INPLASY

Comparative Effectiveness of Cryopreserved and Fresh Oocyte Strategies in Donor IVF Cycles. Systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 July 2025 and was last updated on 14 July 2025.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aim to compare clinical outcomes—specifically pregnancy and live birth rates—across four major IVF pathways using donor oocytes, evaluating how the timing and location of cryopreservation and fertilization influence reproductive efficacy. The study further explores how institutional practices shape patient care quality and highlights evidence gaps where future guidelines should be developed.Study Question 1: Does the timing and location of fertilization (in the oocyte bank vs. in the recipient center) impact pregnancy and live birth outcomes in donor oocyte IVF cycles?Study Question 2: Are thaw–refreeze cycles involving both gametes associated with reduced reproductive outcomes compared to single-thaw or fresh cycles?Study Question 3: Do commercial models offering guaranteed blastocyst packages affect clinical flexibility and patient-tailored IVF planning?Study Question 4: What is the ethical and clinical impact of shifting fertilization and blastocyst production to the gamete bank?Study Question 5: How do different IVF strategies with donor oocytes compare in terms of cost-effectiveness and resource utilization for couples and medical centers?Study Question 6: To what extent does sperm quality—particularly the use of fresh versus cryopreserved semen—affect fertilization, blastocyst development, and pregnancy outcomes in donor oocyte cycles?

Rationale In recent years, the global demand for donor oocytes has substantially increased, driven by delayed childbearing, advancements in assisted reproductive technologies (ART), and broader access to fertility treatments. This surge has outpaced supply, generating widespread shortages across fertility clinics and gamete banks.[1-3] In response, many ART providers have implemented cryopreservation strategies, batch allocation systems, and centralized oocyte banking to optimize logistics, reduce waste, and manage cross-border distribution. However, these evolving practices have also given rise to critical questions regarding clinical efficacy, patient autonomy, and the commercial motives behind policy development.

Condition being studied Recent data show a progressive shift toward bank-mediated fertilization and blastocyst production, with some fertility networks now offering packages that guarantee two blastocysts—rather than delivering 10 vitrified donor oocytes for in-laboratory use by the treating center. This change, often paired with a 30% price increase, is marketed as more efficient but may reduce flexibility, biological transparency, and cost-effectiveness for couples. In contrast, traditional approaches, where 10 oocytes are sent to the clinical lab and fertilized 2 by 2, offer enhanced adaptability. They allow physicians to assess fertilization and blastulation efficiency in real-time, using fresh, normospermic semen and opting for re-storage if developmental parameters fall below standard. This strategy better aligns with individualized medicine principles and ensures better control over embryo quality monitoring and cycle tailoring.

METHODS

Search strategy Search Strategy and PRISMA Compliance This systematic review and meta-analysis were conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A PRISMA flow diagram was used to illustrate the study selection process21.
Systematic searches were conducted in the following databases from January 1, 2015, to April 30, 2025: PubMed/MEDLINE, Embase, Scopus, Cochrane Central Register of Controlled Trials , (CENTRAL), Web of Science, National and international ART registries (SART, CDC, ESHRE, HFEA).

Participant or population The search terms included combinations of: ("donor oocyte" OR "egg donation") AND ("cryopreservation" OR "vitrification" OR "refreezing") AND ("IVF" OR "assisted reproduction") AND ("pregnancy rate" OR "live birth rate") AND ("fresh sperm" OR "cryopreserved sperm") AND ("embryo transfer"). Additional manual searches of references from eligible full-texts and gray literature (conference proceedings, registry data, institutional reports) were performed to identify missing studies.

Intervention Inclusion criteria:
• Studies reporting clinical pregnancy or live birth rates from donor oocyte IVF cycles
• Comparative data involving at least two of the following arms:
1. Cryopreserved oocytes shipped and fertilized fresh at the receiving center
2. Fresh oocytes fertilized with cryopreserved sperm and cryopreserved post-blastulation
3. Cryopreserved oocytes fertilized with thawed sperm and re-frozen embryos
4. Fresh oocytes + fresh sperm with direct transfer
• Studies involving human participants, aged 20–45 years
• Retrospective cohorts, prospective cohorts, case-control studies, and registry-based analyses
Exclusion criteria:
• Case reports, animal studies, reviews, editorials
• Missing or non-comparable outcome data
• Studies reporting only biochemical pregnancy without clinical or live birth outcomes.

Comparator
• Study design and location
• Sample size per arm
• Type and number of freezing/thawing cycles
• Sperm source and preparation method
• Embryo development and transfer timing
• Outcomes: Clinical pregnancy rate, live birth rate, miscarriage rate, blastulation rate
• Stratification by donor and recipient age groups (<30 vs ≥30 years)
Statistical Analysis and Meta-Analytic Model Pooled risk ratios (RRs) and adjusted odds ratios (aORs) were calculated22-25 using a random-effects model (DerSimonian-Laird) due to clinical heterogeneity24.

Study designs to be included Systematic review with meta analysis.

Eligibility criteria Inclusion criteria:
• Studies reporting clinical pregnancy or live birth rates from donor oocyte IVF cycles
• Comparative data involving at least two of the following arms:
1. Cryopreserved oocytes shipped and fertilized fresh at the receiving center
2. Fresh oocytes fertilized with cryopreserved sperm and cryopreserved post-blastulation
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Information sources Systematic searches were conducted in the following databases from January

1, 2015, to April 30, 2025: PubMed/MEDLINE, Embase, Scopus, Cochrane Central Register of Controlled Trials , (CENTRAL), Web of Science, National and international ART registries (SART, CDC, ESHRE, HFEA).

Main outcome(s)
Including:
• Study design and location
• Sample size per arm
• Type and number of freezing/thawing cycles
• Sperm source and preparation method
• Embryo development and transfer timing
• Outcomes: Clinical pregnancy rate, live birth rate, miscarriage rate, blastulation rate
• Stratification by donor and recipient age groups (<30 vs ≥30 years).

Additional outcome(s) Two independent reviewers performed screening, selection, and data abstraction. Discrepancies were resolved by consensus or third-party adjudication.

Data management Statistical Analysis and Meta-Analytic Model Pooled risk ratios (RRs) and adjusted odds ratios (aORs) were calculated22-25 using a random-effects model (DerSimonian-Laird) due to clinical heterogeneity24.

Quality assessment / Risk of bias analysis Risk of Bias Assessment (ROBINS-I) The ROBINS-I tool was used to assess the risk of bias in non-randomized studies across seven

domains: 1.
Confounding 2. Selection of
participants 3. Classification of
interventions 4. Deviations from intended
interventions 5. Missing
data 6. Measurement of
outcomes 7. Selection of reported

results Each domain was scored as low, moderate, serious, or critical
risk. A heatmap and summary bar plots were used to visualize risk distribution across studies and study
arms22. Certainty of Evidence (GRADE) The GRADE approach was applied to assess the certainty of evidence for each primary outcome across
arms23. Domains evaluated

included: • Risk of
bias •
Inconsistency •
Indirectness •
Imprecision • Publicationbias.

Strategy of data synthesis Statistical Analysis and Meta-Analytic Model Pooled risk ratios (RRs) and adjusted odds ratios (aORs) were calculated22-25 using a random-effects model (DerSimonian-Laird) due to clinical heterogeneity24.
• Heterogeneity was assessed using I^2 statistics 25.
• Forest plots were generated for primary outcomes (clinical pregnancy, live birth).
• Subgroup analyses were performed based on age group and number of cryopreservation steps.
• Sensitivity analyses excluded studies at high risk of bias.
All statistical analyses were performed using R (metafor, meta packages) and Python (statsmodels, matplotlib) to ensure replicability.

Subgroup analysis
• Subgroup analyses were performed based on age group and number of cryopreservation steps.
• Sensitivity analyses excluded studies at high risk of bias.

Sensitivity analysis • Sensitivity analyses excluded studies at high risk of bias.

Language restriction English.

Country(ies) involved Italy.

Keywords Donor oocyte, IVF, cryopreservation, embryo transfer, thaw-refreeze, live birth rate, systematic review, meta-analysis, PRISMA.

Contributions of each author
Author 1 - Francesco MAria Bulletti - Francesco Maria Bulletti conceptualized and supervised the study from data analysis to preparation of the manuscript.
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