

Oocytes on ice: Exploring the advancements in elective egg freezing for women

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ABSTRACT

Introduction: Female fecundity decreases significantly after the age of 32, and rapidly so after age 37. There is no treatment to prevent this decline. Furthermore, globally, women are getting married later and the age at which they have their first child is increasing. As of July 2023, elective egg freezing (EEF) or oocyte cryopreservation (OC) for age-related fertility decline, commenced in Singapore. With medical advancements in OC, EEF is no longer considered experimental. The aim of this review is to examine the existing literature around EEF with regard to reproductive outcomes and its safety, to better guide clinicians in counselling young single women.

Method: Published studies were examined to increase understanding on optimal age for EEF, ideal number of oocytes for a live birth, recommended OC protocols, cryopreservation techniques affecting thaw survival or fertilisation, oocyte storage and pregnancy risks.

Results: Models predict that EEF should be performed at age <37 years and to achieve a 70% chance of live birth, women would need 14, 15 and 26 mature oocytes at ages 30–34, 35–37 and >38 years, respectively. An antagonist stimulation protocol with an agonist trigger would minimise ovarian hyperstimulation syndrome and duration of stimulation without affecting outcomes. Oocyte vitrification in comparison to slow freezing increases thaw survival, fertilisation and clinical pregnancy rates. No increased risks exist for the woman, future pregnancy or child when compared with conventional IVF.

Conclusion: EEF is a viable option for single women desiring fertility preservation. Financial costs are significant, but returns are worthwhile if oocytes are utilised.

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Keywords: age-related infertility, elective egg freezing, obstetrics and gynaecology, oocyte cryopreservation, social egg freezing

CLINICAL IMPACT

What is New

- Elective egg freezing (EEF) is safe with minimal risk for women, and studies reviewed report no increase in adverse outcomes with vitrified oocytes.
- Average vitrified-warmed oocyte efficacy is 6%.
- There is significant financial outlay with EEF.

Clinical Implications

- For a 70% chance of live birth, women would need 14, 15 and 26 oocytes at ages 30–34, 35–37 and 38–40 years, respectively.
- Chances of live birth using a younger cryopreserved oocyte follow the age of the oocyte rather than the woman's age at transfer.

has become a viable option for single women to preserve their fertility.¹ It is well known that female fertility decreases gradually, but significantly after the age of 32 and even more rapidly after age 37.^{2,3} As the ovaries age, reduction in oocyte quantity and increased aneuploidy rates due to poorer oocyte quality account for this decreased fecundity.⁴ The problem with female age-related fertility decline is that there is no known preventive treatment; conversely, the mean age of women marrying and getting pregnant is increasing worldwide.⁵ Statistics show that the median age of first-time marriages has been steadily rising over the years.^{5,6} In the 1970s, the mean age of European women having their first child was 27 years; in the year 2020, it had risen to 30 years. The US Centers for Disease Control and Prevention data have also shown birth rates declining among women in their 20s but increasing for women in their 30s and 40s.⁷ The total fertility rate worldwide is declining, where Taiwan, Hong Kong, South Korea and Singapore have the lowest fertility rates.^{5,8,9} The reasons

INTRODUCTION

Elective egg freezing (EEF), otherwise known as oocyte cryopreservation for age-related fertility loss,

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behind delayed childbearing are complex but the most cited reasons are the lack of a suitable partner, and professional and financial matters.^{2,3,10-12}

In 1986, the first successful oocyte cryopreservation with subsequent fertilisation and pregnancy was reported,¹³ but the major change in acceptability of oocyte cryopreservation only came with the shift in cryopreservation of gametes from slow freezing to vitrification. It was found that during cryopreservation, oocytes were more vulnerable to damage from ice crystal formation due to its meiotic spindle apparatus and higher water content. As vitrification in comparison to slow freezing limited the formation of ice crystals, post-thaw survival rates of oocytes increased significantly, supporting the feasibility of this technique for fertility preservation.^{4,14-16} As more studies became available, together with medical advancements, in the years 2012 to 2013, the European Society for Human Reproduction and Embryology and American Society for Reproductive Medicine no longer considered oocyte cryopreservation experimental for age-related fertility decline.^{1,10,17} Given the inevitable decrease in female fecundity coupled with later childbearing, EEF could provide the opportunity for women to preserve their fertility as an alternative to unsuccessful fertility attempts at an advanced maternal age in the future.¹⁸

METHOD

We conducted a search on PubMed using the keywords “oocyte cryopreservation”, “elective egg freezing” and “fertility preservation”. Relevant studies published in English were included. The studies were examined for reported optimal age for EEF, ideal number of oocytes for a live birth, recommended OC protocols, cryopreservation techniques affecting thaw survival or fertilisation, oocyte storage and pregnancy risks.

RESULTS

Chances of conception and optimal timing of cryopreservation

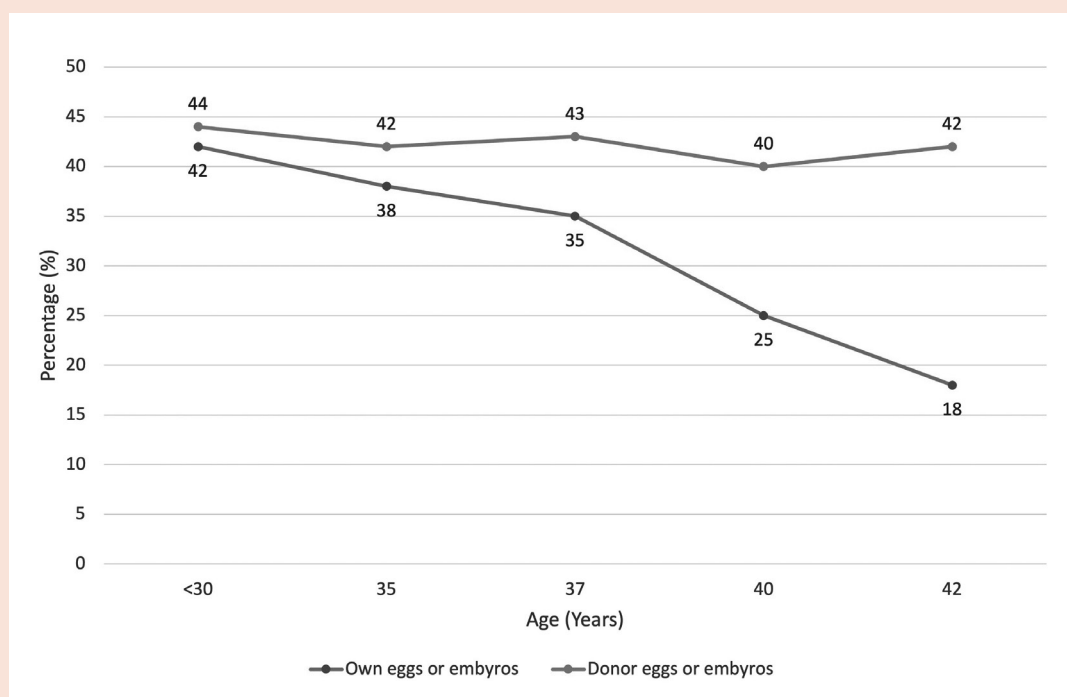
The overall chance of a live birth through in vitro fertilisation (IVF) techniques is approximately 35% to 40%.^{19,20} It is recognised that the chance of a live birth through conventional IVF whereby fresh oocytes are fertilised with the partner's sperm to become embryos, followed by subsequent embryo transfer, decreases with increasing age. At age 32 years, the percentage of embryo transfers resulting in a live birth is around 40%. At 37, 40 and 42 years, this decreases to roughly 35%, 25% and 18%, respectively (Fig. 1).^{19,20} When evaluating oocytes

specifically, it has been found that reproductive outcomes of cryopreserved oocytes were similar to fresh oocytes. The reproductive outcomes of autologous fresh oocyte cycles compared to autologous cryopreserved oocyte cycles revealed no significant differences in rates of implantation, pregnancy or live birth.^{21,22} A recent retrospective cohort study examined 543 patients who underwent 800 EEF cycles.²² It found that cryopreserved oocytes resulted in a 39% live birth rate per patient, which was comparable to age-matched IVF outcomes.²² Crawford et al. analysed specific age groups and reported live birth rates in cryopreserved oocyte cycles at 34%, 28% and 17% for women who did so at ages 30–34, 35–39 and above 40 years, respectively, which were similar to age-matched fresh oocyte cycles.²¹ In keeping with the importance of age, with the usage of younger donor oocytes, regardless of the patient's current age, it is known that the percentage of embryo transfers resulting in a live birth remains stable at about 40%,^{21,23} performing according to the donor's (younger oocyte) age rather than the recipient's age (Fig. 1).

The data in Fig. 1 emphasise how crucial the woman's age at the time of oocyte cryopreservation is, begging the question on the optimal timing of EEF. There is still disagreement on the ideal age for EEF, but a predictive model reported the highest probability of live birth rates (>74%) in women who froze their oocytes at <34 years.²⁴ When analysing women 25–30 years old, as they were still young, the increase in live birth rate in comparison to expectant management was lesser than 3%. The largest improvement in probability of live birth compared to no action (51.6% versus 21.9%) occurred when EEF was performed at age 37. When using this same model on women aged 40 years and above, with or without oocyte cryopreservation, live birth rates were low.²⁴ Therefore, the younger the age at which oocyte cryopreservation is performed, the better the outcomes. Ideally, the woman should be 30–35 years old, though improvement in reproductive outcomes with EEF has been shown for women up to 37 years old.

Optimal number of oocytes to be attained

Very few studies have examined the ideal number of cryopreserved mature oocytes required to achieve a live birth. The aforementioned live birth rates stratified by the woman's age are used to analyse live birth rate per embryo transfer. However, cryopreserved mature oocytes need to not only survive the thawing process, but achieve fertilisation first. Survival rates of cryopreserved oocytes

Fig. 1. Percentage of embryo transfers resulting in live birth rates.⁷

have improved with the advent of vitrification but vary between studies.¹ Thaw survival rates with vitrification have been reported to be between 66% and 94%.²⁵ After thawing, mean fertilisation rates range between 66% and 79%.²⁵ To further complicate this process, increasing age is associated with lower fertilisation rates due to poorer oocyte quality.²⁶ Even after fertilisation, aneuploidy rates increase with age. Biopsies of blastocysts show that aneuploidy rates are approximately 30%, 44% and 70% at <35, 35–40, and 40 years and above, respectively.^{27,28} Additionally, increasing maternal age has been found to be associated with a decline in IVF success rates independent of embryo ploidy.²⁹ Therefore, when considering the chances of oocytes resulting in a live birth, it is complex and the above factors such as surviving thaw, fertilisation and aneuploidy rates all influence live birth, with age playing an important role.

Currently, there is a lack of good quality evidence to counsel patients on the ideal number of oocytes to achieve 1 live birth with EEF.^{10,17} With the abovementioned factors in mind, Doyle et al. estimated that the average vitrified-warmed oocyte to live born child efficiency is 6% but is heavily dependent on age. When a woman is <34 years old, this efficiency per oocyte reaches up to 8%, falling to 7% and 4% at ages 35–37 and 37–40 years, respectively. At 40 years and above, this efficiency decreases to 1–2%. Recently,

several studies have created models to predict the probabilities of live births based on the numbers of cryopreserved oocytes and age-stratified efficiencies. Doyle et al. reported that for a 70% chance of live birth, a woman would need 14, 15 and 26 mature oocytes at ages 30–34, 35–37 and 38–40 years, respectively.³⁰ Another study by Goldman et al. reported that women 34 and 37 years of age would need to cryopreserve 10 and 20 mature oocytes respectively to achieve a 75% chance of a live birth.³² Studies also examined the older age group and estimated that a 42-year-old would need to freeze 61 mature oocytes to achieve a reasonable chance of live birth.^{30–32} Although these models are far from perfect, they are useful counselling tools for women undergoing EEF. The optimal number of oocytes to cryopreserve is dependent heavily on age as they influence fertilisation, aneuploidy and therefore, live birth rates. These models also explain why EEF at age 40 is controversial as the chance of a 40-year-old woman attaining 60 oocytes with ovarian stimulation is extremely low.

Understanding the processes and risks involved during EEF

Women keen to proceed with EEF must visit a fertility specialist to assess and ensure they are in good health prior to proceeding. Basic fertility investigations, including those for markers of

ovarian reserve will be performed. As these procedures can take a mental toll on the woman, psychological counselling is encouraged.

EEF requires processes akin to IVF and the ideal protocol should aim to reduce time, minimise risk to the woman and limit financial burden while maximising oocyte yield. The processes of EEF can be divided into the following:

1) Ovarian stimulation and monitoring (Fig. 2)

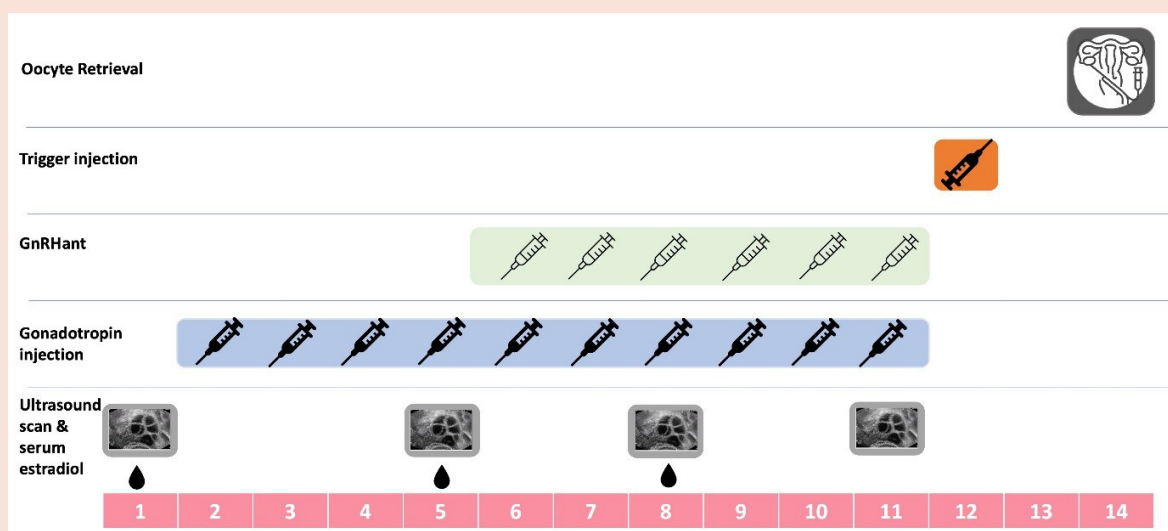
Ovarian stimulation typically commences on the day after menses start. Hormonal medications such as progestins or oestrogens may be given prior to ovarian stimulation to control the start date of the woman's menses. Ovarian stimulation entails gonadotropin administration, which is typically given in the form of daily self-administered subcutaneous injections. These gonadotropins cause multifollicular development in the ovaries. Every woman requires a different dosage of gonadotropins depending on her age and ovarian reserve; therefore, this dose will be individualised upon seeing the fertility specialist. On average, a woman requires 10 to 14 days of gonadotropin injections.

Monitoring a woman's response to ovarian stimulation is performed through transvaginal ultrasound scans and serum estradiol levels. Once the gonadotropin injections commence, she would return every 2 to 5 days for monitoring. The woman's response is gauged through ultrasound measurement of the number and size of ovarian follicles, and increasing estradiol levels.

2) Prevention of ovulation (Fig. 2)

Avoidance of ovulation through the prevention of a premature luteinising hormone (LH) surge is key for controlled ovarian stimulation (COS) in IVF. During the early follicular phase in a natural menstrual cycle, the growing ovarian follicle produces estradiol that initially exerts negative feedback on the pituitary gland, limiting its secretion of LH. However, as the level of estradiol rises, this shifts to a positive feedback via the hypothalamus and pituitary gland, resulting in the LH surge and ovulation. During COS, plasma estradiol is produced in increasing quantities by the multiple ovarian follicles. These high estradiol levels would be at risk of resulting in a LH surge. Failure to control this surge will lead to spontaneous ovulation and decreased oocyte yield.³³ Traditionally, gonadotropin-releasing hormone agonists (GnRHa) were used in COS to prevent the premature LH surge.³⁴ As GnRHa initially cause a flare effect prior to suppression of the hypothalamus pituitary axis, they need to be administered at least a week before ovarian stimulation and continued alongside gonadotropin injections. In recent years, GnRH antagonists (GnRHant) have been favoured over GnRHa as being competitive blockers to GnRH receptors—a rapid reduction in LH occurs following GnRHant administration. Therefore, the usage of GnRHant in COS results in a shorter duration of injections with no difference in the prevention of the LH Surge.^{35–38} GnRHant need only be started around day 6 to 9 of ovarian stimulation, or when the ovarian follicles have reached approximately 12 mm in size. For women undergoing EEF, it would be sensible to

Fig. 2. Ovarian stimulation and monitoring, preventing ovulation, and administering trigger injections.



GnRHant: gonadotropin-releasing hormone antagonists

use a GnRHant protocol for the prevention of the LH surge as it reduces the duration of injections, lowers the risk of ovarian hyperstimulation syndrome (OHSS) and improves cost effectiveness, without compromising on the outcomes.

3) Trigger injection (Fig. 2)

Once at least 4 of the measured ovarian follicles reach 17–17.5 mm in size, the trigger injection is administered, and this marks the end of the COS. When GnRHant are used for the prevention of a premature LH surge, the trigger injection can either be a GnRHa or human chorionic gonadotropin (HCG). The trigger injections cause maturation of the oocyte within a follicle, in preparation for the oocyte retrieval (OR) and have equal efficacy. OHSS is the most common adverse event experienced with COS. To a certain extent, all ovarian stimulation protocols cause some degree of hyperstimulation, but exogenous or endogenous HCG (from pregnancy) is known to be the triggering factor for OHSS. Mild OHSS is common and consist of symptoms, such as nausea or bloatedness. Moderate to severe OHSS is uncommon with reported incidences of 3–8% but it can be life-threatening due to severe third spacing.^{39,40} Globally, the incidence of OHSS has reduced significantly due to the advent of GnRHant protocols with agonist triggers and better cryopreservation techniques allowing the ability to “freeze all” embryos for later transfer, avoiding exogenous HCG from trigger injections and endogenous HCG from pregnancy respectively.^{2,39–41} Although the risk of OHSS is not completely eliminated, if an antagonist stimulation protocol with an agonist trigger is used for EEF, without proceeding on to a fresh embryo transfer as oocytes are cryopreserved, one would expect the risk of OHSS to be minimal since HCG exposure is avoided.⁴² Considering the expected normal to good ovarian response in these younger women attending for EEF,⁴² it would be prudent for the trigger injection used to be GnRHa, rather than HCG, to mitigate the risk of OHSS.

4) Oocyte retrieval (OR)

After approximately 36 hours following the trigger injection, the OR takes place. OR is a minor day surgery and is performed under sedation in an operating theatre. Ovarian follicles are aspirated using a needle under transvaginal ultrasound guidance. Follicular fluid is collected and handed to the embryologists for subsequent identification and vitrification of oocytes. The woman can return home on the day of the oocyte retrieval.

Women planning to embark on EEF must understand the risks associated with ORs.

When evaluating the risks of ORs, based on a large retrospective analysis of 23,827 ORs, the incidence of any complication was 0.4%.⁴³ The most common complication was hemoperitoneum at 0.23% due to damage of ovarian vessels, bleeding from ruptured follicles or direct trauma to pelvic organs. These risks were higher in patients with polycystic ovarian syndrome, history of pelvic surgery and pre-existing bleeding disorders such as Von Willebrand disease. The incidence of infective complications was 0.04% and women with previous pelvic inflammatory disease, severe endometriosis or known pelvic adhesions were at higher risk. Bladder injury was reported in 0.01% of ORs. Other rare and important complications include ovarian torsion, which could potentially compromise the woman's ovarian reserve if unrecognised.⁴³

Oocyte cryopreservation thaw survival and fertilisation rates: Slow freezing versus vitrification

Following OR, any oocytes obtained are then cryopreserved. Among the reproductive cells, one of the biggest challenges was to freeze human oocytes due to their large size, high water content, low surface area to volume ratio, and presence of the meiotic spindle. There are two techniques applied to cryopreserve human oocytes: controlled slow rate freezing and ultrarapid cooling by vitrification. Slow freezing allows cells to be cooled to very low temperatures with gradual cell dehydration, by combining penetrating and non-penetrating cryoprotectants in a controlled manner using a programmable freezer. Slow freezing uses low concentrations of cryoprotectants with slow decreases in temperature. In contrast, vitrification is considered a superfast cooling method forming an extremely viscous supercooled liquid without the formation of ice crystals. Vitrification requires high concentrations of cryoprotectants.^{4,14–16}

Initially, slow freezing was used for cryopreservation of oocytes. However, oocyte survival and fertilisation rates were not ideal due to ice crystal formation. With the development of vitrification, whereby ice crystal formation is minimised, these rates were found to improve significantly, thus allowing oocyte cryopreservation to become widely accepted. In a meta-analysis including 10 studies on oocyte cryopreservation, significantly higher oocyte survival rates post-thaw with vitrification (85%) compared to slow freezing (65%) were reported.⁴⁴ After thaw, higher fertilisation rates with vitrification (79%) compared to slow freezing (74%) were also found.⁴⁴ Examining clinical pregnancy and live birth rates, the Human Oocyte Preservation Experience (HOPE) Registry also confirmed better clinical outcomes in

vitrification compared to slow-freezing cycles. Clinical pregnancy rates (62.6% vs 32.4%) and live birth rates (52.1% vs 25.0%) were also increased with vitrification compared to slow freezing.⁴⁵

Besides the cryopreservation technique, age plays an important role in thaw survival and fertilisation rates. In a large cohort of 1468 women who underwent EEF, oocyte thaw survival rate with vitrification was 94.6% in ≤ 35 -year-old women. However, in ≥ 36 -year-old women, oocyte thaw survival rate was 82.4%. This study further substantiated that oocyte vitrification is an efficient option for EEF, but results are heavily age-dependent.⁴⁶

Oocyte storage, usage and subsequent embryo transfer

In terms of storage, the maximum duration of storage for oocytes is unknown. It has been reported that human oocytes can be safely cryopreserved for several years through the slow-freezing method, based on results of live birth rates from oocytes stored in liquid nitrogen.⁴⁷ There was a report of a live twin birth after IVF from oocytes that were cryopreserved for almost 12 years using slow freezing.⁴⁸ More importantly, in a large cohort study that included 41,783 vitrified-warmed oocytes from 5362 oocyte donation cycles between 2013 and 2021, oocyte survival rate (90.2%) and fertilisation rate (70%), were found to be unaffected by the time spent by these vitrified oocytes in vapour-phase nitrogen tanks.⁴⁹

In existing studies, there is a heterogeneity of data on the proportion of women who have returned to use their oocytes. Cobo et al. reported 12.1% of women returned with a mean time of 2.1 years of storage.³¹ In 2021, Blakemore et al. reported a return rate of 30–40% with a mean storage duration of 4–8 years.⁵⁰

Thaw survival rates of oocytes with vitrification have been reported to range from 66–94% and are centre dependent.²⁵ After thawing, mean fertilisation rates with partner's sperm then range between 66–79% depending on age.²⁵ Successfully fertilised oocytes form embryos and these embryos can then be transferred back into the woman. Embryo transfers are minor procedures and typically performed with the woman awake. A speculum is inserted into the vagina for visualisation of the cervix. A thin catheter is loaded with her embryo and placed into the uterine cavity under ultrasound guidance. Approximately 16 days later, to test for pregnancy, the woman then returns for a serum b-HCG. As previously mentioned, at age 32, the percentage of embryo transfers that result in a live birth is around 40%. At ages 37, 40 and 42,

this decreases to 35%, 25% and 15%, respectively. These success rates are comparable to the age at which the oocytes were collected, not the current age of the woman.^{19,20}

Pregnancy risks

Concerns exist around the safety of cryopreserved oocytes, in comparison to fresh oocytes with regard to pregnancy, fetal and childhood outcomes. To our knowledge, there are no studies reporting long-term follow-up of children born following EEF to date. Reassuringly, existing literature show no significant differences in perinatal, genetic or neonatal outcomes when vitrified oocytes were compared to natural conception or following IVF with fresh oocytes.^{51–53} Cobo et al. compared 1027 children born from vitrified oocytes with 1224 children born from fresh oocytes, and found no significant differences in obstetric outcomes, APGAR scores, birth weight, structural birth defects or perinatal mortality.⁵³ In addition, aneuploidy rates in cryopreserved oocytes did not differ with time or when compared with fresh oocytes.^{4,54,55}

Typical risks of pregnancies conceived with IVF must not be forgotten.^{2,10,56} Recognised early pregnancy complications include increased risk of congenital anomalies and multiple pregnancies. Data from cohort studies found that pregnancies conceived through IVF have a 30–40% increase in congenital malformations compared to women who conceived naturally.^{56,57} The exact cause is unknown but for a background prevalence of 5%, the absolute risk of congenital anomalies in IVF pregnancies would be approximately 7%.^{56,57} The goal of IVF is a birth of a single healthy child. Assisted reproductive techniques have shown a 20 times higher chance of multiple pregnancy than with spontaneous conception (1%), especially when more than 1 embryo is transferred.^{56–59} Along with multiple pregnancies, obstetric complications increase, therefore nowadays, an elective single embryo transfer is employed to avoid this risk as far as possible.^{56–59} Later in pregnancy, incidence of pre-eclampsia, gestational diabetes, preterm birth, intrauterine growth restriction and caesarean section are also increased in pregnancies conceived through IVF.^{56–59} The age at which the woman chooses to use the cryopreserved oocytes are also of importance. With older mothers getting pregnant, very advanced maternal age, otherwise known as vAMA, has been researched. Independent of other factors, being pregnant at ages 45 years and above was associated with significant obstetric morbidity and mortality.^{60,61} Even if these younger oocytes are used and transferred back in a woman with vAMA, her current age alone poses additional significant risk that she needs to be aware of.

Women should be warned against delaying pregnancy too long, and prior to embryo transfers, older women's health status should be rechecked.

Financial concerns and cost-effectiveness

The financial cost of oocyte cryopreservation cannot be overlooked. As EEF is not medically indicated, costs are typically not covered by government subsidies. The total cost will differ from one fertility centre to another, and prior to commencing EEF, the woman should undergo financial counselling. The average cost of EEF is estimated to be USD 9400 (ranging from USD 7000–15,225) in the US.⁶² If performed when the woman is younger, it is thought to be more cost-effective for women thinking of delaying their childbearing desires to late 30s or 40s, due to the cost of fertility treatments in the future. A number of studies have looked at age at EEF and cost-effectiveness.^{4,10} These studies differ in conclusion with some recommending the most cost-effective period of EEF being at the age 35, while others at age 37 as doing so at a very young age may prove to be more costly. For instance, Hirshfeld-Cytron et al. discussed the possibility of EEF at age 25 being less cost-effective in the long run due to higher chance of pregnancy without fertility and storage costs.⁶² As the speed at which age-related fertility declines also varies for each individual, women must be aware that more than 1 cycle of ovarian stimulation may be required to achieve an adequate number of oocytes for a reasonable chance of pregnancy in the future, especially if she desires more than 1 child.¹⁰ Progestin-primed ovarian stimulation (PPOS) is an up-and-coming novel approach to prevent the LH surge and premature ovulation during COS.^{63,64} Oral progestins have been used in place of GnRHant injections with comparable results with respect to the LH surge suppression, mature oocytes retrieved and pregnancy rates.^{63,64} In the future, if more robust evidence emerges for the use of PPOS, significant costs could be saved for EEF as the cost of oral progestins are significantly cheaper than GnRHant injections.

One must not forget that not only does annual storage fees (USD 100–1500 in 2024) become an accruing cost, expenses are also needed for thawing, fertilisation and eventual embryo transfer procedures (average of USD 3000).⁶² Even though EEF may prove to be a costly procedure with a relatively low return to usage, it could be viewed as an insurance policy in the event that pregnancy is delayed for longer than expected. Akin to regular insurance policies where premiums are paid regularly, storage fees are paid regularly as well and returns are more than worthwhile if the insurance or in this case, oocytes are claimed.

CONCLUSION

In light of medical advancements, EEF for age-related fertility loss is now accepted as a safe and viable option for women, with appropriate counselling.^{1,3} Success rates with usage of embryos fertilised with younger oocytes have been shown to be comparable to the age at which oocytes are cryopreserved, rather than the age of the woman at the time of the transfer. The hormonal stimulation needed for EEF have minimal risks due to newer stimulation protocols reducing the risk of OHSS. Furthermore, operative complications with oocyte retrievals are <0.5%. With better cryopreservation techniques, thaw survival rate of oocytes can reach up to 90%. It is reassuring that no increased risk to pregnancy and perinatal outcomes exist so far. However, given the complex variables and considerations involved in EEF, a thorough consent process must be in place to ensure women understand their individual success rates, processes of EEF, possible risks associated with the procedure, financial costs, and regulations around usage in the future.^{1,2} Studies have shown that a significant proportion of women underestimate age-related fertility decline and reliable information is not widely available.⁶⁵ Providing knowledge around the inevitable age-related fertility decline, coupled with robust consent processes, will allow women the reproductive autonomy to choose if EEF is suitable for them.

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