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REVIEW

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Maternal and fetal outcomes in women with uterine congenital abnormalities: a systematic review and meta-analysis

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Abstract

Background Congenital uterine anomalies (CUA) are structural abnormalities resulting from disrupted Müllerian duct development and have been associated with adverse reproductive and obstetric outcomes. However, the magnitude of these risks and variation across anomaly subtypes remain incompletely defined.

Objectives To evaluate the association between CUA and adverse maternal and fetal outcomes and to examine subtype-specific risk patterns using contemporary evidence.

Methods We conducted a systematic review and meta-analysis of studies identified from MEDLINE, Web of Science, and Cochrane CENTRAL. Eligible studies compared women with imaging- or surgically confirmed CUA to those with normal uterine anatomy and reported at least one predefined obstetric outcome. Random-effects meta-analyses were used to estimate pooled odds ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic, and certainty of evidence was evaluated using GRADE.

Results Thirty studies comprising over 3.3 million pregnancies were included. Compared with women with normal uterine anatomy, CUA were associated with increased odds of miscarriage (OR 1.45, 95% CI 1.13–1.86), preterm birth < 37 weeks (OR 3.74, 95% CI 1.99–7.02), fetal malpresentation (OR 19.28, 95% CI 6.27–59.24), and caesarean delivery (OR 3.52, 95% CI 1.11–11.09). Heterogeneity ranged from low to high across outcomes (I^2 0.0–94.9%). Subtype-specific patterns were observed, with septate uterus more frequently associated with miscarriages, and unicornuate and didelphys uteri associated with higher risks of preterm birth and malpresentation. Sensitivity analyses supported the robustness of findings for preterm birth.

Conclusions Congenital uterine anomalies are associated with increased risks of adverse pregnancy outcomes, with distinct subtype-specific patterns. Septate uterus is primarily associated with early pregnancy loss, whereas unicornuate and didelphys uteri are more strongly associated with later gestational complications. These findings support classification of pregnancies complicated by CUA as high risk and highlight the need for tailored antenatal surveillance and subtype-specific clinical management.

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Introduction

Congenital uterine anomalies (CUAs) arise from abnormal Müllerian duct development and encompass a heterogeneous group of structural variants – most commonly septate, bicornuate, unicornuate, and didelphys uteri [1, 2]. The estimated prevalence of CUA in the general female population is approximately 3–6% [3, 4], but CUAs are substantially overrepresented among women with infertility, recurrent pregnancy loss (RPL), and adverse obstetric outcomes [5]. Importantly, the pattern and magnitude of risk vary by anomaly subtype. Septate and unicornuate uteri are consistently associated with poorer reproductive and perinatal outcomes than fusion anomalies such as bicornuate or didelphys uteri [4, 6].

Multiple mechanisms have been proposed to link CUAs with adverse outcomes. Structural distortion of the uterine cavity, reduced functional volume, impaired endometrial receptivity, abnormal placentation, and altered uterine contractility may all contribute to higher risks of miscarriage, fetal growth restriction, preterm birth, malpresentation, and caesarean delivery [7]. These pathophysiological differences across subtypes likely underlie the observed heterogeneity in outcomes, underscoring the clinical importance of subtype-specific risk stratification [8].

Previously conducted observational studies and meta-analyses have shown a relationship between CUA and adverse outcomes. Among these adverse outcomes, fetal growth abnormalities represent a particularly complex and less well-characterized domain. While associations between congenital uterine anomalies and reduced fetal size are increasingly reported, the underlying biological mechanisms remain insufficiently defined and are often inconsistently interpreted across studies.

A key challenge in this area is the distinction between fetal growth restriction (FGR) and small-for-gestational-age (SGA), which are frequently used interchangeably in the literature but represent fundamentally different entities. FGR reflects a pathological process, most commonly driven by placental insufficiency, whereas SGA is a statistical definition based on fetal size and may include constitutionally small but otherwise healthy fetuses [9]. Emerging evidence suggests that congenital uterine anomalies are associated with increased risks of both SGA and clinically defined FGR, with adjusted risk estimates for growth restriction approaching two-fold in some large cohort studies [10, 11]. However, the underlying mechanisms remain uncertain. While abnormal uterine morphology may impose mechanical constraints on fetal growth, leading to SGA phenotypes, it is unclear whether these anomalies also contribute to placental dysfunction sufficient to result in true FGR. Notably, the majority of studies in this field report SGA outcomes without standardized diagnostic criteria for FGR, limiting mechanistic interpretation [11, 12]. In non-anomalous pregnancies, FGR and severe SGA are strongly associated with placental lesions such as maternal vascular malperfusion and fetal vascular malperfusion, which reflect impaired uteroplacental and fetoplacental circulation [13]. However, studies of congenital uterine anomalies rarely include systematic placental histopathological evaluation. As a result, direct evidence linking specific uterine anomaly subtypes to defined placental lesions is lacking [14]. This represents a critical gap in the literature, as it remains unclear whether growth abnormalities in these pregnancies are primarily driven by placental pathology or by structural and biomechanical constraints of the uterine environment

Chang et al. [15] found high rates of first trimester miscarriage and preterm birth, and reduced live birth rates in women with CUA. Recent studies with national data have identified specific risks of fetal malpresentation, operative birth and preterm birth that are notably high in CUA pregnancies [16–18]. However, it is still unclear which are clinically significant. A large part of the evidence is retrospective and inconsistent in its anomaly classification and variable outcomes. Past syntheses often precede the contemporary classification systems (ESHRE/ESGE 2013 consensus and the revised 2021 ASRM schema) and lack the ability to incorporate the data of the assisted reproductive technology (ART) cohorts or large-scale population databases [1, 19, 20]. Previous reviews have frequently focused on isolated reproductive endpoints (such as miscarriage or infertility outcomes) rather than providing an integrated assessment of both maternal and fetal outcomes across the continuum of pregnancy [4].

In the meantime, the growing awareness of CUA in the normal antenatal medical check-up has increased the demands of evidence-based information on risk stratification, sensitization, and delivery planning. Recent European guidelines suggest that pregnancies with uterine anomalies are to be considered at risk but no specific management-informing data are available [21, 22]. The presence of more modern, larger cohorts and better methodological provides an opportunity to have a more rigorous, up-to-date synthesis of outcomes in women with CUA.

This study aimed to systematically evaluate the association between congenital uterine anomalies and adverse obstetric outcomes, including miscarriage, preterm

birth, fetal malpresentation, and caesarean delivery, compared with women with normal uterine anatomy, and to explore differences across anomaly subtypes where data were available. We thus performed a systematic review and meta-analysis of maternal and fetal outcome in pregnancy complicated by congenital uterine anomalies. The review was conducted using PRISMA 2020 guidelines.[17] and observational study recommendations (MOOSE) [23, 24]. In addition to observational studies, we included randomized and non-randomized intervention studies to capture evidence on surgical management, particularly septum resection; however, these were synthesised narratively and not pooled with observational data to avoid methodological heterogeneity. This approach enabled a comprehensive evaluation of both the natural history and interventional outcomes associated with congenital uterine anomalies while maintaining analytical rigor and producing clinically relevant estimates to inform patient counselling, antenatal management, and future guideline development.

Materials and methods

Study design and registration

We performed a systematic review and meta-analysis in accordance with the PRISMA 2020 statement [23]. The review protocol, detailing the study objectives, eligibility criteria, and planned analytical approach, was developed a priori before study selection and data extraction. Although the protocol was not prospectively registered in PROSPERO, the predefined methodology was followed throughout the conduct of the review. This report adheres to PRISMA guidelines, including a PRISMA flow diagram for study selection (Fig. 1).

Eligibility criteria

Participants: Studies of women of reproductive age (≈15–49 years) who were pregnant or attempting conception (including those undergoing ART) with a confirmed diagnosis of a congenital uterine anomaly were eligible [4, 22].

Exposure (CUA): Included studies had to classify CUAs using a recognized system (e.g. American Society for Reproductive Medicine [ASRM]; European Society of Human Reproduction and Embryology/European Society for Gynaecological Endoscopy [ESHRE/ESGE]) [20, 22]. Congenital uterine anomalies were identified using recognized diagnostic modalities reported in the original studies, including hysterosalpingography (HSG), 3D transvaginal ultrasonography, hysteroscopy, magnetic resonance imaging (MRI), or combined imaging approaches. Studies using multimodal assessment were considered to provide greater diagnostic precision and

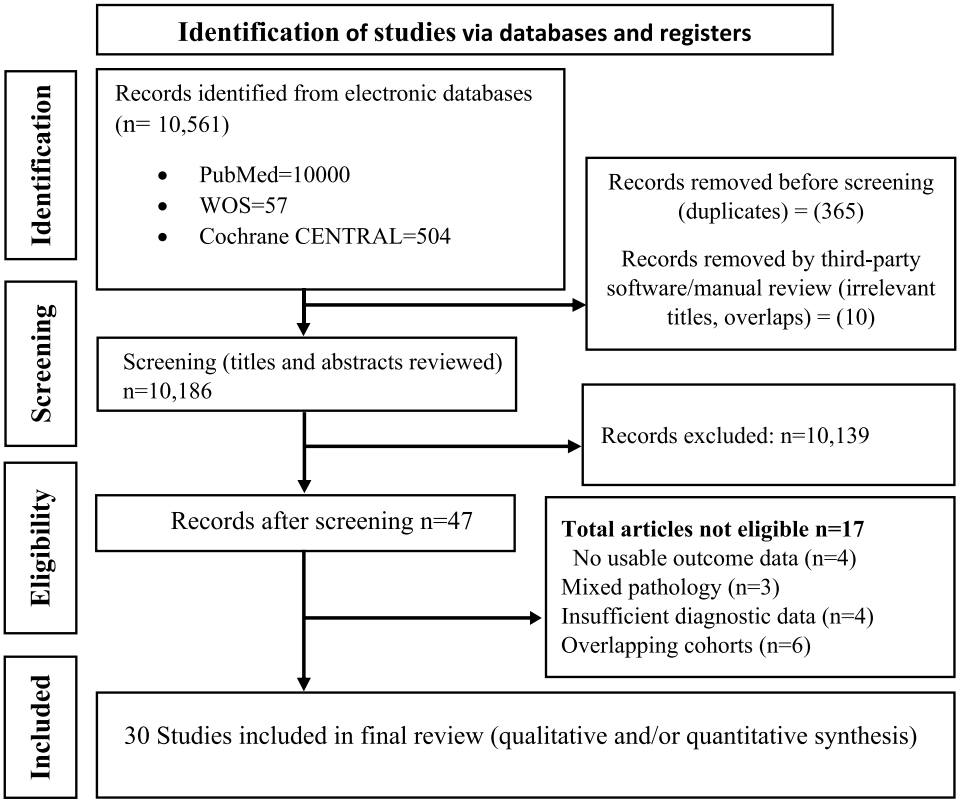

Fig. 1 PRISMA flow diagram

more reliable subtype classification. The arcuate uterus was only considered when it was explicitly stated in the study as a congenital anomaly, and was treated independently in the sensitivity-analyses due to remaining controversy about its clinical significance).

Comparators: Eligible comparator groups for quantitative synthesis (meta-analysis) included: (1) women with normal uterine anatomy (no anomaly), (2) comparisons between different CUA subtypes, and (3) surgical intervention versus no intervention or preoperative baseline (in studies of septum resection). Comparative studies contributed to pooled analyses where outcome definitions and study populations were sufficiently comparable; where pooling was not appropriate, these studies were synthesised narratively. Studies without comparator groups (e.g., single-arm cohorts) were included in the systematic review and synthesised narratively, where they provided relevant evidence on prevalence, classification, or intervention outcomes.

Studies were grouped into predefined evidence domains according to their primary contribution to the review. Comparative obstetric outcome studies contributed to the quantitative synthesis and meta-analysis. Diagnostic, prevalence, infertility, and classification studies were retained to provide contextual evidence regarding anomaly identification, subtype characterization, and population characteristics and were synthesised narratively. Intervention studies evaluating surgical management of congenital uterine anomalies were also retained for structured narrative synthesis. Only comparative obstetric outcome studies meeting predefined eligibility criteria contributed to pooled effect estimates.

Outcome: The studies had to have at least one prespecified outcome: miscarriage; live birth; preterm birth (<37 weeks); stillbirth; fetal growth restriction or small-for-gestational-age (SGA); fetal malpresentation (non-cephalic presentation at ≥37 weeks); caesarean delivery; or ART outcomes (clinical pregnancy, implantation rate, ongoing pregnancy, live birth in ART context). When reported, severe maternal morbidity was also taken into account. We accepted study-specific outcome definitions (e.g., each study SGA threshold) but attempted to use standard definitions where feasible.

Designs of Study: We incorporated primary research studies; randomized controlled trials (RCTs), non-randomized intervention studies, prospective or retrospective cohort studies, and case-control studies. Case reports and small case series (less than 10 cases) were omitted as well as reviews, editorials, conference abstracts, and studies that studied acquired uterine pathology only (fibroids, adenomyosis, intrauterine adhesions). Studies were eligible for inclusion in the systematic review if they met the predefined population, exposure, and outcome criteria, regardless of study design. However, only studies with an appropriate comparator group were included in the quantitative synthesis (meta-analysis). Non-comparative studies (e.g., single-arm cohorts, diagnostic studies, and post-intervention series) were included in the review and synthesised narratively where they contributed relevant evidence on prevalence, classification, or intervention outcomes.

Timeframe and Language: We restricted the search to articles published between January 2015 and December 2025 to identify the recent studies based on the use of modern classification and imaging. Only publications in English were included. The final database search was performed on 31 December 2025, and no additional eligible studies were identified thereafter.

Search strategy

The search strategy was developed with the help of a medical librarian. We searched MEDLINE (Ovid), Web of Science, and Cochrane CENTRAL for studies published from January 2015 to December 2025. The search terms were used as a combination of controlled vocabulary and keywords of congenital uterine anomalies (e.g. Mullerian anomaly, septate uterus, unicornuate uterus) and pregnancy/reproductive outcomes (miscarriage, preterm birth, infertility, IVF etc.). The entire strategy of the search is presented in Supplementary Appendix. Reference lists of any other eligible studies were also handsearched in the included studies and any other relevant reviews.

Study selection

All the records were identified and imported into reference management software and all duplicates were eliminated. Relevance Titles and abstracts were screened by two reviewers. Independent evaluation of full-text articles of potentially eligible studies was then conducted against the inclusion criteria. Any discrepancies on one of the stages were resolved either through discussion or through third party adjudication. The PRISMA flow diagram (Fig. 1) summarizes the process of selection of the studies.

Data extraction

Data were extracted independently by two reviewers using a standardized form. Such extracted data were: study characteristics (First author, year, country, design, setting); participant characteristics (age, parity, infertility or RPL history); CUA subtype and classification; diagnostic modality; surgical intervention details (where appropriate); ART protocol details (where appropriate); outcome definitions; follow-up period; and outcome data (event rates or effect estimates with confidence intervals). When primary outcome was available or derivable, we obtained unadjusted 2×2 contingent data. In cases

where several measures of the effects were reported (e.g., adjusted ORs), we collected those to be used in qualitative synthesis but used crude data in primary meta-analyses so as to maximize comparability. The second reviewer cross-checked all data extraction and consensus were used to resolve any discrepancies.

Risk of bias assessment

Two reviewers independently assessed risk of bias for each study using design-appropriate tools. For RCTs, we used the Cochrane ROB 2 tool [25]; for non-randomized intervention studies, ROBINS-I [26]; for observational cohort and case–control studies, the Newcastle–Ottawa Scale [27]. We interpreted NOS scores ≥ 7/9 as indicative of lower risk of bias (higher quality). We also considered key biases such as confounding (e.g., failure to adjust for maternal age, ART use) and outcome misclassification. Disagreements in risk-of-bias ratings were resolved by discussion. Table 3 presents a summary of risk-of-bias assessments.

Data synthesis and statistical analysis

We performed a qualitative narrative synthesis for all 30 included studies, structured by analytic domain (natural history vs infertility vs surgical) and by CUA subtype where applicable. Study characteristics and findings are summarized in Table 1 (study characteristics) and Table 2 (population, exposure, comparator, and outcome categories). Pre–post intervention studies evaluating surgical correction (e.g., septum resection) were included to capture interventional outcomes; however, these studies were not included in the quantitative synthesis and were analysed separately within the narrative synthesis.

For quantitative synthesis, we conducted meta-analyses when at least two studies provided comparable outcomes and study populations. Primary meta-analyses focused on the four principal obstetric outcomes: miscarriage, preterm birth < 37 weeks, fetal malpresentation, and caesarean delivery. We used DerSimonian–Laird random-effects models to account for between-study heterogeneity [51]. Pooled effect sizes were expressed as odds ratios (OR) with 95% confidence intervals. We calculated crude ORs from raw event counts for each study (2 × 2 tables) to ensure consistency. Between-study heterogeneity was assessed using Cochran's Q and the I^2 statistic (with $I^2 > 50\%$ indicating substantial heterogeneity) [52]. We also reported τ^2 as the estimate of between-study variance.

We performed prespecified subgroup and sensitivity analyses to explore heterogeneity. Subgroup analyses (where data allowed) included stratification by CUA subtype, diagnostic method (imaging-only vs surgical confirmation), and study risk of bias rating. Sensitivity analyses were conducted to investigate the effects of the exclusion of outlier studies (e.g. cohorts with very high baseline risk) and studies conducted on ART populations. We also performed sensitivity analyses excluding all studies that included arcuate uteri to assess the impact of classification variability on pooled estimates.

Although fetal growth restriction (FGR) and small-for-gestational-age (SGA) are clinically important outcomes, they were not included in the primary meta-analyses due to substantial heterogeneity in their definitions across studies. SGA was variably defined using different percentile thresholds (e.g., <10th, <5th), while FGR was inconsistently reported and often lacked standardized diagnostic criteria incorporating fetal Doppler parameters or consensus definitions. This variability limited comparability and increased the risk of outcome misclassification in pooled analyses. Therefore, these outcomes were synthesised narratively to preserve interpretability.

We evaluated the certainty of evidence for each primary outcome using GRADE. Evidence was downgraded for risk of bias, inconsistency, indirectness, imprecision, or publication bias as applicable (Guyatt et al., 2008). All statistical analyses were conducted using Review Manager (RevMan 5.4) and R (v4.0) software (R Core Team, 2020)

Publication bias was assessed for outcomes with a sufficient number of studies (k ≥ 10) using visual inspection of funnel plots and Egger's regression test. For outcomes with fewer studies, formal assessment was not performed due to limited statistical power, and any interpretation of potential small-study effects was undertaken with caution.

Results

Study selection and characteristics

The database search yielded 10,561 records, of which 365 were duplicates. After screening titles/abstracts, 47 full-text articles were assessed for eligibility, and 30 studies met all inclusion criteria (Fig. 1). The most common reasons for exclusion at full text were: wrong population (e.g. anomalies not congenital or no appropriate comparator), ineligible study design (e.g. case series without controls), or publication outside the date range.

The 30 included studies encompassed > 3.3 million total pregnancies (range per study: 21 to 1.4 million) and were published 2015–2025. Table 1 summarizes key characteristics. Nineteen studies were retrospective cohorts [6, 15–18, 21, 28, 31–38, 40, 42, 46, 50], five were prospective cohorts [30, 44, 47, 48, 53], one was an RCT of septum resection [5], one a non-randomized pre–post-surgical study [21], and four were cross-sectional or diagnostic accuracy studies [6, 29, 38, 40]. Geographic representation was broad: 10 studies from Europe [5, 6, 16, 21, 36–38]' [32]' [39], 8 from Asia [15, 18, 31, 33, 34, 44, 47, 48], 7 from North America [17, 29, 30, 35, 40, 46,

Table 1 Characteristics of included studies ($n = 30$)

StudyID	Citation	Citation	Module (Domain)	Design	Setting/Country	Sample Size (N)	Study Period	Comparator Type	Quantitative Synthesis?	Primary Contribution to Review
Buicu2025	Buicu et al., 2025 [28]	Buicu et al., 2025	A (Obstetric outcomes)	Retrospective cohort	Romania	62	2010–2017	Normal uterus	Yes	Obstetric Outcome Study (Meta-analysis)
Mandelbaum	Mandelbaum et al. [17],	Mandelbaum et al.	A (Obstetric outcomes)	Registry cross-sectional	USA	50,180	2016–2019	CUA subtype comparisons	Yes (Exploratory)	Obstetric Outcome Study (Subtype Analysis)
Tellum2022	Tellum et al., 2022 [29]	Tellum et al., 2022	A (Obstetric outcomes)	Population cohort	Denmark	>1.4 million births	1997–2018	Normal uterus	Yes	Obstetric Outcome Study (Meta-analysis)
Khander2017	Khander et al. [30],	Khander et al.	A (Obstetric outcomes)	Retrospective cohort	USA	283	2005–2016	Normal uterus	Yes	Obstetric Outcome Study (Meta-analysis)
Matthews2019	Matthews & Chasen [16],	Matthews & Chasen	A (Obstetric outcomes)	Retrospective cohort	USA	132	2005–2018	Normal uterus	Yes	Obstetric Outcome Study (Meta-analysis)
Naeh2021	Naeh et al. [18],	Naeh et al.	A (Obstetric outcomes)	Retrospective cohort	Israel	167 pregnancies	2010–2017	Normal uterus	No	Obstetric Outcome Study (Narrative Subtype Comparison)
Qian2023	Qian et al. [31],	Qian et al.	A (Obstetric outcomes)	Retrospective cohort	China	336	2015–2021	Normal uterus vs hemiuterus	Yes	Obstetric Outcome Study (Meta-analysis)
Żyła2015	Żyła et al. [32],	Żyła et al.	A (Obstetric outcomes)	Retrospective cohort	Poland	94	1994–2012	Normal uterus	Yes	Obstetric Outcome Study (Meta-analysis)
Wang2025	Wang et al. [33],	Wang et al.	A (Obstetric outcomes)	Retrospective cohort	China	21 twin pregnancies	2013–2022	Normal uterus (twins)	No	Obstetric Outcome Study (Sensitivity Analysis)
Cai2021	Cai et al. [34],	Cai et al.	B (Infertility/ART)	Retrospective cohort	China	348	NR	IVF controls	Yes	ART-Related Reproductive Outcome Evidence
Prior2018	Prior et al. [35],	Prior et al.	B (Infertility/ART)	Retrospective cohort	UK	2,375	NR	IVF controls	Yes	ART-Related Reproductive Outcome Evidence
Rikken2021_RCT	Rikken et al. [5],	Rikken et al.	C (Surgical)	Multicentre RCT	Netherlands	80	NR	Septum resection vs expectant	No	Surgical Intervention Evidence
Rousseau2021	Rousseau et al. [36],	Rousseau et al.	C (Surgical)	Pre-post study	Belgium	31	NR	Pre vs post surgery	No	Surgical Intervention Evidence

Table 1 (continued)

StudyID	Citation	Citation	Module (Domain)	Design	Setting/Country	Sample Size (N)	Study Period	Comparator Type	Quantitative Synthesis?	Primary Contribution to Review
Zizolfi2025	Zizolfi et al. [37],	Zizolfi et al.	C (Surgical)	Retrospective cohort	Italy	107	NR	Pre-post	No	Surgical Intervention Evidence
Chang2023	Chang et al. [15],	Chang et al.	C (Surgical)	Retrospective cohort	China	348	NR	Single-arm	No	Surgical Intervention Evidence
DiSpiezio2021	Di Spiezio Sardo et al. [21]	Di Spiezio Sardo et al.	D (Classification)	Consensus/ Narrative	Europe	NR	NR	None	No	Classification and Clinical Context Evidence
Carriles2024	Carriles et al. [38],	Carriles et al.	E (Prevalence)	Prospective cohort	Spain	993	NR	None	No	Prevalence Evidence
Ludwin2019	Ludwin et al. [39],	Ludwin et al.	D (Diagnostic)	Retrospective cohort	Poland	261	NR	None	No	Diagnostic/ Classification Evidence
Ludwin2020	Ludwin et al. [6],	Ludwin et al.	D (Diagnostic)	Diagnostic accuracy	Poland	100	2014–2016	Method comparison	No	Diagnostic/ Classification Evidence
McCormack2016	McCormack et al. [40],	McCormack et al.	D (Diagnostic)	Cross-sectional cohort	Australia	200	NR	None	No	Diagnostic Evidence
Priya2015	Priya & Vijayalakshmi [41],	Priya & Vijayalakshmi	E (Prevalence)	Cross-sectional	India	1,500	2009–2014	None	No	Prevalence Evidence
Okonkwo2022	Okonkwo et al. [42],	Okonkwo et al.	D (Diagnostic accuracy)	Diagnostic accuracy	Nigeria	88	NR	Hysteroscopy reference	No	Diagnostic Accuracy Evidence
Shiva2018	Shiva et al. [43],	Shiva et al.	D (Diagnostic accuracy)	Diagnostic accuracy	Iran	789	NR	Office hysteroscopy	No	Diagnostic Accuracy Evidence
Tammam2015	Tammam et al., 2015 [44]	Tammam et al.	D (Diagnostic)	Diagnostic implementation	Egypt	226	NR	Diagnostic reference	No	Diagnostic Evidence
Russo2022	Russo et al. [45],	Russo et al.	E (Observational)	Retrospective cohort	Italy	664	NR	None	No	Contextual Reproductive Outcome Evidence
Busnelli2024	Busnelli et al. [46],	Busnelli et al.	E (RPL cohort)	Retrospective cohort	Italy	442	NR	None	No	Recurrent Pregnancy Loss Context Evidence
Anbumani2015	Anbumani et al. [47],	Anbumani et al.	E (Prevalence)	Cross-sectional	India	5,228	2009–2014	None	No	Prevalence Evidence
Joshi2021	Joshi et al. [48],	Joshi et al.	E (Prevalence)	Retrospective cohort	India	NR	NR	None	No	Prevalence and Infertility Context Evidence

Table 1 (continued)

StudyID	Citation	Citation	Module (Domain)	Design	Setting/Country	Sample Size (N)	Study Period	Comparator Type	Quantitative Synthesis?	Primary Contribution to Review
Liston2017	Liston et al., 2017 [49]	Liston et al.	E (Descriptive)	Registry descriptive	UK	NR	NR	None	No	Descriptive Clinical Context Evidence
Roepke2017	Rasmark-Roepke et al. [50],	Rasmark-Roepke et al.	E (Registry cohort)	Registry-based cohort	Sweden	7,842	2003–2012	None	No	Population Context Evidence

Studies were classified according to their primary contribution to the review. Comparative obstetric outcome studies contributed to the quantitative synthesis and pooled meta-analysis. Diagnostic, prevalence, infertility, classification, and surgical intervention studies were retained to provide contextual, mechanistic, or methodological evidence and were synthesised narratively

50], 2 from the Middle East [43, 53], 2 from Australia [16, 40], and 1 from Africa [42].

CUA subtypes evaluated included septate, bicornuate, unicornuate, didelphys, and (in some studies) arcuate uteri [5, 6, 16–18, 39]. Diagnosis was confirmed by modern imaging (3D ultrasound or MRI) in most recent studies, sometimes combined with hysteroscopic or laparoscopic findings (Table 2). Several studies focused on specific subpopulations: two in ART populations (women undergoing IVF) [28, 36], and six, in women investigated for RPL or infertility [6, 21, 34, 39, 46, 48]—these often reported CUA prevalence or diagnostic test accuracy rather than pregnancy outcomes.

Most studies compared outcomes in women with CUA to women with normal uteri (control groups drawn from the general obstetric population or matched fertility clinic patients) [15–18, 30, 31, 36, 42, 47, 50]. Three studies compared different anomaly subtypes without control groups [16–18]. Three surgical studies compared post-metroplasty outcomes to pre-surgery baseline or no surgery [5, 21, 39]. No study reported outcomes for untreated versus treated anomalies in a randomized fashion except the one RCT of septum resection [5].

Table 1 presents detailed study characteristics, including module/domain, design, setting, sample size, comparator, inclusion in quantitative synthesis, and notes. In brief, Module A (natural history of obstetric outcomes) included population-based and hospital-based cohort studies evaluating spontaneous pregnancy outcomes in women with CUA. Module B comprised studies in infertility or RPL settings (including prevalence surveys and diagnostic accuracy studies). Module C encompassed studies of surgical intervention (mostly septum resection) and subsequent reproductive outcomes.

Table 2 provides an overview of each study's population, exposure (anomaly or intervention), comparator category, exposure ascertainment, confounding control, and synthesis classification. Notably, 10 studies were considered suitable for meta-analysis of obstetric outcomes, while 20 were synthesized narratively due to incompatible outcomes or lack of comparators.

Risk of bias: Risk-of-bias assessments are summarized in Table 3 and Fig. 2. Overall, 13 studies were rated Moderate risk, 8 Serious, 6 Some concerns, 2 Low–Moderate, and 1 Critical/High. The sole RCT (septum resection) had "some concerns" [5] (open-label design with potential deviations). Common limitations in cohort studies were retrospective design, potential selection bias, and unmeasured confounding (only 12/28 observational studies adjusted for key confounders like age or IVF use). Many diagnostic studies had "some concerns" due to patient selection and lack of blind outcome assessment [29, 38]. One technical case series was deemed at critical risk of bias (no comparator) [40]. These limitations temper the strength of causal inferences.

Obstetric outcomes in women with CUA

In the pooled analyses, women with congenital uterine anomalies had higher odds of adverse obstetric outcomes compared with women with normal uterine anatomy (Table 4A). The pooled odds of preterm birth < 37 weeks were increased (OR 3.74, 95% CI 1.99–7.02; $I^2 = 68.1\%$; k = 5; Fig. 3A). Caesarean delivery was also more common among women with CUA (OR 3.52, 95% CI 1.11–11.09; $I^2 = 94.9\%$; k = 5; Fig. 3B). Fetal malpresentation was associated with the largest pooled effect estimate (OR 19.28, 95% CI 6.27–59.24; $I^2 = 23.6\%$; k = 2; Fig. 4A), although this estimate should be interpreted cautiously because one contributing study defined malpresentation as breech presentation only. Miscarriage was also more common among women with CUA (OR 1.45, 95% CI 1.13–1.86; $I^2 = 0.0\%$; k = 3; Fig. 4B).

Squares represent individual study effect estimates, with size proportional to the inverse-variance weight of each study. Horizontal lines indicate 95% confidence intervals. Diamonds represent pooled estimates derived using random-effects models. The vertical dashed line represents the line of no effect (OR = 1). Values greater than 1 indicate higher odds of the outcome among women with congenital uterine anomalies.

Between-study heterogeneity is quantified using the I^2 statistic and τ^2. Variation in effect sizes across studies

Table 2 Population, exposure, comparator, and outcome classification of included studies (structured summary of study context and analysis approach)

StudyID	Population	Exposure/Intervention	Comparator	Exposure ascertainment	Confounding control	Synthesis contribution
Buicu2025	Delivering women	CUA (any)	Normal uterus	Imaging/surgical	Adjusted	Meta-analysis + Narrative
Mandelbaum_NIS	Registry deliveries	CUA subtypes	Subtype referent	ICD coding	Adjusted	Meta-analysis + Narrative
Tellum2022	National cohort	CUA	Normal uterus	Registry coding	Adjusted	Meta-analysis + Narrative
Khander2017	Pregnant women	CUA subtype	Normal uterus	Imaging	NR	Meta-analysis + Narrative
Matthews2019	Unicornuate pregnancies	Unicornuate uterus	Normal uterus	Imaging	Unadjusted	Meta-analysis + Narrative
Naeh2021	CUA pregnancies	Subtypes	Normal uterus	Surgical/imaging	NR	Narrative (comparative; not pooled)
Qian2023	Hemi-uterus pregnancies	Hemi-uterus	Normal uterus	Imaging	Adjusted	Meta-analysis + Narrative
Żyła2015	Uterine malformations	CUA subtypes	Normal uterus	Imaging	NR	Meta-analysis + Narrative
Wang2025	Twin pregnancies	Unicornuate uterus	Normal twins	Imaging	NR	Narrative (sensitivity only)
Cai2021	IVF pregnancies	Didelphys uterus	ART controls	Imaging	Matched	Meta-analysis + Narrative
Prior2018	ART cohort	CUA	ART controls	Imaging	Unadjusted	Meta-analysis + Narrative
Rikken2021_RCT	Septate uterus	Septum resection	Expectant	Diagnosis NR	RCT	Narrative (comparative; not pooled)
Rousseau2021	Septate uterus	Septoplasty	Pre–post	Imaging	Unadjusted	Narrative (comparative; not pooled)
Zizolfi2025	Surgical cohort	Metroplasty	Pre–post/none	NR	NR	Narrative (non-comparative)
Chang2023	Post-surgery cohort	Metroplasty	None	Hysteroscopy	Adjusted	Narrative (non-comparative)
DiSpiezio2021	Complex anomaly	Septum treatment	None	ESHRE/ESGE	NA	Narrative (non-comparative)
Carriles2024	General cohort	Septate prevalence	None	Multiple criteria	NA	Narrative (non-comparative)
Ludwin2019	Infertility cohort	Septate definitions	None	Classification systems	Unadjusted	Narrative (non-comparative)
Ludwin2020	Imaging dataset	T-shaped uterus	None	CUME criteria	NA	Narrative (non-comparative)
McCormack2016	RPL clinic	Uterine anomalies	None	Imaging	NA	Narrative (non-comparative)
Okonkwo2022	Infertility cohort	Diagnostic tests	Reference standard	Accuracy study	NA	Narrative (comparative; diagnostic)
Shiva2018	RPL/IVF	Diagnostic test	Reference standard	Imaging vs hysteroscopy	NA	Narrative (comparative; diagnostic)
Tammam2015	Hospital cohort	3D-TVUS	Reference/none	Imaging	NA	Narrative (non-comparative)
Russo2022	Infertility cohort	Septum metrics	None	Imaging	Unadjusted	Narrative (non-comparative)
Busnelli2024	RPL cohort	Screening	None	Imaging	NR	Narrative (non-comparative)
Anbumani2015	Infertility cohort	Prevalence	None	Imaging	NA	Narrative (non-comparative)
Joshi2021	Infertility cohort	Müllerian anomalies	None	Imaging	NR	Narrative (non-comparative)

Table 2 (continued)

StudyID	Population	Exposure/Intervention	Comparator	Exposure ascertainment	Confounding control	Synthesis contribution
Priya2015	Community sample	Uterine anomalies	None	Imaging	NA	Narrative (non-comparative)
Liston2017	Caesarean cohort	Incidental CUA	None	Intraoperative	NA	Narrative (non-comparative)
Roepke2017	Registry cohort	RPL patterns	None	Registry coding	Adjusted	Narrative (non-comparative)

reflects differences in study design, population characteristics, and classification of uterine anomalies.

Figures 3, 4 illustrate the overall risk differences for key outcomes; notably, most pregnancies in women with CUA still resulted in live birth, but the absolute risk of preterm delivery was substantially higher (e.g. ~15% vs ~3% in one cohort【46†Outcome】【46†Relative effect】), and the absolute risk of malpresentation was markedly elevated (e.g. ~25% vs ~3–4%【46†Outcome】【46†Key evidence】). GRADE summary has been presented as Table 5.

Narrative synthesis

This section summarises findings from studies not included in quantitative pooling and reports subtype-specific patterns described across the literature.

A number of studies categorised outcomes by subtype of anomaly, but subtype meta-analysis was not conducted due to inconsistency in comparator groups. In most cases, unicornuate and didelphys uteri were associated with less favourable late-gestation outcomes. In the largest study [17], unicornuate uterus was associated with increased risks of preterm birth (aOR 1.48, 95% CI 1.35–1.62) and fetal malpresentation (aOR 1.39, 95% CI 1.28–1.50) compared with arcuate uterus. Septate uteri were more frequently associated with miscarriage and showed a smaller increase in the risk of preterm birth and malpresentation. Bicornuate uteri showed a moderate increase in risk.

Two studies explicitly compared subtypes without using normal uteri as a reference group. Naeh et al. [18] reported higher risks of preterm birth and malpresentation in didelphys and unicornuate uteri compared with septate uteri. Subtype comparisons were limited by variability in study design, sample size, and adjustment for confounders. No head-to-head randomised trials comparing surgical correction across subtypes were identified.

Two studies conducted in ART populations [34, 35] reported associations between CUA and lower live birth rates and higher preterm birth rates in IVF pregnancies. One study reported that septate uterus was associated with early pregnancy loss in ART cohorts but not with late pregnancy complications, whereas studies in natural conception cohorts reported associations with both early and late adverse outcomes.

Sensitivity analyses

Multiple sensitivity analyses were performed to investigate the strength of the findings (Table 4B). To begin with, the omission of the hemi-uterus study [31] reduced the pooled OR of preterm birth to about 3.1 as compared to the initial pooled OR of about 3.9, but it was still statistically significant. Omission of the ART cohort [35] of the preterm analysis provided an OR of approximately 5.06 (95% CI 3.12–8.21) with no heterogeneity (I2 0%), which implies that in non-ART groups the relative risk of preterm birth could be even greater. The addition of the small Wang [54] twin study (as an exploratory sensitivity) to the preterm meta-analysis provided an OR of approximately 5.45 (95% CI 2.27–13.06) high heterogeneity indicating that the gestation of twins in a unicornuate uterus presents unprecedented risk.

For caesarean delivery, removing the Qian [31] cohort dramatically lowered the pooled OR (from ~3.7 to ~1.8, 95% CI 0.70–4.66) and reduced heterogeneity (I^2 90% vs 96%), suggesting that the very high baseline caesarean rate in that study was an outlier influencing the meta-analysis. Removing the ART cohort increased the caesarean OR to ~5.62 (95% CI 1.02–30.86), but again with extreme heterogeneity. Notably, when including the twin data, the caesarean OR was ~3.26 (95% CI 0.96–11.06; $k = 5$), which is similar to the primary estimate but still with wide CI.

Overall, sensitivity analyses revealed that the relationship between CUA and preterm birth was strong in all assumptions (remaining 3- to 5-fold). The effect size of caesarean delivery was extremely case-mix dependent, as without the high-risk group cases the finding lost its statistical significance, which suggests that baseline risk factors (e.g. the use of prophylactic caesarean when malpresentation is observed in certain centers) have a potent impact on this outcome. Comprehensively, none of the sensitivity tests negated the direction of the original results.

Publication bias

Publication bias was not formally assessed because there were few studies per outcome (k = 4 in both preterm

Table 3 Risk-of-bias assessment of included studies (overall judgments and primary concerns)

StudyID	Risk of Bias Tool	Overall RoB	Key concerns (briefly)
Buicu2025	NOS (cohort)	Serious	Small single-center retrospective; likely residual confounding; limited adjustment
Mandelbaum	ROBINS-I (registry)	Moderate	ICD coding misclassification; delivery-only data; residual confounding
Tellum2022	ROBINS-I (registry cohort)	Moderate	Registry exposure/outcome misclassification possible; most key confounders adjusted
Khander2017	NOS (cohort)	Moderate	Retrospective design; heterogeneity in anomaly types; minimal adjustment for confounding
Matthews2019	NOS (cohort)	Serious	Very small sample; incidental anomaly detection bias; limited control of confounding
Naeh2021	NOS (cohort)	Moderate	Retrospective; comparator is general population (possible residual confounding)
Qian2023	NOS (cohort)	Moderate	Retrospective; selected population (hemi-uterus); some matching but residual confounding likely
Wang2025	NOS (cohort)	Serious	Extremely small N (case series of twins); high imprecision; likely selection bias
Żyła2015	NOS (cohort)	Serious	Older data; limited reporting detail; potential selection bias (single hospital)
Cai2021	NOS (cohort, ART matched)**	Moderate	Well-matched controls; however, only ART context – residual ART-related confounding
Prior2018	NOS (cohort, ART)**	Moderate	Unadjusted comparisons; potential ART confounding; anomaly ascertainment NR
Rikken2021_RCT	Cochrane ROB 2 (RCT)	Some concerns	Open-label design; possible deviations from intended intervention; potential selective reporting
Rousseau2021	NOS (pre–post study)	Serious	No concurrent control; confounding by indication (only poor prognosis patients); regression to mean
Zizolfi2025	NOS (cohort)	Serious	Limited outcome reporting; likely selection bias (who underwent surgery); unclear comparator group
Chang2023	NOS (cohort)	Serious	Post-surgery cohort without internal control; possible prognostic-factor bias; no randomization
DiSpiezio2021	JBI case series/tech note	Critical/High	Technical step-by-step report; no comparator or outcomes; cannot infer effect on fertility
Carriles2024	JBI prevalence (cross-sec)	Moderate	Large prospective sample; some selection bias possible (volunteers); verification bias in diagnostics
Ludwin2019	JBI/QUADAS-2 (classification)	Low–Moderate	Within-cohort comparisons; potential measurement error in classification; moderate representativeness
Ludwin2020	JBI/QUADAS-2 (criteria)	Low–Moderate	Standardized imaging study; applicability issues to general population; measurement cutoff subjectivity
McCormack2016	JBI cross-sectional	Moderate	Clinic-based RPL cohort (not generalizable); no external control; possible selection bias
Okonkwo2022	QUADAS-2 (diag. accuracy)	Some concerns	Limited sample; patient spectrum bias (infertile only); flow/timing of reference standard not fully clear
Shiva2018	QUADAS-2 (diag. accuracy)	Some concerns	Selected high-risk population; unclear blinding of index vs reference test; acceptable overall
Tammam2015	QUADAS-2 (implementation)	Some concerns	Single-center implementation study; incomplete reference standard for all; otherwise acceptable
Russo2022	JBI/QUADAS-2 (classif/outcome)	Some concerns	Retrospective; multiple anomaly definitions (complex analysis); confounding by reproductive history
Busnelli2024	NOS (cohort; RPL clinic)	Some concerns	Retrospective single-cohort study; selection bias (RPL patients); heterogeneity in outcomes definitions
Anbumani2015	JBI cross-sectional	Moderate	Large descriptive study; potential selection bias (hospital-based screening); no reference standard confirmation
Joshi2021	NOS/JBI (retro cohort)	Moderate	Infertility clinic cohort; anomaly ascertainment heterogeneity; confounding (e.g. age) not clearly addressed
Priya2015	JBI cross-sectional	Moderate	Community ultrasound survey; no comparator; limited verification of anomaly findings; large sample helps reliability
Liston2017	JBI case series (descriptive)	Serious	Incidental findings at surgery; likely incomplete case capture; no comparison; high risk of selection bias
Roepke2017	ROBINS-I (registry)	Moderate	National register data; some confounders adjusted; coding validity concerns; outcomes broad (RPL incidence)

Note: Overall risk-of-bias judgments: Low–Moderate (between low and moderate), Some concerns (applies primarily to QUADAS-2 diagnostic studies), Moderate, Serious, or Critical/High. Key concerns highlight dominant potential biases per study

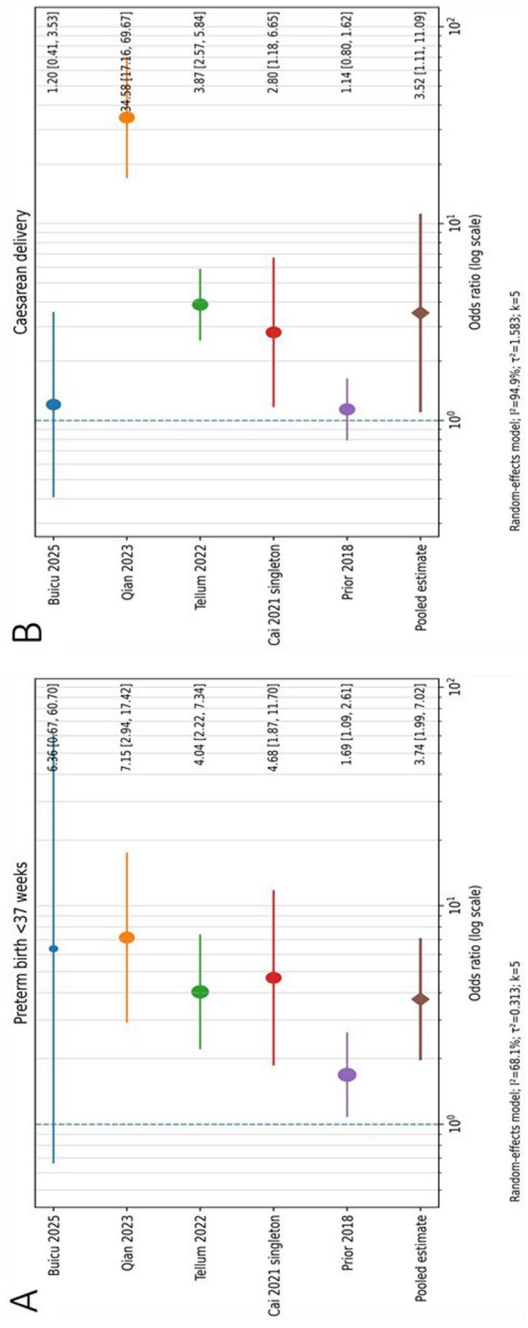

Fig. 2 Risk of bias summary across studies

Table 4A Pooled odds ratios for primary obstetric outcomes (CUA vs normal uterus)

Outcome	k	Pooled OR (95% CI)	Heterogeneity (I^2, τ^2)	P
Miscarriage	3	1.45 (1.13–1.86)	$I^2 = 0.0\%$; $\tau^2 = 0.000$	<0.05
Preterm birth < 37w	5	3.74 (1.99–7.02)	$I^2 = 68.1\%$; $\tau^2 = 0.313$	<0.001
Malpresentation	2	19.28 (6.27–59.24)	$I^2 = 23.6\%$; $\tau^2 = 0.232$	<0.0001
Caesarean delivery	5	3.52 (1.11–11.09)	$I^2 = 94.9\%$; $\tau^2 = 1.583$	0.034

Note: Random-effects model (DerSimonian–Laird). *k* = number of studies. Malpresentation defined variably (Buicu: breech only; Qian: any non-cephalic) – interpret pooled estimate with caution

birth and caesarean). Funnel plots did not show obvious asymmetry due to the limited number of points, and formal statistical assessment was not performed due to limited number of studies. We view these findings with caution; having less than 10 studies, the tests of publication bias are underpowered and can be unreliable. There might also exist smaller studies with negative findings that were unpublished. Nevertheless, this concern is partially addressed by the fact that a number of large population studies were included. We had no evidence of selective reporting in studies (data were typically reported once collected and the outcomes of interest were provided).

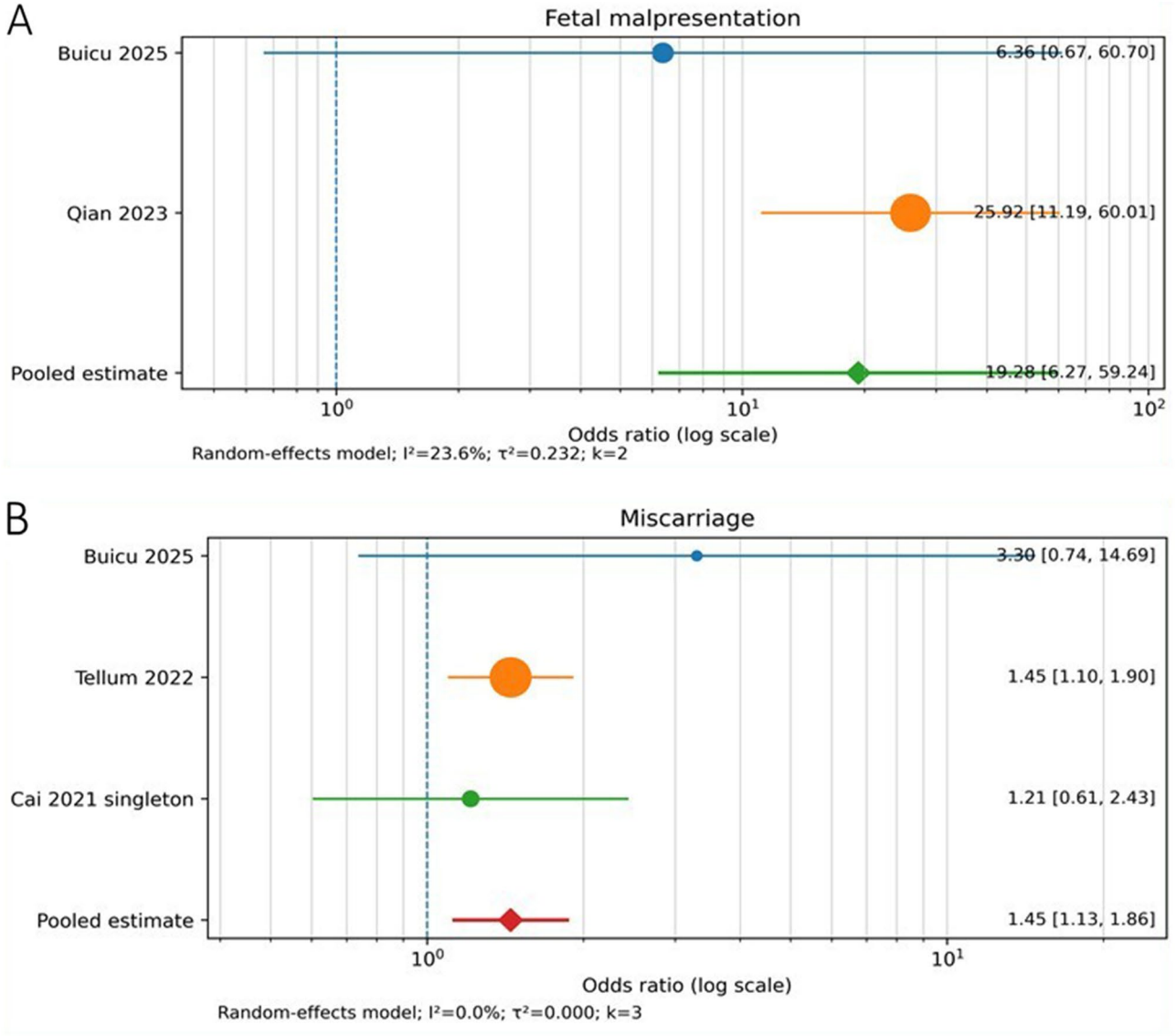

Fig. 3 **A**-**B**: forest plots showing study-level and pooled odds ratios (ORs) with 95% confidence intervals (CIs) for (**A**) preterm birth < 37 weeks (**B**) caesarean delivery

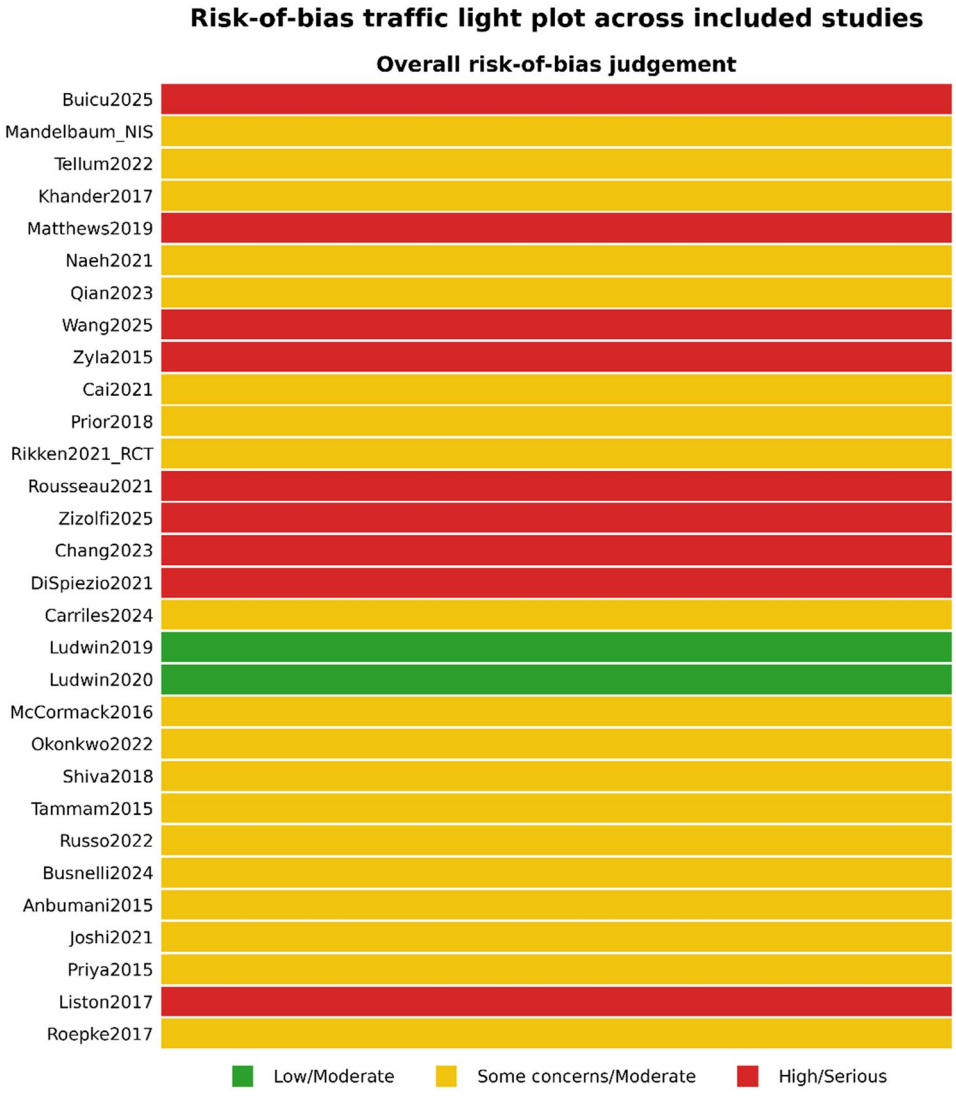

Fig. 4 **A**-**B**: forest plots showing study-level and pooled odds ratios (ORs) with 95% confidence intervals (CIs) for (**A**) fetal malpresentation, and (**B**) miscarriage among women with congenital uterine anomalies compared with women with normal uterine anatomy

Outcomes of surgical intervention

Five studies investigated reproductive outcome following surgical repair of a uterine anomaly, mostly resection of the septum. The sole RCT [5] did not find any significant difference in live birth rate between women who received hysteroscopic septum resection and those who received expectant management during the 12-month period. We did not pool RCT and observational data of surgery in our meta-analysis, but rather narratively synthesized them. Most observational pre-post studies [36] have reported better pregnancy outcomes following resecting the septum, although they are highly susceptible to bias (no controls at the same time). An example of this is a pre- post study where live birth rate rose by approximately 30% prior to septoplasty to approximately 60% following the procedure although it lacked a control group, thus, could have been a regression to the mean or continued fertility treatment. It is therefore possible to draw only tentative conclusions about surgery: septum resection might possibly reduce the miscarriage rates in women who have recurrent loss with a septate uterus as several case series studies have shown but strong-evidence randomized controlled trials did not provide support to a definite benefit in the case of unexplained infertility. It was observed that all the surgical articles did not cover any interventions on other types of anomalies (e.g. Strassman metroplasty on bicornuate uteri) in the contemporary era.

Other outcomes

Not many studies were found to report on stillbirth, SGA/fetal growth restriction, or severe maternal morbidity, and the data were too sparse to be pooled. According to Tellum et al. [29], CUA increased the incidence

Table 4B Sensitivity analyses for preterm birth and caesarean delivery

Outcome	Sensitivity scenario	k	Pooled OR (95% CI)	I^2 (%)	P
Preterm birth < 37 weeks	Primary model	5	3.74 (1.99–7.02)	68.1	<0.001
Preterm birth < 37 weeks	Exclude Qian 2023	4	3.12 (1.64–5.91)	62.5	<0.001
Preterm birth < 37 weeks	Exclude Prior 2018	4	4.84 (3.15–7.43)	0.0	<0.001
Preterm birth < 37 weeks	Exclude Wang 2025	4	3.92 (1.75–8.75)	76.5	0.001
Caesarean delivery	Primary model	5	3.52 (1.12–11.07)	94.9	0.032
Caesarean delivery	Exclude Qian 2023	4	2.00 (0.94–4.28)	85.8	0.073
Caesarean delivery	Exclude Prior 2018	4	4.77 (1.32–17.22)	92.3	0.017
Caesarean delivery	Exclude Wang 2025	4	3.71 (0.93–14.72)	96.2	0.062

Note: k refers to the number of studies included in each sensitivity model. The "Exclude Wang 2025" scenario corresponds to the previous singleton-focused model before inclusion of the twin gestation cohort. sensitivity analyses were performed by sequentially excluding individual studies from the primary meta-analysis model. The association between congenital uterine anomalies and preterm birth remained statistically significant across all sensitivity analyses. For caesarean delivery, pooled estimates varied according to study exclusion, consistent with the substantial between-study heterogeneity observed in the primary analysis

of placenta previa and postpartum bleeding, which was not consistently recorded in other studies. Perinatal mortality was only reported in one study [28] with no significant difference between CUA and controls (probably because of a small sample)[(46+Outcome)]. Goyal et al. [55] reported those cases of surgical complications of metroplasty without outcome comparisons. Therefore, the main findings of our review are informative with regard to miscarriage, preterm birth, malpresentation, and caesarean delivery; we do not have enough evidence to make conclusions concerning other maternal or neonatal outcomes.

Overall risk-of-bias assessment of the 30 studies included in the systematic review. Each horizontal bar represents the overall methodological quality judgment assigned to an individual study following critical appraisal using study-design–specific assessment tools. Green indicates low/moderate risk of bias, yellow indicates some concerns/moderate risk of bias, and red indicates high/serious risk of bias.

Discussion

The systematic review confirms that congenital uterine anomalies (CUA) are associated with increased risks of adverse pregnancy outcomes. Women with uterine malformations have an increased risk of miscarriage, preterm birth, and other adverse pregnancy outcomes [28, 32]. In a cohort of 62 women (26 with CUA and 36 controls) it was found that approximately 54% of pregnancies in the anomaly group proceeded to a live birth and 46% to miscarriage or loss compared to a much greater live birth in the control group. Similarly, a comparative study of unicornuate uteri revealed significantly low live-birth rates and high risks of ectopic pregnancy, miscarriage, and preterm birth in women with unicornuate uterus compared to controls [29]. The results highlight that congenital uterine defect - in particular, more severe anomalies - have a significant adverse impact on reproductive outcomes, despite the fact that the prognosis of an individual patient may differ based on the type of anomaly and patient history.

In our findings, preterm birth is one of the key complications related to anomalies of the uterus. In the literature, about 25–30% of women with CUA give birth

Table 5 GRADE summary of findings

Outcome	Studies (k)	Participants/pregnancies	Pooled effect estimate	Heterogeneity	Certainty of evidence	Main reasons for downgrading
Miscarriage	3	As reported across contributing studies	OR 1.45 (95% CI 1.13–1.86)	I^2 = 0.0%	Low	Observational evidence; residual confounding and outcome-definition variation
Preterm birth < 37 weeks	5	As reported across contributing studies	OR 3.74 (95% CI 1.99–7.02)	I^2 = 68.1%	Very low	Observational evidence; serious inconsistency; residual confounding; population heterogeneity
Fetal malpresentation	2	As reported across contributing studies	OR 19.28 (95% CI 6.27–59.24)	I^2 = 23.6%	Very low	Few studies; imprecision; variable outcome definition; residual confounding
Caesarean delivery	5	As reported across contributing studies	OR 3.52 (95% CI 1.11–11.09)	I^2 = 94.9%	Very low	Serious inconsistency; wide confidence interval; indication bias; institutional practice variation

Note: Certainty of evidence was assessed using GRADE. Because the evidence was derived predominantly from observational studies, the initial certainty was rated as low and downgraded where applicable for risk of bias, inconsistency, imprecision, indirectness, and potential publication bias. OR = odds ratio; CI = confidence interval; CUA = congenital uterine anomalies; k = number of studies. **Population:** Women with congenital uterine anomalies. **Comparison:** Women with normal uterine anatomy or the reference comparator defined in the original study. **Outcomes:** Miscarriage, preterm birth (<37 weeks), fetal malpresentation, and caesarean delivery

to preterm babies, which is which is substantially higher than the overall obstetric population [17, 18]. An example is a national inpatient sample study of more than 50,000 births of women with CUA: the rate was 26.8% preterm births, with a high rate of very preterm (<33 week) births in some subgroups of anomalies. Smaller clinical series also note that preterm labor is one of the most frequent complications in anomaly pregnancies: In one of the single-center studies, 55% of pregnancies with different uterine anomalies were associated with preterm delivery. Among women with uterine anomalies with a history of preterm birth, the risk of recurrence is particularly great – 60% in one group of studies [30]. The high risk of preterm birth is biologically plausible due to the small size of the uterine cavity and cervical insufficiency that is common in the malformations [56–58]. There is also some emerging evidence that anomalies can also interfere with normal uterine contractility and blood supply, also leading to early labor [37].

Fetal malpresentation was another consistently elevated risk in women with congenital uterine anomalies. Abnormal uterine anatomy often constrains fetal movement and growth, leading to a high incidence of non-cephalic presentations (such as breech) at term [18, 31]. In a tertiary care cohort, *42–43%* of pregnancies in women with CUA had a malpresentation at delivery, a striking contrast to the ~4% breech rate in unselected populations. Malpresentation in turn contributes to the markedly high rates of cesarean delivery observed in this patient group. Virtually all large studies of obstetric outcomes in women with uterine malformations report a 65–80% overall cesarean section rate [18, 28, 32]. Although fetal malpresentation is a recognised indication for caesarean delivery, the magnitude of association between these outcomes is not necessarily proportional. Caesarean delivery is influenced by multiple obstetric factors beyond presentation, including prior caesarean section, fetal condition, and clinical practice patterns, which may contribute to the observed differences in effect size. Indicatively, cesarean section has been reported to be 63.5% in the case of anomaly-related pregnancy in the case of an Israeli single-center study [18], and 78% among women with Mullerian duct anomalies in a Polish series. Even within the framework of the contemporary practice in obstetrics, the majority of clinicians choose surgical delivery due to the high rate of breech presentation and other complications in such pregnancies. Interestingly, a recent study that involved anatomically "hemi-uterus" anomalies (unicornuate, didelphic, complete bicornuate) reported a cesarean section rate of more than 90% in the anomaly cohort with malpresentation being the most frequent manifestation [31]. These findings suggest the clinical reality congenital uterine anomalies, often require operative delivery as a measure of their optimization of maternal-fetal outcomes.

The stronger association observed for fetal malpresentation compared with caesarean delivery likely reflects differences in the clinical nature of these outcomes. Malpresentation represents a more direct anatomical consequence of uterine cavity distortion, whereas caesarean delivery is influenced by multiple additional obstetric and institutional factors, including prior caesarean delivery, gestational age, fetal condition, and local delivery practices. Consistent with this pattern, Qian et al. [31] reported markedly increased risks of malpresentation in women with hemi-uterus, while caesarean delivery reflected broader obstetric decision-making beyond fetal presentation alone. Similarly, Tellum et al. [29] observed increased caesarean delivery rates in unicornuate uterus, but with more moderate adjusted effect estimates than those observed for malpresentation. Although external cephalic version may be technically challenging in structurally distorted uterine cavities, this outcome was inconsistently reported across studies. Collectively, these findings suggest that congenital uterine anomalies may have a more direct anatomical relationship with fetal presentation than with delivery mode, which remains influenced by broader obstetric and clinical decision-making factors.

There were interesting intergroup differences - and inconsistencies - of obstetric risk profile between different subtypes of anomalies. In the national sample, every subtype posed unique risks: e.g. uterine didelphys had the highest preterm birth rate (almost 35% of births were preterm), but septate uteri presented a higher risk of maternal complications (such as hemorrhage). The review revealed that anomalies with the unilateral or hemi-uterus configuration (unicornuate and didelphic uteri, and complete bicornuate uteri) are likely to have a similar pattern of unfavorable obstetric outcomes, with the risks of preterm birth, prelabor rupture of membranes, malpresentation, and following cesarean birth being notably high [31]. This is in line with the fact that, a small and single-sided uterine cavity has restricted space and irregular vascular supply to a developing fetus. A septate uterus - an abnormality in the middle of an otherwise normally sized uterus - could, however, have different risk profile, being more closely linked to first-trimester miscarriage and potentially less late-pregnancy complications such as malpresentation. In fact, septate uteri are traditionally associated with frequent pregnancy loss (they are usually mentioned as the most frequent uterine anomaly with the highest miscarriage rate) and the relatively low frequency of preterm birth or fetal growth retardation [36]. It should be stated though that the evidence regarding the difference of subtypes is not consistent. In a single retrospective study that directly

compared the outcomes of women with unification defects of the bicornuate type ($n = 4061$), didelphys type ($n = 1758$), and unicornuate type ($n = 2365$), and women with canalization defects of the septate uterus type ($n = 1758$), the majority of the obstetric outcomes were not statistically different, despite controlling confounders [18]. In that study, the initial difference in very preterm birth and placental abruption was higher in septate uteri compared with fusion defects but was not observed when adjusted with multivariate analysis. Therefore, whereas large population data indicate that each subtype of anomaly is associated with distinct risks, smaller controlled studies suggest that patient factors and underlying risk (not necessarily the subtype itself) can contribute to a significant number of the outcome differences. And this is a position that our review endorses: high-risk obstetric care should be given to women with any major congenital uterine anomaly, but the type of complication to expect may differ to some degree depending on the type of anomaly.

The managerial implications of these results are multifaceted. In the case of septate uterus - the most prevalent malformation in women with recurrent spontaneous abortion - the research question has always been whether surgery can enhance its prognosis. The evidence we included contradicted on this fact. On the one hand, several observational studies and case series indicate that hysteroscopic septum resection has the potential to significantly lower the rate of miscarriage and the number of live births in women with a septate uterus [36]. A recent pre-post study of 101 patients, e.g., showed a decreased miscarriage rate from 35.6% pre-surgery to 14.8% after septoplasty and the live-birth rate doubled (18% to 37%) in the first year after surgery. These results have encouraged a number of clinicians to recommend septum resection in patients with recurrent pregnancy loss or infertility due to a uterine septum. The first randomized controlled trial (the TRUST trial) reported no superiority of septum resection over expectant management in support of better reproductive outcomes [5]. In that multicenter RCT, live birth was seen in 31% of women who were randomized to the septum resection and 35% of those who were randomized to the expectant management and there was no significant difference in miscarriage or preterm birth in both groups. The null finding of the trial has been disputed, partly because of the characteristics of its inclusion criteria (many participants had small, partial septa) and sample size, but offers the strongest evidence to date challenging the utility of elective septoplasty in the behavior of pregnancy [5, 36]. So, the importance of septum resection is controversial: although the results provided by observational studies are rather encouraging, high-quality evidence has not proved the existence of an overt reproductive advantage. In the case of other types of anomalies, evidence-based interventions are even more limited. Such operations as surgical "unification" of bicornuate or didelphys uteri (metroplasty) are now rarely performed, and none of the included studies assessed such operations. Some patients with unicornuate uteri or other anomalies at risk of second-trimester loss may benefit from cervical cerclage or close cervical surveillance, as suggested by case series [28]. Nevertheless, there are no strong data regarding preventive measures (prophylactic cerclage) in conditions where congenital anomalies of the uterus are present, and this monitoring should be personalized in the absence of guidelines.

One complication in the synthesis of the literature regarding the congenital anomalies of the uterus is the non-homogeneity of the methods and classification systems of diagnosis across the investigations. Most of the earlier researches employed hysterosalpingography or two-dimensional ultrasound to detect abnormalities, which are not effective in describing the anatomy of the uterus and unable to differentiate between some of the subtypes [44]. Conversely, three-dimensional ultrasound and MRI have been applied in much more recent studies, and they significantly advance the accuracy of the diagnoses of Mullerian abnormalities [42, 43]. The extensive use of 3D transvaginal ultrasounds has probably elevated the number of previously unknown anomalies and enabled more optimal subclassification of the anomaly types [42]. Inconsistent reporting may occur even when there is improved imaging as a result of variation in the criteria used to classify the image. The ESHRE/ESGE classification system employs stricter anatomical criteria, which may result in a greater proportion of uteri being classified as septate compared with the older ASRM system, where similar morphologies may have been categorised as normal (arcuate). [6, 22, 39]. Ludwin et al. [39] compared the two classification systems on the same population and concluded that the ESHRE/ESGE criteria recognized septate uteri in much more women than the traditional criteria, which may be over diagnosing minor variants of septum. This lack of consistency has practical, clinical consequences: it can result in over-treatment (surgery on milder abnormalities, which might not have posed any problems), or, conversely, in being unable to compare studies that defined what a significant uterine abnormality is differently. According to some authors, the absence of a universal definition of anomalies, such as a septate uterus, is one of the problems preventing the formulation of effective conclusions regarding the effectiveness of management [36]. Thus, future research must endeavor to employ standardized, evidence-based diagnostic criteria of congenital uterine anomalies and present findings in defined subtype, to increase comparability and application of findings.

Limitations

The findings of this review should be interpreted in light of both study-level and review-level limitations.

Limitations of included studies: Most included studies were observational in design, with inherent risks of residual confounding and selection bias. There was considerable heterogeneity in study populations, classification of congenital uterine anomalies, and outcome definitions. In addition, variability in diagnostic modalities and inconsistent reporting of adjusted effect estimates may have influenced the pooled estimates. Some of them were small-scale studies or single-center series that reduced the statistical power and generalizability (e.g., some of the cohorts contained less than 30 cases of anomalies [16, 28]. Some studies did not have a proper internal control group of women without anomalies, which makes it hard to measure the excess risk due to the anomaly itself [15, 37]. Inconsistency in outcome definitions and patient population was also high. For example, some studies were based exclusively on women with recurrent miscarriage or infertility only [46, 48], and others on all pregnant women with an anomaly irrespective of obstetric history [17]. Such variability may introduce selection bias and limit comparability across studies. Also, a study relying on administrative data or registries can be misclassified; one validation study reported concerns over the quality of diagnostic coding of uterine anomalies, and pregnancy loss in regular medical records [50]. In a large U.S. hospital data set analysis, bicornuate uteri represented a surprisingly large percentage of cases (more than 70), probably due to over-coding of bicornuate cases against other anomalies in practice. These peculiarities of coding and identifying the cases may bias risk estimates by the subtype. Considering such constraints, quantitative estimates of risk used in this review (e.g., a three times increased risk of preterm delivery or miscarriage due to a uterine defect) be should be interpreted with caution. The actual extent of risk can vary in more strictly defined groups.

Limitations of the present review: At the review level, the number of studies contributing to some of the assessed outcomes was limited, restricting the precision of pooled estimates and precluding robust assessment of publication bias. Differences in study design and reporting also limited the ability to perform subgroup and sensitivity analyses for certain outcomes. Furthermore, inclusion of studies across diverse clinical settings may have contributed to inter-study heterogeneity. Data on the risk of uterine rupture in subsequent pregnancies following caesarean delivery in women with congenital uterine anomalies were limited and inconsistently reported across studies. However, despite the uncertainty that must be admitted, the pattern of directional results in different studies increases the conclusion that the congenital uterine anomalies produce a clinically significant effect on the results of the pregnancies.

An additional limitation is that the review protocol was not prospectively registered in PROSPERO. Although the methodology, eligibility criteria, and planned analyses were defined a priori and adhered to throughout the review process, the absence of formal protocol registration may limit external verification of methodological decisions and introduces the potential for unrecognized reporting bias.

Conclusion

This review synthesizes current evidence indicating that congenital uterine anomalies are associated with adverse pregnancy outcomes and highlights that persistent gap in the existing literature remain. Major congenital uterine anomalies, including septate, bicornuate, unicornuate, and didelphys uteri, are associated with increased risks of miscarriage, preterm birth, malpresentation, and caesarean delivery. Nevertheless, the severity of these risks, as well as the effectiveness of interventions (septum resection), is rather ambiguous because of the limitations in the number of available robust studies. The additional high-quality studies, such as larger prospective cohorts and randomized trials are urgently required to sharpen our perception of the outcome variability between the subtypes of anomalies and what kind of therapeutic intervention could possibly raise reproductive success in this group. In the future, enhanced standardization of the diagnosis and classification of uterine anomalies [39] will be essential; this will allow researchers and clinicians to align terminology when evaluating the effects of these rare yet significant disorders. By addressing these evidence gaps, we can better counsel patients with congenital uterine anomalies and develop management strategies to optimize their chances for a healthy pregnancy outcome.

Abbreviations

PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PTB	preterm birth
ART	assisted reproductive technology
TVUS	transvaginal ultrasound
RPL	recurrent pregnancy loss
RM	recurrent miscarriage
HSG	hysterosalpingography
HS	hysteroscopy
SIS	saline infusion sonography
NR	not reported
AFS	American Fertility Society
CUME	Congenital Uterine Malformation by Experts
TVS	transvaginal sonography
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
JBI	Joanna Briggs Institute tool
CUA	Congenital uterine anomalies
ESHRE/ESGE	European Society of Human Reproduction and Embryology/ European Society for Gynecological Endoscopy
RCT	Randomized Controlled Trials
OR	Odd Ratio

Author contributions
I.F -Literature search, Data extraction, Supervision T.H - Literature search, Screening, Data extraction M.K - Conceptualization, risk-of-bias evaluation, figure and table preparation, manuscript revision, supervision. C. N.A-Statistical analysis, outcome stratification, manuscript drafting C.P.U- Statistical analysis, outcome stratification, manuscript drafting, Manuscript review E.G.A- Supervision, final manuscript review, approval of submission version, guarantor of overall content integrity.

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Data availability
Data are available upon reasonable request. All data generated or analyzed during this study are included in this article.

Declarations

Ethical approval and consent to participate
The study was approved by Kampala International University Research Ethics Committee (KIU REC). All methods described herein were performed in accordance with the relevant guidelines and regulations of KIU REC. The review did not involve the collection of primary data from human participants. Therefore, consent to participate was not applicable.

Consent for publication
This study is a systematic review and meta-analysis based exclusively on data extracted from previously published studies. No individual participant data, images, or other identifying information were collected or reported; therefore, consent for publication was not required.

Competing interests
The authors declare no competing interests.

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