



SAEBGPP 2025

SURVEY AND EVIDENCE BASED GOOD PRACTICE POINTS

Embryo Transfer Practices in India

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(Col) Pankaj Talwar VSM

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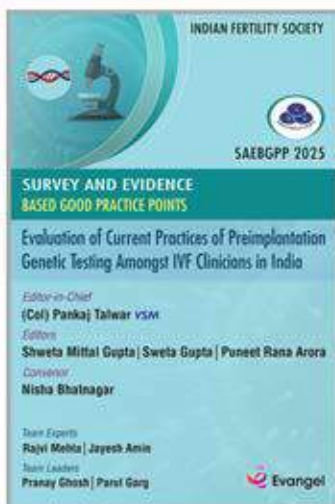
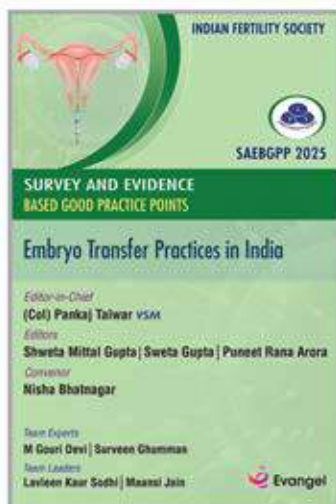
Nisha Bhatnagar

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Dedicated to

This work is lovingly dedicated to all gynecologists of India — those who continue to serve with compassion, courage, and commitment; those who balance science with empathy; those who stand by their patients through hope, uncertainty, and healing; and those who strive every day to raise the standards of women's health and reproductive care in our country.

Your tireless efforts inspire this entire initiative.



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Preface



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The SAEB (Survey and Evidence-Based) Good Practice Points initiative was conceived with the vision of bringing together clinicians, embryologists, researchers, and educators across India to create practical, implementable, and ethically sound guidelines that address real-world challenges in reproductive medicine. Each chapter in this compendium represents months of dedicated teamwork, data collection, expert deliberation, and collaborative refinement.

An important driving force behind this initiative has been the vision of the IFS President, who recognised the prevailing lacunae and knowledge gaps arising from the absence of India-specific recommendations. This endeavour reflects the commitment to develop guidance that is rooted in our own population data, clinical realities, and diversity of practice settings.

The strength of this work lies in its collective wisdom. By combining survey-driven insights with a rigorous evidence-based approach, we have attempted to bridge the gap between everyday clinical practice and evolving scientific knowledge. These GPP documents are not meant to replace existing guidelines; rather, they aim to complement them by offering context-specific recommendations tailored to the Indian ART landscape.

It is our hope that this consolidated effort will support clinicians in making informed decisions, encourage uniformity of care, and ultimately contribute to improved patient outcomes. We extend our gratitude to everyone who contributed to this initiative and made this work possible.



Acknowledgments

We extend our heartfelt appreciation to all the experts, clinicians, embryologists, and young team members who worked tirelessly on each of the eleven SAEB GPP projects. Your commitment to scientific rigor, your enthusiasm for learning, and your willingness to collaborate have been the foundation of this initiative.

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We thank the reviewers, statisticians, and mentors who provided constructive feedback at every stage, ensuring that each chapter meets the highest academic and practical standards. Special appreciation is extended to the editorial and organizational teams whose behind-the-scenes efforts—coordination, communication, formatting, plagiarism checks, and preparation of final deliverables—were indispensable.

To every participant who contributed time, expertise, and passion: this work stands as a testament to your dedication to improving ART practice in India.

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Embryo Transfer Practices in India

INTRODUCTION

Embryo transfer is the final and perhaps the most crucial step in the process of IVF-ET. The success of the procedure depends on a number of factors, including patient factors, the preparation of the endometrium, and the expertise of the practitioner. Many of these factors have been covered in various international guidelines, but evidence has to be updated and newer perspectives remain to be analyzed, such as the best endometrial preparation methods for frozen embryo transfer, the usefulness of 3D ultrasound/color Doppler, any advantage of sequential embryo transfer, etc. This project includes a survey carried out to understand embryo transfer-related practices among IVF consultants across India, and the assimilation of this knowledge with the evidence available in literature to design some good practice points.

PICO 1: DOES PERFORMING A MOCK ET IMPROVE IVF OUTCOMES?

Draft Recommendation

- There is insufficient evidence whether Mock ET done routinely improves pregnancy outcomes in IVF.
- However, it allows the determination of the most suitable ET catheter for each patient and improves chances for an easy transfer.
- It is associated with extra costs and hospital visits.

Summary of Evidence

A review of published randomized trials evaluating the effectiveness of mock ET was conducted by Yusuf Beebeejaun et al.,¹ two randomized trials were identified, reporting data from 499 women. Mock embryo transfer increased pregnancy rates, confirmed by ultrasound (OR 1.80, 95% CI 1.07–3.05) when compared to routine care.

Amol Borkar et al., conducted a single-center randomized controlled trial for the effect of mock embryo transfer before the first IVF cycle. The primary outcome was clinical pregnancy rate (detection of cardiac activity on the ultrasound scan), and the secondary outcome measures were live birth rate, miscarriage and multiple pregnancy rates, difficult ETs, and rate of blood or mucus on the catheter tip. The clinical pregnancy rate was similar between the Mock ET and control groups, and no significant difference was seen in the live birth rate or other secondary outcomes, concluding that Mock ET prior to the first IVF cycle may not improve the success rate in young women without risk factors for a difficult embryo transfer. They observed that a Mock ET procedure will require additional resources, including catheter costs, staff availability, appointments, and extra visits for the subjects. It was concluded that Mock ET should be reserved for subjects with risk factors for potentially difficult ET.


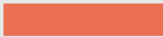

Moossavifar et al., conducted a retrospective study including 160 treatment cycles in 141 patients, with the purpose of determining the consistency of the type of ET (easy or difficult) during mock ET prior to the treatment cycle with the real ET.³ The overall clinical pregnancy rate, both for difficult and easy transfers, was 35%. They observed that Mock ET before the beginning of the treatment cycle is highly consistent with real ET and provides each patient with the highest chance of having an easy transfer. It also allows determination of the most suitable transfer catheter for each patient.

Research Gaps




- Only moderate to poor quality evidence is available on the subject.
- There is a lack of agreement among various studies with regard to the usefulness of routine use of Mock ET before an IVF treatment cycle.

Survey Results from India

Q 1. Do you routinely perform a mock embryo transfer prior to the actual procedure?

Choices	Percentage	Count
Yes, for all patients to assess the uterine cavity and optimal catheter placement	 65.94%	273
I perform Mock ET only if I anticipate difficulty in embryo transfer	 26.09%	108
No, I do not do Mock ET	 7.97%	33
	Total	414
	Unanswered	2

Q 2. Roughly, how frequently do you experience difficult ET (difficulty in crossing the internal os, blood in the catheter, multiple attempts, etc) in your practice?)

Choices	Percentage	Count
<10% of transfers	 86.99%	361
10–20% of transfers	 12.05%	50
>20%	 0.96%	4
	Total	415
	Unanswered	1

Integration with Evidence and Good Practice Points

The majority of clinicians either do a Mock ET for all cases (65.94%) or do it if they anticipate difficulty in embryo transfer (26.09%).

86.99% experience difficulty in <10% transfers, and 12.05% experience difficulty in 10–20% transfers.

An individual choice is thus justifiable, keeping in mind that difficult ETs are fairly uncommon. Even though success rates are not improved by doing a Mock ET,

if there is difficulty in the mock procedure, the clinician is prepared to deal with it by using the appropriate ET catheter or modifications of the procedure.

PICO 2: DOES THE TYPE OF OUTER ET CATHETER (SOFT OR FIRM) AFFECT THE IVF OUTCOME?

Draft Recommendation

Soft embryo transfer catheters may be preferred for all embryo transfer (ET) cases except when there is difficulty in negotiating the cervix/internal os with a soft catheter, since most studies have shown significantly higher pregnancy rates with a soft ET catheter in comparison with firm or semi-rigid catheters.

Summary of Evidence

The type of outer ET catheter (soft or firm) is among several factors studied that can potentially improve IVF results. The American Society for Reproductive Medicine (ASRM) guideline published in 2017 states that there is good evidence to recommend the use of a soft embryo transfer catheter to improve IVF-ET pregnancy rates (Grade A).⁴

In a recent systematic review and meta-analysis published by Tyler et al.,⁵ a total of 27 RCTs compared ET outcomes using soft versus hard catheters. Overall, there was a significant increase in clinical pregnancy with the use of a soft catheter (RR 1.122, 95% CI 1.028–1.224, $I^2 = 57.66\%$) but no difference was found for ongoing pregnancy ($n = 3$, RR 1.138, 95% CI 0.904–1.432, $I^2 = 32.46\%$) or live birth rates ($n = 2$, RR 2.222, 95% CI 0.457–10.806, $I^2 = 94.13\%$). The quality of evidence was moderate.




In a recent retrospective study by Puryan et al.,⁶ the pregnancy outcomes of embryo transfers using soft catheters vs firm catheters were compared. 1,224 cycles from patients aged 18–40 years, in which day 5 frozen-thawed ET cycles of elective single ET (e-SET) and elective double ET (e-DET) were selected. All embryo transfers in the study population were performed by the same two experienced clinicians, and variants of the same brand of catheters were used. There were no statistically significant differences in the clinical and ongoing pregnancy rates of cycles using either soft or firm ET catheters.

Research Gaps

- The study populations in most of these reports are not homogeneous with regard to other factors related to success (e.g., fresh or thawed ET, experience of the physician, etc).
- There is disagreement between the evidence from RCTs and some well-designed, though retrospective studies.

Survey Results from India

Q 3. How frequently do you use an outer catheter with a stylet/metal outer catheter in your practice?

Always in anticipated difficult embryo transfers	 70.29%	291
Never	 22.95%	95
Always in all embryo transfers	 6.76%	28
	Total	414
	Unanswered	2

Integration with Evidence and Good Practice Points

The survey revealed that 70.29% practitioners used an outer ET catheter with a stylet/metal outer catheter only when a difficult ET was anticipated. 22.9% never used an outer ET catheter with a stylet/metal outer catheter, and only 6.76% used them for all embryo transfers. This is in consonance with recommendations available from the literature.

PICO 3: DOES THE USE OF ULTRASOUND GUIDANCE FOR ET IMPROVE IVF OUTCOMES?

Draft Recommendations

Robust evidence is present in favor of the routine use of abdominal ultrasound for guidance during embryo transfer to improve pregnancy and live-birth rates.

Summary of Evidence

There is good evidence based on 10 RCTs to recommend trans-abdominal (TA) ultrasound guidance during embryo transfer (fresh transfer, frozen embryo transfer, and donor cycles) to improve clinical pregnancy rate and live-birth rate in comparison to the clinical touch method (Grade A evidence).⁷⁻⁹ No study reported any adverse effects of ultrasound-guided embryo transfer, and in no study were any detrimental effects on clinical pregnancy rates or embryo implantation rates seen. A recent meta-analysis compared 2D, 3D and 4D ultrasound-guided embryo transfer and found no significant difference in pregnancy rates.¹⁰

Research Gaps

Publication bias may confound the results of all systematic reviews and meta-analyses, as studies showing positive results are more likely to be published.

Survey Results from India

Q 4. Do you perform ET under 2D ultrasound guidance?

Choices	Percentage	Count
Always	97.84%	407
Sometimes	1.20%	5
Never	0.72%	3
Rarely	0.24%	1
	Total	416

Q 5. Do you perform ET under 3D ultrasound guidance?

Choices	Percentage	Count
Never	82.45%	343
Rarely	11.06%	46
Sometimes	4.81%	20
Always in all embryo transfers	1.68%	7
	Total	416

Integration with Evidence and Good Practice Points

The survey showed that 97.84% practitioners always performed ET under 2D ultrasound guidance and only 1.68% performed it under 3D ultrasound. 82.45% practitioners never used 3D ultrasound guidance, 11.06% rarely, and 4.81% sometimes. This practice is in alignment with evidence available from the literature.

PICO 4: DOES THE METHOD OF ENDOMETRIAL PREPARATION FOR FROZEN EMBRYO TRANSFER (FET) AFFECT THE IVF OUTCOMES?

Draft Recommendations

The committee does not recommend any one protocol over another for improving the chances of live birth.

Natural cycle protocol for endometrial preparation (or its modifications) may be associated with better IVF outcomes than HRT cycles (with and without GnRHa down-regulation) in terms of higher live birth rate and lower miscarriage rate, as well as lower antepartum hemorrhage rate. However, the evidence is insufficient and of low certainty.

Summary of Evidence

The results of a network meta-analysis by Hanglin Wu et al.,¹¹ which included both cohort studies and RCTs, reported that artificial cycle (AC) was found to be less efficacious than total natural cycle (tNC) (OR 0.81, 95% CI 0.70 to 0.93, $I^2 = 75.6\%$) and modified natural cycle (mNC) (OR 0.85, 95% CI 0.77 to 0.93, $I^2 = 33.5\%$) in terms of live birth, but not in terms of clinical pregnancy. AC+GnRHa was found to be more efficacious than AC in terms of live birth and clinical pregnancy. Patients who received AC were found to be at an increased risk of miscarriage, pregnancy induced hypertension (PIH), preterm births, and postpartum hemorrhage (PPH) than those after tNC and mNC. No statistically significant differences were observed between tNC and mNC at the level of all the pregnancy outcomes.

In the COMPETE trial¹² (Comparison of Endometrial Preparation Protocols for Frozen Embryo Transfer), 902 women with a regular menstrual cycle were randomly assigned to receive either NC ($n = 448$) or HRT ($n = 454$) for endometrial preparation. In the NC group, 101 women received HRT because of no ovulation, while in the HRT group, 29 women received NC because of spontaneous ovulation. The number of live births was 242 (54.0%) in the NC group versus 195 (43.0%) in the HRT group (RR 1.26, 95% CI 1.10–1.44). Miscarriage rates (RR 0.61, 95% CI 0.41–0.89) and the antepartum hemorrhage rates (RR 0.63, 95% CI 0.42–0.93) were lower in the NC group, with other obstetric and perinatal outcomes not significantly different. The live birth rate was higher with a strategy starting with the NC protocol for endometrial preparation compared to HRT, in women undergoing FET with regular menstrual cycles. However, the permitted crossover between arms limits the certainty in directly assessing NC versus HRT efficacy.

A recent Cochrane meta-analysis included 32 RCTs comparing different cycle regimens for fET in 6352 women.¹³ The certainty of the evidence was moderate to very low. It was concluded that, as the evidence was often of low certainty, and the

confidence intervals were wide and therefore consistent with possible benefit and harm, it is uncertain whether one cycle regimen is more effective and safer than another in preparation for FET in subfertile women.


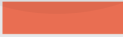


Though the absence of any medical intervention is an advantage of tNC, this protocol entails frequent visits to the clinic for endocrine and Ultrasound monitoring and a high risk of cycle cancellation of 6%, which can be overcome in many cases by mNC.¹⁴ In a recent RCT by Mackens et al., mNC fET was associated with fewer visits for blood samplings compared with tNC fET.¹⁵

Research Gaps

- Only one large RCT is available. The systematic reviews have also included observational studies, which largely restrict the interpretation of these results.
- Heterogeneity exists in most studies as regards drug dosage and timing, freezing method, transfer policy, and luteal phase support, etc.

Survey Results from India

Q 6. When preparing the endometrium for fET, what is your preferred method in the majority of cases?

Choices	Percentage	Count
Hormone replacement cycle without GnRHa suppression	 55.45%	229
Hormone replacement cycle after GnRHa suppression	 33.41%	138
Natural/modified natural	 8.47%	35
Stimulated cycle	 2.66%	11
	Total	413
	Unanswered	3

Integration with Evidence and Good Practice Points

A vast majority of practitioners continue to use HRT as a preferred method for endometrial preparation for fET—55.45% without GnRHa down-regulation and 33.41% after GnRHa down-regulation. Only 8.47% use tNC/mNC, and 2.66% use stimulated cycles as a preferred method. A change of preference may be desirable in regularly menstruating women, though the available evidence is not of good

quality. tNCs are associated with higher cancellation rates and more frequent blood samplings, which may be overcome in mNC and stimulated cycles.

PICO 5: DOES THE NUMBER OF DAYS OF ESTROGEN REPLACEMENT IN AN HRT CYCLE AFFECT IVF OUTCOMES?

Draft Recommendation

- At least 11 days of estrogen exposure before progesterone supplementation in artificial frozen-thawed embryo transfer (FET) cycles should be given for the best treatment outcomes in terms of pregnancy rates, implantation rates, and live birth rates. However, good outcomes have been reported with as few as 7 days.
- The maximum number of days of estrogen exposure before starting Progesterone in an artificial cycle for FET may be limited to 35 days (though it has been reported up to 40 days or more).
- Patients with thin endometrium may require longer periods of estrogen therapy to achieve appropriate endometrial thickness.

Summary of Evidence

The definite time period of estrogen priming in an artificial cycle before FET to get a favorable outcome is difficult to ascertain, as the data from different studies show a wide range of duration from 7 to 65 days. In a retrospective study involving donor oocytes, Borini et al., in 2001 studied the pregnancy and implantation rates in 520 patients for a total of 835 transfer cycles.¹⁶ Recipients were divided into five groups depending on the duration of Estradiol administration: Group A (6–10 days), Group B (11–20 days), Group C (21–30 days), Group D (31–40 days), and Group E (>40 days). This study concluded that endometrial receptivity is tolerant to a wide duration of E2 treatment (until 2 months), as no significant difference was seen in pregnancy and implantation rates between groups. There was a higher number of miscarriages in Group A (41%), ($p < 0.05$) vs. Group B (15%), and vs. Group E (1%). Increased abortion rate in the shortest E2 exposure may be due to more stimulation of the surface epithelium required for attachment than the stromal compartment, which is required for sustained implantation. The best results in terms of pregnancy rates and implantation rates were achieved with a treatment range of 11 to about 40 days.

Another retrospective study of autologous non-genetically tested embryo transfer by Bourdon et al., in 2018 showed that prolonged exposure to estradiol, i.e., > 32 days, was associated with significantly lower live birth rates and increased miscarriage rates after autologous frozen-thawed blastocyst transfer.¹⁷

A retrospective study by Jiang et al., in 2022 analyzed 4,142 FET cycles and compared the 7-day and 14-day estrogen administration (provided an endometrial thickness of 8 mm was achieved).¹⁸ No significant difference in cumulative LBR was observed when comparing seven vs fourteen days of estrogen administration before starting progesterone supplementation (47.6% vs. 48.8%, $P=0.537$).

A recent review article by Wei et al., summed up that shorter periods of estrogen exposure may increase the risk of early miscarriage, even though it may allow the endometrium to reach the desired thickness.¹⁹ Secondly, longer estrogen exposure durations do not appear to be beneficial for the average patient and increase the incidence of adverse events, such as vaginal bleeding. However, prolonged estrogen exposure may be attempted in patients with a thin endometrium.





A systematic review of all the studies till 2023 done by Zhang Y et al., concluded that clinicians can be flexible in scheduling estrogen supplement procedure between 7 and 36 days before Progesterone administration.²⁰

Research Gaps





- The studies done to assess the optimal duration of estrogen exposure are almost all retrospective studies, and there are no randomised controlled trials done on the topic. Hence, the evidence available is of inferior quality.
- The heterogeneous nature of the population studied.
- Earlier studies were done mostly in donor oocyte cycles, with very few done on autologous blastocyst transfers.

Survey Results from India

Q7. What is your minimum number of replacement days of estrogen in an HRT cycle for fET?

Choices	Percentage	Count
Minimum 12 days	 45.91%	191
Minimum 10 days	 26.92%	112
Minimum 14 days	 15.14%	63
I transfer the embryos once endometrial thickness is 8 mm or more, regardless of the number of days of estrogen replacement	 12.02%	50
Total		416

Q 8. What is the maximum duration of estrogen you use for the preparation of the endometrium in HRT cycles for fET?

Choices	Percentage	Count
20 days	 54.63%	224
25 days	 33.66%	138
30 days	 9.76%	40
35 days	 1.95%	8
	Total	410
	Unanswered	6

Integration with Evidence and Good Practice Points

The largest percentage of practitioners (45.91%) gives estrogen replacement for a minimum of 12 days, 26.92% for a minimum of 10 days, 15.4% for a minimum of 14 days, and 12.02% practitioners transfer the embryos as soon as the endometrium is 8 mm thick, regardless of the number of days of replacement. The literature, however, suggests that too short an estrogen replacement may be associated with higher miscarriage rates.

54.6% practitioners give estrogen replacement for a maximum of 20 days, 33.6% for a maximum of 25 days, 9.76% for a maximum of 30 days, and only 1.95% up to 35 days.

Evidence from literature suggests that cycles may not be cancelled even if the required endometrial thickness is not reached in 35 days or more.

PICO 6: DOES THE CHOICE/ROUTE/DOSE OF ESTROGEN AFFECT THE IVF OUTCOMES IN A HORMONE REPLACEMENT (HRT) CYCLE FOR FROZEN EMBRYO TRANSFER (FET)?

Draft Recommendation 6A

There is not enough evidence in the literature to support either estradiol valerate/estradiol hemihydrate or 17 beta estradiol for endometrial preparation in artificial fET cycles.

Summary of Evidence

In artificial FET cycles, the endometrium is prepared for implantation with exogenous estrogen, which is available as estradiol valerate and estradiol

hemihydrate. The former is metabolized in the intestine and liver to estradiol (the active component) and valeric acid. The latter is a hydrate of estradiol and is already in the active form. It does not get further metabolized, thereby causing less load on the liver.

The strongest predictors of estrogenic activity are endometrial thickness and implantation rates. In a prospective randomized comparative trial by Ingale et al., where a total 103 patients undergoing frozen embryo transfer cycles were studied, there was no statistically significant difference in endometrial growth in both groups (10.9 ± 2.5 mm vs 10.9 mm ± 2.2 mm; $P = 1.0000$) but there was significant difference in implantation rate (87.7% vs 71.1%; $P = 0.0444$) and ongoing pregnancy rate (75.5% vs 53.33%, $P = 0.0244$) between estradiol hemihydrate and estradiol valerate group respectively.²¹ Though the clinical pregnancy rate was also higher in the estradiol hemihydrate group (75.5% vs 60%), it was not statistically significant ($P=0.1074$).





In a retrospective study comparing estradiol valerate with estradiol hemihydrate in HRT cycles in 2,529 Indian women, Banker et al., observed that the endometrial thickness achieved by both compounds is adequate, though there is a significant increase (of 0.351 mm; $P < 0.0001$) in thickness in the hemihydrate group, but it did not translate into any clinically significant outcome.²²

Research Gaps

Only one randomized control trial and one retrospective study are available, and the results are contradictory.

Survey Results from India

Q 9. What is your most preferred choice of estrogen for the preparation of the endometrium in HRT cycles for fET?

Choices	Percentage	Count
Estradiol valerate (oral)	 41.16%	170
Estradiol hemihydrate (oral)	 29.30%	121
Combination of the above	 26.39%	109
17 beta Estradiol gel (transdermal administration)	 3.15%	13
	Total	413
	Unanswered	3

Integration with Evidence and Good Practice Points

As per the survey, a comparable number of practitioners prefer oral estradiol valerate/oral estradiol hemihydrate or a combination of these with transdermal gel (41.16%, 29.03% and 26.39% respectively). Very few (3.15%) prefer transdermal 17 beta estradiol gel alone. Evidence from the literature also does not support one form of treatment over the other.

Draft Recommendation 6B

Oral estradiol is the most preferred route of administration, which is non-inferior to transdermal or vaginal preparations in terms of clinical pregnancy rates.

Vaginal route achieves higher serum concentrations of estrogen than transdermal estrogen in HRT-fET cycles, but transdermal estrogen is associated with higher endometrial thickness, shorter treatment duration, and better tolerance.

Non-oral routes can be used effectively in HRT-fET cycles, especially in patients with chronic hepatic and renal dysfunction, high-risk factors for thrombosis, and dyslipidemia.

Summary of Evidence

Oral estrogen is metabolized both in the intestines and liver and converted to estrone and estrone sulfate, whereas the transdermal route circumvents the hepatic metabolism and produces the most stable steady-state levels of estradiol.

In two randomized controlled trials by Davar R et al.,²³ and Kahraman S et al.,²⁴ there was no significant difference between transdermal estradiol and oral estradiol in the thickness of the endometrium on the day of progesterone administration or in the clinical outcomes.

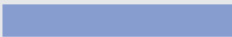



A prospective monocentric cohort study by Corroenne R et al., studied 318 cycles in 215 patients, 119 (37.4%) using transdermal estrogen and 199 (62.6%) using vaginal estrogen.²⁵ They reported no difference in clinical pregnancy rates between the transdermal and vaginal routes, but transdermal estrogen was associated with higher endometrial thickness, shorter treatment duration, fewer side effects, higher patient satisfaction, and lower levels of serum estradiol concentration in artificial FET cycles compared to the vaginal route. However, another study claimed that patients who were given estrogen orally were more satisfied than those who were given estrogen transdermally.²⁶

Research Gaps

Very few studies are available, and there is not much uniformity in comparison groups as far as the dosage and frequency of estrogen used are concerned.

Survey Results from India

Q 10. What is your preferred route of estrogen administration for the preparation of the endometrium in HRT cycles for fET?

Choices	Percentage	Count
Oral	 66.99%	278
Combination of the above	 27.47%	114
Transdermal	 5.06%	21
Vaginal	 0.48%	2
	Total	415
	Unanswered	1

Integration with Evidence and Good Practice Points

The survey shows that a majority of practitioners prefer to give estrogen by the oral route (66.99%), followed by a combination of oral/vaginal/transdermal route (27.47%). Transdermal or vaginal routes are less preferred (5.06% and 0.48% respectively).

This is in agreement with evidence from the literature, which shows that the oral route is the most preferred and non-inferior one. However, no good evidence is available to support the combination of various routes.

Draft Recommendations 6C

There is no standardized recommendation on the maximal dose of exogenous estrogen used for endometrial preparation for FET. Women given higher doses in a stepwise-escalation regimen tend to show lesser endometrial thickness and may be more prone to have low birth weight babies, placental anomalies, and retroplacental haematomas.

Summary of Evidence

Mackens et al., elaborated that while preparing the endometrium, estradiol is commonly administered as two distinct regimens.²⁷ The first regimen involves

a fixed high dose right from the start (6 mg/day), aiming to effectively prevent the formation of unexpected dominant follicles. Conversely, the second regimen follows a stepwise incremental approach, commencing at 2 mg or more and gradually escalating to higher doses.





Two retrospective studies examined the impact of a fixed dose regimen (FDR) compared to a stepwise-escalation regimen (SER) on pregnancy outcomes; however, these studies employed SER with an initial dosage of 6 mg or higher.^{28,29} The findings revealed similar CPR between the two groups.²⁸ Nevertheless, the stepwise-escalation group exhibited significantly lower average birth weight, a significantly higher occurrence of low-birth-weight infants, and a significantly higher prevalence of placental anomalies, including bilobed placentas, accessory lobes, and retroplacental hematomas.²⁹ The poor obstetric outcomes and placental abnormalities are likely to be caused by the excessive administration of total estrogen doses. Furthermore, both studies have demonstrated a significant reduction in endometrial thickness within the stepwise-escalation group compared to the fixed-dose group.

Research Gaps

- A lot of heterogeneity in all the studies with different doses, routes, and regimens, as well as cut-offs of endometrial thickness.
- Most studies are retrospective, and no large RCTs are available.

Survey Results from India

Q 11. What is the maximum daily dose of estrogen you use for preparation of the endometrium in HRT cycles for fET?

Choices	Percentage	Count
12 mg	 60.05%	248
10 mg	 18.89%	78
8 mg	 14.53%	60
14 mg	 6.54%	27
	Total	413
	Unanswered	3

Integration with Evidence and Good Practice Points

The survey shows that a majority (60.05%) of practitioners give a maximum estrogen dose of 12 mg/day, followed by 18.89% giving a maximum dose of 10 mg/day and 14.53% giving a maximum of 8mg/day. Only 6.54% go up to 14 mg/day. As per evidence from literature, a fixed dose schedule of 6mg/day is as good as higher doses. Higher estrogen doses may be harmful, especially in stepwise escalating regimens.

PICO 7: DOES THE MAXIMUM ENDOMETRIAL THICKNESS ACHIEVED IN AN HRT CYCLE FOR FROZEN EMBRYO TRANSFER (FET) AFFECT THE IVF OUTCOMES?

Draft Recommendations

- Based on the current evidence, live birth rates (LBR) vary significantly across ET ranges, peaking at approximately 10 mm in fET cycles.
- Both excessively thin (<8 mm) and thick (>14 mm) endometria may be detrimental to outcomes.

Summary of Evidence

Several studies have evaluated the association between endometrial thickness (ET) and outcomes in IVF-ET. The evidence remains heterogeneous, although certain trends have emerged.

In a retrospective observational study of 768 FET cycles, El-Toukhy et al., found that both thin (<7 mm) and excessively thick (>14 mm) endometria were associated with lower pregnancy rates.³⁰ Optimal live birth rates were achieved with an ET of 9–14 mm, which was significantly more favorable than ET in the 7–8 mm range.

One of the largest retrospective cohort studies to date, using data from 33 assisted reproductive technology (ART) clinics across Canada (2013–2019), analyzed over 96,000 autologous embryo transfers (fresh and frozen).³¹ In FET cycles, a significant increase in live birth rates with increasing ET was demonstrated. Specifically, live birth rates improved from 15.1% with ET <6 mm to 30.8% at ET 10mm, though the effect tapered off beyond 7 mm. However, beyond 10 mm, further increases in ET did not confer additional benefit, indicating a plateau in clinical outcomes. However, an endometrial thickness <6 mm was clearly associated with a dramatic reduction in live birth rates in fresh and frozen embryo transfer cycles.

A 2020 systematic review and meta-analysis by Gao et al., including 30 studies (9 prospective, remainder retrospective), provided further insight.³² Among FET

studies, lower ET - particularly <8 mm—was associated with significantly reduced pregnancy rates (OR 0.66; 95% CI 0.45–0.99; $P=0.042$) and higher miscarriage rates.





A recent retrospective cohort study by Huang et al., analyzed data from 80,585 ART cycles, including 25,683 fresh IVF-ET, 33,112 FET, and 1,071 PGT-ET cycles.³³ Primary outcomes included live birth rates (LBR) and clinical pregnancy rates (CPR) across ET ranges. They concluded that the relationship between ET and LBR was non-linear, with no single cut-off value. LBR varied significantly across ET ranges, peaking at approximately 12 mm in fresh IVF-ET cycles and around 10 mm in FET and PGT-ET cycles. Miscarriage rates (MR) showed no significant differences across ET groups.

Research Gaps

- Heterogeneity in the nature of studies.
- The available data is largely retrospective, and no large prospective studies are available.
- The relationship between endometrial thickness and miscarriage rates warrants further investigation through prospective, controlled studies.

Survey results from India

Q 12. What is the minimum ET below which you would cancel an fET cycle?

Choices	Percentage	Count
<7 mm	 62.32%	258
<6 mm	 16.43%	68
<8 mm	 16.18%	67
<5 mm	 5.07%	21
	Total	414
	Unanswered	2

Integration with Evidence and Good Practice Points

The survey shows that the majority of practitioners (62.32%) cancel the fET if the endometrial thickness is below 7 mm. A cut-off of 6 mm and 8 mm was taken by 16.43% and 16.18% practitioners, respectively. Only 5.07% use 5 mm as a cut-off.

The evidence from literature also indicates that success rates are compromised with ET less than 7–8 mm.

PICO 8: DOES THE PLACEMENT OF THE INNER CATHETER AFFECT IVF OUTCOMES?

Draft Recommendations

- The placement of the embryo transfer (ET) catheter and its distance from the uterine fundus significantly impact IVF outcomes.
- Evidence supports ultrasound-guided ET with the catheter tip ideally placed 10–20 mm from the uterine fundus, correlating with improved clinical pregnancy rates compared to placement less than 10 mm or greater than 20 mm.

Summary of Evidence

D'Angelo et al., reviewed current ET practices extensively. They recognized catheter placement as a critical aspect of ET but highlighted the current lack of universally standardized exact distances.³⁴ The review indicated poorer outcomes when catheter placements were either too close or too distant from the fundal endometrium.

The Practice Committee of ASRM systematically reviewed randomized controlled trials⁴ to establish best practices for embryo transfer. While the guideline did not specify an exact numerical optimal distance, it clearly emphasized avoiding catheter tip placement too close to the uterine fundus.

Selvamani et al., conducted a retrospective analysis involving 150 IVF cycles.³⁵ Patients were grouped based on catheter tip distance from the uterine fundus into four categories: <10 mm, 10–15 mm, 15–20 mm, and >20 mm. Clinical pregnancy rates were highest (62.3–82.2%) in groups with catheter placements between 10–20 mm from the fundus. Placements closer (<10 mm) or farther (>20 mm) significantly reduced pregnancy rates. The study strongly recommended an ideal embryo deposition zone of 10–20 mm from the fundus.

Research Gaps

- Most studies are retrospective and involve relatively small sample sizes. Furthermore, patient anatomical differences and practitioner experience, potentially influencing outcomes, have not been adequately standardized or accounted for across the reviewed studies.
- There is a lack of consistency in comparative placements, with some studies assessing exact distances from the fundus and others dividing the uterine cavity into areas.

Survey Results from India

Q 13. Where do you place your inner catheter tip during USG-guided embryo transfer?

Choices	Percentage	Count
1–2 cm from the fundus	80.43%	333
Approximate miduterine cavity	17.15%	71
I do not measure the distance from the fundus	1.93%	8
At the fundus	0.48%	2
	Total	414
	Unanswered	2

Integration with Evidence and Good Practice Points

As per the survey, 80.43% practitioners place the tip of the inner catheter 1–2 cm from the fundus, and 17.15% place it approximately in the mid-uterine cavity. Only a minority do not measure the distance from the fundus (1.93 %) or keep it at the fundus (0.48%). Therefore, a vast majority are following the policy recommended in the literature.

PICO 9: DOES THE USE OF TOCOLYTICS/ANTI-PROSTAGLANDINS AT THE TIME OF EMBRYO TRANSFER IMPROVE IVF OUTCOMES?

Draft Recommendations

- Atosiban has shown some promise in improving implantation and pregnancy outcomes, particularly in women with RIF, by reducing uterine contractility during ET.
- In contrast, the use of anti-prostaglandins like NSAIDs lacks robust evidence and may carry potential risks.
- The decision to use tocolytics or anti-prostaglandins should be tailored to individual patient profiles, particularly those with recurrent implantation failure, excessive uterine contractions, or difficult embryo transfers.

Summary of Evidence

Uterine quiescence, characterized by reduced myometrial activity, is essential for successful embryo transfer (ET) in IVF cycles. Excessive uterine peristalsis during ET may displace embryos, reduce endometrial receptivity, and lead to implantation failure, particularly in patients with recurrent implantation failure (RIF). Oxytocin and prostaglandin F₂ α (PGF₂ α) are key mediators of uterine contractility. Atosiban, a selective vasopressin and oxytocin receptor antagonist, suppresses uterine contractions, thereby enhancing conditions for implantation. Anti-prostaglandins, such as Nonsteroidal anti-inflammatory drugs (NSAIDs) or COX inhibitors, reduce PGF₂ α synthesis and uterine activity, promoting a stable endometrial environment. These agents may also reduce inflammation and improve embryo-endometrial synchrony.

A systematic review and meta-analysis by Schwarze et al., included four randomized controlled trials (RCTs) and two nonrandomized trials, encompassing over 1,700 women.³⁶ The analysis demonstrated that Atosiban administration was associated with increased clinical pregnancy rates, with pooled odds ratios (OR) of 1.47 (95% CI: 1.18–1.82) in RCTs and 1.50 (95% CI: 1.10–2.05) in nonrandomized trials.

A comprehensive systematic review and meta-analyses by Tyler et al., which focused on interventions to optimize the embryo transfer in ART, reported that Atosiban use in ART was associated with improved clinical pregnancy rates in women with repeated implantation failure (RR \approx 1.7), but no significant benefit was observed in unselected populations.³⁷ Live birth rates also improved in RIF subgroups (RR 2.1), whereas miscarriage, multiple pregnancy, and ectopic rates were unaffected. Evidence quality was moderate to low due to heterogeneity across studies.

A prospective, randomized, double-blind controlled clinical trial was conducted by Tang et al.,³⁸ 194 infertile women with RIF undergoing fresh embryo transfer were randomly allocated into the Atosiban ($n=97$) and the placebo ($n=97$) groups. Women in the treatment group received Atosiban intravenously about 30 minutes before embryo transfer with a bolus dose of 6.75 mg over one minute. Those in the placebo group received only normal saline infusion for the same duration. There was no significant difference in the live birth rate between the atosiban and placebo groups (42.3% *vs* 35.1%, $P=0.302$, RR = 1.206). No significant differences were found between the two groups in the positive pregnancy test, clinical pregnancy, ongoing pregnancy, miscarriage, multiple pregnancy, ectopic pregnancy, and implantation rates.

A recent retrospective study by Yang et al., also concluded that Atosiban was not linked to an increased likelihood of biochemical pregnancy or clinical pregnancy, nor a reduced risk of abortion or ectopic pregnancy ($p > 0.05$).³⁹ No beneficial effect of Atosiban was observed in any of the subgroups based on maternal age, number of previous embryo transfers (ETs), endometrial thickness, or embryo stage in the subgroup analysis of the primary outcome.


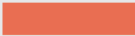


Prostaglandins, particularly $\text{PGF}_2\alpha$, play a role in stimulating uterine contractions. NSAIDs, which inhibit prostaglandin synthesis, have been considered to reduce uterine contractility during ET. However, evidence supporting their efficacy in improving implantation rates is limited. A Cochrane review of randomized controlled trials (2019), including 11 studies with 1,884 women, found no clear benefit of NSAIDs (such as piroxicam, indomethacin, aspirin, or ibuprofen) on outcomes like clinical pregnancy or miscarriage.⁴⁰ Moreover, concerns about potential adverse effects on endometrial receptivity and embryo development have limited the widespread adoption of NSAIDs for this purpose.

Research Gaps





- Large-scale, multicenter randomized controlled trials are not available.
- Most studies do not address the most effective dosing regimens, optimal timing of administration, and long-term safety of these interventions in ART cycles.

Survey Results from India

Q 14. Do you administer tocolytics (e.g, nifedipine, Atosiban) before or after embryo transfer to reduce the risk of uterine contractions?

Choices	Percentage	Count
No, I do not use tocolytics in my practice for embryo transfer	 37.68%	156
Before embryo transfer if I anticipate difficulty	 34.54%	143
Routinely before embryo transfer	 19.81%	82
After a difficult embryo transfer	 7.97%	33
	Total	414
	Unanswered	2

Q 15. Do you administer NSAIDs/anti-prostaglandins before or after embryo transfer to reduce the risk of uterine contractions?

Choices	Percentage	Count
Never	 43.80%	180
Sometimes	 26.76%	110
Rarely	 18.98%	78
Always	 10.46%	43
	Total	411
	Unanswered	5

Integration with Evidence and Good Practice Points

Among Indian practitioners, 37.68% do not use tocolytics at the time of embryo transfer. 34.54% use it if they anticipate a difficult transfer, 19.81 % use it routinely, and 7.97% after a difficult transfer. On the other hand, a majority (43.08%) of Indian practitioners do not use NSAIDs/anti-prostaglandins in their practice of ET, 26.76% use them sometimes, 18.98% rarely, and only 10.06% always. This is in consonance with the evidence from the literature. There is some evidence in literature (though low quality) to support the Use of tocolytics before ET selectively, but not for the Use of NSAIDs/anti-prostaglandins.

PICO 10: DOES SEQUENTIAL EMBRYO TRANSFER IMPROVE IVF OUTCOMES?

Draft Recommendations

- Sequential embryo transfer (SEQET) may be considered as an alternative to conventional cleavage-stage embryo transfer (CET) in the presence of an adequate number of embryos, but evidence is less convincing when compared with blastocyst transfer and in women with a history of recurrent implantation failure.
- SEQET is more likely to benefit when frozen-thawed embryo transfer (FET) is done.

Summary of Evidence

Successful implantation requires effective cross-talk between a competent embryo and a receptive endometrium. Emerging evidence suggests that transferring

a cleavage-stage embryo may enhance the likelihood of implantation for a subsequently transferred blastocyst by improving synchrony with the endometrial “implantation window,” enhancing endometrial receptivity through signalling molecules from the early embryo, and endometrial injury-induced release of favorable cytokines.

A well-designed randomized controlled trial (RCT) study was done for women with repeated IVF failures (RIF).⁴¹ Participants were allocated in a 1:1 ratio to either SEQET on day 3 and day 5 (study group, n=100) and conventional day 5 FET (n=100, control group). The frozen-thawed embryos were transferred to hormone replacement therapy-prepared endometrium in both groups. Clinical pregnancy rates were significantly higher in the SEQET group (40%) compared to the day 5 group (19%) ($P<0.001$).

Zhang et al., (2021) conducted a systematic review to evaluate the efficacy of SEQET in improving IVF outcomes.⁴² Twelve studies were included: 2 randomized controlled trials, 3 prospective cohort studies, 6 retrospective cohort studies, and 1 case-control study. Of these, 8 studies (n=2,658) compared sequential transfer with cleavage-stage transfer, while 4 studies (n=513) compared it with blastocyst transfer. Notably, two-thirds of the studies enrolled only women with recurrent implantation failure (RIF). SEQET significantly improved clinical pregnancy rates in comparison to CET (RR 1.42, 95% CI 1.26–1.60; $P<0.01$) across both RIF and non-RIF populations [RIF group: RR 1.58 (95% CI 1.17–2.13; $P<0.01$), non-RIF group: RR 1.44 (95% CI 1.20–1.66; $P<0.01$)]. Two studies (n=531) reported a significantly higher live birth rate in the sequential group (RR 1.99, 95% CI 1.47–2.71; $P<0.01$). There was a trend toward increased multiple pregnancies, although not reaching statistical significance (RR 1.47, 95% CI 1.01–2.16; $P=0.05$). However, SEQET did not show a significant advantage over blastocyst transfer alone.





A recent systematic review and meta-analysis included 23 studies (clinical trials or observational studies), most of them high quality.⁴³ SEQET showed significant improvement in clinical and chemical pregnancy rates ($P<0.000010$) in comparison to the CET group, as well as the implantation rates ($P=0.002$) and live births ($P=0.006$). In comparing SEQET to blastocyst transfer, SEQET was associated with a significant increase in the clinical pregnancy rate ($P=0.003$) but not live birth rates. In addition, the analysis of patients with RIF was done for SEQET in comparison to CET and blastocyst transfers separately. SEQET improved clinical pregnancy and implantation rates compared to CET, but did not show any advantage in comparison to blastocyst transfer. Subgroups were made for fresh embryos and frozen embryos, and data were analyzed separately. The transfer of frozen-thawed embryos showed improved implantation with SEQET relative to CET and also contributed to a higher clinical pregnancy rate when compared to blastocyst transfer.

Research Gaps

- Most studies have high heterogeneity in study populations and selection bias.
- Limited data on key variables such as patient age and ovarian reserve.

Survey Results from India

Q 16. Do you practice sequential embryo transfer (SET), where embryos are transferred in stages (e.g., day 3 followed by day 5)?

Choices	Percentage	Count
No, I prefer doing an embryo transfer on day 5	 67.23%	279
Only for specific cases	 25.30%	105
No, I prefer doing an embryo transfer on day 3	 5.06%	21
Yes, routine for patients with a high number of embryos	 2.41%	10
	Total	415
	Unanswered	1

Integration with Evidence and Good Practice Points

Only 2.41% practitioners routinely perform sequential embryo transfer when a high number of embryos is available, and 25.30 % do it for specific cases. A majority of practitioners (67.23%) prefer to do a day 5 embryo transfer, and only 5.06% prefer a day 3 transfer. This is in consonance with evidence from the literature.

PICO 11: DOES CHECKING THE HORMONAL PROFILE IN FET (FROZEN-THAWED EMBRYO TRANSFER) CYCLES IMPROVE IVF OUTCOMES?

Draft Recommendations

- P4 levels before starting progesterone do not seem to affect the IVF outcomes in artificial (hormone replacement) cycles for fET.

- In Natural Cycle (NC)/modified natural cycle (mNC)/Stimulated cycles for fET, progesterone level cut-off of 1.0 to 1.5 ng/mL may be used before starting progesterone supplementation.

Summary of Evidence





There is a general consensus that premature progesterone elevation leads to premature luteinization of the endometrium and is associated with adverse IVF outcomes. Most of this inference is derived from the studies and meta-analyses done in fresh embryo transfer cycles following ovarian stimulation, where it was found that premature elevation of Progesterone before trigger injection was associated with decreased embryo implantation rates due to alterations in endometrial receptivity and embryo-endometrial asynchrony.⁴⁴ Hormonal blood sampling may be useful to assess adequate follicular estradiol production, and to detect premature ovulation characterized by an early progesterone rise, generally considered as more than 1.0 ng/mL.⁴⁵ In a review of 36 studies, Jreij et al indicated that an arbitrary value of 1.5 ng/mL as a cut-off for the serum progesterone concentration prior to trigger administration in fresh embryo transfers gave the best results.⁴⁶ Frozen-thawed embryo transfers (fET) are considered to be a better strategy because they may prevent adverse outcomes related to premature luteinization in fresh IVF-ET cycles. No studies have been done to assess the effect of progesterone elevation before starting progesterone supplementation in different methods of endometrial preparation for fET cycles. The results of the fresh ET cycles may be extrapolated to natural cycle (NC)/modified natural cycle (mNC)/stimulated cycles for fET, whereas it is unlikely to be useful in artificial (hormone replacement) fET cycles.

Research Gaps





No studies are available to support the practice of checking progesterone levels before starting progesterone supplementation in different endometrial preparation methods for fET cycles.

Survey Results from India

Q 17. Do you check P4 levels before starting progesterone in fET cycles?

Choices	Percentage	Count
Yes, I do it routinely	 44.10%	183
Only in NC/mNC/stimulated cycles	 31.33%	130
Only if there are ultrasound findings to suggest raised progesterone	 18.31%	76
Never	 6.27%	26
	Total	415
	Unanswered	1

Q 18. In fET cycles, what cut-off for serum P4 levels do you use on the day of starting progesterone?

Choices	Percentage	Count
1.5 ng/dL	 43.58%	180
1.0 ng/dl	 38.98%	161
0.8 ng/dl	 9.20%	38
I do not check serum P4 levels	 8.23%	34
	Total	413
	Unanswered	3

Integration with Evidence and Good Practice Points

44.1% practitioners check serum P4 levels routinely before starting progesterone in fET cycles. 31.33% and 18.31% check only in NC/mNC/stimulated cycles, and if there are ultrasound findings suggestive of raised progesterone, respectively. 6.27% practitioners do not check serum P4 levels. It may be suggested that checking P4 levels in artificial cycles is unnecessary.

As regards cut-off levels, 45.38% would cancel a transfer if levels exceed 1.5 ng/dL, 38.98% if levels exceed 1.0 ng/dL, and 9.2% if levels exceed 0.8 ng/dL. Evidence from literature suggests that cancellation of fET at P4 levels between 0.8 and 1.0 ng/dL may not be justified.

PICO 12: IN FET CYCLES, DOES ASSESSMENT OF UTERINE ARTERY DOPPLER AND ENDOMETRIAL BLOOD FLOW, AS COMPARED TO STANDARD ENDOMETRIAL ASSESSMENT, IMPROVE OUTCOMES?

Draft Recommendation

Doppler ultrasound is an accessible, cost-effective, and non-invasive method to assess endometrial receptivity. While reduced perfusion and abnormal uterine artery flow are linked to infertility, findings are not consistent across studies regarding the routine use in ART and infertility management.

Summary of Evidence


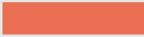


A cohort study published in the International Journal of Reproductive Biomedicine suggests that the endometrial perfusion in zone 2/3 improves the pregnancy rate as compared to flow restricted to Zone 1. Uterine artery doppler PI was found to be significantly different between the positive and negative clinical pregnancy groups in this study.^{47,48} A prospective cohort study developed a multi-parameter Endometrial Receptivity (ER) score, including both qualitative blood flow classification based on Applebaum criteria and quantitative FI index, and found that the overall score correlated positively with CPR.² A recent meta-analysis by Siargkas et al., indicated that women with lower uterine artery pulsatility index (PI) and higher peak systolic velocity (PSV) measured prior to embryo transfer have higher clinical pregnancy rates.⁴⁹ This association is strongest when Doppler measurements are taken early in the ART cycle, preferably during the natural menstrual phase, before any pharmacological intervention. In a study by Wang et al., no relationship was found between pregnancy outcomes and color Doppler imaging parameters.⁵⁰

Research Gaps

- Available evidence is contradictory, and no recent Cochrane review or RCTs are available.
- Operator variability is an additional problem difficult to overcome while making comparisons.

Survey Results from India

Q 19. In the FET cycle, do you check for endometrial blood flow in zone 3/4 and uterine artery PI before starting progesterone?

Choices	Percentage	Count
Only in case of previous failed IVF/ poor endometrial characteristics	 39.90%	164
Yes, routinely	 28.95%	119
I do endometrial blood flow but not uterine artery PI	 24.82%	102
Never	 6.33%	26
	Total	411
	Unanswered	5

Integration with Evidence and Good Practice Points

Only 28.95% Indian Practitioners use these modalities routinely in their practice, while 39.90% do so only in cases of failed IVF or in the presence of poor endometrial characteristics. 24.82% check only the endometrial blood flow, and 6.3% never use these modalities. The difference in acceptance of this technology is likely due to a lack of good evidence for or against this technique of studying endometrial receptivity.

PICO 13: DOES THE PRESENCE OF FLUID IN THE ENDOMETRIAL CAVITY INTERFERE WITH IMPLANTATION?

Draft Recommendation

Evaluation for cause, persistence, and volume should be done. Spontaneous resolution is reported to be associated with a good outcome. Consider aspiration if persistent or >3.5 mm.

It is not clear whether aspiration of fluid improves the IVF outcomes. Recurrence of the problem in a subsequent cycle is not seen in around half of the cancelled cycles.

Summary of Evidence

Evidence regarding the impact of endometrial cavity fluid (ECF) on implantation is inconsistent. A meta-analysis reported a statistically significant reduction in pregnancy rates associated with ECF, with a greater adverse effect when fluid size exceeded 3.5 mm.⁵¹ An RCT found that endometrial fluid aspiration combined with diosmin increased the likelihood of fresh embryo transfer but did not significantly improve pregnancy rates compared with conservative management.⁵² A retrospective study published in fertility and sterility sought to evaluate FET cases in which patients experienced persistence of fluid within the endometrial cavity, to better formulate best practice strategies for clinical care.⁵³ The majority (78.2%) of cycles affected by endometrial fluid during the follicular phase experienced spontaneous resolution. Of these, 63.1 of % cycles had a positive pregnancy test, while the remaining 36.9% did not. In cases where endometrial fluid did not spontaneously resolve, 81.5% cycles were cancelled, and 18.5% underwent aspiration of the endometrial fluid. Of patients whose cycles were cancelled, 41.5% did not experience further episodes of fluid accumulation. Of patients undergoing aspiration of endometrial fluid, 50% had persistence or recurrence of endometrial fluid resulting in cancellation of the cycle, and the other 50% experienced resolution. Following resolution of endometrial fluid after aspiration, 1 of 6 patients (16.7%) had a positive pregnancy test, whereas 5 had negative tests. They concluded that in cases where spontaneous resolution of ECF occurred, the outcomes were not affected, whereas even if the ECF did not reappear after aspiration, outcomes remained poor. Another retrospective study observed better outcomes in fresh embryo transfer cycles with ECF when it was associated with good prognostic factors, such as small and transient accumulation of fluid and polycystic ovarian syndrome as an etiological factor, but a poorer outcome was observed in fET cycles.⁵⁴





Research Gaps

The quality of available evidence is poor, and the evidence is contradictory.

Large multicenter RCTs and meta-analyses are needed to clarify the impact of ECF on implantation, optimal management in fresh vs frozen cycles, and the independent effect of aspiration versus other interventions.

Survey Results from India

Q 20. What would you do for endometrial fluid seen on the day of starting progesterone during fET?

Choices	Percentage	Count
Aspiration of endometrial fluid when detected (sent for culture) and continue monitoring	 45.17%	187
Course of antibiotics and continue monitoring	 28.74%	119
Cancel ET	 20.77%	86
Aspiration of fluid on day of transfer followed by transfer of embryos	 5.31%	22
	Total	414
	Unanswered	2

Integration with Evidence and Good Practice Points

A majority of consultants (45.17%) aspirate the ECF, send it for culture, and continue to monitor, whereas 28.74% give a course of antibiotics and continue to monitor. 20.77% cancel the fET and only 5.31% aspirate the fluid on the day of embryo transfer and proceed with the ET. Evidence from the literature says that in a majority of cases, spontaneous resolution of fluid seen early in the fET cycle will occur, therefore making observation a good option. The benefit that comes from aspiration is doubtful. Cancellation may not be followed by recurrence of the same problem in a subsequent cycle.

PICO 14: DOES ASPIRATION OF MUCUS BEFORE ET IMPROVE IVF SUCCESS RATES?

Draft Recommendation

Aspiration of mucus before embryo transfer should be done to improve the clinical pregnancy rate (CPR) and live birth rate (LBR).

Summary of Evidence

The guidelines published by the American Society for Reproductive Medicine (ASRM) in 2017 stated that removal of mucus from the cervical canal prior to ET




improves CPR and LBR (Grade B evidence).⁴ Two retrospective studies by Michael and Ahmady and McNamee et al., reported a significant increase in pregnancy rate if the cervical mucus was removed.^{55,56} In a prospective, nonrandomized study, Eskandar et al reported an increased clinical pregnancy rate by aspirating the cervical mucus.⁵⁷ Mains et al., published a review on optimizing the technique of ET, which suggested removal of cervical mucus to overcome plugging and bacterial contamination.⁵⁸

Research Gaps

Multicenter RCTs and systematic reviews are needed as better quality evidence regarding the benefit of cervical mucus removal before embryo transfer.

Survey Results from India

Q 21. Do you routinely aspirate mucus before embryo transfer?

Choices	Percentage	Count
Always	 40.39%	166
In cases with excessive mucus	 36.74%	151
Never	 22.87%	94
	Total	411
	Unanswered	5

Integrations of Evidence and Good Practice Points

Aspiration of cervical mucus is routinely done by 40.39% of clinicians, and aspiration is only done in cases with excessive mucus by 36.74%. 22.87% never aspirate cervical mucus. Available evidence, however, suggests that aspiration of mucus before embryo transfer will improve the CPR and live birth rate.

PICO 15: HOW DOES BED REST AFTER ET INFLUENCE IVF OUTCOMES?

Draft Recommendations

Encouragement of normal activities is recommended after embryo transfer, as there is no evidence to suggest that bed rest improves fertility outcomes, and there is some evidence to suggest that bed rest may have negative effects on IVF outcomes.

Summary of Evidence

Embryo transfer (ET) is a critical step in the in vitro fertilization process, and there is ongoing debate regarding the necessity and duration of bed rest after ET to enhance the chances of implantation and successful pregnancy. Even though the concept of rest seems to find many takers among patients, scientific evidence questions the efficacy of this practice. It is common knowledge that prolonged bed rest may lead to discomfort, fatigue, increased psychological stress, and even the risk of deep vein thrombosis in women who are prone to it.

Extensive research, including randomized controlled trials and systematic reviews carried out since the beginning of IVF, has evaluated the impact of bed rest on IVF outcomes. The randomised controlled trial (RCT) by Gaikwad et al., evaluated the influence of 10 minutes of bed rest after ET on live birth rates in women undergoing IVF with donor oocytes.⁵⁹ Live birth rates (56.7% vs 41.6%) were observed to be significantly higher in the no rest group as compared to the rest group. Malhotra et al., also conducted an RCT wherein one hundred and eighty women, 90 in each group, were randomised to 15 minutes rest after ET (Group A) or early ambulation (Group B).⁶⁰ Pregnancy rates were comparable in both groups, even though absolute numbers were higher in the group ambulating early after embryo transfer.

Almost all meta-analyses, including recent ones by Bede Tyler et al.,³⁷ have concluded that there is no statistically significant benefit of enforced bed rest on pregnancy rates. In fact, this meta-analysis showed that recommending bed rest post-ET significantly reduced clinical pregnancy rates. More recently, a systematic review and meta-analysis by Purata et al., suggested that bed rest after ET is not beneficial in terms of achieving a live birth, indicating insufficient evidence to support routine bed rest in this context.⁶¹

Research Gaps

- Most studies are small and have high heterogeneity in study populations.
- Key variables such as patient age, source of gametes, ovarian reserve, whether fresh or frozen transfers, etc., have not been taken into account.

Survey Results from India

Q 22. Do you advise bed rest to your patient after embryo transfer?

Choices	Percentage	Count
Up to 30 minutes	45.19%	188
No bed rest is advised	37.26%	155
30–60 minutes	17.55%	73
	Total	416

Integration of Evidence and Good Practice Points

Bed rest up to 30 minutes is advised by 45.19 % practitioners. 17.55% practitioners advise bed rest for 30–60 minutes, and 37.26% do not advise any bed rest after ET. Evidence from literature does not support bed rest after ET, and there is some evidence to suggest that bed rest may have negative effects on IVF outcomes. A change of policy may be recommended.

PICO 16: DOES THE ROUTINE PRE-IVF HYSTEROSCOPY IMPROVE IVF OUTCOME?

Draft Recommendations

- Screening hysteroscopy is currently not recommended for routine clinical use before IVF.
- Screening hysteroscopy can be considered in patients with recurrent implantation failure.

Summary of Evidence

Effectiveness, safety, need, and impact of hysteroscopy (HSC) on uterine microenvironment were studied in a large systematic review and meta-analysis⁶²





A total of 14 RCTs were included. Five studies evaluated the effect of hysteroscopy on live birth rate and concluded that it had an overall positive effect on live birth rate. Fourteen studies evaluated the effect of HSC on clinical pregnancy rates, and preoperative HSC was associated with significant improvements in pregnancy rates for both first-time IVF/ICSI patients and repeat IVF/ICSI patients. Eight studies showed no significant difference in the effect of HSC on miscarriage rates. A multicenter, randomised controlled trial (inSIGHT trial) by Smit et al., enrolled 750 patients scheduled for their first IVF cycle, and hysteroscopy did not improve the live birth rates in women with a normal transvaginal ultrasound.⁶³ The TROPHY trial, a large multicenter randomised control trial, also suggested that no improvement in live birth rates is present after hysteroscopy in women with 2–4 failed IVF cycles (RR 1.0, 95% CI 0.79–1.25; $p=0.96$).⁶⁴ As per the ‘Good practice recommendations on add-ons in reproductive medicine’ published by ESHRE in 2023, screening hysteroscopy is currently not recommended for routine clinical use.⁶⁵ Screening hysteroscopy can be considered in patients with recurrent implantation failure.

Research Gaps

In most studies, there is no uniformity on the day of the cycle and the duration before IVF when hysteroscopy was performed, as well as the characteristics of the study population.

Survey Results from India

Q 23. Do you routinely do pre-IVF hysteroscopy?

Choices	Percentage	Count
In patients with previous recurrent implantation failure	 42.31%	176
In patients with history of previous one implantation failure	 39.66%	165
Yes, in all patients	 14.66%	61
Never	 3.37%	14

Integrations of Evidence and Good Practice Points

42.31% of clinicians do pre-IVF hysteroscopy in patients with RIF, 39.66 % do pre-IVF hysteroscopy in patients with a history of one previous implantation failure, and 14.66% do pre-IVF hysteroscopy in all patients. 3.37% do not do routine pre-IVF hysteroscopy. However, clinical evidence from a literature search recommends that pre-IVF hysteroscopy may be done in patients with recurrent implantation failure. Routine use of pre-IVF hysteroscopy is not recommended.

KEY GOOD PRACTICE POINTS

1. Does performing a Mock ET improve IVF outcomes?

- There is insufficient evidence whether Mock ET done routinely improves pregnancy outcomes in IVF.
- However, it allows the determination of the most suitable ET catheter for each patient and improves chances for an easy transfer.
- It is associated with extra cost and hospital visits.

The majority of Indian clinicians either do a Mock ET for all cases (65.94%) or do it if they anticipate difficulty in embryo transfer (26.09%). 86.99% experience difficulty in <10% transfers, and 12.05% experience difficulty in 10 to 20% transfers.

An individual choice is thus justifiable, keeping in mind that difficult ETs are fairly uncommon. Even though success rates are not improved by doing a Mock ET, if there is difficulty in the mock procedure, the clinician is prepared to deal with it by using the appropriate ET catheter or modifications of the procedure.

2. Does the type of outer catheter (soft or firm) affect the IVF outcome?

Soft embryo transfer catheters may be preferred for all embryo transfer (ET) cases except when there is difficulty in negotiating the cervix/internal os with a soft catheter, since most studies have shown significantly higher pregnancy rates with a soft ET catheter in comparison with firm or semi-rigid catheters.

The survey revealed that 70.29% Indian practitioners used an outer ET catheter with a stylet/metal outer catheter only when a difficult ET was anticipated, 22.9% never used an outer ET catheter with a stylet/metal outer catheter, and only 6.76% used them for all embryo transfers. This is in consonance with recommendations available from the literature.

3. Does the use of ultrasound guidance for ET improve IVF outcomes?

Robust evidence is present in favor of the routine use of abdominal ultrasound for guidance during embryo transfer to improve pregnancy and live-birth rates.

The survey showed that 97.84% Indian practitioners always performed ET under 2D ultrasound guidance and only 1.68% performed it under 3D ultrasound. 82.45% practitioners never used 3D ultrasound guidance, 11.06% rarely, and 4.81% sometimes. This practice is in alignment with evidence available from the literature.

4. Does the method of endometrial preparation for frozen embryo transfer (fET) affect the IVF Outcomes?

The committee does not recommend any one protocol over another for improving the chances of live birth.

Natural cycle protocol for endometrial preparation (or its modifications) may be associated with better IVF outcomes than HRT cycles (with and without GnRHa down-regulation) in terms of higher live birth rate and lower miscarriage rate, as well as lower antepartum hemorrhage rate. However, the evidence is insufficient and of low certainty.

A vast majority of practitioners continue to use HRT as a preferred method for endometrial preparation for fET—55.45% without GnRHa down-regulation and 33.41% after GnRHa down-regulation. Only 8.47% use tNC/mNC, and 2.66% use stimulated cycles as a preferred method. A change of preference is desirable in regularly menstruating women. tNCs are associated with higher cancellation rates and more frequent blood samplings, which may be overcome in mNC and stimulated cycles.

5. Does the number of days of estrogen replacement in an HRT cycle affect IVF outcomes?

- At least 11 days of estrogen exposure before progesterone supplementation in artificial frozen-thawed embryo transfer (FET) cycles should be given for the best treatment outcomes in terms of pregnancy rates, implantation rates, and live birth rates. However, good outcomes have been reported with as few as 7 days.
- The maximum number of days of estrogen exposure before starting Progesterone in an artificial cycle for FET may be limited to 35 days (though it has been reported up to 40 days or more).

- Patients with thin endometrium may require longer periods of estrogen therapy to achieve appropriate endometrial thickness.

The largest percentage of Indian practitioners (45.91%) gives estrogen replacement for a minimum of 12 days, 26.92% for a minimum of 10 days, 15.4% for a minimum of 14 days, and 12.02% practitioners transfer the embryos as soon as the endometrium is 8 mm thick, regardless of the number of days of replacement. The literature, however, suggests that too short an estrogen replacement may be associated with higher miscarriage rates.

54.6% practitioners give estrogen replacement for a maximum of 20 days, 33.6% for a maximum of 25 days, 9.76% for a maximum of 30 days, and only 1.95% up to 35 days. Evidence from literature suggests that cycles may not be cancelled even if the required endometrial thickness is not reached in 35 days or more.

6. Does the choice/route/dose of estrogen affect the IVF outcomes in a hormone replacement (HRT) cycle for frozen embryo transfer (fET)?

There is not enough evidence in the literature to support either estradiol valerate/estradiol hemihydrate or 17 beta estradiol for endometrial preparation in artificial fET cycles.

As per the survey, a comparable number of practitioners prefer oral estradiol valerate/oral estradiol hemihydrate or a combination of these with transdermal gel (41.16%, 29.03% and 26.39% respectively). Very few (3.15%) prefer transdermal 17 beta estradiol gel alone. Evidence from the literature also does not support one form of treatment over the other.

- Oral estradiol is the most preferred route of administration, which is non-inferior to transdermal or vaginal preparations in terms of clinical pregnancy rates.

Vaginal route achieves higher serum concentrations of estrogen than transdermal estrogen in HRT-fET cycles, but transdermal estrogen is associated with higher endometrial thickness, shorter treatment duration, and better tolerance.

Non-oral routes can be used effectively in HRT-fET cycles, especially in patients with chronic hepatic and renal dysfunction, high-risk factors for thrombosis, and dyslipidemia.

The survey shows that a majority of practitioners prefer to give estrogen by the oral route (66.99%), followed by a combination of oral/vaginal/transdermal route (27.47%). Transdermal or vaginal routes are less preferred (5.06% and 0.48% respectively). This is in agreement with evidence from the literature, which shows that the oral route is the most preferred and non-inferior one. However, no good evidence is available to support the combination of various routes.

- There is no standardized recommendation on the maximal dose of exogenous estrogen used for endometrial preparation for FET. Women given higher doses in a stepwise-escalation regimen tend to show lesser endometrial thickness and may be more prone to have low birth weight babies, placental anomalies, and retroplacental haematomas.

The survey shows that a majority (60.05%) of practitioners give a maximum estrogen dose of 12 mg/day, followed by 18.89% giving a maximum dose of 10 mg/day and 14.53% giving a maximum of 8 mg/day. Only 6.54% go up to 14 mg/day. As per evidence from literature, a fixed dose schedule of 6mg/day is as good as higher doses. Higher estrogen doses may be harmful, especially in stepwise escalating regimens.

7. Does the maximum endometrial thickness achieved in an HRT cycle for frozen embryo transfer (fET) affect the IVF outcomes?

- Based on the current evidence, live birth rates (LBR) vary significantly across ET ranges, peaking at approximately 10 mm in fET cycles.
- Both excessively thin (<7 mm) and thick (>14 mm) endometria may be detrimental to outcomes.

The survey shows that the majority of practitioners (62.32%) cancel the fET if the endometrial thickness is below 7 mm. An equal number use a cut-off of 6 mm and 8 mm (16.43% and 16.18% respectively), and only 5.07% use 5mm as a cut-off. The evidence from literature also indicates that success rates are compromised with ET less than 7–8 mm.

8. Does the placement of the inner catheter affect IVF outcomes?

- The placement of the embryo transfer (ET) catheter and its distance from the uterine fundus significantly impact IVF outcomes.
- Evidence supports ultrasound-guided ET with the catheter tip ideally placed 10–20 mm from the uterine fundus, correlating with improved clinical pregnancy rates compared to placement less than 10 mm or greater than 20 mm.

As per the survey, 80.43% practitioners place the tip of the inner catheter 1 to 2 cm from the fundus, and 17.15% place it approximately in the mid-uterine cavity. Only a minority do not measure the distance from the fundus (1.93%) or keep it at the fundus (0.48%). Therefore, a vast majority are following the policy recommended in the literature.

9. Does the use of tocolytics/anti-prostaglandins at the time of embryo transfer improve IVF outcomes?

- Atosiban has shown some promise in improving implantation and pregnancy outcomes, particularly in women with RIF, by reducing uterine contractility during ET.
- In contrast, the use of anti-prostaglandins like NSAIDs lacks robust evidence and may carry potential risks.
- The decision to use tocolytics or anti-prostaglandins should be tailored to individual patient profiles, particularly those with recurrent implantation failure, excessive uterine contractions, or difficult embryo transfers.

Among Indian practitioners, 37.68% do not use tocolytics at the time of embryo transfer, 34.54% use them if they anticipate a difficult transfer, 19.81% use them routinely, and 7.97% after a difficult transfer. On the other hand, a majority (43.08%) of Indian practitioners do not use NSAIDs/anti-prostaglandins in their practice of ET, 26.76% use them sometimes, 18.98% rarely, and only 10.06% always. This is in consonance with the evidence from literature, which shows some evidence (though low quality) to support the use of tocolytics before ET selectively, but there is not enough evidence to support the use of NSAIDs/anti-prostaglandins.

10. Does sequential embryo transfer improve IVF outcomes?

Sequential embryo transfer (SEQET) may be considered as an alternative to conventional cleavage-stage embryo transfer (CET) in the presence of an adequate number of embryos, but evidence is less convincing when compared with blastocyst transfer and in women with a history of recurrent implantation failure.

Only 2.41% practitioners routinely perform Sequential embryo transfer when a high number of embryos are available, and 25.30% do it for specific cases. A majority of practitioners (67.23%) prefer to do a Day 5 embryo transfer, and only 5.06% prefer a day 3 transfer. This is in consonance with evidence from the literature.

11. Does checking the hormonal profile in fET (frozen-thawed embryo transfer) cycles improve IVF outcomes?

- P4 levels before starting progesterone do not seem to affect the IVF outcomes in artificial (hormone replacement) cycles for fET.
- In natural cycle (NC)/modified natural cycle (mNC)/stimulated cycles for fET, Progesterone level cut-off of 1.0–1.5 ng/mL may be used before starting progesterone supplementation.

44.1% practitioners check Serum P4 levels routinely before starting Progesterone in fET cycles. 31.33% and 18.31% check only in NC/mNC/stimulated cycles, and if there are ultrasound findings suggestive of raised progesterone, respectively. 6.27% practitioners do not check serum P4 levels. It may be suggested that checking P4 levels in artificial cycles is unnecessary. As regards cut-off levels, 45.38% would cancel a transfer if levels exceed 1.5 ng/dL, 38.98% if levels exceed 1.0 ng/dL, and 9.2% if levels exceed 0.8ng/dL. Evidence from literature suggests that cancellation of fET at P4 levels between 0.8 and 1.0 ng/dL may not be justified.

12. In FET cycles, does assessment of uterine artery doppler & endometrial blood flow, as compared to standard endometrial assessment, improve outcomes?

Doppler ultrasound is an accessible, cost-effective, and non-invasive method to assess endometrial receptivity. While reduced perfusion and abnormal uterine artery flow are linked to infertility, findings are not consistent across studies regarding the routine use in ART and infertility management.

Only 28.95% Indian practitioners use these modalities routinely in their practice, while 39.90% do so only in cases of failed IVF or in the presence of poor endometrial characteristics. 24.82% check only the endometrial blood flow, and 6.3% never use these modalities. The difference in acceptance of this technology is likely due to a lack of good evidence for or against this technique of studying endometrial receptivity.

13. Does the presence of fluid in the endometrial cavity interfere with implantation?

- Evaluation for cause, persistence, and volume should be done. Spontaneous resolution is reported to be associated with a good outcome. Consider aspiration if persistent or >3.5 mm.
- It is not clear whether aspiration of fluid improves the IVF outcomes. Recurrence of the problem in a subsequent cycle is not seen in around half of the cancelled cycles.

A majority of consultants (45.17%) aspirate the ECF, send it for culture, and continue to monitor, whereas 28.74% give a course of antibiotics and continue to monitor. 20.77% cancel the fET and only 5.31% aspirate the fluid on the day of embryo transfer and proceed with the ET. Evidence from the literature says that in a majority of cases, spontaneous resolution of fluid seen early in the fET cycle will occur, therefore making observation a good option. The benefit that comes from aspiration is doubtful. Cancellation may not be followed by recurrence of the same problem in a subsequent cycle.

14. Does aspiration of mucus before ET improve IVF success rates?

Aspiration of mucus before embryo transfer should be done to improve the clinical pregnancy rate (CPR) and live birth rate (LBR).

Aspiration of cervical mucus is routinely done by 40.39% of clinicians, and aspiration is only done in cases with excessive mucus by 36.74%. 22.87% never aspirate cervical mucus. Available evidence, however, suggests that aspiration of mucus before embryo transfer will improve the CPR and live birth rate.

15. How does bed rest after ET influence IVF outcomes?

Encouragement of normal activities is recommended after embryo transfer, as there is no evidence to suggest that bed rest improves fertility outcomes, and there is some evidence to suggest that bed rest may have negative effects on IVF outcomes.

Bed rest up to 30 minutes is advised by 45.19 % practitioners. 17.55% practitioners advise bed rest for 30 to 60 minutes, and 37.26% do not advise any bed rest after ET. Evidence from literature does not support bed rest after ET, and there is some evidence to suggest that bed rest may have negative effects on IVF outcomes.

16. Does the routine pre-IVF hysteroscopy improve IVF outcome?

- Screening hysteroscopy is currently not recommended for routine clinical use before IVF.
- Screening hysteroscopy can be considered in patients with recurrent implantation failure.

42.31% of clinicians do pre-IVF hysteroscopy in patients with RIF, 39.66% do pre-IVF hysteroscopy in patients with a history of one previous implantation failure, and 14.66% do pre-IVF hysteroscopy in all patients. 3.37% do not do routine pre-IVF hysteroscopy. However, clinical evidence from a literature search recommends that pre-IVF hysteroscopy may be done in patients with recurrent implantation failure. Routine Use of pre-IVF hysteroscopy is not recommended.

SURVEY QUESTIONNAIRE OF EMBRYO TRANSFER**Basic Demographic Questions**

1. In which city do you practice?
2. Do you practice in
 - a. Corporate Sector
 - b. Private IVF Centre
 - c. Government Institution Centre
 - d. Other (Please specify)
3. Approximately how many embryo transfers (ET) do you perform every month?
 - a. <10
 - b. 11 to 20
 - c. 21 to 30
 - d. > 30

PICO Q 1 - Does performing a mock ET improve IVF outcomes?

1. Do you routinely perform a mock embryo transfer prior to the actual procedure?
 - a. Yes, for all patients to assess the uterine cavity and optimal catheter placement
 - b. No, I do not do Mock ET
 - c. I perform mock ET only if I anticipate difficulty in embryo transfer
2. Roughly, how frequently do you experience difficult ET (difficulty in crossing internal os, blood in the catheter, multiple attempts, etc) in your practice?
 - a. < 10% of transfers
 - b. 10% to 20% of transfers
 - c. >20%

PICO Q 2 - Does the type of outer catheter (soft or firm) affect the IVF outcome?

3. How frequently do you use an outer catheter with stylet / metal outer catheter in your practice?
 - a. Always in all embryo transfers
 - b. Always in anticipated difficult embryo transfers
 - c. Never

PICO Q 3 – Does the use of ultrasound guidance for ET improve IVF outcomes?

4. Do you perform ET under 2D ultrasound guidance?
 - a. Always
 - b. Sometimes
 - c. Rarely
 - d. Never
5. Do you perform ET under 3D ultrasound guidance?
 - a. Always in all embryo transfers
 - b. Sometimes
 - c. Rarely
 - d. Never

PICO Q 4 – Does the method of endometrial preparation for frozen embryo transfer (fET) affect the IVF outcomes?

6. When preparing the endometrium for fET, what is your preferred method in majority of cases?
 - a. Hormone replacement cycle without GnRHa suppression
 - b. Hormone replacement cycle after GnRHa suppression
 - c. Natural / modified natural
 - d. Stimulated cycle

PICO Q 5 – Does the number of days of estrogen replacement in an HRT cycle affect IVF outcomes?

7. What is your minimum number of replacement days of estrogen in an HRT cycle for fET?
 - a. Minimum 10 days
 - b. Minimum 12 days
 - c. Minimum 14 days
 - d. I transfer the embryos once endometrial thickness is 8 mm or more, regardless of the number of days of estrogen replacement

Survey Q 8: What is the maximum duration of estrogen you use for preparation of endometrium in HRT cycles for fET?

- a. 20 days
- b. 25 days
- c. 30days
- d. 35 days

PICO Q 6 - Does the choice / route / dose of estrogen affect the IVF outcomes in an HRT cycle for fET?

- 9. What is your most preferred choice of estrogen for preparation of endometrium in HRT cycles for fET?
 - a. Estradiol valerate (oral)
 - b. Estradiol hemihydrate (oral)
 - c. 17 beta Estradiol gel (transdermal administration)
 - d. Combination of the above
- 10. What is your preferred route of estrogen administration for preparation of endometrium in HRT cycles for fET?
 - a. Oral
 - b. Transdermal
 - c. Vaginal
 - d. Combination of the above
- 11. What is the maximum daily dose of estrogen you use for preparation of the endometrium in HRT cycles for fET?
 - a. 8 mg
 - b. 10 mg
 - c. 12 mg
 - d. 14 mg

PICO Q 7 - Does the maximum endometrial thickness achieved in an HRT cycle for fET affect the IVF outcomes?

- 12. What is the minimum ET below which you would cancel an FET cycle ?
 - a. < 5mm
 - b. < 6 mm
 - c. < 7mm
 - d. < 8 mm

PICO Q 8 - Does the placement of the inner catheter affect IVF outcomes?

13. *Where do you place your inner catheter tip during USG guided Embryo Transfer?*
- 1 to 2 cm from the fundus
 - Approximate mid uterine cavity
 - At the fundus
 - I do not measure the distance from the fundus

PICO Q 9 – Does Use of tocolytics /anti-prostaglandins at the time of embryo transfer improve IVF outcomes?

14. Do you administer tocolytics (e.g, nifedipine, atosiban) before or after embryo transfer to reduce the risk of uterine contractions?
- Routinely before embryo transfer
 - After a difficult embryo transfer
 - Before embryo transfer if I anticipate difficulty
 - No, I do not use tocolytics in my practice for embryo transfer
15. Do you administer NSAIDs / anti-prostaglandins before or after embryo transfer to reduce the risk of uterine contractions?
- Always
 - Sometimes
 - Rarely
 - Never

PICO Q 10 - Does sequential embryo transfer improve IVF outcomes?

16. Survey Q 16 (PICO Q 10) Do you practice sequential embryo transfer (SET), where embryos are transferred in stages (e.g., Day 3 followed by Day 5)?
- Yes, routinely for patients with a high number of embryos
 - Only for specific cases
 - No, I prefer doing an embryo transfer on Day 3
 - No, I prefer doing an embryo transfer on Day 5

PICO Q 11 - Does checking the hormonal profile in fET cycles improve IVF outcomes?

17. Do you check P4 levels before starting progesterone in fET cycles?
- Yes, I do it routinely
 - Only in NC / mNC / stimulated cycles
 - Only if there are ultrasound findings to suggest raised progesterone

- d. Never

Survey Q18: In FET cycles, what cut-off for serum P4 levels do you use on the day of starting progesterone?

- a. 0.8 ng/dl
- b. 1.0 ng/dl
- c. 1.5 ng/dL
- d. I do not check Serum P4 levels

PICO Q 12 – In FET cycles, does assessment of Uterine artery doppler & endometrial blood flow compared to standard endometrial assessment improve IVF outcomes?

- 19. In FET cycles, do you check for Endometrial blood flow in Zone 3/4 & Uterine artery PI before starting progesterone in Frozen Embryo transfer cycle?
 - a. Yes, routinely
 - b. Never
 - c. Only in case of previous failed IVF / poor endometrial characteristics
 - d. I do endometrial blood flow but not uterine artery PI

PICO Q 13 – Does the presence of fluid in the endometrial cavity interfere with implantation?

- 20. What would you do for endometrial fluid seen on day of start of progesterone during fET?
 - a. Aspiration of endometrial fluid when detected (sent for culture) and continue monitoring.
 - b. Course of antibiotics and continue monitoring
 - c. Aspiration of fluid on day of transfer followed by transfer of embryos
 - d. Cancel ET

PICO Q 14 - Does aspiration of mucus before ET improve IVF success rates?

- 21. Do you routinely aspirate mucus before embryo transfer?
 - a. Always
 - b. Never
 - c. In cases with excessive mucus

PICO Q 15 - How does bed rest after ET influence IVF outcomes?

- 22. Do you advise bed rest to your patient after embryo transfer?

- a. No bed rest is advised
- b. Up to 30 minutes.
- c. 30 to 60 minutes.

PICO Q 16 – Does routine Pre-IVF Hysteroscopy improve IVF outcomes?

23. Do you routinely do pre-IVF hysteroscopy?
- a. Yes, in all patients
 - b. In patients with history of previous one implantation failure
 - c. In patients with previous recurrent implantation failure
 - d. Never

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Embryo Transfer Practices in India

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