

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### Interventional procedure overview of hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids

Uterine fibroids are non-cancerous growths that develop in or around the womb (uterus). This procedure is done for fibroids inside the womb, using general, local or spinal anaesthesia. A thin tube with a camera on the end (hysteroscope) is inserted through the vagina and cervix and into the womb. Instruments are passed through the hysteroscope to cut the fibroid into small pieces (morcellation). The pieces of fibroid are removed through the hysteroscope. The aim is to reduce symptoms caused by fibroids.

## Contents

[Introduction](#)

[Description of the procedure](#)

[Efficacy summary](#)

[Safety summary](#)

[The evidence assessed](#)

[Validity and generalisability of the studies](#)

[Existing assessments of this procedure](#)

[Related NICE guidance](#)

[Additional information considered by IPAC](#)

[References](#)

[Literature search strategy](#)

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

[Appendix](#)

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
Food and Drug Administration	FDA
Health Related Quality of Life	HRQOL
International Federation of Gynecology and Obstetrics	FIGO
Manufacturer and User Facility Device Experience database	MAUDE
Uterine Fibroid Symptom and Quality of Life	UFS-QOL

## Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

## Date prepared

This overview was prepared in November 2020 and updated in June 2021.

## Procedure name

- Hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids

## Professional societies

- Royal College of Obstetricians and Gynaecologists
- British Society for Gynaecological Endoscopy.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Description of the procedure

### Indications and current treatment

Uterine fibroids (also known as uterine leiomyomas or myomas) are benign tumours of the uterus. They can be asymptomatic or cause symptoms including heavy periods or bleeding between periods. They can be associated with fertility problems and miscarriage.

Treatment depends on whether the fibroids cause symptoms, and if the person would like to become pregnant in the future. For symptomatic fibroids, treatment options include medication, interventional radiology and surgery. Interventional radiology treatments include uterine artery embolisation and MRI-guided focused ultrasound. Surgery includes hysterectomy, myomectomy, endometrial ablation techniques and myolysis.

This procedure is used for submucosal fibroids, which develop in the muscle layer beneath the inner lining of the uterus and grow into the uterine cavity. This includes pedunculated fibroids, which are attached to the uterus with a narrow stalk of tissue.

### What the procedure involves

Hysteroscopic mechanical tissue removal aims to remove submucosal uterine fibroids under visual guidance using a hysteroscope inserted into the uterus. It is intended to reduce the risks of traumatic injury to the uterus and the risk of inadvertent fluid overload associated with traditional procedures. An intended advantage of the procedure over thermal ablation techniques is avoiding the risk of thermal injury.

Hysteroscopic mechanical tissue removal for uterine fibroids is usually done with the patient under general or spinal anaesthesia, typically as a day-case procedure. A hysteroscope is inserted into the uterus through the cervix and saline is pumped through a small channel in the hysteroscope to distend the uterus. A morcellator is passed through the hysteroscope and used to cut and simultaneously aspirate the morcellated fibroid tissue. The aspirated tissue can be collected for histological analysis.

Different devices are available for this procedure.

## Efficacy summary

### Improvement in symptoms and patient satisfaction

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

In a non-randomised comparative study of 29 patients with submucosal fibroids, a satisfactory outcome (when the patient subjectively reported reduced menstrual bleeding and considered the operation to have improved menstrual symptoms at 3-month follow up) was reported for 93% of patients who had hysteroscopic morcellation and 85% of those who had loop resection ( $p=0.841$ ). A satisfactory outcome was reported for all patients when uterine fibroid protrusion was more than 60% (Lee M, 2016).

In a case series of 73 patients with submucosal fibroids, 84% (54/73) of patients were satisfied with the procedure, 6% (4/73) were neutral and 9% (6/73) were dissatisfied. Failure to control abnormal uterine bleeding was reported in 33% (24/73) of patients, with persistence of at least 1 symptom in 21% (15/73) of patients and recurrence of symptoms in 18% (13/73) of patients (Maheux-Lacroix S, 2017).

In a randomised controlled trial of 74 patients with fibroids or polyps, comparing an office setting with an ambulatory setting, the overall UFS-QOL symptom score improved from 67.5 ( $\pm 15.4$ ) at baseline to 22.3 ( $\pm 22.6$ ) at 12-month follow up ( $p<0.01$ ). Overall, 89% of patients were satisfied or very satisfied and 96% of patients would recommend the treatment to other patients with similar symptoms (Rubino R, 2015).

### **Fibroid volume reduction**

In a systematic review of 498 patients with fibroids or polyps, the total removal rate was higher for hysteroscopic morcellation than conventional resectoscopy (96% compared with 86%, OR 4.28, 95% CI 1.68 to 10.9,  $p=0.002$ ;  $I^2=0\%$ ; 3 studies) (Yin X, 2018).

In a systematic review of 650 patients with fibroids or polyps, hysteroscopic morcellation was associated with lower odds of incomplete removal of lesions when randomised trials were meta-analysed (OR 0.12, 95% CI 0.03 to 0.54,  $p=0.006$ ;  $I^2=0\%$ ; 3 studies). This effect was not statistically significant in observational studies or when all studies were compared (Shazly S, 2016).

In a case series of 278 patients with fibroids or polyps, the mean percentage of fibroids removed was 87% (Scheiber M, 2016).

In a case series of 244 patients with fibroids, polyps or other intrauterine pathology, complete resection of fibroids was reported for 66% (63/95) of patients. The completeness of resection of pathology was associated with symptom resolution for fibroids ( $p=0.005$ ). Increasing fibroid size was negatively correlated with complete removal. (Arnold A, 2016).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

In the case series of 73 patients, 100% of pathology was removed in 71% (49/69) of patients. Less than 50% of pathology was removed in 1 patient, 50% to 74% was removed in 13% (9/69) of patients, and 75% to 99% was removed in 15% (10/69) of patients. A second procedure was needed for 4 patients because the maximum saline deficit was reached before the resection was complete; these patients all had submucosal fibroids of 40 mm or larger (Maheux-Lacroix S, 2017).

In the randomised controlled trial of 74 patients with fibroids or polyps, comparing an office setting with an ambulatory setting, the overall percentage of pathology removal for fibroids was 96% and 64% of fibroids had 100% removal (Rubino R, 2015).

### **Quality of life**

In the randomised controlled trial of 74 patients with fibroids or polyps, comparing an office setting with an ambulatory setting, the overall HRQOL score improved from 38.7 ( $\pm 23.3$ ) at baseline to 83.9 ( $\pm 24.4$ ) at 12-month follow up ( $p < 0.01$ ) (Rubino R, 2015).

### **Subsequent surgery**

In the case series of 73 patients, 27% (20/73) of patients had further related surgery: 19% (14/73) had operative hysteroscopy (11 fibroid resections, 1 polyp resection, 2 endometrial ablations), 12% (9/73) had a hysterectomy and 3% (2/73) had laparoscopic myomectomy. Multivariate cox proportional hazards analysis showed a total pathology size of 50 mm or more was associated with an increased risk of needing a subsequent surgical procedure (hazard ratio 2.9,  $p = 0.02$ ) (Maheux-Lacroix S, 2017).

In a case series of 320 patients with submucosal fibroids, 17% (53/320) had a repeat morcellation procedure 3 months after the initial procedure because of incomplete resection. Of the 130 patients with FIGO type 0 fibroids, 14% (18/130) of patients had a hysterectomy within 3 years of the procedure. A hysterectomy was done within three years in 9% (11/126) of patients with FIGO type 1 fibroids and 18% (11/63) of patients with FIGO type 2 fibroids (Vidal-Mazo C, 2019).

In the case series of 244 patients with fibroids, polyps or other intrauterine pathology, 6% (5/85) of women with fibroids had a subsequent hysterectomy (Arnold A, 2016).

### **Pregnancy**

Pregnancy was reported in 1 patient who had hysteroscopic morcellation of fibroids, 2 patients who had removal of polyps and 2 who had removal of

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

pregnancy products in the case series of 244 patients with fibroids, polyps of other intrauterine pathology (Arnold A, 2016).

Pregnancy was reported in 71% (44/62) of patients in a case series of 62 patients with intrauterine pathology and infertility or recurrent pregnancy loss. The mean time to pregnancy was 8 months after the procedure. Of the 50 pregnancies in 44 patients, 39 (78%) resulted in a live birth, with 1 pregnancy ongoing at the last follow up. Of the 67 lesions in patients who became pregnant, 14 (21%) were fibroids. Of the 31 lesions in patients who did not become pregnant, 5 (16%) were fibroids (Bhalani V, 2016).

## **Safety summary**

### **Unspecified operative and postoperative complications**

There was no statistically significant difference in the rate of operative and postoperative complications between hysteroscopic morcellation and conventional resection in the systematic reviews of 650 patients and 498 patients respectively with fibroids or polyps (Shazly S, 2016; Yin X, 2018).

A review of the FDA MAUDE database estimated the overall complication rate of hysteroscopic surgery for removal of intrauterine polyps or fibroids with use of a reciprocating morcellator to be less than 0.1% (119/180,000). Although the true denominator is unknown, the total number of units sold (180,000) was used as a surrogate for the estimated number of procedures performed. Of the 119 adverse events, 37 (31%) were categorised as major and the rest were minor. The number of reports for specific adverse events have been included in the summaries below (Haber, 2015).

### **Prolapsed fibroid**

Pain caused by a prolapsed fibroid was reported in 3% (2/73) of patients in the case series of 73 patients. This happened 1 and 2 months respectively after the initial procedure and both were successfully treated by combined vaginal and hysteroscopic resection of the remaining fibroid (Maheux-Lacroix S, 2017).

A prolapsed submucosal fibroid was reported in 1% (3/255) of patients at 2 to 12 weeks after surgery in the case series of 244 patients. One patient needed unplanned emergency surgery and a blood transfusion for haemorrhage, with vaginal resection of the prolapsed submucosal fibroid. The second patient had offensive vaginal discharge, which resolved after the prolapsed submucosal fibroid was removed vaginally. The third woman had a 60 mm prolapsed

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

submucosal fibroid detected on laparoscopic hysterectomy for persistent abnormal uterine bleeding (Arnold A, 2016).

### **Bowel damage**

Bowel damage was reported in 12 patients who had hysteroscopic morcellation in a review of the Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database: 2 of these patients needed temporary colostomies and were admitted into the intensive care unit (Haber K, 2015).

### **Death**

Death was reported in 2 patients who had hysteroscopic morcellation in the review of the FDA MAUDE database. One patient had multiple comorbidities such as chronic hypertension and obesity; the patient desaturated during anaesthesia and was diagnosed with pulmonary embolism and died. The second patient was an elderly woman who 'was not well'; she was readmitted the day after her procedure and died shortly after. An exact cause of death was not reported (Haber K, 2015).

### **Fluid deficit or fluid overload**

Fluid overload that needed treating by intubation and admission to the intensive care unit was reported in 11 patients in the review of the FDA MAUDE database. Uncomplicated fluid overload that resolved spontaneously or with conservative treatment was reported in 19 patients in the same review (Haber K, 2015). Hysteroscopic morcellation was halted in 1 patient because of an imminent fluid overload in the randomised controlled trial of 60 patients who had hysteroscopic morcellation or conventional hysteroscopic resection (Van Dongen H, 2008).

In the systematic review of 650 patients with fibroids or polyps, hysteroscopic morcellation was associated with a smaller fluid deficit when randomised trials were meta-analysed (weighted mean difference -36.16, 95% CI -60.66 to -11.67,  $p=0.004$ ;  $I^2=0\%$ ; 2 studies). This effect was not statistically significant in observational studies or when all studies were compared (Shazly S, 2016).

In the non-randomised comparative study of 29 patients with submucosal fibroids, the mean fluid deficit was 1,005 ml for hysteroscopic morcellation and 225 ml for loop resection ( $p=0.003$ ) (Lee M, 2016).

In the case series of 278 patients with fibroids or polyps, the mean fluid deficit was 287 ml (Scheiber M, 2016).

In the case series of 244 patients with fibroids, polyps or other intrauterine pathology, the median fluid deficit for patients with fibroids was 880 ml (range 20 to 2,536) (Arnold A, 2016).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.



## **Hysterectomy**

Hysterectomy was reported in 6 patients in the review of the FDA MAUDE database: 3 were because of excessive blood loss, 2 were at the patient's request after the diagnoses of uterine perforation and a failed endometrial ablation, and 1 was because of device failure (see below) (Haber K, 2015).

## **Uterine perforation**

Uterine perforation that needed no additional surgery or treatment was reported in 28 patients in the review of the FDA MAUDE database (Haber K, 2015).

## **Pelvic infection**

Pelvic infection was reported in 4 patients in the review of the FDA MAUDE database (Haber K, 2015).

## **Postoperative bleeding**

Postoperative bleeding that could be controlled with non-invasive measures was reported in 6 patients in the review of the FDA MAUDE database (Haber K, 2015).

## **Device failure**

Device failure, including metal shavings and broken pieces of device visualised in the uterine cavity, poor visualisation, failure of outflow, and a defective device that would not activate, was reported in 25 patients in the review of the FDA MAUDE database. In 1 reported case the blade fell into the uterine cavity, could not be retrieved and a hysterectomy was done. The review estimated that 180,000 procedures were done during the study period (Haber K, 2015).

## **Disseminated peritoneal leiomyomatosis**

Disseminated peritoneal leiomyomatosis was described in 1 patient in a case report. The patient had a total laparoscopic hysterectomy at least 4 years after hysteroscopic morcellation of fibroids. At the time of the hysterectomy, the patient had an approximate 14-week size, globular retroverted uterus with multiple fibroids and severe adhesive disease. There were numerous individual deposits throughout the peritoneum and omentum that appeared to be consistent with fibroids. In addition, there was leiomyomatous disease on the ovaries bilaterally and a large cyst on the left ovary. Pathology from surgery showed a benign serous cystadenoma, endometriosis, and diffuse peritoneal leiomyomatosis (Benton A, 2018).

## **Other**

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

Hospital admission because of an unknown cause was reported in 3 patients in the review of the FDA MAUDE database (Haber K, 2015). Self-resolving dyspnoea was reported in 1 patient in the case series of 73 patients (attributed to anaesthesia without any evidence of fluid overload) (Maheux-Lacroix S, 2017).

## **Anecdotal and theoretical adverse events**

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, professional experts did not describe any anecdotal adverse events. They considered that the following was a theoretical adverse event: potential theoretical risk of spread of malignant tissue via tubal ostia into peritoneum.

## **The evidence assessed**

### **Rapid review of literature**

The medical literature was searched to identify studies and reviews relevant to hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids. The following databases were searched, covering the period from their start to 13 April 2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the [literature search strategy](#)). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The [inclusion criteria shown in the following table](#) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

## Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	<p>Clinical studies were included. Emphasis was placed on identifying good quality studies.</p> <p>Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study.</p> <p>Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.</p>
Patient	Patients with uterine fibroids.
Intervention/test	Hysteroscopic mechanical tissue removal (morcellation).
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

## List of studies included in the IP overview

This IP overview is based on about 1,500 patients who had hysteroscopic morcellation from 2 systematic reviews, 2 randomised controlled trials (1 is also included in the systematic review and the other compares 2 different healthcare settings), 1 non-randomised comparative study, 3 cohort studies, 2 case series and 1 case report (Yin X, 2018; Shazly S, 2016; Van Dongen H, 2008; Lee M, 2016; Maheux-Lacroix S, 2017; Vidal-Mazo C, 2019; Scheiber M, 2016; Arnold A, 2016; Rubino R, 2015; Bhalani V, 2016; Benton A, 2018). In addition, there is a review of 119 adverse events reported on the FDA MAUDE database (Haber K, 2015).

Other studies that were considered to be relevant to the procedure but were not included in the main [summary of the key evidence](#) are listed in the [appendix](#).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Summary of key evidence on hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids

### Study 1 Yin X (2018; published online 2019)

#### Study details

<b>Study type</b>	Systematic review and meta-analysis
<b>Country</b>	Not reported for individual studies
<b>Recruitment period</b>	Search date: 1 May 2019
<b>Study population and number</b>	n=498 (5 studies); 215 hysteroscopic morcellation, 183 conventional resectoscopy Patients with endometrial polyps or fibroids
<b>Age</b>	Mean ranged from 37 to 51 years
<b>Patient selection criteria</b>	3 databases (Web of Science, PubMed and Medline), were searched, to identify all relevant studies that evaluated hysteroscopic tissue removal system efficacy and safety for the treatment of endometrial polyps or myomas, compared with conventional resectoscopy. Additional publications that had not been identified in the electronic searches were examined manually. The search was limited to English language publications. The following search strategy was used for the literature search: (“hysteroscopic” or “hysteroscopy” or “hysteroscopic surgery”) AND (“myoma” or polyps”). Studies were included in the analysis if they were retrospective, observational and prospective randomised controlled trials and if the patients had endometrial lesions including endometrial polyps or submucous fibroids, the intervention comprised of hysteroscopic tissue removal systems while the control group had conventional resectoscopy with monopolar or bipolar electro-surgical system, at least 1 of 5 outcomes were reported (success rate, fluid deficit, operation time, complications and complete removal). Studies were excluded if the identified publication described a non-comparative study or was a letter, case report, or review. Additionally, if the outcomes ‘data of interest’ were not described clearly, the study was also excluded.
<b>Technique</b>	Hysteroscopic morcellation devices: Truclear (Smith & Nephew, US), Myosure (Hologic, US), Intrauterine Bigatti Shaver (Karl Storz, Germany). Conventional resectoscopy: 2 studies used a 26 Fr bipolar electro-surgical system (Karl Storz SE & Co KG), 1 study used an 8.5 mm bipolar resectoscope (Gynecare Versapoint), and 2 studies used an 8.6 mm monopolar resectoscope (Olympus Corp).
<b>Follow-up</b>	Not reported.
<b>Conflict of interest/source of funding</b>	One of the authors is a consultant for Karl Storz SE & Co KG and the developer of the Intrauterine Bigatti Shaver. Another author is a consultant for Karl Storz SE & Co KG. No financial industry support was received for this study.

#### Analysis

Study design issues: Systematic review and meta-analysis. Data was extracted from the included studies using a standard ‘Preferred Reporting Items for Systematic Reviews and Meta-Analyses’ data extraction form. If the IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

relevant data was not clear, the corresponding author of the original trial was contacted by email for missing or further information. The risk of bias was assessed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. Data synthesis was done using Rev Man 5.2 (Cochrane Collaboration, London, UK). Continuous data was presented as mean value and standard deviation, and the weighted mean difference and 95% confidence interval (CI) was calculated. Dichotomous data was expressed as odds ratios (ORs) with 95% CIs. The heterogeneity in outcomes across trials was assessed using the chi-squared and  $I^2$  tests. An  $I^2$  value of more than 50% was considered to indicate substantial heterogeneity, which prompted use of a random effects model for the analysis. Otherwise, a fixed effects model was applied. Publication bias was assessed with a funnel plot.

Study population issues: Of the 5 studies, 3 reported fibroids as the primary lesion.

One study of 84 patients with polyps was also included in the Shazly S et al., 2016 systematic review.

## Key efficacy findings

Number of patients analysed: 498

### Operation time

There was no statistically significant difference in operation time between hysteroscopic morcellation and conventional resectoscopy (mean difference  $-0.33$  minutes,  $p=0.83$ ; 5 studies).

Operation time for polypectomy only was statistically significantly shorter for hysteroscopic morcellation than conventional resectoscopy (mean difference  $-2.93$ min, 96% CI  $-4.25$  to  $-1.61$ ,  $p<0.0001$ ; 3 studies).

There was no statistically significant difference for fibroid complete removal time ( $p=0.46$ ).

### Total removal rate

The pooled results showed that the success rate was higher with hysteroscopic morcellation than with conventional resectoscopy, (147/154 [95.5%] compared with 107/124 [86.3%]; odds ratio 4.28, 95% CI 1.68 to 10.91;  $p=0.002$ ;  $I^2=0\%$ ,  $p=0.83$ ; 3 studies).

## Key safety findings

### Fluid deficit

All 5 studies showed that the fluid deficit was higher with hysteroscopic morcellation than with conventional resectoscopy (mean difference 158.98 mL, 95% CI 41.4 to 276.5;  $p=0.008$ ), but no fluid overload syndrome was reported. Fluid deficit was statistically significantly higher for fibroids treated by hysteroscopic morcellation ( $p=0.02$ ), but not for polyps ( $p=0.88$ ).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

The authors noted that a possible explanation for the higher fluid deficit in the hysteroscopic morcellation group could be that 1 of the studies used a fast and high pressure fluid pumping device to maintain a clear view, and to prevent bleeding inside the uterine cavity.

### **Complications**

Four studies reported intraoperative and postoperative complication rates, including perforation, via falsa and bleeding. There was no statistically significant difference between hysteroscopic morcellation and conventional resectoscopy (odds ratio 0.31, 95% CI 0.08 to 1.19; p=0.09).

## Study 2 Shazly S (2016)

### Study details

<b>Study type</b>	Systematic review and meta-analysis
<b>Country</b>	France, the Netherlands, Spain, Belgium, UK
<b>Recruitment period</b>	Search date: August 2015
<b>Study population and number</b>	n=650 (238 hysteroscopic morcellation, 412 electrosurgical resection); 7 studies Patients with endometrial polyps or submucous fibroids
<b>Age</b>	Mean age ranged from 38 to 55 years
<b>Patient selection criteria</b>	Studies that compared electrosurgical resection with hysteroscopic morcellation for treating uterine cavity lesions were included. Randomised controlled trials and prospective and retrospective studies were considered eligible. Case reports, case series, and noncomparative studies were excluded. There were no limitations based on foreign language or date of publication.
<b>Technique</b>	Devices: Truclear (Smith & Nephew, US) and Myosure (Hologic, US).
<b>Follow-up</b>	Range from none to 3 months
<b>Conflict of interest/source of funding</b>	None for authors of the systematic review.

### Analysis

Study design issues: Systematic review and meta-analysis. The main outcomes were total procedure time, fluid deficit between fluid instillation and collection, and complete removal of the lesion. Analyses of long-term outcomes and pain scores were not possible because of insufficient data. The Newcastle-Ottawa scale was used to assess observational studies and the Cochrane Risk of Bias Tool was used to assess randomised controlled trials. Of the 7 included studies, 4 were randomised controlled trials (1 of which included patients with fibroids) and 3 were retrospective observational studies (2 of which included patients with fibroids).

Study population issues: An endometrial polyp was the primary lesion in 4 studies. One study included only patients with submucous fibroids, whereas the remaining 2 studies included patients with both polyps and fibroids. The documented polyp sizes ranged from 9.2 to 17 mm and 9.7 to 25.4 mm for fibroids. Abnormal uterine bleeding was the most common presentation followed by infertility.

One study of 84 patients with polyps was also included in the Yin X et al., 2018 systematic review.

### Key efficacy findings

Number of patients analysed: 650 (238 hysteroscopic morcellation, 412 electrosurgical resection)

#### Incomplete removal of lesion – submucosal fibroids and polyps

- All studies (4 studies; 203 morcellation, 212 resection): odds ratio=0.29, 95% CI=0.05 to 1.53, p=0.14

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

- Randomised controlled trials (3 studies; 169 morcellation, 163 resection): odds ratio=0.12, 95% CI=0.03 to 0.54, p=0.006; I<sup>2</sup>=0%
- Retrospective observational studies (1 study; 34 morcellation, 49 resection): odds ratio=1.24, 95% CI 0.49 to 3.13

### **Number of insertions – submucosal fibroids and polyps**

- All studies (2 studies [both randomised controlled trials]; 74 morcellation, 70 resection): weighted mean difference=-3.04, 95% CI=-7.86 to 1.78, p=0.22

### **Procedure time – submucosal fibroids only**

- All studies (2 studies [both retrospective observational studies]; 62 morcellation, 221 resection); weighted mean difference=-13.44, 95% CI -38.13 to 11.25, I<sup>2</sup>=97%



## Key safety findings

### Fluid deficit (ml) – submucosal fibroids and polyps

- All studies (3 studies, 4 cohorts; 129 morcellation, 286 resection): weighted mean difference=-170.33, 95% CI=-382.04 to 41.38, p=0.18
- Randomised controlled trials (2 studies; 74 morcellation, 70 resection): weighted mean difference=-36.16, 95% CI=-60.66 to -11.67, p=0.004; I<sup>2</sup>=0%
- Retrospective observational studies (1 study, 2 cohorts; 55 morcellation, 216 resection): weighted mean difference=-269.55, 95% CI -607.82 to 68.71

### Operative and postoperative complications – submucosal fibroids and polyps

- All studies (3 studies; 140 morcellation, 148 resection): weighted mean difference=0.72, 95% CI=0.20 to 2.57, p=0.62
- Randomised controlled trials (2 studies; 106 morcellation, 99 resection): weighted mean difference=0.41, 95% CI=0.07 to 2.49, p=0.33
- Retrospective observational studies (1 study; 34 morcellation, 49 resection): weighted mean difference=1.52, 95% CI 0.40 to 5.71

## Study 3 Van Dongen H (2008) – included in 2015 overview

### Study details

<b>Study type</b>	Randomised controlled trial
<b>Country</b>	The Netherlands
<b>Recruitment period</b>	2005 to 2006
<b>Study population and number</b>	n=60 (30 hysteroscopic morcellation [10 fibroids] versus 30 conventional hysteroscopic resectoscopy [12 fibroids]) Women with intrauterine polyps or submucous fibroids (type 0 or 1).
<b>Age</b>	Mean 49 years
<b>Patient selection criteria</b>	Intrauterine polyp or type 0 or type 1 submucous fibroid smaller than 30 mm in diameter and an indication for removal (abnormal uterine bleeding, dysmenorrhoea, infertility). Exclusion criteria were type 2 fibroids, suspicion of malignancy before surgery, or contraindications for hysteroscopic surgery.
<b>Technique</b>	All procedures were done in an inpatient setting with the patients under general or spinal anaesthesia. Hysteroscopic morcellator (Smith and Nephew, USA) was used with normal saline solution for distension and irrigation. Conventional resectoscopy used sorbitol (4%) for distension and irrigation.
<b>Follow-up</b>	Not reported
<b>Conflict of interest/source of funding</b>	Financial support was received from Smith and Nephew, USA.

### Analysis

Study design issues: Randomisation was done using sealed opaque envelopes. The procedures were done by 6 residents in training for obstetrics and gynaecology. The primary outcome measure was the operating time, defined as the time between the introduction of the hysteroscope until the removal of the instrument at the end of the procedure. Intention-to-treat analysis.

Study population issues: There were no significant differences in baseline characteristics (age, median parity, menopausal state, indication for surgery, preoperative diagnosis, size of intrauterine abnormality) between the groups. Most patients had polyps rather than fibroids – the results were not separated by indication.

Other issues: The authors noted that no learning curve was observed. They also noted that approximately 20% of resectoscopy procedures had to be taken over by the trainer, compared with 3% of the morcellator procedures. This study is included in the systematic review by Shazly (2016).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Key efficacy findings

Number of patients analysed: 60 (30 hysteroscopic morcellation, 30 conventional resectoscopy)

### Mean operating time (minutes)

- Hysteroscopic morcellation=10.6 (95% CI 7.3 to 14.0)
- Conventional resection=17.0 (95% CI 14.1 to 19.9), p=0.008

### Median number of insertions

- Hysteroscopic morcellation=1 (range 1–2)
- Conventional resection=7 (range 3–50)

Multiple linear regression analysis showed that operating time increased significantly, in both groups, when volume of intrauterine lesions increased.

## Key safety findings

### Mean total distension fluid used (ml)

- Hysteroscopic morcellation=3413 (95% CI 2209 to 4617)
- Conventional resection=5050 (95% CI 4106 to 5994), p=0.041

### Mean total fluid deficit (ml)

- Hysteroscopic morcellation=409 (95% CI 229 to 589)
- Conventional resection=545 (95% CI 406 to 684), p=0.224

## Complications

- 1 patient allocated to conventional resectoscopy did not undergo the intended procedure because of a perforation during cervical dilation.
- Hysteroscopic morcellation was aborted prematurely in 1 patient with submucous type 1 fibroid because of an imminent fluid overload.
- Histological analysis of the specimens revealed that 2 patients in the hysteroscopic morcellation group had malignant endometrial carcinoma (both were diagnosed with fibroid type 0 before the surgery). Both patients were treated primarily with the hysteroscopic morcellator and subsequently (after diagnosis) had a radical hysterectomy with bilateral salpingo-oophorectomy.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 4 Lee M (2016)

### Study details

<b>Study type</b>	Non-randomised comparative study
<b>Country</b>	China
<b>Recruitment period</b>	2011 to 2014
<b>Study population and number</b>	n=29 (15 hysteroscopic morcellation, 14 hysteroscopic monopolar loop resection) Patients with submucosal fibroids
<b>Age</b>	Not reported
<b>Patient selection criteria</b>	All patients who had hysteroscopic resection of submucosal fibroids were selected and case notes reviewed.
<b>Technique</b>	Hysteroscopic morcellation device: Myosure (Hologic, US). Normal saline was used as the distending medium. Loop resection: monopolar energy was used and glycine was the distending medium.
<b>Follow-up</b>	3 months
<b>Conflict of interest/source of funding</b>	None

### Analysis

Follow-up issues: no losses to follow-up were described. Two patients from the morcellation group and 1 from the conventional group were excluded due to the need for multiple procedures including endometrial ablation or laparoscopic ovarian cystectomy during the same operation. One patient in the conventional resection group had a uterine perforation that needed surgical repair and was excluded from data analysis.

Study design issues: Retrospective, single centre non-randomised comparative study. The choice of procedure was dependent on the operator. Those patients with prolonged operating time because of multiple operations for other indications or complications were excluded from the final analysis. Postoperatively, a satisfactory outcome was considered when the patient subjectively reported reduced menstrual bleeding and considered the operation to have improved menstrual symptoms at 3-month follow-up.

Study population issues: The mean size of fibroids resected was 3.3 cm (range 2 to 5 cm) for the conventional technique and 3.5 (range 1.5 to 6 cm) for hysteroscopic morcellation ( $p=0.470$ ).

Study is also included in systematic review by Yin X et al. (2018).

Other issues: All hysteroscopic morcellation procedures were done between 2013 and 2014 after the procedure was introduced in the department.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Key efficacy findings

Number of patients analysed: 25 (13 hysteroscopic morcellation, 12 conventional hysteroscopic resection)

### Duration of procedure (minutes)

- Hysteroscopic morcellation=36.6 (range 17 to 72)
- Loop resection=53.6 (range 39 to 102), p=0.005

### Mean difference in haemoglobin levels before and 3 months after procedure (g/l); n=9 in both groups

- Hysteroscopic morcellation=+17.0 (range -4 to +40)
- Loop resection=+21.5 (range +1 to +44), p=0.235

### Satisfactory outcome

- Hysteroscopic morcellation=93.3%
- Loop resection=84.6%, p=0.841

### Satisfactory outcome when uterine fibroid protrusion >60%

- Hysteroscopic morcellation=100%
- Loop resection=100%

### Comparison of outcomes for small and large fibroids

Fibroid size	Hysteroscopic morcellation	Loop resection	p value
Small (3 cm or less)	n=9	n=5	
Duration of procedure (mins)	27.6 (14 to 45)	53.4 (29 to 76)	0.019
Patient satisfaction	9 (100%)	4 (80%)	0.797
Large (more than 3 cm)	n=4	n=7	
Duration of procedure (mins)	57 (40 to 66)	65 (39 to 102)	0.527
Patient satisfaction	3 (75%)	6 (85.7%)	0.788

## Key safety findings

### Mean fluid deficit (ml)

- Hysteroscopic morcellation=1,005 (range 40 to 2,600)

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

- Loop resection=225 (range 0 to 1,000), p=0.003

**Mean fluid deficit (ml) for small fibroids (3 cm or less)**

- Hysteroscopic morcellation (n=9) = 634.4 (range 40 to 1,600)
- Loop resection (n=5) = 80 (range 0 to 200), p=0.019

**Mean fluid deficit (ml) for large fibroids (more than 3 cm)**

- Hysteroscopic morcellation (n=4) = 1,839 (range 556 to 2,600)
- Loop resection (n=7) = 328.6 (range 0 to 1,000), p=0.024

**Complications**

- Hysteroscopic morcellation: no intraoperative or postoperative complications that could lead to an extended hospital stay.
- Loop resection: 1 uterine perforation

No patient in either group developed any complication associated with excessive fluid absorption.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 5 Maheux-Lacroix S (2017)

### Study details

<b>Study type</b>	Cohort study
<b>Country</b>	Australia
<b>Recruitment period</b>	2011 to 2016
<b>Study population and number</b>	n=73 Women with abnormal uterine bleeding associated with benign submucosal fibroids
<b>Age</b>	Mean 43 years
<b>Patient selection criteria</b>	Inclusion criteria: women with abnormal uterine bleeding who had a hysteroscopic resection by mechanical morcellation of a benign submucosal fibroid confirmed at histopathology. Abnormal uterine bleeding was defined by having at least 1 of the following International Federation of Gynecology and Obstetrics (FIGO) standardised symptoms: heavy menstrual bleeding, inter-menstrual bleeding, post-coital bleeding, or post-menopausal bleeding. Exclusion criteria included viable pregnancy, active pelvic infection, an in situ intra-uterine device, concomitant endometrial ablation or resection, and malignancy or pre-malignancy (endometrial hyperplasia) at histopathology.
<b>Technique</b>	Device: Myosure LITE or XL (Hologic, US) Paracervical or cervical block with local anaesthesia with or without epinephrine was used according to surgeons' preferences. All resected specimens were sent for histologic examination.
<b>Follow-up</b>	Mean 32 months (range 6 to 54)
<b>Conflict of interest/source of funding</b>	One author is the recipient of a Training Award from the Fonds de Recherche Quebec-Sante. One author is a paid consultant for Hologic and is a member of their Medical Advisory Committee in Australia. He has no shares or equity in the company.

### Analysis

Follow-up issues: Patients with a minimum of 6 months after their index surgery were contacted by email (2 attempts) or phone (2 attempts). There were 92 women eligible for the study but 19 were lost to follow-up, leaving 73 (79%) included in the analysis.

Study design issues: Prospective, multicentre cohort study. The main aim was to assess the need for repeat surgical intervention after the procedure. Other outcomes included patient satisfaction, symptom resolution, postoperative complications and predictors of negative outcomes. Medical records including medical notes, operation report and histopathology results were reviewed to confirm the nature and indication for subsequent surgery. A failure to control abnormal uterine bleeding was defined as either the persistence or the recurrence of at least one of the following symptoms: heavy menstrual bleeding, inter-menstrual bleeding, post-coital bleeding or post-menopausal bleeding).

Study population issues: Of the 19 patients who were lost to follow-up, 12 (63%) were nulliparous compared with 23 (31%) in the included group ( $p=0.0114$ ). All other baseline characteristics were similar. Patients had

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

type 0, 1 or 2 fibroids. More than 1 fibroid was removed in 28% of patients and 14% (10/73) also had a polyp removed. The mean total size of pathology at the time of index surgery was 42 mm.

## Key efficacy findings

Number of patients analysed: 73

4 patients needed a second procedure because the maximum saline deficit was reached before the resection was completed. These patients all had submucosal fibroids of 40 mm or more.

### Percentage of pathology removed

- 100%=71% (49/69)
- 75 to 99%=15% (10/69)
- 50 to 74%=13% (9/69)
- <50%=1% (1/69)

### Patient satisfaction

- Satisfied=84% (54/73)
- Neutral=6% (4/73)
- Dissatisfied=9% (6/73)

### Failure to control abnormal uterine bleeding=33% (24/73)

- Persistence of at least 1 symptom=21% (15/73) [reported in paper as 23%]
- Recurrence of symptoms=18% (13/73) [reported in paper as 20%]

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.



**Any subsequent related surgery=27% (20/73)**

- Operative hysteroscopy=19% (14/73) (11 resection of fibroid, 1 resection of polyp, 2 endometrial ablation)
- Hysterectomy=12% (9/73)
- Laparoscopic myomectomy=3% (2/73)

**Estimated cumulative incidence of subsequent related surgery by size of fibroid**

Pathology size	Estimated cumulative incidence (%) ± standard deviation		
	1 year	2 years	3 years
All	15±4	23±5	30±6
<50 mm	10±4	15±5	21±6
50 mm and above	25±9	38±10	54±17

Multivariate cox proportional hazards analysis showed a total pathology size of 50 mm or more was associated with an increased risk of needing a subsequent surgical procedure (hazard ratio 2.9, p=0.02). Having 2 or more fibroids resected was also associated with an increased risk but it did not reach statistical significance (hazard ratio 1.8, p=0.1). There was no association found when comparing type 2 fibroids to other pathology (p=0.57).

For women who had a hysterectomy, multiple fibroids were reported and histopathologically confirmed in all cases and adenomyosis in 66% (6/9) of patients.

**Key safety findings****Postoperative complications=7% (5/73)**

- Pain caused by a prolapsed fibroid=2.7% (2/73) (1 and 2 months respectively after initial procedure; both patients had an incomplete resection that was successfully treated by combined vaginal and hysteroscopic resection of the remaining fibroid)
- Pelvic infection=2.7% (2/73) (treated with antibiotics)
- Self-resolving dyspnoea=1.4% (1/73) (attributed to anaesthesia without any evidence of overload)

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 6 Vidal-Mazo C (2019)

### Study details

<b>Study type</b>	Cohort study
<b>Country</b>	Spain
<b>Recruitment period</b>	2013 to 2018
<b>Study population and number</b>	n=320 (353 myomas) Premenopausal patients with submucosal fibroids and symptoms of abnormal uterine bleeding or infertility
<b>Age</b>	Mean 43 years
<b>Patient selection criteria</b>	Patients with 1 or more submucosal fibroids confirmed by hysteroscopy and pathological study. Indications for hysteroscopy included anormal uterine bleeding and infertility. Fibroids of FIGO type 0, 1 and 2 were included. Fibroids larger than 5 cm were excluded.
<b>Technique</b>	Device: Myosure The procedures were done in office and patients were discharged at the end of the procedure. Oral sedation was used with paracervical anaesthesia. Patients were instructed to take an oral analgesic before the procedure. No patient had prophylactic antibiotics. In case of incomplete resection, a re-morcellation was offered 3 months later. All resected samples were sent for histological examination.
<b>Follow-up</b>	Up to 5 years
<b>Conflict of interest/source of funding</b>	None

### Analysis

**Follow-up issues:** All patients had a follow up visit 3 to 6 months after the procedure and were invited to attend an annual review. There were 99 women remaining to be evaluated (31%) in the second year. In the third year, 176 (55%) patients had not been evaluated and at the fourth and fifth year of follow-up, 75% of patients had not yet completed the study.

**Study design issues:** Prospective cohort study. The aim of the study was to evaluate the clinical recurrence of submucosal fibroids after hysteroscopic morcellation, and to study the characteristics associated with clinical recurrence after 5 years of follow-up. The FIGO classification was used to characterise the fibroids; if there were more than 1, the fibroid of greater hysteroscopic complexity was classified, and the size was calculated as the total sum of all fibroids.

**Study population issues:** Of the 319 patients with reported FIGO fibroid type, 130 (41%) had type 0, 126 (40%) had type 1 and 63 (20%) had type 2 fibroids. The mean size of submucosal fibroid was 24.6 mm. Abnormal uterine bleeding was the indication in 290 (91%) patients and infertility in 30 (9%).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Key efficacy findings

Number of patients analysed: 320

16.6% (53/320) of patients had a repeat morcellation procedure 3 months after the initial procedure because of incomplete resection.

### Outcomes by fibroid type, n (%)

Type	Post procedure	2 year review	3 year review	4 year review	5 year review
FIGO 0	n=130				
<i>Not evaluated</i>	1 (0.8%)	33 (25.4%)	61 (46.9%)	93 (71.5%)	114 (87.7%)
<i>Discharged</i>	109 (83.9%)	87 (66.9%)	64 (49.2%)	32 (24.6%)	14 (10.8%)
<i>Hysterectomy</i>	6 (4.6%)	7 (5.4%)	5 (3.8%)	0 (0%)	0 (0%)
<i>Recurrence</i>	14 (10.8%)	3 (2.3%)	0 (0%)	5 (3.8%)	5 (3.8%)
FIGO 1	n=126				
<i>Not evaluated</i>	1 (0.8%)	38 (30.2%)	64 (50.8%)	90 (71.4%)	105 (83.3%)
<i>Discharged</i>	88 (69.8%)	74 (58.7%)	58 (46%)	35 (27.8%)	21 (16.7%)
<i>Hysterectomy</i>	4 (3.2%)	7 (5.6%)	0 (0%)	1 (0.8%)	0 (0%)
<i>Recurrence</i>	27 (26.2%)	7 (5.6%)	4 (3.2%)	0 (0%)	0 (0%)
FIGO 2	n=63				
<i>Not evaluated</i>	1 (1.6%)	28 (44.4%)	51 (81%)	57 (90.5%)	62 (98.4%)
<i>Discharged</i>	35 (55.6%)	25 (39.7%)	7 (11.1%)	6 (9.5%)	1 (1.6%)
<i>Hysterectomy</i>	6 (9.5%)	4 (6.4%)	1 (3.2%)	0 (0%)	0 (0%)
<i>Recurrence</i>	21 (33.3%)	6 (9.5%)	3 (4.8%)	0 (0%)	0 (0%)

## Key safety findings

The paper states that there were no complications related to surgery or clinical follow up.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 7 Scheiber M (2016)

### Study details

<b>Study type</b>	Case series
<b>Country</b>	US (34 centres)
<b>Recruitment period</b>	Not reported
<b>Study population and number</b>	n=278 (187 fibroids [33%], 372 polyps [67%] Women with indications for hysteroscopic myomectomy or polypectomy
<b>Age</b>	Mean 44 years
<b>Patient selection criteria</b>	Inclusion criteria: age 18 to 65 years, identification of intrauterine pathology using ultrasound, saline infusion sonography, or hysteroscopic examination, with polyps of any size or submucosal fibroids 6 cm or less in diameter. Exclusion criteria: pregnancy, intrauterine device in situ at the time of the procedure, current use of anticoagulant or antiplatelet medication in addition to low-dose aspirin, active pelvic inflammatory disease or pelvic/vaginal infection, known or suspected coagulopathy or bleeding disorder, increased fluid overload risk (such as history of predisposing cardiac, hepatic, or renal dysfunction), or other comorbid condition that, in the opinion of the investigator, could limit the ability to participate or affect the scientific integrity of the study.
<b>Technique</b>	Device: MyoSure Hysteroscopic Tissue Removal System (Hologic Inc., US) General anaesthesia was used for 71% of procedures. Of the 278 patients, 250 were treated in an ambulatory surgery centre or hospital outpatient department and 28 were treated in physician offices.
<b>Follow-up</b>	Not reported
<b>Conflict of interest/source of funding</b>	The 2 authors received compensation for speaking engagements by Hologic Inc. Neither author had any other potential conflicts of interest, financial or otherwise.

### Analysis

Study design issues: Prospective, single-arm, multicentre registry. The aim of the study was to assess the feasibility of hysteroscopic morcellation across a diverse set of facilities, including both surgical and office-based settings. The primary efficacy endpoint was the percentage of lesions removed. Secondary outcomes included procedure time, cutting time, fluid deficit, and the need for mechanical cervical dilation. A 5-point Likert scale was used to evaluate physician postoperative satisfaction with the morcellation system, with a score of 5 indicating “very satisfied,” and a score of 1 indicating “very dissatisfied.” The safety endpoint assessed the incidence of adverse events observed before discharge from the recovery room or reported by the patient after discharge. Study physicians were asked to report the occurrence of specific adverse events, which were cramping, nausea, pain, haemorrhage, pulmonary distress, cervical tearing, fibroid recurrence, vaginal bleeding, vomiting, fluid overload, infection, reaction to anaesthetic agents, and uterine perforation.

Study population issues: Most patients (73%) were premenopausal. Of the 278 patients, 74% were treated for abnormal uterine bleeding, and 15% were treated for infertility. The mean fibroid diameter was 2.2 cm (range

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

0.3 to 5.5 cm). Fibroids were most commonly located in the anterior section of the uterus (26% of the total). Polyps were most commonly located in the posterior uterus (24% of the total).

## Key efficacy findings

Number of patients analysed: 278

### Operative parameters and observations

Parameter	All sites	n	Office	n	Ambulatory surgical centre or hospital outpatient department	n	p value
% pathology removed, by patient	95.4±13.2	278	96.8±14.1	28	95.2±13.1	250	0.5436
% polyp removed, by lesion	99.3±5.8	331	99.3±6.1	27	99.9±0.4	304	0.0900
% fibroid removed, by lesion	86.8±24.1	157	94.8±17.6	18	85.8±24.7	139	0.1368
Resection time, min	6.0±9.0	229	8.9±15.6	21	5.8±8.1	208	0.0978
Time in post-anaesthesia care unit, min	55.4±37.1	207	36.8±24.7	16	57.0±37.5	191	0.0263
Physician satisfaction score 4 to 5, %	95	278	89	28	96	250	0.1470

Of 245 patients for whom cervical dilation information was recorded, mechanical dilation was done in 215 patients (87.7%) and mean dilation was 0.9 cm (range 0.3 to 2.8 cm).

## Key safety findings

- Mean fluid deficit=287±453 ml
- Adverse events=1.8% (5/278) of patients (3.6% in office setting and 1.6% in ambulatory surgical centre or hospital outpatient department, p=0.4143); 4 patients had mild cervical trauma and 1 patient had moderate postoperative pedal oedema. All adverse events were described as mild and resolved spontaneously.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 8 Arnold A (2016)

### Study details

<b>Study type</b>	Cohort study
<b>Country</b>	Australia
<b>Recruitment period</b>	2013 to 2015
<b>Study population and number</b>	n=244; 255 procedures (102 fibroids, 98 polyps, 22 mixed pathology, 16 pregnancy tissue, 17 preinvasive or invasive endometrial abnormalities) Women who had hysteroscopic removal of intrauterine pathology
<b>Age</b>	Median 44 years (range 22 to 82)
<b>Patient selection criteria</b>	Women aged $\geq 18$ years needing a hysteroscopic procedure involving resection of endometrial pathology were included in the study. Exclusion criteria included viable pregnancy, active pelvic infection, and an intrauterine contraceptive device remaining in situ.
<b>Technique</b>	MyoSure Lite or MyoSure XL device (Hologic, US).
<b>Follow-up</b>	Median 3.6 months
<b>Conflict of interest/source of funding</b>	One author is a paid consultant for Hologic and is a member of their speakers' bureau. He has no shares or equity in the company. One author received a travel grant from Hologic to present this study at a meeting. No funding was received to conduct this study.

### Analysis

Study design issues: Prospective cohort study. Surgical data included the need for and extent of cervical dilatation; pathology type, size, and location; percentage of pathology removed, noted as complete (100% of abnormal tissue removed visually) or as an estimated visual assessment of tissue removal, defined as 75% to 99%, 50% to 74%, and <50% and surgical vision, defined as 100%, 75% to 99%, 50% to 74%, and <50% by the operating surgeon; fluid deficit; and any intraoperative complications. When there were multiple pathologies within the endometrial cavity, all pathologies were combined to calculate the size of total pathology. Postoperative data included final pathological diagnosis, resolution of symptoms when seen at follow-up as indicated clinically, and whether further surgery was planned or had been done.

Study population issues: The most common indication for treatment was abnormal bleeding (82%), followed by infertility (6%) and retained products of conception (4%); the indication was not reported for 8% of patients.

### Key efficacy findings

Number of patients analysed: 244 (255 procedures)

Complete resection of fibroids=66% (63/95) of patients

The reasons for incomplete resection of fibroids included maximal fluid deficit reached in 13 (41%), technical issues in 2 (6%), poor vision in 6 (19%), calcified pathology in 3 (9%), and no documented reason in 8 (25%).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Procedure information

Variable	Fibroids (n=102)	Polyps (n=98)	Mixed pathology (n=22)	Pregnancy tissue (n=16)	Preinvasive or invasive (n=17)	p value
Final histology, n (%)	29 (28) type 0; 38 (37) type 1; 17 (17) type 2; 18 (18) not documented		16 (73) polyps and fibroids; 4 (18) benign endometrium; 1 (4.5) septum; 1 (4.5) adenomyoma	16 products of conception	9 (53) preinvasive; 8 (47) invasive	
Median duration of activation of morcellation device, min:s (range)	4:33 (0:09 to 22:45)	0:28 (0:02 to 9:50)	2:03 (0:23 to 13:18)	1:16 (0:17 to 8:33)	0:56 (0:22 to 3:16)	<0.001
Median size of pathology, mm (range)	40 (10 to 150)	20 (3 to 70)	30 (10 to 80)	25 (8 to 45)	20 (5 to 70)	<0.001
Median saline deficit, ml (range)	880 (20 to 2,536)	200 (10 to 2,500)	525 (40 to 2,440)	900 (70 to 2,500)	256 (40 to 1,900)	<0.001
Complete resection of pathology, n (%)	63 (66); 18 (62) type 0; 27 (71) type 1; 11 (65) type 2	91 (92)	16 (76)	13 (87)	15 (88)	

Completeness of resection data was missing for 12 procedures (7 fibroids, 3 polyps, 1 mixed pathology and 1 pregnancy tissue)

Complete resection of pathology was statistically significantly more likely for polyps compared with fibroids (92% vs 66%;  $p < 0.001$ ). The completeness of resection of pathology was associated with symptom resolution for fibroids ( $p = 0.005$ ), but not for polyps ( $p = 0.431$ ).

Multivariable logistic regression analysis was done for possible factors associated with incomplete resection of a fibroid, including total size of pathology, size of the largest fibroid, operator skill level, and subtype of fibroid (0, 1, or 2). The size of the largest leiomyoma ( $p < 0.005$ ) and the seniority of the surgeon ( $p < 0.012$ ) were the only statistically significant factors associated with the likelihood of complete resection with a single procedure. Increasing leiomyoma size was negatively correlated with complete removal.

### Completeness of resection of fibroids according to fibroid size

- <20 mm=90%
- 20 to 29 mm=89%
- 30 to 39 mm=83%
- ≥40 mm=48%

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Pregnancy

Pregnancy occurred in 5 women to the time of follow-up (2 who had polyp removal, 2 who had removal of pregnancy products, and 1 who had fibroid removal).

## Repeat procedures

3 women, who had completely resected pathology, had a repeat procedure at 12 to 18 months after the initial procedure because of new pathology. An additional 6 women had a repeat procedure scheduled after incomplete removal of pathology at the first operation, and 1 woman, who had 15 fibroids, had 3 procedures over an 8 week period to completely resect pathology.

## Hysterectomy

6% (5/85) of women with a fibroid had a subsequent hysterectomy. Of the 5 women, 2 had a complete submucous fibroid resection but persistent symptoms of abnormal uterine bleeding. Final pathology showed intramural fibroids with no submucous component. The other 3 women had an incomplete fibroid resection at the primary hysteroscopic procedure, and all 3 had laparoscopic hysterectomy, with diffuse leiomyomatosis in 1, a 60-mm prolapsed submucosal fibroid in 1, and intramural fibroids in 1.

## Key safety findings

- There were no intraoperative complications
- Postoperative complications=1% (3/255)

All 3 patients with postoperative complications had incomplete removal of fibroid at the index surgery and then sustained a prolapsed submucosal fibroid at 2 to 12 weeks after surgery. One patient needed unplanned emergency surgery and a blood transfusion for haemorrhage, with vaginal resection of the prolapsed submucosal fibroid. The second patient had offensive vaginal discharge, which resolved after the prolapsed submucosal fibroid was removed vaginally. The third woman had a 60 mm prolapsed submucosal fibroid (mentioned above) detected on laparoscopic hysterectomy for persistent abnormal uterine bleeding.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.



## Study 9 Rubino R (2015) – included in 2015 overview

### Study details

<b>Study type</b>	Randomised controlled trial (comparing an office setting against an ambulatory surgical centre)
<b>Country</b>	US
<b>Recruitment period</b>	Not reported
<b>Study population and number</b>	n=74 patients (42 fibroids, 66 polyps) Pre or peri-menopausal women with submucosal fibroids or polyps and abnormal uterine bleeding
<b>Age</b>	Mean 41 years
<b>Patient selection criteria</b>	Intrauterine polyps or submucosal fibroids which were compatible with office-based treatment based on 1 or more of the following criteria: 1 or more polyps, with at least 1 of the polyps $\geq 1.5$ cm and $\leq 3.0$ cm diameter with a broad based attachment to the uterine wall; up to 2 type 0 or type 1 fibroids with at least 1 of them being $\geq 1.5$ cm and none of them being $>3.0$ cm; polyps plus up to 2 type 0 or type 1 fibroids with at least 1 of the fibroids being $\geq 1.5$ cm and $\leq 3.0$ cm and none of the fibroids being $>3.0$ cm. Exclusion criteria: known or suspected cancer; contraindication or allergy to local anaesthetic; history of chronic narcotic use; previous uterine artery embolisation; presence of intrauterine device at the time of the procedure; active pelvic inflammatory disease or pelvic/vaginal infection; type 2 submucosal fibroids, fundal type 1 fibroids, submucosal fibroids $>3.0$ cm or highly vascularised fibroids.
<b>Technique</b>	All procedures were done using the Myosure hysteroscopic tissue removal system (Hologic, US).
<b>Follow-up</b>	12 months
<b>Conflict of interest/source of funding</b>	Study was sponsored by Hologic Inc.

### Analysis

Study design issues: patients were randomised to have the procedure either in an 'office' setting or in an ambulatory surgical centre. Different levels of analgesia were used in each setting. Each patient completed the Health Related Quality of Life (HRQOL) questionnaire and the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire prior to treatment and 12 months after treatment.

Study population issues: In this study, 61% (66/108) of the abnormalities in the 74 patients were polyps. Patient reported outcome data are not presented separately for those women with fibroids only.

### Key efficacy findings

Number of patients analysed: 74

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

**Percentage pathology removal for fibroids**

- Overall=95.9%±6.8% (range 75%–100%)
- Office setting=94%±8.6% (range 75%–100%)
- Ambulatory surgical centre=99.8%±0.4% (range 99%–100%)

**Proportion of fibroids with 100% removal**

- Overall=63.6%
- Office setting=52%
- Ambulatory surgical centre=83.3%

**Mean resection time (seconds)**

- Overall=143.0±293.3
- Office setting=189.3±376.9
- Ambulatory surgical centre=82.2±77.4

**UFS-QOL symptom severity (higher scores indicate more severe symptoms) and HRQOL scores (higher scores indicate better quality of life)**

	Overall	Office	surgical centre
UFS-QOL symptom score before procedure	67.5±15.4	68.3±16.3	66.4±14.0
UFS-QOL score at 12-months follow-up	22.3±22.6	39.1±24.7	38.2±21.1
UFS-QOL symptom severity improvement	45.2±23.2 p<0.01	42.7±24.0 p<0.01	48.3±21.6 p<0.01
HRQOL score before procedure	38.7±23.3	39.1±24.7	38.2±21.2
HRQOL score at 12-months follow-up	83.9±24.4	81.1±28.1	87.6±17.9
HRQOL improvement	45.5±25.1 p<0.01	42.3±25.3 p<0.01	49.4±24.3 p<0.01

**Patient satisfaction (proportion of patients who reported that they were 'satisfied' or 'very satisfied')**

- Overall=89.2%
- Office setting=88.6%
- Ambulatory surgical centre=96.9%

**Proportion of patients who would recommend treatment to other patients having similar symptoms**

- Overall=95.9%
- Office setting=95.5%
- Ambulatory surgical centre=100%

**Key safety findings**

- Adverse events=2.7% (2/74; 1 patient experienced pain that was described as mild and 1 patient had diarrhoea and food poisoning).

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 10 Bhalani V (2016)

### Study details

<b>Study type</b>	Case series
<b>Country</b>	US (2 clinics)
<b>Recruitment period</b>	Not reported
<b>Study population and number</b>	n=62 Women with intrauterine pathology and infertility or recurrent pregnancy loss
<b>Age</b>	Mean 37 years (range 28 to 46)
<b>Patient selection criteria</b>	Inclusion criteria: women aged 45 years or less (or over 45 if using egg donation at the time of hysteroscopic intervention), documented history of infertility for at least 6 months if aged 35 years or more or at least 12 months if aged less than 35 years, recurrent (2 or more) clinical pregnancy losses, postoperative follow-up at least 6 months with documented efforts to conceive, or confirmed fetal heartbeat or other pregnancy verification within 6 months of procedure.
<b>Technique</b>	Device: Myosure Hysteroscopic Tissue Removal System (Hologic Inc., US).
<b>Follow-up</b>	At least 6 months
<b>Conflict of interest/source of funding</b>	2 authors have previously received remuneration from Hologic Inc., the device manufacturer.

### Analysis

Study design issues: Retrospective case series, from 2 private infertility clinics. The main outcomes were the incidence of pregnancy and subsequent live births during follow-up. Secondary outcomes included mean time to pregnancy, age at pregnancy, lesion size and number, and proportion of pathology removed. The authors noted that the total number of fibroids identified was insufficient to correlate with pregnancy outcomes.

Study population issues: Diagnosed reasons for infertility were diverse and often multifactorial. Ovarian dysfunction (55%), male factor (31%) and endometriosis (16%) were more commonly identified than strictly uterine factors (8%). Indications for treatment included polyps as well as fibroids. There were 98 lesions in the 62 patients, most of which (75%) were polyps. There were only 19 fibroids (the number of patients is unclear because at least 1 patient had multiple fibroids). No patient had concurrent polyps and fibroids. Fibroids were classified as type 0 (74%) and type 1 (26%) according to the FIGO classification.

### Key efficacy findings

Number of patients analysed: 62

Percentage of fibroid tissue removed during hysteroscopic morcellation=95.5%

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Fertility outcomes

Fertility outcomes	Site 1 (n=33)	Site 2 (n=29)	Total (n=62)	p value
Pregnancy, number (%)	22 (67)	22 (76)	44 (71)	0.7737
Mean time to pregnancy, months ( $\pm$ standard deviation)	11.9 $\pm$ 7.6	4.9 $\pm$ 4.3	8.4 $\pm$ 7.0	0.0005
Range, number (%)				
1 to 3 months	1 (3)	11 (38)	12 (27)	0.0007
4 to 6 months	5 (15)	4 (18)	9 (20)	0.9999
7 to 12 months	8 (24)	5 (23)	13 (30)	0.5477
>12 months	8 (24)	2 (9)	10 (23)	0.0880
Mean age at pregnancy, years	37.5 $\pm$ 3.9	35.7 $\pm$ 4.1	36.8 $\pm$ 4.0	0.0582
Pregnant, age >35 years, number (%)	17 (77)	9 (41)	26 (59)	0.0130
Outcome, number (% of pregnancies)	n=24	n=26	n=50	
Live birth, living child	21 (88)	18 (69)	39 (78)	0.1754
Stillbirth, antepartum (>20 weeks)	2 (8)	0 (0)	2 (4)	0.2253
Spontaneous abortion ( $\leq$ 20 weeks)	1 (4)	6 (23)	7 (14)	0.1004
Ectopic pregnancy	0 (0)	1 (4)	1 (2)	0.9999
Ongoing at last follow-up	0 (0)	1 (4)	1 (2)	0.9999

## Pathology observations in patients who became pregnant

Lesion characteristic	Site 1 (35 lesions)	Site 2 (32 lesions)	Total (67 lesions)
Lesion type, number (% of all lesions)			
Fibroid	5 (14)	9 (28)	14 (21)
Polyp	27 (77)	20 (63)	47 (70)
Other (for example, synechia)	3 (9)	3 (9)	6 (9)
Mean lesion size, cm			
Fibroid	2.1 $\pm$ 1.2	2.2 $\pm$ 1.5	2.1 $\pm$ 1.3
Polyp	1.4 $\pm$ 0.8	1.5 $\pm$ 0.9	1.4 $\pm$ 0.8
Amount of lesion removed, %			
Fibroid	94.0 $\pm$ 13.2	97.1 $\pm$ 7.6	95.8 $\pm$ 9.9
Polyp	100	100	100

## Lesion parameters in patients who conceived compared with those who remained infertile after hysteroscopic morcellation

Lesion characteristic	Pregnant (n=44)	Not pregnant (n=18)	p value
Lesion type, number (% of all lesions)	n=67 lesions	n=31 lesions	
Fibroid	14 (21)	5 (16)	0.7843
Polyp	47 (70)	26 (84)	0.2130
Other (for example, synechia)	6 (9)	0 (0)	0.1724
Multiple polyps present, number (% of patients)	5 (11)	4 (22)	0.2297
Mean lesion size, cm			
Fibroid	2.1 $\pm$ 1.3	2.5 $\pm$ 0.9	0.5427
Polyp	1.4 $\pm$ 0.8	1.3 $\pm$ 1.1	0.6992
Fibroid location, number (% of fibroids)	n=14 fibroids	n=5 fibroids	
Anterior	4 (29)	2 (40)	0.9999

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

Fundal	2 (14)	0 (0)	0.9999
Lateral wall	2 (14)	1 (20)	0.9999
Lower uterine segment	3 (21)	1 (20)	0.9999
Posterior	3 (21)	1 (20)	0.9999
Polyp location, number (% of polyps)	n=47 polyps	n=26 polyps	
Anterior	10 (21)	7 (27)	0.5787
Fundal	9 (19)	7 (27)	0.5565
Lateral wall	10 (21)	4 (15)	0.7576
Lower uterine segment	7 (15)	3 (12)	0.9999
Posterior	11 (23)	5 (19)	0.7739
Amount of lesion removed, %			
Fibroid	95.8±9.9	100±0.0	0.0039
Polyp	100±0.0	100±0.0	0.9999

## Key safety findings

No intraoperative or perioperative adverse events were recorded for any patient.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 11 Haber K (2015)

### Study details

<b>Study type</b>	Review of US Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database
<b>Country</b>	US
<b>Recruitment period</b>	Database search=June 2014
<b>Study population and number</b>	n=119 events Women who had hysteroscopic surgery to remove an intrauterine polyp or fibroid with a reciprocating morcellator.
<b>Age</b>	Not reported
<b>Patient selection criteria</b>	The database was searched for the following key words: 'Myosure', 'Truclear', 'hysteroscopic reciprocating morcellator', 'Interlace' and 'hysteroscope', 'Myosure' and 'hysteroscopy', 'Smith & Nephew' and 'hysteroscope'.
<b>Technique</b>	The Truclear hysteroscopic morcellator (Smith & Nephew, USA) and the Myosure tissue removal system (Hologic, USA) were used.
<b>Follow-up</b>	Not reported
<b>Conflict of interest/source of funding</b>	Not reported

### Analysis

Study design issues: Reports were reviewed individually for annotations of patient injury or death and were categorised by date reported, date of occurrence, type of morcellation device, type of complication, brief description and who reported the incident. Each company was contacted to provide an estimate of the number of units sold to date in the USA as a surrogate of the number of procedures performed. Duplicate reports were identified and removed.

Limitations of the FDA MAUDE database include the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone because of under-reporting of events, inaccuracies in reports, lack of verification that the device caused the reported event, and lack of information about frequency of device use.

Study population issues: Women treated for polyps were also included.

### Key efficacy findings

No efficacy findings were reported.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Key safety findings

### Adverse events reported on FDA MAUDE database

Major complications	Truclear	Myosure	Total
Death	0	2	2
Bowel damage	3	9	12
Admission to intensive care unit	1	13	14
Hysterectomy	1	5	6
Unknown cause of admission	1	2	3
Total	6	31	37

Minor complications	Truclear	Myosure	Total
Uncomplicated fluid overload (resolved spontaneously or with intravenous Lasix)	1	18	19
Pelvic infection	0	4	4
Uterine perforation (needing no additional surgery or treatment)	6	22	28
Postoperative bleeding (controlled with non-invasive measures)	1	5	6
Device failure	9	16	25
Total	17	65	82

2 patients with bowel damage needed temporary colostomies and were admitted into the intensive care unit.

2 patients had a hysterectomy 'per patient request' after the diagnoses of uterine perforation and a failed endometrial ablation. 3 patients needed hysterectomy because of excessive blood loss.

11 patients with fluid overload needed intubation and admission to the intensive care unit.

Device failure included metal shavings and broken pieces of device visualised in the uterine cavity, poor visualisation, failure of outflow, and a defective device that would not activate. In 1 reported case, the blade fell into the uterine cavity and could not be retrieved. A hysterectomy was done and the patient did well postoperatively.

Of the 2 deaths, 1 was in a patient with multiple comorbidities such as chronic hypertension and obesity; the patient desaturated during anaesthesia and was diagnosed with pulmonary embolism and died. The second patient was an elderly woman who 'was not well'; she was readmitted the day after her procedure and died shortly after. An exact cause of death was not reported.

It is estimated that approximately 80,000 Myosure devices have been sold since FDA approval in 2009 and an estimated 100,000 Truclear procedures have been done since 2004.

Estimated complication rate=0.07% (119/180,000); 0.1% for the Myosure hysteroscopic morcellator and 0.02% for the Truclear device.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Study 12 Benton A (2018)

### Study details

<b>Study type</b>	Case report
<b>Country</b>	US
<b>Recruitment period</b>	Procedure was done in 2013
<b>Study population and number</b>	n=1 Patient with disseminated peritoneal leiomyomatosis after hysteroscopic fibroid morcellation
<b>Age</b>	Age at time of procedure not reported
<b>Patient selection criteria</b>	Not applicable
<b>Technique</b>	Mechanical hysteroscopic myomectomy
<b>Follow-up</b>	Not reported (period between procedure and referral was at least 4 years).
<b>Conflict of interest/source of funding</b>	None

### Key safety findings

The patient presented for laparoscopic hysterectomy in the setting of infertility and known uterine fibroids. As part of her infertility work-up and treatment, the patient had a laparoscopy, which showed a pelvis free of fibroids, and a mechanical hysteroscopic myomectomy in 2013. The pathology report from the procedure was consistent with leiomyoma. The patient was unable to conceive and she continued to have heavy menstrual bleeding and developed symptomatic anaemia. She had a repeat dilation and curettage without hysteroscopy in 2017 and a large posterior fibroid was noted.

She then had a total laparoscopic hysterectomy, bilateral salpingectomy, and left oophorectomy. At the time of the procedure, the patient had an approximate 14-week size, globular retroverted uterus with multiple fibroids and severe adhesive disease. There were numerous individual deposits throughout the peritoneum and omentum that appeared to be consistent with fibroids. In addition, there was leiomyomatous disease on the ovaries bilaterally and a large cyst on the left ovary. Pathology from surgery returned showing a benign serous cystadenoma, endometriosis, and diffuse peritoneal leiomyomatosis.

The authors concluded that hysteroscopic mechanical morcellation of symptomatic fibroids can cause intraperitoneal spillage of intrauterine contents, which could result in intra-abdominal pathology.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.



## Validity and generalisability of the studies

- The randomised controlled trial comparing hysteroscopic morcellation with conventional resection included a high proportion of patients with polyps rather than fibroids; the results were not reported separately (Van Dongen H, 2008).
- The review of events reported on the MAUDE database used the number of devices sold as a surrogate for the number of procedures done to calculate an approximate complication rate. It also included patients who were treated for polyps as well as those treated for fibroids (Haber K, 2015).
- The randomised controlled trials included only type 0 and type 1 submucous myomas smaller than 3 cm (Van Dongen H, 2008; Rubino R, 2015). Most of the other studies included some patients with type 2 fibroids. Where stated, all studies included submucosal fibroids only.
- Most studies reported a follow-up period of 12 months or less. One study had a mean follow-up of 32 months (Maheux-Lacroix S, 2017). One study reported a follow-up period of up to 5 years, but most patients had not yet reached the 3-year follow-up evaluation (Vidal-Mazo C, 2019).
- Different devices were used for the procedure. Only 1 of the systematic reviews included studies that used the Intrauterine Bigatti Shaver device (Yin X, 2018).
- The indications for treatment varied between studies. One study only included premenopausal patients (Vidal-Mazo C, 2019) and 1 only included pre- or peri-menopausal patients (Rubino R, 2015).
- There are data from the UK, Europe, US, Australia and China.

## Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Related NICE guidance

Below is a list of NICE guidance related to this procedure (some are not relevant to type 0 and type 1 fibroids).

### Interventional procedures

- Ultrasound-guided high-intensity transcutaneous focused ultrasound for symptomatic uterine fibroids. NICE interventional procedures guidance 657 (2019). Available from <http://www.nice.org.uk/guidance/IPG657>
- Magnetic resonance image-guided transcutaneous focused ultrasound for uterine fibroids. NICE interventional procedures guidance 413 (2011). Available from <http://www.nice.org.uk/guidance/IPG413>
- Uterine artery embolisation for fibroids. NICE interventional procedures guidance 367 (2010). Available from <http://www.nice.org.uk/guidance/IPG367>
- Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids. NICE interventional procedures guidance 30 (2003). Available from <http://www.nice.org.uk/guidance/IPG30>
- Laparoscopic laser myomectomy. NICE interventional procedures guidance 23 (2003). Available from <http://www.nice.org.uk/guidance/IPG23>

### NICE guidelines

- Heavy menstrual bleeding: assessment and management. NICE guideline 88 (2018). Available from <http://www.nice.org.uk/guidance/NG88>

## Additional information considered by IPAC

### Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Professional expert questionnaires for hysteroscopic morcellation of uterine fibroids were submitted and can be found on the [NICE website](#).

### **Patient commentators' opinions**

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

### **Company engagement**

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

### **Issues for consideration by IPAC**

None other than those described above.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## References

1. Yin X, Cheng J, Ansari SH et al. (2018) Hysteroscopic tissue removal systems for the treatment of intrauterine pathology: a systematic review and meta-analysis. *Facts, Views & Vision in ObGyn* 10: 207–13, published online Jul 24 2019
2. Shazly SAM, Laughlin-Tommaso SK, Breitkopf DM et al. (2016) Hysteroscopic morcellation versus resection for the treatment of uterine cavity lesions: a systematic review and meta-analysis. *Journal of Minimally Invasive Gynecology* 23: 867–77
3. van Dongen H, Emanuel MH, Wolterbeek R et al. (2008) Hysteroscopic morcellator for removal of intrauterine polyps and myomas: a randomized controlled pilot study among residents in training. *Journal of Minimally Invasive Gynecology* 15: 466–71
4. Lee MMH, Matsuzono T (2016) Hysteroscopic intrauterine morcellation of submucosal fibroids: preliminary results in Hong Kong and comparisons with conventional hysteroscopic monopolar loop resection. *Hong Kong Medical Journal* 22: 56–61
5. Maheux-Lacroix S, Mennen J, Arnold A et al. (2018) The need for further surgical intervention following primary hysteroscopic morcellation of submucosal leiomyomas in women with abnormal uterine bleeding. *Aust N Z J Obstet Gynaecol* 58: 570–75
6. Vidal-Mazo C, Forero-Diaz C, Lopez-Gonzalez E et al. (2019) Clinical recurrence of submucosal myoma after a mechanical hysteroscopic myomectomy: Review after 5 years follow up. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 243: 41–45
7. Scheiber MD, Chen SH (2016) A prospective multicenter registry of patients undergoing hysteroscopic morcellation of uterine polyps and myomas. *Journal of Gynecologic Surgery* 32: 318–23
8. Arnold A, Ketheeswaran A, Bhatti M et al. (2016) A prospective analysis of hysteroscopic morcellation in the management of intrauterine pathologies. *Journal of Minimally Invasive Gynecology* 23: 435–41
9. Rubino RJ, Lukes AS (2015) Twelve-month outcomes for patients undergoing hysteroscopic morcellation of uterine polyps and myomas in an office or ambulatory surgical center. *Journal of Minimally Invasive Gynecology* 22: 285–90
10. Bhalani V, Chang A, Adkins C et al. (2016) Fertility outcomes after hysteroscopic morcellation of intrauterine leiomyomas and polyps. *The Journal of Reproductive Medicine* 61: 327–35

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

11. Haber K, Hawkins E, Levie M et al. (2015) Hysteroscopic morcellation: review of the manufacturer and user facility device experience (MAUDE) database. *Journal of Minimally Invasive Gynecology* 22: 110–14
12. Benton A, Sood S, Wagner S et al. (2018) Disseminated peritoneal leiomyomatosis following hysteroscopic leiomyoma morcellation. *Journal of Gynecologic Surgery* 34: 319–21

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	13/04/2021	Issue 4 of 12, April 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	13/04/2021	Issue 4 of 12, April 2021
International HTA database (INAHTA)	13/04/2021	-
MEDLINE (Ovid)	13/04/2021	1946 to April 12, 2021
MEDLINE In-Process (Ovid)	13/04/2021	1946 to April 12, 2021
MEDLINE Epubs ahead of print (Ovid)	13/04/2021	April 12, 2021
EMBASE (Ovid)	13/04/2021	1974 to 2021 April 09

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

### Literature search strategy

Number	Search term
1	Uterine Neoplasms/ and Leiomyoma/
2	((uter* or intrauter*) adj4 (neoplasm* or tumour* or tumor* or growth* or fibroma* or leiomyoma* or leiomyoma* or angioliomyoma* or angiomyoma* or myofibroma* or leyomyoma or lesion*)).tw.
3	(fibromyoma* or fibroleiomyoma).tw.
4	((fibroid* or myoma*) adj4 (tumour* or tumor* or uter* or intrauter* or submucos* subseros* or intramural* or pedunculated or cervical)).tw.
5	or/1-4
6	Morcellation/
7	(hysteroscop* adj5 (morcellat* or cut* or suck* or suction* or remov* or myomectom* or excis* or shav*)).tw.
8	Hysteroscopy/ and uterine myomectomy/
9	(transcervical adj4 resection).tw.
10	TCRE.tw.
11	Myosure*.tw.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

12	Truclear*.tw.
13	Bigatti*.tw.
14	Symphion*.tw.
15	or/6-14
16	5 and 15
17	animals/ not humans/
18	16 not 17

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

## Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the [summary of the key evidence](#). It is by no means an exhaustive list of potentially relevant studies.

### Additional papers identified

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in key evidence summary
Bigatti G, Franchetti S, Rosales M et al. (2014) Hysteroscopic myomectomy with the IBS® Integrated Bigatti Shaver versus conventional bipolar resectoscope: a retrospective comparative study. <i>Gynecol Surg</i> 11: 9–18	Retrospective non-randomised comparative study n=127	The results show no difference in terms of cervical dilatation, resection time, and fluid deficit between the 2 groups, but, for fibroids less than 3 cm and type 2 fibroids, the device has been able to treat respectively 94% and 63% of cases in a single step procedure. The overall number of second procedures was statistically significantly less in the hysteroscopic morcellation group than in the conventional resectoscopy group (p=0.0067).	Study is included in systematic review by Yin et al, 2018.
Bigatti G; Ferrario C; Rosales M; et al. (2012) IBS® Integrated Bigatti Shaver versus conventional bipolar resectoscopy: a randomised comparative study. <i>Gynecol Surg</i> 9: 63–72	RCT n=100 (22 patients with fibroids)	There were no complications in the hysteroscopic morcellation group. The smaller IBS device is easier to apply than the conventional resectoscope. Surgery is not interrupted by tissue chips removal making total operating time shorter. It is postulated that resection of fibroids without the use of electrical current could	Most patients had polyps. Study is included in systematic review by Yin et al, 2018.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.



		significantly reduce the postoperative adhesion formation. Further studies are needed to tailor the indication potential of this approach.	
Bigatti G, Ferrario C, Rosales M et al. (2012) A 4-cm G2 cervical submucosal myoma removed with the IBS® Integrated Bigatti Shaver. <i>Gynecol Surg</i> 9:453–56	Case report n=1	The device was able to remove in a 2-step procedure a very large cervical type 2 submucosal fibroid, considered 1 of the most difficult cases to approach by conventional resectoscopy.	Case report
Bigatti G. (2011) IBS® Integrated Bigatti Shaver, an alternative approach to operative hysteroscopy. <i>Gynecological surgery</i> 8: 187 - 91	Case series n=44 (15 myomas, 2 polyps and myomas) FU=not reported	There were 2 overload complications: 1 was caused by a malfunctioning of the fluid management system. The second complication happened during a 3 cm type 2 fibroid resection.	Studies with more patients or longer follow-up are included.
Cohen S, Greenberg JA. (2011) Hysteroscopic morcellation for treating intrauterine pathology. <i>Reviews in Obstetrics and Gynecology</i> 4: 73–80	Review	Hysteroscopic morcellation allows for the use of smaller diameter hysteroscopes that need less cervical dilation and less anaesthesia than traditional hysteroscopic resection.	No meta-analysis. A more recent systematic review is included.
Emanuel MH, Wamsteker K (2005) The Intra Uterine Morcellator: a new hysteroscopic operating technique to remove intrauterine polyps and myomas. <i>Journal of Minimally Invasive Gynecology</i> 12: 62–6	Non-randomised comparative study n=200 (28 vs 172) FU=3 months	Complete removal of fibroid in a single procedure=93% (26/28). Mean operating time (minutes) <ul style="list-style-type: none"> <li>• Hysteroscopic morcellation=16.4 (95% CI 12.6 to 20.2)</li> <li>• Conventional resection=42.2 (95% CI 39.7 to 44.7)</li> </ul> Fluid loss deficit (ml) <ul style="list-style-type: none"> <li>• Hysteroscopic morcellation=660.0</li> </ul>	Included in systematic review by Shazly et al., 2016.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

		<p>(95% CI 418.6 to 901.4)</p> <ul style="list-style-type: none"> <li>Conventional resection=741.8 (95% CI 645.9 to 837.7)</li> </ul> <p>All patients were symptom free at follow-up.</p>	
<p>Fonge YN, Carter AS, Hoffman MK et al. (2020) Obstetrical outcomes are unchanged after hysteroscopic myomectomy in women with submucosal fibroids. American Journal of Obstetrics and Gynecology MFM 2: 100192</p>	<p>Case control study n=277</p>	<p>Overall, women with submucosal uterine fibroids who have hysteroscopic removal have similar birth outcomes to those who do not.</p>	<p>Only a small proportion of patients had hysteroscopic morcellation.</p>
<p>Friedman JA, Wong JMK, Chaudhari A et al. (2018) Hysteroscopic myomectomy: a comparison of techniques and review of current evidence in the management of abnormal uterine bleeding. Current Opinion in Obstetrics &amp; Gynecology 30: 243-251</p>	<p>Review</p>	<p>Although the hysteroscopic morcellators have been associated with shortened operative time and a decreased learning curve, the data are limited for their use on type 2 fibroids. The evidence suggests that no one technique should be used for all patients, but rather a choice of technique should be taken on a case-by-case basis, depending on the myoma number, size, type, and location.</p>	<p>A systematic review and meta-analysis is included.</p>
<p>Georgiou D, Tranoulis A, Jackson TL (2018) Hysteroscopic tissue removal system (MyoSure) for the resection of polyps, sub-mucosal leiomyomas and retained products of conception in an outpatient setting: A single</p>	<p>Case series n=124</p>	<p>98% (107/109) of polyps and 74% (14/19) of fibroids were completely resected. 7% (9/124) of women experienced severe pain during the procedure, while 17% and 73% reported moderate and mild pain respectively. 99% (123/124) of women would have the procedure</p>	<p>Most of the patients had polyps rather than fibroids.</p>

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

UK institution experience. European Journal of Obstetrics, Gynecology, and Reproductive Biology 231: 147-151		again in the future or recommend it to a friend, for a similar pathology removal.	
Hamerlynck TWO, Dietz V, Schoot BC (2011) Clinical implementation of the hysteroscopic morcellator for removal of intrauterine myomas and polyps. A retrospective descriptive study. Gynecological Surgery 8: 193-196	Case series n=315 (37 fibroids)	In 37 patients who had hysteroscopic morcellation for fibroids, mean installation time was 9 min, mean operating time 18 min, and median fluid deficit, 440 mL. 8% (3/37) procedures were converted to resectoscopy, related to a type 2 myoma. All procedures were uneventful. Hysteroscopic morcellation for removal of type 0 and 1 myomas $\leq 3$ cm, and removal of polyps appears safe and effective.	Studies with more patients or longer follow-up are included.
Indraccolo U, Bini V, Favilli A (2020) Likelihood of accomplishing an in-patient hysteroscopic myomectomy in a one-step procedure: a systematic review and meta-analysis. BioMed Research International 2020: 4208497	Systematic review and meta-analysis 63 references	There is no single hysteroscopic technique proven to be unequivocally superior to the others for treating submucous fibroids with intramural development in one-surgical step. Nevertheless, despite the heterogeneity found among the clinical series analysed, it seems that all the techniques used to deal with the intramural portion of myomas work better than the slicing technique, achieving a higher rate of procedures accomplished in a single surgical time and a lower number of complications.	Only 1 study on hysteroscopic morcellation was included in the meta-analysis.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

Li C, Dai Z, Gong Y et al. (2017) A systematic review and meta-analysis of randomized controlled trials comparing hysteroscopic morcellation with resectoscopy for patients with endometrial lesions. <i>Int J Gynecol Obstet</i> 136: 6-12	Systematic review and meta-analysis n=392 (4 trials)	Hysteroscopic morcellation is associated with a higher operative success rate and a shorter operative time among patients with endometrial lesions than is resectoscopy. More high-quality trials are required to validate these results.	Only 1 trial included patients with fibroids (Van Dongen et al., 2008)
Liang Y, Ren Y, Wan Z et al. (2017) Clinical evaluation of improved MyoSure hysteroscopic tissue removal system for the resection of type II submucosal myomas. <i>Medicine</i> 96: e9363	Case series n=53 FU=6 months	Success rate=96% The low rate of 1-time complete resection for type II submucosal myomas could be improved by combining new apparatus with the MyoSure system. Meanwhile, the advantages of the MyoSure system, including the efficiency and safety, were maintained.	Studies with more patients or longer follow-up are included.
Lukes AS, Roy KH, Presthus JB et al. (2015) Randomized comparative trial of cervical block protocols for pain management during hysteroscopic removal of polyps and myomas. <i>International Journal of Women's Health</i> 7: 833-839	RCT (comparing pain management) n=40 (patients had polyps or fibroids)	Pain during hysteroscopic morcellation of intrauterine polyps and type 0 or 1 myomas can be successfully managed with a local anaesthetic. Two different pain management protocols, a combination para/intracervical block and an intracervical block, were both associated with low pain scores.	Study focuses on pain management, and only a small proportion of the lesions were fibroids.
Miller C, Glazerman L, Roy K et al. (2009) Clinical evaluation of a new hysteroscopic morcellator – retrospective case review. <i>The Journal of Medicine</i> 2: 163–6	Case series n=11 (6 fibroids)	Mean morcellation time for complete resection: <ul style="list-style-type: none"> <li>• Type 0 fibroids=2 minutes 19 seconds</li> <li>• Type I fibroids=9 minutes 10 seconds</li> </ul>	Larger studies are included.

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

		<p>Mean fluid deficit (ml):</p> <ul style="list-style-type: none"> <li>Type 0 fibroids=205 (range 200–210)</li> <li>Type I fibroids=1300 (range 500–1900)</li> </ul>	
<p>Noventa M, Ancona E, Quaranta M et al. (2015) Intrauterine morcellator devices: the icon of hysteroscopic future or merely a marketing image? A systematic review regarding safety, efficacy, advantages, and contraindications. <i>Reproductive Sciences</i> 22: 1289–96</p>	<p>Systematic review n=8 studies</p>	<p>The available evidence allows us to consider intrauterine morcellation devices as a safe, effective, and cost-effective tool for the removal of intrauterine lesions such as polyps, myomas (type 0 and type 1), and placental remnants. Further studies are needed to confirm the available evidence and to validate the long-term safety of procedures for which current data are not exhaustive (placental remnants removal).</p>	<p>No meta-analysis. All relevant studies have been described in the overview, either in the key evidence summary or the appendix.</p>
<p>Ota K, Takahashi T, Kamo N et al. (2020) Successful management of a submucosal fibroid using a hysteroscopic morcellator system in a patient with a history of total proctocolectomy: A case report. <i>Journal of Obstetrics and Gynaecology Research</i></p>	<p>Case report n=1</p>	<p>Case report of patient with multiple fibroids, including a submucosal type 1 fibroid, who had previously had a total proctocolectomy with intestinal pouch-anal anastomosis for ulcerative colitis. Because there was a high risk of permanent colostomy in the event of a bowel injury, an electrode-free, operative hysteroscopy using the Intrauterine Bigatti Shaver (IBS), a hysteroscopic morcellator system, was used to prevent thermal bowel injury. The fibroid was completely removed with no complications.</p>	<p>Case report – no safety events identified</p>

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

<p>Pakrashi T, Ressler IB, Sroga JM et al. (2013) Hysteroscopic enucleation of type II submucosal uterine leiomyomas using a TRUCLEAR hysteroscopic morcellator: case report and review of the literature. <i>Journal of Laparoendoscopic &amp; Advanced Surgical Techniques</i> 23: 378-382</p>	<p>Case report n=1</p>	<p>Case report - complete enucleation of a Type II leiomyoma</p> <p>Hysteroscopic uterine leiomyoma enucleation should only be performed in experienced hands. Inadvertent enucleation of a Type II leiomyoma with a THM device is described, with review of key surgical principles that guided safe resection.</p>	<p>Case report – no safety events identified</p>
<p>Rothenberg S, Nayak S, Sanfilippo JS (2014) Clinical use of the intrauterine morcellator: a single academic center's experience. <i>Open Journal of Obstetrics and Gynecology</i> 4: 326–32</p>	<p>Case series n=28 (18% fibroids)</p>	<p>Mean operative time (minutes)=47±20.9 Mean fluid deficit (ml) = 785±956.7</p> <p>Complication rate=6%</p>	<p>Small study with mixed indications – only 18% of patients had fibroids.</p>
<p>Rubino RJ, Roy KH, Presthus J et al. (2017) Abnormal uterine bleeding control by sequential application of hysteroscopic lesion morcellation and endometrial ablation. <i>The Journal of Reproductive Medicine</i> 62: 102–10</p>	<p>Case series n=26 FU=12 months</p>	<p>Sequential hysteroscopic morcellation and endometrial radiofrequency ablation of intrauterine lesions in women with abnormal uterine bleeding increases amenorrhea rate, alleviates bleeding symptoms, and improves quality of life, with an acceptable safety profile.</p>	<p>Small case series in which hysteroscopic morcellation was followed by endometrial radiofrequency ablation.</p>
<p>Spies JB, Bradley LD, Guido R et al. (2010) Outcomes from leiomyoma therapies. Comparison with normal controls. <i>Obstet Gynecol</i> 116: 641–52</p>	<p>Non-randomised comparative study n=375</p>	<p>At 12 months after treatment, all 3 therapies (hysterectomy, myomectomy, uterine artery embolisation) resulted in substantial symptom relief, to near normal levels, with the greatest improvement after hysterectomy.</p>	<p>Only a small proportion of patients had hysteroscopic myomectomy and it is unclear if any had morcellation.</p>

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.

<p>Vitale SG, Sapia F, Rapisarda AMC et al. (2017) Hysteroscopic morcellation of submucous myomas: a systematic review. BioMed Research International 2017: 6848250</p>	<p>Systematic review n=8 studies</p>	<p>The available studies differ regarding methodology and inclusion and exclusion criteria.</p> <p>Hysteroscopic tissue removal systems reduced operative time compared to traditional resectoscopy in some studies, whereas others did not find significant differences.</p> <p>Despite the availability of few randomised controlled trials and the cost of the instrument, this seems to be a feasible surgical option in terms of operative time and complications.</p> <p>Nevertheless, the type of submucous fibroid remains the biggest challenge: type 0 and 1 are easier to manage than type 2.</p>	<p>No meta-analysis.</p> <p>All included studies have been described in the overview, either in the key evidence summary or the appendix.</p>
<p>Yin X, Cheng J, Ansari SH, et al. (2018) Hysteroscopic tissue removal systems for the treatment of intrauterine pathology: a systematic review and meta-analysis. Facts Views Vis Obgyn. 10: 207–213</p>	<p>Systematic review and meta-analysis n=498 (5 studies)</p>	<p>Hysteroscopic tissue removal systems showed a significantly higher success rate of complete endometrial pathology removal (<math>p=0.002</math>) and a significantly shorter operation time for polyp removal (<math>p&lt;0.0001</math>) compared to conventional resectoscopy. No significant differences, in terms of complications rate, were found (<math>p=0.09</math>).</p> <p>The fluid deficit was significantly higher in the tissue removal system group, compared to conventional resectoscopy (<math>p=0.02</math>).</p>	<p>Of the 5 included studies, 2 used the Integrated Bigatti shaver device.</p>

IP overview: hysteroscopic mechanical tissue removal (hysteroscopic morcellation) for uterine fibroids.