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Review

Beyond Survival: Integrating Fertility Preservation into Gynaecologic Cancer Management

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Abstract

As survival rates among patients with gynaecological cancers continue to improve, fertility preservation has become an increasingly important aspect of comprehensive cancer care, particularly for younger women diagnosed during their reproductive years. The impact of treatment on fertility varies according to cancer type, stage, and modality, necessitating individualised preservation strategies. Fertility preservation is both feasible and safe in carefully selected patients with early-stage gynaecological cancers. Oocyte and embryo cryopreservation remain the most widely accepted techniques, particularly when time allows for ovarian stimulation. Fertility-sparing surgeries, such as radical trachelectomy and conservative management of early endometrial cancer, have shown promising oncological and reproductive outcomes. However, barriers including access, timing, and awareness continue to limit broader implementation. In modern society, fertility-preserving strategies should form an integral part of treatment planning for reproductive-aged women with gynaecological malignancies. Early referral to a fertility specialist, patient-centred counselling, and a coordinated multidisciplinary approach are essential to optimise both oncological and reproductive outcomes. Further research and education are required to refine guidelines and expand access to fertility-preserving care. This review presents the current fertility preservation options available to women with gynaecological cancers, including cervical, ovarian, and endometrial malignancies, and highlights the importance of early multidisciplinary intervention in delivering personalised care.

Keywords: fertility preservation; cervical cancer; endometrial cancer; ovarian cancer; ovarian tissue preservation; artificial intelligence; atypical hyperplasia

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1. Introduction

Gynaecological cancers, while more common in postmenopausal women, also affect a substantial number of women during their reproductive years. Rising incidence in this age group, together with societal trends toward delayed childbearing, has made fertility preservation an increasingly critical aspect of cancer care [1,2]. Although survival rates have improved, standard treatments; surgery, chemotherapy, and radiotherapy, often compromise ovarian reserve and uterine integrity, placing future fertility at risk. Balancing oncological safety with reproductive outcomes has therefore become a central challenge in oncofertility, driving the search for effective alternatives within routine cancer pathways.

This review summarises current fertility preservation strategies in gynaecological malignancies, including conservative surgical approaches and assisted reproductive technologies, with attention to their indications, efficacy, limitations, and ethical implications. By integrating recent advances and emerging trends, it aims to support clinicians in providing informed, individualised, and patient-centred care for women facing the dual challenge of cancer treatment and fertility preservation.

2. Materials and Methods

This study was conducted as a narrative review of the literature. We performed a comprehensive search of Medline (via PubMed) and Embase databases for studies published between January 1990 and June 2025. The search strategy combined controlled vocabulary and free-text terms related to fertility preservation, oncofertility, fertility-sparing surgery, assisted reproductive technologies, cryopreservation, uterine transplantation, and artificial intelligence in infertility.

Eligible articles included randomised controlled trials, systematic reviews and meta-analyses, cohort and cross-sectional studies, and high-quality narrative reviews that reported on:

- Fertility-sparing surgical techniques in gynaecological malignancies.
- Fertility-preservation strategies, including ovarian tissue, oocyte, and embryo cryopreservation.
- Medical gonadal protection during oncological treatment.
- Pregnancy and oncological outcomes following fertility-sparing management.
- Post-family planning management and long-term follow-up.
- Emerging interventions such as uterine transplantation and applications of artificial intelligence in reproductive medicine.

Studies were selected based on their relevance to the scope of this review and the quality of evidence. A total of 143 articles were included.

Case reports, case series, conference abstracts, and non-peer-reviewed publications were excluded because of their high risk of bias and limited evidentiary value. Additional references were identified through manual searches of the bibliographies of included articles and relevant society guidelines (e.g., ESGO, ESMO, NCCN, ASCO).

3. Discussion

Chemotherapy-induced ovarian failure represents a key mechanism underlying infertility in women undergoing treatment for gynaecological malignancies. It is characterised by disruption of both endocrine and reproductive ovarian function following exposure to cytotoxic agents. The pathophysiology is multifactorial and includes direct DNA damage to oocytes, accelerated activation and subsequent depletion of primordial follicles, and impairment of ovarian stromal and vascular integrity. These processes lead to premature exhaustion of the follicular reserve and may result in temporary or permanent ovarian insufficiency. The degree of gonadotoxicity varies according to patient age, baseline ovarian

reserve, and the type and cumulative dose of chemotherapeutic agents, with alkylating agents associated with the highest risk [3].

These considerations are central to fertility preservation counselling, as they directly influence both the urgency and selection of appropriate interventions. However, individual risk prediction remains challenging, reflecting the heterogeneous and predominantly observational nature of the available evidence.

The selection of a fertility preservation strategy for women with gynaecological malignancies depends on a combination of patient, disease, and treatment-related factors, and should be individualised. Age and ovarian reserve are key considerations; younger patients and those with higher anti-Müllerian hormone (AMH) levels and antral follicle count (AFC) are more likely to achieve favourable outcomes with oocyte or embryo cryopreservation. The time available before starting cancer treatment is also important, as stimulation-based approaches usually require 10–14 days or longer and may not be feasible in urgent situations. In these cases, ovarian tissue cryopreservation can be considered given its shorter timeframe. Pubertal status further influences the choice, with ovarian tissue preservation often the only option for prepubertal girls [1].

Cancer-related factors, including tumour type, stage, histology, and the risk of ovarian involvement, also need to be considered when assessing the safety of fertility-preserving approaches. The expected gonadotoxicity of planned treatments helps guide how proactive fertility preservation should be. Where immediate systemic therapy is required, options that do not involve ovarian stimulation are generally preferred to avoid delays. It is also important to recognise that delays often occur earlier in the pathway, particularly between diagnosis and referral for fertility counselling, rather than during the preservation procedure itself. Patient preferences, including ethical and personal considerations, should be taken into account when planning management [1].

3.1. Endometrial Cancer

Endometrial cancer is the most frequently diagnosed gynaecological malignancy in high-income countries and predominantly affects postmenopausal women. In the United States, the number of new cases in 2025 is projected to reach 69,120, with an estimated 13,860 deaths [2]. Although the mean age at diagnosis is approximately 62 years, 4–14% of cases occur in women of reproductive age, many of whom wish to preserve fertility [4]. According to guidelines from the European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO), and the European Society of Pathology (ESP), fertility-sparing treatment may be considered in carefully selected patients [5]. Specifically, conservative management can be offered to women with atypical endometrial hyperplasia or grade 1 endometrioid carcinoma without evidence of myometrial invasion [5–10]. Given the complexity of management, such treatment should be undertaken in specialised centres with appropriate expertise [5,9,11–13].

Accurate evaluation of myometrial invasion (MI) is critical when considering fertility preservation. Transvaginal ultrasound (TVUS) provides cost-effective assessment with sensitivity comparable to other imaging modalities [14–16], while contrast-enhanced magnetic resonance imaging (MRI) offers superior evaluation of cervical stromal involvement and lymph node status. MRI is therefore the preferred tool for selecting candidates for fertility-sparing treatment [5,17–19]. Based on current guidelines the eligibility criteria for conservative management in endometrial cancer are summarised in Table 1 [5,11,20].

Progestin-based therapy, including oral agents and the levonorgestrel-releasing intrauterine device (LNG-IUD), remains the cornerstone of conservative management. In women with stage IA endometrioid endometrial cancer, prolonged hormonal therapy until completion of childbearing does not appear to compromise oncological outcomes [21].

A large population-based analysis of the National Cancer Database showed that women younger than 40 years with stage IA disease treated with progestins had 5-year survival rates comparable to those undergoing hysterectomy [22].

Table 1. Patient selection criteria for fertility -sparing management in endometrial cancer.

No.	Selection Criterion
1	Well-differentiated endometrioid endometrial carcinoma histologically diagnosed and confirmed by an experienced pathologist
2	No evidence of myometrial invasion as confirmed by imaging studies, ideally MRI or high-resolution TVUS
3	No evidence of lymph node metastases (both pelvic and para-aortic) or synchronous ovarian cancer
4	No contraindications to pregnancy or hormonal therapy.
5	Continuous input from GO MDT and fertility specialist
6	Patients compliant to close monitoring and informed about the potential necessity of a future hysterectomy in the event of treatment failure

TVUS: transvaginal ultrasound; GO MDT: Gynaecology Oncology multidisciplinary team.

The optimal dose and duration of progestin therapy remain uncertain. Commonly used regimens include megestrol acetate (MA) 160 mg/day and medroxyprogesterone acetate (MPA) 400–600 mg/day [5,9,11,17,23]. Some studies suggest a higher risk of recurrence with MA, although findings are inconsistent. Treatment duration is not standardised, with reported time to complete response varying across studies [23,24].

The levonorgestrel-releasing intrauterine device (LNG-IUD) provides continuous local progestin delivery while minimising systemic exposure [13]. Its use in fertility-preserving management has increased, either alone or in combination with systemic progestins [8,13,20]. A Cochrane review found insufficient evidence to establish superiority between LNG-IUD and oral progestins in atypical hyperplasia [25]. Combination therapy may improve outcomes, although evidence remains limited and requires further validation in patients with endometrial cancer [5].

Given the association between insulin resistance and endometrial cancer, metformin has been explored as an adjunct to hormonal therapy. While preclinical studies suggest potential anti-proliferative effects [26,27], clinical evidence remains limited and is largely derived from small or observational studies [13].

Hysteroscopic resection, combined with oral or intrauterine progestin therapy, is an established fertility-preserving option for selected women with early-stage endometrial cancer [5,28]. The procedure involves removal of the visible lesion and surrounding endometrium, followed by adjuvant hormonal therapy [5,29].

Close surveillance is essential in fertility-preserving management. Treatment response is typically assessed with repeat endometrial sampling following initiation of hormonal therapy [18]. The optimal monitoring strategy remains uncertain, although the National Comprehensive Cancer Network (NCCN) recommends endometrial biopsy every 3–6 months using either pipelle sampling or dilatation and curettage [11]. Given the risk of recurrence, definitive surgical management is recommended after completion of childbearing, although ovarian preservation may be considered in selected patients [5].

Molecular and genetic profiling is increasingly being explored in treatment planning. A meta-analysis of 27 studies suggested that immunohistochemical markers may help predict response to progestin therapy [30]. Higher oestrogen receptor (ER) and progesterone receptor (PR) expression has been associated with favourable outcomes [30–32]. However, findings remain inconsistent, and their clinical utility is not yet fully established.

Reported clinical outcomes vary considerably across studies. While complete response rates are often high, recurrence remains a significant concern, and pregnancy outcomes are variable [33]. These findings are largely derived from retrospective studies with heterogeneous patient populations, including differences in stage, treatment protocols, and follow-up duration [33]. Combination therapy with oral progestins and the levonorgestrel-releasing intrauterine device may improve response rates, although evidence remains limited.

Hysteroscopic resection combined with hormonal therapy has been associated with favourable oncological and reproductive outcomes in selected patients [34]. Pregnancy rates appear to improve with the use of assisted reproductive technologies, although available data are limited [34]. However, most available evidence is derived from retrospective studies with heterogeneous populations, and prospective data remain limited. The criteria and outcomes for fertility-sparing management in endometrial cancer are summarised in Table 2.

Table 2. Fertility-sparing treatment options and supporting evidence in endometrial cancer.

Fertility-Sparing Methods in Endometrial Cancer			
Method	**Indication**	**Key Consideration**	**Evidence Level**
Oral progestins (MPA, MA)	Stage IA, grade 1 endometrioid EC	Variable response; risk of recurrence	Retrospective studies and systematic reviews [5,11,17,20,23,33]
LNG-IUD	Local progestin delivery	Reduced systemic exposure	Limited comparative evidence [8,13,25,33]
Combined oral progestins + LNG-IUD	Selected patients	May improve response in selected cases	Observational studies [5,8,13,33]
Progestins + metformin (adjunct)	Investigational	Potential benefit in selected patients	Limited evidence [13,26,27]
Hysteroscopic resection (± progestins or LNG-IUD)	Localised disease	Requires specialised expertise	Small observational studies [5,28,29,34]

MPA: Medroxyprogesterone Acetate; MA: Megestrol Acetate; LNG-IUD: Levonorgestrel intrauterine device: EC; Endometrial cancer.

3.2. Ovarian Cancer

Ovarian cancer is the eighth most common cancer in women worldwide, with an estimated 313,959 new cases and 207,252 deaths reported in 2020 [35]. It remains the most lethal gynaecological malignancy, largely due to late-stage presentation and the absence of effective population-based screening. Fertility-sparing treatment is therefore limited to carefully selected patients, typically young women with early-stage disease and favourable histological subtypes. According to guidelines from the National Comprehensive Cancer Network (NCCN) and the European Society of Gynaecological Oncology (ESGO), fertility-sparing surgery (FSS) may be considered in stage IA–IC, grade 1–2 epithelial ovarian cancers of serous, mucinous, or endometrioid histology, as well as in borderline ovarian tumours (BOTs) [36–40]. The selection criteria for fertility-sparing management based on tumour type and stage are summarised in Table 3 [41–47].

Women with germ cell and borderline ovarian tumours are generally considered good candidates for fertility-sparing management, as reproductive outcomes are often favourable. Evidence suggests high pregnancy rates following treatment for malignant ovarian germ cell tumours, with a low risk of premature ovarian insufficiency [43]. Fertility-sparing surgery is also considered safe in selected patients with early-stage granulosa cell tumours, whereas outcomes in Sertoli–Leydig cell tumours appear more limited [42,44,48]. However,

long-term oncological outcomes vary according to tumour type and stage, highlighting the importance of careful patient selection, counselling, and follow-up [49,50].

Table 3. Favourable selection criteria for consideration of fertility sparing management based on the type and the stage of ovarian tumours.

Epithelial Ovarian Cancer		
Borderline ovarian tumours		• All stages (if non-invasive implants confirmed)
Ovarian serous carcinoma	Low-grade	• Stage IA and C1 • Selected Stage IC2
	High-grade	• Stage IA in high grade serous carcinoma • Selected Stage IC1 and IC2
Mucinous ovarian carcinoma	Expansile subtype	• Stage IA, IC1 and IC2 • Selected Stage IC3
	Infiltrative subtype	• Stage IA • Selected Stage IC1 and IC2
Endometrioid Ovarian carcinoma	Low-grade	• Stage IA and IC1 in low grade tumour • Selected Stage IC2
	High-grade	• Stage IA • Selected Stage IC1 and IC2
Clear cell Ovarian carcinoma		• Stage IA and IC1 • Selected Stage IC2
Non-Epithelial		
Ovarian Sex cord-stromal tumours		
Granulosa cell tumour		• Stage IA and IC1 • Selected Stage IC2 and IC3
Sertoli-Leydig cell tumour		• Stage IA (in well and moderately differentiated tumours) • Selected Stage IC1
Germ cell ovarian tumours		
Dysgerminoma		• All stages
Immature ovarian teratoma		• All stages
Yolk sac tumour		• All stages

Evidence on reproductive outcomes in epithelial ovarian cancer (EOC) remains limited. While fertility-sparing surgery may be considered in selected patients with early-stage disease, reported outcomes vary across studies [45,46,51,52]. Most available data are derived from retrospective analyses with heterogeneous patient populations and treatment approaches [46]. Fertility-sparing surgery is not recommended in advanced-stage disease (stage II–IV), where it is associated with inferior oncological outcomes [53–55]. In such cases, standard management includes cytoreductive surgery followed by adjuvant therapy [41,47]. Fertility preservation options such as oocyte or embryo cryopreservation should be discussed prior to treatment initiation, ideally within a multidisciplinary set-

ting [56]. Overall, the current evidence base is largely retrospective and characterised by heterogeneous patient selection, which limits the strength of conclusions.

Fertility-preservation counselling should also be offered to women with hereditary predispositions to gynaecological malignancies, including those with BRCA mutations and Lynch syndrome. These patients often face complex decisions regarding the timing of risk-reducing surgery, such as prophylactic salpingo-oophorectomy, which may significantly impact reproductive potential. Counselling should therefore address disease risk, optimal timing of surgical intervention, and implications for family planning. In addition, the potential transmission of pathogenic variants to offspring should be considered, and discussion of preconception and preimplantation genetic testing is essential to support informed reproductive choices [57,58]. The key criteria and reproductive outcomes for fertility-sparing management of ovarian tumours are summarised in Table 4.

Table 4. Fertility-sparing treatment considerations and supporting evidence in ovarian.

Fertility-Sparing considerations in Ovarian Cancer			
Approach	**Indication**	**Key Consideration**	**Evidence Level**
USO	Borderline tumours; selected early-stage epithelial ovarian cancer	Standard fertility-sparing surgical approach	Retrospective studies [41,45,46,51,52]
Cystectomy	Selected borderline ovarian tumours	Higher recurrence risk compared to USO	Retrospective studies [45,51,52]
FSS for MOGCTs	All stages	High cure rates and favourable reproductive outcomes	Systematic reviews [43]
FSS for BOT	All stages (selected cases)	Good reproductive outcomes; recurrence risk varies	Retrospective studies [45,51,52]
FSS for early-stage epithelial ovarian cancers	Early-stage disease (IA–IC, selected cases)	Outcomes variable; careful selection required	Meta-analyses [46]
FSS for sex cord-stromal tumours (granulosa, Sertoli–Leydig)	Early-stage disease	Outcomes depend on subtype	Small retrospective studies [42,44,48]

USO: Unilateral Salpingo-Oophorectomy; BOT: Borderline Ovarian Tumour; FSS: Fertility-Sparing Surgery; MOGCTs: Malignant Germ Cell Tumours.

3.3. Cervical Cancer

Cervical cancer is the fourth most common malignancy in women worldwide and remains a major global health challenge. It is the leading gynaecological cancer in many low- and middle-income countries and ranks second globally in both incidence and mortality [59]. By 2025, approximately 13,360 new cases and 4320 deaths are projected annually [59]. Notably, around 40% of cases occur in women under 45 years of age, many of whom express a desire for fertility preservation [60]. As a result, fertility-sparing surgery (FSS) has become an important option in carefully selected patients. The principal fertility-preserving procedure is radical trachelectomy, which may be performed via abdominal, vaginal, laparoscopic, or robotic-assisted approaches [61–63].

For women with stage IA1 disease without lymphovascular space invasion (LVSI), cervical conisation or simple trachelectomy with negative margins is generally sufficient [64]. Patients with stage IA2 or small ($\leq$2 cm) stage IB1 tumours without high-risk features may be candidates for radical trachelectomy with pelvic lymphadenectomy [65,66]. ESGO guidelines emphasise the importance of comprehensive preoperative assessment, includ-

ing magnetic resonance imaging (MRI) to evaluate tumour size and exclude parametrial involvement [67]. MRI remains the preferred modality for local staging, while positron emission tomography–computed tomography (PET–CT) may be useful in selected cases, particularly for detecting nodal or distant disease [62].

Oncological outcomes following fertility-sparing surgery for early-stage cervical cancer are generally favourable, although available data are largely derived from retrospective studies [62,65]. Reproductive outcomes are also encouraging; however, reported rates vary across studies and may be influenced by patient selection [68,69]. Women remain at increased risk of second-trimester miscarriage and preterm birth, likely due to cervical insufficiency following trachelectomy [70]. Cervical cerclage and close obstetric surveillance are therefore recommended in subsequent pregnancies. It should be noted that most outcome data are based on women actively attempting conception and may therefore overestimate overall reproductive success [71]. It should be noted that much of the available evidence is based on retrospective data, and prospective studies remain limited.

Fertility-sparing management is not recommended in patients with tumours > 2 cm, high-risk histological subtypes, or advanced-stage disease, as oncological outcomes are significantly compromised in these settings [71,72]. In such cases, radical surgery or definitive chemoradiotherapy remains the standard of care. The main criteria and treatment options for fertility-sparing management in cervical cancer are summarised in Table 5.

Table 5. Fertility-sparing treatment options and supporting evidence in cervical cancer.

Fertility-Sparing Methods in Cervical Cancer			
Approach	**Indication**	**Key Consideration**	**Evidence Level**
Cervical conisation	Stage IA1 without LVSI	Requires negative margins	Retrospective studies [64]
Simple trachelectomy	Stage IA1 (selected cases)	Option when margins are clear	Retrospective studies [64]
Radical trachelectomy (abdominal, vaginal, laparoscopic, robotic assisted)	Stage IA2 and $\leq$2 cm stage IB1 tumours	Requires pelvic lymphadenectomy; increased obstetric risks	Retrospective studies and systematic reviews [61–63,65,66]

LVSI: Lymphovascular Space Invasion.

3.4. Psychological and Social Implications of Cancer-Associated Infertility

The threat of infertility resulting from cancer, or its treatment imposes a significant psychological burden on women of reproductive age [72]. Young survivors may experience grief, emotional distress, and a sense of identity loss. Fertility, often closely tied to personal aspirations and societal expectations, becomes a central concern for many women diagnosed during their reproductive years [73]. The resulting stigmatisation, low self-esteem, and depression may also negatively affect sexual health and function [74]. Despite the availability of effective fertility-preservation strategies, many patients do not receive timely counselling. Missed opportunities are frequently attributed to inadequate referral pathways, limited interdisciplinary collaboration, or time constraints prior to the initiation of treatment. Addressing this gap requires a multidisciplinary team (MDT) approach that integrates oncologists, reproductive endocrinologists, psychologists, and patient navigators to ensure comprehensive care [75].

3.5. Fertility Preservation Modalities

Fertility preservation modalities have advanced considerably in recent years, offering women with gynaecological malignancies the opportunity to pursue parenthood following cancer treatment. The principal approaches include oocyte and embryo cryopreservation,

ovarian tissue cryopreservation, ovarian suppression with gonadotropin-releasing hormone (GnRH) analogues, and conservative surgical interventions [76].

3.5.1. Embryo Cryopreservation

Embryo cryopreservation remains the most validated and widely adopted fertility-preservation strategy for women undergoing gonadotoxic therapy. The process involves controlled ovarian stimulation, oocyte retrieval, and in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI), followed by cryogenic storage of the resulting embryos [77]. This method is primarily applicable to post-pubertal women with a male partner or those electing to use donor sperm. Reported live birth rates per thawed embryo transfer cycle range from 22% to 45%, depending on maternal age and embryo quality [78].

The principal strengths of embryo cryopreservation lie in its well-established efficacy, standardisation, and broad availability in reproductive medicine centres. However, several limitations must be considered. Completion of ovarian stimulation requires a 10–14-day delay, which may not be feasible for patients requiring urgent initiation of oncological treatment [79]. Ethical, moral, or religious objections to embryo storage may also restrict its acceptability for some women. In addition, for patients with hormone-sensitive malignancies, elevated oestrogen levels during stimulation may increase oncological risk. The concurrent use of aromatase inhibitors, such as letrozole, within stimulation protocols has been shown to reduce oestrogen exposure and mitigate this risk [80,81].

3.5.2. Oocyte Cryopreservation

Oocyte cryopreservation is a key fertility-preservation strategy, particularly for single women or for those declining embryo storage for personal, ethical, or religious reasons [82]. The introduction of vitrification has markedly improved outcomes, with post-thaw oocyte survival rates now exceeding 90% and fertilisation rates comparable to those of fresh oocytes [83]. In a study by Martinez et al. [84], fertilisation rates reached 76.6%, with an average of 1.8 ± 0.7 embryos transferred per patient among 11 women with malignancies; four achieved full-term live births without adverse perinatal events. Similarly, Alvarez et al. [85] reported the first successful live birth following oocyte cryopreservation in a patient with invasive ovarian carcinoma.

This approach enhances reproductive autonomy while avoiding the ethical and legal complexities of embryo freezing. However, as with embryo cryopreservation, a controlled ovarian stimulation phase of approximately 10–14 days is required [86]. For patients with hormone-sensitive tumours, such as breast cancer, stimulation protocols incorporating gonadotropin-releasing hormone (GnRH) antagonists and aromatase inhibitors have been shown to reduce oestrogen exposure. Despite these adaptations, oocyte cryopreservation may not be feasible for patients requiring immediate initiation of cancer treatment, and success rates may be lower in women with diminished ovarian reserve [87].

3.5.3. Ovarian Tissue Cryopreservation and Transplantation

Ovarian tissue cryopreservation (OTC) and subsequent transplantation have become established fertility-preservation options, particularly for patients who are not suitable candidates for oocyte or embryo cryopreservation [88]. Increasing evidence supports both their efficacy and safety, with the additional advantage of restoring endocrine function. OTC is now included in clinical practice guidelines, including those from the American Society for Reproductive Medicine (ASRM) and the American Society of Clinical Oncology (ASCO) [75,89], although access remains limited to specialised centres.

OTC is particularly relevant for prepubertal girls, patients requiring urgent gonadotoxic treatment, and those with contraindications to ovarian stimulation, such as oestrogen-sensitive tumours. It may also be considered in women with reduced ovarian reserve or

when oocyte retrieval is not feasible [90]. Current recommendations suggest offering OTC to selected patients, particularly those under 35–38 years of age and those undergoing treatment for haematological malignancies or paediatric cancers [91].

The procedure involves laparoscopic retrieval of ovarian cortical tissue, which is then cryopreserved using either slow freezing or vitrification [92,93]. Following completion of cancer treatment and confirmation of remission, tissue transplantation is usually performed orthotopically, although heterotopic approaches may be considered in selected cases [94–97]. Restoration of ovarian function generally occurs within 3–6 months after transplantation [98].

Clinical outcomes are summarised in Table 6. Overall, available data are encouraging, with restoration of ovarian function and increasing numbers of pregnancies and live births reported. Outcomes appear more favourable in patients who undergo cryopreservation at a younger age, and a considerable proportion of pregnancies occur spontaneously [56,94,95,99].

Table 6. Clinical outcomes following ovarian tissue cryopreservation and transplantation.

Outcome	Reported Findings	Key Consideration	References
Restoration of ovarian function	Frequently achieved in a substantial proportion of patients	Typically occurs within 3–6 months following transplantation	[98,100]
Clinical pregnancy rate	35–44%	Higher in patients undergoing cryopreservation at younger age (<35 years)	[56,95,99]
Live birth rate	26–32.3%	Variable depending on patient selection and follow-up duration	[56,94,95]
Mode of conception	51–69% spontaneous pregnancies	Reflects restoration of endocrine and ovarian function	[95]
Duration of graft function	Up to >10 years reported in selected cases	May require repeated or sequential transplantation	[92,100,101]
Perinatal outcomes	No significant increase in congenital anomalies reported	Limited long-term data; outcomes generally comparable to general population	[100]

A key limitation of OTC is follicular loss during the initial post-transplant period due to ischaemia, which can significantly reduce follicle survival before revascularisation occurs [102]. Another important concern is the potential risk of reintroducing malignant cells, particularly in haematological malignancies where ovarian involvement may be present [103]. In contrast, this risk appears lower in early-stage solid tumours, including cervical, borderline ovarian, and endometrial cancers [104].

OTC offers several advantages over other fertility-preservation methods, including the restoration of endocrine function and the possibility of spontaneous conception. Importantly, it does not require ovarian stimulation and therefore avoids delaying cancer treatment [94,105,106]. However, the technique requires surgical intervention and may involve more than one procedure. Its use also remains limited by restricted availability, variable expertise, and the need for further long-term outcome data [107].

Emerging approaches, including artificial ovaries, in vitro folliculogenesis, and improved tissue screening techniques, are being explored to improve both safety and efficacy. As experience grows, OTC is increasingly recognised as an important component of oncofertility care [98,108].

3.5.4. Oocyte In Vitro Maturation (IVM)

In vitro maturation (IVM) offers a stimulation-free approach in which immature oocytes are retrieved and subsequently matured in vitro. This technique is particularly valuable for patients requiring urgent initiation of chemotherapy or for those unable to undergo standard ovarian stimulation, including adolescents with an immature hypothalamic–pituitary–gonadal axis [109]. While IVM reduces treatment delays, it is associated with lower success rates compared with conventional IVF, due to challenges in oocyte cryopreservation and reduced fertilisation efficiency. Consequently, IVM remains an investigational method reserved for selected clinical cases [110].

3.5.5. Primordial and Pre-Antral Follicle Culture

This experimental strategy aims to support the in vitro growth and maturation of early-stage follicles through all developmental stages to generate fertilised oocytes. It holds particular promise for prepubertal girls and for patients at high risk of ovarian cancer cell contamination. The technique requires a complex, multistep culture system designed to replicate the physiological follicular niche. Although significant progress has been made in animal models, particularly in rodents, clinical application in humans has not yet been achieved [111].

3.5.6. Uterine Transplantation

Uterine transplantation has emerged as a transformative option for women with absolute uterine factor infertility (AUFI), including cancer survivors who have undergone hysterectomy. The procedure involves transplantation of a uterus from a living or deceased donor into a recipient, followed by immunosuppressive therapy and the use of assisted reproductive techniques to achieve pregnancy [112]. Uterus transplantation remains investigational but has achieved clinical success, with more than 140 procedures performed worldwide and over 70 live births reported [113]. For gynaecological cancer survivors, uterine transplantation offers a pathway to gestational motherhood that would otherwise be impossible without surrogacy. However, its application in this subgroup remains rare, with only one live birth in a cancer survivor reported to date [114].

Selection criteria for uterine transplantation are stringent: candidates must be in remission for at least five years, be under 40 years of age, and have cryopreserved embryos available [115]. The procedure carries significant risks, including surgical complications such as thrombosis, fistula formation, and ureteric injury, as well as rejection episodes and long-term side effects associated with immunosuppressive therapy. In addition, the use of immunosuppression during pregnancy raises concerns regarding foetal exposure and potential long-term consequences [116].

Despite these challenges, uterine transplantation offers unique psychosocial and reproductive benefits. It enables gestation, fostering maternal bonding and alleviating the psychological burden associated with surrogacy or adoption [117]. As surgical techniques advance and ethical frameworks continue to evolve, uterine transplantation may become a more widely accepted option for carefully selected cancer survivors, particularly those with pre-treatment embryo cryopreservation and no contraindications to immunosuppression [118].

3.6. The Use of Artificial Intelligence in Infertility

Artificial intelligence (AI) is an emerging tool in reproductive medicine with potential to enhance fertility preservation for patients with gynaecological malignancies. In this context, AI applications may help optimise ovarian stimulation protocols to reduce treatment

delays and improve oocyte yield, which is particularly important when time before cancer therapy is limited [119–123].

AI-driven models can assist in predicting ovarian response and individualising stimulation regimens, thereby improving efficiency and minimising risks such as ovarian hyperstimulation syndrome. This is especially relevant in oncofertility, where the need for rapid initiation of cancer treatment often constrains fertility preservation options [124–127].

AI also shows promise in improving embryo and gamete selection by providing more objective assessments, which may enhance assisted reproductive technology outcomes following cancer treatment. However, most current evidence is derived from general infertility populations, and data specific to patients with gynaecological malignancies remain limited [128–133].

Future applications may include AI-based risk stratification tools to predict treatment-related gonadotoxicity and long-term reproductive outcomes, allowing more tailored fertility preservation counselling. Ethical considerations, including data bias, transparency, and patient privacy, must also be addressed before wider clinical implementation [134–139]. Overall, AI represents a promising area for future development in oncofertility, although further validation in cancer-specific populations is required before routine clinical use.

3.6.1. Gamete Selection

Oocyte Selection

Wang et al. (2019) reported that reproductive success, whether spontaneous or assisted, is strongly influenced by oocyte quality [122]. At present, the estimated pregnancy rate per retrieved oocyte is only ~4.5% [123]. AI-based oocyte selection in IVF has the potential to improve outcomes by reducing reliance on subjective morphological assessment, which is constrained by inter-observer variability and limited predictive accuracy.

Image-based machine learning algorithms can extract subtle morphological and dynamic features not readily discernible to the human eye, thereby standardising and enhancing oocyte quality assessment [140]. Early studies suggest that AI can improve predictive accuracy for oocyte maturation and fertilisation outcomes by analysing parameters such as cytoplasmic granularity, zona pellucida thickness, and spindle morphology [119]. Cavalera et al. (2018), for instance, applied particle image velocimetry (PIV) combined with a feed-forward neural network to analyse cytoplasmic movements in mouse oocytes, achieving 91% accuracy in distinguishing competent from incompetent oocytes [132].

Despite these promising results, current AI models face important limitations. Many are trained on relatively small, single-centre datasets, raising concerns about generalisability and algorithmic bias [141]. Furthermore, most lack interpretability, producing predictions without transparent reasoning. This "black box" nature reduces clinician confidence and presents barriers to clinical adoption [133]. While AI holds promise for standardising oocyte evaluation, it should be regarded as an adjunct to, rather than a replacement for, clinical judgement. Progress in this field will require large-scale, multicentre trials and the development of explainable AI frameworks to ensure safe, equitable, and reproducible implementation in reproductive medicine.

Sperm Selection

AI is also being applied to sperm analysis, aiming to overcome the subjectivity of manual assessment and the limited reproducibility of computer-assisted sperm analysis (CASA) [129]. Deep learning models have demonstrated superior accuracy in identifying high-quality sperm compared with conventional methods [130]. For example, Sato et al. (2022) reported a YOLOv3-based system that improved consistency in sperm selection during intracytoplasmic sperm injection (ICSI) [128]. These advances may be particularly

valuable for male cancer survivors seeking fertility care, where optimising sperm selection is critical to improving ART outcomes.

3.6.2. Embryo Selection

Embryo selection is central to ART success but remains largely subjective, relying on morphological assessment by embryologists. AI, particularly deep learning, offers greater precision by integrating time-lapse imaging and genetic data to predict implantation potential [140]. These models can quantify dynamic parameters such as cleavage timing and blastocyst expansion, linking them with implantation and live birth outcomes [131]. Olawade et al. (2025) reviewed AI systems using deep learning, showing improved accuracy over traditional methods in predicting implantation from time-lapse imaging [125]. These approaches may improve prediction of embryo viability and implantation outcomes. Diakiw et al. (2022) also demonstrated that deep learning could predict embryo euploidy with moderate accuracy from blastocyst images, highlighting the potential for non-invasive AI-based genetic screening in IVF [135].

Despite advances, the clinical value of AI-assisted embryo selection remains unproven, with no prospective trials showing improved live birth rates [141]. In a recent double-blind randomised controlled trial, Illingworth et al. (2024) reported no significant difference between AI-based and morphology-based selection (Nature Medicine) [136].

3.6.3. Ethical Considerations

Transparency and Explainability

The use of AI in infertility care must align with the ethical principles of beneficence, non-maleficence, autonomy, and justice, yet its implications require scrutiny. A key concern is transparency: many models function as "black boxes," generating outputs without clear reasoning, which undermines clinician trust and limits adoption [133]. In reproductive medicine—where decisions such as embryo selection carry profound emotional and moral weight—it is essential that both patients and clinicians understand how AI contributes to outcomes.

Bias, Privacy, and Clinical Judgement

Ethical challenges also include data privacy, patient consent, and bias arising from small or non-representative datasets, which limit generalisability and risk reinforcing socioeconomic and racial disparities [120,121,134,137,139]. Over-reliance on algorithmic recommendations could further undermine clinical judgement, particularly in complex cases. At present, AI should therefore be viewed as a tool to complement, not replace, expert decision-making.

Regulation, Commercialisation, and Accountability

Regulatory oversight in reproductive medicine remains limited, and algorithm-driven gamete selection raises concerns regarding eugenics and fairness. Priorities for future research include large multicentre validation trials and the development of explainable AI to ensure clinical reliability and equity [142]. Commercialisation adds further complexity, as many proprietary tools restrict peer review, prioritise profit over patient welfare, and leave accountability unclear when adverse outcomes occur—whether responsibility lies with the developer, clinician, or healthcare organisation remains unresolved [143].

Despite advances in fertility preservation, several challenges remain in clinical practice. Access to specialised oncofertility services varies widely, with clear regional disparities and limited availability in low- and middle-income countries. The cost of procedures such as cryopreservation and assisted reproduction can also be a significant barrier, particularly

where public funding is limited or absent. In addition, the need to make decisions soon after a cancer diagnosis may limit the opportunity for thorough counselling and timely referral.

More broadly, the use of advanced techniques, including ovarian tissue cryopreservation and newer technologies, is often dependent on local expertise, infrastructure, and regulatory frameworks, which are not uniformly available. These limitations, together with ongoing uncertainties around long-term outcomes and cost-effectiveness, highlight the need for a more realistic integration of fertility preservation into routine cancer care. Efforts to improve accessibility, resource allocation, and equitable delivery of these services remain essential.

4. Conclusions

Fertility-sparing treatment represents a safe and feasible option for appropriately selected patients with gynaecological malignancies. Success depends on clearly defined oncological criteria, early referral to fertility specialists, and multidisciplinary collaboration across oncology, pathology, radiology, and reproductive medicine. Alongside established strategies such as embryo and oocyte cryopreservation, ovarian tissue cryopreservation has emerged as a promising modality, particularly for young patients and those requiring urgent treatment. Assisted reproductive technologies continue to evolve, and artificial intelligence may further enhance personalisation of care, embryo selection, and treatment outcomes. Nevertheless, important challenges remain, including limited long-term data, risks of recurrence, ethical considerations, and unequal access to fertility-preservation services. Continued innovation, rigorous clinical validation, and careful oversight will be essential to translate advances into safe, effective, and patient-centred care. AI offers promising applications in reproductive medicine, particularly in optimising stimulation protocols and embryo selection, but its clinical role remains experimental and requires further validation. For now, AI should be regarded as a supportive tool that complements, rather than replaces, clinical expertise.

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