

From Preservation to Creation: The Expanding Frontier of Fertility Preservation – Proceedings of the 2nd Montreux Reproductive Summit, 29-30 August 2025

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ABSTRACT

Fertility preservation (FP) has become an essential dimension of modern medicine, reflecting the paradigm shift from survival alone to survivorship. Once confined to oncology, FP now spans a broad spectrum of medical, social, and technological contexts. Surgical innovations, including fertility-sparing surgery and ovarian transposition, allow reproductive potential to be safeguarded without compromising oncological safety. Cryobiology has been transformed by the transition from slow-freezing to vitrification, establishing oocyte and embryo cryopreservation as gold-standard approaches with outcomes comparable to fresh cycles. Alongside onco-fertility, “social freezing” has emerged as a tool of reproductive autonomy, though it raises counselling and ethical challenges related to age, expectations, and equity of access. Resilience in FP also requires psychosocial support: while emotional distress is common, evidence shows that interventions such as mindfulness and structured counselling improve mental health even if conception outcomes remain unchanged. In parallel, ovarian tissue cryopreservation for patients unable to undergo stimulation and immature testicular tissue banking extend possibilities, with early clinical successes highlighting future translational pathways. Uterus transplantation has emerged as the first-line treatment of congenital absence of a uterus and can restore fertility after a hysterectomy performed for cervical cancer. Looking ahead, regenerative approaches, including stem-cell-based strategies, 3D bio-printing of genital tissues, tissue engineering, and artificial uterus systems, signal the next frontier, while underscoring the need for further research as well as robust ethical, legal, and safety frameworks. FP thus represents a multidisciplinary and rapidly evolving field that integrates oncology, reproductive medicine, gynaecology, transplantation surgery, psychology, and laboratory disciplines. Its trajectory is defined by both technological innovation and the imperative to align medical progress with patient autonomy, equity, and long-term quality of life.

Introduction

Historically, the management of life-threatening diseases such as cancer focused primarily on curative and life-saving treatments, often neglecting long-term quality of life considerations, including reproductive health. Over the past two decades, major advances in oncologic therapies have markedly improved survival rates in both children and reproductive-aged adults. This paradigm shift, from survival alone to survivorship, has positioned fertility preservation (FP) as a critical component of modern comprehensive care.^{1,2}

Professional societies have played a pivotal role in shaping FP as a discipline. The American Society of Clinical Oncology (ASCO) first issued evidence-based clinical practice guidelines in 2006,³ with updates in 2013 and 2018,¹ highlighting the integration of FP into the standard of oncological care, with also the latest recommendations of the International Society of Fertility Preservation (ISFP).⁴ In parallel, the European Society of Human Reproduction and Embryology (ESHRE) and European Society for Gynaecological Endoscopy (ESGE)

together with European Society of Gynaecological Oncology (ESGO) have been equally instrumental in establishing FP as a core element of reproductive medicine in Europe. These European Societies have produced several influential guidelines, most notably the 2020 update on ovarian tissue cryopreservation (OTC),⁵ the 2022 good practice recommendations on oocyte and embryo cryopreservation, and fertility sparing treatment of gynaecological cancers,^{6,7} ensuring that clinicians across Europe adopt harmonised, evidence-based practices.

Beyond oncology, FP has also become a tool of reproductive autonomy. Increasing numbers of individuals are seeking to delay parenthood for personal, professional, or social reasons, commonly referred to as “social freezing.” This expansion of FP from a purely medical intervention to a broader societal practice underscores the dual medical and ethical dimensions of the field.

Given this convergence of medical necessity and reproductive choice, FP is no longer a niche concern but

an international priority requiring input from oncologists, reproductive endocrinologists, psychologists, ethicists, and policymakers. The field encompasses surgical innovation, advances in cryobiology, psychosocial support, and even advanced technologies such as 3D bioprinting and artificial gestation.⁸

This review provides a comprehensive, multidisciplinary analysis of FP, structured into five thematic domains: (1) the revolution of fertility-sparing surgery (FSS), (2) stress management and resilience, (3) innovations in cryopreservation and social freezing, (4) germline tissue preservation and long-term outcomes, and (5) technological advances in artificial reproductive organs. The objective is to offer an updated, scientifically rigorous, and internationally relevant resource that reflects the joint contributions of ASCO, ESHRE, ISFP and other organisations in shaping the present and future of FP.

Revolutionising Fertility Surgery and Preservation (Figure 1)

The Role of Fertility-Sparing Surgery in Oncology

FSS is a crucial strategy in modern gynaecological oncology, preserving reproductive potential without compromising oncologic safety.⁹ While oocyte cryopreservation is a reliable FP option for women undergoing chemotherapy and/or radiotherapy, OTC offers an alternative for adolescents and for patients who cannot undergo ovarian stimulation or whose cancer treatment cannot be delayed. For women with early-stage cervical cancer, procedures such as conisation or trachelectomy can be performed to remove the cancerous tissue with a margin while preserving the major part of the uterus.¹⁰ This allows the patient to subsequently carry a pregnancy, though any subsequent birth would be associated with a considerable risk of preterm birth.¹⁰ Similarly, for early-stage ovarian cancer that is confined to one ovary, the affected ovary can be removed while

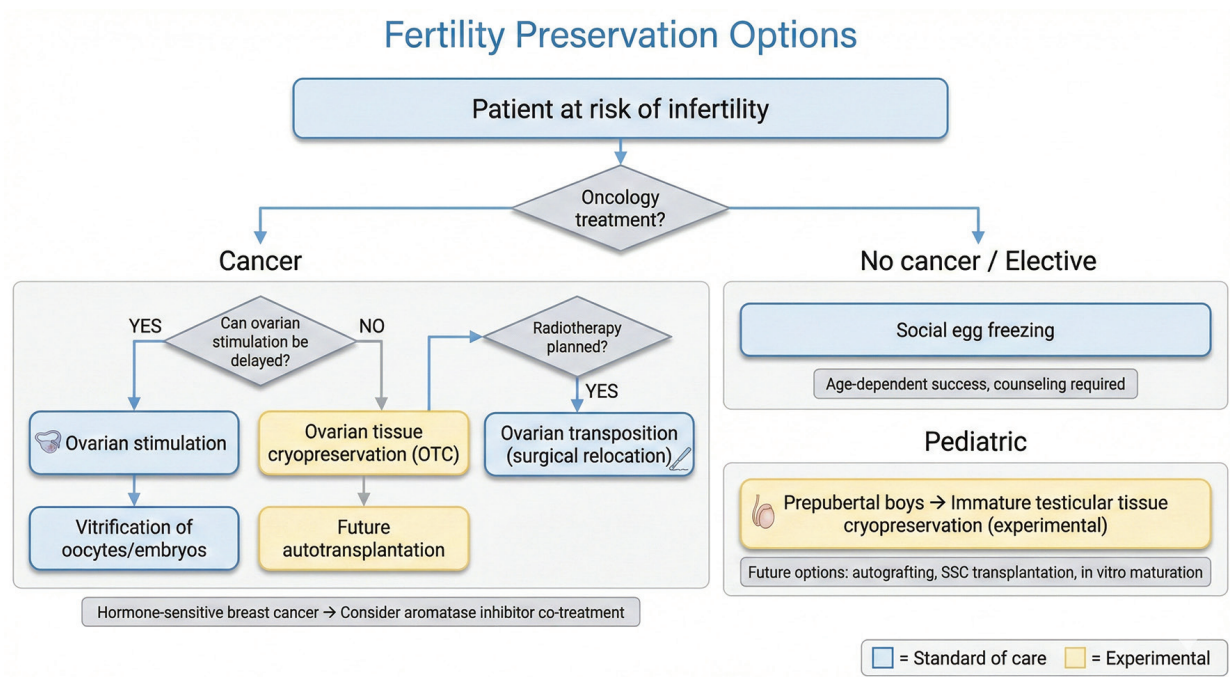


Figure 1. Clinical decision flowchart for fertility preservation options. Decision pathway for fertility preservation according to oncologic status, treatment timing, and age. Standard approaches include ovarian stimulation with vitrification, ovarian tissue cryopreservation, and ovarian transposition during radiotherapy. Social egg freezing is proposed in non-oncologic elective settings. Immature testicular tissue cryopreservation remains experimental in prepubertal boys.

Blue boxes represent the standard of care and yellow boxes experimental approaches.

This figure was generated using an AI-based image generation tool (Gemini, Google), based on an original conceptual prompt developed by the authors.

the contralateral is left intact. For patients with early-stage focal endometrial cancer, hysteroscopic resection and staging followed by progestin administration can be applied, preserving the uterus, ovaries and fallopian tubes.^{11,12} The indications for FSS are expanding to include certain early-stage epithelial ovarian cancers and borderline ovarian tumours, even in the presence of peritoneal implants, depending on histologic subtypes and prognostic factors.^{7,9} For patients with high-grade epithelial ovarian cancer where FSS is not a safe option, the ovaries and Fallopian tubes may be removed while the uterus is conserved to allow for future pregnancy through egg donation.⁹ Recently, the option to preserve the uterus in cases of incidental diagnosis of uterine smooth muscle tumours of uncertain malignant potential following myomectomy was also explored.¹³

Ovarian Tissue Freezing, Transplantation and Gonadoprotection

OTC and subsequent auto-transplantation represent a cornerstone innovation in FP, particularly for patients who cannot undergo ovarian stimulation or where treatment must be initiated urgently.^{14,15} Cortical ovarian tissue, rich in primordial follicles, can be laparoscopically harvested in minutes without delaying oncologic therapy and stored for future transplantation. A number of live births have now been reported worldwide after orthotopic transplantation, with restoration of both endocrine function and spontaneous fertility, confirming OTC as a clinically effective option in appropriately selected candidates.¹⁶ International guidelines now consider OTC a standard of care for prepubertal girls, adolescents, and young women at high gonadotoxic risk, provided that tissue quality, oncologic safety, and multidisciplinary evaluation are ensured.¹⁷ Cryopreserved ovarian tissue typically resumes function within 3–6 months after reimplantation, with graft longevity varying from 2 to more than 10 years depending on patient age, follicular reserve, and tissue volume.^{14,16,18,19} Importantly, OTC offers an integrated approach to endocrine recovery: resumption of menstrual cycles mitigates vasomotor symptoms, low bone density, sexual dysfunction, and cardiovascular risk associated with treatment-induced ovarian insufficiency, while simultaneously enabling the possibility of natural conception.²⁰

In parallel, gonadoprotective strategies aim to reduce treatment-related ovarian damage at the source.^{21–23} Previously published pharmacologic gonadoprotection using gonadotropin-releasing hormone agonists

during chemotherapy has been shown to decrease rates of premature ovarian insufficiency in hormone receptor–negative cancers, although it does not replace established methods of FP.^{22,23} Very recent studies in mice investigated the effects of temsirolimus and antimüllerian hormone as gonadoprotective agents.^{21,24} This pharmacological association proved to protect fertility and the ovarian reserve against cyclophosphamide-induced damage in a murine model²¹ and needs to be evaluated on human ovarian tissue.

The combined availability of OTC, transplantation, pharmacologic suppression, and surgical repositioning reflects a modern, multimodal gonadoprotection framework. These strategies are increasingly coordinated within onco-fertility programs to ensure that decisions are timely, evidence-based, and aligned with each patient's reproductive goals, autonomy, and oncologic safety.

Ovarian Transposition: A Specialised Surgical Solution

OT is a surgical intervention to protect the ovaries from damage caused by pelvic or craniospinal radiation.^{25,26} The procedure involves moving the ovaries above and to the side of the central pelvic area, away from the radiation field. The preferred surgical approach is laparoscopy due to its association with a more rapid recovery and less postoperative pain compared to a traditional laparotomy. It is important to note that OT is not a beneficial option for patients receiving concomitant gonadotoxic chemotherapy, as systemic agents will still damage the ovaries regardless of their location.^{25,26}

The Shift to Minimally Invasive Techniques

The field of gynaecological surgery is experiencing a significant shift away from large-incision laparotomy toward minimally invasive techniques like laparoscopy and robotic-assisted surgery. These methods utilise small incisions and high-definition cameras, resulting in reduced pain, shorter recovery times, and lower risks of infection and blood loss. For complex gynaecological surgeries, such as those for uterine fibroids, robotic surgery offers surgeons enhanced dexterity, precision, and vision, further improving patient outcomes.²⁷ This progression in surgical technology is not simply a matter of technical refinement; it is a direct response to a demand for better patient outcomes and a more efficient transition to subsequent therapies. By facilitating a faster recovery, these techniques allow a patient to move more quickly to the next phase of their treatment, whether it

be chemotherapy or radiation. The continuous evolution of surgical techniques, from the macro level of choosing a minimally invasive approach to the microsurgery and supermicrosurgery technique (i.e., anastomosing lymph vessels), demonstrates a deep commitment to improving the patient experience and making complex procedures safer and more feasible.

The Integration of Oncology and Reproductive Medicine

The comprehensive ASCO guidelines and the recommendations for early referral of cancer patients to reproductive specialists highlight a fundamental change in the standard of care.²⁸ The development and refinement of surgical techniques that prioritise FP alongside oncological safety are a direct result of this shift. As long-term cancer survival has become more common, the medical community has recognised that the goal of care extends beyond survival to encompass the patient's long-term quality of life and future family-building aspirations.²⁹ This evolution demonstrates how a major medical advancement in one field, such as oncology, can act as a catalyst, fundamentally reshaping clinical practice and protocols in another, namely reproductive medicine. The integration of these two disciplines is not just a theoretical concept; it is now an established clinical reality driven by a more patient-centric model of care. While advances in FSS and coordinated onco-reproductive care have transformed clinical pathways, they do not exhaust the lived experience of FP. Beyond technical success and oncological safety, patients must navigate uncertainty, time pressure, and altered life trajectories, making psychological resilience and supportive care integral components of contemporary FP.

Operational Strategies For Urgent Fertility Preservation

Operationally, resilient ovarian stimulation strategies minimise waiting and compress time-to-yield without compromising oncology care: random-start protocols and luteal-phase starts enable immediate initiation and are unlikely to delay neoadjuvant chemotherapy; contemporary reviews and randomised data indicate comparable oocyte/embryo outcomes, with luteal-phase stimulation sometimes increasing mature oocyte counts in poor responders.³⁰⁻³² For hormone-sensitive breast cancer, co-treatment with aromatase inhibitors during stimulation reduces oestradiol exposure without clear detriment to overall effectiveness, aligning

oncologic prudence with reproductive goals.^{33,34} When stimulation is inadvisable or time is critically short, alternative resilient options include *in vitro* maturation, explicitly recognised in the 2025 ASCO guideline update as an emerging method, and OTC,³⁵ which can be performed with zero delay and yields meaningful restoration of fertility and endocrine function in appropriate candidates.²⁹

Stress Management and Resilience in Fertility Preservation

Stress management in FP is best conceived as building clinical resilience across physiology, timelines, and care pathways. Psychologically, high perceived stress and anxiety are common at diagnosis, yet large prospective meta-analyses show that pre-treatment emotional distress does not reduce *in vitro* fertilization pregnancy rates, while failure predicts later distress; targeted interventions such as mindfulness-based programmes and guided relaxation reliably improve anxiety and depressive symptoms even if they do not consistently alter conception outcomes.^{36,37} Systems-level resilience further depends on early counselling and fast-track access: the 2025 ASCO update emphasises immediate, universal fertility risk discussions with referral at diagnosis, and real-world programmes show that dedicated onco-fertility navigation and Electronic Health Record-enabled pathways increase referrals and shorten time to consultation.^{29,38} The shift to standardised freeze-all vitrification ensures that prompt preservation does not sacrifice quality, with guideline data supporting oocyte cryopreservation outcomes comparable to fresh in modern practice.³⁹

The Psychological Toll of Fertility Challenges

The prospect of infertility or the emotional burden of fertility treatment and preservation can have a profound negative impact on mental health.⁴⁰ Patients often experience heightened psychological distress, including anxiety, depression, grief, and a sense of loss, particularly if a FP procedure is impossible, fails, or results in complications.⁴¹ This emotional turmoil can be exacerbated by social interactions, with unsolicited questions from friends or family about family planning being experienced as particularly painful reminders of the challenge.⁴¹ This heightened emotional distress can be a primary reason why some patients, despite being eligible, do not pursue FP.

The Paradox of Hope and Burden

The decision to undergo FP creates a complex emotional dynamic. On one hand, the completion of a procedure can lead to positive feelings of hope, happiness, and peace of mind.⁴¹ Many survivors describe it as an “insurance” or a “backup plan” that gives them a sense of control and “more time” to consider future family-building goals. However, this sense of hope can be a double-edged sword. The stored material itself can become a source of new uncertainties and a substantial psychological distress throughout survivorship, as patients may constantly worry about whether the material is sufficient, the storage is appropriate, or if future assisted reproductive technologies will be successful.⁴¹ This paradox means that while the act of preservation offers a psychological buffer, the hope it provides can be replaced by emotional distress if the stored material becomes a necessity rather than a backup, or if the process ultimately fails.⁴¹

Ethical Boundaries and Social Justice in Fertility Preservation

The session interrogated how far FP should extend and when to pause, arguing for an “embedded ethics” approach that integrates normative analysis into clinical and technological development rather than bolting it on post-hoc. It problematises the medical/social dichotomy, often used to separate onco-fertility from age-related “elective” use, by showing how indications, expectations, and constraints blur across contexts, a point developed in sociological and bioethics scholarship that documents the porous, politicised line between “medical” and “social” egg freezing.^{42,43} Within this frame, major professional bodies now deem planned oocyte cryopreservation ethically permissible if delivered with robust counselling about uncertainties, risks, and age-contingent success, and they call for standardised information provision and equitable pathways in FP programmes.^{42,43} Evidence syntheses underscore that outcomes remain highly age-dependent and that real-world live-birth rates after thaw are modest, which should recalibrate consent conversations and expectations; recent meta-analysis and commentary report overall live-birth around 28% (≈52% if <35 years; ≈19% if ≥40 years) and stress that “no guarantees” is the honest headline.^{5,44} Demographically, the age at which people freeze eggs is trending downward, consistent with earlier, more prognostically favourable banking, but variation in who accesses services remains wide.⁴⁵ High-quality consent requires addressing persistent

fertility-knowledge gaps and numeracy about age-related decline, while decision-quality studies show that tailored, durable education (as opposed to one-off interventions) is needed to avoid overconfidence; decisional regret is non-negligible and correlates with low oocyte yield and poorer counselling.^{46–50} The analysis also centres distributive justice: costs, variable insurance coverage, and workplace policies shape who can act on reproductive planning, with ethnographic and policy studies documenting cross-national inequities and the ambivalence of employer-sponsored benefits vis-à-vis autonomy.⁵¹ Beyond cisgender women, transgender and gender-diverse people face additional barriers, including timing of counselling, dysphoria-exacerbating procedures, legal hurdles, and cost, requiring adapted consent processes and programme design.^{52–54} Finally, the talk situates temporal and intergenerational questions (storage duration, disposition, posthumous use) within a broader Ethical-Legal-Social-Implication map, urging governance that anticipates downstream identities and kinship claims rather than reacting to them.⁵⁵ Overall, the synthesis argues that ethically defensible FP couples evidence-based clinical practice with upstream ethics, equitable access, realistic framing of probabilities, and sensitivity to gendered burdens and diverse family-making trajectories. This multidimensional concept of resilience, psychological, ethical, and social, finds its concrete expression in the laboratory. Advances in cryobiology, particularly vitrification, have enabled FP to move from an emergency response to cancer toward a broader framework of anticipatory reproductive planning, including social egg freezing.

Innovations in Cryopreservation and Social Freezing

The Vitrification Revolution: From Inefficient Freezing to Gold Standard

The history of oocyte cryopreservation is defined by the transition from slow freezing to vitrification. Slow-freezing, which cools cells at a rate of 0.3 °C per minute, may lead to intracellular ice crystal formation that can damage the delicate cellular structure.⁵⁶ Slow-freezing cools cells at 0.3 °C/min cause damaging ice crystals and lead to poor oocyte survival and developmental competence.⁵⁷ This method was largely inefficient for oocytes, resulting in low survival and compromised developmental outcomes.

In contrast, vitrification, or ultra-rapid freezing, cools at an astonishing rate of over 15,000 °C per minute.⁵⁶ This rapid cooling, combined with high concentrations of

cryoprotectant agents like ethylene glycol and dimethyl sulfoxide, prevents ice crystal formation and transforms the intracellular solution into a glass-like, amorphous solid and is especially suitable for small uniform structures like oocytes and embryos. This technical advancement has revolutionised the field, achieving a typical oocyte survival rate of 85-90% and yielding fertilisation and pregnancy rates comparable to those of fresh oocytes. Vitrification has become the current method of choice for cryopreserving metaphase II oocytes.

Social Egg Freezing: Clinical Trends and Outcomes

The widespread adoption of social egg freezing is a direct consequence of the technical success of vitrification. The success of this technique in achieving post-thaw survival and pregnancy rates comparable to fresh eggs removed the primary technical barrier, enabling the societal trend of delayed childbearing to be addressed with a viable medical solution.

A retrospective cohort study on social egg freezing revealed several key facts. The mean age at the time of

freezing was 37.1 years, and an average of 9.5 eggs were frozen per retrieval.⁵⁸ The study reported a live birth rate of 35% per embryo transfer, a figure comparable to a comprehensive literature review of fresh cycles.⁵⁸ A crucial finding was that freezing 15 or more eggs significantly increased the live birth rate, regardless of the patient's age at the time of freezing.⁵⁸ The utilisation rate of the frozen eggs during the study period, however, was found to be low, with only 16% of women returning to use them (Figure 2).⁵⁸

The Counselling Imperative

The data on social freezing highlights a critical tension: the average age of patients and the number of eggs frozen often fall short of the levels required for a significantly high live birth rate. Furthermore, the low utilisation rate suggests that for many, the "backup plan" serves its primary purpose by simply existing, alleviating psychological pressure and allowing them to pursue other family-building options.⁴¹ This reality creates a crucial counselling challenge. Clinics must

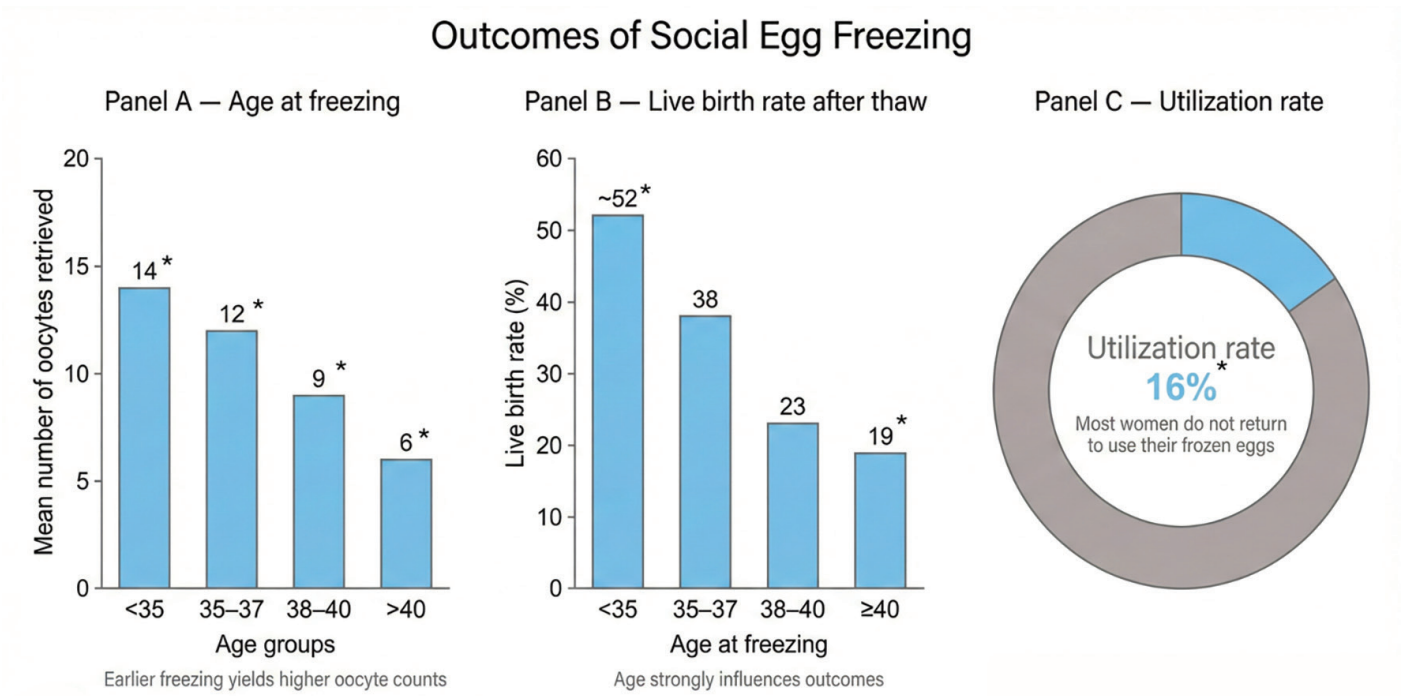


Figure 2. Outcomes of social egg freezing. Age-stratified oocyte yield and live birth rates were derived from published cohort data and meta-analyses and are summarised graphically. *Values marked with an asterisk correspond to figures directly reported in the cited studies; remaining values represent synthesised estimates derived from age-stratified cohort data and meta-analyses.

Panel A shows the mean number of oocytes retrieved according to age at freezing, with earlier freezing associated with higher yield.⁵⁸

Panel B illustrates age-dependent live-birth rates after thaw, with the best outcomes in women who froze eggs before age 35.^{5,44,45,74}

Panel C displays the overall utilisation rate of 16%, indicating that most women do not return to use their frozen eggs.⁵⁸

This figure was generated using an AI-based image generation tool (Gemini, Google), based on an original conceptual prompt developed by the authors.

transparently present data on costs, success rates, and the low likelihood of utilisation to ensure that patients can make a truly informed decision. The discrepancy between patient hope and clinical reality underscores the importance of transparent communication and shared decision-making in this rapidly growing sector of reproductive medicine.

Future Directions in Germline Tissue and Long-Term Outcomes

Immature testicular tissue (ITT) cryopreservation has become a possible fertility-preservation option for prepubertal boys and for peripubertal patients without recoverable sperm, and it is now implemented internationally under research protocols, including in non-malignant conditions; an international ORCHID-NET survey reported cryobanking activity across 16 centres and >3,000 paediatric samples worldwide, and 2025 ESHRE good-practice recommendations reaffirm the experimental status while emphasising the need for refining indications.^{59,60} Restorative pathways under evaluation include autografting of thawed tissue fragments, spermatogonia stem-cell transplantation (SSCT),⁶¹ and ex vivo maturation strategies (organotypic culture, organoids with selected testicular cells or “artificial testis”) to generate haploid germ cells; proof-of-concept spans animal models with donor sperm and live offspring after testis-tissue grafting in mice⁶² and other mammals, fertile offspring after *in vitro* spermatogenesis in mice and, more recently, rats^{62–64} and functional sperm and live progeny after autologous grafting of cryopreserved prepubertal tissue in rhesus macaques.⁶⁵ In human tissue, xenograft studies of ITT consistently showed survival of Sertoli cells and spermatogonia but limited germ-cell recovery,^{62,63,66,67} although the potential to reinitiate spermatogenesis based on the development of pachytene spermatocytes, spermatid and sperm-like cells and survival of functional Leydig cells producing testosterone was observed.⁶⁸ Long-term organotypic culture of cryopreserved prepubertal biopsies can advance cells through meiosis with haploid cells detected, albeit at low efficiency and with immature somatic support.⁶⁹ Translation to the clinic hinges on mitigating oncologic risk and improving engraftment biology: malignant cell carryover is a central barrier, and fluorescence- or magnetic-activated cell sorting are promising to decontaminate testicular cell suspensions and enrich human spermatogonia in preclinical assays; contemporaneous workflows now

assess residual cancer cells in banked tissue from boys with haematologic malignancies. For SSCT, delivery into the rete testis under ultrasound guidance remains the preferred technique from primate and cadaveric work,^{70,71} and a 2025 human feasibility report of an ultrasound-guided rete-testis approach underscores procedural practicality.⁷² However, clinical efficacy and safety (epigenetics, tumour seeding) still require prospective trials with long-term follow-up. Expert perspectives on clinical implementation of autotransplantation of cryopreserved testicular tissue have been published recently,⁶¹ and pilot clinical trials are ongoing. Emerging consensus is that pilot, ethically approved autografting/SSCT studies are approaching readiness under strict eligibility and contamination-control criteria, even as ITT banking itself is increasingly offered within structured programmes and framed with counselling about uncertain timelines to clinical use.^{59,60,73}

Long-Term Reproductive Outcomes of Fertility Preservation of Oocytes and Embryos

Long-term cohort studies are essential for understanding the true efficacy of FP. A large population-based study in the Netherlands, with a 10-year follow-up period, provides critical data on utilisation and live birth rates.⁷⁴ The study found a cumulative utilisation rate of 25.5%, meaning about one-quarter of the women had returned to use their cryopreserved oocytes or embryos.⁷⁴ The cumulative live birth rate was 34.6% per patient, with comparable live birth rates for cryopreserved oocytes and embryos.⁷⁴ These long-term data are invaluable for improving patient counselling and providing a more realistic perspective on the likelihood of future success.⁷⁴

The data reveal a key distinction between patient-level and population-level success. While the individual live birth rates per ET are encouraging at 35%, the low overall utilisation rate suggests that for many patients, the preserved material is not ultimately used.⁷⁴ This points to a more nuanced view of success, one that must also account for patient readiness, life circumstances, and the psychological value of the procedure as a “safety net,” independent of its clinical use.⁴¹

The Scientific Debate: Female Germline Stem Cells

A fundamental and ongoing scientific debate centres on the existence and regenerative potential of female germline stem cells (FGSCs) in the adult mammalian ovary.⁷⁵ The “classical theory” posits that the ovarian follicle pool is finite and fixed at birth, while the

“oocyte regeneration theory” suggests that FGSCs can generate new oocytes throughout life. Proponents of the regeneration theory have cited evidence from mouse models where bone marrow-derived cells can restore oocyte production, as well as more recent findings using advanced single-cell RNA sequencing (scRNA-seq) to identify rare germline cells in human ovarian cortical tissue.⁷⁵ However, critics argue that the human ovary lacks the active stem cell niches seen in rodents, making extrapolation difficult and citing methodological flaws in some early studies.⁷⁵

This debate is not merely an academic exercise; it is the theoretical foundation for future reproductive medicine. If the existence of FGSCs is definitively proven, it could shift the future of FP from a “preservation” model to a “regeneration” model.⁷⁵ The debate is ongoing.

Stem-Cell Horizons For Fertility Preservation and Germline Restoration

This talk mapped a translational arc from today’s regenerative adjuncts to speculative future platforms for making gametes, emphasising where evidence is mature versus experimental. In clinical translational work, mesenchymal stem cells (MSCs) are being explored as paracrine “bioreactors” to mitigate reproductive tract injury; preclinical and early clinical data suggest benefits in models of intrauterine adhesions, endometrial injury, and ovarian insufficiency, with secretome-based or exosome-based strategies increasingly favoured for safety and manufacturability. Recent systematic reviews highlight trophic, immunomodulatory, and pro-angiogenic mechanisms, and a 2025 meta-analysis cautiously supports MSCs for intrauterine adhesions while calling for larger RCTs and long-term follow-up.⁷⁶⁻⁷⁸ Parallel laboratory routes seek to restore or produce sperm *ex vivo*: in mice, air–liquid interface organ culture can complete spermatogenesis to fertile offspring, whereas in human ITT, long-term organotypic culture yields limited meiotic progression and rare haploid cells to date, underscoring a persistent efficiency gap.⁶⁹ A second research stream, pluripotent-stem-cell-based *in vitro* gametogenesis (IVG), is complete in rodents, where primordial germ cell-like cells (PGCLCs) give functional sperm and oocytes, and healthy offspring, but remains partial in humans: 2024 studies reconstitute key epigenetic reprogramming steps and derive PGCLCs, including from men with non-obstructive azoospermia, yet do not achieve fully competent human gametes. Stem-cell embryo models provide third-pillar systems for discovery: human

blastoids and post-implantation models recapitulate lineage specification and endometrial attachment *in vitro*, while mouse blastoids trigger decidualisation after transfer without normal embryonic development; human gastruloids have recently been shown to generate PGCLCs, refining early germline ontogeny maps.^{79,80} Looking ahead, “programmable development” is moving from concept to practice via microfluidic/morphogen engineering and optogenetic control of signalling, enabling real-time patterning in human pluripotent stem-cell systems and seeding visions of feedback-controlled morphogenesis, opportunities that heighten, rather than diminish, the need for rigorous safety metrics.^{81,82} Governance is catching up: UK guidance and recent ethics reports press for bespoke oversight of stem-cell-based embryo models and prospective IVG, emphasise prohibitions on transfer, and call for benchmarks of “normality” plus per-gamete risk assessment, given that bulk testing cannot assure the safety of individual gametes or embryos. Overall, current patient-facing translation rests on MSC-based regeneration and the first SSC/tissue autografts under strict protocols, whereas IVG and embryo-like models remain research tools; the field’s trajectory demands parallel investment in manufacturing standards, long-term safety/epigenetic surveillance, and adaptive regulation.

Technological Advances in Artificial Organs and Reproductive Medicine (Figure 3)

3D Bioprinting For Reproductive Tissues and Organs

3D bioprinting is a ground-breaking technology that is enabling the creation of patient-specific extracellular tissues and organ models that mimic the complex architecture and functionality of the extracellular matrix and structure of human reproductive organs. This technology offers a wide range of potential applications, from personalising fertility treatments to the development of fully functional artificial organs for transplantation.^{83,84}

The development of these bioengineered organs is not just a biological challenge but is fundamentally an engineering one, dependent on advances in biomaterials science. Bioprinting relies on “bioinks” made from a combination of cells and biomaterials like gelatin, alginate, and decellularised extracellular matrix. For ovarian regeneration, GelMA bioink has been used in mouse models to create microporous scaffolds that support folliculogenesis and vascularisation, enabling mice to give birth. For uterine regeneration, alginate-

based bioinks have been used to create scaffolds for endometrial repair.⁸⁵ Much work is also directed towards proper recellularisation of this bio-printed scaffolds to accomplish fully functional reproductive tissues and organs.

The Artificial Uterus (Ectogestation)

An artificial uterus is a device designed to allow a fetus to develop outside the maternal body, a concept known as ectogestation or ectogenesis. While still experimental, proof-of-concept studies have demonstrated its feasibility in large animal models for an artificial uterus of use during a pregnancy time before fetal viability outside the uterus but well after organogenesis. In a landmark study, extremely premature lamb fetuses supported in a fluid-filled “biobag” system connected to an extracorporeal oxygenator survived and showed normal growth and organ development for up to four weeks.⁸⁶ However, extending ectogestation to stages before organogenesis would be vastly more challenging, as recreating the intricate biochemical, mechanical, and spatial cues of the early uterine environment remains far beyond current capabilities. The coordinated processes of implantation,

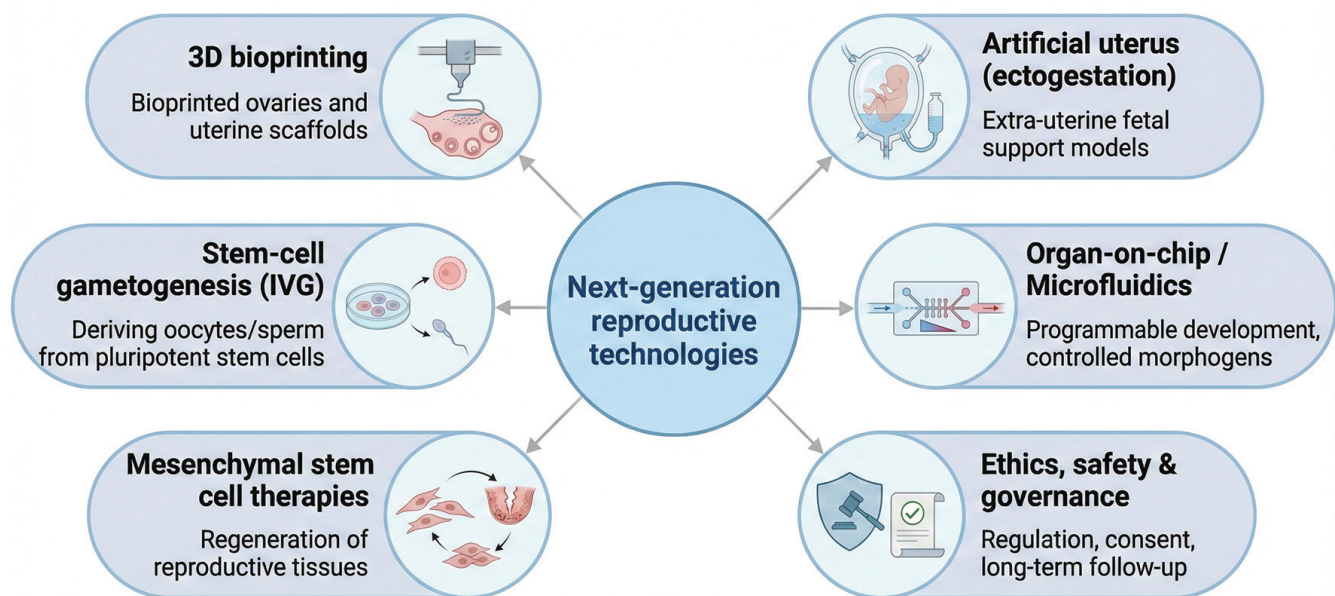
placenta formation, and early organ development rely on dynamic, bidirectional interactions between embryo and uterus that would be extremely difficult to replicate ex utero.

Bioethical and Technical Challenges

The development of these advanced reproductive technologies is not without significant challenges. Technically, replicating the intricate cellular architecture, vascular networks, and hormonal environment of native tissues remains a formidable hurdle. There are also significant safety concerns with bio-printed organs, including biomaterial degradation and the potential for implant rejection or cancer.⁸⁷ Since these organs are custom-made, traditional pre-implantation safety testing is impossible, which adds to the dilemma.⁸⁷

Beyond the technical hurdles, these technologies introduce complex ethical and legal questions. The artificial uterus, in particular, has the potential to redefine the concept of fetal “viability,” the stage at which a fetus can survive independently of the mother.⁸⁸ This could shift the moral and legal landscape of neonatal care and

“Future Technologies in Fertility Preservation”



Hub-and-spoke map of emerging technologies in fertility preservation, spanning bioprinting, stem-cell gametogenesis, organ-on-chip engineering, artificial uterus systems, and ethics/regulatory frameworks.

Figure 3. Future technologies in fertility preservation. Hub-and-spoke map of emerging technologies in fertility preservation, including 3D bioprinting of ovarian and uterine scaffolds, artificial uterus systems for ectogestation, stem-cell–based gametogenesis, organ-on-chip engineering, mesenchymal stem-cell therapies, and ethics/regulatory governance.

This figure was generated using an AI-based image generation tool (Gemini, Google), based on an original conceptual prompt developed by the authors.

abortion rights, as the existence of an external womb might sever the long-held link between viability and the function of the mother's body.⁸⁸ Furthermore, the increased visibility of gestation through ectogestation could be used to restrict women's reproductive liberties.⁸⁹ Similarly, bioprinting raises ethical concerns about the source of cells used, the need for fully informed consent, and the potential for social and economic disparities in access to these high-cost technologies. The development of these technologies is an example of innovation outpacing existing legal and ethical frameworks, and it requires a proactive, multi-stakeholder dialogue to ensure they are introduced responsibly.

Conclusion

FP has evolved into a multidisciplinary field that unites oncology, reproductive medicine, psychology, and bioengineering. Advances in surgery, cryopreservation, and emerging technologies such as stem cell-based regeneration, 3D bioprinting, and artificial uterus models are expanding possibilities for patients facing infertility risks. Yet, these innovations bring ethical and clinical challenges that require transparent counselling, equitable access, and robust regulatory frameworks. The goal is not only to safeguard fertility but also to align medical progress with patient autonomy, safety, and long-term quality of life.

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