Hysteroscopic Sterilisation by Tubal Cannulation and Placement of Intrafallopian Implant

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The Medical Services Advisory Committee is an independent committee established to provide advice to the Australian Government Minister for Health and Ageing on the strength of evidence on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice helps to inform Government decisions about which medical services should attract funding under Medicare.

This report was prepared by the Medical Services Advisory Committee with the assistance of Dr Emma Bryan, Dr Bruce Hollingsworth, Dr Claire Harris, Ms Elizabeth Burrows and Ms Emily Petherick (Centre for Clinical Effectiveness, Monash Institute of Health Services Research and Health Economics Unit, Centre for Program Evaluation) of Monash University. Bianca Ledbrook and Linda Marshall of the Department of Health and Ageing and edited by Dr Alana Mitchell (ScienceLink Pty Ltd). The report was endorsed by the Commonwealth Minister for Health and Ageing on 2 March 2005.

Publication approval number: 3420

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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Executive summary

The procedure

Hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant (HSTCPII) is a method for permanent sterilisation of females. An intrafallopian implant is inserted hysteroscopically into each fallopian tube where a local response causes tissue to infiltrate the implant. As a result, the fallopian tubes are blocked, preventing sperm from reaching the egg. The procedure is carried out using local anaesthesia, so it could potentially be undertaken as an outpatient procedure. HSTCPII is currently performed in Australia only on admitted patients.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. The MSAC advises the Australian Government Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. A team from the Monash Institute of Health Services Research and the Monash Health Economics Unit was engaged to conduct a systematic review of the literature on HSTCPII. A supporting committee with expertise in this area then evaluated the evidence and provided advice to the MSAC.

MSAC's assessment of hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant

Clinical need

Two thirds of Australian women aged between 18 and 49 (about 2,750,000 women) rely on some form of temporary or permanent birth control. For the year 1995, approximately 19 per cent (528,000) of these women relied on permanent sterilisation as their primary method of birth control (Australian Bureau of Statistics 2002). For women over the age of 35, sterilisation is the most frequently used method of birth control (Yusuf & Siedlecky 1999).

Safety

The main safety issues with respect to HSTCPII are perforation of the fallopian tube, expulsion of the intrafallopian implant, pain and bleeding. Other potential safety issues include changes in menstrual pattern, ectopic pregnancy and infection.

The incidence of perforation decreased markedly from approximately three per cent in the earliest studies to less than one per cent in the Pivotal study when the method was changed to discontinue the use of a support catheter. Expulsion of the intrafallopian implant affected 2.7 per cent (14/518) of patients in the Pivotal study, however, only two of the 14 patients with expulsion exhibited symptoms, and those symptoms abated on removal of the inserts. When observed, pain and bleeding were usually mild. No evidence was presented in the studies to indicate significant changes in menstrual pattern. No pregnancies were reported, so ectopic pregnancy was not an issue.

Overall, HSTCPII appears to be relatively safe, however, this is based on short-term data and it is only with extensive use and further long-term studies that the true safety profile of HSTCPII will be elucidated. At which time comparisons with the known problems associated with its main comparator, laparoscopic tubal ligation (LTL), can be made.

Effectiveness

Forty articles were identified in the original literature search, 38 of which contained no data on HSTCPII. One of the two remaining articles did not assess the primary effectiveness outcome of pregnancy; leaving only one published study that met the inclusion criteria. Two unpublished study reports supplied by the manufacturer (one of which incorporated data from the published study) were also included in the current review.

To date, no pregnancies have been reported in patients who have relied on the intrafallopian implant as their primary form of contraception. However, further long-term follow-up and additional studies are required to fully establish the effectiveness of the intrafallopian implant over time. One condition of a recommendation by the US Food and Drug Administration's Center for Devices and Radiological Health (2002) for premarket approval of the Essure system was that the manufacturer follow the subjects for five years. It is the stated intention of the manufacturer to collect data from patients in the Phase II and Pivotal studies for five years post-implantation.

In total, 86 per cent (194/227) of patients who commenced the Phase II study and 83 per cent (430/518) of patients from the Pivotal study currently rely on the intrafallopian implant as their primary method of contraception. One patient with unilateral placement in the Phase II trial relied on the intrafallopian implant as the sole method of contraception due to proximal tube occlusion in the contralateral tube. Two patients with unilateral placement in the Pivotal study were also able to rely on the device for contraception due to possession of a unicornuate uterus. It should be noted that approximately 15 per cent of patients are unable to rely on the implants for contraception, often due to anatomical factors.

Overall, HSTCPII appears to be a relatively effective procedure, which has not been associated with any pregnancies to date. However, as with safety considerations, further follow-up data and additional studies are required to ascertain the full effectiveness of HSTCPII.

Cost-effectiveness

There is no evidence concerning the rate of substitution of HSTCPII for LTL, let alone potential conversions from vasectomy if sterilisation is viewed from the perspective of the couple. There are potential costs surrounding issues of the procedures being reversible. In addition, there is no reporting of economic outcomes such as pregnancies avoided per HSTCPII procedure.

Given the additional costs of HSTCPII over LTL of between $776 and $1,021 per procedure, and of HSTCPII over vasectomy of between $1,461 and $2,012 per procedure, it is estimated that, at minimum substitution rates, additional costs to the Australian health system of between $7.29 and $9.78 million would result from the introduction of HSTCPII. A more realistic scenario estimates additional annual actual procedure costs over and above those currently carried out, at between $18.25 and $24.68 million. Depending on technology uptake, additional health care costs could be as high as $45 million.

Recommendation

The MSAC recognised that hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant is an evolving technology but as there was presently insufficient evidence pertaining to its safety, effectiveness and cost-effectiveness, the MSAC recommended that public funding for the procedure should not be supported at this time.

The Minister for Health and Ageing accepted MSAC's advice on the safety, effectiveness and cost-effectiveness of this technology. However, as more Australian data are due to become available shortly, the Minister approved a continuation of interim reimbursement until November 2007, to allow further assessment to occur.

The Minister for Health and Ageing accepted this recommendation on 2 March 2005.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant (HSTCPII). The MSAC evaluates new and existing health technologies and procedures for which funding is sought under Medicare Benefits arrangements in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. The MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

The MSAC's terms of reference and membership are in Appendix A. The MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer issues and health administration.

Background

Hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant (HSTCPII)

The procedure

Preliminary procedures

The manufacturer recommends that certain procedures be followed before women undergo HSTCPII. Initially patients are required to receive adequate counselling regarding the implications of permanent, irreversible sterilisation and the full range of birth control options available to them. Patients should also be informed that HSTCPII is a relatively new procedure for which there is less clinical data available than for the more established methods of sterilisation.

The manufacturer also recommends that patients be tested for gonorrhoea and chlamydia infections before undergoing HSTCPII, as these could potentially interfere with the effectiveness of the intrafallopian implant. A pregnancy test is also performed.

Intrafallopian implant

This assessment reviews the safety, effectiveness and cost-effectiveness of Essure, the only intrafallopian implant currently available. The Essure intrafallopian implant is a small, flexible, dynamically-expanding microcoil (Figure 1) comprising a stainless steel inner coil, a nickel titanium (nitinol) expanding super elastic outer coil and polyethylene (PET) fibres wound in and around the inner coil. PET has been widely used in implants and prostheses for more than 40 years.

The Essure permanent birth control system consists of the intrafallopian implant, a disposable delivery device and a disposable split introducer (Figures 1 and 2). The intrafallopian implant is attached to a delivery wire contained in a release catheter for ease of insertion (Shellock 2002). It is four centimetres long and 0.8 mm in diameter in its wound down configuration (Figure 1). When released from the delivery system, the outer coil expands to a 1.5 to 2.0 mm diameter to anchor the implant in the fallopian tube. A local tissue response is elicited, causing tissue ingrowth in the intrafallopian implant (Shellock 2002). This local fibrotic response occludes the tube, preventing sperm from reaching the egg (Shellock 2002).

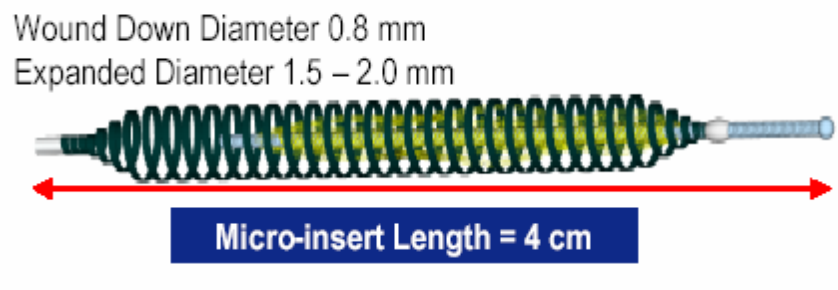

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Figure 1 Essure micro-insert (shown in its expanded configuration).

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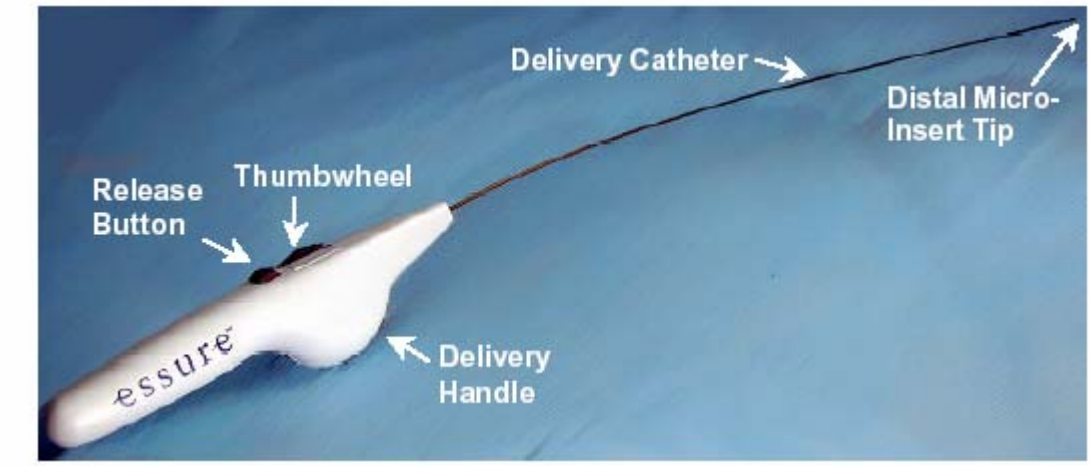

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Figure 2 Essure delivery system.

Hysteroscopic placement of intrafallopian implant

The implant is inserted into the fallopian tube using a hysteroscope of diameter 3.5 to 5.5 mm. Local anaesthesia is preferred, although the procedure can be performed without any analgesia.

It is possible to perform HSTCPII in outpatient departments if the necessary equipment and resources to deal with adverse events are available. However, in Australia, it is only performed on patients admitted to hospital for two reasons. The first is the requirement for documentation of consent, device placement and registration of the device being inserted. The second is that the necessary expertise in operative hysteroscopy using fluid distension generally exists only within operating suites in hospitals.

During the procedure, a single-toothed tenaculum grips the cervix to steady it at which point a mild 'nip' or slight discomfort may be felt. Saline at the tip of the hysteroscope at low pressure can then be used to dilate the cervix if required. The hysteroscope is advanced through the cervix into the uterine cavity and placed against the tubal ostium. A small amount of pressure is applied to open the ostium, facilitating advancement of

the implant into the fallopian tube. Marks on the side of the implant guide the distance for insertion. The intrafallopian implant is placed in the proximal section of the fallopian tube lumen where it is released. The procedure is repeated for the contralateral fallopian tube.

Assessment of fallopian tube occlusion

Complete occlusion of the fallopian tube takes time. Patients are advised to use alternative birth control methods for the first three months post-placement, at which time a pelvic X-ray is carried out to assess tubal occlusion and placement of the intrafallopian implant. In patients for whom the X-ray suggests suboptimal placement, a hysterosalpingogram (HSG) is recommended. If bilateral occlusion has not been achieved after three months, a repeat HSG is performed at six months to check for occlusion. Patients are advised to continue using alternative birth control during this time.

Training requirements

Competence in diagnostic hysteroscopy is the minimum eligibility requirement for gynaecologists wishing to train in HSTCPII. Training includes a module that incorporates theory of placement, clinical data, patient selection and counselling information. On completion of theoretical training, trainees initially work on anatomical models before progressing to patients. For the first five cases, or until competency has been demonstrated, trainees are supervised by a preceptor. To ensure that qualified gynaecologists carry out HSTCPII, data concerning the gynaecologist intending to perform the procedure is required by the manufacturer before sale of the intrafallopian implant.

Contraindications

HSTCPII may not be suitable for all women requesting permanent sterilisation. The primary contraindications are abnormalities in the uterine cavity or fallopian tubes, which may present difficulties in visualising the tubal ostia and/or cannulation of the proximal tube. It is thought that five per cent of women presenting for HSTCPII have problems with both fallopian tubes and ten per cent have problems with one tube only. The most appropriate form of sterilisation for these women is laparoscopic tubal ligation (LTL).

In addition, HSTCPII is not recommended as a post-partum or post-abortion procedure as fallopian tubes have an increased susceptibility to perforation at these times.

Recent or active pelvic infection, untreated acute cervicitis, unexplained or severe bleeding, gynaecological malignancy, allergy to contrast material or nickel and current use of corticosteroids are also contraindications. In these cases patients are advised to seek alternative forms of birth control or sterilisation.

History of hysteroscopic sterilisation

Many different materials and devices have been trialed for use in hysteroscopic sterilisation, including sclerosing agents, plugs and other occlusive devices, electrocautery, laser treatment and cryocoagulation.

For example silver nitrate, quinacrine and tetracycline, phenol atrabrine paste, gelatin-resorcinol-formaldehyde, methylcyanoacrylate (using the Femcept system), bismuth polyurethane and several other chemicals have been tested as sclerosing agents (Kerin et al 2001, Maubon et al 2000). However, none has proved both safe and effective for use in humans.

Many occlusive devices have been investigated, including silicone formed-in-place plugs (Ovabloc), microcoils, hydrogel (P-Block), ceramic plugs, Hosseinian plugs, the Hamou tubal device and many others (Kerin 1995, Maubon et al 2000, Neuwirth 1995). These devices were all deemed unsuitable for use due to various problems with inaccurate placement, expulsion and unwanted pregnancies (Kerin 1995, Neuwirth 1995, Shoupe 2000).

Electrocautery, laser treatment and cryocoagulation are not used due to high failure rates and concerns regarding safety and effectiveness (Kerin 1995, Maubon et al 2000, Neuwirth 1995, Wilson 1996).

Intended purpose

Female sterilisation remains one of the most widely used methods of permanent birth control worldwide (Kerin 1995, Rioux & Daris 2001). The purpose of HSTCPII is to provide permanent birth control to women without a requirement for abdominal incisions or general anaesthesia.

Clinical need / burden of disease

Two thirds of Australian women aged between 18 and 49 (about 2,750,000 women) rely on some form of temporary or permanent birth control. During 1995, approximately 19 per cent (528,000) of these women relied on permanent sterilisation as their primary method of birth control (Australian Bureau of Statistics 2002). As summarised in Table 1, sterilisation is the most frequently used method of birth control for women over the age of 35 (Yusuf & Siedlecky 1999).

Table 1 Reliance on tubal ligation or hysterectomy as the primary method of birth control in 1995

Age	Number of women using contraception ('000s)	Proportion of women relying on sterilisation (%)
18-19	111.3	0.0
20-24	441.1	0.0
25-29	428.6	3.6
30-34	453.7	10.7
35-39	476.5	21.6
40-44	448.2	36.1
45-49	392.6	49.9
Total	**2751.9**	**19.2**

Source: Australian Bureau of Statistics (2002)

Existing procedures and comparator

The most widely used method of female sterilisation is tubal ligation, which requires incisional surgery and general anaesthesia (Kerin et al 2001). Tubal sterilisation can be performed post-partum, post-abortion or at a time unrelated to pregnancy as an interval procedure. The timing of the procedure will influence both the surgical approach and the method of tubal occlusion (American College of Gynecology 1996). Tubal ligation used as an interval procedure is the comparator for this report as HSTCPII is indicated for use as an interval procedure only.

In developed countries tubal ligation is generally performed laparoscopically. The limited resources for the purchase and maintenance of laparoscopic equipment in developing countries make minilaparotomy the more common surgical approach (Kulier et al 2002). In this report, only LTL has been considered as a relevant comparator for the Australian situation. The most common methods of LTL in Australia use rings or Filshie clips.

Marketing status of the device / technology

The Essure device is currently listed in the Australian Register of Therapeutic Goods as AUSTL 72090.

Current reimbursement arrangement

Pending the outcome of this report, interim funding currently provides reimbursement for the HSTCPII procedure via Medicare Benefits Schedule (MBS) Item number 35633: 'Hysteroscopy with uterine adhesiolysis or polypectomy or tubal catheterisation (including for insertion of a device for sterilisation) or removal of IUD which cannot be removed by other means, 1 or more of ' (Commonwealth Department of Health and Aged Care 2001).

Approach to assessment

The objective of this review was to evaluate research evidence on the effectiveness, safety and cost-effectiveness of HSTCPII.

Review of literature

The medical literature was searched to identify relevant studies and reviews of HSTCPII for the period 1966 to 2002. Searches were conducted using the databases shown in Table 2. An Internet search of health technology assessment agency websites and clinical trial register websites was undertaken. The sites searched are listed in Appendices D and E.

Table 2 Electronic databases accessed for this review

Database	Period/Issue covered
Cochrane Library including: The Cochrane Database of Systematic Reviews (CDSR) Database of Abstracts of Reviews of Effectiveness (DARE) The Cochrane Controlled Trials Register (CCTR)	Issue 4, 2002
CINAHL (OVID)	1982 to September, week 4, 2002
Current Contents (OVID)	Week 27, 1993 to week 25, 2002
Medline (OVID)	1966 to October, week 3, 2002
PreMedline (OVID)	October 28, 2002
EMBASE (OVID)	November 11, 2002

Search terms

The search terms used to identify the literature are presented in Table 3. The same terms were used to identify studies assessing safety and/or effectiveness. The search strategy is presented in Appendix C.

Table 3 Search terms used to identify literature for HSTCPII

Effectiveness terms[a]	Safety filter[a]	Cost-effectiveness filter[a]
MeSH terms:	**MeSH terms:**	**Textwords:**
Sterilization, Tubal/	Safety/	economic$.tw
Fallopian tube$.tw	Intraoperative Complications/	cost$.tw
Textwords:	Postoperative Complications/	
Essure.tw	Mortality/	
STOP.tw	**Textwords:**	
Micro?coil$.tw	complicat$.tw	
Micro?implant$.tw	adverse event$.tw	
Micro?insert$.tw		
Intra?tubal device$.tw		
Tubal plug$.tw		
Contraceptive device$.tw		
Tubal sterili?ation.tw		
Transcervical sterili?ation.tw		
Hysteroscopic sterili?ation.tw		
Tubal occlusion$.tw		
Permanent contraception$.tw		
Permanent birth control.tw		
Surgical sterili?ation.tw		
Sterili?$.tw		
Pregnancy prevent$.tw		
Fallopian tube$.tw		

[a] '$' represents a truncation symbol that replaces a series of letters at the end of a word segment so that any letters following the symbol are searched; ? represents a single letter; MeSH = Medical Subject Heading

Selection criteria

The following criteria were developed *a priori* to determine eligibility of relevant studies.

Subject characteristics

Inclusion: Women seeking tubal sterilisation as an interval procedure

Exclusion: Tubal sterilisation as a post-abortion/post-partum procedure

Characteristics of the intervention

Inclusion: HSTCPII using prefabricated plugs (Essure device previously known as the Selective Tubal Occlusion Procedure (STOP))

Exclusion: *In situ* casts and destruction of the tubal mucosa by chemocaustics, endoelectrocaustics or tissue adhesives

Characteristics of the comparison intervention

Inclusion: LTL using rings (Falope, Yoon) or clips (Filshie, Hulka)

Exclusion: Non-tubal female sterilisation; LTL using salpingectomy, fimbriectomy and electrocoagulation; reversible sterilisation

Characteristics of the outcome

Inclusion: Clinically relevant outcomes (primary outcome: prevention of pregnancy; secondary outcomes: failure of technical approach, quality of life, delay in return to normal activity, pain etc), safety (adverse events related to the procedure and/or device) and cost-effectiveness

Exclusion: Not defined

Characteristics of study design

Inclusion: Health technology assessments, systematic reviews, meta-analyses and randomised controlled trials (RCTs) will be sought initially. If unavailable, other controlled trials, comparative studies and cohort studies will be assessed. If these are also unavailable, case series will be evaluated

Exclusion: Case series of less than 25 patients, case reports, narrative reviews, abstracts, editorials, and letters

Characteristics of the publication (date, language, specific journals)

Inclusion: English language only

Assessment of validity

Critical appraisal refers to the process of evaluating the study design of included articles. The most rigorous study design for assessing the validity of therapeutic interventions is considered to be an RCT (Guyatt et al 1993, Sackett et al 2000).

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the Australian National Health and Medical Research Council (NHMRC 2000).

These dimensions (Table 4) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature on a particular intervention. The last two require expert clinical input as part of their determination.

Table 4 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design[a].
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *p*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the "null" value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

[a] See Table 6

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. Study design susceptibility to bias is shown in Table 5.

Table 5 Susceptibility to bias[a]

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

[a] Modified from NHMRC (2000)

The National Health Service (NHS) Centre for Reviews and Dissemination (2001) in the United Kingdom (UK) lists criteria that can be used to evaluate the validity of evidence from the various study designs. The relevant validity criteria used in this review for assessing quality of evidence are listed in Table 6.

Table 6 Validity criteria according to study design

Study design	Validity criteria
Primary studies[a]	
RCT	Randomised method Allocation concealment Similar groups at baseline Specified eligibility criteria Blinding of patients, investigators and outcome assessors Proportion lost to follow-up Point estimates and measure of variability presented for the primary outcome measure Intention to treat analysis
Cohort	Prospective/retrospective Comparable groups at inception Intervention/treatment reliably ascertained Identification and adjustment for confounding factors Blind outcome assessment Sufficient duration of follow-up Proportion lost to follow-up
Case-control	Explicit definition of cases Adequate details of selection of controls Comparable groups with respect to confounding factors Interventions and other exposures assessed in same way for cases and controls Possibility of over-matching i.e. cases and controls matched according to factors related to exposure Appropriate statistical analysis
Case series	Explicit description of patients Explicit inclusion/exclusion criteria All patients included Sufficient follow-up Outcomes assessed objectively Explicit description of techniques
Secondary studies[b]	
Systematic reviews	Focused research question Explicit inclusion/exclusion criteria Explicit and comprehensive search strategy Validity of included trials appraised Homogeneity between studies assessed Summary of main results Strengths and limitations

[a] Primary study criteria modified from NHS Centre for Reviews and Dissemination (2001)
[b] Secondary study criteria modified from Evidence Based Medicine Toolkit, University of Alberta (http://www.med.ualberta.ca/ebm/ebm.htm)

Critical appraisal of published systematic reviews

Critical appraisal of any identified systematic reviews is to be performed using recognised qualitative criteria as described in Table 6 (Chalmers & Altman 1995, Sackett et al 2000). Qualitative criteria are designed to assess whether a given systematic review was performed in the optimal way to minimise bias. These criteria assess whether the systematic review contained an explicit statement of the objectives and methods and whether the methods are reproducible. Specific criteria assess whether the review asked a focused question, if the eligibility criteria for included trials were explicit, what search strategy was used, how the validity of included trials was assessed and whether results of included trials were similar.

Expert advice

A supporting committee with expertise in obstetrics and gynaecology, reproductive medicine, general practice and epidemiology was established to evaluate the evidence and provide advice to the MSAC from a clinical perspective. In selecting members for supporting committees, the MSAC's practice is to approach appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the supporting committee is provided in Appendix B.

Results of assessment

Search results

An Internet search of health technology assessment agency and clinical trial websites failed to identify any relevant literature.

The medical literature was also searched to identify relevant studies. An initial assessment of the abstracts allowed for the exclusion of articles that did not meet the selection criteria for inclusion outlined in the Effectiveness section. Studies that met the inclusion criteria and ambiguous or unclear references were included for examination of the full text in the next assessment stage. Two reviewers examined each citation for inclusion. Discrepancies in selection were discussed and resolved through consensus. A final decision to reject or accept articles was based on a thorough reading of the complete article. Only studies that successfully passed this process were included.

The search for studies on HSTCPII identified 40 articles of which 38 were rejected on the basis of their abstracts, leaving two articles to be assessed in full text. One of the two met the inclusion criteria and was eligible for critical appraisal in the Effectiveness section (Appendix F). Appendix G lists the 39 articles that were excluded from further assessment in the Effectiveness section and the reasons for exclusion. The reasons were: obsolete device (8), not tubal sterilisation (21), LTL (5), Food and Drug Administration (FDA) regulations (1), editorial (1), no pregnancy data (1) and animal study (2). Five articles were used to assess safety. These included the article used in the assessment of effectiveness plus two references from among the 40 articles identified by the search.

Four study reports were also made available by the manufacturer of Essure. They included the Phase IA, Phase IB, Phase II and Pivotal studies. All four contained information on safety of the intrafallopian implant and two (Phase II and Pivotal studies) also contained relevant data on effectiveness. In addition, the manufacturer provided further safety and effectiveness data on request.

Data included in this review

This review considered Essure, the only intrafallopian implant currently available in Australia. Three versions of the implant have been used at various times in clinical trials. Initially the implant was known as STOP (selective tubal occlusion procedure). The three versions of STOP were alpha, beta and gamma. The gamma version of STOP was recently renamed Essure. The Safety section includes data derived from studies of several versions of the implant. The Effectiveness section includes only data pertaining to Essure.

Is HSTCPII safe?

The Phase IA study was a peri-hysterectomy study to assess the placement of the STOP implants, the safety and effectiveness of the delivery systems and to estimate acute tubal occlusion. The patient population was comprised of women with benign conditions for hysterectomy who were willing to undergo placement of the STOP implant directly preceding hysterectomy.

Valle et al (2001) includes the results of the Phase IB study, which was carried out in the United States and in Mexico, and examined the safety, effectiveness and local tissue response of the STOP implant. Patients scheduled for elective hysterectomy agreed to participate in this study. The intrafallopian implant was inserted and the resultant local tissue response was evaluated after the hysterectomy performed between one and 13 weeks later. There is doubt about the validity of this study due to inconsistency regarding the number of patients reported. Valle et al (2001) stated a sample size of 33, which has been used in this review, however a larger number of patients is reported at one point in the published results. There were also 30 additional patients reported in the Phase IB study (provided by the manufacturer) than in Valle et al (2001). This discrepancy may have arisen due to the reports being prepared at different times during the study follow-up.

Kerin et al (2001) published the results of the Australian section of the Phase II study, which was a large international multi-centre study. As with the Pivotal study, it included a case series of women seeking permanent birth control who were fitted with an intrafallopian implant using hysteroscopy. Further descriptions of these studies are provided in the assessment of effectiveness. Note that since the current review was completed, the full results of the Phase II study have been published [Kerin et al, 2003. *Human Reproduction*, 18 (6), pp1223-1230].

The main safety issues are perforation of the fallopian tube, expulsion of the intrafallopian implant, pain and bleeding. Other potential safety issues include changes in menstrual pattern and ectopic pregnancy. There is also a small risk of infection with any procedure involving instrumentation of the uterine cavity. However, no incidences of infection were recorded in the studies. Tables 7 and 8 summarise the main safety issues identified from the published literature and the study reports, respectively.

Table 7 Adverse events reported in the published literature

Adverse Event	Valle et al, 2001[a]	Kerin et al, 2001[b]
Perforation rate	9.1% (3/33)[c]	1.5% (2/130)
Expulsion rate	Not reported	0
Proximal band detachment	0	2.3% (3/130)
Pain	Post-procedure: 65% (abated within 4 days)	During procedure: 72.3% (94/130) Post-procedure: 10.5% (12/114)
Bleeding	34% (abated within 1 week)	5.3% (6/114 after 3 months)
Other	None	Device tip detachment: 0.7% (1/130)

[a] See also Phase 1B study, Table 8
[b] Subset of patients from the Phase II study, Table 8
[c] Two due to support catheter, resulting in a design change

Table 8 Adverse events reported in the studies

Adverse event	Proportion of women affected in the:			
	Phase IA study	Phase IB study[a]	Phase II study[b]	Pivotal study
Perforation rate	5.5% (4/73)	3 cases	2.6% (6/227)	0.8% (4/518) (1 was diagnosed on day of placement)
Expulsion rate	Not applicable	Not reported	0.4% (1/227)	2.7% (14/518)
Proximal band detachment	0.0%	0.0%	1.3% (3/227)	0.4% (2/518)
Pain	Not applicable	Post-procedure: 61.8% (21/34[c]) (Abated within 4 days)	During placement: 67.4% (153/227) Post-procedure: 76.1% (156/205[d]) (Abated within 1 week for 99% of these patients)	During placement: 82.6% (426/516[e]) Post-procedure: 71.1% (367/516[e])
Post-procedure bleeding	Not reported	41.2% (14/34[c]) (Abated within 7 days)	83.4%[c] (171/205[d]) (Abated within 1 week in 96% of cases)	6.8% (35/518)
Other	Not reported	None	Fever: 2.0% (4/205[d]) Retained implant fragment: 0.4% (1/227)	Hypervolemia: 0.4% (2/518)

[a] It is unclear from this study how many patients were included. The study report stated that 49 patients underwent attempts at intrafallopian implant placement
[b] Kerin et al, 2001 contained a subset of these data (Table 7)
[c] Number of patients for whom results were available
[d] Number of patients that completed the one-week post-procedure questionnaire
[e] Number of patients for whom pain data were available

Perforation

Table 9 summarises the reasons for the 17 perforations observed across the four included studies. Seven perforations were related to the support catheter, as a result of which its design was modified during the Phase II study. Subsequently the perforation rate in the Pivotal study was less than one per cent. The intrafallopian implant was removed successfully from four of the six patients who suffered perforations in the Phase II study. For one of the four, removal of the implant two years post procedure due to menstrual pain caused the pain to abate. The two patients who retained the intrafallopian implants experienced no sequelae.

Table 9 Reasons for perforation in the studies

Study	№ patients	№ patients with a perforation (%)	Reasons for perforation					
			Support catheter	Pre-existing tubal occlusion	Poorly defined ostia	Prior tubal ligation[a]	Inexperienced operator	Unknown
IA	73	4 (5.5)	1	0	0	1	0	2
IB	49[b]	3 (6.1)	2	0	0	0	1	0
II	227	6 (2.6)	4	2	0	0	0	0
Pivotal	518	4 (0.8)	0	2	2	0	0	0

[a] Prior tubal ligation was an exclusion criterion for the study
[b] The number of patients receiving intrafallopian implant placement as quoted in the study report

Expulsion of the intrafallopian implant

In the Phase IA study, insertion of the intrafallopian implant was followed immediately by hysterectomy. This left no opportunity for expulsion. No expulsions were reported in the Phase IB study.

Expulsion of the intrafallopian implant was observed in one patient (0.4 per cent) in the Phase II study. This patient had an unsuccessful second attempt at intrafallopian implant insertion and the patient's husband subsequently underwent a vasectomy. Fourteen patients (2.7 per cent) in the Pivotal study had expulsion of an intrafallopian implant. Two of these experienced symptoms as a direct result of the intrafallopian implant being expelled into the uterus. The unspecified symptoms were reported to have abated after removal of the expelled implants.

Adverse tissue response

Histological analysis of fallopian tubes from the Phase IB study demonstrated that the tissue reaction was confined to the area immediately adjacent to the intrafallopian implant and did not extend into the fallopian tube wall. In addition, there was no evidence of peri-tubal adhesions or serositis.

One potential concern with both expulsion of the intrafallopian implant and perforation of the fallopian tubes is adverse local tissue reaction elicited by the intrafallopian implant in areas other than the fallopian tube. In each of four cases for whom the intrafallopian implant was placed into the peritoneal cavity in the Phase II study, no adverse tissue reactions were observed. This is potentially due to the fact that in its unexpanded state, the outer coil prevents the PET fibre from coming into contact with surrounding tissue. However, further long-term research is required to assess the local tissue response to incorrectly placed intrafallopian implants.

Distal location

One patient from the Phase II study had unsatisfactory distal intrafallopian implant placement diagnosed on the three-month HSG. Laparoscopic bilateral salpingectomy was used to retrieve both intrafallopian implants.

Damage to the intrafallopian implant

Three patients (1.3 per cent) in the Phase II study and two (0.4 per cent) in the Pivotal study experienced proximal band detachment from the intrafallopian implant.

Kerin et al (2001) also reported three proximal band detachments, indicating that all of the detachments observed in the Phase II trial occurred in the Australian arm of the study. The manufacturing process of the intrafallopian implant was altered in response to reporting of this complication. In one woman from the Phase II study, X-ray revealed that the proximal band was in the uterus.

An investigator in the Phase II study attempted to remove the intrafallopian implant hysteroscopically due to dissatisfaction with intrafallopian implant placement. The attempt caused the distal ball tip of the intrafallopian implant to break. Consequently, hysteroscopic removal of the intrafallopian implant was not recommended.

Pain

Placement of the intrafallopian implant was usually carried out without the use of a general anaesthetic in the Phase II and Pivotal studies. Pain during placement was reported by 67 per cent (153/227) and 83 per cent (426/516) of patients, respectively. The pain was rated as less than or equal to expected in 67 per cent of patients and greater than expected in 26 per cent of the patients in the Phase II study. Eleven per cent of patients failed to answer the question on pain. However, there is some ambiguity in the reported results as these percentages add up to 104. In the Pivotal study the majority of the patients described the pain experienced as mild or moderate with only four per cent stating that the pain was severe. One patient in the Phase II study experienced severe leg pain during the procedure.

In the Phase IB, Phase II and Pivotal studies, patients were asked to complete a daily diary for seven days. They were also asked to complete a questionnaire one week after intrafallopian implant placement to assess bleeding, pain and any other adverse events. Patients in the Phase II and Pivotal studies also kept diaries for up to six months post-procedure to record their experiences with the intrafallopian implant. Any post-procedural pain was compared to the pain that the woman normally experienced during menstruation. The reports of pain do not provide data concerning duration or frequency, only whether patients experienced, or did not experience, pain. In the absence of a copy of the questionnaire, interpretation of the responses was not possible.

Post-procedural pain was observed in 65 per cent (actual numbers not given) of patients in the study by Valle et al (2001). Although the Phase IB study was essentially the Valle et al (2001) study, the results were slightly different with 62 per cent (21/34) of patients experiencing post-procedural pain. Both studies reported that the pain resolved within four days. No pain was reported during pelvic examination before hysterectomy.

Seventy six per cent (156/205) of patients in the Phase II study who completed the one week post-procedure questionnaire, reported post-procedural pain. In 99 per cent of cases this was resolved within one week. The pain was described as continuous by 43 per cent of the patients experiencing pain. Four per cent reported pain during sexual activity, seven per cent during urination, 20 per cent during menstruation, 19 per cent during exercise and 56 per cent of patients reported pain during 'other' activities, (for instance on standing, sitting, resting, during all activities, etc). Of the patients experiencing pain, 67 per cent took medication. This took the form of non-steroidal anti-inflammatory drugs (NSAIDs) in 48 per cent of cases while others chose narcotics (50 per cent) or other drugs (2 per cent). Fourteen per cent (27/195) of patients who kept a post-procedure diary recorded more pain than normal during menstruation. The majority of these patients experienced the increased pain in the first month post-procedure. The

number of patients experiencing greater menstrual pain decreased with time to nine during the second month, and four during the third.

Kerin et al (2001) reported that 89 per cent (102/114) of patients (a subset of the Phase II study) with implant placement reported no pain or unusual symptoms in any follow-up visit. Reported events were relatively rare. They included pain greater than normal during intercourse in the first week (seven patients); pain greater than normal in the first month post intrafallopian implant placement (five patients); pain greater than normal during menstruation in the first month after placement (10 patients) and pain or bleeding beyond three months post-procedure (six patients).

Seventy-one per cent (367/516) of patients who had completed the one week questionnaire in the Pivotal study reported post-procedural pain, 98 per cent of those stating that the pain was of mild to moderate intensity. Only two per cent of patients experienced severe post-procedural pain.

Bleeding

Information on bleeding was collected from the patient diaries. Bleeding was assessed compared to normal menses. Data were recorded as a patient experiencing or not experiencing bleeding but not on the duration or frequency of events.

Thirty four per cent of patients experienced mild post-procedural bleeding in Valle et al (2001) and 41 per cent (14/34) in the Phase IB study. As these two reports describe the same study, it is unclear why these numbers differ. Valle et al (2001) did not report the actual numbers of patients used to derive the percentage. Due to the underlying conditions requiring hysterectomy, only bleeding additional to that expected was recorded. Such bleeding generally abated within one week.

Eighty three per cent (171/205) of respondents reported post-procedural bleeding in the Phase II study. Twenty seven per cent of cases resolved within one day, 64 per cent in three days and 96 per cent within one week. In some patients bleeding could be a result of normal menstruation.

Seven per cent (35/518) of patients experienced post-procedural bleeding in the Pivotal study. On the day of the procedure, one patient was reported to have experienced excessive bleeding but no details were provided of its quantity or severity. As described in Table 10, 24 per cent (106/441) of patients at the three-month follow-up visit reported intermenstrual bleeding that lasted between one and two days.

The extent of post-procedural bleeding differed markedly between the studies, ranging from seven per cent in the Pivotal study to 84 per cent in the Phase II study. This difference may be attributable to different classifications for post-procedure bleeding.

Table 10 Severity of intermenstrual bleeding 3 months post-placement in the Pivotal study

Severity	Number[a]	Per cent
Spotting	68	15.4
Light bleeding	19	4.3
Moderate	10	2.3
Heavy	6	1.4

[a] The total number of patients was 441

Changes in menstrual pattern

There has been debate in previous literature concerning changes in menstrual pattern following tubal sterilisation. Fewer than five per cent of patients in the Phase II study experienced irregular menses or changes in flow after HSTCPII. In the Pivotal study, nine patients experienced a persistent increase in menstrual flow and eight experienced a decrease.

Ectopic pregnancy

No ectopic pregnancies were reported in either the published literature on HSTCPII or in the relevant study reports. A meta-analysis by Mol et al (1995) in which different methods of contraception and associated risk of ectopic pregnancy were assessed found that women who became pregnant after tubal sterilisation had a nine-fold greater risk of ectopic pregnancy than women who had not undergone tubal sterilisation [Odds Ratio = 9.3, 95% CI: 4.9, 18.0]. The actual numbers of patients experiencing ectopic pregnancy in both the sterilised and non-sterilised groups were not reported. In addition, the only confounder considered was age.

Tubal spasm

Tubal spasm resulting in failed intrafallopian implant placement was reported in ten patients in the Pivotal study and no patients in the other studies.

Cooper et al (1985) investigated the incidence of tubal spasm during attempted hysteroscopic sterilisation using formed-in-place silicone plugs. Of 403 procedures performed in 340 patients, tubal spasm was observed in 9.2 per cent (37/403). In 57 per cent (21/37) of these cases, the spasm remitted. In the remaining 43 per cent (16/37), unremitting tubal spasm was responsible for failure of placement. Tubal spasm was associated with increased discomfort for the patients during the procedure.

Post-procedural pelvic surgery

The manufacturers of the Essure Permanent Birth Control System recommend that electrocautery be avoided in surgical procedures on the uterine cornua and fallopian tubes. The manufacturers also recommend that electrocautery within four centimetres of the intrafallopian implant be used with caution due to potential risks of contact with the metallic surface of the intrafallopian implant (Conceptus Inc. 2002).

In addition, intrauterine procedures such as endometrial biopsy, dilation and curettage, and hysteroscopy have the potential to disrupt the ability of the intrafallopian implant to prevent pregnancy. There may be other, unestablished risks associated with the use of the procedures listed above.

A study of the safety of magnetic resonance imaging (MRI) after insertion of the Essure intrafallopian implant (Shellock 2002) established that MRI using a 1.5 Tesla magnet caused no injury due to movement or heating of the metallic insert in patients with the intrafallopian implant. However, images of the area immediately adjacent to the intrafallopian implant would be obscured during MRI (Shellock 2002).

Subsequent In Vitro Fertilisation

Although potential patients are given counselling about the permanency of HSTCPII, it remains possible that many patients may want to conceive after receiving the

intrafallopian implant. Reversal would require a cornual resection with tubal reimplantation or in vitro fertilisation (IVF), with IVF being the more likely of these options. No data are available regarding the success rate or risks to the patient and/or the fetus with IVF after HSTCPII. However, one naturally-conceived pregnancy in a patient who had the beta version of the STOP device progressed to term with no serious adverse events while the device was *in situ*.

Comparator safety

The main safety issues with LTL are the requirement for general anaesthetic, the insertion of a large trocar into the abdominal cavity and laparoscopy related risks. The study findings of less frequent adverse events with HSTCPII than LTL can be attributed to the former technology obviating such risk factors. The adverse events reported in the literature for HSTCPII generally occur in the short term as operative problems with insertion and expulsion and short term post-procedural pain. Although longer-term data are required to confirm the apparent safety of HSTCPII, expert opinion suggests that there is a low theoretical risk of longer-term complications.

The manufacturer of Essure provided considerable data on the incidence of side effects for LTL. These studies examined the rates of adverse events in case series of women receiving one or other of these technologies. The manufacturer did not provide data comparing adverse events between LTL and HSTCPII directly and the evaluation did not identify such comparative studies in the literature. An RCT of the two procedures would be difficult to undertake and evaluate and is unlikely to be conducted as a head-to-head comparison. In addition, the laparoscopic data in the literature may not be presented in a way that clearly identifies early complications and side effects.

While this reasoning seems to make a case for enhanced safety of HSTCPII, no conclusion can be drawn due to a number of factors. Firstly, the time scale of follow-up in the HSTCPII Phase II and Pivotal studies was relatively short. As of October 2002, only 17 per cent of patients in the Phase II study and no patients in the Pivotal study had been followed-up for three years. Mortality data relating to the use of tubal sterilisation were collected at the time of death irrespective of when the procedure had taken place.

Secondly, because there have been no direct comparative studies of HSTCPII and LTL in comparable groups, it is unclear whether the patient groups in the studies of the separate technologies are sufficiently similar to allow robust conclusions to be drawn. For example, the seven mortality studies of tubal sterilisation quoted by the manufacturer predominantly assessed mortality due to tubal sterilisation in general, rather than LTL using rings or clips specifically.

In addition, the LTL studies could have included women who were receiving tubal ligation post-partum or post-abortion, which are contraindicated for the use of HSTCPII. A proportion of these women may have received tubal sterilisation while undergoing a general anaesthetic for caesarean section, which introduces further comparative difficulties. Finally, the populations used in the Phase II and Pivotal studies for HSTCPII were highly selected whereas the populations in the mortality studies were generally representative of all women undergoing tubal sterilisation.

The limitations of the currently available data prevent the performance of a direct statistical comparison of the safety of HSTCPII and LTL.

Is HSTCPII effective?

Critical appraisal of primary studies

The Phase IA and IB studies are not included in the assessment of effectiveness as HSTCPII was performed on patients either during (Phase IA) or before (Phase IB) hysterectomy, as a result of which pregnancy was not applicable as a primary outcome measure.

Study and patient characteristics

Only one published study (Kerin et al 2001) met the inclusion and exclusion criteria for this review. The study characteristics are summarised in Table 11. The study by Kerin et al (2001) was carried out in Australia and followed 130 patients with the intrafallopian implant for 1,894 women-months. The average age of the patients was 35 years with 95 per cent between 31 and 39 years. On average, patients had experienced 2.8 pregnancies and 2.4 births.

The characteristics of the study reports are provided in Table 12. The Phase II study of 227 patients, including some from Kerin et al (2001), was conducted in the USA, Europe and Australia. The study generated 3,974 woman-months of data from the 206 patients that had at least one intrafallopian implant from this study. The average age of patients was 35, with more than 90 per cent between 28 and 45 years of age. On average, patients had experienced 2.6 pregnancies and 2.2 births. With respect to follow-up, patients were seen three, six, 12 and 18 months post-procedure, then yearly for up to five years post-reliance on the intrafallopian implant. Earlier forms of the protocol required patients to be followed-up at three, four, five and six months post-procedure. Four- and five- month data from these patients have been included in the six-month visit.

The protocol was altered such that the 24-month visit was post-reliance on the intrafallopian implant, not post-procedure. However two patients were analysed according to the original protocol. The number of patients included in follow-up data declined rapidly over time, apparently due to insufficient time having elapsed for completion of some visits.

The Pivotal study was a multi-centre study conducted in the USA, Europe and Australia. The study enrolled 522 patients (518 of whom received a placement attempt) and incorporated more than 4,300 woman-months of use of the intrafallopian implant. With respect to follow-up, patients were seen three, six, 12 and 18 months post-procedure. They were also followed-up at three and six months as well as two, three, four and five years post-reliance on the intrafallopian implant. The average age of patients in the study was 32. On average, patients had experienced three pregnancies and 2.3 births. The patients included in the Pivotal study were not included in the Phase II study.

In all studies, an HSG was performed at three months post-procedure to assess tubal occlusion. Patients for whom bilateral occlusion was unsuccessful were advised to continue with alternative contraception for a further three months at which time HSG was repeated. If bilateral tubal occlusion had still not been achieved by six months, patients were advised to consider an alternative sterilisation procedure. The manufacturer has indicated that the HSG will be replaced by a pelvic X-ray to assess tubal occlusion. In the reported trials all patients had both pelvic X-ray and HSG. Based on the findings of

these two tests, the investigators established pelvic X-ray criteria which indicated the need for further investigation by HSG. HSG is associated with greater risk than pelvic X-ray, including the potential for recanalising the fallopian tube.

Table 11 Characteristics of published studies

Study	Location	Enrol-ment period	Study population					
			Sample size	Duration of follow-up %	Women-months	Age (years)	Gravidity	Parity
Kerin et al, 2001	Australia	Not reported	130	3 months: 95.6% (109/114[a]) 6 months: 93.0% (106/114) 12 months: 68.4% (78/114) 18 months: 21.9% (25/114)	1,894	Average: 35 Range: 21-43 95%: 31-39 (123/130)	Average: 2.8	Average: 2.4

[a] Number of patients with at least one intrafallopian implant

Table 12 Characteristics of study reports

Study	Location	Enrol-ment period	Study population					
			Sample size	Duration of follow-up %	Women-months	Age (years)	Gravidity	Parity
Phase II	USA Europe Australia	Ended in June 2000	Total: 227 Screened: 231 ≥ 1 implant: 206	3 months: 98.5% (203/206) 6 months: 96.6% (199/206) Post-reliance: 12 months: 95.1% (196/206) 18 months: 93.7% (193/206) 24 months: 92.7% (191/206) 36 months: 16.5% (34/206)	3,974 (206 patients with ≥ 1 implant)	Average: 35 Range: 23-45 < 28: 7.0% (16/227) 28-33: 23.3% (53/227) 34-45: 69.6% (158/227)	Mean±SD: 2.6±1.3 Median: 2	Mean± SD: 2.2±0.89 Median: 2
Pivotal	USA Europe Australia (13 sites)	Trial initiated in May 2000	Total: 518 USA: 320 Europe: 65 Australia: 133 Screened: 522	6 months: 92.6% (441/476) Post-reliance: 12 months: 96.8% (461/476) 18 months: 63.9% (304/476) 24 months: 4.4% (21/476)	> 4,300 (in 476 patients with the implants for 3-12mths) 2,140 (in patients relying on the implants)	Average: 32 Range: 21-40 21-33: 62.0% (321/518) 34-40: 38.0% (197/518)	Mean±SD[a]: 3.05±1.49 Median: 3 Range: 1-11	Mean± SD[a]: 2.28± 0.96 Median: 2 Range: 1-6

[a] Based on 522 patients screened

Study validity

The Kerin et al (2001) study, and the Phase II and Pivotal studies were all post-test case series (level IV evidence), which have the most potential for bias. Details of the validity of these studies are reported in Tables 13 and 14. Stringent selection criteria were used when enrolling patients in each. Although this has the potential to introduce bias, the patients enrolled in the three studies possessed similar characteristics to those who would ultimately be offered the intrafallopian implant.

One potential source of selection bias in the Phase II study is the exclusion of women who were considered to be unsuitable for intrafallopian implant. The direction of this bias cannot be assessed as no details were given for what constituted 'not suitable for device placement'.

Table 13 Validity of published study

Criterion	Kerin et al, 2001
Study design	Prospective
Explicit patient criteria for inclusion	Yes
Explicit description of patients	Yes
Objective assessment of outcomes	Yes
Adequate duration of follow-up[a]	Yes
All patients included in the analysis	Yes
Explicit description of techniques	Yes

[a] At the time of study publication, further follow-up was intended

Table 14 Validity of study reports

Criterion	Phase II study	Pivotal study
Study design	Prospective	Prospective
Explicit patient criteria for inclusion	Yes	Yes
Explicit description of patients	Yes	Yes
Objective assessment of outcomes	Yes	Yes
Intended adequate duration of follow-up[a]	Yes	Yes
All patients included in the analysis	Yes	Yes
Explicit description of techniques	Yes	Yes

[a] Further follow-up was intended

Summary of results

The results are presented in Tables 15 and 16. Effectiveness was only measured after completion of the three-month visit as patients needed to use alternative contraception for three months post-intrafallopian implant placement.

Table 15 Results of published study

Outcome	Kerin et al, 2001[a]
Pregnancy rate	0
Bilateral placement rate at first attempt	Not reported
Final bilateral placement rate	85.4% (111/130) 3.6% (4/111) with unsatisfactory implant placement on HSG
Bilateral occlusion rate	3 months: 80.8% (105/130) 6 months: 82.3% (107/130)
Patients relying on implant for contraception	Mean: 17 months (based on 108[b] women) > 12 months: 77.7% (101/130)
Unilateral placement rate	2.3% (3/130)

[a] contains a subset of the patients from the Phase II study
[b] 107 had bilateral occlusion and 1 patient had unilateral occlusion with contralateral proximal tube occlusion

Table 16 Results of study reports

Outcome	Phase II study[a]	Pivotal study
Pregnancy rate	0	0[b]
Bilateral placement rate at first attempt	86.3% (196/227)	86.1% (446/518)
Final bilateral placement rate	88.1% (200/227) 3.0% (6/200) with unsatisfactory implant placement on HSG	Time of procedure: 90.0% (464/518) 3 month HSG: 93.1% (432/464[c])
Bilateral occlusion rate	3 month HSG: 93.5% (187/200 of patients with satisfactory implant placement) 6 month HSG: 96.5% (193/200)	3 month HSG: 89.9% (417/464[c]) 6 month HSG: 92.7% (430/464[c])
Nº of patients relying on implant for contraception	85.5% (194[d]/227)	83.0% (430/518)
Unilateral placement rate	2.6% (6/227)	1.9% (10/518) Unicornuate uterus <1% (2/518)

[a] a subset of the patients in this study were included in Kerin et al, (2001)
[b] 4 luteal phase pregnancies conceived before completion of the 3-month alternative contraception phase
[c] 450 patients had HSGs
[d] 193 patients had bilateral occlusion and 1 patient had unilateral occlusion with contralateral proximal tubal occlusion

Pregnancy is the primary outcome measure for this review. No pregnancies were reported after placement of the intrafallopian implant. The four luteal phase pregnancies diagnosed were conceived before completion of the 3-month alternate contraception phase. The four women concerned chose not to continue with the pregnancy.

An interesting secondary outcome is the bilateral placement rate of the intrafallopian implant at the first attempt. Table 16 shows that in both the Phase II and Pivotal studies, 86 percent of patients received bilateral placement at the first attempt. After a second attempt, this figure increased to 88 percent in the Phase II study and 90 per cent in the Pivotal study. The reasons for failure of placement are reported in Table 17. The most common reasons relate to anatomical factors and not to the intrafallopian implant or the procedure. It is important to note that HSTCPII as a method of sterilisation is not feasible for approximately 15 per cent of women.

Table 17 Reasons for failed intrafallopian implant placement

Reasons for failed intrafallopian implant placement[a]	Phase II study[b]	Pivotal study[c]
Anatomical including: - stenotic tubes - endometrium preventing visualisation - lateral/tortuous tubes - occluded tubes - no visible ostium/scarring - uterine adhesions	13	78
Procedure-related including: - tubal spasm - visualisation - inability to cannulate or advance catheter - suspicion of a perforation/placement in endometrial tissue	7	19
Implant-related: - catheter performance	5	1
Unknown	2	1

[a] There may be more than one reason per patient
[b] 227 attempted placements with a total number (i.e. first plus second attempts) of 27 failures
[c] 518 attempted placements with a total number (i.e. first plus second attempts) of 99 failures

Of the 464 patients in the Pivotal study with bilateral placement, 21 (4.5%) experienced an adverse event that initially prevented them from relying on the intrafallopian implant. As shown in Table 18, 12 of these patients were ultimately unable to rely on the intrafallopian implant. At least eight patients chose alternative forms of sterilisation.

Table 18 Adverse events preventing reliance on the intrafallopian implant among women with bilateral placement in the Pivotal study

Event	Number[a] of patients with adverse event	Management		Other outcomes	№ patients ultimately unable to rely on implant
		Successful second attempt	Laparoscopic sterilisation		
Expulsion	14 (3.0%)	9	4	1[b]	5[c] (1.1%)
Perforation	4 (0.9%)	0	3	1[d]	4 (0.9%)
Proximal implant location and perforation	1 (0.2%)	0	1	0	1 (0.2%)
Proximal implant location	2 (0.4%)	0	0	2[e]	2 (0.4%)
Total	21 (4.5%)	9	8	4	12 (2.6%)

[a] Of the 464 patients with bilateral placement
[b] One patient required laparotomy due to pre-existing Crohn's disease
[c] In earlier versions of the protocol which are applicable to these five patients, patients were not allowed to have a second insertion attempt if the initial attempt resulted in expulsion of the intrafallopian implant
[d] Patient requested second procedure
[e] Awaiting women's decision to undergo laparoscopic sterilisation

Ninety four per cent (187/200) of patients with bilateral placement were shown to have bilateral occlusion on their three-month HSG in the Phase II study and 90 per cent (417/464) in the Pivotal study. This increased to 97 per cent (193/200) and 93 per cent (430/464), respectively, after six months. Eighty six per cent (194/227) of patients who commenced the Phase II study and 83 per cent (430/518) of patients from the Pivotal study are currently relying on the intrafallopian implant as their primary method of contraception.

Of the two patients with unilateral placement in the Phase II trial, one was relying on the intrafallopian implant as their sole method of contraception due to proximal tube occlusion in the contralateral tube. Two of the 10 patients in the Pivotal study with unilateral placement were able to rely on the device due to a unicornuate uterus.

Comparator effectiveness

The main comparator for HSTCPII is LTL. In Australia, LTL is generally performed using rings or Filshie clips. A direct comparison of the effectiveness of these two procedures is not possible, as no head-to-head studies have been performed. In addition, LTL is indicated as a post-partum and post-abortion procedure as well as an interval procedure. HSTCPII is only indicated as an interval procedure.

Nardin et al (2002) have published a systematic review of the different techniques for the interruption of tubal patency for female sterilisation. No differences were observed between the use of rings or clips in the yearly incidences of unintended pregnancy. Overall, 1.5 per cent of patients per year receiving LTL using rings had an unintended pregnancy compared to two per cent of patients per year receiving LTL using clips. No failures were observed in a study that assessed Hulka clips versus Filshie clips (Nardin et al 2002).

Technical failures were observed in 1.6 per cent of patients receiving LTL using clips compared with 7.3 per cent of patients receiving LTL using rings (Nardin et al 2002). Technical failures were classified as those for which a second method was required to complete tubal ligation. No technical failures were observed in the studies directly comparing the use of Hulka and Filshie clips (Toplis et al 1988 cited in Nardin et al 2002).

The global pregnancy rate for patients after tubal ligation by any method has been reported as approximately 1.33 per 1000 patients (Maubon et al 2000).

The long-term failure rate of HSTCPII to prevent pregnancy has not been assessed. Follow-up for at least 10 years would be needed to allow comparison with long-term failure rates of LTL. However, an RCT comparing the two procedures would be difficult to undertake and evaluate and is unlikely to be conducted as a head-to-head comparison.

Quality of life

Adverse events

Adverse events occurring in the day following the procedure for the Phase II study included vasovagal responses (two patients), severe leg pain (one patient) and severe post-operative pain (one patient). Other symptoms reported in the one-week post-procedure questionnaire of the Phase II study included awareness of something foreign in the body, bloating, night sweats, aches, fainting, fatigue and abdominal tightness. Four patients (2%) reported fever, which resolved within 12 hours. It is important to note that details of the reliability of the one-week questionnaire were not provided. It is not clear how data were collected, ie if the questionnaire was administered in person, by telephone, etc.

Potentially serious hypervolaemia was observed in two of the 518 patients in the Pivotal study. Hypervolaemia is an abnormal increase in the volume of circulating plasma in the body. It is a known risk with HSTCPII due to the introduction of high volumes of distension fluid into the uterine cavity over a relatively short period of time.

Intrafallopian implant tolerance

In the Phase II study, 90 per cent (205/227) of participants completed the patient questionnaire at one week after intrafallopian implant placement. Ninety per cent of these 205 rated tolerance of the intrafallopian implant as good to excellent. Table 19 presents levels of patient satisfaction with the use of intrafallopian implants at various points of follow-up.

Table 19 Intrafallopian implant tolerance in the Phase II study (N=227)

Follow-up time point (months)	Respondents	Excellent	Very good	Good	Fair	No response
3	89.4% (203/227)	87.7% (178/203)	8.9% (18/203)	2.0% (4/203)	1.0% (2/203)	0.5% (1/203)
6	87.7% (199/227)	89.9% (179/199)	6.5% (13/199)	2.0% (4/199)	0.5% (1/199)	1.0% (2/199)
12	68.7% (156/227)	88.5% (138/156)	8.3% (13/156)	2.6% (4/156)	0.0%	0.6% (1/156)
18	30.8% (70/227)	90.0% (63/70)	8.6% (6/70)	1.4% (1/70)	0.0%	0.0%
24	4.4% (10/227)	90.0% (9/10)	10.0% (1/10)	0.0%	0.0%	0.0%

The majority of patients rated tolerance of the intrafallopian implant as excellent at each of the time points analysed. However, the significance of this finding is difficult to assess because a copy of the relevant question was not provided. The most negative response reported was 'fair'. It is unclear whether a more negative response than 'fair' was available to patients. If not, then a rating of 'fair' would indicate the number of patients who were most unhappy with the intrafallopian implant.

Patients in the Pivotal study were asked to rate their comfort with use of the intrafallopian implant. A total of 4,300 woman-months of data were accumulated. The results are reported in Table 20. The majority of patients rated the tolerance of the intrafallopian implant very highly.

Table 20 Overall patient tolerance of the intrafallopian implant in the Pivotal study

Follow-up	Respondents	Excellent	Very Good	Good	Fair	Poor
3-months post implant placement	82.4% (427/518)	82.9% (354/427)	12.2% (52/427)	4.0% (17/427)	0.7% (3/427)	0.2% (1/427)
3-months relying on implant	43.2% (224/518)	87.9% (197/224)	11.2% (25/224)	0.9% (2/224)	0.0%	0.0%
6-months relying on implant	9.7% (50/518)	90.0% (45/50)	8.0% (4/50	2.0% (1/50)	0.0%	0.0%

Time taken to return to normal functioning

The Pivotal study reported time taken for patients to return to normal functioning after placement of the intrafallopian implant (Table 21). Overall, the majority of patients returned to normal physical functioning within three days. Data are not available for 10.8 per cent (56/518) of patients. Reasons for the lack of these data were not provided, therefore the possibility that these patients had yet to return to normal functioning cannot be ruled out.

Table 21 Number of days after HSTCPII before return to normal physical functioning

Number of days before returning to normal functioning	Number of patients[a] (%)
<1	132 (28.6)
1	144 (31.2)
2	77 (16.7)
3	49 (10.6)
4	22 (4.8)
5	12 (2.6)
6	10 (2.2)
7	6 (1.3)
>7	10 (2.2)

[a] data are available for 462 of the 518 patients in the Pivotal study

What are the economic considerations?

General framework

The framework for the economic evaluation of any medical technology considered by the MSAC is the comparison of the costs and benefits of that technology relative to the current alternative treatment for patients. The approach taken is to calculate an incremental cost effectiveness ratio $(C_i-C_c)/(O_i-O_c)$ where C_i is the total cost of resources associated with the intervention, C_c is the total cost of resources used by the comparator, O_i is the outcome associated with the intervention, and O_c is the outcome associated with the comparator. The broad perspective is a societal one that includes costs borne by governments and individuals.

Where there are two comparators or patient groups, a weighted average of cost and outcome can be calculated based on the proportion of patients who are likely to receive each of the comparator treatments.

This analysis refers to costs and effects for HSTCPII using the Essure device.

Economic evaluation

A literature review of economic evidence was conducted using Medline (1966 to date) as well as economic databases such as HEED (Health Economic Evaluations Database) and Embase. The results of the review are summarised in Appendix H. There is limited literature in this area.

Garcia et al (2000) looked at microlaparoscopic versus standard laparoscopic tubal sterilisation in the USA and found that costs were comparable at about US$1,500 (A$2,670[1]), but that the degree of satisfaction was higher, and the discomfort was less, with microsurgery. Using hospital charges, Hatasaka et al (1997) found that minimally-invasive tubal ligation under sedation and local anaesthetic cost US$1,615 (A$2,875) and conventional techniques under general anaesthetic cost US$2,820 (A$5,020).

Trussell et al (1995) estimated the economic value of several methods of contraception including tubal ligation and vasectomy. They listed public costs for tubal ligation at US$1,190 (A$2,118) and for vasectomy at US$353 (A$628). Overall cost savings for the two contraceptive methods over a five-year period were US$11,750 (A$20,915) for tubal ligation and US$13,900 (A$24,742) for vasectomy. Ashraf et al (1994) listed costs for vasectomy at US$587 (A$1,045), and for tubal ligation at US$1,281 (A$2,280), with mean costs per patient per year of US$55 (A$98) for vasectomy and US$118 (A$210) for tubal ligation.

Hughes and McGuire (1996) examined family planning services in the UK, including female sterilisation and vasectomy. They estimated costs at £212 (A$600)[2] for female sterilisation, and £178 (A$504) for vasectomy. Cost per pregnancy avoided for female

[1] 1 US$ = A$1.78
[2] 1 £ = A$2.83

sterilisation was £22 (A$62) and for vasectomy £18 (A$51). The inclusion of costs saved by the avoidance of unwanted pregnancies gave net resource savings of £780 (A$2,207) and £784 (A$2,219) respectively. In terms of couple-years of protection (the time unit provided by one unit of protective cover divided by 365, adjusted by failure rates), female sterilisation and vasectomy are among the most cost-effective forms of contraception, saving £7,597 (A$21,500) and £7,643 (A$21,630) respectively.

We did not locate any studies of the cost-effectiveness of HSTCPII.

Cost per case and financial implications for Australia

The submission from the manufacturer listed various total cost scenarios for HSTCPII in Australia. These ranged from $2,265 to $2,646 per patient (Table 22). Costs for LTL were estimated at between $1,392 and $1,725. Given comparative settings, these differences amount to between $776 and $1,021. Public funding differences were towards the lower end of the range.

Table 22 Cost scenarios for HSTCPII

Item	Cost of LTL - public[a] ($A)	Cost of LTL - private ($A)	Cost of HSTCPII - public ($A)	Cost of HSTCPII - private ($A)
Prostheses	27	91	1,200	1,200
Hospital costs	1,183	1,540	795	1,231
Diagnostics etc	88	-	83	28
Community health services	94	94	187[b]	187[b]
Total	1,392	1,725	2,265	2,646

[a] Public costs: Medicare Benefits Schedule (MBS), National Hospital Cost Data Collection (NHCDC). Private costs: MBS, private sector per diem payments

[b] Includes cost of HSG of $107 (based on the relevant MBS item). It was estimated that one third of women who had a pelvic X-ray would require a HSG

The submission provided a calculation of the number of patients expected to convert from LTL to HSTCPII. The estimates were based on current figures for LTL and a projection of the number of LTL cases for the next two years. The conversion figures are based on a survey commissioned by Conceptus in the USA and Australia.

The submission also used vasectomy as a comparator in terms of numbers likely to convert to HSTCPII. Diagnosis related group (DRG) costs range from $634 (private) to $804 (public), giving a range of cost differences between HSTCPII and vasectomy of $1,461 to $2,012.

Taking the minimum estimates of potential conversions to HSTCPII of six per cent for vasectomy and 28 per cent for LTL, and minimum estimated cost differences, additional costs would be $7.29 million for 7,450 procedures.[3] At the upper range of cost estimates, additional costs would be $9.78 million.

[3] 2001/2 numbers of procedures for vasectomy are given as 36,618, and for LTL 18,761 – a total of 55,379 sterilisation procedures.

Perhaps a more realistic estimate for conversions (based on aggregated ratings four, and five from the U.S. survey and 'likely' from the Australian survey, as suggested in the submission[4]) would be 21 per cent for vasectomy, and 48 per cent for LTL, leading to higher annual procedure costs over and above those for current procedures of between $18.25 and $24.69 million for 16,695 HSTCPII procedures. The most pessimistic scenario considered here (aggregated ratings three, four, and five from the U.S. survey and 'very likely' from the Australian survey) would result in conversion rates of 45 per cent for vasectomy and 60 per cent for LTL and additional costs of $32.9 to $44.8 million for 27,735 HSTCPII procedures.

Table 23 reports sensitivity analysis and cost projections versus conversion rates for LTL (with cost differences with HSTCPII of $776 and $1,021) and vasectomy (with cost differences with HSTCPII of $1,461 and $2,012).

Table 23 Sensitivity Analysis for conversion rates to HSTCPII

Rate of conversion	LTL with cost differences with HSTCPII of:		Vasectomy with cost differences with HSTCPII of:	
	$1,021	$776	$2,012	$1,461
0.05	N/A	N/A	$3,683,368	$2,675,366
0.10	N/A	N/A	$7,370,599	$5,354,540
0.15	N/A	N/A	$11,061,694	$8,037,522
0.20	N/A	N/A	$14,756,652	$10,724,313
0.25	$4,789,355	$3,640,947	$18,455,474	$13,414,913
0.30	$5,747,226	$4,369,137	$22,158,160	$16,109,322
0.35	$6,705,097	$5,097,326	$25,864,711	$18,807,541
0.40	$7,662,968	$5,825,516	$29,575,127	$21,509,570
0.45	$8,620,839	$6,553,705	$33,289,408	$24,215,408
0.50	$9,578,710	$7,281,895	$37,007,555	$26,925,057
0.55	$10,536,581	$8,010,084	$40,729,567	$29,638,517
0.60	$11,494,452	$8,738,273	$44,455,445	$32,355,788
0.65	$12,452,323	$9,466,463	$48,185,190	$35,076,870
0.70	$13,410,194	$10,194,652	$51,918,801	$37,801,763
0.75	$14,368,065	$10,922,842	$55,656,280	$40,530,469
0.80	$15,325,936	$11,651,031	$59,397,625	$43,262,987
0.85	$16,283,807	$12,379,221	$63,142,839	$45,999,317
0.90	$17,241,678	$13,107,410	$66,891,920	$48,739,460

Abbreviations: N/A; not applicable

It is not possible to undertake a cost-effectiveness analysis in the absence of data for HSTCPII on outcomes in terms of pregnancies avoided. The submission from the manufacturer used 'disability days averted' in a cost-effectiveness analysis, which is not a recognised measure of health gain and is of uncertain economic significance. Even if disability days averted represented a loss of income for the community with a cost difference with LTL of between $776 and $1,021 it would require the average female

[4] This is a seven-point scale ranging from 'not at all likely to convert', then scaling from one to five finishing with the option of 'very likely to convert'.

wage to be $259 to $340 per day before the additional expenditure created a cost saving in terms of income gains. In fact, at the existing average wage for women of $104 per day, the average loss to society would be $464 to $709 per patient. At the minimum estimated conversion figure of 14,848 from LTL to HSTCPII, this would lead to overall societal losses of between $6.9 million and $10.5 million.

Key areas of economic uncertainty

Key areas of uncertainty within the economic analysis included the following:

- The number of women who will convert from LTL to HSTCPII.
- The number of women, as part of a couple, who will undertake HSTCPII in preference to their partners undergoing vasectomy.
- The long term costs of those wishing to reverse the procedure. Women would potentially have to progress to IVF after HSTCPII whereas LTL and vasectomy are potentially reversible.
- The costs of adverse events and contraceptive failure (e.g. normal delivery, miscarriage, abortion).
- The outcome evidence in terms of pregnancies avoided, is not available for HSTCPII.
- The potential benefits of HSTCPII such as greater effectiveness, which patients may be willing to pay for have not been quantified.
- The number of women who are attracted to HSTCPII as a form of permanent sterilisation but who would not have considered permanent sterilisation by another means.
- The number of women who may consider other forms of contraception, permanent or otherwise, if HSTCPII fails.

Summary

There is no evidence concerning the rate of substitution of HSTCPII for LTL or (if sterilisation is viewed from the perspective of the couple) the potential conversions from vasectomy. There are also potential costs surrounding issues of the procedures being reversible. In addition, there is no evidence, in terms of economic outcomes, for pregnancies avoided with HSTCPII.

Given the cost differences between HSTCPII and LTL, and between HSTCPII and vasectomy, it is estimated that additional health care costs would lie between $7.29 and $9.78 million at minimum rates of conversion. Perhaps a more realistic estimate for conversion rates based on aggregated ratings from the Australian survey in the submission would be 21 per cent for vasectomy and 48 per cent for LTL. This would lead to higher additional annual actual procedure costs, over and above the cost of procedures currently carried out, ranging from $18.25 to $24.69 million for 16,695

procedures. Depending on the rate of uptake, additional health care costs could be as high as $45 million.

Conclusions

Safety

The main safety issues with respect to HSTCPII include perforation of the fallopian tube, expulsion of the intrafallopian implant, pain and bleeding. Other potential safety issues include changes in menstrual pattern, ectopic pregnancy and infection. The incidence of perforation decreased markedly from approximately three per cent in the earlier studies to less than one per cent in the Pivotal study after the procedure was modified to discontinue the use of the support catheter. Expulsion of the intrafallopian implant affected 2.7 per cent (14/518) of patients in the Pivotal study. However only two of the 14 patients with expelled implants exhibited any symptoms and these abated following removal of the implant. Pain and bleeding, when observed, were usually mild. No evidence was presented in the studies that indicated significant changes in menstrual pattern. Since no pregnancies were reported, ectopic pregnancy was not an issue.

Overall, HSTCPII appears to be relatively safe, however, this is based on short-term data and it is only with extensive use and further long-term studies that the true safety profile of HSTCPII will be elucidated. At which time comparisons with the known problems associated with its main comparator, laparoscopic tubal ligation (LTL), can be made.

Effectiveness

No pregnancies have been reported in patients who have relied on HSTCPII as their primary form of contraception. However, further long-term follow-up is required to establish fully the effectiveness of the intrafallopian implant over a reasonable amount of time. A condition of a recommendation by the FDA for pre-market approval of the Essure system was that the manufacturer follows study subjects for five years (US Food and Drug Administration and the Center for Devices and Radiological Health, 2002). It is the stated intention of the manufacturer to collect data from patients in the Phase II and Pivotal studies for five years post-implantation.

A total of 86 per cent (194/227) of patients who commenced the Phase II study and 83 per cent (430/518) of patients from the Pivotal study are currently relying on the intrafallopian implant as their primary method of contraception. One patient with unilateral placement in the Phase II trial was relying on the intrafallopian implant as their sole method of contraception due to proximal tube occlusion in the contralateral tube. In addition, two patients in the Pivotal study with unilateral placement were able to rely on the device due to a unicornuate uterus. However, it must be noted that approximately 15 per cent of patients are unable to rely on the implant for contraception, often due to anatomical factors. These patients must use alternative forms of birth control.

Overall, HSTCPII appears to be a relatively effective procedure, which has not been associated with any pregnancies to date. However, as with safety, further follow-up data are required to ascertain the longer-term effectiveness of HSTCPII.

Cost-effectiveness

The rates of substitution of HSTCPII for LTL, and for vasectomy if sterilisation is viewed from the perspective of the couple, are unknown. There are also potential costs surrounding issues of the procedures being reversible. In addition there is no evidence, in terms of economic outcomes, for pregnancies avoided with HSTCPII.

At minimum rates of substitution and with the additional costs of HSTCPII over LTL of between $776 and $1,021 per procedure, and of HSTCPII over vasectomy of between $1,461 and $2,012 per procedure, it is estimated that the introduction of HSTCPII to the Australian health system would give rise to additional overall health care costs of between $7.29 and $9.78 million.

A more realistic estimate for conversion rates based on aggregated ratings from the Australian survey in the submission may be 21 per cent for vasectomy and 48 per cent for LTL. This would lead to higher annual procedure costs, over and above the cost of procedures currently carried out, from $18.25 to $24.69 million for 16,695 procedures. Depending on the rate of technology uptake, additional health care costs could be as high as $45 million per annum.

Recommendation

The MSAC recognised that hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant is an evolving technology but as there was presently insufficient evidence pertaining to its safety, effectiveness and cost-effectiveness, the MSAC recommended that public funding for the procedure should not be supported at this time.

The Minister for Health and Ageing accepted MSAC's advice on the safety, effectiveness and cost-effectiveness of this technology. However, as more Australian data are due to become available shortly, the Minister approved a continuation of interim reimbursement until November 2007, to allow further assessment to occur.

The Minister for Health and Ageing accepted this recommendation on 2 March 2005.

Appendix A MSAC terms of reference and membership

The MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related to new or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to the AHMAC.

The membership of the MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumer issues, and health administration and planning:

Member	Expertise or Affiliation
Dr Stephen Blamey (Chair)	General surgery
Associate Professor John Atherton	Cardiology
Professor Bruce Barraclough	General surgery
Professor Syd Bell	Pathology
Dr Michael Cleary	Emergency medicine
Dr Paul Craft	Clinical epidemiology and oncology
Dr Kwun Fong	Thoracic medicine
Professor Jane Hall	Health economics
Dr Terri Jackson	Health economics
Ms Rebecca James	Consumer health issues
Professor Brendon Kearney	Health administration and planning

Member	Expertise or Affiliation
Associate Professor Richard King	Internal medicine
Dr Ray Kirk	Health research
Dr Michael Kitchener	Nuclear medicine
Dr Ewa Piejko	General practice
Ms Sheila Rimmer	Consumer representative
Professor Jeffrey Robinson	Obstetrics and gynaecology
Professor John Simes	Clinical epidemiology and clinical trials
Professor Bryant Stokes	Neurology
Professor Ken Thomson	Radiology
Dr Douglas Travis	Urology

Appendix B Supporting committee

Supporting committee for MSAC application 1055 - Hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant

Professor Ian Fraser AO (Chair) MD, BSc(Hons), FRANZCOG, CREI Professor in Reproductive Medicine Department of Obstetrics and Gynaecology University of Sydney	Member of MSAC
Professor Justin Beilby MD, MBBS, FRACGP, MPH Professor of General Practice Department of General Practice University of Adelaide, South Australia	Co-opted by MSAC
Dr Ray Kirk BSc, MSc, PhD Director, NZHTA Clinical Senior Lecturer in Public Health Otago University NZ Health and Technology Assessment Unit Dept of Public Health & General Practice Christchurch, NZ	Co-opted MSAC member
Dr Anthony Lawrence BSc(Hons), MB, BS(Hons), MRCOG, FRANZCOG Specialist in Obstetrics and Gynaecology Glen Waverley Specialist Centre Glen Waverley, Victoria	Co-opted by MSAC
Professor Roger Pepperell MD, MGO, FRACP, FRANZCOG Professorial Fellow Department of Obstetrics and Gynaecology University of Melbourne, Melbourne	Nominated by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Ms Beth Walker BA (Welfare Studies), GradCert (Housing Management and Policy) Executive Officer Consumers' Health Forum Stuart Park, Darwin, Northern Territory	Nominated by the Consumers' Health Forum of Australia

Appendix C Search strategy

Search terms for MEDLINE	
1	Essure.tw
2	STOP.tw
3	Microcoil$.tw
4	Micro-coil$.tw
5	Microimplant$.tw
6	Micro-implant$.tw
7	Microinsert$.tw
8	Micro-insert$.tw
9	Intratubal device$.tw
10	Intra-tubal device$.tw
11	Tubal plug$.tw
12	Contraceptive device$.tw
13	Or/1-12
14	Exp sterilisation, tubal/
15	Tubal sterili?ation$.tw
16	Transcervical sterili?ation$.tw
17	Hysteroscopic sterili?ation$.tw
18	Tubal occlusion$.tw
19	Or/14-18
20	Permanent contracept$.tw
21	Permanent birth control.tw
22	Sterili?$.tw
23	Surgical sterili?$.tw
24	Pregnancy prevent$.tw
25	Or/20-24
26	Exp fallopian tubes/
27	Fallopian tube$.tw
28	26 or 27
29	25 and 28
30	19 or 29
31	13 and 30
32	Limit 31 to (human and female)

Appendix D Health Technology Assessment agency websites

Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé (AÉTMIS). http://www.aetmis.gouv.qc.ca/ (Accessed 4 November 2002)

Alberta Heritage Foundation for Medical Research (AHFMR). http://www.ahfmr.ab.ca/index.html (Accessed 4 November 2002)

Agency for Healthcare Research and Quality. http://www.ahrq.gov/ (Accessed 4 November 2002)

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical. http://www.racs.edu.au/open/asernip-s.htm (Accessed 4 November 2002)

The Centre for Health Services and Policy Research (CHSPR). http://www.chspr.ubc.ca/ (Accessed 4 November 2002)

Canadian Coordinating Office for Health Technology Assessment (CCOHTA). http://www.ccohta.ca/ (Accessed 4 November 2002)

Danish Institute for Health Technology Assessment (DIHTA). http://www.dihta.dk/ (Accessed 4 November 2002)

EUROSCAN. http://www.ad.bham.ac.uk/euroscan/index.asp (Accessed 4 November 2002)

Finnish Office for Health Care Technology Assessment. http://www.stakes.fi/finohta/e/ (Accessed 4 November 2002)

Health Council of the Netherlands. http://www.gr.nl/engels/welcome/frameset.htm (Accessed 4 November 2002)

Minnesota Health Technology Advisory Council. http://www.health.state.mn.us/htac/ (Accessed 4 November 2002)

Institute for Clinical Systems Improvement. http://www.icsi.org/talist.htm (Accessed 4 November 2002)

Institute of Technology Assessment of the Austrian Academy of Science. http://www.oeaw.ac.at/ita/welcome.htm (Accessed 4 November 2002)

International Network of Agencies for Health Technology Assessment (INAHTA). http://www.inahta.org/ (Accessed 4 November 2002)

International Society of Technology Assessment in Health Care (ISTAHC). http://www.istahc.org/ (Accessed 4 November 2002)

Medical Technology Assessment Group (M-TAG). http://www.m-tag.net/ (Accessed 4 November 2002)

Medical Technology & Practice Patterns Institute (MTPPI). http://www.mtppi.org/ (Accessed 4 November 2002)

NHS Centre for reviews and dissemination, University of York. http://nhscrd.york.ac.uk/welcome.html (Accessed 4 November 2002)

The National Coordinating Centre for Health Technology Assessment (NCCHTA). http://www.hta.nhsweb.nhs.uk/ (Accessed 4 November 2002)

National Horizon Scanning Centre. http://www.bham.ac.uk/PublicHealth/horizon/ (Accessed 4 November 2002)

National Institute for Clinical Excellence (NICE). http://www.nice.org.uk/ (Accessed 4 November 2002)

New Zealand Health Technology Assessment (NZHTA). http://nzhta.chmeds.ac.nz/ (Accessed 4 November 2002)

The Swedish Council on Technology Assessment in Health Care (SBU). http://www.sbu.se/admin/index.asp (Accessed 4 November 2002)

The Norwegian Centre for Health Technology Assessment (SMM). http://www.oslo.sintef.no/smm/news/FramesetNews.htm (Accessed 4 November 2002)

Swiss Science Council/Technology Assessment (SWISS/TA). http://www.ta-swiss.ch/ (Accessed 4 November 2002)

TNO Prevention and Health (TNO). http://www.health.tno.nl/homepage_pg_en.html (Accessed 4 November 2002)

Veterans Affairs Technology Assessment Program (VATAP). http://www.va.gov/resdev/ps/pshsrd/mdrc.htm#HealthCareTechnologyAssessment (Accessed 4 November 2002)

WHO Health Technology Assessment Programme (Collaborating Centres). http://www.who.int/pht/technology_assessment/index.html (Accessed 4 November 2002)

Appendix E Clinical trials register websites

Centre Watch Clinical Trials Listing Service. http://www.centerwatch.com/ (Accessed 4 November 2002)

Clinical Trials.com. http://clinicaltrials.com/ (Accessed 4 November 2002)

Clinical Trials.gov. http://clinicaltrials.gov/ (Accessed 4 November 2002)

Current Controlled Trials. http://www.controlled-trials.com/ (Accessed 4 November 2002)

FDA Clinical trials links. http://www.fda.gov/oc/oha/default.htm#clinical (Accessed 4 November 2002)

NHMRC Clinical Trials Registry. http://www.ctc.usyd.edu.au/6registry/reg1.shtml (Accessed 4 November 2002)

Society for Clinical Trials. http://www.sctweb.org/ (Accessed 4 November 2002)

Trials Central. http://www.trialscentral.org/ (Accessed 4 November 2002)

UK National Research Registry. http://www.update-software.com/National/ (Accessed 4 November 2002)

Appendix F Study included in the effectiveness analysis

Kerin, J.F., Carignan, C.S. & Cher, D. 2001. 'The safety and effectiveness of a new hysteroscopic method for permanent birth control: Results of the first Essure PBC clinical study', *Australian & New Zealand Journal of Obstetrics & Gynaecology*, 41 (4), 364-370.

Appendix G Studies excluded from the effectiveness analysis

Animal Studies

Post, J.H., Cardella, J.F., Wilson, R.P. et al, 1997. 'Experimental nonsurgical transcervical sterilization with a custom-designed platinum microcoil', *Journal of Vascular & Interventional Radiology*, 8 (1, Part 1), 113-118.

Schmitzrode, T., Ross, P.L., Timmermans, H. et al, 1994. 'Experimental nonsurgical female sterilization - transcervical implantation of microspindles in fallopian tubes', *Journal of Vascular & Interventional Radiology*, 5 (6), 905-910.

Editorial

Squires, S. 2000. 'Tests of non-surgical contraception appear effective', *Los Angeles Times* (Health) S5.

FDA regulations

Dickey, R.P. 1977. 'The effect of recent FDA legislation on contraceptive development and safety', *International Journal of Gynaecology & Obstetrics*, 15 (2), 111-114.

LTL

Bhiwandiwala, P.P., Mumford, S.D. & Feldblum, P.J. 1983. 'Menstrual pattern changes following laparoscopic sterilization with different occlusion techniques: A review of 10,004 cases', *American Journal of Obstetrics & Gynecology*, 145 (6), 684-694.

Chi, I., Mumford, S.D. & Laufe, L.E. 1980. 'Technical failures in tubal ring sterilization: Incidence, perceived reasons, outcome, and risk factors', *American Journal of Obstetrics & Gynecology*, 138 (3), 307-312.

Seiler, J.S. 1986. 'Laparoscopic tubal sterilization combined with removal of an intrauterine contraceptive device. A report of 49 cases', *Journal of Reproductive Medicine*, 31 (5), 339-342.

Thranov, I., Hertz, J.B., Kjer, J.J. et al, 1992. 'Hormonal and menstrual changes after laparoscopic sterilization by falope-rings or filshie-clips', *Fertility & Sterility*, 57 (4), 751-755.

DeStefano, F., Peterson, H.B., Layde, P.M. et al, 1982. 'Risk of ectopic pregnancy following tubal sterilization', *Obstetrics & Gynecology*, 60 (3), 326-330.

No pregnancy data

Valle, R.F., Carignan, C.S., Wright, T.C. et al, 2001. 'Tissue response to the STOP microcoil transcervical permanent contraceptive device: Results from a prehysterectomy study', *Fertility & Sterility*, 76 (5), 974-980.

Not tubal sterilisation

Alvarez, F., Brache, V., Fernandez, E. et al, 1988. 'New insights on the mode of action of intrauterine contraceptive devices in women', *Fertility & Sterility*, 49 (5), 768-773.

Archibong, E.I. & Sobande, A.A. 2000. 'Ectopic pregnancy in Abha, Saudi Arabia. A continuing conundrum', *Saudi Medical Journal*, 21 (4), 330-334.

Botash, R.J. 1997. 'Loss of radiopacity may impede localization of intrauterine contraceptive device', *Clinical Imaging*, 21 (5), 372-374.

Brown, S., Vessey, M. & Stratton, I. 1988. 'The influence of method of contraception and cigarette smoking on menstrual patterns', *British Journal of Obstetrics & Gynaecology*, 95 (9), 905-910.

Brunham, R.C., Binns, B., McDowell, J. et al, 1986. 'Chlamydia trachomatis infection in women with ectopic pregnancy', *Obstetrics & Gynecology*, 67 (5), 722-726.

Burkman, R.T. 1997. 'The intrauterine contraceptive device: An acceptable alternative to sterilization in young women', *American Journal of Obstetrics & Gynecology*, 177 (4), 977-978.

Chi, I.C. 1995. 'Intrauterine contraceptive device - status report', *Advanced Drug Delivery Reviews*, 17 (2), 165-178.

Coste, J. & Job-Spira, N. 1988. 'Epidemiologic aspects of extrauterine pregnancy', *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction*, 17 (8), 991-1001.

Fernandez, R., Nelson, P., Delgado, J. et al, 2001. 'Increased adhesiveness and internalization of neisseria gonorrhoeae and changes in the expression of epithelial gonococcal receptors in the fallopian tube of copper T and norplant (R) users', *Human Reproduction*, 16 (3), 463-468.

Grimes, D.A. 2000. 'Intrauterine device and upper-genital-tract infection', *Lancet*, 356 (9234), 1013-1019.

Kanter, E. 1975. 'Letter: Tubo ovarian abscess associated with laparoscopic tubal cauterization and the intrauterine contraceptive device', *American Journal of Obstetrics & Gynecology*, 121 (2), 291.

Lete, I., Morales, P. & de Pablo, J.L. 1998. 'Use of intrauterine contraceptive devices in nulliparous women: Personal experience over a 12-year period', *European Journal of Contraception & Reproductive Health Care*, 3 (4), 190-193.

Lindblom, B. & Hamberger, L. 1981. 'Copper and contractility of the human fallopian tube', *American Journal of Obstetrics & Gynecology*, 141 (4), 398-402.

Margolis, M. & McLennan, M.K. 1993. 'Radiology rounds. Intrauterine contraceptive device', *Canadian Family Physician*, 39 2113, 2283-2284.

Molland, J.R., Morehead, D.B., Baldwin, D.M. et al, 1996. 'Immediate postpartum insertion of the norplant contraceptive device', *Fertility & Sterility*, 66 (1), 43-48.

Portuondo, J.A., Ochoa, C., Gomez, B.J. et al, 1984. 'Fertility and contraception of 6 patients with ovarian pregnancy', *International Journal of Fertility*, 29 (4), 254-256.

Sheikh, H.H. & Yussman, M.A. 1976. 'Electrocardiographic monitoring during hysterosalpingography', *Obstetrics & Gynecology*, 48 (1), 90-92.

Tancer, M.L., Delke, I. & Veridiano, N.P. 1981. 'A fifteen year experience with ectopic pregnancy', *Surgery, Gynecology & Obstetrics*, 152 (2), 179-182.

Vandekerckhove, P., Watson, A., Lilford, R. et al, 2000. 'Oil-soluble versus water-soluble media for assessing tubal patency with hysterosalpingography or laparoscopy in subfertile women', *Cochrane Database of Systematic Reviews*, (2), CD000092.

Wollen, A.L., Flood, P.R. & Sandvei, R. 1990. 'Altered ciliary substructure in the endosalpinx in women using an IUCD', *Acta Obstetricia et Gynecologica Scandinavica*, 69 (4), 307-312.

Wollen, A.L., Sandvei, R., Mork, S. et al, 1994. 'In situ characterization of leukocytes in the fallopian tube in women with or without an intrauterine contraceptive device', *Acta Obstetricia et Gynecologica Scandinavica*, 73 (2), 103-112.

Obsolete device

Almstrom, H. & Brundin, J. 1989. 'Sonographic localization of an intramurally placed intratubal device-the P-block', *European Journal of Obstetrics, Gynecology & Reproductive Biology*, 33 (2), 155-160.

Assaf, A., Abdin, F., Elkady, A. et al, 1993. 'Histopathological effects of silicone rubber 'ovabloc' on the human fallopian tube', *International Journal of Gynaecology & Obstetrics*, 43 (2), 181-189.

Brundin, J. 1987. 'Observations on the mode of action of an intratubal device, the P-block', *American Journal of Obstetrics & Gynecology*, 156 (4), 997-1000.

Cooper, J.M., Rigberg, H.S., Houck, R. et al, 1985. 'Incidence, significance and remission of tubal spasm during attempted hysteroscopic tubal sterilization', *Journal of Reproductive Medicine*, 30 (1), 39-42.

Loffer, F.D. 1982. 'What's new in female sterilization? The silicone tubal plug is', *Arizona Medicine*, 39 (7), 442-445.

Neuwirth, R.S. 1995. 'Update on transcervical sterilization', *International Journal of Gynaecology & Obstetrics*, 51 (Suppl.1), S23-28.

Van der Leij, G. & Lammes, F.B. 1996. 'Office hysteroscopic tubal occlusion with siloxane intratubal devices (the Ovabloc method)', *International Journal of Gynaecology & Obstetrics*, 53 (3), 253-260.

Van der Leij, G. & Lammes, F.B. 1997. 'Radiographic aspects of office hysteroscopic tubal occlusion with siloxane intratubal devices (the Ovabloc method)', *International Journal of Gynaecology & Obstetrics*, 59 (2), 123-131.

Appendix H Critical appraisal of literature on economic costs

Study	Assumptions	Costs	Outcomes measured	Results
Ashraf et al, 1994 USA	Comparison of contraceptive methods	Acquisition costs (drugs or surgery); costs of visits and monitoring; costs of adverse events and contraceptive failure	Pregnancy-free years	Vasectomy: US$55 per woman per pregnancy-free year Tubal ligation: US$118 per woman per pregnancy-free year
Garcia et al, 2000 USA	Microlaparoscopic (n=16) versus standard (n=34) laparoscopic tubal sterilisation	Standard laparoscopy: US$1,535 Microlaparoscopy: US$1,523	Post operative discomfort, patient satisfaction	With microlaparoscopy, costs were comparable, patient satisfaction was higher and discomfort significantly less
Hatasaka et al, 1997 USA	Minimally-invasive tubal ligation under sedation and local anaesthetic (n=7) versus conventional technique under general anaesthetic (n=7)	Hospital charges: Minimally-invasive technique: US$1,615 Conventional technique: US$2,820	Recovery time, patient satisfaction, complications	Recovery time was longer after general anaesthetic. There was no difference in complications and satisfaction
Hughes & McGuire, 1996 UK	Family planning services: oral contraceptives, diaphragm, IUD, spermicide, injection, implant, condom Hospital provision: female sterilisation, vasectomy	Female sterilisation: £212 Vasectomy: £178	Sterilisation failure rate (number of expected pregnancies per year per 100 users) Couple-years of protection (the time unit provided by one unit of protective cover divided by 365), adjusted by failure rates	Cost per pregnancy avoided: Female sterilisation: £22 Vasectomy: £18 Net resource savings including costs averted from unwanted pregnancies: Female sterilisation: £780 Vasectomy: £784 In terms of couple-years of protection, savings were: Female sterilisation: £7,597 Vasectomy: £7,643
Trussell et al, 1995 USA	15 contraceptive methods including tubal ligation and vasectomy	Include method use, side effects, and costs of unintended pregnancies. Public payer unit cost: Tubal ligation-US$1,190 Vasectomy-US$353	Failure rate	Vasectomy saved US$13,899 and avoided 4.2 pregnancies over a 5-year period Tubal ligation saved only US$11,750 and avoided a similar number of pregnancies to vasectomy

Abbreviations

AE	adverse event
AHMAC	Australian Health Ministers' Advisory Council
DRG	diagnosis related group
FDA	Food and Drug Administration
HSG	hysterosalpingogram
HSTCPII	hysteroscopic sterilisation by tubal cannulation and placement of intrafallopian implant
IUD	intrauterine device
IVF	in vitro fertilisation
LTL	laparoscopic tubal ligation
MRI	magnetic resonance imaging
MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NSAIDs	non-steroidal anti-inflammatory drugs
RCT	randomised controlled trial
STOP	selective tubal occlusion procedure

References

American College of Gynecology, 1996. 'ACOG technical bulletin. Sterilization'. Number 222-April 1996 (replaces no. 113, February 1988). American college of obstetricians and gynecologists', *International Journal of Gynaecology & Obstetrics*, 53 (3), 281-288.

Ashraf, T., Arnold, S.B. & Maxfield, M. 1994. 'Cost effectiveness of levonorgestrel subdermal implants, comparison with other contraceptive methods available in the United States', *Journal of Reproductive Medicine*, 39 (10), 791-798.

Australian Bureau of Statistics. 2002. *Australian social trends 1998, family formation: Family planning* [Internet]. Australian Bureau of Statistics, Available from: http://www.abs.gov.au/ausstats/abs%40.nsf/94713ad445ff1425ca25682000192af2/3aebe08dcac76b81ca2569ad000402a8!OpenDocument [Accessed 28 November 2002].

Commonwealth Department of Health and Aged Care. 2001. Medicare Benefits Schedule 1 November 2001. Commonwealth Department of Health and Aged Care, Canberra.

Chalmers, I. & Altman, D.G. 1995. Systematic reviews, BMJ Publishing Group, London.

Conceptus Inc. 2002; *Conceptus Essure draft instructions for use* [Internet]. Conceptus Inc., Available from: http://www.fda.gov/ohrms/dockets/ac/02/briefing/3881b1_03.pdf [Accessed 28 November 2002].

Cooper, J.M., Rigberg, H.S., Houck, R. et al, 1985. 'Incidence, significance and remission of tubal spasm during attempted hysteroscopic tubal sterilization', *Journal of Reproductive Medicine*, 30 (1), 39-42.

Garcia, A.R., Steinmetz, I., Barker, B. et al, 2000. 'Economic and clinical outcomes of microlaparoscopic and standard laparoscopic sterilisation', *Journal of Reproductive Medicine*, 45 (5), 372-376.

Guyatt, G.H., Sackett, D.L. & Cook, D.J. 1993. 'User's guide to the medical literature. II. How to use an article about therapy or prevention. A: Are results of the study valid?', *Journal of the American Medical Association*, 270 (21), 2598-2601.

Hatasaka, H.H., Sharp, H.T., Dowling, D.D. et al, 1997. 'Laparoscopic tubal ligation in a minimally invasive surgical unit under local anesthesia compared to a conventional operating room approach under general anesthesia', *Journal of Laparoendoscopic and Advanced Surgical Techniques*, 7 (5), 295-299.

Hughes, D. & McGuire, A. 1996. 'The cost effectiveness of family planning provision', *Journal of Public Health Medicine*, 18 (2), 189-196.

Kerin, J.F. 1995. 'New methods for transcervical cannulation of the fallopian tube', *International Journal of Gynaecology & Obstetrics*, 51 (Suppl.1), S29-39.

Kerin, J.F., Carignan, C.S. & Cher, D. 2001. 'The safety and effectiveness of a new hysteroscopic method for permanent birth control: Results of the first Essure PBC clinical study', *Australian & New Zealand Journal of Obstetrics & Gynaecology*, 41 (4), 364-370.

Kulier, R., Boulvain, M., Walker, D. et al, 2002. 'Minilaparotomy and endoscopic techniques for tubal sterilisation', *Cochrane Database of Systematic Reviews*, Issue 4, 2002.

Maubon, A., Thurmond, A.S., Laurent, A. et al, 2000. 'Fallopian tube catheterisation for sterilization', *Seminars in Interventional Radiology*, 17 (3), 295-301.

Mol, B.W., Ankum, W.M., Bossuyt, P.M. et al, 1995. 'Contraception and the risk of ectopic pregnancy: A meta-analysis', *Contraception*, 52 (6), 337-341.

Nardin, J.M., Kulier, R., Boulvain, M. et al, 2002. 'Techniques for the interruption of tubal patency for female sterilisation', *Cochrane Database of Systematic Reviews*, Issue 4, 2002.

Neuwirth, R.S. 1995. 'Update on transcervical sterilization', *International Journal of Gynaecology & Obstetrics*, 51 (Suppl.1), S23-28.

NHMRC. 1999. *A guide to the development, implementation and evaluation of clinical practice guidelines*, National Health and Medical Research Council, Canberra.

NHMRC. 2000. *How to use the evidence: Assessment and application of scientific evidence.* National Health and Medical Research Council, Canberra.

NHS Centre for Reviews and Dissemination. 2001. *Undertaking systematic review of research on effectiveness. CRD's guidance for those carrying out or commissioning reviews.* [Internet]. NHS Centres for Reviews and Dissemination. Available from: www.york.ac.uk/inst/crd/report4.htm [Accessed 28 November 2002].

Rioux, J.E. & Daris, M. 2001. 'Female sterilization: An update', *Current Opinion in Obstetrics & Gynecology*, 13 (4), 377-381.

Sackett, D.L., Straus, S.E., Richardson, W.S. & Haynes, R.B. 2000. *Evidence-based medicine: How to practice and teach EBM*, 2nd edn, Harcourt Livingstone, London.

Shellock, F.G. 2002. 'New metallic implant used for permanent contraception in women: Evaluation of MRI safety', *American Journal of Roentgenology*, 178 (6), 1513-1516.

Shoupe, D. 2000. 'Contraceptive vaginal rings, antiprogestins, and hysteroscopic tubal ligation', *Contraception*, 11 (4), 729-741.

Trussell, J., Leveque, J.A., Koenig, J.D. et al, 1995. 'The economic value of contraception: A comparison of 15 methods', *American Journal of Public Health*, 85 (4), 494-503.

U.S. Food and Drug Administration and the Center for Devices and Radiological Health. 2002, *Obstetrics and gynecology devices panel - July 22 and 23, 2002* [Internet]. U.S. Food and Drug Administration and the Center for Devices and Radiological Health, Available from: http://www.fda.gov/cdrh/panel/summary/obgyn07222002.html [Accessed 28 November 2002].

Valle, R.F., Carignan, C.S., Wright, T.C. et al, 2001. 'Tissue response to the STOP microcoil transcervical permanent contraceptive device: Results from a prehysterectomy study', *Fertility &Sterility*, 76 (5), 974-980.

Wilson, E.W. 1996. 'Sterilization', *Baillieres Clinical Obstetrics & Gynaecology*, 10 (1), 103-119.

Yusuf, F. & Siedlecky, S. 1999. 'Contraceptive use in Australia: Evidence from the 1995 national health survey', *Australian & New Zealand Journal of Obstetrics & Gynaecology*, 39 (1), 58-62.