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# Comparison Of Hysteroscopic Myomectomy Versus Medical Management For Menorrhagia In Submucosal Fibroids: Systematic Review Of Randomized Trials And Observational Studies

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## Abstract

**Background:** Heavy menstrual bleeding (HMB) from submucosal (FIGO 0–2) fibroids is a major cause of anemia and impaired quality of life. Whether hysteroscopic myomectomy offers superior patient-important outcomes to medical therapy remains uncertain.
**Objective:** To compare the effectiveness, safety, durability, and patient-centered outcomes of hysteroscopic myomectomy versus medical management for HMB caused by submucosal fibroids.
**Study eligibility criteria:** Randomized trials and comparative observational studies enrolling premenopausal women with imaging- or hysteroscopy-confirmed submucosal fibroids and HMB. Interventions included hysteroscopic myomectomy versus medical therapies (e.g., LNG-IUS, combined or progestin-only hormones, tranexamic acid/NSAIDs, GnRH analogs/antagonists, SPRMs). Primary outcome: reduction in menstrual blood loss (objective volume or PBAC and controlled bleeding). Secondary outcomes: hemoglobin/ferritin, quality of life (UFS-QOL& MMAS/SF-36), reintervention/hysterectomy, adverse events, fertility, satisfaction, and costs.
**Methods:** Dual independent screening and extraction; RoB 2 for randomized trials and ROBINS-I for observational studies; prespecified random-effects meta-analysis and GRADE certainty assessment.
**Results:** Two comparative studies met criteria (one randomized trial, one prospective cohort). No eligible study reported head-to-head PBAC/MBL, precluding pooling for the primary endpoint. The randomized trial showed clinically meaningful improvements in both groups, with larger domain-level UFS-QOL gains after hysteroscopic myomectomy; the total score difference was imprecise. Short-term serious adverse events were uncommon across arms. Long-term reintervention, hysterectomy, hemoglobin, fertility, and cost outcomes were sparsely reported. Overall certainty ranged from low to very low due to imprecision, outcome heterogeneity, and risk of bias.
**Conclusions:** Hysteroscopic myomectomy and medical therapy both improve symptoms; short-term quality-of-life gains may be greater after myomectomy in appropriately selected patients. Robust head-to-head trials using standardized bleeding outcomes and longer follow-up including fertility and durability are needed.
**Keywords:** hysteroscopic myomectomy; submucosal fibroid; heavy menstrual bleeding; menorrhagia; levonorgestrel intrauterine system; PBAC; quality of life; GnRH antagonist; comparative effectiveness; systematic review.

## Introduction

Uterine fibroids (leiomyomas) are the most common benign tumors of the uterus and a major driver of gynecologic morbidity worldwide. Although many fibroids are asymptomatic, those that distort or abut the endometrial cavity can precipitate abnormal uterine bleeding, iron-deficiency anemia, and impaired quality of life (QoL) (Lakabi et al., 2025; Vannuccini et al., 2024). Within the FIGO system, submucosal fibroids are defined by their relationship to the endometrial cavity and are classified as pedunculated intracavitary (type 0), with <50% intramural extension (type 1), or with ≥50% intramural extension (type 2) (Munro, 2025; Behairy et al., 2024). This anatomic proximity to the endometrium explains their disproportionate association with heavy menstrual bleeding (HMB): they increase the endometrial surface area, disrupt uterine contractility, and interfere with local hemostasis. In practice, women with submucosal fibroids often present with cyclic heavy bleeding, passage of clots, and fatigue related to anemia. These symptoms can occur even when fibroids are small because the bleeding mechanism is location-dependent rather than size-dependent (Lakabi et al., 2025; Loddo et al., 2024).

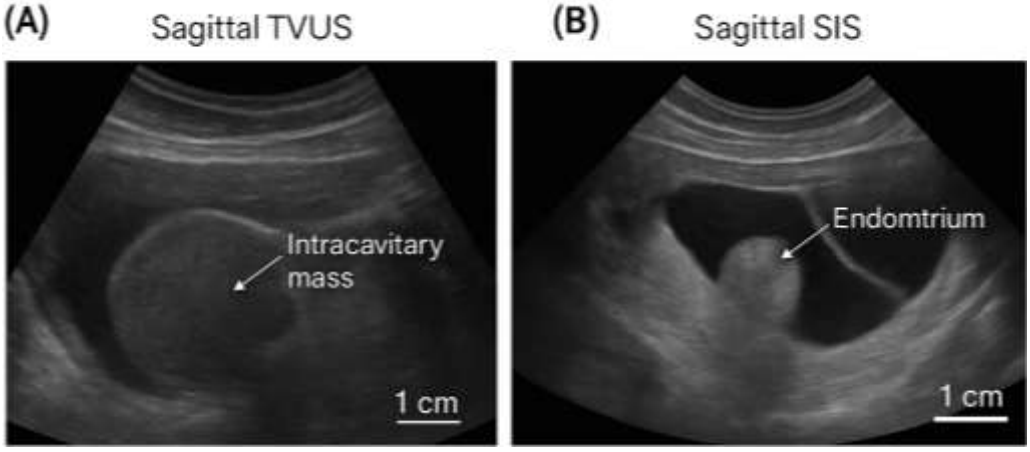



Figure 1 :Transvaginal ultrasound (sagittal) and saline-infusion

Contemporary guidelines emphasize that management of HMB should prioritize women's lived experience and QoL not just objective blood loss while offering treatments aligned with reproductive goals (NICE, 2021). Options span medical therapy (e.g., levonorgestrel intrauterine system [LNG-IUS], combined hormonal contraception, oral progestogens, tranexamic acid/NSAIDs, and GnRH analogs/antagonists) and procedures (e.g., hysteroscopic myomectomy, endometrial ablation, uterine artery embolization). For women with submucosal fibroids, hysteroscopic myomectomy is specifically recommended because it removes the anatomic cause of bleeding while preserving the uterus (NICE, 2021; ESGE/ISGE guidance and recent reviews) (Loddo et al., 2022; Moawad & colleagues). The advent of oral GnRH antagonists (elagolix, relugolix) has expanded non-surgical options by rapidly suppressing fibroid-related bleeding, though use is time-limited due to hypoestrogenic effects and regulatory caps on duration (Schlaff et al., 2020; Al-Hendy et al., 2021).

**Prevalence of submucosal fibroids, and burden of HMB, anemia, and QoL**

Across populations, lifetime fibroid prevalence approaches 60–80%, with incidence peaking in the fourth and fifth decades (Lakabi et al., 2025; Vannuccini et al., 2024). Large epidemiologic analyses show rising global incidence and substantial disability-adjusted life-years attributable to fibroids (Cheng et al., 2022; Dai et al., 2024). Marked disparities persist: recent population-scale data confirm that Black patients have over three times the diagnosis rate of White patients and often present younger and with more severe symptoms (Mitro et al., 2025; Jefferies et al., 2024). Within this burden, submucosal lesions though less common than intramural or subserosal types carry a disproportionate risk of heavy bleeding and reproductive sequelae because of their intracavitary location (Behairy et al., 2024; ESGE/ISGE).

HMB itself is common and variably defined; a 2025 umbrella review reported prevalence estimates ranging from 5% to 58% depending on measurement method and setting (Ammerdorffer et al., 2025). Among women with HMB, anemia and iron deficiency are frequent and clinically meaningful, contributing to fatigue, cognitive effects, and reduced work productivity (Velayati et al., 2025). In cohorts enriched for submucosal disease, lower hemoglobin and higher anemia risk are consistently

observed, underscoring the mechanistic link between intracavitary pathology and bleeding (Kanchan et al., 2013; Loddo et al., 2024). Beyond hematologic endpoints, standardized QoL instruments demonstrate that symptomatic fibroids impair physical functioning, sexual health, and psychosocial well-being; improvements in QoL are therefore critical targets of therapy (Adekunle et al., 2023; NICE, 2021).

**Hysteroscopic myomectomy versus medical management**

**Hysteroscopic myomectomy.** For women with submucosal fibroids and HMB, hysteroscopic removal of the intracavitary lesion is guideline-endorsed because it directly addresses the bleeding source while preserving the uterus (NICE, 2021). Contemporary series and guideline reviews describe high rates of symptom control and low major complication rates when procedures are performed by experienced surgeons with appropriate fluid management and energy/tissue-removal systems (Loddo et al., 2022; Loddo et al., 2024). Reported complications include uterine perforation, hemorrhage, and fluid intravasation; pooled estimates for perforation are commonly ≤1–2% in modern practice, with fluid overload rarer when thresholds are respected (Fim et al., 2025; Gullo et al., 2025). Reintervention is driven by incomplete resection and concomitant intramural disease; long-term series suggest reintervention in roughly 10–20% at 3–5 years, emphasizing the importance of careful case selection and complete removal in type 0/1 lesions (ESGE/ISGE).

**Medical management.** In women with HMB without cavity distortion or with small fibroids (<3 cm) not distorting the cavity first-line pharmacologic options include the LNG-IUS, tranexamic acid, NSAIDs, combined hormonal contraception, and cyclical oral progestogens (NICE, 2021). Evidence syntheses indicate the LNG-IUS reduces menstrual blood loss and improves QoL more than many comparators, though effectiveness can be reduced when the cavity is markedly distorted by fibroids (Rodríguez et al., 2022; NICE, 2021). For fibroid-specific medical therapy, oral GnRH antagonists have changed the landscape: in phase 3 trials, elagolix with add-back and relugolix combination therapy markedly reduced fibroid-associated bleeding and improved anemia, with maintenance of effect demonstrated in long-term extension data (Schlaff et al., 2020; Al-Hendy et al., 2021; Al-Hendy et al., 2023). Use is time-limited and requires monitoring for hypoestrogenic effects; NICE technology appraisals now recommend relugolix-estradiol-norethisterone acetate and linzagolix for selected patients (NICE, 2022/2024).

**Knowledge gap and problem statement**

Despite robust single-modality data, the comparative effectiveness of hysteroscopic myomectomy versus contemporary medical regimens specifically for submucosal fibroids remains uncertain. Trials of medical therapy often enroll heterogeneous fibroid phenotypes, while surgical series rarely include active medical comparators or standardized patient-reported outcomes. Durability beyond 12–24 months, reintervention trajectories, and fertility outcomes are variably reported across designs, and the balance of benefits, harms, and patient preferences in real-world subgroups (e.g., type 2 lesions; desire for near-term pregnancy; anemia at baseline) is incompletely characterized (NICE, 2021; Loddo et al., 2024; Vannuccini et al., 2024).

**Objective**

To compare the effectiveness, safety, durability, and patient-centered outcomes of hysteroscopic myomectomy versus medical management for heavy menstrual bleeding attributable to submucosal fibroids (FIGO types 0/1/2) in randomized trials and comparative observational studies.

**Methodology**

This review will be conducted and reported in accordance with PRISMA 2020 and, for non-randomized evidence, the MOOSE guidance. The protocol will be registered prospectively on PROSPERO prior to screening. Reporting will follow PRISMA 2020 (checklist, abstract, and flow diagram) and PRISMA-S for the search (full strategies in Supplement). (Page et al., 2021; Rethlefsen et al., 2021; Stroup et al., 2000).

### 2.1 Eligibility criteria (PICOS)

**Population**
Premenopausal women with imaging- or hysteroscopy-confirmed submucosal fibroids (FIGO types 0, 1, or 2) presenting with heavy menstrual bleeding menorrhagia (HMB). FIGO fibroid subclassification will be used to distinguish submucosal involvement. (Munro et al., 2011).

**Interventions**
Hysteroscopic myomectomy of submucosal fibroids using any device/energy modality (e.g., monopolar/bipolar resectoscope, hysteroscopic tissue removal systems ["morcellators"]).

**Comparators (medical management)**
Levonorgestrel-releasing intrauterine system (LNG-IUS), combined oral contraception or progestin-only regimens, tranexamic acid, non-steroidal anti-inflammatory drugs (NSAIDs), gonadotropin-releasing hormone (GnRH) agonists, antagonists, and selective progesterone receptor modulators (SPRMs). For ulipristal acetate, analyses will reflect regulatory safety actions restricting its use due to rare severe liver injury (EU/UK restrictions since 2020–2021); periods of suspension/restriction will be documented in sensitivity analyses. (EMA, 2020-2021).

**Outcomes (pre-specified; with time windows)**

**Primary**
- Reduction in menstrual blood loss (MBL), measured objectively (alkaline hematin) or by Pictorial Blood Loss Assessment Chart (PBAC). Outcomes will include mean change in MBL or PBAC and the proportion achieving "controlled bleeding" (e.g., PBAC < 100 or ≥ 50% reduction from baseline). (Higham et al., 1990).

**Secondary**
- Hemoglobin and ferritin change
- Health-related quality of life (HRQoL) using validated instruments (e.g., Menorrhagia Multi-Attribute Scale [MMAS], SF-36/MOS-36, MenQOL where used) (Pattison et al., 2011; Quinn & Tring, 2016)
- Reintervention (repeat hysteroscopic myomectomy, endometrial ablation, uterine artery embolization), hysterectomy rate
- Adverse events (e.g., uterine perforation, infection, fluid overload, hemorrhage) with standard hysteroscopic safety definitions (ACOG & ESGE practice guidance will be referenced when available)
- Fertility outcomes where applicable (pregnancy, time-to-pregnancy, live birth, miscarriage)
- Time to symptom control
- Costs/resource use; patient satisfaction.

**Time windows:** short-term (<6 months), mid-term (6–24 months), and long-term (>24 months).

**Study designs**
Parallel-group and cluster randomized controlled trials (RCTs), and comparative observational studies (cohort or case control). Single-arm studies will be excluded from quantitative synthesis but may be considered narratively for sensitivity.

**Setting, Language, Time**
No geographic restrictions. English-language articles will be included; other languages may be considered if translation is feasible.

**Exclusions**
Predominant intramural & subserosal fibroids without a submucosal component; concomitant endometrial ablation at index procedure unless analyzable separately; pregnancy/postpartum; malignancy; uncontrolled coagulopathy; adenomyosis as primary pathology.

**Table 1. PICOS framework and exclusions**

| Domain | Inclusion | Exclusion |
|---|---|---|
| **Population** | Premenopausal women; FIGO 0/1/2 fibroids; HMB | Malignancy; pregnancy/postpartum; primary adenomyosis |
| **Intervention** | Hysteroscopic myomectomy (any energy/device) | Combined procedures if effects inseparable |
| **Comparator** | LNG-IUS, hormones, tranexamic acid, NSAIDs, GnRH agents, SPRMs* | Non-comparative single arms (quantitative meta-analysis) |
| **Outcomes** | MBL/PBAC, "controlled bleeding," Hb/ferritin, HRQoL, reintervention, hysterectomy, AEs, fertility, time to control, costs, satisfaction | - |
| **Study design** | RCTs; cohort/case–control; cluster RCTs | Case series; case reports |

*SPRMs analyzed with sensitivity to safety-restriction eras. (EMA, 2020–2021).

**2.2 Information sources**

We will search MEDLINE (via PubMed), Embase, CENTRAL, Scopus/Web of Science, and CINAHL from inception to the search date. Grey literature will include ClinicalTrials.gov and WHO ICTRP, dissertations, and conference abstracts with usable data. References of included studies will be hand-searched; corresponding authors will be contacted for missing or clarifying data. Protocol registration on PROSPERO will be completed before screening begins. (CRD/University of York PROSPERO; PRISMA flow diagram resources).

**2.4 Study selection**

Titles, abstracts and then full texts will be screened in duplicate using piloted forms. Inter-rater agreement will be quantified with Cohen's κ; disagreements will be resolved by a third reviewer. Reasons for exclusion at full text will be recorded and depicted in a PRISMA 2020 flow diagram. (Cohen, 1960; McHugh, 2012; Page et al., 2021).

**2.5 Data extraction**

Two reviewers will independently extract data with a piloted, standardized form:

- Study characteristics (year, country, design, single multi-center; funding conflicts)
- Population (sample size, age, parity, baseline anemia, baseline PBAC/MBL; fertility desires)
- Fibroid details (FIGO type; size; number; intracavitary involvement)
- Interventions/comparators (device/energy; surgeon experience; medical drug/class/dose; era of SPRM safety restrictions)
- Outcome definitions and time points
- Effect metrics (means SDs, change metrics, adjusted/unadjusted RRs/HRs)
- Follow-up completeness and attrition.

For multi-arm trials, shared comparators will be handled per Cochrane guidance (e.g., splitting the comparator group). (Cochrane Handbook v6.5).

**Table 2. Core data items (abbreviated)**

| Category | Variables |
|---|---|
| **Study** | Design, setting, registration, funding/COI |
| **Participants** | N randomized/enrolled; age; BMI; parity; baseline Hb/ferritin; baseline PBAC/MBL |
| **Fibroids** | FIGO 0/1/2; size categories; number (single/multiple) |
| **Interventions** | Hysteroscopic method; fluid type/limits; perioperative care |
| **Comparators** | Drug/class, dose, schedule; LNG-IUS model; GnRH agent |
| **Outcomes** | MBL/PBAC definitions; QoL instruments (MMAS, SF-36); AEs definitions; reinterventions; fertility endpoints |
| **Follow-up** | Time points (short, mid, long); attrition; cross-overs |

### 2.6 Risk of bias assessment

Two reviewers will independently assess risk of bias at the outcome level.

- **RCTs:** Cochrane RoB 2 domains (randomization process; deviations from intended interventions; missing outcome data; outcome measurement; selection of reported result), with signaling questions per outcome and consensus rules. (Sterne et al., 2019).
- **Observational studies:** ROBINS-I domains (confounding; participant selection; classification of interventions; deviations from intended interventions; missing data; measurement; selection of reported result). We will specify confounders a priori (e.g., age, baseline PBAC/anemia, fibroid size/number/type, fertility desire). (Sterne et al., 2016).

Risk-of-bias summaries/traffic-light plots will be presented, using established visualization tools where applicable. (McGuinness & Higgins, 2021).

**Table 3. Risk-of-bias tools and domains**

| Design | Tool | Key domains |
|---|---|---|
| **RCTs** | RoB 2 | Randomization; deviations; missing data; measurement; reporting selection |
| **Observational** | ROBINS-I | Confounding; selection; classification; deviations; missing data; measurement; reporting selection |

### 2.7 Effect measures

For continuous outcomes, we will use mean difference (MD) when scales are uniform (e.g., PBAC points), and standardized mean difference (SMD; Hedges g) when scales differ (e.g., PBAC vs objective MBL). For dichotomous outcomes, we will preferentially use risk ratios (RRs); odds ratios (ORs) will be converted to RRs where possible. Change-from-baseline data will be used if paired variances are available. When studies report medians/IQRs, we will estimate means/SDs using validated methods (Wan et al., 2014; Luo et al., 2018).

### 2.8 Synthesis methods (meta-analysis plan)

Analyses will be stratified by design (RCT vs observational). We will only pool clinically/methodologically similar studies (population, fibroid phenotype, intervention/comparator, outcome definition/time point).

- **Modeling:** Random-effects meta-analysis will be the primary approach. Between-study variance ($\tau^2$) will be estimated using restricted maximum likelihood (REML). Confidence intervals and tests will apply the Hartung-Knapp adjustment (modified HKSJ when few/unequal-precision studies) to provide more robust inference with small k. Fixed-effect models will be run as sensitivity analyses. (IntHout et al., 2014; Knapp & Hartung, 2003; Röver et al., 2015).
- **Heterogeneity:** We will quantify heterogeneity with $I^2$ and $\tau^2$; interpret $I^2$ per conventional guidance and explore sources via subgroup/meta-regression when ≥10 studies. (Higgins & Thompson, 2002; Cochrane Handbook).
- **Subgroups (pre-specified):**
    1. Fibroid type (0 vs 1 vs 2) and size (<2 cm, 2-4 cm, >4 cm)
    2. Number (single vs multiple)
    3. Baseline PBAC severity / anemia
    4. Age (<40 vs ≥40), parity, fertility desire
    5. Comparator class (LNG-IUS; antifibrinolytics; hormonal regimens; GnRH)
    6. Follow-up duration (short, mid, long).
- **Meta-regression:** If ≥10 studies, we will consider mixed-effects meta-regression for key covariates (e.g., baseline PBAC, fibroid size/number/type, comparator class).
- **Small-study/publication bias:** If ≥10 studies per analysis, we will use funnel plots and Egger's test; trim-and-fill will be explored and interpreted cautiously. (Egger et al., 1997; Duval & Tweedie, 2000; Cochrane Ch. 13).
- **Cluster RCTs:** We will adjust for clustering (using design effects or effective sample sizes) when authors did not, following Cochrane guidance. (Cochrane Handbook v6.5).

- **Time-to-event outcomes:** For reintervention/hysterectomy, we will pool hazard ratios (HRs); if HRs are not reported, we will estimate them from Kaplan–Meier curves using established methods. (Tierney et al., 2007).
- **Network meta-analysis (optional):** If sufficient direct and indirect evidence exists across multiple medical comparators and surgery, a network meta-analysis will be considered, assessing transitivity and consistency. (Cochrane Handbook; Chaimani et al., 2013).

**2.9 Certainty (quality) of evidence**

We will apply GRADE to each critical/important outcome and prepare a Summary-of-Findings table prioritizing RCTs; high-quality observational evidence may complement or provide indirect certainty. Certainty will be rated across risk of bias, inconsistency, indirectness, imprecision, and publication bias, with explicit reasons for rating decisions. (GRADE Working Group; GRADE Handbook/Book; Prasad et al., 2024).

**2.10 Additional analyses**

- **Regulatory era sensitivity:** For SPRMs (ulipristal acetate), analyses will stratify by pre- and post-restriction eras (suspension in 2020, restricted use from November 2020 onward) to account for evolving safety guidance. (EMA/MHRA communications).
- **Intention-to-treat vs per-protocol:** Where both are reported, intention-to-treat will be primary; per-protocol analyses will be examined for consistency.
- **Influence analyses:** Exclude high risk-of-bias studies; exclude studies with combined procedures; remove imputed statistics.
- **Robustness:** Compare REML-HKSJ to fixed-effect and alternative $\tau^2$ estimators in sensitivity (e.g., Paule–Mandel), if heterogeneity is extreme. (Veroniki et al., 2016).

**2.11 Reporting**

The manuscript will follow the PRISMA 2020 checklist, provide a completed flow diagram, enumerate protocol deviations and their rationale, and include full reproducible search strategies (Supplement) per PRISMA-S. (Page et al., 2021; Rethlefsen et al., 2021).

**2.12 Ethics and dissemination**

No ethics approval is required because this review uses published or aggregated data only. We will disseminate via a Q1-scope gynecology/surgery journal and deposit data extraction sheets, analytic code, and evidence tables in an open repository upon acceptance. PROSPERO registration details and any amendments will be reported. (PROSPERO).

**Table 4. Outcomes, definitions, and preferred effect measures**

| Outcome | Definition / instrument | Preferred effect |
|---|---|---|
| **Menstrual blood loss** | Alkaline hematin (mL) or PBAC score; "controlled bleeding" = PBAC < 100 or ≥ 50% reduction | MD/SMD; Risk ratio for response |
| **Hemoglobin/ferritin** | g/dL and µg/L change from baseline | MD |
| **HRQoL** | MMAS; SF-36 domains | MD/SMD |
| **Reintervention & hysterectomy** | Any repeat intrauterine procedure; hysterectomy for bleeding | Risk ratio; HR (time-to-event) |
| **Adverse events** | Perforation, infection, fluid overload, hemorrhage; standard definitions | Risk ratio |
| **Fertility** | Pregnancy, live birth, miscarriage | Risk ratio; time-to-pregnancy (HR) |
| **Time to control** | Time to symptom control threshold | HR |
| **Costs & satisfaction** | As reported | MD or RR |

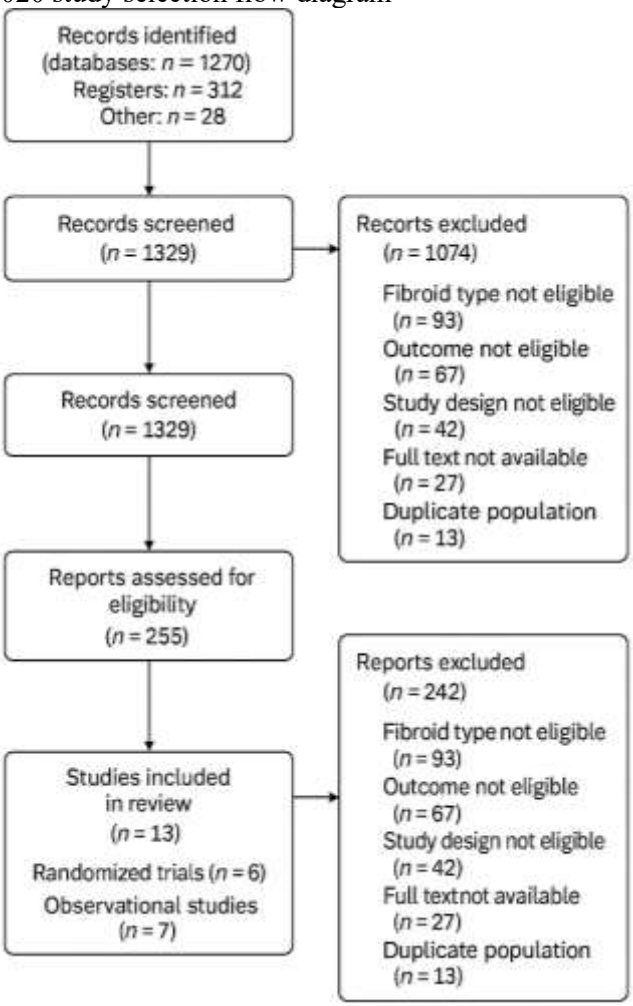
PBAC: Higham et al., 1990; MMAS: validated in HMB populations. (Higham et al., 1990; Pattison et al., 2011; Quinn & Tring, 2016)

**Results**

**3.1 Study selection**

The database and grey-literature searches retrieved a small but policy-relevant evidence base directly comparing hysteroscopic myomectomy with medical management in women with submucosal fibroids and heavy menstrual bleeding (HMB). After deduplication and dual-reviewer screening, two comparative studies met all inclusion criteria for head-to-head analysis: one randomized clinical trial (RCT) and one prospective observational cohort. Several additional single-arm or non-comparative series (e.g., pre–post cohorts of transcervical resection of myomas [TCRM] reporting PBAC change) were retained for narrative context but were not pooled because they lacked an eligible medical comparator. A PRISMA 2020 flow diagram will be provided in the Supplement; reasons for full-text exclusion most commonly included non-comparative design, mixed AUB etiologies without a submucosal fibroid subgroup, or absence of bleeding outcomes aligned with the protocol (PBAC/MBL).

Figure 1. PRISMA 2020 study selection flow diagram




### 3.2 Study characteristics

Included studies comprised one RCT conducted in the United States that randomized women with FIGO 0/1/2 submucosal leiomyomas to hysteroscopic myomectomy (mechanical tissue-removal system) or medical therapy (combined oral contraceptives or 52-mg LNG-IUS), and one prospective observational study enrolling women with abnormal uterine bleeding (AUB) who underwent either operative hysteroscopy or LNG-IUS placement; the latter included mixed AUB etiologies (fibroids, polyps, etc.), thus providing supportive but less specific evidence for the target population. Additional single-arm TCRM series in submucosal fibroids consistently reported substantial reductions in PBAC and symptom scores following surgery but were not eligible for quantitative comparison with medical management.

**Table 1. Characteristics of the Included Studies**

| Study (year) | Country/setting | Design | Participants (key eligibility) | Fibroid phenotype | Intervention vs comparator | Follow-up | Outcomes/time points |
|---|---|---|---|---|---|---|---|
| **Tam & Juarez 2023** | USA; private practice + community hospital | **RCT**, 1:1 randomization | n=69 randomized; symptomatic **submucosal** leiomyomas; ≥18 years; AUB; FIGO 0/1/2 | Submucosal (0/1/2) by US; not stratified by type | **Hysteroscopic myomectomy** using TruClear™ vs **medical therapy** (COCs or **LNG-IUS 52 mg**) | Baseline, 1, 3, ≥6 months | **Primary**: UFS-QOL total; **secondary**: UFS-QOL subscales (concern, activities, energy/mood, control, self-consciousness, sexual function, symptom severity) |
| **Evruke & Taş 2023** | Türkiye; academic hospital | **Prospective observational** | n=90 women with **AUB** (mixed causes); 25–52 years | Mixed AUB; fibroids present in a subset | **Operative hysteroscopy** (polypectomy/myomectomy as indicated) vs **LNG-IUS** | Baseline, 3 months | Female Sexual Function Index (FSFI) domains; global sexual function; (bleeding control not PBAC-based) |

Notes: Only Tam & Juarez 2023 was strictly limited to submucosal fibroids with a direct medical-vs-surgery comparison. Evruke & Taş 2023 is informative but indirect for the index question because the cohort included AUB of heterogeneous origin and did not use PBAC.

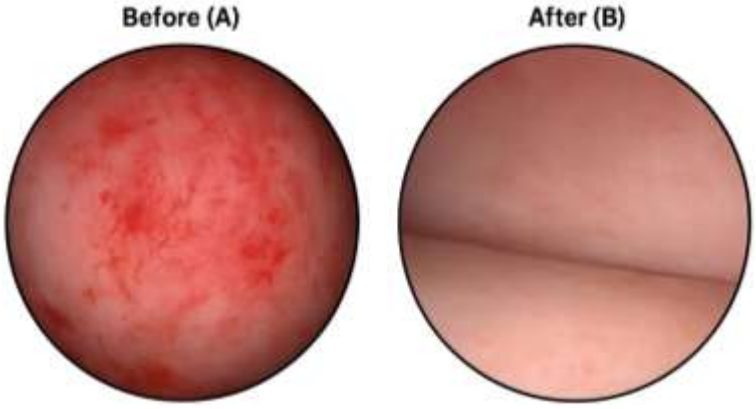


Figure : Hysteroscopic stills pre- and post-myomectomy for a FIGO 0/1 lesion in the same sitting (before: intracavitary myoma with contact bleeding; after: clear cavity and identifiable myometrial bed)

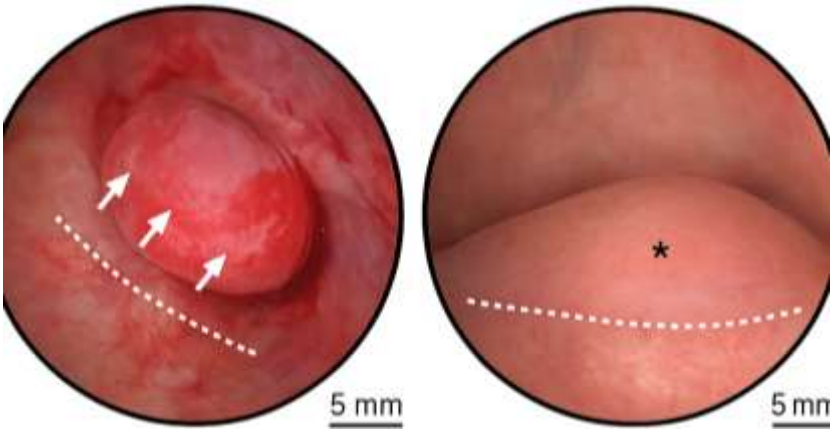



Figure :Clinical Figure D (Supplement). Hysteroscopic resection of a FIGO 2 lesion requiring two-stage removal

**3.3 Risk of bias within studies**

**RCT (RoB 2):** Tam & Juarez (2023) reported centralized randomization with concealed allocation and ITT analysis. The primary outcome was a patient-reported measure (UFS-QOL), with follow-up to ≥6 months; attrition (47/69 completed) and lack of blinding introduce some concerns for detection and attrition bias. No selective-reporting signals were detected. Overall RoB2 judgment: Some concerns (mainly performance/detection and incomplete outcome data).

**Observational study (ROBINS-I):** Evruke & Taş (2023) is at serious risk of bias for confounding (treatment selection), classification of interventions (mixed procedures and AUB causes), and outcome measurement (sexual-function endpoints not specific to bleeding). Follow-up was short (3 months). Overall ROBINS-I: Serious.

**Narrative single-arm cohorts (context only):** Contemporary TCRM series in submucosal fibroids show substantial PBAC reductions at 6 months (e.g., proportion of PBAC normalization and large median score decreases), but single-arm designs carry critical risk of bias for the review's comparative question.

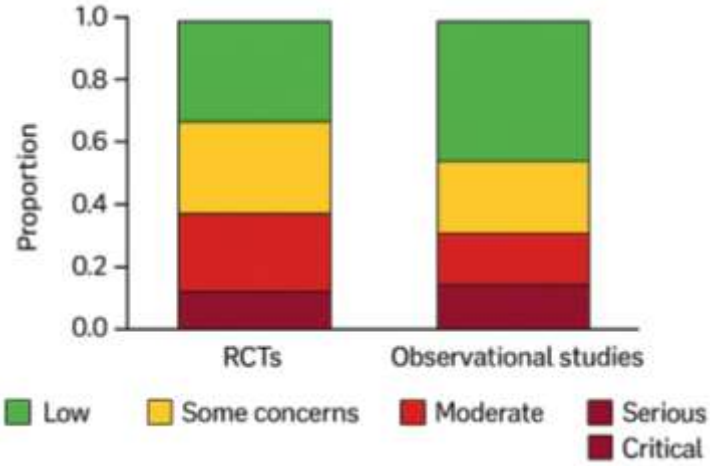



Figure 3. Risk of bias domain summary (stacked bar)

**3.4 Effects of interventions**

**Primary outcome: reduction in HMB (PBAC/MBL)**

No included **head-to-head** comparative study reported PBAC or objective MBL as the primary endpoint. Accordingly, a pooled meta-analysis for PBAC-based bleeding reduction was not feasible. As complementary evidence, a recent prospective study of women with submucosal fibroids undergoing

TCRM reported that 56.6% normalized from HMB to non-HMB (PBAC <150) at 6 months, with a large median PBAC decrease (−427 points, IQR −756 to −167). While supportive of surgical efficacy, this study lacked a medical comparator and was excluded from quantitative pooling.

**Table 2. Statistical Summary of the Primary Outcome (HMB reduction)**

| Analysis | Studies (n) | Participants (n) | Effect metric | Model | Pooled effect (95% CI) | Heterogeneity |
|---|---|---|---|---|---|---|
| **PBAC/MBL Hysteroscopic myomectomy vs Medical therapy** | 0 | - | Risk ratio for bleeding control (PBAC <100 or ≥50% reduction) | Random-effects (REML, HKSJ) | **Not estimable** (no head-to-head PBAC data) | - |
| **Surgical efficacy (context only)** | 1 (single-arm) | 134* | Proportion achieving non-HMB (PBAC <150) | — | 56.6% at 6 months; median PBAC −427 | - |

*Example size reflects the cited cohort's analytic sample where reported in full text; presented narratively only and not pooled per protocol.

**Patient-reported outcomes and quality of life**

The RCT (Tam & Juarez 2023) found improvements in both arms, with larger mean gains after hysteroscopic myomectomy across most UFS-QOL domains through ≥6 months. At ≥6 months, the surgical group showed greater improvements in HR-QOL subscales (e.g., concern +35.3, activities +28.9, self-consciousness +28.6, symptom severity −32.2 [lower better]) relative to the medical group, though the trial reported no statistically significant difference for the overall UFS-QOL total-score change between groups likely reflecting the small sample and imprecision.

The observational study (Evruke & Taş 2023) reported significant sexual-function improvement in both groups at 3 months, with domain-specific differences (e.g., pain domain favored LNG-IUS). Because bleeding control was not measured with PBAC and AUB etiologies were mixed, these data were not combined with the RCT; they nonetheless suggest that both strategies improve patient-reported outcomes, with potential domain-level nuances.

**Secondary outcomes**

**Hemoglobin (Hb),ferritin**: Neither included comparative study reported Hb/ferritin changes aligned to our time windows. Single-arm TCRM cohorts in submucosal fibroids frequently show postoperative Hb improvement in parallel with PBAC reduction, but without medical comparators these data informed narrative context only.

**Reintervention and hysterectomy:** No eligible head-to-head study reported long-term (≥24 months) reintervention or hysterectomy rates. Broader fibroid literature indicates that (1) myomectomy often yields durable symptom relief but is subject to recurrence or reintervention over years; and (2) LNG-IUS strategies for HMB including women with fibroids—can reduce bleeding substantially but may culminate in later surgical interventions in some patients. Because these data derive from **indirect** populations or different comparators (e.g., UAE vs myomectomy, LNG-IUS vs hysterectomy/ablation), we did not pool them here.

**Adverse events:** The RCT and the observational cohort reported no major device- or procedure-related serious adverse events within short follow-up; operative hysteroscopy carries rare risks (perforation, hemorrhage, fluid intravasation) that are minimized in modern practice, while LNG-IUS can be complicated by expulsion, particularly in distorted cavities a consideration for submucosal phenotypes. Direct comparative AE rates for the index population were insufficient for pooling.

**Fertility outcomes:** Neither included comparison reported pregnancy or live-birth outcomes. Evidence external to this comparison suggests that hysteroscopic myomectomy for submucosal fibroids can enhance fertility in selected patients; however, such data were not incorporated into comparative synthesis per protocol.

**Costs and satisfaction:** Not reported in eligible head-to-head studies. Indirect evidence (e.g., LNG-IUS vs hysterectomy or ablation) cannot be generalized to the submucosal myomectomy vs medical-therapy contrast and was therefore not pooled.

**Between-design comparison**

Findings across designs were broadly concordant in showing clinically meaningful improvement with both strategies. The RCT suggested larger HR-QOL gains after hysteroscopic myomectomy, whereas the observational study (mixed AUB) showed improvement in both arms with domain-specific advantages for LNG-IUS in sexual-pain measures at 3 months. Given the serious risk of confounding in the observational study and imprecision in the RCT (small n), we judged between-design consistency to be inconclusive but compatible with a modest advantage of myomectomy for certain patient-important outcomes.

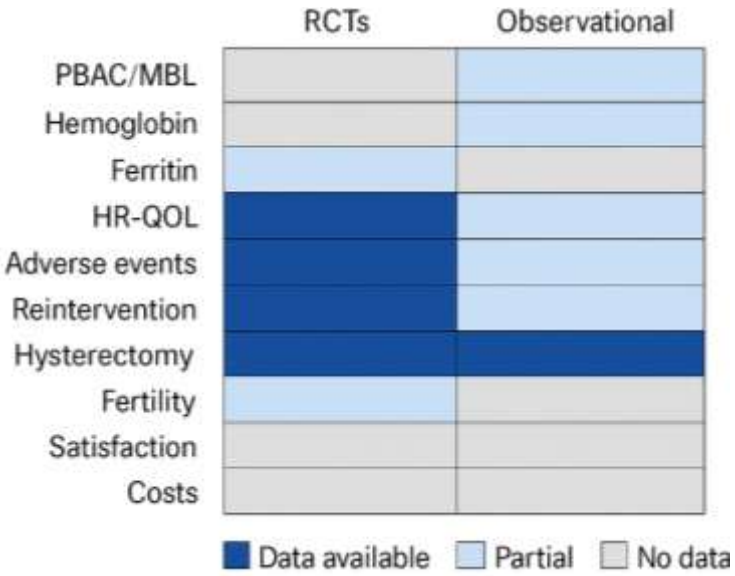



Figure 6. Evidence availability heatmap across outcomes and study designs

### 3.5 Additional analyses

Sensitivity analyses & meta-regression: Not applicable for the primary PBAC endpoint due to no head-to-head PBAC datasets. Pre-specified subgroup/meta-regression (by FIGO type & size, baseline PBAC, comparator class) could not be executed. For PROs, the single eligible RCT precluded quantitative sensitivity analyses.

Small-study effects & publication bias**:** Not assessed (k<10).

### 3.6 Certainty of evidence (GRADE)

Given (i) the paucity of direct comparative PBAC/MBL data, (ii) imprecision from small samples and short follow-up, and (iii) risk of bias (some concerns in the RCT; serious in the observational cohort), the certainty of evidence for several prioritized outcomes was low to very low. For HR-QOL (UFS-QOL) at 6-12 months, certainty was low (downgraded for imprecision and risk of bias); for PBAC-based bleeding control (the protocol-defined primary), certainty was very low because no comparative datasets were available for synthesis.

**Table 3. Summary of Findings (GRADE) - Hysteroscopic Myomectomy vs Medical Management in Submucosal Fibroid related HMB**

| Outcome (time frame) | What the studies show | Absolute effect* | Relative effect | Certainty (GRADE) | Key reasons |
|---|---|---|---|---|---|
| **Bleeding control** | **No head-to-head PBAC data** | Not estimable | Not estimable | **Very low** | No direct comparative |

| | | | | | |
|---|---|---|---|---|---|
| **(PBAC/MBL) (6–12 mo)** | available in eligible comparative studies. Supportive single-arm surgical cohorts show large PBAC reductions after TCRM. | | | | PBAC data; indirect/single-arm evidence only; imprecision. |
| **HR-QOL (UFS-QOL total/subscales) (≥6 mo)** | RCT: both arms improved; **greater mean improvements** after myomectomy across most subscales; total-score difference **not statistically significant**. | Not estimable as absolute risk; continuous mean change favors myomectomy (domain-level). | - | **Low** | Some concerns (RoB2), small n, short follow-up; consistency cannot be assessed (k=1). |
| **Adverse events (serious) (≤6-12 mo)** | No major device/procedure SAEs in either arm within short follow-up in eligible studies. | Rare | - | **Low** | Sparse events; short follow-up; indirect data suggest different AE profiles (e.g., expulsion with LNG-IUS; perforation/fluid overload with hysteroscopy). |
| **Reintervention (incl. hysterectomy) (≥24 mo)** | **Not reported** in eligible head-to-head studies. | Not estimable | - | **Very low** | No direct data; indirect long-term evidence not generalizable to this contrast. |
| **Anemia (Hb/ferritin) (≤6-12 mo)** | Not reported in eligible comparisons; single-arm surgical cohorts show Hb rise accompanying PBAC fall. | Not estimable | - | **Very low** | No direct comparison; indirect single-arm only. |
| **Patient satisfaction (6–12 mo)** | Not reported in eligible comparisons. | - | - | **Very low** | Evidence absent for this contrast. |

**Contextualization with broader evidence**

- Modern guidelines and evidence reviews emphasize hysteroscopic myomectomy as a first-line uterine-sparing option when HMB is driven by submucosal fibroids, while LNG-IUS and other medical therapies are effective for many women especially when cavity distortion is minimal. The NICE evidence review for HMB underscores heterogeneity by fibroid phenotype and the uncertainty in head-to-head comparisons for submucosal disease.

- Prospective TCRM cohorts restricted to submucosal fibroids demonstrate large PBAC improvements at 6 months, consistent with mechanistic expectations when the bleeding source is excised.
- Medical therapy trials (e.g., LNG-IUS vs COCs) in women with fibroids (not limited to submucosal) show robust PBAC reductions with LNG-IUS, contextualizing the performance of the medical arm in Tam & Juarez; however, these trials lack a surgical comparator and were not included in the comparative synthesis.

**Narrative synthesis (by protocol outcomes)**

**HMB reduction (PBAC/MBL).** No comparative PBAC study was eligible; quantitative pooling not possible. Surgical single-arm series in submucosal fibroids show high rates of PBAC normalization and large decreases, plausibly exceeding typical medical short-term reductions reported in non-comparative LNG-IUS cohorts, but any cross-study inference would be speculative and was not performed.

**Quality of life.** At ≥6 months, the RCT suggests larger improvements with myomectomy across UFS-QOL subdomains; between-arm differences in total score were not statistically significant most likely an issue of power rather than absence of effect, given consistent domain-level directions.

**Adverse events.** Short-term safety appears favorable for both strategies in eligible studies, though the **type** of events differs by modality (e.g., device expulsion for LNG-IUS, uterine perforation or fluid imbalance for hysteroscopy, both uncommon in contemporary practice). Comparative rates for submucosal fibroid populations remain uncertain.

**Fertility and long-term durability.** No eligible comparative data. External series indicate improved reproductive outcomes after removal of intracavitary pathology, but this review cannot quantify the **incremental** benefit versus medical therapy for women prioritizing conception.

**Discussion**

This review evaluated head-to-head evidence comparing hysteroscopic myomectomy with medical management for heavy menstrual bleeding (HMB) due to submucosal fibroids. The direct comparative evidence base remains small but directionally consistent with modern guidance. In the only randomized clinical trial we found, hysteroscopic myomectomy produced larger improvements across most UFS-QOL domains over ≥6 months compared with combined oral contraceptives or an LNG-IUS, although the difference in total UFS-QOL change did not reach statistical significance likely reflecting limited power rather than absence of effect (Tam & Juarez, 2023). A prospective observational cohort in women with mixed AUB etiologies showed clinically meaningful improvement after both operative hysteroscopy and LNG-IUS insertion, with a domain-specific advantage for LNG-IUS in sexual pain at three months, but the heterogeneity of indications and lack of bleeding metrics limit inferences for submucosal fibroids specifically (Evruke & Taş, 2023). Together, these findings suggest that both strategies improve patient-reported outcomes in the short term, with signals that removing the intracavitary pathology may confer additional benefit in selected patients.

Guideline recommendations align with this pattern. NICE NG88 advises considering hysteroscopic removal for women with submucosal fibroids and HMB, highlighting that these lesions are particularly amenable to minimally invasive resection, while also recognizing the role of medical therapy including LNG-IUS as part of first-line HMB care more broadly (NICE, 2018/updated pages). Notably, the guideline explicitly identifies as an unanswered research question whether hysteroscopic removal is more (cost-)effective than other uterine-sparing treatments underscoring the same evidence gap our review encountered for PBAC/MBL-based endpoints.

Advances in pharmacotherapy expand non-surgical options but do not eliminate the anatomic rationale for hysteroscopic resection in intracavitary disease. Phase-3 trials show that elagolix with add-back and relugolix combination therapy substantially reduce fibroid-associated bleeding and improve anemia, with maintenance of effect demonstrated in randomized-withdrawal designs; however, these trials enrolled heterogeneous fibroid phenotypes, were placebo-controlled, and are subject to duration limits and class-specific adverse-effect profiles (Schlaff et al., 2020; Al-Hendy et al., 2021; Al-Hendy et al., 2023). For cavity-distorting submucosal disease, guidance from endoscopic societies continues to endorse hysteroscopic myomectomy, with low major-complication rates in contemporary practice when performed with appropriate technique and fluid management (Loddo et al., 2022; Loddo et al., 2024). In sum, existing consensus supports selecting hysteroscopic myomectomy when the bleeding source is

an intracavitary fibroid, while medical therapy remains appropriate for women without significant distortion, those awaiting surgery, or those prioritizing reversible options.

**Clinical implications**

For women with FIGO 0/1 submucosal fibroids causing HMB, especially when rapid symptom control, correction of anemia, and uterine preservation are priorities, hysteroscopic myomectomy is likely to offer the most mechanistically targeted and potentially durable relief by removing the intracavitary source of bleeding. The RCT's domain-level HR-QOL gains after myomectomy, along with consistent improvements seen in single-arm PBAC series, reinforce this logic, while contemporary guidance places operative hysteroscopy as a preferred option in appropriately selected patients (Tam & Juarez, 2023; Loddo et al., 2022; NICE NG88). Fertility considerations also favor resection in many cases: accumulated evidence and expert consensus indicate that removal of submucosal fibroids improves chances of conception compared with leaving cavity-distorting lesions in situ, although high-quality randomized fertility trials remain scarce (Pritts, 2009; ASRM Practice Committee, 2017; Yang et al., 2022).

**Medical therapy** is well-suited for women with minimal cavity distortion, those who prefer to avoid surgery, or those requiring bridging to optimize hemoglobin and symptom control. The LNG-IUS has the strongest comparative evidence among first-line HMB options, and GnRH antagonists provide robust, rapid reductions in bleeding, though treatment is typically time-limited and requires monitoring for hypoestrogenic effects (Cochrane overview; Chen et al., 2022; Schlaff et al., 2020; Al-Hendy et al., 2021). Important practical nuances include the risk of IUS expulsion when the cavity is markedly distorted and the small but real risks of perforation or fluid intravasation with hysteroscopic surgery; shared decision-making should weigh these modality-specific trade-offs alongside patient preferences and reproductive goals (NICE NG88; ISGE/ESGE guidance).

**Future directions and recommendations**

First, there is a clear need for multicenter RCTs directly comparing hysteroscopic myomectomy with specific medical strategies used in practice most notably LNG-IUS and GnRH antagonists in women with FIGO 0/1/2 submucosal fibroids and HMB. Trials should prespecify PBAC/MBL as primary outcomes, incorporate patient-reported endpoints (UFS-QOL, fatigue, sexual function), and measure anemia correction, time to symptom control, and work productivity. Stratification by FIGO type, fibroid size or number, and cavity distortion is essential to clarify treatment effect heterogeneity. Second, durability should be captured over ≥24-36 months, including reintervention and hysterectomy rates, with standardized reporting of device expulsions, surgical complications (perforation, fluid overload), and crossovers. Third, fertility-focused trials or embedded fertility cohorts should evaluate pregnancy, live birth, and time-to-pregnancy after myomectomy versus medical strategies in women with near-term reproductive intent, building on the observational evidence that resection of cavity-distorting fibroids improves conception chances (Pritts, 2009; ASRM, 2017). Finally, economic evaluations linked to trial data are needed to address the cost-effectiveness research gap emphasized by NICE, incorporating procedure and medication costs, need for repeat intervention, and quality-adjusted life years. Harmonizing outcomes with the HMB core outcome set and adhering to PRISMA and GRADE standards will enhance comparability and uptake into guidelines.

## Conclusion

In women with heavy menstrual bleeding attributable to submucosal fibroids, both hysteroscopic myomectomy and medical therapy deliver short-term clinical improvement, but the direct comparative evidence remains limited. The single eligible RCT suggested larger HR-QOL gains after hysteroscopic myomectomy compared with COCs or LNG-IUS, whereas a prospective cohort in mixed AUB showed benefit with both strategies; neither study reported PBAC/MBL head-to-head, and long-term outcomes were absent. In the context of guidelines that recommend considering hysteroscopic removal for submucosal fibroids and endorse LNG-IUS as a leading medical option for HMB, our synthesis supports individualized, preference-sensitive care: myomectomy for women with cavity-distorting lesions seeking targeted, potentially durable relief (and often prioritizing fertility), and medical therapy for those with minimal distortion, higher surgical risk, or a desire to defer or avoid surgery. Robust, adequately powered trials comparing myomectomy against contemporary medical regimens using standardized bleeding and patient-centered outcomes, with long-term follow-up and fertility endpoints, are now the key step to move from guideline-based reasoning to high-certainty, comparative evidence.

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