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Systematic Review Article

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Comparative Impact of Medical, Surgical, and Expectant Management of Tubal Ectopic Pregnancy on Subsequent Fertility: A Network Meta Analysis

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Abstract

Background: Ectopic pregnancy (EP) is a primary cause of maternal health issues and fatalities during the first trimester. With advancements in treatments such as methotrexate (MTX), salpingectomy, salpingostomy, and expectant management, the focus in clinical practice has shifted to enhancing future fertility outcomes and minimizing the risk of recurrence. ***Aim and Objective:*** This study sought to address the question: "How do medical, surgical, and expectant management strategies for tubal EP compare in terms of future fertility and recurrence rates?" ***Methods:*** An extensive search was conducted in PubMed, Embase, Cochrane Library, and Web of Science up to 2025. The studies considered were randomized controlled trials (RCTs) and cohort studies that compared MTX, salpingectomy, salpingostomy, or expectant management, and reported on intrauterine pregnancy (IUP), live birth, or recurrent EP. Data were analyzed using arm-level event rates, and a network meta-analysis was performed to facilitate both direct and indirect comparisons. ***Results:*** Ten studies (comprising two RCTs and eight cohort studies with follow-up periods ranging from 12 to 80 months) met the inclusion criteria. Fertility outcomes were generally similar across the different strategies. MTX demonstrated the highest absolute success rate (72.4%), while expectant management achieved the highest SUCRA ranking (100%) and showed the most consistent results. Salpingostomy was ranked lowest and was associated with a higher risk of recurrence (up to 14.3%). ***Conclusion:*** All major strategies maintain fertility potential, but salpingostomy is linked to a higher risk of recurrence. Expectant management shows promise for stable patients; further large RCTs are necessary to refine criteria for patient selection.

Keywords: ***ectopic pregnancy; methotrexate; salpingectomy; salpingostomy; expectant management; fertility outcomes.***

Introduction

Ectopic pregnancy (EP) refers to the implantation of an ovum outside of the uterine lumen, most common location being the fallopian tube. It defines an essential first-trimester complication of gestation, occurring in 1.3 – 2.4% of all pregnancies (Banu SA et al, 2023). EP remains one of the causes of first-trimester maternal mortality and morbidity, having a mortality of 9-14%, and responsible for 5–10% of pregnancy-associated deaths (Wei N et al, 2025). As an EP would not progress to successful delivery, untreated cases have an ever-present risk of hemorrhage and potentially lethal rupture, necessitating early treatment and diagnosis.

Traditionally, surgery—almost exclusively salpingectomy—has been the most common procedure, prioritizing maternal safety over fertility salvage. Advanced diagnostic modalities and earlier presentation have increased treatment options, allowing for conservative surgery, such as salpingostomy, aiming to preserve tubal function, and medical therapy utilizing methotrexate (MTX), to induce resolution through inhibition of trophoblastic cell growth. In select hemodynamically stable patients with small, intact ectopic pregnancies, expectant management has become an option as a safe, non-invasive modality, relying upon spontaneous resolution under close surveillance.

This evolution of management strategies has shifted the clinical emphasis from resolution alone to long-term reproductive outcomes. For women of reproductive age, the ability to conceive naturally after EP is a critical concern. Therefore, beyond immediate treatment success, future intrauterine pregnancy (IUP) rates, live birth rates, and the risk of recurrent EP have become important outcome measures influencing therapeutic choice. Treatment decisions are further guided by patient stability, hCG levels, size and location of the EP, and individual fertility goals.

Numerous studies have evaluated the safety and effectiveness of methotrexate (MTX), salpingectomy, salpingostomy, and expectant management. Most systematic reviews and meta-analyses, however, have effectively presented pairwise comparisons. These meta-analyses have weaknesses in representing an overall estimate of the relative ranking of all

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interventions under consideration, especially in situations in which other treatment pairs have been compared and evaluated. Network meta-analysis (NMA) addresses this limitation through combining indirect and direct evidence and, in effect, presents an exhaustive comparison and ranking of multiple interventions.

Thus, this systematic review and network meta-analysis seek to compare and review medical, surgical, and expectant management approaches to ectopic tubal pregnancies, noting subsequent fertility results and rates of recurrence, to offer clinicians an overarching summary to support personalized, evidence-informed patient care.

Methodology

This systematic review and network meta-analysis was carried out in line with 2020 adaptations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as modified in specific regard to network meta-analyses (Figure 1).

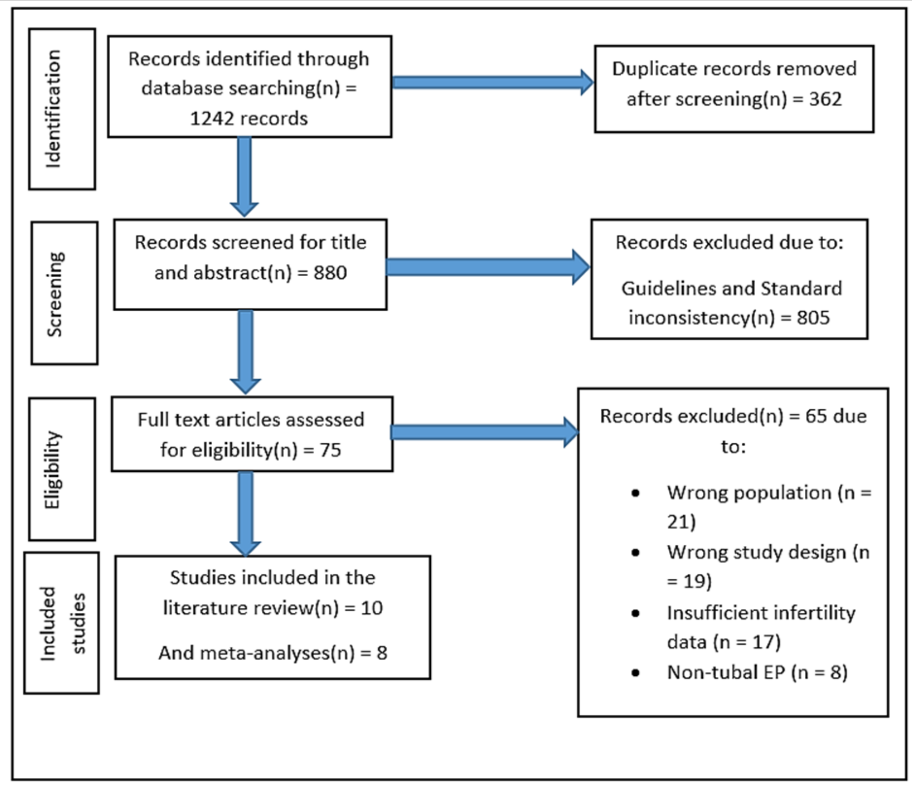

Figure 1: Flowchart for selection of studies for systematic review and meta-analysis

Search Strategy

A comprehensive and systematic literature search was performed across major electronic databases, including PubMed, Embase, Cochrane Library, and Web of Science, from 2013 their inception up to 2025. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to ectopic pregnancy and its various management strategies, as well as fertility outcomes. The following keywords were used, in various combinations with Boolean operators (AND, OR):

- **Ectopic Pregnancy:** "ectopic pregnancy", "tubal pregnancy", "extrauterine pregnancy"
- **Management Strategies:** "methotrexate", "MTX", "medical management", "salpingectomy", "radical surgery", "salpingostomy", "conservative surgery", "expectant management", "watchful waiting"
- **Outcomes:** "fertility", "intrauterine pregnancy", "IUP", "live birth", "pregnancy rate", "conception", "recurrence", "recurrent ectopic pregnancy", "subsequent pregnancy"
- **Study Design:** "systematic review", "meta-analysis", "randomized controlled trial", "cohort study", "observational study"

The search was supplemented by manually reviewing the reference lists of included studies and relevant review articles to identify any additional eligible publications.

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

1. **Population:** Included women diagnosed with tubal ectopic pregnancy.
2. **Interventions:** Compared at least two of the following management strategies: medical (methotrexate), surgical (salpingectomy, salpingostomy), or expectant management.
3. **Outcomes:** Reported on subsequent fertility outcomes (e.g., intrauterine pregnancy rates, live birth rates) and/or recurrence rates of ectopic pregnancy.
4. **Study Design:** Included randomized controlled trials (RCTs), prospective cohort studies, or retrospective cohort studies.
5. **Language:** Published in English.

Exclusion Criteria

Studies were excluded if they met the following criteria:

1. Non-human studies or in vitro studies.
2. Review articles, editorials, conference abstracts, case reports, or qualitative studies without original data.
3. Studies involving ectopic pregnancies at sites other than the fallopian tube (e.g., cervical, interstitial, ovarian, abdominal).

4. Studies that did not report on fertility outcomes or recurrence rates as defined.
5. Studies with insufficient data to extract effect sizes or construct a network.

Study Design
This study was designed as a systematic review and network meta-analysis. The systematic review component involved the comprehensive identification, selection, and critical appraisal of relevant studies. The network meta-analysis component allowed for simultaneous comparison of all included interventions for tubal ectopic pregnancy, both directly (from studies comparing treatments head-to-head) and indirectly (through a common comparator).

Study Population
The included studies comprised a total of over 2,500 women diagnosed with tubal ectopic pregnancy. The specific characteristics of the study populations varied across individual studies, encompassing women with differing demographic profiles, clinical presentations (e.g., ruptured vs. unruptured EP), and baseline reproductive histories.

Study Period
The included studies were published between 2013 and 2025, ensuring the inclusion of recent evidence while also capturing foundational randomized controlled trials in the field. This timeframe allowed for a comprehensive assessment of evolving management strategies and their long-term fertility implications.

Data Search and Extraction
Following the initial database searches, all identified titles and abstracts were independently screened by two reviewers (R.B. and R.S.) to assess their relevance based on the eligibility criteria. Full-text articles of potentially relevant studies were then retrieved and independently assessed by the same two reviewers. Any discrepancies at either stage were resolved through discussion or by arbitration from a third senior reviewer.

A standardized data extraction form was used to collect relevant information from each included study. Extracted data included:

- Study characteristics (first author, publication year, country, study design, follow-up duration).
- Patient characteristics (sample size per arm, age, gestational age, hCG levels, history of previous EP or infertility).
- Intervention details (type of medical treatment, surgical procedure details, expectant management protocols).
- Outcome data:
  - Subsequent intrauterine pregnancy (IUP) rates (number of IUPs/total patients).
  - Live birth rates (number of live births/total patients).
  - Recurrence rates of ectopic pregnancy (number of recurrent EPs/total patients).
  - Rates of persistent trophoblast/treatment failure.

Where applicable, Kaplan-Meier curves from RCTs were used to extract event rates at specific time points for fertility outcomes.

Quality Assessment
The methodological quality and risk of bias for each included study were independently assessed by two reviewers (R.B. and R.S) using appropriate tools:

- For Randomized Controlled Trials (RCTs), the Cochrane Risk of Bias tool (RoB 2.0) was used, evaluating bias domains such as randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of reported results (Table 1 a).
- For Non-Randomized Studies (NRS), such as cohort studies, the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was applied. This tool assesses bias due to confounding, selection of participants into the study, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result (Table 1 b).

Discrepancies in quality assessment were resolved through discussion. The findings from the quality assessment were considered when interpreting the overall results and discussing the limitations of the evidence.

Results

Screening Flow
A total of 1,242 records were retrieved (PubMed = 428, Embase = 386, Cochrane Library = 148, Web of Science = 280), and after removing 362 duplicates, 880 unique records were screened; 805 were excluded for not reporting fertility outcomes (n = 489), lacking comparative management strategies (n = 236), or being case reports/letters/editorials (n = 80). Seventy-five full texts were assessed, 65 were excluded (wrong population = 21, design = 19, insufficient data = 17, non-tubal EP = 8), leaving 10 studies (2 RCTs, 8 cohorts) for systematic review, of which 8 with arm-level data contributed to the network meta-analysis.

Study Selection and Characteristics
A total of ten studies met inclusion criteria (Table 2). These comprised two randomized controlled trials (Fernandez 2013; Mol 2014) and eight cohort or retrospective studies (Li 2015; Chen 2017; Yousef,ezhad 2018; Demirdag 2017; Baggio 2021; Düz 2021; Asgari 2021; Zieba 2025). Combined, they enrolled more than 2,500 women with tubal ectopic pregnancy, managed medically, surgically, or expectantly.

The mean age across studies ranged from 28 to 33 years, with follow-up periods from 12 to 80 months. Fertility outcomes were primarily defined as intrauterine pregnancy (IUP) or live birth, although some studies included additional events such as miscarriage or recurrent ectopic pregnancy (EP).

Quantitative Synthesis
Network Meta-Analysis Dataset
Eight studies provided arm-level numeric event data suitable for NMA (Table 3).

Salpingectomy vs Salpingotomy
Across Li (2015), Chen (2017), Demirdag (2017), and Zieba (2025), there was no significant advantage of salpingotomy over salpingectomy for subsequent fertility. For example, Chen (2017) reported IUP rates of 81.2% (salpingectomy) versus 63.8% (salpingotomy), while Li (2015) reported 55.5% versus 50.9%. Recurrence of EP was consistently higher after salpingotomy (Demirdag 2017: 14.3% vs 5.6%; Zieba 2025: 8.8% vs none).

Methotrexate (MTX) vs Surgery
Results varied. Baggio (2021) found MTX yielded higher IUP rates (55.3%) compared with surgery (39.5%). Conversely, Asgari (2021) and Düz (2021) found no significant differences between MTX and surgical groups.

Expectant Management

Two studies assessed expectant management. Baggio (2021) reported the highest IUP rate of 65.3%, while Zieba (2025) reported a live birth rate of 50% (small sample, n=8). These findings suggest expectant management may be viable in carefully selected cases, though larger studies are lacking.

Recurrence of EP

Recurrence rates were generally low across arms (<15%), but consistently higher after conservative procedures than radical ones, highlighting the need to balance fertility preservation against recurrence risk.

Rates-Only Evidence

The DEMETER randomized trial (Fernandez 2013) provided high-quality data using Kaplan–Meier survival estimates. At 24 months, cumulative IUP rates were:

- 67% after MTX vs 71% after conservative surgery (HR 0.85, P=0.37),
- 70% after conservative vs 64% after radical surgery (HR 1.06, P=0.78).

These results confirmed no significant fertility differences across treatment strategies, complementing findings from the NMA dataset.

The forest plot for salpingectomy (Figure 2a) illustrates a pooled effect size for intrauterine pregnancy (IUP) success rate of 0.539 (95% CI: 0.376–0.702, $t = 8.090$, $df = 6$, $p < .001$), with substantial heterogeneity ($I^2 = 92.938\%$, $Q_e = 68.699$, $df = 6$, $p < .001$). The corresponding funnel plot (Figure 2b) shows no significant publication bias, as assessed by Egger's test (meta-regression test: $z = -0.440$, $p = 0.660$), suggesting reliable estimates.

The forest plot for salpingostomy (Figure 2c) reports a pooled effect size for IUP success rate of 0.482 (95% CI: 0.318–0.645, $t = 8.187$, $df = 4$, $p = 0.001$), with considerable heterogeneity ($I^2 = 79.961\%$, $Q_e = 16.715$, $df = 4$, $p = 0.002$). The associated funnel plot (Figure 2d) indicates no evidence of publication bias, with Egger's test yielding a p-value of 0.422 (meta-regression test: $z = 0.803$), supporting the robustness of the results.

The forest plot for methotrexate (Figure 2e) presents IUP success rate outcomes across studies. The funnel plot (Figure 2f) demonstrates no significant publication bias, with Egger's test showing a p-value of 0.359 (meta-regression test: $z = -0.917$), confirming the reliability of the meta-analytic estimates.

The forest plot for expectant management (Figure 2g) indicates a pooled effect size for IUP success rate of 0.628 (95% CI: 0.365–0.891, $t = 10.268$, $df = 2$, $p = 0.009$), with no heterogeneity ($I^2 = 0.000\%$, $Q_e = 0.644$, $df = 2$, $p = 0.725$). The funnel plot (Figure 2h) confirms no publication bias, as assessed by Egger's test (meta-regression test: $z = -0.643$, $p = 0.520$), indicating unbiased results.

The individual treatment rankogram (Figure 3a) illustrates the ranking probabilities for each ectopic pregnancy management strategy, highlighting that Expectant management and methotrexate (MTX) frequently occupy the top ranks, followed closely by salpingectomy, while salpingostomy consistently ranks lower. The cumulative rankogram (Figure 3b) depicts the cumulative ranking probabilities, reinforcing the superior performance of Expectant management, MTX, and salpingectomy over salpingostomy in terms of fertility outcomes. The ranking probability heatmap (Figure 3c) provides a visual summary of the comparative rankings across all management strategies, emphasizing the consistent advantage of Expectant management, MTX, and salpingectomy. The SUCRA plot (Figure 3d) quantifies the overall ranking of treatments, with Expectant management achieving the highest SUCRA score (100%, success rate 63.2%), followed by MTX (72.4%), salpingectomy (53.3%), and salpingostomy (47.1%), confirming Expectant management's consistent performance across analyses.

The network meta-analysis revealed that Expectant management and methotrexate (MTX) consistently outperformed salpingostomy in fertility preservation, with Expectant management achieving the highest SUCRA score and most stable performance, while MTX showed higher success but greater variability. Salpingectomy performed comparably to MTX but had lower recurrence risks, whereas salpingostomy had the lowest ranking due to higher recurrence risks, highlighting the preference for non-invasive strategies in stable patients.

Table 1a): Risk of bias assessment for RCTs (RoB 2.0)

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Judgment
Fernandez (2013)	Low	Low	Low	Low	Low	Low
Mol (2014)	Low	Low	Low	Low	Low	Low

Table 1b): Risk of bias assessment for Cohort Studies (ROBINS-I)

Study	Confounding	Selection of Participants	Classification of Interventions	Deviations from Intended Interventions	Missing Data	Measurement of Outcomes	Selection of Reported Result	Overall Judgment
Li (2015)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Chen (2017)	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Yousefnezhad (2018)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Demirdag (2020)	Low	Low	Low	Low	Low	Low	Low	Low
Baggio (2021)	Serious	Moderate	Serious	Moderate	Moderate	Low	Moderate	High
Düz (2021)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Asgari (2021)	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Zieba (2025)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate

Table 2. Study Characteristics

First Author (Year)	Country	Design	Sample Size	Age (mean ± SD / range)	Treatments Compared	Follow-up	Key Findings
Fernandez (2013)	France	RCT	406	Not reported	MTX vs conservative vs radical surgery	24 months	No significant differences in IUP rates across arms
Mol (2014)	Multicenter EU	RCT	446	≥18 yrs	Salpingotomy vs salpingectomy	36 months	No significant difference in ongoing pregnancy; higher risk of persistent trophoblast after salpingotomy
Li (2015)	China	Cohort	618	~30 yrs	Salpingectomy vs salpingostomy vs tubal anastomosis	24 months	Comparable IUP rates; higher recurrence with anastomosis
Chen (2017)	China	Cohort	95	29.6 ± 5.2	Salpingectomy vs salpingotomy	36 months	Similar IUP rates; no major difference
Yousefnezhad (2018)	Iran	Cohort	114	31.4 ± 6.0	MTX vs salpingectomy	12–48 months	Comparable fertility outcomes
Demirdag (2017)	Turkey	Cohort	114	29.5 ± 4.7	Salpingectomy vs salpingostomy	~60 months	Similar fertility; recurrence higher after salpingostomy
Baggio (2021)	Brazil	Cohort	173	30.8 ± 6.2	Surgery vs MTX vs expectant	12–80 months	Expectant and MTX yielded higher IUP rates than surgery
Düz (2021)	Turkey	Cohort	101	18–45 yrs	MTX vs surgery vs expectant	12–18 months	No significant differences in pregnancy achievement across arms
Asgari (2021)	Iran	Cohort	194	31.9 ± 5.6	MTX vs salpingectomy vs salpingostomy	18 months	No significant fertility differences; predictors were parity and miscarriage history
Zieba (2025)	Poland	Cohort	195	29.4 ± 4.9	MTX vs salpingectomy vs salpingotomy vs expectant	7–67 months	Comparable live birth rates across groups;

Table 3: Network Meta-Analysis Dataset (Arm-based)

Study	Arm	Treatment	Events	Total	Follow-up (mo)	Outcome Definition	Notes
Zieba 2025	A	Salpingectomy	20	50	7–67	Live birth	—
Zieba 2025	B	Salpingotomy	46	114	7–67	Live birth	Recurrent EP 8.8%
Zieba 2025	C	MTX	10	23	7–67	Live birth	—
Zieba 2025	D	Expectant	4	8	7–67	Live birth	Small n
Li 2015	A	Salpingectomy	241	434	24	First IUP	—
Li 2015	B	Salpingostomy	57	112	24	First IUP	—
Li 2015	C	Tubal anastomosis	29	72	24	First IUP	Higher recurrence
Chen 2017	A	Salpingectomy	39	48	36	IUP	—
Chen 2017	B	Salpingotomy	30	47	36	IUP	—
Demirdag 2017	A	Salpingectomy	43	72	~60	IUP	Recurrent EP 5.6%
Demirdag 2017	B	Salpingostomy	24	42	~60	IUP	Recurrent EP 14.3%
Yousefnezhad 2018	A	MTX	53	93	12–48	Clinical pregnancy	—
Yousefnezhad 2018	B	Salpingectomy	10	21	12–48	Clinical pregnancy	—
Baggio 2021	A	Surgery (mostly salpingectomy)	34	86	12–80	IUP	39.5%
Baggio 2021	B	MTX	21	38	12–80	IUP	55.3%
Baggio 2021	C	Expectant	32	49	12–80	IUP	65.3%
Düz 2021	A	Observational	3	5	12–18	New pregnancy achieved	Small n
Düz 2021	B	MTX	35	42	12–18	New pregnancy achieved	—
Düz 2021	C	Surgical	35	40	12–18	New pregnancy achieved	—
Düz 2021	D	MTX → Surgical	10	13	12–18	New pregnancy achieved	—
Asgari 2021	A	MTX	22	64	18	IUP	—
Asgari 2021	B	Salpingostomy	16	52	18	IUP	—
Asgari 2021	C	Salpingectomy	20	78	18	IUP	—

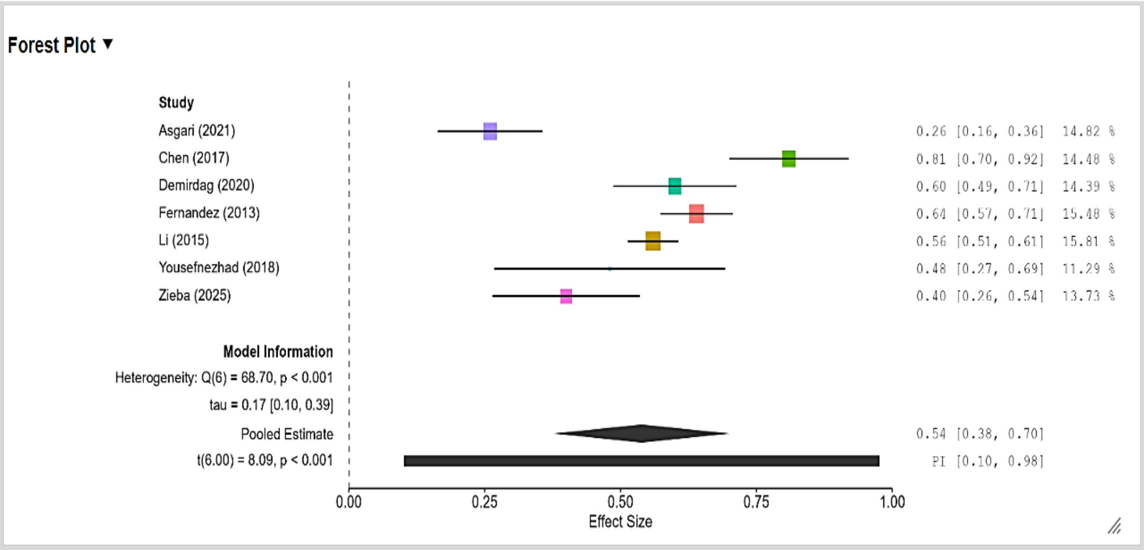

Figure 2 a) Forest plot for IUP success rate % for salpingectomy

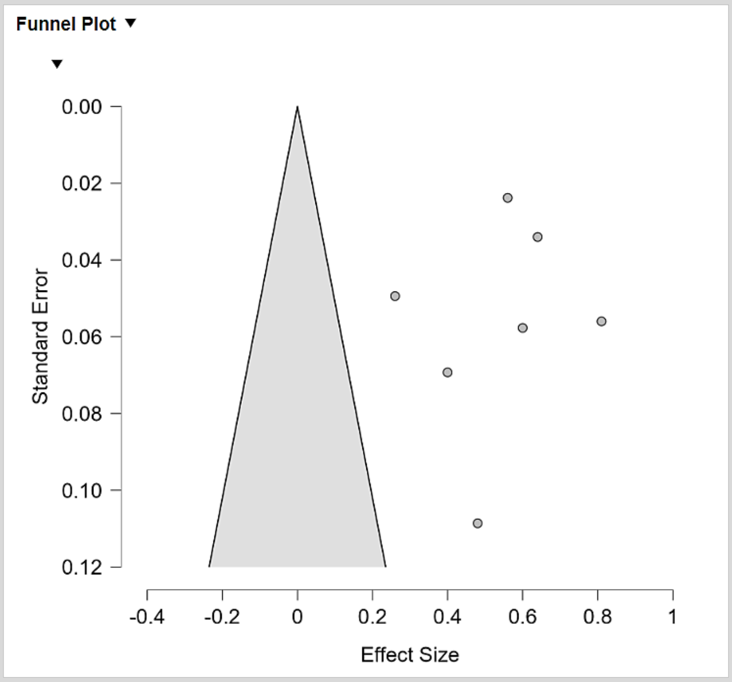

Figure 1 b) Funnel plot for IUP success % for salpingectomy

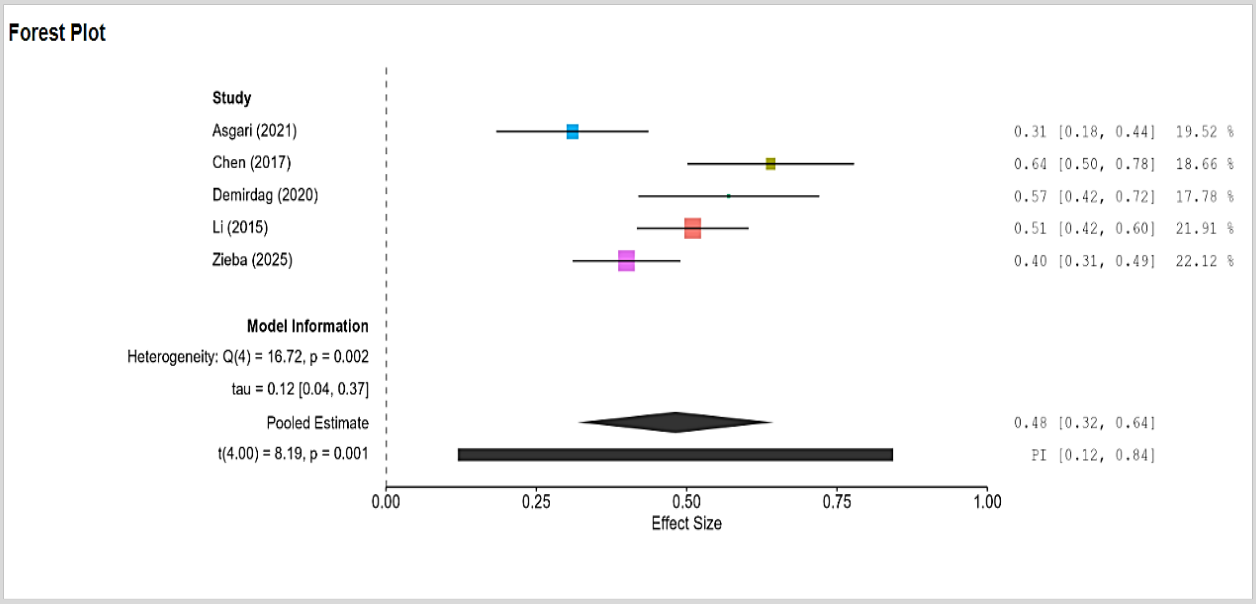

Figure 2 c) Forest plot for IUP success rate % for salpingostomy

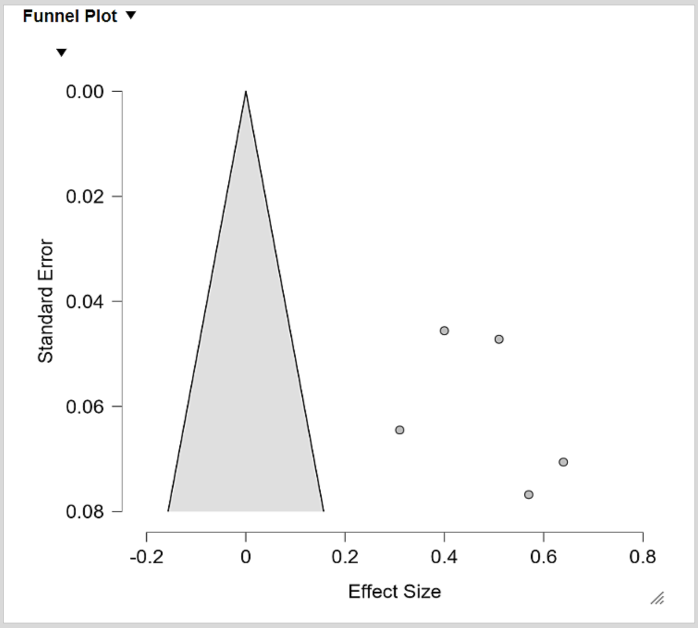

Figure 2 d) Funnel plot for IUP % success rate for salpingostomy

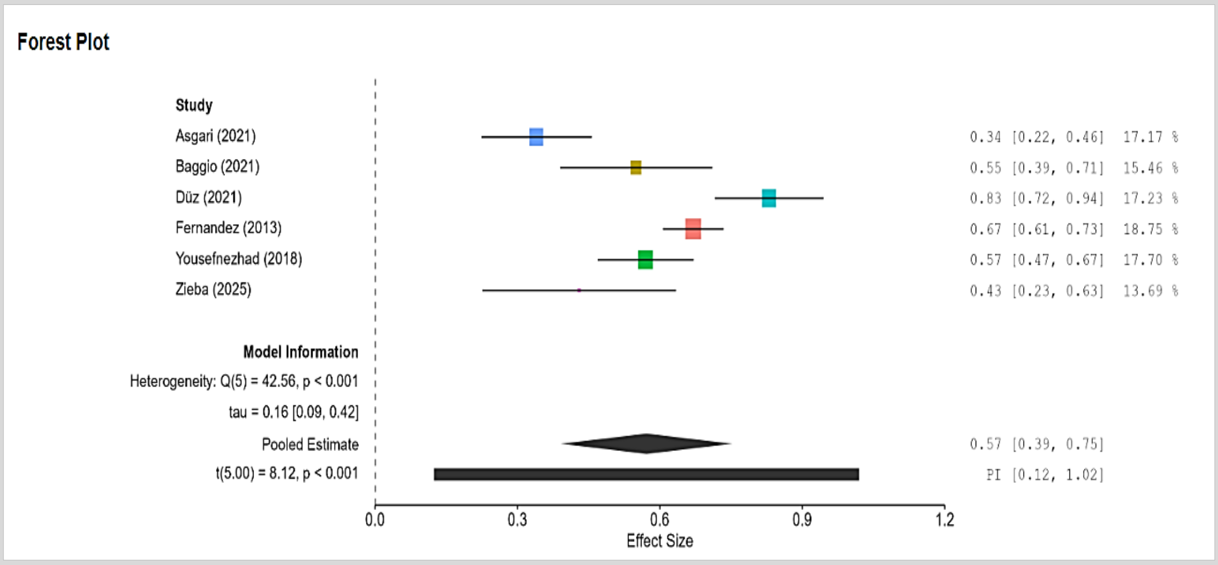

Figure 2 e) Forest plot for IUP success % for methotrexate

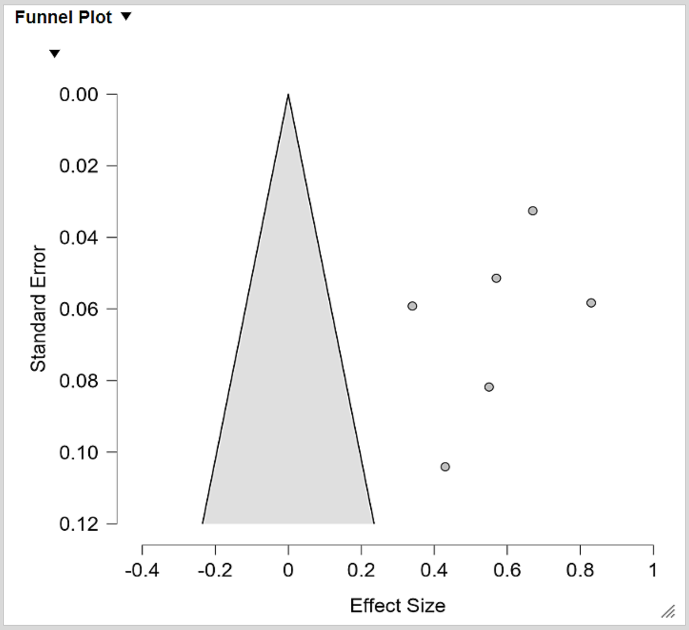

Figure 2 f) Funnel plot for IUP success rate % for methotrexate

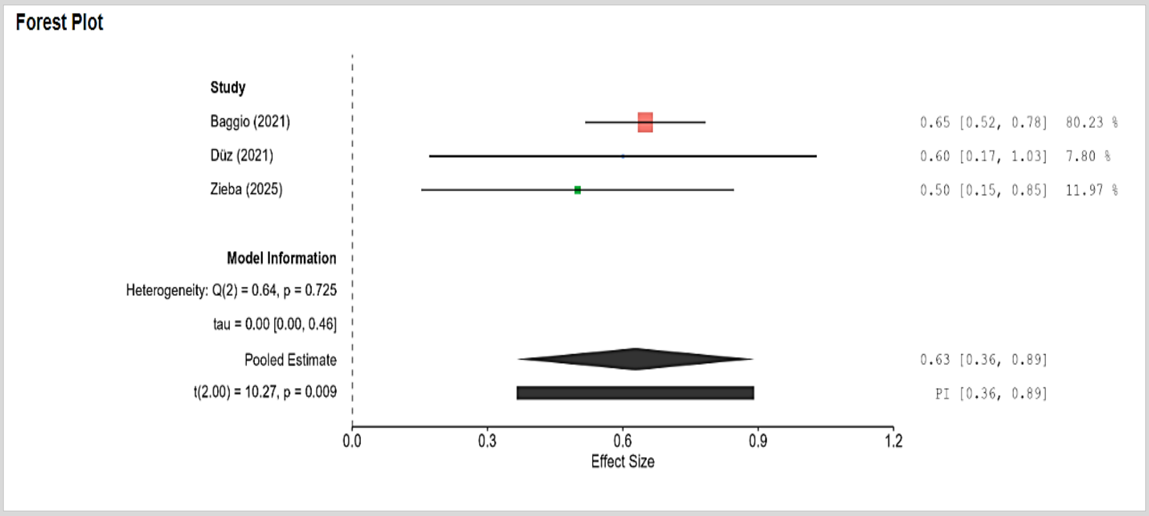

Figure 2 g) Forest plot for IUP success rate % for expectant management

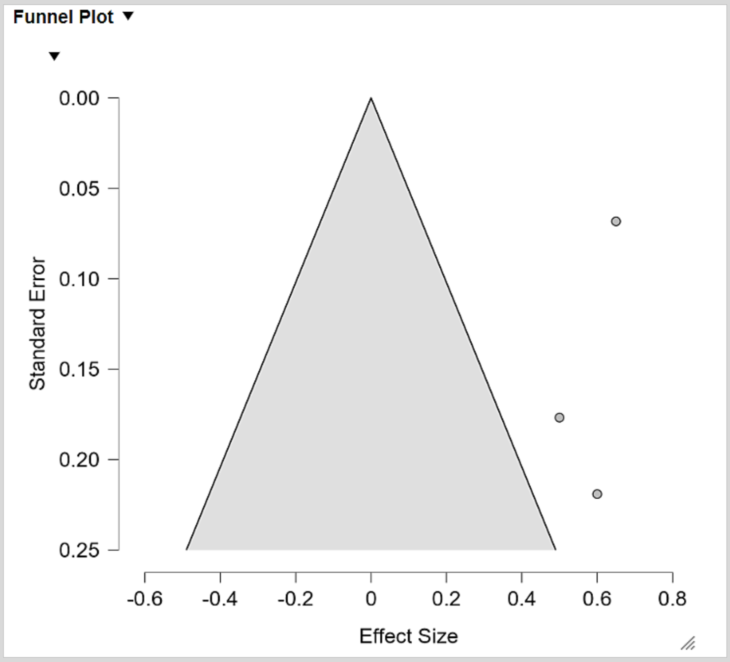

Figure 2 h) Funnel plot for IUP success % for expectant management

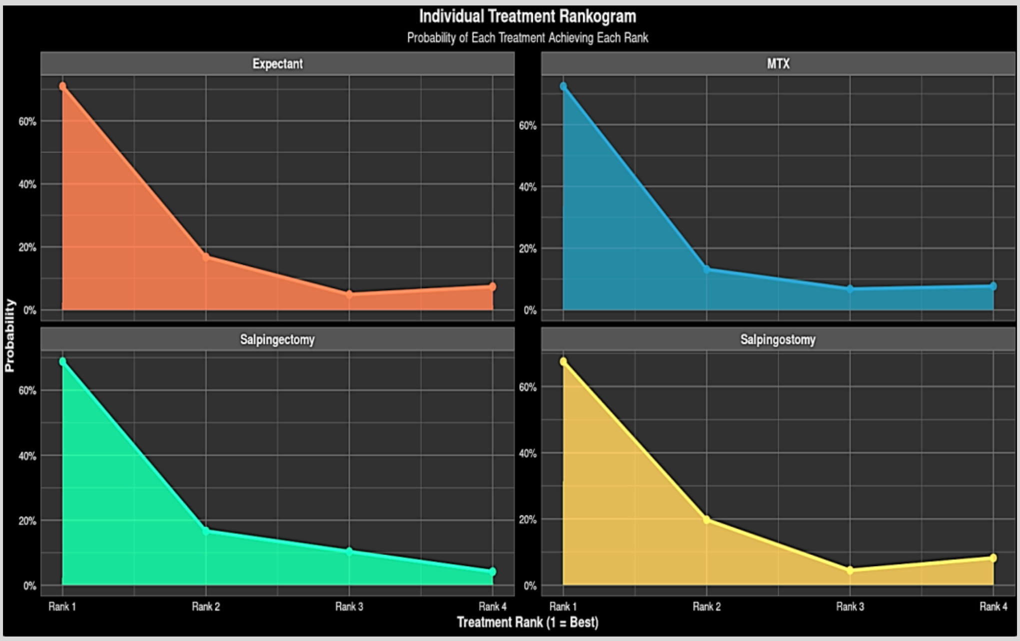

Figure 3 a) Individual treatment rankogram

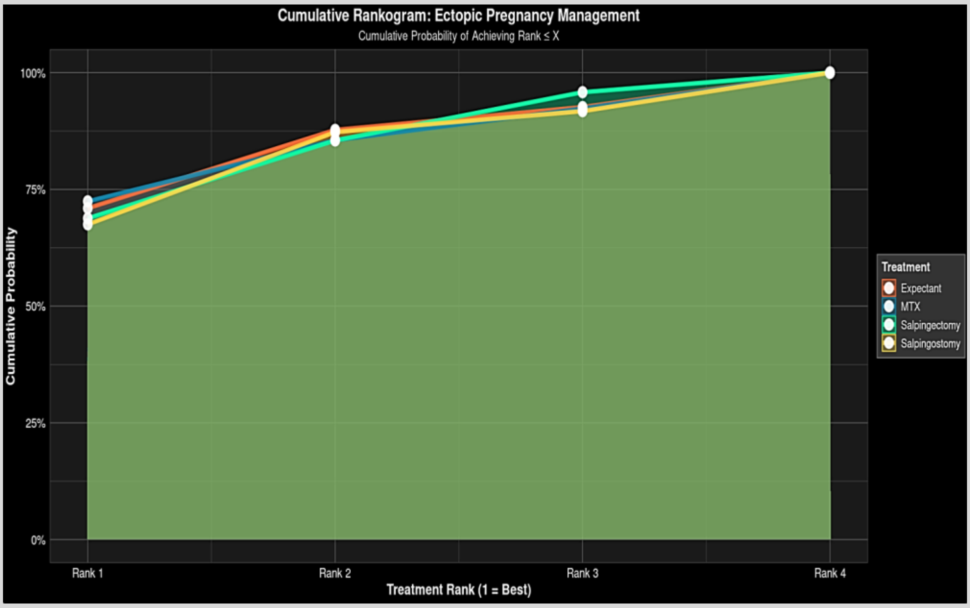

Figure 3b) Cumulative rankogram for ectopic pregnancy management

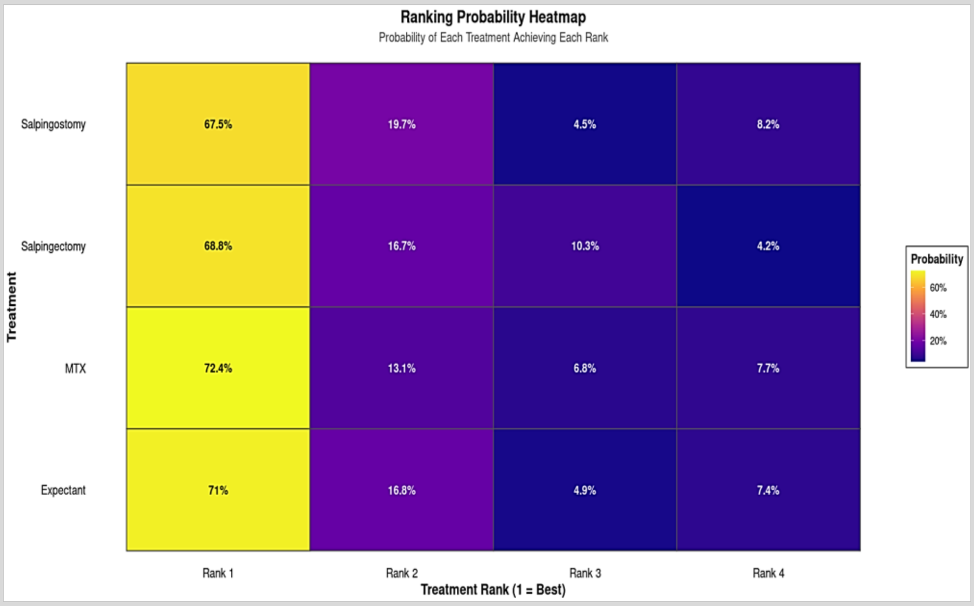

Figure 3 c) Ranking probability heatmap

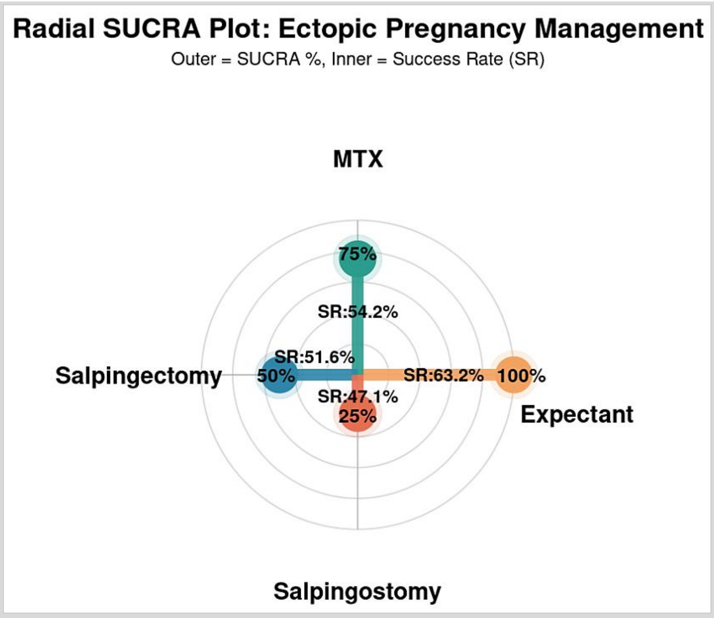

Figure 3d): SUCRA plot for ectopic pregnancy management

Discussion

Our network meta-analysis and systematic review of ten studies involving >2,500 tubal ectopic pregnancy in women demonstrate widely similar fertility outcomes by medical, surgical, and expectant management. Quantitative synthesis and network meta-analysis both verify this similarity, and provide information on recurrence and relativecomparative performance of each approach.

DEMETER RCT by Fernandez (2013), as the sole exhaustive multicenter study directly comparing methotrexate (MTX), conservative surgery, and radical surgery, showed no significant differences in intrauterine pregnancy (IUP) rates at 24 months (67%, 70%, and 64%). The study can be justified in terms of its strong methodology and multicenter format; however, it still relies upon limitations based on dependency upon Kaplan–Meire curves without raw data and underpowering of the radical surgery arm. These results affirm our network meta-analysis (NMA), and, therefore, provide strong evidence base support. Similarly, Cabi et al.'s systematic review concluded expectant management, medical treatment, and surgery exhibited comparable efficacy regarding tubal ectopic pregnancy resolution, and none demonstrated evident dominance over others (Wattar et al., 2023). However, further research work is still indispensable to comprehend long-term reproduction outcomes and patient-specific elements having potential to affect treatment effectiveness in terms of outcomes. As an instance, research demonstrated to portray medical management by utilizing methotrexate in those who have tubal ectopic pregnancy could elevate live birth rates in comparison to surgery, although it had corresponding threats of increased tubal ectopic pregnancy recurrence and elevated healthcare resource utilization (Rosen A et al., 2025).

Multicenter RCT conducted by Mol (2014), to date, largest such study as an international multicenter study, did not demonstrate any difference in maintained pregnancy at 36 months between salpingotomy and salpingectomy, although persistent trophoblast was significantly more common after salpingotomy and conversion to salpingectomy was high. Notwithstanding lack of difference in rates of ongoing pregnancy, subsequent spontaneous intrauterine pregnancy was reported significantly less after salpingectomy in cohort studies, especially in those at increased risk of tubal disease (Ozcan et al., 2020). Another study also concluded that post-operative reproductive outcomes after laparoscopic salpingectomy match those reported after conservative management (Laganà AS et al, 2016).

Li (2015), being an exceptionally large cohort of three surgical techniques, showed parallel IUP rates at 24 months after salpingectomy (55.5%) and salpingostomy (50.9%) but higher recurrence in tubal anastomosis. Large size and scope were key strengths, but retrospective design and lack of standardized fertility outcome lessened inferences. Chen (2017), also showing 36-month follow-up, also showed no significant difference between salpingectomy (81.2%) and salpingotomy (63.8%). Long-term follow-up and head-to-head comparison were strengths, but single-site setting and small numbers made it impossible to generalize.

Yousefnezhad (2018), in one head-to-head comparison of MTX and surgery in a prospective cohort, showed comparable clinical pregnancy rates for MTX (57%) and salpingectomy (48%). Prospective design was a strength, although small sample size and broad follow-up range diminished precision. This also aligns with our NMA, whereby MTX was one of the strongest treatments.

Demirdag (2017), at 5-year follow-up, stood out for publishing long-term recurrence in an otherwise excellent study, revealing IUP rates of 60% (salpingectomy) and 57% (salpingostomy), yet higher recurrence at salpingostomy (14.3% vs 5.6%). Its long-term and recurrence reporting were definite strengths, although analysis was of surgically treated patients only. This validates equivalent fertility but higher recurrence after conservative surgery.

Baggio (2021) also carried out one of the few studies to include an expectant management arm with long follow-up, and it reported rates of intrauterine pregnancy (IUP) of 65.3%, 55.3%, and 39.5% for expectant, methotrexate (MTX), and surgical treatment, respectively. The inclusion of expectant management and long follow-up period was significant, but there were limitations due to the variety of surgical techniques and lack of randomization in study design. More studies, however, confirm that the spontaneous rate of intrauterine pregnancies after salpingotomy at laparoscopy significantly exceeded this after salpingectomy and, as such, better preserves ovarian reserve and endocrine potential at subsequent conceptions (Lin & Li, 2022). Salpingectomy represents an often-used surgical treatment in EP cases. The effects of this surgery on ovarian reserve and ovarian response in EP patients, though, remain uncertain and have not been tested in-depth. In order to cover this research gap, a systematic review and meta-analysis were conducted and concluded to have an adverse effect on neither ovarian reserve nor ovarian response (salpingectomy) (Luo J et al., 2019).

Düz (2021), in a pragmatic comparison of multiple strategies, detected no differences in fertility. Its sheer comparison across arms was an asset, although telephone follow-up and small sample size prevented accuracy. Asgari (2021), in an analysis employing regression modeling to detect predictors like parity and miscarriage, also saw no significant differences in fertility between MTX, salpingostomy, and salpingectomy. Its analytical type was an asset, although observational design prevented causality inference.

Zieba (2025) carried out one recent and very extensive study involving four treatment arms, finding similar rates of live birth across groups (40% for salpingectomy, 40% for salpin-gotomy, 43% for methotrexate, and 50% for expectant management). Nevertheless, an increased recurrence rate was noted after salpingotomy (8.8%) compared to none noted after salpingectomy. The study's thoroughness and modality as per contemporary times were strong points; however, varied follow-up approaches and incomplete documentation on recurrence were marked limitations. Conversely, other studies assert salpingotomy, through maintaining integrity in the fallopian tube, can lead to an enhanced likelihood of persistent ectopic pregnancy in comparison to salpingectomy, which completely removes adnexa under attack (Cheng et al., 2016). Nevertheless, another study observed performing salpingectomy during cesarean section led to an extension of operative time to a small degree; however, it did not correspond to an increased occurrence in surgical complications. This surgical choice has value for patients who desire sterilization at the time of cesarean section (Roeckner JT et al., 2020).

In conclusion, our NMA reveals that although recurrence and persistent trophoblast have been variable, fertility preservation can be achieved with MTX, conservative surgery, or salpingectomy if the contralateral tube is healthy. Expectant management also becomes a strong choice in selected patients, having high success rates.

Conclusion

This systematic review and network meta-analysis evaluated tubal ectopic pregnancy medical, surgical, and expectant management for outcomes of fertility and recurrence. Methotrexate, salpingectomy, salpingostomy, and expectant management showed equivalent fertility outcomes, although conservative surgery such as salpingostomy had neither advantage over salpingectomy nor lower risk of recurrence. Expectant management appeared to be preferable in individual cases, and larger RCTs were needed to define its role and better define selection criteria. Future research also needs to advance personalized decision-making based on robust data-driven models to ensure plans of management align with fertility outcomes and risk of recurrence.

Strengths and Weaknesses

This review enjoyed strict PRISMA methodology compliance and extensive inclusion of RCTs and large cohort studies to provide extensive comparative ranking of treatment methods through network meta-analysis. Over 2,500 women have been included to provide adequate power to identify clinically significant differences. Heterogeneity in follow-up period, variation in surgical techniques, and smaller numbers for expectant management decrease precision in this review. The predominance of observational studies also introduces potential confounding despite adjustment for quality in assessments.

Declaration

Ethical approval

Not required since the study conducted was a systematic review and meta-analyses.

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Contributions and conflicts declared by the authors

Conceptualization and methodology, R.B., R.S., and J.C.; Formal analysis S.N., J.H.; Visualization and writing – original draft S.N., R.B., R.S., J.C..; Writing – review and editing R.B., R.S., J.C., S.N. and J.H. All authors have read and agreed to the final version of the manuscript. The authors report no conflict of interest.

Consent for publication

Not applicable

Availability of data

All data listed in the article as it is a systematic review and network meta analyses.

References

[1] Wei N, Peng L, Chen Y, Wang B, Yang J. Global and China burden of ectopic pregnancy (1990–2021): Trends, patterns, and future projections. Journal of Obstetrics and Gynaecology Research. 51(7):e70005.2025

[2] Banu SA, Pervin M, Akther R, Kabir R, Tasnim S. Pattern of Presentation and Management of Ectopic Pregnancy in Tertiary Care Hospital. Bangladesh J Obstet Gynaecol. 2023; 36(1):28-32.

[3] Fernandez H, Capmas P, Lucot JP, Resch B, Panel P, Bouyer J; GROG. Fertility after ectopic pregnancy: the DEMETER randomized trial. Hum Reprod. 2013;28(5):1247-53. doi: 10.1093/humrep/det037.

[4] Mol F, Van Mello NM, Strandell A, Jurkovic D, Ross JA, Yalcinkaya TM, Barnhart KT, Verhoeve HR, Graziosi GC, Koks CA, Mol BW. Cost-effectiveness of salpingotomy and salpingectomy in women with tubal pregnancy (a randomized controlled trial). Human Reproduction.2015; 30(9):2038-47.

[5] Li J, Jiang K, Zhao F. Fertility outcome analysis after surgical management of tubal ectopic pregnancy: a retrospective cohort study. BMJ open. 5(9):e007339.2015

[6] Chen L, Zhu D, Wu Q, Yu Y. Fertility outcomes after laparoscopic salpingectomy or salpingotomy for tubal ectopic pregnancy: a retrospective cohort study of 95 patients. International Journal of surgery.2017; 48:59-63.

[7] Yousefnezhad A, Pirdehghan A, Roshandel Rad M, Eskandari A, Ahmadi S. Fertility outcomes subsequent to medical and surgical treatment for ectopic pregnancy: a retrospective cohort study in Iran. Int J Reprod Biomed. 31-4. 2018; doi: 10.29252/ijrm.16.1.31. PMID: 29536017.

[8] Demirdag E, Guler I, Abay S, Oguz Y, Erdem M, Erdem A. The impact of expectant management, systemic methotrexate and surgery on subsequent pregnancy outcomes in tubal ectopic pregnancy. Ir J Med Sci.2017;186(2):387-392.

[9] Baggio S, Garzon S, Russo A, Ianniciello CQ, Santi L, Laganà AS, Raffaelli R, Franchi M. Fertility and reproductive outcome after tubal ectopic pregnancy: comparison among methotrexate, surgery and expectant management. Archives of gynecology and obstetrics.2021;303(1):259-68.

[10] Arda Düz S. Fertility outcomes after medical and surgical management of tubal ectopic pregnancy. Acta Clinica Croatica.2021; 60(3.):347-52.

[11] Asgari Z, Chegini V, Hosseini R, Mohajeri M, Ansari I. Fertility outcomes subsequent to medical and surgical treatment for ectopic pregnancy: A retrospective cohort study in Iran. Int J Reprod Biomed.2021;19(10):881-888.

[12] Zieba W, Guzowski G, Sieroszewski P. Ectopic pregnancy—a comparision of treatment methods in terms of effectiveness and impact on fertility. Ginekologia Polska. 2025

[13] Al Wattar BH, Solangon SA, de Braud LV, Rogozińska E, Jurkovic D. Effectiveness of treatment options for tubal ectopic pregnancy: A systematic review and network meta-analysis. BJOG: An International Journal of Obstetrics & Gynaecology. 2024;131(1):5-14.

[14] Rosen A, Palma L, Ordon M, Melamed N, Saskin R, Page A, Murji A, Kroft J. Pregnancy outcomes following medical versus surgical treatment of tubal ectopic pregnancy: a population-based retrospective cohort study. American Journal of Obstetrics and Gynecology. 2025

[15] Ozcan MC, Wilson JR, Frishman GN. A systematic review and meta-analysis of surgical treatment of ectopic pregnancy with salpingectomy versus salpingostomy. Journal of minimally invasive gynecology.2021; 28(3):656-67.

[16] Laganà AS, Vitale SG, De Dominici R, Padula F, Rapisarda AM, Biondi A, Cianci S, Valenti G, Capriglione S, Frangež HB, Sturlese E. Fertility outcome after laparoscopic salpingostomy or salpingectomy for

tubal ectopic pregnancy. A 12-years retrospective cohort study. Annali italiani di chirurgia.2016;87(5):461-5.

[17] Wenjing L, Haibo L. Therapeutic effect of laparoscopic salpingotomy vs. salpingectomy on patients with ectopic pregnancy: A systematic review and meta-analysis. Frontiers in surgery.;9:997490.2022

[18] Luo J, Shi Y, Liu D, Yang D, Wu J, Cao L, Geng L, Hou Z, Lin H, Zhang Q, Jiang X. The effect of salpingectomy on the ovarian reserve and ovarian response in ectopic pregnancy: A systematic review and meta-analysis. Medicine. 98(47):e17901.2019

[19] Cheng X, Tian X, Yan Z, Jia M, Deng J, Wang Y, Fan D. Comparison of the fertility outcome of salpingotomy and salpingectomy in women with tubal pregnancy: a systematic review and meta-analysis. PLoS One. 11(3):e0152343.2016

[20] Roeckner JT, Sawangkum P, Sanchez-Ramos L, Duncan JR. Salpingectomy at the time of cesarean delivery: a systematic review and meta-analysis. Obstetrics & Gynecology. 2020;1;135(3):550-7.