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INVITED ARTICLE

An Update on Fertility Preservation From the Asian Society for Fertility Preservation

Volkan Turan[1] | Mohd Faizal Bin Ahmad[2] | Wen Di[3] | Debra Gook[4] | Nalini Kaul[5] | Seok Hyun Kim[6] | Jennifer Ko[7] | Thi Minh Chau Le[8] | Jung Ryeol Lee[6,9] | Wen Li[10] | Joyce Mathew[11] | Virgilio Novero[12] | Porntip Sirayapiwat[13] | Nao Suzuki[14] | Chii-Ruey Tzeng[15] | Budi Wiweko[16] | Takai Yasushi[17] | Ozgur Oktem[18]

[1]Department of Obstetrics and Gynecology, Istanbul Health and Technology University School of Medicine, Istanbul, Turkey | [2]Department of Obstetrics & Gynaecology, National University of Malaysia, Kuala Lumpur, Malaysia | [3]Department of Obstetrics and Gynecology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China | [4]Reproductive Services, Royal Women's Hospital, and University of Melbourne Department of Obstetrics and Gynaecology, Melbourne, Australia | [5]Mother and Child Hospital, New Delhi, India | [6]Seoul National University College of Medicine, Seoul, Republic of Korea | [7]Department of Obstetrics and Gynecology, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, China | [8]Tu Du Hospital, Ho Chi Minh City, Vietnam | [9]Seoul National University Bundang Hospital, Seoul, Republic of Korea | [10]The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China | [11]Department of Obstetrics and Gynecology, National University Hospital, Kent Ridge, Singapore | [12]Section of Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Philippines Manila, Manila, Philippines | [13]Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand | [14]St Marianna University School of Medicine, Kawasaki, Japan | [15]Taipei Medical University, Taipei City, Taiwan | [16]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia | [17]Department of Obstetrics and Gynecology, Saitama Medical University, Saitama, Japan | [18]Department of Obstetrics and Gynecology, Istanbul Koc University School of Medicine, Istanbul, Turkey

Correspondence: Volkan Turan (volkanturan@yahoo.com)

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ABSTRACT

Fertility preservation (FP) is a rapidly expanding field in reproductive medicine with still limited data on outcomes. FP aims to protect the fertility of children, women, and men who face the potential risk of fertility loss for various medical conditions, including but not limited to cancer and its gonadotoxic treatment forms. Therefore, it is crucial to provide evidence-based recommendations to assist health professionals in discussing FP options. Our aim was to provide a guideline for multidisciplinary medical staff in considering the availability of FP options and to help them decide whether to provide FP. The objective of any FP intervention is to minimize or eliminate primary disease burden and to ensure the maintenance or preserving reproductive health. Therefore, people who are at risk of losing fertility should be evaluated for and counseled about future reproductive risks. Embryo, oocyte, and ovarian tissue cryopreservation are the established FP options in adult females, with ovarian tissue cryopreservation the only option for prepubertal girls. A wide range of variables affect the choice of the FP strategy. These include age and ovarian reserve of women, the time available before the initiation of cancer treatment, pubertal status, and cancer type and stage. In males, sperm cryopreservation is a highly effective method in adolescent and adult males, while testicular tissue cryopreservation, which is experimental, is the only available option for prepubertal males. This review addressed the important clinical questions and provided answers for FP in females, males, and children according to the indications and availability of FP.

1 | Purpose

The purpose of this review is to provide evidence-based information regarding the indications of fertility preservation for women, men, and children, and to outline the available options for these candidates.

2 | Methodology

The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Figure 1).

We searched the published articles in PubMed up to January 2026 containing key words "fertility preservation," "controlled ovarian hyperstimulation," (COH) "embryo cryopreservation," "cancer," "frozen embryo transfer," "pregnancy outcome," "live birth," "chemotherapy," "radiotherapy," "oocyte cryopreservation," "ovarian tissue cryopreservation," "sperm cryopreservation," "children," "BRCA," and "ovarian reserve." We excluded abstracts, editorials, commentaries, case reports, and case series with fewer than 10 participants, letters, experimental studies in animals, or conference proceedings because the data are usually difficult to assess. Systematic reviews, randomized clinical trials (RCTs), prospective or retrospective cohort studies, and case–control studies were included. The search was limited to full-length manuscripts published in English in peer-reviewed journals. The data were extracted by two reviewers independently (V.T. and O.O.) All recommendations in this review were based on data from the available literature, mostly RCTs, which were the mainstay to achieve evidence in clinical research, and were developed by expert consensus. Each recommendation was listed, and authors were asked to consider whether they agreed or disagreed, and disagreements were solved by discussion with the working group.

3 | Adult Women

3.1 | Target Group

- *Cancer patients*: Before receiving gonadotoxic chemotherapy regimens and pelvic radiotherapy [1, 2].
- *Before ovarian surgery*: For conditions such as benign and malignant tumors of the ovary, and endometriosis.
- *Low ovarian reserve*: Defined as anti-Mullerian hormone levels <1.5 ng/mL regardless of age or advanced maternal age (>40 years) with a normal anti-Mullerian hormone level.
- Family history of early menopause
- *Genetic factors*: Turner's syndrome, FMR-1 gene mutation, galactosemia, and *BRCA* mutation carriers.
- *Systemic connective tissue disorders*: Systemic lupus erythematosus and other autoimmune diseases requiring cytotoxic chemotherapy agents for immune suppression.

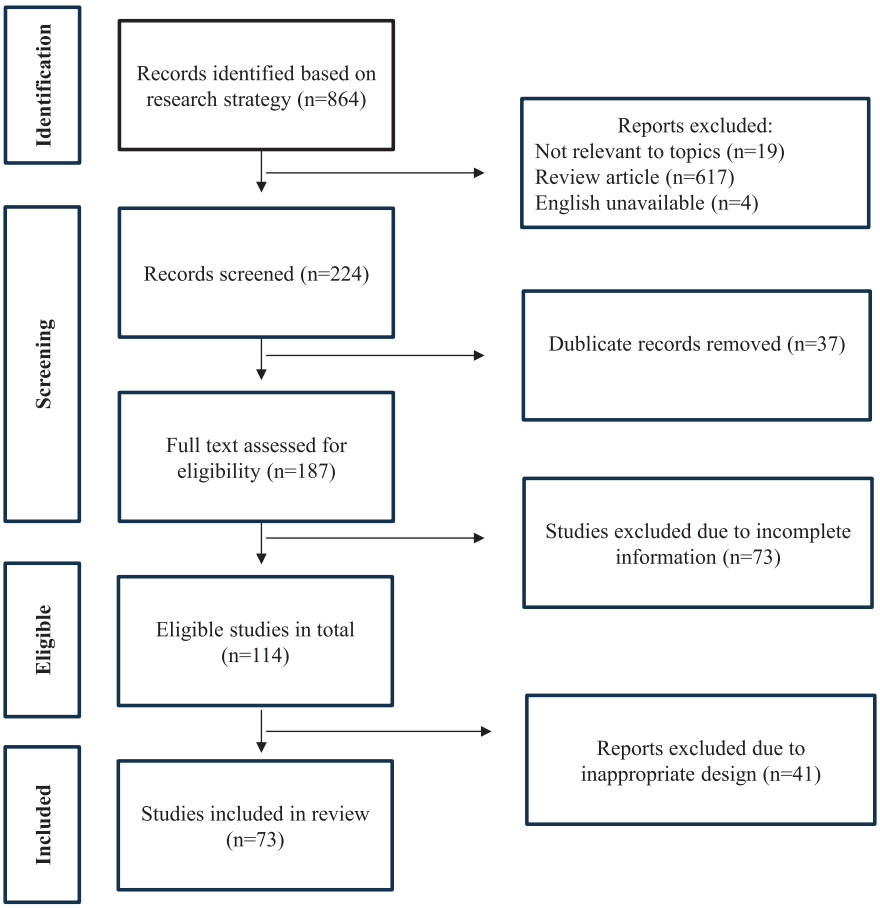

FIGURE 1 | Study selection and inclusion process for the review.

- *Hematopoietic stem cell transplantation (HSCT)*: Diseases requiring high-dose chemotherapy and/or radiation therapy for myeloablation, such as thalassemia, sickle cell anemia, or Fanconi anemia.
- *Social reasons*: Elective fertility preservation for women who postpone childbearing for various reasons.
- For transgender patients who wish to preserve fertility before transitioning.

Effects of chemotherapy agents and radiotherapy on gonads [3, 4] are shown in Tables 1 and 2.

3.1.1 | Target Users of the Review

This review is aimed at multidisciplinary healthcare professionals who are involved in information provision and decision-making with women who are scheduled to undergo gonadotoxic treatments and those considering fertility preservation for other reasons. This includes gynecologists, medical oncologists, hematologists, pediatricians (specialized in genetics, endocrinology, oncology, rheumatology, and hematology), radiation oncologists, general surgeons, urologists, paramedical and reproductive biologists (including embryologists), and geneticists [5].

TABLE 1 | Effects of chemotherapy agents on gonads.

Gonadotoxicity level	Chemotherapy agents
High	Alkylating agents[a] (cyclophosphamide,[b] busulfan > 500 mg/m^2, chlorambucil > 300 mg/m^2, melphalan > 100 mg/m^2, procarbazine > 5 mg/m^2, ifosfamide > 16 g/m^2)
Moderate	Anthracyclines (doxorubicin, daunorubicin), platinum derivatives (cisplatin, carboplatin)
Low	Antimetabolites (methotrexate, 5-fluorouracil), vinca alkaloids (vinblastine, vincristine)
Very low/none	Imatinib, tamoxifen
Unknown	Monoclonal antibodies, immune checkpoint inhibitors, and PARP inhibitors

[a]Dose is based on the cyclophosphamide equivalent dose.
[b]Age younger than 20 years with total cumulative dose greater than 7.5 g/m^2 or age older than 40 years with total cumulative dose greater than 5 g/m^2.

3.1.2 | Review Scope

The field of fertility preservation has rapidly expanded in the last two decades as a consequence of the increasing recognition of the importance of loss of fertility after treatment for cancer and other serious diseases. There has been a widespread provision of fertility preservation strategies for many women and young girls, along with ever-improving success rates of enabling technologies of oocyte/embryo vitrification and ovarian tissue cryopreservation. Rapid development of the fertility preservation field in daily clinical practice, together with limited data on outcomes, has led to the preparation of an evidence-based guideline of fertility preservation in females and males for healthcare professionals.

Clinicians should provide up-to-date information to patients at initial consultation for the following issues:

1. Impact of cancer, other diseases, and their treatment modalities on reproductive functioning and fertility.
2. Available options to preserve fertility.
3. Treatment options post-cancer treatment for infertility.
4. Follow-up post cryopreservation and fertility preservation.
5. Risk associated with pregnancy after cytotoxic treatments.
6. Other options for childbearing and parenting.

3.2 | Recommendations

1. Embryo cryopreservation:
   - Well-established fertility preservation option with the highest success rate (see Table 3).

TABLE 2 | Effects of radiotherapy on gonads.

Radiation dose (gray)	Effect on ovaries	Radiation dose (gray)	Effect on testes
≤ 0.6	No effect	0.1	Spermatogenesis disruption
≤ 1.5	No effect under 40 years of age	0.65	Oligo-azoospermia
2	50% reduction in follicular pool	1.2	Permanent oligo-azoospermia
2.5–5.0	60% risk of premature ovarian failure	20	Leydig cell dysfunction
20.3	Effective sterilization dose (age 0)		
18.4	Effective sterilization dose (age 10)		
16.5	Effective sterilization dose (age 20)		
14.3	Effective sterilization dose (age 30)		
6.0	Effective sterilization dose (age 40)		

TABLE 3 | Advantages and disadvantages of fertility preservation methods.

Method	Advantages	Disadvantages
Embryo cryopreservation	Reliable, long-established, ~100% embryo survival rate	Requires stable partner/donor sperm, 2-week COH period
Oocyte cryopreservation	Does not require marriage/donor sperm	Requires experienced centers (60%–90% oocyte survival rate), 2-week COH period
Ovarian tissue cryopreservation	Enables freezing multiple follicles simultaneously; does not require ovarian stimulation; restores hormonal function posttransplantation	Requires surgery; follicular loss due to ischemic damage; risk of transplanting metastatic cells in cancer cases
GnRH analog suppression	Easy to administer	Conflicting outcomes; not a primary method for fertility preservation
Ovarian transposition	Protects against pelvic radiation-induced failure	Requires surgery; does not guarantee full protection from radiation scatter
Sperm cryopreservation	Simple and cost-effective	Not applicable for prepubertal boys
Testicular tissue cryopreservation	Only option for prepubertal boys	Requires surgery; experimental

Abbreviation: COH, controlled ovarian hyperstimulation.

- Women should be informed about the risk of losing reproductive autonomy and possible legal issues with ownership of cryopreserved embryos.
- Women should be informed of the attrition from oocyte to embryos that are appropriate for cryopreservation.
- Women should be informed that there is no guarantee of a pregnancy from their cryopreserved embryos.
- In some countries, there is an imposed time limit for the use of embryos.

2. Oocyte cryopreservation:
   - This is a well-established fertility preservation option [6].
   - It is an option for single women and those who do not wish to use donor/partner sperm.
   - Married women may opt to have their oocytes frozen without inseminating them with their partner's sperm due to legal issues with ownership of cryopreserved embryos.
   - Women with a partner should be offered the option to cryopreserve oocytes or to split the oocytes to attempt both embryo and oocyte cryopreservation.
   - Women should be informed of the attrition associated with oocyte cryopreservation.
   - Women should be informed that there is no guarantee of a pregnancy from their cryopreserved oocytes.
   - In some countries, there is an imposed time limit for the usage of oocytes.

- For both embryo and oocyte cryopreservation:
  - A COH process of approximately 2 weeks is required. Early referral is crucial to avoid delays in cancer treatment.
  - Early referral allows for consecutive stimulations, enabling the collection of more oocytes and embryos safely [7].
  - Flexible protocols have been developed for oocyte retrieval (random start ovarian hyperstimulation). Controlled ovarian stimulation can now be initiated randomly anytime during the follicular or luteal phase, regardless of the cycle day. This reduces treatment delays and achieves cycle and pregnancy outcomes comparable to conventional protocols [8].
  - Estrogen-sensitive cancers (e.g., breast and endometrial cancer):
    - These patients may have high estrogen levels during ovarian stimulation, potentially increasing the risk of recurrence.
    - Using tamoxifen (a selective estrogen receptor modulator) or aromatase inhibitors during stimulation is recommended in most countries [9, 10]. Combining letrozole (an aromatase inhibitor) or tamoxifen with gonadotropins in breast cancer patients yields similar cycle outcomes without increasing recurrence rates [9, 10].
    - However, caution should be exercised when using tamoxifen with gonadotropins because the teratogenic and genotoxic potential of this drug has been shown in animal studies, although no human data is available [11, 12].
    - Although still limited, available data did not show an increase in the post-pregnancy recurrence rates of breast cancer in women who underwent COH regardless of estrogen receptor and *BRCA* mutation status [13–15].
    - To minimize the risk of ovarian hyperstimulation syndrome, gonadotropin-releasing hormone (GnRH) antagonist protocols and triggering of final maturation with a GnRH agonist should be considered.
  - Post-cancer therapy:
    - Pregnancy is not recommended within the first 6 months due to potential adverse effects on the fetus.
    - Although no evidence suggests pregnancies within 2 years increase cancer risk, waiting 24 months may reduce recurrence risk. Discussing with the oncology team regarding the pregnancy plan and optimal time is strongly recommended.
    - Chemotherapy is not recommended before 14 weeks of pregnancy as it can harm the developing baby or cause a miscarriage [16].

- Pregnancy after breast cancer seems to be safe regardless of *BRCA* mutation and estrogen receptor status [17, 18].
- The recommended duration of contraception after completion of tamoxifen treatment has been extended from 2 to 9 months due to possible genotoxic effects of the drug [11, 12].

3. Ovarian transposition:
   - Ovarian transposition (oophoropexy) is recommended for patients requiring pelvic radiation therapy as part of cancer treatment.
   - Patients must be informed that scattered radiation may still affect the ovaries, and this technique is not always successful [19]. Other established fertility preservation methods, such as embryo, oocyte, or ovarian tissue cryopreservation, should be considered as alternative or additional options.
   - The procedure should be planned as close as possible to the time of radiotherapy to minimize ovarian displacement risks.
4. Conservative gynecological surgery:
   - Radical trachelectomy is recommended for cervical cancers limited to Stages 1A2–1B, with a tumor size smaller than 2 cm and invasion not exceeding 10 mm [20].
   - Cystectomy may be performed for early-stage ovarian cancers [21].
   - For other gynecological malignancies, less radical surgeries aimed at preserving reproductive organs are suggested, considering the grade and stage of the cancer.
   - Medical treatment should be recommended for women with endometrioid endometrial carcinoma with Grade 1, Stage 1A without myometrial invasion [22].
   - In any case where conservative treatment is being considered for gynecologic cancer, fertility preservation options such as embryo, oocyte, and ovarian tissue cryopreservation should also be considered, depending on the patient's individual situation.
5. Ovarian suppression:
   - The use of GnRH analogs or other ovarian suppression agents for fertility preservation is inconclusive [23, 24].
   - If proven fertility-preserving techniques cannot be applied, GnRH analogs may be considered to reduce the risk of chemotherapy-induced premature ovarian failure in young breast cancer patients [25].
   - However, these methods should never replace established fertility-preserving techniques such as embryo, oocyte, and ovarian tissue cryopreservation [2, 26, 27].
6. Ovarian tissue cryopreservation and transplantation:
   - This method was removed from the experimental category in 2019 and is an established fertility preservation option [28].
   - Currently, more than 200 live births have been reported through spontaneous or in vitro fertilization using this method [29].
   - Advantages:
     - Does not require ovarian stimulation, enabling rapid application.
     - Can be performed after chemotherapy, with current data suggesting no impact [30].
     - It is the only option available for prepubertal children in conjunction with oocyte in vitro maturation.
     - Restores endocrine function in addition to fertility.
     - Can, in some cases, allow for spontaneous conception when transplanted later.
   - Limitations:
     - Its safety is debated in cases such as ovarian tumors, leukemia, non-Hodgkin lymphoma, advanced cancers, and neuroblastoma due to the risk of micro-metastases [31, 32].
     - There is a risk of malignant contamination within the tissue [33].
     - Up to 50%–60% follicular loss occurs after transplantation of ovarian tissue due to ischemia before neovascularization develops [31].
     - Lack of standardization in the procedure
   - Ovarian tissue cryopreservation should be recommended based on the patient's age (≤36), ovarian reserve, and potential efficacy [2].
   - Previous chemotherapy or *BRCA* mutations are not contraindications. However, in *BRCA* mutation carriers, the tissue should be removed post-pregnancy [2, 26].

Advantages and disadvantages of fertility preservation methods and the flowchart for the management of these patients are presented in Table 3 and Figure 2, respectively.

7. Uterine transposition.

Uterine transposition can be considered for young females with pelvic cancer requiring pelvic radiotherapy [34]; however, it is an extensive surgical procedure requiring special training and experience, and further evaluation and prospective clinical trials are needed to confirm the effectiveness of this technique in preserving fertility.

4 | Adult Men

4.1 | Target Group

- *Cancer patients*: Before chemotherapy and radiotherapy treatments that may damage gonadal cells [35–38].
- *Before surgeries resulting in loss of reproductive function*: Such as testicular removal or surgeries for testicular tumors.
- *Low sperm count (cryptozoospermia)*: In cases where sperm is present in very limited amounts.
- *Systemic connective tissue disorders*: Requiring cytotoxic agents for treatment.
- *Genetic conditions*: Such as Klinefelter syndrome or cystic fibrosis.
- Transitioning males.

4.1.1 | Guidance for Target Group

Interdepartmental collaboration is essential to inform the target group about fertility preservation. Medical oncologists,

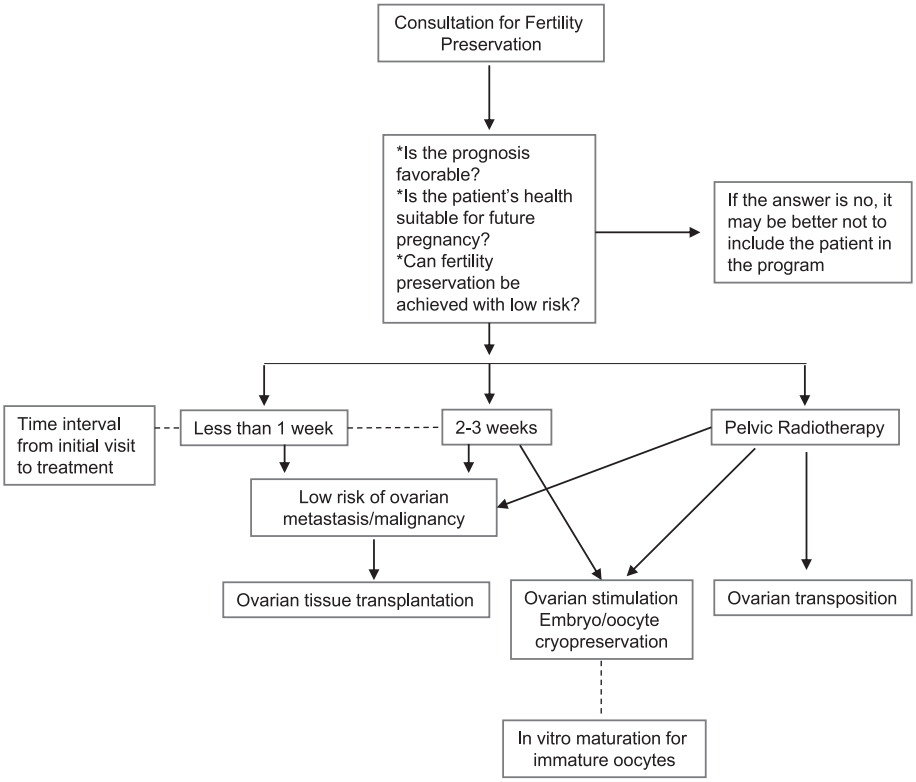

FIGURE 2 | Management of women for fertility preservation.

hematologists, pediatricians (in fields such as genetics, endocrinology, oncology, rheumatology, and hematology), and urologists should consult patients with reproductive endocrinologists and ensure they are comprehensively informed.

4.2 | Recommendations

1. Sperm cryopreservation:
   - Sperm cryopreservation is a highly effective method and should be offered to postpubertal males before cancer treatment.
2. Hormonal suppression for gonadal protection:
   - This method has not proven successful in men and therefore is not recommended [39].
3. Other methods to preserve male fertility:
   - Techniques such as testicular tissue cryopreservation for prepubertal males and subsequent autotransplantation are currently experimental strategies and are used only in clinical trials.
4. Post-chemotherapy:
   - Patients should be informed that sperm obtained after starting treatment may carry a high risk of genetic damage.
   - Sperm collection before treatment is strongly recommended to avoid compromising sperm quality and DNA integrity, even after a single cycle of therapy.
   - Although sperm count and quality may already be reduced in some patients before treatment, this should not deter patients from considering sperm cryopreservation.
   - Intracytoplasmic sperm injection (ICSI) can help preserve fertility even in severe cases, using limited sperm samples [37].
   - It is recommended that men should not discard sperm until they are certain that they have returned to normal fertility and have completed their family.
   - Although it is very difficult to give a specific time to recovery of "normal sperm," 12–24 months of continued contraception should be recommended to attempt to conceive spontaneously, depending on the type of cancer and cancer treatment combination [40].

5 | Children

- Proven methods such as semen and oocyte cryopreservation are recommended for postpubertal adolescents, with parental consent being mandatory.

1. Girls:
   - The only option for fertility preservation in prepubertal girls is cryopreservation of ovarian tissue.
   - Recent studies have reported successful retrieval of mature oocytes following controlled ovarian stimulation in peripubertal girls [41]. However, there is no data on the fertilization potential and pregnancy outcomes of these oocytes.
   - Due to the immaturity of the hypothalamic–pituitary axis, stimulation should include LH supplementation, and oocyte maturation should be triggered with hCG.
   - The impact of ovarian stimulation during the peripubertal stage on growth and puberty (e.g., thelarche) should also be evaluated.

- The psychological impact of ovarian stimulation and ovum collection should be discussed with the adolescent and parents by a qualified psychologist or counselor before proceeding.

2. Boys:
   - Testicular tissue cryopreservation is the only available option for prepubertal boys; however, it remains experimental. Although it has been shown to be successful in primates, to date, there have not been any children born using human sperm from cryopreserved prepubertal testicular tissue [2].

Author Contributions

Volkan Turan: design, planning, writing – original draft. **Mohd Faizal Bin Ahmad:** design, planning, writing – original draft. **Wen Di:** design, planning, writing – original draft. **Debra Gook:** design, planning, writing – original draft. **Nalini Kaul:** design, planning, writing – original draft. **Seok Hyun Kim:** design, planning, writing – original draft. **Jennifer Ko:** design, planning, writing – original draft. **Thi Minh Chau Le:** design, planning, writing – original draft. **Jung Ryeol Lee:** design, planning, writing – original draft. **Wen Li:** design, planning, writing – original draft. **Joyce Mathew:** design, planning, writing – original draft. **Virgilio Novero:** design, planning, writing – original draft. **Porntip Sirayapiwat:** design, planning, writing – original draft. **Nao Suzuki:** design, planning, writing – original draft. **Chii-Ruey Tzeng:** design, planning, writing – original draft. **Budi Wiweko:** design, planning, writing – original draft. **Takai Yasushi:** design, planning, writing – original draft. **Ozgur Oktem:** design, planning, writing – original draft.

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The authors have nothing to report.

Consent

All authors consented to participate.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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