

Thermal Balloon Endometrial Ablation for Dysfunctional Uterine Bleeding

An Evidence-Based Analysis

September 2004



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The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

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Abbreviations

CI	Confidence interval
DUB	Dysfunctional uterine bleeding
EA	Endometrial ablation
HMB	Heavy menstrual bleeding
ICER	Incremental cost-effectiveness ratio
MEA	Microwave endometrial ablation
OR	Odds ratio
QALY	Quality adjusted life year
QoL	Quality of life
RB	Rollerball
RCT	Randomized controlled trial
TBEA	Thermal balloon endometrial ablation
TCRE	Transcervical resection of the endometrium
WMD	Weighted mean difference

Executive Summary

Objectives

The objective of this review was to evaluate the effectiveness and cost-effectiveness of thermal balloon endometrial ablation (TBEA) for dysfunctional uterine bleeding (DUB).

Background: Condition and Target Population

Abnormal uterine bleeding is defined as an increase in the frequency of menstruation, duration of flow or amount of blood loss. (1) DUB is a diagnosis of exclusion when there is no pelvic pathology or underlying medical cause for the increased bleeding. (1) It is characterized by heavy prolonged flow with or without breakthrough bleeding. It may occur as frequent, irregular, or unpredictable bleeding; lengthy menstrual periods; bleeding between periods; or a heavy flow during periods. Menorrhagia, cyclical HMB over several consecutive cycles during the reproductive years, is the most frequent form of DUB.

The incidence of DUB has not been reported in the literature. For Ontario, an expert estimated that about 15% to 20% of women over 30 years have DUB. The prevalence increases with age and peaks just before menopause. (1) Using 2001 Ontario census-based population estimates, there are about 2 million women between the ages of 30 and 49 years; therefore, of these, about 290,965 to 387,953 may have DUB.

The Technology Being Reviewed: Thermal Balloon Endometrial Ablation

Since the 1990s, second-generation endometrial ablation (EA) techniques developed, the aim to provide simpler, quicker, and more effective treatment options for menorrhagia compared with first-generation EA techniques and hysterectomy. (2) Compared with first-generation techniques these depend less on the people operating them and more on the actual devices to ensure safety and efficacy.

TBEA relies on the transfer of heat from heated liquid within a balloon that is inserted into the uterus. (2) It does not require a hysteroscope for direct visualization of the uterus and can be performed under local anesthesia. In order to use TBEA, patients with DUB cannot have a long (>10–12 cm) or irregularly shaped uterine cavity, because the balloon must be in direct contact with the uterine wall to cause ablation. For Ontario, an expert estimated that about 70% of patients with DUB considered for EA would have a uterus suitable for TBEA based on these criteria. If 70% of Ontario women between 30 and 49 years of age with DUB have a uterus suitable for TBEA, then about 203,675 to 271,567 women may be eligible. However, some of these women will be successfully treated by drugs or will want amenorrhea (the cessation of their periods) and therefore choose to have a hysterectomy.

Review Strategy

The standard Medical Advisory Secretariat search strategy was used to locate international health technology assessments and English-language journal articles published from January 1996 to June 2004. A Cochrane systematic review from 2004 was identified that examined the effectiveness and cost-effectiveness of TBEA for heavy menstrual bleeding. (2) Another literature search was done to update information from the systematic review.

Summary of Findings

A 2004 systematic review of the literature by Garside et al. (2) in the United Kingdom, found that overall,

there were few significant differences between outcomes for first-generation techniques and TBEA. The outcomes were bleeding, postoperative complications, patient satisfaction, quality of life, and repeat surgery rates. Significant differences were reported most often by one study by Pellicano et al., (3) but this was a level 2 study with methodological weaknesses. Furthermore, according to Garside et al., there was considerable clinical and methodological heterogeneity among the studies in the systematic review. Therefore, a quantitative synthesis using meta-analysis was not done. In Garfield and colleagues' review:

- TBEA had significantly shorter operating and theatre times ($P < .05$, $< .01$, and $.0001$).
- TBEA had fewer intraoperative adverse effects (e.g., reported rates of uterine perforation with RB ablation: from 1% to 5%; TBEA: 0%; rates of cervical laceration with RB: 2% to 5%; TBEA 0%).
- They found no studies have directly compared second-generation techniques and hysterectomy; therefore, the comparison can only be indirectly inferred from studies of first-generation techniques and hysterectomy.
 - Compared with hysterectomy, TCRE and RB are quicker to perform and result in shorter hospitalization stays and a faster return to work.
 - Hysterectomy results in more adverse effects.
 - Satisfaction with hysterectomy is initially higher, but there is no difference after 2 years.
- Studies (level 2 evidence) published after Garside's systematic review support these conclusions.
- A study with level 2 evidence reported a significantly higher risk overall of intraoperative complications for RB compared with TBEA ($P < .001$). This included uterine perforation (RB, 5%; TBEA, 0%) and suspicion of perforation (RB, 2%; TBEA, 0%).
- A multicentre long-term case series (level 4 evidence) that examined avoidance of hysterectomy after TBEA for menorrhagia reported that 86% of women who had TBEA did not require a hysterectomy, and 75% did not have any further surgery during a follow-up period of 4 to 6 years. (4)
- Several TBEA studies did not provide justification for using general anesthesia over local anesthesia.
- Patient preferences for different treatments will depend on a woman's desire for amenorrhea as an outcome and/or avoidance of major surgery. *Hysterectomy is the only procedure that can guarantee amenorrhea. TBEA will not totally replace hysterectomy in the treatment of DUB, because some women may want cessation of menstruation.*
- Ensuring that patient expectations are consistent with the outcomes achievable with TBEA is important to obtain high levels of satisfaction. Vilos et al. (5) noted that up to one-half of patients who underwent a second attempt at TBEA might have avoided the second procedure with *proper preoperative counselling*. Meyer et al. (6) noted that one consideration for patients with menorrhagia (and no structural lesions) is to return to normal or less blood loss rather than amenorrhea. Patients may have distinct concepts of menstrual bleeding depending on cultural background, and maintaining an acceptable menstrual flow instead of amenorrhea may represent a healthier status. (7)
- A budget impact analysis suggests that the net annual budget outlay for TBEA would be between \$1.4 million in savings and \$2.8 million in additional outlays. (Note: Not all savings would be realized directly by the Ministry of Health and Long-Term Care, because much of the savings would accrue to the global budgets of hospitals).

Conclusions

- TBEA is effective, safe, and cost-effective for patients with DUB.
- For women who are not worried about amenorrhea, first-generation techniques offer advantages over hysterectomy.
- TBEA is a better alternative to first-generation techniques for DUB, because it is associated with fewer intraoperative adverse effects.

Objective

The objective of this review was to evaluate the effectiveness and cost-effectiveness of thermal balloon endometrial ablation (TBEA) for dysfunctional uterine bleeding (DUB).

Background

Clinical Need – Target Population and Condition

Abnormal uterine bleeding is defined as an increase in the frequency of menstruation, duration of flow, or amount of blood loss. (1) DUB is a diagnosis of exclusion when there is no pelvic pathology or underlying medical cause for the increased bleeding. (1) It is characterized by heavy prolonged flow with or without breakthrough bleeding. It may occur as frequent, irregular, or unpredictable bleeding; lengthy menstrual periods; bleeding between periods; or a heavy flow during periods. (1) DUB may occur with or without ovulation. (1) Menorrhagia, cyclical heavy menstrual bleeding occurring over several consecutive cycles during the reproductive years, is the most frequent form of DUB.

Objectively, menorrhagia is defined as blood loss of more than 80 mL per menstrual cycle. (1) Monthly blood loss over 60 mL may cause iron deficiency anemia. (1) Objective measurement is difficult, and some studies have shown that 35% to 60% of women who present with a complaint of menorrhagia have objectively measured blood loss in the normal range. However, there are also some women who do not seek help, even though they can be shown to have “abnormally heavy” blood loss.

Menorrhagia is an embarrassing and debilitating condition for many women that may have physical, emotional, and social impacts in addition to affecting a woman’s ability to carry out her normal activities. (2) Coulter et al. (8) studied 348 women in general practice and found that over one-half said menorrhagia was the cause of anxiety or depression and moodiness or irritability. Over one-third reported that menorrhagia interfered with relationships, sexual intercourse, and hobbies or holidays. (8) For 14% of the women, menorrhagia had an impact on their ability to carry out their job. (8) Anemia is common in women with menorrhagia, which may further deteriorate their quality of life.

It is estimated that 9% to 30% of reproductive age women experience menorrhagia. (1) In the United Kingdom, 1 in 20 women aged 30 to 49 years consults her general practitioner about menorrhagia annually. (2) Referrals for menstrual disorders account for about 20% of all those to specialist gynecology services in the United Kingdom. (2) There, heavy menstrual bleeding is the presenting complaint in about one-half of all hysterectomies. (9) The Royal College of Obstetricians and Gynecologists reported that 42% of hysterectomies in the United Kingdom are done to manage DUB. (5)

In Ontario, an expert estimated that about 15% to 20% of women over 30 years have DUB. Using 2001 Ontario census-based population estimates, there are about 2 million women between the ages of 30 and 49 years; therefore, of these, about 290,965 to 387,953 Ontario may have DUB. The incidence of DUB has not been identified in the literature, nor was an expert able to estimate its incidence in Ontario.

In Quebec, DUB and menstrual pain (dysmenorrhea) were the main indications for 16.2% of the hysterectomies performed there in 1996 to 1997. (10).

Existing Treatment Options Other Than Technology Being Reviewed

Treatment options generally start with the least invasive method (drugs) and may progress through minimally invasive first-generation or global second-generation endometrial ablation (EA) procedures. Hysterectomy is the last technique in this increasingly invasive stepwise approach.

Although medical management remains the first line of therapy, there is uncertainty about its effectiveness and acceptability. (11) Coulter et al. demonstrated that few patients choose to continue medical treatment. (12) Cooper et al. analyzed follow-up data from a trial of transcervical resection of the endometrium (TCRE) versus medical treatment and found that only 10% of patients who were allocated to medical treatment chose to continue with it after 5 years. (13) Nath Roy suggested the decision to discontinue medical treatment might be due to genuine lack of effectiveness, or inappropriate and non-evidence-based use of drugs. (11;14) Despite the availability of a variety of drugs for DUB, there is marked variation in practice and ongoing debate about the most appropriate therapy. (11;15;16)

EA techniques do not guarantee amenorrhea (cessation of menstruation). EA can be used to treat premenopausal women with DUB who do not want to conceive and who have no other major endometrial pathology. EA can provide relief from DUB without removing an otherwise healthy uterus.

First-Generation Endometrial Ablation Techniques

First-generation EA techniques were introduced in the early 1980s. They use electrical, thermal, or laser energy and require a high degree of surgical skill. (17) Examples include TCRE, rollerball, and laser ablation. All first-generation ablation techniques require training and direct visualization of the endometrium using a hysteroscope. Furthermore, to minimize the depth of endometrial lining, thinning agents or hormones may be used prior to ablation. Although it is possible to perform first-generation EA procedures using a local anesthetic, this is rare. (2) Possible adverse effects with first-generation EA techniques include the following:

- Electrosurgical burns
- Uterine perforation
- Hemorrhage
- Gas embolism
- Infection
- Fluid overload (which can cause congestive heart failure, hypertension, hemolysis [a breakdown of the red blood cells], pulmonary and brain edema, coma, and death)

The incidences of complications following first-generation ablation techniques are reported to include a rate of emergency hysterectomy of 6.6 per 1000 procedures and blunt uterine perforation in 14.7 per 1000 procedures. (2)

An expert estimated that the most commonly used first-generation EA technique in Ontario is hysteroscopic rollerball ablation.

Hysterectomy

Hysterectomy, the total or partial (leaving the cervix) removal of the uterus, is the only treatment that guarantees cessation of menstruation. Hysterectomy can be done abdominally, vaginally, or laparoscopically. The vaginal and laparoscopic approaches have been reported to cause fewer complications and shorter hospital stays compared with the abdominal approach. (10) However, hysterectomy is associated with perioperative and postoperative complications, including incontinence and other urinary problems, fatigue, infection, pelvic pain, and sexual problems. Hysterectomy requires general anesthesia, longer operating times than first-generation EA procedures, and a hospital stay of

several days. Full recovery may take 4 to 6 weeks. (2) Overall, 1 in 30 women reportedly experience a major adverse event during or soon after the procedure. (2) (Table 1)

Table 1: Adverse Events After Hysterectomy*

Very Common (> 1/10)	Common (>1/100, <1/10)	Uncommon (>1/1000, <1/100)
Sepsis	Hemorrhage	Death
Pyrexia	Blood transfusion	Fluid overload
Wound hematoma	Anemia	Visceral damage
Hypergranulation	Vault hematoma	Respiratory/heart complications
Urinary tract infection	Anesthetic	Deep vein thrombosis
	Gastrointestinal obstruction	
	Diarrhea	

**Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

During the fiscal year 2002 to 2003 in Ontario, physicians were paid on a fee-for-service basis for 4,467 EA procedures (exact technique not specified) and 12,695 hysterectomies (total or subtotal, abdominal or vaginal). An examination of the diagnostic codes for the hysterectomies during this year shows 4,917 of the hysterectomies were done because of “disorders of menstruation.”

In Ontario during 1999 to 2000, vaginal hysterectomies were about one-half as common as abdominal hysterectomies (ratio of vaginal to abdominal, 0.4). (18) Overall, 72% of the hysterectomies done in Ontario in women under 40 years (excluding those performed for cancer, HIV, or endometriosis) were total or included removal of the ovaries. (18)

Second-Generation Endometrial Ablation Techniques

Since the 1990s, second-generation ablation techniques developed with the aim to provide simpler, quicker, and more effective treatments for menorrhagia compared with first-generation techniques and hysterectomy. (2) These techniques are not as operator dependent as first-generation techniques and rely heavily on the devices to ensure safety and efficacy. (2) Examples of new second-generation techniques include thermal hot water balloon endometrial ablation (TBEA), intrauterine free saline solution, electrocoagulating multielectrode balloon, 3-D bipolar electrocoagulation probe, microwave devices, and different cryoprobes. (19) Preliminary results on TBEA were published as early as 1994. (20)

Early on, it was believed that EA might replace hysterectomy for DUB. However, diffusion of EA has not been reported to be that straightforward. For example, Bridgman and Dunn analyzed hospital admission data in the United Kingdom between 1989 and 1990, and then 1995 and 1996, and concluded that EA was not replacing hysterectomy. (21)

Conversely, Garside et al. (2) stated that the number of EAs in the United Kingdom increased, while the number of hysterectomies fell. Using Hospital Episode Statistics codes, Garside et al. reported the numbers of hysterectomies and EA procedures in England between 1990 and 2000. Nazar Amso, through personal communication to Garside et al. in 2002, suggested that the rise in the number of EA procedures for 1997 coincides with the introduction of second-generation devices into clinical practice:

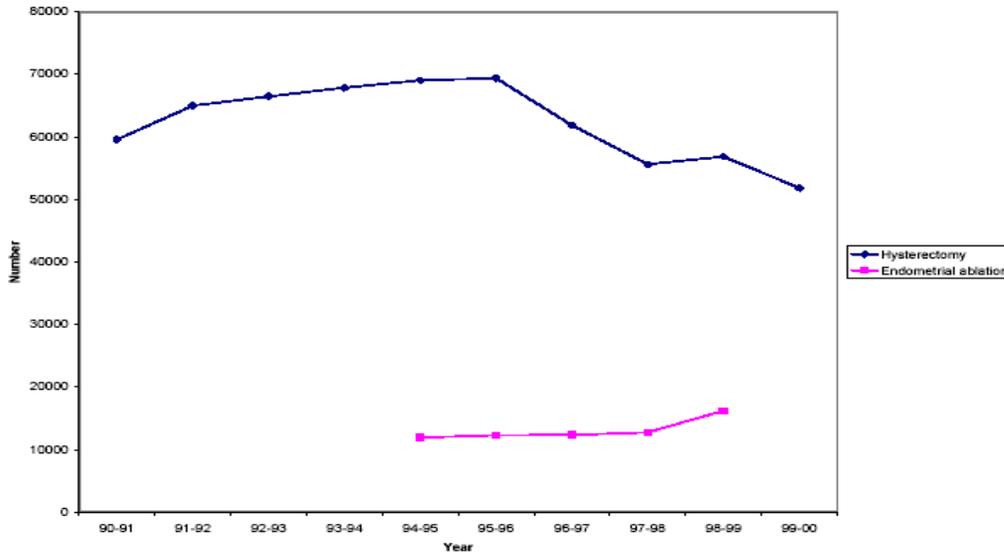


Figure 1: Number of Hysterectomies and Endometrial Ablations in England.

**Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

Garside and colleagues noted that although there may appear to be a trend toward more EA procedures and fewer hysterectomies, the figures may mask more complex, local variations. (2)

In the United States, Farquhar et al. (22) examined the diffusion of EA in 6 states from 1990 to 1997. The rate increased in all states, whereas the rates of hysterectomy fell in 3, remained the same in 2, and rose in 1 state. The ratio of hysterectomies to EAs decreased in all states. Farquhar et al. proposed that EA is being used as an adjunct therapy, rather than a replacement menorrhagia. Furthermore, the authors suggested that the availability of EA might decrease the threshold for surgical treatment.

New Technology Being Reviewed: Thermal Balloon Endometrial Ablation

TBEA relies on the transfer of heat from heated liquid within a balloon that is inserted into the uterus. (2) (Figure 2, Appendix 1). A thermal balloon cannot be used in patients with DUB who have a long (>10 cm to 12cm) or irregularly shaped uterine cavity, because the balloon must be in direct contact with the uterine wall to cause ablation.

In Ontario, an expert estimated about 70% of patients with DUB considered for EA would have a uterus suitable for TBEA (i.e., excluding large or abnormally shaped uteri). If 70% of Ontario women between 30 and 49 years of age with DUB have a uterus suitable for TBEA, then about 203,675 to 271,567 women may be eligible. However, some of these patients will be successfully treated by drugs or will want amenorrhea and therefore choose to have a hysterectomy.

Regulatory Status

The following 3 systems are licensed by Health Canada as Class 3 devices:

- Cavaterm *plus* System (Wallsten Medical SA; Morges, Switzerland), Licence 27440
- Thermablate EAS (MDMI Technologies Inc.; Richmond, BC, Canada), Licence 62542
- Thermachoice Uterine Balloon Therapy System (Gynecare, A Division of Ethicon Inc.; Somerville, NJ, United States), Licence 9897

MenoTreat (Lina Medical) is available in Europe but is not licensed by Health Canada.

Literature Review on Effectiveness

Objective

- To assess the effectiveness and cost-effectiveness of TBEA for DUB.

Questions Asked

- Is TBEA more effective and cost-effective than first-generation EA techniques or hysterectomy?
- Are there fewer postsurgical complications after TBEA than first-generation EA techniques and hysterectomy?
- Is quality of life (QoL) better after TBEA than after first-generation EA techniques or hysterectomy?

Methods

Inclusion criteria

- English-language articles (1996–June 2004)
- Journal articles that report primary data on the effectiveness or cost-effectiveness of TBEA obtained in a clinical setting, or analysis of primary data maintained in registries or databases
- Study design and methods clearly described
- Systematic reviews, randomized controlled trials (RCTs), non-randomized controlled trials and/or cohort studies that have ≥ 20 patients, cost-effectiveness studies

Exclusion criteria

- Duplicate publications (superseded by another publication by the same investigator group, with the same objective and data)
- Non-English-language articles
- Non-systematic reviews, letters, and editorials
- Animal and in-vitro studies
- Case reports
- Studies that do not examine the outcomes of interest

Intervention

- TBEA
- Controls do not undergo TBEA but receive optimal first-generation EA medical management

Literature Search

- Cochrane database of systematic reviews
- ACP Journal Club
- DARE
- INAHTA
- EMBASE
- MEDLINE
- Reference section from reviews and extracted articles

Outcomes of Interest

- Time without DUB
- Time to second EA procedure and/or hysterectomy for DUB
- QoL
- Postsurgical complications
- Economic analysis data

Results of Literature Review

Summary of Existing Health Technology Assessments

No studies were identified that directly compared TBEA to hysterectomy for the treatment of DUB. An overall summary of results comparing hysterectomy with first-generation EA techniques/TCRE (adapted from Lethaby et al., (23)) and first-generation EA techniques/TCRE with TBEA (partially adapted from Garside et al. (2)) are shown in Appendix 2.

National Health Service Research and Development Health Technology Assessment Programme (NHS R&D), United Kingdom, 2004

“The effectiveness and cost-effectiveness of microwave and thermal balloon EA for heavy menstrual bleeding: a systematic review and economic modelling.” (2)

For this study, Garside et al. (2), conducted a systematic review and compared microwave endometrial ablation (MEA) and TBEA for heavy menstrual bleeding (HMB) with existing first-generation EA techniques used in the United Kingdom. These earlier techniques were transcervical resection of the endometrium (TCRE), rollerball (RB) ablation, and hysterectomy.

The authors included systematic reviews, RCTs, and controlled trials of MEA and TBEA versus TCRE, RB or TCRE and RB combined. A comprehensive literature search was done up to August 2002. Cochrane reviews that examined treatments for HMB were also included.

According to the authors, there was considerable clinical and methodological heterogeneity among the studies included in the review. Therefore, they did not do a quantitative synthesis through meta-analysis.

Garside et al. identified the previously published systematic reviews:

- Eight Cochrane reviews examined treatments for HMB: 5 looked at the evidence for various medical methods (drugs) of controlling HMB, and 1 examined the use of preoperative thinning agents before hysteroscopic surgery.
- Two reviews were included in the evaluation by Garside et al.: endometrial destruction techniques for HMB and TCRE and RB compared with hysterectomy for HMB.

Cochrane Systematic Review of first-generation EA Techniques Versus Hysterectomy

- Five RCTs comprising 752 patients were included in the Cochrane review. (23) Follow-up ranged from 1 to 4 years (median, 2 years).
- There was a significant advantage in improved HMB and satisfaction rates up to, but not beyond, 2 years (OR 0.31 [95% CI, 0.16–0.59]) for women undergoing hysterectomy.
- Duration of surgery and hospital stay, and time to return to work were all shorter following EA:
 - Duration of surgery (weighted mean difference [WMD] 23.1 minutes (95% CI, 23.8–22.3))
 - Length of hospital stay WMD 4 days (95% CI, 4.9– 4.8)
 - Time to return to work WMD 4.6 weeks (95% CI, 4.8–4.4)
- Most minor and major adverse effects were more likely with hysterectomy. These were sepsis, blood transfusion, urinary retention, anemia, fever, hematoma, and hypergranulation tissue.
- Only fluid overload was more likely with first-generation EA.
- There were no differences between the groups for other adverse effects.

The reviewers concluded that first-generation EA techniques offered an alternative to hysterectomy for HMB and that effectiveness and satisfaction rates for both procedures were high. Permanent relief from symptoms offset the higher rate of complications and longer recovery period for hysterectomy. Costs were lower for EA; however, owing to retreatment in the EA group, the difference narrowed over time, with EA costing between 5% and 11% less than hysterectomy at 4 years.

Cochrane Systematic Review of Endometrial Destruction Techniques

- Two RCTs comparing TBEA with RB were included in the Cochrane review. (24) Three follow-up papers were published on one of these studies at 12, 24, and 36 months. One study comparing MEA with combined TCRE and RB was also included.
- Six other RCTs were included: 3 comparing first-generation methods, and 2 comparing other second-generation techniques (Vesta system, heated saline hydrotherm ablator) with first-generation techniques.
- Combined, the studies had 1,595 patients. Follow-up was from 6 to 15 months (median, 12 months).
- For RCTs comparing TBEA and RB:
 - Amenorrhea was more likely in the RB group at 12 and 36 months (OR 0.55 [95% CI, 0.31–0.99]; and OR 0.55 [95% CI, 0.25–0.97]), but not at 24 months.
 - Additional surgery was significantly more likely in the RB group at 24 months (OR 0.35 [95% CI, 0.12–0.99]), but not at 12 or 36 months. Other outcomes were not significantly different.
 - For the MEA group, most outcomes were not significantly different from the TCRE group. The odds of hemorrhage were lower in the MEA group (OR 0.14 [95% CI, 0.02–0.8]), but equipment failure was more likely (OR 4.07 [95% CI, 1.1–15]).
 - There were differences in the text and graph figures for some of the included study findings; attempts to contact the authors to clarify these data were unsuccessful.

The reviewers concluded that second-generation techniques compared favourably with first-generation techniques, but that equipment problems needed to be resolved.

Because the systematic review included only RCTs, did not include an economic assessment, and had

done the primary search in 2001, Garside et al. (2) did a new search for the assessment .

Update to Cochrane Review by Garside et al.

- In this update, (2) 14 publications were identified.
- Three were of MEA and 11 were of TBEA.
- Two of the MEA papers reported on the same trial at 12 and 24 months follow-up.
- Four of the TBEA papers reported the same trial at 12, 24, 36, and 60 months follow-up.
- Three trials were provided by industry. Wallsten Medical (Cavaterm) provided a translation of a small RCT comparing TBEA with RB ablation that was originally published in German and confidential unpublished trial details of an RCT comparing TBEA with TCRE. Garside and colleagues omitted the details of the second study from the public version of the assessment. Microsulis Medical (MEA equipment) provided details of an RCT they did as part of their submission for approval to the United States Food and Drug Administration.
- Therefore, 2 MEA and 8 TBEA trials were included in the review, although data were taken from all of the published reports of these trials.
- Most of the included studies are RCTs. Two are observational studies. (25;26) Details of all of the studies are shown in Table 2, in Appendix 3.
- The methods of the reports of RCTs are summarized in Table 3, in Appendix 3.

To assess effectiveness, the studies measured a wide range of outcomes of surgery. In general, the outcomes can be grouped into the following categories:

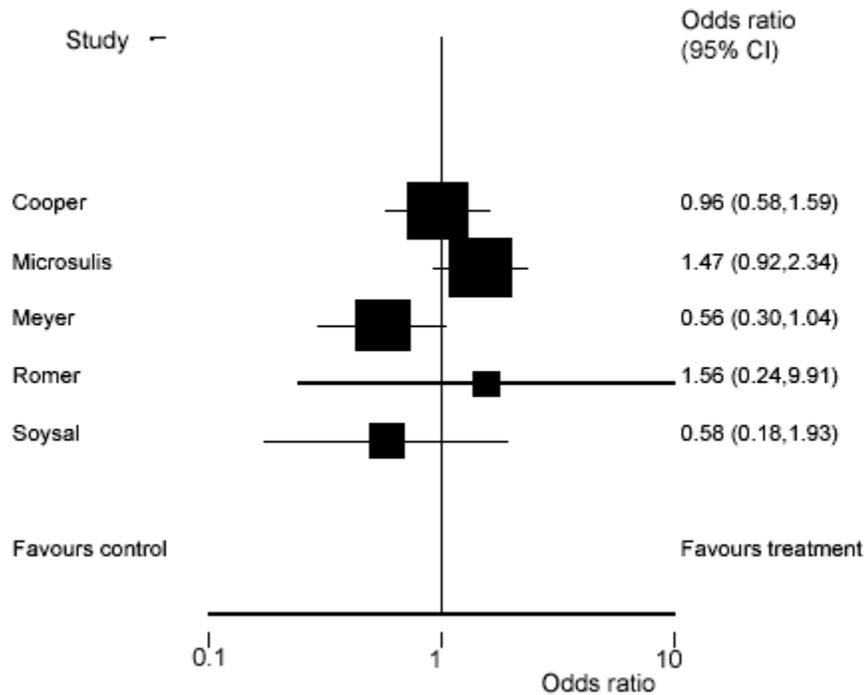
- Bleeding
- Premenstrual syndrome (PMS)
- Dysmenorrhea
- Anemia/hemoglobin
- Satisfaction
- QoL
- Operation details
- Further surgery
- Adverse effects (perioperative and postoperative)

Of note, how outcomes were reported differed among studies. (2) For example, some bleeding outcomes used mean pictorial blood loss assessment chart scores, or changes in these, whereas other investigators reported the number of women with various bleeding patterns. Therefore, it was not possible to compare results across studies or to combine them for meta-analysis.

Bleeding

Table 4 (Appendix 3) displays the rates of postoperative amenorrhea. Figures 3 and 4 below show the findings for amenorrhea at 12 and 24 months for first-generation and second-generation EA techniques. The size of the data points indicates the relative size of each study. In most cases, the confidence intervals cross the centre line indicating that differences were not statistically significant. The significant difference detected by Meyer et al. at 12 months (TBEA versus RB) is not seen in the forest plot, because the data were recalculated on an intent-to-treat basis, whereas the original study analysis excluded the patients who were lost to follow-up.

Figure 3: Forest Plot of Amenorrhea at 12 months: First-Generation Versus Second-Generation Endometrial Ablation Techniques. Random effects model, results not pooled. TBEA studies are Meyer, Romer and Soysal.*



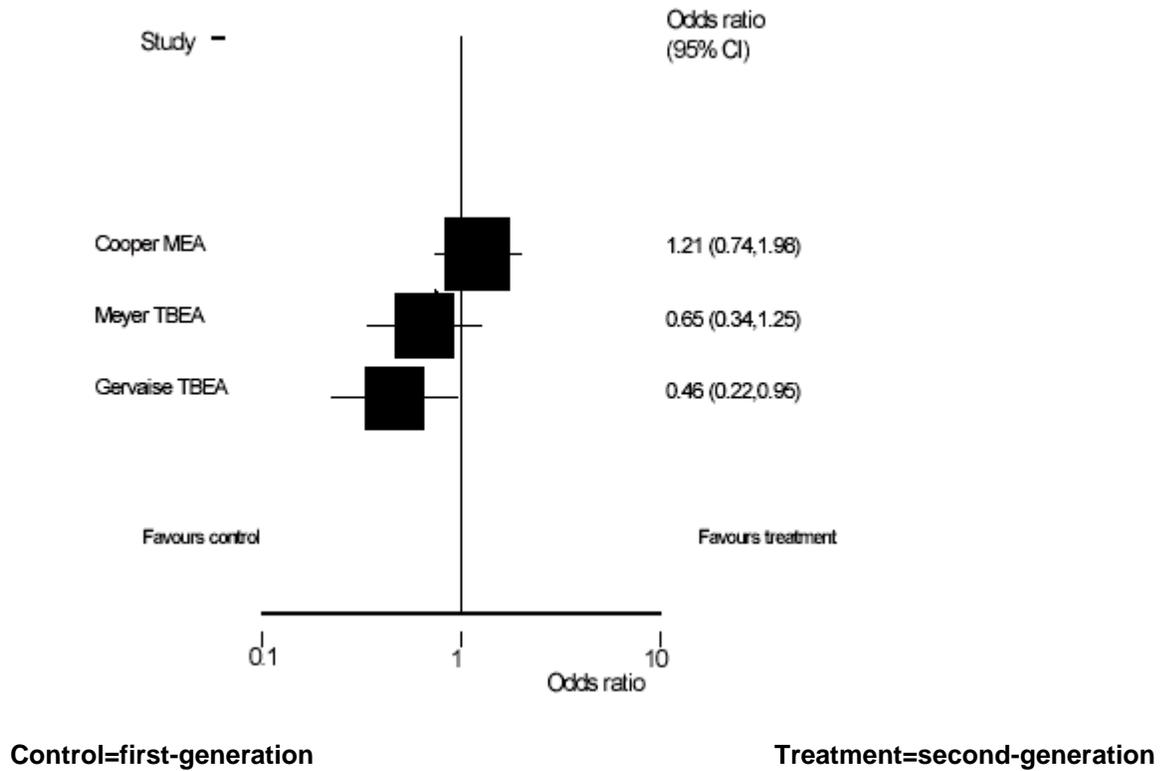
Control=first-generation

Treatment=second-generation

* TBEA indicates thermal balloon endometrial ablation

Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)

Figure 4: Forest Plot of Amenorrhea at 24 Months: First-Generation Versus Second-Generation Endometrial Ablation Techniques. Random effects model, results not pooled. TBEA studies are Meyer and Gervaise.*



**Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

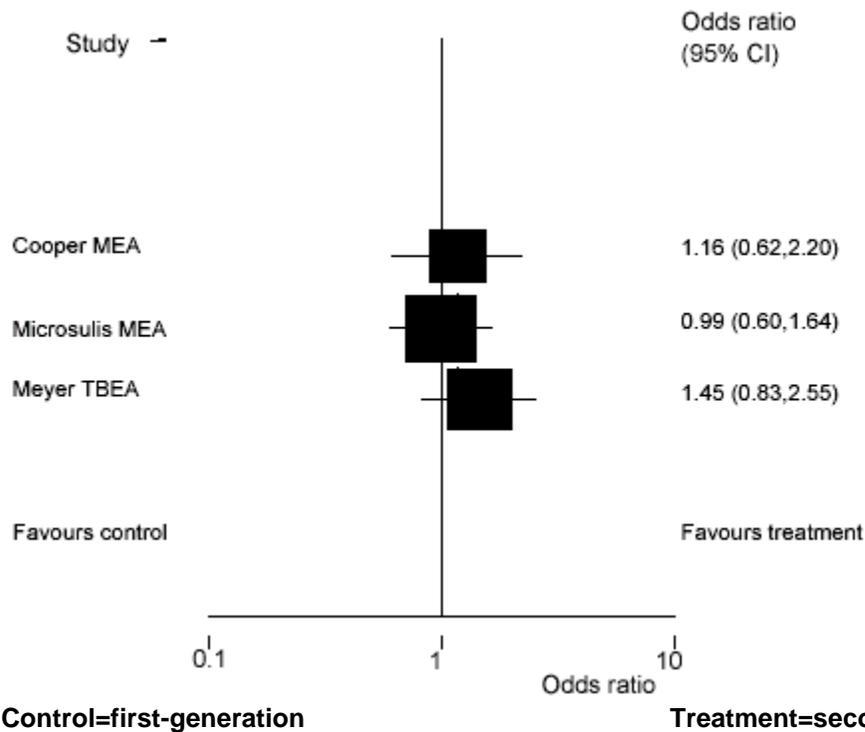
Table 5 (Appendix 3) shows other recorded outcomes for bleeding. No trial reported statistically significant differences between the groups for recurrent menorrhagia. Bongers et al. (26) (TBEA versus TCRE) reported the number of patients undergoing reintervention surgery who cited menorrhagia or metrorrhagia as a reason, *but it is not clear if other women may have also suffered these symptoms but not have undergone repeat surgery.*

Dysmenorrhea

Four trials reported on postoperative dysmenorrhea (Table 6, Appendix 3). *None of the trials reported using a validated pain score.* Bongers et al. (26) (TBEA versus TCRE) reported that 4% of women who had TCRE underwent a repeat procedure due to dysmenorrhea. However, they did not say if other patients had dysmenorrhea but did not opt for further surgery.

Garside et al. (9) provided a funnel plot (Figure 5) on dysmenorrhea rates at 12 months for first-generation versus second-generation EA techniques. The data points were produced from numbers describing dysmenorrhea as the same or worse as preoperatively. In all of the cases, the confidence intervals cross the central line indicating no statistically significant differences between the groups. The results were not combined owing to clinical heterogeneity between the trials.

Figure 5: Forest Plot of Dysmenorrhoea 12 months Postoperatively: First-Generation Versus Second-Generation Endometrial Ablation. Random Effects Model, Results Not Pooled. The TBEA Study in the Figure is Meyer.*



*Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. *Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168.* (2)

Premenstrual Syndrome Symptoms

Meyer et al. (6) (TBEA versus RB) reported the number of women who did not have PMS symptoms at 12, 24, and 36 months after the operation, and the number of women who had moderate or severe PMS at 12 months (TBEA 30%, RB 24%) and 24 months (TBEA 25%, RB 22%). There were no statistically significant differences in PMS symptoms between the groups.

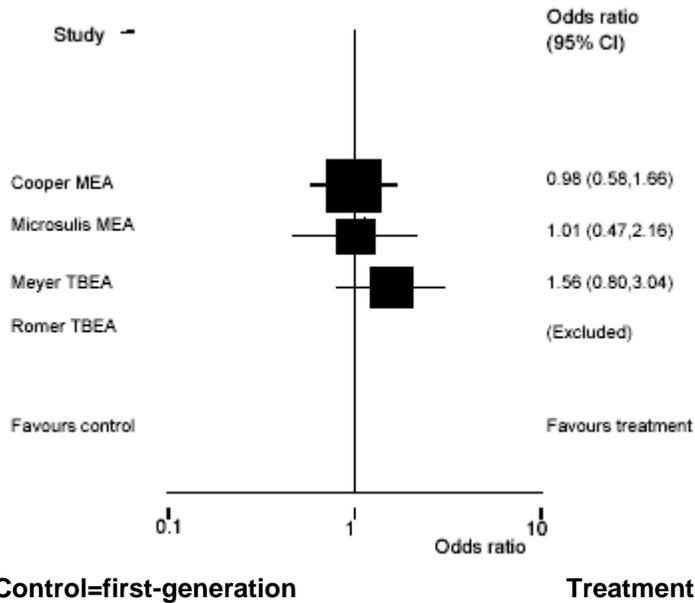
Satisfaction With Treatment

Table 7 (Appendix 3) displays data on satisfaction with treatment results. Using this data, Garside et al. (9) provided Figures 6 and 7 below to show the satisfaction rates at 12 and 24 months for first-generation versus second-generation EA techniques. (2) The data points were produced by combining the categories of “perfectly satisfactory” and “satisfactory” in the study by Bongers et al.; (26) “satisfied” and “very satisfied” in the study by Meyer et al.; (6) and “totally satisfied” and “generally satisfied” in the study by Cooper et al. (2) The size of the data points indicates the relative size of each study.

Bongers et al. (26) found a statistically significant effect for satisfaction in favour of TBEA at 12 months, but not at 24 months. Meyer et al. (6) found satisfaction to favour second-generation techniques significantly at 24 months (OR 1.93 [95% CI, 1.05–3.56]), but not at 12 months. Other studies did not note such a difference. (2) Garside et al. did not statistically combine the results because there was

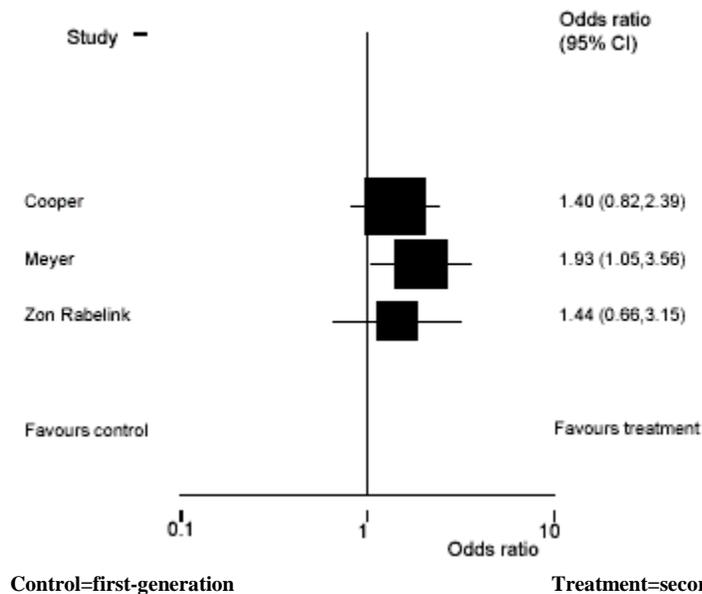
clinical heterogeneity between the trials. (2)

Figure 6: Forest Plot of Satisfaction at 12-Month Follow-Up: First-Generation Versus Second-Generation Endometrial Ablation Techniques. Random Effects, Results Not Pooled. TBEA Studies are Meyer and Romer.*



*Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. *Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168.* (2)

Figure 7: Forest Plot of Satisfaction at 24-Month Follow-up: First-Generation Versus Second-Generation Endometrial Ablation. Random Effects, Results Not Pooled. TBEA Studies are Meyer and Zon Rabelink.*



*Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. *Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

Quality of Life

Table 8 (Appendix 3) shows various aspects of QoL reported in the included studies, of which only 2 studies used measures relating to QoL. (2) Meyer et al. (6) (TBEA versus RB) reported a significant postoperative decrease in the proportion of women unable to work outside the home at all times of follow-up, with 4% of women in both arms unable to work outside the home at 36 months. In addition, whereas 2/3 of women reported that HMB had a severe impact on their lives before the operation, this was reduced to 1% in both arms at 36 months. The differences between the groups were not significant.

According to Garside et al., only the MEA study by Cooper et al. used a QoL instrument validated in HMB, the SF-36. (2)

Operation Details

Table 9 (Appendix 3) shows the results for duration of operations. Two studies reported on the percentage of operations that took less than 30 minutes to do. For TBEA, this was 65% to 100%. For TCRE and RB, this was 24% to 53%. These differences were significant in both studies ($P < .05$). Meyer et al. reported that 2% of TBEA and 14% of RB procedures took more than 50 minutes ($P < .05$).

Procedure times were significantly different in the study by Soysal et al. (TBEA versus RB), $P < .0001$; and Gervaise et al. (TBEA vs. TCRE), $P < .05$. Zon-Rabelink et al. (TBEA versus RB) reported that the mean operating time for TBEA was significantly shorter than for RB ($P < .001$) but did not provide data.

Bongers et al. (26) (TBEA versus TCRE), Brun et al. (TBEA versus RB), and Romer (TBEA versus RB)

did not report operating times.

Adverse Effects

Tables 10 and 11 on the following pages show the intraoperative and postoperative adverse effects reported in the trials. (2) Overall, there appear to be fewer perioperative adverse effects with second-generation techniques. Postoperative adverse effects are similar.

Table 10: Intraoperative Adverse Effects Reported in Trials Comparing TBEA and First-Generation EA Techniques*

Study, Year	Treatment	Intent to treat (No. reported on)	Intraoperative adverse effects No. (%)							
			Procedure Abandoned	Equipment Failure	Fluid Overload	Cervical Laceration or burn	Uterine Perforation or Laceration	Hemorrhage	Electrolyte Imbalance	Total Intraoperative Events
Meyer et al. 1998	TBEA	134 (125)	-	-	0	0	0	0	-	0
	RB	126 (114)	-	-	2 (1)	1 (1)	1 (1)	0	-	4 (3)
Gervaise 1999	TBEA	73 (73)	-	-	0	0	0	0	-	0
	TCRE	74 (74)	-	-	0	0	0	0	-	0
Pellicano 2002	TBEA	40 (46)	-	-	0	0	0	0	-	0
	TCRE/RB	42 (50)	-	-	5 (12)	1 (2)	2 (5) †	0	-	8 (19)
Romer 1998	TBEA	10 (10)	-	-	-	-	-	-	-	-
	RB	10 (10)	-	-	-	-	-	-	-	-
Soysal 2001	TBEA	48 (45)	-	-	0	0	0	0	0	0
	RB	48 (48)	-	-	2 (4)	1 (2)	0	0	0	5(10)
Zon- Rabelink 2001	TBEA	77 (77)	-	-	0	0	0	0	0	0
	RB	62 (60)	-	-	No	Yes	Yes	No	Yes	-

TBEA indicates thermal balloon endometrial ablation; EA, endometrial ablation; RB, rollerball ablation; TCRE, transcervical resection of the endometrium.

†Both patients had an emergency hysterectomy at the time of the procedure due to uterine perforation.

*Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. *The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

Table 11: Postoperative Adverse Effects Reported in Trials Comparing TBEA and First-Generation EA Techniques*

Study, Year	Treatment	Follow-up time post-procedure	Postoperative adverse effects Number (%)									Total Postoperative (cumulative)	
			Endometritis	Urinary tract infection	Hema-tometra	Urinary incontinence	Fever	Hemorrhage	Pain	Symptomatic Hydrosalpinx	CIN grade 1		
Meyer et al. 1998	TBEA n=126 RB n=114	12	3 (2) 1 (1)	1 (1) 0	- -	- -	- -	- -	- -	- -	0 1 (1)	- -	4 (3) 3 (3)
Loffer et al. 2001	TBEA n=122 RB n=105	24	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -	4 (3) 3 (3)
Loffer et al. 2002	TBEA n=114 RB n=99 TBEA n=61 RB n=61	36 60	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	4 (3) 3 (3) - -
Gervaise 1999	TBEA n=44 TCRE n=47	24	0 2 (4)	- -	- -	- -	- -	- -	- -	- -	- -	- -	0 2 (4)
Pellicano 2002	TBEA n=40 TCRE/RB n=42	3	- -	0 1 (2)	- -	- -	- -	1 (2) 2 (5)	5 (12) 4 (10)	- -	- -	- -	6 (14) 13 (31)
	TBEA n=40 TCRE/RB n=42	12	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -	6 (14) 13 (31)
	TBEA n=40 TCRE/RB n=42	24	- -	- -	- -	- -	- -	- -	- -	- -	1 (3) 1 (3)	- -	7 (17) 14 (34)
	TBEA n=40 TCRE/RB n=42		- -	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -
Romer 1998	TBEA n=10 RB n=10	12	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -
Soysal 2001	TBEA n=45 RB n=48	12	2 (4) 1 (2)	- -	1 (2) 2 (4)	- -	- -	- -	- -	- -	- -	- -	3 (7) 3 (6)
Zon-Rabelink 2001	TBEA n=77 RB n=60	12	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -

TBEA indicates thermal balloon endometrial ablation; EA, endometrial ablation; RB, rollerball ablation; TCRE, transcervical resection of the endometrium.

**Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

Repeat Endometrial Ablation

Table 12 in Appendix 3 shows the percentage of patients who had a repeat EA or hysterectomy at different follow-up times. To report the most conservative success rate, percentages based on the number of patients available for follow-up were reported by Garside et al. (2) in the text and shown in the table in parentheses. Data presented on an intent-to-treat basis are shown in square brackets in the table. For studies with multiple follow-up periods, the figures are cumulative for repeat procedures.

In all studies, treatment failure resulted in more hysterectomies than repeat ablation. Meyer et al. (6) (TBEA versus RB) reported 1 RB procedure in the intervention arm at 36 months. However, there was no repeat TCRE/RB in the control arm. At 60 months follow-up, Meyer et al. reported that 2 patients in each of the intervention (TBEA 3%) and control arms (RB 3%) had undergone repeat RB ablation. Bongers and colleagues (TBEA versus TCRE) reported 4 (5%) repeat TCREs in the control arm and 0 in the TBEA arm at 24 months. (2)

At 24 months, Gervaise et al. (TBEA versus TCRE) reported that 5 (7%) patients in the control arm had a repeat TCRE, versus 0 patients in the TBEA arm.

Hysterectomy

Overall, by 12 months, 1% to 10% (median, 6%) of the patients in all of the studies had a hysterectomy following initial TBEA (Table 12, Appendix 3). (2) At 24 months, this increased to 3% to 12% (median, 10%). (9) Only Meyer et al. (6) reported follow-up data at 36 months: 6% of patients who had TBEA needed a hysterectomy after the initial TBEA. At 60 months, the follow-up data from Meyer et al. showed that 9% of patients who had TBEA required hysterectomy.

For patients who underwent TCRE or RB, 2% to 16% (median, 8%) had a hysterectomy by 12 months. At 24 months, the figure was 1% to 20% (median, 8%). Only Meyer et al. (6) reported follow-up data at 36 months: 10% of RB patients later required a hysterectomy. Furthermore, the follow-up data from Meyer et al. showed that at 60 months, 5% of patients who had RB subsequently required hysterectomy.

Pellicano et al. (3) (TBEA versus TCRE/RB) only reported a “total repeat surgery” figure (i.e., not broken down to type of repeat surgery: e.g., hysterectomy, RB, or TCRE). By 12 months, 5% of patients undergoing TBEA, and 10% of patients undergoing TCRE and RB, had an “additional procedure.” This rose to 6% and 15%, respectively, at 24 months. This difference in repeat surgery rates was statistically significant ($P < .01$) in favour of TBEA.

Zon-Rabelink (2) reported the percentage of patients who had “intervention therapy” during 2 years of follow-up: 17% and 15% of patients undergoing TBEA and TCRE, respectively. It is unclear if this refers only to further ablations and hysterectomies or to other gynecological procedures or drug treatments.

Thermal Balloon Endometrial Ablation Versus Hysterectomy

Garside et al. did not identify any studies that directly compared second-generation EA techniques and hysterectomy as treatments for DUB. However, as discussed earlier, the prior systematic review by Lethaby et al. (23) concluded that first-generation EA techniques offered an alternative to hysterectomy for HMB and that effectiveness and satisfaction rates for both procedures were high. Permanent relief from symptoms offset the higher rate of complications and longer recovery for hysterectomy.

Given the conclusions from the initial systematic review of EA techniques by Lethaby et al., (24) and the updated systematic review by Garside et al., (2) the following was concluded:

- Any comparison between second-generation techniques and hysterectomy can only be indirectly inferred from studies of first-generation techniques and hysterectomy.
- Compared with hysterectomy, TCRE and RB are quicker to perform and result in shorter hospitalization stays and a faster return to work.
- Hysterectomy is associated with more adverse effects and is more expensive, although the need for retreatment leads this difference to decrease over time.
- Satisfaction with hysterectomy is initially higher, but there is no significant difference after 2 years.

Summary of Effectiveness From Garside et al.

Garside et al. (2) examined 2 systematic reviews and 10 controlled trials in the review. The systematic reviews were of good quality, and the controlled trials were of variable quality. Two trials investigated MEA, and 8 looked at TBEA. The comparators were either TCRE or RB or combined technique.

There were few significant differences between first-generation techniques and TBEA in patient outcomes, including bleeding, postoperative complications, patient satisfaction, QoL measures, and repeat surgery rates. Significant differences were reported most often by Pellicano et al., (3) but this was a level 2 study with methodological weaknesses.

Second-generation techniques had significantly shorter operating and theatre times. There appeared to be fewer intraoperative adverse effects with second-generation techniques, whereas postoperative complications for the first- and second-generation techniques were similar.

Garside et al. found no studies directly comparing second-generation techniques and hysterectomy, so similarities and differences for these can only be indirectly inferred from studies of first-generation techniques and hysterectomy.

Thus, it appears that, compared with hysterectomy, TCRE and RB are quicker to do and result in shorter hospitalization stays and a faster return to work. Satisfaction with hysterectomy is initially higher, but there is no significant difference after 2 years. Finally, hysterectomy is associated with more adverse effects.

The authors also noted that it is not possible to predict which patients will become amenorrhagic. If the patient decides that amenorrhea is the preferred outcome, then hysterectomy is the most effective technology.

Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS), December 2002

“Endometrial ablation techniques in the treatment of dysfunctional uterine bleeding” (10)

Lessard and Framarin (10) reviewed and summarized first- and second-generation EA techniques to treat DUB in Quebec. The following is a commentary from the report.

AETMIS developed these classifications to determine the status of technologies it assesses:

- Experimental: A procedure whose effectiveness has yet to be established and should only be used in research projects.

- Innovative: Technology that has passed the experimental stage; but, due to lack of experience, certain indications for its use and various aspects of its application are not yet clearly defined.
- Accepted: Well-established technology with a long history of use and generally accepted knowledge of its effectiveness in its applications.

First-Generation Endometrial Techniques

Transcervical Resection of the Endometrium

- According to AETMIS, TCRE is an *accepted* technique.
- The results of a meta-analysis of 6 RCTs and several other studies showed that this technique is safe, with reproducible results.
- TCRE effectively reduces the quantity of menstrual flow and yields a high level of satisfaction.

Rollerball Ablation

- According to AETMIS, RB ablation is an *accepted* technique.
- It is similar to TCRE on efficacy, the level of satisfaction, and the reoperation rate.
- RB ablation is the easiest first-generation technique to master and the quickest to perform.
- It causes fewer intraoperative complications than does TCRE, and it carries a lower risk of uterine perforation and fluid absorption because the tip of the RB is blunt.

Laser Ablation

- Laser ablation is comparable to TCRE on efficacy, the level of satisfaction and the reoperation rate.
- Its main drawbacks are its cost and the length of the procedure.
- It requires more surgical skill, but it causes fewer intraoperative complications than does TCRE.
- In Quebec, laser EA *stopped being performed* about 10 years ago.

Second-Generation Endometrial Techniques

Most manufacturers market second-generation ablation techniques as procedures that can be performed on an outpatient basis. (10) Most of these techniques can be done without visual hysteroscopic monitoring. However, the physician should make a diagnosis based on a visual examination prior to treatment, supported by a pathophysiological study including a hysteroscopy and at the very least an endometrial biopsy. (10) It is also advisable to perform a hysteroscopy after treatment to check that the uterine cavity was actually treated. (10)

Compared with first-generation techniques, the second-generation techniques assessed in the AETMIS report offered the advantage of being quick, easy, and amenable to local anesthesia or narcosis, and they caused fewer intraoperative complications. (10) However, there were complications, including hematometra, infection, and internal organ injury. (10)

Thermal Balloon Endometrial Ablation

- Of all of the second-generation techniques, only TBEA is *accepted* according to AETMIS.
- The long-term results of a RCT and of several other studies indicate that this technique is comparable to TCRE on efficacy and the reoperation rate.
- Few studies have examined the level of satisfaction.
- TBEA is reserved for normal uterine cavities and causes pain due to uterine distention.
- Uterine retroversion appears to be associated with a greater risk of treatment failure.

- Contraindications to TBEA are an active genital or urinary tract infection and any anatomic abnormality or disease that can cause myometrial weakening.
- When the AETMIS report was being drafted, the use of TBEA was still not widespread in Quebec.

Microwave Endometrial Ablation

- According to AETMIS, this technique is *innovative*.
- There is less evidence on MEA than on the first-generation techniques or TBEA.
- The medium-term results from a RCT and those of a few non-RCTs indicate MEA compares with TCRE on efficacy, the level of satisfaction, and the reoperation rate.
- As of yet, there are no published long-term results of large RCTs. Such results would enable one to determine better the impact of the therapeutic effects and the reoperation rate, which seems to plateau within 3 years of the initial procedure.
- There is a potential for EA to be incomplete in patients whose uterine cavity is hypertrophied or highly deformed.
- The cervix must be dilated to 9 mm to insert the waveguide; dilatation may be painful, even with local anesthesia.

Hydrothermal Ablation

- According to AETMIS, this technique is *innovative*.
- There are few data on this technique and no published long-term results of large RCTs.
- Published reports indicate that this technique and TCRE are similar on efficacy and the reoperation rate.
- Few studies have examined the level of satisfaction.
- Contraindications include active genital or urinary tract infection and any anatomic abnormality, and any condition that can cause myometrial weakening.
- The cervix must be dilated to 8 mm to insert the device; dilation may be painful, even with local anesthesia.

Cryoablation

- According to AETMIS, this is an *innovative* technique.
- There are few data on this technique and no published long-term results of large RCTs.
- Based on the results of 1 RCT, cryoablation is comparable to TCRE on efficacy, the level of satisfaction, and the reoperation rate.
- Hysterosonography is performed to confirm that the cryosurgical probe is properly positioned in the uterine cavity and to monitor the growth of the ice crystal during the treatment cycles.
- Contraindications are an active genital or urinary tract infection and any anatomic abnormality, or any condition that can cause myometrial weakening (e.g., Cesarean section or transmural myomectomy).

Impedance-Controlled Ablation

- According to AETMIS, this is an *innovative* technique.
- There are few data and no published long-term results of large RCTs.
- Based on the results of 1 RCT, impedance-controlled ablation compared well with TCRE on efficacy, the level of satisfaction, and the reoperation rate.
- It can be performed at any time during the menstrual cycle, even during menstruation.
- It is contraindicated in the presence of an active genital or urinary tract infection and any anatomic abnormality or any condition that can cause myometrial weakening.
- If the uterine cavity is less than 4 cm long, the treatment will cause burning of the walls of the cervix.
- The cervix must be dilated to 8 mm to insert the device; dilation may be painful, even with local anesthesia.

Endometrial Laser Intrauterine Thermotherapy

- According to AETMIS, this is an *experimental* technique.
- There are few clinical data on its efficacy and safety.

Conclusions

- First-generation techniques offer considerable advantages over hysterectomy.
- Results from studies indicated that TBEA are comparable to first-generation techniques on efficacy and the reoperation rate.
- Of all of the second-generation techniques, only TBEA is accepted in Quebec.

Summary of Medical Advisory Secretariat Review

The Medical Advisory Secretariat searched MEDLINE and EMBASE after the literature search cut-off date for the most recent systematic review, from August 2002, for studies comparing TBEA with any first-generation EA technique or hysterectomy. This search yielded 96 citations; of these, 9 studies met the inclusion criteria. The quality of the included articles is presented in Table 13.

Table 13: Quality of Evidence of Studies

Study Design	Level of Evidence	No. of Eligible Studies
Large RCTs*, systematic reviews of RCTs	1	
Large RCT unpublished but reported to an international scientific meeting	1(g)†	
Small RCT	2	3
Small RCT unpublished but reported to an international scientific meeting	2(g)	
Non-RCT with contemporaneous controls	3a	
Non-RCT study with historical controls	3b	
Non-RCT presented at an international conference	3(g)	
Surveillance (database or register)	4a	
Case series (multi-site)	4b	1
Case series (single site)	4c	5
Retrospective review, modeling	4d	
Case series presented at an international conference	4(g)	

*RCT indicates randomized controlled trial.

†g indicates grey literature.

Randomized Controlled Trials Comparing TBEA With Rollerball Ablation

In a single-centre RCT from the Netherlands, Zon-Rabelink et al. (27;28) examined the efficacy, safety, and patient satisfaction of TBEA compared with RB for DUB in 137 patients (level 2 evidence). The inclusion criteria were as follows:

- DUB
- Medical treatment failed or contraindicated
- Premenopausal
- No desire for hysterectomy
- No desire for fertility

The exclusion criteria were as follows:

- Diagnostic hysteroscopy with malignancy, leiomyomata, polyps, or uterine cavity anomaly
- Follicle stimulating hormone >20U/L and irregular menstrual cycle
- Abnormal Pap smear

All of the patients were pretreated with a drug at 6 weeks and 2 weeks prior to ablation to reduce endometrial thickness, uterine volume, and vascularity. One hysteroscopist did all of the procedures using general anesthesia.

The end points of the study were menstrual blood loss as judged by a blood pictorial card, the relative reduction of the menstrual blood loss, and QoL as judged by a score list. The end points were measured at 6, 12, and 24 months after EA. The following scoring definitions were used:

- Amenorrhea/spotting: < 20
- Hypomenorrhea: 20–80
- Eumenorrhea: 80–185
- Hypermenorrhea: ≥ 185

Success was defined as having a menstrual blood loss score of less than 185. Failure was defined as having a menstrual score of 185 or higher, or needing intervention due to an insufficient menstrual reduction during the follow-up period. If a patient had a hysterectomy for other reasons and the 2 preceding menstrual scores were less than 5, this was not considered a failure.

The QoL score was filled in over the same period as the menstrual pictorial card.

The trial was designed to show the equivalence of both treatments at 2 years postoperatively and to compare them on technical and safety aspects. The authors said that TBEA "... is supposed to be equivalent to RB if the success rate for TBEA is at most 15% lower than the success rate for RB. ... Assuming a success rate of 85% for RB and accepting 80% probability (power) that the 95% confidence interval does not exceed the difference 15%, 71 patients for each arm were required." The authors further noted that, "Because practically no dropouts were expected, a total number of about 140 patients were enrolled in the study."

After they enrolled 139 patients, they excluded 1 patient owing to a low mean preoperative menstrual score of 93. A second patient who was allocated to RB had a thick endometrial lining, despite the drug pretreatment. This patient was treated with a loop resectoscope and excluded from the study. After randomization, 60 patients were enrolled in the RB group, and 77 were enrolled in the TBEA group. No

significant differences were observed between the groups at baseline. During the follow-up period of 2 years, some patients had intervention therapy, and 1 patient was lost.

Table 14: Rates of Intervention: TBEA Compared With Rollerball Ablation*

Intervention	Rollerball Ablation (N=60)	TBEA (N=70)
	n (%)	n (%)
None	51 (85)	64 (91)
Repeat TBEA	1 (2)	0 (0)
Repeat rollerball ablation	0 (0)	1 (1)
Repeat loop resection	0 (0)	1 (1)
Oac (optical aspirating curette?)**	1 (2)	1 (1)
Mirena (levonorgestral-releasing intrauterine contraceptive)	0 (0)	2(3)
Hysterectomy		
Due to menorrhagia	2 (3)	8 (10)
Due to dysmenorrhea	3 (5)	0 (0)
Due to other reasons	1 (2)	0 (0)
Lost to follow-up	1 (2)	0 (0)

*TBEA indicates thermal balloon endometrial ablation

Reprinted from European Journal of Obstetrics, Gynecology, & Reproductive Biology, 114(1), Zon-Rabelink IAA, Vleugels MPH, Merkus HMWM, de Graaf R. Efficacy and satisfaction rate comparing endometrial ablation by rollerball electrocoagulation to uterine balloon thermal ablation in a randomised controlled trial, pp. 97-103, Copyright 2004, with permission from Elsevier.

The only significant difference between postoperative menstrual scores at 6, 12, and 24 months after TBEA or RB favoured TBEA after 24 months ($P = .01$). The reduction in menstrual blood loss at 24 months postoperatively was also significantly higher for TBEA patients. Success rates were equivalent for each group ($P = .01$) at 1 (RB 79%; TBEA 79%) and 2 years (RB 76%; TBEA 78%) postoperatively.

The QoL scores 2 years postoperatively showed that the rate of satisfaction was not statistically significantly different between groups (75% for RB patients and 80% for TBEA patients; $P = .53$).

Limitations to the study by Zon-Rabelink et al. (27;28) included the following:

- The rationale for the sample size calculation is unclear. The authors stated that they were testing *equivalence*, defined as a TBEA success rate that was at most 15% lower than the success rate for RB. The total sample size was 137.
- 60 patients were enrolled to RB and 77 to TBEA. It is unclear why the study arms were unbalanced.
- There were no details about the QoL scoring system.
- It is unclear if the patient filled in the QoL and pictorial form.
- An intent-to-treat-analysis was not discussed.
- Blinding was not discussed.
- The method of randomization was not discussed.

In a second publication of the *same patient groups*, Zon Rabelink et al. (27) reported safety data for the 2 procedures. A significantly higher risk of intraoperative complications was found for RB compared with TBEA ($P < .001$). The complications are shown in Table 15.

Table 15: Complications in Rollerball Ablation and TBEA*

Complications	Rollerball Ablation	TBEA
	(N=62)	(N=77)
	n (%)	n (%)
None	54 (87)	77 (100)
Perforation of uterus	3 (5)	0 (0)
Laceration of cervix	3 (5)	0 (0)
Electrolyte imbalance	1 (2)	0 (0)
Suspicion of perforation	1 (2)	0 (0)
Other	0 (0)	0 (0)

*TBEA indicates thermal balloon endometrial ablation

Reprinted from European Journal of Obstetrics, Gynecology, & Reproductive Biology, 110(2), Zon-Rabelink IAA, Vleugels MPH, Merkus HMWM, de Graaf R. Endometrial ablation by rollerball electrocoagulation compared to uterine balloon thermal ablation. Technical and safety aspects., pp. 220-223, Copyright 2003, with permission from Elsevier.

In patients who had TBEA, only technical complications were observed. All of the technical disturbances (16% in RB and 17% in TBEA) were minor and did not harm the patients (no *P* value reported).

The mean operation time in minutes (“inclusive to general anesthesia time”) for TBEA was 18 (SD 5, median 17, range 12–41). For RB ablation, it was 35 (SD 13, median 34, range 17–75). The mean operation time for RB ablation was significantly longer than for TBEA (*P* < .001).

More postoperative pain medication was prescribed after TBEA (*P* = .01). After both procedures, complaints during the first 6 weeks were minimal, except pain. The authors reported that 97% of patients in the RB ablation group and 95% of patients in the TBEA group had no complaints (no *P* value). The number of patients with postoperative complaints and the type of complaints are shown in Table 16.

Table 16: Postoperative Complaints: TBEA Compared With Rollerball Ablation*

Complaint	Rollerball Ablation	TBEA
	(N=62)	(N=77)
	n (%)	n (%)
None	60 (97)	73 (95)
Pain	0 (0)	3 (4)
Nausea	1 (2)	0 (0)
Infection	1 (2)	0 (0)
Pain + nausea + headache	0 (0)	1 (1)

TBEA indicates thermal balloon endometrial ablation

Reprinted from European Journal of Obstetrics, Gynecology, & Reproductive Biology, 110(2), Zon-Rabelink IAA, Vleugels MPH, Merkus HMWM, de Graaf R. Endometrial ablation by rollerball electrocoagulation compared to uterine balloon thermal ablation. Technical and safety aspects., pp. 220-223, Copyright 2003, with permission from Elsevier.

The limitations of this study are the same as those in the study by Zon-Rabelink et al. (27;28)

Randomized Controlled Trials Comparing Thermal Balloon Endometrial Ablation With Laser Endometrial Ablation

In the United Kingdom, Hawe et al. (29) conducted a single-centre RCT (N=72) to compare the effectiveness of TBEA with neodymium yttrium garnet (Nd:YAG) laser EA (level 2 evidence). The

inclusion criteria were as follows:

- Higham blood loss score >100
- Measured premenopausal gonadotrophin levels
- Uterine length < 12 cm
- No intrauterine pathology
- Normal endometrial biopsy
- Normal cervical cytology
- Completed family (i.e., no more pregnancies planned)
- Using a reliable form of contraception

Exclusion criteria were as follows:

- Endometrial hyperplasia and malignancy
 - Active pelvic infection and intrauterine pathology
- The 72 patients were recruited after being referred to a gynecology outpatient department. The primary outcome measure was amenorrhea rate. Secondary measures were menstrual status (other than amenorrhea), patient satisfaction, acceptability, health-related QoL, sexual activity, operative details, and morbidity. Patients completed a preoperative and follow-up questionnaire at 6 and 12 months after the surgery. A pictorial blood loss assessment chart was completed preoperatively and at 6 and 12 months after the surgery. The questionnaires used closed and open-ended questions and included validated health questionnaires (e.g., EQ-5D, Short Form [SF]-12, and sexual activity [SAQ]). Patients, nurses, and the patients' general practitioners were blinded to the treatment arm. A nurse in the outpatient department, blinded to the treatment allocation, assessed outcomes with a questionnaire at 6 months. Then, the patient was told which treatment she had received.

TBEA does not require hormonal pretreatment. However, all women were given a drug 4 to 5 weeks before surgery to ensure blinding and because endometrial thinning treatment is preferable prior to EA. A sample size of 34 women in each arm was required for 80% power to detect an amenorrhea rate of 68% (rate from a pilot TBEA study), versus 32% (rate from an unpublished laser EA study) at 12 months. (29)

Of the 72 patients enrolled, 37 were randomized to TBEA and 35 to laser EA. One patient in the laser arm was excluded because fibroids were found at the time of surgery, leaving 34 patients in the laser EA arm. Questionnaires were completed at 6 and 12 months by 100% and 91% of the TBEA group, and 97% and 96% of the laser EA group.

There were no significant differences in patient characteristics at baseline.

Amenorrhea rates for TBEA and laser EA at 6 months were 40.5% and 37% ($P = .673$). At 12 months, they were 29% and 39% ($P = .95$).

The authors reported that there were no significant differences in visual analogue scores of menstrual loss reduced or pictorial blood loss assessment scores between the groups.

Table 17: Blood loss Assessment: TBEA and Laser Endometrial Ablation*

Blood Loss Assessment	TBEA	Laser EA*
Visual analogue scale scores of menstrual loss reduced at 12 months from baseline	80.5% $P \leq .0001$	83.5% $P \leq .0001$
Pictorial blood loss assessment chart scores reduced at 6 months	92% $P \leq .0001$	94% $P \leq .0001$

*TBEA indicates thermal balloon endometrial ablation; EA, endometrial ablation

From Hawe J, Abbott J, Hunter D, Phillips G, Garry R. A randomised controlled trial comparing the Cavaterm endometrial ablation system with the Nd:YAG laser for the treatment of dysfunctional uterine bleeding. *BJOG: an International Journal of Obstetrics & Gynaecology* 2003; 110(4):350-357

For patients who continued to menstruate at 12 months, treatment with TBEA was associated with a significant reduction in the number of days bleeding (from 7.2 to 3.4; $P < .0001$), increased cycle length (from 24 to 30 days; $P = .02$), a 60% reduction in dysmenorrhea score (from 62 to 25; $P < .0001$), and a 60% reduction in PMS score (from 55 to 22; $P = .04$). The authors reported similar findings in the laser EA group. There were no significant differences between the groups; however, the study was not designed to measure these end points.

There were also no statistically significant differences in patient satisfaction at 6 and 12 months (P value not reported). The authors reported that both procedures were acceptable to patients. However, “Outcomes that reached statistical significance were that patients felt more positive about laser EA (mean difference 1.27 [95% CI, 0.43–2.1], $P = .04$), and felt laser EA was safer (mean difference 0.87; 95% CI, 0.12 –1.63) and more agreeable (mean difference 1.08 [95% CI, 0.29–1.87], $P = .08$) than TBEA.” (29) Again, however, the study was not designed to measure these end points.

Hawe and colleagues reported that there were no major intraoperative complications in either group. All women were treated as day patients, except 1 in the TBEA group who required overnight admission for pain on her right side.

In the TBEA group, there was balloon failure in 2 cases, which required further catheter use. In the laser EA group, 3 patients had fluid “absorption.” Blood loss was excessive in 1 of these patients. It was managed using an intrauterine 30 mL balloon catheter, which was left in situ for 4 hours to stop the blood loss. Postoperatively, 4 (11%) and 2 (6%) patients in the TBEA and laser EA groups, respectively, had oral antibiotics for suspected endometritis.

At 12 months, 3 (9%) patients in the TBEA group required a hysterectomy, and 1 patient needed a repeat ablation procedure (laser EA). For the patient who underwent a repeat ablation procedure, there was active endometrium in areas suggesting that the balloon had not been inserted to the full cavity length in the original treatment.

In the laser EA group, 5 (14.7%) patients had had hysterectomies, 1 before 6 months (stage 4 endometriosis), and 4 between 6 and 12 months. Another 2 patients were listed for surgery between 6 and 12 months postoperatively, but were still on the waiting list at the time of the 12 month-data collection.

Both groups of patients showed improvement in their physical and mental component scores of the SF-12 at 6 and 12 months after the surgery. Both treatments were associated with an increase from baseline in the SF-12 physical score (TBEA not significant, no P value provided; laser EA, $P = .003$); and SF-12 mental health score (TBEA, $P = .001$; laser EA, $P = .04$). The patients’ own assessment of health (EQ-5D VAS) improved from baseline in both groups (TBEA, $P = .02$; laser EA, not significant, no P value). EQ-5D index scores also improved (TBEA not significant, no P value; laser EA, $P = .02$). Note, the study was

not initially designed to measure these end points.

The percentage of patients who were sexually active during the trial was 68%, 73%, and 76.5% in the TBEA group; and 82%, 75%, and 75% in the laser EA group, at baseline, 6, and 12 months, respectively. The main reason for no sexual activity was the lack of a partner.

There were no significant changes in the pleasure, habit, and discomfort scores for TBEA patients between baseline and 6 months, and between baseline and 12 months after the procedure (*P* values not provided). In the laser EA group, there were no significant changes in the discomfort scores at 6 and 12 months. However, there were significant changes for pleasure (6 months, *P* = .01; 12 months, *P* = .05) and habit (6 months, *P* = .05; 12 months, *P* = .02) for patients who received laser EA. When results were compared between the TBEA and laser EA groups, there were no statistically significant differences (no *P* value). These comparison groups were not stratified a priori to test these end points; therefore, they probably were not adequately statistically powered to detect differences.

Limitations to the study by Hawe et al. were as follows:

- The study was designed to detect an amenorrhea rate of 68% (rate from a pilot TBEA study) versus 32% (rate from an unpublished laser EA study) at 12 months. Therefore, all other statistical comparisons should be considered hypothesis generating. The same sample size to detect differences in amenorrhea rate was used throughout the study and incorrectly assumes the study was powered to detect differences without a priori stratification.
- Patients in the laser EA group had a lower QoL at baseline (Euro QoL-5D) compared with those in the TBEA group. The statistically significant improvement in score reported at 6 and 12 months may have been due to regression to the mean.

Case Series of Thermal Balloon Endometrial Ablation

Mettler (30) conducted a single-arm, prospective study of women who had TBEA (level 4c evidence). Follow-up of patients extended to 48 months. The inclusion criteria were as follows:

- Age over 40 years
- Menorrhagia and hypermenorrhea
- Failed hormonal treatment

Seventy patients were evaluated. Group A comprised 10 patients with adenomyosis and an enlarged fibroid uterus in addition to menorrhagia and hypermenorrhea. Patients were preoperatively informed that the effectiveness of the procedure could not be guaranteed, but that a successful EA would rule out the need to do a hysterectomy. If ablation failed, a hysterectomy would be performed. Group B had 60 patients with normal Pap smears, no distortion of the uterine cavity, no polyps or myomas in the uterine cavity, no pelvic inflammatory disease, and no long-term steroid use.

Patients were contacted at 3, 9, and 48 months postablation to assess bleeding and well-being. Table 18 shows the number of hysterectomies and bleeding patterns at 48 months.

Table 18: Patient Characteristics in a Prospective Case Series (30)

	Group A (N=10)	Group B (N=60)
	n (%)	n (%)
Hysterectomies following failure	5 (50)	-
Bleeding patterns at 48 months		
Amenorrhea	-	35 (58)
Hypomenorrhea	5 (50)	20 (33)
Eumenorrhea	-	5 (9)

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No complications were reported intraoperatively, postoperatively, or during the 4-year follow-up. All patients were treated on an inpatient basis and discharged on the next day or the day after that.

Limitations of the study by Mettler were as follows:

- It used a case series study design.
- Included were women who are generally considered ineligible for TBEA (group A), and who had a higher hysterectomy rate than those in group B.

In another case series, Jarrell and Olsen (31) examined the medical records of 28 patients with menorrhagia who underwent TBEA and were followed-up by telephone interview to determine overall patient satisfaction after the procedure (level 4c evidence). Follow-up time was ranged from 16 to 28 months. All patients had menometrorrhagia, menorrhagia, or DUB as a preoperative diagnosis.

Table 19: Patient Satisfaction With Thermal Balloon Endometrial Ablation (31)

Patient Satisfaction	Number of Patients
Very satisfied	7
Satisfied	9
Neutral	1
Dissatisfied	4
Very dissatisfied	7

From Jarrell A, Olsen ME. Patient satisfaction with thermal balloon endometrial ablation. A retrospective review. *Journal of Reproductive Medicine* 2003; 48(8):635-636

Jarrell and Olsen reported that 68% of patients had less bleeding, while 32% had no change. Forty-three percent of women had fewer menstrual cramps. None reported an increase in bleeding or cramping after the procedure. Thirteen patients (46%) had hysterectomies within 1 year of TBEA. The mean time to hysterectomy was 4.7 months. Patient satisfaction is shown in Table 19.

Limitations of the study by Jarrel and Olsen were as follows:

- It used a case series study design.
- Information about the status of 5 patients who were excluded from the study was not reported.
- It was unclear if authors examined records of consecutive patients.

Baruah and Etherington (32) conducted a prospective case series of 42 patients with DUB who received TBEA (level 4c evidence). The inclusion criteria were as follows:

- Menorrhagia that had failed to respond to medical treatment

- No suspicion of any malignant or premalignant disease
- Completed families

Exclusion criteria were as follows:

- Submucous fibroids (> 2x2 cm)
- Intrauterine septa
- Premalignant disease
- Uterine cavity >12 cm long
- Desire to retain fertility

Women were asked to grade the heaviness of their menstrual bleeding using a score of 1 to 10 (with 10 being severe bleeding), and the number of days of flow, flooding, and clots.

All except 2 of the TBEAs were performed under general anesthetic. No reason was provided for using general instead of local anesthetic.

Thirty-seven patients were discharged within 6 hours of having the procedure, and 5 patients were discharged within 24 hours. The procedure was abandoned for 1 patient because perforation occurred during uterine sounding (to assess position and length of the cavity before beginning).

The patients were reviewed at 4, 8, and 12 months after receiving TBEA. They were asked specific questions about menstrual flow and pattern, dysmenorrhea, and satisfaction (rated from 1 to 10, where 10 was maximum satisfaction).

The women ranged in age from 32 to 53 years (median, 43 years). Of the 42 patients, 41 completed the 4-month follow-up, 26 completed the 8-month follow-up, and 19 completed the full 12-month review.

Results consisted of descriptive statistics. Menorrhagia was reported by 3 patients (7.3%) at 4 months, 2 patients (7.6%) at 8 months and 1 patient (5.2%) at 12 months after receiving TBEA. At 4, 8 and 12 months patients rated their mean (SD) satisfaction as 5.63 (2.91), 6.9 (3.68) and 7.42 (3.18) respectively. At 4, 8, and 12 months, 4 (9.7%), 4 (15.3%), and 2 (10.5%) patients respectively reported having no dysmenorrhea.

Limitations to the study by Baruah and Etherington were as follows:

- It used a case series study design.
- It was unclear if patients were enrolled consecutively.
- There was no discussion of using general versus local anesthesia.

Feitoza et al. (7) examined the long-term outcome, level of satisfaction, and change in QoL in patients with abnormal uterine bleeding who were treated with TBEA in a single institution (level 4c evidence).

The charts of 157 women who were treated with TBEA for menorrhagia were reviewed retrospectively. Inclusion criteria were as follows:

- Heavy or prolonged menstrual bleeding
- Uterine size \leq 10cm (based on sounding the uterus and the absence of submucous myomas)
- Dysfunctional bleeding

Exclusion criteria consisted were as follows:

- Abnormal bleeding that was associated with ovulatory dysfunction

- Hematologic disease
- Use of anticoagulants
- Lost to follow-up
- Denied research authorization

Forty-seven patients had TBEA as first-line therapy, and 120 patients had at least 1 previous failed treatment (hormone therapy, n=106; curettage, n=22; EA, n=2; nonsteroidal anti-inflammatory drugs, n=18; some patients had more than 1 previous therapy). This information was not available for 4 patients.

Patients were followed-up by telephone. They were asked about postprocedure bleeding, onset of pregnancy after ablation, need for further therapy, change in QoL, and level of satisfaction with TBEA. Menstrual blood loss was assessed indirectly with the use of pad/tampon counts in the heaviest day of bleeding and the number of days of bleeding per cycle. QoL was assessed by asking patients to rank their QoL before and after TBEA using a scale of 1 to 10, where 1 was worst and 10 was best. Patients were asked to classify their satisfaction with the TBEA as “not satisfied,” “satisfied,” and “very satisfied.” Treatment was considered successful if the patient reported eumenorrhea, hypomenorrhea, or amenorrhea. Recurrent menorrhagia and the need for hysterectomy were considered treatment failures. Women who had a hysterectomy reported in the charts were not considered for the telephone interview to avoid recall bias. This is because level of satisfaction with TBEA and hysterectomy could have been confounded.

TBEA was performed by 1 of the 5 gynecologic surgeons with the use of general anesthetic, except when clinically contraindicated. An initial curettage with frozen section histopathologic evidence was done in all cases where histologic information was not available previously. Hysteroscopy was done at the discretion of the treating physician.

From the initial 175 women identified, 4 denied research authorization, 16 were excluded due to hematologic disorders or the use of anticoagulants, and 14 were excluded because of missing follow-up data. Clinical follow-up data were obtained from the charts of all 141 eligible patients. A telephone interview was consented to by 132 women and eventually obtained from 119 women.

The median follow-up time was 18 months (range, 6–44 months). The mean age was 42.5 years (range, 27–56 years). Of the 141 patients, 82 (58%) were premenopausal, 58 (41%) were perimenopausal, and 1 patient (0.8%) was postmenopausal and receiving hormone replacement therapy. TBEA was performed with general anesthesia in 139 patients (98%) and with local anesthesia and intravenous sedation in 2 patients (2%). Pretreatment with hormones to induce endometrial thinning was not used.

Post-TBEA menstrual patterns as a function of time are shown in Table 20.

Table 20: Post-TBEA Menstrual Patterns as a Function of Time

Menstrual pattern	Months after TBA						Last follow-up (n = 141)
	3 (n = 137*)	6 (n = 129)	9 (n = 113)	12 (n = 96)	18 (n = 73)	24 (n = 53)	
Amenorrhea (No.)	40 (29%)	32 (24%)	25 (22%)	25 (26%)	19 (26%)	15 (28%)	34 (24%)
Hypomenorrhea (No.)	60 (43%)	63 (48%)	56 (49%)	47 (48%)	32 (43%)	19 (35%)	41 (29%)
Eumenorrhea (No.)	26 (18%)	27 (20%)	29 (25%)	22 (22%)	18 (24%)	14 (26%)	50 (35%)
Menorrhagia (No.)	11 (8%)	7 (5%)	3 (2%)	2 (2%)	4 (5%)	5 (9%)	16 (11%)
Hysterectomy (n/N)	4/141 (3%)	11/141 (8%)	14/141 (10%)	15/141 (1%)	18/141 (13%)	19/141 (13%)	21/141 (15%)

*Excludes the four patients who underwent hysterectomy for menorrhagia <3 months after TBA.

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The outcome after TBEA was reported for all patients that were available for each follow-up. However, hysterectomies were reported cumulatively (i.e., hysterectomies reported at 18 months were the sum of the procedures that were performed at 3, 6, 9, and 12 months). During the follow-up, 60% to 74% of the patients were either amenorrheic or hypomenorrheic after TBEA, and fewer than 11% reported menorrhagia. A reduction in days per cycle and pad counts per day was seen after TBEA ($P < .001$ for each). (See Table 21.)

Table 21: Change in Menstrual Bleeding After TBEA.*

Menstrual bleeding	Before TBA	After TBA	P value
Days/cycle (No.)			
Mean \pm SD	9.6 \pm 5.1	3.1 \pm 2.7	<.0001
Median (range)	7 (3-30)	3 (0-14)	
Pads/d (No.)			
Mean \pm SD	12.8 \pm 6.1	2.5 \pm 2.5	<.0001
Median (range)	12 (1-30)	2 (0-12)	

*TBEA indicates thermal balloon endometrial ablation

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The level of satisfaction with TBEA and the change in QoL that resulted from the procedure were obtained from 119 patients. On the basis of pre- and post-TBEA scores, QoL improved ($P < .0001$). (See Table 22.)

Table 22: QoL Scores Before and After TBEA*

QoL score	Before TBA	After TBA	P value
Mean \pm SD	2.8 \pm 1.7	9 \pm 1.16	<.0001
Median (range)	3 (1-9)	9 (6-10)	

*TBEA indicates thermal balloon endometrial ablation

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A significant correlation was observed between the level of satisfaction with TBEA and the resulting bleeding pattern ($P < .007$). Patients with amenorrhea or hypomenorrhea were more likely to be “very satisfied” with the procedure (84% and 89%, respectively). (See Table 23.)

Table 23: Satisfaction and Resultant Bleeding After TBEA*

Menstrual flow after TBA	Level of satisfaction with TBA (No.)		
	Not satisfied	Satisfied	Very satisfied
Amenorrhea	1	4	27
Hypomenorrhea	1	3	34
Eumenorrhea	0	23	22
Menorrhagia	3	0	0

*TBEA indicates thermal balloon endometrial ablation

Reprinted from the *American Journal of Obstetrics & Gynecology*, 189(2), Feitoza SS, Gebhart JB, Gostout BS, Wilson TO, Cliby WA. Efficacy of thermal balloon ablation in patients with abnormal uterine bleeding, pp453-457, Copyright 2003, with permission from Elsevier (7)

Of note, a reduction in blood loss to eumenorrhea was adequate for high levels of patient satisfaction and improvement in QoL.

Twenty-eight of 141 patients (20%) underwent subsequent treatment during the follow-up:

- Myomectomy: 1 patient
- Hormonal therapy: 6 patients
- Hysterectomy: 21 patients

The indications for the 21 hysterectomies were as follows:

- Persistent menorrhagia: 14 patients
- Dysmenorrhea: 4 patients
- Cervical carcinoma in situ: 1 patient
- Uterine prolapse: 1 patient
- Ovarian endometrioma: 1 patient

Histopathologic findings reported fibroid tumours in 10 patients, adenomyosis in 2 patients, and endometriosis in 3 women.

The only complication that was attributed to TBEA was a case of mild endometritis that required less than

24 hours of hospitalization and responded to antibiotic therapy. No deaths were related to TBEA.

Limitations to the study by Feitoza et al. were as follows:

- Retrospective design and lack of control group.
- Recall bias for grading the QoL scores before TBEA. To quantify QoL, the authors used a descriptive version of an analog scale. Of note, patients self-reported a very low pretreatment QoL score. This provides insight into the disabling effect that HMB has on otherwise healthy women.
- Attrition rate.
- No justification for use of general versus local anesthesia.
- Patients who had hysterectomies soon after TBEA demonstrated that *structural lesions might have been present that contributed to the failure and need for hysterectomy. A detailed preprocedure evaluation should be done to determine the patients who may be best served by hysterectomy rather than TBEA.*

Ensuring that patient expectations are consistent with the outcomes achievable with TBEA is important to obtain high levels of satisfaction. Vilos et al. (5) said that up to one-half of patients who underwent a second attempt at TBEA might have avoided the second procedure with *proper preoperative counselling*. Hysterectomy is the only procedure that can guarantee amenorrhea. Meyer et al. (6) suggested that one consideration for patients with menorrhagia (and no structural lesions) is to be returned to normal or less blood loss, rather than amenorrhea. Patients may have distinct concepts of menstrual bleeding depending on cultural background, and maintaining an acceptable menstrual flow instead of amenorrhea may represent a healthier status. (7)

In another case series, Alaily et al. (33) prospectively evaluated the efficacy and safety of TBEA for the treatment of DUB (level 4c evidence). Patients with a mean age of 43 years were treated under general anesthesia. All of the women had menorrhagia and either had failed medical therapy or were unwilling or unable to continue with it. They were suitable for either hysterectomy or EA and were given the option of TBEA. Alaily and colleagues said that during pre-TBEA counselling, patients were informed that the aim of TBEA is either to stop periods or to reduce the amount of blood loss (i.e., back to normal or light periods), because it was previously shown that an expectation of amenorrhea leads to higher reoperation rates despite lighter periods being achieved. (34)

Inclusion criteria were as follows:

- Normal uterine cavity on hysteroscopic examination
- Normal endometrial histology and cervical cytology
- No desire to maintain fertility

Exclusion criteria were as follows:

- Undiagnosed uterine bleeding
- Gross uterine abnormality
- Pregnancy or the desire to become pregnant
- Uterine cavity length greater than 12 cm or less than 4 cm
- Suspicion of uterine wall weakness (previous Cesarean section)

There was no preoperative endometrial preparation. The surgeon used intraoperative curettage to thin the endometrium and obtain a final sample for histological diagnosis.

Follow-up assessments at 3, 6, 12, and 24 months post-TBEA included questions on pictorial menstrual charts. Alternatively, because most of the women did not continue to use the charts, they were asked

about their bleeding pattern, including if there was any bleeding, the number of days of bleeding, the interval between periods, the date of the last menstrual period, and a subjective assessment of each day's heaviest bleeding.

A recognized QoL questionnaire was not used. The patients' subjective assessment of satisfaction with the operation was assessed as "excellent," "good," "moderate," or "no improvement."

Seventy-seven patients completed a 12-month follow-up; of these, 62 completed 24 months of follow-up. No immediate intraoperative complications were reported. The treatment was a day procedure in 65 patients, and 12 returned home on the next day. The 12 patients stayed overnight for these reasons:

- Postoperative pain
- "Home was far away"
- "Intercurrent disease"
- "Late in the evening before they felt well"

The first few patients in the case series experienced moderate to severe postoperative pain that required narcotic analgesia. The rest of the patients were prescribed postoperative oral analgesia routinely for 3 days as above. The authors reported that this regimen appeared to be adequate.

Postoperative morbidity was minimal. One patient presented as an emergency 9 months after TBEA, due to sudden onset of acute lower abdominal pain. Transvaginal ultrasound revealed hematometra (blood in the uterus), which was treated by cervical dilation and drainage under general anesthesia. After drainage, the patient had amenorrhea. Three hysterectomies were performed abdominally for persistent HMB, which was considered a treatment failure. Histopathological examination was normal, and there was no evidence of thermal destruction of endometrium. Four other patients were treated subsequently by the insertion of a levonorgestrel-releasing intrauterine system with improvement.

After 1 year, 27 of 77 (35%) patients were amenorrheic; 28 of 61 (46%) patients were amenorrheic in their second year of follow-up. (Table 24.) Treatment was considered successful if there was subjective perception of reduced menstrual blood loss either to a "normal" pattern, "light" periods, or amenorrhea.

Table 24: Type of Bleeding Reported by Patients 12 months and 2 years Post-TBEA*

Bleeding	12 months (N=77)	2 years (N=61)
	n (%)	n (%)
Heavy	8 (10)	6 (10)
Normal	7 (9)	3 (5)
Light	35 (46)	24 (39)
Amenorrhea	27 (35)	28 (46)

*TBEA indicates thermal balloon endometrial ablation

Used with permission from Taylor & Francis Ltd., www.tandf.co.uk/journals; Alaily AB, Auld BJ, Diab Y. Endometrial ablation with the Cavaterm thermal balloon. Journal of Obstetrics & Gynaecology 2003; 23(1):51-54

The authors reported a 72% reduction of dysmenorrhea and premenstrual symptoms; however, no further data were reported.

They also reported that most of the patients felt satisfied after receiving TBEA. The results on satisfaction

are shown in Table 25.

Table 25: Patients' Long-Term Level of Satisfaction With Thermal Balloon Endometrial Ablation

Follow-up	Satisfied	Not Satisfied
	n (%)	n (%)
12 months	69 (90%)	8 (10%)
2 years	55 (90%)	6 (10%)

Adapted with permission from Taylor & Francis Ltd., www.tandf.co.uk/journals; Alaily AB, Auld BJ, Diab Y. Endometrial ablation with the Cavaterm thermal balloon. *Journal of Obstetrics & Gynaecology* 2003; 23(1):51-54

Limitations to the study by Alaily et al. included the following:

- It was a case series design, and there was no control group.
- Suspicion of uterine wall weakness as an exclusion criterion when the authors said, "There was no firm data to either support or refute this." (33)
- There was no justification for use of general versus local anesthesia.

Amso et al. (4) conducted a multicentre long-term (4 to 6 years) case series (level 4b evidence) of patients with menorrhagia who underwent TBEA. The primary outcome measure was avoidance of hysterectomy. Secondary outcome measures were the need for other surgical procedures (e.g., TCRE, RB ablation, or repeat TBEA), the impact of patient- and treatment-dependent variables on avoidance of hysterectomy, and current bleeding pattern in women who had not undergone hysterectomy.

The group of patients treated with TBEA and analyzed for long-term follow-up was selected from a prior clinical study by the same investigators. (35) Inclusion criteria of the prior study were as follows:

- Severe menorrhagia as evidenced by their pad counts and subjective assessment of their bleeding
- Failed or unwilling to continue with medical therapy
- Completed their family
- Suitable for either ablation or hysterectomy

Exclusion criteria of the prior study were as follows:

- Pathology distorting the uterine cavity
- Atypical endometrial hyperplasia
- Suspected genital tract infection or malignancy
- Uterine cavity depth > 12cm
- Previous EA

Ten centres participated. Patients were eligible for inclusion if the following applied:

- They were treated by TBEA between June 1994 and August 1996.
- The starting balloon pressure gradient was > 150 mm Hg.
- They were not taking hormone replacement therapy in the first year as part of another study.
- The 12-month follow-up data for the original study were complete.
- They had signed an informed consent form.

Patients were excluded if the following applied:

- They were treated with TBEA with a starting gradient pressure of < 150 mm Hg.
- They were treated outside the clinical study protocol outlined above.
- The data recording of the 12-month follow-up was not complete.

- They did not agree to take part or sign the informed consent form.

Based on these criteria, 260 women from 10 participating centres were eligible for inclusion in the study. The women were mailed a questionnaire asking them about their current menstrual history and, where applicable, the date of cessation of their periods and any adverse events or disease since their first TBEA, as well as if further surgery had taken place. Of the 260 questionnaires sent to patients for long-term follow-up, 188 replies were received (72%). One of the patients had incomplete information and was excluded from the hysterectomy and menstrual status life table analysis.

Of the 187 patients entered in the life table analyses, the time elapsed between the initial TBEA and their response to the questionnaire was between 4 and 5 years in 38 patients, between 5 and 6 years in 122 patients, and between 6 and 7 years in 27 patients.

Current Bleeding Pattern

Of the 162 patients who had not had a hysterectomy, 76 (46.9%) were amenorrheic, 48 (30%) had light bleeding, 22 (13.6%) had normal periods, and 14 (8.5%) had heavy bleeding. The bleeding pattern was unknown in 2 patients (1%). Twenty of 76 women became amenorrheic within 3 months, while the overall median time to amenorrhea was 4.6 quarters or 1.15 years (1 quarter = 0.25 years). In patients who continued to bleed, the mean duration of bleeding was 3.8 days for the light bleeders, 4.6 days for the normal menstrual group, and 9 days for the continuing menorrhagia group.

In patients who had one ablation only and had not undergone hysterectomy (n=141), 63 (45%) had no periods, 44 (31%) had light bleeding, 21 (15%) had normal menses, and 12 (8.5%) had heavy periods. The outcome of patients who had repeat ablation (n=21) was as follows: 13 (62%) became amenorrheic, 4 (19%) had light bleeding, 1 (5%) had normal menses, and 2 (10%) continued to have heavy periods.

Further Surgery

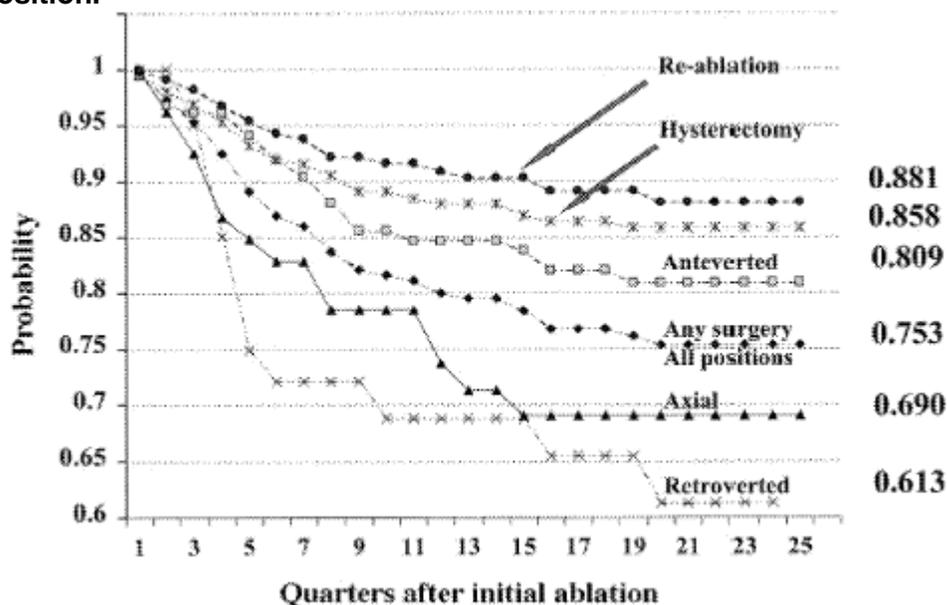
In women who responded to the questionnaire, 25 (13.3%) had undergone hysterectomy, and 21 (11.2%) had undergone repeat ablation during the follow-up period. The most common indication for hysterectomy was continued menorrhagia (n=20). Other indications included fibroids (n=2) and bleeding with unclear reason (n=1). None had cancer as an indication. In 2 women, the indications for hysterectomy were unknown. The largest proportion of patients requiring hysterectomy (18.8% [6/32]) comprised women with a retroverted uterus (i.e., tipped or tilted backward away from the belly), followed by those with an axial uterus (14% [6/42]). The least affected (11.7% [13/111]) were women with an anteverted uterus (i.e., tilted forward). None of the women who had repeat ablation had hysterectomy.

Of 21 repeat ablations, 7 were for women who had spotting only, 11 were for women with light periods, and 3 were for women who had a normal menstrual pattern after the initial procedure. Seven repeat ablations were carried out in each of the uterine position groups. Of patients who had a second ablation, 13 women were amenorrheic at the time of the follow-up, and 7 continued to bleed. Of these 7, 4 had light bleeding, 1 bled normally, 2 continued to have heavy bleeding. In 1 patient, the severity of bleeding was unknown. The impact of uterine position on the probability of not having a reablation in women who did not have hysterectomies was 77% for the retroverted uterus group, 83% for the axial position group, and 94% for women with an anteverted uterus.

Life Table Analysis

At 4 to 6 years after the first TBEA, the probability of avoiding hysterectomy was 86% for all women (95% CI, 81%–90.5%). The probability of avoiding reablation was 88% (95% CI, 83.4%–92.8%) for all women who did not have a hysterectomy. The probability of avoiding *any* surgery (hysterectomy or reablation) was 75% (95% CI, 69.4%–81.2%). The probability of avoiding further surgery varied according to a woman's uterine position. It was the lowest for those with a retroverted uterus (61%), increased to 69% for the axial position, and was highest (80%) in women with an anteverted uterus. (Figure 8, next page.)

Figure 8: Probability of Not Having a Reablation, Hysterectomy, or Both, and Uterine Position.*



*From Amso NN, Fernandez H, Vilos G, Fortin C, McFaul P, Schaffer M et al. Uterine endometrial thermal balloon therapy for the treatment of menorrhagia: long-term multicentre follow-up study. *Human Reproduction* 2003; 18(5):1082-1087, by permission of Oxford University Press and the author(4)

At 4 to 6 years follow-up, the probability of amenorrhea in women who had not had hysterectomy was 52.1% (95% CI, 43.1%–52.7%).

One limitation of this study by Amso et al. (4) was its case series design.

Summary of Findings

- A systematic review from the United Kingdom (2) found that overall, there were few significant differences between the patient outcomes of first- and second-generation techniques (including TBEA), such as postsurgical complications, bleeding, patient satisfaction, QoL measures, and repeat surgery rates. The review found that TBEA had significantly shorter operating and theatre times, and apparently fewer intraoperative adverse effects (e.g., uterine perforation, hemorrhage).
 - There are no studies directly comparing second-generation techniques and hysterectomy; therefore, this comparison can only be indirectly inferred from studies of first-generation techniques and hysterectomy.
 - Compared with hysterectomy, TCRE and RB ablation are quicker to perform and result in shorter hospitalization stays and a faster return to work.
 - Hysterectomy results in more adverse effects.
 - Satisfaction with hysterectomy is initially higher, but there is no difference after 2 years.
- Studies (level 2 evidence) published after the United Kingdom systematic review support these conclusions.
- A multicentre long-term case series (4) (level 4 evidence) that examined avoidance of hysterectomy after TBEA for menorrhagia found that 86% of women undergoing TBEA did not require hysterectomy, and 75% did not have any further surgery during a follow-up of 4 to 6 years.
- Several TBEA studies did not justify using general anesthesia instead of local anesthesia.

- Patient preferences for treatments will depend on a woman's desire for amenorrhea as an outcome and/or avoidance of major surgery. Ensuring that patient expectations are consistent with the outcomes achievable with TBEA is important to obtain high levels of satisfaction. Vilos et al. (5) noted that up to one-half of patients who underwent a second attempt at TBEA might have avoided the second procedure with proper preoperative counselling. Hysterectomy is the only procedure that can guarantee amenorrhea. TBEA will not replace hysterectomy in the treatment of DUB, because some patients may want cessation of menstruation.
- Several studies examining the efficacy of EA used amenorrhea rate as an outcome measure. (36) The justification is that amenorrhea is an end point that is not open to interpretation. Other menstrual outcomes, such as hypomenorrhea and eumenorrhea, are subjective and open to interpretation by patients and investigators.
- Meyer et al. (6) suggested that one consideration for patients with menorrhagia (and no structural lesions) is to be returned to normal or less blood loss, rather than amenorrhea. Patients may have distinct concepts of menstrual bleeding depending on their cultural backgrounds, and maintaining an acceptable menstrual flow instead of amenorrhea may represent a healthier status. (7)

Economic Analysis

Objective and Methods

The Ontario Health Technology Advisory Committee asked the Medical Advisory Secretariat to analyze the cost-effectiveness of TBEA for DUB as part of the larger evidence-based assessment.

The methods are described fully in the main methods section of this review.

Results of Literature Review on Economics

Update to Cochrane Review by Garside et al.

Garside et al. (2) used a deterministic Markov model to assess the cost-effectiveness of TBEA. A list of assumptions and costs used in the model is listed in Tables 26 to 31 (Appendix 3). The authors cautioned that many of these values might be subject to uncertainty. For example, the utility values were taken from the only published cost-utility study found to have obtained values from women with menorrhagia. In addition, estimates of reintervention were problematic, because of the generally short-term follow-up and the different ways in which the studies reported on postoperative bleeding. To examine the impact of uncertainty in these parameters, the authors did a sensitivity analysis.

Garside and colleagues presented the total costs for the modeled cohort of 1000 women across 10 years. Table 32 shows the results of the cost-effectiveness analysis for TBEA compared with each of the other procedures examined. TBEA costs less and accrues more quality-adjusted life years (QALYs) compared with only TCRE, TCRE with RB, and only RB. TBEA costs less and generates fewer QALYs compared with hysterectomy.

Table 32: Summary of Cost-Utility Analysis for TBEA at 10 years.*

Procedure	Total costs (£)	Total QALYS*	ICER*
TBEA*-baseline	1,323,925	8,361	-
TCRE*	1,731,734	8,357	TBEA dominates
TCRE + rollerball	1,785,045	8358	TBEA dominates
Rollerball	1,752,359	8,360	TBEA dominates
Hysterectomy	2,320,512	8,774	2,410

TBEA indicates thermal balloon endometrial ablation;

ICER, incremental cost-effectiveness ratio; QALYs, quality adjusted life years; TCRE, transcervical resection of the endometrium.

*Used with permission. Garside R, Stein K, Wyatt K, Round A, Price A. The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling. *Health Technology Assessment (Winchester, England) 2004; 8(3):iii-168. (2)*

Garside and colleagues made several conclusions based on their analysis:

- If amenorrhea is the preferred outcome, hysterectomy is the most effective technology, although it has higher costs.
- The cost-utility ratio for hysterectomy versus EA is within the range considered by decision makers to represent acceptable value for money.

- More sophisticated modelling studies may improve estimates of cost-effectiveness; for example, by taking into account population heterogeneity, and permitting the exploration of issues relevant to implementation, such as waiting times and detailed budget impact.
- Given the importance of the utility values in determining the cost-effectiveness of treatments for HMB, further research to establish utilities for the states of HMB, its surgical treatment, convalescence, and complications of treatment would be valuable.
- Future studies of HMB should use validated QoL measures and established modes of measuring patient satisfaction with the procedure and the outcomes.
- Alternative models of care for EA should be further investigated, including different operators (non-consultant medical staff and specialist nurses) and different settings (office versus operating theatre).

In France, Fernandez et al. (37) evaluated the direct medical costs for vaginal hysterectomy, hysteroscopic EA, and TBEA to treat menorrhagia. Included were patients who had severe menorrhagia as evaluated on a pictorial chart (> 150 for Higham score). These patients had either failed medical therapy with progestins or were unwilling or unable to continue medical treatment for severe menorrhagia lasting more than 1 year. Patients with myomas (uterine fibroids) were excluded.

Patients were contacted 24 to 36 months after surgery to collect data on treatment success, subsequent interventions, medical visits, gynecological problems, and satisfaction with the procedure.

One hundred and forty-seven patients were included in the study. Of these, 47 had TBEA, 50 had a vaginal hysterectomy, and 50 had a hysteroscopic EA. Fernandez and colleagues concluded that overall, TBEA and EA can be considered equally clinically effective, and that differences relate to cost.

Mean operating time was about 2 hours for hysterectomy, 1 hour for EA, and 46 minutes for TBEA. Patients who had TBEA had the highest number of follow-up visits (mean, 5.9). This could be explained by the newness of the procedure. The mean number of follow-up visits for EA and hysterectomy were 3.9 and 2.2, respectively.

The total cost for hysterectomy was higher than for the other 2 procedures, due to the need for all patients to be hospitalized. The other 2 procedures were mostly outpatient procedures; therefore, they cost less. When only the procedures were considered (i.e., excluding the cost of the device), TBEA had the lowest cost. When devices were included, EA had the lowest cost.

The cost of hospitalization was lowest for thermocoagulation, because only 4 of 47 patients required an overnight stay, compared with 14 of 50 patients for EA. Patients who had TBEA had slightly more follow-up visits compared with those who had EA or a hysterectomy.

The cost of reinterventions was higher for TBEA than for EA, because all 7 reinterventions were hysterectomies, whereas the preferred intervention after failure of EA was a second EA. Therefore, the total cost per patient rose by €782 per patient for reinterventions after TBEA, but only by €165 after EA.

Table 33: Mean cost (€) per patient. From: Fernandez et al. (37)

Resources	Thermo-coagulation	Hysterectomy	Ablation
Patients (n)	47	50	50
Primary procedure only (excl. devices and materials)	169	520	225
Primary procedure only (incl. devices and materials)	626	617	281
Medical visits	178	66	120
Total cost (without re-intervention)	922	5315	1098
Total cost (with re-intervention)	1704 (1320) ^a	5321	1263

^aWith therapeutic strategies used in 2001.

From Fernandez H, Kobelt G, Gervaise A. *Economic evaluation of three surgical interventions for menorrhagia. Human Reproduction* 2003; 18(3):583-587, by permission of Oxford University Press and the author

Fernandez et al. found hysterectomy was more effective than either of the 2 outpatient procedures, but as Table 33 shows, it was also more expensive. The incremental cost per patient (including reintervention) was €3,617 compared with TBEA (labelled thermocoagulation in the table), and €4,058 compared with EA. The 2 outpatient procedures have about the same cure rate (80%), but within the conditions of this study, EA had a lower cost (by €441); therefore, the authors say it would be preferred on cost grounds.

Fernandez et al. cautioned that the study represented experimental conditions for TBEA and that the cost of reintervention may have been overstated. They also noted that the incremental effectiveness of hysterectomy compared with ablation (i.e., the proportion of additional patients that are cured) is 20%. Therefore, the incremental cost-effectiveness (i.e., the cost per additional patient cured with hysterectomy compared with ablation) is high, €20,290.

Limitations to the economic analysis by Fernandez et al. were as follows:

- The economic analysis was not based on a RCT. Effectiveness was estimated from patients' answers on the follow-up questionnaire.
- The scoring definition of the satisfaction level was not based on a validated questionnaire.
- The reintervention rates after TBEA may have reflected the introduction of a new procedure rather than current clinical practice.
- The interventions were performed between 1995 and 1997, and patient management patterns may have changed since then.
- Data about reinterventions and medical appointments were obtained from patients 2 to 3 years after the procedure and may include recall bias.
- All of the costs related to the procedure (e.g., follow-up treatments, cost of treating complications) were not included. These costs are more frequent after hysterectomy.
- Information on sick leave and other indirect costs of the treatments was not available.

Ontario-Based Economic Analysis

Demographics

Based on previously noted estimates that 15% to 20% of women over age 30 may have DUB, there are between 291,000 and 388,000 women aged 30 to 49 years in Ontario that have DUB (source for population estimates: Ontario Population estimates for Ontario 2001, August 2002). Of these, about 70% have suitable uteri for TBEA. Thus, the potential population that suffers from DUB ranges from 200,000 to 270,000; however, most of these women would be presumably treated with the pharmacopeia designed to deal with this problem (e.g., prostaglandins).

There are about 10,000 annual surgical procedures designed to treat DUB in Ontario. About 50% are total hysterectomies, and the rest are largely first-generation EA techniques. There is also a waiting list of about 2,000 patients for EA. Estimates by London Health Sciences Centre suggests that the number of patients annually treated surgically for DUB in Ontario could increase by up to 50% in the future if second-generation EA techniques are fully funded. However, if this increase is not realized, these new EA techniques would largely be done in place of the existing volume of hysterectomies done for DUB and first-generation endometrial procedures.

Budget Impact Analysis

Fixed Assumptions

- About 3,750 hysterectomy patients per year will opt for second-generation ablation techniques if available. This equals 75% of 5,000 annual hysterectomy treatments for DUB.
- Control units will be purchased out of the ministry's medical equipment fund.
- All 5,000 first-generation techniques will be replaced by second-generation techniques.
- Waiting lists will be eliminated in 2 years if second-generation techniques are funded.

Varied Assumptions

- Diffusion pressure is minimal: TBEA replaces most of the existing volume of hysterectomies for DUB and first-generation EA procedures.
- Diffusion pressure is intense: There is a 50% increase in caseload due to introduction of a technical fee that allows TBEA to be delivered in the offices of physicians.

The following information relates to the capital/equipment costs associated with the 3 major competitors in the market for second-generation EA technology. All costs are in Canadian currency.

- Thermachoice control unit (with umbilical, cable, and power cord) is \$15,000; the balloon is \$745.
- Thermablate control unit (excluding power supply and stand) is \$6,000; the balloon is \$550 to \$700.
- Cavaterm central unit (including power supply, circulation system, operator's keyboard, and treatment monitor) is \$18,300; the balloon is \$669.

Because the Ministry of Health and Long-Term Care has access to a special medical equipment fund from the federal government, it is likely that capital costs associated with the control unit would be purchased with these monies. Therefore, the incremental cost associated with TBEA would largely involve the cost of the disposable balloon, which is assessed liberally in the foregoing analysis at \$750 per procedure.

(Note: If there is diffusion pressure beyond the existing volume of surgical procedures for DUB, then the incremental cost for the extra procedures would increase to over \$964 to account for added Ontario Health Insurance Policy [OHIP] physician fees.)

To assess the budget impact of funding TBEA, it is also necessary to assess cost avoidance, particularly because replacing the more costly hysterectomy procedures should produce large savings to the system. The following information is used to calculate the average cost of a total hysterectomy to treat DUB.

- \$3,454 is the expected hospitalization costs for hysterectomy (PAC-10 weight of 0.9069)

Medical professional fees:

- \$420.70: physician reimbursement for hysterectomy (FSC=\$757)
- \$211.86: anesthetist reimbursement (18 units at \$11.77/unit)
- \$99.96: surgical assistant reimbursement (14 units at \$10.20/unit). (Note: A surgical assistant is used 70% of the time.)
- \$733 is the total for expected medical professional fees.

- \$4,187 is the expected total cost for hysterectomy excluding drug costs (e.g., lifetime hormone replacement costs).

Calculations

Annual Outlays

- \$750: incremental cost per case (without capitalization costs and OHIP fees)
- 8,750: estimated annual TBEA treatments under scenario A: minimal diffusion pressure (8,750: 5,000 first-generation techniques + 3,750 hysterectomy treatments)
- \$6.6 million: total outlay for TBEA excluding capital costs

Annual Cost Avoidance

- \$8 million: net savings from shifting 3,750 hysterectomy treatments to TBEA
 - (+) \$750 estimated cost of disposable balloon for TBEA
 - (+) \$1,100 estimated average facility cost for outpatient procedures
 - (+) \$214 physician OHIP fee (\$772) for ablation procedures
 - (-) \$4,187 total cost of hysterectomy
- -\$1.4 million (net annual savings)

One-time Outlays

- \$4.1 million: cost of clearing EA waiting list of 2,000 patients
→ (\$750 balloon cost + \$214 physician's fee + \$1,100 facility fee) x 2,000 patients

Other Offsets and Unknowns

- Lifetime hormone replacement therapy costs for hysterectomy patients could be large as lifetime costs are added across annual cohorts of hysterectomy patients. Consequently, this is a potentially large source of cost-avoidance if TBEA is funded.
- Avoided costs for future treatments of menorrhagia in TBEA recipients
- Large indirect cost savings associated with either reduced loss of work associated with menorrhagia and avoided hysterectomy recovery (6 weeks)
- Potential diffusion pressure: Based on the London Health Sciences Centre estimates, TBEA could experience a 50% volume increase if a technical fee is instituted.
 - Would permit physicians to find it feasible financially to treat patients in their offices
 - Outlays could increase to over \$10.8 million excluding capital costs

Ⓜ (\$6.6 million base increase + (4,375 pts. x [\$750 + \$214.35 phys. fee])

Ⓜ + \$2.8 million net annual outlay under this scenario

Based on this analysis, we estimate that the net annual budget outlay for TBEA will range from \$1.4 million in savings to \$2.8 million in additional outlays. (Note: Not all savings will be realized directly by the ministry, because much of the savings will accrue to hospitals' global budgets.)

These cost estimates are largely consistent with a cost comparison published in France in 2003. (37)

The control units for TBEA vary in cost from \$6,000 to \$18,000, depending on the make.

Based on statistics gathered from London Health Sciences Centre, a typical user of this technology might do 8 procedures per week, or about 400 per year. Given that we expect there to be close to 8,750 procedures per year in Ontario under scenario A (limited diffusion), this would translate to 22 control units (8,750/400) for the entire province. Under Scenario B (full expected diffusion; i.e., 50% increase), there about 33 control units would be needed.

Due to variations in price per control unit, the outlay for machines could be between \$132,000 and \$396,000 under Scenario A, and between \$198,000 and \$594,000 under Scenario B.

To amortize the cost of the machine per procedure over the course of a single year, the add-on to the ministry's remuneration cost for the first year would be from \$50 to \$75 per procedure (i.e., negligible).

Existing Guidelines for Use of Technology

Canada

The Society of Obstetricians and Gynaecologists of Canada (SOGC) released clinical practice guidelines in August 2001 (1) on global Endometrial Ablation. It said, "Although all devices are promising and have produced impressive preliminary results, the long term efficacy, complication rates and effectiveness have not been established."

United Kingdom

The National Institute for Clinical Excellence (NICE) in April 2004 (38) noted that TBEA is recommended as a treatment option for patients with HMB in cases where it has been decided (by the patient and the clinician responsible for her treatment) that surgical intervention is appropriate for the management of the condition.

They also suggested that the choice of surgical treatment for HMB should be made jointly by the woman and the clinician responsible for treatment. The decision should be made after an informed discussion taking into account the desired outcome of the treatment (such as reduced menstrual bleeding or complete cessation of menstrual bleeding), the relative benefits of all other treatment options and the adverse events associated with them, as well as the women's clinical condition, anatomical suitability, and preferences.

Appraisal/Policy Development

Policy Considerations/Implications

Patient Outcomes

- Patient preferences for treatments will depend on a woman's desire or priority for amenorrhea as an outcome and/or avoidance of major surgery. (39;40) Hysterectomy is the only procedure that can guarantee amenorrhea. TBEA will not totally replace hysterectomy in the treatment of DUB, because some women may want cessation of menstruation.
- Ensuring that patient expectations are consistent with the outcomes achievable with TBEA is important to obtain high levels of satisfaction. Vilos et al. (5) noted that up to one-half of patients who underwent a second attempt at TBEA might have avoided the second procedure with proper preoperative counselling. Meyer et al. (6) suggested that one consideration for patients with menorrhagia (and no structural lesions) is to be returned to normal or less blood loss, rather than amenorrhea. Patients may have distinct concepts of menstrual bleeding depending on their cultural backgrounds, and maintaining an acceptable menstrual flow instead of amenorrhea may represent a healthier status. (7)

Demographics

- In Ontario, an expert estimated the prevalence of DUB at 15% to 20% of women over 30 years of age. However, some of these patients will be treated by drugs or want amenorrhea, and therefore will choose to have a hysterectomy.

- The incidence of DUB has not been identified in the literature, nor was an expert in the field able to estimate the incidence of DUB in Ontario.
- Only a certain number of women with DUB are eligible for TBEA (i.e., larger and abnormal uteri are a contraindication for TBEA).
- In Ontario, an expert estimated that about 70% of patients with DUB considered for EA would have a uterus suitable for TBEA (i.e., excluding large or abnormally shaped uteri).

Diffusion

- In the United Kingdom, NICE stated that the impact of second-generation EA techniques on the National Health Service budget will depend on the number of women eligible for each technique and the uptake rates, which will be greatly influenced by the preferences of patients and clinicians.

- United States Aetna – March 2004 (41)

- Aetna considers thermoablation (e.g., thermal fluid filled balloon, heated saline) medically necessary for women who meet all of the following selection criteria:
 - Menorrhagia unresponsive to or a contraindication to either hormonal therapy or other pharmacotherapy; or dilation and curettage. (Note: The degree of severity and persistence of the menorrhagia and the failure of prior treatment should be such that the woman would otherwise be a candidate for a hysterectomy.)
 - Endometrial sampling has excluded cancerous, precancerous, or structural abnormalities (e.g., polyps, fibroids) that require surgery.
 - Pap smear and gynecologic examination have excluded significant cervical disease.

- In Quebec in December 2002, Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) noted the following:

“Of the second generation ablation techniques, only thermal balloon endometrial ablation is considered accepted. The long-term results of a randomized, controlled trial and those of several other studies indicate that this technique compares with transcervical resection of the endometrium in terms of efficacy and the reoperation rate. Very few studies have examined the level of satisfaction. Further more, this technique seems to be reserved for normal uterine cavities and causes pain due to uterine distention. Uterine retroversion appears to be associated with a greater risk of treatment failure. Among the contraindications to thermal balloon endometrial ablation, particular mention should be made of an active genital or urinary tract infection and any anatomic abnormality or any disease that can cause myometrial weakening. When this report was being drafted, the use of thermal balloon endometrial ablation was still not very widespread in Quebec.” (42)

- The AETMIS report noted that EA is a surgical procedure that is growing in popularity. (10) According to Regie de L'assurance maladie de Quebec statistics, the number of Quebec women aged 15 to 84 treated by EA increased sharply between 1995 and 1999. The number of these procedures rose from 1,007 to 1,830 annually, an increase of almost 82%.
- Most EAs in Quebec are done on women aged 35 and over. (10)
- The number and proportion of EAs in this age group is increasing. (10) The proportion of Quebec women aged 35 and over at the time of EA rose from 81.3% in 1995 to 87.8% in 1999.
- Regional variations in the frequency of EA in Quebec may be related to whether or not the patients live in an urban area. (10) Women living in rural areas who have abnormal uterine bleeding may have more difficulty obtaining an alternate form of treatment. “In borderline cases, the medical personnel and the patient herself may opt for a hysterectomy (to avoid the frequent travel required for aftercare by a specialist).” (10)

- Farquhar et al. (22) suggested that EA is being used as an adjunct to, rather than a replacement therapy for, menorrhagia. Furthermore, they suggested the availability of EA might decrease the threshold for surgical treatment.

Cost

To recap, according to the manufacturers, the device costs in Canadian dollars are as follows:

- Thermachoice control unit (including umbilical cable and power cord): \$15,000; balloon catheter: \$745
- ThermaBlate control unit (excluding power supply and stand): \$6,000; cartridge: \$550–\$700
- Cavaterm central unit (including power supply, circulation system, operator’s keyboard, and treatment monitor): \$18,300; catheter/balloon: \$669

Stakeholder Analysis

- TBEA requires less surgical skill and experience than first-generation techniques. Therefore, more gynecologists might want to offer TBEA, which in turn might lead to greater access of TBEA to patients.
- In February 2002, the Ontario Women’s Health Council wrote the report, *Achieving Best Practices in the Use of Hysterectomy*. One recommendation was to “make hysteroscopic and global endometrial ablation procedures more widely available to women through Ontario by designating funding and situating these procedures in outpatient centres and ambulatory surgical facilities.”

System Pressures

- There is a code in place for the professional fee for EA (S772). There is no restriction on where this is done (i.e., it now may be done outside a hospital); *but, in the absence of a technical fee, it is likely that few, if any, procedures are done outside of a hospital.*
- If TBEA is approved for funding, administering TBEA will require training and knowledge of the indications and contraindications for TBEA; and pretreatment counselling to ensure that *patient expectations are consistent with the outcomes achievable with TBEA.*
- The availability of TBEA may lead patients to seek treatment earlier than if hysterectomy was the only procedure available.
- Patients who are conventionally treated first by drug therapy could undergo TBEA and bypass drug treatment. Although medical management remains the first line of therapy for DUB, there is uncertainty about its effectiveness and acceptability. (11)
- If TBEA is approved for funding, hospitals may undergo changes in infrastructure (e.g., TBEA outpatient clinics may be created rather than performing the procedure in the operating room).
- If TBEA is approved for funding, the procedure might be able to be done in a gynecologist’s office. A recent abstract presented at the Society of Obstetricians and Gynecologists of Canada concluded that global ablation technologies (including TBEA) are safe and well tolerated in an office setting under local anesthesia. (43)

Conclusions

- TBEA is an effective, safe, and cost-effective technology for patients with DUB. For women who are not worried about amenorrhea, first-generation techniques offer advantages over hysterectomy.
- TBEA is a better alternative to first-generation techniques for DUB, because it is associated with fewer intraoperative adverse effects.

Glossary

Abnormal uterine bleeding:	An increase in frequency of menstruation, duration of flow or amount of blood loss.
Amenorrhea:	Absence or abnormal stoppage of menstruation.
Dysfunctional uterine bleeding (DUB):	A subcategory of abnormal uterine bleeding, this is a diagnosis of exclusion when there is no pelvic pathology or underlying medical cause.
Dysmenorrhea:	Painful menstruation.
Endometrial ablation:	Removal or destruction of the endometrium.
Endometritis:	Inflammation of the endometrium.
Endometrium:	Mucous membrane lining the uterus, whose thickness and structure vary with the phase of the menstrual cycle.
Eumenorrhea:	Normal menstruation.
Hematometra:	An accumulation of blood in the uterus.
Hydrosalpinx:	A collection of watery fluid in a fallopian tube, occurring as the end stage of pus in the fallopian tube.
Hypomenorrhea:	Menstruation in which the flow is less than the normal amount but at regular intervals, with the period of flow lasting the same or less time than average.
Hysterectomy:	Removal of the uterus and cervix (total) or removal of the uterus only (subtotal). It may also be associated with the removal of the ovaries and fallopian tubes (bilateral salpingo-oophorectomy). Hysterectomy can be done via the abdomen or vagina depending on the surgeon, the indication for surgery, the nature of the disease, and patient characteristics. Hysterectomy may also be done with a laparoscope, thereby allowing a procedure to be performed vaginally that otherwise could have only be performed through larger abdominal incisions.
Hysteroscope:	Instrument using fiber optic technology that allows direct visualization of the uterine cavity. Channels in the instrument allow other instruments to be inserted to perform ablations.
Menorrhagia:	Menstruation with an excessive flow but at regular intervals and of usual duration.

Menstruation:

Cyclic, physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus; it is under hormonal control and normally recurs at approximately four-week intervals, in the absence of pregnancy during the reproductive period (puberty through menopause). The menstrual cycle stops when the thickened endometrium is sloughed off.

Metrorrhagia:

Uterine bleeding, usually of variable amount, occurring at completely irregular but frequent intervals, the period of flow sometimes being prolonged.

Surgical tissue coagulation:

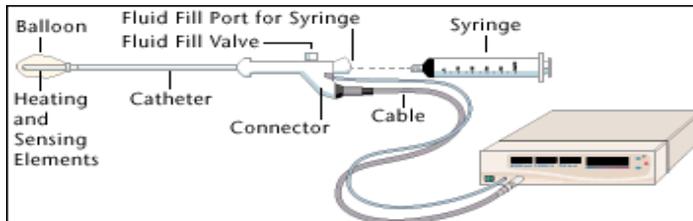
In surgery, the disruption of tissue by physical means to form an amorphous residuum, as in thermocoagulation.

Transcervical resection of the endometrium: Removal of some of the endometrial tissue via the cervix.

Appendices

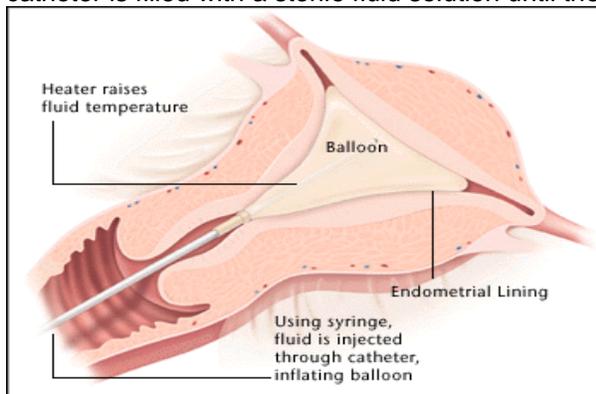
Appendix 1

Figure 2: Example of thermal endometrial ablation therapy. The procedure works by ablating the endometrial lining of the uterus, in three phases: 1) insertion and balloon inflation; 2) heating, ablation, and monitoring; 3) deflation and removal.



Insertion and Inflation

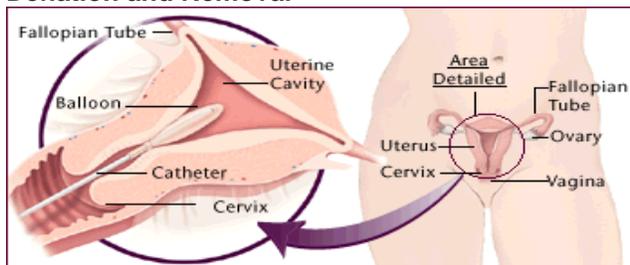
The balloon catheter is inserted vaginally, through the cervix, into the uterus. Inflation occurs when the catheter is filled with a sterile fluid solution until the pressure reaches 160 to 170 mm of mercury.



Ablation and Monitoring

A heating element inside the balloon raises the temperature to about 87 degrees C and maintains it for about 8 minutes. The controller continuously monitors and displays catheter pressure, regulates fluid temperature, and controls therapy time. If any of the preset parameters are exceeded, the device is automatically deactivated, and the procedure is immediately terminated.

Deflation and Removal



When the controller signals that treatment is complete, the balloon is deflated and the catheter is withdrawn and discarded.

Above figures used with permission from Gynecare, a division of Ethicon Inc. From: <http://www.gynecare.com/>

Appendix 2

Summary of Results: Hysterectomy Versus Endometrial Resection or First-Generation Endometrial Ablation Techniques. Adapted from Lethaby et al. (23)

Outcome	Study, Year	Result [OR (95% CI)] or Weighted mean difference when reported	Comment and (P values when reported)
Proportion with improvement in blood loss Within 1 year of follow-up	Dwyer et al., 1993	0.13 (0.03–0.48)*	Favours hysterectomy
	Gannon et al., 1991	0.11 (0.02–0.86)*	Favours hysterectomy
	Pinion, 1994	0.11 (0.04–0.31)*	Favours hysterectomy
At 2 years of follow-up	Crosignani et al., 1997	0.10 (0.00–5.41)	
At 4 years of follow-up	Pinion et al., 1994	0.15 (0.01–2.38)	
Proportion satisfied with treatment At 1 year follow-up	Dwyer et al., 1993	0.40 (0.16–0.99)*	Favours hysterectomy
	O'Connor et al., 1997	0.64 (0.22–1.85)	
	Pinion et al., 1994	0.32 (0.05–1.86)	
At 2 year follow-up	Crosignani et al., 1997	0.38 (0.08–1.79)	
	Dwyer et al., 1993	0.23 (0.09–0.59)*	Favours hysterectomy
	O'Connor et al., 1997	0.42 (0.13–1.41)	
At 3 years follow-up	O'Conner et al., 1997	0.32 (0.08–1.37)	
At 4 years of follow-up	Pinion et al., 1994	0.52 (0.21–1.26)	
Proportion with improvement in QoL Improvement with pain 2 years after surgery	Dwyer et al., 1993	0.51 (0.15–1.98)	
Improvement in general health 1 year after surgery	Pinion et al., 1994	0.26 (0.11–0.63)*	
Improvement in general health 4 years after surgery	Pinion et al., 1994	0.36 (0.13–1.01)	
Improvement in previous symptoms 1 year after surgery	Pinion et al., 1994	0.43 (0.15–1.28)	
Duration of surgery	Crosignani et al., 1997	WMD > -10* (data from graph)	Favours TCRE/ablation
	Dwyer et al., 1993	WMD > -10*	Favours TCRE/ablation
	Gannon et al., 1991	WMD > -10*	Favours TCRE/ablation
	O'Connor et al., 1997	WMD > -10*	Favours TCRE/ablation
	Pinion et al., 1994	WMD > -10*	Favours TCRE/ablation
Duration of hospital stay (days)	Crosignani et al., 1997	WMD ~ -5* (data from graph)	Favours TCRE/ablation
	Dwyer et al., 1993	WMD ~ -5*	Favours TCRE/ablation
	Gannon et al., 1991	WMD ~ -5*	Favours TCRE/ablation
	O'Connor et al., 1997	WMD ~ -5*	Favours TCRE/ablation
	Pinion et al., 1994	WMD ~ -5*	Favours TCRE/ablation
Time to return to work (weeks)	Crosignani et al., 1997	WMD ~ -3* (data from graph)	Favours TCRE/ablation
	Dwyer et al., 1993	WMD ~ -10*	Favours TCRE/ablation
	Gannon et al., 1991	WMD ~ -7*	Favours TCRE/ablation
	O'Connor et al.,	WMD ~ -5*	Favours TCRE/ablation

	1997		
Adverse events – short term before discharge			
Sepsis	Dwyer et al., 1993	0.12 (0.06–0.27) *	Favours TCRE/ablation
	Gannon et al., 1991	0.11 (0.02–0.61) *	Favours TCRE/ablation
	O'Connor et al., 1997	0.04 (0.01–0.21) *	Favours TCRE/ablation
	Pinion et al., 1994	0.22 (0.12–0.40)*	
Hemorrhage	O'Connor et al., 1997	0.04 (0.00–0.51) *	Favours TCRE/ablation
	Pinion et al., 1994	1.11 (0.33–3.75)	
Blood transfusion	Dwyer et al., 1993	0.35 (0.08–1.42)	
	O'Connor et al., 1997	0.04 (0.00–0.51)*	Favours TCRE/ablation
	Pinion et al., 1994	0.23 (0.05–1.19)	
Urinary retention	Dwyer et al., 1993	0.13 (0.02–0.64)*	Favours TCRE/ablation
	Gannon et al., 1991	0.12 (0.02–0.94)*	Favours TCRE/ablation
Anemia	Dwyer et al., 1993	0.12 (0.03–0.43)*	Favours TCRE/ablation
Fever	Dwyer et al., 1993	0.12 (0.06–0.27)*	Favours TCRE/ablation
Vault hematoma	Dwyer et al., 1993	0.19 (0.05–0.73)*	Favours TCRE/ablation
	Gannon et al., 1991	0.14 (0.00–7.09)	
	Pinion et al., 1994	0.11 (0.03–0.38)*	Favours TCRE/ablation
Wound hematoma	Pinion et al., 1994	0.11 (0.04–0.32)*	Favours TCRE/ablation
Adverse events – long term after discharge			
Sepsis	O'Connor et al., 1997	0.19 (0.08–0.47)*	Favours TCRE/ablation
Hematoma	Dwyer et al., 1993	0.13 (0.01–2.11)	
	O'Connor et al., 1997	0.96 (0.17–5.46)	
Diarrhea	Dwyer et al., 1993	0.13 (0.00–6.68)	
Hemorrhage	Dwyer et al., 1993	7.24 (0.14–365.04)	
Proportion requiring further surgery for HMB			
Within 1 year after surgery	Crosignani et al., 1997	7.95 (0.16–401.66)	
	Dwyer et al., 1993	8.15 (2.54–26.13)*	Favours hysterectomy
	Gannon et al., 1991	8.76 (1.16–66.17)*	Favours hysterectomy
	O'Connor et al., 1997	2.96 (0.76–11.51)	
	Pinion et al., 1994	9.23 (4.16–20.47)*	Favours hysterectomy
At 2 years after surgery	Crosignani et al., 1997	8.36 (0.85–82.75)	
	Dwyer et al., 1993	10.53 (4.94–22.41)*	Favours hysterectomy
	O'Connor et al., 1997	4.10 (10.52–11.07)*	Favours hysterectomy
At 3 years after surgery	O'Connor et al., 1997	4.45 (1.78–11.15)*	Favours hysterectomy
At 4 years after surgery	Pinion et al., 1994	9.84 (4.92–19.67)*	Favours hysterectomy

*statistically significant

OR=Odds ratio

WMD=Weighted mean difference

CI=Confidence Interval

From Lethaby A, Shepperd S, Cooke I, Farquhar C. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. The Cochrane Database of Systematic Reviews 1999, Issue 2. Art. No.: CD000329. DOI: 10.1002/14651858.CD000329, This version first published online: 26 April 1999 in Issue 2, 1999

Date of Most Recent Substantive Amendment: 15 January 1999. Copyright Cochrane Library. Reproduced with permission from the Cochrane Library and the author.

Summary of Outcomes: First-Generation Endometrial Ablation Techniques/TCRE Versus Second-Generation Endometrial Ablation Technique TBEA.

Outcome	Study, Year (Type)	Result OR (95% CI) or % (intent to treat)	Comment (P value When Reported)
Amenorrhea after surgery			
12 months	Meyer et al., 1998 Romer et al., 1998 Soysal et al., 2001 Alaily et al., 2003 (case series) Baruah et al., 2003 (case series)	0.56 (0.30–1.04) 1.56 (0.24–9.91) 0.58 (0.18–1.93) TBEA: 35% TBEA: 10.5%	No statistically significant differences
24 months	Meyer et al., 1998 Gervaise et al., 1999 Alaily et al., 2003 (case series)	0.36 (0.20–0.65)* 0.90 (0.42–1.95) TBEA: 46%	Favoured first-generation
36 months	Meyer et al., 1998	TBEA: 12% RB: 19%	
60 months	Meyer et al., 1998	TBEA: 14% RB: 10%	
4–6 years	Amso et al., 2003 (case series)	TBEA: 46.9%	
18 months (median)	Feitoza et al., 2003 (case series)	TBEA: 60%–74% of patients were either amenorrheic or hypomenorrheic.	
4 months	Baruah et al., 2003 (case series)	TBEA: 7.3%	
8 months	Baruah et al., 2003 (case series)	TBEA: 15.3%	
48 months	Mettler, 2002 (case series)	TBEA: 58% (also: 33% reported hypomenorrhea; and 9% reported eumenorrhea)	
16–28 months	Jarrell et al., 2003 (retrospective case series)	TBEA: 57% of women reported amenorrhea or “very decreased bleeding.”	
Menorrhagia after surgery	Study, Year (Type)	%	
1 month	Gervaise et al., 1999	TBEA: 11 TCRE 12	
4 months	Baruah et al., 2003 (case series)	TBEA: 7.3	
8 months	Baruah et al., 2003 (case series)	TBEA: 7.6	
12 months	Alaily et al., 2003 (case series) Baruah et al., 2003 (case series)	TBEA: 10 TBEA: 5.2	
24 months	Bongers et al., 2000 Gervaise et al., 1999	TBEA: 9 TCRE: 12 TBEA: 5 TCRE: 15	

	Meyer et al., 1998	TBEA: 8 RB: 9	
	Alaily et al., 2003 (case series)	TBEA: 10	
36 months	Meyer et al., 1998	TBEA: 6 RB: 4	
60 months	Meyer et al., 1998	TBEA: 2 RB: 1	
18 months (median)	Feitoza et al., 2003 (case series)	TBEA: 2	
4–6 years	Amso et al., 2003 (case series)	TBEA: 8.5	
Reduction in blood loss after surgery	Study, Year	Median values of the % reduction in menstrual score relative to preoperative values	P Value
6 months	Zon Rabelink et al., 2004	TBEA: 75% RB: 83%	.42
12 months	Zon Rabelink et al., 2004	TBEA: 79% RB: 86%	.64
24 months	Zon Rabelink et al., 2004	TBEA: 91%* RB: 87%	.03
Dysmenorrhea after surgery	Study, Year	OR (95% CI) or % (intent to treat)	Comments
12 months	Meyer et al., 1998 (pain “same or worse”)	1.45 (0.83–2.55)	
24 months	Bongers et al., 2000	TBEA: 0 TCRE: 4	
36 months	Meyer et al., 1998 (pain “moderate”)	TBEA: 9 TCRE: 5	
Satisfaction with Treatment after surgery	Study, Year (Type)	OR (95% CI) or % (intent to treat)	Comments
12 months	Meyer et al., 1998 Bongers et al., 2000 Romer et al., 1998	1.56 (0.80–3.04) 2.35 (1.23–4.50)* “all patients were satisfied”	Favoured TBEA
	Alaily et al., 2003 (case series)	TBEA: 90%	
	Baruah et al., 2003 (case series) (scale of 1–10, 10 = complete satisfaction)	TBEA mean score: 7.42 (SD, 3.18)	
24 months	Meyer et al., 1998 Bongers et al., 2000 Zon Rabelink et al., 2001	1.93 (1.05–3.56)* 1.44 (0.74–2.82) 1.44 (0.66–3.15)	Favoured TBEA
	Zon Rabelink et al., 2004	TBEA: 80% RB: 75%	P = .53
	Alaily et al., 2003 (case series)	TBEA: 90%	

36 months	Meyer et al., 1998	TBEA: 6% RB: 4%	
Median 18 months (median)	Feitoza et al., 2003 (case series)	TBEA 71% "very satisfied" 25% "satisfied" 4% "not satisfied"	
4 months	Baruah et al., 2003 (case series) (Scale of 1–10, where 10= complete satisfaction)	TBEA Mean score 5.63 (SD, 2.91)	
8 months	Baruah et al., 2003 (case series) (scale of 1–10, where 10= complete satisfaction)	TBEA Mean score 6.9 (SD, 3.68)	
60 months	Meyer et al., 1998	TBEA: 42% RB: 44%	
Quality of Life After Surgery	Study, Year (Type)	%	P value
12 months	Meyer et al., 1998 (impact of symptoms on life)	<u>Severe Impact</u> Pre-TBEA: 66 post-TBEA: 3 pre-RB: 67 post-RB: 2	
36 months	Meyer et al., 1998 (impact of symptoms on life—% intent to treat)	<u>Severe Impact</u> Pre-TBEA: 66 post-TBEA: 1 pre-RB: 67 post-RB: 1 <u>Moderate Impact</u> Pre-TBEA: 28 post-TBEA: 7 pre-RB: 20 post-RB: 6 <u>Minor Impact</u> Pre-TBEA: 1 post-TBEA: 75 pre-RB: 1 post-RB: 64	
18 months (median)	Feitoza et al., 2003 (case series)	Pre-TBEA: mean, 2.8 (SD, 1.7)* Post-TBEA: mean, 9.0 (SD, 1.16)	< .0001
Operating Time, Minutes	Study, Year	Mean (SD) or % as a function of time	P value
	Meyer et al., 1998	TBEA: 71% < 30 minutes* RB: 28.6% < 30 minutes	< .05
	Gervaise et al., 1999	TBEA: 20.3* RB: 44.8	< .05
	Pellicano et al., 2002	TBEA: 24 (4)* TCRE/RB: 37 (6)	< .01
	Soysal et al., 2001	TBEA: 11.5 (0.8)* RB: 37.3 (7.5)	.0001

Time/Recovery	Study, Year (Type)	Mean (SD) or %	Comments
Postoperative stay, days	Pellicano et al., 2002	TBEA: 1.0 (0.4) TCRE/RB: 1.3 (0.6)	
	Meyer et al., 1998 (< 30 min % ITT)	TBEA: 65% RB: 24%	
	Gervaise et al., 1999 (< 30 min % ITT)	TBEA: 100% TCRE: 53%	
	Alaily et al., 2003 (case series)	TBEA: 84% had day case procedures	
	Baruah et al., 2003 (case series)	TBEA: 88.1% discharged within 6 hours; 12% discharged within 24 hours.	
Time to return to work, days	Pellicano et al., 2002	TBEA: 0.7 (0.1) TCRE/RB: 0.9 (0.3)	NS
Adverse events: intraoperative	Study, Year	%	P value
Fluid overload	Bongers et al., 2000	TBEA: 0 TCRE: 26	
	Meyer et al., 1998	TBEA: 0 RB: 1	
	Gervaise et al., 1999	TBEA: 0 TCRE: 0	
	Pellicano et al., 2002	TBEA: 0 TCRE/RB: 12	
	Soysal et al., 2001	TBEA: 0 RB: 4	.05
	Zon Rabelink et al., 2001	TBEA: 0 RB: "no"	
Cervical laceration/burn	Meyer et al., 1998	TBEA: 0 RB: 1	
	Brun et al., 2002	TBEA: 3 TCRE: not reported	
	Gervaise et al., 1999	TBEA: 0 TCRE: 0	
	Pellicano et al., 2002	TBEA: 0 TCRE/RB: 5	
	Soysal et al., 2001	TBEA: 0 RB: 2	
	Zon Rabelink et al., 2001	TBEA: 0 RB: "yes"	
	Zon Rabelink et al., 2004	TBEA: 0 RB: 5	

Uterine perforation/laceration	Bongers et al., 2000	TBEA: not reported RB: 1	
	Meyer et al., 1998	TBEA: 0 RB: 1	
	Gervaise et al., 1999	TBEA: 0 TCRE: 0	
	Pellicano et al., 2002	TBEA: 0 RB: 5	
	Soysal et al., 2001	TBEA: 0 RB: 0	
	Zon Rabelink et al., 2001	TBEA: 0 RB: "yes"	
	Zon Rabelink et al., 2004	TBEA: 0 RB: 5	
Suspicion of perforation	Zon Rabelink et al., 2004	TBEA: 0 RB: 2	
Hemorrhage	Meyer et al., 1998	TBEA: 0 RB: 0	
	Gervaise et al., 1999	TBEA: 0 TCRE/RB: 0	
	Pellicano et al., 2002	TBEA: 0 RB: 0	
	Soysal et al., 2001	TBEA: 0 RB: 0	
	Zon Rabelink et al., 2001	TBEA: 0 RB: No	
Electrolyte imbalance	Zon Rabelink et al., 2001	TBEA: 0 RB: "yes"	
	Zon Rabelink et al., 2004	TBEA: 0 RB: 2	
	Mettler, 2002 (case series)	TBEA: 0	
Adverse events: Postoperative	Study, Year	%	
Pain	Zon Rabelink et al., 2004	TBEA: 4 RB: 0	
Nausea	Zon Rabelink et al., 2004	TBEA: 0 RB: 2	
Infection	Zon Rabelink et al., 2004	TBEA: 0 RB: 2	
Pain + nausea + headache	Zon Rabelink et al., 2004	TBEA: 1 RB: 0	
Endometritis	Meyer et al., 1998 (12 mos.)	TBEA: 2 RB: 1	
	Gervaise et al., 1999 (24 mos.)	TBEA: 0 TCRE/RB: 4	
	Soysal et al., 2001 (12 mos.)	TBEA: 4 RB: 2	

	Feitoza et al., 2003 (median 18 months) (case series)	TBEA: 1 patient had "mild" endometritis	
Urinary tract infection	Meyer et al., 1998	TBEA: 1 RB: 0	
	Pellicano et al., 2002	TBEA: 0 RB: 2	
Hematometra	Meyer et al., 1998 (12 mos.)	TBEA: 0 RB: 1	
	Soysal et al., 2001 (12 mos.)	TBEA: 2 RB: 4	
Fever	Pellicano et al., 2002 (3 mos.)	TBEA: 2 RB: 5	
Hemorrhage	Pellicano et al., 2002 (3 mos.)	TBEA: 12 RB: 10	
Symptomatic hydrosalpinx	Meyer et al., 1998 (12 mos.)	TBEA: 0 RB: 1	"not significant"
	Mettler, 2002 (case series)	TBEA: 0 (postoperative complications overall)	
Repeat Surgery	Study, Year (Time Frame)	%	
Hysterectomy % ITT	Bongers et al., 2000 (12 mos.)	TBEA: 10 TCRE: 16	"not significant"
	Bongers et al., 2000 (24 mos.)	TBEA: 12 TCRE: 20	
	Brun et al. 2002 (3 mos.)	TBEA: not reported TCRE: not reported	
	Meyer et al., 1998 (12 mos.)	TBEA: 1 RB: 2	
	Meyer et al., 1998 (24 mos.)	TBEA: 3 RB: 8	
	Meyer et al., 1998 (36 mos.)	TBEA: 6 RB: 10	
	Meyer et al., 1998 (60 mos.)	TBEA: 9 RB: 5	
	Gervaise et al., 1999 (24 mos.)	TBEA: 10 RB: 1%	
	Pellicano et al., 2002 (12 mos.)	TBEA: not reported TCRE: not reported	
	Pellicano et al., 2002 (24 mos.)	TBEA: not reported TCRE/RB: not reported	
	Romer et al., 1998 (12 mos.)	TBEA: not reported TCRE/RB: not reported	
	Soysal et al., 2001 (12 mos.)	TBEA: 9 RB: 8	
	Zon Rabelink et al., 2001	TBEA: not reported RB: not reported	
	Zon Rabelink et al., 2004 Due to menorrhagia	TBEA: 10 RB: 3	
	Due to dysmenorrhea	TBEA: 0 RB: 5	
Due to "other reasons"	TBEA: 0 RB: 2		
	Baruah et al., 2003 (12 mos.) (case series)	TBEA: 4.7	
	Feitoza et al., 2003 (case series; median 18	TBEA: 10 for persistent	

	months after surgery)	menorrhagia; 3 for dysmenorrhea	
	Mettler, 2002 (48 mos.; case series)	TBEA: 0 (for group B with TBEA indications)	
	Jarrell et al., 2003 (16–28 months; retrospective case series, N=28)	TBEA: 46	
	Amso et al., 2003 (4–6 years; case series)	TBEA: 10.6 for menorrhagia	
Repeat ablation	Amso et al., 2003 (4–6 years; case series)	TBEA: 11.2	
	Zon Rabelink et al., 2004 (24 mos.)	TBEA: 1 RB: 2	
	Baruah et al., 2003 (12 mos.) Case series	TBEA: 2.3	
Total repeat surgery (% ITT) (hysterectomy &/or repeat ablation)	Bongers et al., 2000 (12 mos.)	TBEA: 10 TCRE: 21	
	Bongers et al., 2000 (24 mos.)	TBEA: 12 TCRE: 36	
	Brun et al. 2002 (3 mos.)	TBEA: not reported TCRE: not reported	
	Meyer et al., 1998 (12 mos.)	TBEA: 1 RB: 2	
	Meyer et al., 1998 (24 mos.)	TBEA: 3 RB: 8	
	Meyer et al., 1998 (36 mos.)	TBEA: 7 RB: 10	
	Meyer et al., 1998 (60 mo).	TBEA: 11 RB: 7	
	Gervaise et al., 1999 (24 mos.)	TBEA: 10 RB: 8	
	Pellicano et al., 2002 (12 mos.)	TBEA: 4 TCRE: 8	
	Pellicano et al., 2002 (24 mos.)	TBEA: =4 TCRE/RB: 10	
	Romer et al., 1998 (12 mos.)	TBEA: 0 TCRE/RB: 0	
	Soysal et al., 2001 (12 mos.)	TBEA: 8 RB: 8	
	Zon Rabelink et al., 2001	TBEA: not reported RB: not reported	

*statistically significant
OR=Odds ratio
CI=Confidence Interval

Appendix 3

Table 2: Characteristics of Trials Reported in All Included Papers and Treatments*

Author/ Date/ Design	No. pts	Average age (years)	Women with Fibroids excluded?	Intervention	Control treatment	Pre-treatment	Surgeon experience	Anaesthetic	Length of Follow up (months)
Cooper et al 1999 RCT	263	MEA 41.1 (SD 6.7) TCRE/RB 42.0 (SD 8.4)	No	Microwave	TCRE / RB	3.6mg goserelin 5 weeks prior	At least 50 prior TCRES, at least 5 prior MEAs	100% GA	12
Bain et al 2002 RCT	263	MEA 41.4 (SD 5.4) TCRE/RB 42.2 (SD5.8)	No	Microwave	TCRE / RB	3.6mg goserelin 5 weeks prior	At least 50 prior TCRES, at least 5 prior MEAs	GA	24
Microsulis 2002 RCT	322	Not stated	No	Microwave	RB	Leuprolide acetate depot 3-5 weeks prior	Not stated	GA: MEA 37% RB 76%	12
Meyer et al 1998 RCT	275	TBEA 40.2 (SD 4.9) 30-51 RB 40.9 (SD 5.2) 29-50	Yes	Thermachoice™ thermal balloon	RB	None stated	All had extensive experience of rollerball .	GA: TBEA 53% RB 84%	12
Grainger et al 2000 RCT	255	Not stated	Yes	Thermachoice™ thermal balloon	RB	3 minute curettage using 5mm curette prior to ablation	All experienced in rollerball and trained in TBEA	Not stated	24
Loffer 2001 RCT	255	Not stated	Yes	Thermachoice™ thermal balloon	RB	Timed 3 minute suction curettage given to all prior to ablation	All experienced in rollerball and trained in TBEA	Local, local with sedation and general. More GA with RB	36
Loffer et al 2002 RCT	255	TBEA 40.4 RB 40.9	Yes	Thermachoice™ thermal balloon	RB	3 minute suction curettage	All experienced in rollerball and trained in TBEA	Not stated	60
Gervaise 1999 Non-random CT	147	TBEA 46.3 (+/- 1.4) 34-66 TCRE 47.4 (+/- 0.2) 34-65	Yes	Thermachoice™ balloon	TCRE	None	Not stated	General TCRE General and local (38%) for TBEA	18

TCRE indicates transcervical resection of the endometrium; MEA, microwave endometrial ablation; TBEA, thermal balloon endometrial ablation; RB, rollerball ablation; RCT, randomized controlled trial; CT, controlled trial

Table 2: Characteristics of Trials Reported in All Included Papers and Treatments (cont'd)

Author/ Date/ Design	No. pts	Average age (years)	Women with Fibroids excluded?	Intervention	Control treatment	Surgery pre-treatment	Surgeon experience	Anaesthetic	Length of Follow up (months)
Pellicano 2002 RCT	96	TBEA 42.6 (+/-4.4) TCRE/RB: 43.2 (+/-3.5)	Submucous	Cavaterm™ balloon	TCRE/RB	Treatment group none Control group GnRH 6 and 2 weeks prior to surgery.	Surgeons "proficient" in TCRE.	Spinal anaesthesia	24
Romer 1998 RCT	20	TBEA 42 (37-52) RB 40 (37-50)	Yes	Cavaterm™ balloon	RB	2x monthly injections of GnRH (leuprolide 3.75mg) operation 2 weeks after injection.	Not stated	All GA	9-15 months
Soysal et al 2001 RCT	96	TBEA 43.6 (+/-2.5,40-49) RB 44.3 (+/-2.6,40-49)	No - all pts had fibroids	Thermachoice™ balloon	RB	2x monthly injections of GnRH analogue (3.6mg goserelin acetate)	One experienced surgeon performed all rollerball, TBEA by staff surgeons supervised by residents	All RB GA, all TBEA local.	12
Zon-Rabelink 2001 RCT	139	Not stated	Not stated	Thermachoice™ balloon	RB	Pre-treatment with Zoladex 6 and 2 weeks prior to surgery.	Not stated	Not stated	24

Key

RB = Rollerball
 TCRE = Trans cervical Resection
 TBEA = Thermal Balloon Endometrial Ablation
 MEA = Microwave Endometrial Ablation
 GA = General Anaesthetic

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Table 3: Methodological Characteristics of Included Controlled Trials*

Author/ Date	No. of pts	Adequate allocation to groups	Blinding	Comparability of groups	Same intervention to all pts?	% loss to follow up	Sample size calc.	ITT	Generalisability	Main outcome measured independently	Inter-centre variability	Conflicts of interest
Cooper et al 1999	263	Yes	Yes	Yes	Yes	12 months 9% 24 months 5%	Yes	Stated that it is, but some data points appear to use different denominators – missing data?	High	Yes	Not applicable	Yes
Microsulis 2002	322	Uncertain	Uncertain	Uncertain	Uncertain	7%	Uncertain	Yes	Low	Yes	Yes	Yes
Meyer et al 1998	275	Yes	Uncertain	Yes	Yes	12 months 11% 24 months 17% 36 months 22% 60 months 46%	Yes	No. pts lost between randomisation and treatment are excluded, in addition some data points appear to use different denominators – missing data?	High	Yes for bleeding – uncertain for satisfaction	None found	Yes
Gervaise 1999	147	No	No	No – 27% of women given TCRE and 7% given TBEA were post-menopausal.	Yes	None	No	N/A	Medium	Uncertain	N/A	None
Pellicano 2002	96	Yes	Uncertain	Yes	Yes	29% at 2 yrs	No	No	High	Yes		
Romer 1998	20	Uncertain	Uncertain	Yes	Yes	None	Uncertain	N/A	Low	Uncertain	N/A	None
Soysal et al 2001	96	Yes	Uncertain	Yes	Yes	None	No	3 pts allocated to TBEA did not receive treatment and were excluded – no other LTFU	High	Yes	No	None
Zon-Rabelink 2001	139	Yes	Yes	Uncertain	Yes	2% at 2 yrs	No	No	Low	Yes	Not stated	None

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Table 4: Postoperative Amenorrhea - % (intent to treat %)*

	Immediate post/op		12 months		24 months		36 months		60 months	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
MEA Cooper et al 1999	-	-	40 (36)	40 (36)	-	-	47 (44)	41 (40)	-	-
MEA Microsulis 2002	-	-	55 (55)	46 (46)	-	-	-	-	-	-
TBEA Meyer et al 1998	-	-	15 (14)	27 (22)	15 (13)	26 (21)	15 (13)	26 (21)	23 (10)	33(14)
TBEA Gervaise et al 1999	25 (25)	38 (38)	-	-	-	-	36 (22)	38 (24)	-	-
TBEA Pellicano 2002	-	-	-	-	-	-	-	-	-	-
TBEA Romer 1998	-	-	40 (40)	31 (30)	-	-	-	-	-	-
TBEA Soysal et al 2001	-	-	11 (10)	17 (17)	-	-	-	-	-	-
TBEA Zon-Rabelink 2001	-	-	-	-	-	-	-	-	-	-

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Table 5: Results: Type of Postoperative Bleeding* - % (% intent to treat)*

	Length FU	Intervention	Spotting	Hypomenorrhoea	Eumenorrhoea	Menorrhagia	Metrorrhagia
Cooper et al 1999	12	MEA TCRE /RB	- -	- -	- -	- -	- -
	24	MEA TCRE /RB	- -	- -	- -	- -	- -
Microsulis 2002	12	MEA RB	- -	- -	- -	- -	- -
	12	TBEA RB	- -	- -	- -	- -	- -
Meyer et al 1998	24	TBEA RB	11(9) 13 (10)	45 (40) 30 (22)	21 (19) 21 (16)	9 (8) 12 (9)	- -
	36	TBEA RB	10 (8) 16 (12)	39 (33) 26 (19)	29 (24) 25 (18)	7 (6) 6 (4)	- -
	60	TBEA	10 (4)	38 (17)	25 (11)	5 (2)	-
		TCRE	11 (5)	25 (11)	28 (12)	3 (1)	-
Gervaise et al 1999	1	TBEA	25 (25)	22 (22)	38 (38)	11 (11)	4 (4)
		TCRE	38 (38)	31 (31)	13 (13)	12 (12)	5 (5)
	24	TBEA TCRE	36 (22) 38 (38)	16 (10) 28 (28)	34 (20) 17 (17)	9 (5) 15 (15)	4 (3) 2 (2)
Romer 1998	12	TBEA	-	50 (50)	10 (10)	-	-
		RB	-	60 (60)	10 (10)	-	-
Pellicano et al 2002	12	TBEA TCRE/RB	- -	- -	- -	- -	- -
	24	TBEA TCRE/ RB	- -	- -	- -	- -	- -
Soysal et al 2001	12	TBEA	-	-	-	-	-
		RB	-	-	-	-	-
Zon-Rabelink 2001	12	TBEA	-	-	-	-	-
		RB	-	-	-	-	-
	24	TBEA	-	-	-	-	-
		RB	-	-	-	-	-

*Spotting is slight discharge of blood through vagina.

Hypomenorrhoea is menstruation in which the flow is less than the normal amount, but at regular intervals, with the period of flow lasting the same or less time than average.

Eumenorrhoea is normal menstruation.

Menorrhagia is menstruation with an excessive flow, but at regular intervals and of usual duration.

Metrorrhagia is uterine bleeding, usually of variable amount, occurring at completely irregular but frequent intervals, and the period of flow is sometimes prolonged.

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Table 6: Postoperative Menstrual Pain - % (% intent to treat)

	Length FU	Intervention	Dysmen. Decreased	Dysmen. Same or worse	Dysmen.	Pain recurs	Mean pain score (mean, range)	Mild dysmen.	Moderate dysmen.	Severe dysmen.
Cooper et al 1999	12	MEA	-	21 (19)	-	-	1 (0-9)	-	-	-
		TCRE/RB	-	18 (16)	-	-	1 (0-7)	-	-	-
	24	MEA	-	18 (17)	-	-	0 (0, 6) +	-	-	-
		TCRE/RB	-	22 (22)	-	-	1 (0, 8)+	-	-	-
Microsulis 2002	12	MEA	-	-	31 (31)	-	-	-	-	-
		RB	-	-	31 (31)	-	-	-	-	-
Meyer et al 1998	12	TBEA	70 (64)	30 (27)*	-	-	-	-	-	-
		RB	75 (62)	25 (20)*	-	-	-	-	-	-
	24	TBEA	-	-	-	-	-	-	-	-
		RB	-	-	-	-	-	-	-	-
	36	TBEA	-	-	-	-	-	-	-	-
		RB	-	-	-	-	-	-	-	-
	60	TBEA	-	-	-	-	-	21 (9)	21 (9)	5 (4)
		RB	-	-	-	-	-	26 (12)	13 (5)	8 (4)
Gervaise et al 1999	1	TBEA	-	-	-	-	-	-	-	-
		TCRE	-	-	-	-	-	-	-	-
	24	TBEA	-	-	-	-	-	-	-	-
		TCRE	-	-	-	-	-	-	-	-
Pellicano et al 2002	12	TBEA	-	-	-	1 (2)	-	-	-	-
		TCRE/RB	-	-	-	7 (14)	-	-	-	-
	24	TBEA	-	-	-	2 (4)	-	-	-	-
		TCRE/RB	-	-	-	9 (18)	-	-	-	-
Romer 1998	12	TBEA	-	-	-	-	-	-	-	-
		RB	-	-	-	-	-	-	-	-
Soysal et al 2001	12	TBEA	-	-	-	-	-	-	-	-
		RB	-	-	-	-	-	-	-	-
Zon-Rabelink 2001	24	TBEA	-	-	-	-	-	-	-	-
		RB	-	-	-	-	-	-	-	-

* Calculated from given categories "Dysmenorrhoea unchanged" and "dysmenorrhoea increased."

+ Median, (25th, 75th percentile)

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Table 7: Satisfaction With Treatment and its Acceptability % (% intent to treat)

	Length FU	Intervention	Very satisfied	Satisfied	Not very satisfied	Not satisfied	Excellent	Good	Moderate	Totally or generally satisfied	Cure or acceptable improvement	Treatment acceptable	Menstrual loss acceptable	Recommend treatment ?
Cooper et al 1999	12	MEA	-	-	-	-	-	-	-	77 (69)	78 (70)	94 (84)	-	91 (81)
		TCRE/RB	-	-	-	-	-	-	-	75 (69)	76 (70)	90 (84)	-	89 (82)
	24	MEA	-	-	-	-	-	-	-	79 (74)	-	-	96 (89)	90 (84)
		TCRE/RB	-	-	-	-	-	-	-	67 (64)	-	-	88 (84)	90 (87)
Microsulis 2002	12	MEA	-	98 (98)*	-	2 (2)	-	-	-	-	-	99 (99)+	-	-
		RB	-	99 (99)*	-	1 (1)	-	-	-	-	-	100 (100)*	-	-
Meyer et al 1998	12	TBEA	86 (78)	10 (9)	-	4 (4)	-	-	-	-	-	-	-	-
		RB	87 (72)	12 (10)	-	1 (1)	-	-	-	-	-	-	-	-
	24	TBEA	86 (77)	10 (9)	-	4 (3)	-	-	-	-	-	-	-	-
		RB	87 (66)	11 (9)	-	2 (1)	-	-	-	-	-	-	-	-
36	TBEA	88 (72)	9 (6)	-	3 (2)	-	-	-	-	-	-	-	-	
	RB	92 (67)	6 (4)	-	2 (1)	-	-	-	-	-	-	-	-	
60	TBEA	-	93 (42)	-	-	-	-	-	-	-	-	-	-	
	RB	-	100 (44)	-	-	-	-	-	-	-	-	-	-	
Gervaise et al 1999	1	TBEA	-	-	-	-	-	-	-	-	-	-	-	-
		TCRE	-	-	-	-	-	-	-	-	-	-	-	-
	24	TBEA	-	-	-	-	-	-	-	-	-	-	-	-
		TCRE	-	-	-	-	-	-	-	-	-	-	-	-
3	TBEA	-	-	-	-	27 (59)	13 (28)	0	-	-	-	-	-	
		TCRE/RB	-	-	-	-	21 (42)	12 (24)	9 (18)	-	-	-	-	
Pellicano et al 2002	12	TBEA	-	-	-	-	20 (43)	10 (22)	5 (11)	-	-	-	-	
		TCRE/RB	-	-	-	-	12 (24)	12 (24)	10 (20)	-	-	-	-	
24	TBEA	-	-	-	-	16 (35)	12 (26)	5 (11)	-	-	-	-		
		TCRE+RB	-	-	-	-	2(4)	18 (36)	3 (6)	-	-	-		
Romer 1998	12	TBEA	-	100 (100)	-	-	-	-	-	-	-	-	-	
		RB	-	100 (100)	-	-	-	-	-	-	-	-	-	
Soysal et al 2001	12	TBEA	-	-	33 (31)	-	-	-	-	-	-	-	-	
		RB	-	-	39 (39)	-	-	-	-	-	-	-	-	
Zon Rabelink 2001	24	TBEA	-	80 (80)	-	-	-	-	-	-	-	-	-	
		RB	-	75 (73)	-	-	-	-	-	-	-	-	-	

**"Very satisfied" and "satisfied" combined.

+ "Acceptance of operation positive"

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Table 8: Preoperative and Postoperative Impact of Symptoms on Life % (% intent to treat)*

	Length FU	Intervention	Unable to work outside the home		2 or more days work absence		Severe impact on life		Moderate impact on life		Minor impact on life	
			Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
Cooper et al 1999	12	MEA TCRE/RB	-	-	36 (36) 37 (37)	3 (3) 7 (6)	-	-	-	-	-	-
	24	MEA TCRE/RB	-	-	-	-	-	-	-	-	-	-
Microsulis 2002	12	MEA RB	-	-	-	-	-	-	-	-	-	-
Meyer et al 1998	12	TBEA	40 (37)	4 (4)	-	-	70 (66)	3 (3)	-	-	-	-
		RB	38 (33)	3 (2)	-	-	79 (67)	2 (2)	-	-	-	-
	24	TBEA	40 (37)	1 (1)	-	-	-	-	-	-	-	-
		RB	38 (36)	3 (2)	-	-	-	-	-	-	-	-
	36	TBEA	40 (33)	4 (4)	-	-	70 (66)	2 (1)	28 (28)	8 (7)	2 (1)	90 (75)
		RB	38 (36)	5 (4)	-	-	79 (67)	2 (1)	20 (20)	8 (6)	1 (1)	90 (64)
60	TBEA RB	-	-	-	-	-	-	-	-	-	-	
Gervaise et al 1999	1	TBEA TCRE	-	-	-	-	-	-	-	-	-	-
	24	TBEA TCRE	-	-	-	-	-	-	-	-	-	-
Pellicano 2002	3	TBEA TCRE/RB	-	-	-	-	-	-	-	-	-	-
	12	TBEA	-	-	-	-	-	-	-	-	-	-
		TCRE/RB	-	-	-	-	-	-	-	-	-	-
24	TBEA RB	-	-	-	-	-	-	-	-	-	-	
Romer 1998	12	TBEA RB	-	-	-	-	-	-	-	-	-	
Soysal et al 2001	12	TBEA RB	-	-	-	-	-	-	-	-	-	
Zon Rabelink 2001	24	TBEA RB	-	-	-	-	-	-	-	-	-	

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Table 9: Operation Details

	Intervention	<30mins - % (%ITT)	>50mins - % (%ITT)	Mean (SD) Operating time -mins	Mean (SD) Theatre time-mins	Mean (SD) Post operative stay -hrs	Fully recovered in 4 wks - % (%ITT)	Return to normal domestic activities-days	Return to work-days	Resumption of sexual activity - days
Cooper et al 1999	MEA	-	-	11.4 (10.5)	20.9 (11.3)	13.4 (17.6)hrs	72 (67)	-	-	-
	TCRE/RB	-	-	15.0 (7.2)	26.2 (8.7)	16.7 (21.2)hrs	66 (61)	-	-	-
Microsulis 2002	MEA	-	-	3.45 (1.02)+	41.7(25.4)*	-	-	-	-	-
	RB	-	-	20.26 (15.6)+	50.0 (23.0)*	-	-	-	-	-
Meyer et al 1998	TBEA	71 (65)	2 (2)	-	-	-	-	-	-	-
	RB	27 (24)	18 (14)	-	-	-	-	-	-	-
Gervaise 1999	TBEA	100 (100)	-	20.3	-	-	-	-	-	-
	TCRE	53 (53)	-	44.8	-	-	-	-	-	-
Pellicano 200298	TBEA	-	-	24 (4.0)	-	1.0 (0.4)days	-	4.1 (+-1.8)	0.7 (+-0.1)	9.6 (+-0.6)
	TCRE/RB	-	-	37 (6.0)	-	1.3 (0.6)days	-	6.2 (+-3.3)	0.9 (+-0.3)	9.8 (+-0.7)
Romer 1998	TBEA	-	-	-	-	-	-	-	-	-
	RB	-	-	-	-	-	-	-	-	-
Soysal et al 2001	TBEA	-	-	11.5 (+-0.8)	-	-	-	-	-	-
	RB	-	-	37.3 (+-7.5)	-	-	-	-	-	-
Zon-Rabelink 2001	TBEA	-	-	-	-	-	-	-	-	-
	RB	-	-	-	-	-	-	-	-	-

* Given as "anaesthetic time" and excluding one centre whose patients all had GA.

+ Given as "treatment time"

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Table 12: Repeat Surgery – Number (%) [intent to treat %]*

	Length FU	Intervention	Total repeat surgery	Hysterectomy	TCRE	Other ablation
Cooper et al 1999	12	MEA n=116 TCRE/RB n=124	9 (9) [8] 11 (9) [8]	8 (7) [6] [^] 11 (9) [8] [^]	1 (1) [1] [*] -	1 (1) [1] 0 [#]
	24	MEA n= 120 TCRE/RB n= 129	- -	- -	- -	- -
Microsulis 2002	12	MEA n= 215 RB n= 107	1 (<1) [<1] 1 (1) [1]	1 (<1) [<1] 1 (1) [1]	0 0	0 0
	24	TBEA n= 125 RB n= 114	2 (2) [1] 3 (3) [2]	2 (2) [1] 3 (3) [2]	- -	- -
Meyer 1998	24	TBEA n=122 RB n= 105	4 (3) [3] 11 (10) [8]	4 (3) [3] 11 (10) [8]	- -	- -
	36	TBEA n=114 RB n=99	9 (8) [7] 14 (14) [10]	8 (7) [6] 14 (14) [10]	1 (1) [1] 0	- -
	60	TBEA n= 61 RB n= 61	15 (25) [11] 10 [†] (16) [7]	13 (21) [9] 7 (11) [5]	2 (3) [1] 2 (3) [1]	- -
	24	TBEA n=73 TCRE n=74	7 (10) [10] 6 (8) [8]	7 (10) [10] 1 (1) [1]	0 5 (7) [7]	- -
Pellicano et al 2002	12	TBEA n= 37 TCRE/RB n= 38	2 (5) [4] 4 (10) [8]	- -	- -	- -
	24	TBEA n=35 TCRE/RB n= 33	2 (6) [4] 5 (15) [10]	- -	- -	- -
Romer 1998	12	TBEA n= 10 RB n= 10	0 0	- -	- -	- -
Soysal 2001	12	TBEA n= 45 RB n= 48	4 (9) [8] 4 (8) [8]	4 (9) [8] 4 (8) [8]	- -	- -
	24	TBEA n= 77 RB n= 60	- -	- -	- -	- -

*In addition, 4 women had a TCRE as a primary procedure instead of MEA, due to equipment failure.
[#] 1 woman had MEA as her primary procedure having been allocated to TCRE group.
[^] In addition, 1 woman allocated to each group had hysterectomy as primary procedure.
[†] In addition, 2 women the TBEA group underwent hysterectomy at the time of the primary procedure (see Table 17)
^{*} Includes 1 D&C

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Table 26: Assumptions Used in the Model

Assumptions	Value	Source	Justification for source
Transitions			
Background death rate (Death)	0.001234	Life Tables	UK figures – starting age 42 as given in the studies included in this assessment, and increasing year on year.
Complications after hysterectomy	0.035	VALUE study ⁴⁶	Large UK observational study
Death after hysterectomy (direct cause)	0.00025	VALUE study ⁴⁶	Large UK observational study
Median length of complications after hysterectomy	2 months	Clinician estimate	
Length of convalescence period post hysterectomy	2 months	Lethaby et al 2002 ⁵²	Mean time of return to work/normal activities in systematic review of hysterectomy
Waiting time – mean (median)	94 (54) days	HES 2000/01 ⁷³ Table 5 Q07	UK data set
Complications after TCRE + rollerball			
Complications after TCRE + rollerball	0.0398	MISTLETOE study ⁵⁴	Large UK observational study
Death after TCRE + rollerball (direct cause)	0.0002	MISTLETOE study ⁵⁴	Large UK observational study
Complications after rollerball			
Complications after rollerball	0.0200	MISTLETOE study ⁵⁴	Large UK observational study
Death after rollerball (direct cause)	0	MISTLETOE study ⁵⁴	Large UK observational study
Complications due to TCRE alone			
Complications due to TCRE alone	0.0606	MISTLETOE study ⁵⁴	Large UK observational study
Death after TCRE alone	0.0003	MISTLETOE study ⁵⁴	Large UK observational study
Median length of complications following 1 st generation techniques	1 month	Professional estimate	
Complications due to MEA			
Complications due to MEA	0.0007	Case series 1433 women ⁷²	Large UK observational study
Death after MEA (direct cause)	0	Case series 1433 women ⁷²	Large UK observational study
Complications due to TBEA			
Complications due to TBEA	0.0023	See Table 23 page 88	European survey of complications in 5800 women
Death after TBEA (direct cause)	0	Adverse effect evidence in this report (Table 17 and 83)	Systematic review of controlled trial evidence
Median length of complications after 2 nd generation techniques	1 month	Professional estimate	
TBEA treatment failure (recurrent menorrhagia)			
TBEA treatment failure (recurrent menorrhagia)	0.11	Gervaise data (immediate post-op) ³⁶	Controlled trial. Only data available for immediate post-operative failure rates
TBEA treatment failure years 2 and 3			
TBEA treatment failure years 2 and 3	0.1	See Table 19	RCTs in this assessment
Proportion of women with recurrent menorrhagia who undergo hysterectomy			
Proportion of women with recurrent menorrhagia who undergo hysterectomy	0.6	5 year follow up women undergoing TCRE (vs medical management) ⁴³	Long term RCT data for TCRE
Proportion of women with recurrent menorrhagia who repeat ablation.			
Proportion of women with recurrent menorrhagia who repeat ablation.	0.4	5 year follow up women undergoing TCRE (vs medical management) ⁴³	Long term RCT data for TCRE

Table 26: Assumptions Used in the Model (cont'd)

Proportion of women with second EA failure who undergo hysterectomy within 6 months	0.9	Professional estimate	
Complications after repeat TCRE or rollerball ablation	Twice the rate after 1 st ablation	Maclean-Fraser et al 2002 ⁷⁰ and professional estimate	Comparative case series study of primary and repeat ablations. Only data on complications after repeat ablation.
Death after repeat TCRE/ rollerball ablation to	0.0003	MISTLETOE study ³⁴	Large UK audit
First year return of menorrhagia post TCRE/rollerball	0.11	Effectiveness data median at 12 months (Table 8 page 66)	RCT data, best available evidence
Second and third year return of menorrhagia following TCRE/RB	0.1	Effectiveness data median at 24 months (Table 8 page 66) plus repeat surgery rate (Table 19, page 86)	RCT data, best available evidence
First year return of menorrhagia post TBEA/MEA	0.11	Effectiveness data median at 12 months (Table 8 page 66)	RCT data, best available evidence
Second and third year return of menorrhagia following TBEA/MEA	0.1	Effectiveness data median at 24 months (Table 8 page 66) plus repeat surgery rate (Table 19, page 86)	RCT data, best available evidence
Discount rates			
Costs	6%	NICE	As recommended by the National Institute for Clinical Excellence (NICE).
Benefits	1.5%	NICE	As recommended by the National Institute for Clinical Excellence (NICE)
Health state utilities:	Value	Source	Justification for source
Chronic states			
Menorrhagia	0.55	Sculpher 1998 ³⁰	Median value based on interviews with 60 women with menorrhagia
Premenopausal following recovery from successful TCRE	0.9	Sculpher 1998 ³⁰	Median value based on interviews with 60 women with menorrhagia
Premenopausal following recovery from hysterectomy	0.95	Sculpher 1998 ³⁰	Median value based on interviews with 60 women with menorrhagia
Dead	0		Usual value

Table 26: Assumptions Used in the Model (cont'd)

Temporary States			
Complications after Hysterectomy	0.55	Assumption	Same as menorrhagia
Hysterectomy	0.63	Assumption	One third less than recovery after hysterectomy
Convalescence after Hysterectomy	0.95	Sculpher1998 ³⁰	Median value based on interviews with 60 women with menorrhagia
MEA/ Convalescence after MEA	0.85	Sculpher1998 ³⁰	Convalescent states post ablation assumed to be the same for all types of ablation. Based on the Sculpher1998 ³⁰ score for TCRE
TBEA/ Convalescence after TBEA	0.85	Sculpher1998 ³⁰	Convalescent states post ablation assumed to be the same for all types of ablation. Based on the Sculpher1998 ³⁰ score for TCRE
TCRE and rollerball/ Convalescence after TCRE and rollerball	0.85	Sculpher1998 ³⁰	Median value based on interviews with 60 women with menorrhagia

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Table 27: Surgical Management: Assumptions Used in the Cost-Effectiveness Model

Procedure	Data	Source	Justification
Abdominal Hysterectomy			
Length of stay (median)	4 days	Local median waiting time (Mid Devon PCT residents) and expert opinion	UK data based on all women, uncomplicated menorrhagia will be shorter
Day cases	0%	HES 2000/01 table5 Q07	UK data set
Duration of surgery	59 mins	Lethaby 2000 ²²	Good quality systematic review
% under general anaesthetic	100%	Assumed	
1st generation EA			
Waiting time – mean (median)	79 (45)	HES 2000/01 table5 Q17	UK data set
Length of stay – weighted mean	2.0	Lethaby 2000 ²²	Good quality systematic review
Day cases	60%	HES 2000/01 table5 Q17	UK data set
Duration of surgery - TCRE	40.9 mins	Median from Effectiveness data in this report (Table 16 page 80)	RCT data – best available evidence
Duration of surgery – RB	50 mins	Effectiveness data in this report (Table 16 page 80)	RCT data – best available evidence
Duration of surgery – TCRE/RB	31.6 mins	Median from Effectiveness data in this report (Table 16 page 80)	RCT data – best available evidence
% under General anaesthetic	78%	Lethaby 2002 ⁹	Systematic review
2nd generation EA			
Waiting time – mean (median)	80 (50)	HES 2000/01 table5 Q16	UK data set
Length of stay – mean (median)	1.6 (1)	HES 2000/01 table5 Q16	UK data set
Day cases	65%	HES 2000/01 table5 Q16	UK data set
Duration of surgery MEA	31.3 mins	Effectiveness data for theatre in this report (Table 16 page 80)	Median from RCT data – best available evidence
Duration of surgery TBEA	18.6 mins	Effectiveness data for theatre in this report (Table 16 page 80)	Median from RCT data – best available evidence
% under general anaesthetic	52%	Bain et al 2001 ²⁷	Partially randomised study of LA vs. GA among 98 women in the UK

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Table 28: Thermal Balloon Equipment Costs*

Equipment	Cost (£)	Life-time	Source	Notes
Thermal Balloon				
Cavaterm™ control unit	3990	10 years	Manufacturer	
Cavaterm™ disposable balloon catheter	280	Single use	Manufacturer	
Thermachoice™ generator	6000	10 years	Manufacturer	Cost from manufacturer, life time assumed.
Thermachoice™ disposable balloon catheter	335-350	Single use	Manufacturer	The list price is £350, manufacturers informs that due to various discounts, £335 is the UK average price
Thermachoice™ cost of surgical devices	290	Per patient	Manufacturer	Calculated from cost given in Euros

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Table 29: Staff Costs

Staff	Cost/minute (£)	Source
Surgeon (consultant)	0.77	Southampton University Hospital
Anaesthetist (consultant)	0.77	Southampton University Hospital
Anaesthetist nurse (Grade H)	0.28	Southampton University Hospital
Instrument nurse (Grade G)	0.25	Southampton University Hospital
Trolley nurse (Grade G)	0.25	Southampton University Hospital
Circulating nurse (Grade G)	0.25	Southampton University Hospital
Recovery nurse	0.25	Southampton University Hospital
Senior house officer	0.29	Southampton University Hospital
Registrar	0.26	Southampton University Hospital
Nurse practitioner	0.28	Southampton University Hospital

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Table 30: Costs of Anesthesia and Ward Costs

Resource	Cost £	Source
General anaesthetic	1.08 per minute	Microsulis submission
Local anaesthetic	7.7 per minute	Microsulis submission
Inpatient bed	231 per day	Southampton University Hospital – estimated from own cost +50%

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Table 31: Total Procedure Costs

Procedure	Baseline price (£)
Hysterectomy	2096
TCRE	1110
TCRE/RB	1027
RB	1190
MEA	942
TBEA	826

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