

BMJ Open First and second-generation endometrial ablation devices: A network meta-analysis

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ABSTRACT

Objective First-generation and second-generation endometrial ablation (EA) techniques, along with medical treatment and invasive surgery, are considered successful lines of management for abnormal uterine bleeding (AUB). We set out to determine the efficacy of first and second-generation ablation techniques compared with medical treatment, invasive surgery and different modalities of the EA techniques themselves.

Design Systematic review and network meta-analysis using a frequentist network.

Data sources We searched Medline (Ovid), PubMed, ClinicalTrials.gov, Cochrane CENTRAL, Web of Science, EBSCO and Scopus for all published studies up to 1 March 2021 using relevant keywords.

Eligibility criteria We included all randomised controlled trials (RCTs) that compared premenopausal women with AUB receiving the intervention of second-generation EA techniques.

Data extraction and synthesis 49 high-quality RCTs with 8038 women were included. We extracted and pooled the data and then analysed to estimate the network meta-analysis models within a frequentist framework. We used the random-effects model of the netmeta package in R (V.3.6.1) and the 'Meta-Insight' website.

Results Our network meta-analysis showed many varying results according to specific outcomes. The uterine balloon ablation had significantly higher amenorrhoea rates than other techniques in both short (hydrothermal ablation (risk ratio (RR)=0.51, 95% CI 0.37; 0.72), microwave ablation (RR=0.43, 95% CI 0.31; 0.59), first-generation techniques (RR=0.44, 95% CI 0.33; 0.59), endometrial laser intrauterine therapy (RR=0.18, 95% CI 0.10; 0.32) and bipolar radio frequency treatments (RR=0.22, 95% CI 0.15; 0.31)) and long-term follow-up (microwave ablation (RR=0.11, 95% CI 0.01; 0.86), bipolar radio frequency ablation (RR=0.12, 95% CI 0.02; 0.90), first generation (RR=0.12, 95% CI 0.02; 0.90) and endometrial laser intrauterine thermal therapy (RR=0.04, 95% CI 0.01; 0.36)). When calculating efficacy based only on calculated bleeding scores, the highest scores were achieved by cryoablation systems (p-score=0.98).

Conclusion Most second-generation EA systems were superior to first-generation systems, and statistical superiority between devices depended on which characteristic was measured (secondary amenorrhoea rate, treatment of AUB, patient satisfaction or treatment

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ A strength of our study is that we used a network meta-analysis model constructed using a frequentist framework, so we were able to make many more head-to-head comparisons than the limited number of studies available would have otherwise allowed.
- ⇒ Another strength was our inclusion of only randomised controlled trials in this analysis, resulting in minimal epidemiological bias.
- ⇒ Another strength was the large number of outcomes used to compare the devices.
- ⇒ A limitation of our study was the difficulty of excluding menopausal and perimenopausal women from the analysis because of a lack of documentation or a consistent definition of these terms in some of the included studies.

of dysmenorrhoea). Although our study was limited by a paucity of data comparing large numbers of devices, we conclude that there is no evidence at this time that any one of the examined second-generation systems is clearly superior to all others.

INTRODUCTION

Abnormal uterine bleeding (AUB) refers to excessive, sustained or random bleeding from the uterus that occurs without systemic disease of haemostasis, intrauterine contraception, pregnancy or demonstrable pelvic pathology. It may be ovulatory or anovulatory.^{1 2} AUB is a common gynaecological condition affecting many premenopausal women, severely disrupting their physical, social and psychological quality of life.³ Annually, 1 in 20 women of reproductive age consults their gynaecologists concerning heavy menstrual bleeding (AUB).^{4 5} AUB accounts for over one-third of performed hysterectomies in North America and Europe yearly. In addition to hysterectomy, AUB may sometimes be treated medically or with less invasive surgical techniques.⁶



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Medical regimens are often considered the first-line approach for treating AUB, including hormonal (oestrogen or progesterone-based therapies) and non-hormonal treatments (tranexamic acid or non-steroidal anti-inflammatory drugs). Hormonal options may be oral contraceptives or intrauterine devices releasing levonorgestrel (Mirena). These therapies have the potential to decrease menstrual bleeding effectively.⁷ In women resistant to medical therapy, surgical procedures may provide alternative treatment options for managing AUB.⁸ The most common surgical techniques in women without a desire for future pregnancies are hysterectomy and endometrial ablation (EA).⁹

Hysterectomy is a major surgical procedure associated with high success rates in managing AUB and increased patient satisfaction. However, it has a significant surgical recovery, longer operating time and higher economic costs. As it involves the removal of the uterus, it may cause psychological distress to some women. Naturally, many patients seek less invasive approaches, and it is generally understood that these less invasive procedures may have a lower success rate.^{8–12} Consequently, many practitioners reserve hysterectomy for circumstances where other less invasive medical and surgical approaches have failed.¹³

EA is a minimally invasive surgical technique that is an efficacious substitute for hysterectomy in some women suffering from AUB.¹⁴ Currently, EA is broadly separated into two different generations. The first-generation endometrial ablative techniques are hysteroscopic methods, including rollerball ablation, laser ablation and transcervical resection of the endometrium. These techniques are effective but also require considerable hysteroscopic training and may involve a learning curve for a surgeon to reach the maximum results. Moreover, several studies have found that complications are more common with first-generation EA techniques, including uterine perforation, bleeding and water intoxication.^{15 16} Despite an increase in complications that seem mainly related to the hysteroscopic portion of the procedure, first-generation procedures overall have resulted in a notable decline in the number of performed hysterectomies. In a 1-year follow-up, they may have secondary amenorrhoea rates as high as 90%.¹⁷ Due to the complication rates and necessity for a high level of expertise, second-generation endometrial ablative techniques were developed and have largely been substituted over the last two decades as they preclude the use of hysteroscopy in expertise in this area. Second-generation techniques are also generally associated with quicker recovery and lower complication rates and can generally be performed under local anaesthesia in an office or surgery centre setting.^{18 19} The devices of second-generation endometrial ablative techniques can destroy the endometrium through different methods without needing a hysteroscopy. The most common three methods use high-temperature fluids within a balloon (Thermachoice and Cavaterm), bipolar radiofrequency electrical energy (Novasure)^{20 21} and application of microwave energy (Microsulis).¹⁵ Several studies report

satisfaction rates of up to 90% at 1 year following different second-generation devices, similar to first-generation results performed with hysteroscopy.^{21–26}

One very important question regarding second-generation techniques involves which techniques are more effective than others. A recent network meta-analysis showed that microwave and bipolar radiofrequency ablative devices are more effective in managing AUB than a thermal balloon or hydrothermal ablation.²⁷ Prior to this, other studies have revealed that bipolar radiofrequency electrical energy is superior to both thermal balloon and microwave ablation in terms of quality of life, patient satisfaction and the rate of amenorrhoea.^{28–30}

Despite these high levels of efficacy, studies consistently show that approximately 20% of patients receiving EA will ultimately require a hysterectomy to relieve their symptoms.¹³ Two recent meta-analyses of randomised clinical trials (RCTs) have reported that total hysterectomy was superior to EA regarding cost and clinical efficacy.^{31 32} In addition, the levonorgestrel intrauterine system also may have several advantages compared with EA, such as ease of installation by almost any practitioner and the fertility-sparing reversibility of the system.^{33 34} Recently, Beelen *et al* found the intrauterine levonorgestrel system resulted in a notable decline in blood loss in women with AUB.³⁵

The selection of the ideal EA system for optimal results continues to be a pressing subject in gynaecology. In addition, our authors noted a plethora of new data in recent years since the publication of the last meta-analysis on this topic. As a result, we sought to perform this systematic review and network meta-analysis, enrolling all studies comparing second-generation EA techniques with the first generation, medical therapy, surgical procedures and others to determine which technique can achieve more patient satisfaction and lower rates of amenorrhoea and bleeding.

METHODS

Patient and public involvement

Although we were influenced by the questions of our patients to theorise this analysis, no patients or members of the public were involved in the study.

We conducted our study in strict accordance with the Cochrane Handbook guidelines for systematic reviews of interventions. We reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and the extension for network meta-analyses.^{36 37} Although outcomes were formulated entirely prior to data extraction, no formal protocol was established for this study.

Search strategy and data collection

We conducted our search through electronic databases: Medline (PubMed), Cochrane CENTRAL, Web of Science, EBSCO and Scopus for all published studies up until 1 March 2021, using a mix of the following keywords and their synonyms: “Menorrhagia”, “uterine bleeding”,

“Endometrial Ablation”, “Thermal balloon” and “radio-frequency”. We also searched for any published results from ongoing studies on the ongoing trials registry of the US National Institutes of Health (<http://www.clinicaltrials.gov>). Our full search strategy can be found in online supplemental file 1.

Duplicates were removed using EndNote software, then all retrieved citations were assessed for eligibility through two steps: titles and abstracts and then full texts. Those that matched our criteria were included in our study. For other related documents, we manually screened the references of the included studies to search for additional qualifying studies.

SELECTION CRITERIA

To maximise the included sample size without affecting the quality of evidence provided by our research, we limited our analysis to RCTs. We included all studies that met the following criteria: population: premenopausal women with AUB; intervention: second-generation EA techniques; study design: RCTs; outcomes: rates of amenorrhoea, dysmenorrhoea, heavy bleeding, bleeding score and patient satisfaction. No restrictions for age, sex, site or publication date were applied. We excluded studies that included menopausal or perimenopausal women, cross-sectional studies, case reports, case series, non-English articles, reviews, editorials, letters and studies in which the full text was unavailable. We included all second-generation EA devices in our treatment network without merging into duplicate nodes. The decision to exclude non-English studies was based on the low number of non-English studies and the comparative quality of these studies when considered for inclusion.

Data extraction

We extracted the data related to the following:

1. Summary of the included studies, including inclusion criteria, follow-up duration, primary outcomes, study design, study groups and conclusion.
2. Baseline characteristics of the enrolled population, including sample size, age, pain score, bleeding score and body mass index.
3. Outcomes of interest including rates of amenorrhoea, dysmenorrhoea, heavy bleeding, patient satisfaction and bleeding score, defined as the amount and severity of menstrual blood loss measured through multiple scales such as a 5-point scale and pictorial blood loss assessment chart.
4. Quality assessment domains.

Two authors (GJM and AM) extracted data manually in duplicate, and a third author was assigned to resolve any discrepancies between the two datasets (SG).

Quality assessment

We used the Cochrane risk tool to assess the quality of included interventional studies. The tool is reported in Chapter 8.5 of the Cochrane Handbook for systematic

reviews of Interventions V.5.1.0. The tool consists of the following assessment items: sequence generation, allocation sequence concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and any other bias. Author judgements fall into three categories: low, unclear or high risk of bias for each item. We used the quality assessment table in part 2, Chapter 8.5 of the same book.³⁸

At least two authors (GJM, AM) were involved with the quality assessment to ensure an unbiased assessment. In the case of disagreements, an additional author (SG) was added to discuss the rating until a consensus could be reached.

Statistical analysis

Outcomes were considered short term if the follow-up period was less than 1 year and long term if more than 1 year. We compared second-generation techniques, surgery, medical treatment and first-generation techniques such as rollerball ablation, transcervical endometrial resection and endometrial laser ablation. We compared treatments for the indications of dysmenorrhoea and AUB, and compared bleeding score outcomes in addition to patient satisfaction as an outcome.

For dichotomous outcomes, a frequentist network meta-analysis was performed using the meta and netmeta packages of R software, V.3.6.1. and pooled as a risk ratio (RR) with 95% CIs. While for continuous outcomes, data were pooled as a standardised mean difference using Meta-Insight, a web-based tool for network meta-analysis powered by Rshiny, with all calculations performed using the R package netmeta (please see online supplemental files 2 and 3 for complete Netameta R Scripts for continuous and dichotomous outcomes). If the source study did not provide median values of continuous outcomes, instead of mean values, we used Wan *et al*'s method to convert median values to respective mean values.³⁹ Statistical heterogeneity between studies was assessed by the I^2 test and the p value of the X^2 test. The fixed-effects model was used for homogeneous outcomes, while the random-effects model was applied for heterogeneous outcomes. Network geometry was computer generated to be presented graphically. Nodes represent each treatment class included in this review. A solid line means a direct comparison, and line thickness represents the number of comparisons between nodes.

In the case of multiarm studies, we approached them by combining relevant groups and with careful attention paid to avoid double-counting of participants. We found that measurement scales between studies were universally compatible for all of our measured outcomes, with means or SDs used by all included studies. Also, to assess the inconsistency of the network, we obtained direct evidence from each pair of compared treatments using only those studies that directly compared the two individual treatments. We used a random-effects model (DerSimonian and Laird approach) for this purpose. Additionally, we

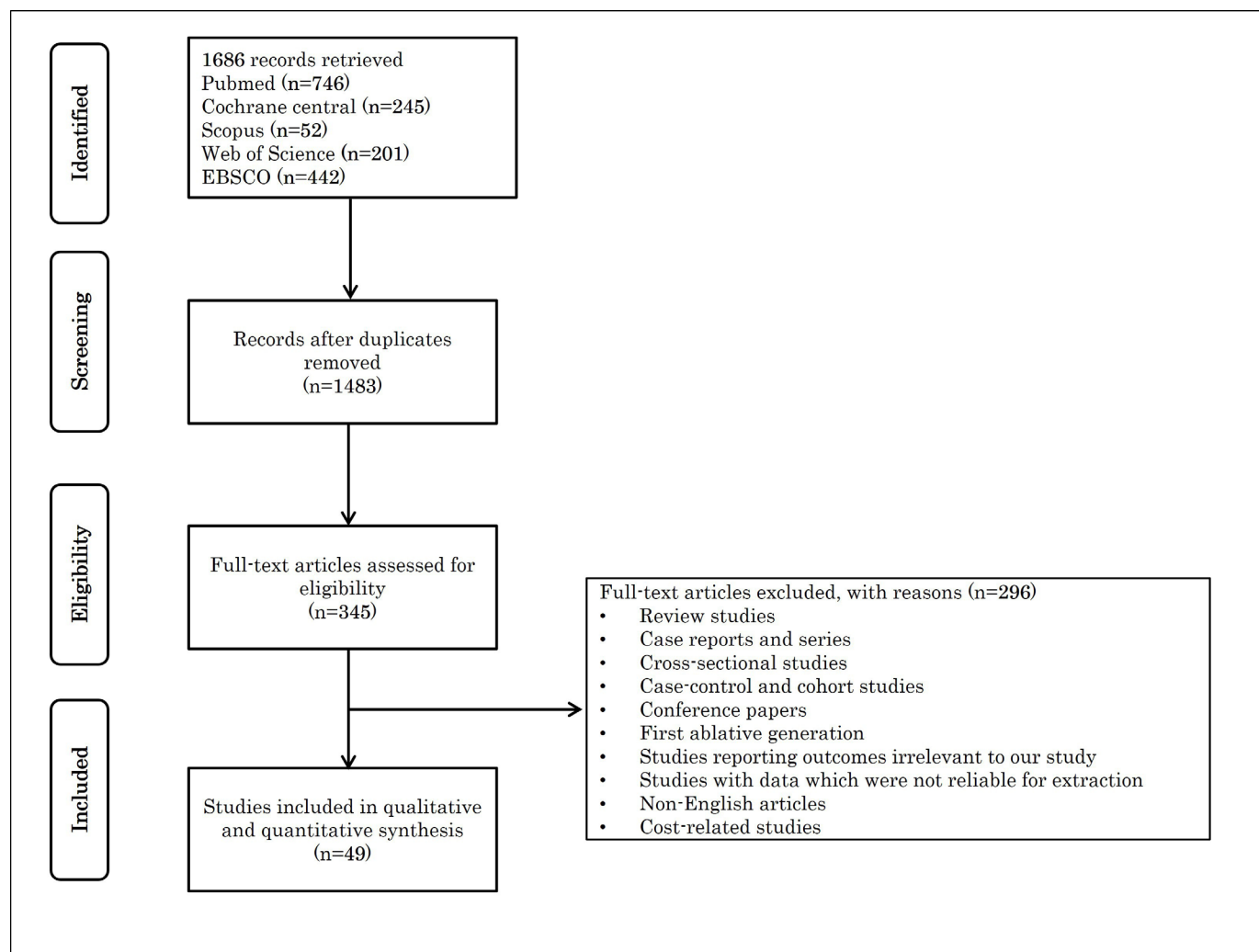


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

assessed the risk of publication bias using the Egger's test and funnel plots.

RESULTS

Literature search results

Our search retrieved 1686 citations through database searching. After removing the duplications, 1483 records were assessed for eligibility, and 1138 records were excluded by title or abstract screening. The remaining 345 were eligible for full-text screening. We finally included 49 RCT studies in our network meta-analysis.^{15 20 21 24 26 28 30 33 35 40–79} The flow of data collection and screening process is shown in [figure 1](#).

Summary of the included studies

We included 49 studies; 21 of these studies compared first-generation and second-generation techniques, 10 of these studies compared second-generation techniques and medical treatment, and 4 studies compared second-generation techniques and surgery. 17 studies compared outcomes only between different second-generation techniques. The total sample size was 8038 patients with mean

age ranging from 39.7 years to 49.5 years. The follow-up duration of the included studies ranged from less than 1 year to 10 years, although 1-year and 2-year follow-ups were the most frequent. Summaries of the included trials and baseline characteristics of their enrolled patients are shown in online supplemental tables 1 and 2, respectively. Furthermore, all the extracted datasets used for the meta-analysis have been provided in online supplemental file 4.

Quality assessment

A full description of the quality of assessments made for the included RCTs can be found in online supplemental table 3. The overall risk of bias was low for most studies, and no evidence for exclusion from the analysis because of high levels of bias was seen in any included trial.

Outcomes

Rate of amenorrhoea

In the short term, 40 datasets with 5588 patients were included. Compared with the first-generation techniques, the uterine balloon ablation techniques were statistically superior to some of the other modalities, such as hydro-thermal ablation (RR=0.51, 95% CI 0.37; 0.72), microwave

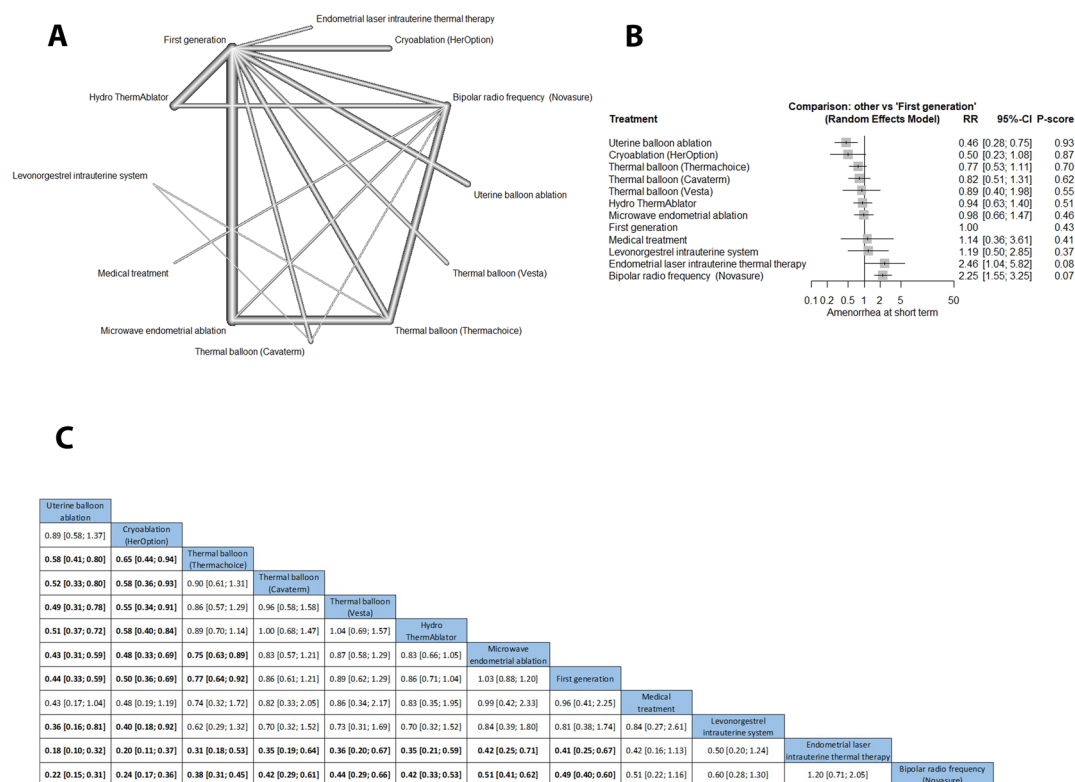


Figure 2 Network meta-analysis results of rate of amenorrhoea in short-term follow-up. (A) Network graph showing direct evidence between the assessed modalities. (B) A forest plot generated by comparing all modalities with the first-generation techniques; p-score used for ranking. (C) The league table represents the network meta-analysis estimates for all modalities comparisons, the results are relative risk (RR) with 95% CI, bold items are statistically significant.

ablation (RR=0.43, 95% CI 0.31; 0.59), first-generation techniques (RR=0.44, 95% CI 0.33; 0.59), endometrial laser intrauterine therapy (RR=0.18, 95% CI 0.10; 0.32) and bipolar radiofrequency treatments (RR=0.22, 95% CI 0.15; 0.31). The order of the modalities in terms of reducing the rate of amenorrhoea according to p-score was: uterine balloon ablation, cryoablation, dextrose solution balloon ablation, saline balloon ablation, multielectrode balloon ablation (Vesta), hydrothermal ablation, microwave ablation, first-generation ablation, medical treatment, the levonorgestrel intrauterine system, endometrial laser intrauterine thermal therapy, then bipolar radiofrequency ablation. Regarding head-to-head comparisons, uterine balloon ablation, endometrial cryoablation, dextrose solution balloon ablation, saline balloon ablation, hydrothermal ablation and first generation were significantly superior to endometrial laser intrauterine thermal therapy and bipolar radiofrequency ablation. Also, chemical ablation, multielectrode balloon ablation and microwave ablation were significantly superior to endometrial laser intrauterine thermal therapy and bipolar radiofrequency ablation, as shown in figure 2A–C. According to the Egger's test and by visual inspection of the funnel plot, there was no publication

bias ($p=0.9324$), as shown in online supplemental figure 1.

In the long term, 16 datasets with 2558 patients were included. Compared with the first-generation techniques, saline balloon uterine ablation was significantly superior to some of other modalities, such as microwave ablation (RR=0.11, 95% CI 0.01; 0.86), bipolar radiofrequency ablation (RR=0.12, 95% CI 0.02; 0.90), first generation (RR=0.12, 95% CI 0.02; 0.90) and endometrial laser intrauterine thermal therapy (RR=0.04, 95% CI 0.01; 0.36). The order of the modalities in terms of decreasing the rate of amenorrhoea in the long term according to p-score was: saline balloon uterine ablation, hydrothermal ablation, saline solution balloon ablation, the levonorgestrel intrauterine system, dextrose solution balloon ablation, bipolar radiofrequency ablation, microwave ablation, first-generation ablation techniques, then endometrial laser intrauterine thermal therapy. Regarding head-to-head comparisons, hydrothermal ablation was significantly superior to microwave ablation, bipolar radiofrequency ablation, first-generation ablation techniques and endometrial laser intrauterine thermal therapy. Also, all assessed modalities were significantly superior to endometrial laser intrauterine thermal

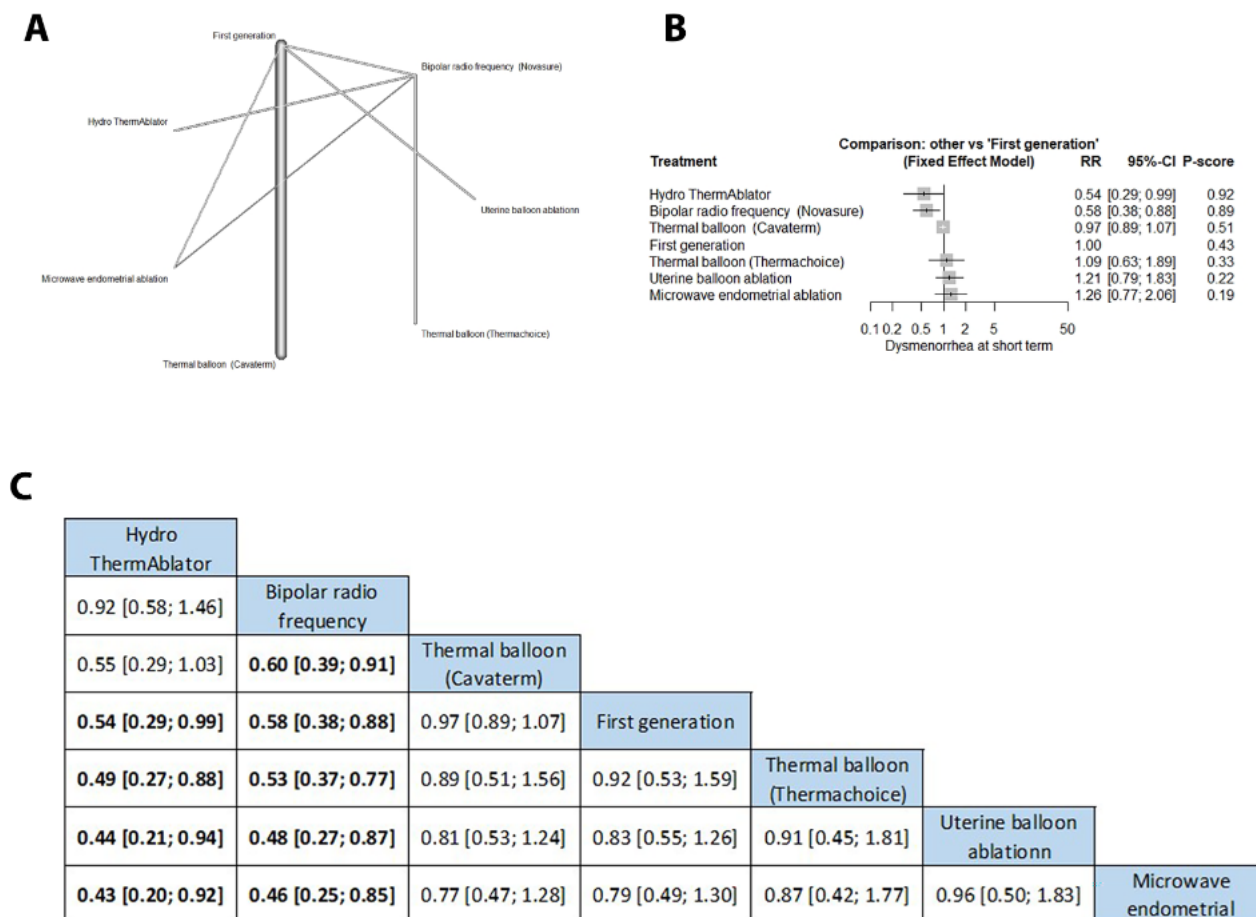


Figure 3 Network meta-analysis results of rate of dysmenorrhoea in short-term follow-up. (A) Network graph showing direct evidence between the assessed modalities. (B) A forest plot generated by comparing all modalities with the first-generation techniques; p-score used for ranking. (C) The league table represents the network meta-analysis estimates for all modalities comparisons, the results are relative risk (RR) with 95% CI, bold items are statistically significant.

therapy, as shown in online supplemental figure 2A–C. According to the Egger's test and by visual inspection of the funnel plot, there was no publication bias ($p=0.8195$), as shown in online supplemental figure 3.

Rate of dysmenorrhoea

In the short term, 15 datasets with 1864 patients were included. Compared with first-generation ablation techniques, hydrothermal ablation was significantly superior to some of the other modalities, including first-generation ablation techniques (RR=0.54, 95% CI 0.29; 0.99), dextrose solution balloon ablation (RR=0.49, 95% CI 0.27; 0.88), saline solution balloon ablation (RR=0.44, 95% CI 0.21; 0.94) and microwave ablation (RR=0.43, 95% CI 0.20; 0.92). The order of the modalities in terms of decreasing the rate of dysmenorrhoea according to p-score was: hydrothermal ablation, bipolar radiofrequency ablation, saline balloon ablation, first-generation ablation techniques, dextrose solution balloon ablation, uterine balloon ablation, then microwave ablation. Regarding head-to-head comparisons, bipolar radiofrequency ablation was significantly superior to saline balloon ablation, first-generation ablation techniques, dextrose solution balloon ablation, uterine balloon ablation and

microwave ablation, as shown in figure 3A–C. According to the Egger's test and by visual inspection of the funnel plot, there was no publication bias ($p=0.9694$), as shown in online supplemental figure 4.

Rates of AUB

In the short term, 27 datasets with 4594 patients were included. Compared with first-generation ablation techniques, saline balloon ablation was significantly superior to bipolar radiofrequency ablation (RR=0.45, 95% CI 0.21; 0.98). The order of the modalities in terms of decreasing the rate of AUB according to the p-score was: saline balloon ablation, dextrose solution balloon ablation, endometrial laser intrauterine thermal therapy, hydrothermal ablation, multielectrode balloon ablation, microwave ablation, endometrial laser ablation, first-generation ablation techniques, the levonorgestrel intrauterine system, bipolar radiofrequency ablation, uterine balloon ablation and finally endometrial cryoablation. Regarding head-to-head comparisons, dextrose solution balloon and hydrothermal ablation were significantly superior to first-generation ablation techniques, as seen in figure 4A–C. According to the Egger's test and by visual inspection of

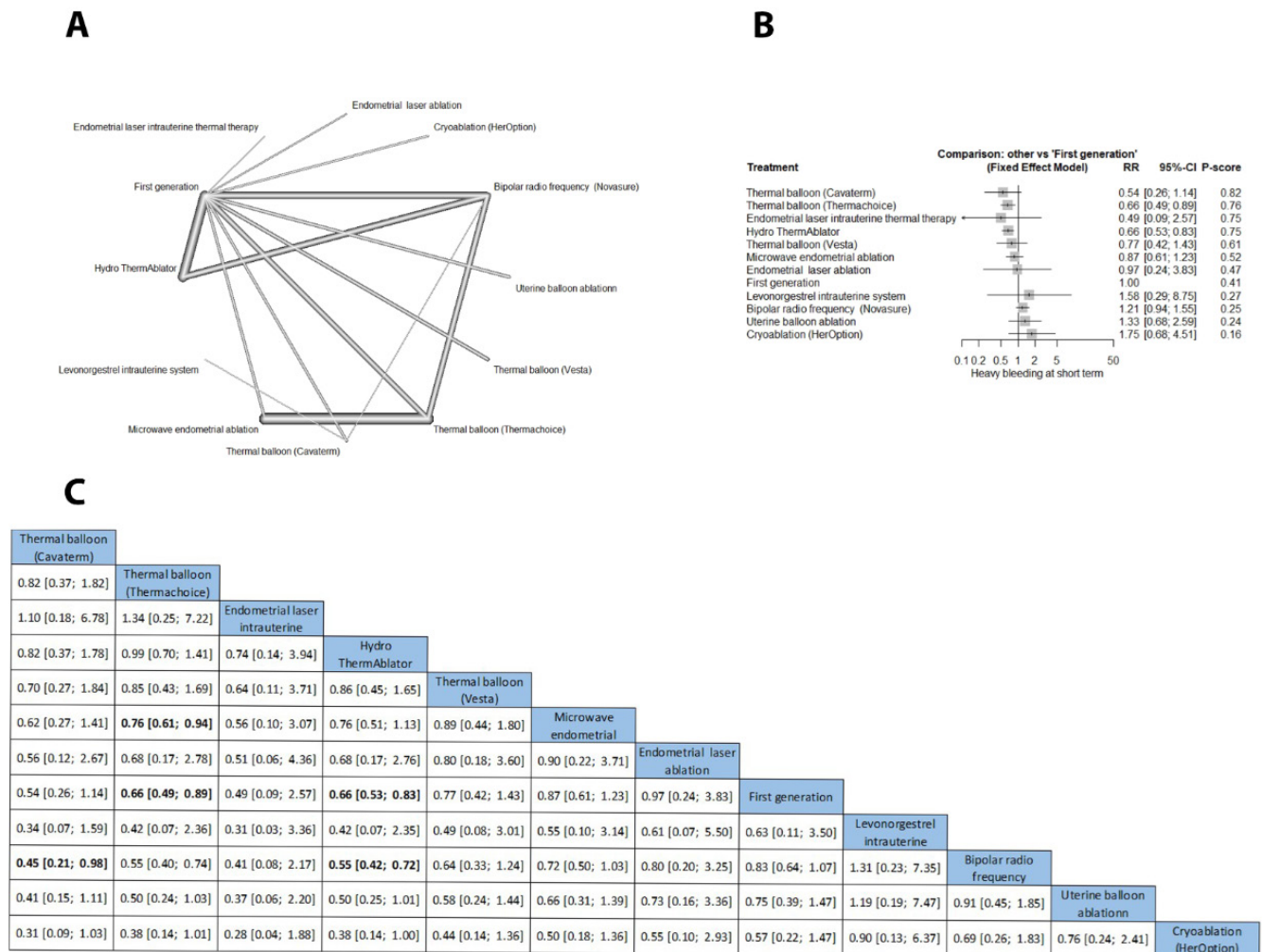


Figure 4 Network meta-analysis results of rate of abnormal uterine bleeding in short-term follow-up. (A) Network graph showing direct evidence between the assessed modalities. (B) A forest plot generated by comparing all modalities with the first-generation techniques; p-score used for ranking. (C) The league table represents the network meta-analysis estimates for all modalities comparisons, the results are relative risk (RR) with 95% CI, bold items are statistically significant.

the funnel plot, there was no publication bias ($p=0.9779$), as shown in online supplemental figure 5.

In the long term, eight datasets with 1586 patients were included. Hydrothermal ablation was significantly superior to some of the other modalities, such as first generation ($RR=0.41$, 95% CI 0.21; 0.81) and uterine balloon ablation ($RR=0.35$, 95% CI 0.14; 0.86). The order of the modalities in terms of decreasing the rate of heavy bleeding in the long term according to p-score was: hydrothermal ablation, endometrial laser intrauterine thermal therapy, microwave ablation, first-generation ablation techniques, then uterine balloon ablation, as seen in online supplemental figure 6A–C.

Rate of satisfaction

In the short term, 34 datasets with 4821 patients were included. Compared with first-generation ablation techniques, levonorgestrel intrauterine system and dextrose solution ablation techniques were significantly superior to most other modalities. The order

of the modalities in terms of decreasing the rate of satisfaction according to p-score was: the levonorgestrel intrauterine system, saline solution balloon ablation, uterine balloon ablation, microwave EA, hydrothermal ablation, endometrial laser ablation, first-generation ablation techniques, medical treatment, endometrial laser intrauterine thermal therapy, endometrial cryoablation, bipolar radiofrequency ablation, dextrose solution ablation, hysterectomy and hydrothermal ablation. Regarding head-to-head comparisons, uterine balloon ablation was significantly superior to dextrose solution and hydrothermal ablation, as seen in figure 5A–C. Also, microwave EA was superior to hydrothermal ablation. According to the Egger's test and by visual inspection of the funnel plot, there was no publication bias ($p=0.4874$), as shown in online supplemental figure 7.

In the long term, 17 datasets with 2829 patients were included. Compared with first-generation ablation

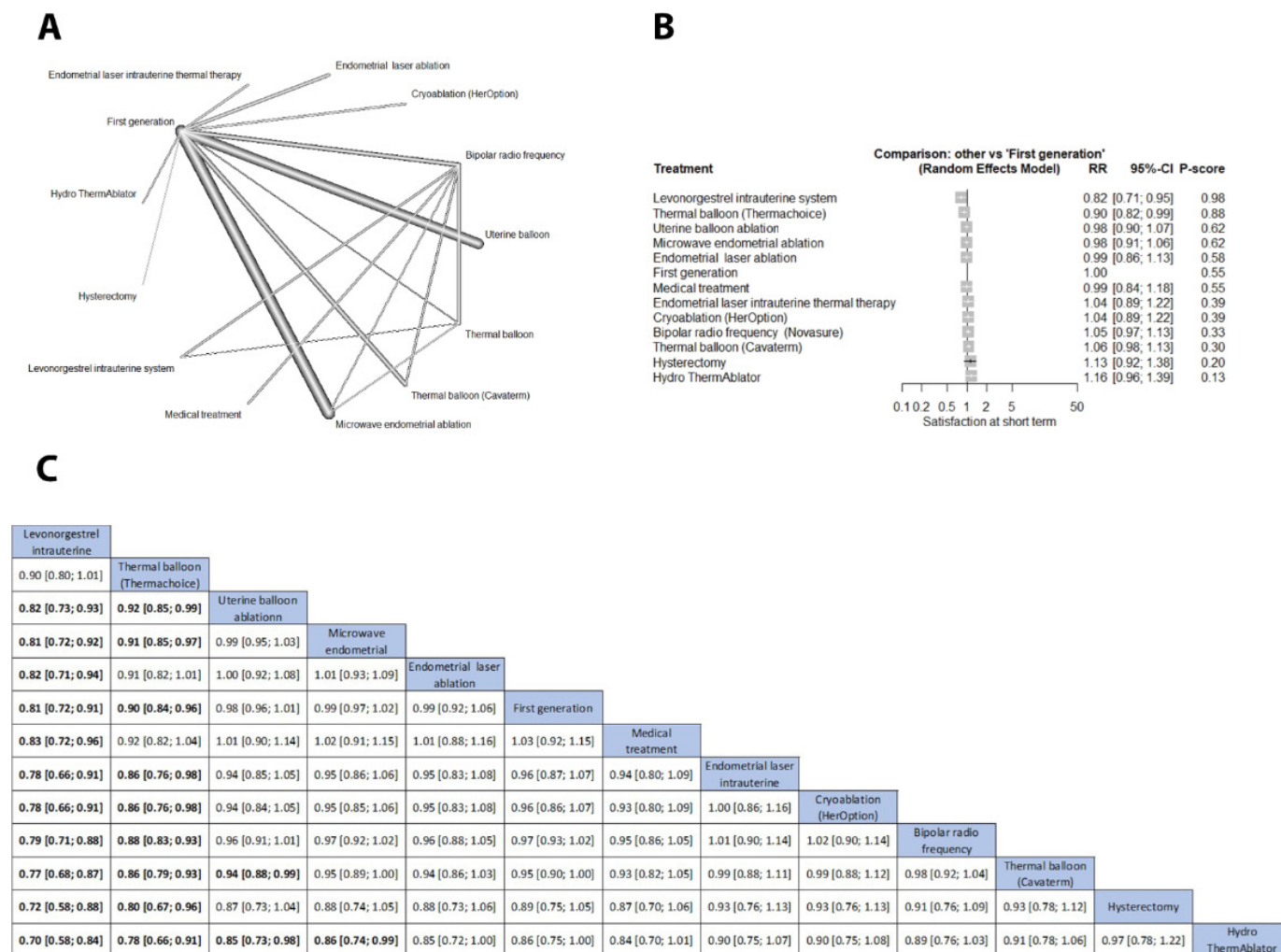


Figure 5 Network meta-analysis results of rate of patient satisfaction in short-term follow-up. (A) Network graph showing direct evidence between the assessed modalities. (B) A forest plot generated by comparing all modalities with the first-generation techniques; p-score used for ranking. (C) The league table represents the network meta-analysis estimates for all modalities comparisons, the results are relative risk (RR) with 95% CI, bold items are statistically significant.

techniques, the saline balloon ablation technique was significantly superior to all the other modalities. The order of the modalities in terms of decreasing the rate of satisfaction according to p-score was: saline balloon ablation, uterine balloon ablation, hydrothermal ablation, first-generation ablation techniques, endometrial laser intrauterine thermal therapy, hysterectomy, microwave EA, thermal ablation, levonorgestrel intrauterine system and bipolar radiofrequency. According to the Egger's test and by visual inspection of the funnel plot, there was no publication bias ($p=0.4596$), as shown in online supplemental figure 8.

Bleeding score

In the short term, 29 datasets with 4349 patients were included. Endometrial cryoablation was superior to all the other modalities except saline balloon ablation and microelectrode balloon ablation. The order of the modalities in terms of decreasing bleeding scores according to the p-score was cryoablation HerOption, saline balloon

ablation, thermal balloon ablation, bipolar radiofrequency, laparoscopic supracervical hysterectomy, dextrose solution balloon ablation, hydrothermal ablation, microwave EA, first-generation ablation and medical treatment, as shown in figure 6A–C.

DISCUSSION

We identified 49 interventional studies assessing the effect of second-generation techniques compared with first-generation ablation, medical treatment, surgery and the other second-generation modalities in 8038 women suffering from AUB.

Regarding amenorrhoea in the short term, the uterine solution balloon ablation showed significant superiority over other different treatment modalities in head-to-head and network analysis. This contradicts some previous analyses, such as Daniels *et al* in 2012,⁸⁰ who expressed higher rates of amenorrhoea with bipolar radiofrequency and microwave ablation techniques than thermal balloon

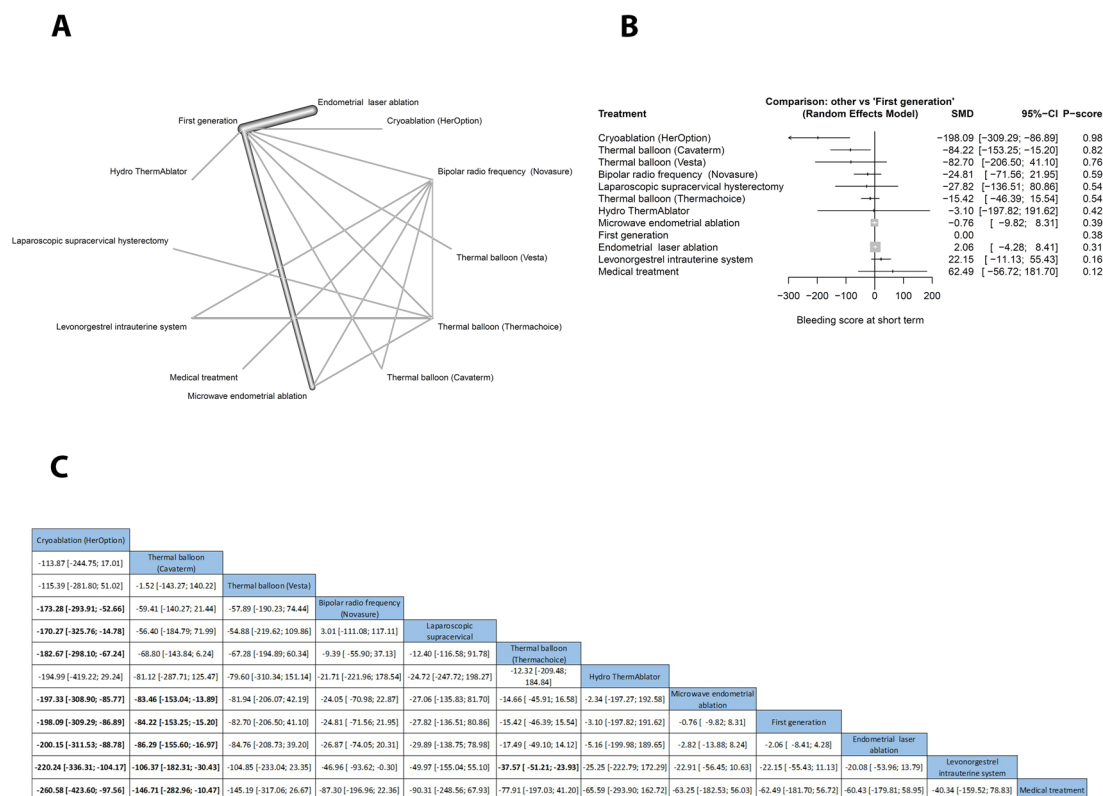


Figure 6 Network meta-analysis results of total bleeding score in short-term follow-up. (A) Network graph showing direct evidence between the assessed modalities. (B) A forest plot generated by comparing all modalities with the first-generation techniques; p-score used for ranking. (C) The league table represents the network meta-analysis estimates for all modalities comparisons, the results are standardised mean difference (SMD) with 95% CI, bold items are statistically significant.

ablation. In the long term, uterine balloon ablation was significantly superior to some other modalities in this network analysis. In contrast, hydrothermal ablation was significantly superior to others in head-to-head comparisons. This is consistent with recent analyses by Smith *et al* in 2014 and Clark *et al* in 2011, who found no significant difference between saline solution balloon ablation or bipolar radiofrequency in amenorrhoea rates at 6 months.^{79 81} These results also contradicted an earlier analysis that found bipolar radiofrequency EA superior to balloon EA and hydrothermal ablation, respectively.^{29 48} We found that endometrial laser intrauterine thermal therapy was one of the least advantageous techniques in both the short and long term when compared with other methods, saline solution balloon ablation, endometrial cryoablation, dextrose solution balloon ablation, uterine balloon ablation, hydrothermal ablation, first-generation ablation techniques chemical ablation, multielectrode balloon ablation and microwave ablation. Only one included study showed superior endometrial laser intrauterine thermal therapy results over other techniques reported here.⁸⁰

Hydrothermal ablation was significantly superior to other lines as first-generation ablation techniques

dextrose solution balloon ablation, uterine balloon ablation and microwave ablation, in terms of decreasing the rate of dysmenorrhoea in the short term. At the same time, bipolar radiofrequency (Novasure) was significantly superior to them in head-to-head comparisons. Bipolar radiofrequency ablation was more effective than saline solution balloon ablation in reducing dysmenorrhoea.⁴¹

Regarding heavy bleeding in only short-term follow-up, saline balloon ablation was more beneficial than bipolar radiofrequency ablation. In longer-term follow-up, hydrothermal ablation was significantly superior to first-generation and uterine balloon ablation.

Regarding patient satisfaction rates, we found hydrothermal ablation was significantly inferior to dextrose solution balloon ablation and the levonorgestrel intrauterine system, uterine balloon ablation and microwave ablation. This is similar to other studies that found that both bipolar radiofrequency ablation and uterine balloon ablation showed high satisfaction rates and low bleeding rates,⁴⁸ and that patients are generally more satisfied following bipolar radiofrequency ablation than hydrothermal ablation procedures.⁴⁹

Strengths and limitations

We aimed to generate direct and indirect high-quality evidence using network meta-analysis. We conducted an extensive literature search guided by the Cochrane Handbook of systematic reviews, including all RCTs that reported targeted study groups and outcomes, ensuring a large sample size. Despite these strong points, our limitations included a large number of included devices and procedures, many of which showed superiority in small areas, making clinical relevance difficult. In addition, although studies containing menopausal or perimenopausal women were excluded, not all studies specifically mentioned what definition of perimenopausal was used. As a result, some confounding errors from a perimenopausal population may limit the utility of our data. We would very much like to see more clinical trials with larger sample sizes and more detailed descriptions of the intervention techniques and clear protocols. We feel this would help to achieve clearer evidence in the field.

CONCLUSION

The overall risk of bias for our analysis was low, consistent with a moderate level of evidence for our findings. We found that most second-generation EA systems were superior to first-generation systems. Statistical superiority between devices depended on which characteristic was measured (secondary amenorrhoea rate, treatment of AUB, patient satisfaction or treatment of dysmenorrhoea). There is no evidence now that one second-generation system is superior or inferior to others.

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Contributors All authors listed attest to substantial contributions to the conception or design of the work; or the acquisition, analysis or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content. All authors listed have given final approval of the version to be published and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Planning and concept of the paper were mainly performed by GJM, AM and MG. Data extraction and tabulation were mainly performed by SG, AK, GB, HU, CM and JP. Analysis of data was performed mainly by GB, HU, JP, AA and CC. Analysis and interpretation were performed mainly by GJM, AM, AA, JP and AK. Final draft and discussion were performed mainly by CC, HU, GB and SG. Revisions were addressed by many authors but mainly GJM, AM and CM. GM is the author responsible for the overall content as the guarantor, and accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Patient consent for publication Not applicable.

Ethics approval Not applicable.

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