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A SYSTEMATIC REVIEW COMPARING HYSTERECTOMY TO LESS INVASIVE TREATMENTS FOR ABNORMAL UTERINE BLEEDING

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Abstract

Study Objective—To compare hysterectomy and less invasive alternatives for abnormal uterine bleeding (AUB) in 7 clinically important domains

Design—Systematic review

Setting—Randomized clinical trials (RCTs) comparing bleeding, quality of life, pain, sexual health, satisfaction, need for subsequent surgery, and/or adverse events between hysterectomy and less invasive treatment options

Patients—Women with AUB, predominantly from ovulatory disorders and endometrial causes

Interventions—Systematic review of the literature (from inception to January 2011) comparing hysterectomy to alternatives for AUB treatment. Eligible trials were extracted into standardized forms. Trials were graded using a predefined 3-level rating and the strengths of evidence for each outcome were evaluated with the GRADE system.

Measurements and Main Results—Nine RCTs (18 articles) were eligible. Endometrial ablation, levonorgestrel intrauterine system (LNG-IUS), and medications were associated with lower risk of adverse events but higher risk of additional treatments than hysterectomy. Compared to ablation, hysterectomy had superior long-term pain and bleeding control. Compared to LNG-IUS, hysterectomy had superior control of bleeding. No other differences between treatments were found.

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Conclusion—Less invasive treatment options for AUB result in improvement in quality of life but carry significant risk of retreatment secondary to unsatisfactory results. While hysterectomy is the most effective treatment for AUB, it carries the highest risk for adverse events.

Keywords

Abnormal uterine bleeding; dysfunctional uterine bleeding; hysterectomy; systematic review

INTRODUCTION

Abnormal uterine bleeding (AUB) affects up to 30% of women during their reproductive years. (1–4) AUB has a substantial impact on women's quality of life, associated loss of productivity, and major health care costs. (5–8)

AUB is a symptom of several different underlying conditions, which have been newly classified by the International Federation of Gynecology and Obstetrics (FIGO) Menstrual Disorders Group. (9,10) Under this system, causes of AUB are classified as polyps (AUB-P), adenomyosis (AUB-A), leiomyomas (AUB-L), malignancy and premalignant conditions (AUB-M), coagulaopathy (AUB-C), ovulatory disorders (AUB-O), endometrial disorders (AUB-E), iatrogenic (AUB-I), and “not classified” (AUB-N). Because of confusion surrounding the term “dysfunctional uterine bleeding” or “DUB”, this term is not included in the naming system and women who were formerly described as having “DUB” generally fit into the ovulatory disorders and endometrial hemostatic disorders categories if coagulopathy has been excluded. (9,10) Although hysterectomy is considered the “definitive” treatment for AUB regardless of etiology, less invasive options are increasingly available, including medical therapy, the levonorgestrel intrauterine system (LNG-IUS), and endometrial ablation. Better characterization of the relative efficacy of these alternatives compared to hysterectomy will improve patient counseling, facilitate informed decision-making, and reduce the burden of unnecessary procedures on both the patient and the health care system.

The Systematic Review Group of the Society of Gynecologic Surgeons (SGS SRG) performed a systematic review of randomized control trials (RCTs) comparing hysterectomy with other treatment modalities for women with AUB presumed secondary to ovulatory (AUB-O) or endometrial dysfunction (AUB-E) under this new FIGO classification system. The objective of this study was to determine the relative efficacy of less invasive treatments compared to hysterectomy for bleeding control, change in quality of life, pain, sexual health, patient satisfaction, additional needed treatments, and adverse events. The systematic review was conducted with the goal of producing an evidence-based guideline on decision-making around hysterectomy for AUB-O and AUB-E. (If JMIG chooses to publish the clinical practice guidelines will insert the location of the guideline in the journal here)

Materials and Methods

Data Source—The SGS SRG, including gynecologic surgeons and systematic review methodologists, performed a systematic search to identify RCTs comparing treatments for AUB in women with ovulatory disorders (AUB-O), endometrial hemostatic dysfunction (AUB-E), or fibroids (AUB-L). A working document defining parameters for a literature search was created. (11) We searched MEDLINE from inception to January 14, 2011 for English language human studies. We included search terms for AUB, menorrhagia, fibroids, hysterectomy, myomectomy, uterine artery embolization, ablation, intrauterine devices, medical therapies, RCTs, and related terms. Details of the full search were reported in a previous publication. (12)

Study selection and data extraction—We included RCTs that compared hysterectomy (via any route) to endometrial ablation, LNG-IUS, or medical therapies as treatments of AUB secondary to presumed ovulatory disorders (AUB-O) or endometrial hemostatic dysfunction (AUB-E), and reported an outcome of interest. We excluded RCTs that included only participants with AUB attributed to fibroids (AUB-L), though studies that included women with AUB-L in addition to AUB-O and AUB-E were not excluded. This review was conducted as part of a broader systematic review that addressed all treatments for AUB secondary to ovulatory disorders (AUB-O), endometrial hemostatic dysfunction (AUB-E), or fibroids (AUB-L).

Data from studies were extracted by members of the SRG, most of whom had experience from a prior systematic review.(13, 14) Individual extractions were confirmed by a second member and discrepancies were resolved by consensus among all members of the SRG. Complete details on the definitions of variables of interest, outcome classification, and coding have been published.(12) In brief, 114 outcomes were identified and ranked as “critical”, “important”, and “low-importance” for clinical decision-making. Using a ballot system all members of the SGS SRG used a structured process (explained in detail in a previous publication of the review group) to grade the importance of each outcome with a scale suggested by the GRADE Working Group (12, 15, 16). “Critical” and “important” outcomes were organized into 7 overarching domains considered in this review (bleeding, quality of life, pain, sexual health, patient satisfaction, need for subsequent surgical treatment, and adverse events).(12) Adverse events were categorized as “major” [need for urgent re-operation/conversion to another surgery (hysterectomy or laparotomy), cystotomy, ureteral injury, bowel injury, pelvic or vaginal vault hematoma, death, myocardial infarction/respiratory event, deep vein thrombosis/thromboembolism, pulmonary embolus/thromboembolic event, stroke, admission to the intensive care unit, and “other”] and “minor” [wound infection, pelvic infection/cuff cellulitis, febrile morbidity, “other infection” (which included urinary tract infection, pneumonia, other infections), wound hematoma/wound rupture (which also included wound hematoma/seroma and unspecified hematomas), need for transfusion, re-admission without re-operation, fluid overload, uterine perforation, ileus or obstruction, non-urgent surgery presumed secondary to complications from the initial procedure. Re-operations which were not presumed secondary to complications from the initial procedure were not reliably reported (for example, subsequent surgery for ovarian cysts or adhesions) and therefore not included.

We assessed the methodological quality of each study using predefined criteria from a three-category system modified from the Agency for Healthcare Research and Quality.(15) Studies were graded as good (A), fair (B), or poor (C) quality based on the likelihood of biases and the completeness of reporting. Grades for different outcomes could vary within the same study. We decided a priori that meta-analyses would be performed only when three or more trials used similar interventions and outcome definitions. To grade the overall *strength of evidence*, we followed the Grades for Recommendation, Assessment, Development and Evaluation (GRADE) system, with four ratings: high, moderate, low, and very low. (16) As part of a public vetting process, the review and guidelines were presented for public comment at the 36th SGS Annual Scientific Meeting April 2010 and posted on the SGS website, where public comments were solicited for 4 weeks.

RESULTS

The literature search identified 5,503 citations. Screening of citations and potentially relevant full-text articles resulted in 117 eligible articles (115 which were extracted) and 81 distinct RCTs relevant to the broader review. (Figure 1) *This review is based upon the 18*

articles from 9 trials that directly compared hysterectomy with another intervention and met our eligibility criteria. (Table 1)

Hysterectomy versus endometrial ablation (Table 2)

Seven RCTs (six rated as “B” quality and one rated as “A” quality) with 1,167 women, compared hysterectomy to endometrial ablation with follow-up from 4–48 months.(17–26) Two of the seven trials included women with submucous myomas (AUB-L-SM). (23,26). In the hysterectomy arm of these seven trials, 49% (n=395) had a TAH, 26% (n=206) had a TVH, and 25% (n=199) had a laparoscopic approach to hysterectomy. All trials utilized resectoscopic methods of endometrial ablation [4 used resection only, one resection or laser (20), one resection or rollerball (23), and one electrodesiccation or thermal balloon (25)]. Overall quality of the evidence for these studies was low to moderate for each outcome domain. The heterogeneity in specific outcomes reported precluded meta-analyses for this comparison.

Bleeding control (critical importance)—Seven studies reported bleeding outcomes. Amenorrhea rates for the endometrial ablation groups ranged from 13–64%, versus an implied 100% following hysterectomy in most studies (one study reported one woman who had bleeding following hysterectomy). (25) Because of the heterogeneity of outcomes measures between studies comparing hysterectomy and ablation (different questionnaires), there were insufficient data to systematically compare bleeding control outcomes other than amenorrhea for the evidence profiles. The strength of evidence was moderate that bleeding is better controlled following hysterectomy than ablation.

Quality of life (critical importance)—Six studies evaluated quality of life. Overall, studies showed significant improvement above baseline in quality of life scores after treatment with both ablation and hysterectomy. Several studies found no difference between treatment arms in scores on various validated quality of life assessment tools. (18,19,21,24,25) However, these studies were not powered to detect differences in quality of life scores, thus lack of statistical significance does not confirm no difference in effect. Three studies found statistically significant differences in various SF-36 dimensions favoring hysterectomy: pain(19), general health (23,24), vitality (23,24), and social function (24). It should be noted that two of these three studies compared ablation specifically to minimally invasive methods of hysterectomy (the Zupi et al hysterectomies were LASH and the Croisignani et hysterectomies were TVH).(23,24) The strength of evidence was moderate revealing no difference between hysterectomy and ablation in post-operative quality of life.

Pain (critical importance)—Five trials assessed pain beyond the immediate post-operative period. (18,19,22,24,25). Improvement in “dysmenorrhea” was more prevalent in the hysterectomy group than the ablation group at 4 months post-procedure. (18) Three studies found pelvic pain was less prevalent in the hysterectomy group (5–19%) than the ablation group (24–64%) at 2–3 years follow-up, though only one study tested this statistically and found a significant difference.(19,24,25) One study found no difference in the proportion experiencing pain at 4 years. (22) The strength of evidence on pain beyond the post-operative period was low and favored hysterectomy over ablation.

Sexual health (high importance)—Five trials reported comparisons of sexual health outcomes.(18, 22–24, 26) These studies showed no difference in overall effect on sexual satisfaction and sexual health rating, although only one study used a validated questionnaire. (23) The quality of evidence for sexual health was low and revealed no difference in the effect of hysterectomy compared to ablation.

Satisfaction (high importance)—Five trials compared general satisfaction between ablation and hysterectomy and four of which defined satisfaction rate as the primary outcome. (18–20, 22, 23, 25, 26) Outcome measures varied among studies. The majority of women in both treatment arms reported being satisfied with their treatment option (50–95% for ablation, 52–96% for hysterectomy) at 1–4 years follow-up. Three trials found no differences in satisfaction between the hysterectomy and ablation group. (23, 25, 26) Two trials found significantly greater satisfaction after hysterectomy than ablation. One trial reported more women “very satisfied” 1 year after hysterectomy (88% vs. 78%, $p<0.05$), but no significant difference at 4.8 years, possibly due to reduced statistical power due to dropouts. Another study found that at 4 months, 95% of the hysterectomy group was “quite satisfied” or “very satisfied” compared to 79% of ablation group ($p=0.002$). (19) Overall, the quality of evidence was very low for satisfaction outcomes which were not different between hysterectomy and ablation.

Additional treatment (Moderate importance)—The need for additional treatment after endometrial ablation, with either repeat ablation or hysterectomy, was reported as an outcome in seven trials. (17–20, 22–26) At 1–4 years follow-up, 16–42% of participants assigned to ablation had undergone an additional surgical treatment for bleeding with 10–29% treated with hysterectomy. Overall, the quality of evidence regarding additional treatments was moderate and favored hysterectomy over ablation.

Hysterectomy versus the levonorgestrel-intrauterine system (Table 3)

One “A” quality RCT (with six publications) compared hysterectomy to LNG-IUS. (27–32) A total of 236 women with heavy menstrual bleeding were followed for 6 months to 10 years after treatment. In the hysterectomy group 20% ($n=21$) had a TAH, 28% ($n=30$) had a TVH, and 52% ($n=56$) had a laparoscopic approach to hysterectomy. Women with submucous fibroids and women with “irregular bleeding” as a main complaint were excluded; 49% of participants had uterine fibroids. Overall quality of the evidence for these studies was moderate for each outcome domain.

Bleeding control (critical importance)—The proportion of participants who reported amenorrhea or oligomenorrhea with the LNG-IUS still “in-situ” was 51% (41/81) at 12 months and 75% (43/57) at 5 years. Women who discontinued use of the LNG-IUS ($n=50$, 42%) did so because of inter-menstrual bleeding (70%) and heavy bleeding (30%). Overall, the evidence favored hysterectomy over LNG-IUS for bleeding control.

Quality of life measures (critical importance)—Both the EuroQOL-5D and the SF-36 were used to measure quality of life. (27–29) Overall, the evidence revealed no differences in quality of life outcomes between hysterectomy and LNG-IUS.

Pain (critical importance)—At 6 and 12 month follow-up, a greater proportion of participants in the LNG-IUS group reported lower abdominal pain. At 12 months, this difference was statistically significant (30% LNG-IUS vs. 14% hysterectomy, $p=0.02$). No difference was found at 5 years. (31) Overall, the evidence on pain revealed no differences between hysterectomy and LNG-IUS.

Sexual health (high importance)—Sexual function was compared between LNG-IUS and hysterectomy at 6 months, 1 year, and 5 years using McCoy sex scale scores (30) Compared to hysterectomy, the LNG-IUS group reported more sexual problems at 6 months ($p=0.03$), however, this effect was not seen at 12 months or 5 years. No differences were found in sexual problems at other time points or in sexual satisfaction scores at any time

point. Overall, evidence for sexual health revealed no differences between hysterectomy and LNG-IUS.

Satisfaction (high importance)—Satisfaction rates at 5 years were very high for both the LNG-IUS group (93%) and the hysterectomy group (94%). (29) Overall, the evidence regarding satisfaction showed no difference in satisfaction between LNG-IUS and hysterectomy.

Additional treatment (Moderate importance)—Among women randomized to LNG-IUS, 20% had undergone hysterectomy by 12-months, 42% by 5 years, and 46% by 10 years. Overall, the evidence on additional treatments favored hysterectomy over LNG-IUS.

Hysterectomy versus medications (Table 4)

One RCT (rated as “A” or “B” quality for different outcomes) compared hysterectomy to medical therapy in 63 women with AUB presumably from DUB. The participants were followed for 2 years. (33,34) In the hysterectomy group 36% (n=10) had a TAH and 64% (n=18) had a TVH. The trial did not mandate a specific medication regimen and therapies used in this study included combined oral contraceptive pills (38%), cyclic progestin (16%), continuous progestin (6%), conjugated estrogen with progestin (25%), and conjugated estrogen alone (6%); 53% received a prostaglandin synthetase inhibitor, usually with a hormonal therapy. Overall quality of the evidence for these studies was low to very low for each outcome domain.

Bleeding control (critical importance)—Measures of bleeding control were not reported for this trial.

Quality of life measures (critical importance)—No differences were found in the change of any SF-36 scores between medication and hysterectomy groups.(33) Overall, the quality of evidence for quality of life measures was low and revealed no differences between hysterectomy and medications.

Pain (critical importance)—No differences were found in pain between groups. (34) Overall, the quality of evidence for pain outside the post-operative period was very low and revealed no differences between hysterectomy and medications.

Sexual health (high importance)—No differences were found in SF-36 sexual satisfaction scores between groups. (33) Overall, the quality of evidence on sexual health outcomes was low and revealed no differences between hysterectomy and medications.

Satisfaction (high importance)—No differences were found in change in satisfaction with symptom level between groups. (33) Overall, the quality of evidence for satisfaction was low and revealed no differences between hysterectomy and medications.

Additional treatment (Moderate importance)—At 2 year follow-up, 53% of the group randomized to medication had “crossed-over” to the hysterectomy group. (33) One patient in the hysterectomy arm required a trachelectomy 15 months after hysterectomy for persistent bleeding. Although “additional treatment” can be inferred from “crossed-over” to hysterectomy, it was not specifically assessed nor reported as an explicit “outcome” for this study. Therefore an evidence profile was not generated.

Adverse events

Adverse events are listed in Table 5, however reporting of adverse events was not standardized across studies and not all studies presented data on each adverse event listed. We combined the hysterectomy arms of all nine trials (ablation vs. hysterectomy, LNG-IUS vs. hysterectomy, and medications vs. hysterectomy) to obtain the complication totals for hysterectomy. In total, there were 57 “major” complications and 225 “minor” complications in the hysterectomy group which consisted of 724 patients. Rates/proportions are reported for each individual complication and not the composite of “major” and “minor” complications because one patient could have multiple complications and artificially inflate the overall complication rate. The most common “major” complication was pelvic or vaginal vault hematoma (n=28, 3.9%), with urinary tract injuries (n=7, 1% for cystotomy and n=1, 0.1% for ureteral injuries), and bowel injuries (n=2, 0.3%) being present but uncommon.

For the studies comparing ablation to hysterectomy, adverse events were reported in seven studies (n=1167). In patients randomized to ablation, there were a total of seven major complications and 69 minor complications. The most common “major” complication was conversion to a different surgery or urgent re-operation, but this occurred in only 1% of patients (n=6). The most common “minor” complication was fluid overload, which occurred in 4% of patients (n=23). Two studies statistically compared adverse events between hysterectomy and ablation groups. One found no significant differences in complications between ablation and hysterectomy. (24) The second found no difference in intra-operative complications, but a higher rate of complications in the hysterectomy group pre-discharge ($p<0.001$) and post-discharge ($p=0.004$). (26) There appears to be a trend to a higher rate of major and minor complications for hysterectomy than for ablation. Overall, the quality of evidence regarding adverse events was moderate and favored ablation over hysterectomy for minimizing adverse events.

One study compared the LNG-IUS to hysterectomy. In this study, one major complication (a recurrent thromboembolic event) occurred in the LNG-IUS group (1%) and no minor complications. There were 12 major complications and 32 minor complications among patients receiving hysterectomy in this study and the authors reported that 30% of participants in the hysterectomy group had “post-operative complications”. Overall, the evidence for adverse events was moderate quality and favored LNG-IUS over hysterectomy.

In the one trial that compared medications to hysterectomy, there were no reported complications in the medication group. In the hysterectomy group, there were 3 major complications and 1 minor complication. Overall, the quality of evidence for adverse events was low and favored medication over hysterectomy.

DISCUSSION

Designing and interpreting research on AUB treatment is challenging. Many different treatment modalities are available and AUB is associated with a wide spectrum of symptoms. Our review provides a concise assessment of the efficacy of less invasive options for managing AUB, predominantly from ovulatory dysfunction or endometrial hemostatic dysfunction, as compared to hysterectomy within seven important clinically-relevant outcome domains. Despite the high prevalence of AUB and a variety of available treatments, we found only 9 RCTs reported in 18 articles which compared hysterectomy directly to other “less invasive” treatment options. We identified important trade-offs between the relative benefits and harms of hysterectomy and endometrial ablation, LNG-IUS, and medications.

Regardless of the comparator, hysterectomy was favored over other options for elimination of bleeding symptoms and need for additional treatment. Hysterectomy was also favored over ablation for pelvic pain resolution outside of the immediate postoperative period. However, these superior outcomes were achieved with the tradeoff of higher risks of adverse events. While hysterectomy is more efficacious for treatment of many AUB symptoms, we found less invasive options including endometrial ablation and LNG-IUS to be comparable to hysterectomy in achieving outcomes related to patient satisfaction and quality of life improvement. Consistent with our finding, a previous meta-analysis of individual patient data from 17 trials (six which compared hysterectomy to ablation, one which compared hysterectomy to LNG-IUS, 3 which compared ablation to LNG-IUS, and seven which compared ablation techniques) concluded that patients undergoing hysterectomy were more satisfied than patients undergoing endometrial ablation. However, satisfaction rates were very high for both groups and absolute differences were small.(35)

A limitation to our comparison of hysterectomy versus endometrial ablation is that all of the RCTs identified involved resectoscopic endometrial ablation techniques, which, while still used, have largely been replaced by a number of non-resectoscopic ablation techniques. Thus the applicability of the available trials to current practice is unclear. However, two recent reviews comparing non-resectoscopic to resectoscopic endometrial ablation techniques found no difference in amenorrhea rates, satisfaction rates, and rates of additional surgical interventions.(35, 36)

Because of the limited body of evidence comparing medical therapies to hysterectomy, we are unable to make definitive conclusions on the relative effectiveness of individual medical therapy compared to hysterectomy. Many different medication types were used in the “medication arm” of the one RCT which directly compared medications to hysterectomy, which may help with the broad comparison of “medication vs. hysterectomy” but did not allow direct comparison of individual medical therapies to hysterectomy in terms of effectiveness. Most of the data concerning effectiveness of medical therapies are derived from RCTs comparing specific medications to either placebo or each other, which were outside of the scope of our review. Given that medications arguably represent the “least invasive” alternative to hysterectomy, the lack of evidence in this area highlights the importance of future research.

For this review, we chose to include only evidence from RCTs which compared hysterectomy to uterine-preserving treatments. Although this reduced the body of evidence, using the hysterectomy comparison arm as a prerequisite for study inclusion provided a means to standardize populations across trials and to reduce the clinical heterogeneity and selection bias that stems from recruitment for treatments with varying interventional risks. However, we were challenged by the inconsistency across studies in the definitions of the study populations. There are multiple etiologies of AUB and although we reviewed trials of treatment of women with AUB presumed secondary to ovulatory dysfunction or endometrial hemostatic dysfunction (AUB-O or AUB-E), it was not always clear how the studies identified the cause of bleeding, especially whether or not they investigated possible coagulopathies as a cause (AUB-C). Additionally, two of the studies comparing ablation to hysterectomy included patients with submucous myomas, (AUB-L-SM) which could affect bleeding and treatment effectiveness. Another obstacle is that the term “DUB”, which was used in most of these trials, is used inconsistently by clinicians, researchers, and experts on AUB. (9) This is why an expert group from FIGO has recommended discontinued use of the terms “dysfunctional uterine bleeding” and “DUB” and why we have not used these terms throughout this manuscript.

In addition to the small number of trials, this review was limited lack of consistency in the eligibility criteria of individual trials, and the extensive heterogeneity of studied outcomes. As discussed in greater detail in a previous publication (12), the extreme heterogeneity in specific outcomes across trials limited the interpretability of their conclusions. Likewise, the sparseness of data made it difficult to come to definitive conclusions about the efficacy of hysterectomy versus alternative treatments or to rank treatments. A clear example of this challenge was studying the efficacy in bleeding control. For most women seeking treatment for AUB, a reduction in their amount of bleeding to an acceptable level or a “normalization of menses” by their personal standards would likely constitute a satisfactory outcome. Unfortunately, amenorrhea was the only outcome that was reported in a consistent fashion across studies, allowing direct comparisons between hysterectomy and other treatments. We could not compare treatments in terms of “reduction in bleeding” or “normalization of menses”. Studies tended to report overall patient *satisfaction* with their interventions, but it is unclear how this may correlate with “satisfaction” with their menstrual bleeding. There is a need to standardize and validate outcome measures that are responsive to important symptoms from AUB (12, 37) and to use them consistently going forward.

We generated clinical practice guidelines for the treatment of AUB-O and AUB-E based on our systematic review (see accompanying article). Because limitations in the current body of literature comparing hysterectomy to other options allowed us to make only “weak” recommendations, we offer suggestions to address these shortcomings with additional higher quality research. Treatments not yet compared against hysterectomy, like newer endometrial ablation techniques, need to be studied in appropriate trials before we can confidently appraise their relative value. Additionally, although some studies used minimally invasive approaches to hysterectomy, overall the majority of hysterectomies for the ablation comparisons were performed abdominally (49%). It is possible that outcomes may vary by method of hysterectomy and the studies involved in this review did not stratify results by hysterectomy type. Given emphasis on increasing the proportion of hysterectomies performed by minimally invasive approaches (total vaginal hysterectomy and laparoscopic and robotic approaches to hysterectomy), the outcomes of these methods need to be more clearly studied relative to non-hysterectomy options for AUB. (38) Also, studies looking at outcomes of treatment for women with AUB should be powered to detect a meaningful difference in symptoms related to bleeding and disease-specific quality of life. (39)

In summary, in comparing hysterectomy to the “less invasive” options of endometrial ablation, LNG-IUS, and medications, we identified tradeoffs between treatment effectiveness and risk of serious adverse events. Given the many options available for the treatment of AUB, it is important that clinicians are aware of the relative advantages and disadvantages of each option and able to discuss this with patients seeking treatment for AUB. Each patient should receive counseling about the efficacy as well as burden and risk of each management option in the context of her disease manifestations to facilitate an informed choice based on the available evidence.

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Figure 1.
Study Selection Process

Table 1

Summary of studies, comparators, primary outcomes, sample size and power

Study (Study quality rating) ^a	N	Mean Age	Hysterectomy	Comparator	1° Outcomes (Time), Sample size and power summary
Hysterectomy vs. Ablation					
Gannon 1991(17)(B) United Kingdom	54	40 years	TAH	TCER (pretreated with IM MPA)	Unclear (12 mo) Primary outcome, power, and sample size unclear
Dwyer 1993(18)(B) United Kingdom	196	40 years	TAH	TCER	Satisfaction (4 mo) Needed 100 per group to detect a 10% difference $\beta=0.1$, $\alpha=0.05$
Sculpher 1996(19)(B) United Kingdom	155				Satisfaction (2.8 y) Primary outcome, power, and sample size unclear
Pinion 1994(20) (B) United Kingdom	204	40 years	Hysterectomy (87 TAH, 12 TVH)	TCER or laser endometrial ablation (pretreated with GnRH analog)	Satisfaction (12mo) Needed 160 per group to detect a 20% difference $\beta=0.2$, $\alpha=0.05$
Alexander 1996(21)(B) United Kingdom	204				Psychosocial outcomes (12 mo) Power and sample size unclear
Aberdeen 1999(22)(B) United Kingdom	151				Satisfaction (4.8 years) Power and sample size unclear, may be same as Pinion et al
Corisignani 1997(23)(B) Italy ^b	92	46 years	TVH	TCER or rollerball ablation	Satisfaction (2 yr) Needed 43 per group to detect a 25% difference $\beta=0.2$, $\alpha=0.05$
Zupi 2003(24)(A) Italy	181	43 years	LASH	TCER (pretreated with GnRH analog)	HRQoL: SF-36, (2 yr) — Sample size not calculated for this outcome. Needed 90 per group to detect a 50% difference in satisfaction, $\beta=0.2$, $\alpha=0.05$
Dickersin 2007(25)(B) USA	237	NR	Hysterectomy (30 TAH, 70 TVH, 18 laparoscopic)	Endometrial ablation (hysteroscopic using coagulation or vaporization or nonresectoscopic using thermal balloon)	Problem solved, resolution of primary complaint, bleeding, pain, and fatigue measured by SF-36 (12 mo) Needed 121 per group to detect a 7.4 point difference in MCS, 9 point difference in pain, and a 10 point difference in general health and energy, $\beta=0.1$, $\alpha=0.05$. Sample size for bleeding Scale score, but data on Ruta scale score. Not included in paper.
O'Connor 1997(26)(B) United Kingdom ^b	202	40 years	Hysterectomy (28 TAH, 28 TVH)	TCER (pretreated, mixed)	Satisfaction rate and subsequent re-operation (2 yr) Needed 200 total (2:1 ablation to hysterectomy ratio) to detect a 15% difference in "rate of further gynecologic surgery, $\beta=0.1$, $\alpha=0.05$
Hysterectomy vs. LNG-IUS^b All studies conducted in Finland					
Hurskainen 2001(27) (A)	236	43 years	Hysterectomy (21 TAH, 30 TVH, 56 laparoscopic)	LNG- IUS	EuroQoL-5D (12 mo) Needed 115 per group to detect a 7.5% difference in score, $\beta=0.2$, $\alpha=0.05$
Hurskainen 2004(28) (A)	236				EuroQoL-5D (12 mo) Power and sample size needed for multivariable logistic regression unclear.

Study (Study quality rating) ^a	N	Mean Age	Hysterectomy	Comparator	1° Outcomes (Time), Sample size and power summary
Hurskainen 2004(29) (A)	232				EuroQoL-5D (5 yr) Needed 115 per group to detect a 7.5% difference in score, $\beta=0.2$, $\alpha=0.05$
Halmesmaki 2007(30) (A)	232				McCoys sex scale scores (5 yr) Power and sample size not reported
Heliövaara-Peippo 2009(31)(A)	232				Likert scores on back/abdominal pain (5yr) Power and sample size not reported
Heliövaara-Peippo 2010(32)(A)	221				Lower urinary tract symptoms (10 yr) Retrospective power calculation showed 164 hysterectomy group and 71 in LNG-IUS group would give 80% power to detect a 15% difference in symptoms with $\alpha=0.05$
Hysterectomy vs. Medication All studies conducted in USA					
Kuppermann 2004 (33)(A)	63	41 years	Hysterectomy (10 TAH, 18 TVH)	Medical therapy ^c	Mental health score of SF-36 (2 yr) Needed 30 per group to detect a 6.8 unit difference with $\beta=0.1$, $\alpha=0.05$
Learman 2004(34) (B)					“Clinical outcomes” (2 yr) Power and sample size not reported

Note: mo = month; yr = year; IM MPA = intramuscular medroxyprogesterone acetate; HRQoL = health-related quality of life; MOS SF-36 = Medical Outcomes Study – Short-Form 36; LNG-IUS = Levonorgestrel intrauterine system; TAH = Total abdominal hysterectomy; TCER = Transcervical resection of endometrium; TVH = Total vaginal hysterectomy; LASH = Laparoscopic supracervical hysterectomy.

^a Study Quality Rating - Quality of the evidence determine by rating the quality of the study, the quality of the assessment of the particular outcome within a study, the consistency (refers to treatments showing similar effect for each outcome across all or most studies), the directness (refers to applicability of the results to the population of interest), and other factors such as imprecision or sparseness of the evidence.

A - Good quality: Prospective, no obvious biases or reporting errors, complete reporting of data. Intervention studies must also be prospective.

B - Fair quality: Problems with study/paper unlikely to cause major bias. Intervention studies can also be either prospective or retrospective.

C - Poor quality: Prospective or retrospective. Cannot exclude possible significant biases. Poor methods, incomplete data, reporting errors.

^b Included participants with AUB presumed secondary to ovulatory (AUB-O) or endometrial dysfunction (AUB-E) and fibroids (AUB-L)

^c Medical therapy could include: combined oral contraceptive pills (38%), cyclic progestin (16%), continuous progestin (6%), Conjugated estrogen with progestin (25%), Conjugated estrogen alone (6%), 53% received a prostaglandin synthetase inhibitor, usually with a hormonal therapy

Table 2

Summary of data comparing ablation to hysterectomy

Outcome	Study, year	Length of Follow-up (months)	Ablation	Hysterectomy	SUMMARY OF FINDINGS
Bleeding control [7 studies, n=1167] Summary: Moderate quality evidence showed no difference; outcome of critical importance					
Amenorrhea ^a	Gannon 1991(17)	12	16/25 (64%)	Only measured in ablation arm	6 of 7 trials evaluated amenorrhea as an outcome in the ablation group. Amenorrhea rates ranged from 13–64% and hypomenorrhea rates ranged from 24–77%
	Dwyer 1993(18)	4	13/99 (13%)		
	Pinion 1994(20)	12	21/96 (22%)		
	Aberdeen 1999(22)	48	33/73 (45%)		
	Corsignani 1997(23)	24	8/41 (20%)		
	O'Connor 1997(26)	12	48/104(46%)		
Hypomenorrhea ^a	Dwyer 1993(18)	36	11/54 (21%)	Only measured in ablation arm	Proportion of patients with "excessive" bleeding appears greater in ablation group than the hysterectomy group, though statistical testing was not performed for this outcome
	Pinion 1994(20)	4	76/99 (77%)		
	Aberdeen 1999(22)	12	59/96 (61%)		
	Corsignani 1997(23)	48	29/73 (40%)		
"Excessive" bleeding ^a	Dickersin 2007(25)	24	10/41 (24%)		
Amount		12	10/107 (9%)	3/103 (3%)	
Unpredictability		48	7/47 (15%)	0/51 (0%)	
		12	6/107 (6%)	1/103 (1%)	
		48	5/47 (11%)	0/51 (0%)	
Duration		12	19/107 (18%)	1/103 (1%)	
		48	8/47 (17%)	0/51 (0%)	
Frequency		12	16/107 (15%)	2/103 (2%)	
		48	5/47 (11%)	0/51 (0%)	
Quality of Life [6 studies, n=1116] Summary: Moderate quality evidence showed no difference; outcome of critical importance					
SF-36 (Pain) ^b	Sculpher 1996(19)	33	73.2	83.1 ^c	No difference in SF-36 physical component, mental component, or emotional scores. No difference in EuroQol5D scores. Findings of some studies suggest greater SF-36 dimension scores for pain, general health, vitality, and social function for hysterectomy group compared to ablation group. Pinion found better health in the hysterectomy group 1 year post-operatively. Other studies found no difference in "General Health Questionnaire" score (Dwyer), Hospital
	Corsignani 1997(23)	24	69.6	75.9	
	Zupi 2003(24)	24	58.6	60.1	

Outcome	Study, year	Length of Follow-up (months)	Ablation	Hysterectomy	SUMMARY OF FINDINGS
SF-36 (General Health) ^b	Sculpher 1996(19)	33	74.4	79.7	
	Corsignani 1997(23)	24	61.3	71.2	
	Zupi 2003(24)	24	59.6	69.4 ^c	
SF-36 (Vitality) ^b	Sculpher 1996(19)	33	60.8	62.3	
	Corsignani 1997(23)	24	52.3	63.6 ^c	
SF-36(Social Function) ^b	Zupi 2003(24)	24	61.0	72.3	
	Sculpher 1996(19)	33	84.4	90.4	
	Corsignani 1997(23)	24	70.1	80.4 ^d	
Health much better compared to 1 year ago?	Zupi 2003(24)	24	67.3	88.5 ^c	
	Pinion 1994(20)	12	46/96 (48%)	65/89(73%) ^c	Anxiety and Depression Scores (Alexander).
Pain [5 studies, n=818] Summary: Low quality evidence favored hysterectomy; outcome of critical importance					
Improve Dysmenorrhea ^a	Dwyer 1993(18)	4	53/85 (62%)	81/84 (96%) ^e	Dickerson et al found a higher proportion in the ablation group reported "moderate/severe" pain 2 years post-operatively. Statistical testing was not performed for most comparisons, though it appears that more participants in the ablation groups than hysterectomy groups reported pelvic pain at follow-up.
Pelvic pain present ^a	Sculpher 1996(19)	33	46/72 (64%)	13/70 (19%) ^e	
	Aberdeen 1999(22)	48	14/77 (18%)	10/68 (15%)	
	Zupi 2003(24)	24	9/38 (24%)	2/39 (5%) ^e	
	Dickersin 2007(25)	24	30/106 (28%)	7/107(7%) ^c	
Sexual Health [5 studies, n=879] Summary: Low quality evidence showed no difference; outcome of high importance					
Return to sexual activity ^f	Dwyer 1993(18)	4	3 wks	6 wks ^c	Participants in the ablation group reported faster return to sexual activity. No differences in sexual satisfaction or sexual rating between groups.
	Zupi 2003(24)	24	3 wks	3 wks	
	O'Connor 1997(26)	24	4 wks	6 wks ^c	
Increased sexual satisfaction	Dwyer 1993(18)	4	19/85 (22%)	12/81 (15%)	
	Aberdeen 1999(22)	48	19/69 (28%)	22/69 (32%)	
Sexual Rating Scale ^g	Corsignani 1997(23)	24	44.8	48.5	
Satisfaction [5 studies, n=935] Summary: Very low quality evidence showed no difference; outcome of high importance					

Outcome	Study, year	Length of Follow-up (months)	Ablation	Hysterectomy	SUMMARY OF FINDINGS
Satisfied ^a	Sculpher 1996(19)	33	65/82 (79%)	69/73 (95%) ^c	The majority of participants randomized to either ablation or hysterectomy were satisfied. One study showed statistically greater satisfaction among the hysterectomy group compared to the ablation group.
	Aberdeen 1999(22)	48	69/73 (95%)	67/72 (93%)	
	Corsignani 1997(23)	24	33/38 (87%)	37/39 (95%)	
	Dickersin 2007(25)	48	53/107 (50%)	54/103 (52%)	
	O'Connor 1997(26)	12	90/104 (87%)	42/46 (91%)	
		24	74/86 (86%)	36/38 (94%)	
		36	46/54 (75%)	27/28 (96%)	
Additional Treatment [7 studies, n=1167] Summary: Moderate quality evidence favored hysterectomy; outcome of moderate importance					
Repeat ablation ^a	Sculpher 1996(19)	33	10/88 (11%)	N/A hyst arm	At 1–4 years post-operatively, 2–19% of the ablation groups had undergone repeat ablation.
	Gannon 1991(22)	12	4/25 (16%)		
	Aberdeen 1999(23)	48	19/102 (19%)		
	Dickersin 2007(25)	48	2/110 (2%)		
	O'Connor 1997(26)	24	14/119 (12%)		
		33	18/88 (20%)	N/A hyst arm	
Hysterectomy	Aberdeen 1999(22)	48	24/102 (24%)		At 1–4 years postoperatively, 10–29% of the ablation groups had undergone a hysterectomy.
	Corsignani 1997(23)	24	4/41 (10%)		
	Dickersin 2007(25)	48	32/110 (29%)		
	O'Connor 1997(26)	24	12/119 (10%)		
		24	12/89 (14%)	1/92 (1%)	
	Zupi 2003(24)	24			
"Further surgical needs"					

^a Results reported as proportion with the outcome

^b Results reported as score on the SF-36

^c Groups statistically different with a p-value less than or equal to 0.01

^d Groups statistically different with a p-value less than 0.05 but greater than 0.01

^e statistical testing of difference between groups not reported

^f Results reported as number of weeks between date of surgery and date of return to sexual activity

^g Results reported as Revised Sabbatsberg Sexual Rating Scale score

Table 3

Summary of data comparing LNG-IUS to hysterectomy. All data from one RCT (several publications) with a total of 236 participants.

Outcome	Study Year	Length of Follow-up (months)	LNG-IUS	Hysterectomy	SUMMARY OF RESULTS
Bleeding control					
Summary: Moderate quality evidence favored hysterectomy; outcome of critical importance					
Amenorrhea/oligomenorrhea ^a	Hurskainen 2004(29)	12	41/81 (51%)	Only measured LNG-IUS arm	Data were analyzed "as treated". Included only women with the LNG-IUS still in situ.
		60	43/57 (75%)		
Quality of life					
Summary: Moderate quality evidence showed no difference; outcome of critical importance					
Change in SF-36 score					
Physical Health	Hurskainen 2004(29)	60	-1.4	-2.0	No differences in change in any quality of life scores (pretreatment minus post-treatment) between LNG-IUS and hysterectomy groups
Mental Health			8.4	8.1	
Physical Role Function			8.9	8.9	
Pain			12.8	13.4	
General Health			3.6	4.4	
Vitality			9.4	10.0	
Social Function			8.7	9.0	
Emotional Role			16.2	12.9	
EuroQol-5D ^b	Hurskainen 2004(29)	60	0.08	0.10	
STAI ^c	Hurskainen 2004(29)	60	-2.4	1.9	
BDI ^d	Hurskainen 2004(29)	60	-1.2	-1.4	
Pain					
Summary: Moderate quality evidence showed no difference; outcome of critical importance					
Lower abdominal pain ^a	Heliövaara-Peippo 2009(31)	6	35/114 (31%)	19/103 (18%)	Greater proportion of LNG-IUS group with lower abdominal pain at 12 months. No difference in proportion with lower abdominal pain at 6 months and 5 years. No difference in back pain between groups at any time point.
		12	33/111 (30%)	15/108 (14%) ^e	
		60	18/116 (16%)	17/113 (15%)	
Back pain ^a	Heliövaara-Peippo 2009(31)	6	40/114 (35%)	31/104 (30%)	
		12	46/111 (41%)	32/109 (29%)	
		60	44/116 (38%)	41/113 (36%)	

Outcome	Study Year	Length of Follow-up (months)	LNG-IUS	Hysterectomy	SUMMARY OF RESULTS
Sexual Health					
Summary: Moderate quality evidence showed no difference; outcome of high importance					
McCoy Sex Scale Score ^g	Halmesmaki 2007(30)	6	23.87	24.51	Compared to hysterectomy, the LNG-IUS group reported more sexual problems at 6 months ($p=0.03$), however, this effect was not seen at 12 months or 5 years. No differences were found in sexual problems at other time points or in satisfaction scores at any time point.
		12	23.25	24.25	
		60	22.8	23.95 ^f	
Sexual problems ^h		6	4.25	3.83	
		12	4.2	4.1	
		60	4.48	4.38	
Satisfaction with partner ⁱ		6	16.23	16.47	
		12	15.95	16.62	
		60	15.95	16.62	
Satisfaction					
Summary: Moderate quality evidence showed no difference; outcome of high importance					
Very/mostly satisfied	Hurskainen 2004(29)	60	93%	94%	Both treatment options resulted in high satisfaction rates.
Additional Treatment					
Summary: Moderate quality evidence favored hysterectomy; outcome of moderate importance					
Hysterectomy	Hurskainen 2004(29)	12	24/119 (20%)	N/A	At 5 years post-randomization, 42% of patients in the LNG-IUS had undergone subsequent hysterectomy
		60	50/119 (42%)		

Note: LNG-IUS = Levonorgestrel IUS; SF-36 (Short-form 36)

^aResults reported as proportion with the outcome

^bEuroQol = European quality of life scale (Scale range 0–1) = higher scores indicate better function

^cSTAI = STAI (State-Trait Anxiety Inventory) = Spielberger and colleagues' 20-item state anxiety scale, ranging from 20 to 80. Higher scores indicate worse or more anxiety

^dBDI = BDI (Beck Depression Index) = Beck's depression inventory is a 13-item scale 0–39. Higher scores indicate worse or more depression

^eDifference between groups statistically significant with a p-value of 0.02

^fDifference between groups statistically significant with a p-value of 0.03

^gResults reported as score on the McCoy Sex Scale: This scale contains 3 subscales: sexual satisfaction (5 items; subscale range, 5–35), sexual problems (2 items; subscale range, 2–14), and participant satisfaction with the partner (3 items; subscale range, 3–21). McCoy Sex Scale Sexual satisfaction (subscale range 5–35) = higher scores indicate more satisfaction

^hResults reported as score on the sexual problems subscale of the McCoy Sex Scale: Sexual problems (subscale range 2–14) = higher scores indicate more symptoms/problems

ⁱResults reported as score on participant satisfaction with the partner subscale of the McCoy Sex Scale: Satisfaction with partner (subscale range 3–21) = higher scores indicate more satisfaction.

Table 4
Summary of data comparing medications to hysterectomy. All data from one RCT with a total of 63 participants.

Outcome	Study Year	Length of Follow-up (months)	Meds ^a	Hysterectomy ^a	SUMMARY OF RESULTS
Bleeding control					
Not reported					
Quality of life					
Summary: Low quality evidence showed no difference; outcome of critical importance					
Change in SF-36 score					No differences in change in any quality of life scores (pretreatment minus post-treatment) between medication and hysterectomy groups
Physical Health	Kuppermann 2004(33)	24	9	7	
Mental Health			4	7	
Pain					
Summary: Very low quality evidence showed no difference; outcome of critical importance					
Pelvic pain	Learman 2004(34)	24	-1.8	-2.2	No difference in pelvic pain and lower back pain between groups
Lower back pain			-1.3	-1.7	
Sexual Health					
Summary: Low quality evidence showed no difference; outcome of high importance					
Change in SF-36 score	Kuppermann 2004(33)	24	18	17	No difference in sexual satisfaction between groups
Sexual satisfaction					
Satisfaction					
Summary: Low quality evidence showed no difference; outcome of high importance					
Change in SF-36 score	Kuppermann 2004(33)	24	46	40	No difference in satisfaction with treatment between groups in intention to treat analyses.
Satisfaction with symptom level					
Additional Treatment					
Not assessed as an "outcome" for this study; therefore evidence profile not generated; outcome of moderate importance					
Hysterectomy	Kuppermann 2004(33)	24	17/32 (53%)	N/A	At 2 year follow-up, 53% of the group randomized to medication had undergone subsequent hysterectomy
Trachelectomy for persistent bleeding			N/A	1/31 (3.2%)	

^aNo differences were significant (P > 0.05)

Table 5

Adverse events for hysterectomy, ablation, LNG-IUS, and mediations

	Hyst ^a	Ablation	LNG-IUS	Meds
Total n	724	579	116	32
Number of studies	9	7	1	1
“Major” complications (number) ^b	57	7	1	0
Additional intra-operative procedures or urgent re-operation ^c	13 (1.8%)	6 (1%)	0	None reported
Cystotomy ^d	7 (1%)	0	0	
Ureteral injury	1 (0.1%)	0	0	
Bowel injury	2 (0.3%)	0	0	
Pelvic hematoma or vaginal vault hematoma	28 (3.9%)	1 (0.2%)	0	
“Cardiorespiratory event” ^e	3 (0.4%)	0	0	
Deep vein thrombosis or thromboembolism	0	0	1 (0.9%)	
“Thromboembolic event” ^e	2 (0.3%)	0	0	
Other ^f	1 (0.1%)	0	0	
“Minor” complications (number) ^b	225	69	0	0
Infection			No minor complications reported for LNG-IUS or medications	
Wound infection	46 (6.4%)	0		
Pelvic infection or cuff cellulitis ^g	25 (3.5%)	10 (1.7%)		
Febrile morbidity	37 (5.1%)	4 (0.7%)		
Other infection ^h	64 (8.8%)	18 (3.1%)		
Wound hematoma or wound rupture ⁱ	25 (3.5%)	5 (0.9%)		
Need for transfusion	17 (2.4%)	4 (0.7%)		
Re-admission not re-operation	4 (0.6%)	3 (0.5%)		
Uterine perforation	0	8 (1.4%)		
Fluid overload	0	23 (4.0%)		
Ileus or obstruction	5 (0.7%)	1 (0.2%)		
Non-urgent surgery presumed secondary to complications from initial procedure ^j	2 (0.3%)	1 (0.2%)		

^aNote: we included in the hysterectomy numbers the 50 patients in the LNG-IUS vs. hysterectomy studies (28–32) who were randomized to LNG-IUS and underwent subsequent hysterectomy because complications specifically after hysterectomy were presented. We did not include the 16 patients in the Learman study (33,34) who were randomized to medications and underwent subsequent hysterectomy in the hysterectomy numbers because whether or not they had complications secondary to hysterectomy was not specifically reported.

^bTotal number of major and minor complications given. Percent/proportion not presented because one patient could have multiple complications and this distinction was not clear in the papers. Dividing the number of major complications by the number of patients would provide an inflated complication rate.

^cIncluded unplanned intra-operative surgical procedures (not treatment failure) such as conversion to laparotomy if laparoscopic or vaginal hysterectomy, laparoscopy if vaginal hysterectomy, laparoscopy if ablation, hysterectomy if ablation, urgent post-operative laparotomy

^dCystotomy includes 1 vesicovaginal fistula (28–32)

^eNo deaths, MIs, stroke, pulmonary embolus, or admission to the ICU were specifically reported. One study reported 3 “cardiorespiratory events” and 2 “thromboembolic events” which were classified as such.(25)

^fOther – One study reported new onset seizures after surgery (34)

^gPelvic infection includes endometritis

^hOther infection included urinary tract infection, upper respiratory tract infection, peritonitis

ⁱWound hematoma or wound rupture includes “hematoma/seroma” and unspecified hematomas

^jNon-urgent surgery presumed secondary to complications from initial procedure – does not include “additional treatment” for AUB