

台灣婦産科醫學會

The oocyte cryopreservation: medical vs. social reasons

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# Conflict of interest statement

This speech was delivered without any commercial or financial relationships that could be interpreted as potential conflicts of interest.

# Outline

- 1. Time line of key milestones in the history of oocyte freezing
- 2. Medical Oocyte Cryopreservation
- 3. Social Oocyte Cryopreservation
- 4.Conclusion



# THE ONGOING EVOLUTION OF OOCYTE VALUATION: FROM QUANTITY TO QUANTIFICATION OF QUALITATIVE ASSESSMENTS

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# Medical Oocyte Cryopreservation

Initially, this is recommended for individuals facing gonadotoxic treatments, such as chemotherapy, which may impair fertility.

### Gonadotoxicity risk of various oncologic treatments/regimens.

High (>80% likelihood of causing permanent amenorrhea)	Conditioning chemotherapy for bone marrow transplantation Total body irradiation Alkylating agents Pelvic radiotherapy Brachytherapy for cervical cancer
Intermediate (60-80% likelihood of causing permanent amenorrhea)	Escalated therapy (e.g., BEACOPP) for Hodgkin's lymphoma Adjuvant chemotherapy agents for breast cancer
Low	Anti-metabolites Vinca alkaloids Anthracyclines Topoisomerase inhibitors

### Indications for Medical Oocyte Freezing

Medical oocyte cryopreservation is recommended when fertility is at risk due to disease or medical treatment.

**Oncology (Cancer-related Indications)** 

- Patients undergoing gonadotoxic treatments that may damage ovarian function:
  - Chemotherapy: Alkylating agents (e.g., cyclophosphamide) and other cytotoxic drugs.
  - Radiotherapy: Pelvic or whole-body irradiation.
  - Surgery: Oophorectomy (removal of ovaries) or surgeries affecting ovarian blood supply.
  - Bone Marrow or Stem Cell Transplantation: High-dose chemotherapy with myeloablative regimens.

Genetic and Autoimmune Conditions Affecting Ovarian Reserve

- Genetic disorders:
  - Turner syndrome (mosaic karyotypes may still have ovarian function).
  - BRCA1/BRCA2 mutation carriers (who may undergo risk-reducing oophorectomy).
  - Fragile X (FMR1)premutation carriers.
- Autoimmune diseases:
  - Systemic lupus erythematosus (SLE)
  - Rheumatoid arthritis
  - Myasthenia gravis
- Metabolic disorders:
  - Galactosemia (associated with premature ovarian failure).

### Indications for Medical Oocyte Freezing

Medical oocyte cryopreservation is recommended when fertility is at risk due to disease or medical treatment.

#### **Gynecological Disorders Affecting Fertility**

- Ovarian endometrioma with diminish ovarian reserve
- Previous ovarian surgery with diminish ovarian reserve



#### **Chronic Medical Conditions**

- Patients with conditions requiring longterm gonadotoxic medications or those at risk of infertility due to systemic disease:
  - Sickle Cell Disease:
    - May require bone marrow transplant or repeated blood transfusions.
  - Thalassemia Major:
    - Iron overload from repeated transfusions may lead to ovarian insufficiency.
  - Chronic Kidney Disease (CKD) and Dialysis Patients:
    - May experience anovulation or premature menopause.



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Trends in Adolescent and Young Adult Cancer Incidence and Mortality Rates for All Cancers Combined by Age and Sex, 1975 to 2017.



With continued improvement in cancer mortality, there has been an increasing focus on improving care and quality of life in the context of long-term survivorship

Fertility preservation counseling has increasingly become a standard component of cancer therapy, particularly for patients of reproductive age.

- Professional Guidelines and Recommendations:
  - American Society of Clinical Oncology (ASCO): Recommends that healthcare providers discuss the possibility of infertility with patients treated during their reproductive years and refer them to reproductive specialists as appropriate.
  - American Society for Reproductive Medicine (ASRM): Advises that oncologists address the risks of infertility with patients and provide information about options for fertility preservation prior to cancer treatment.
  - National Comprehensive Cancer Network (NCCN): Includes guidelines suggesting that fertility preservation be part of the initial discussion with patients undergoing cancer treatment.

#### NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY

#### Adolescent and Young Adult (AYA) Oncology, Version 2.2024

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Initiate Early Discussions: Healthcare providers should discuss potential risks to fertility and available preservation options with patients prior to starting cancer treatment.

Timely Referrals: For patients interested in fertility preservation, referrals to reproductive specialists should be made promptly, ideally within 24 hours, to facilitate timely decision-making and interventions.

Fertility Preservation Methods:

Fertility preservation counseling has increasingly become a standard component of cancer therapy, particularly for patients of reproductive age.



More than ever, young people will survive cancer and can look forward to the future. Cancer treatment can affect future fertility, pregnancy, and family planning choices. Our mission is to provide meaningful, evidence-based information on reproductive health issues for girls, adolescents, young women, and others who have faced cancer or cancer treatment.

# Infertility risk and fertility Family planning and birth Fertility and pregnancy CED Calculator Learn More Learn More Learn More Learn More Learn More

#### **About Us**

We are actively engaged in research to improve reproductive health and fertility in cancer survivors. Our research group is located at UC San Diego Moores Cancer Center and is funded by the California Breast Cancer Research Program.



# Cancer Related Infertility Score Predictor(CRISP)

CRISP calculates population-based infertility risk (for females) based on age, cancer treatment, and the most current data available. Individual risks may vary

Name: (optional) 🕦	Drug Treatments * 🕦
Danny	Please select all applicable treatments:
Age: * 🕦	TDM1 (trastuzumab emantasine)
38	TH (taxane, trastuzumab)
30	CEF (Cyclophosphamide, Epirubicin, Fluorouracil)
Cancer Type: * 🕦	CMF (Cyclophosphamide, Methotrexate, Fluorouracil)
	FAC (Fluorouracil, Adriamycin, Cyclophosphamide)
Breast	□ KP (TDM-1, pertuzumab)
	□ TAC (taxane, doxorubicin, cyclophosphamide)
Cancer Treatment Types: *	TC (taxane, cyclophosphamide)
	TCH (taxane, carboplatin, trastuzumab)
Chemotherapy Regimen	TCHP (taxane, carboplatin, trastuzumab, pertuzumab)
□ Hormone	AC (Adriamycin, Cyclophosphamide)
Radiation	AC-T (Adriamycin, Cyclophosphamide, Taxol)
Single Chemotherapy Drug	Carboplatin and Taxane
Surgery	Is your treatment not listed? Please request it here.
Transplant	Joar a council of internation request the of

# Cancer Related Infertility Score Predictor(CRISP)



CRISP calculates population-based infertility risk (for females) based on age, cancer treatment, and the most current data available. Individual risks may vary

<b>Reproductive Risk Summary f</b>	or Danny
Age: <b>38</b> Cancer Type: <b>Breast</b>	
Estimated Infertility	Risk is MODERATE
Risk based on your treatment:	Compare to 1% risk of primary ovarian insufficiency in young women without cancer
Why? As part of your cancer treatment you received:	
CEF (Cyclophosphamide, Epirubicin, Fluorouracil) 41 - 50% risk of Amenorrhea (12 months) Low risk Moderate risk High risk Unknown risk	

https://oncofertilityrisk.com/en/infertility/



# **Fertility Preservation Option**



The recommended ovarian stimulation protocols for fertility preservation aim to maximize oocyte yield while minimizing treatment delays and potential complications.

#### Timing of Stimulation:

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**Random-Start Protocols:** To avoid delaying cancer treatment, random-start protocols allow initiation at any point in the menstrual cycle, this flexibility enables timely oocyte retrieval without compromising outcomes.

#### Choice of Stimulation Agents:

**GnRH Antagonist Protocols:** offer a shorter duration of stimulation and reduce the risk of ovarian hyperstimulation syndrome (OHSS).

**Letrozole Co-Administration:** In hormonesensitive cancers (e.g., certain breast cancers), combining letrozole, with gonadotropins can minimize estrogen exposure during stimulation. This approach reduces potential stimulation of hormonesensitive tumors.

#### Triggering Final Oocyte Maturation:

**GnRH Agonist Trigger:** Using a GnRH agonist for final oocyte maturation induction decreases the risk of OHSS compared to human chorionic gonadotropin (hCG) triggers. This method is particularly beneficial for cancer patients who may have an elevated thromboembolic risk.

#### Adjunctive Measures:

**Anticoagulant Prophylaxis:** Patients with additional risk factors for thrombosis may require anticoagulant prophylaxis during ovarian stimulation to mitigate the risk of thromboembolic events.

TAOG 2025 Annual Meeting 合灣婦產科醫學會 Totana Anaclather of Obstatries and Operations ORIGINAL ARTICLE

Random-start ovarian stimulation with aromatase inhibitor for fertility preservation in women with Japanese breast cancer

WILEY Reproductive Medicine and Biolog

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- February 2012 to August 2017. The study entailed 50 cycles with 34 patients who underwent fertility preservation due to breast cancer.
- GnRH antagonist protocol with AI (letrozole 2.5 or 5 mg/d) for ovarian stimulation. GnRH agonist and FSH/HMG were co-administered until the final trigger.



Characteristics of breast cancer. A, Stages of breast cancer. B, Intrinsic subtypes of breast cancer



WILEY Reproductive Medicine and Biology

# Random-start ovarian stimulation with aromatase inhibitor for fertility preservation in women with Japanese breast cancer

	FPS (n = 29)	LPS (n = 21)	Р
Age at OPU (y)	35.3 ± 4.0	37 ± 3.1	0.12
AMH (ng/mL)	3.8 ± 2.5	3.5 ± 2.5	0.66
No. of days stimulated	9.0 ± 1.9	11.3 ± 2.6	<0.001
Total FSH/HMG dose (IU)	1290.5 ± 586.2	1957.1 ± 1030.2	0.0056
No. of retrieved oocytes	8.7 ± 6.0	10.0 ± 6.8	0.48
Mature (MII) oocytes (%) Fertilization rate (%)	83.3 (125/150)	81.7 (49/60)	0.84
IVF	62.5 (35/56)	47.1 (48/102)	0.069
ICSI	70.3 (26/37)	90.0 (36/40)	1

TABLE 2 No. of frozen oocytes and embryos

TABLE 1 Characteristics of EPS and LPS

	FPS (n = 29)	LPS (n = 18)	Ρ
No. of frozen oocytes	7.4 ± 5.1 (n = 18)	5.0 ± 5.4 (n = 7)	0.31
No. of frozen embryos	3.2 ± 1.9 (n = 11)	4.4 ± 2.9 (n = 11)	0.27







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Human Reproduction, 2024, **39(12)**, 2693–2701 https://doi.org/10.1093/humrep/deae243 Advance Access Publication Date: October 30, 2024 Original Article

#### Infertility

Outcomes of female fertility preservation with cryopreservation of oocytes or embryos in the Netherlands: a population-based study

STUDY DESIGN, SIZE, DURATION: A retrospective observational study was performed in the Netherlands. Data were collected between 2017 and 2019 from 1112 women who cryopreserved oocytes or embryos more than 2 years ago in the context of fertility preservation in 10 IVF centers in the Netherlands

MAIN RESULTS :Cryopreservation of oocytes versus embryos resulted in comparable numbers of used embryos (median of 2) for transfer and comparable live birth rates (33.9% and 34.6%, respectively). The 5-year utilization rate was 12.3% and the 10-year utilization rate was 25.5%. The cumulative clinical pregnancy rate was 35.6% and the cumulative live birth rate was 34.6% per patient. Those who had fertility preservation due to benign diseases returned earlier to use their cryopreserved embryos or oocytes.



Oncological Benign Non-medical

Female age at first oocyte retrieval—median and range

Oncological	17-42	30
Benign	16-39	30
Non-medical	22-44	36
Total	16-44	32





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Distribution of different indications. (A) Distribution of oncological indications; (B) distribution of benign indications.





Number of fertility preservation cycles with cryopreservation of embryos and oocytes in the Netherlands.







Time after cryopreservation of oocytes or embryos (years)

In comparison with the oncological and the non-medical group, women with a benign indication used their cryopreserved oocytes or embryos relatively more often within 5 years (17.1%,  $P \le 0.05$ ), with a median period of 23 months (range 2–88).



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In total, 205 embryo transfer procedures in 96 patients were performed with an average of  $1.08 \pm 0.3$  embryos per transfer procedure.





Journal of the Formosan Medical Association

journal homepage: www.jfma-online.com

**Original Article** 



Pathways to motherhood: A single-center retrospective study on fertility preservation and reproductive outcomes in patients with breast cancer



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Methods: This retrospective review evaluated 42 patients with breast cancer who underwent fertility preservation at our center from January 2012 to December 2022. Of 42 patients, 26 underwent oocyte cryopreservation; 17, embryo cryopreservation; and 2, ovarian tissue cryopreservation.

Utilization rates varied: oocyte cryopreservation was at 7.69%; embryo cryopreservation had a higher rate of 52.94%.



	Oocyte cryopreservation	Embryo cryopreservation
Not attempting to conceive yet	19	5
Receiving cancer treatment	2	2
Death	1	0
Follow-up loss	3	1
Not married	11	1
No desire of conceiving although married	2	1
Attempting pregnancy	7	12
Pregnancy success (number of live births)	4 (5)	5 (7) <sup>b.</sup>
CO IVF success	1	Х
CE IVF success	Х	4 (5)
Nature conception	2 (3)	2
Another IVF success	1 <sup>a.</sup>	0
Try nature conception	1	0
CO/CE IVF cycle failure	1 <sup>a.</sup>	6
Plan to IVF recently	2	2
Utilization rates (%)	2/26 (7.69%)	9/17 (52.94%)

Current status of patients and oocytes and embryos utilization.

Abbreviations: CO, cryopreserved oocytes; CE, cryopreserved embryos; IVF, in vitro fertilization.

<sup>a</sup> The patient received another IVF (after cancer treatment) and got live birth.

<sup>b</sup> One patient got twice live birth via nature conception. One patient got twice live birth, one via cryopreserved embryos and another via nature conception.

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Medical Freezing Social Freezing



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### 奇美醫院冷凍解凍卵子臨床結果

使用率				
	使用	儲存	銷毀	活產率
Medical Freezing(25)	2(8%)	18(72%)	5(20%)	2(100%)
Social Freezing(69)	4(5.8%)	63(91.3%)	2(2.9%)	2(50%)
Total	6(6.4%)	81(86.2%)	7(7.4%)	4(66.6%)
	使用	儲存	銷毀	活産率
Medical Freezing(25)	8%	72%	20%	100%
Social Freezing(69)	5.80%	91.30%	2.90%	50%
Total	6.40%	86.20%	7.40%	67%



# Medical Oocyte Cryopreservation

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#### Impact on Chemotherapy Initiation:

- No Significant Delay
- Research indicates that FP does not significantly delay the start of chemotherapy. A study involving breast cancer patients found no substantial difference in the time to treatment between those who underwent FP and those who did not.
  - Cancer 2021;127:3872-3880

#### Effect on Patient Outcomes:

- No Negative Impact on Survival
- Studies have demonstrated that FP procedures do not adversely affect survival outcomes. For instance, research involving young women with breast cancer showed that FP is safe and does not increase the risk of mortality in the ensuing decades.
  - JAMA Oncol. 2021;7(1):86-91.



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# Oocyte cryopreservation for fertility preservation in women with ovarian endometriosis

Fertility preservation strategies such as oocyte or ovarian tissue cryopreservation should be considered, particularly for women at risk of diminished ovarian reserve due to endometriomas or planned surgical intervention

## Impact of Endometrioma on Fertility

- Ovarian Reserve Reduction
  - Endometriomas can damage ovarian tissue, reducing the ovarian reserve due to inflammation, oxidative stress, and surgical removal of cysts.
- Disrupted Ovulation
  - Endometriomas may alter the hormonal environment, leading to impaired ovulation or lower-quality oocytes.
- Inflammation and Adhesion Formation
  - Chronic inflammation caused by endometriosis leads to pelvic adhesions, distorting the pelvic anatomy and affecting the normal functioning of reproductive organs.
- Impaired Follicular Development
  - Endometriomas may interfere with follicle development and ovulatory processes, reducing fertility potential.

- Poor Oocyte Quality
  - Endometriomas contribute to oxidative stress and inflammatory mediators in the ovarian microenvironment, leading to reduced oocyte quality.

#### Impact on ART

Endometriomas may negatively affect the outcomes of IVF by reducing the number and quality of retrieved oocytes and embryos.

#### Altered Endometrial Receptivity

 The inflammatory environment associated with endometriosis can compromise endometrial receptivity, reducing the likelihood of successful implantation.

#### Co-existing Infertility Factors

 Women with endometriomas often have other forms of endometriosis or pelvic conditions, further compounding infertility

### Scenario 1:

A33-Year-Old Woman with Bilateral Ovarian Endometriomas

#### Background:

- A33-year-old woman is referred for infertility evaluation after trying to conceive for two years.
- Ultrasound reveals bilateral ovarian endometriomas (left ovary: 5 cm, right ovary: 4 cm).
- Serum AMH level is low (1.2 ng/mL), and antral follicle count (AFC) is reduced.
- She experiences moderate pelvic pain but no acute symptoms.

#### Key Issues:

- Decreased ovarian reserve.
- Bilateral cysts increasing the complexity of surgical management.
- Desire for fertility preservation.

#### Human Reproduction, Vol.28, No.8 pp. 2140-2145, 2013

Advanced Access publication on April 26, 2013 doi:10.1093/humrep/det123

human reproduction **ORIGINAL ARTICLE Infertility** 

Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve<sup>†</sup> Aprospective cohort study including 30 women with endometrioma >2 cm were age matched with 30 healthy women without ovarian cysts.Women with endometrioma underwent laparoscopic excision with the stripping technique. Serum AMH level and antral follicle count (AFC) were determined preoperatively, 1 and 6 months after surgery

# Ovarian reserve in women with or without endometrioma

Markers of ovarian reserve in women before and after endometrioma excision

	Endometrioma (n = 30)	Control (n = 30)	P value
Age (in years)	29.0 (5.4)	30.1 (4.4)	0.39
Nulligravid (%)	15 (50)	10 (33.3)	0.19
AMH (in ng/ml)	2.81 (2.15)	4.20 (2.26)	0.02
Total AFC	9.73 (4.77)	14.7 (4.11)	<0.01

Values are the mean (SD). AMH, anti-Müllerian hormone; AFC, antral follicle count.

**Preoperative** 6 months I month (n = 30)after after surgery surgery (n = 30)(n = 26)2.07 (1.47)<sup>0.18</sup> 1.82(1.29)<sup>0.02</sup> AMH (in ng/ml) 2.81 (2.15) 11.0 (5.37)<sup>0.28</sup>  $10.4(4.16)^{0.63}$ Total AFC 9.73 (4.77)

Values are mean (SD). Superscripts are P values compared with preoperative values.

human reproduction **ORIGINAL ARTICLE Infertility** 

Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve<sup>†</sup> Both the presence of eomas and their removal negatively affect ovarian reserve. The detrimental impact on ovarian reserve is not temporary but sustained over 6–9 months. Excision of bilateral endometriomas might be associated with a greater loss of ovarian reserve.

#### Markers of ovarian reserve in women before and after endometrioma excision, according to laterality

	Preoperative $(n = 15)$	I month after surgery $(n = 15)$	6 months after surgery $(n = 14)$
Unilateral only			
AMH (in ng/ml)	2.04 (1.38)	2.03 (1.18) <sup>0.50</sup>	1.76 (1.18) <sup>0.40</sup>
Total AFC	11.73 (4.56)	12.0 (4.16) <sup>0.91</sup>	10.57 (2.56) <sup>0.31</sup>
	Preoperative $(n = 15)$	I month after surgery (n = 15)	6 months after surgery (n = 12)
Bilateral only			
AMH (in ng/ml)	3.58 (2.53)	2.11 (1.76) <sup>0.05</sup>	1.88 (1.45) <sup>0.02</sup>
Total AFC	7.73 (4.22)	10.0 (6.35) <sup>0.10</sup>	10.2 (5.67) <sup>0.09</sup>
	X		

Values are the mean (SD). Superscripts are P values compared with preoperative values.

#### Reproductive BioMedicine Online (2011) 23, 740-746



ARTICLE

Laparoscopic stripping of endometriomas negatively affects ovarian follicular reserve even if performed by experienced surgeons 43 normoovulatory women were studied by endocrine (AMH, FSH, LH, inhibin B, oestradiol) and ultrasonographic (antral follicle count) methods before surgery, and 3 and 9 months after surgery. The operation was performed by experienced laparoscopists, particularly aware of the need to avoid damaging the healthy part of the ovary.

Table 2Hormone concentrations before laparoscopic stripping of ovarian endome-<br/>trioma(s) and after 3 and 9 months.

Hormone	Before LPS	After LPS		P-value
		3 months	9 months	
FSH (IU/l) LH (IU/l) Oestradiol (pg/ml) Inhibin B (pg/ml) AMH (ng/ml)	$\begin{array}{c} 6.6 \pm 2.0 \\ 5.0 \pm 2.0 \\ 35.2 \pm 24.5 \\ 51.6 \pm 31.3 \\ 3.0 \pm 0.4 \end{array}$	$7.8 \pm 3.4 \\ 4.5 \pm 1.7 \\ 33.5 \pm 29.3 \\ 47.4 \pm 23.0 \\ 1.4 \pm 0.2$	$8.0 \pm 3.7 \\ 4.2 \pm 2.0 \\ 32.9 \pm 26.6 \\ 44.5 \pm 26.0 \\ 1.3 \pm 0.3$	NS NS NS <0.0001

Values are mean ± SD. AMH = anti-Müllerian hormone; LPS = laparoscopic stripping; NS = not statistically significant.

Overall, the data show that laparoscopic stripping of endometriomas reduces ovarian reserve. The significant decrease of AMH after surgery confirms that part of the healthy ovarian pericapsular tissue, containing primordial and preantral follicles, is removed or damaged despite all the surgical efforts to be atraumatic. Ţ

For fertility preservation in reproductive-age women with ovarian endometrioma, surgical intervention like cystectomy may not be the optimal choice due to potential damage to ovarian reserve.

> Surgery might be necessary in cases where the endometrioma causes significant pain, rapid growth, or poses other health risks. In such scenarios, presurgical fertility preservation options like oocyte or embryo cryopreservation should be considered.

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### Scenario 1: A33-Year-Old Woman with Bilateral Ovarian Endometriomas

- 1. Avoid Immediate Surgery (If Pain Is Manageable):
  - Surgery may further reduce ovarian reserve, particularly with bilateral cysts.
  - Proceed with a non-surgical approach initially, focusing on fertility preservation.

#### 2. Fertility Preservation:

- Oocyte or Embryo Cryopreservation:
  - Initiate ovarian stimulation and retrieve as many oocytes as possible before any surgical intervention.

#### 3. Medical Management for Pain:

 Consider hormonal suppression (e.g., progestins like dienogest) to manage pain while planning fertility preservation.

#### Reassess After Fertility Preservation:

- If surgery becomes necessary (e.g., for symptom control or to reduce cyst size), perform laparoscopic cystectomy with meticulous care to preserve ovarian tissue.
- Use hemostatic sealants instead of coagulation to minimize ovarian damage.

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# Medical Oocyte Cryopreservation

Medical Oocyte Freezing is both a medically sound and ethically justified option, empowering women to safeguard their reproductive potential amidst life-saving medical treatments.

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# Social Oocyte Cryopreservation

Social oocyte cryopreservation (SOC) is performed for non-medical reasons to extend reproductive options. The primary indications include personal, professional, and social factors that may delay childbearing.



# Common reasons why women pursue social oocyte freezing

- 1. Absence of a Suitable Partner
- 2. Delaying Childbearing for Career or Education
- 3. Declining Ovarian Reserve with Age
- 4. Personal or Lifestyle Preferences
- 5. Family History of Early Menopause or Infertility
- 6. Uncertainty About Future Parenthood
- 7. Desire for Biological Children Without Immediate Parenthood
- 8. Ethical or Religious Considerations Regarding Embryo Freezing





#### human reproduction

#### **ORIGINAL ARTICLE** Fertility control

A major increase in oocyte cryopreservation cycles in the USA, Australia and New Zealand since 2010 is highlighted by younger women but a need for standardized data collection

#### STUDY DESIGN, SIZE, DURATION: A

trinational retrospective cohort study was performed of 31 191 OC cycles and 972 oocyte thaw (OT) cycles undertaken in the USA (2010–2016) and 3673 OC and 517 OT cycles undertaken in Australia/New Zealand (Aus/NZ;2010–2015). There has been a dramatic rise in the number of OC cycles performed each year (+880% in the USA from 2010 to 2016 and +311% in Aus/NZ from 2010 to 2015).



Number of cycles and patients undergoing oocyte cryopreservation in the USA (2010–2016) and Australia/New Zealand (2010–2015).



Across both regions, most women undergoing OC were aged in their late 30s, but the average age decreased over time (USA: 36.7 years vs 34.7 years in 2010 and 2016, respectively).



Women's age at time of oocyte cryopreservation. (A) Data are presented for mean age of women at time of oocyte cryopreservation in the USA (2010–2016) and (B) Australia/New Zealand (2010–2015).



# Data about oocyte cryopreservation for fertility preservation and oocyte donation from SART, ESHRE and ANZARD registries





#### All SART Member Clinics - 2022 Retrieval and Transfer Tables



Age of Woman at time of Egg Freezing	< 35	35 - 37	38 - 40	41 - 42	> 42
Number of Egg Freezing Cycles Initiated	11995	8800	5147	1324	720
Number of Egg Freezing Retrievals	11546	8392	4786	1198	619
% of Egg Freezing Cycle Cancellations	3.7 %	4.6 %	7.0 %	9.5 %	14.0 %
Mean # of Oocytes Per Retrieval	18.3	15.0	12.3	10.0	6.7
Mean # of Oocytes Frozen Per Retrieval	14.2	11.6	9.4	7.8	5.2

# Social (Elective) Oocyte Cryopreservation

#### Egg Quantity Declines with Age

- Women are born with about 1–2 million eggs
- By age 35, only about 10% (100,000 eggs) remain.
- By age 40, most women have less than 10,000 eggs, many of which are chromosomally abnormal.

#### Egg Quality Drops with Age

- The rate of aneuploidy (chromosomal abnormalities) increases:
- Under 35 y/o: ~20% of eggs are abnormal.
- At 40 y/o: ~80% of eggs are abnormal.
- At 43+ y/o: ~90–95% are abnormal.



#### Female Egg Quality by Age



# How Old Is Too Old to Freeze Eggs?

There is no strict age limit for egg freezing, but the success rate significantly declines with age. Generally, freezing eggs after 38– 40 years old is much less effective.



Successful elective and medically indicated oocyte vitrification and warming for autologous in vitro fertilization, with predicted birth probabilities for fertility preservation according to number of cryopreserved oocytes and age at retrieval

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#### Patient(s)

Women undergoing autologous IVF treatment using vitrified and warmed oocytes. A total of 1,283 vitrified oocytes were warmed for 128 autologous IVF treatment cycles.

#### Conclusion(s)

Treatment outcomes using autologous oocyte vitrification and warming are as good as cycles using fresh oocytes. These results are especially reassuring for infertile patients who must cryopreserve oocytes owing to unavailability of sperm or who wish to limit the number of oocytes inseminated.

Characteristic	Vitrified oocytes	Fresh oocytes	<i>P</i> value
Cycles (n)	128	2,963	
Age (y) at oocyte retrieval	34.9	35.5	NS
BMI (kg/m <sup>2</sup> )	24.6	25.9	.006
No. of MII oocytes inseminated	8.0	10.1	.0002
Fertilization per MII inseminated (%)	69.5	71.7	NS
Blastocyst-stage ET (%)	50.9	66.1	.001
Implantation per embryo transferred (%)	41.2	35.4	NS
Clinical pregnancy per transfer cycle (%)	54.4	45.1	.050
Pregnancy loss per clinical pregnancy(%	29.0	20.1	NS
Live birth/ongoing pregnancy per transfer cycle (%)	38.6	36.0	NS

### Predicted probability of having at least one kid from egg freezing by maternal age and number of eggs frozen



# RBMO

REVIEW



# Planned oocyte cryopreservation: the state of the ART





#### BIOGRAPHY

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#### **KEY MESSAGE**

Planned oocyte cryopreservation increases reproductive autonomy and promotes social justice by allowing women to postpone childbearing while maintaining the option of a biological child.Based on current evidence, cryopreserving 20 mature oocytes at <38 years of age provides a 70% chance of one live birth; however, larger studies are needed.

# **BWH Egg Freezing Counseling Tool (EFCT)**

Predicts likelihood of live birth for elective egg freezing in women.



- Since limited data exist regarding live births following elective egg freezing, the BWH Egg Freezing Counseling Tool was developed from a surrogate population of presumably fertile women (egg donor, male-factor, and tubal-factor only infertility).
- No number of frozen eggs can guarantee a live birth.
  - IVF stimulation cycles produce a variable number of eggs, even among women of similar ages. Older women typically obtain fewer eggs per stimulation cycle.
- May be less reliable for women ≥39 years old.
- May overestimate live birth rates for women undergoing non-elective egg freezing for medical reasons, such as cancer.
- Data are retrospective and from a single academic institution in an insurance-mandated state.
- Individual IVF clinics with different thaw survival and live birth rates may need to modify and customize this model.
- Has yet to be prospectively validated.



Reproductive Biology and Endocrinology

#### RESEARCH

#### **Open Access**

# Usage and cost-effectiveness of elective ocyte freezing: a retrospective observational study

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645 women with 840 oocyte retrieval cycles for elective oocyte freezing from November 2002 to December 2020. The overall usage rate was 8.4% (54/645).

	Total	Age ≤ 35	Age 36-39	Age ≥ 40	P value
Thawing cases	54	11	26	17	
Usage rate	54/645 (8.4)	11/189 (5.8)	26/263 (9.9)	17/193 (8.8)	0.650
Storage duration, y	3.0 (1.4–4.7)	3.4 (2.6–4.3)	3.1 (2.2–5.2)	2.8 (1.2–4.3)	0.817
Survival rate of all oocytes	382/518 (73.7)	100/147 (68.0)	205/262 (78.2)	77/109 (70.6)	0.159
Fertilization rate	220/332 (66.3)	61/85 (71.8)	110/177 (62.1)	49/70 (70.0)	0.545
Implantation rate	29/122 (23.8)	9/34 (26.5)	16/66 (24.2)	4/22 (18.2)	0.988
Clinical pregnancy rate/transfer	21/52 (40.4)	8/16 (50.0)	9/26 (34.6)	4/10 (40.0)	0.943
Ongoing pregnancy rate/transfer	18/52 (34.6)	7/16 (43.8)	8/26 (30.8)	3/10 (30.0)	0.958
At least 1 live birth/thawed case	17/54 (31.5)	6/11 (54.5)	8/26 (30.8)	3/17 (17.6)	0.320
Cumulative live birth/thawed case	21/54 (38.9)	7/11 (63.6)	11/26 (42.3)	3/17 (17.6)	0.045







TSMC Taking Over Intel's Fabs? A High-...

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# Why so few women in Taiwan use their frozen eggs



Many believe that Taiwan's legal restrictions on fertility treatment are to blame for the comparatively low usage rate. The Assisted Reproduction Act, which was adopted in 2007, stipulates that artificial insemination is limited to married heterosexual couples where one of the partners is infertile. This means that single women and same-sex couples are prevented from having children from their thawed eggs.



# TAIPEI 🗰 TIMES



Only about 4 percent of children in Taiwan are born out of wedlock, compared with about 40 percent in the US where it is more accepted.

#### **RISING TREND**

Demand for egg freezing in Taiwan has surged, with the number of women aged between 35 and 39 opting for the technology up 86 percent over the past three years, according to a study by National Taiwan University Hospital.

# RBMO



ARTICLE

'Why have women not returned to use their frozen oocytes?': a 5-year follow-up of women after planned oocyte cryopreservation



#### BIOGRAPHY

Avi Tsafrir is currently a Senior Clinician at the IVF Unit, Shaare-Zedek Medical Center, and Lecturer at the Hebrew University, Jerusalem. He is also the Coordinator of Fertility Preservation at Shaare Zedek. His research interests are infertility at an advanced reproductive age, fertility preservation and decision making in medicine.

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The most common reasons for not using cryopreserved oocytes approximately 5 years after planned oocyte cryopreservation were achieving pregnancy without cryopreserved oocytes, or preferring not to have a child without a partner. Many women who initially expressed disinterest in single parenthood by choice eventually attempted to conceive using donor sperm.



WHAT YOU NEED TO KNOW ABOUT OOCYTE CRYOPRESERVATION?

Its efficacy, safety, costs, benefits, and risks, including the unknown long-term health effects for offspring.

# Subsidies for egg freezing !

Several countries have implemented subsidies or public funding programs to support elective egg freezing for non-medical reasons.

- France: France is the first country to offer elective egg freezing for non-medical reasons under public health coverage.
- Israel: The Israeli government provides public funding for up to two cycles of egg freezing, reflecting progressive policies toward fertility preservation.
- Japan: The Tokyo Metropolitan Government has expanded its subsidy program for elective egg freezing to address the country's declining fertility rate.
- South Korea: The Seoul Metropolitan Government subsidizes 50% of egg freezing expenses for women aged 20 to 49.





Tokyo's Fertility Program Is Overwhelmed by How Many Women Want to Freeze Their Eggs



More than 7,000 women have registered for information sessions about the new programme, which offers up to 300,000 yen (S\$2,715) toward the costs of egg-freezing, and 1,800 women have applied since October, according to the Tokyo Metropolitan Government.

### Freezing is Just the First Step—Don't Forget the Next One!

I froze my eggs when I was 28, thinking I was securing my future. !



My eggs are still frozen, and I know egg freezing is a tool, not a guarantee !



### Don't Just Freeze Your Eggs—Hatch Them!

1.4

0.8

0.6

Booyoung Group, a construction firm based in Seoul, offers employees a bonus of 100 million Korean won (approximately \$75,000) for each child born.



In 2024, South Korea's fertility rate experienced a slight uptick, rising to 0.75 from 0.72 in 2023—the first increase in nine years.

South Korea's fertility rate ticked up ...while marriages increased 14.8% last year... year on year in 2024 Fertility rate (births per woman) Number of marriages 400,000 300,000 200,000 100,000 2020 2000 2005 2010 2015 2020 2000 2010 2015 2005

Source: KOSIS, Statistics Korea

Source: Statistics Korea, CEIC

# Subsidies for egg freezing amiss !

- Is it reasonable or necessary to use government funds to subsidize egg freezing when the usage is so low?
- Why not use these funds to improve support for parents or other things?
- Research in many nations has shown that the main reason women have their eggs frozen is not career or study considerations, but the lack of a partner
- Regulatory mechanism for egg freezing is lacking ! (There were cases of equipment malfunctions at reproduction institutions in the US resulting in the loss of eggs and even embryos. )





Check for updates

### Planned oocyte cryopreservation to preserve future reproductive potential: an Ethics Committee opinion



Ethics Committee of the American Society for Reproductive Medicine American Society for Reproductive Medicine, Washington, D.C.

- 1. Planned OC serves legitimate interests in reproductive autonomy.
- 2. Planned OC is relatively new, and uncertainties exist regarding its efficacy, appropriate use, and long-term effects.
- 3. Providers should ensure that individuals who request planned OC are informed about its efficacy, safety, costs, benefits, and risks, including the unknown long-term health effects for offspring. Because of the uncertainties that accompany this developing procedure, there are distinct obligations regarding disclosure and informed decision-making.
- 4. Providers should disclose their own clinic-specific statistics, or lack thereof, for successful freeze-thaw and live birth. Patients should be informed that medical benefits are uncertain and harms that are not fully understood may emerge from planned OC.

# Take Home Message

- Egg freezing is not a guarantee of future fertility, but when done at the right time, it can significantly increase reproductive options.
- Medical egg freezing should be assessed early and initiated promptly, without delaying cancer treatment or affecting survival outcomes.
- Social egg freezing requires thorough informed consent and risk communication to prevent unrealistic expectations about success rates.
- Policy initiatives should balance women's reproductive autonomy with the fair allocation of societal resources.

