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Arcuate vs Septate Uterus and Reproductive Outcomes: A Systematic Review and Meta-analysis of Spontaneous and IVF Pregnancies (2000–2025)

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ADMINISTRATIVE INFORMATION

Support - Personal.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 September 2025 and was last updated on 29 September 2025.

INTRODUCTION

Review question / Objective Uterine anomalies, particularly arcuate and septate uteri, have long been suspected to contribute to reproductive failure. This systematic review and meta-analysis aimed to clarify their impact on infertility, implantation failure, miscarriage, and IVF outcomes.

Rationale This systematic review and meta-analysis aim to provide a comprehensive assessment of their effect on spontaneous and IVF pregnancies by:
• Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.
• Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
• Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

Condition being studied We included RCTs, prospective and retrospective observational studies, and systematic reviews with meta-analyses reporting on reproductive outcomes (implantation failure, live birth) in women with arcuate or septate uteri. We excluded case reports, editorials, and non-English publications.

METHODS

Search strategy We searched PubMed, Embase, CINAHL Complete, MEDLINE, PsycInfo, Global Health, Cochrane Library, Scopus, and UpToDate from 1980 through March 2025 (full queries in Supplementary 1). No language or study-design filters were applied.

Participant or population
• Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.

• Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
• Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

Intervention
• Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.
• Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
• Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

Comparator
• Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.
• Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
• Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

Study designs to be included Meta-analyses were conducted in RevMan 5.4.1 and R 4.3.2 (metafor). We used a random-effects model (DerSimonian–Laird), calculated risk ratios (RR) with 95% CI, and examined heterogeneity by I^2. Publication bias was assessed via Egger's regression. Subgroup analyses were performed by study design.

Eligibility criteria We included RCTs, prospective and retrospective observational studies, and systematic reviews with meta-analyses reporting on reproductive outcomes (implantation failure, live birth) in women with arcuate or septate uteri. We excluded case reports, editorials, and non-English publications.

Information sources We searched PubMed, Embase, CINAHL Complete, MEDLINE, PsycInfo, Global Health, Cochrane Library, Scopus, and UpToDate from 1980 through March 2025 (full queries in Supplementary 1). No language or study-design filters were applied.

Main outcome(s)
• Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.

• Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
• Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

Additional outcome(s)
• Evaluating the impact of septate and arcuate uteri on implantation failure and live birth rates in spontaneous and IVF pregnancies.
• Examining whether the presence of fibrotic septal tissue alters decidualization and trophoblast function, thereby compromising embryo survival.
• Assessing the efficacy of surgical intervention (hysteroscopic metroplasty) in improving reproductive outcomes.

Data management Selection process and data collection Two reviewers (CB, FMB) independently screened titles/abstracts and extracted full texts. Disagreements were resolved by a third reviewer (EG). Data were collected in standardized REDCap form.

Quality assessment / Risk of bias analysis Risk of bias was assessed using Cochrane RoB 2 for RCTs and ROBINS-I for non-RCTs. Overall evidence certainty was graded by GRADE.

Strategy of data synthesis Meta-analyses were conducted in RevMan 5.4.1 and R 4.3.2 (metafor). We used a random-effects model (DerSimonian–Laird), calculated risk ratios (RR) with 95% CI, and examined heterogeneity by I^2. Publication bias was assessed via Egger's regression. Subgroup analyses were performed by study design.

Subgroup analysis
Meta-analysis
• Implantation failure: septate uteri RR 1.75 (1.40–2.10; I^2 = 45%) spontaneous; RR 1.60 (1.30–1.90; I^2 = 50%) IVF. Arcuate uteri: RR 1.10 (0.90–1.30) spontaneous; RR 1.05 (0.85–1.25) IVF (Fig 3).
• Live birth: septate uteri RR 0.70 (0.60–0.80; I^2 = 40%) spontaneous; RR 0.75 (0.65–0.85; I^2 = 42%) IVF. Arcuate uteri: RR 0.95 (0.85–1.05) spontaneous; RR 0.90 (0.80–1.00) IVF (Fig 4).
• Secondary outcomes: miscarriage and preterm birth pooled in Supplementary 2, 3.
Subgroup and sensitivity analyses Results were consistent across RCTs vs observational studies and after excluding high-risk bias studies.

Sensitivity analysis Meta-analyses were conducted in RevMan 5.4.1 and R 4.3.2 (metafor). We used a random-effects model (DerSimonian–Laird), calculated risk ratios (RR) with 95% CI, and

examined heterogeneity by I^2. Publication bias was assessed via Egger's regression. Subgroup analyses were performed by study design.

Language restriction English.

Country(ies) involved Italy.

Keywords septate uterus, arcuate uterus, uterine anomalies, miscarriage, infertility, IVF, meta-analysis, hysteroscopic surgery.

Dissemination plans Scientific article.

Contributions of each author

Author 1 - Francesco Maria Bulletti - Conceptualization. Manuscript drafting. Final revision.
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