *www.rcog.org.uk/files/rcog-corp/uploaded-files/NEBSterilisationFull060607.pdf* (accessed 8 August 2012).
13. Vilos GA, Ternamian A, Dempster J, Laberge PY, the Society of Obstetricians and Gynaecologists of Canada. Laparoscopic entry: A review of techniques, technologies, and complications. SOGC Clinical Practice Guideline No. 193, May 2007. *Journal of Obstetrics & Gynaecology Canada* 2007;29(5):433-447.
14. Famuyide AO, Hopkins MR, El-Nashar SA, Creedon DJ, Vasdev GM, Driscoll DJ, et al. Hysteroscopic sterilization in women with severe cardiac disease: experience at a tertiary center. *Mayo Clinical Proceedings* 2008;83(4):431-438.
15. Scarabin C, Dhainaut C. The ESTHYME study. Women's satisfaction after hysteroscopic sterilization (Essure micro-insert). A retrospective multicenter survey. *Gynecologie, Obstetrique & Fertilite* 2007;35(11):1123-1128.

16. Occhino JA, Hannigan TL, Baggish MS, Gebhart JB. Resident duty-hour restrictions and their effect on operative experience in obstetrics and gynecology. *Gynecologic & Obstetric Investigation* 2011;72(2):73-78.

17. Essure US Physician training manual. Available from: *www.essuremd.com/Portals/essuremd/PDFs/PST/CC1687_Essure_Training_Manual.pdf* (accessed 28 February 2012).

18. Food & Drug Administration. Post-Approval Study ESS-305. Available from: *www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm?c_id=112&t_id=367828* (accessed 8 August 2012).

19. Food & Drug Administration, Department of Health and Human Services. Approval Order, Essure System, 2002. Available from: *www.accessdata.fda.gov/cdrh_docs/pdf2/P020014a.pdf* (accessed 28 February 2012).

20. U.S. Food and Drug Administration CfDaRH. Summary of safety and effectiveness data. Essure System. Available from: *www.accessdata.fda.gov/cdrh_docs/pdf2/P020014b.pdf* (accessed 3 April 2012).

21. Zurawin RK, Zurawin JL. Adverse events due to suspected nickel hypersensitivity in patients with essure micro-inserts. *Journal of Minimally Invasive Gynecology* 2011;18(4):475-482.

22. Lessard CR, Hopkins MR. Efficacy, safety, and patient acceptability of the EssureTM procedure. *Patient Preference & Adherence* 2011;5:207-212.

23. Langenveld J, Veersema S, Bongers MY, Koks CA. Tubal perforation by Essure: three different clinical presentations. *Fertility & Sterility* 2008;90(5):2011.e5-2011.e10.

24. Essure® The Alternative to Incision. HSG Protocol. US Physician Training Manual, 2003. Available from: *www.essuremd.com/Portals/0/Skins/Conceptus_Skin/PDFs/TR-0671-101-HSG-Protocol.pdf* (accessed 8 August 2012).

25. Radiological Society of North America. Hysterosalpingography. RadiologyInfo, The radiology information resource for patients, reviewed 2012. Available from: *www.radiologyinfo.org/en/pdf/hysterosalp.pdf* (accessed 8 August 2012).

26. Shah V, Panay N, Williamson R, Hemingway A. Hysterosalpingogram: an essential examination following Essure hysteroscopic sterilisation. *British Journal of Radiology* 2011;84(1005):805-812.

27. American College of Obstetricians and Gynecologists. Use of hysterosalpingography after tubal sterilization. Committee Opinion No. 458. *Obstetrics & Gynecology* 2010;115(6):1343-1345.

28. Zite N, Borrero S. Female sterilisation in the United States. *European Journal of Contraception and Reproductive Health Care* 2011;16(5):336-340.

29. Connor VF. Essure: a review six years later. *Journal of Minimally Invasive Gynecology* 2009;16(3):282-290.

30. Shavell VI, Abdallah ME, Diamond MP, Kmak DC, Berman JM. Post-Essure hysterosalpingography compliance in a clinic population. *Journal of Minimally Invasive Gynecology* 2008;15(4):431-434.

31. Mino M, Arjona JE, Cordon J, Pelegrin B, Povedano B, Chacon E. Success rate and patient satisfaction with the Essure sterilisation in an outpatient setting: a prospective study of 857 women. *BJOG* 2007;114(6):763-766.

32. Oliveira M, Johnson D, Switalski P, Taraschi S, Canet N, Roberts D, et al. Optimal Use of 3D and 4D Transvaginal Sonography in Localizing the Essure® Contraceptive Device. *Journal of Diagnostic Medical Sonography* 2009;25(3):163-167.

33. Wittmer MH, Brown DL, Hartman RP, Famuyide AO, Kawashima A, King BF. Sonography, CT, and MRI appearance of the Essure microinsert permanent birth control device. *American Journal of Roentgenology* 2006;187(4):959-964.

34. Thiel J, Suchet I, Tyson N, Price P. Outcomes in the ultrasound follow-up of the Essure micro-insert: complications and proper placement. *Journal of Obstetrics & Gynaecology Canada:* 2011;33(2):134-138.

35. Thiel JA, Suchet IB, Lortie K. Confirmation of Essure microinsert tubal coil placement with conventional and volume-contrast imaging three-dimensional ultrasound. *Fertility & Sterility* 2005;84(2):504-508.

36. Levy B, Levie MD, Childers ME. A summary of reported pregnancies after hysteroscopic sterilization. *Journal of Minimally Invasive Gynecology* 2007;14(3):271-274.

37. Kerin JF, Cooper JM, Price T, Herendael BJ, Cayuela-Font E, Cher D, et al. Hysteroscopic sterilization using a micro-insert device: results of a multicentre Phase II study. *Human Reproduction* 2003;18(6):1223-1230.

38. Cooper JM, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. *Obstetrics & Gynecology* 2003;102(1):59-67.

39. Al-Safi ZA, Shavell VI, Hobson DT, Berman JM, Diamond MP. Analysis of adverse events associated with essure hysteroscopic sterilization reported to the maude database, 2002–2011. *Fertility and Sterility* 2011; Conference: 67th Annual Meeting of the American Society for Reproductive Medicine, ASRM 2011 Orlando, FL, United States. Conference Publication: (var. pagings):S113.

40. A new method of permanent birth control: the Essure permanent birth control system. Patient information booklet, 2002. Available from: *www.fda.gov/ohrms/dockets/ac/02/briefing/3881b1_04.pdf* (accessed 28 February 2012).

41. Levie M, Chudnoff SG. A comparison of novice and experienced physicians performing hysteroscopic sterilization: an analysis of an FDA-mandated trial. *Fertility & Sterility* 2011;96(3):643-648.

42. National Institute for Health and Clinical Excellence (NICE). Hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implants, 2009. Available from: *www.nice.org.uk/nicemedia/live/11118/45506/45506.pdf*.

43. Fleming N, Morris M, Pymar H, Smith T. Canadian contraception consensus [Part 3], Society of Obstetricians and Gynaecologists of Canada. Chapter 11: Contraception—Meeting special needs. *Journal of Obstetrics & Gynaecology* 2004;26:347-387.

44. Health Canada – Medical Devices Active Licence Listing. Conceptus Essure permanent birth control system, 2012. Available from: *http://webprod3.hc-sc.gc.ca/mdll-limh/dispatch-repartition do?type=active&lang=eng* (accessed 1 March 2012).

45. Conceptus I. "Health Canada Approves Conceptus' Third Generation Essure(R) Permanent Birth Control System." *Medical News Today MediLexicon, Intl,* 2007. Available from: *www.medicalnewstoday.com/releases/91107.php* (accessed 28 February 2012).

46. Minister of Justice. Medical Devices Regulations, 2011. Available from: *http://laws-lois.justice.gc.ca/PDF/SOR-98-282.pdf* (accessed 3 April 2012).

47. Austen L. *Essure – Hysteroscopic Tubal Occlusion for Female Sterilization. Executive Summary.* Health Technology Assessment and Innovation Department of Surgery, Alberta Health Services – Calgary Zone and University of Calgary 2012.

48. U.S. Food and Drug Administration, Department of Health & Human Services. Approval Order, Adiana Permanent Contraception System, 2007. Available from: *www.accessdata.fda.gov/cdrh_docs/pdf7/P070022a.pdf* (accessed 28 February 2012).

49. National Institute for Health and Clinical Excellence, Interventional Procedures Programme. Interventional procedure overview of hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implants, 2008 Available from: *www.nice.org.uk/nicemedia/live/11118/43367/43367.pdf* (accessed 17 February 2012).

50. United Nations, Department of Economic and Social Affairs, Population Division. World Contraceptive Use 2009. *United Nations* (accessed 8 August 2012).

51. Fisher W, Boroditsky R, Morris B. The 2002 Canadian Contraception Study: Part 1. *Journal of Obstetrics & Gynaecology* 262004:580-590.

52. Fisher WA, Black A. Contraception in Canada: a review of method choices, characteristics, adherence and approaches to counselling. *CMAJ* 2007;176(7):953-961.

53. Fisher W, Boroditsky R, Morris B. The 2002 Canadian Contraception Study: Part 2. *Journal of Obstetrics & Gynaecology Canada* 2004;26(7):646-56.

54. Canadian Federation for Sexual Health. Sexual Health in Canada Baseline 2007. *Canadian Federation for Sexual Health* 2007. Available from: *http://synthesis.womenshealthdata.ca/uploads/topic225_0.pdf* (accessed 8 August 2012).

55. BC Women's Hospital Reproductive Medicine Program. Referral for Essure Sterilization, 2012. Available from: *www.bcwomens.ca/NR/rdonlyres/A17B176C-71C5-40AB-8F6F-55E293983C6B/58550/Ezzurereferralandeligibilityforms.pdf* (accessed 8 August 2012).

56. U.S. Food and Drug Administration. Professional labeling—Conceptus Essure permanent birth control system; Instructions for use, 2012. Available from: *www.accessdata.fda.gov/cdrh_docs/pdf2/P020014c.pdf* (accessed 28 February 2012).

SECTION TWO: Technology Effectiveness/Efficacy

Carmen Moga MD, MSc; Maria Ospina, PhD, MSc; Christa Harstall, MLS, MHSA

This health technology assessment report has been produced in response to a request from Alberta Health (AH) as part of the Alberta Health Technologies Decision Process (AHTDP) to perform an evaluation of the scientific evidence on the safety and efficacy/effectiveness of hysteroscopic tubal sterilization (HTS) used for permanent birth control.

Objective and scope

To perform a review and critical appraisal of the published primary research concerning the safety and efficacy/effectiveness of HTS as a method used for elective permanent birth control.

Research questions

The **T**echnology (**T**) section of the report attempts to address the following questions:

- What is the scientific evidence on the safety of HTS procedures currently licensed by Health Canada (that is, the Essure® system)?
- What is the scientific evidence on the efficacy/effectiveness of HTS with the Essure® system, the rate of success, the quality of life, and the satisfaction level of women and providers?

The methodological approach to answer these questions was established a priori and included a structured review and critical appraisal of the scientific research on HTS with Essure® for permanent birth control. Appendices provide the following information:

- Appendix A—A detailed description of the literature strategy (data sources, dates searched, and search terms) and literature selection (inclusion and exclusion criteria).
- Appendix B—A list of excluded studies.
- Appendix C—A synopsis of characteristics of the included studies.
- Appendix D—Quality appraisal results of the included studies.

Project scope

The scope of the **T** section of the report was defined as follows:

Population: women seeking permanent tubal sterilization

Intervention: HTS using the Essure® system

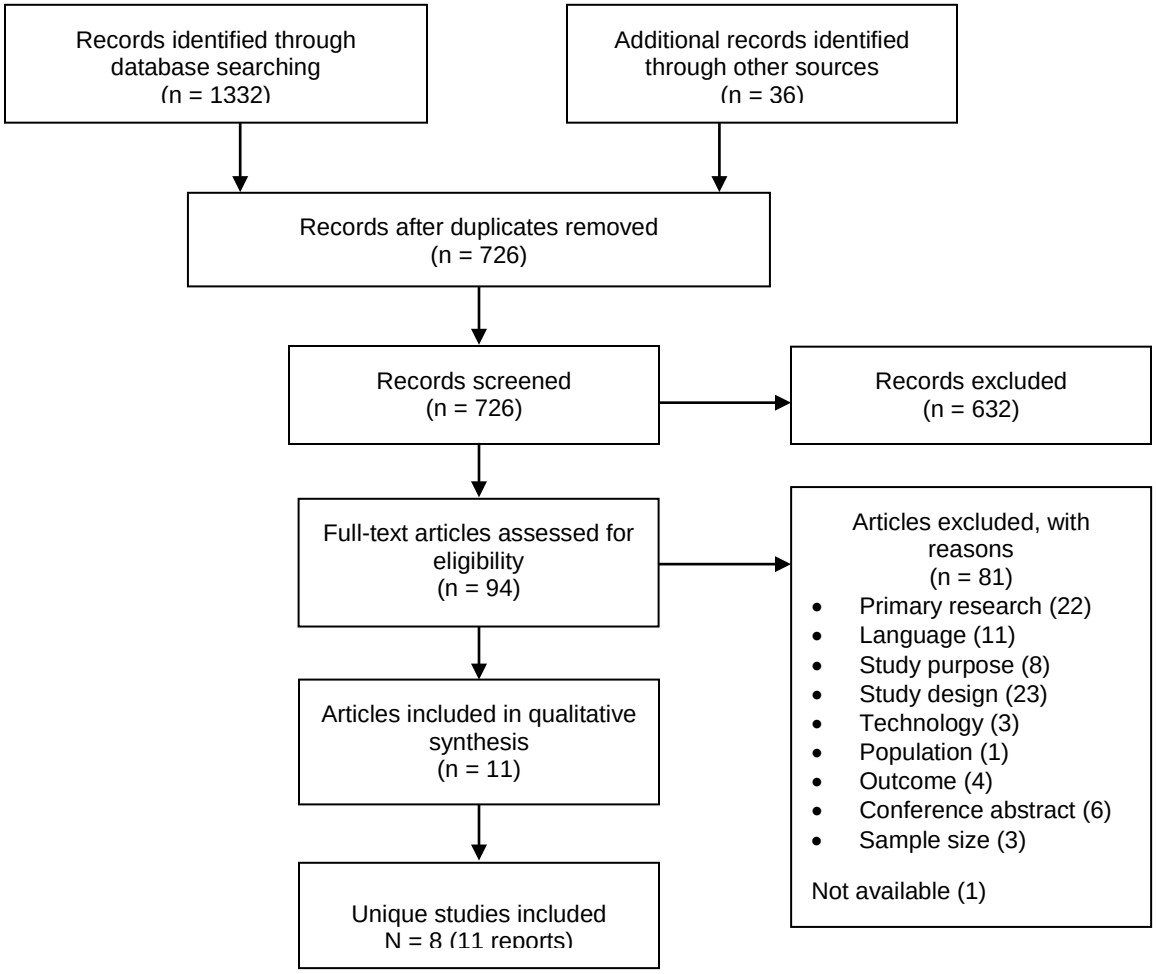
Outcome measures: the main outcomes were the success and failure rates of bilateral tubal occlusion, the incidence of unintended pregnancies, adverse events that prevented reliance on the implants for contraception, adverse events reported on day of the placement procedure, short- and long-term follow-up, health-related quality of life, and other women-related outcomes, including tolerance and satisfaction.

Results

Results of literature search

A search of electronic databases for articles published between 2006 and February 2012 (see Appendix T.A) identified 726 citations. Two independent reviewers conducted the screening and selection of studies for inclusion. After screening of titles and abstracts, the full text of 93 potentially relevant articles was retrieved and evaluated for eligibility in the review. Eight case series studies[1-8] were included (see Figure T.1). Three reports[9-11] were identified as multiple publications. In cases of multiple publication studies, the degree of detail of reporting the efficacy/effectiveness results of the procedure determined the selection. The information provided in the multiple publications was included with the data reported in the main published study.

Figure T.1: Selection of included studies



Study characteristics

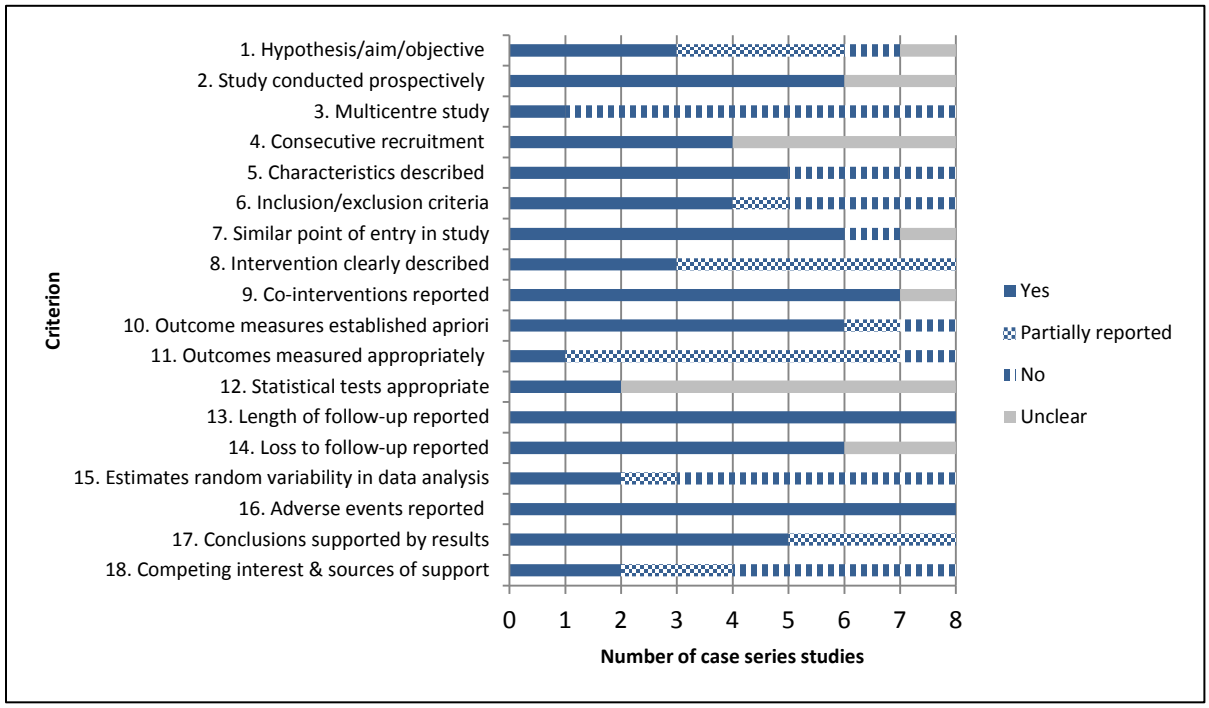
The eight case series studies[1-8] were published between 2006 and 2011. Six studies[1,2,4-6,8] collected data prospectively. In two studies,[3,7] the method of data collection was unclear. One study[6] was a

multicentre study. Studies were conducted in the USA,[5,8] Spain,[4,7] the UK,[1,3] The Netherlands,[6] and Sweden.[2] In terms of sample size, two studies[4,6] had 1145 and 857 cases, respectively, four studies[1,3,5,8] had between 100 and 175 cases, and two studies[2,7] had 28 and 61 cases, respectively. The women's mean age was between 35 and 39.6 in six studies (range from 22 to 49 years). In two studies,[3,8] the women's age was not reported. The women's body mass index was reported in three studies,[1,5,6] and ranged from 17 to 53 kg/m^2. The parity was reported in four studies,[2,4-6] and ranged from 0 (nulliparous) to 8. No information was reported about gravity. In terms of comorbidity, in one study,[2] half the cases had diabetes mellitus, obesity, or previous abdominal or pelvic surgeries, which are contraindications for laparoscopic tubal sterilization, and in one study,[5] one third of the cases had had prior abdominal or pelvic surgery. However, the results were not reported separately for the higher risk groups.

Reporting and risk of bias

The reporting and risk of bias varied across studies (see Figure T.2, Appendix T.D, Table T.D.1). On an 18-criteria checklist,[12] two studies[2,3] met four and seven criteria, respectively; five studies[4-8] met 10 to 14 criteria; one study[1] reported 15 criteria. The hypothesis, aim, or objective of the study was clearly stated in three studies.[1,4,6] In four studies, cases were recruited consecutively[1,5-7], while it was unclear in four studies[2-4,8] how women had been enrolled. In five studies,[1,2,4-6] at least two relevant characteristics of the cases (age, parity, gravity, ethnicity, comorbidity) were described; the remaining three studies[3,7,8] did not report any of those characteristics. Only four studies[1,5,7,8] provided an explicit description of the studies' inclusion and exclusion criteria, while one study[4] only reported the inclusion criteria and three studies[2,3,6] did not describe the criteria. Six studies[1,3-5,7,8] included cases which were at a similar point based on their clinical status; in one study[6] the clinical status of cases was unclear and in another study[2] half of the included cases had other comorbidities. The most relevant characteristics of the HTS intervention (description of technical parameters and process of insertion of the Essure® system, the average time per procedure, provider's training, and setting of intervention) were reported in three studies,[1,4,7] while the remaining studies[2,3,5,6,8] partially reported only two characteristics. In all but one study[6] it was reported that women received anti-inflammatory medication prior to the intervention. The main outcome measures (that is, measurement of the efficacy/effectiveness) were reported in the introduction or methods section in six studies.[1,4-8] In only one study,[5] the test used at three months follow-up to determine the bilateral occlusion of the fallopian tubes was the standard test HSG. In six studies[1,3,4,6-8] the tests included abdominal X-ray or ultrasonography while HSG was performed only after unsatisfactory placement of micro-inserts and in one study[2] the tests used were abdominal X-ray or ultrasound. In terms of appropriateness of the statistical tests used to assess the relevant outcomes, only two studies[1,5] described clearly the statistical tests in the methods section of the publication. All studies provided an adequate description of the length of follow-up when reporting the outcome data and two studies[2,3] were unclear about the losses to follow-up. Two studies[1,6] reported the estimates of the random variability for all relevant outcomes, while in five studies,[3-5,7,8] the estimates were partially reported. All studies reported safety outcomes at different follow-up periods. In five studies,[1,2,4,7,8] the conclusions of the study were supported by the reported results, while in three studies,[3,5,6] the conclusions were partially supported by the reported results. Only two studies[2,8] declared both competing interest and source of support, two studies[6,7] reported only one aspect, competing interest or source of support, and four studies[1,3-5] did not provide any competing interest or source-of-support information. Three co-authors of three studies[2,6,8] declared provision of consultancy for the manufacturer of the Essure® system.

Figure T.2: Reporting and risk of bias, case series studies (n = 8)



Individual study characteristics and efficacy/effectiveness outcomes

Eight case series studies, six prospective studies,[1,2,4-6,8] and two studies[3,7] with unclear design included 2566 women who underwent HTS with the Essure® system in hospital outpatient settings or a medical office (see Appendix T.C.1).[8] In one study,[7] the 28 included women had an IUD device in place at the time of HTS. In all studies, women were pre-medicated with oral or intramuscular NSAIDs and in some cases with NSAIDs and opioids or benzodiazepines one half to two hours prior to HTS intervention. Paracervical block local anesthesia was administered to all women in two studies.[5,8] In two studies[1,2] the anesthesia was used early in the study, then only for cases of severe pain, and in one study it was used only for extreme anxiety and severe pain.[4] In two studies[6,7] it was reported that anesthesia was not necessary. The procedures were conducted by gynecologists experienced in hysteroscopy in four studies[3-6] and by surgeons in two studies.[1,2] In one study,[5] approximately half of the procedures were conducted by residents, fellows, or attending physicians learning the HTS procedure. The time necessary to perform the HTS was reported in six studies[1,2,4-7] and ranged from 5 to 70 minutes. In five studies,[1,4-7] the mean time was between 6.8 and 14 minutes. In one study,[2] conducted between 2002 and 2007, the authors noted that the longer operating time (mean 30 minutes) was due to a learning curve, since the procedures performed toward the end of the study were of shorter duration. Another reason for an increased duration of operating time might have been the use of an old version of the Essure® device. The recovery time to home discharge was reported in three studies[1,2,7] and ranged between 25 minutes and four hours. In two studies, women returned to normal activity after the HTS procedure on the same day[4] or after 48 hours.[3]

Women who had bilateral placement of micro-inserts were followed-up at three months by HSG and/or abdominal x-ray and/or pelvic or vaginal ultrasound to confirm the occlusion of the fallopian tubes and reliance of the woman on the sterilization method. When occlusion had not been achieved, the women were followed up again at six months.[1,4,8] Other follow-ups were conducted at various times, ranging from the first two hours after HTS procedure up to 67 months after the procedure. Follow-ups focused on efficacy/effectiveness outcomes (verification of occlusion at six months) and safety outcomes (adverse events related to HTS intervention and adverse events reported post-intervention at short-, medium- and long-term (that is, women followed-up at two weeks, at three months, and at more than three months, respectively), as well as information about satisfaction of women and providers with the HTS procedure.

Bilateral placement of the Essure® micro-inserts was achieved in 2362 women after the first attempt (range 85 to 95% from the total number of women in each study) and in 58 women after the second attempt (see Table T.1, Appendix T.C.1). Reported reasons for failure of bilateral placement of micro-inserts after the first attempt included:

- anatomical factors—blocked tubes (eight cases), stenotic tubes (five cases), bicornuate uterus (one case), extremely lateral tubes (one case)
- operative factors—incorrect positioning of the devices (nine cases), obstructive view (six cases), obstruction due to presence of IUD (four cases), tubular spasm (four cases), inability to access the uterine cavity and optimally site the hysteroscope (two cases), non-identification of one tubal ostia (two cases)
- women's factors—obesity (three cases), anxiety (one case), pain (one case)

The interventions were conducted by gynecologists with experience in hysteroscopy in three studies,[3,4,6] in two studies by surgeons,[1,2] and in one study[5] by an experienced hysteroscopist and residents learning the procedure. In two studies[7,8] the providers' qualifications were not reported.

The device was considered optimally positioned when three to eight coils were visible in the uterine cavity at the tubal ostia at the end of procedure.[1-4,6] In all studies, 2410 of 2566 women were followed up at three months to confirm the occlusion of the fallopian tubes and reliance of women on the sterilization method. HSG, which is considered the standard test for documenting the location of micro-inserts and for confirming the occlusion of fallopian tubes, was used as a single test in only one study.[5] In seven studies,[1-4,6-8] other tests used at the three-month follow-up to identify the location and retention of the micro-inserts were pelvic x-ray or transvaginal ultrasound or x-ray and transvaginal ultrasound (see Table T.1, Appendix T.C.1). In the majority of the studies HSG was used only after suspected unsatisfactory placement of micro-inserts, such as if more than 10 or fewer than three coils remained visible during hysteroscopic insertion, when the insertion was not possible in both tubes, if the procedure time was longer than 15 minutes, when women experienced prolonged pain after the procedure, or when the other tests used provided unclear results.

Occlusion of the fallopian tubes was achieved in 2329 women at three months and in 12 women at six months (see Table T.1, Appendix T.C.1). Unilateral placement of the Essure® system was reported in 29 women. Among the reported reasons were: presence of stenotic tubes, previous salpingectomy, and unicornuate uterus. Ninety women were lost to follow-up in six studies and 24 women reported in seven studies had laparoscopic tubal sterilization after failing to achieve bilateral occlusion of the fallopian tubes. Six pregnancies were reported in three studies.[4-6] The reasons were undiagnosed pregnancy at time of HTS (one case), incorrectly positioned device (one case), and

non-compliance with the protocol (four cases). Four studies reported no pregnancies[1,2,7,8] during a follow-up period of three months[8] while one study[2] reported no pregnancies at one to five years of follow-up.

Table T.1: HTS with the Essure® system—efficacy outcomes

Author Sample size N	Bilateral placement N (%)	Unilateral placement N	Failed placement; LTS N (%)	Confirmed bilateral occlusion of the fallopian tubes N	Lost to follow-up N	Pregnancy N (length follow-up)
Andersson 2009[2] N = 61	58/61 (95%) 1st attempt: 52/61 (85%) 2nd attempt: 6 of 61	–	3/61 (5%) LTS: n = 4	At three mo.: 57/58 X-ray (n = 38) or ultrasound (n = 20); HSG (n = 1)	0	0 (mean 23 mo. [range seven to 67])
Chapa 2011[8] N = 161	158/161 (98%) 1st attempt: 154/161 (96%) 2nd attempt: 4/161	–	3/161 (2%) LTS: n = 3	At three mo.: 125/158 HSG; 139/154 TUV At six mo.: 2/158 HSG	31	0/127 (at three mo.)
Levie 2006[5] N = 102	98/102 (96%) 1st attempt: 97/102 (95%) 2nd attempt: 1/102	–	4/102 (4%) LTS: n = 1	At three mo.: 89/98 HSG Other: 1/98 (time NR)	7	1 (before three mo.)
Mascaro 2008[7] N = 28	27/28 (93%) 1st attempt: 20 IUD + (71%) + 5 IUD- 2nd attempt: 2 IUD-	1/28	1/28 (4%) LTS: n = 0	At three mo.: 26/27 IUD+: 19 X-ray + TVU IUD-: 5 X-ray + TVU & 2 HSG	1	0 (NR)
Mino 2007[4] N = 857	830/857 (97%) 1st attempt: 812/857 (95%) 2nd attempt: 18/857	15/857	12/857 (1%) LTS: n = 0; n = 3*[9]	At three mo.: 835/845 X-ray ± HSG At six mo.: 9/845 HSG (n = 77 HSG)	0	1 (undiagnosed at time of HTS)
Sinha 2007[1] N = 112	103/112 (92%) 1st attempt: NR 2nd attempt: NR	–	9/112 (8%) LTS: n = 8	At three mo.: 81/82 abdominal X-ray (n = 16) or HSG (n = 65) At 6 mo.: 1/82 HSG	21	NR
Veersema 2011[6] N = 1145	1059/1145 (92%) 1st attempt: 1034/1145 (90%) 2nd attempt: 25/1145	13/1145	73/1145 (7%) LTS: NR; n = 3*[11]	At three mo.: 1037/1059 TVU ± HSG	22	4/1037 (at 24 mo.)
Vellayan 2006[3] N = 100	87/100 (87%) 1st attempt: 85/100 (85%) 2nd attempt: 2/100	–	13/100 (13%) LTS: n = 2	Unclear; 79/83 uncomplicated bilateral placement: X-ray or HSG	Unclear: (4+4†)	NR

*LTS interventions reported in multiple publications

†Not clearly stated in the publication

HSG – hysterosalpingography; HTS – hysteroscopic tubal sterilization; IUD – intrauterine device (IUD+ = user; IUD- = non user); LTS – laparoscopic tubal sterilization; mo. – month; N, n – number; NR – not reported; TVU – transvaginal ultrasound

Andersson et al. (2009)[2] conducted a prospective case series study in a hospital outpatient department of obstetrics and gynecology enrolling 61 women with a mean age of 39.6 years (range 30 to 46) and parity mean 2.4 (range 1 to 5). Thirty-seven women included in the study had contraindications for laparoscopic tubal sterilization: diabetes mellitus, obesity, previous abdominal or pelvic surgery, or another medical disease (no details provided). The purpose was to evaluate the short- and long-term results of HTS with the Essure® system in the outpatient setting. Women were on day three to 10 of their menstrual cycle, if possible, and had a pregnancy test on the day of procedure. Women received oral analgesics (NSAIDs or opioids) one hour prior to the intervention. Paracervical block local anesthesia was administered in 44 women. One surgeon, with attendance and support of a trained nurse, performed all procedures. The mean duration of the intervention was 30 minutes (range 7 to 70) and the recovery time to home discharge was approximately two hours. Follow-up was at three months by x-ray or ultrasound. No losses to follow-up were reported. A follow-up questionnaire was administered one to five years after the procedure. Data were reported for successful bilateral device placement on the first and second attempts (device was considered optimally positioned when three to eight coils were visible at the tubal ostia), satisfactory occlusion confirmed at three months follow-up, satisfaction with the procedure, adverse reactions related to the procedure, and short- and long-term follow-up. Women's tolerance was determined through a visual analogue scale, but details about the scale were not provided.

Bilateral placement of the micro-insert was achieved in 58 of 61 women (52 at first attempt and six at second attempt). Reasons for failure at first attempt were material defects (two cases), tubular spasm (four cases), obstructed view (two cases), and failure to pass the cervix (one case). Satisfactory placement of micro-inserts was confirmed at the three-month follow-up in 57 of 58 women; x-ray was performed in 38 women and ultrasound in 20 women. One woman had an HSG, which confirmed unilateral patency of the fallopian tube. Four women underwent laparoscopic tubal sterilization, three of them after failing the first attempt, and one had a unilateral procedure at the three-month follow-up. No pregnancies were reported during a follow-up of one to five years (mean follow-up 23 months [range 7 to 67]).

Chapa et al. (2011)[8] conducted a prospective case series study in a community-based private obstetrics–gynecology medical office, which included 161 women of reproductive age (mean age was not reported). The main purpose was to determine the ability of in-office two-dimensional transvaginal ultrasound (TVU) compared with subsequent HSG to predict proper tubal occlusion and micro-insert location. The secondary purpose was to determine the rate of bilateral placement of the Essure® micro-insert, to report follow-up results at three months by HSG and to report pregnancy rate. All women were pretreated with a progestogen-only contraceptive 10 days before the HTS, underwent a urine pregnancy test before the Essure® attempt, and received an analgesic 30 minutes prior the intervention. Women also received paracervical block local anesthesia. The TVU was conducted at three months in 139 women. These women were referred for a confirmation HSG test. The HSG was conducted in 125 women at three months and repeated in two women at six months. Optimal placement of the micro-insert was considered when three to eight coils trailing into the uterine cavity were visible. Thirty-one women were lost to follow-up, 19 for the TVU evaluation, and another 12 did not present for the HSG test. Data were reported for rate of successful placement of the Essure® inserts and reliance in the sterilization.

Bilateral placement of the micro-insert was achieved in 158 of 161 women, 154 women at first attempt and four women at second attempt. Of the 158 women with bilateral placement, 139 had TVU and 130 of them showed a desirable location of the device. All 139 women were referred for a

confirmation of bilateral tubal occlusion by HSG. Only 127 women had the procedure and 125 of them showed bilateral occlusion of the fallopian tubes. Two women showed tubal patency and were followed up at six months when they showed occlusion of the fallopian tubes. Three women had laparoscopic bilateral tubal ligation after an unsuccessful placement of the micro-inserts at first attempt. Reason of failure of the micro-insert placement was not reported. No pregnancies were reported during a three-month follow-up of 127 women.

Levie et al. (2006)[5] conducted a prospective case series study in a university outpatient office, including 102 consecutive women with a mean age of 35 years (range 22 to 44), mean BMI of 30.3 kg/m^2 (range 18.6 to 51) and mean parity of 3 (range 0 to 8). Most participants were of Hispanic origin; 45 women had had prior abdominal or pelvic surgery, 38 women had had at least one Cesarean section, 17 women had sexually transmitted disease history, and six women had polypectomies at the time of the Essure® placement. The purpose was to evaluate the efficacy of performing the Essure® HTS in an office-based setting using only NSAIDs administered intramuscularly one half hour prior to the intervention, and paracervical block local anesthesia. All procedures were provided under the supervision of a senior faculty member with expertise in hysteroscopy. Residents, fellows, or attending physicians learning the procedures conducted approximately half of the procedures. The mean duration of intervention was 12.4 minutes; the average time was 17.2 minutes for the first 13 cases. Recovery time after intervention was not reported. The satisfactory bilateral placement of micro-inserts was confirmed at three months by HSG. Six women were lost to follow-up at three months. One woman who failed bilateral tubal occlusion underwent laparoscopic tubal sterilization. Data are reported for successful completion of the procedure.

Bilateral placement of the micro-insert was achieved in 98 of 102 women, 97 women at first attempt and one woman at second attempt. Four failures were reported due to anatomical factors (bicornuate uterus, extremely lateral tubes, severe obesity, and polypectomy of a polyp obscuring the tubal ostia) and absence of visualization of tubal ostia. Confirmed bilateral occlusion of the fallopian tubes was obtained by HSG in 90 women, 89 of them at the three-month follow-up and one at a subsequent unreported follow-up time. At the three-month follow-up, one woman had a free Essure® coil in the uterine cavity; this was removed and the woman underwent laparoscopic tubal ligation. Pregnancy was reported at eight weeks after HTS procedure in one woman who had had the procedure performed on day 14 of her cycle while she was sexually active without contraception.

Another study, published in 2010 by Levie et al.,[10] included 209 women provided with office-based HTS. Only the adverse events (that is, pain) related to the intervention were reported, but no details were available on the three-month follow-up test used to measure the placement of the micro-inserts. Pain was assessed with a Likert-type scale of 0 to 10, with 0 indicating no pain and 10 indicating the worst pain. A standardized pain score (SPS) was also calculated.

Mascaro et al. (2008)[7] conducted a case series study in an office setting of a tertiary university hospital, including 28 consecutive intrauterine device (IUD) users (multiload and T-shaped) aged 26 to 44 years. Eight women required IUD removal before HTS intervention. Data collection was unclear. The purpose was to evaluate the feasibility of the Essure® procedure in IUD users and the use of the IUD as an alternative, non-definitive contraceptive method for a three-month period post-HTS. Women received oral NSAIDs approximately one hour prior to the intervention. Administration of local anesthesia was not necessary. The mean duration of intervention was 8.7 minutes (range 5 to 20), with a recovery time to home discharge of approximately 25 minutes. The

follow-up was conducted at three months in 27 women by pelvic x-ray to locate the micro-insert, and TVU to identify the location and retention of the micro-insert. Only two HSGs were performed in suspected unsatisfactory placements. One woman was lost to follow-up. Data were reported for successful completion of the procedure and reliability of the procedure at the three-month follow-up.

Bilateral placement of the micro-insert at first attempt was achieved in 20 women who had an IUD in place and in five women after an IUD was removed. Two cases were successful at second attempt. The reasons for failure of correct bilateral micro-insert placement with an IUD in place were anatomic (visual obstructed by uterine bleeding (one case), no visible ostium (one case), stenotic tubes (two cases)) and procedure-related (IUD obstructed uterotubal junction (two cases), and IUD descended (two cases)). The confirmation of bilateral occlusion of the fallopian tubes was obtained in 26 of 27 women by x-ray and by TVU in 19 users of IUD and five women without the IUD in place. Two women with an IUD in place had confirmation of the bilateral occlusion by HSG. One woman showed a unilateral stenotic tube with spontaneous expulsion of the Essure®. A total of 19 women benefitted from IUD contraceptive protection during the three months after the procedure. The IUDs were removed without difficulty after confirming the bilateral tubal occlusion. No pregnancies were reported (length of follow-up not stated).

Mino et al. (2007)[4] conducted a prospective case series study in a hospital outpatient department. The study enrolled 857 women with a mean age of 36 years (range 22 to 49), parity of two in the majority of cases, and normal gynecological physical examination and pelvic sonography. The purpose was to evaluate the success rate of the HTS with the Essure® system and women's satisfaction following the procedure. The vast majority of women used at least one cycle of oral contraception prior to the procedure. Women were medicated with NSAIDs and benzodiazepine one hour prior to the intervention. Paracervical local anesthesia was administered only for extreme anxiety and pain in half of the women. The procedures were performed by two hysteroscopists; mean duration of the intervention was 6.8 minutes (range 5 to 18). The majority of women returned to normal activity the same day. Satisfactory bilateral placement of micro-inserts was confirmed at three months by x-ray. HSG was used only in 77 women if more than 10 or fewer than three coils remained visible during hysteroscopic insertion, if the insertion was not possible in both fallopian tubes, or when the plain radiological image was not conclusive. Pelvic ultrasound was later introduced for inconclusive x-rays. All women completed the follow-up. The adverse events related to the procedure and at short term were recorded.

Bilateral placement of the micro-insert was achieved in 830 of 857 women; 812 women at first attempt and 18 women at second attempt. Unilateral placement was achieved in 15 women (14 had had a previous salpingectomy and one had a unicornuate uterus). Failed placement was reported in 12 women, with previous tubal occlusion confirmed by subsequent HSG. At the three-month follow-up, by x-ray and/or HSG, 835 of 845 women had confirmed bilateral occlusion; nine women obtained confirmation by HSG at six months. After plain radiological follow-up at three months, HSG was indicated in 77 women. One pregnancy was reported in an undiagnosed woman at the time of HTS.

The **Mino et al.** study has another publication, **Arjona et al.** (2008),[9] which included 1630 women and evaluated their satisfaction with and tolerance of HTS. All women completed a self-assessment diary and were contacted by the study team after discharge. Satisfaction was evaluated with a visual analog scale (VAS; 100-mm line) rating from 0 (absolutely dissatisfied) to 10 (highly satisfied) and by

a verbal rating scale ranging from very satisfied to very unsatisfied. Women's tolerance and discomfort were measured with an ordinal Likert-type scale immediately after the procedure.

Sinha et al. (2007)[1] conducted a prospective case series study in an outpatient hysteroscopy clinic at a teaching hospital including 112 consecutive women with a mean age of 36 years (range 23 to 48) and mean BMI of 27 kg/m^2 (range 17 to 53). The purpose was to determine the feasibility and women's satisfaction with HTS using the Essure® system without general anesthesia or conscious sedation. Fifty-one women were in the secretory phase of the menstrual cycle at the time of intervention. Intrauterine pathology was recorded at hysteroscopy in nine women and the uterus was enlarged clinically in eight women. Women received oral analgesics (NSAIDs [most of them] or opioids) one hour prior the intervention, and local anesthesia. Two experienced surgeons performed the HTS. Mean duration of the intervention was 14 minutes (range 3 to 50) with a recovery time to home discharge of 30 minutes to four hours. Follow-up was at three months by HSG or x-ray. Data were reported for successful completion of the procedure defined as satisfactory bilateral tubal placement of the Essure® inserts (three to eight intrauterine coils visible) at the three-month follow-up and adverse events related to the procedure at short- and medium-term follow-ups. A postal questionnaire was administered three months after the procedure to 84 women, to determine women's satisfaction with the procedure.

Bilateral placement of the micro-inserts was achieved in 103 of 112 women. Reasons for failure included: anatomic factors (four cases), women's factors (two cases), and operative factors (two cases). The satisfactory placement of micro-inserts was confirmed at a three-month follow-up in 81 out of 82 women; HSG was performed in 65 women and abdominal x-ray in the first 16 women. Twenty-one women were lost to follow-up. In one woman, occlusion of the fallopian tubes was observed at six months follow-up with HSG. No pregnancies were reported to date. Length of follow-up was not reported.

Veersema et al. (2011)[6] conducted a prospective multicentre case series study in four outpatient teaching hospital departments that included 1145 consecutive women with a mean age of 39.2 years, a mean BMI of 25 kg/m^2 and a parity of two in the majority of cases. The purpose was to evaluate the protocol for confirmation of satisfactory Essure® placement at three months using transvaginal ultrasound (TVU). Women were advised to take an NSAID on the evening before the procedure and one hour prior to undergoing the HTS procedure. No one received local or general anesthesia. Nine appropriately trained gynecologists, with experience in office hysteroscopy and training in HTS using the Essure® system, performed all procedures. The mean duration of the intervention was 7.2 minutes. Duration of recovery time was not provided. One hundred sixty-four women were scheduled to undergo an additional TVU examination at four weeks after the procedure. These tests were followed by HSG at three months after difficult placement of the micro-inserts, when the procedure time was longer than 15 minutes, when an incorrect number of coils protruded into the uterine cavity (none or more than 10), or when women experienced prolonged pain after the procedure. However, the extra TVU confirmation tests at four weeks did not reduce the number of HSGs at three months. Twenty-one women were lost to follow-up at three months. Data were reported for rate of successful placement of the Essure® inserts, effectiveness of HTS, and adverse events related to HTS. The Veersema et al.[6] study had another publication, **Langenveld et al.** (2008),[11] which reported results of a subset of 149 women treated at two outpatient centres.

Bilateral placement of the micro-insert was achieved in 1059 of 1145 women, 1034 women at first attempt and 25 women at second attempt. Unilateral placement was achieved in 13 women. There

were 98 failures at the first attempt and 73 failures after the second attempt. The reasons for failure at HSG conducted on 164 women at the three-month follow-up were incorrect positioning of one or two devices and expulsion (two cases), perforations of the tube (seven cases), and tubal patency (five cases). At the three-month follow-up, 1037 of 1059 women had confirmation of bilateral occlusion of the fallopian tubes by TVU and or HSG. Twenty-two women were lost to follow-up. No interventions for laparoscopic tubal ligation were reported, however three cases were reported in the multiple publication by Langenveld et al.[11] At 24 months of follow-up, four pregnancies were reported from a total of 1037 women. Reasons were: the device incorrectly positioned or absent (one case), and non-compliance with the protocol (three cases).

Vellayan et al. (2006)[3] conducted a case series study that included 100 women, in an outpatient hysteroscopy clinic of a teaching hospital. The characteristics of participants were not reported and data collection was unclear. The purpose was to report the experience with the Essure® technique in terms of success rates, complications, and acceptability to women. The procedure was conducted in the first half of the menstrual cycle, when possible. Also, when appropriate, women were advised to take oral contraceptives to avoid bleeding at the time of procedure. A urine pregnancy test was performed prior to HTS. Women were medicated two hours prior to the intervention with oral analgesics, NSAIDs, acetaminophen, or opiates. The first 37 procedures were conducted with the Essure® old device and 63 with a modified Essure® device introduced in April 2004. Intracervical block local anesthesia was used for the first cases. Three consultant gynecologists experienced in diagnostic and operative outpatient hysteroscopy provided all procedures. Two nurses were also required, one to attend the woman and one to assist the surgeon. The recovery time to home discharge was 30 minutes. The follow-up of 97 women was done at three months by plain abdominal x-ray or by HSG if the x-ray was inconclusive, if fewer than three or more than eight coils were seen in the uterine cavity at the end of the procedure, or if the women experienced undue pain during the insertion, suggesting an increased risk of possible perforation. A telephone survey was conducted with 37 women at 48 hours after intervention, to assess satisfaction, well-being, and post-intervention adverse events. Data were reported for successful completion of the procedure, satisfactory placement of the micro-insert at the three-month follow-up, and short-term potential adverse events.

Bilateral placement of the micro-insert was achieved in 87 of 100 women, 85 cases at first attempt and two cases at second attempt. Eighty-three cases were considered uncomplicated. The x-ray or HSG was performed in 79 women to confirm device positions. The duration of follow-up was not clearly reported. The placement of micro-inserts failed in 13 women (seven during the first 30 insertions and six during the next 30 insertions), the majority of cases due to pre-existing tubal damage—pain (one case), obesity (one case), and failed cannulation (11 cases). Eight women had blocked tubes, two women declined HSG and chose a different contraception method, and one woman failed to attend tests. In two women the device migrated distally into the peritoneal cavity and both devices were removed by laparoscopy. The number of participants lost to follow-up was not clearly reported. Information on pregnancies was not reported.

Safety outcomes

Adverse events related to HTS intervention were reported in four studies[1-3,6] and two multiple publications[9,10] (see Table T.2, Appendix T.C.1).

Adverse events that prevented reliance on Essure® included perforation of the fallopian tubes and uterus (nine),[1,3,6] expulsion of micro-inserts (14),[6,9] intramyometrial placement of device (two),[9] and

migration of the device to abdominal cavity (three).[9] One case of nickel allergy was reported in one study[9], but the duration of follow-up was unclear. No micro-insert expulsions or suspected uterine perforations or other complications were encountered in one study.[8]

At time of procedure, vasovagal reactions were reported in three studies[1,2,9] and involved 24 women. The episodes were minor, self-limiting,[1] and resolved during the procedure[2] without medication.[9] Light bleeding was reported in two cases.[2] Pain with or without abdominal discomfort was the most prevalent symptom reported in four studies[1,2,9,10] by 454 women representing 13 to 75% of the surveyed women in each study. The severity of pain ranged from similar to more pain than normal menstruation pain. In one study[2] the pain tolerance on a visual analogue pain score (VAS) was 5.4 (range 1 to 10) during the procedure (details about the scale used were not provided). In one study[10] the overall average pain reported for the procedure was 2.6 ±2.05; 95% CI (2.3 to 2.9) while the overall average reported menses pain was 3.6 ±2.63; 95% CI (3.2 to 3.9). In the same study, on a standardized pain score (SPS), 70% of women felt that the average pain experienced during the procedure was equal to or less than the typical pain they experienced with their menses and the average pain for the procedure was statistically significant lower than average menses pain ($p<0.001$).

No major complications, such as infections, uterine or tubal perforation, hemorrhage, or other adverse events, were reported during the procedure in one study.[7]

Table T.2: Adverse events related to HTS intervention

Outcome; study	Number AE/women
AE that prevented reliance on Essure®	
Expulsion of micro-inserts	
Arjona 2008[9†]	12/1615
Veersema 2011[6]	2/1145
Perforation of the fallopian tubes	
Sinha 2007[1]	1/112
Veersema 2011[6]	7/1145
Vellayan 2006[3]	1/100
Migration of device to abdominal cavity	
Arjona 2008[9†]	3/1615
Intramyometrial placement of devices	
Arjona 2008[9†]	2/1615
Nickel allergy	
Arjona 2008[9†]	1/1615
AE reported during the intervention	
Vasovagal reaction	
Andersson 2009[2]	3/61
Arjona 2008[9†]	16/1630
Sinha 2007[1]	5/112
Light bleeding	
Andersson 2009[2]	2/61

Pain	
Andersson 2009[2]	36/61 (required additional analgesia) Pain tolerance self-reported on VAS: mean = 5.4 (range 1 to 10)
Arjona 2008[9†]	50/1630 more pain than with menstruation 166/1630 pain similar to that with normal mestruation
Levie 2010[10]*	Pain (mean ± SD): 2.6 ±2.05; 95% CI (2.3 to 2.9) (on a pain scale 0 to 10; 0 = no pain, 10 = the worst pain possible) SPS (mean ± SD): -0.20 ±0.843; 95% CI (-0.313 to -0.0839) Average pain lower than average menses pain: 145/209
Sinha 2007[1]	Pain or discomfort (survey): 57/76 (95% CI 64 to 84%); severe pain: 10/57

*Multiple publication of Levie 2006[5] (N = 102); †Multiple publication of Mino 2007[4] (N = 857)

AE – adverse event; CI – confidence interval; HTS – hysteroscopic tubal sterilization; SD – standard deviation; SPS – standardized pain score; VAS – visual analogue pain scale

Short-term adverse events (occurring immediately after the intervention and up to two weeks after) (see Table T.3, Appendix T.C.1) were reported in four studies[1,3,4,13] and one multiple publication[9]. Pain was the most prevalent event. Most cases of pain (231 women) were reported in the first 48 hours after the HTS,[1-3,9] while 10 women reported pain at three days after intervention[4] and nine women had pain four or more days after intervention.[4] In one study, three women experienced pain at six days and at two weeks after intervention in one study.[3] In most cases, women required analgesia to cope with pain.[1,2,4] Nausea or uterine cramping was reported by 15 women in one study.[2] In one study,[3] three surveyed women felt they would have preferred to have had more pain relief and one would have preferred to have had general anesthesia. In one study, 31 of 76 surveyed women experienced vaginal bleeding or discharge with a median duration of three days, two women reported urinary tract infection, and two women reported new pain or discomfort with sexual intercourse.

Medium-term adverse events (up to three months follow-up) (see Table T.3, Appendix T.C.1) were reported in one study[1] that surveyed 76 women; these consisted of subsequent abnormal menstrual periods (23 cases) or persistent change of menstrual period at the three-month follow-up (20 cases). In one study,[4] there were no reports of changes in the volume or pattern of menstruation or discomfort during sexual intercourse, nor were there any notable lifestyle modifications following the HTS procedure.

Long-term adverse events (at more than three months follow-up) (see Table T.3, Appendix T.C.1) were reported in two studies.[2,9] In one study,[2] 17 women surveyed at seven to 67 months after the HTS intervention reported changes in the pattern of subsequent menstrual periods.

Table T.3: Self-reported adverse events: short-, medium-, and long-term post-HTS intervention

Author Sample size	AE post-intervention short-term (up to two weeks)	AE post-intervention medium-term (up to three months)	AE post-intervention long-term (at more than three months)
Andersson 2009[2] N = 61 (BP: N_1 = 58)	• Nausea or uterine cramping n = 1 • Pain requiring analgesia first two hours n = 9 • Pain tolerance self-reported on VAS, first two hours: mean 3.5 (range 0 to 6)	NR	• Subsequent menstrual periods (survey at seven to 67 months): heavier 9/50, lighter 8/50
Mino 2007[4] N = 857 (BP: N_1 = 830)	• Pain requiring analgesia n_{total} = 77; three days n_1 = 10, ≥4 days n_2 = 9	No AE	NR
Arjona 2008[9]* N = 1630 (BP: N_1 = 1612)	• Pain requiring analgesia one or two days: 113/1612	NR	NR
Sinha 2007[1] N=112 (BP: N_1 = 103)	• Post-intervention pain that required analgesia n = 71 • Post-intervention pain (survey): 60/76 (95% CI 68 to 88); severe pain n = 6; pain lasting < four hours 37/60; pain lasting > eight hours 8/60 • Vaginal bleeding or discharge 31/76 (Me duration three days) • Urinary tract infection 2/76 • New pain or discomfort with sexual intercourse 2/76	• Subsequent menstrual period abnormal 23/76 (heavier loss [5], lighter loss [1], delayed [3], NR [14]) • Persistent change of menstrual period at three months (survey): 20/76 (heavier loss [14], irregular [2] intermenstrual bleeding [1], amenorrhea [3])	NR
Vellayan 2006[3] N=100 (BP: N_1=87)	• Pain at 48 hours: no pain or mild pain 24/37, moderate pain 8/37, severe pain 6/37 • Pain at six days n = 1 • Pain at two weeks n = 2	NR	NR

*Multiple publication of Mino 2007[4]

AE – adverse event; BP – bilateral placement of micro-inserts; HTS – hysteroscopic tubal sterilization; Me – median; VAS – visual analogue pain scale; N, n – number women; NR – not reported

Women' satisfaction and tolerance

The satisfaction with and tolerance of the HTS procedure was reported in four studies[1-4] and one multiple publication.[9] Three studies did not survey the women.[5,6,8] In one study,[7] a high level of women's satisfaction was reported, however no information is provided about how this was measured.

In one study,[3] a telephone survey with 37 of 100 women conducted 48 hours after HTS indicated satisfaction with the level of care received, and all but one participant indicated they would recommend the procedure to a friend.

In one study,[4] overall satisfaction at the three-month follow-up was rated very high by 806 out of 857 women surveyed and high by 51 of the total surveyed. In the multiple publication by Arjona et al. (2008),[9] the satisfaction was assessed by a 10-point VAS (a 100-mm line with end anchors, where 0 = absolutely dissatisfied and 10 = highly satisfied). The HTS procedure was well tolerated and rated excellent or very good by 1398 of 1615 women. The survey, conducted the first and second day after HTS, showed that 1516 of 1612 women were very satisfied with and 96 were somewhat satisfied with the procedure. None of the 722 women contacted at the end of the follow-up period (at >18 months) reported dissatisfaction with their HTS. On the VAS scale, 658 of 722 women were highly satisfied (VAS: 10); the lowest VAS rating score was 8. The most positive aspects noted by the respondents were avoidance of an operation (380 women), the method's quickness and comfort (144 women), the fact that HTS is a definitive procedure (131 women), and the possibility of returning quickly to a normal life (32 women).

In one study,[1] a postal survey was administered to 84 women (total 112) at a three-month follow-up. More than 90% of the 76 respondents were satisfied with their overall experience of the outpatient HTS procedure and subsequent radiological testing and would recommend the HTS procedure to others, and 42 women reported that the HSG is an "acceptable" test. A reason for non-satisfaction with HSG at the three-month follow-up was the painfulness of the test (22 of 58 women). The degree of HSG pain was considered mild by 14 women, moderate by six women, and severe by two women. The most common reason given by women for choosing the Essure® method over other sterilization procedures was the desire to avoid general anesthetic (55 women), although nine women indicated that they would have preferred general anesthesia. Other reasons in favor of HTS were: avoidance of surgical incisions (45 women), no need for hospital stay (25 women) and convenience (25 women). Reasons for disliking the HTS procedure were presence of "too many people around" (four women) and discomfort (three women).

In one study,[2] a survey of 50 out of 61 women at a mean follow-up of 23 months (range 7 to 67 months) after the HTS procedure showed overall satisfaction with the procedure. All respondents indicated that they would recommend the procedure to others.

Physicians' satisfaction with the HTS intervention

In one study,[5] the authors stated that the HTS procedure has a short learning curve to achieve proficiency and can be performed by a general obstetrician or gynecologist, after an appropriate training course and supervision for the first several procedures. The time required for HTS is short and this aspect improves office productivity. In one study,[4] two hysteroscopists described the HTS procedure as very difficult in 15% of the total cases, mainly due to the presence of anatomical tubal anomalies or tubal spasm. Other less prevalent reasons were marked uterine retroflexion, difficulty of ostium visualization, tubal obstruction, and menstrual bleeding.

Comparison between sterilization with the Essure® system and with other methods of sterilization

At the time of writing this review, no randomized controlled trials or studies comparing the Essure® HTS method with other methods of sterilization had been published within the previous five years.

A comparative study would be useful for comparing women's outcomes—efficacy, safety, and satisfaction—with the Essure® HTS and with other widely used sterilization methods such as laparoscopic tubal sterilization (considered the gold standard against which other methods of permanent female sterilization are judged). However, several limitations exist with conducting this

type of study. It would be a comparison of two methods of sterilization with clearly different surgical approaches (hospital admission and general anesthesia versus outpatient office and no anesthesia) and the procedures are suitable in different populations of women, who may also have different perceptions of tolerance and satisfaction.[9]

A multicentre study published by Duffy et al. in 2005 compared the Essure® system with laparoscopic sterilization.[14] A total of 59 women underwent the Essure® placement in outpatient facilities; 48 of them had bilateral placement of the system after two attempts and 34 women were relying on the Essure® system for sterilization at the three-month follow-up with HSG. One woman became pregnant during the follow-up period. In the comparative group, 24 women had successful laparoscopic tubal sterilization in day surgery facilities. The primary outcome was women's satisfaction, as judged by the study participants who had had a successful procedure and had completed questionnaires on days seven and 90. Satisfaction at 90 days with the Essure® placement was 94%, and with laparoscopy it was 80%, with no statistically significant difference between the two groups. Six out of 48 women experienced adverse events immediately post-operatively in the Essure® group, compared with six women out of 24 in the laparoscopy group. The majority of women who had problems in the laparoscopy group at 90 days were those who developed inflammation or infection (four out of six) from their surgical wounds, while the majority of women in the Essure® group suffered from pain (five out of six) at 90 days (however, 13 women were lost to follow-up). The authors concluded that sterilization using the Essure® system can be performed for the majority of women and, when successful, is associated with a higher degree of self-reported satisfaction as compared to the satisfaction of those who underwent laparoscopy. Women who underwent the Essure® placement spent less time in hospital, had a better tolerance of the procedure, and described less severe post-operative pain. However, all the women in the laparoscopy group had general anesthesia, while 30% in the Essure® group had local anesthesia and the others in the Essure® group underwent the procedure without any anesthesia.

No comparative study was found to compare the HTS using the Essure® system with another transcervical method of sterilization. Presently no other method of HTS is licensed by Health Canada.

Other publications

Three HTA reviews[14-16] were published between 2006 and 2010. A synopsis of the objectives, searches, inclusion and exclusion criteria, main findings, and review conclusions is available in Appendix T.C.2.

The Alberta Heritage Foundation for Medical Research (AHFMR) rapid review[14] was published in 2006. The review included one non-controlled comparative study and five prospective case series studies. Two studies were the FDA Premarket Approval (PMA) multicentre case series studies. The report concluded that, based on the quick overview of weak evidence with very short-term follow-up periods, the Essure® system appears to be adequate in terms of safety and effectiveness under controlled conditions. However, the ultimate clinical outcome of interest is prevention of pregnancy during the length of the women's fertility cycle and this would require longer-term studies. Evidence from longer-term comparative trials is necessary before this procedure is to be introduced into routine practice.

The National Institute for Health and Clinical Excellence (NICE) in the UK published an update overview[15] of hysteroscopic sterilization by tubal cannulation in 2008 and issued guidance for use of

the procedure in September 2009. The overview included one non-controlled comparative study, six prospective case series studies, and six case reports that focused on HTS using the Essure® system. Two studies were the FDA Premarket Approval (PMA) multicentre case series studies. The quality of the included studies was not reported. The guidance indicated that current evidence on the safety and efficacy of hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants was adequate to support the use of this procedure, provided that normal arrangements are in place for clinical governance and audit. The intervention was usually performed with the woman under local anesthesia and/or intravenous sedation. Confirmation of satisfactory placement of the micro-inserts was done by appropriate imaging with x-ray or ultrasound scanning initially, followed by HSG in selected women, or by HSG as a routine test to ensure that the fallopian tubes were occluded.

In 2010 the Finnish Office for Health Technology Assessment published the results from an HTA review[16] conducted to update the evidence on the efficacy and safety of the Essure® system, by updating the AHFMR 2006 review.[14] Only one new prospective case series study was found by the searches. The quality appraisal of the included studies was not reported. In Finland, the Registry on Sterilization included 848 Essure® procedures and 23,978 laparoscopic sterilizations between January 2002, when the Essure® system was introduced, and December 2007. The linkage to other health registries showed no pregnancies with the Essure® system but 103 pregnancies (0.3%) with laparoscopic sterilization using the Filshie clip. The Essure® procedure can be provided in an ambulatory setting, under pain medications. Tubal occlusion was demonstrated by transvaginal ultrasound, hysterosalpingosonography, HSG, or pelvic radiography. The authors concluded that long-term Essure® data on safety, efficacy, effectiveness, and pregnancy rates were still unavailable.

Discussion

The Essure® procedure for permanent contraception is the only HTS method of female sterilization approved for use as of November 2001 by Health Canada.

Transcervical sterilization using the Essure® system is a permanent, irreversible, minimally invasive, non-incisional approach to sterilization by bilateral occlusion of the fallopian tubes. The mode of action is a combination of mechanical insertion of the implant (expansion of outer coil for acute anchoring, and space filling/mechanical blockage of tubal lumen), and tissue in-growth into and around the micro-insert for device retention and obstruction of fallopian tubes. Compared with laparoscopic tubal ligation, which is the current standard procedure for female sterilization, HTS does not need to be performed in an operating room, requires less anesthesia, and has a shorter recovery period by avoiding general anesthesia, surgical incisions, and entry into the peritoneal cavity. Sterilization, however, is not immediate, and women are required to use alternate contraception for approximately three months, until tubal occlusion is demonstrated by HSG, pelvic radiography, or transvaginal ultrasound assessment. Success rates of HTS with Essure® depend upon the compliance of women to use alternative modes of contraception during the first three months after insertion. HSG is the gold standard recommended test to determine whether tubal occlusion is complete and the device is located in the right position.

Since its introduction on the market, the design of the Essure® system has been improved several times. This aspect was emphasized in two of the published studies,[2,3] with the authors noting an improvement of the technical success rates of micro-inserts placement as the series progressed.

The adoption of new technologies is always associated with a learning curve. The Essure® procedure requires a provider trained in hysteroscopy, practice of the procedure on a simulator, and three to five proctored cases before competency is achieved. Increase in the experience of the operator using the device, and adoption of a good technique, affect success rates. Furthermore, the minor changes and modifications to the Essure® system since it was first introduced to the market were considered important factors for affecting the success of the intervention.[1,2,4] In the hands of a trained professional, the technique is fast, with a reported mean procedure time in five of the included studies of between 6.8 and 14 minutes, partly due to the fact that most cases can be completed without anesthesia. The adherence to the Essure® HSG protocol by the gynecologist and the radiologist performing the HSG is another important factor of success.

Published research evidence on the effectiveness and safety of HTS with Essure® is available from case series studies with short follow-ups. Due to the short follow-up periods, no evidence is available about the long-term nature of the tissue response to the Essure® micro-insert and the maintenance of its effectiveness in avoiding pregnancies over all of a woman's reproductive years.

Eight case series studies published from 2006 onwards, with recruitment beginning in 2002, had a combined sample size of 2566 women and met the inclusion criteria of the present review. Six studies included women with mean ages between 35 and 39.6 years (range 22 to 49 years). The bilateral placement of micro-inserts was performed mainly in outpatient settings and was achieved in 2420 cases, most of them (that is, 2362 women) at first attempt. The rate of successful bilateral placement of Essure® micro-inserts at first attempt was between 71 and 96%. The successful bilateral placement of the micro-inserts after first and second attempts was between 87 and 98%, which is in line with previously reported success rates by the manufacturer and in other earlier published studies. In all studies, the women were followed up at three months for confirmation of bilateral occlusion of the fallopian tubes, and in three studies 12 women with unsuccessful occlusion were reassessed at six months. Occlusion of the fallopian tubes was confirmed in 2342 women, most of them (that is, 2329 cases) at the three-month follow-up.

The HSG was used as a single test to assess the occlusion of the fallopian tubes and the proper placement of the device in one case series study, while in the other seven case series studies women had pelvic radiography and transvaginal ultrasound (TVU) tests at the three-month follow-up. X-ray and TVU can locate the device and visualize its relationship with surrounding tissues. However, they cannot assess the occlusion of the fallopian tubes. Among the reasons stated for replacing HSG with these tests were: increasing the compliance of women, and convenience. The HSG was used only in cases of suspected unsatisfactory placement of the micro-inserts. Although the pelvic radiography and TVU were less invasive, not all women adhered to the three-month follow-up, indicating the need for better communication with and counseling of women about the importance of the follow-up examination. Six unintended pregnancies were reported in three case series studies with follow-ups from three to 24 months, mainly due to non-adherence to the manufacture's protocol. Ninety women were reported as lost to follow-up.

Not all women are candidates for the Essure® procedure, and failures were attributed to various reasons, including anatomic reasons (stenotic or previously occluded tubes, unsuspected tubal or uterine abnormalities and primary tubal occlusion). A total of 24 women who failed the procedure underwent laparoscopic tubal sterilization. In one study, one case of nickel sensitization was reported. The prevalence of allergic reactions to the nitinol (nickel-titanium alloy) was found to be very small since the introduction of the Essure® system, so much so that the manufacturer removed

from the Essure® protocol the requirement for nickel testing before the HTS intervention. Participants in two studies[2,5] had comorbidities which are usually contraindications for laparoscopic tubal sterilization (that is, diabetes mellitus, obesity, and previous abdominal or pelvic surgeries). No study included women that carried other high surgical risks, such as heart and pulmonary diseases.

The main safety issues related to the Essure® system were: expulsion of micro-inserts (14 cases), vasovagal reactions (24 cases), perforation of the fallopian tubes (nine cases), migration of the device to the abdominal cavity (three cases), light bleeding (two cases), and intramyometrial placement of device (two cases). Most of the cases were found after the intervention by HSG, at the one-week to three-month follow-ups. These findings emphasize the need for a careful follow-up of women who undergo the procedure.

The information about adverse events and safety was mainly self-reported, collected by surveys conducted at various follow-up times, however the authors did not survey all women who underwent the Essure® procedures, which may raise the question of potential underreporting of adverse events. A total of 454 women, representing 13 to 75% of participants in each study, experienced pain during intervention, and 231 women reported pain in the first 48 hours. The pain was usually mild. The most prevalent short- and medium-term adverse events experienced included pain, vaginal bleeding or discharge, and changes in menstrual patterns.

The surveys also assessed the satisfaction with and tolerance of the Essure® procedure and reported favourable satisfaction with the Essure® technique. Among the reasons for increased satisfaction were the convenience, avoidance of an operation room, avoidance of general anesthetic and surgical incisions, quickness and comfort, irreversibility, and rapid return to normal life.

It was emphasized[1,3,4,6,7] that proper timing of the procedure (during the early proliferative phase of the menses cycle) provides better visualization of the tubal ostium and can help avoid luteal phase pregnancies. It is still unclear whether timing the procedure to coincide with a specific time in the menstrual cycle makes it easier or increases successful bilateral placement of the Essure® device.[17,18]

All women were pre-medicated with NSAIDs prior to undergoing HTS with Essure®. The use of non-steroidal anti-inflammatory agents prior to the procedure has been suggested to work by decreasing tubal spasm during the procedure, and appears to increase the success rate of Essure® placement;[7,17,19] however, the results are unclear as to the effect of NSAIDs, because none of the studies were randomized or powered to detect a difference in success rates.

For women using an IUD for contraception, the results from one case series study[7] which included a small number of women indicated that providers may consider placing the Essure® device while leaving the IUD in situ for contraceptive reasons until occlusion of the fallopian tubes is demonstrated at the three-month follow-up. Some common limitations that affect the ability to complete the procedure properly in IUD users were related to undiagnosed anatomic tubal defects such as stenosis or occlusion, or to blockage of tubal ostia by the IUD device and the need, in some cases, to remove the IUD device prior to performing HTS with Essure®.

Some counseling issues are specific to the Essure® technique and need to be implemented before proceeding with HTS. The irreversibility of the procedure brings potential ethical and legal issues to the forefront. These issues can be avoided if the autonomy of the woman is respected, and if couples receive sufficient counseling before the intervention so they may fully understand the advantages and risks of the intervention. The woman's mental capacity to provide informed consent to undergo the procedure must be assessed. The guidelines published by the Society of Obstetricians

and Gynaecologists of Canada in April 2004 considered transcervical sterilization an effective, safe, and less invasive technique, but virtually impossible to reverse. The recommendation was to inform couples about all the different sterilization procedures that were available to them before they made the decision about their procedure of choice.

Strengths and limitations

The present review builds on and updates a 2006 rapid HTA review[14] prepared by AHFMR in response to a request from Alberta Health & Wellness for evidence on the efficacy/effectiveness, efficiency, and safety of HTS (the Essure® system) used for permanent birth control. A comprehensive literature search was conducted for studies published from 2006 up to March 2012 and for grey literature publications. Only full text, English articles were included; conference abstracts were excluded. The corresponding author of one included study[6] was contacted for more details. Two reviewers screened the abstracts of published studies, applied the pre-determined inclusion criteria in selecting the studies, and assessed the risk of bias of the included studies. One reviewer did the data extraction.

Case series studies were the only evidence base found to be eligible for inclusion. Evidence from case series studies is considered to be weak, since this study design is prone to biases related to selection, detection, performance, and attrition. Six of the eight studies met 10 to 15 of the 18 quality criteria used to evaluate the robustness of the results of the studies.

Most of the studies reported short-term outcomes. Limited information was reported about the quality of life, satisfaction, and tolerance with the HTS using the Essure® system. When it was available, the satisfaction and tolerance information was recorded mostly in a subset of participants. Information about the long-term adverse events and effectiveness of the Essure® system in relation to the number of pregnancies after the procedure is available mainly from the manufacturer's databases, and is based on ad-hoc reports provided by users or providers. All included studies in the present review were conducted in countries with developed market economies, and the "western" context may increase the clinical relevance and applicability of the results to our Canadian population. On the other hand, the period of enrolment for women in the eight case series studies was between 2002 and 2009, meaning that in the majority of the studies[1-5] some of the early procedures were conducted with the old device, which might have affected the success rates of micro-insert placement and the generalizability of these results to today's context.

The experience and expertise of providers of the HTS interventions was reported in detail in few of the publications.

None of the included studies focused on HTS with Essure® performed simultaneously with another intrauterine procedure, such as endometrial ablation, myomectomy, uterine synechiae resection or polipectomy.

The present review does not focus on alternative sterilization options, such as vasectomy, that are available to couples in Canada. In the Canadian Contraception Study, conducted in 2002 on a national sample of women aged 15 to 44 years, 13% of the surveyed women reported reliance on male sterilization (vasectomy), while female sterilization was used by only 7% of them.

Conclusions

Based on current evidence, HTS using the Essure® system can be an alternative to laparoscopic sterilization in women in whom visualization of both tubal ostia is possible and in whom exists the anatomical possibility to place the micro-inserts. At relatively short follow-up periods, the

intervention seems to be adequate in terms of safety and effectiveness, with few reported failures or cases of major adverse events. One important disadvantage of the intervention is its irreversibility and the potential of regret in younger women downstream. The intervention prevents pregnancies to at least at the same levels as do the traditional methods available for female sterilization. However, the nature of the tissue, cellular, and fibrotic response and ability of the tissue response to maintain occlusion of the fallopian tubes is not known over longer periods of time. This is more important if the Essure® system is provided to younger women who need to rely on permanent fertility control throughout their reproductive years.

Good communication and compliance with the protocol by professionals and women are important factors that impact the success of the intervention. The Essure® system has the advantages of avoiding surgical incisions and general anesthesia, and promising a faster recovery time. The hysteroscopic approach could probably be a clear indication in women who have a relative contraindication to laparoscopy due to morbid obesity, intra-abdominal adhesions, and/or cardiopulmonary diseases, or who have contraindications for general anesthesia. Several sterilization options are available to couples and these options need to be compared to the Essure® system over the longer term using a risk/benefit approach. Appropriate education and counseling are key, due to the irreversibility of the Essure® system.

Appendix T.A: Methodology

The project was conducted in accordance with an a priori protocol developed by the IHE HTA unit.

Search Strategy

The IHE Research Librarian (DC) conducted a search of electronic databases to retrieve articles published between 2006 and February 29, 2012. The searches were limited to human studies. The reference lists of retrieved articles were also searched. Grey literature was identified through an internet search using Google, as well as by searching the websites of other HTA agencies, guidelines databases, and regulatory and licensing agency (Health Canada and the United States Food and Drug Administration) databases.

Table T.A.1: Search strategy

Database	Edition or date searched	Search Terms ††
Core Databases		
MEDLINE (includes in-process articles) (OVID interface)	29 February 2012	1 Hysteroscopy/ 2 (hysteroscop* or transcervical or Essure or Adiana).tw. 3 exp Sterilization, Tubal/ or exp Sterilization, Reproductive/ 4 sterili?ation.tw. 5 1 or 2 6 3 or 4 7 5 and 6 8 limit 7 to animals 9 7 not 8 **(376 results)**
Embase	29 February 2012	1 Hysteroscopy/ 2 (hysteroscop* or transcervical or Essure or Adiana).tw. 3 female sterilization/ or uterine tube sterilization/ 4 sterili?ation.tw. 5 1 or 2 6 3 or 4 7 5 and 6 8 limit 7 to animals 9 7 not 8 **(513 results)**
Cochrane Library (including Cochrane Reviews, CENTRAL, DARE, HTA, and Economic Studies)	29 February 2012	#1 MeSH descriptor Hysteroscopy, this term only #2 (hysteroscop* or transcervical or Essure or Adiana) #3 MeSH descriptor Sterilization, Tubal, this term only #4 MeSH descriptor Sterilization, Reproductive, this term only #5 (sterili*ation) #6 (#1 OR #2) #7 (#3 OR #4 OR #5) #8 (#6 AND #7) **(39 results)**
Web of Science	29 February 2012	# 3 #1 and #2 # 2 TS=(sterili*ation) # 1 TS=(hysteroscop* or transcervical or Essure or Adiana) **(315 results)**

CINAHL	5 March 2012	S7 S5 and S6 S6 S3 or S4 S5 S1 or S2 S4 (sterili*ation) S3 (MH “Sterilization, Sexual”) OR (MH “Sterilization Tubal S2 (hysteroscop* or transcervical or Essure or Adiana) S1 (MH "Hysteroscopy") **(89 results)**
Guidelines		
AMA Clinical Practice Guidelines *www.topalbertadoctors.org/cpgs.php*	12 March 2012	Browsed list of topics **(0 results)**
NICE Guidance *www.nice.org.uk/*	12 March 2012	sterilization or sterilisation or hysteroscopic or transcervical **(1 result)**
CMA Infobase http://mdm.ca/cpgsnew/cpgs/index.asp	12 March 2012	sterilization or sterilisation or hysteroscopic or transcervical **(0 results)**
National Guideline Clearinghouse *www.ngc.gov*	12 March 2012	sterilization or sterilisation or hysteroscopic or transcervical **(3 results)**
Society of Obstetricians and Gynecologists Canada *www.sogc.org/index_e.asp*	12 March 2012	Browsed list of guidelines **(0 results)**
Coverage/Regulatory/Licensing Agencies		
Alberta Health *www.health.gov.ab.ca*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical **(0 results)**
Medical Devices Active Licence Listing *www.mdall.ca/*	12 March 2012	Essure or Adiana or hysteroscopic or permanent birth control or permanent contraceptive or sterilization or sterilisation **(2 results)**
Health Canada *www.hc-sc.gc.ca*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical **(0 results)**
US Food and Drug Administration Databases *www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive **(2 results)**
Aetna Clinical Policy Bulletins *www.aetna.com/about/cov_det_policies.html*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(1 result)**
HTA resources		
INESS *www.inesss.qc.ca/*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(0 results)**

CADTH www.cadth.ca/index.php/en/	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(2 results)**
Institute for Clinical and Evaluative Sciences (ICES), Ontario *www.ices.on.ca/*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(0 results)**
Health Technology Assessment Unit at McGill *www.mcgill.ca/tau/*	12 March 2012	Browsed list **(0 results)**
Medical Advisory Secretariat *www.health.gov.on.ca/english/providers/program/mas/mas_mn.html*	12 March 2012	Browsed list **(0 results)**
Dissertations		
Proquest Dissertations and Theses	13 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive* or permanent birth control **(0 results)**
Search Engines		
Google	14 March 2012	tubal occlusion OR permanent contraceptive OR permanent birth control OR sterilisation OR sterilization -pubmed Essure OR Adiana OR hysteroscopic OR transcervical **(8 results)**
NHS Evidence	14 March 2012	Hysteroscopic sterilization or transcervical sterilization or Essure or Adiana **(2 results)**

††,*, #, and ? are truncation characters that retrieve all possible suffix variations of the root word, for example, surg* retrieves surgery, surgical, surgeon, etc.

Searches separated by semicolons have been entered separately into the search interface.

Literature selection

Two reviewers (CM and MO) screened titles and abstracts and retrieved relevant articles. The same two reviewers determined eligibility of key studies according to the inclusion and exclusion criteria below. Disagreements were resolved by consensus.

Inclusion criteria

Study design: health technology assessments, systematic reviews, and randomized controlled trials will be sought initially. If unavailable, non-randomized controlled trials, comparative studies and cohort or case-control studies will be assessed. If these are also unavailable, single group descriptive studies before-and-after or case series studies will be evaluated. Case reports will be evaluated for safety issues in the absence of other research evidence.

Note: An article is deemed to be a systematic review if it meets all of the following criteria as defined by Cook et al. (1997):[20]

- focused clinical question

- explicit search strategy
- use of explicit, reproducible, and uniformly applied criteria for article selection
- critical appraisal of the included studies
- qualitative or quantitative data synthesis

Population: women seeking permanent tubal sterilization.

Intervention: hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implant, as currently licensed by Health Canada.

Comparator: different techniques used to permanently interrupt tubal patency (for example, laparoscopic tubal ligation, transcervical sterilization).

Setting: any setting (for example, outpatient setting, ambulatory clinic, surgery unit).

Outcome of interest: numeric data on at least one of the following:

- Safety: adverse events that prevent reliance on the implants for contraception, adverse events per procedure reported on day of placement procedure, adverse events reported on short- and long-term follow-up by body systems (for example, genitourinary, abdominal, musculo-skeletal, nervous/psychiatric)
- Efficacy/effectiveness: *primary outcome*: success/failure rate (incidence of unintended pregnancy); *secondary outcomes*: failure of or difficulties with technical approach, health-related quality of life, other woman-important outcomes (tolerance, satisfaction), providers' satisfaction

Language: limited to English. Non-English language articles are excluded unless they are thought to add substantively to the English-language evidence base.

Publication period: January 2006 to February 2012.

Exclusion criteria

Studies are excluded if they meet any of the following criteria:

Study design: conference abstracts, letters, news, editorial comments; studies that included less than 25 women for examination of the efficacy/effectiveness; studies that did not assess tubal occlusion at three months following the procedure; economic evaluation and modeling studies; studies that assess the diagnostic accuracy or utility or reliability of the pelvic x-ray or transvaginal ultrasound or hysterosalpingography (HSG) for confirmation of correct device placement at three months after intervention; animal studies; in vitro studies.

Intervention: tubal female sterilization other than HTS: surgical cutting and ligation of the fallopian tubes with or without a section of tube being removed (salpingectomy), or fallopian tubes mechanically blocked using clips or rings, or electrically coagulated, or blocked due to a reaction induced by chemicals.

Comparator: non-tubal female sterilization, reversible sterilization.

Outcomes: studies that did not report data on any of the pre-defined outcomes.

Quality assessment

Two reviewers (CM and MO) assessed methodological quality of the case series studies using the IHE's quality assessment checklist for case series studies.[12] Disagreements were resolved by consensus. Ratings of individual items on the checklist were summarized both narratively and graphically. Quality assessment results were not used as inclusion or exclusion criteria.

Data extraction

One reviewer (CM) extracted data according to a predetermined data extraction form. Extracted information included: publication and study characteristics (for example, setting, study population, intervention, training of provider), numeric outcome data for efficacy/effectiveness (successful completion of intervention at first and second attempt, reliance on intervention for contraception, pregnancy), numeric outcome data for adverse events (intervention-related adverse events, post-intervention adverse events at short-, medium- and long-term follow-up), other woman-important outcomes (quality of life, satisfaction, tolerance). Extracted information from health technology assessment reviews included: search strategy, study selection and characteristics, quality assessment, results, and conclusions.

Data analysis and synthesis

Data from the included studies was summarized narratively. No statistical pooling of outcome data was performed due to study design. Outcomes were presented in tabular form for comparison.

Appendix T.B: Excluded Studies

Six hundred thirty-two articles were excluded that, on the basis of their abstract, clearly did not meet the inclusion criteria. Copies of the full text of 94 potentially eligible studies were retrieved. Closer examination of the studies revealed that 81 of them did not meet the inclusion criteria specified by the protocol. Consequently those studies were excluded. The primary reasons for exclusion were as follows:

1. The article was not primary original research or secondary research (that is, a systematic review) (n = 22).
2. The article was not published in English (n = 11).
3. The study did not evaluate the safety and or efficacy/effectiveness of HTS as a method for elective permanent sterilization (n = 8).
4. The study was a case report (n = 21) or a non-randomized comparative study that compared the exposure of participants but not the intervention (n = 2).
5. The study did not focus on the technology of interest (n = 3).
6. The study did not focus on the population of interest (n = 1).
7. The study did not report quantitative data on the safety and/or efficacy/effectiveness of Essure® (n = 4).
8. The report was a conference abstract (n = 6).
9. The primary research study did not include at least 25 women for the assessment of efficacy/effectiveness (n = 3).
10. The study was not available (n = 1).

1. The article was not primary original research or secondary research (n = 22).

- Lessard CR, Hopkins MR. Efficacy, safety, and patient acceptability of the Essure™ procedure. *Patient Preference & Adherence* 2011;5:207-212.
- Herbst SJ, Evantash EG. Clinical performance characteristics of the Adiana® system for permanent contraception: the first year of commercial use. *Revue Obstetricale et Gynecologique* 2010;3(4):156-162.
- Basinski CM. A review of clinical data for currently approved hysteroscopic sterilization procedures. *Revue Obstetricale et Gynecologique* 2010;3(3):101-110.
- Palmer SN, Greenberg JA. Transcervical sterilization: a comparison of essure(r) permanent birth control system and adiana(r) permanent contraception system. *Revue Obstetricale et Gynecologique* 2009;2(2):84-92.
- Beerthuizen R. State-of-the-art of non-hormonal methods of contraception: V. Female sterilization. *European Journal of Contraception & Reproductive Health Care* 2010;15(2):124-135.
- Di Spiezio SA. Bettocchi S, Spinelli M, Guida M, Nappi L, Angioni S, et al. Review of new office-based hysteroscopic procedures 2003-2009. *Journal of Minimally Invasive Gynecology* 2010;17(4):436-448.
- Castano PM, Adekunle L. Transcervical sterilization. *Seminars in Reproductive Medicine* 2010;28(2):103-109.
- Connor VF. Essure: a review six years later. *Journal of Minimally Invasive Gynecology* 2009;16(30):282-290.

- Sagili H, Divers M. Hysteroscopic sterilisation with Essure: a promising new alternative to tubal ligation? *Journal of Family Planning & Reproductive Health Care* 2008;34(2):99-102.
- Qureshi NS. The feasibility, success and patient satisfaction associated with outpatients hysteroscopic sterilization. *BJOG* 2007;114(11):1449-1450.
- Valle RF. Re: Case report of failed tubal occlusion using Essure pbc (permanent birth control) hysteroscopic sterilisation procedure. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 2007;47(2):155-156.
- Valle RF. Tubal perforation by ESSURE microinsert: clearly not a tubal perforation but a cornual-uterine perforation. *Journal of Minimally Invasive Gynecology* 2006;13(5):487-488.
- Glasser MH. Tubal perforation by ESSURE microinsert: a tubal perforation? *Journal of Minimally Invasive Gynecology* 2006;13(5):487.
- Haneke K, Sokal D. Transcervical sterilization. *Current Opinion in Obstetrics & Gynecology* 2008;20(2):182-183.
- Transcervical sterilization. *Clinical Privilege White Paper* 2006;236:1-12.
- Siristatidis C, Chrelias C, Salamalekis G, Kassanos D. Office hysteroscopy: Current trends and potential applications: A critical review. *Archives of Gynecology and Obstetrics* 2010;282(4):383-388.
- Hurskainen R, Hovi SL, Gissler M, Grahn R, Kukkonen-Harjula K, Nord-Saari M, Makela M. Hysteroscopic tubal sterilization: a systematic review of the Essure system. *Fertility and Sterility* 2010;94(1):16-19.
- Smith RD. Contemporary hysteroscopic methods for female sterilization. *International Journal of Gynecology and Obstetrics* 2010;108(1):79-84.
- Abbott J. Transcervical sterilization. *Current Opinion in Obstetrics and Gynecology* 2008;20(2):183-184.
- Hysteroscopic sterilization leaves patients satisfied. *Contemporary OB/GYN* 2007;52(10):24.
- Jelsema RD. Hysteroscopic tubal sterilization... "greatest benefit" of hysteroscopic tubal sterilization. *Contemporary OB/GYN* 2007;52(1):32.
- Pregnancy after hysteroscopic sterilization. *Contemporary OB/GYN* 2007;52(8):21.

2. The article was not published in English (n = 11).

- Grosdemouge I, Engrand JB, Dhainault C, Marchand F, Martigny H, Thevenot J, et al. Essure implants for tubal sterilisation in France. *Gynecologie, Obstetrique & Fertilite* 2009;37(5):389-395.
- Revel A, Nadjary M, Shushan A. Essure—a novel method of sterilization. *Harefuah* 2008;147(2):107-110.
- Scarabin C, Dhainaut C. The ESTHYME study. Women's satisfaction after hysteroscopic sterilization (Essure micro-insert). A retrospective multicenter survey. *Gynecologie, Obstetrique & Fertilite* 2007;35(11):1123-1128.
- Haute Autorité de santé. Male and female sterilization techniques: Summary of ANAES

assessments (May 2005). *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction* 2006;35(6):551-570.

- Gibon E, Lopes P, Linet T, Martigny H, Orieux C, Philippe HJ. Hysteroscopic fallopian tube sterilization procedure: feasibility and one-year follow-up. *Gynecologie, Obstetrique & Fertilite* 2006;34(3):202-208.
- Paredes AG, Oliver AR, Parra JF. Hysteroscopic tubal sterilization with essure intratubal device: Analysis of results and complications. *Revista Iberoamericana de Fertilidad y Reproduccion Humana* 2010;27(6):525-529.
- Bernardo R, Vazquez-Camino F. Essure as a method of permanent female sterilization. *Clinica e Investigacion en Ginecologia y Obstetricia* 2010;37(6):223-232.
- Varo B, Hidalgo JJ, Rubio JM, Marza A, Oltra D, Monzo A, Romeu, A. Essure hysteroscopic tubal sterilization: Our first clinical experience. *Revista Iberoamericana de Fertilidad y Reproduccion Humana* 2010;27(2):125-129.
- Lassere J. Nickel induced allergic dermatitis and Essure device. *Nouvelles Dermatologiques* 2010;29(3 Part 1):142-143.
- Wischnik A. A proven hysteroscopic sterilization procedure—ESSURE. *Internistische Praxis* 2008;48(1):458-459.
- Agostini A, Crochet P, Blanc K, Collette E, Cravello L, Blanc B. Vaginoscopic hysteroscopy. *Gynecologie Obstetrique Fertilite* 2006;34(5):420-422.

3. The study did not evaluate the safety and or efficacy/effectiveness of HTS as a method for elective permanent sterilization (n = 8).

- Panel P, Grosdemouge I, Houllier M, Renouvel F, Friederich L, Le Tohic A. Bipolar hysteroscopic procedures and placement of Essure microinserts for tubal sterilization: a case control study. *Fertility & Sterility* 2011;95(7):2422-2425.
- Legendre G, Gervaise A, Levaillant JM, Faivre E, Deffieux X, Fernandez H. Assessment of three-dimensional ultrasound examination classification to check the position of the tubal sterilization microinsert. *Fertility & Sterility* 2010;94(7):2732-2735.
- Veersema S, Vleugels MP, Moolenaar LM, Janssen CA, Brolmann HA. Unintended pregnancies after Essure sterilization in the Netherlands. *Fertility & Sterility* 2010;93(1):35-38.
- Lopes P, Gibon E, Linet T, Philippe HJ. Hysteroscopic tubal sterilization with Essure intratubal devices: a case-control prospective with inert local anesthesia or without anesthesia. *European Journal of Obstetrics, Gynecology, & Reproductive Biology* 2008;138(2):199-203.
- Levy B, Levie MD, Childers ME. A summary of reported pregnancies after hysteroscopic sterilization. *Journal of Minimally Invasive Gynecology* 2007;14(3):271-274.
- Kerin JF, Munday D, Ritossa M, Rosen D. Tissue encapsulation of the proximal Essure micro-insert from the uterine cavity following hysteroscopic sterilization. *Journal of Minimally Invasive Gynecology* 2007;14(2):202-204.
- Nichols M, Carter JF, Fylstra DL, Childers M, Essure System U.S. Post-Approval Study

Group. A comparative study of hysteroscopic sterilization performed in-office versus a hospital operating room. *Journal of Minimally Invasive Gynecology* 2006;13(4):447-450.

- Xia EL, Li TC, Yu D, Huang XW, Zheng J, Liu YH, Zhang M. The occurrence and outcome of 39 pregnancies after 1621 cases of transcervical resection of endometrium. *Human Reproduction* 2006:21(12):3282-3286.

4. The study was a case report (n = 21) or non-randomized comparative study that compared the exposure of participants but not the intervention (n = 2).

- Belotte J, Shavell VI, Awonuga AO, Diamond MP, Berman JM, Yancy AF. Small bowel obstruction subsequent to Essure microinsert sterilization: a case report. *Fertility & Sterility* 2011;96(1):e4-6.
- Solt I, Ioffe Y, Elmore RG, Solnik MJ. Group A streptococcal peritonitis and ruptured tubo-ovarian abscess three years after Essure® insertion: a case report. *Journal of Women's Health* 2011;20(5):781-783.
- Borley J, Shabajee N, Tan TL. A kink is not always a perforation: assessing Essure hysteroscopic sterilization placement. *Fertility & Sterility* 2011;95(7):2429.
- Moawad N, Mansuria S. Essure perforation and chronic pelvic pain. *Journal of Minimally Invasive Gynecology* 2011;18(3):285-286.
- Brown WW, III. An unusual complication of hysteroscopic sterilization. *Journal of Ultrasound in Medicine* 2011;30(5):707-709.
- Bjornsson HM, Graffeo CS, Davis SS. Ruptured ectopic pregnancy after previously confirmed tubal occlusion by the Essure procedure. *Annals of Emergency Medicine* 2011;57(3):310-311.
- Al-Safi Z, Shavell VI, Katz LE, Berman JM. Nickel hypersensitivity associated with an intratubal microinsert system. *Obstetrics & Gynecology* 2011;117(2 Pt 2):461-462.
- Mahmoud MS, Fridman D, Merhi ZO. Subserosal misplacement of Essure device manifested by late-onset acute pelvic pain. *Fertility & Sterility* 2009;92(6):2038.
- Gerritse MB, Veersema S, Timmermans A, Brolmann HA. Incorrect position of Essure microinserts 3 months after successful bilateral placement. *Fertility & Sterility* 2009;91(3):930-935.
- Hur HC, Mansuria SM, Chen BA, Lee TT. Laparoscopic management of hysteroscopic essure sterilization complications: report of 3 cases. *Journal of Minimally Invasive Gynecology* 2008;15(3):362-365.
- Booker CJ, Yarwood RL, Dodson WC. Dislodged Essure microinsert. *Fertility & Sterility* 2008;89(4):964-965.
- Famuyide AO, Hopkins MR, El-Nashar SA, Creedon DJ, Vasdev GM, Driscoll DJ, et al. Hysteroscopic sterilization in women with severe cardiac disease: experience at a tertiary center. *Mayo Clinic Proceedings* 2008;83(4):431-438.
- Tatalovich JM, Anderson TL. Hysteroscopic sterilization in patients with a Mirena intrauterine device: transition from extended interval to permanent contraception. *Journal of Minimally Invasive Gynecology* 2010;17(2):228-231.

- Moses AW, Burgis JT, Bacon JL, Risinger J. Pregnancy after Essure placement: report of two cases. *Fertility & Sterility* 2008;89(3):724.
- Podolsky ML, Desai NA, Waters TP, Nyirjesy P. Hysteroscopic tubal occlusion: sterilization after failed laparoscopic or abdominal approaches. *Obstetrics & Gynecology* 2008;111(2 Pt 2):513-515.
- Beckwith AW. Persistent pain after hysteroscopic sterilization with microinserts. *Obstetrics & Gynecology* 2008;222(2 Pt 2):511-512.
- Ory EM, Hines RS, Cleland WH, Rehberg JF. Pregnancy after microinsert sterilization with tubal occlusion confirmed by hysterosalpingogram. *Obstetrics & Gynecology* 2008;111(2 Pt 2):508-510.
- Lannon BM, Lee SY. Techniques for removal of the Essure hysteroscopic tubal occlusion device. *Fertility & Sterility* 2007;88(2):497.
- Hastings-Tolsma M, Nodine P, Teal SB, Embry J. Pregnancy outcome after transcervical hysteroscopic sterilization. *Obstetrics & Gynecology* 2007;110(2 Pt 2):504-506.
- Karthigasu KA, Garry R, Hart R. Case report of failed tubal occlusion using Essure pbc (permanent birth control) hysteroscopic sterilisation procedure. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 2006;46(4):365-367.
- Omurtag K, Pauli S, Session D. Spontaneous intrauterine pregnancy after unilateral placement of tubal occlusive microinsert. *Fertility & Sterility* 2009;92(1):393-397.
- Pyke R, Blackwood LR. Complication of the essure implant sterilization procedure: A case report. *Journal of Gynecologic Surgery* 2008;24(1):37-42.
- Arjona JE, Serrano JJ, Povedano B, Carrasco S, Castelo-Branco C. Unintended pregnancy after long-term Essure microinserts placement. *Fertility and Sterility* 2010;94(7):2793-2795.

5. The study did not focus on the technology of interest (n = 3).

- Anderson TL, Vancaillie TG. The Adiana System for permanent contraception: safety and efficacy at 3 years. *Journal of Minimally Invasive Gynecology* 2011;18(5):612-616.
- Vancaillie TG, Anderson TL, Johns DA. A 12-month prospective evaluation of transcervical sterilization using implantable polymer matrices. *Obstetrics & Gynecology* 2008;112(6):1270-1277.
- Lawrie TA, Nardin JM, Kulier R, Boulvain M. Techniques for the interruption of tubal patency for female sterilization. *Cochrane Database of Systematic Reviews*, Issue 2, 2011.

6. The study did not focus on the population of interest (n = 1).

- Savage UK, Masters SJ, Smid MC, Hung YY, Jacobson GF. Hysteroscopic sterilization in a large group practice: experience and effectiveness. *Obstetrics & Gynecology* 2009;114(6):1227-1231.

7. The study did not report quantitative data on the safety and/or efficacy/effectiveness of Essure® (n = 4).

- Franchini M, Boeri C, Calzolari S, Imperatore A, Cianferoni L, Litta P, et al. Essure

transcervical tubal sterilization: a 5-year x-ray follow up. *Fertility & Sterility* 2011;95(6):2114-2115.

- Panel P, Grosdemouge I. Predictive factors of Essure implant placement failure: prospective, multicenter study of 495 patients. *Fertility & Sterility* 2010;93(1):29-34.
- Shavell VI, Abdallah ME, Diamond MP, Berman JM. Placement of a permanent birth control device at a university medical center. *Journal of Reproductive Medicine* 2009;54(4):218-222.
- Shavell VI, Abdallah ME, Diamond MP, Kmak DC, Berman JM. Post-Essure hysterosalpingography compliance in a clinic population. *Journal of Minimally Invasive Gynecology* 2008;15(4):431-434.

8. The report was a conference abstract (n = 6).

- Castillo JR, Sanchez EV, Canizares BP, Cara MD, Gonzalez JL, Berral JEA. Long term efficacy of female sterilization with Essure device. *Human Reproduction* 2011;26:1247.
- Sanchez EV, Castillo JER, Berral JEA, Canizares BP, Gonzalez JL, Cara MD. Pregnancy outcomes and perinatal results of unintended pregnancies following Essure AE sterilization: descriptive study of 10 cases. *Human Reproduction* 2011;26:1247.
- Zapata M, Chen A, Rible R, Parvataneni R. Analysis of hysteroscopic sterilization versus the intrauterine device as long-term contraception. *Contraception* 2010;82(2):201.
- Sakinci M, Aksu T. Hysteroscopic tubal sterilization; research on safety and effectiveness of microinsert method. *Human Reproduction* 2007;22:1173-1174.
- Kerin JF. Tissue encapsulation of the essure device from the uterine cavity after hysteroscopic sterilization. *Obstetrics and Gynecology* 2006;107(4):3S.
- Kerin JF. Hysteroscopic sterilization—A safe choice for high-risk women. *Obstetrics and Gynecology* 2006;107(4):15S.

9. The primary research study did not include at least 25 women for the assessment of efficacy/effectiveness (n = 3).

- Detollenaere RJ, Vleugels MPH, Van Eijndhoven HWF. Combining NovaSure endometrial ablation and Essure hysteroscopic sterilization: A feasibility study to evaluate the confirmation tests. *Gynecological Surgery* 2011;8(1):59-63.
- Agostini A, Crochet P, Petrakian M, Estrade JP, Cravello L, Gamerre M. Hysteroscopic tubal sterilization (Essure) in women with an intrauterine device. *Journal of Minimally Invasive Gynecology* 2008;15(3):277-9.
- Wittmer MH, Famuyide AO, Creedon DJ, Hartman RP. Hysterosalpingography for assessing efficacy of Essure microinsert permanent birth control device. *American Journal of Roentgenology* 2006;4:955-958.

10. The study was not available (n = 1).

- Finnish Office for Health Care Technology Assessment. *ESSURE sterilization (Project record)*. Helsinki: Finnish Office for Health Care Technology Assessment (FinOHTA) 2007.

Appendix T.C: Study Characteristics

Table T.C.1: Case series studies

Author, year, country, objective, design, setting, enrollment, study period, follow-up(s) Manufacturer (device characteristics) Characteristics intervention Funding & competing interest	Population characteristics Inclusion criteria Exclusion criteria	Efficacy results	Safety results/adverse events Authors' conclusion
Andersson et al. 2009[2] Sweden *Objective(s)*: to evaluate the short- and long-term results of hysteroscopic sterilization in an outpatient setting Case series, prospective, single centre *Setting*: university hospital outpatient department, obstetrics & gynecology *Enrollment*: NR *Study period*: 2002 to 2007 *Follow-up*: at three months; survey up to five years after procedure (mean follow-up: 23 months [range 7 to 67]) *Device characteristics & intervention*: Essure® Permanent Birth Control System, Conceptus Inc., San Carlos, CA, USA *Pre-intervention preparations*: one hour prior the intervention, NSAIDs or opioids *Anesthesia*: local, paracervical block early in the study (44/61); then administered only if severe pain *Time procedure* (mean, min.): 30	*Enrolled/analyzed (n)*: 61/61 *Age (mean)*: 39.6 yr (range 30 to 46) *BMI*: NR *Parity (mean)*: 2.4 children (range 1 to 5) *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity*: n = 37 with contraindications for LTS: diabetes mellitus, obesity, medical disease (details NR), previous abdominal or pelvic surgery *Inclusion criteria*: NR *Other specifications*: included women on days three to 10 of the menstrual cycle, if possible; with pregnancy test on the day of procedure *Exclusion criteria*: NR	*Bilateral placement*: 58/61 (95%) *1st attempt*: 52/61 *2nd attempt*: 6/61 *Unilateral*: – *Failed placement*: 3/61 *Reason failure, first attempt* (n): material defects (2); tubular spasm (4); obstructed view (2); failure to pass the cervix (1) *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: 57/58 confirmed by X-ray or ultrasound, HSG in one woman demonstrated unilateral patency due to incorrect device placement *LTS*: after first attempt (3); unilateral LTS at three-month follow-up (1) *Pregnancy*: no pregnancy reported (source: survey) *Lost to follow-up*: all women participated in the follow-up at three months *Satisfaction women*: survey 50/61; overall satisfaction with the procedure, all women will recommend the procedure to others	*AE that prevented reliance on Essure® for contraception*: NR *AE related to intervention*: vasovagal reactions (3/61), light bleeding (2/61); pain requiring additional analgesia (36/61); self- reported pain on VAS: mean 5.4 (range 1 to 10) (no details reported about the scale) *AE post-intervention short-term*: nausea or uterine cramping (15/61); analgesia needed in the first two hours (9/61); self-reported pain on VAS during the first two hours: mean 3.5 (range 0 to 6); no postoperative complications related to the procedure *AE post-intervention medium-term:* NR *AE post-intervention long-term*: survey at seven to 67 months (50/61 responses): subsequent menstrual periods heavier (9/50); lighter (8/50) *Authors' conclusion*: Essure® sterilization is a safe effective method for female sterilization that is feasible in the outpatient setting. *Other notes*: The procedures performed toward the end of the study were of shorter duration and

(range 7 to 70) *Recovery time*: approximately two hours *Provider, qualification*: surgeon; NR *Funding*: Swedish Medical Research Council, the Karolinska Intitutet Foundation, Stockholm *Competing interest*: consulting fees for teaching about Essure® procedure		*Satisfaction provider*: NR	associated with lower pain scores on a VAS.
Chapa et al. 2011[8] USA *Objective(s)*: to determine the ability of in-office two-dimensional TVU to predict proper tubal occlusion/micro-insert location compared with subsequent HSG; secondary outcomes: to determine the rate of bilateral placements, HSG follow-up at three months, and clinical pregnancy rate (*note: Only the secondary outcomes are abstracted*) Case series, prospective, single centre *Setting*: community-based, private obstretics & gynecology medical office *Enrollment*: NR *Study period*: March 2007 to December 2009 *Follow-up*: at three months *Device characteristics & intervention*: Essure®, Conceptus, Inc., model ESS 305 *Pre-intervention preparations*: all women, oral medroxyprogesterone acetate for the immediate 10 days preceding the HTS; urine pregnancy test before the HTS; 30 minutes prior	*Enrolled/analyzed (n)*: 161/161 *Age (mean)*: NR *BMI*: NR *Parity (mean)*: NR *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity*: NR *Inclusion criteria*: women of reproductive age desiring permanent sterilization *Exclusion Criteria*: history of prior tubal surgery, a stated allergy to nickel/contrast media, women who were < six weeks postpartum	*Bilateral placement*: 158/161 (98%) *1st attempt*: 154/161 *2nd attempt*: 4/161 *Unilateral*: – *Failed placement*: 3/161 *Reason failure*: NR *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: HSG 125/158, TVU 139/154 ; at six-month: HSG 2/127 *LTS*: after first attempt (3) *Pregnancy*: 0/127 *Lost to follow-up*: HSG: 31; *reason*: NR *Satisfaction women*: NR *Satisfaction provider*: NR	*AE that prevented reliance on Essure® for contraception*: no micro-insert expulsions or suspected uterine perforations were encountered up to the three-month follow-up *AE related to intervention and post-intervention short-term*: NR *AE post-intervention medium-term*: NR *AE post-intervention long-term*: NR

the procedure: analgesic (toradol and acetaminophen/hydrocodone). *Anesthesia*: deep lower uterine (paracervical) block *Time procedure* (mean, min.): NR *Recovery time*: NR *Provider, qualification*: NR *Funding*: no funding *Competing interest*: medical consultant, member of the Advisory Panel for Conceptus Inc. (one author)			
Levie et al. 2006[5] USA *Objective(s)*: to evaluate the efficacy of performing the Essure® HTS in an office-based setting using only NSAID and local anesthesia Case series, prospective, single centre *Setting*: university outpatient office *Enrollment*: NR *Study period*: NR *Follow-up*: at three months *Device characteristics & intervention*: Essure® *Pre-intervention preparations (n)*: 30 minutes prior the intervention: intramuscular NSAIDs 99/102 *Anesthesia (n)*: paracervical block 101/102 *Time procedure* (mean ± SD): 12.4 min. ±6.35; first 13 cases: 17.2 min.; next 89 cases: 11.2 min. ±6.46 *Recovery time*: NR	*Enrolled/analyzed (n)*: 102/102 *Age (mean ± SD)*: 35 yr ±5.9 (range 22 to 44) *BMI(mean ± SD)*: 30.3 kg/m^2 ±6.9 (range 18.6 to 51) *Parity (mean ± SD)*: 3 ±1.28 (0 to 8) *Gravity (mean)*: NR *Ethnicity (n)*: hispanic (63), black (27), white (5), Asian (1) other (6) *Comorbidity (n)*: prior abdominal/pelvic surgery (45); Cesarean section (≥1) (38); STD history: chlamydia (10), gonorrhea (4), PID/salpingitis/TOA (3); polypectomy at the time of the Essure® placement (6) *Inclusion criteria*: desire for permanent sterilization *Exclusion criteria*: no women were excluded on the bases of historical factors	*Bilateral placement*: 98/102 (96%) *1st attempt*: 97/102 *2nd attempt*: 1/102 *Unilateral*: – *Failed placement*: 4/102 *Reason failure*: anatomical factors: bicornuate uterus (1), extremely lateral tubes + severe obesity (1), polypectomy of a polyp obscuring the tubal ostia (1); absence of visualization of tubal ostia (1) *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: 89/98 confirmed by HSG; repeated HSG other follow-up time: 1/98 *LTS*: at three-month (one free coil in the uterine cavity) *Pregnancy*: one woman; *reason*: misinformed staff regarding last menstual period, HTS performed on day 14 of her cycle, absence of contraception after HTS *Lost to follow-up*: seven women; *reason*: declined HSG (4); changed contact information (3)	*AE that prevented reliance on Essure® for contraception*: NR *AE related to intervention and post-intervention short-term*: no complications reported *AE post-intervention medium-term*: NR *AE post-intervention long-term*: NR *Authors' conclusion*: The results show that office-based HTS is a feasible and effective method for permanent sterilization. It is easily performed in an outpatient setting without the need for general anesthesia or sedation.

Provider, qualification: all procedures were done under the supervision of a senior faculty member with expertise in hysteroscopy (primary investigator); approximately half of procedures were done by residents, fellows, or attending physicians learning the procedure *Funding*: NR *Competing interest*: NR		*Satisfaction women*: NR *Satisfaction provider*: short time required to perform the procedure; significant improvement in office productivity; short learning curve to achieve proficiency; procedure can be recommended for general obstetrics/gynecology after an appropriate training course and supervision for the first several procedures	
Levie et al. 2010[10] This study is a multiple publication of Levie et al. 2006[5]. *Objective*: to assess pain and women's satisfaction (tolerability) with office-based hysteroscopic sterilization. *Study period*: June 2003 to June 2006 *Device characteristics & intervention*: *Time procedure* (n): ≤8 min (97), >8 min (109) *Funding*: no funding *Note: Study does not provide information about the follow-ups at three months or other time; only the AE related to the intervention are abstracted in table*	*Enrolled/analyzed (n)*: 209/209 *Age (mean ± SD)*: 35.1 yr ±5.2 *BMI (mean ± SD)*: 30.5 kg/m^2 ±6.6 (range 17 to 50.1) *Parity (mean ± SD)*: 2.7 ±1.0 (0 to 6) *Gravity (mean)*: NR *Ethnicity (n)*: hispanic (63), black (27), white (5), Asian (1) other (6) *Comorbidity (n)*: prior abdominal surgery (97) *Ethnicity (n)*: Hispanic (136), black (62), white (6), other (5)	*Placement status* Successful (n): 198/209 Unsuccessful (n): 11/209 *No other efficacy results reported*	*AE that prevented reliance on Essure® for contraception*: NR *AE related to intervention*: overall average pain: 2.6 ±2.05; 95% CI (2.3 to 2.9) (on a pain scale with 0 indicating no pain and 10 indicating the worst pain possible); standardized pain score (SPS—see legend for details): 145/209 felt that average pain experienced during the procedure was equal to or less than the typical pain they experience with their menses; overall SPS -0.20 ±0.843; 95% CI (-0.313 to -0.0839); the average pain for the procedure was statistically significantly lower than average menses pain (p<0.001); most pain for the procedure: 124 women reported pain scores lower than menses pain scores SPS: -0.040 ±0.827; 95% CI (-0.153 to 0.0725) (p = 0.32) *Authors' comment*: Higher pain scores statistically significant were found (by multivariate analysis & logistic regression) in hispanic etnicity (only by multivariate analysis), higher education, a history of pregnancy termination, longer procedural time; SPS higher pain scores statistically significant (multivariate analysis and multivariate ligistic regression): history of

			Cesarean section (only multivariate analysis), higher household income, longer procedural times.
Mascaro et al. 2008 [7] Spain *Objective(s)*: to evaluate the feasibility of Essure® procedure in IUD users and the use of the IUD as an alternative nondefinitive cotraceptive method for three months post-HTS Case series, unclear, single centre *Setting*: office, tertiary university hospital *Enrollment*: consecutive *Study period*: December 2004 to April 2007 *Follow-up*: at three months *Device characteristics & intervention*: Essure®, Conceptus Inc., Montain View, CA *Pre-intervention preparations*: one hour prior the intervention: oral NSAID *Anesthesia*: no local anesthesia needed *Time procedure* (mean, min.): 8.7 ±4.4 (range 5 to 20) *Recovery time*: approximately 25 minutes *Provider, qualification*: NR *Funding*: NR *Competing interest*: no competing interest	*Enrolled/analyzed (n)*: 28/28 *Age (mean)*: NR (range 26 to 44 yr) *BMI*: NR *Parity (mean)*: NR *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity*: NR *Inclusion criteria*: IUD users requesting a definitive sterilization method and willing to use an IUD for three months after device placement *Exclusion criteria*: all conditions considered contraindication for the Essure® procedure as defined in the instructions for use, except for use of an IUD for contraception after micro-insert placement procedure Whenever possible, micro-insert placement was performed during the early proliferative phase of the menstrual cycle, to enhance visualization of uterine cavity and fallopian tubal ostia.	*Bilateral placement*: 27/28 (93%) *1st attempt*: 25 women (20 IUD users + five after removal of IUD) *2nd attempt*: two women after removal of IUD *Unilateral*: one woman (showed unilateral stenotic tube with spontaneous expulsion of the Essure®) *Failed placement in IUD users (1st attempt)*: 8/28 *Reason failure*: anatomic: defect visual by uterine bleeding (1), no visible ostium (1), stenotic tubes (2); procedure related: IUD obstructs uterotubal junction (2), IUD descended (2) *Failed placement at three-month follow-up*: 1/27; *reason*: incorrect placement *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: 26/27 (19 in IUD users (X-ray and TVU) + five after removal of IUD (X-ray and TVU) + two after removal of IUD (HSG)) *LTS*: no case reported *Pregnancy*: no pregnancy reported (duration of follow-up not clearly reported) *Lost to follow-up*: one woman; *reason*: NR *Satisfaction women*: high, no other information reported *Satisfaction provider*: NR	*AE that prevented reliance on Essure® for contraception*: no tubal perforations were reported *AE related to intervention*: no major complications (infections, uterine or hemorrhage) or adverse events were reported *AE post-intervention short-term*: NR *AE post-intervention medium-term*: NR *AE post-intervention long-term*: NR *Authors' conclusion*: HTS with Essure® micro-inserts in IUD users is feasible and likely safe and reliable; could be an option for the three-month follow-up period for women who are not good candidates for alternative methods of contraception (e.g., obese women, smokers, women older than age 35). *Other notes*: the main causes that prevented micro-insert placement in IUD user were: ostia blocked by IUD arms and inadequate visualization due to bleeding or malpositioned IUD; women had the copper-containing Multiload or a "T-shaped" IUD (considered not very flexible).

Mino et al. 2007 [4] Spain *Objective(s)*: to evaluate the success rate of the Essure® procedure in a large cohort of women at a single centre and to capture physician assessment of the procedure, as well as information regarding women's satisfaction Case series, prospective, single centre *Setting*: Outpatient teaching hospital *Enrollment*: NR *Study period*: January 2003 to January 2005 *Follow-up*: at three months *Device characteristics & intervention*: Essure® Permanent Birth Control System, Conceptus Inc., San Carlos, CA, USA *Pre-intervention preparations*: one hour prior the intervention with NSAIDs & benzodiazepine *Anesthesia (n)*: paracervical only for extreme anxiety and pain (433) *Time procedure* (mean, min.): 6.8 (range 5 to 18) *Recovery time (n)*: returned to normal activity same day (719), the day following the procedure (132), more than one day afterward (6) *Provider, qualification*: two hysteroscopists *Funding*: NR *Competing interest*: NR	*Enrolled/analyzed (n)*: 857/857 *Age (mean)*: 36 yr (range 22 to 49) *BMI*: NR *Parity (n)*: nulliparous (4), one (45), two (552), three (216), four or more (40) *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity*: NR *Inclusion criteria*: desire for permanent sterilization and normal gynecological physical examination and pelvic sonography *Exclusion criteria*: NR	*Bilateral placement*: 830/857 (97%) *1st attempt*: 812/857 *2nd attempt*: 18/857 *Unilateral*: 15/857; *Reason*: previous salpingectomy (14), unicornuate uterus (1) *Failed placement*: 12/857 (bilateral [5/12], unilateral [7/12]); in all cases occlusion was confirmed by subsequent HSG at three-month follow-up: (a) four expulsions of the Essure® device, subsequently replaced at a second attempt; (b) two partial expulsions, one of which subsequently replaced; (c) one false passage insertion between endometrium and myometrium which was subsequently placed correctly; (d) one intra-abdominal device migration; (e) one device insertion in pregnant woman *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: 835/845 confirmed by abdominal X-ray ±HSG; at six-month: 9/845; in total 77 women had HSG *LTS*: no case reported *Pregnancy*: one woman pregnant at the time of Essure® insertion (used oral contraceptive for three months prior to device insertion), underwent a termination of the pregnancy. No other pregnancies reported, duration of follow-up *Lost to follow-up*: all women completed the follow-up *Satisfaction women*: overall satisfaction was very high (806/857) and high (51/857) at three-month	*AE that prevented reliance on Essure® for contraception*: NR *AE related to intervention*: procedure more painful than normal menses, 33/857; procedure of equal discomfort, 103/857; little or no discomfort, 721/857 *AE post-intervention short-term*: pain which necessitated oral analgesic, 77/857 (day of procedure [33], two days [23], three days [10], four or more days [9]) *AE post-intervention medium-term*: no changes in the volume or pattern of menstruation, discomfort during sexual intercourse, and any notable lifestyle modifications following the procedure (n = 857, up to three-month follow-up) *AE post-intervention long-term*: NR *Authors' conclusion*: The procedure is quick and well tolerated and it permits a rapid return to normal activity producing a high degree of women's satisfaction.

		follow-up *Satisfaction provider*: the hysteroscopists described the procedure as very difficult in 127/851 (15%) of the cases, mainly due to anatomical tubal anomalies or tubal spasm	
Arjona et al. 2008[9] This study is a multiple publication of Mino et al. 2007.[4] *Objective(s)*: to evaluate women's satisfaction, adverse effects and tolerance of hysteroscopic sterilization. *Study period*: January 2003 to June 2006 *Follow-up*: day one, three months, up to 42 months *Device characteristics & intervention*: Essure® Permanent Birth Control System, Conceptus Inc., Mountain View, CA, USA *Recovery time*: most women (number NR) did not need recovery time. All women were discharged same day *Provider, qualification*: gynecologist *Funding*: Andalusia Health Service	*Enrolled/analyzed (n)*: 1630/varies with duration of follow-up *Age (mean ± SD)*: 36.6 yr ±5.7 (range 32 to 41) *Gravity (mean ± SD)*: 2.4 ±1.2	*Pregnancy*: three cases diagnosed in the first 90 days after procedure. No other pregnancies reported, among the 1419 women who have ≥18 months of follow-up (until June 2007) *Lost to follow-up*: 15 women, due to failure in the procedure *Satisfaction women*: pain: procedure well tolerated (rated excellent or very good): 1398/1615; at survey, first and second day (n = 1612): very satisfied with the procedure 1516/1612; somewhat satisfied 96/1612; no women reported dissatisfaction; at 18 months* (n = 722): highly satisfied (VAS: 10) 658/722; lowest rating was 8 on a scale from 0 (absolutely dissatisfied) to 10 (highly satisfied); most positive aspects (n): avoidance of an operating room (380), quick and comfortable procedure (144), definitive procedure (131), normal life (32), other (34)	*AE that prevented reliance on Essure® for contraception* (n = 1615): intramyometrial placement of the devices (two, found at three-month by HSG); expulsion of one micro-insert (12); migration of device to abdominal cavity (3); nickel allergy (1) *AE related to intervention* (n = 1615): vasovagal syncope resolved with medication: 16/1615; pain (survey) similar to normal menstruation (rated good): 166/1615; more pain than with menstruation was rated fair or poor by 50 women *AE post-intervention short-term* (n = 1612): returned to daily activity the day after: 239/1612; needed more than one day to recover: 20/1612; needed oral analgesics for one or two days: 113/1612 *AE post-intervention medium-term*: NR *AE post-intervention long-term*: (up to 42 months follow-up) NR *Authors' conclusion*: The Essure® micro-inserts can be placed in a usual gynecologic consultation room in standard conditions without any type of anesthesia or sedation and are associated with high overall women's satisfaction and tolerance.

Sinha et al. 2007[1] UK *Objective(s)*: to determine the feasibility and women's satisfaction with sterilization using the Essure® system without general anesthesia or conscious sedation Case series, prospective, single centre *Setting*: teaching hospital outpatient hysteroscopy clinic *Enrollment*: consecutive *Study period*: August 2002 to June 2006 *Follow-up*: at three months *Device characteristics & intervention*: Essure® Permanent Birth Control System, Conceptus Inc., San Carlos, CA, USA *Pre-intervention preparations (n)*: one hour prior the intervention: oral analgesics NSAIDs or opioids (104/112) *Anesthesia*: local up to March 2006 when protocol was changed to use vaginoscopy without local anesthesia and local anesthetic was used only if necessary *Time procedure* (mean, min.): 14 (range 3 to 50); vaginoscopically: 11 (range 5 to 20); (p = 0.2) *Recovery time*: 30 minutes to four hours *Provider, qualification*: two experienced surgeons (number of interventions per surgeon: 88/112 and 24/112), one nurse for support and	*Enrolled/analyzed (n)*: 112/112 *Age (mean)*: 36 yr (range 23 to 48) *BMI(mean)*: 27 kg/m^2 (range 17 to 53) *Parity (mean)*: NR *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity* (n = 21): menstrual disorders (12), intrauterine pathology recorded at hysteroscopy (9), submucous fibroids (5), endometrial polyps (1), uterine anomalies (2), cervical stenosis (1) *Inclusion criteria*: NR *Exclusion criteria*: women with desire to preserve their fertility; unable to consent to the procedure; positive urinary pregnancy tests on admission; suspected lower genital tract infection	*Bilateral placement*: 103/112 (92%) (95% CI 85 to 96) *1st attempt*: NR *2nd attempt*: NR *Unilateral*: no case reported *Failed placement*: 9/112 *Reason failure (n)*: anatomic factors (inability to access the uterine cavity [1], nonidentification of one tubal ostia [2], stenosis of tubal ostia [2]); woman factors (obesity + large uterus [1], anxiety [1]); operative factors (poor visualization of tubal ostia [1], inability to optimally site hysteroscope [1]); six of nine failures occurred in the first 14 women *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: 81/82 (95% CI 93 to 100) confirmed by abdominal X-ray (first 16 procedures) or HSG (65); at six-month: 1/82 confirmed by HSG *LTS*: eight women who failed procedure; one woman had Mirena® intrauterine system *Pregnancy*: to date, no pregnancies have been reported (length of follow-up not stated) *Lost to follow-up*: 21 women, *reason*: NR *Satisfaction women*: postal survey at three-month follow-up 84/112; response rate: 76/84. More than 90% of respondents were satisfied with their overall experience of the outpatient procedure and subsequent radiological testing and would recommend it; 42/58 reported the HSG to be an "acceptable" test. Main reason for non-satisfaction: painful	*AE that prevented reliance on Essure® for contraception*: uterine perforation following blind cervical dilatation in women with cervical stenosis (1/112) *AE related to intervention*: minor self-limiting vasovagal reactions (5/112); survey results (76 responses): pain or discomfort (57/76 (95% CI 64 to 84%), 10/57 described having severe pain *AE post-intervention short-term*: oral or intramuscular analgesia 71/112; survey results (76 responses): post-operative pain 60/76 (95% CI 68 to 88); described having severe pain (6/60); pain lasted < four hours (37/60); pain lasted > eight hours (8/60) *AE post-intervention medium-term*: survey results (76 responses): at three months: vaginal bleeding or discharge 31/76, duration Me = three days; urinary tract infection treated with antibiotics 2/76; subsequent menstrual period abnormal 23/76 (heavier loss [5], lighter loss [1], delayed [3], not specified [14]); menstrual period persistent change at three months 20/76 (heavier loss [14], irregular [2] intermenstrual bleeding [1], amenorrhea [3]); new pain or discomfort with sexual intercourse (2/76) *AE post-intervention long-term*: NR *Authors' conclusion*: The procedure conducted without sedation and general anesthesia was found successful and safe and associated with high rates of women's satisfaction; if practical, women should be scheduled to have their procedures done in the proliferative phase of the menstrual cycle to optimize successful

distraction *Funding*: NR *Competing interest*: NR		test (22/58). Reasons for choosing HTS: desire to avoid general anesthetic (55/76), avoidance of surgical incisions (45/76), no need for hospital stay (25/76), convenience (25/76). Reasons for disliking of HTS: too many people around (4/76), discomfort (3/76). *Satisfaction provider*: NR	placement of Essure® devices, especially if the uterus is clinically enlarged.
Veersema et al. 2011[6] Netherlands *Objective(s)*: to evaluate the protocol for confirmation of satisfactory Essure® placement using TVU; to analyze the rate of success of placement and effectiveness of the method Case series, prospective, multicentre (five centres) *Setting*: outpatient departments, teaching hospitals *Enrollment*: consecutive *Study period*: March 2005 to December 2007 *Follow-up*: TVU at four weeks and HSG at three months *Device characteristics & intervention*: Essure®, Conceptus Inc., Mountain View, CA *Pre-intervention preparations*: NSAID on the evening before the procedure and one hour before intervention *Anesthesia*: no use of local or general anesthesia *Time procedure* (mean, min. CI): 7.2 (95% CI 7.0 to 7.4); successful bilateral placement: 6.7 (95% CI 6.52 to 6.94); unsuccessful placement:	*Enrolled/analyzed (n)*: 1145/1145 *Age (mean ± SD)*: 39.2 yr ±4.7 (95% CI 38.9 to 39.5) *BMI(mean ± SD)*: 25.1 kg/m^2±5.1 (95% CI 24.8 to 26.0) *Parity (n)*: nulliparous (116), one (159), two (543), three (225), more than three (92) *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity*: NR *Inclusion criteria*: NR *Exclusion criteria*: NR Note: 35 IUDs were left in situ during the HTS procedure and were removed at the three-month follow-up	*Bilateral placement*: 1059/1145 (92%) *1st attempt*: 1034/1145 *2nd attempt*: 25/1145 *Unilateral*: 13/1145; *Reason*: NR *Failed placement*: 98/1145 after first attempt; final failure 73/1145 *Reason failure*: incorrect positioning of one or two devices (two expulsions, seven perforations, five tubal patency) *Satisfactory occlusion (at three-month & other follow-ups)*: at three-month: 1037/1059 confirmed by TVU ± HSG (rely on sterilization due to missing data) *LTS*: NR; 3 LTS reported in the multiple publication by Langenveld et al. 2008[11] *Pregnancy*: 4/1037 at 24 months; *Reason* (one device was absent or incorrectly positioned, three women were noncompliant with the protocol) *Lost to follow-up*: 22 women, *reason*: NR *Satisfaction women*: NR *Satisfaction provider*: NR	*AE that prevented reliance on Essure® for contraception*: expulsion two cases showed by HSG at the three-month follow-up; perforation seven cases showed at HSG at three-month follow-up; in multiple publication[11]: tubal perforation (3), one was diagnosed at one week, the device was removed hysteroscopically followed by LTS on one tube, the second was diagnosed at three months and woman underwent LTS; third case was diagnosed at seven months, device was was left in situ and woman underwent LTS *AE related to intervention*: NR *AE post-intervention short-term*: NR *AE post-intervention medium-term*: NR *AE post-intervention long-term*: NR *Authors' conclusion*: Transvaginal ultrasound (TVU) can be performed in an outpatient setting; in women in whom placement is unsatisfactory or in whom transvaginal ultrasound cannot confirm satisfactory placement, a complementary HSG is required; the Dutch protocol for confirmation of Essure® HTS reduced the number of HSGs and is associated with high woman compliance; in cases of difficult placement, the extra TVU confirmation

11.84 (95% CI 10.26 to 12.70); successful single placement in women with only one tube: 5.82 (95% CI 3.76 to 7.88) *Recovery time*: NR *Provider, qualification*: nine apropriately trained gynecologists with experience in office hysteroscopy trained in HTS with Essure® *Funding*: NR *Competing interest*: consultancy for Conceptus, source Langenveld et al. 2008[11]			at four weeks did not reduce the number of HSGs thus, the need for routine TVU after a difficult HTS procedure should be abandoned, with sole reliance on the three-month HSG as a confirmatory test.
Vellayan et al. 2006[3] UK *Objective(s)*: to report the experience with Essure® technique in terms of success rates, complications, and woman acceptability Case series, unclear design, single centre *Setting*: outpatient hysteroscopy clinic from teaching hospital *Enrollment*: NR *Study period*: November 2002 to November 2005 *Follow-up*: at 48 hours after intervention (telephone survey); at three months *Device characteristics & intervention*: Essure® Permanent Birth Control System: 37 procedures were perfomed with the old device and 63 with the modified Essure® device (introduced in April 2004) *Pre-intervention preparations*: two hours prior the intervention: oral	*Enrolled/analyzed (n)*: 100/100 *Age (mean)*: NR *BMI*: NR *Parity (mean)*: NR *Gravity (mean)*: NR *Ethnicity*: NR *Comorbidity (n)*: intrauterine pathology recorded at hysteroscopy: uterine anomalies: subseptate or bicornuate uterus (2) *Inclusion criteria*: all women referred with a request for permanent contraception *Other specifications*: procedure timed if possible for the first half of the menstrual cycle; urine pregnancy test performed prior to the procedure *Exclusion criteria*: NR	*Bilateral placement*: 87/100 (87%) *1st attempt*: 85/100 *2nd attempt*: 2/100 Uncomplicated bilateral placements reported: 83/100 *Unilateral*: no case reported *Failed placement*: 13/100 (seven during the first 30 procedures and six during the next 30) *Reason failure (n)*: pain (1), obesity (1), failed cannulation (11) (due to blocked tubes [8], declined HSG and opted for a different contraception [2], failed to attend tests [1]); three of five women who had repeated procedures following first failed attempt had tubal blockage on subsequent assessment; three incorrect device placements with initial old devices: in one woman the procedure was successful on second attempt; in one woman, one device migrated distally into the peritoneal cavity and the other device perforated the tube near the cornua—both devices were removed by laparoscopy); in one women one	*AE that prevented reliance on Essure® for contraception*: perforation (1) diagnosed by X-ray at three months *AE related to intervention (n)*: NR *AE post-intervention short-term*: at 48 hours after intervention, telephone survey (37): no pain or mild pain (24/37), moderate pain (8/37), severe pain (6/37); three women would have preferred more pain relief; pain at six days (1); pain at two weeks after procedure (2) *AE post-intervention medium-term (n)*: NR *AE post-intervention long-term*: NR *Authors' conclusion*: Essure® hysteroscopic sterilization is a simple, reproducible procedure that, after appropriate training, can be performed by any gynecologist with experience in outpatient hysteroscopy; the insertion failure was more common with the older devices and was due to pre-existing tubal damage in the majority of cases; the satisfaction survey revealed that the procedure was associated with low

analgesics NSAIDs or opiate *Anesthesia*: NR *Time procedure* (min.): NR *Recovery time*: 30 minutes of the procedure; time to return to normal work, 48 hours on average *Provider, qualification*: three consultant gynecologists experienced in diagnostic and operative outpatient hysteroscopy; two nurses (one attended the woman and one assisted the surgeon and monitored the irrigation fluid) *Funding*: NR *Competing interest*: NR		device incorrectly placed was removed by laparoscopy *Satisfactory occlusion (at three-month & other follow-ups)*: not clearly reported; 79 of 83 uncomplicated cases had abdominal X-ray or HSG to confirm device position; HSG was used in cases of suspected perforation or incorrect placement *LTS*: two cases *Pregnancy*: NR *Lost to follow-up (n)*: not clearly reported (4+4[†]); *reason*: partially reported: failed to attend for assessment (2), awaiting the three-month follow-up (2) *Satisfaction women*: at 48 hours after intervention, telephone survey (37): would recommend this procedure to a friend (36/37), were satisfied with the care they received (37/37) *Satisfaction provider*: NR	pain scores and high satisfaction levels.

*Follow-up period not clearly stated in the publication

[†]Not clearly stated in the publication

AE – adverse event; CI – confidence interval; HSG – hysterosalpingography; HTS – hysteroscopic tubal sterilization; IQR – interquartile range; IUD – intrauterine device; LTS – laparoscopic tubal sterilization; Me – median; N, n – number; NR – not reported; PID – pelvic inflammatory disease; SD – standard deviation; SPS – standardized pain score (obtained by taking the log of the pain score plus 1 divided by the log of the menstrual score plus 1; one point was added to the score to avoid zero values in the denominator, and the log was used to ensure a normal distribution of scores); STD – sexually transmitted disease; TOA – tubo-ovarian abscess; TVU – transvaginal ultrasonography; VAS – visual analogue pain score

Table T.C.2: HTA reports on hysteroscopic tubal sterilization

Study	Inclusion and exclusion criteria; studies included	Main findings; conclusions
Alberta Heritage Foundation for Medical Research[14] Hysteroscopic Tubal Sterilization (Essure® system) Canada June 2006 **Objective**: To review the clinical research evidence on the efficacy/ effectiveness, efficiency, and safety of HTS used for permanent birth control Systematic literature searches from 1999 to February 2006	**Inclusion criteria:** • Intervention: HTS • Device: Essure® system • Indication: permanent method of contraception for women • Publication limits starting with 1999 • Best level of evidence available • Language: English • Abstract of the study: available **Exclusion criteria:** • Studies that did not provide information on the effectiveness and safety or efficiency of the Essure® system • Studies with a follow-up period less than three months, which did not assess tubal occlusion at three months • Number of women included in the study: less than 25 • Conference abstracts • In vitro studies **Studies included** (efficacy/ effectiveness and safety): • Primary studies (number of women): one non-controlled comparative study (n = 48), three prospective case series (range 33 to 100), two multicentre studies referred to in one HTA report (n_1 = 518, n_2 = 227) • Secondary studies: three HTA reviews	The published research evidence on effectiveness and safety is mainly available from case series studies of no more than three months duration. Results from three prospective case series (n = 223): **Efficacy/Effectiveness** Three-month follow-up reported: n = 201 (HSG: n = 126, X-ray: n = 75) *Bilateral placement* success rate: 95% (211/223), 94% at first attempt *Pregnancies*: None reported **Safety** (number women) *Immediate post implantation* Discomfort (51); uterine cramps (mild to moderate) (40); severe localized pelvic pain (8); nausea and vomiting (3); vasovagal reaction (2); suspected tubal perforation (1); cervical bleeding (1) *During week one* Bleeding or spotting (57); pain (31); infection in perineum (1); headache (1) *At three months post implantation* Migration of the micro-device (10); pain with different abdominal location (5); tubal perforation and micro-insert adherent to the sigmoid colon (1); possible salpingitis (1) The long-term nature of the tissue response to the Essure® micro-insert is not known. The Essure® system appears to be adequate in terms of safety and effectiveness under controlled conditions. However, the ultimate clinical outcome of interest is prevention of pregnancy during the length of the women's fertility cycle and this would require longer-term studies. Several sterilization options are available to couples; these options need to be compared to the Essure® system over the longer term using a risk/benefit approach.

HSG – Hysterosalpingography; HTA – health technology assessment; HTS – hysteroscopic tubal sterilization; n – number of participants; NR – not reported

Table T.C.2: HTA reports on hysteroscopic tubal sterilization (cont'd)

Study	Inclusion and exclusion criteria; studies included	Main findings; conclusions
National Institute for Health and Clinical Excellence[15] Interventional procedure overview of hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants UK November 2008 **Objective**: To review the published literature evidence on the efficacy and safety of hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants The overview was prepared to assist members of the Interventional Procedures Advisory Committee in making recommendations about the safety and efficacy of an interventional procedure Rapid review of literature. Searches up to July 2008, updated March 2009	**Inclusion criteria**: Women wanting sterilization • Intervention: hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants • Outcome: relevant to the safety and/or efficacy • Clinical studies, emphasis on good quality studies **Exclusion criteria**: No clinical outcomes reported • Reviews, editorials, laboratory or animal studies • Conference abstracts, unless they reported specific adverse events that were not available in the published literature • Non-English-language articles unless they were thought to add substantively to the English-language evidence base **Studies included**: Essure® system Primary studies (Essure® system): six case series studies; one non-controlled comparative study; five case reports	**Efficacy/Effectiveness*** *Bilateral placement success* rate (range, (total number)): 86 to 99% (1830/1937) (six studies) *Tubal occlusion confirmed* by HSG or position of the micro-inserts confirmed by X-ray, at three months after the procedure (range, [total number]): 92 to 99% (1721/1779) (six studies) *Pregnancies* (number from total pregnancies): 64 out of an estimated 50,000 procedures; reasons: non-compliance (30/64), misread X-ray or HSG (18/64), undetected pregnancy at the time of procedure (8/64), a prior device design no longer available (1/64) (retrospective study, pregnancies reported by the device manufacturer from 1997 to December 2005) **Safet* (number women)** *Procedural complications:* 0 to 11 % (77/2692) (six studies) *Minor adverse events related to a vasovagal reaction*: 0.1 to 4.5% (28/2516) (five studies) *Unsatisfactory micro-insert placement (including expulsion and migration to the abdominal cavity*): 1 to 4% (41/2349) (three studies) *Perforation*: 13/905 (four studies) *Pain*: similar to normal menstruation: 166/1615 (one study); more pain than normal menstruation: 51/1615 (one study); pain during the procedure: severe pain 10/76 (one study); postoperative severe pain: 27/583 (two studies) *Vaginal bleeding or discharge after the procedure*: 127/583 (two studies); abnormal subsequent menstrual period: 23/76 (one study) Current evidence on the safety and efficacy of hysteroscopic sterilization by tubal cannulation and placement of intrafallopian implants is adequate to support the use of this procedure, provided that normal arrangements are in place for clinical governance and audit.[21]

* Only information about the Essure® system is abstracted

HSG – hysterosalpingography

Table T.C.2: HTA reports on hysteroscopic tubal sterilization (cont'd)

Study	Inclusion and exclusion criteria; studies included	Main findings; conclusions
Finnish Office for Health Technology Assessment[16] Hysteroscopic tubal sterilization: a systematic review of the Essure® system Finland 2010 **Objective**: To update the evidence of the efficacy and safety of the Essure® system The review is based on the results of the Alberta Heritage Foundation for Medical Research (AHFMR) report[14] with updated research evidence from a systematic literature search of published evidence from 2004 to April 2008	**Inclusion criteria**: NR **Exclusion criteria**: NR **Studies included**: AHFMR report: six studies One new prospective cohort study (n = 102)	**Efficacy/Effectiveness** In general the published studies suggest that the Essure® method is well tolerated and effective in the short term. Some uncertainty comes from the relatively low follow-up rates. *Bilateral placement* success rate: 81 to 98%, with up to two attempts. *Pregnancies*: device manufacturer reported 64 out of an estimated 50,000 procedures from 1997 to December 2005 (retrospective study) **Safety** Based on two case series studies* (n = 745): *tubal perforation*: 1 to 3%; *intraperitoneally placed implants*: 0.5 to 3%; *pain*, day of placement: 1 to 13%; *stomach cramps*: 30%; *nausea*: 11%; *bleeding or spotting*: 7% As a foreign body, the Essure® micro-insert may cause tissue encapsulation, observed in 17% of cases at 12-month follow-up and 25% of cases at 13 to 43 months of follow-up. Long-term data on safety, efficacy, effectiveness and pregnancy rates are still unavailable. The Essure® system appears to be safe, permanent, irreversible, and a less invasive method of contraception than is laparoscopic sterilization.

*Studies were the FDA Premarket Approval (PMA) multicentre case series studies[22,23]

n – number of participants; NR – not reported

Appendix T.D: Quality Appraisal Results

Table T.D.1: Quality appraisal results—case series studies

Study	Criterion								
	1. Is the hypothesis/aim/objective of the study clearly stated?	2. Was the study conducted prospectively?	3. Were the cases collected in more than one centre?	4. Were participants recruited consecutively?	5. Are the characteristics of the participants included in the study described?	6. Are the eligibility criteria (i.e., inclusion and exclusion criteria) for entry into the study clearly stated?	7. Did participants enter the study at a similar point on their co-morbidity/clinical status?	8. Was the intervention of interest clearly described?	9. Were additional interventions (co-interventions) reported in the study?
Andersson et al. 2009[2]	Partial	Yes	No	Unclear	Yes	No	No	Partial	Yes
Chapa et al. 2011[8]	Partial	Yes	No	Unclear	No	Yes	Yes	Partial	Yes
Levie et al. 2006[5]	Partial	Yes	No	Yes	Yes	Yes	Yes	Partial	Yes
Mascaro et al. 2008[7]	Unclear	Unclear	No	Yes	No	Yes	Yes	Yes	Yes
Mino et al. 2007[4]	Yes	Yes	No	Unclear	Yes	Partial	Yes	Yes	Yes
Sinha et al. 2007[1]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Veersema et al. 2011[6]	Yes	Yes	Yes	Yes	Yes	No	Unclear	Partial	Unclear
Vellayan et al. 2006[3]	No	Unclear	No	Unclear	No	No	Yes	Partial	Yes

Table T.D.1: Quality appraisal results—case series studies (cont'd)

Study	Criterion								
	10. Are the outcome measures established a priori?	11. Were the relevant outcomes measured with appropriate objective and/or subjective methods?	12. Were the statistical tests used to assess the relevant outcomes appropriate?	13. Was the length of follow-up reported?	14. Was the loss to follow-up reported?	15. Does the study provide estimates of the random variability in the data analysis of relevant outcomes?	16. Are the adverse events related to the intervention reported?	17. Are the conclusions of the study supported by results?	18. Are both competing interests and sources of support for the study reported?
Andersson et al. 2009[2]	Partial	No	Unclear	Yes	Unclear	Partial	Yes	Yes	Yes
Chapa et al. 2011[8]	Yes	Partial	Unclear	Yes	Yes	No	Yes	Yes	Yes
Levie et al. 2006[5]	Yes	Yes	Yes	Yes	Yes	No	Yes	Partial	No
Mascaro et al. 2008[7]	Yes	Partial	Unclear	Yes	Yes	No	Yes	Yes	Partial
Mino et al. 2007[4]	Yes	Partial	Unclear	Yes	Yes	No	Yes	Yes	No
Sinha et al. 2007[1]	Yes	Partial	Yes	Yes	Yes	Yes	Yes	Yes	No
Veersema et al. 2011[6]	Yes	Partial	Unclear	Yes	Yes	Yes	Yes	Partial	Partial
Vellayan et al. 2006[3]	No	Partial	Unclear	Yes	Unclear	No	Yes	Partial	No

References

1. Sinha D, Kalathy V, Gupta JK, Clark TJ. The feasibility, success and patient satisfaction associated with outpatient hysteroscopic sterilisation. *BJOG* 2007;114(6):676-683.
2. Andersson S, Eriksson S, Mints M. Hysteroscopic female sterilization with Essure in an outpatient setting. *Acta Obstetricia et Gynecologica Scandinavica* 2009;88(6):743-746.
3. Vellayan M, Baxter A, Connor M, Brown V. The Essure hysteroscopic sterilisation procedure: Initial experience in Sheffield, UK. *Gynecological Surgery* 2006;3(4):303-307.
4. Mino M, Arjona JE, Cordon J, Pelegrin B, Povedano B, Chacon E. Success rate and patient satisfaction with the Essure sterilisation in an outpatient setting: a prospective study of 857 women. *BJOG* 2007;114(6):763-766.
5. Levie MD, Chudnoff SG. Prospective analysis of office-based hysteroscopic sterilization. *Journal of Minimally Invasive Gynecology* 2006;13(2):98-101.
6. Veersema S, Vleugels M, Koks C, Thurkow A, van d, V, Brolmann H. Confirmation of Essure placement using transvaginal ultrasound. *Journal of Minimally Invasive Gynecology* 2011;18(2):164-168.
7. Mascaro M, Marino M, Vicens-Vidal M. Feasibility of Essure placement in intrauterine device users. *Journal of Minimally Invasive Gynecology* 2008;15(4):485-490.
8. Chapa HO, Bakker K, Sandate J, Silver L, Antonetti AG. Essure sterilization with sonographic confirmation test: Protocol description and clinical outcomes using ultrasound as an Essure confirmation test. *Journal of Gynecology & Surgery* 2011;27(2):57-62.
9. Arjona JE, Mino M, Cordon J, Povedano B, Pelegrin B, Castelo-Branco C. Satisfaction and tolerance with office hysteroscopic tubal sterilization. *Fertility & Sterility* 2008;90(4):1182-1186.
10. Levie M, Weiss G, Kaiser B, Daif J, Chudnoff SG. Analysis of pain and satisfaction with office-based hysteroscopic sterilization. *Fertility & Sterility* 2010;94(4):1189-1194.
11. Langenveld J, Veersema S, Bongers MY, Koks CA. Tubal perforation by Essure: three different clinical presentations. *Fertility & Sterility* 2008;90(5):2011.e5-2011.e10.
12. Moga C, Guo B, Schopflocher D, Harstall C. Development of a quality appraisal tool for case series studies using a modified Delphi technique. Methodology paper. Edmonton, AB: Institute of Health Economics, 2012. Available from: *www.ihe.ca* (accessed 8 August 2012).
13. Alpizar F. Quinacrine sterilization (QS) in Costa Rica: 694 cases. *International Journal of Gynaecology & Obstetrics* 2003;83(Suppl 2):S141-145.
14. Moga C, Harstall C, Alberta Heritage Foundation for Medical Research. Hysteroscopic tubal sterilization (Essure (TM) system) TechNote 57, June 2006. Edmonton, AB: Alberta Heritage Foundation for Medical Research (AHFMR).
15. National Institute for Health and Clinical Excellence IPP. Interventional procedure overview of hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implants,

2008. Available from: *http://publications.nice.org.uk/hysteroscopic-sterilisation-by-tubal-cannulation-and-placement-of-intrafallopian-implants-ipg315* (accessed 17 February 2012).

16. Hurskainen R, Hovi S-L, Gissler M, Grahn R, Kukkonen-Harjula K, Nord-Saari M, et al. Hysteroscopic tubal sterilization: a systematic review of the Essure system. *Fertility and Sterility* 2010;94(1):16-19.
17. Castano PM, Adekunle L. Transcervical sterilization. *Seminars in Reproductive Medicine* 2010;28(2):103-109.
18. Levy B, Levie MD, Childers ME. A summary of reported pregnancies after hysteroscopic sterilization. *Journal of Minimally Invasive Gynecology* 2007;14(3):271-274.
19. Lessard CR, Hopkins MR. Efficacy, safety, and patient acceptability of the EssureTM procedure. *Patient Preference & Adherence* 2011;5:207-212.
20. Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: Synthesis of best evidence for clinical decisions. *Annals of Internal Medicine* 1997;126:376-380.
21. National Institute for Health and Clinical Excellence (NICE). Hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implants, 2009. Available from: *www.nice.org.uk/nicemedia/live/11118/45506/45506.pdf*.
22. Kerin JF, Cooper JM, Price T, Herendael BJ, Cayuela-Font E, Cher D ea. Hysteroscopic sterilization using a micro-insert device: results of a multicentre Phase II study. *Human Reproduction* 2003;18(6):1223-1230.
23. Cooper JM, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. *Obstetrics & Gynecology* 2003;102(1):59-67.

SECTION THREE: Economic Analysis

Charles Yan, PhD; Anderson Chuck, PhD, MPH

Objectives and Scope

The objectives for the economic analysis were to determine the cost-effectiveness of hysteroscopic tubal sterilization (HTS) compared to that of laparoscopic tubal sterilization (LTS) and to determine the budget impact of HTS. The proposed methods used to inform these questions include a review of the economic literature, an Alberta based cost-effectiveness analysis, and a budget impact analysis.

Literature review

Search strategy

The literature review was an update to the previous TechNote of HTS conducted by the Alberta Heritage Foundation for Medical Research (AHFMR) in 2006.[1] Selected databases were searched for economic evaluation studies of HTS. Databases searched include Medline, EMBASE, CINAHL, Cochrane Database of Systematic Reviews, Web of Science, and grey literature. To supplement the electronic searches, reference lists of retrieved articles were also reviewed to find further studies. The literature search summary is presented in Appendix E.A.

Selection criteria

The search was limited to human and English language publications. Eligible studies were those met the following predefined inclusion/exclusion criteria:

Inclusion criteria:

- Study design: Cost minimization studies (that is, comparison of costs only) or economic evaluation studies including studies of cost-effectiveness, cost-utility, or cost-benefit analyses. This can include economic studies conducted as part of health technology assessment reports, systematic reviews, randomized and non-randomized controlled trials, and observational cohort or modelling studies.
- Population: women seeking permanent tubal sterilization
- Interventions and comparators: HTS versus laparoscopic tubal ligation
- Language: English
- Search period: from January 2006 onward

Exclusion criteria:

- Abstracts, case studies, narrative reviews, letters, and editorials
- Studies that reported the cost and outcomes of only one strategy (without a comparator)

Outcomes of interest

- Rate of procedure success
- Rate of pregnancy averted
- Quality adjusted life years (QALYs)
- Costs per patient

- Additional costs per unit outcome achieved

Quality assessment

A formal quality assessment of economic studies was conducted with the Quality of Health Economic Studies (QHES) instrument.[2] The QHES instrument was designed to evaluate health economic analyses, including the analysis of cost minimization, cost-effectiveness, and cost utility. It includes a weighting system to score and aggregate across individual criteria thereby providing a summative index of quality. The quality index ranges from 0 to 100, with a score of 75 or greater indicating acceptable quality.

Data Extraction

Data extracted from studies include study objective, health interventions under investigation, cost components, health outcome measures, results, and conclusions.

Economic analysis

The primary economic analysis consisted of an economic evaluation and a budget impact analysis.

Economic evaluation

Cost-effectiveness analysis (CEA) is an analytic approach for contrasting incremental health benefits with the incremental resource expenditures associated with competing health technologies. A CEA was conducted to evaluate the cost-effectiveness of alternative protocols for conducting HTS procedures in women seeking permanent birth control. A decision analytic simulation model was developed to comparatively evaluate the procedures in terms of their costs and health outcomes.

The CEA adopted a payer perspective and considered direct medical service costs to the Alberta health system, including costs of physician, inpatient, and outpatient resources, including the costs of the device. The time horizon adopted for the analysis considered costs from initial procedure to confirmative diagnosis. All analyses were conducted using Microsoft Excel 2010 and TreeAge Pro 2010 (TreeAge Software Inc.; Williamstown, MA).

Protocols

The CEA compared three alternative protocols.

- The first HTS protocol is the one currently conducted in Calgary (HTS – Calg, see Figure E.1). This procedure is currently not conducted elsewhere in Alberta.
- The second HTS protocol is the one conducted in Saskatchewan (HTS – Sask, see Figure E.2).
- The third protocol is LTS, currently conducted in Alberta (LTS, see Figure E.3).

Figure E.1: Clinical pathway and resources used for HTS, using Calgary Protocol

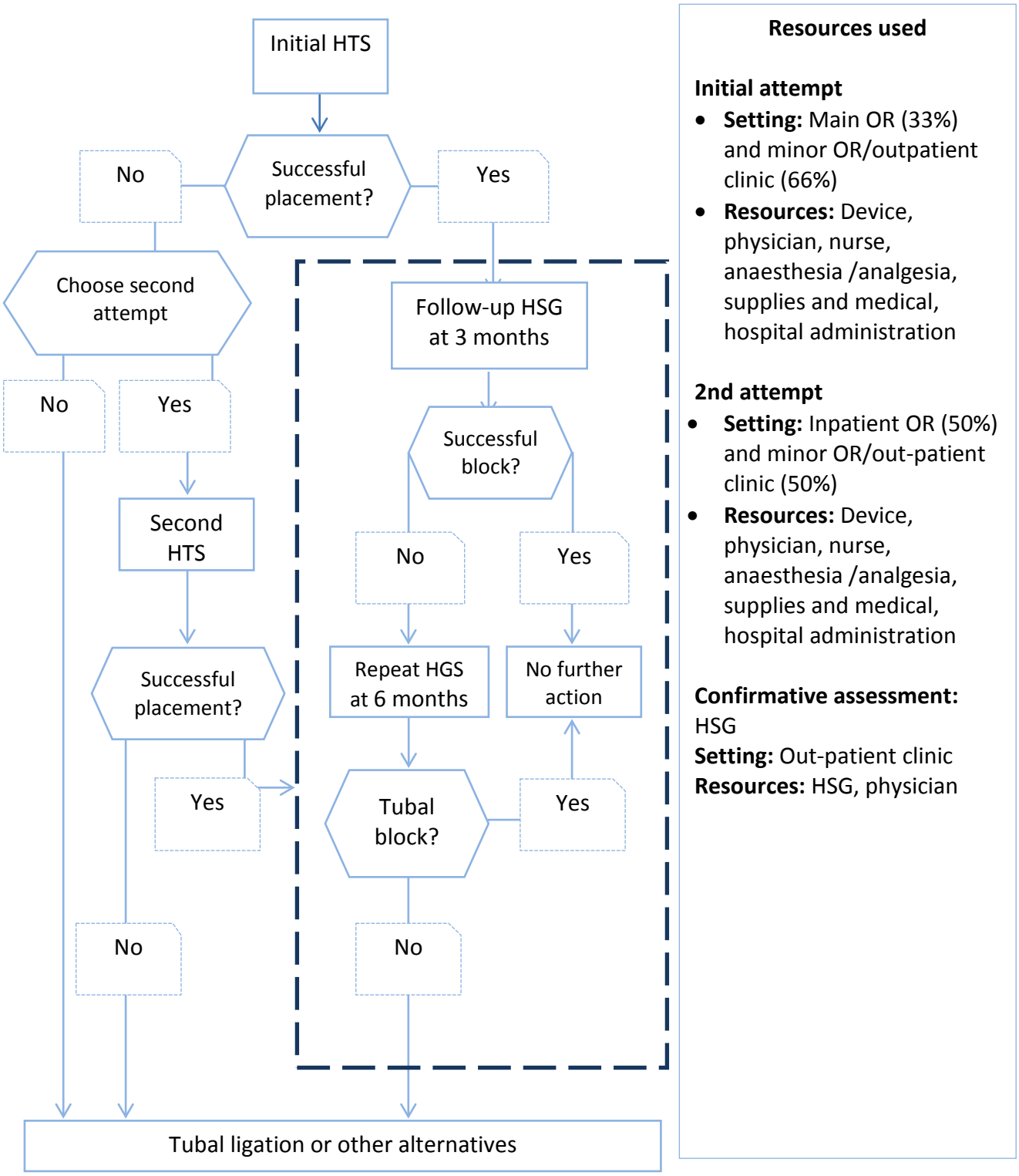
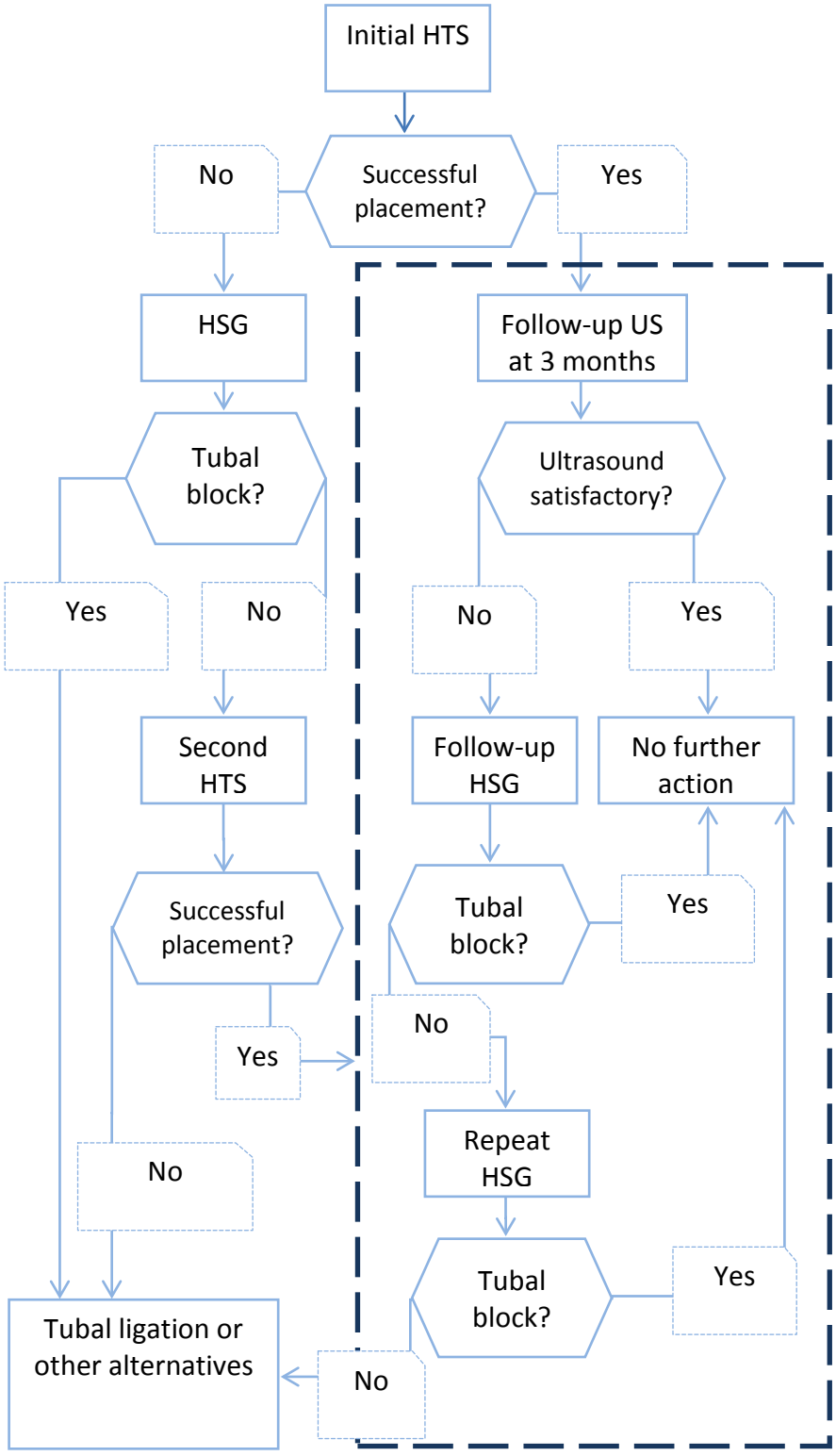


Figure E.2: Clinical pathway and resources used for HTS, using Saskatchewan Protocol



Resources used

Initial attempt

- **Setting*:** Outpatient clinic
- **Resources:** Device, physician, nurse, analgesia, supplies and medical, hospital administration

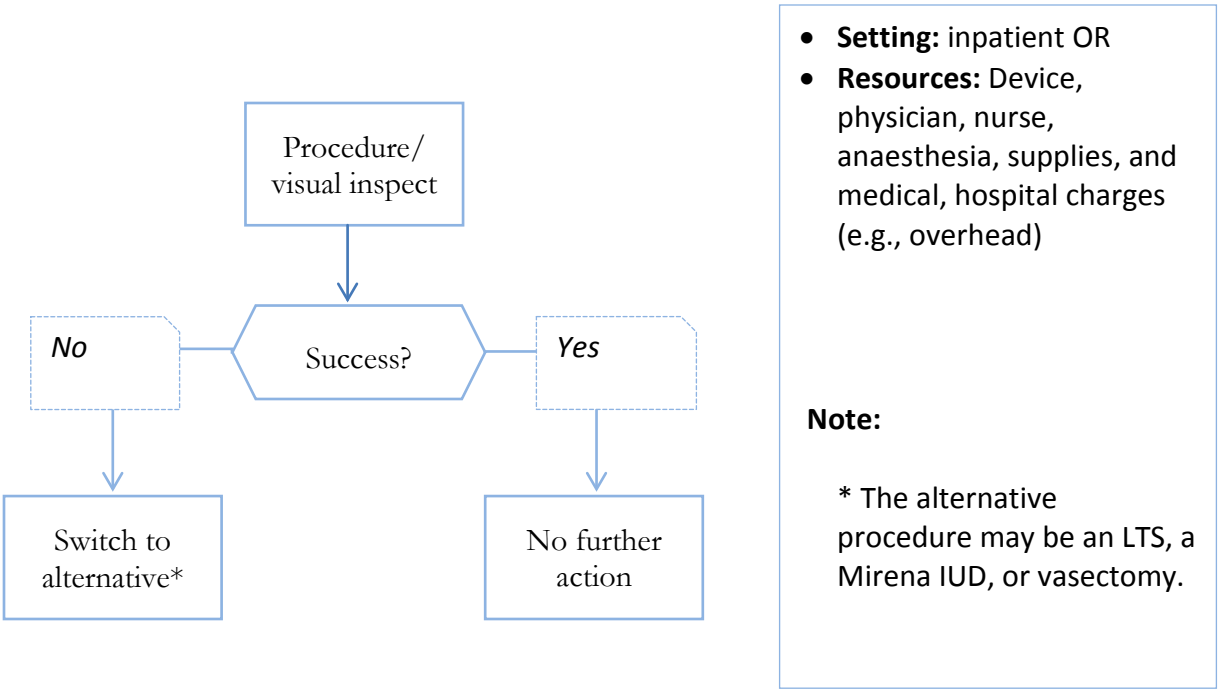
2nd attempt

- **Setting*:** Inpatient OR
- **Resources**: Device, physician, nurse, supplies, anaesthesia and medical, hospital administration

Confirmative assessment: Ultrasound (US) and HSG if necessary.
Setting*: Hospital radiology dep't/US office
Resources: US – radiologist
HSG – physician

*: Settings presented here are for information purposes. These settings will be replaced with those adopted in the Calgary protocol to reflect an Alberta context.

Figure E.3: Clinical pathway and resources used for LTS in Alberta



Model inputs

Data obtained from the pilot study of HTS procedures in Calgary was used to populate the HTS protocols. Calgary data was applied to the Saskatchewan protocol to assess the cost-effectiveness of the Saskatchewan protocol within the Alberta context. As shown in Figure E.1, 33% of initial HTS procedures were performed in the inpatient operation room (OR) setting while 66% were performed in an outpatient OR setting. If a second HTS was attempted, 50% of the procedures were performed in an inpatient OR setting. Not all HTS procedures can be conducted on an outpatient basis due to the heterogeneity in the complexity of the patient population. Hence the current mix already reflects the number that have been deemed clinically suitable to have the procedure conducted on an outpatient basis.

Table E.1 shows the probability inputs associated with each clinical outcome outlined in Figures E.1 through E.3. Health service resources considered in the analysis are shown in Table E.2 and reflect the costs in 2012 Canadian dollars. Given that all costs and outcomes occur within one year, no discounting was applied.

Costs pertaining to HTS were primarily obtained from the Calgary pilot study supplemented by data obtained from the Alberta schedule of medical benefits. Hospital facility costs were obtained from the literature. Cost data for LTS were obtained from three provincial administrative databases. The Physician Claims database provided data about billing services to physicians for conducting LTS. The Discharge Abstract Database (DAD) provided data on inpatient hospital costs while the Ambulatory Care Classification System (ACCS) database provided data on outpatient hospital costs. The DAD and the ACCS contain patient-specific cost information including drug and supply costs, functional centre direct costs (for example, salaries, medical and surgical supplies), and indirect costs

(for example, facilities management, registration, patient food services, and health records). These costs were estimated by identifying cases of LTS using Canadian Classification of Health Interventions (CCI) codes, with each procedure having a corresponding cost in the database (see Table E.2). Given that LTS could be conducted in either an inpatient or an outpatient setting, costs for hospital-related services were calculated using a weighted average between inpatient and outpatient procedures.

Table E.1: Clinical and epidemiological data inputs

Parameter	Base case	Lower limit*	Upper limit*	Dist	Source
Probability of pregnancy (HTS)	0.2%	0.18%†	0.22%††	Beta	Connor (2009)[3]
Probability of pregnancy (LTS)	1.31%	1.08%	1.54%	Beta	Peterson (1996)[4]
HTS technical success	95%	88.11%‡	100%¶	Beta	Expert opinion
LTS technical failures	4.38%	1.61%	7.28%	Beta	Aranda (1985) and Argeuta (1980), as cited in Lawrie (2011)[5]
Success of second HTS attempt	50%	47.37%[6]	70%	Beta	Expert opinion
Tubal occlusion, first HSG	97.60%	95.83%‡	100%¶	Beta	Weighted average from [6-10]
Tubal occlusion, second HSG	100%	98%‡‡	100%	Triangular	Expert opinion
Choosing second attempt following first attempt failure	70%	63%†	77%††	Triangular	Expert opinion
Satisfactory HSG, following unsuccessful initial HTS	99.67%	89.7%†	100%¶	Triangular	Expert opinion
Satisfactory HSG, following unsatisfactory US	72.09%	64.88%†	79.3%††	Beta	Thiel (2011)[11]
Satisfactory US	85.90%	77.31%†	94.49%††	Beta	Thiel (2011)[11]
Rate of conducting HTS in inpatient OR for initial attempt	33%	0%¶	100%¶		Expert opinion
Rate of conducting HTS in inpatient OR for second attempt	50%	0%¶	100%¶		Expert opinion

* – Values of lower and upper limit were used in deterministic sensitivity analysis.

‡ – Published studies[6-10] indicated a range from 88.11 to 94.31% for HTS success rate and 95.83 to 100% for tubal occlusion in 1st HSG; the lowest value from Cooper[6] was used as lower limit.

¶: – The lower and upper limit was assumed to be 0% and 100%, respectively.

‡‡ – assumption

† – assume to be 10% lower than base case value

†† – assume to be 10% higher than base case value

Table E.2: Cost per procedure associated with HTS and LTS (2012)¶

Cost	Main OR	Minor OR/ outpatient clinic¶¶	Lower limit*	Upper limit*	Dist	Source
HTS						
Device	$1,100.00	$1,100.00	$880.00	$1,320.00		OFIA
Supplies	$26.43	$28.32	$21.14	$31.72	Gamma	OFIA
Facility**	$679.97	$438.61	$543.98	$815.96	Gamma	OFIA
Obstetrician	$136.37		$109.10	$163.64	Gamma	SOMB
Analgesic	$69.00	–	$55.20	$82.80	Gamma	OFIA
RN	$100.00	–	$80.00	$120.00	Gamma	OFIA
RN	–	$25.00	$20.00	$30.00	Gamma	SOMB
Physician follow-up	$18.40	$18.40	$14.72	$22.08		SOMB
HSG	$192.00	$192.00	$153.60	$230.40		SOMB
Follow-up ultrasound	$118.21	$118.21	$94.57	$141.85		OFIA
LTS						
Hospital‡	$1,576.18 (SD: 346)		$1,112.66§	$1,891.41	Gamma	AH data
Physicians	$449.56 (SD: 107)		$359.65	$539.48	Gamma	AH data

¶ – All costs were adjusted to 2013 Canadian dollars using the Alberta Consumer Price Index; inputs assigned gamma distribution are used in the probabilistic sensitivity analysis.

¶¶ – Costs associated with HTS were determined to be equivalent regardless of whether the procedure was conducted in a minor OR or the outpatient clinic.

* – Lower (upper) limit was assumed to be 20% lower (higher) than base case, and is used in deterministic sensitivity analysis.

** – Facility costs are estimated based on costs for HTS minus the cost of supplies and surgical assistants. OFIA combined facility costs with the cost of the device. Our estimate excludes the cost of the device.

‡ – These contain patient-specific costs, including drug and supply costs, functional centre direct costs (salaries, medical, and surgical supplies) and indirect costs (e.g., facilities management, registration, patient food services, and health records).

§ – From OFIA; used in sensitivity analysis.

SOMB – schedule of medical benefits, Alberta

OFIA – operational and financial impact analysis, AHS

Model outputs

The outputs generated from the model were:

- Overall rate of successful sterilization associated with each protocol
- Total costs associated with each protocol
- Incremental costs per additional outcome (i.e., permanent sterilization)

Criteria for cost-effectiveness

The criteria for concluding that an alternative is cost-effective are as follows:

1. Alternatives that are both more costly and less effective compared to other alternatives are dominated and are considered NOT cost-effective. These are eliminated from further consideration.
2. Alternatives that are less costly and more effective compared to other alternatives are dominant and are considered cost-effective. These are included for further consideration.
3. Alternatives that are both more costly and more effective (or less costly and less effective) are not dominant and their cost-effectiveness is uncertain:
    a. Within these alternatives there can be a situation of extended dominance. That is, among these alternatives there are some alternatives that are more cost efficient than others. Alternatives that are dominated by extension are not considered cost-effective and are excluded from further consideration.
    b. For the remaining alternatives that are not dominated by extension, cost-effectiveness is dependent on whether decision-makers deem the additional effectiveness to be worth the additional costs; this is referred to as the cost-effectiveness threshold.

Sensitivity analysis

It is important to provide information regarding the degree of variability (that is, uncertainty) in potential costs and effectiveness to enable decision-makers to evaluate the *credible* range of potential costs and outcomes. Therefore, a probabilistic sensitivity analysis was conducted using 5000 Monte Carlo simulations using the ranges and distributions listed in Tables E.1 and E.2 to generate the distribution of potential costs and effectiveness associated with each alternative procedure.

As previously mentioned, the AHS OFIA estimate of the outpatient facility cost associated with HTS was derived from case costing patients from select centres, whereas the outpatient facility cost for LTS in the present analysis was taken from provincial databases, which is a weighted average across all centres adjusting for patient case mix. We tested the impact of the higher cost estimate in a one-way sensitivity analysis. A one-way sensitivity analysis was also conducted to determine the impact on the cost-effectiveness results if patients paid for the HTS device.

Budget impact analysis (BIA)

The BIA was conducted to assess the cost impact of replacing eligible LTS procedures with HTS. Patients undergoing LTS accompanying another surgical procedure (for example, Cesarean section) were not considered eligible for HTS. Data estimating the number of eligible LTS patients for HTS (that is, observed demand) were extracted from the DAD for LTS conducted as inpatient procedures and from the ACCS for LTS conducted as outpatient procedures, based on the CCI codes listed in Table E.3. Estimates were generated using 2008-2012 data. Cost and clinical inputs applied in the BIA model were identical to the data used in the CEA.

Table E.3: CCI codes used to identify patients undergoing LTS

Description	CCI code		
Method	**Laparoscopic approach**	**Endoscopic vaginal approach**	**Open approach**
Fallopian Tube Occlusion using band (ring)	1.RF.51.DA-FA	1.RF.51.FJ-FA	1.RF.51.LA-FA
Fallopian Tube Occlusion using bipolar electrode	1.RF.51.DA-AL	1.RF.51.FJ-AL	1.RF.51.LA-AL
Using clips (e.g., plastic)	1.RF.51.DA-FF	1.RF.51.FJ-FF	1.RF.51.LA-FF
Using ligature (and transection or resection)	1.RF.51.DA-LV	1.RF.51.FJ-LV	1.RF.51.LA-LV
Fallopian Tube Occlusion using coil (e.g., micro-insert)	—	1.RF.51.FJ-GE	—

Sensitivity analysis

Deterministic one-way sensitivity analysis was conducted to evaluate the change to the budget impact when varying model inputs. These included the cost of the Essure® device, the rate of procedure success, the proportion of HTS procedures conducted in the inpatient OR, and the cost of follow-up and confirmatory diagnosis.

Results

Review of economic studies

Search results

The literature search identified 92 references. After reviewing the titles and abstracts/summaries, 14 of these were retrieved for further review. Of the 14 studies, four studies met the final inclusion/exclusion criteria. See Appendix E.B for information about data extraction from included studies and Appendix E.C for the quality assessment scores of included studies.

Evidence from the economic literature

Thiel et al. (2008)[14] compared the health service costs of women who received Essure® (n = 108) with the health service costs of those receiving LTS (n = 104) in Saskatchewan, Canada. HTS procedures were conducted in the outpatient setting while LTS was conducted in the inpatient OR setting. Cost components included in their analysis were nursing, inpatient and outpatient OR resources, anaesthesia, Essure® micro-insert coils or Filshie clips and disposables, ancillary hospital charges, ultrasound, and HSG. The results showed that the cost per case was $1,288 (standard deviation = $2,450) for Essure® and $1,398 (standard deviation = $36) for LTS. Compared to LTS, HTS was $111 cheaper per case ($p<.01$). The authors concluded that Essure® was net cost saving compared to LTS. The study was assessed with a quality score of 70.

Kraemer et al. (2009)[15] compared the costs of Essure® to those of laparoscopic bilateral tubal ligation (LBTL) in outpatient settings in the USA, using a decision tree model. Cost components included in their analysis were costs of procedure, ectopic pregnancy, induced abortion, spontaneous abortion, and live birth over a five-year period. The results showed that the costs per case were US$2,367 for Essure® and US$3,545 for LBTL, resulting in a cost saving of $1,178. The study

concluded that Essure® was associated with cost savings over five years when compared to LBTL. The study was assessed with a quality score of 77.

Hopkins et al. (2007)[16] compared the health service costs of women who received Essure® (n = 43) with the health service costs of those receiving LTS (n = 44) in an inpatient OR setting in the USA. Cost components included in the analysis were physician and hospital costs. The results showed that the total costs per case were US$2,700 for HTS and US$2,880 for LTS, with a difference of US$180 (p = 0.038). The study was assessed with a quality score of 73.

Franchini et al. (2009)[17] conducted a prospective study that compared the health service costs of women receiving Essure® (n = 25) with the health service costs of those receiving LTS (n = 24) in an inpatient OR setting in Italy. The cost components considered in the study were operation room resources, recovery unit and hospital stay, material, physician services, nursing, administrative staff, laboratory testing, overhead, and ancillary services. The results showed that compared to LTS, HTS was associated with higher costs for operating theatre resources (€1,411.96 ±36.9 versus €893.73 ±213.56, p<.0001)); but were associated with lower total health costs (€1,830.96 ±43.69 versus €2,704.83 ±246.43, p<.0001)). The study concluded that HTS was less expensive than LTS, mainly as a result of low support before, during, and after the procedure. The study was assessed with a quality score of 70.

Economic evaluation

Cost, outcomes, and cost-effectiveness

Table E.4 presents results of the cost-effectiveness analysis. The protocol associated with the lowest cost was LTS, followed by HTS – Sask., with HTS – Calg. being the most costly. The protocol associated with the highest success rate was HTS – Sask., followed by HTS – Calg. and LTS.

When contrasting the costs and outcomes between alternatives, compared to LTS, the cost per additional successful sterilization was $3,588 for HTS – Sask. and $4,789 for HTS – Calg. Compared to HTS – Calg., HTS – Sask. is more effective and less costly.

Table E.4: Total costs, success rate, and cost-effectiveness

Cost and outcomes			
Procedure	**Cost**	**Success rate**	
LTS	$2,025.74	0.9437	
HTS – Sask.	$2,125.13	0.9714	
HTS – Calg.	$2,129.19	0.9653	
Incremental cost-effectiveness			
Procedure	**ΔCost**	**Δ Success rate**	**ICER**
HTS – Calg. versus HTS – Sask.	$4.06	-0.0061	HTS – Sask. dominates HTS – Calg.
HTS – Sask. versus LTS	$99.39	0.0277	$3,588.09
HTS – Calg. versus LTS	$103.45	0.0216	$4,789.35

Sensitivity analysis

Figures E.4 to E.6 show the scatter plots of the incremental costs and effectiveness for: HTS – Calg. versus LTS; HTS – Sask. versus LTS; and HTS – Sask. versus HTS – Calg. Compared to LTS, 44% and 49% of the simulated costs and outcomes showed that HTS – Calg. and HTS – Sask. were more costly and more effective, respectively. Compared to HTS – Calg., 42% of the simulated costs and outcomes showed that HTS – Sask. is more costly and less effective.

Figure E.4: Incremental cost-effectiveness, HTS – Calg. versus LTS

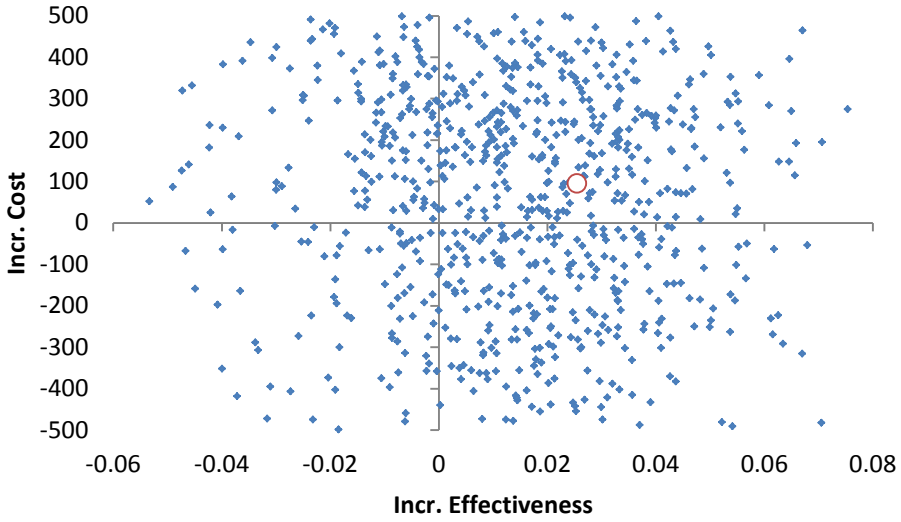


Figure E.5: Incremental cost-effectiveness, HTS – Sask. versus LTS

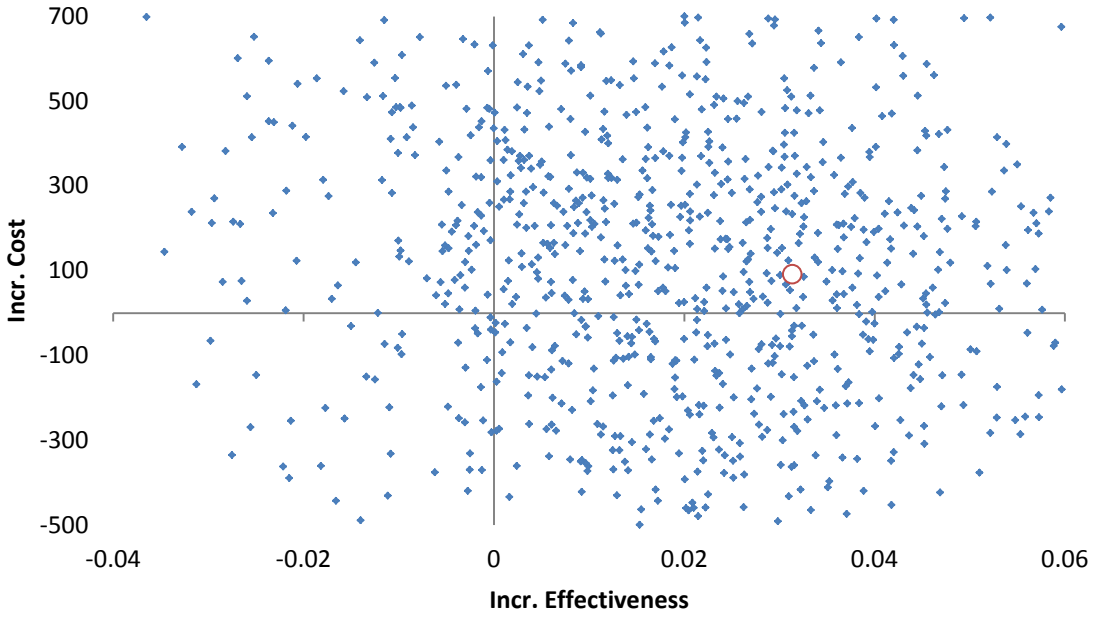


Figure E.6: Incremental cost-effectiveness, HTS – Calg. versus HTS – Sask.

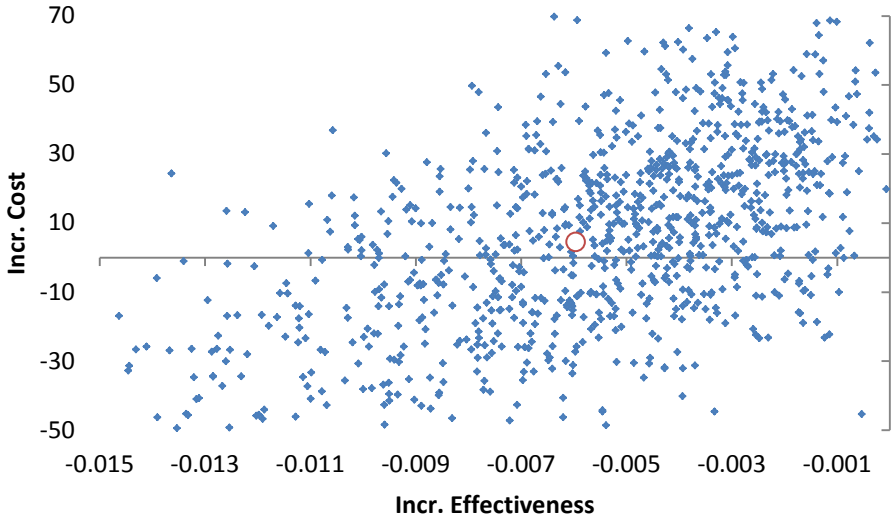


Table E.5 shows the cost-effectiveness results when using the LTS costs taken from the AHS OFIA. Compared to LTS, the cost to produce one additional successful sterilization for HTS has now increased by $16,733 for HTS – Sask. and by $21,459 for HTS – Calg. Table E.6 shows the cost-effectiveness results if patients pay for the HTS device. The results indicate that HTS – Sask. is the most cost-effective strategy because it is both less costly and more effective than either HTS – Calg. or LTS.

Table E.5: Sensitivity analysis using AHS OFIA LTS costs*

Cost and outcomes			
Procedure	**Cost**	**Success rate**	
LTS	$1,562.22	0.9437	
HTS – Sask.	$2,125.13	0.9714	
HTS – Calg.	$2,129.19	0.9653	
Incremental cost-effectiveness			
Procedure	**ΔCost**	**Δ Success rate**	**ICER**
HTS – Calg. versus HTS – Sask.	$4.06	-0.0061	HTS – Sask. dominates HTS – Calg.
HTS – Sask. versus LTS	$562.91	0.0277	$20,321.66
HTS – Calg. versus LTS	$566.97	0.0216	$26,248.61

* – In this scenario, LTS cost in base case analysis ($1,576) is replaced with that from AHS OFIA ($1,112).

Table E.6: Sensitivity analysis assuming HTS device cost not paid by public sources*

Cost and outcomes			
Procedure	**Cost**	**Success rate**	
LTS	$2,025.74	0.9437	
HTS – Sask.	$972.93	0.9714	
HTS – Calg.	$990.69	0.9653	
Incremental cost-effectiveness			
Procedure	**ΔCost**	**Δ Success rate**	**ICER**
HTS – Calg. versus HTS – Sask.	$17.76	-0.0061	HTS – Sask. dominates HTS – Calg.
HTS – Sask. versus LTS	-$1,052.81	0.0277	HTS – Sask. dominates LTS
HTS – Calg. versus LTS	-$1,035.05	0.0216	HTS – Calg. dominates LTS

* – Cost of HTS device is assumed to be paid by patients.

Budget impact analysis

Table E.7 shows the number of LTS procedures conducted in Alberta from 2009 to 2012. The potential LTS procedures that could be replaced by HTS procedures are listed in rows 1 and 4. Adding the total LTS procedures from rows 1 and 4 gives a total of 1593 LTS procedures that could instead have been HTS procedures in 2012. It is also estimated that 20 to 30% of women are contraindicated for LTS (EAG, personal communication) providing an additional 531 eligible women, for a total of 2124.

Table E.7: Number of LTS procedures conducted in Alberta, based on CCI coding

Type of Procedure	Inpatient Procedures					Outpatient Procedures			
	08/09	09/10	10/11	11/12		08/09	09/10	10/11	11/12
1. tubal ligation only	14	27	25	12		2077	1873	1789	1577
2. tubal ligation plus C-section	1765	1734	1729	1708					
3. tubal ligation plus procedures related to neoplasms of uterus or ovary	9	14	12	4		41	35	37	31
4. tubal ligation for overweight	2	2	2	1		2	2	1	3
5. tubal ligation plus procedures related to diseases of the digestive system	8	9	9	5		51	46	35	48
6. tubal ligation plus procedures related to diseases of the genitourinary system	30	31	27	29		329	358	377	369
7. tubal ligation plus procedures related to pregnancy with abortive outcome, maternal disorders predominantly related to pregnancy, or complications of labour and delivery	61	64	53	38		37	41	20	35
Total	1889	1881	1857	1797		2537	2355	2259	2063

The budget impact (using the cost results from Table E.5) is as follows:

- If the policy were to not provide public funding for HTS and to cease current limited provision, the budget impact is approximately $46,842 in cost savings.
- If the policy were to fund HTS for those women contraindicated for LTS, the budget impact is approximately $1,130,600.
- If the policy were to fund HTS for all women, the budget impact is approximately $2,033,783.

Sensitivity analysis

Figures E.7 and E.8 show the results of the sensitivity analysis testing if changes in input parameters significantly change the budget impact. The hospital costs of LTS, the Essure device costs, HTS success rate (first HTS attempt), physician costs, and facility costs for HTS were identified as the top five drivers to the budget impact. The unit cost per procedure if varying the five inputs is presented in Appendix E.D.

Figure E.7: Cost per HTS procedure, using Calgary protocol

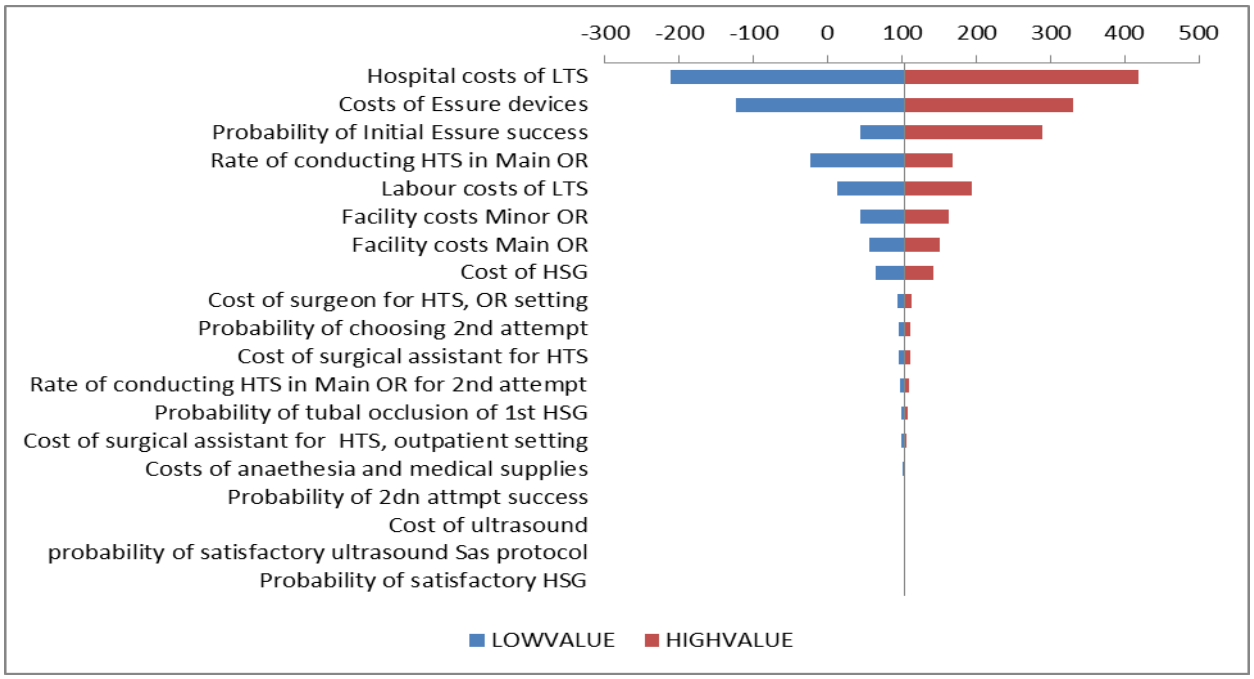
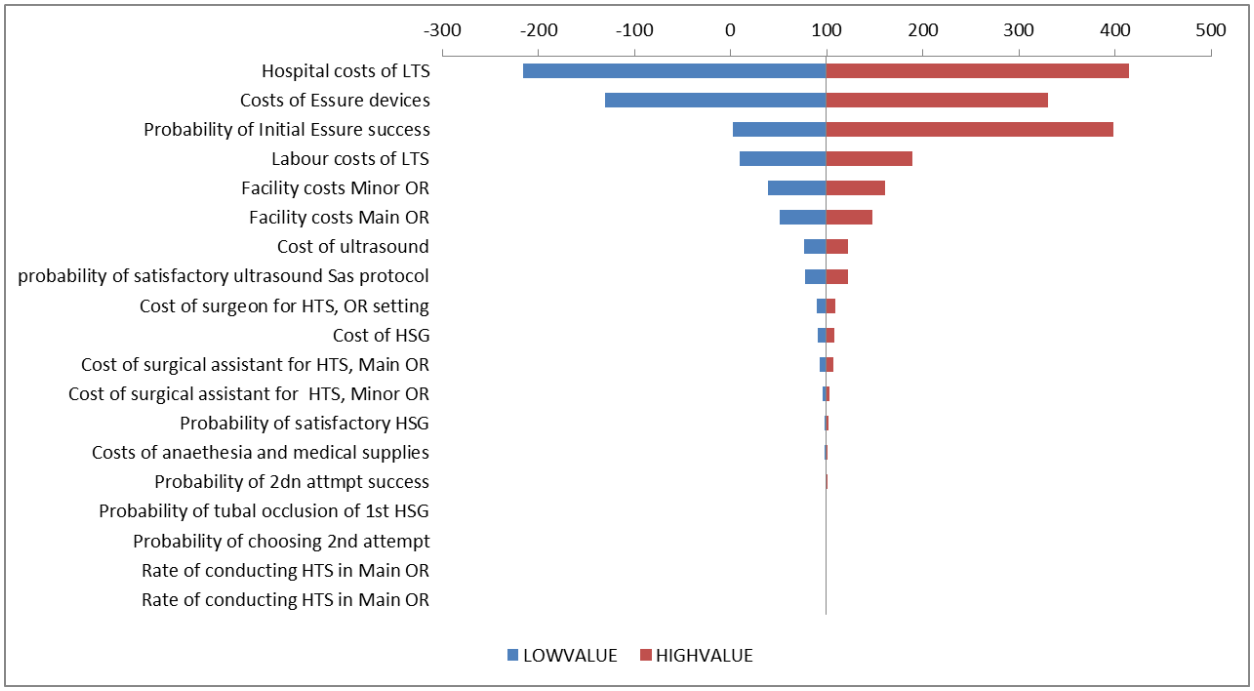


Figure E.8: Cost per HTS procedure, using Saskatchewan protocol



Discussion

The objective of the economic analysis as to determine the cost-effectiveness and budget impact of HTS compared to LTS (for LTS procedures clinically suitable for HTS). The economic analysis based on Alberta data shows that both the Calgary and Saskatchewan HTS protocols were found to be cost-adding when compared to LTS. Establishing cost-effectiveness, however, should not be solely dependent on an assessment of costs, because decisions based solely on cost implications run the risk of adopting a technology that provides insufficient value for money or not adopting a technology that is associated with significant benefit.

When examining outcomes—which was defined as achieving a successful sterilization[1]—both HTS alternatives were more effective than LTS, with HTS – Sask. being the most effective. When considering both the costs and outcomes combined, compared to LTS, the cost per additional successful sterilization was $3,588 for HTS – Sask. and $4,789 for HTS – Calg.[2] However, the sensitivity analysis indicates that the cost per additional successful sterilization could be as high as $20,322 and $26,249 (see Table E.5).

Thus, HTS does not dominate LTS by being both less costly and more effective (not unequivocally cost-effective), but rather there is a trade-off regarding whether the additional effectiveness is worth the additional cost.

The evidence from the literature review, which was limited to only a few studies, showed that HTS is less costly than LTS, with comparable effectiveness. Our results differ from these studies due to the fact that LTS was assumed to be an inpatient procedure (where the patient is admitted to a hospital or clinic for treatment and requires an overnight stay) in three of the four published studies, while it is almost exclusively an outpatient procedure (where the patient is admitted to a hospital or clinic for treatment and does not require overnight stay) in Alberta, which significantly decreases the cost of LTS in Alberta. Moreover, HTS is performed in a hospital surgical setting in Alberta, while the published studies evaluated HTS being performed in a non-hospital setting.

Given that HTS is more costly but also more effective than LTS, determining whether HTS is cost-effective is dependent on the opportunity cost of its adoption. Replacing eligible LTS procedures with HTS will not free the resources that could be used to fund its adoption. An assessment of opportunity costs would therefore entail examining the health benefits foregone from displacing or contracting other services elsewhere in the health system to obtain the resources needed to adopt HTS.

---

[1] Note that the technical failure rate for LTS is lower than HTS. However, HTS was found to be more effective because patients that fail the first HTS attempt can undergo a second HTS procedure (which is associated with additional costs) whereas there are no repeat LTS procedures.

[2] This suggests that HTS-Sask. provides greater value than HTS-Calg. because it costs less to achieve the same unit of outcome (that is, better technical efficiency). The degree of variability in costs shown in the probabilistic sensitivity analysis suggests that HTS-Sask. and HTS-Calg. are similar and the cost difference between the algorithms negligible. However, because HTS-Sask. is associated with better effectiveness, HTS-Sask. is associated with better value for money compared to HTS-Calg.

The budget impact, if the policy were to fund all women or only those contraindicated for LTS, is approximately $2,033,783 or $1,130,600, respectively. The cost savings, if the limited number of HTS procedures were to cease, is approximately $46,842. It should be mentioned that these estimates are based on observed demand and do not account for potential unobserved demand for HTS. That is, the analysis only considers the number of HTS procedures usurped from LTS (including those estimated to be contraindicated for LTS), but not those potentially usurped from other forms of contraception (for example, vasectomy, intra-uterine devices). These other contraceptive modalities were beyond the scope of this report as the project charter specifically focused on LTS only. This is an important distinction, because the data shows that the number of LTS procedures conducted in Alberta is decreasing at a rate of approximately 4% per year (see Table E.7).

Caveats

The findings should be evaluated in light of the following caveats:

1. Results are specific to the patient population where HTS is a suitable alternative to LTS.
    a. Budget impact only reflects observed demand—it does not account for unknown demand.
    b. Cost-effectiveness of HTs compared to the cost-effectiveness of other forms of permanent contraception is unknown.
2. The payer perspective ignores other benefits. It did not account for patient preference and benefits to other sectors. HTS is less invasive than LTS, potentially resulting in women not only having a stronger preference for HTS but also in their being able to return to their daily activities sooner. An economic value is associated with both the preference for a less invasive procedure and the productivity gains resulting from returning to work sooner, although it should be acknowledged that LTS is not associated with a significant loss in time from work.
3. The analysis did not account for differences in complications between LTS and HTS. LTS may be associated with greater risk of intra-operative complications than HTS. However, in a study comparing HTS with LTS on the rate of adverse events, no statistically significant difference was found between the two procedures.[7] We did not include it in our main analysis, with the exception that immediate complications associated with LTS are reflected in our costing of LTS because these costs would be reflected in the administrative databases used to estimate costs of LTS. Put in another way, our cost estimate for LTS may, in fact, be biased higher when compared to HTS, as the data used to estimate the cost of HTS did not account for the risk (albeit small) of complications. Nevertheless, we conducted a scenario analysis to examine whether an increase in the risk of severe bowel injury during LTS would change the results based on a published risk estimate of 0.15%[18] and an average cost of

$23,228 (CMG code 803).[3] The results indicate that accounting for severe bowel injury had minimal impact to the results and did not change our conclusions.

4. Cost calculation excluded the cost associated with receiving other permanent sterilization alternatives if HTS (or LTS) were unsuccessful, due to their being no data to elucidate what alternatives (if any) were being received. Thus, cost-effectiveness is affected by how well clinicians assess patient suitability, to maximize the likelihood of success.
5. No data is available about the long-term effectiveness, safety, or durability of the HTS device, and the analysis assumes the device need not be replaced.
6. Physician training costs for HTS were not considered in the analysis due to uncertainty in how HTS services would be operationalized across the province. However, the impact of physician training on total costs is likely minimal. As discussed in the T-section of this report, the duration of professional training for gynecologists to perform HTS is about two days and the learning curve is between five and seven cases.
7. Any reported cost savings to the health system is a finding that is independent from whether the health system has the resource management tools in place to be able to extract resultant savings.

Conclusion

In Alberta, HTS is more costly and more effective than LTS. Identifying the services that would be displaced, expanded, or contracted in the health system to obtain the resources needed to adopt HTS, and examining the associated foregone health benefits of such action, is important because the value for money associated with HTS is dependent on determining whether its associated health benefits are worth the additional cost.

[3] Refers to extensive procedures for injury or complication of treatment. The cost for CMG 803 was estimated to be $21,547 in 2007 Canadian dollars[19] and adjusted to 2012 Canadian dollars using the Alberta consumer price index. The average cost added to LTS after accounting for treating severe bowel injury is approximately $35 (that is, 0.15% × $23,228).

Appendix E.A: Literature search summary

Table E.A.1: Literature search summary – Hysteroscopic tubal sterilization - Economics

Database	Edition or date searched	Search Terms ††
Core Databases		
MEDLINE (includes in-process articles) (OVID interface)	2 March 2012	1 Hysteroscopy/ 2 (hysteroscop* or transcervical or Essure or Adiana).tw. 3 exp Sterilization, Tubal/ or exp Sterilization, Reproductive/ 4 sterili?ation.tw. 5 1 or 2 6 3 or 4 7 5 and 6 8 exp "Costs and Cost Analysis"/ 9 (cost* or economic* or expensive*).tw. 10 (expenditures or price or fiscal or financial or burden or efficiency or pay or valuation or spending or resource*).ti 11 8 or 9 or 10 12 7 and 11 **(37 results)**
Embase (OVID interface)	2 March 2012	1 Hysteroscopy/ 2 (hysteroscop* or transcervical or Essure or Adiana).tw. 3 female sterilization/ or uterine tube sterilization/ 4 sterili?ation.tw. 5 1 or 2 6 3 or 4 7 5 and 6 8 limit 7 to animals 9 7 not 8 10 Health economics/ or exp economic evaluation/ or exp health care cost/ or cost/ 11 (cost* or economic* or expensive*).tw. 12 (expenditures or price or fiscal or financial or burden or efficiency or pay or valuation or spending or resource*).ti. 13 or/10-12 14 13 and 9 **(56 results)**
Cochrane Library (including Cochrane Reviews, DARE, CENTRAL, Technology Assessments, Economic Studies)	5 March 2012	#1 MeSH descriptor Hysteroscopy, this term only #2 (hysteroscop* or transcervical or Essure or Adiana) #3 MeSH descriptor Sterilization, Reproductive, this term #4 MeSH descriptor Sterilization, Tubal, this term only #5 (sterili*ation) #6 (#1 OR #2) #7 (#3 OR #4 OR #5) #8 (#6 AND #7) #9 (cost* or economic* or expenditures or price or fiscal or financial or burden or efficiency or pay or valuation or spending) #10 (#9 AND #8) **(17 results)**

Web of Science	5 March 2012	# 7 #6 AND #3 # 6 #4 OR #5 # 5 TI =(cost* or economic* or expenditures or price or fiscal or financial or efficiency or pay or valuation) # 4 TS=(cost-benefit or benefit-cost or cost effectiv* or cost utility or economic evaluat* or economic analys* or cost analys* or costs analys* or "cost of illness") # 3 #1 and #2 # 2 TS=(sterili?ation) # 1 TS=(hysteroscop* or transcervical or Essure or Adiana) **(24 results)**
CINAHL	5 March 2012	S9 S7 and S8 S8 economic* or cost* S7 S5 and S6 S6 S3 or S4 S5 S1 or S2 S4 (sterili*ation) S3 (MH "Sterilization, Sexual") OR (MH "Sterilization, Tubal") S2 (hysteroscop* or transcervical or Essure or Adiana) S1 (MH "Hysteroscopy") **(5 results)**
Guidelines		
AMA Clinical Practice Guidelines *www.topalbertadoctors.org/cpgs.php*	12 March 2012	Browsed list of topics **(0 results)**
NICE Guidance *www.nice.org.uk/*	12 March 2012	sterilization or sterilisation or hysteroscopic or transcervical **(1 result)**
CMA Infobase *http://mdm.ca/cpgsnew/cpgs/index.asp*	12 March 2012	sterilization or sterilisation or hysteroscopic or transcervical **(0 results)**
National Guideline Clearinghouse *www.ngc.gov*	12 March 2012	sterilization or sterilisation or hysteroscopic or transcervical **(3 results)**
Society of Obstetricians and Gynaecologists Canada *www.sogc.org/index_e.asp*	12 March 2012	Browsed list of guidelines **(0 results)**
Coverage/Regulatory/Licensing Agencies		
Alberta Health *www.health.gov.ab.ca*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical **(0 results)**
Medical Devices Active License Listing *www.mdall.ca/*	12 March 2012	Essure or Adiana or hysteroscopic or permanent birth control or permanent contraceptive or sterilization or sterilisation **(2 results)**
Health Canada *www.hc-sc.gc.ca*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical **(0 results)**
US Food and Drug Administration Databases *www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive **(2 results)**

Aetna Clinical Policy Bulletins *www.aetna.com/about/cov_det_policies.html*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(1 result)**
HTA resources		
INESS *www.inesss.qc.ca/*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(0 results)**
CADTH www.cadth.ca/index.php/en/	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(2 results)**
Institute for Clinical and Evaluative Sciences (ICES), Ontario *www.ices.on.ca/*	12 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control **(0 results)**
Health Technology Assessment Unit at McGill *www.mcgill.ca/tau/*	12 March 2012	Browsed list **(0 results)**
Medical Advisory Secretariat *www.health.gov.on.ca/english/providers/program/mas/mas_mn.html*	12 March 2012	Browsed list **(0 results)**
Dissertations		
Proquest Dissertations and Theses	13 March 2012	Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive* or permanent birth control **(0 results)**
Search engines		
Google	14 March 2012	transcervical sterilization OR hysteroscopic sterilization OR Essure OR Adiana economic OR cost -pubmed **(3 results)**
NHS Evidence	14 March 2012	Hysteroscopic sterilization or transcervical sterilization or Essure or Adiana **(2 results)**

[††],*, #, and ? are truncation characters that retrieve all possible suffix variations of the root word, for example, surg* retrieves surgery, surgical, surgeon, etc.

Searches separated by semicolons have been entered separately into the search interface.

Appendix E.B: Summarized evidence

Table E.B.1: Summarized evidence from selected studies

#	Item	Description
1	Study	Authors/publish year: Thiel et al[14]/2008; country: Canada; study type: retrospective cohort study; setting: ambulatory for Essure®/OR for LTS; study perspective: na
	Objective	To compare the cost of Essure® system with the traditional laparoscopic tubal sterilization (LTS)
	Population	Women seeking permanent tubal sterilization
	Intervention	Essure® system versus laparoscopic tubal sterilization
	Time horizon/ discount rate	Short time/na
	Currency/ price year	Canadian $/na
	Outcomes measure	Not stated. The study compared the cost per case.
	Cost components	Nursing, OR including anaesthesia, Essure® micro-insert coils or Filshie clips, and disposables, and ancillary including hospital charges, ultrasound, and hysterosalpingography
	Results	
	Outcomes	108 women underwent the hysteroscopic sterilization and 104 women underwent laparoscopic tubal sterilization. The success rate at the first attempt was 95% (103 out of 108) for the Essure® and 100% for the laparoscopic tubal sterilization.
	Costs	The cost (SD) per case was $1,288 ($2,450) for Essure® system and $1,398 ($36) for laparoscopic tubal sterilization. The difference ($111) in costs was statistically significant (p<0.01).
	Marginal analysis	na
	Conclusion	The Essure® procedure was associated with a significant cost saving.
2	Study	Authors/publish year: Kraemer et al[15]/2008; country: USA; study type: cost comparison; setting: office for Essure®/outpatient for LBTL; study perspective: Medicaid provider
	Objective	To compare the costs of the Essure® system to those of laparoscopic bilateral tubal ligation (LBTL)
	Population	Women seeking permanent tubal sterilization
	Intervention	Essure® system versus LBTL
	Time horizon/ discount rate	5 years/3%
	Currency/ price year	US$/2008
	Outcomes measure	Not stated. The study compared the cost per case.
	Cost components	Procedure, ectopic pregnancy, induced abortion, spontaneous abortion, and live birth
	Results	
	Outcomes	na
	Costs	Total costs per patient were $2,367 for Essure® and $3,545 for LBTL, with a saving of $1,178.
	Marginal Analysis	na

	Conclusion	Essure® was associated with significant cost savings over five years compared to LBTL.
3	Study	Authors/publish year: Hopkins et al[16]/2007; country: USA; study type: retrospective cohort study; setting: hospital OR; study perspective: na
	Objective	To compare the costs of the Essure® system with those of laparoscopic tubal sterilization (LTS)
	Population	Women seeking permanent tubal sterilization
	Intervention	Essure® system versus laparoscopic tubal sterilization
	Time Horizon/discount rate	Short time/na
	currency/ price year	US $/na
	Outcomes measure	Not stated. The study compared the cost per case.
	Cost components	Physician and hospital costs; a breakdown of the costs was not provided.
	Results	
	Outcomes	The study assessed 43 women who underwent the hysteroscopic sterilization and 44 women who underwent laparoscopic tubal sterilization.
	Costs	The total cost was $2,700 for the Essure® system and $2,880 for laparoscopic tubal sterilization, with a difference of $180.
	Marginal Analysis	na
	Conclusion	The Essure® procedure had significant cost savings compared to those of laparoscopic tubal sterilization.
4	Study	Authors/publish year: Franchini et al[17]/2009; country: Italy; study type: prospective cohort study; setting: hospital OR; study perspective: na
	Objective	To compare the costs of the Essure® system with those of laparoscopic tubal sterilization (LTS)
	Population	Women seeking permanent tubal sterilization
	Intervention	Essure® system versus laparoscopic tubal sterilization
	Time Horizon/discount rate	Short time/na
	Currency/ price year	€
	Outcomes measure	Not stated: The study reported the costs per case
	Cost components	OR, recovery unit □and hospital stay, material, physician, nurse and staff, laboratory testing
	Results	
	Outcomes	The study assessed□25 women in the Essure hysteroscopic sterilization and 24 women in the laparoscopic tubal sterilization.
	Costs	The Essure® system was associated with significantly higher costs of the operating theatre than those of LTS (€1,411.96 ±36.9 versus €893.73 ±213.56); and with significantly lower total health□costs than□LTS (€1,830.96±43.69 versus €2,704.83 ±246.4).
	Marginal Analysis	na
	Conclusion	Essure® was less expensive than LTS

Appendix E.C: QHES instrument

Table E.C.1: QHES instrument

#	Questions	QHES Scores			
		Thiel, 2008[14]	Kraemer, 2009[15]	Hopkins, 2007[16]	Franchini, 2009[17]
1	Was the study objective presented in a clear, specific, and measurable manner?	7	7	7	7
2	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	0	4	0	0
3	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial—best, expert opinion—worst)?	7	7	7	8
4	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	1	1	1
5	Was uncertainty handled by: (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	8	9	8	8
6	Was incremental analysis performed between alternatives for resources and costs?	6	6	6	6
7	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	5	5	5
8	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond one year discounted (3 to 5%) and justification given for the discount rate?	7	7	7	7
9	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	8	8	8
10	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes.	0	0	0	0

11	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	0	0	0	0
12	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	8	8	8
13	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	5	7	5	4
14	Did the author(s) explicitly discuss the direction and magnitude of potential biases?	0	0	3	0
15	Were the conclusions/recommendations of the study justified and based on the study results?	8	8	8	8
16	Was there a statement disclosing the source of funding for the study?	0	0	0	0
	TOTAL POINTS	**70**	**77**	**73**	**70**

Appendix E.D: Unit cost and ICER of HTS

Table E.D.1: Unit cost and ICER of HTS over a range of inputs

Device	Low value: $880			High value: $1,320		
	LTS	Calgary	SAS	LTS	Calgary	SAS
Cost	$2,026	$1,901	$1,895	$2,026	$2,357	$2,356
Incr*		-$124	-$131		$331	$330
ICER**		Dominating LTS	Dominating LTS		$15,324	$11,913
Facility costs	**Low value: $544**			**High value: $816**		
	LTS	Calgary	SAS	LTS	Calgary	SAS
Cost	$2,026	$2,082	$2,077	$2,026	$2,176	$2,173
Incr*		$56	$1,089		$51	$147
ICER**		$2,593	$39,314		$2,361	$5,307
LTS hospital costs	**Low value: $1,113**			**High value: $1,891**		
	LTS	Calgary	SAS	LTS	Calgary	SAS
Cost	$1,562	$2,129	$2,125	$2,341	$2,129	$2,125
Incr*		$567	$563		-$212	-$216
ICER**		$26,250	$20,325		Dominating LTS	Dominating LTS
LTS physician costs	**Low value: $360**			**High value: $539**		
	LTS	Calgary	SAS	LTS	Calgary	SAS
Cost	$1,936	$2,129	$2,125	$2,116	$2,129	$2,125
Incr*		$193	$189		$14	$9
ICER**		$8,935	$6,823		$648	$325
Success rate	**Low value: 88%**			**High value: 100%**		
	LTS	Calgary	SAS	LTS	Calgary	SAS
Cost	$2,026	$2,315	$2,424	$2,026	$2,069	$2,028
Incr*		$289	$398		$43	$2
ICER**		$13,380	$14,368		$1,991	$72

* – incremental cost

** – The incremental health outcome used to calculate ICER is constant over the range of cost inputs; that is, the incremental success rate compared to LTS is 0.0216 for HTS – Calg. and 0.0277 for HTS – Sask. (see Table E.4 for details).

References

1. Moga C, Harstall C. *Hysteroscopic Tubal Sterilization (Essure System)*. Edmonton, AB: Alberta Heritage Foundation for Medical Research, 2006.
2. Ofman JJ, Sullivan SD, Neumann PJ, et al. Examining the value and quality of health economic analyses: implications of utilizing the QHES. *Journal of Managed Care Pharmacy* 2003;9(1):53-61.
3. Connor VF. Essure: A review six years later. *Journal of Minimally Invasive Gynecology* 2009:16(3):282-290.
4. Peterson HB, Xia Z, Hughesa JM, et al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. *American Journal of Obstetrics and Gynecology* 1996;174(4):1161-1170.
5. Lawrie TA, Nardin JM, Kulier R, et al. Techniques for the interruption of tubal patency for female sterilisation. *Cochrane Database of Systematic Reviews* 2011;(2):CD003034.
6. Cooper JM, Carignan CS, Cher D, et al. Microinsert nonincisional hysteroscopic sterilization. *Obstetrics & Gynecology* 2003;102(1):59-67.
7. Duffy S, Marsh F, Rogerson L, et al. Female sterilisation: a cohort controlled comparative study of ESSURE versus laparoscopic sterilisation. *BJOG* 2005;112(11):1522-1528.
8. Sinha D, Kalathy V, Gupta JK, et al. The feasibility, success and patient satisfaction associated with outpatient hysteroscopic sterilisation. *BJOG* 2007;114(6):676-683.
9. Vancaillie TG, Anderson TL, Johns DA. A 12-month prospective evaluation of transcervical sterilization using implantable polymer matrices. *Obstetrics & Gynecology* 2008;112(6):1270-1277.
10. Vleugels MPH, Veersema S. Hysteroscopic sterilisation in the outpatient department without anaesthesia. *Gynecological Surgery* 2005;2(3):155-158.
11. Thiel J, Suchet I, Tyson N, et al. Outcomes in the ultrasound follow-up of the Essure micro-insert: complications and proper placement. *Journal of Obstetrics & Gynaecology Canada* 2011;33(2):134-138.
12. Woolhandler S, Campbell T, Himmelstein DU. Costs of Health Care Administration in the United States and Canada. *New England Journal of Medicine* 2003;349(8):768-775.
13. Chuck A. Cost-effectiveness of 21 alternative cervical cancer screening strategies. *Value in Health* 2010;13(2):169-179.
14. Thiel JA, Carson GD. Cost-effectiveness analysis comparing the essure tubal sterilization procedure and laparoscopic tubal sterilization. *Journal of Obstetrics & Gynaecology Canada* 2008;30(7):581-585.
15. Kraemer DF, Yen PY, Nichols M. An economic comparison of female sterilization of hysteroscopic tubal occlusion with laparoscopic bilateral tubal ligation. *Contraception* 2009;80(3):254-260.
16. Hopkins MR, Creedon DJ, Wagie AE, et al. Retrospective cost analysis comparing Essure hysteroscopic sterilization and laparoscopic bilateral tubal coagulation. *Journal of Minimally Invasive Gynecology* 2007;14(1):97-102.

17. Franchini M, Cianferoni L, Lippi G, et al. Tubal sterilization by laparoscopy or hysteroscopy: which is the most cost-effective procedure? *Fertility & Sterility* 2009;91(4 Suppl):1499-1502.

18. MAGRINA JF. Complications of laparoscopic surgery. *Clinical Obstetrics and Gynecology* 2002;45(2).

19. Alberta Health and Wellness. *Alberta Case Cost Report for 2006/2007 Hospital Activity*. Alberta Health and Wellness, 2009.

Author Contribution Statements

Dr. Carmen Moga contributed to authoring the background section and conducted the study conception, design, literature selection, quality assessment, and data extraction, analysis, and interpretation of the technology effects and effectiveness section.

Dr. Maria Ospina contributed to the literature selection and quality assessment of studies of the technology effects and effectiveness section.

Ms. Christa Harstall contributed to the study conception, design, data analysis, and interpretation of the technology effects and effectiveness section and revision of background and technology effects and effectiveness sections for critical content.

Dr. Charles Yan contributed to the study conception, design, data analysis, and interpretation of the economic analysis section.

Dr. Anderson Chuck contributed to the study conception, design, data analysis, and interpretation of the economic analysis section and was the project lead of the STE review.

Ms. Dagmara Chojecki contributed by developing and executing the literature search for the STE review.

This report is an evidence assessment of the clinical effectiveness and safety of hysteroscopic tubal sterilization, and the value for money associated with adopting hysteroscopic tubal sterilization in Alberta.

Institute of Health Economics
1200 – 10405 Jasper Avenue
Edmonton AB Canada T5J 3N4
Tel. 780.448.4881 Fax. 780.448.0018
info@ihe.ca

www.ihe.ca

ISBN 978-1-926929-35-4 (on-line)