

GLOBAL VALUE DOSSIER SITE OF SERVICE SHIFT FOR GYNECOLOGY PROCEDURES

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List of Abbreviations

ACOG	American College of Obstetricians and Gynecologists
AE	Adverse Event
AUB	Abnormal Uterine Bleeding
CI	Confidence Interval
D&C	Dilation and Curettage
D&E	Dilation and Evacuation
ER	Emergency Room
GBP	Pound sterling
GnRH	Gonadotropin-Releasing Hormone
GVD	Global Value Dossier
HMB	Heavy Menstrual Bleeding
HOPD	Hospital Outpatient Department
ICER	Incremental Cost-Effectiveness Ratio
IMB	Intermenstrual Bleeding
IUA	Intrauterine Adhesion
MEPS	Medical Expenditures Panel Survey
mHTR	Mechanical Hysteroscopic Tissue Removal
MRI	Magnetic Resonance Imaging
NHS	National Health Service
OPT	Outpatient versus Inpatient Polyp Treatment (trial)
OR	Odds Ratio
PALM–COEIN	Polyp, Adenomyosis, Leiomyoma, Malignancy–Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, Not yet classified
PMB	Postmenopausal Bleeding
QALY	Quality-adjusted Life Year
QoL	Quality of Life
RCT	Randomized Controlled Trial
RPOC	Retained Products of Conception
RR	Relative Risk
SCPMG	Southern California Permanente Medical Group
SD	Standard Deviation
SIS	Saline Infusion Sonohysterography
TVUS	Transvaginal Ultrasonography
UAE	Uterine Artery Embolization
UK	United Kingdom

UPS	Uterine-Preserving Surgery
US	United States of America
USD	United States Dollar
VAS	Visual Analog Scale

1 Executive Summary

Surgical procedures are generally associated with lower costs if performed in a physician's office than if performed in an operating room.^{1,2,3}

Published evidence suggests clinical and economic benefits associated with shifting gynecologic surgery for structural causes of abnormal uterine bleeding (AUB) from hospitals to gynecologists' offices. In hospitals, these surgical procedures are performed under general anesthesia but they can be performed with local or no anesthesia in the office. The clinical benefits of this site of service shift are reviewed in this Global Value Dossier (GVD). In addition, the safety of office gynecologic procedures and patients' treatment satisfaction are investigated. Emphasis is placed on evidence involving mechanical hysteroscopic tissue removal (mHTR) devices, especially the TruClear™ system as a successful treatment device.

1.1 Clinical Impact of the Site of Service Shift

Clinical impact: Gynecologic surgery in the office for the treatment of AUB is generally as successful as surgery in the hospital.

Three studies, one from the UK and two from the US, provided a direct comparison between sites of service for gynecologic surgery. In a multi-center US trial, mHTR performance in the office was compared with that in ambulatory surgical centers (ASCs) and hospital outpatient departments (HOPD).¹¹⁶ Office, compared with ASC/HOPD, procedures removed more pathologies by patient (97% versus 95%) and more fibroids (95% versus 86%) and almost as many polyps (99% versus 100%).¹¹⁶ Women treated in the office spent significantly less time in post-anesthesia care units (37 min versus 57 min, $p=0.0263$) and were significantly less likely to receive general anesthesia (7% versus 78%, $p<0.0001$). This study demonstrated the clinical success of mHTR and of performing gynecologic surgery in the office.

A further US study comparing mHTR in the office and the ASC setting showed that mHTR removed similar levels of pathology in both settings.¹¹⁷ In the office, 97% of all pathologies (100% in ASCs), 94% of fibroids (100% in ASCs) and 100% of polyps (100% in ASCs) were removed. As no difference was statistically significant, mHTR, similarly to the results summarized above, proved to be clinically successful with little difference between settings. This study demonstrated a high level of clinical success in removing intrauterine pathologies can be achieved in the office.

The UK OPT trial compared outpatient with inpatient polypectomy.⁴² Outpatient polypectomy was performed under local anesthesia, usually directly after diagnosis, which made the outpatient setting similar to the office in the US. At 6 months, 73% of women treated in the office/outpatient setting reported successful treatment response, compared with 80% of inpatients. In the office/outpatient setting, polypectomy was performed slightly faster (11 min versus 12 min) although this difference was not statistically significant. Overall, office/outpatient treatment was non-inferior to inpatient polypectomy.

Safety: Gynecologic surgery performed in the office is safe and has a low rate of complications, similar to the rate observed in the hospital. Effective approaches exist to manage pain in office procedures.

Several protocols exist to implement gynecologic procedures safely in the office setting.^{1,5,6} In a head-to-head comparison conducted by Scheiber *et al.*, mHTR was associated with adverse event rates of 1.6% in the ASC/HOPD and of 3.6% in the office ($p=0.4143$).¹¹⁶ All adverse events were mild and resolved spontaneously so mHTR was considered to be safe in both the ASC/HOPD setting and the office. The other head-to-head comparisons reported

lower complication rates in the office, of 0% versus 2.0% and 2.4% versus 3.1%, respectively.^{42,117} Single-arm studies confirmed the generally low rate of complications in the office.^{124,125,126} However, office treatment was associated with higher levels of pain during the procedure as less anesthesia are used than in the hospital settings where women are treated under general anesthesia. Women treated in the office/outpatient setting reported higher pain scores associated with polypectomy than if treated in the inpatient setting.^{42,62} Up to 32% of patients treated in the office reported unacceptable levels of pain, with the surgeon's lack of hysteroscopic experience as a statistically significant predictor of unacceptable pain during the procedure and cramps after discharge, and dysmenorrhea as a statistically significant predictor of cramps after discharge.^{63,128} Effective, often multimodal approaches have been developed to manage pain in the office and relatively simple solutions, such as reducing waiting times or playing music during the procedure, may help reduce patient anxiety and pain.^{123,127}

Patient satisfaction: Women report similar satisfaction with office and hospital procedures.

Head-to-head comparisons showed that satisfaction with office treatment is similar to satisfaction with hospital treatment. Rubino *et al.* reported similar improvements of quality of life in both settings.¹¹⁷ The proportion of women satisfied with their treatment was not statistically different between the settings higher and similar proportions of women would undergo future treatment or recommend the procedure to a friend for both settings.¹¹⁷ In the UK, office treatment was associated with slightly higher though not statistically significant differences in quality of life at 6 months.⁴ Again, similar proportions of women would undergo future treatment or recommend the procedure to a friend. Among US women presenting with early pregnancy failure, almost 70% chose the office over the operating room although treatment satisfaction did not differ between treatment settings.⁹⁰ Single-arm studies confirmed these findings and reported that generally >90% of women treated in an office preferred office over inpatient procedures and would undergo the procedure again or recommend it to a friend.^{124,129}

1.2 Health Economic Impact of the Site of Service Shift

Shifting gynecologic surgery from hospitals to offices is associated with substantial cost savings for healthcare payers and providers, particularly because operating room and anesthesia costs can be avoided.

A cost-effectiveness analysis was conducted as part of the OPT trial.¹³¹ The analysis was conducted from the perspective of the UK NHS and was based on UK reference costs, which were applied to the resource use observed in the OPT trial. Patient-reported treatment effectiveness and quality of life were used to assess the benefit of office/outpatient and inpatient treatment. Office/outpatient treatment was associated with absolute cost savings of GBP 660 (95% confidence interval [CI] 516 to 781) and GBP 669 (95% CI 517 to 833) at 6 and 12 months, respectively.¹³¹ Despite higher costs, inpatient treatment was associated only with small gains in patient-reported effectiveness and quality-adjusted life years (QALYs). Consequently, incremental cost-effectiveness ratios of GBP 1,1 million and GBP 446,000 per QALY gained on the inpatient arm were obtained.¹³¹ These values are substantially higher than commonly quoted willingness-to-pay thresholds in the UK, indicating that office/outpatient treatment is likely to be cost-effective compared with inpatient treatment. Only at a willingness-to-pay threshold of GBP 90,000 per QALY gained would treatment in the two different settings start to become equally cost-effective.

Cost comparisons, which mostly used setting-specific charges and fees, confirmed the potential for cost savings to healthcare payers and providers associated with conducting gynecologic surgery in the office. Estimates of cost savings ranged from 18% in a

comparison of an office/outpatient with a see-and-treat approach for AUB from the perspective of the UK NHS to >90% in a comparison of office with inpatient diagnostic hysteroscopy from the perspective of a US healthcare payer.^{126,135} Key drivers of cost savings in the office were reduced or even absent costs for operating room time and staff as well as for anesthesia and anesthesiologists.^{90,129,134,135}

1.3 Conclusion

Overall, the available published evidence demonstrates that office gynecologic surgery is feasible, successful and safe for a range of indications and using a range of procedures, including particularly mechanical hysteroscopic tissue removal (mHTR). The clinical success in removal of intrauterine pathologies is comparable between office and inpatient settings. Unlike inpatient procedures, no general anesthesia is required during office procedures although several effective, multimodal approaches to pain management in the office have been developed.

Importantly, there is clear evidence that office treatment is associated with substantial cost savings, to both healthcare payers and providers, compared with inpatient treatment. Combined with the clinical success of office procedures, these findings imply that shifting gynecologic surgery from the operating room to the office may help healthcare systems to provide women with high-quality treatment at reduced costs.

2 Current Care Paradigm

Gynecologic surgical procedures are increasingly shifting away from operating rooms and inpatient settings to the physician's office.^{1,2} This site of service shift is part of a broader trend, in the US and elsewhere, to reduce healthcare expenditure while improving treatment quality and patient satisfaction.^{1,2} Analyses of price variation by site of service have identified much higher costs (from an additional 21% up to an additional 258%) for the same procedure when performed in a hospital outpatient setting compared with the office, thereby identifying site of service shifts as a promising way to rein in costs.³

This Global Value Dossier (GVD) documents the site of service shift to the office for a subset of gynecological surgery procedures, namely procedures for the diagnosis and removal of intrauterine pathology in the treatment of abnormal uterine bleeding (AUB). These procedures can be performed successfully and safely in the office (Sections 4.1 and 4.2) where they are associated with improved patient satisfaction (Section 4.3) and cost savings (Section 5) compared with hospital or outpatient procedures.² It should be noted at the outset that office procedures are preferred over inpatient procedures by most women: In the Outpatient versus Inpatient Polyp Treatment (OPT) trial, 81% of 399 women presenting with AUB and an endometrial polyp expressed a preference for office treatment.⁴ In additional qualitative interviews, women showed a willingness to accept higher levels of short-term pain experienced in the office for a faster response to their medical problem. With regard to safety of office procedures, some variation in clinical practice, particularly of pain management, is still observed but standards and recommendations, including those published by the American College of Obstetricians and Gynecologists (ACOG) and the Institute of Medicine, are available to perform office gynecologic procedures safely and successfully.^{5,6}

This trend towards the office was set by hysteroscopy. In 1992, Gimpelson suggested that hysteroscopy be moved to the office to save time and money for both patients and physicians.⁷ He listed fibroids, endometrial polyps and retained products of conception (RPOC) as indications that could easily be diagnosed and treated in offices. In 2000, Isaacson published a review of indications easily diagnosed and treated in office hysteroscopy and urged gynecologists to use office hysteroscopy to save time and money.⁸ He also discussed office hysteroscopy as a means to improve patient outcomes, particularly as office hysteroscopy does require no or only local anesthesia. In a review of office hysteroscopic procedures between 2003 to 2009, Di Spiezio Sardo *et al.* reviewed the scientific literature and concluded that office hysteroscopy was successfully used for a range of treatment goals, including tubal sterilization, metroplasty, emptying hematometra and removal of uterovaginal packing.⁹ In 2016, Mairos and Di Martino concluded that office hysteroscopy is the gold standard surgical treatment for intrauterine pathology.¹⁰ They concluded that office hysteroscopy was an important contribution to patient safety as the risk of adverse events (AEs) associated with inpatient admission and of complications associated with general or regional anesthesia was reduced.

The first section provides the context for this GVD and outlines the clinical and economic burden of AUB and its causes (Section 2.1). Treatment strategies, including current guidelines, and surgical procedures to diagnose and remove intrauterine pathological tissue are discussed in Section 2.2. A particularly successful treatment device, the TruClear™ system for mechanical hysteroscopic tissue removal (mHTR), is presented in Section 3. Treatment is increasingly shifting to offices and the clinical benefits of this shift are described in Section 4. As the shift to offices is not only clinically but also economically beneficial, the health economic impact of treating women in the office, not in the operating room, is presented in Section 5.

2.1 Burden of Abnormal Uterine Bleeding and Intrauterine Pathology

Key messages

Abnormal uterine bleeding affects a large number of women worldwide and is associated with a substantial clinical and economic burden.

A number of factors, including endometrial polyps, uterine fibroids and retained products of conception, can cause abnormal uterine bleeding. Treatment for these structural causes is generally successful and has the potential to reduce the burden on women and healthcare systems.

As part of recent market dynamics, a shift in certain gynecological procedures to the office has been observed. This shift can result in clinical and economic benefits to patients and healthcare systems.

Short summary

Abnormal uterine bleeding affects between 9 to 14% of women during their reproductive years and is associated with increased healthcare resource use, direct and indirect costs as well as decreased quality of life.^{16,18}

Endometrial polyps, uterine fibroids and retained products of conception are among the main structural causes of abnormal uterine bleeding.^{11,12} The prevalence of endometrial polyps ranges from 8 to 35% and that of uterine fibroids ranges from 3 to 51% while retained products of conception complicate an estimated 1% of all pregnancies.^{39,40,41,44,52} All three conditions are associated with impaired fertility and reduced quality of life in affected women. Treatment of fibroids alone has been estimated to cost USD 5.9 to 34.4 billion per year in the US.⁵⁸

The clinical and economic burden of abnormal uterine bleeding can be reduced when treatment is timely, convenient, clinically effective and safe. Women and healthcare systems stand to benefit from effective and safe treatment for these conditions.^{2,19,24,61} Additional clinical and economic benefits for patients and payers are contributed by recent shifts of gynecologic surgery, including surgery for intrauterine pathologies, to offices.^{2,24}

AUB is a common condition in women before and after menopause. AUB includes both heavy menstrual bleeding (HMB) as well as intermenstrual bleeding (IMB). Bleeding is abnormal when it occurs irregularly, is untimely, or is associated with excessive blood loss.^{11,12} AUB may cause iron deficiency, fatigue, mood disorders or social embarrassment, thereby affecting women's general health and quality of life (QoL).^{13,14,15}

AUB may be experienced by between 9 to 30% of women between menarche and menopause.^{12,15,16} In a US study using the full-year household component of the Medical Expenditures Panel Survey (MEPS) from 2002 to 2010, the number of non-pregnant women of reproductive age affected by AUB (defined by International Classification of Diseases-9 code group 626) was extrapolated to the corresponding total US population.¹⁷ Of the 57,484 women included from MEPS, 2.4% reported AUB in an annual survey. Extrapolated to the corresponding US population of 56.2 million (95% confidence interval [CI]: 54.3 to 58.0 million), an average of 1.4 million (95% CI: 1.3 to 1.5 million) non-pregnant US women of reproductive age were affected by AUB. In this study, AUB was also found to be associated

with an increased likelihood of poor physical (odds ratio [OR] 1.3 [95% CI 1.1 to 1.6]) and mental (OR 1.3 [95% CI 1.1 to 1.5]) health as measured by the SF-12 Physical and Mental Component Scores.

AUB is associated with QoL losses and significant costs to healthcare systems.¹⁵ US women who reported heavier blood flow than 12 months before were more likely to visit their general physician (OR 1.5 [95% CI 1.2 to 1.9]) or the emergency room (ER) (OR 1.8 [95% CI 1.4 to 2.4]) and to require any surgery (OR 1.6 [95% CI 1.1 to 2.2]) than women whose blood flow was lighter or steady.¹³ A further US study confirmed these results and reported incidence rate ratios of 2.7 (95% CI 2.6 to 2.8) for hospitalizations, 1.4 (95% CI 1.3 to 1.4) for ER visits and of 1.3 (95% CI 1.3 to 1.3) for outpatient visits in women with HMB compared with women without HMB.¹⁸ On average, annual costs of USD 6,439 (standard deviation [SD]: USD 8,682) were recorded for women with HMB, considerably more than for women without HMB (USD 3,832 [SD: USD 8,308], $p < 0.001$). Total work loss costs were also higher for women with HMB (USD 623 [SD 1,593]) than without (USD 549 [SD 2,480], $p < 0.001$).¹⁸

The personal and economic burden of AUB necessitates adequate treatment. To aid treatment and therapy decisions, the PALM–COEIN classification system for causes of AUB was developed (Table 2-1), which uses medical history, physical examination and, where appropriate, laboratory testing and imaging techniques for diagnosis.¹⁹

Table 2-1 PALM–COEIN classifications system for causes of AUB²⁰

PALM (structural causes)	COEIN (non-structural causes)
Polyp (AUB-P)	Coagulopathy (AUB-C)
Adenomyosis (AUB-A)	Ovulatory dysfunction (AUB-O)
Leiomyoma (AUB-L)	Endometrial (AUB-E)
Submucosal myoma (AUB-L _{sm})	Iatrogenic (AUB-I)
Other myoma (AUB-L _o)	Not yet classified (AUB-N)
Malignancy and hyperplasia (AUB-M)	

Treatment options for AUB include using expectant management, medical therapy or surgical procedures.^{20,21} Surgical procedures are particularly relevant to the treatment of structural causes of AUB (PALM), notably for polyps, fibroids (also called leiomyomas or myomas) and malignancy/hyperplasia. For these conditions, current technology allows removal of intrauterine pathology quickly, safely and thoroughly, possibly in the same step as diagnosing the conditions, e.g. when using hysteroscopy, and in offices.^{19,20,21} The same technologies can be used to remove RPOC, e.g. after miscarriage.^{22,23}

Advances in technology and the commitment to improving patient outcomes while reducing treatment costs have led to a shift in the setting of gynecologic procedures, from the operating room to offices.^{19,24,25} Procedures to diagnose and remove pathologic intrauterine tissue have been a prominent part of this site of service shift and have been shown to be a successful, safe treatment of AUB and its structural causes.^{1,2,19,25,26,27}

2.1.1 Burden of Endometrial Polyps

Endometrial polyps are localized outgrowths of the endometrium, containing endometrial glands, blood vessels and stroma (Table 2-2). The outgrowth can be pedunculated or sessile and usually extends towards the internal cervical os although some polyps project through the external cervical os, into the vagina.^{28,29,30} The etiology of endometrial polyps is not fully understood but likely multifactorial, possibly including genetic factors such as anomalies on chromosomes 6 and 12.^{29,31,32} Polyps likely originate as stromal or glandular overgrowths and may be associated with overexpression of estrogen and progesterone receptors.^{29,30}

Endometrial polyps are usually asymptomatic but they have some oncogenic potential. A 2010 review reported a prevalence of 0.2 to 23.8% for premalignant and of 0 to 12.9% for malignant tissue in endometrial polyps, with a pooled prevalence of 0.8% and 3.1%, respectively.³³ Higher age and post-menopausal status as well as AUB were identified as possible risk factors for malignancy. These results were confirmed by a further 2010 review.³⁴ For premalignant and malignant polyps, a pooled prevalence of 5.4% and 1.7% were reported for postmenopausal and premenopausal women (relative risk [RR] 3.9 [95% CI 2.9 to 5.1]), respectively. Women with symptomatic bleeding were more likely to have neoplasia in their polyps than women without symptomatic bleeding (4.2% versus 2.2%, RR 2.0 [95% CI 1.2 to 3.1]).³⁴

Table 2-2 Histological subtypes of endometrial polyps³²

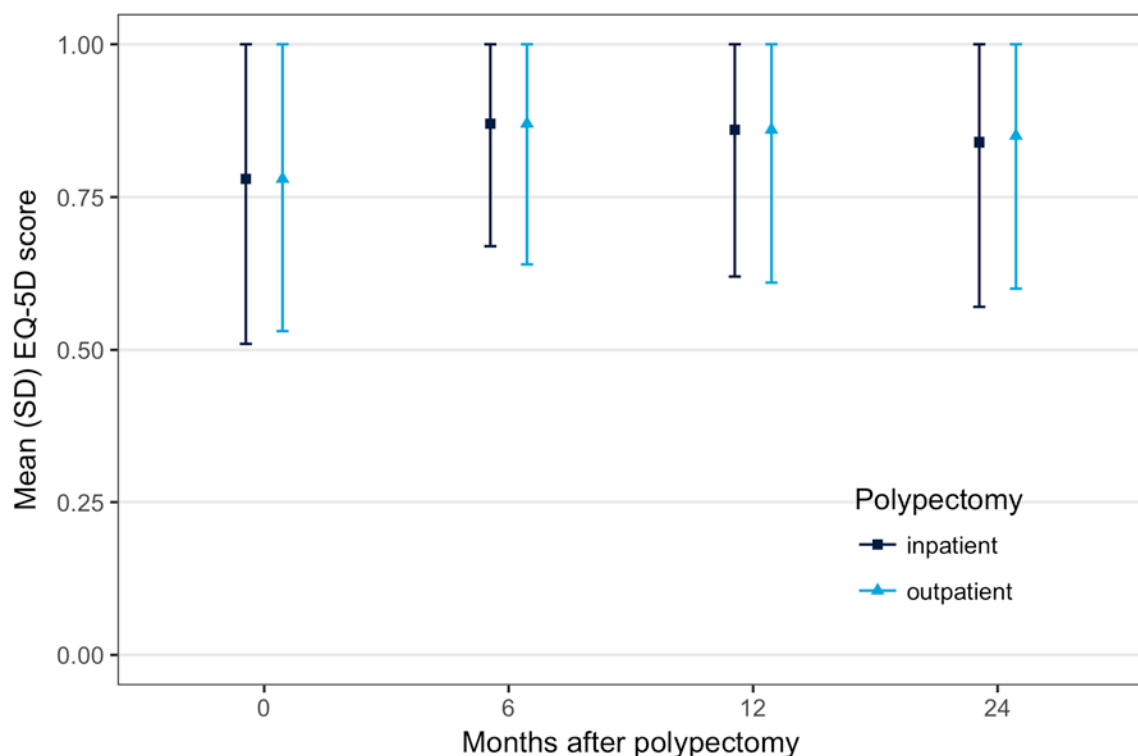
Subtype	Explanation
Adenomyomatous	Varying amounts of smooth muscle cells and fibrous tissue; "atypical" forms with benign endometrial glands and stroma; likelihood of association with endometrial cancer transformation approx. 9%
Atrophic	Typical after menopause; usually regressive alterations of functional or hyperplastic type
Functional	Glandular alterations similar to surrounding endometrium; respond to hormonal stimuli of menstrual cycle
Hyperplastic	Arise in endometrial layer because of unbalanced estrogen stimulation; associated with diffuse endometrial hyperplasia
Pseudopolyps	Small sessile lesions; detected only in secretory phase of menstrual cycle and disappear with menstrual flow

Endometrial polyps can be associated with impaired fertility. The exact mechanisms are not fully understood but reduced levels of molecular markers of endometrial receptivity, mechanical interference with sperm transportation and increased inflammation in the uterine cavity have been suggested as possible causes.^{35,36,37} However, fertility was found to improve after hysteroscopic polypectomy. In a randomized controlled trial (RCT) of 215 Spanish women who had been infertile for ≥ 24 months, women undergoing hysteroscopic polypectomy were compared with women who received only a polyp biopsy.³⁸ Women who underwent polypectomy were more likely than untreated women to become pregnant (63% versus 28%, RR 2.1 [95% CI 1.5 to 2.9]) and, after intrauterine insemination, treated women became pregnant faster than untreated women. A review of the surgical management of endometrial polyps confirmed these results, reporting post-polypectomy natural conception rates of approximately 40 to 80%, even in previously subfertile women.³⁶

The prevalence of endometrial polyps depends on the study population.^{29,33,36} In an analysis of Danish Civil Registry data, an overall prevalence of 7.8% (95% CI 5.6 to 9.9%) was observed, with higher prevalence in post- (11.8%) than in pre-menopausal (5.8%) women.³⁹ In infertile women presenting for in vitro fertilization, a prevalence of 32% was observed, similar to the 35% observed in infertile women undergoing hysteroscopy as part of an infertility work-up.^{40,41}

QoL is impaired for women with symptomatic polyps, usually due to AUB. In a trial comparing QoL for women treated with in- and outpatient polypectomy, both groups reported a baseline EQ-5D score of 0.78 (ranging from -0.59 as the worst imaginable to 1 as the best imaginable health state).⁴² After polyp removal under direct hysteroscopic vision, using miniature mechanical or electrosurgical instruments, treatment was found to improve QoL. In both groups, QoL increased in response to polypectomy and remained above baseline 2 years after treatment, with slightly higher long-term QoL for outpatient-treated patients (Figure 2-1).

Figure 2-1 QoL scores before and after polypectomy



Source: Cooper *et al.* (2015)⁴²

2.1.2 Burden of RPOC

A second type of pathologic intrauterine tissue that can cause AUB is RPOC. The term describes fetal or placental tissue that develops after conception but persists after the pregnancy was terminated or delivered.^{43,44}

In addition to its association with AUB, RPOC is a risk factor for infertility. While the mechanism is not fully understood, a suggested pathway is that the trophoblastic tissue leads to formation of intrauterine adhesions (IUA), thereby impairing fertility.⁴⁵ Similar to endometrial polyps, resection of RPOC can improve fertility. In a study of women treated for RPOC with an operative hysteroscope or a bipolar resectoscope, 50% achieved subsequent

pregnancy, within a median 29 weeks (range 2 to 295).⁴⁶ Of the women who become pregnant, 89.0% had either vaginal or cesarean delivery of their pregnancy. The cause of RPOC was not related to the success of surgical treatment for improvement of fertility outcomes. In women undergoing uterine re-evacuation with dilation and curettage (D&C) or tissue removal via hysteroscopic resection, conception rates of 87.8% and 90.3% were reported for women with a previous spontaneous vaginal delivery and abortion, respectively.⁴⁷

As RPOC is difficult to diagnose, estimates of its prevalence and incidence are associated with substantial uncertainty.⁴⁸ RPOC is estimated to complicate approximately 1% of all pregnancies and is more common after early pregnancy termination than after vaginal or cesarean delivery.⁴⁴ A higher prevalence was reported in a prospective study following-up women after delivery or miscarriage.⁴⁹ At a median time of 6 weeks after delivery/miscarriage, a sonographic examination was performed and showed a prevalence of 6.3% for residual trophoblastic tissue (Table 2-3). In an additional 5.7% of women, RPOC was considered possible. RPOC was particularly prevalent after 2nd trimester pregnancy loss, with 40.0% of women with highly suspicious and 36.7% with possibly trophoblastic tissue.

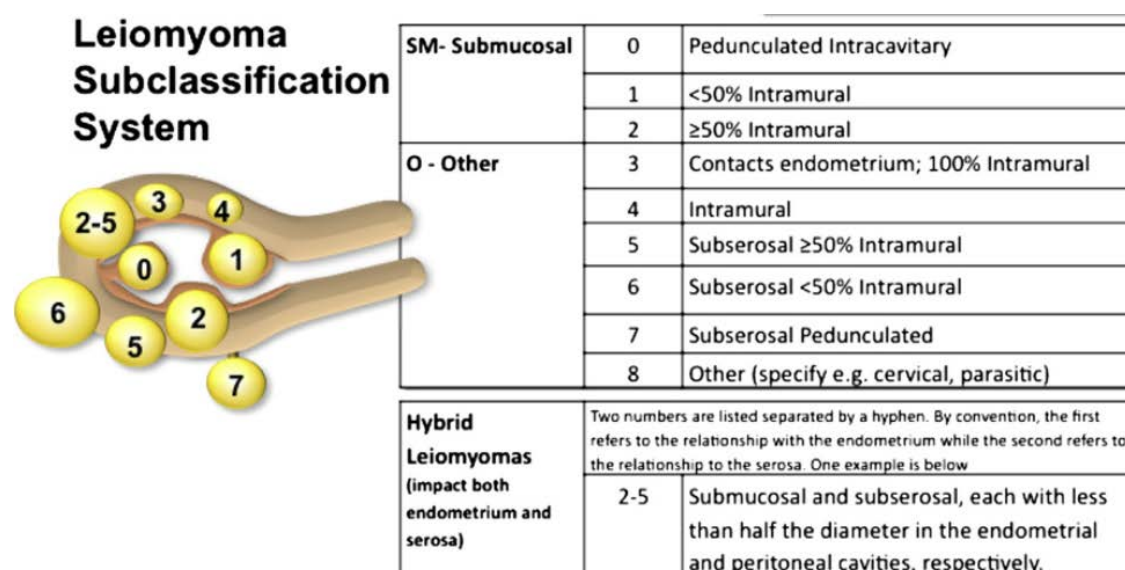
Table 2-3 **Prevalence of trophoblastic tissue after delivery/miscarriage⁴⁹**

Last pregnancy	N	Sonographic findings on residual tissue (%)		
		Highly suspicious	Possible	Absent
Termination of pregnancy	25	36.0	24.0	40.0
1 st trimester pregnancy loss	157	17.8	10.8	71.3
2 nd trimester pregnancy loss	15	40.0	36.7	33.3
3 rd trimester deliveries	873	2.7	3.9	93.4
<i>Total</i>	1,070	6.3	5.7	88.0

2.1.3 **Burden of Fibroids**

Uterine fibroids are monoclonal tumors that originate in the muscular layer of the uterus (the myometrium). The cellular origins of fibroids are not fully understood but stem cell mutation during hormone-induced growth cycles, followed by involution of myometrial smooth-muscle cells, are a likely cause.^{50,51} Some current classification systems distinguish fibroids subtypes by their location in the myometrium, with submucosal, intramural and subserosal fibroids as the main subtypes (Figure 2-2).²⁰

Figure 2-2 FIGO leiomyoma subclassification system



FIGO, International Federation of Gynecology and Obstetrics. Reproduced from AAGL (2012a)²⁰.

Fibroids are a common condition although prevalence and incidence vary by geography and ethnicity.²⁰ In the US, a prevalence of 35% and 51%, respectively, was reported for women with and without a previous diagnosis of fibroids.⁵² By the age of 50 years, the cumulative incidence of fibroids was estimated at nearly 70% for white and more than 80% for black women. In 2004, an estimated 443,000 women with employer-sponsored insurance in the US had clinically significant fibroids.⁵³

While fibroids usually grow slowly and are rarely malignant, they are associated with AUB and reduced fertility, with 4.1% and 5.9% of women with ≥2 and ≥3 recurrent pregnancy losses, respectively, being diagnosed with fibroids.^{50,54} In a 2009 meta-analysis, the clinical pregnancy rate was lower (RR 0.85 [95% CI 0.73 to 0.98]) and the spontaneous abortion rate higher (RR 1.68 [95% CI 1.37 to 2.05]) in women with fibroids than without.⁵⁵ Surgical removal of fibroids can restore fertility, at least in some patients. In the first 3 years after myomectomy, the cumulative probability of conception was 49%, 36% and 33% in women with pedunculated submucous, sessile submucous and intramural fibroids, respectively.⁵⁶ Of note was the 3-year cumulative conception rate of 43% observed in previously infertile women. Similarly, after hysteroscopic resection of submucous fibroids, women with recurrent miscarriage had a decreased probability of mid-trimester loss (22% before versus 0% after resection, $p < 0.01$) and an increased probability of giving live birth (23% before versus 52% after resection, $p < 0.05$).⁵⁷

Fibroids are associated with considerable healthcare costs. For 2010, the estimated direct costs of fibroids, including medications, inpatient admission or outpatient visits as well as surgery, were USD 4.1–9.4 billion in the US.⁵⁸ Costs for surgical management ranged from USD 0.83–4.3 billion, with hysterectomy alone contributing USD 0.77–3.6 billion. In addition to these high direct costs, the annual work time lost to fibroid-related absenteeism or short-term disability was estimated at USD 1.5–17.2 billion, with women untreated for fibroids contributing USD 0.97–6.5 billion. An additional USD 0.24–7.8 billion was contributed by obstetric complications attributable to fibroids, for a total annual fibroid-related cost of USD 5.9–34.4 billion.

Fibroids also reduce QoL in affected women. In a US survey, 79% of women stated they were afraid that their fibroids might grow and 69% stated that they were afraid that there was “something inside them that does not belong there”.⁵⁹ With regard to employment, 26% of women stated that fibroid-related conditions prevented them from carrying out professional responsibilities and 24% stated that they were prevented from fulfilling their full potential at work. Fear and anger were identified as central issues related to fibroids, with many women having a negative self-image and worrying about their attractiveness.⁶⁰ Nearly half of women felt helpless because of their fibroids and 20% reported a lack of adequate support although, similar to endometrial polyps, treatment can improve QoL.^{60,61}

2.2 Current Care and Treatment Options

Key messages

Endometrial polyps, retained products of conception and submucosal fibroids should be treated with minimally invasive procedures when possible.

Gynecologic procedures are increasingly shifting to physicians' offices, where they can be performed safely, effectively, at lower cost and in line with women's treatment preferences.

Mechanical hysteroscopic tissue removal, e.g. using the TruClear™ system, is a minimally invasive procedure that can be successfully used in the office.

Short summary

A range of minimally invasive procedures are available for treatment of uterine pathological tissue. These generally safe and successful procedures are hysteroscopy-based and include hysteroscopic polypectomy for endometrial polyps, hysteroscopic resection for retained products of conception and hysteroscopic myomectomy for uterine fibroids.^{20,21,32,69,70}

Gynecologic surgery has benefited from technological advances, particularly the development of mechanical hysteroscopic tissue removal.^{19,24,94} These procedures can be used in offices, thereby contributing further to patient satisfaction and cost savings that have resulted from a broader shift of gynecologic procedures to offices.^{1,4,5}

2.2.1 Current Guidelines and Treatment Patterns

For each guideline and treatment review, the recommendations and findings most relevant to the GVD are presented here.

2.2.1.1 Endometrial Polyps

Expectant management is recommended only for asymptomatic polyps while medical management is generally not recommended.^{21,33} Surgical treatment is recommended for symptomatic endometrial polyps and can be considered also for asymptomatic polyps if the polyp is large or possibly malignant, or if the polyp might impair fertility.^{21,26,33} Hysteroscopic polypectomy is considered the gold standard for the removal of endometrial polyps.^{21,26,32,33,36}

Guideline: In their 2012 guideline, the American Association of Gynecologic Laparoscopists (AAGL) made the following recommendations with regard to the management of endometrial polyps (Level C evidence omitted)²¹:

- Level A (good and consistent scientific evidence)
 - Expectant management of polyps, particularly of small and asymptomatic polyps, is reasonable.
 - Surgical removal of polyps is recommended for infertile patients to increase the likelihood of natural conception of assisted reproductive technology.
- Level B (limited or inconsistent scientific evidence)
 - Medical treatment for polyps is not recommended.
 - Hysteroscopic polypectomy remains the gold standard for treatment.
 - Removal for histologic assessment is appropriate in symptomatic post-menopausal women.

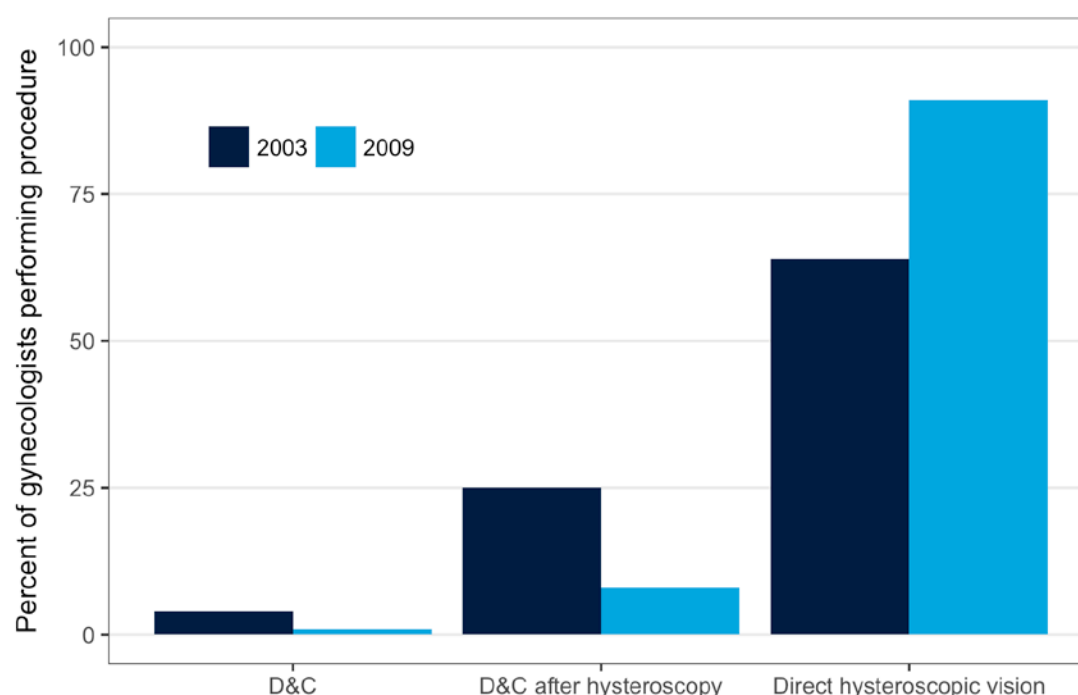
The guideline recommends against the use of the traditional surgical treatment option, blind D&C, if hysteroscopic treatment can be performed. Hysterectomy should be used judiciously and only after consultation with the patient to reduce costs and the risk of ensuing morbidity.

Diagnosis and treatment: With regard to *diagnosis*, transvaginal ultrasonography (TVUS) is the least invasive but also least accurate procedure to identify endometrial polyps. The addition of color-flow or power Doppler as well as 3-dimensional TVUS may improve accuracy compared with 2-dimensional TVUS.^{21,26,30,32,36} Saline infusion sonohysterography (SIS) is a more accurate procedure that uses a sterile normal saline solution to distend the endometrial cavity.²⁶ Although more accurate than TVUS, SIS has a lower sensitivity and is associated with more patient discomfort compared with hysteroscopy with guided biopsy, which is considered the diagnostic gold standard.^{21,26,30,32}

With regard to *surgical treatment*, blind D&C used to be the most frequent treatment for endometrial polyps and is still a common procedure.^{30,62,63,64} However, blind removal of polyps is no longer recommended as it is associated with uterine trauma and can miss pathologic tissue in up to 50% of cases.^{30,36} Similar to diagnostic procedures, hysteroscopic polypectomy is now considered the gold standard.³⁶ The procedure is safe and clinically successful in outpatient and offices, at lower costs than in inpatient settings.^{32,26} General anesthesia can be avoided using hysteroscopic procedures and advances in hysteroscopic technology, e.g. mechanical systems, allow treatment of even large polyps.^{30,36} The advent of mechanical tissue removal technologies, e.g. the TruClear™ system, has further improved the success of hysteroscopic polypectomy by allowing for simultaneous tissue cutting and removal while being quicker and better accepted by patients than electrosurgical resection.^{26,30,36,65}

Recent data on treatment patterns were available from a Dutch survey of 585 gynecologists (no US data were available).⁶⁶ A trend towards hysteroscopic polypectomy, at the expense of D&C, was observed (Figure 2-3). This trend was accompanied by a shift towards local or no anesthesia, from 22% of gynecologists performing polypectomies with local or no anesthesia in 2003 to 46% in 2009. The shift towards outpatient hysteroscopic polypectomy was considered an improvement in medical practice, in line with recommendations from the literature.

Figure 2-3 Trends in polyp removal procedures among Dutch gynecologists



Source: van Dijk *et al.* (2012)⁶⁶.

2.2.1.2 RPOC

Generally, treatment reviews (no guideline was identified) for management of RPOC recommended hysteroscopic procedures which are associated with a low risk of IUA and good fertility outcomes.^{44,48,67} As no country-specific information was identified, treatment reviews and patterns are described in this subsection without regard to geography.

Diagnosis and treatment: With regard to *diagnosis*, clinical, laboratory and ultrasound methods are available.⁴³ Diagnosis based on the clinical presentation alone is less accurate than ultrasound, which is considered sufficient for most cases.⁴³ For complicated cases, magnetic resonance imaging (MRI) or computed tomography might have to be used.⁴³

With regard to *treatment*, blind D&C used to be the most frequent treatment for RPOC. However, blind D&C may cause endometrial trauma and lead to IUA, thereby adding physiological to the psychological burden of women who have experienced a pregnancy loss.^{44,49,67,68} As early as 1997, hysteroscopic RPOC removal was suggested to be preferable to blind D&C.⁶⁹ A recent systematic review of long-term complications and reproductive outcomes after surgical management included five cohort studies, considered to be of poor to average methodological quality.⁴⁸ IUA was reported in 330 women who were surgically treated for RPOC and who had been hysteroscopically evaluated. The pooled prevalence of IUA was clearly lower in women treated with hysteroscopic resection than in women treated with blind or ultrasound-guided D&C (12.8% vs 29.6%, $p < 0.001$).

In a review of medical data of 177 women undergoing either blind D&C or hysteroscopic resection for suspected RPOC, hysteroscopic resection was associated with faster time to conception and fewer new infertility problems (Table 2-4).⁴⁴ On average, women treated with hysteroscopic resection conceived 5 months earlier than women treated with blind D&C and were half as likely to experience a new infertility problem.⁴⁴

Table 2-4 Fertility after blind D&C and hysteroscopic resection for RPOC⁴⁴

Outcomes	Hysteroscopic resection (n=83)	D&C (n=94)	p-value
Reproductive outcome following RPOC			
Desired pregnancy, %	53.0	58.5	0.280
Conceived, %	92.8	92.6	0.340
Months to conception, mean (SD)	7.4 (7)	12.9 (16.8)	0.037
New infertility problem, %	12.0	24.5	0.034
Pregnancy outcome following RPOC			
Delivery, %	80.7	88.3	–
Abortion, %	19.3	11.7	–
Placental complications, %	13.3	4.3	0.177
Birth weight in gram, mean (SD)	2,984 (485.7)	3,055 (528.4)	0.551
Gestational age at delivery in weeks, mean (SD)	38.1 (4.2)	38.2 (2.5)	0.811

Similar findings were reported by a study of 95 women with pregnancy loss, of whom 42 were treated with ultrasound-guided dilation and evacuation (D&E) before the healthcare provider switched to using hysteroscopic resection, with which the remaining 53 patients were treated.⁷⁰ Treatment with hysteroscopic resection was associated with a higher likelihood of conception and live birth and with shorter conception times (Table 2-5). Women treated with hysteroscopic resection conceived after a median time of 27 months, compared with 34 months for women treated with ultrasound-guided D&E, with an advantage of more than 12 months for patients aged <35 years (14 versus 27 months). It was concluded that the direct visualization of the uterine cavity and simplicity of hysteroscopic resection, without inflicting trauma to the endometrium, made the procedure attractive for the management of RPOC. A review of management of first trimester pregnancy loss concluded that management, including surgery, can be moved from the operating room to the office without a loss in clinical success and safety.²³

Table 2-5 Fertility outcomes after D&E and hysteroscopic resection for RPOC ⁷⁰				
Outcome	Hysteroscopic resection (n=45)	D&E (n=37)	p-value	Hazard ratio (95% CI)
Reproductive outcome				
Conception, %	68.8%	59.5	0.035	–
Conception in patients aged <35 years, %	78.1	66.6	0.028	–
First trimester spontaneous miscarriage, %	6.9	15.0	0.227	–
Second trimester spontaneous miscarriage, %	3.4	0.0	0.382	–
Live births, %	57.8	45.9	–	–
Months to conception				
All patients, median (range)	27 (7 to 39)	34 (10 to 36)	–	1.79 (1.04 to 3.22)
Patients aged <35 years, median (range)	14 (7 to 33)	27 (11 to 33)		1.90 (1.08 to 3.79)

2.2.1.3 Uterine fibroids

Generally, guidelines and treatment reviews pointed out that currently no medication is available for the successful treatment of fibroids although medication, e.g. gonadotropin-releasing hormone (GnRH) agonists and selective progesterone-receptor modulators, can be used to prepare women for surgery.^{71,72,73,74} Among surgical procedures, hysterectomy was recommended in most cases as the definitive method of treatment. However, an increased preference for retaining the uterus, not only for future fertility but also in response to a changed perception of the uterus as a sexual organ and a source of vitality, led to changes in women's preferences and increased the attractiveness of uterine-preserving procedures.^{59,73} As a result of preference changes and technologic development, hysteroscopic procedures have gained a place in current guidelines and treatment recommendations as alternatives to hysterectomy.

Guidelines: In their 2012 guidelines, AAGL made the following recommendations for management of fibroids (Level C evidence omitted)²⁰:

- Level A (good and consistent scientific evidence)
 - Women with type II (European Society of Gynecological Endoscopy classification) fibroids and HMB, who have completed childbearing, can generally be treated effectively with endometrial ablation.
 - Cervical preparation techniques can reduce trauma associated with hysteroscopic surgery.
- Level B (limited or inconsistent scientific evidence)
 - Expectant management can be used if fertility enhancement is not a treatment goal.

- HMB can be treated effectively using hysteroscopic myomectomy if the fibroid is removed completely. In addition to hysteroscopic myomectomy, endometrial ablation can be performed if future fertility is irrelevant.
- If hysteroscopic myomectomy is expected to damage a large portion of the endometrium but women desire future fertility, submucous fibroids should be removed using abdominal procedures.

Among surgical treatments, uterine artery embolization (UAE) is recommended to be used cautiously whereas endometrial ablation can be used successfully in a selective subset of patients. If feasible, hysteroscopic myomectomy is considered the most efficacious treatment if fertility is to be retained. Care has to be taken to avoid IUAs, which negatively affect fertility.²⁰

ACOG published a practice bulletin on alternatives to hysterectomy as the most radical treatment of fibroids (Level C evidence omitted)¹¹:

- Level A (good and consistent scientific evidence)
 - Women with symptomatic fibroids can be treated safely and effectively with abdominal myomectomy.
 - If women wish to retain their uteri, UAE is a safe and effective alternative to hysterectomy.
- Level B (limited or inconsistent scientific evidence)
 - Hysteroscopic myomectomy is considered an acceptable method for treatment of AUB caused by submucosal fibroids. Note that hysteroscopic myomectomy is considered the first-line conservative surgical treatment for symptomatic fibroids in more recent guidelines, e.g. the guidelines published by the Society of Obstetricians and Gynaecologists of Canada.⁵⁰

GnRH agonists are considered potentially beneficial in preparing for surgery as are the newer GnRH antagonists, which have the advantage of not inducing steroidal flare. However, for treatment of fibroids, no simple, inexpensive and safe long-term medication is currently available so surgical procedures must be used in the management of most fibroids.¹¹

Diagnosis and treatment: With regard to *diagnosis*, a combination of various procedures, including TVUS, SIS, MRI and hysteroscopy, can be used.²⁰ Hysteroscopy, SIS and MRI are generally more accurate than hysterosalpingography and TVUS and all three are considered highly sensitive and specific for the diagnosis of submucous fibroids. MRI is considered the best technique to characterize the relationship of submucous fibroids with the myometrium and uterine serosa.²⁰

With regard to *treatment*, the available data indicate that hysterectomy is still the most frequent surgical treatment for fibroids in the US. In a study of 13,263 commercially insured women aged 25 to 54 years who had sought treatment for fibroids, treatment patterns were analyzed and extrapolated to the US using MEPS survey weights.⁵³ The extrapolated results showed that approximately 443,000 commercially insured women in the US sought treatment for fibroids (Table 2-6).

Table 2-6 Treatments for uterine fibroids in US women aged 25 to 54 years ⁵³		
Treatment	Number of patients	Percentage
All treatments		
Only surgical	74,499	16.8
Only prescription drug	99,332	22.4

Table 2-6 Treatments for uterine fibroids in US women aged 25 to 54 years⁵³

Treatment	Number of patients	Percentage
Surgical and prescription drug	188,021	42.4
None	81,594	18.4
<i>Total</i>	443,445	100
Surgical treatments		
Hysterectomy only	207,102	78.9
Myomectomy only	26,304	10.0
Uterine artery embolization only	7,849	3.0
Endometrial ablation only	10,790	4.1
Multiple	10,475	4.0
<i>Total</i>	262,519	100

Almost 60% of patients received surgical treatment, and only 10% of these underwent a myomectomy. The authors suggested that less radical and less expensive treatment options be pursued in the US.

Additional data on treatment patterns were reported by an analysis of premenopausal women.⁷⁵ The women selected for the study had presented to a gynecologic clinic and reported, in baseline interviews, to have been diagnosed with fibroids and AUB or pelvic pressure. Among women without prior uterus-preserving surgery (UPS, i.e. no hysterectomy), almost three-quarters did not require surgery over a mean 3.7 years of follow-up (Table 2-7).

Table 2-7 Treatment for uterine fibroids in premenopausal women⁷⁵

Treatment during follow-up	Percentage of patients	Mean years of follow-up
No uterus-preserving surgery before baseline (n=719)		
Hysterectomy	15	5.0
Myomectomy	7	4.8
Uterine artery embolization	3	5.1
Endometrial ablation	1	4.2
No surgery	74	3.7
Prior myomectomy (n=159)		
Hysterectomy	19	5.8
Myomectomy	10	6.0
Uterine artery embolization	3	3.9
Endometrial ablation	1	8.0

Table 2-7 Treatment for uterine fibroids in premenopausal women⁷⁵

Treatment during follow-up	Percentage of patients	Mean years of follow-up
No surgery	65	3.8
Prior uterine artery embolization (n=29)		
Hysterectomy	20	3.7
No surgery	79	3.3
Prior endometrial ablation (n=59)		
Hysterectomy	15	6.2
Myomectomy	3	8.0
Uterine artery embolization	2	3.2
No surgery	80	3.0

Hysterectomy was performed in 15% of these women over a mean follow-up of 5.0 years, a percentage similar to that in women with prior myomectomy, UAE or endometrial ablation. Myomectomy was the second-most popular surgery but much less frequent than hysterectomy, with percentages ranging from 3 to 10%. In additional analyses, medical and complimentary treatment (exercise, herbs, diet changes, acupuncture, physical therapy) were found to be similarly effective but UPS-treated women reported statistically significantly greater improvements in pelvic pressure, bladder pain and frequent urination.⁷⁵

Despite its frequent use in the US, hysterectomy is the least preferred procedure among US women. In a survey of almost 1,000 women aged 29 to 59 years without prior hysterectomy, more than three in four women stated that a fibroid treatment option without invasive surgery was important.⁵⁹ A majority of women, particularly women aged <40 years, stated a preference to keep their uterus regardless of future pregnancy plans. These women expressed a clear interest in alternatives to hysterectomy and are likely to benefit from minimally invasive, uterus-sparing treatment options such as mHTR.²⁴

In a subsequent study of a commercial insurance claims database, clinical and non-clinical factors associated with receiving UPS or hysterectomy were explored.⁷⁶ In a multivariable analysis, younger women were found to be more likely to undergo UPS than older women and this relationship increased with the proportion of black residents in the ZIP code area, presumably because fibroids occur at younger ages in black women and younger women were more likely to express a desire for maintaining fertility. Women with higher income or higher education were more likely to undergo UPS as were women residing in the Northeast US (compared with Midwest, South and West). Among clinical characteristics, infertile women and women with menstrual disorders were more likely to undergo UPS, reflecting the effectiveness of UPS in the treatment of these conditions.

2.2.2 Diagnostic and Surgical Procedures for Removal of Intrauterine Tissue

Table 2-8 Overview procedures for removal of intrauterine tissue	
Procedure	Description
Resectoscopy (electrical tissue removal)	<p>Uses electrical energy (monopolar or bipolar) to remove tissue</p> <p>Successfully removes fibroids and endometrial polyps but less successful than mechanical hysteroscopic tissue removal in complete removal of tissue and operating time^{79,80,89}</p> <p>Has complication risk from distending media and thermal injury; requires multiple insertions to remove cut tissue^{24,81}</p>
Mechanical hysteroscopic tissue removal	<p>Uses mechanical energy to cut and remove tissue simultaneously</p> <p>Faster and more effective than earlier gynecologic surgical procedures, particularly resection^{95,96,97,98}</p> <p>Has very good safety profile as little/no dilation is necessary and no electrical energy is used^{24,95}</p>
Dilation and curettage	<p>Uses a curette to scrape off intrauterine tissue</p> <p>Historically performed blindly, which misses up to 87% of lesions^{29,108,109,110}</p> <p>Associated with adverse events such as bladder perforation and preterm births^{111,112}</p>

2.2.2.1 Resectoscopy

Hysteroscopic resectoscopes were modified from urologic resectoscopes and their use was first described in 1978.⁷⁷ Resectoscopes contain a sheath with inflow and outflow ports, are equipped with continuous flow and offer good irrigation during operation but require assembly by an experienced user before surgery.²⁴ Traditionally, resectoscopy is conducted as monopolar high-frequency electrosurgery during which the women has to be grounded and non-electrolytic, non-conducting distending media have to be used.²⁴ Bipolar resectoscopes, which require saline distending media, have become available in recent years. They are considered less dangerous than monopolar resectoscopes, due to the better safety profile of electrolytic compared with non-electrolytic distending media, although this contention has not yet been proven in clinical practice.^{24,78}

Hysteroscopic resectoscopy was found to be an effective procedure for treatment of AUB in women with a normally sized uterus with at most two fibroids.⁷⁹ Outpatient treatment with a monopolar mini-resectoscope was recently found to be a safe and effective treatment of endometrial polyps.⁸⁰ However, the use of a non-electrolytic medium was considered a possible limitation of this device. Although rare, sorbitol and glycine, which are used as distending media in monopolar resectoscopy, may lead to life-threatening changes in blood electrolyte levels in case of excessive intravasation through uterine vessels.⁸¹ Possible complications include hyponatremia, pulmonary and cerebral edema and heart failure so close monitoring of fluid in- and outflow is required at all times during resection.^{81,82,83,84} Isotonic fluid media used in bipolar electrosurgery, such as physiological saline, have a lower risk of hyposmolarity and hyponatremia but excessive fluid absorption of these media continues to be a risk factor for cardiac failure and pulmonary edema.⁸⁴ In addition to fluid-related complications, the use of electric energy (not only in hysteroscopic resection but also in procedures such as endometrial ablation) may lead to thermal injury of the surrounding

endometrial tissue, e.g. in case of a device malfunction, stray currents or improper usage.^{85,86,87,88}

Resectoscopes require multiple insertions through the cervix as cut tissue needs to be removed periodically. The need for multiple insertions can prolong procedures and increase the risk of perforation, cervical trauma and excess fluid intravasation.⁸¹ Removal of the resectoscope is also necessary if gas bubbles or surgical debris block the field of vision.^{24,81} These issues make resectoscopy an inconvenient procedure that is difficult to learn and requires considerable practice.⁸¹

Electrical resection was found in a recent systematic review to be less successful than mHTR in removing endometrial lesions although no differences in complication rates were observed.⁸⁹ In the meta-analysis of RCTs comparing mHTR (TruClear™ system) with mono- or bipolar resection of endometrial lesions, the OR for complete removal of lesions was 4.5 (95% CI 1.9 to 10.4) in favor of mHTR. Similarly, for total operating time, mHTR an advantage over resection as mHTR was, on average, 5 minutes (95% CI 2.7 to 7.2 minutes) faster. Although the meta-analysis was based on only four trials, it showed a clear disadvantage of hysteroscopic resection compared with mHTR in two important domains of surgery, namely complete removal of pathology and operating time. The higher success rate of mHTR was attributed to better visualization while the shorter operating time was assumed to result from lower fluid deficits and less time spent on re-insertions of the hysteroscope.^{24,50,89,93,95} Faster procedure and recovery times associated with mHTR, compared with eHTR, suggest that mHTR may be the more attractive choice for the office as time savings are an incentive for both patients and providers to choose the office in the first place.^{2,27,90}

2.2.2.2 Mechanical Hysteroscopic Tissue Removal

Developed to overcome the shortcomings and risks of electrical tissue removal the first mHTR system (TruClear™) was approved by the Food and Drug Administration in 2005, with a second system (MyoSure™) approved in 2009.^{24,91} During mHTR, a hysteroscope is inserted through the cervix into the uterus. Saline is used to distend the uterus and a tissue removal device, inserted through the hysteroscope, is used to resect the tissue, thereby reducing the number of necessary insertions.^{24,81,92}

Several studies comparing mHTR and electrical resection are available. A prospective randomized trial was conducted to compare mHTR and bipolar resectoscopy for removal of larger endometrial polyps in a day surgery setting.⁹³ The 84 women included in the study had ≥1 endometrial polyp with a diameter ≥1 cm and were randomly assigned to either bipolar resection or mHTR (TruClear™ 8.0). Again, mHTR was found to be superior to resection with regard to treatment success and safety (Table 2-9). Although mHTR was associated with a longer installation time, its shorter operating time led a shorter overall procedure time. Fewer insertions were required for mHTR and no uterine perforations associated with (re-) insertion were observed for mHTR, compared with 5% of resectoscopic procedures. Mechanical hysteroscopic tissue removal successfully and completely removed all endometrial polyps whereas resectoscopy removed 95% of polyps.

Mechanical hysteroscopic tissue removal was shown in several trials and reviews to be superior to earlier gynecologic surgical procedures with regard to speed, safety and clinical success (see Section 1.1.1.4).⁹⁴ An analysis of 105 mHTR procedures (TruClear™ 8.0 system) in women with histologically confirmed RPOC showed that complete removal of RPOC was achieved in the first attempt in 94% of patients.⁹⁵ No AE was observed in 86% of procedures and the median procedure time was only 20 minutes (range 10 to 60 minutes). Similarly, the MyoSure™ system, although less successful than the TruClear™ system, was found to

completely resect 92% of endometrial polyps and 87% of RPOC (but only 66% of fibroids) in an analysis of 255 procedures.⁹⁶

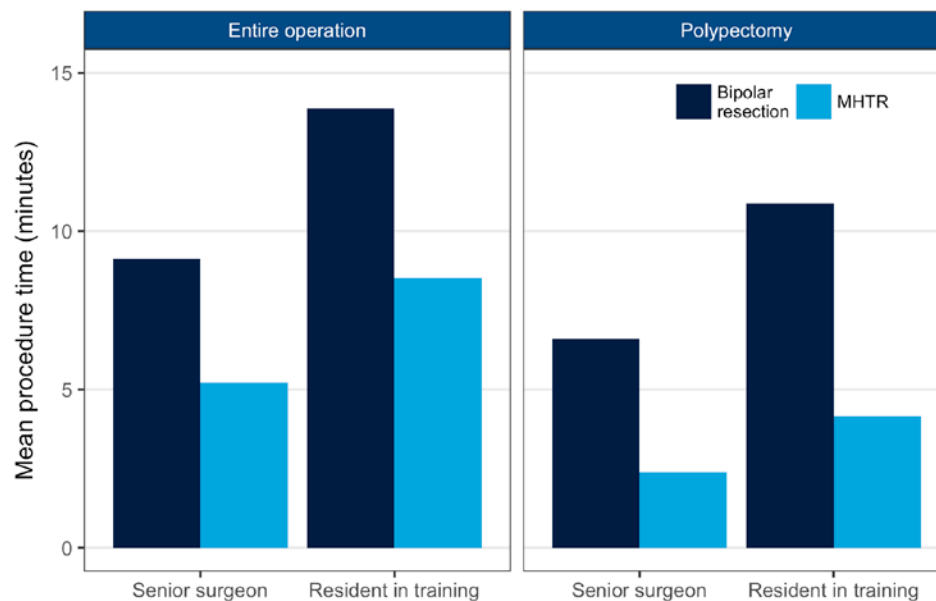
	Resectoscopy (n=40)	Mechanical hysteroscopic tissue removal (n=44)	p-value
Procedure time in minutes, median (interquartile range)	12.2 (8.8 to 16.0)	9.5 (7.6 to 12.2)	0.72
Installation time in minutes, median (interquartile range)	4.5 (3.9 to 6.0)	5.2 (4.3 to 6.3)	0.66
Operating time in minutes, median (interquartile range)	6.0 (3.8 to 11.7)	4.0 (2.5 to 7.1)	0.028
Fluid deficit in mL, median (interquartile range)	200 (110 to 290)	165 (58 to 333)	0.115
Number of insertions, median (interquartile range)	2 (2 to 5)	1 (1 to 1)	<0.001
Perforation, %	7.5	2	0.34
Dilation	2.5	2	–
(Re-) Insertion	5	0	–
Polyp removal, %			0.22
Complete	95	100	–
Incomplete	5	0	–

A retrospective analysis of 311 US women treated for AUB and endometrial polyps using either hysteroscopic resection (microscissors, micrograspers, VersaPoint™) or mHTR (TruClear™) showed that treatment with mHTR was likely associated with long-term benefits.⁹⁷ Overall, 21% of patients treated with hysteroscopic resection and 15% of patients treated with mHTR had recurrent AUB, with median times to recurrence of 2.2 and 1.4 years, respectively. The 4-year cumulative incidence of recurrent AUB was lower for mHTR than for hysteroscopic resection (HR 1.12 [95% CI 0.64 to 1.98]) as was the overall cumulative incidence of recurrent endometrial polyps (HR 3.3 [95% CI 0.94 to 11.49]) although the differences between treatments were not statistically significant. Of the women with recurrent AUB, 81% had subsequent treatment for AUB (37% expectant management, 20% medical treatment, 30% hysteroscopy and polypectomy, 2% hysteroscopic polypectomy followed by endometrial ablation, 2% hysteroscopic polypectomy followed by levonorgestrel intrauterine device, 4% endometrial ablation, 4% D&C). Hysterectomy was ultimately performed in 19% of women with recurrent AUB.

An RCT in 133 women diagnosed with endometrial polyps confirmed the advantage of mHTR over electrosurgical resection.⁹⁸ Women were randomized to treatment with either the TruClear™ 5.0 system or resectoscopy with a bipolar device and treated either by staff experienced in handling the respective device or by staff currently undergoing training for the respective device. The success rate for complete polyp removal was much higher for mHTR

(92%) than for bipolar resection (77%), with no resident in training able to perform bipolar resection without verbal or practical assistance, compared with 22% of residents who used mHTR without practical assistance. Mechanical hysteroscopic tissue removal clearly outperformed bipolar resection with regard to the time required for polypectomy and the entire operation (Figure 2-4). Both experienced surgeons and residents in training performed procedures 2 to 3 minutes faster, on average, when using mHTR compared with using bipolar resection. Again, faster operating times suggest that mHTR is preferable to bipolar resection in the office.^{2,27}

Figure 2-4 Operating and polypectomy times for bipolar resection versus mHTR



mHTR, mechanical hysteroscopic tissue removal. Source: Pampalona et al. (2015)⁹⁸.

2.2.2.3 Endometrial Sampling

Endometrial sampling is a procedure used to diagnose irregularities in the uterine cavity, e.g. to investigate AUB or suspected endometrial cancer.^{99,100} Although TVUS is often the initial step, endometrial sampling becomes necessary when tissue specimens are required for histologic analysis, particularly if the endometrial thickness equals or exceeds an agreed threshold (often 4 to 5 mm).^{101,102,103,104} Hysteroscopy-assisted endometrial sampling is the gold standard and strongly recommended if endometrial thickness is ≥ 10 mm and negative Pipelle sampling.^{101,102,103} In a comparison of 105 women presenting with symptoms of menorrhagia, postmenopausal bleeding (PMB) and infertility, diagnostic hysteroscopy had a sensitivity of 97.3% (95% CI: 90.4 to 99.6%) and a specificity of 92.0% (95% CI: 73.9% to 98.8%) for the detection of uterine pathologies, much higher than TVUS and SIS for all conditions investigated in the study.¹⁰⁵

In a systematic review and meta-analysis of 27 studies comparing D&C, hysteroscopically-guided biopsy and endometrial hysteroscopic resection for the diagnosis of endometrial cancer, a risk of 33% (95% CI: 26 to 40%) was estimated for missing endometrial cancer with D&C.¹⁰⁶ The corresponding risk for hysteroscopically-guided biopsy and hysteroscopic resection were 45% (95% CI: 33 to 59%) and 6% (95% CI: 0.8 to 32%), respectively. A further meta-analysis, of 12 studies in postmenopausal women with AUB, estimated a sensitivity of 100% for D&C versus 90% for hysteroscopy in the diagnosis of endometrial cancer, 92%

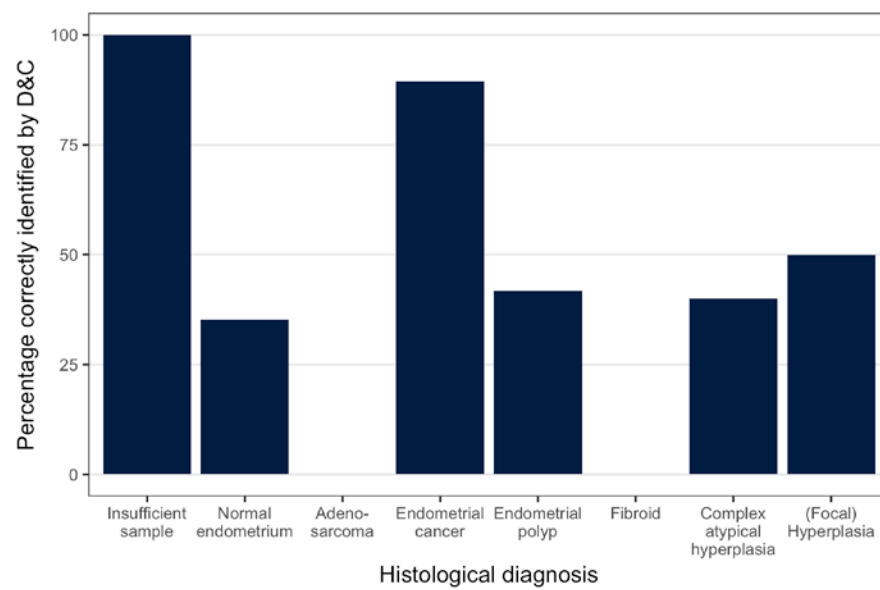
versus 82% for cancer or atypical hyperplasia and 39% for endometrial disease (for endometrial disease, no D&C data were available).¹⁰³ The specificity for both procedures was approximately 100% for all three conditions.

2.2.2.4 Instruments (curette, forceps, graspers)

A commonly used procedure in this category is D&C: after medical and/or mechanical dilation of the cervix, a curette is inserted into the uterus to scrape off pathologic tissue.¹⁰⁷ The procedure used to be performed blindly and was the standard treatment for AUB despite D&C generally being considered ineffective in removing pathologic tissue from the uterus.²⁹ In a prospective study of 105 women with postmenopausal bleeding and an endometrium thickness ≥ 5 mm, diagnosis and removal of pathologic tissue using D&C were evaluated using hysteroscopy.¹⁰⁸ Diagnostic agreement between D&C and hysteroscopy was good for women without focally growing lesions but poor in women with focally growing lesions (Figure 2-5). D&C diagnosed less than half of endometrial polyps and no fibroids or adenosarcomata. In addition, whole or partial uterine lesions remained in 87% of women after D&C, indicating that D&C lacks sensitivity in the detection and removal of intrauterine pathologic tissue. These results were confirmed by a study comparing blind and directed biopsy in 319 postmenopausal women with AUB.¹⁰⁹ Blind biopsy showed a sensitivity of 11% and a specificity of 93%, with an accuracy of only 59% in detecting endometrial polyps. Blind biopsy or D&C are therefore no longer recommended and all D&C procedures should be supported by hysteroscopy.^{29,110}

In addition to possible but rare AEs such as cervical tears, bladder or bowel perforation or IUA, D&C has also been linked to impaired subsequent fertility outcomes.^{48,111,112} A recent systematic review and meta-analysis of case-control and cohort studies identified ORs of 1.3 (95% CI 1.2 to 1.4), 1.7 (95% CI 1.2 to 2.4) and 1.7 (95% CI 1.5 to 1.9) for preterm births at <37 , <32 and <28 weeks for women with a history of D&C, compared with women without a history of D&C.¹¹² As ORs increased with the number of previous D&Cs, the authors considered the relation between preterm births and D&C to be causal (also see Table 2-4 and Table 2-5). More modern procedures, e.g. mHTR with its better safety profile and higher clinical success rate, have widely replaced D&C procedures in many countries and settings, including the office.

Figure 2-5 Diagnostic agreement between D&C and hysteroscopy



Source: Epstein *et al.* (2001)¹⁰⁸

3 Review of the TruClear™ System

Key messages

The TruClear™ system offers a complete technology platform for the diagnosis and removal of a range of intrauterine pathologies

The TruClear™ system is the only system that uses mechanical energy to remove pathology such as polyps and fibroids with pathology-optimized devices and offers continuous flow to help maintain clear visualization throughout the procedure.

The hysteroscopic tissue removal system has been optimized to enhance hysteroscopic tissue removal and contribute to added patient safety.

Key benefits of the TruClear™ system

Patient friendly hysteroscope design, requiring little to no dilation with the TruClear™ 5C hysteroscope

The only system with pathology-optimized tissue removal devices available in two different sizes

Continuous flow through the uterine cavity during diagnostic and operative procedures to maintain a clear field of view

Hysteroscopic fluid management system, designed with patient safety in mind

The TruClear™ system is a complete operative hysteroscopy system and part of the gynecologic portfolio of Medtronic. The system consists of

- The TruClear™ 5C hysteroscope, which is the newest hysteroscope to the family of products and offers several advantages:
 - Enables both operative and diagnostic procedures in the office, ambulatory surgery center (ASC) and operating room, eliminating the need for scope changes
 - Patient-friendly instrumentation, with an anatomically-designed distal end for gentle introduction into the uterine canal and uterine cavity with little to no dilation
 - Longer scope length means access to the entire uterine cavity, including the fundal wall and cornua
 - Used with the TruClear™ INCISOR™* device and the TruClear™ ULTRA Mini device
- The TruClear™ 8.0 hysteroscope set, which is most frequently utilized in the operating room or ASC setting and offers several benefits:
 - Large working channel offers capability to use additional hysteroscopy instruments
 - Option to use TruClear™ obturator for gentle introduction of the sheath into the uterine cavity
 - Used with the TruClear™ INCISOR™* Plus device and the TruClear™ ULTRA Plus device

- The family of TruClear™ devices includes pathology-optimized devices in two different sizes that allow simultaneous tissue cutting and aspiration to meet your needs for a full spectrum of procedures
 - The TruClear™ INCISOR™* devices are optimized for treatment of soft tissue such as polyps
 - The TruClear™ ULTRA devices are optimized for treatment of dense tissue such as fibroids
- The hysteroscopic fluid management system, which can be used in most hysteroscopic procedures although it may not be widely used in clinical practice, was designed with patient safety in mind and includes:
 - High maximum flow rate contributes to optimized visualization and facilitates maintained uterine distension
 - High speed response to changes in uterine pressure
 - Continuous deficit monitoring for accurate measurement
 - Flexible suction contributes to clear visualization and maintained distension
 - Reliable audible alarms for patient safety, including over pressure, under pressure and fluid deficit thresholds
- The TruClear™ system and TruClear™ devices are intended for intrauterine use by trained gynecologists to hysteroscopically resect and remove tissue such as submucous myomas, endometrial polyps and retained products of conception. The TruClear™ system enables a full spectrum of procedures, including:
 - Polypectomy
 - Myomectomy
 - RPOC evacuation
 - Diagnostic visual D&C
 - Endometrial biopsy.

The TruClear™ system was shown to be successful in the treatment of polypectomy, myomectomy and RPOC evacuation.^{95,96,113} TruClear™ meets demands for an easy-to-use, effective treatment of intrauterine pathology while simultaneously improving the treatment safety when compared with earlier procedures.

TruClear™ also fulfills women's preferences for uterine-saving, office procedures and might be able to reduce the frequency of hysterectomies which, although often not clinically indicated, expensive and disliked by women, continue to be widely used.^{2,4,20} TruClear™ is therefore in a good position to satisfy patient preferences and reduce both the clinical and economic burden associated with AUB and intrauterine pathology.

4 Clinical Impact of Shifting Gynecologic Procedures to the Office

Key messages on clinical success

Studies show that gynecologic surgery, including mechanical hysteroscopic tissue removal, in the office/outpatient setting is as successful as the corresponding inpatient procedures.

In office procedures, mechanical hysteroscopic tissue removal removed over 95% of pathologic tissue.^{116,117}

Office procedures are generally successful without general anesthesia.

Key messages on safety

Office gynecologic procedures including mechanical hysteroscopic tissue removal are safe and have low rates of adverse events.

Adverse events were observed in <5% of office surgical procedures and were generally mild and resolved spontaneously.^{30,116,117,124} No serious adverse events were reported in head-to-head comparisons of office with inpatient treatment.

Pain is the most common adverse event in office surgery but effective anesthesia algorithms exist for prevention and treatment of pain. The convenience of office procedures tends to outweigh pain in women's treatment decisions.

Key messages on patient satisfaction

Women are generally very satisfied with office treatment and would recommend the procedure to a friend.

In addition to convenience, privacy concerns and wanting to stay awake during the procedure were found to motivate the choice for treatment in the office.

4.1 Note on Definitions Used

This section presents evidence on the clinical effectiveness of shifting gynecologic procedures away from inpatient settings.

A challenge when interpreting the published evidence is the lack of consistent definitions of clinical settings across studies. Different studies define "outpatient" and "office" settings differently. For example:

- Gambadauro *et al.* labeled polypectomy performed during operative hysteroscopy, without cervical dilation or anesthesia and short post-procedure observation times, as both "outpatient" and "office" procedures, with procedures performed in the hysteroscopic unit of a Spanish hospital.¹¹⁴
- Di Spiezo Sardo *et al.*, in their review of "outpatient" hysteroscopies, explicitly treated "outpatient" and "office" settings as synonyms.¹¹⁵
- Cooper *et al.*, in the OPT trial, use "outpatient" and "office" interchangeably.³⁰

The settings where procedures were performed are therefore described in some detail for the studies presented in the following sections. A study was considered for inclusion in the following sections if it contributed data on gynecologic procedures in non-inpatient settings, using local or no anesthesia and little or no cervical dilation, and quickly released patients

after the procedure. The term “office” is used for a setting that fulfils these requirements (but the use of “office” is flagged whenever a study uses different terminology).

Only a few studies presented a direct comparison of outcomes between settings and these studies are presented first as they are most relevant to illustrate the benefits of shifting the site of gynecologic procedures. Single-arm studies and reviews are presented subsequently, to provide additional information.

4.2 Clinical Outcomes of Office Gynecologic Procedures

Short Summary

Three head-to-head comparisons of gynecologic procedures of inpatient and office/outpatient settings were available.^{42,116,117} Office mechanical hysteroscopic tissue removal removed 97% of total pathologic tissue, 95% of fibroids and 99% of polyps, similar to treatment success of removal in ambulatory surgery centers/hospital outpatient departments for total pathologic tissue and polyps and more successfully for fibroids.¹¹⁶

Office mechanical hysteroscopic tissue removal was comparable to removal in ambulatory surgery centers, removing 97% of pathologic tissue and almost 100% of polyps (differences between office and center treatments were small and not statistically significant).¹¹⁷

A UK trial of inpatient (general anesthesia) and office/outpatient (local anesthesia) polypectomy showed that 73% of women in the outpatient and 80% of women in the inpatient group were successfully treated (difference not statistically significant).⁴² Outpatient treatment was non-inferior to inpatient treatment and recommended to be more widely established.

4.2.1 Direct Comparisons of Clinical Effectiveness in Different Settings

4.2.1.1 mHTR of Polyps and Fibroids in Office versus ASC/HOPD Setting (Scheiber et al.)

In a prospective multicenter registry study of women undergoing mHTR for uterine polyps and fibroids, clinical outcomes were compared for procedures performed in ASCs, hospital outpatient departments (HOPD) with procedures performed in obstetrics/gynecology offices.¹¹⁶ In 34 US institutions (7 offices, 12 academic hospitals/ASCs, 15 nonacademic hospitals/ASCs), women aged 18 to 65 years were enrolled prospectively if ultrasound, SIS or hysteroscopic examination had revealed intrauterine pathology.

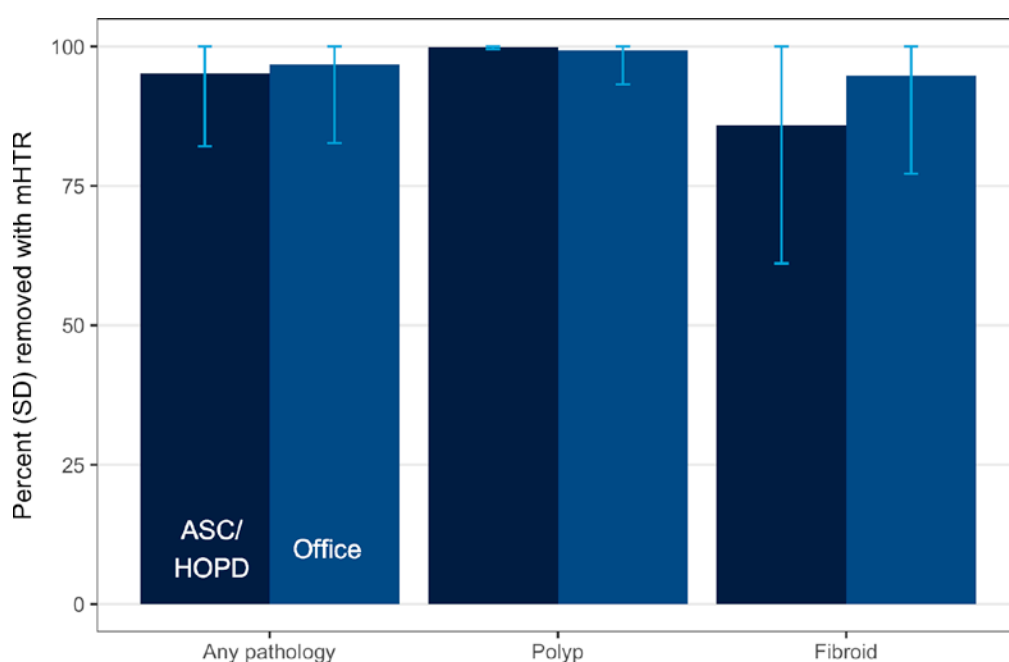
The primary efficacy endpoint of mHTR procedures was the percentage of lesions removed. Additional endpoints included total procedure time, total cutting time, fluid deficit and the necessity for mechanical cervical dilation. In addition, safety was assessed using the incidence of AEs prior to and after patient discharge (reported in Section 4.3).

In total, 278 women were treated. Most patients (n=250) were treated in an ASC/HOPD setting. The majority of patients were premenopausal (73%) and treated for AUB (74%). In total, 559 pathologies (33.5% fibroids, 66.5% polyps) were removed. The mean diameter of fibroids was 2.2 cm (SD 1.2 cm, range 0.3 to 5.5 cm), the mean diameter of polyps was 1.3 cm (SD 1.0 cm, range 0.1 to 7.0 cm). Across sites, 95.4% (SD 13.2%) of pathologic tissue was removed. For both total pathologic tissue removed by patient and fibroids removed, office procedures outperformed ASC/HOPD procedures (96.8% [SD 14.1%] versus 95.2% [SD 13.1%] and 94.8% [SD 17.6%] versus 85.8% [24.7%]) but ASC procedures were slightly superior in removing polyps (99.3% [SD: 6.1%] versus 99.9% [0.4%]) although differences were not statistically significant (Figure 4-1). No statistically significant differences were

observed for fluid deficit, physician satisfaction and resection time between sites but patients treated in the office spent statistically significantly less time in post-anesthesia care units than patients treated in ASC/HOPD-settings (36.8 min [SD 24.7 min] versus 57.0 min [SD 37.5 min], $p=0.0263$). While patients treated in the office were more likely to receive oral sedation (18% versus <1%), cervical blocks (54% versus 10%) or intravenous sedation (61% versus 20%), they were much less likely to receive general anesthesia (7% versus 78%).

It was concluded that mHTR was a feasible and successful procedure in both settings, which were considered reflective of general US community practice. Of note, the clinical effectiveness of office mHTR matched that of ASC/HOPD procedures while sparing many patients general anesthesia.

Figure 4-1 Pathology removed by mHTR in office and ASC/HOPD-settings



ASC/HOPD, ambulatory surgery center/hospital outpatient department; mHTR, mechanical hysteroscopic tissue removal; SD, standard deviation. Source: Scheiber *et al.*¹¹⁶

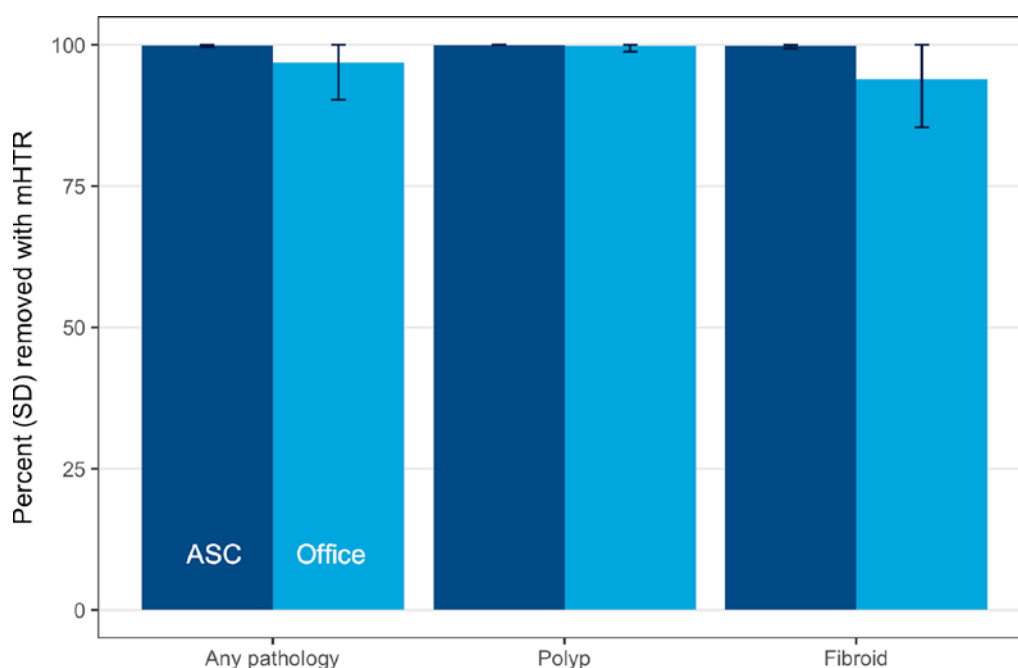
4.2.1.2 mHTR for Polyps and Fibroids in Office versus ASC Setting (Rubino *et al.*)

Similar findings were reported by a multicenter RCT of women undergoing mHTR treatment for uterine polyps and/or submucosal fibroids in eight gynecologic offices or ASCs in the US.¹¹⁷ Women aged 18 to 55 years were enrolled prospectively if they were scheduled for hysteroscopic myomectomy or polypectomy for the treatment of AUB as determined by extensive screening. Uterine pathologies had to be compatible with office treatment, i.e. patients had to have 1) ≥ 1 polyp with ≥ 1 polyp between ≥ 1.5 cm and ≤ 3.0 cm in diameter with a broad-base attachment to the uterine wall, 2) up to 2 type 0 or 1 fibroids with ≥ 1 fibroid ≥ 1.5 cm and no fibroid > 3.0 cm or 3) a combination of 1) and 2). The main endpoint was the percent of pathologic tissue removed, with pain experienced during the procedure and pre-/post-treatment QoL as additional endpoints (see Sections 4.3 and 4.4).

In total, 74 women were treated. Most patients ($n=42$) were treated in the office (with baseline demographics comparable between settings). More pathologies were removed in the ASC setting ($n=55$, of which 41 polyps) than in the office ($n=53$, of which 25 polyps).

Overall, 98.2% (SD 4.9%) of pathologic tissue was removed. ASC procedures removed, on average, more pathologic tissue for any pathology (99.9% [SD 0.3%] versus 96.9% [SD 6.6%]) as well as fibroids (99.8% [SD 0.4%] versus 94.0% [SD 8.6%]) and polyps (100.0% [SD 0%] versus 99.8% [1.0%]) than procedures performed in the office but differences were small and not statistically significant (Figure 4-2). All pathologic tissue was removed in 93.8% of ASC and 74.0% of office procedures, with the difference due to a higher rate for complete fibroid removal in ASC procedures (83.3% versus 52.0%) whereas mHTR in both settings was equally successful for complete removal of polyps (96% of procedures).

Figure 4-2 Pathologic tissue removed by mHTR in office and ASC setting



ASC, ambulatory surgery center; mHTR, mechanical hysteroscopic tissue removal; SD, standard deviation. Source: Rubino *et al.*¹¹⁷

The resection time was longer for office procedures (189.3 sec [SD: 376.9 sec]) than for ASC procedures (82.2 sec [77.4 sec]) although the difference was not statistically significant ($p=0.09$). No statistically significant difference was observed for fluid deficit. It was concluded that mHTR was a clinically successful procedure in both the office and ASC settings.

4.2.1.3 Office versus Inpatient Polyp Treatment (Cooper *et al.*, Clark *et al.*)

Inpatient and office removal of polyps was compared in the OPT trial.^{30,42} Women presenting with AUB at one of 31 UK National Health Service (NHS) outpatient hysteroscopy clinics were eligible for inclusion if an endometrial polyp was identified during office hysteroscopy. For this study, "outpatient" and "office" were used interchangeably as polypectomy was performed with or without minor cervical dilation and local anesthesia.

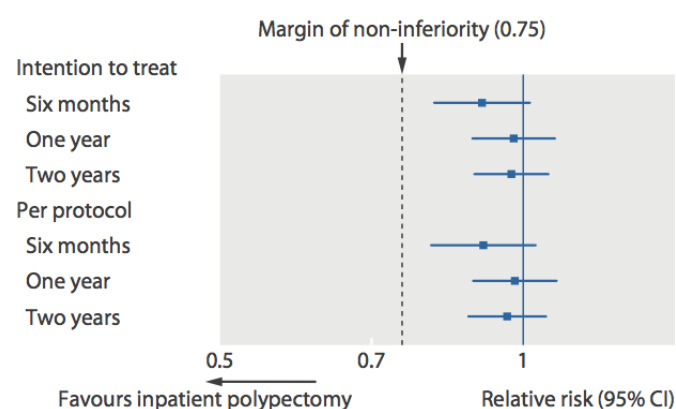
Women were randomly allocated, in a 1:1 ratio, to removal of uterine polyps in either an inpatient or an office/outpatient setting. Patients allocated to office/outpatient treatment usually underwent the procedure immediately after randomization. Office/outpatient polypectomy was performed with local anesthesia while inpatient polypectomy was

performed with regional or general anesthesia, under direct hysteroscopic vision using miniature mechanical or electrosurgical instruments (clinicians were free to use the device of their choice). The primary outcome measure was successful treatment based on women's assessment of their bleeding at six months (success/fail). For women with HMB, a reduction of bleeding to acceptable levels was considered as success. Non-inferiority of treatment success in the office/outpatient compared with the inpatient setting was assessed at a prespecified non-inferiority margin of 25%. Additional outcomes were assessment of bleeding using visual analog scales (VAS) and a Likert scale comparison of pre-/post-treatment bleeding. In addition, pain, procedure acceptability and QoL were assessed (see Sections 4.3 and 4.4).

A total of 507 women underwent inpatient (n=253) or office/outpatient (n=254) polypectomy. Baseline characteristics were comparable between groups. The most frequent presentation was postmenopausal bleeding (45%), followed by HMB (30%) and intermenstrual bleeding (25%). Primary outcome data at 6 months were available for 87% of women and showed that 73% of office/outpatient-treated and 80% of inpatient-treated women reported treatment as successful. The intent-to-treat relative risk of successful treatment for office/outpatient compared with inpatient polypectomy was 0.91 (95% CI: 0.82 to 1.02). Office/outpatient polypectomy was considered non-inferior to inpatient treatment (Figure 4-3). Treatment success did not differ across predefined subgroups but partial or failed removal was more frequent in the office/outpatient setting (19%) than in the inpatient setting (7%) group (relative risk 2.5 [95% CI 1.5 to 4.1]). Over the 2-year period of the trial, 43 and 21 women treated in the office/outpatient and inpatient setting, respectively, had a further polyp removal (relative risk 2.0 [95% CI 1.2 to 3.3]).

It was concluded that office/outpatient polypectomy was a non-inferior alternative to inpatient polypectomy at 6 and 12 months. Procedures in both settings improved clinical symptoms considerably, regardless of the type of AUB (IMB, HMB, PMB) or the type and location of the polyp, although failure of complete polyp removal was more likely in the office/outpatient setting. Office/outpatient treatment was as successful as inpatient treatment in improving generic and disease-specific quality of life. The authors suggested that office hysteroscopic services be established to offer women the chance of an informed decision between inpatient and office polypectomy. This might include both hospital-affiliated ambulatory units as well as community services.

Figure 4-3 Success of office/outpatient polypectomy



Reproduced from Cooper *et al.*⁴²

4.2.2 Reviews and Single-Arm Studies of Office/Outpatient Procedures

4.2.2.1 Review of 5,000 Outpatient Hysteroscopies (Di Spiezio Sardo et al.)

In a review of 5,000 consecutive cases between 1998 to 2003 at two outpatient clinics in the UK, the treatment success of outpatient hysteroscopy for AUB, subfertility, follow-up checks or lost IUDs was evaluated.¹¹⁵ Up to April 1998, hysteroscopies were conducted with a 4 mm telescope (5 mm diagnostic sheath). From May 1998, a 2.9 mm optic (3.5 mm diagnostic sheath) was also used. Similarly, the traditional technique using a Sims speculum and vulsellum were used exclusively before 1999, when they were complemented by the no-touch technique, using a hysteroscope and saline distention media. Hysteroscopies were defined as attempted or not attempted (contraindication or patient chose to cancel the procedure). Attempted hysteroscopies were classified as complete, incomplete (no visualization of the entire uterine cavity) or failed (no examination of uterine cavity possible). Risk factors for hysteroscopy outcomes were retrieved from patient data.

In 4,910 of 5,000 women (98.2%), hysteroscopy was attempted and 91.4% of attempted cases were successful (incomplete: 3.3%, failed: 5.3%). Failure was more likely in post- than in pre-menopausal women and in nulliparous than in parous women (Table 4-1). Traditional insertion was more often associated with failure than the no-touch approach. It was concluded that outpatient hysteroscopy was a simple and safe approach, which was recommended for uptake by the gynecologic community.

Table 4-1 Factors associated with failed hysteroscopy ¹¹⁵		
	Percent of failed hysteroscopies	p-value
Menopausal status		
Pre-menopausal	4.8	<0.001
Post-menopausal	7.6	
Parity		
Nulliparous	6.2	<0.05
Parous	4.8	
Need for cervical dilation (procedure continued with traditional approach, no-touch approach counted as failure)		
Yes	6.6	<0.001
No	3.5	
Need for local anesthesia (procedure continued with traditional approach, no-touch approach counted as failure)		
Yes	7.4	<0.001
No	3.0	
Traditional insertion technique		
Yes	5.5	<0.001
No	0.9	

Table 4-1 Factors associated with failed hysteroscopy¹¹⁵

	Percent of failed hysteroscopies	p-value
Use of a 4mm-optic		
Yes	4.9	<0.01
No	2.7	

4.2.2.2 Success of See-and-Treat Hysteroscopic Polypectomy (Gambadauro et al.)

In a retrospective study of 229 women referred to the outpatient hysteroscopic unit of a Spanish hospital, endometrial polyps were removed using a vaginoscopic approach without cervical dilation or anesthesia.¹¹⁴ Polyps were removed during diagnostic hysteroscopy, where possible, using mechanical (scissors, grasping or biopsy forceps) and electrosurgical (VersaPoint™) devices. Patients were released home shortly after the procedure if removal was successful (otherwise, they were scheduled for hysteroscopic resection on the following day). The authors considered this to be an “office” procedure as no dilation or anesthesia were used and patients were treated quickly after referral.

Access to the uterine cavity was achieved in 97% of cases who underwent office hysteroscopy. See-and-treat polypectomy was successful in 66% of these cases. Success was positively associated with premenopausal status (OR 3.6 [95% CI: 1.3 to 10.1]) as treatment was successful in 77% of premenopausal but only 53% of postmenopausal women. Treatment was negatively associated with pain at hysteroscopy (OR 0.09 [95% CI: 0.03 to 0.21]) and smaller polyp size (OR 0.89 [95% CI: 0.85 to 0.94]). It was concluded that polypectomy can be performed successfully, particularly for smaller polyps and in premenopausal women, in an office-like setting.

4.2.2.3 Hysteroscopy-guided Polyp Removal with mHTR (Abeywardena et al.)

A prospective study of polypectomy under local anesthesia in an office/outpatient setting was conducted in 50 women presenting with PMB, HMB or IMB in the UK.¹¹⁸ After local anesthesia, hysteroscopy was performed to diagnose abnormalities before the outflow channel was replaced with an mHTR device (manufacturer unspecified). Patients were accompanied by a chaperone during the procedure and were assessed by a member of staff before discharge. Overall, office-based mHTR removed polyps completely in 94% of women and partially in 6% of women. The authors concluded that mHTR can be used successfully for office-based polypectomy.

4.2.2.4 Specimen Quality in Office Polypectomy (Franchini et al.)

In a review of 90 consecutive office polypectomies, the specimen quality of histopathological slides was assessed.¹¹⁹ Procedures performed in the office with grasping forceps/microscissors, bipolar electrosurgical probes or mHTR (TruClear™) were evaluated with regard to the adequacy of specimens obtained during the procedures. Adequacy was defined as the percentage of biopsy specimens needed for two pathologists, who were blinded to the polypectomy technique, to make a diagnosis. In addition, agreement/accuracy was defined as the percentage of reports confirmed by a second pair of pathologists.

All 90 specimens were considered adequate and no difference by the type of device used was observed. It was concluded that, regardless of the technique used, office polypectomy is able to deliver histopathological specimen of good quality.

4.3 Safety of Office Gynecologic Procedures

Short summary

Several guidelines outline procedures to establish a safe environment for office surgery. These guidelines stress the need for a safety-oriented mindset and the use of safety checklists. In general, office gynecologic procedures are considered to be safe.^{5,6}

Complication and adverse event rates are not statistically significantly different between office and inpatient procedures.^{42,116,117} When adverse events occur, they are generally mild and resolve spontaneously.^{124,125,126}

Pain is the most frequent adverse event in office procedures and occurs more frequently than in inpatient procedures, which use general anesthesia. However, effective treatment, e.g. a vaginoscopic approach, and anesthesia algorithms exist for prevention and treatment of pain. Pain was also found to be outweighed by the convenience of office procedures.^{42,117,120,126}

4.3.1 General Safety Considerations for Office Gynecologic Procedures

Office gynecologic procedures are generally safe and benefit both patients and providers.⁵ Best practices for office gynecologic procedures can be certified in the US with the Safety Certification in Outpatient Practice Excellence (SCOPE), developed by ACOG as a voluntary certification for interested offices.^{5,6} SCOPE involves two steps: First, offices apply for certification and submit data on patient demographics, medication safety, practice management, quality initiatives and performance indicators before, second, an on-site validation is performed by a SCOPE site visitor whose findings might lead to the office being awarded a certification of up to 3 years.⁶

Pain management during gynecologic procedures performed in the office is crucial to treatment success and patient satisfaction.^{121,122} Local anesthesia is commonly used in the office but recent reviews of the literature suggest that multimodal approaches might be more effective than local anesthesia alone.^{121,122} Multimodal approaches complement anesthesia, which is often given orally, with emotional support provided by a dedicated support person or with visual/auditory distraction, e.g. music.^{122,123} The available evidence is not fully conclusive as heterogeneous study populations, gynecologic procedures and pain regimens limit the comparability of results.¹²² Even so, studies and reviews agree on the importance of patient counseling and selection to target pain management programmes.¹²²

4.3.2 Rates of Complications and Adverse Events

Rates of complications and adverse events for office gynecologic procedures were generally reported as low (pain is considered in more detail in the next subsection) (Table 4-2).

4.3.2.1 Evidence from Head-To-Head Comparisons of Treatment Settings

Scheiber *et al.*, in their trial comparing mHTR in the office and the ASC/HOPD setting reported adverse event (cervical trauma or postoperative pedal edema) rates of 3.6% for office mHTR and 1.6% for ASC/HOPD treatment.¹¹⁶ The difference between settings was not statistically significant ($p=0.4143$), and all AEs were considered mild and resolved spontaneously.

Similar results were reported by Rubino *et al.*, in their comparison of office and ASC mHTR.¹¹⁷ One patient from the office (2.4%) experienced pain and one patient from the ASC setting (3.1%) experienced diarrhea and food poisoning (no relation with gynecologic procedure reported). Again, all AEs were considered mild and did not require hospitalization.

In the OPT trial, four serious AEs occurred in the inpatient group (2% of patients in this group).⁴² AEs were uterine perforations, one of which involved a bowel injury requiring laparotomy and small bowel resection and one of which required an indwelling catheter after inpatient polypectomy. In addition, one woman in the inpatient group had indwelling catheterization following an inpatient removal. One patient in the office/outpatient group experienced a myocardial infarction (no relation with gynecologic procedure reported).

4.3.2.2 Evidence from Single-Arm Studies and Reviews

Single-arm studies and published literature reviews indicate that complication rates for hysteroscopy and polypectomy are low in all settings (Table 4-2).

Study	Procedures	Setting	N	Complication rate (% of procedures)	Type/severity of adverse events
Scheiber <i>et al.</i> , 2016 ¹¹⁶	mHTR for polyps and fibroids	Office	28	3.6	Mild cervical trauma, moderate post-operative pedal edema
		ASC/HOPD	250	1.6	
Rubino <i>et al.</i> , 2015 ¹¹⁷	mHTR for polyps and fibroids	Office	42	2.4	Pain
		ASC	32	3.1	Diarrhea, food poisoning
Cooper <i>et al.</i> , 2015 ⁴²	Polypectomy	Office	242	0.0	Uterine perforation
		Inpatient	233	2.0	
Wortman <i>et al.</i> , 2013 ¹²⁴	Operative hysteroscopy	Office	414	2.7	Febrile infection, uterine perforation, uterine rupture
van Kerkvoorde <i>et al.</i> , 2012 ¹²⁵	Diagnostic and operative hysteroscopy	Office	1,028	7 (short-term) 0.001 (within 1 st year)	Vasovagal attack, nausea/vomiting, lower abdominal pain
Keyhan & Munro, 2014 ¹²⁶	Diagnostic and operative hysteroscopy	Office	639	0.5	Vasovagal attack
Di Spiezio Sardo <i>et al.</i> , 2008 ¹¹⁵	Diagnostic hysteroscopy	Office	5,000	5.4	Vasovagal attacks, shoulder pain, false passage, cervical laceration, panic attack, bleeding, pain

ASC, ambulatory surgery center; HOPD, hospital outpatient department; mHTR, mechanical hysteroscopic tissue removal.

In a retrospective review of 387 women with 414 operative hysteroscopies, conducted mostly with a 9 mm continuous-flow resectoscope for myomectomy, polypectomy or repeat surgery after failed endometrial ablation, procedure data from a physician's private office were analyzed for complications.¹²⁴ Eleven complications were observed in these 414 office operative hysteroscopies (2.7%). Febrile infections were the most common AE (1.9% of all procedures), with most women becoming febrile within 30 minutes after the procedure. One uterine perforation occurred with an active electrode (0.2%) and hospitalization was required for this case. In addition, two uterine ruptures (0.5%) occurred and precluded completion of the procedure. Overall, the office was considered safe for operative hysteroscopic surgery.

Operative and diagnostic office hysteroscopy was also concluded to be safe in a review of 1,028 procedures using a vaginoscopic approach.¹²⁵ Hysteroscopy was performed using a 4.5 mm continuous-flow rigid hysteroscope and saline solution 0.9% as a distention medium. Long-term complications were retrieved from the departmental complications registry and were supplemented by a random sample of medical histories of a third of patients. Overall, 72 complications were observed in 1,028 procedures (7%). The most frequent short-term complication was excessive pain (75% of complications), followed by vasovagal attack (14%) and nausea/vomiting (7%). One case of suspected fever was not confirmed but the same case reported lower abdominal pain 9 days after hysteroscopy. This was the only complication observed within the first year after hysteroscopy, yielding a 1-year complication rate of 0.001% for office hysteroscopy.

A similarly low rate of complications was reported in a review of office diagnostic and operative hysteroscopies between 2005 to 2012.¹²⁶ Women underwent hysteroscopy with a 3 mm continuous-flow hysteroscope, occasionally also with a resectoscope, and were treated with a multimodal local anesthesia protocol. Polyps were usually removed with scissors and forceps. Fibroids were, at the beginning of the study period, removed with bipolar needles or resectoscopes but were increasingly removed using mHTR as the study progressed. In total, 639 procedures in 569 women were eligible for the study. Except for three transient vasovagal reactions, no complications were observed, yielding a complication rate of 0.5%.

4.3.3 Pain during Office Gynecologic Procedures

Pain is the most frequent complication in office gynecologic procedures and is often linked to using no or local anesthesia in office procedures, compared with general anesthesia used in inpatient procedures.^{115,127}

4.3.3.1 Evidence from Head-To-Head Comparisons of Treatment Settings

Rubino *et al.*, in their direct comparison of office and ASC mHTR, used a pain management protocol for office procedures.¹¹⁷ Patients took 800 mg ibuprofen in the night before the procedure and, 1 hour before the procedure, were given oral 10 mg diazepam, 10 mg hydrocodone/acetaminophen and 25 mg promethazine. In addition, topical 2% lidocaine gel was applied to the cervix and a swab coated with 2% lidocaine gel was inserted into the cervical os for 10 min. Patients were also injected superficially at the 12:00 position with 2 mL of 1% lidocaine and 0.25% bupivacaine and received a deep injection (1 to 2 cm) of 10 mL of 1% lidocaine and 0.25% bupivacaine at the 4:00 and 8:00 positions. Patients in the ASC setting received anesthesia according to the respective institutional protocol.

Patients assessed the pain experienced during office mHTR and compared the pain with that experienced during a Pap smear (inpatients did not assess their pain due to different anesthetic regimens). On a 10-point scale, where higher values indicated more pain, women reported a mean pain score of 1.8 (SD 1.8). The difference to the main pain score reported for a Pap smear (1.2 [SD 1.1]) was not statistically significant ($p=0.06$). Combined with the low rate of non-pain complications, office procedures were considered to be safe.

Pain scores were also reported for the OPT trial.^{30,42} Inpatients were usually treated under regional or general anesthesia (local anesthesia was used in 6% of inpatients) whereas patients treated in the office/outpatient setting were treated with local or no anesthesia. No detailed pain management protocol was provided but anesthetics used in the office/outpatient setting included 2% lidocaine, 3% prilocaine, 3% mepivacaine and 3% bupivacaine.³⁰ Patients rated their pain 1 hour after the procedure and on discharge using VAS (0, no pain, to 100, worst imaginable pain).

Table 4-3 Pain scores associated with polypectomy⁴²

	Inpatient	Office/ outpatient	Mean difference (95% CI)
During procedure, mean (SD)	–	45 (26)	–
60 minutes after procedure, mean (SD)	23 (22)	28 (23)	–5 (–10 to 0)
On discharge, mean (SD)	15 (17)	23 (21)	–8 (–12 to –4)

CI, confidence interval; SD, standard deviation. Pain scores measured using visual analog scale, with 0 indicating no pain and 100 indicating worst imaginable pain.

Office/outpatient-treated patients reported a mean pain score of 45 (SD 26) during the procedure (Table 4-3). Both 60 minutes after the procedure and on discharge, pain scores reported by inpatients (treated mostly under general or regional anesthesia) were statistically significantly lower than pain scores reported by office/outpatient-treated patients. Qualitative interviews showed, however, that women in the office/outpatient group experienced mostly short-term pain which was outweighed by the convenience of fast treatment.¹⁴

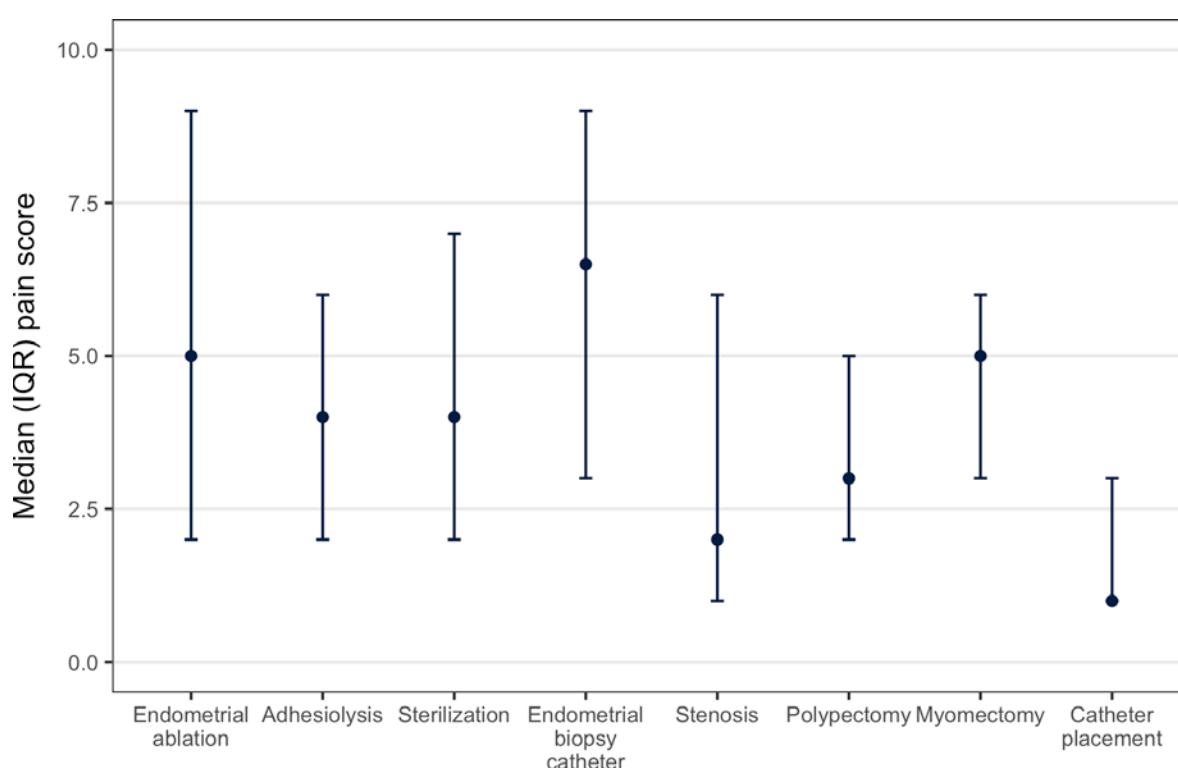
4.3.3.2 Evidence from Single-Arm Studies

In a retrospective study of 639 office diagnostic or operative hysteroscopic procedures, using mostly 3 mm hysteroscopes and 9 mm sheaths for resectoscopy, pain scores associated with the procedure were analyzed.¹²⁶ Women scheduled for hysteroscopy were instructed to use a cyclooxygenase inhibitor and either 600 mg of ibuprofen (3 times daily) or 440 mg sodium naproxen (twice daily) in the 48 hours preceding the procedure. During the procedure, a multiple modality anesthetic protocol was used, beginning with 2% lidocaine gel to coat the speculum before insertion. After speculum placement, approximately 3 mL of 0.5% lidocaine was injected into the cervix, with 1:200,000 adrenaline, via a spinal needle. In addition, a paracervical block was administered using the same spinal needle to inject a total of 20 to 30 mL of 0.5% lidocaine, with 1:200,000 adrenaline. Furthermore, 4% liposomal lidocaine paste was applied to the cervical canal and 10 mL of 2% lidocaine gel was injected

into the endometrial cavity. Hysteroscopy was begun 10 to 20 min after administration of anesthetics.

Patients were asked, at the end of the procedure, to rate the pain experience on a scale from 0 to 10, with higher score indicating more pain. In procedures performed between 2005 to 2009, patients were asked about the maximum pain experienced during hysteroscopy whereas the maximum pain during both administration of anesthesia and hysteroscopy was assessed for procedures after 2009. Patients rated catheter placement as the least painful procedure, with a median pain score of 1 (interquartile range [IQR] 1 to 3) (Figure 4-4). The most painful procedure was endometrial biopsy catheter, with a median pain score of 6.5 (IQR 3 to 9). For myomectomy, a median pain score of 5 (IQR 3 to 6) was reported. Removal of endometrial polyps was rated among the less painful procedures, at a median pain score of 3 (IQR 2 to 5).

Figure 4-4 Pain scores associated with office procedures



IQR, interquartile range. Higher scores indicate more pain. Source: Keyhan & Munro¹²⁶

For operative hysteroscopy, no difference between anesthesia and procedure pain scores was identified but anesthesia was found to be more painful than the procedure itself in diagnostic procedures. It was concluded that a multimodal approach to local anesthesia contributes to successful and comfortable surgery in offices.

Similar results were observed in a UK study of 50 women who underwent polyp removal with mHTR under local anesthesia.¹¹⁸ Women answered a questionnaire on pain experienced during and immediately after polypectomy and follow-up telephone calls were made to assess pain on the first day after the procedure. On the Discrete Quantitative Pain Verbal Rating Scale, which ranges from 0 (no pain) to 10 (worst pain), the mean score was 2.4, which was considered mild.¹¹⁸ The mean pain of the procedure itself (1.9) as well as the pain immediately after (1.4) and on the day after the procedure (1.4) were also mild and lower than

the pain associated with infiltration of local anesthesia (2.6) and cervical dilation (where necessary; 3.4). It was concluded that, overall, patients experienced little pain during and after polyp removal so the procedure was considered to be well tolerated in the office.

A similar study was conducted in 558 women undergoing elective diagnostic office hysteroscopy without anesthesia.¹²⁸ Hysteroscopy was performed using a vaginoscopic approach and a hysteroscope with an outer diameter of 2.9 mm. Pain intensity was assessed by women rating their pain at the end of the procedure and 10 to 15 min after the procedure (at discharge) on a scale of 0 (no pain) to 10 (worst imaginable pain). Unacceptable pain at the end of the procedure and at discharge was defined as a rating ≥ 7 and ≥ 4 , respectively.

Overall, 32% (95% CI 29 to 36%) reported unacceptable pain during the procedure, which was associated with longer procedure time and less experienced physicians. At discharge, 29% (95% CI 25 to 32%) of women reported unacceptable pain, again associated with longer procedure time and less experienced physicians. Further studies suggested that pain was also higher in older and post-menopausal patients and was positively associated with pre-procedure anxiety and waiting time.^{123,127} It was shown that relatively simple methods, e.g. reducing waiting time or playing music during the procedure, can reduce patient anxiety and pain during office-based gynecologic procedures.^{123,127}

4.4 Patient Satisfaction with Office Gynecologic Procedures

Short summary

Improvements in symptoms and quality of life are similar for office and inpatient treatment. Head-to-head comparisons showed that 80% and more of women were satisfied or very satisfied with office treatment, would undergo the procedure again and would recommend office procedures to others.^{4,90,117}

Single-arm studies confirmed these findings and showed that most women felt safe in the office environment and well prepared for the procedure. A lack of satisfaction was often associated with insufficient sedation during or nausea after the procedure, both of which can be easily avoided or treated if guideline recommendations are implemented.^{90,124,129}

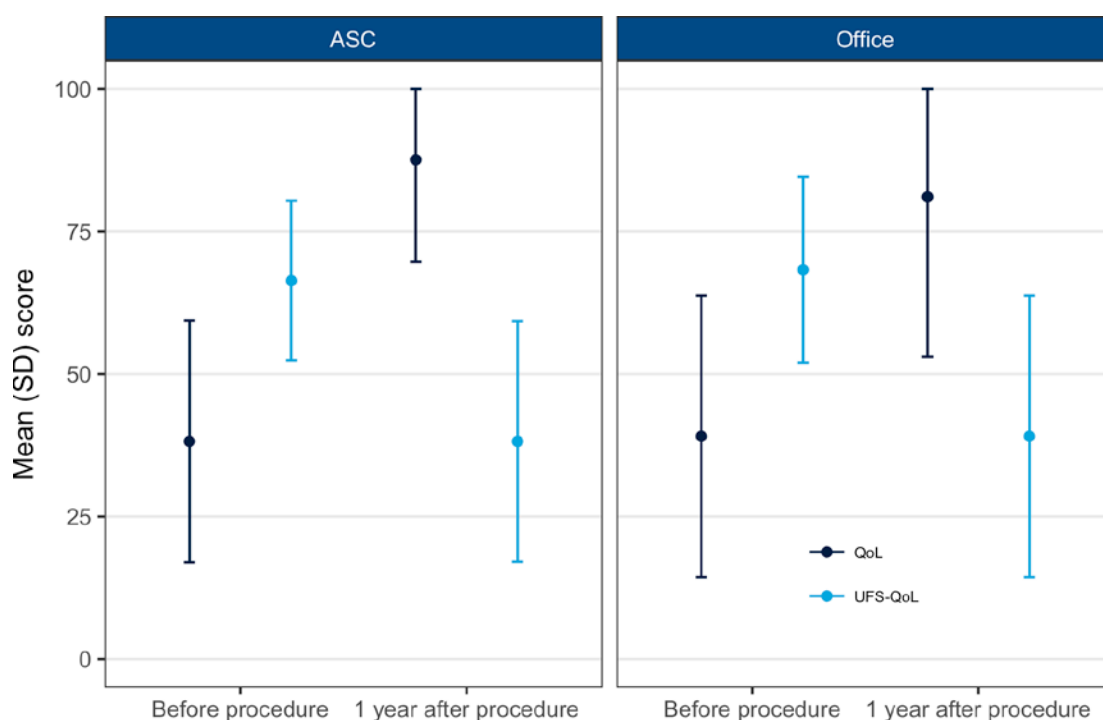
4.4.1 Evidence from Head-To-Head Comparisons of Treatment Settings

Rubino *et al.*, in their study of office versus ASC mHTR, also evaluated patient satisfaction and QoL.¹¹⁷ QoL was assessed using the generic HRQoL questionnaire and the Uterine Fibroids Symptom-Quality of Life (UFS-QoL) symptom severity score before and 1 year after treatment. Patient satisfaction was assessed in a survey 1 year after treatment.

Symptom severity was reduced considerably, with improvements of 42.7 (SD 24.0) and 48.3 (SD 21.6) points for office and ASC treatment, respectively (Figure 4-5). Similarly, QoL score improvements of 42.3 (SD 25.3) and 49.4 (SD 24.3) points were observed for office- and ASC treatment.

Treatment satisfaction was slightly higher for patients treated in the ASC. Of ASC-treated patients, 97% were satisfied or very satisfied with their treatment (office: 89%), 97% would undergo future treatment if they experienced similar symptoms (office: 96%) and all would recommend the treatment to others with the same symptoms (office: 96%). It was concluded that mHTR in both settings is not only clinically effective but also contributes to considerable improvements in QoL and symptom severity, leading to high levels of patient satisfaction.

Figure 4-5 QoL and symptom severity after mHTR treatment by treatment site



ASC, ambulatory surgery center; QoL, quality of life; UFS-QoL, Uterine Fibroid Symptoms Quality of Life. Higher scores indicate higher QoL/more severe symptoms. Source: Rubino *et al.*¹¹⁷

Similar results were reported for the OPT trial.⁴ QoL was assessed at baseline and 6 months after recruitment with the EQ-5D-3L (ranging from -0.59 for a health state worse than death to 1 for a perfect health state) and the disease-specific Menorrhagia Multi-Attribute Scale. Patients also rated procedure acceptability on a Likert scale and in survey questions. In addition, semi-structured interviews were conducted 1 week after treatment in women who had consented to be interviewed.

In both settings, condition-specific QoL was improved 6 months after polypectomy, with no statistically significant difference between settings (Table 4-4). Although 2% of office/outpatient-treated women considered the procedure “unacceptable”, there was no statistically significant difference between groups with regard to recommending treatment to a friend, undergoing the same treatment again or preferring an alternative treatment. Overall, office/outpatient polypectomy was considered an acceptable procedure capable of increasing QoL.

Table 4-4 QoL and treatment satisfaction with polypectomy⁴

	Office/ outpatient	Inpatient	Mean difference (95% CI)
MMAS, mean (SD)			
Baseline	63 (26)	61 (28)	-4 (-14 to 3) [#]
At 6 months	77 (25)	79 (25)	

Table 4-4 QoL and treatment satisfaction with polypectomy⁴

	Office/ outpatient	Inpatient	Mean difference (95% CI)
EQ-5D, mean (SD)			
Baseline	0.79 (0.26)	0.72 (0.30)	0.01 (−0.05 to 0.08) [#]
At 6 months	0.82 (0.25)	0.81 (0.30)	
Operation acceptability, %			
Totally	65	81	0.19 (0.05 to 0.70) [#]
Generally	16	14	
Fairly	17	5	
Unacceptable	2	0	
Exposure embarrassing, %			
Extremely	2	3	1.4 (0.6 to 3.7) [#]
Moderately	10	12	
A little	30	13	
No	59	72	
Recommend to friend, %	93	97	0.45 (0.10 to 2.0)
Same treatment again, %	94	98	0.27 (0.04 to 2.1)
Preferred alternative treatment, %	12	16	1.5 (0.7 to 3.5) [#]

MMAS, Menorrhagia Multi Attribute Scale. Difference at each point in time adjusted for baseline score. Differences >0 favor office polypectomy. # Difference adjusted, among others, for predominant bleeding complaint at consent, type/number/size of polyps, surgeon experience, treatment method, age, BMI and parity.

Office treatment was preferred by many US women presenting for surgical management of early pregnancy failure.⁹⁰ Patients could choose between treatment in the office or the operating room. Patients treated in the office received 1 mg oral lorazepam, 800 mg ibuprofen and/or 100mg propoxyphene napsylate (acetaminophen 650 mg) and were treated with manual vacuum aspiration. Patients treated in the operating room received intravenous sedation, regional anesthesia or general anesthesia and were treated with electric suction, with or without sharp curettage. Before discharge, patients completed a questionnaire rating communication with the care provider and the procedure itself on a 10-point scale, with higher values indicating greater satisfaction. The two scores were combined for a total satisfaction score.

Overall, 165 women were enrolled and 115 chose the office. Satisfaction data were available for 146 women (110 in the office). No statistically significant differences were observed for total satisfaction or the proportion of highly satisfied patients. Similarly, the proportion of patients who would choose the procedure again or recommend it to a friend did not differ statistically significantly between treatment settings. The authors concluded that many women about to undergo surgical treatment for early pregnancy failure prefer the office,

especially those who prioritize treatment safety, staying awake during the procedure and privacy.⁹⁰

4.4.2 Evidence from Single-Arm Studies

In their study of office operative hysteroscopy, Wortman *et al.* contacted patients after treatment (time period unspecified) to conduct a brief patient satisfaction interview.¹²⁴ A total of 255 women (of 387) responded to the telephone survey, of which 99% were satisfied or very satisfied with their office treatment. Women who were somewhat dissatisfied with treatment had been inadequately sedated or experienced prolonged nausea/vomiting after the procedure. Office treatment was preferred by 98% of women. Only 2% would have preferred hospital treatment (including the “somewhat dissatisfied” women) and 98% would recommend office treatment to a friend.

Similarly, in a study of 118 women treated with resectoscopic operative hysteroscopy for fibroids and endometrial polyps, most women viewed the office treatment favorably.¹²⁹ Patients were treated with resectoscopy under local anesthesia and, 1 week after treatment, participated in a telephone interview about their treatment satisfaction. Satisfaction data were available for 102 patients, of which 99% reported that the treatment environment was acceptable and 93% reported that they felt they had enough information and explanation to prepare for the procedure. More than 90% of patients said that no part of the procedure had caused them concern and 91% would recommend the procedure to a friend.

Women treated for endometrial polyps in the UK also expressed satisfaction with their treatment in an office/outpatient setting.¹¹⁸ Of the 50 women, all treated with mHTR, 78% reported they were “totally” satisfied with the procedure, 14% were “generally” and 8% were “fairly” satisfied. All patients considered the procedure to be acceptable, 94% would recommend the procedure to a friend and 96% would undergo the procedure again should another polypectomy be necessary. It was concluded that patients accepted mHTR treatment in an office/outpatient setting well.

5 Health Economic Impact of Shifting Gynecologic Procedures to the Office

Key messages

Studies consistently show that healthcare payers can save costs if gynecologic procedures are shifted to the office.

Cost savings for healthcare payers and providers of up to USD 3,000 per procedure performed in the office instead of the operating room have been reported, without a loss in clinical success.

Mechanical hysteroscopic tissue removal has a superior clinical and safety profile compared with other procedures in published cost analyses and might therefore be associated with even larger cost savings.

Short summary

Cost comparison analyses identified savings of up to USD 3,000 per office procedure.^{90,129,133,134,135} Key drivers of the favorable cost profile for the office were the lower costs for procedure room and staff. In addition, office procedures were performed mostly under local anesthesia, thereby reducing the costs associated with anesthetics and anesthesiologists' fees.

Lower costs for office procedures were associated with clinical success and patient satisfaction similar or even superior to inpatient procedures. Mechanical hysteroscopic tissue removal might reduce costs even further given its excellent clinical and safety profile, reduced procedure times and shorter learning curve.^{89,98,113,130,135}

A cost-effectiveness study of office/outpatient versus inpatient polypectomy identified cost savings of GBP 669 per office procedure after 12 months, from the perspective of the English NHS.¹³¹ To gain an additional quality-adjusted life-year with inpatient versus office/outpatient treatment, healthcare payers would have to pay more than GBP 400,000, a price much higher than healthcare payers' willingness-to-pay thresholds. The favorable position of office/outpatient treatment resulted from its much lower costs to achieve the same treatment success.

Table 5-1 Cost savings associated with the site of service shift to the office

Study	Procedure and setting	Cost data/perspective	Mean savings per procedure with office treatment	
			Absolute	Relative
Hidlebaugh (1996) ¹³³	Office hysteroscopy with suction biopsy versus hospital D&C	Hospital billing data (1994) for anesthesia and operative charges versus office, instrument repair and capital equipment costs	USD 1,737	97%

Table 5-1 Cost savings associated with the site of service shift to the office

Study	Procedure and setting	Cost data/perspective	Mean savings per procedure with office treatment	
			Absolute	Relative
Dalton <i>et al.</i> (2006) ⁹⁰	Office versus operating room evacuation of early pregnancy failure	Resource use estimated from procedure time and patient time at facility; direct and indirect costs institutional database (n.d.)	USD 997	51%
Saridogan <i>et al.</i> (2010) ¹³⁵	Office/outpatient versus inpatient see-and-treat approach for AUB	UK NHS perspective; direct medical costs using NHS reference costs (2008)	GBP 141	18%
Keyhan & Munro (2014) ¹²⁶	Office versus inpatient diagnostic hysteroscopy	Resource use from randomly selected institutional cases; line item costs taken from SCPMG; total cost saving estimated for healthcare payer (2006)	USD 3,411	94%
Moawad <i>et al.</i> (2014) ¹³⁴	Office versus operating room hysteroscopy for AUB	Operating room versus office charges from billing department (n.d.)	USD 3,590	73%
Penketh <i>et al.</i> (2014) ¹²⁹	Office/outpatient versus day case resectoscopic hysteroscopy under general anesthesia	Resource use and staffing, procedure, drug and equipment costs from local (Welsh) and national (UK) sources (2010)	USD 1,003	68%
Diwakar <i>et al.</i> (2016) ¹³¹	Office/outpatient versus inpatient polypectomy (12 months after procedure)	UK NHS perspective; use of standard NHS reference costs; resource use collected prospectively during trial (2012)	GBP 669	42%

AUB, abnormal uterine bleeding; GBP, pounds sterling; n.d., no date; NHS, National Health Service; SCPMG, Southern California Permanente Medical Group; UK, United Kingdom; USD, US dollar.

5.1 Note on Health Economic Terminology

The health economic studies summarized in this section mostly compare costs between different sites of service. For each site of service, (units of) resources used are multiplied with unit costs and the results summed to yield the total cost associated with a procedure. The difference in total costs can then be interpreted as the cost savings associated by choosing the cheaper over the more expensive site of service.

Cost-effectiveness studies, of which one was identified in the literature review for this GVD, follow the same methodology with regard to costs. They go one step further than cost comparison studies in that the costs of a procedure are related to its benefit. A commonly used measure of benefit is the quality-adjusted life-year (QALY). The QALY combines the impact of a procedure on the quantity and quality of life by multiplying life years with their utility.¹³² Utilities are evaluations of health states and are elicited from patients or the general public. A popular instrument to obtain utilities is the EQ-5D questionnaire, which is filled in by respondents whose answers are converted to a utility value, ranging from 0 to 1, with the help of special conversion algorithms.

Benefits, e.g. QALYs, can then be compared across sites of services simply by taking the difference of the procedure benefit between the two sites. If this difference is used to divide the corresponding difference in costs, the incremental cost-effectiveness ratio (ICER) is obtained. The ICER indicates what an additional unit of the benefit, e.g. an additional QALY, would cost at one site of service compared with the other.

5.2 Cost-Effectiveness Analysis of Office/Outpatient Versus Inpatient Polyp Treatment

A cost-effectiveness analysis comparing office/outpatient with inpatient polyp treatment for AUB was performed as part of the OPT trial.^{4,30,42,131}

The analysis was conducted from the perspective of the UK NHS. Two separate methods were used to estimate 1-year costs. First, published NHS Reference costs (2011 to 2012) and Personal Social Services Resource Unit costs (2012) were used. Second, Health and Community Health Services prices, inflated to 2011 to 2012 prices, were used for individual components of office/outpatient and inpatient procedures. For both site of services, the costs of initial outpatient clinic visits, hysteroscopy and polypectomy were included. For office/outpatient procedures, the costs of a follow-up outpatient visit were included. For inpatient procedures, the costs of pre-operative assessment were included. Costs of immediate complications or complications occurring within 1 year after procedure were also considered in the analysis. Surgeon fees were ignored as they were assumed to be the same in both settings. As the time frame of the analysis was only 1 year, costs were not discounted.

Two outcomes were considered, each measured at 6 and 12 months after the procedure. First, patient-reported treatment success was used to calculate the costs per additional patient who was successfully treated. Treatment was defined as successful if AUB had stopped (for women with postmenopausal or intermenstrual bleeding) or was reduced to an acceptable level (for women with HMB). Second, QALYs were used to calculate the cost per QALY gained. QALYs were obtained from EQ-5D-3L surveys at baseline and at 6 and 12 months after the procedure.

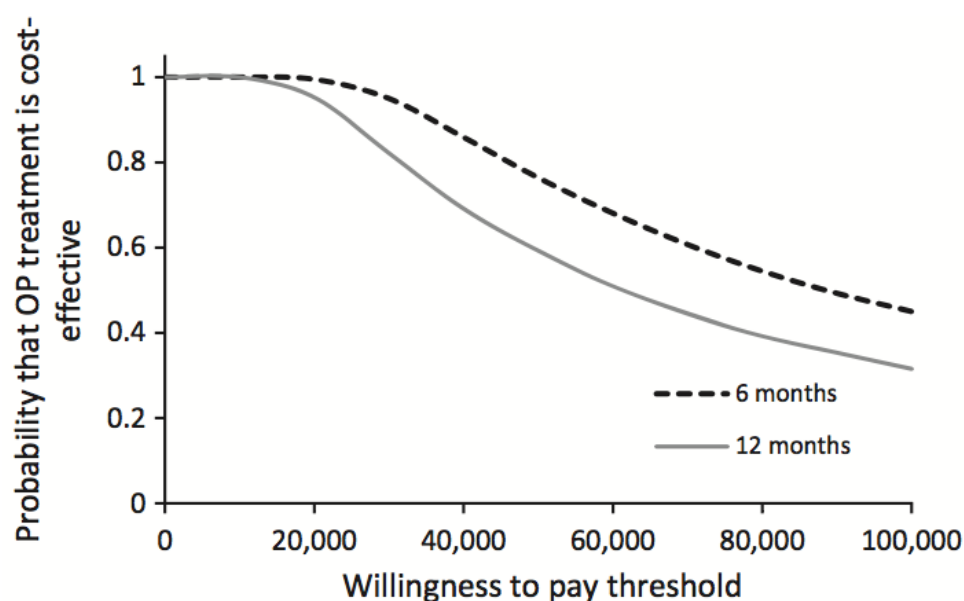
Office/outpatient procedures were associated with lower costs than inpatient procedures, with mean absolute savings of GBP 660 (95% CI GBP 516 to 781) and GBP 669 (95% CI GBP 517 to 833) at 6 and 12 months after polypectomy, respectively (Table 5-2). The higher costs of inpatient procedures were associated with only small and statistically insignificant gains in QALYs and, after 12 months, the gain in treatment success associated with inpatient versus office/outpatient polypectomy was reduced to only 3% (the difference was not statistically significant).

Table 5-2 Cost-effectiveness of office/outpatient versus inpatient polypectomy ¹³¹			
	Office (n=254)	Inpatient (n=253)	Mean difference (95% CI)
6 months after polypectomy			
Overall cost from UK NHS perspective (GBP), mean (SD)	822 (832)	1,482 (681)	−660 (−781 to −516)
Overall QALYs, mean (SD)	0.4087 (0.0984)	0.4093 (0.0937)	−0.0006 (−0.0169 to 0.0150)
Treatment success, %	74 (44)	82 (39)	−7 (−15 to −1)
ICER, treatment success	GBP 9,421 per additional women who feels better with inpatient treatment		
ICER, QALY	GBP 1,099,167 per QALY gained on inpatient arm		
12 months after polypectomy			
Overall cost from UK NHS perspective (GBP), mean (SD))	938 (971)	1,606 (862)	−669 (−833 to −517)
Overall QALYs, mean (SD)	0.8338 (0.1911)	0.8353 (0.1773)	−0.0015 (−0.0345 to 0.0281)
Treatment success, %	81 (39)	85 (36)	−0.03 (−0.09 to 0.04)
ICER, treatment success	GBP 22,293 per additional women who feels better with inpatient treatment		
ICER, QALY	GBP 445,867 per QALY gained on inpatient arm		

CI, confidence interval; GBP, pounds sterling; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

At 6 and 12 months after polypectomy, costs of GBP 9,421 and GBP 22,293 were incurred per women who felt better after inpatient treatment. With regard to QoL, ICERs of GBP 1,099,167 and GBP 445,867 per QALY gained at 6 and 12 months after treatment, respectively, were reported. These ICERs are substantially higher than the commonly quoted willingness-to-pay threshold of the NHS, which ranges between GBP 20,000 to 30,000 per QALY gained. In sensitivity analyses, inpatient treatment was consistently found to be more expensive and the probability that office/outpatient polypectomy was considered cost-effective compared with inpatient polypectomy was over 60%, for both 6 and 12 month-outcomes, at a willingness-to-pay threshold of GBP 40,000 per QALY gained (Figure 5-1). Only at a willingness-to-pay threshold of GBP 90,000 per QALY gained was treatment in both settings likely to be equally cost-effective.

Figure 5-1 Cost-effectiveness of office/outpatient versus inpatient polypectomy



Source: Reproduced from Diwakar *et al.*¹³¹

It was concluded that, as office/outpatient polypectomy offered the same benefits as inpatient polypectomy at a lower cost, office/outpatient treatment was cost-effective compared with inpatient treatment. Given limited NHS resources, office/outpatient treatment was recommended for women presenting with AUB caused by uterine polyps.

5.3 Cost Comparisons of Office and Inpatient Gynecologic Procedures

5.3.1.1 Hidlebaugh *et al.*, 1996

A first cost comparison for office versus hospital hysteroscopy was provided by Hidlebaugh in 1996.¹³³ Attempted office hysteroscopies (with suction biopsy) and hospital diagnostic hysteroscopies (with D&C), performed in an office group practice (1991 to 1995) and a university-affiliated private hospital (1993 to 1994), were reviewed retrospectively. In total, 473 office and 95 hospital procedures in women presenting with AUB were included in the review.

Cost data for office hysteroscopies included costs of disposable equipment, staff salary, instrument repair charges and capital equipment costs (surgical instruments, hysteroscope, light source, insufflators) and were compared with hospital anesthesia, nursing, room, surgical and physician charges. Gynecologists' fees were excluded as they were the same in both sites of service (the same group of gynecologists performed the procedures in both settings).

Over the period of the study, total capital equipment and instrument repair costs of USD 16,359 were incurred in the office. With additional disposable supply costs and staff salaries of USD 27 per procedure, the overall mean cost per office hysteroscopy was USD 62, compared with USD 1,799 (range USD 1,304 to 2,612) per hospital hysteroscopy. As hospital procedures were almost 30 times more expensive and were associated with higher complication rates than office procedures, the office was considered the preferred site of service for hysteroscopy. It was recommended that the value of the office be explained to patients requesting hospitalization, with reference to additional advantages of office

procedures such as avoidance of general anesthesia and less disruption of patients' daily lives.

5.3.1.2 Dalton et al., 2006

In a prospective observational study of 165 US women presenting with early pregnancy failure, participants could choose between office treatment and treatment in the operating room.⁹⁰ Resource use was estimated from patient time spent at the site of service and from the procedure length. Cost data were taken from a cost accounting system (TSI, maintained at the University of Michigan) which provides variable and fixed direct and indirect costs for medical procedures.

Costs of office treatment were 50% lower than costs of treatment in the operating room (Table 5-3). The savings of almost USD 1,000 per procedure performed in the office instead of the operating room resulted from substantial time savings for patients. Procedures were performed almost twice as fast in the office. Patients treated in the office spent, on average, 3 hours less at the healthcare facility, compared with patients treated in the operating room. In general, office treatment was considered an excellent alternative to inpatient treatment for early pregnancy failure because of its effectiveness and reduced resource use.

Table 5-3 failure ⁹⁰	Resource use for office versus hospital management of early pregnancy	
	Office (n=115)	Operating room (n=50)
Total patient time (min), mean (SD)	97 (42)	290 (85)
Total procedure time (min), mean (SD)	10 (4)	19 (10)
Total procedure costs (USD), mean (SD)	968 (426)	1,965 (926)

All differences between office and operating room statistically significant ($p < 0.01$).

5.3.1.3 Moawad et al., 2014

Recent US cost data were provided by Moawad et al. for 130 women undergoing hysteroscopy for AUB in the office or the operating room.¹³⁴ Costs were compared for two treatment strategies: Treating all women in the operating room versus treating women in the office versus referring them to the operating room only if needed. Cost data were obtained from the billing department at the site where the study was conducted (University of Florida Women's Health Center).

Physician fees were assumed to be the same at both sites of service but were incurred twice if a patient was initially treated in the office but then referred to the operating room. As treatment in the operating room was associated with anesthesia costs and hospital fees, the cost per patient, accounting for the share of patients who had been treated with each strategy in the study, was more than twice as high in the operating room compared with the office. Per patient, more than USD 2,000 could be saved if the patient was treated only in the office (USD 1,356) and did not need to be referred to the operating room (USD 4,946). Patients treated in the office first but then referred to the operating room incurred mean costs of USD 3,448 (Table 5-4).

As office hysteroscopy was as successful as but less expensive than hysteroscopy performed in the operating room, office treatment was considered a useful, cost-saving alternative to treatment under general anesthesia, while also increasing operating room availability.

Table 5-4 Hysteroscopy costs in the office and operating room¹³⁴

	Treated only in office	Initially treated in office but referred to operating room
N	75	55
Charges and fees (USD)		
Physician fee	1,356	2x1,356
Anesthesia fee	0	1,190
Hospital fee	0	2,400
Total	1,356	6,302
Charges and fees per patient	1,356	3,448

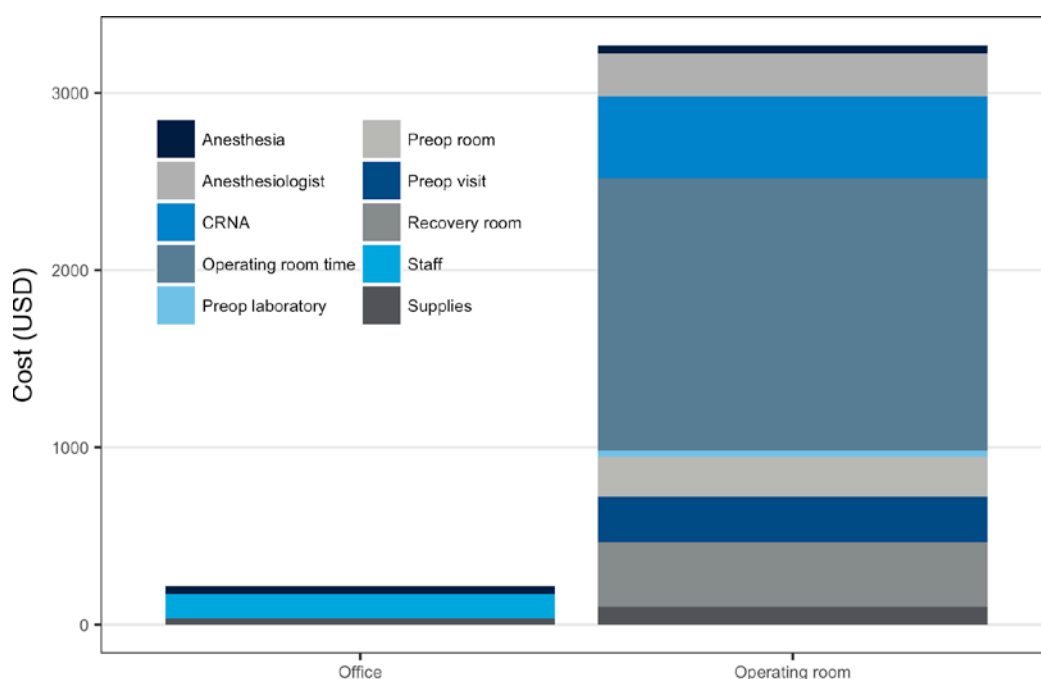
5.3.1.4 Keyhan & Munro, 2014

Further cost data, on diagnostic hysteroscopy using only local anesthesia, was provided by Keyhan & Munro who compared 639 procedures performed in the office or the operating room.¹²⁶ Resource use was obtained from three randomly selected operating room cases and, for the operating room, mean item costs were retrieved from the Southern California Permanente Medical Group (SCPMG). Office costs were determined from a sample of procedures (sample size unspecified) performed in SCPMG centers. Gynecologists' fees and capital costs of instruments and surgical devices were assumed to be the same for both sites of service. Indirect costs, e.g. income lost, were not included.

Performing diagnostic hysteroscopy in the office was associated with savings of more than USD 3,000 per case, compared with the operating room (Figure 5-2). While a hysteroscopy in the operating room was associated with costs of USD 3,627, a hysteroscopy in the office was associated with costs of only USD 216 (6% of the operating room procedure costs). Key drivers of the difference were the time and staffing costs associated with the operating room and the costs pre- and post-operative procedures necessary for patients treated in the operating room. For the 639 procedures analyzed in the study, healthcare payers would have saved almost USD 2 million if hysteroscopies had been performed exclusively in the office.

As direct costs of diagnostic hysteroscopies were substantially lower in the office, it was concluded that considerable cost savings could be achieved by moving hysteroscopy from the operating room to the office. The inclusion of indirect costs was expected to strengthen the case for office procedures even further as inpatient stays were assumed to be associated with more time and income lost than office visits.

Figure 5-2 Costs of diagnostic hysteroscopy in the office and operating room



CRNA, Certified Registered Nurse Anesthetist. Staff costs for the operating room were included in the "operating room time" item. Source: Keyhan & Munro¹²⁶

5.3.1.5 Saridogan et al., 2010

A comparison of the costs of different hysteroscopy service models was provided by Saridogan et al. for the UK.¹³⁵ See-and-treat hysteroscopy for polyps and small fibroids, performed in an office/outpatient setting with oral analgesia or local anesthesia, was compared with outpatient and referral service (office/outpatient diagnostic hysteroscopy followed by day surgery under general anesthesia) and with general anesthesia see-and-treat service, performed in inpatient or day surgery settings.

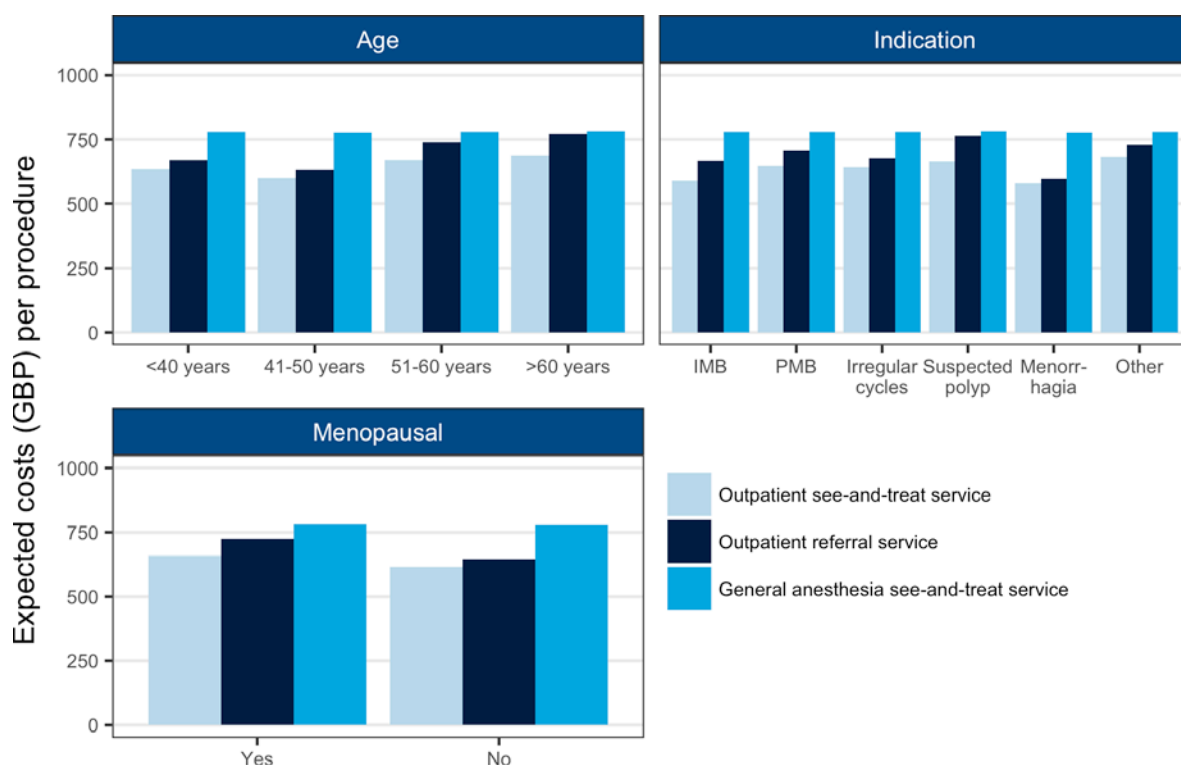
A decision tree was developed to calculate the expected costs for each of the three hysteroscopy service models. The probabilities needed to populate the decision tree, and population data in general, were taken from an audit of 1,109 women referred for hysteroscopy to a tertiary care hospital between 2001 to 2007. All polypectomies and myomectomies were performed with bipolar electrosurgery.

The cost analysis was conducted from the perspective of the UK NHS, and NHS reference costs were used where available. In addition, 2007–2008 elective inpatient reference costs were used and all costs were reported in 2008 GBP. For office/outpatient see-and-treat procedures, an additional cost of GBP 44.27 was assumed to reflect additional consumable costs.

In the base case analysis, the outpatient see-and-treat service model was associated with the lowest expected costs (GBP 638), compared with GBP 687 for the outpatient-referral and GBP 779 for the general anesthesia see-and-treat service model. In all subgroup analyses, the outpatient see-and-treat service model was the least expensive option and associated with savings between GBP 95 and 195 per procedure compared with the general anesthesia see-and-treat service model (Figure 5-3). Sensitivity analyses showed that the outpatient see-and-treat service was associated with lower costs than the outpatient and referral

service model (and, therefore, than the general anesthesia see-and-treat service) over a wide range of costs, treatment patterns and failure rates.

Figure 5-3 Cost comparison for hysteroscopic service models



IMB, intermenstrual bleeding; PMB, post-menstrual bleeding. Source: Saridogan *et al.*¹³⁵

It was concluded that the overall cost savings associated with an office-like, outpatient see-and-treat service would be substantial, given the high number of hysteroscopies performed in the NHS. This service model was recommended for inclusion in clinical guidelines as cost savings were accompanied by avoidance of general anesthesia and reduced procedure risks.

5.3.1.6 Penketh *et al.*, 2014

Further UK data were provided by Penketh *et al.*, in a study comparing costs for resectoscopic operative hysteroscopy service models in 118 women with diagnosed or suspected fibroids and polyps.¹²⁹ Women were treated either in the office (under local anesthesia), as a day case under local anesthesia or as a day case under general anesthesia.

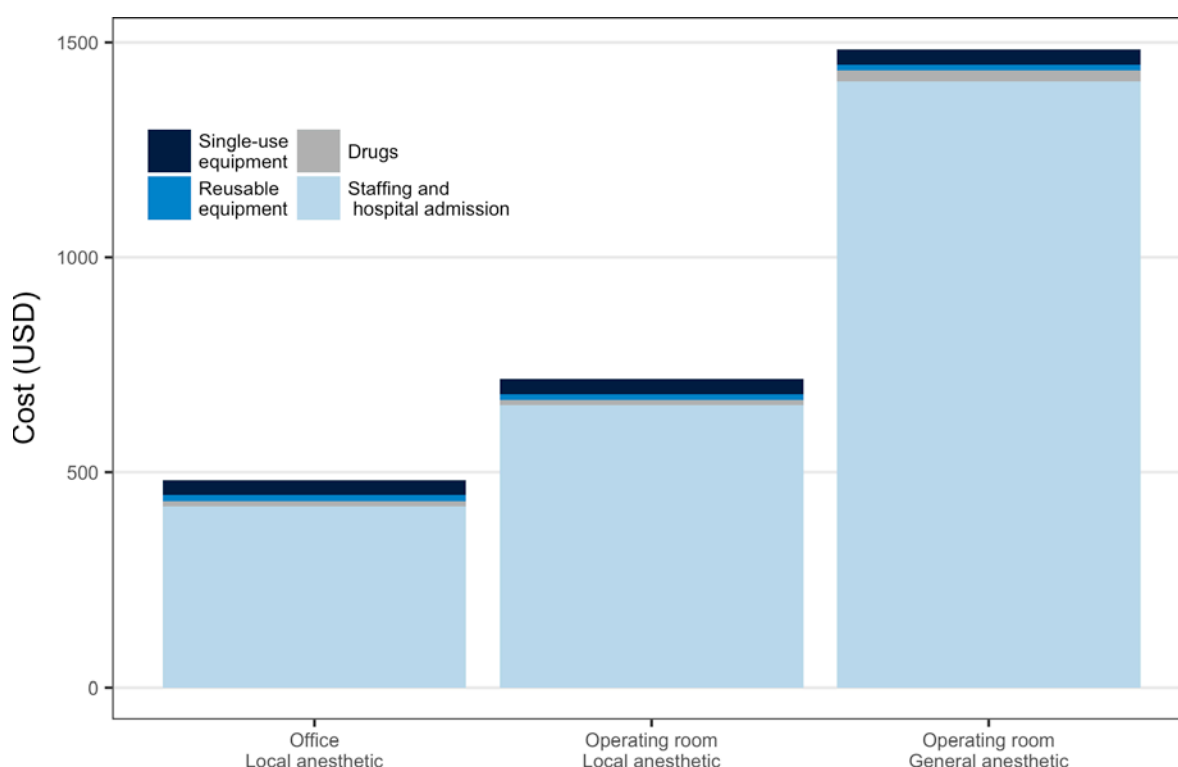
Costs data were obtained from various sources. Staffing costs were obtained from published local and national sources, and were calculated per procedure based on mean procedure time and actual staffing levels. Admission costs for day cases were assumed to be equal to costs for an uncomplicated general medicine bed-day, to avoid duplicating operating room costs. Costs of equipment were obtained from the NHS Supply Chain database and drugs costs from the British National Formulary 61. Although the study was conducted in a UK setting, costs were reported in USD, assuming an exchange rate of USD 1.54 per GBP.

Operative hysteroscopy with monopolar resectoscopes was associated with the lowest total costs when performed in the office (USD 482) compared with operating room procedures

under local (USD 716) or general (USD 1,485) anesthesia (Figure 5-4). The key driver of differences were widely differing costs for staffing and hospital admission.

It was concluded that office hysteroscopic resection was not only safe and well tolerated by patients but also associated with cost savings, compared with procedures performed in the operating room. Moving procedures to the office was suggested to also free up operating room resources.

Figure 5-4 Costs for operative resectoscopic hysteroscopic by site of service



Source: Penketh *et al.*¹²⁹

5.3.1.7 Summary

The available evidence shows that a site for service shift, from inpatient settings and operating rooms towards office/outpatient settings, for gynecologic procedures is associated with substantial cost savings for healthcare payers. Most cost analyses focus on hysteroscopy or electrosurgery and demonstrate a clear cost advantage from a healthcare payer perspective, including savings of hospital charges and fees, for the office. It seems plausible that mechanical hysteroscopic tissue removal, e.g. the TruClear™ system, is associated with even larger cost savings given its superior clinical and safety profile (Section 4). If lower rates of immediate and long-term complications, e.g. when comparing mHTR with electrosurgery, and reduced operating time are taken into account, mHTR devices like the TruClear™ system may potentially offer an even more cost-effective alternative.

6 References

- ¹ Urman RD, Punwani N, Shapiro FE. Office-based surgical and medical procedures: educational gaps. *Ochsner J*. 2012;12(4):383-8. ([PMID: 23267269](#))
- ² Peacock LM, Thomasse ME, Williams VL, Young AE. Transition to office-based obstetric and gynecologic procedures: safety, technical, and financial considerations. *Clin Obstet Gynecol*. 2015;58(2):418-33. ([PMID: 25851846](#))
- ³ Higgins A, Veselovskiy G, Schinkel J. National estimates of price variation by site of care. *Am J Manag Care*. 2016;22(3):e116-21. ([PMID: 26978238](#))
- ⁴ Cooper NA, Middleton L, Smith P, Denny E, Stobert L, Daniels J, Clark TJ. A patient-preference cohort study of office versus inpatient uterine polyp treatment for abnormal uterine bleeding. *Gynecol Surg*. 2016;13(4):313-22. ([PMID: 28003798](#))
- ⁵ Urman RD, Punwani N, Bombaugh M, Shapiro FE. Safety considerations for office-based obstetric and gynecologic procedures. *Rev Obstet Gynecol*. 2013;6(1):e8-e14. ([PMID: 23687556](#))
- ⁶ Weiss PM, Swisher E. Patient safety in the ambulatory OB/GYN setting. *Clin Obstet Gynecol*. 2012;55(3):613-9. ([PMID: 22828094](#))
- ⁷ Gimpelson RJ. Office hysteroscopy. *Clin Obstet Gynecol*. 1992;35(2):270-81. ([PMID: 1638820](#))
- ⁸ Isaacson K. New developments in operative hysteroscopy. *Obstet Gynecol Clin North Am*. 2000;27(2):375-83. ([PMID: 10857127](#))
- ⁹ Di Spiezio Sardo A, Bettocchi S, Spinelli M, Guida M, Nappi L, Angioni S, Sosa Fernandez LM, Nappi C. Review of new office-based hysteroscopic procedures 2003-2009. *J Minim Invasive Gynecol*. 2010;17(4):436-48. ([PMID: 20621007](#))
- ¹⁰ Mairos J, Di Martino P. Office hysteroscopy: an operative gold standard technique and an important contribution to patient safety. *Gynecol Surg*. 2016;13:111-14. ([PMID: 27226786](#))
- ¹¹ American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Gynecology. Practice bulletin no. 96: alternatives to hysterectomy in the management of leiomyomas. *Obstet Gynecol*. 2008;112(1):387-400. ([PMID: 18669742](#))
- ¹² Whitaker L, Critchley HO. Abnormal uterine bleeding. *Best Pract Res Clin Obstet Gynaecol*. 2016;34:54-65. ([PMID: 26803558](#))
- ¹³ Côté I, Jacobs P, Cumming DC. Use of health services associated with increased menstrual loss in the United States. *Am J Obstet Gynecol*. 2003;188(2):343-8. ([PMID: 12592237](#))
- ¹⁴ Cooper KG, Parkin DE, Garratt AM, Grant AM. Two-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. *Br J Obstet Gynaecol*. 1999;106(3):258-65. ([PMID: 10426646](#))
- ¹⁵ Liu Z, Doan QV, Blumenthal P, Dubois RW. A systematic review evaluating health-related quality of life, work impairment, and health-care costs and utilization in abnormal uterine bleeding. *Value Health*. 2007;10(3):183-94. ([PMID: 17532811](#))

- ¹⁶ Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of abnormal uterine bleeding in premenopausal women. *Am Fam Physician*. 2012;85(1):35-43. (PMID: 22230306)
- ¹⁷ Matteson KA, Raker CA, Clark MA, Frick KD. Abnormal uterine bleeding, health status, and usual source of medical care: analyses using the Medical Expenditures Panel Survey. *J Womens Health (Larchmt)*. 2013;22(11):959-65. (PMID: 24050455)
- ¹⁸ Jensen JT, Lefebvre P, Laliberté F, Sarda SP, Law A, Pocoski J, Duh MS. Cost burden and treatment patterns associated with management of heavy menstrual bleeding. *J Womens Health (Larchmt)*. 2012;21(5):539-47. (PMID: 22360696)
- ¹⁹ Tsai MC, Goldstein SR. Office diagnosis and management of abnormal uterine bleeding. *Clin Obstet Gynecol*. 2012;55(3):635-50. (PMID: 22828096)
- ²⁰ American Association of Gynecologic Laparoscopists (AAGL): Advancing Minimally Invasive Gynecology Worldwide. AAGL practice report: practice guidelines for the diagnosis and management of submucous leiomyomas. *J Minim Invasive Gynecol*. 2012a;19(2):152-71. (PMID: 22381967)
- ²¹ American Association of Gynecologic Laparoscopists. AAGL practice report: practice guidelines for the diagnosis and management of endometrial polyps. *J Minim Invasive Gynecol*. 2012b;19(1):3-10. (PMID: 22196255)
- ²² Trinder J, Brocklehurst P, Porter R, Read M, Vyas S, Smith L. Management of miscarriage: expectant, medical, or surgical? Results of randomised controlled trial (miscarriage treatment (MIST) trial). *BMJ*. 2006;332(7552):1235-40. (PMID: 16707509)
- ²³ Allison JL, Sherwood RS, Schust DJ. Management of first trimester pregnancy loss can be safely moved into the office. *Rev Obstet Gynecol*. 2011;4(1):5-14. (PMID: 21629493)
- ²⁴ Emanuel MH. Hysteroscopy and the treatment of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(7):920-9. (PMID: 25937553)
- ²⁵ O'Flynn H, Murphy LL, Ahmad G, Watson AJ. Pain relief in outpatient hysteroscopy: a survey of current UK clinical practice. *Eur J Obstet Gynecol Reprod Biol*. 2011;154(1):9-15. (PMID: 20926175)
- ²⁶ Annan JJ, Aquilina J, Ball E. The management of endometrial polyps in the 21st century. *Obstetrician Gynaecologist*. 2012;14:33-38. <http://onlinelibrary.wiley.com/doi/10.1111/j.1744-4667.2011.00091.x/epdf>. Accessed on July 4, 2017.
- ²⁷ Erickson TB, Kirkpatrick DH, DeFrancesco MS, Lawrence HC 3rd. Executive summary of the American College of Obstetricians and Gynecologists Presidential Task Force on Patient Safety in the Office Setting: reinvigorating safety in office-based gynecologic surgery. *Obstet Gynecol*. 2010;115(1):147-51. (PMID: 20027047)
- ²⁸ Peterson WF, Novak ER. Endometrial polyps. *Obstet Gynecol*. 1956;8(1):40-9. (PMID: 13335063)
- ²⁹ Salim S, Won H, Nesbitt-Hawes E, Campbell N, Abbott J. Diagnosis and management of endometrial polyps: a critical review of the literature. *J Minim Invasive Gynecol*. 2011;18(5):569-81. (PMID: 21783430)
- ³⁰ Clark TJ, Middleton LJ, Cooper NA, Diwakar L, Denny E, Smith P, Gennard L, Stobert L, Roberts TE, Cheed V, Bingham T, Jowett S, Brettell E, Connor M, Jones SE, Daniels JP. A

randomised controlled trial of Outpatient versus inpatient Polyp Treatment (OPT) for abnormal uterine bleeding. *Health Technol Assess*. 2015;19(61):1-194. ([PMID: 26240949](#))

³¹ Vanni R, Dal Cin P, Marras S, Moerman P, Andria M, Valdes E, Deprest J, Van den Berghe H. Endometrial polyp: another benign tumor characterized by 12q13-q15 changes. *Cancer Genet Cytogenet*. 1993;68(1):32-3. ([PMID: 8330280](#))

³² Di Spiezio Sardo A, Calagna G, Guida M, Perino A, Nappi C. Hysteroscopy and treatment of uterine polyps. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(7):908-19. ([PMID: 26165746](#))

³³ Lieng M, Istre O, Qvigstad E. Treatment of endometrial polyps: a systematic review. *Acta Obstet Gynecol Scand*. 2010;89(8):992-1002. ([PMID: 20528202](#))

³⁴ Lee SC, Kaunitz AM, Sanchez-Ramos L, Rhatigan RM. The oncogenic potential of endometrial polyps: a systematic review and meta-analysis. *Obstet Gynecol*. 2010;116(5):1197-205. ([PMID: 20966706](#))

³⁵ Rackow BW, Jorgensen E, Taylor HS. Endometrial polyps affect uterine receptivity. *Fertil Steril*. 2011 Jun 30;95(8):2690-2. ([PMID: 21269620](#))

³⁶ Pereira N, Petrini AC, Lekovich JP, Elias RT, Spandorfer SD. Surgical management of endometrial polyps in infertile women: a comprehensive review. *Surg Res Pract*. 2015;2015:914390. ([PMID: 26301260](#))

³⁷ Afifi K, Anand S, Nallapeta S, Gelbaya TA. Management of endometrial polyps in subfertile women: a systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2010;151(2):117-21. ([PMID: 20430512](#))

³⁸ Pérez-Medina T1, Bajo-Arenas J, Salazar F, Redondo T, Sanfrutos L, Alvarez P, Engels V. Endometrial polyps and their implication in the pregnancy rates of patients undergoing intrauterine insemination: a prospective, randomized study. *Hum Reprod*. 2005;20(6):1632-5. ([PMID: 15760959](#))

³⁹ Dreisler E, Stampe Sorensen S, Ibsen PH, Lose G. Prevalence of endometrial polyps and abnormal uterine bleeding in a Danish population aged 20-74 years. *Ultrasound Obstet Gynecol*. 2009;33(1):102-8. ([PMID: 19115236](#))

⁴⁰ Hinckley MD, Milki AA. 1000 office-based hysteroscopies prior to in vitro fertilization: feasibility and findings. *JSLs*. 2004;8(2):103-7. ([PMID: 15119651](#))

⁴¹ Fabres C, Alam V, Balmaceda J, Zegers-Hochschild F, Mackenna A, Fernandez E. Comparison of ultrasonography and hysteroscopy in the diagnosis of intrauterine lesions in infertile women. *J Am Assoc Gynecol Laparosc*. 1998;5(4):375-8. ([PMID: 9782141](#))

⁴² Cooper NA, Clark TJ, Middleton L, Diwakar L, Smith P, Denny E, Roberts T, Stobert L, Jowett S, Daniels J; OPT Trial Collaborative Group. Outpatient versus inpatient uterine polyp treatment for abnormal uterine bleeding: randomised controlled non-inferiority study. *BMJ*. 2015;350:h1398. ([PMID: 25801579](#))

⁴³ Sellmyer MA, Dessler TS, Maturen KE, Jeffrey RB Jr, Kamaya A. Physiologic, histologic, and imaging features of retained products of conception. *Radiographics*. 2013;33(3):781-96. ([PMID: 23674774](#))

⁴⁴ Ben-Ami I, Melcer Y, Smorgick N, Schneider D, Pansky M, Halperin R. A comparison of reproductive outcomes following hysteroscopic management versus dilatation and curettage of retained products of conception. *Int J Gynaecol Obstet*. 2014;127(1):86-9. ([PMID: 24997472](#))

- ⁴⁵ Ben-Ami I, Ofir T, Melcer Y, Smorgick N, Schneider D, Pansky M, Halperin R. Infertility following retained products of conception: is it the surgical procedure or the presence of trophoblastic tissue? *Eur J Obstet Gynecol Reprod Biol.* 2014;182:132-5. (PMID: 25268782)
- ⁴⁶ Ikkena DE, Bortoletto P, Lawson AK, Confino R, Marsh EE, Milad MP, Steinberg ML, Confino E, Pavone ME. Reproductive outcomes after hysteroscopic resection of retained products of conception. *J Minim Invasive Gynecol.* 2016;23(7):1070-4. (PMID: 27449689)
- ⁴⁷ Melcer Y, Smorgick N, Schneider D, Pansky M, Halperin R, Ben-Ami I. Comparison of reproductive outcomes following retained products of conception after vaginal delivery versus first-trimester abortion. *Gynecol Obstet Invest.* 2015;80(3):206-10. (PMID: 26088169)
- ⁴⁸ Hooker AB, Aydin H, Brölmann HA, Huirne JA. Long-term complications and reproductive outcome after the management of retained products of conception: a systematic review. *Fertil Steril.* 2016;105(1):156-64.e1-2. (PMID: 26453977)
- ⁴⁹ van den Bosch T, Daemen A, Van Schoubroeck D, Pochet N, De Moor B, Timmerman D. Occurrence and outcome of residual trophoblastic tissue: a prospective study. *J Ultrasound Med.* 2008;27(3):357-61. (PMID: 18314513)
- ⁵⁰ Vilos GA, Allaire C, Laberge PY, Leyland N, Vilos AG, Murji A, Chen I. The management of uterine leiomyomas. *J Obstet Gynaecol Can.* 2015;37(2):157-81. (PMID: 25767949)
- ⁵¹ Bulun SE. Uterine fibroids. *N Engl J Med.* 2013;369(14):1344-55. (PMID: 24088094)
- ⁵² Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol.* 2003;188(1):100-7. (PMID: 12548202)
- ⁵³ Lee DW, Gibson TB, Carls GS, Ozminkowski RJ, Wang S, Stewart EA. Uterine fibroid treatment patterns in a population of insured women. *Fertil Steril.* 2009;91(2):566-74. (PMID: 18304543)
- ⁵⁴ Russo M, Suen M, Bedaiwy M, Chen I. Prevalence of uterine myomas among women with 2 or more recurrent pregnancy losses: a systematic review. *J Minim Invasive Gynecol.* 2016;23(5):702-6. (PMID: 27041652)
- ⁵⁵ Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. *Fertil Steril.* 2009;91(4):1215-23. (PMID: 18339376)
- ⁵⁶ Vercellini P1, Zaina B, Yaylayan L, Pisacreta A, De Giorgi O, Crosignani PG. Hysteroscopic myomectomy: long-term effects on menstrual pattern and fertility. *Obstet Gynecol.* 1999;94(3):341-7. (PMID: 10472856)
- ⁵⁷ Saravelos SH, Yan J, Rehmani H, Li TC. The prevalence and impact of fibroids and their treatment on the outcome of pregnancy in women with recurrent miscarriage. *Hum Reprod.* 2011;26(12):3274-9. (PMID: 21954281)
- ⁵⁸ Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol.* 2012;206(3):211.e1-9. (PMID: 22244472)
- ⁵⁹ Borah BJ, Nicholson WK, Bradley L, Stewart EA. The impact of uterine leiomyomas: a national survey of affected women. *Am J Obstet Gynecol.* 2013;209(4):319.e1-319.e20. (PMID: 23891629)
- ⁶⁰ Ghant MS, Sengoba KS, Recht H, Cameron KA, Lawson AK, Marsh EE. Beyond the physical: a qualitative assessment of the burden of symptomatic uterine fibroids on women's emotional and psychosocial health. *J Psychosom Res.* 2015;78(5):499-503. (PMID: 25725565)

- ⁶¹ Fennessy FM, Kong CY, Tempany CM, Swan JS. Quality-of-life assessment of fibroid treatment options and outcomes. *Radiology*. 2011;259(3):785-92. (PMID: [21364084](#))
- ⁶² Clark TJ, Khan KS, Gupta JK. Current practice for the treatment of benign intrauterine polyps: a national questionnaire survey of consultant gynaecologists in UK. *Eur J Obstet Gynecol Reprod Biol*. 2002;103(1):65-7. (PMID: [12039467](#))
- ⁶³ Cooper NA, Barton PM, Breijer M, Caffrey O, Opmeer BC, Timmermans A, Mol BW, Khan KS, Clark TJ. Cost-effectiveness of diagnostic strategies for the management of abnormal uterine bleeding (heavy menstrual bleeding and post-menopausal bleeding): a decision analysis. *Health Technol Assess*. 2014;18(24):1-201. (PMID: [24767431](#))
- ⁶⁴ Penman-Aguilar A, Whiteman MK, Cox S, Posner SF, Meikle SF, Kourtis AP, Jamieson DJ. Complications of common gynecologic surgeries among HIV-infected women in the United States. *Infect Dis Obstet Gynecol*. 2012;2012:610876. (PMID: [22675242](#))
- ⁶⁵ Smith PP, Middleton LJ, Connor M, Clark TJ. Hysteroscopic morcellation compared with electrical resection of endometrial polyps: a randomized controlled trial. *Obstet Gynecol*. 2014;123(4):745-51. (PMID: [24785600](#))
- ⁶⁶ van Dijk LJ, Breijer MC, Veersema S, Mol BW, Timmermans A. Current practice in the removal of benign endometrial polyps: a Dutch survey. *Gynecol Surg*. 2012;9(2):163-8. (PMID: [22611350](#))
- ⁶⁷ Smorgick N, Barel O, Fuchs N, Ben-Ami I, Pansky M, Vaknin Z. Hysteroscopic management of retained products of conception: meta-analysis and literature review. *Eur J Obstet Gynecol Reprod Biol*. 2014;173:19-22. (PMID: [24332096](#))
- ⁶⁸ Dawood A, Al-Talib A, Tulandi T. Predisposing factors and treatment outcome of different stages of intrauterine adhesions. *J Obstet Gynaecol Can*. 2010;32(8):767-70. (PMID: [21050509](#))
- ⁶⁹ Goldenberg M, Schiff E, Achiron R, Lipitz S, Mashlach S. Managing residual trophoblastic tissue: hysteroscopy for directing curettage. *J Reprod Med*. 1997;42(1):26-8. (PMID: [9018641](#))
- ⁷⁰ Rein DT, Schmidt T, Hess AP, Volkmer A, Schöndorf T, Breidenbach M. Hysteroscopic management of residual trophoblastic tissue is superior to ultrasound-guided curettage. *J Minim Invasive Gynecol*. 2011;18(6):774-8. (PMID: [22024264](#))
- ⁷¹ Lethaby A, Vollenhoven B, Sowter M. Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. *Cochrane Database Syst Rev*. 2001;(2):CD000547. (PMID: [11405968](#))
- ⁷² Biglia N, Carinelli S, Maiorana A, D'Alonzo M, Lo Monte G, Marci R. Ulipristal acetate: a novel pharmacological approach for the treatment of uterine fibroids. *Drug Des Devel Ther*. 2014;8:285-92. (PMID: [24591818](#))
- ⁷³ Ciarmela P, Ciavattini A, Giannubilo SR, Lamanna P, Fiorini R, Tranquilli AL, Christman GM, Castellucci M. Management of leiomyomas in perimenopausal women. *Maturitas*. 2014;78(3):168-73. (PMID: [24835002](#))
- ⁷⁴ Gurusamy KS, Vaughan J, Fraser IS, Best LM, Richards T. Medical therapies for uterine fibroids: a systematic review and network meta-analysis of randomised controlled trials. *PLoS One*. 2016;11(2):e0149631. (PMID: [26919185](#))
- ⁷⁵ Jacoby VL, Jacoby A, Learman LA, Schembri M, Gregorich SE, Jackson R, Kuppermann M. Use of medical, surgical and complementary treatments among women with fibroids. *Eur J Obstet Gynecol Reprod Biol*. 2014;182:220-5. (PMID: [25445104](#))

- ⁷⁶ Borah BJ, Laughlin-Tommaso SK, Myers ER, Yao X, Stewart EA. Association between patient characteristics and treatment procedure among patients with uterine leiomyomas. *Obstet Gynecol*. 2016;127(1):67-77. (PMID: [26646122](#))
- ⁷⁷ Neuwirth RS. A new technique for and additional experience with hysteroscopic resection of submucous fibroids. *Am J Obstet Gynecol*. 1978;131(1):91-4. (PMID: [645789](#))
- ⁷⁸ Calabrese S, DE Alberti D, Garuti G. The use of bipolar technology in hysteroscopy. *Minerva Ginecol*. 2016;68(2):133-42. (PMID: [26928415](#))
- ⁷⁹ Emanuel MH, Wamsteker K, Hart AA, Metz G, Lammes FB. Long-term results of hysteroscopic myomectomy for abnormal uterine bleeding. *Obstet Gynecol*. 1999;93(5 Pt 1):743-8. (PMID: [10912978](#))
- ⁸⁰ Dealberti D, Riboni F, Prigione S, Pisani C, Rovetta E, Montella F, Garuti G. New mini-resectoscope: analysis of preliminary quality results in outpatient hysteroscopic polypectomy. *Arch Gynecol Obstet*. 2013;288(2):349-53. (PMID: [23417150](#))
- ⁸¹ Emanuel MH, Wamsteker K. The Intra Uterine Morcellator: a new hysteroscopic operating technique to remove intrauterine polyps and myomas. *J Minim Invasive Gynecol*. 2005;12(1):62-6. (PMID: [15904601](#))
- ⁸² Baumann R, Magos AL, Kay JD, Turnbull AC. Absorption of glycine irrigating solution during transcervical resection of endometrium. *BMJ*. 1990;300(6720):304-5. (PMID: [2106961](#))
- ⁸³ Istre O, Bjoennes J, Naess R, Hornbaek K, Forman A. Postoperative cerebral oedema after transcervical endometrial resection and uterine irrigation with 1.5% glycine. *Lancet*. 1994;344(8931):1187-9. (PMID: [7934539](#))
- ⁸⁴ Umraniar S, Clark TJ, Saridogan E, Miligkos D, Arambage K, Torbe E, Campo R, Sardo AD, Tanos V, Grimbizis G. BSGE/ESGE guideline on management of fluid distension media in operative hysteroscopy. *Gynecol Surg*. 2016;13(4):289-303. (PMID: [28003797](#))
- ⁸⁵ Brown J, Blank K. Minimally invasive endometrial ablation device complications and use outside of the manufacturers' instructions. *Obstet Gynecol*. 2012;120(4):865-70. (PMID: [22996104](#))
- ⁸⁶ Vilos GA, Brown S, Graham G, McCulloch S, Borg P. Genital tract electrical burns during hysteroscopic endometrial ablation: report of 13 cases in the United States and Canada. *J Am Assoc Gynecol Laparosc*. 2000;7(1):141-7. (PMID: [10648756](#))
- ⁸⁷ Vilos GA, McCulloch S, Borg P, Zheng W, Denstedt J. Intended and stray radiofrequency electrical currents during resectoscopic surgery. *J Am Assoc Gynecol Laparosc*. 2000;7(1):55-63. (PMID: [10648740](#))
- ⁸⁸ Munro MG. Mechanisms of thermal injury to the lower genital tract with radiofrequency resectoscopic surgery. *J Minim Invasive Gynecol*. 2006;13(1):36-42. (PMID: [16431321](#))
- ⁸⁹ Li C, Dai Z, Gong Y, Xie B, Wang B. A systematic review and meta-analysis of randomized controlled trials comparing hysteroscopic morcellation with resectoscopy for patients with endometrial lesions. *Int J Gynaecol Obstet*. 2017;136(1):6-12. (PMID: [28099700](#))
- ⁹⁰ Dalton VK, Harris L, Weisman CS, Guire K, Castleman L, Lebovic D. Patient preferences, satisfaction, and resource use in office evacuation of early pregnancy failure. *Obstet Gynecol*. 2006;108(1):103-10. (PMID: [16816063](#))
- ⁹¹ Cohen S, Greenberg JA. Hysteroscopic morcellation for treating intrauterine pathology. *Rev Obstet Gynecol*. 2011;4(2):73-80. (PMID: [22102930](#))

- ⁹² National Institute for Health and Care Excellence. Hysteroscopic morcellation of uterine leiomyomas (fibroids): Interventional procedures guidance [IPG522]. 2015. <https://www.nice.org.uk/guidance/ipg522>. Accessed on February 5, 2017.
- ⁹³ Hamerlynck TW, Schoot BC, van Vliet HA, Weyers S. Removal of endometrial polyps: hysteroscopic morcellation versus bipolar resectoscopy: a randomized trial. *J Minim Invasive Gynecol*. 2015;22(7):1237-43. (PMID: 26192235)
- ⁹⁴ Haber K, Hawkins E, Levie M, Chudnoff S. Hysteroscopic morcellation: review of the manufacturer and user facility device experience (MAUDE) database. *J Minim Invasive Gynecol*. 2015;22(1):110-4. (PMID: 25128851)
- ⁹⁵ Hamerlynck TW, Blikkendaal MD, Schoot BC, Hanstede MM, Jansen FW. An alternative approach for removal of placental remnants: hysteroscopic morcellation. *J Minim Invasive Gynecol*. 2013;20(6):796-802. (PMID: 24183271)
- ⁹⁶ Arnold A, Ketheeswaran A, Bhatti M, Nesbitt-Hawes E, Abbott J. A prospective analysis of hysteroscopic morcellation in the management of intrauterine pathologies. *J Minim Invasive Gynecol*. 2016;23(3):435-41. (PMID: 26803919)
- ⁹⁷ AlHilli MM, Nixon KE, Hopkins MR, Weaver AL, Laughlin-Tommaso SK, Famuyide AO. Long-term outcomes after intrauterine morcellation vs hysteroscopic resection of endometrial polyps. *J Minim Invasive Gynecol*. 2013;20(2):215-21. (PMID: 23295201)
- ⁹⁸ Pampalona JR, Bastos MD, Moreno GM, Pust AB, Montesdeoca GE, Guerra Garcia A, Pruñonosa JC, Collado RC, Torras PB. A comparison of hysteroscopic mechanical tissue removal with bipolar electrical resection for the management of endometrial polyps in an ambulatory care setting: preliminary results. *J Minim Invasive Gynecol*. 2015;22(3):439-45. (PMID: 25497165)
- ⁹⁹ Chambers JT, Chambers SK. Endometrial sampling: When? Where? Why? With what? *Clin Obstet Gynecol*. 1992;35(1):28-39. (PMID: 1544246)
- ¹⁰⁰ Dimitraki M, Tsikouras P, Bouchlariotou S, Dafopoulos A, Liberis V, Maroulis G, Teichmann AT. Clinical evaluation of women with PMB. Is it always necessary an endometrial biopsy to be performed? A review of the literature. *Arch Gynecol Obstet*. 2011;283(2):261-6. (PMID: 20683604)
- ¹⁰¹ Turnbull HL, Akrivos N, Simpson P, Duncan TJ, Nieto JJ, Burbos N. Investigating vaginal bleeding in postmenopausal women found to have an endometrial thickness of equal to or greater than 10 mm on ultrasonography. *Arch Gynecol Obstet*. 2017;295(2):445-50. (PMID: 27909879)
- ¹⁰² Royal College of Obstetricians and Gynaecologists (RCOG), British Society for Gynaecological Endoscopy (BSGE). Management of endometrial hyperplasia: guideline no 67. https://www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg_67_endometrial_hyperplasia.pdf. Accessed on February 23, 2017.
- ¹⁰³ van Hanegem N, Prins MM, Bongers MY, Opmeer BC, Sahota DS, Mol BW, Timmermans A. The accuracy of endometrial sampling in women with postmenopausal bleeding: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2016;197:147-55. (PMID: 26748390)
- ¹⁰⁴ Du J, Li Y, Lv S, Wang Q, Sun C, Dong X, He M, Ulain Q, Yuan Y, Tuo X, Batchu N, Song Q, Li Q. Endometrial sampling devices for early diagnosis of endometrial lesions. *J Cancer Res Clin Oncol*. 2016;142(12):2515-22. (PMID: 27515060)

- ¹⁰⁵ Grimbizis GF, Tsolakidis D, Mikos T, Anagnostou E, Asimakopoulos E, Stamatopoulos P, Tarlatzis BC. A prospective comparison of transvaginal ultrasound, saline infusion sonohysterography, and diagnostic hysteroscopy in the evaluation of endometrial pathology. *Fertil Steril*. 2010;94(7):2720-5. (PMID: 20462577)
- ¹⁰⁶ Bourdel N, Chauvet P, Tognazza E, Pereira B, Botchorishvili R, Canis M. Sampling in atypical endometrial hyperplasia: which method results in the lowest underestimation of endometrial cancer? A systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2016;23(5):692-701. (PMID: 27058769)
- ¹⁰⁷ Mayo Clinic. Tests and procedures: dilation and curettage. Mayo Clinic Website. <http://www.mayoclinic.org/tests-procedures/dilation-and-curettage/home/ovc-20259331>. Updated on October 26, 2016. Accessed on February 5, 2017.
- ¹⁰⁸ Epstein E, Ramirez A, Skoog L, Valentin L. Dilatation and curettage fails to detect most focal lesions in the uterine cavity in women with postmenopausal bleeding. *Acta Obstet Gynecol Scand*. 2001;80(12):1131-6. (PMID: 11846711)
- ¹⁰⁹ Angioni S, Loddo A, Milano F, Piras B, Minerba L, Melis GB. Detection of benign intracavitary lesions in postmenopausal women with abnormal uterine bleeding: a prospective comparative study on outpatient hysteroscopy and blind biopsy. *J Minim Invasive Gynecol*. 2008;15(1):87-91. (PMID: 18262151)
- ¹¹⁰ American College of Obstetricians and Gynecologists. Practice Bulletin No. 149: Endometrial cancer. *Obstet Gynecol*. 2015;125(4):1006-26. (PMID: 25798986)
- ¹¹¹ Bhattee GA, Rahman J, Rahman MS. Bowel injury in gynecologic operations: analysis of 110 cases. *Int Surg*. 2006;91(6):336-40. (PMID: 17256432)
- ¹¹² Lemmers M, Verschoor MA, Hooker AB, Opmeer BC, Limpens J, Huirne JA, Ankum WM, Mol BW. Dilatation and curettage increases the risk of subsequent preterm birth: a systematic review and meta-analysis. *Hum Reprod*. 2016;31(1):34-45. (PMID: 26534897)
- ¹¹³ Shazly SA, Laughlin-Tommaso SK, Breitkopf DM, Hopkins MR, Burnett T2, Green IC, Farrell AM, Murad MH, Famuyide AO. Hysteroscopic morcellation versus resection for the treatment of uterine cavity lesions: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2016;23(6):867-77. (PMID: 27164165)
- ¹¹⁴ Gambadauro P, Martínez-Maestre MA, Torrejón R. When is see-and-treat hysteroscopic polypectomy successful? *Eur J Obstet Gynecol Reprod Biol*. 2014;178:70-3. (PMID: 24792666)
- ¹¹⁵ Di Spiezo Sardo A, Taylor A, Tsirkas P, Mastrogamvrakis G, Sharma M, Magos A. Hysteroscopy: a technique for all? Analysis of 5,000 outpatient hysteroscopies. *Fertil Steril*. 2008;89(2):438-43. (PMID: 17482613)
- ¹¹⁶ Scheiber MD, Chen SH. A prospective multicenter registry of patients undergoing hysteroscopic morcellation of uterine polyps and myomas. *J Gynecol Surg*. 2016;32(6):318-23. (PMID: 27965523)
- ¹¹⁷ Rubino RJ, Lukes AS. Twelve-month outcomes for patients undergoing hysteroscopic morcellation of uterine polyps and myomas in an office or ambulatory surgical center. *J Minim Invasive Gynecol*. 2015;22(2):285-90. (PMID: 25446547)
- ¹¹⁸ Abeywardena AJ, Sivasuriam A. Acceptability of endometrial polyp resection under local anaesthesia. *Sri Lanka J Obstet Gynecol*. 2017;39(1):12-5. (<http://sljog.sljol.info/articles/abstract/10.4038/sljog.v39i1.7806/>)

- ¹¹⁹ Franchini M, Zolfanelli F, Gallorini M, Giarre G, Fimiani R, Florio P. Hysteroscopic polypectomy in an office setting: specimen quality assessment for histopathological evaluation. *Eur J Obstet Gynecol Reprod Biol.* 2015;189:64-7. (PMID: 25879991)
- ¹²⁰ Cooper NA, Smith P, Khan KS, Clark TJ. Vaginoscopic approach to outpatient hysteroscopy: a systematic review of the effect on pain. *BJOG.* 2010;117(5):532-9. (PMID: 20374594)
- ¹²¹ Allen RH, Micks E, Edelman A. Pain relief for obstetric and gynecologic ambulatory procedures. *Obstet Gynecol Clin North Am.* 2013;40(4):625-45. (PMID: 24286993)
- ¹²² Ireland LD, Allen RH. Pain management for gynecologic procedures in the office. *Obstet Gynecol Surv.* 2016;71(2):89-98. (PMID: 26894801)
- ¹²³ Angioli R, De Cicco Nardone C, Plotti F, Cafà EV, Dugo N, Damiani P, Ricciardi R, Linciano F, Terranova C. Use of music to reduce anxiety during office hysteroscopy: prospective randomized trial. *J Minim Invasive Gynecol.* 2014;21(3):454-9. (PMID: 23962572)
- ¹²⁴ Wortman M, Daggett A, Ball C. Operative hysteroscopy in an office-based surgical setting: review of patient safety and satisfaction in 414 cases. *J Minim Invasive Gynecol.* 2013;20(1):56-63. (PMID: 23107759)
- ¹²⁵ van Kerkvoorde TC, Veersema S, Timmermans A. Long-term complications of office hysteroscopy: analysis of 1028 cases. *J Minim Invasive Gynecol.* 2012;19(4):494-7. (PMID: 22564927)
- ¹²⁶ Keyhan S, Munro MG. Office diagnostic and operative hysteroscopy using local anesthesia only: an analysis of patient reported pain and other procedural outcomes. *J Minim Invasive Gynecol.* 2014;21(5):791-8. (PMID: 24681061)
- ¹²⁷ Carta G, Palermo P, Marinangeli F, Piroli A, Necozone S, De Lellis V, Patacchiola F. Waiting time and pain during office hysteroscopy. *J Minim Invasive Gynecol.* 2012;19(3):360-4. (PMID: 22387163)
- ¹²⁸ de Freitas Fonseca M, Sessa FV, Resende JA Jr, Guerra CG, Andrade CM Jr, Crispi CP. Identifying predictors of unacceptable pain at office hysteroscopy. *J Minim Invasive Gynecol.* 2014;21(4):586-91. (PMID: 24423975)
- ¹²⁹ Penketh RJ, Bruen EM, White J, Griffiths AN, Patwardhan A, Lindsay P, Hill S, Carolan-Rees G. Feasibility of resectoscopic operative hysteroscopy in a UK outpatient clinic using local anesthetic and traditional reusable equipment, with patient experiences and comparative cost analysis. *J Minim Invasive Gynecol.* 2014;21(5):830-6. (PMID: 24681168)
- ¹³⁰ Noventa M, Ancona E, Quaranta M, Vitagliano A, Cosmi E, D'Antona D, Gizzo S. Intrauterine morcellator devices: the icon of hysteroscopic future or merely a marketing image? A systematic review regarding safety, efficacy, advantages, and contraindications. *Reprod Sci.* 2015;22(10):1289-96. (PMID: 25878200)
- ¹³¹ Diwakar L, Roberts TE, Cooper NA, Middleton L, Jowett S, Daniels J, Smith P, Clark TJ; OPT trial collaborative group. An economic evaluation of outpatient versus inpatient polyp treatment for abnormal uterine bleeding. *BJOG.* 2016;123(4):625-31. (PMID: 26011792)
- ¹³² Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. *Br Med Bull.* 2010;96:5-21. (PMID: 21037243)
- ¹³³ Hidlebaugh D. A comparison of clinical outcomes and cost of office versus hospital hysteroscopy. *J Am Assoc Gynecol Laparosc.* 1996;4(1):39-45. (PMID: 9050710)

¹³⁴ Moawad NS, Santamaria E, Johnson M, Shuster J. Cost-effectiveness of office hysteroscopy for abnormal uterine bleeding. *JSLS*. 2014;18(3). ([PMID: 25392645](#))

¹³⁵ Saridogan E, Tilden D, Sykes D, Davis N, Subramanian D. Cost-analysis comparison of outpatient see-and-treat hysteroscopy service with other hysteroscopy service models. *J Minim Invasive Gynecol*. 2010;17(4):518-25. ([PMID: 20621013](#))

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