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# Assisted Reproductive Technologies (ART) for Female Infertility: A Review of the Current State of the ART

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## ABSTRACT

Female infertility remains a pervasive global health challenge, with complex etiologies encompassing ovulatory disorders, tubal pathology, diminished ovarian reserve, endometriosis, and unexplained reproductive failure. Over the past four decades, assisted reproductive technologies (ART) have evolved from rudimentary hormonal manipulations to highly sophisticated, precision-driven interventions that transcend biological limitations. This review synthesizes the contemporary landscape of ART for female infertility, delineating advancements in controlled ovarian stimulation protocols, intrauterine insemination, in vitro fertilization, intracytoplasmic sperm injection, and preimplantation genetic testing. It further interrogates the expanding frontier of fertility preservation, including vitrification-based oocyte cryopreservation and oncofertility applications, alongside disruptive innovations such as uterus transplantation, artificial gametogenesis, and AI-enabled embryo morphokinetics. Beyond technical dimensions, the discourse critically engages with the ethical, psychosocial, and cultural complexities that shape ART accessibility and acceptability across diverse sociogeographic contexts. By integrating evidence from recent clinical trials, meta-analyses, and translational research, this review provides a panoramic yet nuanced appraisal of current best practices and future trajectories. In doing so, it underscores the imperative for individualized, patient-centered reproductive care that harmonizes biomedical efficacy with humanistic values.

## INTRODUCTION

Infertility is no longer a whispered sorrow in hushed clinic corridors; it has emerged as a global public health concern, echoing through households and communities with profound emotional, economic, and sociocultural resonance. By 2021, over 110 million women worldwide faced impaired fertility, with the age-standardized prevalence increasing nearly 22% over the past three decades (Wei et al., 2025). In women, infertility is a multifactorial condition rooted in ovulatory disorders, tubal obstructions, endometrial pathologies, endocrine dysregulation, genetic anomalies, and idiopathic factors (Ahmad et al., 2025).

Against this backdrop, assisted reproductive technology (ART) has matured into an alchemical intersection of endocrinology, cellular engineering, and data science. Since the first successful in vitro fertilization (IVF) birth in 1978, ART has expanded from experimental innovation to a mainstream clinical service, transforming reproductive care and offering hope where natural conception has proven elusive (Howles et al., 2012). Over the past few decades, protocols have evolved from conventional ovarian stimulation to highly individualized cycles, integrating biomarkers such as anti-Müllerian hormone (AMH) and antral follicle count (AFC) for optimized gonadotropin dosing (Melo et al., 2025). Ovarian stimulation remains the fulcrum of ART, with GnRH antagonist protocols increasingly favoured for their capacity to mitigate ovarian hyperstimulation syndrome (OHSS) while maintaining pregnancy outcomes comparable to agonist regimens (Omokanye et al., 2019). These refinements align with a broader movement toward patient-tailored reproductive medicine, which blends molecular diagnostics, individualized pharmacology, and noninvasive monitoring.

However, ART is not confined to the realms of IVF and ICSI. Fertility preservation, once a niche intervention for cancer patients has been normalized through vitrification-based oocyte cryopreservation, enables women to decouple reproductive potential from chronological age. Preimplantation genetic testing (PGT) now empowers clinicians to screen embryos for aneuploidy or monogenic disorders, increasing implantation rates and reducing miscarriage risk (Guan et al., 2021).

The next frontier is even more audacious. Advances in artificial gametogenesis suggest a future where oocytes could be generated from somatic cells, whereas uterus transplantation has already culminated in live births, expanding options for women with absolute uterine factor infertility (Ouyang and Wei, 2025).AI-driven embryo selection leverages morphokinetic imaging and predictive analytics to increase the probability of implantation, potentially replacing subjective embryologist grading

(Gleicher et al., 2019).

However, ARTs' proliferation also creates ethical, economic, and equity dilemmas. Despite remarkable technological strides, access remains skewed toward affluent populations in high-resource settings, with many low- and middle-income countries lacking subsidized programs. This inequity forces a reckoning with the principle of reproductive justice, prompting calls for policy frameworks that bridge technological capability with social responsibility (Johansson and Lindström Sol, 2022).

In this review, we review the current state of the art in female infertility management through ART, unpacking its biological underpinnings, technical evolution, and disruptive innovations, while also investigating its societal footprint. By weaving clinical evidence with emerging research, this work aims to present not merely a catalogue of procedures but also a holistic narrative of where ART stands today and where it may journey tomorrow.

Assisted reproductive practice has not only scaled numerically but also diversified technically: global IVF utilization and live–birth outputs continued to rise through 2022-2023, reflecting both broader access in some regions and greater uptake of elective fertility services such as oocyte cryopreservation. Large registry reports and society bulletins document year-to-year increases in cycle volumes and births attributable to ART, highlighting that refinement of stimulation strategies, laboratory protocols and cryotechniques is translating into measurable population-level impact (Mai et al., 2025).

Concurrently, the literature from 2021-2025 highlights two major thrusts reshaping clinical practice. First, vitrification-based oocyte cryopreservation has matured into a clinically robust tool with multiple cohort and registry analyses showing comparable clinical pregnancy and perinatal outcomes versus fresh oocytes in many settings, cementing its role in both oncofertility and elective fertility preservation (Pantos et al., 2024). Second, artificial intelligence and deep learning platforms for embryo assessment and morphokinetic analysis have progressed from proof-of-concept to multicenter validation studies, with systematic reviews and comparative analyses reporting that AI models can match or outperform embryologists for embryo viability prediction in some datasets, a development that promises to standardize selection, reduce subjective bias, and potentially improve live birth rates when integrated responsibly into lab workflows (Olawade et al., 2025).

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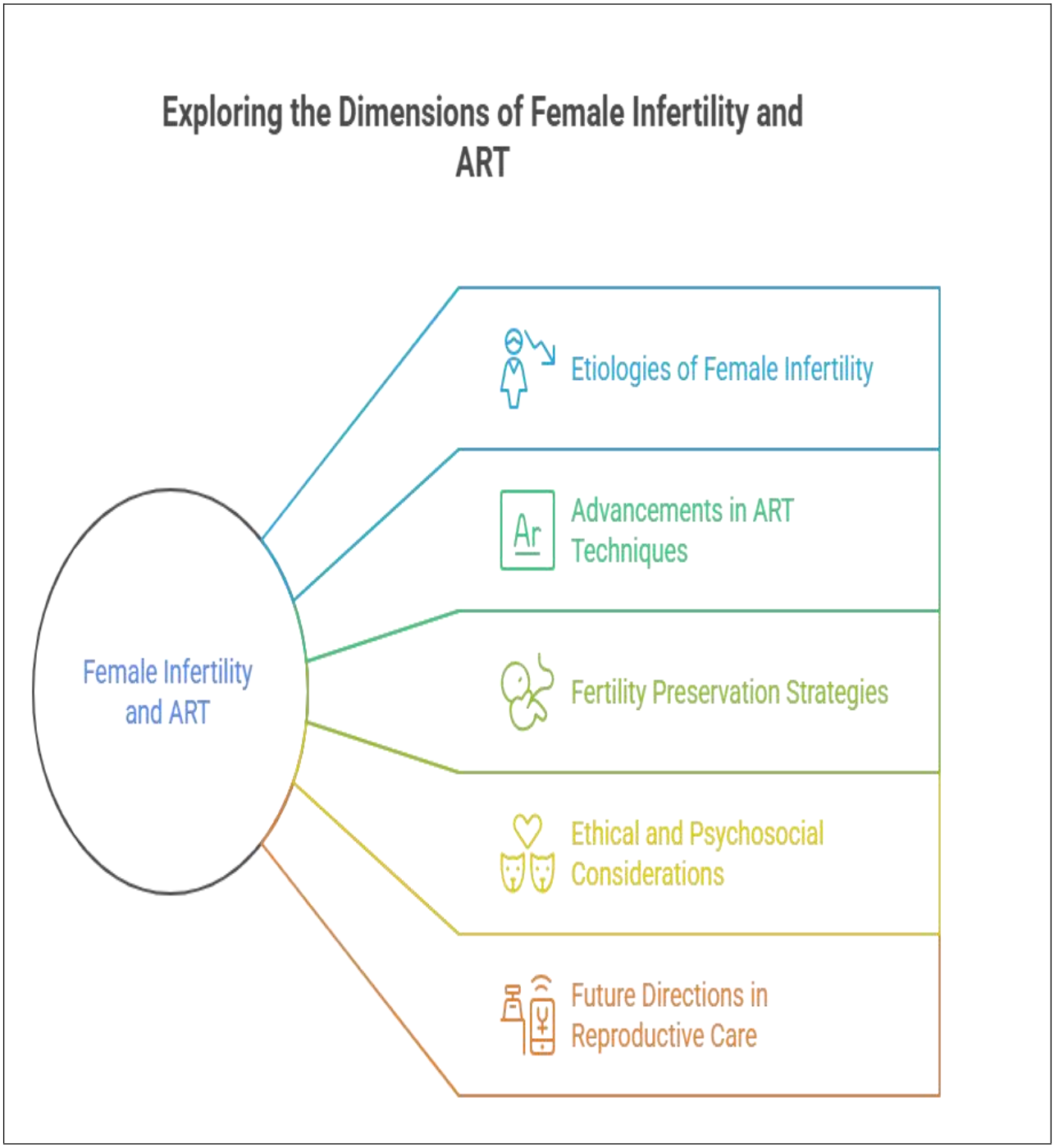


**GRAPHICAL ABSTRACT,ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) FOR FEMALE INFERTILITY: A REVIEW OF THE CURRENT STATE OF THE ART**

## EPIDEMIOLOGY AND ETIOLOGY OF FEMALE INFERTILITY

Infertility is a common, heterogeneous reproductive disorder with broad public health and psychosocial ramifications: contemporary estimates suggest that approximately one in six people worldwide will experience infertility at some point in their lives, underscoring both its ubiquity and the urgent need for equitable access to care. Recent global burden studies place the absolute number of women affected on the order of ~110 million (2021 estimates), with age-standardized prevalence rates remaining substantive across regions. These data reflect not only biological drivers but also changing demographics, delayed childbearing, and differing access to reproductive health services (Liu et al., 2025).

At a practical level, female infertility is multifactorial: major categories include ovulatory disorders, tubal and peritoneal disease, uterine factors, diminished ovarian reserve, endometriosis, and unexplained infertility. Epidemiologic and clinical syntheses consistently report that ovulatory dysfunction (including polycystic ovary syndrome and hypothalamic amenorrhea) comprises a large share of identifiable causes, whereas tubal disease, which is often a sequelae of pelvic infection or prior surgery, remains a leading mechanical impediment to natural conception. Estimates of the proportional contribution vary by population and methodology, but ovulatory disorders and tubal factors together account for a substantial fraction of diagnosed cases encountered in infertility clinics (Bala et al., 2021; Ennab and Atiomo, 2023).

Infectious and inflammatory etiologies retain outsized importance in many settings. Sexually transmitted and reproductive tract infections, untreated chlamydia, gonorrhea, and pelvic inflammatory disease continue to drive tubal damage and account for a sizable and rising share of the infertility burden in some regions, particularly where screening and early treatment are limited. Recent analyses quantifying the global burden attributable to infections reported an increasing absolute number of cases linked to infectious causes between 1990 and 2021, highlighting persistent prevention gaps (Wei et al., 2025; Van Gerwen et al., 2022).

Another dominant theme is the centrality of ovarian aging and diminished ovarian reserve as population-level drivers of female infertility. Anti-Müllerian hormone (AMH) and the antral follicle count (AFC) have become staple biomarkers in both epidemiological studies and clinical practice for estimating the size of the remaining follicle pool, guiding counselling, and individualizing ART strategies. Contemporary cohorts and mechanistic work emphasize that while chronological age is the

single strongest predictor of fecundability, interindividual variation in ovarian reserve and its precipitous decline in some women explain why fertility becomes compromised earlier in a subset of patients (Karaviti et al., 2025).

Endometriosis deserves a separate line: it is common in reproductive-aged women and is linked to reduced fecundity through a constellation of mechanisms, such as ovarian reserve depletion (when ovarian endometriomas are present), pelvic adhesions, an inflammatory milieu impairing gamete/embryo interactions, and altered endometrial receptivity. Epidemiologic syntheses and IVF registry analyses indicate that women with moderate-to-severe endometriosis may have lower oocyte yield and implantation rates, although ART (including IVF) remains a primary route to parenthood for many affected patients (Elizur et al., 2025).

Lifestyle, metabolic, and environmental contributors also modulate risk. Obesity, tobacco exposure, extreme exercise, eating disorders, and metabolic syndrome can all perturb ovulatory function and endometrial physiology; concurrently, emerging evidence implicates environmental toxicants and endocrine disruptors in subfertility trends, although causal links at the population level remain challenging to prove. Male factor infertility also coexists in many couples, and early dropping sperm counts or semen anomalies in the partner will shift both diagnosis and ART planning.

Finally, the epidemiology of infertility is inseparable from social determinants: delayed first pregnancy driven by educational and career trajectories, limited reproductive health access, cultural norms that delay care seeking, and economic barriers to specialty services shape who receives a diagnosis and who ultimately benefits from ART. These intersecting biological and societal vectors explain why prevalence estimates vary modestly between income strata even as the underlying biological vulnerabilities are widespread. The epidemiologic picture, therefore, not only frames clinical decision-making but also motivates public health interventions aimed at prevention, earlier detection, and equitable access to infertility evaluation and treatment (Feng et al., 2025).

## OVERVIEW OF ASSISTED REPRODUCTIVE TECHNOLOGIES

Assisted reproductive technology (ART) represents a sophisticated constellation of biomedical interventions designed to circumvent barriers to natural conception by manipulating gametes, embryos, or reproductive physiology in vitro or in vivo. Since the birth of the first “test-tube baby” in 1978, ART has evolved from a niche experimental procedure into a highly structured, evidence-based branch of reproductive medicine, encompassing a spectrum of techniques that range from minimally

invasive insemination approaches to complex micromanipulation of oocytes and embryos (Uche, 2025). At its core, ART aims to optimize the meeting of gametes and the implantation of a viable embryo by overcoming mechanical, hormonal, or genetic impediments. The armamentarium includes controlled ovarian stimulation (COS) to induce the synchronous maturation of multiple follicles, oocyte retrieval under ultrasound guidance, in vitro fertilization (IVF) with conventional insemination or intracytoplasmic sperm injection (ICSI), embryo culture, and embryo transfer into the uterine cavity. Adjunct modalities such as preimplantation genetic testing (PGT), assisted hatching, and time-lapse morphokinetics increase embryo selection and implantation probability, whereas cryopreservation (via vitrification) allows surplus gametes or embryos to be stored for future use without compromising developmental potential (Zhou et al., 2025; Solomon, 2024).

In addition to these mainstays, ART currently incorporates intrauterine insemination (IUI), a lower-complexity intervention suitable for select cases of mild male factor infertility or unexplained infertility, oocyte donation for women with depleted or nonfunctional ovaries, and gestational surrogacy for those with absolute uterine factor infertility. Innovations in oocyte and ovarian tissue cryopreservation have broadened the reach of ART into oncofertility and elective fertility preservation, empowering women to decouple reproductive planning from chronological age or disease progression. The last decade has witnessed the integration of cutting-edge technologies into ART workflows. Artificial intelligence (AI) and deep learning algorithms are being deployed to analyse embryo morphokinetics with a level of granularity unattainable by the human eye, enabling more objective and potentially more predictive embryo grading. Omics-based profiling, including transcriptomics, metabolomics, and proteomics of follicular fluid and culture media, promises to refine patient stratification and treatment personalization. Even uterus transplantation, once considered a distant dream, has yielded live births, expanding the frontiers of reproductive possibilities (Canosa, 2021; Paya Bosch, 2024).

Importantly, ART is no longer purely a laboratory endeavor; it is embedded within a multidisciplinary clinical framework involving reproductive endocrinologists, embryologists, rologists, genetic counselors, mental health specialists, and legal advisors. This integrated approach reflects the reality that infertility is as much a psychosocial journey as it is a biological condition, requiring patient-centered care that balances technical efficacy with emotional and ethical considerations (Munch et al., 2025).

As global demand increases, ART faces a dual imperative: to continue advancing technologically while ensuring equitable access, affordability, and cultural sensitivity. The present landscape is thus characterized by both unprecedented capability and persistent disparity, a tension that will shape the trajectory of ART in the coming decades.

## CONTROLLED OVARIAN STIMULATION AND OVULATION INDUCTION

Controlled ovarian stimulation (COS) and ovulation induction are the physiologic ignition switches of most assisted reproductive technology (ART) cycles and are designed to coax the ovaries to produce multiple mature oocytes within a single menstrual window. While ovulation induction aims to stimulate the development of one or a few follicles in women with anovulatory disorders (e.g., polycystic ovary syndrome), COS pursues a multifollicular recruitment strategy, maximizing the yield of mature oocytes for IVF or ICSI while preserving endometrial receptivity (Dragotto et al., 2024).

The rationale is simple yet biologically intricate: in a natural cycle, follicular selection is a tightly orchestrated endocrine ballet, with rising follicle-stimulating hormone (FSH) recruiting a cohort and one dominant follicle suppressing its rivals through estradiol and inhibin B feedback (Lewis, 2024). COS pharmacologically disrupts this single-follicle paradigm, sustaining supraphysiologic FSH levels to prevent follicular atresia and allow simultaneous maturation of multiple follicles.

## PHARMACOLOGIC ARMAMENTARIUM

- Gonadotropins (recombinant FSH, urinary FSH, or human menopausal gonadotropin remain the cornerstone of COS and are administered in daily subcutaneous injections titrated to ovarian reserve markers such as anti-Müllerian hormone (AMH) and the antral follicle count (AFC).
- Gonadotropin-releasing hormone (GnRH) analogues, either agonists (for downregulation in long protocols) or antagonists (for rapid suppression in flexible or fixed regimens), are used to prevent a premature luteinizing hormone (LH) surge. Antagonist protocols, which are increasingly favoured in contemporary practice, offer shorter durations, reduced gonadotropin consumption, and a lower risk of ovarian hyperstimulation syndrome (OHSS), especially in high responders.
- Trigger agents such as human chorionic gonadotropin (hCG) or GnRH agonists trigger final oocyte maturation. Agonist triggers are preferred in antagonist cycles for OHSS prevention, although dual triggers (hCG + GnRH agonist) are gaining traction for optimizing oocyte competence.

## PROTOCOL PERSONALIZATION

COS is no longer a one-size-fits-all endeavor. High responders (often young women or those with

polycystic ovarian morphology) benefit from lower gonadotropin doses and antagonist protocols to mitigate OHSS risk, whereas poor responders (low AMH/AFC, advanced reproductive age) may require higher gonadotropin doses, microdose flare protocols, or adjuncts such as growth hormone or androgens. The use of individualized starting doses on the basis of ovarian reserve biomarkers is now recommended in most guideline-based approaches, improving safety without compromising efficacy.

### i. INDUCTION OF OVULATION IN ANOVULATORY WOMEN

For women with WHO Group II anovulation (predominantly PCOS), oral ovulation induction agents such as letrozole, an aromatase inhibitor, are now widely recommended as first-line therapy owing to higher ovulation and live birth rates than clomiphene citrate does, along with a lower risk of multiple pregnancy. Gonadotropins remain an effective second-line option when oral agents fail, although careful ultrasound and hormonal monitoring are mandatory to reduce the risk of multifollicular development and multiple gestation.

### ii. SAFETY AND MONITORING

The principal iatrogenic hazard of COS is OHSS, a potentially life-threatening vascular permeability syndrome driven by hCG-mediated upregulation of vasoactive mediators. Strategies to minimize OHSS include antagonist protocols with agonist triggers, "freeze-all" embryo transfer strategies, and vigilant cycle monitoring via transvaginal ultrasound and serum estradiol.

### iii. EMERGING TRENDS

Recent innovations include dual stimulation (follicular + luteal phase COS) in poor responders to rapidly accrue more oocytes in a single menstrual cycle and mild stimulation IVF protocols aimed at reducing drug burden and cost while maintaining acceptable pregnancy rates. AI-assisted monitoring platforms are also under exploration and are promising for integrating hormonal, ultrasonographic, and patient-specific data to refine stimulation in real time.

In essence, COS and ovulation induction have evolved into precision endocrinology in motion, balancing biological amplification with individualized restraint to optimize oocyte yield, quality, and safety. Their continued refinement remains central to improving ART outcomes across diverse infertility phenotypes.

## INTRAUTERINE INSEMINATION (IUI)

Intrauterine insemination (IUI) is the gentle "first step" in the ART repertoire and represents a bridging strategy between natural conception and more invasive procedures. By bypassing the cervix

and placing washed, motile sperm directly into the uterus at the optimal moment of ovulation, IUI increases the likelihood of gamete encounter in a minimally laboratory-intensive way. The procedure remains intimate and approachable, quick, relatively inexpensive, and emotionally less burdensome than IVF does, making it a comforting option for many couples' initial foray into fertility treatment (Saxena and Mishra, 2024).

### i. INDICATIONS AND MECHANISM

IUI is especially suited for certain diagnoses, such as mild male factor infertility, unexplained or cervical factor infertility, early-stage endometriosis, and ovulatory dysfunction. The underlying logic is simple yet elegant: by concentrating motile sperm and depositing them near the fallopian tubes, IUI enhances fertilization potential even when other barriers are mild (Huniadi et al., 2023).

### ii. SUCCESS RATES

The success story of IUI is modest but meaningful. The average clinical pregnancy rate per cycle is approximately 9%, with a wide range from 5% to 20-25%, depending on the patient profile, stimulation approach, and local protocols (Dias et al., 2024). One real-world study in a low-to-middle income setting reported a 12.4% clinical pregnancy rate and 11.9% live birth rate per cycle, with a cumulative pregnancy probability of 21.6% over three cycles, especially in women under 40 years of age, with a shorter infertility duration and favourable sperm counts.

### iii. PREDICTIVE FACTORS AND LIMITATIONS

Several variables shape the arc of IUI success:

- Sperm quality is foundational. Postwash total motile sperm counts, usually at least 1-5 million, drive outcomes, and higher counts correlate with better results (Nesbit et al., 2022).
- Female age and duration of infertility remain powerful predictors: success wanes beyond the age of 38-40 years, and prolonged infertility is a predictor (Zippl et al., 2022).
- Infertility diagnosis matters: women with ovulatory dysfunction enjoy the highest cumulative pregnancy rates; those with tubal factor or advanced endometriosis fare less well and may be better served by IVF (Wang et al., 2021).
- The cycle number also matters: most pregnancies occur within the first three to four IUI cycles, after which clinicians often recommend transitioning to IVF if outcomes remain elusive (Patil et al., 2024).
- Novel adjuncts such as piroxicam, an NSAID, are emerging as intriguing, but still preliminary,

tweaks. A small randomized trial revealed more than quadrupled pregnancy rates (9% vs. 2.2%) in unexplained infertility patients, possibly due to dampening uterine contractions postinsemination.

**iv. EMOTIONAL FRAME**

IUI's accessibility and the hope it brings make it both an emotional lifeline and a potential source of frustration. Each cycle is deeply personal and carries optimism, anticipation, and sometimes societal or financial strain, especially where donor sperm access or repeated attempts may pose logistical or psychological hurdles (Lucey, 2023).

**IN VITRO FERTILIZATION (IVF)**

In vitro fertilization (IVF) is the most emblematic and transformative branch of ART, where fertilization occurs outside the body, typically in a Petri dish, before the crafted embryo is transferred into the uterus. IVF has steadily become the go-to option when conception has proven elusive through natural or less invasive means, now accounting for approximately 2% of births in the United States. Its live-birth success rate varies dramatically by age: it is approximately 54% for women under 35 years of age and decreases to 4% for those over 42 years of age. The robustness of IVF outcomes has increased in recent years through multiple innovations: preimplantation genetic testing (PGT) helps select chromosomally normal embryos; cutting-edge cryopreservation via vitrification improves the viability of thawed embryos; and AI-driven platforms for embryo evaluation, such as the AIVF EMA system, are cut through human subjectivity and increase implantation success by prescreening embryos with up to a 70% predicted chance of pregnancy (Ukonaho, 2024).

Moreover, a landmark 2025 randomized trial in Denmark revealed that in couples without severe male factor infertility, conventional IVF and ICSI produced virtually identical live birth rates (~47% vs ~43%), suggesting that c-IVF should remain the first-line path unless a male factor warrants otherwise taken together, IVF has evolved into a highly nuanced fusion of biological orchestration, technological refinement, and personalized strategies, delivering more hope and precision than ever before.

**INTRACYTOPLASMIC SPERM INJECTION (ICSI) IN THE FEMALE INFERTILITY CONTEXT**

ICSI is the molecular micromanipulation method of ART, where a single sperm is gently injected straight into the cytoplasm of an oocyte, circumventing the natural acrosome reaction and sperm–egg binding entirely. Born in the early 1990s, this technique revolutionized treatment for severe male

factor infertility, such as teratozoospermia or azoospermia, by placing fertilization in the steady grip of the embryologist's needle rather than the vagaries of nature (Kocur et al., 2025).

In the context of female infertility, or more precisely, in couples where male factor issues are absent, ICSI remains a nuanced tool. A comprehensive meta-analysis of randomized controlled trials revealed that although ICSI significantly lowers the risk of fertilization failure (total fertilization failure) and improves fertilization rates per oocyte, it does not confer a significant advantage in live birth rates compared with conventional IVF in terms of non–male factor infertility (Yang et al., 2024). Another retrospective cohort study similarly discouraged the routine use of ICSI in older women with limited oocyte yield when male factors were not present, citing its invasiveness without clear outcome superiority.

Nevertheless, the reach of ICSI extends beyond standard IVF. Variants such as IMSI and Intracytoplasmic Morphologically Selected Sperm Injection employ ultrahigh magnification (6,000-10,000×) to cherry-pick sperm with superior nuclear morphology. This can reduce fertilization failure and miscarriage rates, especially in cases of repeated (failures) or high sperm DNA fragmentation levels.

On the technological frontier, ICSI may soon be guided by artificial intelligence. A groundbreaking case reported a live birth derived from a fully AI-operated robotic ICSI system capable of independently selecting sperm, immobilizing them via a laser, and executing precise microinjection steps, potentially reducing human fatigue and variability (Hew et al., 2024).

**OOCYTE CRYOPRESERVATION AND FERTILITY PRESERVATION STRATEGIES**

Oocyte cryopreservation, commonly known as egg freezing, has evolved from an experimental fringe technique to a cornerstone of reproductive autonomy. For women seeking to hedge against age-related fertility decline or to preserve reproductive potential before gonadotoxic treatments, this strategy offers both scientific promise and emotional reassurance. Owing to vitrification, an ultrarapid cooling method, egg survival now often exceeds 90%, imprinting cryotechnique as a modern-day cryobiological triumph. Importantly, pregnancy success using frozen-thawed oocytes mirrors that of fresh cycles when performed in young patients, a parity that was once inconceivable (Gil-Arribas et al., 2022).

Recent analyses offer both clarity and pragmatic benchmarks. A systematic review of elective oocyte freezing revealed that freezing at least 8–10 oocytes delivers a meaningful chance of a live birth,

whereas ~20 oocytes substantially increase the probability, especially if vitrified before the age of 35. A large multicenter retrospective study reported clinical pregnancy rates of approximately 50% per transfer and cumulative live birth rates of nearly 40%, even when oocytes were frozen at an average age above 37 years (Walker et al., 2022).

The real-world utility of this tool is illuminated by long-term follow-up. In the Netherlands, a population-based study of women who banked oocytes or embryos reported a 10-year utilization rate of 25.5%, with a cumulative live birth rate of 34.6% per woman reassuring figures for both medical and elective users. Meanwhile, trends in Israel reveal a cultural shift: the average age at first elective egg retrieval dropped from 38.3 to 35.4 between 2011 and 2023, signalling growing awareness and earlier engagement (Shavit et al., 2024).

Fertility preservation extends beyond elective delay. In oncofertility, where women face chemotherapy or radiotherapy, oocyte (and ovarian tissue) freezing has become the standard of care, offering a tangible route to biological parenthood posttreatment. Uptake has swiftly increased, particularly in countries such as Japan, where registry data show that female patients now surpass males in seeking fertility preservation (Kawai et al., 2024).

**PREIMPLANTATION GENETIC TESTING (PGT)**

Preimplantation genetic testing, a molecular magnifier within the ART toolkit, empowers clinicians and patients to prescreen embryos for chromosomal or monogenic defects before uterine placement. This technology involves two main methods: PGT-A (aneuploidy screening) to flag numeric chromosome errors and PGT-M (monogenic testing) to detect single-gene disorders. PGT is rooted in techniques such as next-generation sequencing (NGS) and comparative genomic hybridization, which have greatly enhanced resolution and diagnostic accuracy (Gudapati et al., 2024).

**EFFICACY AND CLINICAL OUTCOMES**

Live birth optimization per transfer: Large-scale data confirm that PGT-A coupled with NGS significantly increases live birth rates per embryo transfer by 48.9% vs. 42.7% in non-PGT-A cases, especially in women aged ≥35 years, and is particularly beneficial in those with diminished ovarian reserve or endometriosis (Sarkar et al., 2023). Cumulative benefits in monogenic conditions: For PGT-M, which targets familial genetic diseases, a systematic review across >5,000 cycles revealed that the live birth rate per embryo transfer was ~22%, with improved outcomes when PGT-M was combined with PGT-A (Poulton et al., 2025).

Recurrent reproductive failure (RRF): Meta-analyses including patients with recurrent implantation failure or pregnancy loss suggest that PGT-A may increase implantation, clinical pregnancy, and live birth rates, particularly in advanced-aged patients, although younger cohorts present more mixed results. Randomized evidence in older women: A 2025 pilot RCT in women aged 35-42 compared morphology-based vs. PGT-A selection. Although not statistically significant (possibly underpowered), the cumulative live birth rate tended to be higher with PGT-A (72% vs. 52%)(Beebeejaun et al., 2025).

**SAFETY AND ETHICAL CONSIDERATIONS**

Large-scale meta-analyses have shown that PGT does not increase adverse obstetric or neonatal outcomes; in fact, some risks, such as low birth weight and very preterm birth, are lower in PGT cohorts, although a slightly elevated risk of gestational hypertension was observed. Early childhood follow-ups (particularly for PGT-M) report developmental outcomes on par with those of naturally conceived peers (Hou et al., 2021).

However, PGT-A remains a subject of critique. Some studies highlight a decreased cumulative live birth rate in younger women, raising concerns about overreliance on the per-transfer metric. Legal and emotional challenges have also surfaced several IVF patients, suggesting that false-positive PGT-A results led to the discarding of embryos that might have resulted in healthy pregnancies (Seckin and Forman 2023).

**EMERGING HORIZONS**

In addition to conventional methods, the field is steering toward noninvasive PGT, leveraging DNA from culture media or spent fluid to infer embryo health without biopsy, and the integration of AI and machine learning, which holds promise for paring subjectivity from genetic assessment workflows. However, these innovations raise ethical questions, especially concerning transparency, bias, and decision-making, necessitating thoughtful regulation and patient counselling. PGT stands at the intersection of precision medicine and reproductive autonomy, offering powerful tools to optimize embryo selection, reduce the emotional toll, and address genetic risks. However, its nuanced benefits, ethical dimensions, and evolving technologies demand shared decision-making and judicious application (Table 1).

**TABLE 1: PREIMPLANTATION GENETIC TESTING AND ASSISTED REPRODUCTIVE TECHNOLOGY**

| Application Context | Benefit Highlighted | Caveats or Controversies |
|---|---|---|
| Advanced-age or diminished reserve | Higher live birth per transfer via euploid embryo selection | Possible lower cumulative outcomes for younger women |
| Recurrent implantation/failures | Enhanced implantation and reduced miscarriage | Data mixed in younger or non-RRF populations |
| Monogenic disorders (PGT-M) | Safe and effective with good live birth outcomes | Largely limited to disease-specific cases |
| Long-term safety | Favorable obstetric and developmental outcomes | Slight increase in some hypertensive disorders |

## THIRD-PARTY REPRODUCTION: DONOR OOCYTES, EMBRYOS, AND SURROGACY

Third-party reproduction offers powerful pathways to parenthood when a woman's own gametes or uterus cannot achieve successful gestation. Donor oocytes stand at the forefront: enabling women with diminished ovarian reserve, advanced age, or genetic concerns to conceive using eggs from younger or otherwise healthy donors. In the U.S., fresh donor cycles boast success rates exceeding 60%, and when fresh cycles are followed by frozen transfers, cumulative rates approach 80%, highlighting the transformative potency of donor egg IVF (Salazar et al., 2023).

Although less frequently discussed, donor embryos provide a "ready-made" solution when both gametes are unavailable or contraindicated, circumventing multiple coordination steps and streamlining decision-making for intended parents. The emotional and ethical appeal of this approach lies in its simplicity and immediacy, although nuanced counselling remains essential. Surrogacy, the most common form of gestation, has increased in both demand and complexity. In the U.S., gestational surrogacy now represents a growing slice of ART, with the overall commercial surrogacy market expanding from approximately USD 22.4 billion in 2024 to USD 129.9 billion by 2034. Globally, surrogacy and third-party reproduction are becoming increasingly mainstream, driven by inclusive family structures (single parents, LGBTQ+ couples) and evolving social norms (UNFPA, 2025).

The outcomes of surrogacy are encouraging: gestational carrier pregnancy rates fall between 19-33% per embryo transfer, with live birth occurring in 30-70% of cases. Babies born via surrogacy tend to have lower preterm and low-birth-weight rates than those born via standard IVF, although

twin pregnancies still carry elevated risks.Legislation remains a moving target. Some countries (e.g., Italy and Spain) restrict or criminalize surrogacy, even across borders, pushing intended parents toward reproductive travel. Other regions, such as parts of Canada, permit altruistic surrogacy while outlawing commercial arrangements, emphasizing reimbursement over profit. Even within countries, legal frameworks differ: for example, the UAE recently liberalized ART by removing marriage prerequisites for non-Muslim couples, decriminalizing surrogacy, and permitting the import of gametes, marking a major shift in Middle Eastern reproductive policy (Ellenbogen et al., 2021).

**EMERGING TECHNOLOGIES: ARTIFICIAL GAMETES, UTERUS TRANSPLANTATION, AND AI-BASED EMBRYO SELECTION**

The frontier of assisted reproduction is rapidly advancing, stretching the boundaries of possibility with once-fictional tools that are becoming scientifically feasible. In in vitro gametogenesis (IVG), the transformation of adult cells (such as skin or blood) into sperm or eggs has moved from speculative to tangible. Visionaries such as Prof. Katsuhiko Hayashi anticipate clinical advances within the next 5-10 years, potentially democratizing genetic parenthood for individuals of any sex, age, or fertility status. These developments, while exciting, come bundled with profound safety, ethical, and regulatory challenges. In the UK, the fertility watchdog HFEA is already sounding alarms on genetic mutations, solo and multiplex parenting, and the need for stringent oversight.

Uterus transplantation represents another improvement in reproductive medicine. Initially, pioneered in Sweden in 2014, the procedure has now been performed in over 80 cases across multiple continents, yielding upwards of 40 live births. Technical success rates exceed 75% for living donors versus deceased donors, and live birth rates in successful grafts often exceed 80%. For example, a Dallas cohort reported a 55% live birth rate per attempted transplant and a 79% live birth rate per technically successful graft. While these results rival those of conventional IVF, transplant recipients face notable risks, including surgical complications, infection, and the side effects of immunosuppression (Brännström et al., 2021).

Moreover, the infusion of artificial intelligence into embryo selection has revolutionized in vitro success paradigms. AI systems such as the AIVF EMA platform leverage morphokinetic data to score embryos with up to 38% higher predictive accuracy than traditional embryologist-grade embryos flagged high by the EMA correlate with an ~70% probability of successful implantation. Other AI models, such as BELA and transformer-based frameworks such as IVFormer, offer objective,

noninvasive assessments of ploidy and implantation potential, sometimes matching or even outperforming human embryologists while processing data at unprecedented speed (Wang et al., 2024). These technologies, IVG, uterus transplantation, and AI-based embryo selection, are more than incremental improvements; they represent seismic shifts in what is possible in reproductive medicine. They promise previously unthinkable freedoms and capabilities but equally demand rigorous safety testing, ethical frameworks, and social dialogue (Table 2).

**TABLE 2: PROMISE AND POTENTIAL FOR IN-VITRO GAMETOGENESIS,UTERUS TRANSPLANTATIONAI-DRIVEN EMBRYO SELECTION**

| Technology | Promise & Potential | Key Caveats & Considerations |
|---|---|---|
| **In-Vitro Gametogenesis (IVG)** | Lab-created gametes from adult cells endless reproductive possibilities, novel family constructs | Unknown genetic safety, ethical ramifications, regulatory uncertainty |
| **Uterus Transplantation** | Gestation enabled for those with uterine absence biological motherhood restored | Surgical risk, immunosuppression, high cost, equitable access issues |
| **AI-Driven Embryo Selection** | Faster, more objective embryo grading higher accuracy, efficiency gains | Black-box concerns, need for interpretability, integration into clinical norms |

## ETHICAL, CULTURAL, AND SOCIOECONOMIC CONSIDERATIONS

The promise of ART is profound, but woven into its fabric are complex ethical and cultural threads that demand sensitive unpacking. In many societies, infertility casts a long shadow: women are often stigmatized and even blamed for childlessness, despite parity in terms of male factor infertility rates. In regions such as the so-called "Africa Infertility Belt," infertile women may face social exclusion, loss of inheritance, or even expulsion from communal rituals, underscoring how reproductive status can define social identity. Humanity's need to be seen and valued often hinges on fertility (Khawaja, 2014).

Economic barriers loom large. ART remains out of reach for most patients because of high costs and disproportionately limited public support. Only approximately 21 countries offer partial public funding for ART; many others set age limits or restrict the number of subsidized cycles. In the United States, an IVF cycle costs, on average, USD 9,200, resulting in per-live-birth costs ranging from USD 33,000

to 41,000, which are too steep for low- and middle-income families. In low-resource settings, this financial divide is even starker: patients face astronomical costs, long waitlists, a lack of trained professionals, and the need to navigate remoteness and bureaucracy. In Brazil, for example, a single IVF cycle in the public sector could equate to several months of income for most citizens (Garcia, 2023).

Geography and education further compound access inequalities. A global review highlights that even where ART is available, its concentration in urban centers, combined with low awareness and cultural misconceptions, leaves rural, less-educated communities sidelined. In sub-Saharan Africa, fertility professionals cited insufficient government support, limited infrastructure, and high costs as principal roadblocks, but innovations such as low-cost IVF protocols and strategic knowledge transfer show promise in forging more equitable pathways.

Ethically, infertility is not just a medical condition; it is also a reproductive justice issue. Denying access to ART limits parental autonomy and disproportionately impacts marginalized groups, including low-income individuals and women. These groups already contend with systemic biases in healthcare, further eroding trust and perpetuating disparities. ART lies at the crossroads of personal desire and societal responsibility: its implementation must tread thoughtfully through issues of consent, equity, and transparency.

## FUTURE PERSPECTIVES AND RESEARCH GAPS

As ART continues to push boundaries, several emerging avenues show transformative promise, although they also reveal gaps demanding rigorous investigation and ethical framing.

### i. NOVEL REPRODUCTIVE PLATFORMS

Artificial ovaries, bioengineered scaffolds seeded with follicles or ovarian cells. could someday bypass the limitations of egg or tissue cryopreservation, particularly for prepubertal girls or cancer survivors. However, human clinical use remains distant, necessitating advances in iPSC-derived oocyte sources, scaffold biocompatibility, and long-term safety studies.

Mitochondrial donation, exemplified in a recent successful pronuclear transfer trial that led to eight healthy births, offers a life-altering route to avoid maternally inherited mitochondrial disease. Nevertheless, questions remain about long-term developmental follow-up, residual maternal mitochondrial DNA, and equitable access under varying regulatory climates.

### ii. PRECISION AND PERSONALIZATION IN ART

AI and imaging analytics are being integrated to optimize ovarian stimulation and embryo selection. However, these systems often rely on limited datasets, lack interpretability, and are seldom validated across diverse clinical contexts. Explainable AI frameworks, expanded imaging methods (such as 3D ultrasound), and multicenter validation studies are urgently needed.

In vitro maturation (IVM), where immature oocytes mature ex vivo, has facilitated over 1,000 live births, particularly in PCOS or fertility preservation contexts. However, comparative effectiveness versus standard stimulation and optimization of culture conditions remain open research frontiers (Das and Sun, 2023).

### iii. DIAGNOSTIC INNOVATION FOR INFERTILITY

Applications of nanotechnology, including biosensors and high-resolution imaging, are advancing our ability to assess sperm, oocyte, or follicular microenvironments. However, translation into routine clinical workflows is still nascent, highlighting the need for reliability, standardization, and implementation studies (Andone et al., 2023).

### iv. ADDRESSING EQUITY, ETHICS, AND PSYCHOSOCIAL DIMENSIONS

Despite technological advances, inequity in access to the ART persists, driven by geography, socioeconomic status, education, and minority group membership. More research is needed on low-cost ART models, rural delivery solutions, and culturally sensitive care, including engaging underrepresented groups such as LGBTQ+ communities and men in ART access studies. Psychological support integration in fertility care has proven beneficial, yet too often overlooked studies report high distress (up to 60%) among infertile women, with minimal utilization of psychiatric or counseling services. Standard guidelines and implementation frameworks are lacking (John et al., 2024).

## CONCLUSION

Assisted reproductive technologies (ART) have evolved from experimental interventions to highly sophisticated, evidence-driven modalities that redefine the possibilities of parenthood for individuals and couples affected by female infertility. In recent decades, advances in ovarian stimulation protocols, gamete manipulation, preimplantation genetic testing, and fertility preservation have significantly improved success rates while expanding the scope of reproductive choices. The integration of emerging frontiers such as artificial gametogenesis, uterus transplantation, and AI-assisted embryo

selection promises to further optimize outcomes, personalize treatment, and potentially overcome biological barriers once they are deemed insurmountable. However, these advancements are accompanied by persistent challenges, including disparities in access, ethical dilemmas surrounding third-party reproduction, and the psychosocial complexities intertwined with infertility care. Bridging these gaps will require multidisciplinary collaboration, patient-centered policies, and continued investment in translational research. In essence, ART stands not merely as a collection of biomedical techniques but also as a dynamic interface where science, ethics, and human aspirations converge, shaping a future where reproductive autonomy is increasingly attainable, equitable, and informed by the best available evidence.

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