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This is an update to a previously published Alberta STE Report.

Alberta STE Reports are 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.
Project Lead
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Declared Competing Interest of Authors
Competing interest is considered to be financial interest or 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.

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**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.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CADTH</td>
<td>Canadian Agency for Drugs and Technologies in Health</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<td>DESH</td>
<td>Dutch Essure® versus Salpingectomy for Hydrosalpinx trial</td>
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<tr>
<td>FDA</td>
<td>United States Food and Drug Administration</td>
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<td>HSG</td>
<td>hysterosalpingography</td>
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<td>HTS</td>
<td>hysteroscopic tubal sterilization</td>
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<td>IVF</td>
<td>in vitro fertilization</td>
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<td>LBTL</td>
<td>laparoscopic bilateral tubal ligation</td>
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<td>LTS</td>
<td>laparoscopic tubal sterilization</td>
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<td>MAUDE</td>
<td>Manufacturer and User Facility Device Experience</td>
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<td>MDR</td>
<td>Medical Device Reports</td>
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<td>OHTAC</td>
<td>Ontario Health Technology Advisory Committee</td>
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<td>OR</td>
<td>odds ratio</td>
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<td>PMA</td>
<td>Premarket Approval</td>
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<td>TVU</td>
<td>transvaginal ultrasound</td>
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Request

This rapid report has been produced in response to a request from Alberta Health to provide an update on the new published research evidence on the efficacy/effectiveness, efficiency, and safety of hysteroscopic tubal sterilization (HTS) using the Essure® system for permanent birth control since the publication of the Institute of Health Economics (IHE) STE report in September 2014. Only updated information related to the Background and T sections of the STE report is included in the present rapid report.

Project Scope

The scope of this rapid 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.

Appendices for this rapid report 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: evidence on effectiveness from new published studies
- Appendix D: evidence on safety from new published studies
- Appendix E: summary of new guidelines recommendations

Technology

The Essure® system is indicated for women who desire permanent fertility control by bilateral occlusion of the fallopian tubes. A particular use of the system is in women who have comorbidities that are contraindications for laparoscopic tubal sterilization (LTS), due to a higher surgical risk. The Essure® system, consisting of two micro-inserts and two delivery catheters, was originally manufactured by Conceptus Inc. (Mountain View, CA, USA), and was acquired by Bayer HealthCare LLC (CA, USA) in June 2013.

With the currently available device, immediate tubal occlusion is not guaranteed, and thus a confirmation test is required at three months. Hysterosalpingography (HSG) is considered the standard test for the determination of tubal occlusion, and can also confirm the satisfactory position of the micro-inserts. An ultrasound can confirm only the satisfactory position of the micro-inserts. To avert the requirement for three-month contraception during the wait period before the confirmation test, the manufacturer of the device developed a third-generation Essure® system (ESS505) by modifying the currently approved ESS305 device to incorporate a synthetic polymer.
hydrogel seal on the distal end of the micro-insert. Exposure to an aqueous environment causes the distal end to swell, potentially enabling immediate tubal occlusion.2

**Confirmation of fallopian tubal occlusion**

Until June 2015, the United States Food and Drug Administration (FDA)-approved Essure® confirmation test of fallopian tubal occlusion was limited to a modified HSG. In June 2015, the FDA approved an algorithm that allows transvaginal ultrasound (TVU) to serve as the confirmation test in lieu of the modified HSG.3 Since 2011, TVU was an accepted method for the Essure® confirmation test in several countries in the European Union and elsewhere. TVU, however, does not provide confirmation of occlusion. Individual physician training and assessment of comprehension is required before users may adopt the TVU/HSG protocol.

**Regulatory status in Canada, the United States, and other countries**

In Canada, the Essure® permanent birth control system was granted a Medical Device License by Health Canada as a Class 3 device in November 2001. The most recently (2006) approved version of the device is the ESS305 system, presently manufactured by Bayer HealthCare LLC (CA, USA). As of January 2016, the status of the Essure® system is unchanged.

In the United States, the Obstetrics and Gynecology Devices Panel recommended Premarket Approval (PMA) for the Essure® system in July 2002. As of January 2016, the status of the Essure® system is unchanged.

The Essure® system is commercially available in other countries, including Australia, several European countries, several Latin and South American countries, and several Asia Pacific countries. According to the manufacturer, about one million Essure® systems have been distributed worldwide.4

**Available Evidence on Efficacy/Effectiveness and Safety**

**Conclusions from the 2014 IHE STE review**

The IHE published a systematic review1 (STE review) in September 2014 based on a comprehensive literature search of electronic databases for articles published between 2006 and February 2012. The conclusions of the review (T section), based on evidence from eight case series studies published between 2006 and 2011,5-12 were that 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. With 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 later regret in younger women. The intervention prevents pregnancies at at least the same level as 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 for longer periods of time are not known. Such information is especially 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 both physicians and patients using the system are important factors that impact the success of the intervention. The Essure® system has the advantages of avoiding surgical incisions and general anaesthesia, and of promising a faster recovery time. The hysteroscopic approach could potentially be a clear indication for women with a relative
contraindication for laparoscopy due to morbid obesity, intra-abdominal adhesions, or cardiopulmonary diseases, or for those with contraindications for general anaesthesia. 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 counselling are key, due to the irreversibility of the Essure® system.

**New available evidence on efficacy/effectiveness and safety**

To update the September 2014 T section of the STE review, a comprehensive literature search of electronic databases was performed for this rapid report, for articles published between 2012 and January 2016 (see Appendix A). The search identified 462 new citations (see Figure 1). A list of the 74 excluded publications is available in Appendix B. The following summarizes the evidence found, from 20 publications, by type of publication.

**Figure 1: Selection of included studies**

A. Evidence from health technology assessments

The Essure® system was reviewed by two Canadian health technology assessment (HTA) agencies, which published their reports in August and December 2012.\(^{13,14}\)

An evidence-based analysis was conducted in 2013 by Health Quality Ontario\(^ {13}\) to determine what the effectiveness and safety of HTS is compared to tubal ligation for permanent female sterilization. The review was based on research literature published between January 2008 and December 2012. A
lack of long-term follow-up for HTS and a paucity of studies that directly compare the two procedures limited the assessment. In addition, optimal placement of the micro-inserts at the time of hysteroscopy varied among studies. The review conducted by Health Quality Ontario found that that HTS is a safe, effective, and less invasive alternative to tubal ligation for female sterilization. The authors concluded that HTS was associated with lower pregnancy rates, lower complication rates, and no significant improvement in patient satisfaction compared to tubal ligation, based on very low quality of the evidence. The Ontario Health Technology Advisory Committee (OHTAC) recommends that: a) HTS be considered as an alternative to tubal ligation for female sterilization; and b) access issues regarding HTS being provided in an outpatient setting be considered as part of the associated implementation strategy.

In August 2012, the Canadian Agency for Drugs and Technologies in Health (CADTH) published a rapid response\textsuperscript{14} on the evidence-based guidelines regarding the Essure\textsuperscript{®} system for hysteroscopic tubal occlusion, based on a limited literature search conducted on key resources published up to August 2012. The review did not meet the definition of a systematic review (see Appendix A, Inclusion criteria), and was excluded from this rapid report.

B. Evidence from quasi-systematic reviews

Four quasi-systematic reviews were published between 2013 and 2015 in the United States,\textsuperscript{15,16} Italy,\textsuperscript{17} and the Netherlands\textsuperscript{18} with the scope to: assess whether HTS is feasible and effective in preventing pregnancy; identify risk factors for failure of HTS;\textsuperscript{18} review the risk of Essure\textsuperscript{®} micro-insert abdominal migration;\textsuperscript{17} identify when and how often pregnancies occur following HTS;\textsuperscript{15} and compare interval laparoscopic bilateral tubal ligation (LBTL) versus HTS in terms of procedure completion rates, reliance, procedure efficacy, pain, and complication rates.\textsuperscript{16} The reviews did not meet the definition of a systematic review (see Appendix A, Inclusion criteria); their results and conclusions are in line with the conclusions of the T section of the 2014 STE review.\textsuperscript{1} The following is a brief summary of the four quasi-systematic reviews and their conclusions as reported by their authors.

Chapelle et al.\textsuperscript{18} conducted a literature search for studies published up to February 2014, and included 37 Essure\textsuperscript{®} studies (26 prospective, nine retrospective, one ambispective, and one with unclear perspective) with a total of 14,126 women. None of the included studies were randomized control trials. The authors stated that they assessed the quality of the included studies using an adapted checklist. However, the authors did not provide the checklist or the individual quality appraisal results in the publication, and no response was received from the corresponding author regarding the quality assessment of the included studies. The reported successful bilateral placement of the micro-inserts in a first attempt was between 81 and 98%. Pregnancy rates after sterilization could not be calculated, and, as the incidence of complications and their severity had not been studied or reported adequately in the included studies, such remained unclear. The authors concluded that HTS with the Essure\textsuperscript{®} system seems feasible, but that the effectiveness and risk factors for failure of sterilization remain unclear, owing to the poor-quality evidence. The authors also stated that the Essure\textsuperscript{®} technique needs a proper evaluation of its feasibility and effectiveness, and that appropriate randomized controlled trials and observational studies with sufficient power as well as complete and long-term (more than 10 years) follow-up data on unintended pregnancies and complications are needed.

Cleary et al.\textsuperscript{15} conducted a literature search for studies published up to March 2012, and included 22 studies published between 2001 and 2012 of women who underwent Essure\textsuperscript{®} placement. The results
of the quality assessment of the included studies only include the level of the evidence based on the type of studies included. A total of 102 pregnancies were reported in 11 studies, of which 15 occurred after imaging confirmation of correct micro-insert placement or tubal occlusion. The remaining 87 pregnancies occurred most frequently in women who did not have any or accurate follow-up imaging, who were not using effective contraception in the first three months after placement, or who were already pregnant at the time of placement. The research evidence is of fair quality; most of the included studies had less than five years of follow-up, with only one study reporting seven years of follow-up. The authors concluded that further studies are needed to address the long-term effectiveness of HTS using the Essure® system.

Ricci et al.\textsuperscript{17} conducted a literature search for studies published between 2002 and December 2013, and included eight studies describing 12 cases of Essure® abdominal migration. The included studies were not critically appraised for quality. According to the authors, various factors may influence the risk of HTS complication, among which are the operator’s experience and anatomical anomalies such as ostium stenosis, occlusion, no visible ostium/scarring, extremely lateral/tortuous tubes, and uterine pathology polyps, adhesions that may make placement of the Essure® micro-inserts difficult. Another risk factor may be represented by using general anaesthesia during the intervention, which may hide pain due to tubal perforation. The authors made the following recommendations for reducing the risks in the case of a complicated procedure:

- The correct placement of both micro-inserts should be ascertained by adequate imaging, and the patient should be strictly followed-up.
- In the case of the occurrence of pelvic or abdominal symptomatology, bowel obstruction or perforation should be immediately excluded.
- In the case of asymptomatic device displacement detected at the three-month follow-up, a laparoscopy should be performed and the device removed, and bilateral laparoscopic sterilization should be performed.
- The removed device should be carefully inspected and compared with a new, unused one through a magnifying glass (because of the small size coils) in order to exclude that fragments were left in the abdomen.
- In cases where the original placement was complicated, the opportunity of removing the contralateral device should also be considered, and a follow-up of the patient is necessary.

The authors also advised that, during pre-sterilization counselling, the patient should be correctly informed about the risk of this rare but relevant complication, as well as about the surgical interventions that could be required to solve it. The rate and the severity of complications of other available sterilization methods should also be taken into account and made comparable with Essure® sterilization for an informed choice.

Ouzounelli and Reaven\textsuperscript{16} conducted a literature search for studies published up to October 2013, and included 18 primary studies (13 on the Essure® system, four on LBTL, and one that compared the Essure® system and LBTL). When contacted by email, the corresponding author stated that the risk of bias/quality assessment of the included studies was conducted, but did not provide the individual assessment results. The analysis was limited by the restricted number of studies involving head-to-head comparisons of the two approaches, and the authors concluded that both LBTL and the Essure® intervention are safe and effective methods of female sterilization, and that both have
high rates of efficacy and low rates of complications. However, when complications do occur, the authors stated that those related to the Essure® intervention were more likely to be minor in nature.

C. Evidence from primary studies

At the time of writing, no randomized controlled trials on the Essure® system have been published. Our updated literature search identified four retrospective case series studies that evaluated the results of HTS with the Essure® system in outpatient settings. These studies were published between 2012 and 2015 in Spain, the United States, Australia, and European countries. One study was a multi-centre study, and two were seven- and five-year follow-up studies of previous publications. The following are brief summaries of the studies’ results and conclusions (see also Appendix C, Table C.1, and Appendix D, Tables D.1 and D.2).

In 2012, Povedano et al. published a retrospective seven-year follow-up study that is a multiple publication of Mino et al. (2007), Arjona et al. (2008), and Rios-Castillo et al. (2013), the latter of which included results from a five-year follow-up. Povedano et al. included 4,306 women who underwent the Essure® sterilization procedure between 2003 and 2010 in a single-office hysteroscopic unit in a teaching hospital in Spain; only 921 of these women were followed-up for seven years. The aim of the study was to analyze the short-, medium-, and long-term complications with the Essure® device. There were 115 recorded complications reported, none of which resulted in the need for hospitalization or discharge later than two hours after the procedure. Vasovagal syncope was the most frequently encountered adverse event, occurring in 85 women. In 19 cases, one micro-insert was expelled, with most expulsions (14 out of 19) being detected before or during the three-month follow-up procedure. The authors concluded that outpatient HTS using the Essure® system is safe with a low rate of complications. In another multiple publication by Arjona et al. (2014) that focused on the prevalence of chronic pain, seven women out of 4,274 presented with chronic pelvic pain that required micro-insert removal. Four of the women classified their pain perceived during the procedure as medium or high. The mean time between placement and removal of the Essure® micro-inserts in the seven women with chronic pain was 29.4 months. The authors concluded that the development of chronic pelvic pain is very uncommon after placement of Essure® micro-inserts, and that removal of the inserts improved the pain.

In 2015, Chudnoff et al. published a multi-centre five-year follow-up retrospective case series study, conducted in 13 centres in Australia, countries from Europe, and the United States. The objective was to describe the long-term safety, tolerability, effectiveness results, prevention of pregnancy, and satisfaction of a phase III trial with the ESS205 Essure® model (an old version that is not presently used), published by Cooper et al. in 2008. Approximately 30% of the initial population did not complete the full five-year follow-up, either because of study termination or loss to follow-up. No pregnancies were reported among the 449 women relying on the Essure® micro-inserts who completed the full duration of follow-up. The majority of adverse events reported during the five years were mild or moderate in severity, as self-rated by participants in the study. Three severe events that involved abdominal pain with very heavy periods and irregular menstrual bleeding were reported in two subjects during follow-up as being possibly related to the procedure or the micro-inserts. Pelvic pain was reported in 7% or less of study participants at any visit (see also Appendix D, Table D.3). No subjects reported persistent pelvic pain of any kind at the three-, four-, and five-year follow-up visits. However, an important caveat mentioned by the authors is that women with preexisting chronic pain (which was seen to be associated with pelvic chronic pain after Essure® placement) were excluded from participation in the study. The authors noted that 43% of
participants in the study were using oral contraceptives before Essure® placement as their birth control modality, which might have masked the abnormal and heavy bleeding, as well as pelvic pain. The Essure® micro-inserts were generally well-tolerated by 382 out of 385 women who participated in a follow-up survey. The comfort was rated by 99% of the women surveyed after five years of use as “good” to “excellent”. A total of 376 out of 384 women were “somewhat” to “very” satisfied.

The authors stated that the findings from the extended follow-up study further support the effectiveness, tolerability, and satisfaction with Essure® micro-inserts.

In 2013, Anderson et al. published a retrospective single-centre case series study, with the aim to determine factors associated with HTS success in 638 women who received the HTS with the Essure® system. The authors also sought to determine if there were any differences related to the setting of the procedure (that is, an operating room versus an office setting). Successful bilateral device placement and occlusion of the fallopian tubes did not differ between the intervention settings. Occlusion of the fallopian tubes was achieved in 88% of the women (89% in the operating room and 86% in the office setting, p-value [p]=0.50; confidence interval [CI] 95% -1.03 to 0.50).

Three pregnancies were reported in the study population. Two women encountered a vasovagal episode, two had a micro-insert expulsion, and one had a malpositioned device.

In 2015, Truong et al. published a retrospective case series study conducted in one academic centre between August 2003 and April 2010, with the aim to evaluate the relationship between hormonal endometrial preparation duration and the placement success rate of the Essure® device in 247 women. The success rate of Essure® placement was 91.5% (94.4 % in the hormonal preparation group and 72.7% in the non-hormonal group; p<0.05), but the duration of hormonal treatment did not affect the rate of successful Essure® placement (p=0.518). The results of the study supported the use of hormonal endometrial preparation prior to HTS. The authors concluded that more studies are needed to validate their findings.

**D. HTS in specific populations**

**The Essure® system in the management of hydrosalpinx before in vitro fertilization**

In infertile women, hydrosalpinx reduces the success rate of in vitro fertilization (IVF). The surgical management of hydrosalpinx before IVF (that is, laparoscopic salpingectomy) improves the outcomes (pregnancy rates), but the procedure is contraindicated in women with dense pelvic adhesions. Tubal occlusion of the fallopian tubes with the Essure® system provides an alternative treatment. Two studies on this population were identified, one systematic review and one retrospective case series studies, published in 2014 in the United Kingdom and France. The following are brief summaries of the studies’ results and conclusions (see also Appendix C, Table C.2, and Appendix D, Table D.1).

In the systematic review, Arora et al. conducted a literature search for studies published up to July 2013, and included 11 studies with a total of 115 women. The majority of the included studies were small case series or single case reports, and only one study had a control group. The objective of the systematic review was to analyze the use of the Essure® system in the management of hydrosalpinx before IVF. The Essure® intervention was chosen as a treatment modality for hydrosalpinx in women with previous pelvic adhesions secondary to abdominopelvic surgery, endometriosis, Crohn’s disease, pelvic inflammatory disease, and tuberculosis, in order to avoid morbidity potentially associated with an operative/surgical intervention. The Essure® micro-inserts were successfully placed in 96.5% of the women in the included studies. Tubal occlusion after Essure®
placement was assessed by HSG in most of the included studies, and was confirmed in 98.1% of the women. Two procedure-related complications were reported, one false passage during Essure® placement because of severe uterocervical angulation secondary to pelvic adhesions, and one case of pyosalpinx. The authors’ conclusion was that the Essure® system seemed to be an effective option for the management of hydrosalpinx before IVF where other operative treatment options were limited by the presence of pelvic adhesions; for this group of women with infertility, the Essure® system could become the preferred alternative intervention. However, for women with hydrosalpinx where presence of pelvic adhesions is not a complicating factor, the Essure® system is considered a nonsurgical option among a range of other surgical options such as laparoscopic salpingectomy or proximal tubal occlusion. Research evidence from a randomized control trial is lacking.

The retrospective case series study by Legendre et al. was published after the systematic review by Arora et al. and was therefore not included in that review. Legendre et al. surveyed hospitals in France to identify those who used the Essure® system for the management of hydrosalpinx prior to IVF, and included forty-three women who had undergone the procedure in seven hospital centres. The bilateral and unilateral occlusion of the fallopian tubes with the Essure® system was successful in 95.3% of the women, and confirmed occlusion of the fallopian tubes via pelvic ultrasound, x-ray, hysteroscopy, or HSG was reported in 74.4%. Three procedure-related complications were reported, expulsion of the device into the uterus in two women, and one case of pyosalpinx. The authors concluded that Essure® placement is an effective method for the occlusion of hydrosalpinges before IVF. The Essure® device should not be used as the first step of the treatment of hydrosalpinx, but only when laparoscopic salpingectomy is contraindicated because of a major risk of bowel injury, such as severe endometriosis or pelvic inflammatory disease with frozen pelvis.

An ongoing randomized trial DESH (Dutch Essure® versus Salpingectomy for Hydrosalpinx) with the aim to evaluate and compare the impact of HTS using the Essure® system with the standard treatment (laparoscopic removal of hydrosalpinx, or salpingectomy) in women before IVF treatment was also reported by Arora et al.

**The Essure® system and hysteroscopic endometrial ablation**

Two retrospective case series studies on a combined procedure consisting of HTS using the Essure® system and hysteroscopic endometrial ablation were identified, both published in France. The following are brief summaries of the studies’ results and conclusions (see also Appendix C, Table C.3, and Appendix D, Tables D.1 and D.2).

In 2014, Levy-Zauberman et al. published a retrospective case series study with the aim to evaluate the efficacy of endometrial ablation (specifically by endometrectomy, the Thermachoice® technique, or the NovaSure® technique) combined with HTS using the Essure® system, as well as the satisfaction with the combined procedure. The procedures were conducted in France between 2002 and 2011 in 131 non-menopausal women with abnormal uterine bleeding. The mean duration of follow-up was 37.8 months (with a range eight to 87 months). The bilateral placement of the Essure® device was achieved in 90.8% of the study population. The bilateral occlusion of the fallopian tubes with the Essure® system was confirmed to be successful using HSG, 3D pelvic ultrasound, or pelvic x-ray tests in 65.6% of the women. A high number of the women were lost to follow-up (25 did not undergo the three-month follow-up after Essure® placement, and 38 were lost to follow-up after the endometrial ablation). Twelve women underwent a hysterectomy, seven of which were a direct consequence of treatment failure (it is not clear if the failure was related to the Essure® micro-inserts). No pregnancies were reported during the follow-up period. The satisfaction
rate was 90.3% (score of 5 to 10 out of 10), and 85% of the women who received the combined procedure would recommend it to a friend. The endometrial ablation and concomitant tubal sterilization by the Essure® micro-inserts were found to be safe and effective. The authors concluded that a subsequent study should be conducted to assess the stability of the results on abnormal uterine bleeding over time, and evaluate if, with more experience, the rate of adequate insert position can be improved. The authors commented that the combined procedure is not approved by the FDA in the United States because it is considered difficult to interpret the results of an HSG (that is, the preferred imaging technique for insert position confirmation) in the case of synechiae caused by endometrial ablation. In France, HSG at the three-month follow-up is not the reference examination test. Starting in June 2015, the FDA accepts TVU as a method for the Essure® placement confirmation test in lieu of HSG.

In 2012, Basinski et al. published a retrospective case series study from a single private practice that included 117 women seeking permanent birth control and menorrhagia reduction between July 2008 and December 2009. The aim of the study was to evaluate the safety and feasibility of using the NovaSure® radiofrequency endometrial ablation technique after HTS using the Essure® system, and to determine if the effectiveness of either procedure was altered by this in-office treatment sequence. The procedures were typically scheduled to be 14 days apart. Bilateral placement of the Essure® micro-inserts was reported in 97.4% of the women, and confirmation of bilateral occlusion of the fallopian tubes was confirmed with HSG at the three-month follow-up in 83 women. Information on satisfaction was obtained from 97 women who underwent Essure® placement and 96 women who had endometrial ablation using the NovaSure® technique. Twenty-two out of 97 women reported a satisfactory decrease in menstrual flow, and three reported ablation failure. Eighty-nine out of 97 women were very satisfied and eight satisfied with the Essure® intervention, while 83 out of 96 women were very satisfied and 11 satisfied with the NovaSure® procedure. All of the women in the study would recommend the Essure® intervention to others, while all but one would recommend the NovaSure® procedure. In-office Essure® placement followed by NovaSure® endometrial ablation at about 14 days apart appeared to be safe, effective, and associated with high patient satisfaction. The authors commented that, despite positive results with Essure® placement followed by the NovaSure® procedure, several concerns remain when considering the performance of a NovaSure® procedure when Essure® micro-inserts were previously placed in a patient. It is unclear: if radiofrequency energy and/or heat transfer from the NovaSure® procedure along the Essure® micro-insert could increase the likelihood of surrounding bowel injury over use of NovaSure® endometrial ablation alone; if the Essure® micro-inserts could cause malfunction of the NovaSure® mesh that is inserted during the procedure; what is the probability that a properly placed Essure® micro-insert will become dislodged or damaged because of adherence to the NovaSure® mesh that is removed after completion of the endometrial ablation procedure; and if the sequence of Essure® placement followed by the NovaSure® procedure could decrease the effectiveness of either intervention.

There are two ongoing multi-centre case series studies on this combined procedure. One study, sponsored by Bayer, aims to evaluate the effectiveness and safety of the Essure® (ESS305 model) system when a NovaSure® procedure is performed following a successful Essure® placement confirmation test. This study includes 200 women and has an estimated completion date of 2021. Another ongoing study with an estimated primary completion date in June 2016 is sponsored by Hologic Inc., and its aim is to evaluate the safety of the NovaSure® procedure in the presence of the Essure® system, following the Essure® placement confirmation test.
E. Sterilization with the Essure® system versus other methods

The updated literature search identified two population-based cohort retrospective studies conducted in the United States and France that compared HTS using the Essure® system and LTS, and one single-centre retrospective comparative study of the Essure® system and LTS conducted in France. The following are brief summaries of the studies’ results and conclusions.

In 2015, Mao et al. published a cohort study using statewide, all-inclusive population data to compare the safety and efficacy of HTS using the Essure® system with LTS. The study included 8,048 women who underwent HTS and 44,278 women who underwent LTS in outpatient settings in New York State between 2005 and 2013.

Compared to the women undergoing LTS, a larger proportion of the women undergoing HTS were 40 years of age and older, had one or more comorbidities, had a higher prevalence of previous pelvic inflammatory disease, and were more likely to have a history of major abdominal surgery or caesarean section.

Surgical iatrogenic complications (HTS 0.2% versus LTS 0.4%; p<0.01) and major medical complications (HTS % value not reported versus LTS 0.1%) following both procedures were rare. After adjusting for patient characteristics and hospital clustering, HTS was associated with lower risk of iatrogenic complications within 30 days after surgery, compared to LTS (odds ratio [OR] 0.35; CI 95% 0.20 to 0.61). Unintended pregnancy occurrence was similar after HTS and LTS (1.2% versus 1.1%; p=0.66), while reoperation (repeated sterilization) risk within one year was higher (10-fold increase) after HTS (2.4% versus 0.2%; p<0.01). Women who underwent HTS were eight times more likely to undergo reoperation at two years after initial surgery (OR 7.96; CI 95% 6.00 to 10.57) and six times more likely at three years (OR 5.88; CI 95% 4.44 to 7.79), compared to women who had undergone LTS. In the subgroup analyses of those who underwent HTS, the higher risk of reoperation persisted in various age groups and in patients with history of pelvic inflammatory disease. Reoperation was determined based on repeated procedures on fallopian tubes. HTS procedures were associated with shorter procedure time (median 36 minutes versus 52 minutes; p<0.01) and less frequent use of general anaesthesia (50.6% versus 75.8%; p<0.01) but higher total charges (median US$7,832 versus US$5,068; p<0.01), compared to LTS procedures.

The authors commented on the major public health impact of HTS, noticing a trend toward increasing the number HTS procedures in New York State from 45 cases to 1,231 cases every year during the review period (2005 to 2013), while the number of LTS procedures decreased from 7,852 to 3,517 annually, over the same period of time. A registry-based study with longer follow-up is warranted to further understand the failure events after an HTS procedure, and to improve the safety and efficacy of the sterilization procedure. Benefits and risks should be discussed with patients for informed decision-making.

In their 2014 study, Fernandez et al. compared the rates of pregnancy among women who underwent HTS with the Essure® system versus LTS in France between 2006 and 2010. The incidence of pregnancy was examined by searching the hospital records related to hospitalization during pregnancy or for giving birth. A limitation of the study was the impossibility to trace pregnancies that did not involve hospitalization at any stage. A total of 39,169 Essure® placements and 70,108 LTS procedures were performed during the study period. The study found that spontaneous and assisted pregnancies occurred less often among women who underwent Essure®
placement than among those undergoing LTS (pregnancy rates in the Essure® group was 0.36% versus 0.46% in the LTS group).

In 2014, Kathy et al. published a retrospective non-controlled study with the aim to compare the success rate, patient satisfaction, discomfort, procedure time, and intraoperative adverse events of HTS using the Essure® system versus LTS using Filshie® Clips in 70 women who underwent the procedures between April 2008 and December 2011 in a district general hospital in France. Placement of the Essure® micro-inserts was achieved in 45 out of 50 women initially scheduled for the procedure. LTS was conducted in five women from the HTS group with unsuccessful placement of the micro-inserts, as well as 20 other women. Bilateral placement of the micro-inserts was achieved in 82% women from the HTS group. The intervention was successful in 100% women who had the LTS procedure. Forty women were assessed with HSG as the confirmation test three months following Essure® placement, and correct placement and bilateral occlusion was confirmed in all forty women. Compared to the LTS group, the operative mean time in the HTS group was significantly shorter (mean time 15.6 minutes versus 35.2 minutes; p<0.001). No pregnancies were reported in the HTS and LTS groups (mean follow-up duration was 18 months in the HTS group and 20 months in the LTS group). The mean postoperative self-reported pain score in the HTS group on a 10-point scale was 3.2 (with a range of 0 to 9) compared to 6.5 (with a range of 1 to 10) in the LTS group (p<0.001). The pain during the HSG confirmation test was described as severe by 15 out of 40 women on a scale of mild, moderate, and severe. Three women stated they would reconsider HTS using the Essure® system on the experience of the HSG test alone. One woman from the HTS group was treated with antibiotics for endometritis, while, in the LTS group, one woman required readmission for analgesia for pain and two women were treated with antibiotics for wound infection. On a three-point scale of satisfaction, 42 women (93%) were “very satisfied” and three women (7%) were “somewhat satisfied” with HTS, while 92% women were “very satisfied” and 8% were “somewhat satisfied” with LTS. The authors concluded that HTS using the Essure® system is a safe and effective alternative to LTS, with statistically significant less procedure-related postoperative pain, significantly shorter operative time, shorter hospital stay, and faster return to normal activities.

F. Third-generation Essure® system

In 2014, Thiel et al. published a case series study on 30 women scheduled to undergo a hysterectomy in Saskatchewan. Women underwent placement of the ESS505 model of the Essure® system (that is, the new, third generation of the device) in the right fallopian tube, and placement of the ESS305 model (that is, the commercially approved, previous version of the device) in the left fallopian tube at 30 (n=10), 60 (n=10), or 90 (n=10) days before a planned hysterectomy. The authors concluded that the modified ESS505 demonstrates a high rate of both immediate- and intermediate-term tubal occlusion in most women (93%) in each of the three study groups. A prospective trial of the safety and effectiveness of the new ESS505 model in women seeking permanent sterilization is planned.

An ongoing multi-centre, multinational clinical study sponsored by Bayer is aiming to evaluate the safety and effectiveness of the ESS505 model to prevent pregnancy in 617 women who are seeking permanent contraception. The study is being conducted in Canada, the Netherlands, Spain, and the United States. The study will determine if the new design modification of the Essure® system provides immediate birth control, thereby removing the three-month waiting period required for the commercially available ESS305 model to be effective. The study started in September 2013, its
primary completion date is September 2016 (that is, the final data collection date for primary outcome measure), and the estimated study completion date is December 2024.

Guidelines and Policies

In 2013, the American College of Obstetricians and Gynecologists published guideline recommendations that support the use of hysteroscopic occlusion techniques followed by a confirmatory HSG for tubal occlusion, based on limited or inconsistent scientific evidence (Level B – recommendations based on limited or inconsistent scientific evidence).34 “Hysteroscopic occlusion techniques, followed by a confirmatory HSG, have at least equal if not superior efficacy to tubal occlusion done via laparoscopy or minilaparotomy. Hysteroscopic procedures require the use of an alternative method of contraception for at least three months after the procedure and until a confirmatory HSG indicates successful tubal occlusion.” The literature search for this guideline was conducted for relevant articles published up to October 2012.

More recently, the American College of Obstetricians and Gynecologists reaffirmed its support for less-invasive tubal occlusion options such as the Essure® system. To improve the use of HTS in the future, the College called for the FDA to take steps toward obtaining more high-quality data on its safety and efficacy/effectiveness, and also called upon clinicians to obtain HSG confirmation of tubal occlusion three months after the operation.4

In September 2014, the Faculty of Sexual & Reproductive Healthcare in the United Kingdom published a clinical practice guideline on male and female sterilization35, 36 which addresses HTS and updates the 2004 Royal College of Obstetricians and Gynaecologists guideline. The guideline is based on published research evidence up to 2014, and includes recommendations for anaesthesia and analgesia for HTS, insertion of the micro-inserts, intraoperative complications with tubal micro-inserts, postoperative complications of HTS, and post-procedure imaging following micro-insert placement, as well as training issues, patient satisfaction, and hysteroscopic sterilization, and other related procedures such as endometrial ablation (see Appendix E).

In April 2015, the Society of Obstetricians and Gynaecologists of Canada published clinical practice guidelines for endometrial ablation in the management of abdominal uterine bleeding.37 The guideline is based on a literature search for publications up to December 2014, and includes a statement on the combined HTS and endometrial ablation procedure, indicating that “combined hysteroscopic sterilization and endometrial ablation can be safe and efficacious while favouring a minimally invasive approach.”

Discussion

The present rapid report builds on and updates the technology effectiveness/efficacy and safety section of a 2014 STE review on HTS using the Essure® system for permanent birth control,1 prepared by the IHE in response to a request from Alberta Health. To find updated information, a comprehensive literature search was conducted for studies published from March 2012 (that is, the date of the last searches conducted for the 2014 IHE review) to January 2016. Only full-text, English language articles were included; conference abstracts were excluded. The corresponding authors of two quasi-systematic reviews16, 18 were contacted for more details about the quality appraisal of the included studies, and the author of a population-based study31 was contacted for more details regarding the analyses of the results. One reviewer screened the abstracts of published
studies, applied the predefined inclusion criteria, conducted brief data extraction, and summarized the research evidence.

**Evidence from HTA reports**

The update review found two Canadian HTA publications: the 2013 review with recommendations\(^{13}\) developed by OHTAC that stated that HTS is considered an alternative intervention to tubal ligation; and the 2012 rapid response\(^{14}\) prepared in 2012 by CADTH, which was excluded.

**Evidence from quasi-systematic reviews**

Four quasi-systematic reviews\(^{15-18}\) were published between 2013 and 2015 that included between eight and 37 primary studies on the Essure\(^\circledR\) system. The objectives of the reviewers were to assess whether HTS is feasible and effective in preventing pregnancy, to identify risk factors for failure of HTS\(^{18}\) to identify when and how often pregnancies occur following HTS\(^{15}\) to review the risk of Essure\(^\circledR\) micro-insert abdominal migration\(^{15}\) and to compare interval laparoscopic bilateral tubal ligation with HTS in terms of procedure completion rates, reliance, procedure efficacy, pain, and complication rates\(^{16}\). None of the identified reviews met the predefined inclusion criteria of a systematic review. One review\(^{17}\) did not include a critical appraisal of the included studies. Although the authors of three reviews\(^{15,16,18}\) indicated in their methods section that they had appraised the quality of the included studies, and that studies were of weak quality, the reviews did not include in the review the results of the appraisals nor clearly provide the quality appraisal checklists. Some of the primary studies included in the reviews were multiple publications, and it was not clear if their outcome results were duplicated in the analysis. Other studies were single case reports. The conclusions of the reviews were, in general, in line with those of the 2014 IHE systematic review; authors stated that, although HTS with the Essure\(^\circledR\) system seems to be effective and safe, further studies are needed to address the long-term effectiveness and safety of the procedure, and to compare the Essure\(^\circledR\) system with other sterilization approaches.

**Evidence from primary studies**

No randomized controlled trial has been conducted to compare the efficacy and safety of HTS using the Essure\(^\circledR\) system with traditional LTS.

Four retrospective case series studies\(^{19-22}\) were published between 2012 and 2015 in Australia, Spain, the United States, and European countries. Two follow-up studies at five\(^{20}\) and seven years\(^{19}\) concluded that HTS using the Essure\(^\circledR\) system is safe and has a low rate of complications. However, not all participants included in the follow-up studies were observed for the entire durations of follow-up. On short-term follow-up, in one study\(^{21}\) the authors did not find any difference between conducting the Essure\(^\circledR\) placement in an operating room or an office setting. In another study,\(^{22}\) the outcome results supported the use of hormonal endometrial preparation prior to HTS; however, the rate of success of fallopian tube occlusion was not affected by the duration of hormonal treatment, and the authors concluded that more studies are needed to validate the findings.

**Evidence from studies on specific populations**

Two studies were conducted on women who underwent Essure\(^\circledR\) placement for hydrosalpinx prior to IVF: one systematic review\(^{27}\) published in 2013 that included 11 case series studies and single case reports; and one retrospective case series study\(^{28}\) published in 2014. The outcome results reported were positive, and the Essure\(^\circledR\) intervention was considered particularly useful in women who have pathology that contraindicate laparoscopic salpingectomy due to previous pelvic adhesions.
secondary to abdominopelvic surgery, endometriosis, Crohn’s disease, pelvic inflammatory disease, or tuberculosis.

Two retrospective case series studies conducted in France and published in 2012 and 2014 evaluated the effectiveness, safety, and satisfaction of women who received the combined procedure of HTS using the Essure® system and hysteroscopic endometrial ablation (specifically by endometrectomy, the Thermachoice® technique, or the NovaSure® technique). Although the combined procedures are performed in countries from Europe, it is considered difficult to interpret the results of an HSG in the case of synechiae caused by endometrial ablation, and, until June 2015, the combined procedures were not approved by the FDA in the United States, where HSG was considered the preferred imaging technique for insert position confirmation. Two ongoing multicentre case series studies are reported, one sponsored by Bayer and one by Hologic Inc., to evaluate the effectiveness and safety of HTS using the Essure® system when a NovaSure® radiofrequency endometrial ablation procedure is performed following a successful Essure® placement confirmation test, and to evaluate the safety of the NovaSure® procedure in the presence of the Essure® micro-inserts following the Essure® placement confirmation test, respectively.

Evidence from comparative studies

Two population-based cohort retrospective studies published in the United States in 2015 and France in 2014 compared HTS using the Essure® system and LTS. In the United States study, the unintended pregnancy rates were similar in patients who underwent HTS and LTS; however, HTS was associated with over 10-fold higher risk of reoperation, defined as repeated procedures on the fallopian tubes. The higher risk of reoperation after HTS was also found in various age groups and patients with history of pelvic inflammatory disease. Compared to LTS, a larger proportion of the women who underwent HTS were 40 years of age and older, had one or more comorbidities, had a higher prevalence of previous pelvic inflammatory disease, and were more likely to have a history of major abdominal surgery or caesarean section, which may have contributed to the failure of the HTS procedure at first or second attempts. The French study found that spontaneous and assisted pregnancies occurred less often among the Essure® group compared to those undergoing laparoscopic tubal ligation. A limitation of this study was the impossibility to trace pregnancies that did not involve hospitalization at any stage.

In another non-controlled comparative study published in 2014, in a single district general hospital in France, HTS using the Essure® system was found to be a safe and effective alternative to LTS. Women receiving HTS reported less procedure-related postoperative pain and shorter operative times and hospital stay, and benefited from a faster return to normal activities, compared to LTS.

Evidence from clinical practice guidelines

Two guidelines published in 2013 by the American College of Obstetricians and Gynecologists and in 2014 by the Faculty of Sexual & Reproductive Healthcare in the United Kingdom support the use of HTS for permanent fertility control. In April 2015, the Society of Obstetricians and Gynaecologists of Canada published clinical practice guidelines for endometrial ablation in the management of abdominal uterine bleeding, and included a statement that supports the combined hysteroscopic sterilization and endometrial ablation procedure. The United Kingdom guideline issued an expert opinion recommendation that states that intra-fallopian micro-insert insertion can be carried out in combination with endometrial ablation.
Strengths and limitations of the new included publications

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.

The recently published primary case series studies have a retrospective design, and some of the variables collected may not have been accurately documented for each patient included. Even if recently published, some of the studies reported results from interventions conducted in earlier years of the technology, up to 2010 or 2011. Not all included studies reported information about the type/generation of the Essure® system used. Since its initial introduction, the manufacturer has reported improvements in the design of the device and better outcomes. Therefore, inaccurate results may result from the synthesis of outcome results from primary studies that used different generations of the device, or analyses of outcomes from the same study over a longer follow-up period that involved different generations of the technology, or analyses of outcomes in all-inclusive population type or ecological studies over a longer period of time (which do not allow for causal conclusions to be drawn because data are not associated with individual persons).

In general, in the publications reviewed, not all participants completed the entire follow-up period, either because of early study termination or loss to follow-up. Also, not all participants were followed-up at three months with the HSG test, which provides confirmation of the occlusion of the fallopian tubes and establishes the correct position of the micro-inserts, or with other tests (for example, x-ray, TVU) that indicate the correct position of the micro-inserts.

In general, the percentages of successful bilateral placement of the Essure® micro-inserts and occlusion of the fallopian tubes reported in the recent studies are in line with those found and reported in the 2014 IHE systematic review. However, the adverse event rates may not be known with certainty because of potential recall and reporting bias, which may have been introduced owing to the nature of the retrospective data collection in most of the new studies, self-reporting, and duration of follow-up.

There is no available information about the quality of life and limited information about the satisfaction and tolerance with HTS using the Essure® system on longer follow-ups from the new publications. When it was available, the satisfaction and tolerance information was recorded mostly in a subset of participants, and indicated positive experience with the device.

Several limitations exist with conducting a non-controlled comparative study of HTS and LTS. It is a comparison of two methods of sterilization with clearly different surgical approaches (hospital admission with general anaesthesia versus outpatient office interventions with no or less anaesthesia) and different target populations, who may also have different perceptions of tolerance and satisfaction.

Some of the authors of the included studies were affiliated with the manufacturer of the Essure® system (Conceputus Inc. or Bayer HealthCare LLC, starting in June 2013), or acted as consultants for the manufacturer, or received funds from the manufacturer to attend scientific meetings and congresses and/or expenses for conducting the studies. These competing interest issues raise the question of reporting and publication bias.

Additional information on adverse events

Adverse events associated with Essure® placement have been a topic of recent interest. Some of the adverse events recently reported by women who underwent HTS using the Essure® system such as
changes in the amount of bleeding and bleeding intervals as well as pelvic pain may have been masked with the use of hormonal contraception before the HTS procedure in some of the women. An important caveat is that women with preexisting chronic pain were excluded from participation in some of the published studies. Because incidence data rely on both the patient reporting pain to their provider and the provider recording this in the medical record, the reported results are likely an underestimate rather than an overestimate of the pain incidence.

In one excluded study published in 2015 by Yunker et al., women with a preexisting diagnosis of any chronic pain such as pelvic, low back, headache, or fibromyalgia were more than six-fold more likely than women without preexisting chronic pain to report either acute or chronic pain after Essure® placement. The authors suggested caution in performing HTS in patients with a history of chronic pain, and emphasized the need for counselling patients that pelvic pain may develop after the procedure.

Beginning in late 2013, the FDA received a significant increase in the number of adverse event reports related to the Essure® system, particularly from patients who received the device in the United States. In response, the FDA prepared a review of studies published up to June 2015 on HTS using the Essure® system, for a meeting in September 2015 of the FDA’s Obstetrics and Gynecology Devices Advisory Panel Center for Devices and Radiological Health, with the aim to discuss the Essure® device, its approved use, effectiveness, and selected reported complications. The following are reported limitations of the studies that involved the Essure® system, as summarized in the FDA review:

- Many studies are retrospective, which may be more susceptible to study bias than prospective studies and could lead to biased estimates of incidence rates.
- Very few studies reported data for a comparison group receiving an alternate sterilization procedure such as tubal ligation, and therefore it is difficult to assess incidence rates and device-related events such as compared to the general population or women who received other sterilization procedures.
- The majority of studies are single-site studies that reported results obtained by physicians with extensive device experience, while some studies were multiple publications that reported on the same study or patient population from a given centre at different time points.
- Study enrolment varied considerably in the numbers of patients included.
- Some studies provided limited follow-up in terms of duration and/or percentage of patients completing follow-up.
- Details about events such as device migration and perforation were lacking in many publications.
- Multiple studies and authors listed affiliation with the manufacturer of the Essure® system, which may introduce a publication bias toward published positive results or competing interest.

The FDA has a passive surveillance system in place of Medical Device Reports (MDRs) for device-associated deaths, serious injuries, and malfunctions. The Manufacturer and User Facility Device Experience (MAUDE) database houses MDRs submitted to the FDA by mandatory reporters (manufacturers, importers, and device-user facilities) and voluntary reports such as healthcare
professionals, patients, and consumers (see Appendix D, Table D.4). Limitations of such a surveillance system as stated in the FDA report include the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. Also, the incidence or prevalence of an event cannot be determined from the reporting system alone due to potential under-reporting of events and lack of information about frequency of device use. Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified, or if the device in question has not been directly evaluated. The MAUDE data is subject to reporting bias, attributable to potential causes such as reporting practice, increased media attention, and/or other agency regulatory actions. The MAUDE data does not represent all known safety information for a reported medical device, and should be interpreted in the context of other available information when making device-related or treatment decisions.

In February 2016, the FDA proposed a boxed warning for the Essure® system, which states that clinicians should inform women about the potential adverse events. This discussion is supposed to happen with a proposed patient checklist that asks the patient to initial that she has been told about: alternatives to the Essure® method of permanent sterilization; the increased risk for an ectopic pregnancy; adverse events such as pelvic pain, excessive fatigue, and hypersensitivity reactions; and the need for a confirmation test at three months after implantation of the micro-inserts. The FDA also requires Bayer to conduct a post-marketing study in the next 15 months that involves an estimated 2,000 women who must be followed for at least three years. The study will compare the adverse events experienced by Essure® device users with those who undergo bilateral tubal ligation.

Conclusions

The majority of new published studies found in this updated literature search support the following:

- HTS using the Essure® system can be an alternative to laparoscopic sterilization for women in whom visualization of both tubal ostia is possible, for women who have the anatomical possibility for micro-insert placement, and for women who have a contraindication for laparoscopic tubal sterilization.

- The intervention prevents pregnancies at least the same levels as 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 for longer periods of time are not known, and the details about medium- and long-term adverse events are lacking from the publications. An increased incidence of adverse events associated with Essure® placement (such as chronic pelvic pain, changes in the amount and intervals of bleeding, perforation, and expulsion of the device) were recently reported in the FDA MAUDE database, and these require further investigation. Further studies are needed to address the long-term effectiveness and safety of the procedure, and to compare HTS using the Essure® system with other approaches of sterilization.

- In specific populations, Essure® placement was found useful in women who have pathology that contraindicates laparoscopic salpingectomy prior to IVF. The combined HTS and endometrial ablation procedure in non-menopausal women with abnormal uterine bleeding were reported successful.

A clinical study is ongoing to evaluate the safety and effectiveness of a third-generation Essure® model (ESS505), which promises a high rate of both immediate-term and intermediate-term tubal Hysteroscopic tubal sterilization (using the Essure® system) – An update
occlusion and avert the requirement for three-month contraception after the procedure by producing an immediate occlusion of the fallopian tubes. Another two ongoing studies are evaluating the effectiveness and safety of the combined Essure® and endometrial ablation procedures.
Appendix A: Methodology

Search Strategy

The IHE Research Librarian (DC) conducted a search of electronic databases to retrieve articles published between 2012 and 12 January 2016. The search was developed and carried out prior to the study selection process.

The searches were limited to human studies. 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 FDA) databases. In addition to the strategy outlined below, reference lists of retrieved articles were reviewed for potential studies.

Table A.1: Databases and search terms used in the search strategy

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<td>sterilization or sterilisation or hysteroscopic or transcervical</td>
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</tr>
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<td>19 January 2016</td>
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</tr>
<tr>
<td>US Food and Drug Administration Databases</td>
<td>19 January 2016</td>
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</tr>
<tr>
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<tr>
<td>HTA resources</td>
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<td>25 January 2016</td>
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</tr>
<tr>
<td>CADTH</td>
<td>27 January 2016</td>
<td>Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control</td>
</tr>
<tr>
<td>Institute for Clinical and Evaluative Sciences (ICES), Ontario</td>
<td>27 January 2016</td>
<td>Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control</td>
</tr>
<tr>
<td>Health Technology Assessment Unit At McGill</td>
<td>27 January 2016</td>
<td>Browsed list</td>
</tr>
<tr>
<td>OHTAS - Health Quality Ontario</td>
<td>27 January 2016</td>
<td>Browsed list</td>
</tr>
<tr>
<td>Dissertations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proquest Dissertations and Theses</td>
<td>27 January 2016</td>
<td>Essure or Adiana or hysteroscopic or transcervical or tubal occlusion or permanent contraceptive or permanent birth control</td>
</tr>
<tr>
<td>Clinical Trials Registries</td>
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<td>WHO Clinical Trials Registry</td>
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<td>Adiana OR Essure</td>
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</tbody>
</table>
Controlled Clinical Trials Meta-registry www.controlled-trials.com/ 27 January 2016 No longer in existence

Search Engines

<table>
<thead>
<tr>
<th>Engine</th>
<th>Date</th>
<th>Search Terms</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
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<td>27 January 2016</td>
<td>tubal occlusion OR permanent contraceptive OR permanent birth control OR sterilisation OR sterilization -pubmed Essure OR Adiana OR hysteroscopic OR transcervical</td>
<td>18 results</td>
</tr>
<tr>
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<td>27 January 2016</td>
<td>Hysteroscopic sterilization or transcervical sterilization or Essure or Adiana</td>
<td>4 results</td>
</tr>
</tbody>
</table>

† “*”, “#”, and “?” are truncation characters that retrieve all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc. Searches separated by semicolons have been entered separately into the search interface.

**Literature selection**

One reviewer (CM) screened titles and abstracts and retrieved relevant articles. The same reviewer determined eligibility of key studies according to the inclusion and exclusion criteria below.

**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):

- 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 intra-fallopian 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, musculoskeletal, 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: February 2012 to January 2016.

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 TVU or 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

No quality assessment of the included studies was conducted due to time limitation.

Data extraction

One reviewer (CM) extracted data according to a predetermined data extraction form. Extracted information was limited due to timing and included: publication and study characteristics (for example, setting, study population, intervention), 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), and other woman-important outcomes (quality of life, satisfaction, tolerance).

Data analysis and synthesis

Data from the included studies was summarized narratively. No statistical pooling of outcome data was performed. New outcomes were presented in tabular form together with the outcomes from studies included in the 2014 IHE STE report, for comparison.
Appendix B: Excluded Studies

Three hundred sixty-eight 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 74 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=11). However, four quasi-systematic reviews\textsuperscript{15-18} were summarized in the report.
2. The article was not published in English (n=5).
3. The study did not evaluate the safety and/or efficacy/effectiveness of HTS as a method for elective permanent sterilization (n=5).
4. The study was a case report or a non-randomized comparative study that compared the exposure of participants but not the intervention (n=6).
5. The study did not focus on the technology of interest (n=1).
6. The study did not focus on the population of interest (n=1).
7. The report was a conference abstract (n=45).

1. The article was not primary original research or secondary research (systematic review) (n=11)


Robinson LLL, Cooper NAM, Clark TJ. The role of ambulatory hysteroscopy in reproduction.


2. The article was not published in English (n=5)


3. The study did not evaluate the safety and/or efficacy/effectiveness of HTS as a method for elective permanent sterilization (n=5)


4. The study was a case report or non-randomized comparative study that compared the exposure of participants but not the intervention (n=6)


Chapa HO, Antonetti AG, Sandate J. Office versus hospital based Essure® procedure: Pareto


5. The study did not focus on the technology of interest (n=1)


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


7. The report was a conference abstract (n=45)

List of excluded conference abstracts available upon request.
Appendix C: HTS with the Essure® System – Evidence on Effectiveness

Table C.1: Evidence from primary studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Bilateral placement</th>
<th>1st attempt</th>
<th>2nd attempt</th>
<th>Unilateral placement</th>
<th>LSTM</th>
<th>Confirmed bilateral occlusion of the fallopian tubes</th>
<th>Lost to follow-up</th>
<th>Pregnancy (length of follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P: Andersson 2009[^2]</td>
<td>N=61</td>
<td>58/61 (95%)</td>
<td>52/61 (85%)</td>
<td>6 of 61</td>
<td>3/61 (5%) LTS: n=4</td>
<td>57/58 x-ray (n=38) or ultrasound (n=20); HSG (n=1)</td>
<td>0</td>
<td>0 (mean 23 mo. [range seven to 67])</td>
<td></td>
</tr>
<tr>
<td>P: Chapa 2011[^6]</td>
<td>N=161</td>
<td>158/161 (98%)</td>
<td>154/161 (96%)</td>
<td>4/161</td>
<td>3/161 (2%) LTS: n=3</td>
<td>125/158 HSG; 139/154 TUV</td>
<td>31</td>
<td>0/127 (at three mo.)</td>
<td></td>
</tr>
<tr>
<td>P: Levie 2006[^2]</td>
<td>N=102</td>
<td>98/102 (96%)</td>
<td>97/102 (95%)</td>
<td>1/102</td>
<td>4/102 (4%) LTS: n=1</td>
<td>89/98 HSG Other: 1/98 (time NR)</td>
<td>7</td>
<td>1 (before three mo.)</td>
<td></td>
</tr>
<tr>
<td>U: Mascaro 2008[^8]</td>
<td>N=28</td>
<td>27/28 (93%)</td>
<td>20 IUD + (71%) + 5 IUD-</td>
<td>2 IUD-</td>
<td>1/28 (4%) LTS: n=0</td>
<td>26/27 IUD+: 19 x-ray + TVU IUD-: 5 x-ray + TVU &amp; 2 HSG</td>
<td>1</td>
<td>0 (NR)</td>
<td></td>
</tr>
<tr>
<td>P: Mino 2007[^9]</td>
<td>N=857</td>
<td>830/857 (97%)</td>
<td>812/857 (95%)</td>
<td>18/857</td>
<td>12/857 (1%) LTS: n=0; n=3^23</td>
<td>835/845 x-ray ± HSG At six mo.: 9/845 HSG (n=77 HSG)</td>
<td>0</td>
<td>1 (undiagnosed at time of HTS)</td>
<td></td>
</tr>
<tr>
<td>P: Sinha 2007[^10]</td>
<td>N=112</td>
<td>103/112 (92%)</td>
<td>NR</td>
<td>NR</td>
<td>9/112 (8%) LTS: n=8</td>
<td>81/82 abdominal x-ray (n=16) or HSG (n=65) At six mo.: 1/82 HSG</td>
<td>21</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>P: Veersema 2011[^11]</td>
<td>N=1,145</td>
<td>1059/1145 (92%)</td>
<td>1,034/1,145 (90%)</td>
<td>25/1,145</td>
<td>13/1145 (7%) LTS: NR; n=3^4</td>
<td>1,037/1,059 TVU ± HSG</td>
<td>22</td>
<td>4/1,037 (at 24 mo.)</td>
<td></td>
</tr>
<tr>
<td>U: Vellayan 2006[^12]</td>
<td>N=100</td>
<td>87/100 (87%)</td>
<td>85/100 (85%)</td>
<td>2/100</td>
<td>13/100 (13%) LTS: n=2</td>
<td>Unclear; 79/83 uncomplicated bilateral placement: x-ray or HSG</td>
<td>Unclear: (4+4^1)</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>
### New R: Povedano 2012

- **N=4,306**
- **7 years follow-up N=921**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no.</td>
<td>4,200/4,306 (97.5%)</td>
</tr>
<tr>
<td>New R</td>
<td>42/4,306</td>
</tr>
<tr>
<td>LTS: NR</td>
<td>77/4,306 (1.7%)</td>
</tr>
<tr>
<td>At three mo.:</td>
<td>4,095/4,306 x-ray</td>
</tr>
<tr>
<td>Unclear number HSG, TVU</td>
<td>134 (at three mo.)</td>
</tr>
<tr>
<td>7 (3 before and 4 after three mo.)</td>
<td></td>
</tr>
</tbody>
</table>

### New R: Chudnoff 2015

- **N=enrolled 518; attempt 507**
- **USA, Europe, Australia**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no.</td>
<td>464/518 (89.6%)</td>
</tr>
<tr>
<td>New R</td>
<td>12/518</td>
</tr>
<tr>
<td>LTS: NR</td>
<td>31/518 (6%)</td>
</tr>
<tr>
<td>No placement: 11/518</td>
<td></td>
</tr>
<tr>
<td>At three mo.:</td>
<td>421/518 HSG</td>
</tr>
<tr>
<td>At six mo.:</td>
<td>16/518 HSG</td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4 (before three mo.)</td>
<td></td>
</tr>
</tbody>
</table>

### At 5-year follow-up:

<table>
<thead>
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<tbody>
<tr>
<td>At three mo.:</td>
<td>4,095/4,306 x-ray</td>
</tr>
<tr>
<td>Unclear number HSG, TVU</td>
<td>134 (at three mo.)</td>
</tr>
<tr>
<td>7 (3 before and 4 after three mo.)</td>
<td></td>
</tr>
</tbody>
</table>

### New R: Anderson 2013

- **N=638 (OR:364 + OS:274)**
- **USA**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no.</td>
<td>609/638 (95.5%)</td>
</tr>
<tr>
<td>(OR 349 + OS 260)/(OR 364 + OS 274)</td>
<td></td>
</tr>
<tr>
<td>New R</td>
<td>NR</td>
</tr>
<tr>
<td>LTS: NR</td>
<td>NR</td>
</tr>
<tr>
<td>At three mo.:</td>
<td>561/638 HSG</td>
</tr>
<tr>
<td>(OR 324 + OS 236)/(OR 364 + OS 274)</td>
<td></td>
</tr>
<tr>
<td>NR (77 did not attend HSG)</td>
<td>3</td>
</tr>
<tr>
<td>0 (1-year follow-up)</td>
<td></td>
</tr>
</tbody>
</table>

### New R: Truong 2015

- **N=271; 247 included in the analysis (24 excluded due to missing data)**
- **USA**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no.</td>
<td>226/247 (91.5%)</td>
</tr>
<tr>
<td>(H 203 + NH 23)/(H 216 + NH 31)</td>
<td></td>
</tr>
<tr>
<td>New R</td>
<td>NR</td>
</tr>
<tr>
<td>H: n=12</td>
<td></td>
</tr>
<tr>
<td>NH: n=9</td>
<td></td>
</tr>
<tr>
<td>LTS: NR</td>
<td>21/247 (8.5%)</td>
</tr>
<tr>
<td>Mini-laparotomy: n=1</td>
<td></td>
</tr>
<tr>
<td>At three mo.:</td>
<td>226/247 HSG</td>
</tr>
<tr>
<td>H: 203/247</td>
<td></td>
</tr>
<tr>
<td>NH: 23/247</td>
<td></td>
</tr>
<tr>
<td>Not clearly stated (24 excluded due to missing data)</td>
<td></td>
</tr>
<tr>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

---

**Note:** studies included in the 2014 IHE systematic review are coloured grey.

**Study design:** P - prospective; R – retrospective; U – unclear

*LTS interventions reported in multiple publications; †Not clearly stated in the publication; ‡ Multiple publication of Mino and Arjona; § Not clearly stated

H: hormonal group; HSG: hysterosalpingography; HTS: hysteroscopic tubal sterilization; IUD: intrauterine device (IUD+ = user; IUD- = non user); LTS: laparoscopic tubal sterilization; mo.: month; N, n: number; n/a: not applicable; NH: non-preparation/non-hormonal group; NR: not reported; OR: operating room; OS: office setting; TVU: transvaginal ultrasound
## Table C.2: Essure® system for management of hydrosalpinx prior to in vitro fertilization

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Bilateral placement</th>
<th>Unilateral placement</th>
<th>Failed placement</th>
<th>Confirmed bilateral occlusion of the fallopian tubes</th>
<th>Lost to follow-up</th>
<th>Summary outcomes: Pregnancy (length of follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arora 2014²⁷</td>
<td>Systematic review</td>
<td>96.5% women</td>
<td>NR</td>
<td>1.9%</td>
<td>Number not clearly stated 98.1% women HSG; ultrasound scan (n=2 women)</td>
<td>NR</td>
<td>2 (before three mo.) 54 pregnancies from 140 embryo transfers performed in 75 women 39 live births 7 preterm births</td>
</tr>
<tr>
<td></td>
<td>N=11 studies (7 case series, 1 case series with control group, and 3 single case reports)</td>
<td>1st attempt: 114</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n=115 women</td>
<td>2nd attempt: 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>New</strong></td>
<td></td>
<td>36/43 (83.7%)</td>
<td>5 (11.6%)</td>
<td>NR</td>
<td>At three mo.: 32/43 (74.4%) HSG: 3; pelvic ultrasound: 18; x-ray: 21; hysteroscopy: 11</td>
<td>2</td>
<td>22 pregnancies from 54 embryo transfers performed in 29 women 14 live births</td>
</tr>
<tr>
<td>Legendre 2014²⁸</td>
<td>Retrospective case series study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=43 women (16 women had a unilateral hydrosalpinx and 27 had bilateral hydrosalpinges)</td>
<td>Survey of 45 French hospital centres; 7 out of 45 performed the procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*For all women, at least one imaging examination was performed.

HSG: hysterosalpingography; IVF: in vitro fertilization; LTS: laparoscopic tubal sterilization; mo.: month; N, n: number; NR: not reported
### Table C.3: Essure<sup>®</sup> system and hysteroscopic endometrial ablation

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Bilateral placement</th>
<th>Unilateral placement</th>
<th>Failed placement</th>
<th>Confirmed bilateral occlusion of the fallopian tubes</th>
<th>Lost to follow-up</th>
<th>Pregnancy (length of follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New R:</strong> Levy-Zauberman 2014&lt;sup&gt;29&lt;/sup&gt;</td>
<td>N=131</td>
<td>119/131 (90.8%)</td>
<td>2/131</td>
<td>10/131 (7.6%) LTS: n=1</td>
<td>Essure&lt;sup&gt;®&lt;/sup&gt; follow-up at three mo.: 106/131 (80.9%) (endometrectomy n=22; Thermachoice&lt;sup&gt;®&lt;/sup&gt; n=75, NovaSure&lt;sup&gt;®&lt;/sup&gt; n=9); Successful n=86, uncertain n=16, inadequate n=4</td>
<td>Essure&lt;sup&gt;®&lt;/sup&gt; at three mo.: n=25</td>
<td>0 (at follow-up mean 37.8 mo.: 0/93)</td>
</tr>
<tr>
<td>Essure&lt;sup&gt;®&lt;/sup&gt; + endometrial ablation (endometrectomy n=27; Thermachoice&lt;sup&gt;®&lt;/sup&gt; n=92, NovaSure&lt;sup&gt;®&lt;/sup&gt; n=12) France</td>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; attempt: 118/131</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; attempt: 1/131</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>New R:</strong> Basinski 2012&lt;sup&gt;30&lt;/sup&gt;</td>
<td>N=117</td>
<td>114/117 (97.4%)</td>
<td>3/117</td>
<td>4 patients with unsuccessful three- or six-mo. placement with HSG test</td>
<td>At three mo.: 83/117 (71%) HSG (n=71 after NovaSure&lt;sup&gt;®&lt;/sup&gt;; n=12 prior to NovaSure&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>6 after completion of both procedures</td>
<td>1 luteal phase pregnancy at time of Essure&lt;sup&gt;®&lt;/sup&gt; placement before NovaSure&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
<tr>
<td>Essure&lt;sup&gt;®&lt;/sup&gt; followed by NovaSure&lt;sup&gt;®&lt;/sup&gt; (interval between interventions 14 days) Intervention conducted by a single physician in a private practice</td>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; attempt: 114/117</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AUB: abnormal uterine bleeding; mo.: months; R: retrospective
## Appendix D: HTS with the Essure® System – Evidence on Safety Studies

### Table D.1: Adverse events related to HTS intervention

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study</th>
<th>Number AE/women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AE that prevented reliance on Essure®</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expulsion of micro-inserts</td>
<td>Arjona 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>12/1,615</td>
</tr>
<tr>
<td></td>
<td>Veersema 2011&lt;sup&gt;11&lt;/sup&gt;</td>
<td>2/1,145</td>
</tr>
<tr>
<td></td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>19/4,306</td>
</tr>
<tr>
<td></td>
<td>New Anderson 2013&lt;sup&gt;121&lt;/sup&gt;</td>
<td>2/638</td>
</tr>
<tr>
<td></td>
<td>New Legendre 2014&lt;sup&gt;128&lt;/sup&gt;</td>
<td>2/43</td>
</tr>
<tr>
<td></td>
<td>New Levy-Zauberman 2014&lt;sup&gt;1229&lt;/sup&gt;</td>
<td>1/131</td>
</tr>
<tr>
<td>Perforation of the fallopian tubes</td>
<td>Sinha 2007&lt;sup&gt;10&lt;/sup&gt;</td>
<td>1/112</td>
</tr>
<tr>
<td></td>
<td>Veersema 2011&lt;sup&gt;11&lt;/sup&gt;</td>
<td>7/1145</td>
</tr>
<tr>
<td></td>
<td>Vellayan 2006&lt;sup&gt;12&lt;/sup&gt;</td>
<td>1/100</td>
</tr>
<tr>
<td></td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>1/4,306</td>
</tr>
<tr>
<td>Migration of device to abdominal cavity</td>
<td>Arjona 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>3/1,615</td>
</tr>
<tr>
<td></td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>2/4,306</td>
</tr>
<tr>
<td></td>
<td>New Levy-Zauberman 2014&lt;sup&gt;1229&lt;/sup&gt;</td>
<td>1/131</td>
</tr>
<tr>
<td>Intramyometrial placement of devices</td>
<td>Arjona 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>2/1,615</td>
</tr>
<tr>
<td></td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>3/4,306</td>
</tr>
<tr>
<td></td>
<td>New Anderson 2013&lt;sup&gt;121&lt;/sup&gt;</td>
<td>1/638 (malpositioned)</td>
</tr>
<tr>
<td></td>
<td>New Arora 2014&lt;sup&gt;127&lt;/sup&gt;</td>
<td>2/115 (false passage) (SR, 11 studies included)</td>
</tr>
<tr>
<td>Pelvic inflammatory disease</td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>2/4,306</td>
</tr>
<tr>
<td></td>
<td>New Legendre 2014&lt;sup&gt;128&lt;/sup&gt;</td>
<td>1/43 (pyosalpinx)</td>
</tr>
<tr>
<td></td>
<td>New Arora 2014&lt;sup&gt;127&lt;/sup&gt;</td>
<td>1/115 (pyosalpinx) (SR, 11 studies included)</td>
</tr>
<tr>
<td></td>
<td>New Levy-Zauberman 2014&lt;sup&gt;1229&lt;/sup&gt;</td>
<td>1/131 (endometritis)</td>
</tr>
<tr>
<td>Nickel allergy</td>
<td>Arjona 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>1/1,615</td>
</tr>
<tr>
<td></td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>2/4,306</td>
</tr>
<tr>
<td>AE reported during the intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasovagal reaction</td>
<td>Andersson 2009&lt;sup&gt;5&lt;/sup&gt;</td>
<td>3/61</td>
</tr>
<tr>
<td></td>
<td>Arjona 2008&lt;sup&gt;23&lt;/sup&gt;</td>
<td>16/1,630</td>
</tr>
<tr>
<td></td>
<td>Sinha 2007&lt;sup&gt;10&lt;/sup&gt;</td>
<td>5/112</td>
</tr>
<tr>
<td></td>
<td>New Povedano 2012&lt;sup&gt;119&lt;/sup&gt;</td>
<td>85/4,306</td>
</tr>
<tr>
<td></td>
<td>New Anderson 2013&lt;sup&gt;121&lt;/sup&gt;</td>
<td>2/638</td>
</tr>
<tr>
<td></td>
<td>Basinski 2012&lt;sup&gt;130&lt;/sup&gt;</td>
<td>2/117</td>
</tr>
<tr>
<td>Light bleeding</td>
<td>Andersson 2009&lt;sup&gt;5&lt;/sup&gt;</td>
<td>2/61</td>
</tr>
<tr>
<td>Pain</td>
<td>Andersson 2009&lt;sup&gt;5&lt;/sup&gt;</td>
<td>36/61 (required additional analgesia) Pain tolerance self-reported on VAS: mean = 5.4 (range 1 to 10)</td>
</tr>
<tr>
<td>Author/Year</td>
<td>Sample Size</td>
<td>AE post-intervention short-term (up to two weeks)</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Andersson 2009*</td>
<td>N=61 (BP: N1=58)</td>
<td>• Nausea or uterine cramping n=1</td>
</tr>
<tr>
<td>Mino 2007§</td>
<td>N=857 (BP: N1=830)</td>
<td>• Pain requiring analgesia n_total=77; three days n1=10, ≥4 days n2=9</td>
</tr>
<tr>
<td>Arjona 2008*</td>
<td>N=1,630 (BP: N1=1,612)</td>
<td>• Pain requiring analgesia one or two days: 113/1,612</td>
</tr>
</tbody>
</table>

*Multiple publication of Mino 20079 (N=857)
†New studies, January 2016 update
‡Essure® + endometrial ablation
§Multiple publication of Levy 20067 (N=102)
AE: adverse event; CI: confidence interval; HTS: hysteroscopic tubal sterilization; SD: standard deviation; SPS: standardized pain score; SR: systematic review; VAS: visual analogue pain scale

**Table D.2: Self-reported adverse events, short-, medium-, and long-term post-HTS intervention**
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Authors</th>
<th>N</th>
<th>Pain at 48 hours</th>
<th>Pain at 6 days</th>
<th>Pain at 2 weeks</th>
<th>Removable device by</th>
<th>Pain at 6 mo., 12 mo., 18 mo., 24 mo., 48 mo., 60 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vellayan 2006</td>
<td>2006</td>
<td>2</td>
<td>N=100 (BP: N=87)</td>
<td>• Pain at 48 hours: no pain or mild pain 24/37, moderate pain 8/37, severe pain 6/37</td>
<td>• Pain at six days n=1</td>
<td>• Pain at two weeks n=2</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>New</td>
<td>Arjona Berral 2014</td>
<td>2014</td>
<td>N=4,274 – multiple publication of Milo/Arjona (above)/Povedano (new)</td>
<td>NR</td>
<td>NR</td>
<td>Pain n=7 (mild [3]; moderate [1]; severe [3])</td>
<td>Removal of device by: laparoscopy (5), hysteroscopy (2); time until removal (months range 4 to 57)</td>
<td></td>
</tr>
<tr>
<td>New</td>
<td>Chudnoff 2015</td>
<td>2015</td>
<td>N=enrolled: 518/attempt: 507</td>
<td>NR</td>
<td>23.6% intermenstrual bleeding</td>
<td>Pelvic pain at three mo.: • dysmenorrhea 20/440 (4.5%) • dyspareunia 10/440 (2.3%) • ovulatory pain 6/440 (1.4%) • other pain 26/440 (5.9%)</td>
<td>Subsequent 4-year follow-up: • n=15 adverse events possibly related to the Essure® micro-inserts, heavy periods with or without pain, irregular periods (continuous, frequent, and varying) with or without pain, dyspareunia, spotting when ovulating Over 5-year follow-up: • irregular bleeding 5 to 12% • heavier menses 17 to 22% • lighter menses 11 to 15% • irregular menses 5 to 12% • n=15 hysterectomy due to menorrhagia/abnormal bleeding (7); pelvic pain (3); dysmenorrhea (2); and 2 cases possibly related to the Essure® micro-inserts: lower abdominal pain and very heavy and irregular periods (1); continuous bleeding (1) Pelvic pain at 6 mo., 12 mo., 18 mo., 24 mo., 48 mo., 60 mo. (range, %): • dysmenorrhea (0.7 to 5.1%) • dyspareunia (1.2 to 3.3%) • ovulatory pain (0.7 to 5.1%) • other pain (1.4 to 5.9%) Recurrent symptoms reported at more than 1 visit: • dysmenorrhea (29/473; 6.1%) • dyspareunia (18/473; 3.8%) • ovulatory pain (14/473; 3.0%) • other pain (25/473; 5.3%)</td>
<td></td>
</tr>
<tr>
<td>New</td>
<td>Anderson 2013</td>
<td>2013</td>
<td>N=638</td>
<td>n=1 persistant post-procedural pain</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>New</td>
<td>Levy-Zauberman 2014</td>
<td>2014</td>
<td>Essure® + endometrial ablation</td>
<td>NR</td>
<td>NR</td>
<td>At average 22 mo.: n=12 hysterectomy (AUB n=7; other pathologies i.e. painful myomas without bleeding, ovarian pathology, endometriosis, cervical malignancy n=5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**New Basinski 2012**

Essure® followed by NovaSure®

N=117

n=1 pelvic pain after Essure®
n=1 admitted to hospital with severe headache, nausea, vomiting, dizziness within one day of a combined procedure of Essure® + NovaSure®

NR

n=2 hysterectomy for continuing chronic pelvic pain; diagnosed with endometriosis at surgery

n=1 severe dysmenorrhea at 10 mo.
after NovaSure® ablation diagnosed with hematometra

*Multiple publication of Mino 2007*

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

### Table D.3: Adverse events reported in two multi-centre case series studies and extended follow-up

<table>
<thead>
<tr>
<th>Event</th>
<th>Phase II Study (N=227) No. (%)</th>
<th>Pivotal Study (N=518) No. (%)</th>
<th>New Phase III Follow-up Study (N=364) No.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse events that prevented reliance on Essure® for contraception</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perforation</td>
<td>7/206 (3.4)</td>
<td>5/476 (1.1)</td>
<td>n/a</td>
</tr>
<tr>
<td>Expulsion</td>
<td>1/206 (0.5)</td>
<td>14/476 (2.9)</td>
<td>n/a</td>
</tr>
<tr>
<td>Other unsatisfactory micro-insert location</td>
<td>1/206 (0.5)</td>
<td>3/476 (0.6)</td>
<td>n/a</td>
</tr>
<tr>
<td>Initial tubal patency</td>
<td>7/200 (3.5)</td>
<td>16/456 (3.5)</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Adverse events per procedures, reported on day of placement procedure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Band detachment</td>
<td>3/233 (1.3)</td>
<td>2/544 (0.4)</td>
<td>n/a</td>
</tr>
<tr>
<td>Vasovagal response/fainting</td>
<td>2/233 (0.9)</td>
<td>7/544 (1.3)</td>
<td>n/a</td>
</tr>
<tr>
<td>Pain</td>
<td>2/233 (0.9)</td>
<td>70/544 (12.9)</td>
<td>n/a</td>
</tr>
<tr>
<td>Cramping</td>
<td>n/a</td>
<td>161/544 (29.6)</td>
<td>n/a</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>n/a</td>
<td>59/544 (10.8)</td>
<td>n/a</td>
</tr>
<tr>
<td>Dizziness/light-headed</td>
<td>n/a</td>
<td>48/544 (8.8)</td>
<td>n/a</td>
</tr>
<tr>
<td>Post-procedural bleeding</td>
<td>n/a</td>
<td>37/544 (6.8)</td>
<td>n/a</td>
</tr>
<tr>
<td>Vaginal spotting</td>
<td>n/a</td>
<td>2/544 (0.4)</td>
<td>n/a</td>
</tr>
<tr>
<td>Hypervolemia</td>
<td>n/a</td>
<td>16/544 (2.9)</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Abdominal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain/cramps</td>
<td>n/a</td>
<td>18/476 (3.8)</td>
<td>n/a</td>
</tr>
<tr>
<td>Gas/bloating</td>
<td>n/a</td>
<td>6/476 (1.3)</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Musculo-skeletal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back-pain/low back pain</td>
<td>n/a</td>
<td>43/476 (9.0)</td>
<td>n/a</td>
</tr>
<tr>
<td>Arm/leg pain</td>
<td>n/a</td>
<td>4/476 (0.8)</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Nervous/psychiatric</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>n/a</td>
<td>12/476 (2.5)</td>
<td>n/a</td>
</tr>
<tr>
<td>Premenstrual syndrome</td>
<td>n/a</td>
<td>4/476 (0.8)</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hysteroscopic tubal sterilization (using the Essure® system) – An update 34
<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
<th>Incidence</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysmenorrhea/menstrual cramps (severe)</td>
<td>n/a</td>
<td>14/476 (2.9)</td>
<td>n/a</td>
</tr>
<tr>
<td>Pelvic/lower abdominal pain (severe)</td>
<td>n/a</td>
<td>12/476 (2.5)</td>
<td>n/a</td>
</tr>
<tr>
<td>Persistent increase in menstrual flow</td>
<td>n/a</td>
<td>9/476 (1.9)</td>
<td>n/a</td>
</tr>
<tr>
<td>Vaginal discharge/vaginal infection</td>
<td>n/a</td>
<td>7/476 (1.5)</td>
<td>n/a</td>
</tr>
<tr>
<td>Abnormal bleeding – timing not specified</td>
<td>n/a</td>
<td>9/476 (1.9)</td>
<td>n/a</td>
</tr>
<tr>
<td>Menorrhagia/prolonged menses (severe)</td>
<td>n/a</td>
<td>5/476 (1.1)</td>
<td>n/a</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>n/a</td>
<td>17/476 (3.6)</td>
<td>n/a</td>
</tr>
<tr>
<td>Pain/discomfort – uncharacterized</td>
<td>n/a</td>
<td>14/476 (2.9)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**Adverse events, extended follow-up**

- **Related to the Essure® micro-inserts**
  - (heavy periods with or without pain, irregular periods [continuous, frequent, and varying] with or without pain, dyspareunia, spotting when ovulating)
  - n/a
  - n/a
  - 60 mo. 15/364

- **Hysterectomy**
  - n/a
  - n/a
  - 60 mo. 1/364

- **Dilatation and curettage for irregular menstrual bleeding**
  - n/a
  - n/a
  - 60 mo. 1/364

- **Bilateral salpingectomy to remove the Essure® micro-inserts**
  - n/a
  - n/a
  - 60 mo. 1/364

- **Pelvic pain: dysmenorrhea**
  - n/a
  - n/a
  - 18 mo. 14/410
  - 24 mo. 22/435
  - 36 mo. 14/422
  - 48 mo. 3/402
  - 60 mo. 14/386

- **Recurrent**
  - n/a
  - n/a
  - 29/473

- **Pelvic pain: dyspareunia**
  - n/a
  - n/a
  - 18 mo. 9/410
  - 24 mo. 9/435
  - 36 mo. 7/422
  - 48 mo. 5/402
  - 60 mo. 8/386

- **Recurrent**
  - n/a
  - n/a
  - 18/473

- **Pelvic pain: ovulatory pain**
  - n/a
  - n/a
  - 18 mo. 10/410
  - 24 mo. 22/435
  - 36 mo. 12/422
  - 48 mo. 6/402
  - 60 mo. 10/386

- **Recurrent**
  - n/a
  - n/a
  - 14/473

- **Pelvic pain: other pain**
  - n/a
  - n/a
  - 18 mo. 11/410
  - 24 mo. 13/435
  - 36 mo. 6/422
  - 48 mo. 11/402
  - 60 mo. 9/386

- **Recurrent**
  - n/a
  - n/a
  - 25/473

*Phase II Study* – prospective, multi-centre, single-arm, non-randomized international study
†Pivotal (Phase III) Study – prospective, multi-centre, single-arm, non-randomized international study

Hysteroscopic tubal sterilization (using the Essure® system) – An update
Extended follow-up Phase III Study[^19] – prospective, multi-centre, single-arm, non-randomized international study

N, n: number of patients; 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 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.

^h Symptoms reported at more than 1 visit.

**MAUDE reports of adverse events**

Figure D.1: Number of MDRs received per year, prior to June 1, 2015, by report source

![MDR Year Received by Report Source*](image)

Source: FDA report (2015)[^3]

MAUDE: Manufacturer and User Facility Device Experience; MDR: Medical Device Reports

**Table D.4: MAUDE reports of adverse events related to Essure® placement between January 2013 and February 2015**

<table>
<thead>
<tr>
<th>Events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All adverse event report*</td>
</tr>
<tr>
<td>- Reported by patients</td>
</tr>
<tr>
<td>- Reported by manufacturers, providers, or others</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Injury†</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>Pain related to injury</td>
</tr>
<tr>
<td>Bleeding related to injury</td>
</tr>
<tr>
<td>Perforation</td>
</tr>
<tr>
<td>Tissue injury</td>
</tr>
<tr>
<td>Puncture</td>
</tr>
<tr>
<td>Hysterectomy following procedure</td>
</tr>
<tr>
<td>Failure to deploy</td>
</tr>
</tbody>
</table>

Source: Mao et al., 31 supplementary information

* Reporting source: the average voluntary reporting rate from patients for medical device in MAUDE is 2%.
† Sum up of percentages of events related to injury was more than 100% because patients could report multiple events.

MAUDE: Manufacturer and User Facility Device Experience.
Appendix E: Summary of New Guideline Recommendations

Source: UK guidelines 35, 36

Legend:
- **Grade A**: Evidence based on randomized controlled trials
- **Grade B**: Evidence based on other robust experimental or observational studies
- **Grade C**: Evidence is limited but the advice relies on expert opinion and has the endorsement of respected authorities
- **GPP (Good Practice Point)**: Where no evidence exists but where best practice is based on the clinical experience of the guideline group

Anaesthesia and Analgesia for Hysteroscopic Sterilization

There is insufficient evidence to recommend the routine use of oral non-steroidal anti-inflammatory drugs (NSAIDs) or intravenous sedation for hysteroscopic sterilization. The use of such pharmacological agents should be based on clinical judgement. (Grade A)

Local anaesthesia is not routinely required prior to hysteroscopic sterilization as it does not alleviate pain associated with the placement of micro-inserts into the fallopian tubes. However, local anaesthesia should be used when dilatation of the cervix is necessary to aid passage of the hysteroscope into the uterine cavity. (Grade A)

Insertion of the Micro-Inserts

The incidence of unsuccessful placement of intra-fallopian implants is reported as ranging between 0% and 19%, following up to two attempts in an outpatient setting. (Grade B)

The likelihood of successful micro-insert placement is increased if the procedure is scheduled during the proliferative phase of the menstrual cycle. (Grade B)

Clinicians should undergo a period of supervised training to become proficient in the hysteroscopic insertion of micro-inserts. (Grade C)

Following sterilization via hysteroscopy and the insertion of intra-fallopian micro-inserts, additional contraception must be used until either successful insert placement and/or tubal occlusion are confirmed, depending upon the confirmatory test employed. (Grade B)

Hysteroscopic sterilization may be safely and effectively undertaken when intrauterine contraception is already in situ (outside the terms of the manufacturer’s instructions for use). Women should be advised to use additional contraception or abstain from intercourse for 7 days before the procedure in case the intrauterine device needs to be removed to gain access to the fallopian tubes. (GPP)

Intraoperative Complications with Tubal Micro-Inserts

Hysteroscopic sterilization via the placement of intra-fallopian micro-inserts is associated with a low level of intraoperative complications in a minority of patients. (Grade B)

Postoperative Complications of Hysteroscopic Sterilization

Hysteroscopic sterilization via the placement of intra-fallopian micro-inserts is associated with a low level of postoperative complications. The majority of post-procedural adverse events are self-limiting, with most women able to return to daily activities 1-2 days following the procedure. (Grade B)
Hysteroscopic sterilization with micro-inserts is contraindicated if there is documented proven patch test for nickel allergy. (GPP)

Post-Procedure Imaging Following Micro-Insert Placement

A confirmatory imaging test should be undertaken 3 months after the insertion of intra-fallopian micro-inserts. This may be via x-ray or transvaginal ultrasound scanning (TVUSS) in the first instance, followed by hysterosalpingogram (HSG) in selected patients where x-ray/TVUSS cannot confirm satisfactory placement. (Grade B)

HSG should be used as a first-line test where the hysteroscopic procedure was considered suboptimal, according to local protocols. (Grade B)

HSG can be used as a routine test to confirm tubal occlusion following insertion of intra-fallopian micro-inserts. (Grade B)

Women who do not attend for confirmatory testing should be informed that they need to continue using additional contraception until tubal occlusion is confirmed. (GPP)

Training Issues in Post-Procedure Imaging of Micro-Inserts

Training in interpretation and performance of confirmatory imaging techniques specifically for sterilization using Essure® is essential, as a number of pregnancies have been attributed to the misinterpretation of images. (GPP)

Efficacy of Micro-Inserts

Available evidence suggests that tubal occlusion by intra-fallopian micro-insert has a low associated failure rate of approximately 1 in 500 at 5 years of follow-up; this includes cases where luteal-phase pregnancy or non-adherence with post-procedural instructions was documented. (Grade B)

Patient Satisfaction with Hysteroscopic Sterilization

Available evidence suggests that the use of intra-fallopian micro-inserts for tubal occlusion is a procedure that is well tolerated by the majority of women and results in good long-term satisfaction in terms of comfort and tolerance of the insert. (Grade B)

Hysteroscopic Sterilization and Other Procedures

Endometrial Ablation

Limited available evidence suggests that intra-fallopian micro-insert insertion can be carried out in combination with endometrial ablation. (Grade C)

Long-Term Complications of Female Sterilization

Ovarian Cancer

Tubal occlusion is not associated with an increased risk of ovarian cancer. Evidence suggests that the procedure may have a protective effect against developing ovarian cancer that persists over time. (Grade A)

Breast Cancer

There is no available evidence of an association between tubal occlusion and breast cancer risk. (Grade A)
Cervical and Endometrial Cancer
Available evidence suggests that there is no association between tubal occlusion and cervical or endometrial cancer risk. (Grade B)

Menstrual and Gynaecological Symptoms
There is no evidence that tubal occlusion results in significant changes to hormone levels. (Grade B)
Evidence suggests that there is an association between tubal occlusion and an increased risk of subsequent hysterectomy but there is no evidence of causation. (Grade B)
Women may report worsening menstrual symptoms following tubal occlusion but there is no evidence to suggest a causal effect. (Grade B)

Female Sterilization Reversal
Fallopian tube re-anastomosis following sterilisation can result in high postoperative patency rates, but may not result in pregnancy or a return to fertility. (Grade B)
To date, reversal of sterilization with micro-inserts cannot be achieved via fallopian re-anastomosis, therefore consideration should be given to in vitro fertilization. (GPP)
References


39. U.S. Food and Drug Administration (FDA) [Internet]. FDA takes additional action to better understand safety of Essure, inform patients of potential risks [February 29, 2016]. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm488313.htm.


Author Contribution Statements

_Carmen Moga_ (MD, MSc) contributed to study conception and design, data analysis and interpretation, and approved the final version for publication.

_Dagmara Chojecki_ (MLIS) contributed to developing and executing the literature search.
This report is an update of the 2014 Alberta STE report, which was an evidence assessment of the clinical effectiveness and safety of hysteroscopic tubal sterilization, and of the value for money associated with adopting hysteroscopic tubal sterilization in Alberta.