Summary

Chapter 1 gives an overview and historical perspective of sterilisation methods and describes the outline of this thesis.

In chapter 2 we conducted a systematic review to evaluate the feasibility, reliability and safety of modern hysteroscopic sterilisation methods. All longitudinal studies addressing hysteroscopic tubal sterilisation were considered for inclusion, both prospective and retrospective. Studies were included if they investigated reliability or safety of sterilisation techniques, risk factors for failure of hysteroscopic sterilisation. Only original studies were included with > 20 patients were included. Descriptive articles, case-series (non-consecutively), reviews, surveys, technical reports were excluded. A total of 45 articles were included: 7 articles concerned Ovabloc, 36 Essure, and 2 Adiana sterilisation.

The Ovabloc Intratubal Device method is an office procedure which can be done using local anaesthesia. A catheter is installed into the ostium and a silicon mixture solidifies with in 5 min into a soft rubber plug. The procedure is repeated on the contra lateral side. A post-procedure x-ray is captured. If after three month a second x-ray shows that the position of the devices has not altered, the patient can rely on Ovabloc for sterilisation.

The Essure is an 4 cm expanding spring device made of a nitinol outer coil and stainless steel innercoil with PET fibers. The microinsert is placed in the proximal section of the fallopian tube under. The PET fibres cause localised tissue ingrowth from the surrounding tube , thereby achieving mechanical occlusion of the tube and anchoring of the device. Different diagnostic tests (hysterosalpingography, x-ray and ultrasound) are described to confirm adequate position and bilateral tubal occlusion after three months.

The Adiana System is a combination of the 60-second application of radiofrequency (F) to the mucosa of the fallopian tube, followed by deployment of a porous silicon 3.5 mm matrix in to the thermal lesion. The procedure is than repeated on the other side. The matrix provides a substrate for tissue ingrowth, leading to tubal occlusion. A three-months hysterosalpingography is indicated to confirm bilateral tubal occlusion. The devices are not radiopaque.

All hysteroscopic sterilisation technique offers distinct advantages over laparoscopic sterilisation or mini-laparotomy with reduced need for anaesthesia and decreased risk for injury to intra-abdominal organs. It can be performed in an office setting with local or no anaesthesia. Patient tolerability and satisfaction was high in all studies despite the large difference in settings and pain management protocols that were used (no anaesthetics, para-cervical block, intravenous sedation and general anaesthesia). The Ovabloc system had a higher placement failure rate, because of higher numbers of unsatisfactory position at the three months control, due to migration or expulsions of the plugs. Also the number of unsuccessful procedures was higher but we have to realise that procedures were performed with larger (8 mm)
single flow instruments, initially with Hyskon or carbon dioxide as distension medium. Long-term data were spare. At least 12 patients, of a group of 1588 patients who relied on, conceived after a satisfactory three months x-ray. In 2009 the method was stopped.

The bilateral placement reliance represents the number of women who were ultimately instructed to that they could rely on the sterilisation divided by the number of intention to treat was similar for both techniques. The three years cumulative pregnancy rate for Adiana was 15/1000, while we calculated a 1/1000 pregnancy rate for commercial use of Essure. Since March 2012 the Essure method is the only available method on the market.

Chapter 3 describes a study to compare the test characteristics of two diagnostic tests for Essure confirmation. The pelvic- x rays, transvaginal ultrasound and HSG imaging was performed in 150 women with successful bilateral placement. The results of transvaginal ultrasound as compared with the results of HSG as the “reference test” showed a sensitivity of 50% and a specificity of 95%. One patient with correct position of the microinserts but with tubal patency on one side could not be identified by ultrasound or x-ray. A second patient with an expulsion of one microinsert was well diagnosed by both ultrasound and x-ray. When we compared diagnostic characteristics of the ultrasound with pelvic X-ray as the reference test (accepting the case with tubal patency as satisfactory) the sensitivity and specificity were 100% and 95%, respectively. In only 8 patients with a satisfactory pelvic x-ray it was not possible to confirm the satisfactory position of the devices with ultrasound. The predictive value of a satisfactory transvaginal ultrasound result is than 99% and the predictive value of an unsatisfactory result is 11%.

In this cohort of 150 women there was no case of perforation of a microinsert. Therefore we developed a new study to estimate the diagnostic accuracy and interobserver reproducibility of pelvic x-rays in the diagnosis of bilateral sterilisation with Essure.

In Chapter 4 six observers evaluated x-rays from 47 patients, including one case with a complete perforation of one device, one case of proximal position and tubal patency on HSG and one abnormal x-ray from the patient with complete expulsion of one device and tubal patency on HSG. Three gynaecologists with experience in Essure sterilisation and x-ray reading and 3 radiologists with specific training in confirmation of Essure sterilisation with x-ray were involved. After evaluation of the results it seemed that the test characteristics of pelvic x-ray as the imaging technique to assess the position of the microinserts were poor, as was the reproducibility. The sensitivity and specificity for x-rays read by gynaecologists was 0.67 (95% CI,0.29–0.96) and 0.79 (95% CI, 0.58–1.00) and for radiologists 1.0 and 0.5 (95% CI, 0.36–0.64). The interobserver agreement in reliability (Fleiss’s k-statistics) of pelvic x-ray of hysteroscopic sterilisation assessment with Essure ranged from slight (k-value: 0.09) for gynaecologists to moderate (k-value: 0.52) for radiologists. Because of the limitations of x-ray compared to ultrasound and the non-superior diagnostic characteristics and poor interobserver agreement, we do not recommend the routine use of pelvic x-ray for the assessment of the positioning of microinserts after hysteroscopic sterilisation. Only if expulsion or perforation of a device is suspected and ultrasound examination is not confirmative a x-ray can be helpful.
In chapter 5 we describe three different types of incorrect position of Essure microinserts detected at 3 months’ follow-up and their appearance on x-ray and by ultrasound. In a series of hundred patients who underwent hysteroscopic sterilisation with Essure three cases were identified with an abnormal position of a microinsert. In case A, both inserts were not clearly visible with vaginal ultrasound while on pelvic X-ray an abnormal configuration of one insert was seen. HSG showed tubal patency. The perforated microinsert was laparoscopically removed. Retrospectively, the patient had experienced abdominal pain for several weeks after the procedure. In Patient B one device was missing which was recognised with all confirmation-tests. Patient had not noticed an expulsion. In a second attempt a new microinsert was placed successfully. In the third patient who had a difficult bilateral placement due to adhesions in the uterine cavity one device was expelled to the uterine cavity. With ultrasound examination one device could not be made clearly visible. X-pelvis showed an abnormal configuration of one device and on HSG there was tubal patency. After hysteroscopic removal of the microinsert a second device was correctly placed. Complications after Essure placement can be detected during the procedure itself or at follow-up. When, during the procedure, there is doubt about the position of a microinsert, a transvaginal ultrasound can be performed at that time. But one should realise that in case of perforation and expulsion, most incorrectly placed microinserts will migrate in the period after the procedure. A majority of cases will not be detected during or directly after the procedure. We advise screening patients with apparent successful bilateral placement but with difficult placement procedures, other suboptimal conditions during the procedure, or abdominal pain earlier than 3 months after the procedure. Initially this can be done with transvaginal ultrasound after the patient’s first period or withdrawal bleeding (approximately 4 weeks), and when in doubt, a pelvic X-ray can be performed.

Because hysteroscopic sterilisation is a rather new method, it is important that all pregnancies are reported and that the cases are reviewed to determine the cause of the unintended pregnancy. Some of the causes might be preventable. Understanding these causes can be helpful to improve the follow-up protocols and reduce the number of failures in the future. In chapter 6 we describe a retrospective analysis of 10 unintended pregnancies after Essure sterilisation in the Netherlands from August 2002 till May 2008. In one case pregnancy already occurred before the procedure (luteal pregnancy). In three cases single placement was followed by HSG after three months and bilateral tubal occlusion was concluded. In the other six cases an abnormal position of a microinsert was recognised after termination of pregnancy although from 1 case data were lacking. In these 5 cases there was non-compliance to the protocol. A procedure with only a single device placement in a patient without a history of salpingectomy of the contra-lateral tube should be considered as unsuccessful and an HSG should not be performed.

With the information we collected from our earlier in the Netherlands. We developed a revised protocol for the follow-up after Essure sterilisation. Objectives were to reduce the need for radiologic confirmation (x-ray examination and HSG), without compromising the effectiveness of Essure. In January 2005, this new protocol for follow-up of Essure sterilisation was introduced in the Netherlands. With the new Dutch protocol, transvaginal ultrasound is used for the 3-month confirmation of tubo-cornual location of the microinserts after an uncomplicated successful bilateral
placement. The criteria for a normal successful bilateral procedure include procedure time of 15 minutes or less, microinsert visible after placement, fewer than 9 coils protruding into the uterine cavity, and no unusual events during the procedure. In all other cases, HSG is still indicated. A procedure with only a single device placement in a patient without a history of salpingectomy of the contra-lateral tube should be considered unsuccessful, and HSG should be abandoned, because of a high risk of false positive confirmation of occlusion of the contra-lateral tube. When findings at ultrasound examination are inconclusive or abnormal location of a microinsert is suspected, HSG is indicated.

In a multicentre study, described in chapter 7 we evaluated the revised protocol based on first-line confirmation using transvaginal ultrasound at 3 months after uncomplicated successful Essure sterilisation and analysed the rate of success of placement and effectiveness of the method. Data of 1145 consecutive cases from 5 clinics were collected and analysed. The overall successful placement rate was 93.6% (1072 of 1145 intentions to treat). In 6% of patients with intention to treat, Essure sterilisation was successfully completed; however, the procedure was not considered straightforward. According to the Dutch protocol, TVU was scheduled at 4 weeks after the procedure, and HSG at 3 months. In 4.5%, the “standard” 3-month TVU was inconclusive; thus, HSG was scheduled as outlined in the protocol. In 50 of these 52 patients, HSG confirmed bilateral occlusion with normal position of the devices. Only in 2 of these patients there was an abnormal positioning of 1 device: 1 expulsion and 1 perforation. Including patients with a successful second attempt and successful single placement. Overall 14.3% of patients (164 of 1145) with intention to treat underwent HSG. In 9 patients, HSG showed evidence of an abnormal position of 1 or 2 devices (2 expulsions and 7 perforations). Finally 1037 patients were instructed to rely on the sterilisation. The 24-months cumulative pregnancy rate was 3.86 per 1000 (4/1037). None of these pregnancies was related to failure of the sterilisation method. Two patients conceived with only one device in situ, one after bilateral placement and ultrasound confirmation and one with bilateral tubal occlusion on HSG after single placement. In two cases there was a perforation of one device after a complicated procedure.

When the device was properly placed; in 1 case the device was absent or incorrectly positioned, and in three cases there was noncompliance with the protocol. The Dutch protocol for confirmation of Essure sterilisation, with transvaginal ultrasound as first-line test, reduced the number of HSGs, thus reducing costs, inconvenience, and discomfort without influencing the effectiveness of the sterilisation. Compared with the FDA protocol, the Dutch control protocol is associated with high patient compliance. In cases of difficult placement, the extra TVU confirmation at 4 weeks did not reduce the number of HSGs. Thus, the need for routine TVU after a difficult hysteroscopic procedure should be abandoned, with sole reliance on the 3-month HSG as a confirmatory test.

After the success of occlusion of the fallopian tubes with microinserts for contraceptive use, a new indication was presented in 2005 to obstruct hydrosalpinges of subfertile woman to improve the results of IVF treatment as an alternative for salpingectomy to improve the chance of ongoing pregnancies in IVF-programs.
Chapter 8 provides a prospective study to investigate the success-rate of proximal tubal occlusion with Essure devices in subfertile women with hydrosalpinges and to observe the results of subsequent treatment with IVF. Ten patients had successful placement of the Essure devices without any complications. Proximal tubal occlusion was confirmed by hysterosalpingography in 9 out of 10 patients. A 40% ongoing pregnancy rate was achieved with 20% live births after one IVF cycle and/or frozen embryo transfer. Our case series shows good pregnancy rates with IVF-ET following Essure placement, and is consistent with others found after laparoscopic salpingectomy.

A significant concern for women with unintended pregnancies and subfertile women wishing to conceive with microinserts in situ, is the trailing of Essure coils into the uterine cavity and its possible effects on implantation as well as on pregnancy. Therefore we collected data of 50 pregnancies in 43 patients in the Netherlands who became pregnant with 1 or 2 Essure microinserts in situ.

In Chapter 9 we analysed the obstetric outcomes of 50 pregnancies in 43 women with 1 or 2 Essure microinserts in place and found a good outcome for ongoing pregnancies. Of 26 unintended pregnancies after hysteroscopic sterilisation with Essure 17 (65.4%) were electively terminated, and 9 (34.6%) resulted in the birth of a healthy baby. Each of the 2 patients with sterilisation regret treated via IVF/ET conceived after the first single embryo transfer. Both delivered a healthy baby. In the IVF-group with pre-procedure closure of hydrosalpinges 15 of 23 pregnancies (65%) were ongoing. Only 2 patients had a microinsert with 5 coils in the uterine cavity. In 1 of these patients, pregnancy ended in miscarriage. In the other patient, pregnancy ended with stillbirth. After removal of the microinserts, dramatically her next pregnancy ended with a second still birth. The number of miscarriages (35%) in the group who underwent IVF/ET after proximal closure of hydrosalpinges is not unexpectedly high and reflects findings reported in the literature. The number of ongoing pregnancies in this group is encouraging and congruent with the literature on pre-IVF salpingectomy or tubal occlusion. It is unlikely that the presence of Essure microinserts interferes with implantation and the developing amniotic sac and foetus.

Chapter 10 is a general discussion on the findings of this thesis and provides the answers to the research questions posed in the outline of this thesis. Furthermore some future perspectives are discussed, including the introduction of new hysteroscopic sterilisation devices and alternative non-ionising confirmation tests.

A recommendation is made to register all data of patients seeking for sterilisation in the Patient Outcome Measurement Tool that has recently been introduced in the Netherlands.