INPLASY

Impact of Uterine Artery Embolization on Subsequent Fertility Outcomes: A Meta-Analysis of 20 Years of Clinical Evidence

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 September 2025 and was last updated on 17 September 2025.

INTRODUCTION

Review question / Objective Uterine fibroids are the most common benign tumors of the uterus, affecting up to 70–80% of women by the age of 50, with a high incidence among women of reproductive age. Their impact on fertility is substantial, resulting from multiple mechanisms including distortion of the uterine cavity, impaired endometrial receptivity, abnormal implantation, and impaired uterine contractility during labor. Symptomatic fibroids have been consistently associated with reduced conception rates, increased pregnancy loss, and higher obstetric complication rates.

Traditional management of fibroids has relied heavily on surgical interventions such as myomectomy or hysterectomy. While hysterectomy completely eliminates reproductive potential, myomectomy carries its own surgical risks, including adhesion formation, uterine rupture in subsequent pregnancies, and the potential reduction of ovarian reserve. In this context, uterine artery embolization (UAE) has emerged since the 1990s as a minimally invasive alternative to surgical approaches. UAE offers significant advantages, including reduced morbidity, shorter recovery time, preservation of uterine architecture, and improved quality of life. Importantly, it has become increasingly appealing to women who desire fertility preservation.

However, the role of UAE in women wishing to conceive remains controversial. Concerns have been raised regarding the possibility of ovarian dysfunction due to non-target embolization, given the known anastomoses between uterine and ovarian circulations. Additional issues include potential endometrial damage, intrauterine adhesions, impaired placentation, and uncertainty regarding long-term reproductive outcomes. Interpretation of the existing evidence is further complicated by heterogeneity in study design,

variations in outcome definitions, limited follow-up durations, and differences in embolic agents and techniques used across studies.

With the increasing age at childbearing and growing demand for minimally invasive procedures, clarifying the reproductive outcomes of UAE is of high clinical relevance. Patients and clinicians alike require clear, evidence-based guidance to weigh the relative risks and benefits of UAE compared with myomectomy or other fertility-preserving options. Furthermore, as UAE has been increasingly utilized not only for fibroids but also for conditions such as adenomyosis and postpartum hemorrhage, understanding its fertility implications in diverse clinical scenarios is critical.

Objective of the Review:
The primary objective of this systematic review and meta-analysis is to evaluate the impact of uterine artery embolization on subsequent fertility outcomes in women with fibroids. Specifically, we aim to:

Assess rates of conception, live birth, and miscarriage following UAE.

Compare reproductive outcomes of UAE with those of myomectomy and other fertility-preserving treatments.

Evaluate obstetric outcomes, including placentation abnormalities, preterm birth, and obstetric complications.

Identify and summarize evidence on adverse reproductive sequelae, such as ovarian dysfunction, endometrial damage, and intrauterine adhesions.

Highlight gaps in the current literature and propose areas for further research to guide clinical decision-making.

Through this comprehensive synthesis, we seek to provide a balanced and evidence-based perspective on the role of UAE in women of reproductive age, supporting clinicians in counseling patients and guiding individualized treatment strategies.

Rationale Uterine fibroids represent the most frequent benign tumors of the female reproductive system, with a lifetime prevalence of 70–80% by the age of 50. Their impact on fertility is multifactorial: they can distort the uterine cavity, alter endometrial receptivity, interfere with implantation, and impair uterine contractility during labor. Women with symptomatic fibroids often experience reduced conception rates, higher pregnancy loss, and increased obstetric complications.

Conventional treatment has traditionally relied on surgical approaches, particularly myomectomy or hysterectomy. While myomectomy may preserve fertility, it carries risks such as postoperative adhesions, uterine rupture in subsequent pregnancies, and potential compromise of ovarian reserve. Hysterectomy, on the other hand, results in permanent infertility. These limitations underscore the need for fertility-preserving alternatives.

Uterine artery embolization (UAE) emerged in the 1990s as a minimally invasive, uterus-sparing technique. It involves selective catheterization and embolization of uterine arteries to induce ischemic necrosis of fibroid tissue while preserving the surrounding myometrium. UAE offers advantages such as shorter recovery, reduced morbidity, and preservation of uterine architecture, making it particularly attractive for women wishing to maintain fertility. However, concerns persist regarding its long-term reproductive impact.

The main apprehensions include potential ovarian dysfunction due to non-target embolization, formation of intrauterine synechiae, alterations in vascularization affecting implantation and placentation, and delayed conception compared to baseline populations. Furthermore, the evidence base is fragmented: studies differ in design, population characteristics, follow-up duration, and outcome definitions. Many are limited case series or retrospective cohorts, with few randomized controlled trials. Such heterogeneity makes it difficult to draw firm conclusions about the role of UAE in fertility preservation.

At the same time, clinical demand for minimally invasive treatments has grown, driven by the trend of delayed childbearing and the increasing expectation of uterus-preserving interventions. Counseling women about treatment options requires robust, evidence-based data comparing UAE with standard alternatives like myomectomy. Without reliable pooled evidence, clinicians face uncertainty in advising patients regarding conception rates, time to fertility recovery, and risks of complications.

This meta-analysis responds to the pressing clinical need for a comprehensive synthesis of 20 years of data on UAE and fertility. By pooling results across diverse populations and study

designs, the review aims to clarify: the likelihood of achieving pregnancy after UAE, the typical time frame to conception, the impact of patient characteristics (especially age), fibroid features, and technical factors on outcomes, and the relative effectiveness of UAE compared with myomectomy in fertility preservation.

Such evidence is crucial to guide individualized treatment planning. Younger women, particularly those under 35 with intramural or subserosal fibroids, may benefit most from UAE, while older patients or those with submucous fibroids may face lower fertility success. Identifying these subgroups can help clinicians recommend UAE appropriately and avoid unrealistic expectations.

In summary, the rationale for this review lies in bridging the current evidence gap. By systematically synthesizing data from observational studies and trials published over the past two decades, the review will provide the most reliable estimates to date of fertility outcomes following UAE. The results will directly support patient counseling, clinical decision-making, and the development of treatment algorithms that balance symptom control, reproductive goals, and long-term safety.

Condition being studied Uterine fibroids (leiomyomas) are the most common benign tumors of the female reproductive tract. They arise from the smooth muscle cells of the myometrium and are hormonally responsive, with growth stimulated primarily by estrogen and progesterone. By the age of 50, between 70% and 80% of women will have developed fibroids, with the highest prevalence during reproductive years. Although many fibroids remain asymptomatic, a significant proportion cause clinical manifestations that adversely affect quality of life and fertility.

Epidemiology and Clinical Burden

Fibroids are especially prevalent among women of reproductive age, often diagnosed during evaluation for abnormal uterine bleeding, pelvic pain, or infertility. Symptomatic fibroids may lead to menorrhagia, pelvic pressure, anemia, and bulk-related symptoms. In terms of reproduction, they are associated with decreased rates of natural conception, increased risk of miscarriage, pregnancy complications, and adverse obstetric outcomes. Their burden is not only medical but also psychosocial and economic, as they contribute to work absenteeism, health care costs, and impaired quality of life.

Pathophysiology and Impact on Fertility

The mechanism by which fibroids impair fertility is multifactorial. Mechanical distortion of the uterine cavity, particularly by submucous fibroids, disrupts implantation and embryo development. Intramural fibroids can alter uterine contractility and endometrial receptivity. In addition, vascular and hormonal alterations associated with fibroids may interfere with successful conception and pregnancy maintenance. Fibroids have also been linked with complications such as preterm delivery, malpresentation, postpartum hemorrhage, and cesarean section.

Conventional Treatment Options

Historically, the mainstay of management has been surgical intervention. Myomectomy removes fibroids while preserving the uterus and is often offered to women desiring fertility. However, it carries surgical risks such as adhesion formation, uterine rupture during pregnancy, and reduction of ovarian reserve. Hysterectomy, while definitive, eliminates reproductive potential entirely. Medical treatments, including gonadotropin-releasing hormone agonists and selective progesterone receptor modulators (e.g., ulipristal acetate), may provide temporary symptom relief but are limited by side effects, lack of long-term efficacy, and contraindications in women actively seeking pregnancy.

Emergence of Uterine Artery Embolization (UAE)

Introduced in the 1990s, UAE has become an established minimally invasive alternative for the treatment of symptomatic fibroids. It involves selective catheterization of the uterine arteries and embolization with particulate agents to induce ischemic necrosis of fibroid tissue, while preserving the surrounding myometrium via collateral circulation. UAE offers several advantages: shorter hospital stays, faster recovery, reduced morbidity, and preservation of the uterus. For these reasons, it is increasingly requested by women wishing to avoid surgery.

METHODS

Search strategy A rigorous and systematic search strategy was applied to identify all available evidence regarding fertility outcomes after uterine artery embolization (UAE) in women with symptomatic uterine fibroids. The review adhered strictly to the PRISMA 2020 reporting guidelines.

Databases and Information Sources

An extensive electronic literature search was conducted across multiple databases:
PubMed/MEDLINE
Embase
Cochrane Library (CENTRAL)

Web of Science
To maximize coverage, additional searches were performed in: MDPI Journals, Taylor & Francis, and CrossRef databases.
Grey literature was explored through: reference lists of relevant reviews and included studies, conference abstracts from major gynecological and interventional radiology meetings, institutional repositories where accessible.
All searches were completed in March 2025 and updated prior to final analysis. No geographical restrictions were applied.
Search Terms and Keywords
The search strategy combined both keywords and Medical Subject Headings (MeSH) terms to improve sensitivity and precision. Boolean operators (AND, OR) were applied to combine concepts. The primary search string included:
("uterine artery embolization" OR "UAE" OR "uterine fibroid embolization")
AND ("fertility" OR "pregnancy" OR "conception" OR "reproductive outcomes" OR "live birth" OR "time to pregnancy")
Additional synonyms for fibroids were included to ensure broader capture: "fibroid" OR "leiomyoma" OR "myoma" OR "uterine tumors"
An example of the MEDLINE search strategy: ("Uterine Artery Embolization"[Mesh] OR "uterine artery embolization" OR UAE OR "uterine fibroid embolization") AND ("Fertility"[Mesh] OR fertility OR "pregnancy outcome" OR "pregnancy rate" OR conception OR "live birth" OR "time to pregnancy" OR reproduction OR "obstetric outcome")
AND ("Fibroid" OR leiomyoma OR myoma OR "uterine neoplasm" OR "uterine tumor")
Filters: Publication date from Jan 2005 to Mar 2025, Humans, English
Search strategies were iteratively refined in collaboration with an experienced medical librarian to optimize sensitivity and specificity.
Time Frame. The review period covered January 2005 – March 2025. This interval was selected because:
1. It reflects the period of maturation of UAE techniques, including the introduction of improved embolic agents.
2. It ensures inclusion of studies with sufficient follow-up (≥6 months) to adequately assess fertility outcomes.
Language and Publication Filters. The review primarily included English-language publications, due to feasibility and resource constraints. Non-English articles identified during screening were documented but not included in the meta-analysis.
Eligibility Criteria
Inclusion criteria
Studies were considered eligible if they met the following requirements:
1. Reported fertility or pregnancy outcomes after UAE.
2. Included women with symptomatic uterine fibroids.
3. Follow-up period of at least 6 months post-procedure.
4. Clear definition of fertility-related outcomes (pregnancy rate, time to conception, live birth, infertility, sterility).
5. Published in peer-reviewed journals.
Exclusion criteria
Studies were excluded if they:
1. Focused on non-fibroid indications (e.g., postpartum hemorrhage, adenomyosis, malignancy).
2. Were case reports with fewer than 5 patients.
3. Provided insufficient fertility-related data for analysis.
4. Were duplicates or overlapping populations.
5. Were conference abstracts without full-text publication.
Screening and Study Selection
A two-stage screening process was applied:
1. Title and abstract screening: Two independent reviewers assessed all retrieved citations.
2. Full-text review: Potentially eligible studies were evaluated in detail.
Disagreements were resolved by discussion; if consensus was not reached, a third senior reviewer adjudicated.
Inter-rater reliability was quantified using the Cohen kappa statistic ($\kappa > 0.8$ = excellent agreement). Reference management software was used to track decisions, create an audit trail, and document reasons for exclusion.
Data Extraction
Standardized data collection forms were used. Extracted data included:
Study characteristics: year, country, design, sample size, follow-up duration.
Patient demographics: age, parity, prior fertility history, baseline infertility.
Fibroid characteristics: number, size, location, volume, and symptom profile.
Procedural details: unilateral vs bilateral UAE, embolic agent type, technical success.
Primary outcomes: pregnancy rates, time to conception, live birth rates.
Secondary outcomes: infertility and sterility rates, pregnancy complications (miscarriage, ectopic pregnancy, preterm birth, intrauterine growth restriction), obstetric outcomes (mode of delivery, placental abnormalities, postpartum hemorrhage), and use of assisted reproductive technologies.
Safety outcomes: post-embolization syndrome, ovarian dysfunction, uterine necrosis, adhesions, amenorrhea.

When studies reported cumulative pregnancy rates, data were extracted at each available time point to allow time-to-event analysis.
Quality Assessment
Risk of bias was independently assessed by two reviewers:
Observational studies: Newcastle-Ottawa Scale (NOS), with scores categorized as high (7–9), moderate (4–6), or low (1–3).
Randomized controlled trials (RCTs): Cochrane Risk of Bias 2 tool (RoB 2), assessing randomization, adherence to interventions, missing data, measurement of outcomes, and selective reporting.
Publication bias was evaluated through funnel plot asymmetry and Egger's regression test, provided ≥10 studies reported the outcome.

Participant or population This review focuses on women of reproductive age who underwent uterine artery embolization (UAE) for symptomatic uterine fibroids and for whom fertility-related outcomes were reported. The target population includes those who:
Were diagnosed with symptomatic uterine fibroids (e.g., abnormal uterine bleeding, bulk symptoms, pelvic pain, infertility).
Expressed an interest in preserving fertility or subsequently attempted conception after UAE.
Had a minimum of six months follow-up post-procedure to allow meaningful evaluation of reproductive outcomes.
Characteristics of participants addressed in the review:
1. Age groups
Women under 30 years
Women between 30–35 years
Women between 35–40 years
Women over 40 years
(Since age was shown to be a major determinant of fertility success after UAE.)
2. Fertility history
Nulliparous women with no prior pregnancies.
Women with prior successful pregnancies (secondary infertility).
Women with pre-existing infertility before UAE.
3. Fibroid characteristics
Varying number (single vs. multiple).
Different sizes (small 10 cm).
Different locations (subserosal, intramural, submucosal).
4. Procedural variations
Unilateral vs. bilateral UAE.
Different embolic agents (polyvinyl alcohol particles, tris-acryl microspheres, mixed).
5. Geographic and clinical settings
Studies included women from diverse backgrounds and countries (e.g., USA, France, Italy, Japan, South Korea, China, Brazil, Romania, UK).
Both single-center and multi-center cohorts were included.
Outcomes of interest in this population
Primary outcomes: pregnancy rates, live birth rates, and time to conception.
Secondary outcomes: infertility and sterility rates, pregnancy complications (miscarriage, ectopic pregnancy, preterm birth, intrauterine growth restriction), and obstetric outcomes (cesarean section, placenta-related complications, postpartum hemorrhage).
In summary, the review population consists of women of reproductive potential, treated with UAE for symptomatic uterine fibroids, and followed to assess fertility and obstetric outcomes. The findings are intended to guide clinicians and patients considering UAE as a fertility-preserving alternative to surgical management.

Intervention The intervention evaluated in this review is uterine artery embolization (UAE), a minimally invasive, uterus-preserving treatment for symptomatic uterine fibroids.
Description of the intervention
UAE is performed by selective catheterization of the uterine arteries under fluoroscopic guidance, followed by the injection of embolic particles to occlude arterial blood flow to the fibroids. This results in ischemic necrosis of fibroid tissue while preserving surrounding myometrium due to collateral circulation.
Procedural variations considered in the review
Because techniques and materials may influence reproductive outcomes, the following aspects were included:
1. Laterality of embolization
Bilateral UAE (standard practice, both uterine arteries targeted).
Unilateral UAE (applied in selected cases with dominant supply from one uterine artery; associated in some studies with better fertility outcomes).
2. Type of embolic agent
Polyvinyl alcohol (PVA) particles.
Tris-acryl gelatin microspheres.
Mixed agents or other newer embolic materials.
3. Technical considerations
Size and dose of particles used.
Fluoroscopy and procedure time.
Operator experience and institutional protocols.
Comparison to other interventions
Where available, studies directly comparing UAE with alternative fertility-preserving treatments were included, especially:
Myomectomy (abdominal, laparoscopic, or hysteroscopic).

Other minimally invasive approaches (e.g., high-intensity focused ultrasound), although data are limited.
Outcomes assessed in relation to the intervention
The review evaluates how UAE, as a fertility-preserving intervention, influences:
Pregnancy rates and time to conception.
Live birth rates and obstetric outcomes.
Rates of infertility and sterility post-intervention.
Procedure-related complications relevant to fertility (ovarian dysfunction, amenorrhea, uterine necrosis, adhesions).

Comparator In this review, the main comparator to uterine artery embolization (UAE) is myomectomy, which has traditionally been considered the gold-standard fertility-preserving surgical treatment for symptomatic uterine fibroids.
Description of comparator
Myomectomy involves the surgical removal of fibroids while preserving the uterus, performed through abdominal, laparoscopic, or hysteroscopic approaches depending on fibroid size, number, and location.
It is widely used in women desiring future fertility, with reported conception rates of 60–70% in published series.
However, it carries potential risks relevant to fertility, including adhesion formation, uterine rupture in subsequent pregnancies, and reduced ovarian reserve.
Other possible comparators (less frequent)
Although myomectomy is the primary comparator, some studies have also reported UAE in relation to:
Expectant management (women with untreated fibroids used as baseline fertility reference).
Medical therapies such as gonadotropin-releasing hormone (GnRH) agonists or ulipristal acetate. These are not definitive fertility-preserving strategies but may serve as secondary comparators.
High-intensity focused ultrasound (HIFU), a noninvasive technique, although limited evidence on fertility outcomes exists.
Rationale for comparator choice
Myomectomy remains the most relevant comparator because:
1. It is widely practiced in women desiring conception.
2. It directly addresses fibroids as the cause of infertility.
3. It provides higher reported pregnancy rates compared to UAE, though with greater surgical morbidity.
4. Both UAE and myomectomy are uterus-preserving interventions, making their comparison directly meaningful for reproductive outcomes.

Study designs to be included The review will include randomized controlled trials (RCTs), prospective and retrospective cohort studies, and systematic reviews/meta-analyses that report fertility outcomes after uterine artery embolization in women with symptomatic fibroids. Case series with ≥5 patients may be considered if they provide relevant reproductive data. Case reports, non-fibroid indications, and studies with insufficient follow-up or incomplete fertility outcomes will be excluded.

Eligibility criteria In addition to the PICOS framework, the following criteria were applied:
Inclusion criteria
Studies reporting fertility or pregnancy outcomes after UAE in women with symptomatic fibroids.
Minimum follow-up of 6 months post-intervention.
Clear definition of reproductive outcomes (e.g., pregnancy rate, live birth, time to conception).
Published in peer-reviewed journals.
Case series with ≥5 patients included if relevant fertility data were available.
Exclusion criteria
UAE performed for non-fibroid indications (e.g., postpartum hemorrhage, adenomyosis, malignancy).
Case reports (<5 patients) or conference abstracts without full publication.
Studies with duplicate populations (in such cases, the most complete dataset was used).
Insufficient fertility-related data or unclear outcome definitions.
Publications in languages other than English, due to feasibility constraints.

Information sources To ensure a comprehensive evidence base, multiple information sources will be consulted for this review.

1. Electronic Databases
A systematic search will be conducted across the following major databases:

PubMed/MEDLINE – for biomedical and clinical research.

Embase – to capture additional European and pharmacological literature not indexed in MEDLINE.

Cochrane Library (CENTRAL) – for controlled trials and systematic reviews.

Web of Science – for broader coverage and citation tracking.
These databases were chosen to maximize sensitivity and specificity, ensuring retrieval of both

clinical and methodological studies on uterine artery embolization (UAE) and fertility outcomes.

2. Supplementary Databases and Publishers
To broaden the search, targeted databases such as MDPI Journals, Taylor & Francis Online, and CrossRef will also be screened. These sources include both peer-reviewed articles and early online publications that may not yet appear in traditional databases.

3. Grey Literature
To reduce the risk of publication bias, grey literature sources will be considered:

Conference abstracts from major gynecological and interventional radiology meetings.

Reference lists of included studies and related reviews.

Institutional repositories and dissertations, where available.
These searches aim to identify studies not formally published in peer-reviewed journals but potentially containing relevant outcome data.

4. Trial Registers
Registries such as ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), and the EU Clinical Trials Register will be consulted to identify ongoing or unpublished trials addressing UAE and fertility. Trial records may provide insights into emerging evidence and reduce selective reporting bias.

5. Contact with Study Authors
Where outcome data are incomplete, ambiguous, or unavailable, efforts will be made to contact corresponding authors directly to obtain additional details, clarifications, or unpublished results. This step is particularly relevant for studies with limited reporting of pregnancy or live birth outcomes.

6. Expert Consultation
An experienced medical librarian will support the development and refinement of the search strategy, ensuring the use of appropriate Boolean operators, keywords, and MeSH terms. Additionally, consultation with clinical experts in gynecology and interventional radiology will help confirm the comprehensiveness of the strategy.

Timeframe
The search will cover studies published between January 2005 and March 2025, reflecting the period of maturation of UAE techniques and sufficient follow-up for fertility assessment.

Language
Due to resource limitations, only English-language publications will be included. Non-English studies will be documented but excluded from final synthesis.

Main outcome(s) The primary outcomes of this review are focused on fertility and reproductive success following uterine artery embolization (UAE) for symptomatic fibroids:

1. Pregnancy rate – proportion of women achieving pregnancy after UAE, reported as pooled percentages with 95% confidence intervals.

2. Time to conception – mean or median interval (in months) from UAE to confirmed pregnancy, assessed through time-to-event analysis when possible.

3. Live birth rate – proportion of achieved pregnancies resulting in live delivery, distinguished from overall pregnancy rates to account for losses.

Secondary outcomes include:

Infertility rate – inability to conceive after ≥12 months of unprotected intercourse post-UAE.

Sterility rate – permanent reproductive failure (e.g., ovarian insufficiency, amenorrhea >24 months).

Pregnancy complications – miscarriage, ectopic pregnancy, preterm delivery, intrauterine growth restriction.

Obstetric outcomes – mode of delivery (vaginal, cesarean), placental abnormalities (placenta accreta, previa), postpartum hemorrhage, maternal morbidity.

Use of assisted reproductive technologies (ART) – frequency of IVF or other ART required to achieve pregnancy after UAE.

Safety outcomes – ovarian dysfunction, uterine necrosis, intrauterine adhesions, and long-term amenorrhea.

Timing of assessment

Outcomes will be evaluated at the longest reported follow-up for each study (minimum 6 months post-procedure).

Time-dependent measures (e.g., conception, live birth) will be analyzed based on available data points across different follow-up intervals.

Effect measures

Dichotomous outcomes (e.g., pregnancy, live birth, miscarriage) will be expressed as risk ratios (RR) or odds ratios (OR) with 95% CI.

Continuous outcomes (e.g., time to conception) will be reported as mean differences (MD) or standardized mean differences (SMD).

Time-to-event outcomes will be summarized using hazard ratios (HR) where available.

Additional outcome(s) Beyond the core fertility and obstetric outcomes, this review will also examine a set of additional outcomes that provide further context for the reproductive and clinical safety profile of uterine artery embolization (UAE).

1. Procedure-related outcomes

Technical success rate of UAE, defined as effective embolization with adequate occlusion of target vessels.

Repeat intervention rates, including need for repeat UAE or subsequent myomectomy/hysterectomy due to persistent or recurrent fibroid symptoms.

Symptom relief and quality of life, where reported, as improved symptom control may indirectly influence fertility planning.

2. Long-term reproductive health

Menstrual cycle patterns, including resumption or alteration of regular menses post-UAE.

Incidence of premature ovarian insufficiency or diminished ovarian reserve, assessed by hormonal or imaging markers.

Amenorrhea (>6 months), temporary or permanent.

3. Maternal and neonatal outcomes

Maternal morbidity during pregnancy and delivery, including uterine rupture, abnormal placentation, or severe postpartum hemorrhage.

Neonatal outcomes, such as birth weight, Apgar scores, and admission to neonatal intensive care, where data are available.

4. Comparative outcomes with alternative treatments

Where studies compare UAE with myomectomy or other fertility-preserving treatments, relative differences in conception, obstetric complications, and maternal morbidity will be summarized.

Timing and effect measures
Additional outcomes will be analyzed at the longest available follow-up, with dichotomous variables reported as risk ratios (RR) or odds ratios (OR), and continuous variables as mean differences (MD) or standardized mean differences (SMD).

These additional outcomes provide a broader evaluation of the safety, durability, and overall reproductive impact of UAE, complementing the primary fertility-focused measures.

Data management To ensure transparency, reproducibility, and accuracy, a structured system will be used for managing records and extracted data throughout the review process.

1. Reference Management
All records retrieved from electronic databases (PubMed, Embase, Cochrane, Web of Science, etc.) will be imported into reference management software (EndNote/Zotero). Duplicate records will be automatically identified and removed, followed by manual verification. Each citation will be assigned a unique identifier to allow consistent tracking throughout the screening and data extraction stages.

2. Screening Process
The screening will be conducted in two stages using Rayyan or Covidence software:

Title/abstract screening: performed independently by two reviewers according to predefined eligibility criteria.

Full-text screening: potentially relevant articles will be uploaded and assessed independently by two reviewers.

Disagreements will be resolved by consensus or adjudication by a third reviewer. Screening decisions and reasons for exclusion will be logged to generate a transparent PRISMA flow diagram.

3. Data Extraction

A standardized data extraction form (created in Excel or Covidence) will be piloted and refined. Extracted variables will include:

Study characteristics (author, year, country, design).

Population details (sample size, age, parity, fibroid features).

Intervention details (UAE technique, embolic agent, laterality).

Comparator information (e.g., myomectomy).

Outcomes (pregnancy rate, time to conception, live birth, infertility, obstetric complications, adverse events).

Two reviewers will independently extract data; discrepancies will be resolved by discussion or third-party arbitration.

4. Data Storage and Security
All extracted data and analysis files will be stored in a secure, backed-up institutional cloud server with restricted access. Version control will be maintained to ensure auditability of any changes.

5. Data Synthesis Preparation
Final cleaned datasets will be formatted for meta-analysis software (Review Manager 5.4 and Stata 17.0). Any missing or unclear outcome data will be addressed by contacting study authors directly.

Quality assessment / Risk of bias analysis To ensure validity and minimize bias, the methodological quality of all included studies will be systematically evaluated using validated tools appropriate for their design.

1. Observational Studies
Most studies addressing fertility after UAE are prospective or retrospective cohorts. For these, the Newcastle-Ottawa Scale (NOS) will be applied. The NOS evaluates three domains:

Selection (representativeness of cohorts, ascertainment of exposure, and outcome at baseline).

Comparability (control for confounders such as age, prior fertility history, fibroid type).

Outcome (assessment method, adequacy of follow-up, loss to follow-up rates).

Scores range from 0 to 9 stars, with 7–9 considered high quality, 4–6 moderate quality, and ≤3 low quality.

2. Randomized Controlled Trials (RCTs)
For RCTs, the Cochrane Risk of Bias 2 (RoB 2) tool will be used. It covers five domains:

Randomization process.

Deviations from intended interventions.

Missing outcome data.

Measurement of outcomes.

Selection of reported results.

Each domain will be rated as “low risk,” “some concerns,” or “high risk of bias.”

3. Systematic Reviews/Meta-analyses
If secondary reviews are included, their quality will be assessed with AMSTAR-2 (A MeaSurement Tool to Assess Systematic Reviews), focusing on methodological rigor and reporting transparency.

4. Process
Two reviewers will independently conduct all assessments. Discrepancies will be resolved through discussion or consultation with a third reviewer. Results will be tabulated, and quality grading will be incorporated into sensitivity and subgroup analyses to evaluate the robustness of findings.

5. Assessment of Publication Bias
When at least 10 studies contribute to an outcome, funnel plot asymmetry will be visually inspected. In addition, Egger’s regression test will be performed to statistically assess small-study effects and reporting bias.

6. Integration with Analysis
Quality ratings will inform interpretation of pooled estimates. Sensitivity analyses excluding low-quality studies (NOS <4 or high risk on RoB 2) will be conducted to test stability of results.

Strategy of data synthesis The analysis will combine quantitative meta-analysis with narrative synthesis to provide a comprehensive evaluation of fertility outcomes after uterine artery embolization (UAE).

1. Data Preparation
Extracted data will be cleaned and standardized before pooling. Pregnancy rates, live births, time to

conception, infertility, and obstetric complications will be prioritized. Continuous outcomes (e.g., time to conception) will be converted into means with standard deviations, and dichotomous outcomes (e.g., pregnancy achieved vs. not achieved) into event rates. When studies report cumulative outcomes, the longest available follow-up will be used.

2. Effect Measures

Dichotomous outcomes (pregnancy, live birth, miscarriage, complications) will be expressed as risk ratios (RR) or odds ratios (OR) with 95% confidence intervals (CI).

Continuous outcomes (e.g., time to conception) will be summarized as mean differences (MD) or standardized mean differences (SMD) depending on measurement scales.

Time-to-event outcomes will be analyzed using hazard ratios (HR) when sufficient data are reported.

3. Statistical Models
Meta-analysis will be conducted using Review Manager (RevMan 5.4) and Stata 17.0.

A random-effects model (DerSimonian-Laird method) will be used where moderate or high heterogeneity is expected (I^2 ≥25%).

A fixed-effects model will be applied only when heterogeneity is minimal (I^2 <25%).

4. Assessment of Heterogeneity
Heterogeneity will be quantified using:

I^2 statistic (25%, 50%, and 75% thresholds for low, moderate, high heterogeneity).

Chi-square test (p <0.10 considered significant due to low power).

Tau^2 estimates for between-study variance.
Sources of heterogeneity will be explored through subgroup analyses.

5. Subgroup Analyses
Where data permit, subgroup analyses will be performed by:

Age groups (40 years).

Fibroid characteristics (size, number, location).

Procedure details (unilateral vs. bilateral UAE, embolic agent type).

Study design (prospective vs. retrospective, single vs. multicenter).

6. Sensitivity Analyses
To test robustness, analyses will be repeated excluding:

Studies with high risk of bias (NOS <4, RoB 2 “high risk”).

Studies with <12 months follow-up.

7. Publication Bias
Assessed visually by funnel plot asymmetry and statistically with Egger’s regression test where ≥10 studies contribute to an outcome.

8. Narrative Synthesis
For outcomes not amenable to pooling a structured narrative summary will be provided, highlighting patterns across studies and methodological quality.

Subgroup analysis To explore sources of heterogeneity and identify patient or procedural factors that influence reproductive outcomes after uterine artery embolization (UAE), pre-specified subgroup analyses will be conducted where sufficient data are available.

1. Age of Participants
Age is one of the strongest predictors of fertility. Subgroups will include:

40 years
Outcomes of interest will include pregnancy rate, time to conception, and live birth rate.

2. Fibroid Characteristics
Fertility outcomes may vary according to fibroid burden and location. Subgroups will include:

Size: 10 cm.

Number: single vs. multiple fibroids.

Location: submucosal, intramural, subserosal.

3. Procedural Factors
Technical differences in UAE can affect fertility preservation. Subgroups will include:

Laterality: unilateral vs. bilateral UAE.

Embolic agent: polyvinyl alcohol (PVA) particles, tris-acryl gelatin microspheres, or mixed/other agents.

Operator experience: high-volume vs. low-volume centers, where reported.

4. Reproductive History

Nulliparous women vs. women with prior successful pregnancies.

Primary infertility vs. secondary infertility.

5. Study Design and Quality

Prospective vs. retrospective cohorts.

Randomized controlled trials vs. observational studies.

High-quality (NOS ≥7 or RoB 2 low risk) vs. moderate/low-quality studies.

Effect Measures in Subgroups
Comparisons will be expressed as risk ratios (RR), odds ratios (OR), mean differences (MD), or hazard ratios (HR), depending on outcome type. Interaction tests will be used to assess whether differences between subgroups are statistically significant.

Interpretation
Subgroup analyses will help identify which patients are most likely to benefit from UAE in terms of fertility preservation and which procedural approaches may optimize reproductive outcomes. Findings will be interpreted cautiously, as subgroup analyses are exploratory and subject to reduced statistical power.

Sensitivity analysis Sensitivity analyses will be performed to evaluate the robustness and reliability of the findings in this review. These analyses are designed to test whether pooled results remain consistent when key methodological decisions or study characteristics are varied.

1. Study Quality

Studies judged to be at high risk of bias (Newcastle-Ottawa Scale <4 for observational studies or "high risk" on RoB 2 for RCTs) will be excluded, and results will be reanalyzed.

The impact of including vs. excluding moderate-quality studies will also be examined to assess whether overall conclusions are driven by lower-quality evidence.

2. Follow-up Duration

Only studies with a minimum follow-up of 12 months will be analyzed separately.

This will help determine whether shorter follow-up periods overestimate or underestimate fertility outcomes, particularly live birth and time-to-conception rates.

3. Study Size

Small studies (<50 participants) may inflate effect estimates due to limited power or selective reporting.

Analyses will be repeated excluding small studies to test for stability of pooled estimates.

4. Publication Type

Analyses will be repeated after excluding conference abstracts, dissertations, or grey literature, ensuring findings are not disproportionately influenced by unpublished or non-peer-reviewed data.

5. Statistical Models

Both fixed-effect and random-effects models will be applied to key outcomes (pregnancy rate, live birth rate).

Differences in pooled results will be documented, helping to assess the impact of heterogeneity assumptions.

6. Comparative Studies Only

Where possible, analyses will be repeated including only studies directly comparing UAE with myomectomy or other interventions.

This will test whether indirect, single-arm studies alter the magnitude of effect.

7. Outcome Definition Variability

Because studies may define fertility outcomes differently (e.g., clinical pregnancy confirmed by ultrasound vs. self-reported conception), analyses will be repeated excluding studies with unclear or non-standardized definitions.

Interpretation
If sensitivity analyses yield results consistent with the primary analyses, confidence in the robustness of findings will increase. Conversely, if significant variation is observed, potential explanations (e.g., methodological weaknesses, population differences, heterogeneity of interventions) will be discussed.

These steps ensure that the review's conclusions are not disproportionately influenced by individual studies, methodological choices, or reporting biases, thereby strengthening the validity and clinical applicability of the evidence.

Language restriction Yes, only studies published in English will be included to ensure accurate interpretation of clinical terminology and methodological details.

Country(ies) involved Romania.

Keywords Uterine artery embolization; fertility; pregnancy outcomes; fibroids.

Dissemination plans The findings of this systematic review and meta-analysis will be disseminated through multiple channels to ensure broad visibility and impact among clinicians, researchers, and policymakers in gynecology and reproductive medicine.

1. Peer-reviewed publication
The primary route of dissemination will be through submission of the full manuscript to the Journal of Clinical Medicine (JCM), an open-access, peer-reviewed journal with a strong track record of publishing high-quality clinical and translational research. This journal was selected due to its international readership, rapid dissemination of research, and specific interest in women's health, interventional radiology, and reproductive outcomes.

2. Conference presentations
Key findings will be presented at relevant national and international conferences, including meetings organized by:

The European Society of Human Reproduction and Embryology (ESHRE),

The International Society of Interventional Radiology (SIR), and

The European Society of Gynaecological Endoscopy (ESGE).

Presentations may include oral communications, poster sessions, and symposia to reach both clinical and academic audiences.

3. Academic and clinical networks
Results will be shared within university networks, teaching hospitals, and collaborating institutions to support evidence-based decision-making in patient care. Educational workshops and seminars may be used to translate findings into clinical practice.

4. Public and patient engagement
Given the growing demand for fertility-preserving treatments among women with symptomatic fibroids, a plain-language summary of findings will be prepared. This summary may be made available through institutional websites, social media platforms, and patient advocacy groups to improve accessibility for non-specialist audiences.

5. Data transparency
Supplementary materials, including extracted datasets and quality assessment tables, will be deposited.

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