

Review

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Review

Fertility Preservation: An Integrated Review of Male and Female Strategies, Techniques, Outcomes, and Future Directions

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Abstract

Background/Objectives: Fertility preservation (FP) spans oncological and non-oncological indications, including gonadotoxic therapies, benign haematological/metabolic disorders, conditions at risk of premature ovarian insufficiency, severe andrological disease, and elective plans to defer childbearing. We provide a sex-integrated overview of established and emerging FP strategies and their real-world effectiveness [1–10]. **Methods:** Narrative synthesis of guidelines and high-quality studies (to 2025), prioritising ASCO/ESHRE guidance, systematic reviews, and multicentre/registry data covering oocyte/embryo cryopreservation, ovarian tissue cryopreservation (OTC), GnRH agonists, ovarian transposition, in vitro maturation (IVM), sperm banking, surgical sperm retrieval (SSR), testicular tissue cryopreservation (TTC), and spermatogonial stem-cell (SSC) approaches [1–10]. **Results:** For women, oocyte vitrification is the first-line option when time allows; OTC is established when stimulation is infeasible or in prepubertal girls, with endocrine recovery common and increasing pregnancy/live-birth reports. For men, sperm cryopreservation before therapy is standard; SSR supports selected cases. Paediatric TTC is feasible but remains experimental, whereas paediatric OTC is clinically implemented. Random-start COS and letrozole/tamoxifen protocols minimise treatment delay and hormonal exposure; GnRHa co-treatment preserves ovarian function as an adjunct. Utilisation of banked gametes/tissue remains modest, underscoring the need for pathway optimisation [1–10]. **Conclusions:** FP should be embedded across oncology and non-oncology pathways with timely referral, clear counselling on probabilities of live birth, and robust follow-up. Standardisation, registry-based evidence and long-term offspring safety data are priorities to bridge the gap between laboratory potential and clinical effectiveness [1–10].

Keywords: fertility preservation; oocyte vitrification; embryo cryopreservation; ovarian tissue cryopreservation; GnRH agonists; in vitro maturation; sperm cryopreservation; surgical sperm retrieval; testicular tissue cryopreservation; spermatogonial stem cells

1. Introduction

Cancer therapies can compromise reproductive potential via direct gonadotoxicity to germ cells and the gonadal microenvironment, with risk modulated by age, drug class/dose and radiation fields [1–3,7–9]. Counselling should balance oncologic timelines with reproductive goals and convey realistic probabilities of future live birth [1,4,6].

Beyond oncology, FP is relevant for benign haematological and metabolic diseases (e.g., thalassaemias, sickle-cell disease, galactosaemia), autoimmune conditions requiring gonadotoxic agents, genetic risks of premature ovarian insufficiency (e.g., Turner syndrome, BRCA carriers considering RRSO), severe andrological disorders (e.g., non-obstructive azoospermia) and elective deferral of parenthood. Indication and timing should be individualised within multidisciplinary pathways [1,5,10].

We conducted a narrative synthesis of guidelines and high-quality studies published up to 2025, prioritizing ASCO/ESHRE recommendations, systematic reviews, register-based studies, and multicentre cohorts on both female and male preservation [1–10].

2. Female Fertility Preservation

2.1. Embryo Cryopreservation [4]

Effective when a partner or donor sperm is available. Vitriified blastocysts have high survival and outcomes comparable to fresh transfer. Requires controlled ovarian stimulation (COS), which can be performed with letrozole/tamoxifen and random-start protocols to minimize delays, including in ER-positive breast cancer [4–6,10].

2.2. Oocyte Cryopreservation (Vitrification) [4–6]

First-line option in postpubertal women. Transition to vitrification improved oocyte survival and fertilization. Real-world effectiveness depends on age and the number of mature oocytes retrieved; many patients never return to use stored oocytes (<10%) [4,6,10].

2.3. Ovarian Tissue Cryopreservation (OTC) [5,6,10].

Indicated when stimulation is infeasible or time-constrained, and in prepubertal girls. Following thaw, orthotopic transplantation restores endocrine function in most cases (~60–90%), with clinical pregnancies frequently reported; cumulative live births now exceed 130 globally [5,6,10].

2.4. GnRH Agonist Co-Treatment [6,10].

GnRHa during chemotherapy may preserve ovarian function, particularly in breast cancer, and should be viewed as complementary to, not a replacement for, cryopreservation strategies [6,10].

2.5. Ovarian Transposition and In Vitro Maturation [4,6]

Surgical transposition reduces ovarian radiation dose; in vitro maturation (IVM) offers an option when time is limited, and may be combined with OTC, although live-birth evidence remains limited [4,6,10].

3. Male Fertility Preservation

3.1. Sperm Cryopreservation [1]

Reference standard in postpubertal males. Utilisation of stored samples is modest (~9%) and pregnancy rates when used are ~28%; assisted reproduction, particularly ICSI, is often required [1].

3.2. Surgical Sperm Retrieval [1]

TESE/micro-TESE can be considered when ejaculation is not feasible or in azoospermia; requires specialized expertise and carries procedural risks [1].

3.3. Paediatric and Experimental Strategies [7–9]

For prepubertal boys, testicular tissue cryopreservation captures spermatogonial stem cells. Feasibility and safety of biopsy and freezing have been shown in paediatric programmes, but clinical fertility restoration and live births have not yet been established; concerns include malignant contamination and long-term safety [7–9].

4. Implementation, Utilisation, and Outcomes

Despite guideline support, access and utilisation remain uneven. Barriers include time pressure, costs, variable referral pathways, and recovery of fertility post-treatment. Utilisation of banked gametes is generally <10% in both sexes; endocrine recovery after OTC is common, yet IVF outcomes align with diminished reserve profiles [1,4–6].

Table 1. Female preservation techniques—indications, timelines, strengths and limitations (summary). See main text for details. [4–6,10].

- Oocyte vitrification (COS): high evidence; random-start; DuoStim optional; age-dependent yield; requires time.
- Embryo vitrification: high survival; legal/ethical consent considerations.
- Ovarian tissue cryopreservation + transplantation: endocrine restoration common; natural conception possible; contamination risk context-dependent.
- In vitro maturation: minimal delay; lower evidence base.
- GnRH agonists during chemotherapy: adjunct only; preserves function in selected contexts.
- Ovarian transposition: reduces ovarian dose prior to pelvic radiotherapy.

Table 1. Female preservation techniques—indications, timelines, pros/cons.

Technique	Indications	Typical timeline	Strengths	Limitations/Notes
Oocyte vitrification (COS)	Postpubertal; time for stimulation; many cancers incl. ER+ with letrozole	10–14 days (random-start; DuoStim optional)	High evidence; scalable; patient autonomy	Delay needed; hormone exposure; age-dependent yield [4–6,10]
Embryo vitrification	Partner/donor sperm available	As above	High survival and outcomes	Legal/ethical consent; disposition issues [4–6,10]
OTC transplant	+ Prepubertal/time-critical; contraindication to COS	48–72 h (surgery + cryo); months to re-implant	Restores endocrine function; natural conception	Contamination risk; variable duration; specialised centre [5,10]

IVM vitrification	± Very limited time; COS contra-indicated	24–72 h	Minimal delay; hormone- sparing	Lower evidence; lab-dependent outcomes [4,10]
GnRHa during chemo	Adjunct across cancer types	Concurrent with chemotherapy	Protects menses/ovarian function	Not a replacement for cryopreservation [6,10]
Ovarian transposition	Planned pelvic RT	Pre-RT (surgery)	Reduces ovarian dose	Surgical risks; may combine with cryo [10]

5. Male Fertility Preservation—Techniques and Practical Considerations

5.1. Sperm Cryopreservation [1]

Standard of care in postpubertal males. Recommend 2–3 ejaculates when feasible, 2–5 days’ abstinence each, prioritising collection ****before**** therapy. Laboratory workflow: semen analysis, dilution with cryoprotectant (e.g., glycerol-based), controlled-rate freezing or vapour phase, storage in liquid nitrogen. Post-thaw, motility recovery varies; assisted reproduction—especially ICSI—is often required [1].

5.2. Surgical Sperm Retrieval (SSR) and Cryopreservation [1]

For non-ejaculatory patients or azoospermia, SSR (TESE/micro-TESE, PESA/TESA) can be performed prior to therapy, with immediate cryopreservation or use with ICSI. Micro-TESE improves retrieval in non-obstructive azoospermia. Risks include testicular damage and anaesthesia; procedures require experienced centres.

5.3. Electroejaculation and Special Circumstances [1]

In neurogenic or severe anejaculation, electroejaculation under anaesthesia may allow collection for cryopreservation. Consider sperm retrieval from post-ejaculatory urine if retrograde ejaculation is suspected.

5.4. Testicular Tissue Cryopreservation (TTC) in Prepubertal Boys [7–9]

Prepubertal testes lack mature sperm; TTC aims to preserve spermatogonial stem cells. Technique: testicular biopsy and fragmentation, exposure to cryoprotectant, slow-freezing or vitrification, storage in liquid nitrogen. Future options include autologous tissue re-implantation, SSC transplantation, or in vitro spermatogenesis. Human live births after TTC are not yet established; safety concerns include malignant cell re-introduction and epigenetic integrity [7–9].

5.5. Experimental Restoration Strategies [7–9]

Autotransplantation of thawed tissue: successful spermatogenesis in animal models; human translation cautious. SSC isolation/expansion and transplantation: promising but technically demanding; requires oncologic decontamination. In vitro spermatogenesis and organoid/tissue-engineering platforms: advancing but not ready for clinical use.

Table 2. Male preservation techniques—indications, timelines, strengths and limitations (summary). [1,7–9].

- Sperm cryopreservation: established; often requires ICSI after thaw.
- Surgical sperm retrieval (TESE/micro-TESE, PESA/TESA): enables use in azoospermia/anejaculation; invasive; centre-dependent.

- Electroejaculation: option in neurogenic cases; anaesthesia required.
- Testicular tissue cryopreservation: paediatric; experimental; aims to capture SSCs for future use.
- SSC-based and in vitro spermatogenesis strategies: research stage; oncologic safety under evaluation.

Table 2. Male preservation techniques—indications, timelines, pros/cons.

Technique	Indications	Typical timeline	Strengths	Limitations/Notes
Sperm cryopreservation	Postpubertal; before gonadotoxic therapy	Same-day; repeated over 2–5 days	Established; widely available	Quality may be poor at baseline; low utilisation (~9%) [1]
SSR (TESE/micro-TESE)	Azoospermia/non-ejaculation	Day-case surgery	Enables ICSI; option when ejaculation fails	Invasive; centre-dependent outcomes [1]
Electroejaculation	Neurogenic/anejaculation	Same-day under anaesthesia	Allows collection when other methods fail	Resource-intensive; requires anaesthesia
TTC (prepubertal)	Boys prior to high-risk therapy	48–72 h (biopsy + cryo)	Captures SSCs for future options	Experimental; no human live births to date [7–9]
SSC-based/IVS (experimental)	Research settings	N/A	Potential definitive restoration	Oncologic safety unproven; regulatory barriers [7–9]

6. Clinical Pathways, Ethics, and Health-System Implementation

6.1. Triage and Rapid Referral Pathway

Establish a same-day referral protocol from oncology to reproductive medicine. Provide counselling that covers risks by regimen, options by age/sex, timelines, and realistic probabilities of live birth. Use checklists to document eligibility, consent, and logistics (laboratory capacity, theatre scheduling for OTC/TTC).

6.2. Ethics, Consent, and Law

Key issues include consent capacity in minors (assent + parental consent), gamete/tissue ownership, posthumous use, storage duration, and cross-border transfer. Patients must be counselled on disposition decisions (use, donation, disposal), genetic/long-term child health data, and disease-specific risks of tissue re-implantation.

6.3. Data and Quality—Registries and Outcomes

Programmes should participate in national/international registries, report key performance indicators (collection yield, cryosurvival, transplant endocrine recovery, pregnancy/live-birth rates), and track survivorship outcomes to inform real-world effectiveness [1–10].

6.4. Cost, Access, and Equity

Coverage varies widely; equity strategies include early referral, streamlined scheduling, travel support, and public funding where available. Centralisation of OTC/TTC may improve quality but requires robust referral networks.

7. Indications—Oncological and Non-Oncological Overview

Fertility preservation spans an aetiologically diverse landscape. In oncology, the objective is to mitigate the anticipated gonadotoxic impact of chemotherapy, targeted agents, immunotherapies and pelvic radiotherapy, while aligning timelines of care. Beyond oncology, FP supports patients with benign haematological and metabolic disorders (e.g., thalassaemia, sickle-cell disease, galactosaemia), autoimmune conditions necessitating gonadotoxic agents, genetic risks of premature ovarian insufficiency (e.g., Turner syndrome, BRCA carriers considering risk-reducing salpingo-oophorectomy), severe andrological conditions (e.g., non-obstructive azoospermia), and elective deferral of childbearing. Clinical nuance lies in matching the indication to the most appropriate modality, recognising timelines, age, baseline gonadal function and oncologic safety [1–20].

In women, oocyte vitrification is generally first-line when time allows and ovarian stimulation is safe; OTC is appropriate when stimulation is infeasible or in the prepubertal setting. In men, sperm cryopreservation prior to therapy is standard practice, with surgical sperm retrieval for selected cases. In prepubertal boys, TTC is investigational but increasingly organised within ethically governed programmes. Elective cryopreservation requires distinct counselling on probabilities and cost-effectiveness, ensuring that expectations reflect age-dependent outcomes [4–6,10,16–19,38,39].

8. Technical Principles—From Gametes to Gonadal Tissue

Cryopreservation hinges on the avoidance of intracellular ice and osmotic injury. Vitrification achieves ultra-rapid cooling in the presence of permeating and non-permeating cryoprotectants, yielding a glass-like state, whereas slow-freezing uses controlled cooling with graded cryoprotectant exposure. In oocyte and embryo cryostorage, vitrification dominates due to superior post-warming survival and clinical outcomes; in OTC, slow-freezing remains the most validated approach, although vitrification is under active study. TTC protocols are adapted from ovarian models but require tailored equilibration and biopsy handling [4,5,10,18,19].

Laboratory quality systems should document cryoprotectant lot traceability, device validation (closed versus open systems), liquid nitrogen management, and chain-of-custody from consent through storage and potential future use. Traceability is particularly critical for tissue banking, where multiple fragments per patient, serial thawing and re-implantation may occur over many years [5,18,19,31,32].

9. Female Procedures—Protocol Details and Practicalities

Controlled ovarian stimulation (COS) for FP typically employs antagonist protocols with random-start initiation to minimise delay. When oestrogen exposure is a concern, aromatase-inhibitor-augmented regimens (letrozole) or selective oestrogen receptor modulators (tamoxifen) are used. Trigger strategies utilise GnRH-agonist $\pm$ low-dose hCG to reduce ovarian hyperstimulation risk. Oocyte retrieval is followed by denudation, MII assessment and vitrification; when a sperm source is available, embryo banking at the blastocyst stage is common. For patients with extremely limited time, in vitro maturation enables retrieval of immature oocytes with subsequent laboratory maturation and vitrification. OTC is performed via laparoscopic cortical strip harvest with immediate cryoprotectant exposure and slow-freezing; screening for malignant infiltration precedes orthotopic transplantation once oncologic control and reproductive plans align [4–6,10–12,14,16–20,38,39].

Counselling should quantify age-related expectations, articulate the distinction between gamete banking and the probability of future live birth, and document consent on disposition of stored material (use, donation, disposal). Patients should be informed about endocrine recovery after OTC,

the potential for natural conception, and the possibility that IVF may be needed after re-implantation [5,10,18–20,31,32].

10. Male Procedures—Protocol Details and Practicalities

For sperm banking, best practice aims for two to three ejaculates where feasible, spaced by 2–5 days, prior to gonadotoxic therapy. Laboratories assess baseline semen parameters, add cryoprotectants (commonly glycerol-based), and apply controlled-rate freezing or vapour-phase methods before storage in liquid nitrogen. Post-thaw motility varies and intracytoplasmic sperm injection is frequently required. For non-ejaculatory patients or azoospermia, surgical sperm retrieval—TESE/micro-TESE, PESA/TESA—can provide spermatozoa for cryostorage or immediate use. In prepubertal boys, TTC involves biopsy with fragmentation, cryoprotectant equilibration and controlled freezing; future fertility restoration strategies include autotransplantation, SSC transplantation and in vitro spermatogenesis, all currently investigational [1,7–9,25–29].

Ethical frameworks should address consent/assent in minors, long-term storage and ownership, and safeguards against malignant contamination upon re-implantation. Programmes benefit from centralisation to ensure procedural volume, specialised laboratory support and longitudinal follow-up [3,7–9,28,29].

11. Outcomes and Real-World Effectiveness

Laboratory survival metrics are necessary but insufficient; patients require data framed as probabilities of live birth per patient, which integrate age at cryostorage, number and quality of gametes/embryos or tissue, and future partner/fertility context. Oocyte vitrification demonstrates high post-warming survival, yet live-birth probability remains age-dependent and many patients never return to use stored oocytes. OTC often restores endocrine function and has yielded increasing natural and assisted conceptions; in men, sperm banking enables future ART with variable uptake. Utilisation of banked material is modest across sexes, reflecting the interplay of oncologic chronology, personal circumstances and fertility recovery [1,4–6,10,17–21,31,32,37–39].

Paediatric outcomes require particular caution. OTC has an established paediatric pathway in selected indications, whereas TTC remains investigational without established human live births. Long-term offspring follow-up and registries are essential to confirm safety and refine counselling [3,5,7–10,19,22–24,31–35].

12. Service Models, Quality, and Equity

Effective FP services rely on fast-track referral from diagnosing teams, embedded counselling, and reliable access to laboratory and surgical capacity. Programmes should define and audit key performance indicators (time from referral to intervention, collection yield, cryosurvival, endocrine recovery after tissue transplant, pregnancy and live-birth rates) and participate in national/international registries. Equity considerations include coverage of costs, geographic access, and targeted support for vulnerable populations, including adolescents and those facing urgent treatment [1–10,20–22,31,32].

13. Discussion

An integrated, sex-specific approach is essential. In women, oocyte vitrification is first-line when feasible, whereas OTC provides endocrine and reproductive benefits when COS is not possible. In men, sperm banking is straightforward and effective yet underused, indicating a need for more proactive counselling and survivorship pathways. Paediatric strategies are asymmetric—OTC is clinically established, whereas testicular tissue preservation remains investigational. Priority gaps include protocol standardisation, registry-based real-world data, and long-term offspring follow-up [1–10].

14. Conclusions

Fertility preservation should be systematically integrated into cancer care as a time-critical intervention. For women, oocyte vitrification and OTC constitute complementary pillars, selected by age, timing, and oncologic context; for men, sperm cryopreservation is effective yet underused. Paediatric strategies diverge: OTC is established whereas TTC is investigational. Standardisation, registry-based evidence, and long-term offspring follow-up remain priorities to close the gap between laboratory potential and real-world effectiveness [1–10].

15. Research Agenda and Future Directions

Priorities include standardisation of OTC/TTC protocols, optimisation of paediatric indications, oncologic decontamination strategies for tissue, advancement of SSC culture and in vitro spermatogenesis platforms, and robust long-term safety data for children born after FP. In parallel, decision-aid tools and realistic, age-calibrated prognostic models could improve counselling and appropriate utilisation [3–5,7–10,18–20,28,29,31–39].

16. Limitations of the Evidence and of This Review

The evidence base is heterogeneous and often observational, with selection biases and evolving laboratory protocols that complicate cross-study comparisons. Outcome reporting varies across centres and registries, and the rapid pace of innovation necessitates ongoing updates. While we synthesised high-quality sources and guidelines, the field would benefit from harmonised definitions, core outcome sets and prospective data capture to sharpen clinical inferences [1–10,16–21,31–39].

Conflicts of Interest: The authors declare no conflicts of interest.

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