

REVIEW

Oocyte vitrification for elective fertility preservation: a SWOT analysis



BIOGRAPHY

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KEY MESSAGE

Elective egg freezing (EEF) is a safe and successful procedure, but low-return usage rates, often due to lack of a partner, result in low cost-effectiveness. While EEF empowers women, education is needed regarding the risks of the procedure, future potential of treatment success and risks of late maternity.

ABSTRACT

Oocyte vitrification, also known as egg freezing, is increasingly being used by women as a precautionary measure against the anticipated decline in fertility. In countries where this procedure is allowed, elective oocyte vitrification has become an integral part of the treatment portfolio of fertility clinics. The widespread tendency towards the postponement of motherhood and the advances in laboratory technologies are encouraging women to consider oocyte vitrification and, by doing so, increase their reproductive autonomy. However, elective oocyte vitrification, or elective egg freezing (EEF), still elicits controversy, not only when EEF is appraised from a cost-efficiency point of view, but also in terms of medical and ethical concerns. In general, although the laboratory tool of vitrification has revolutionized the treatment of infertility, the pros and cons need to be clarified when considering EEF.

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KEY WORDS

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INTRODUCTION

Since the introduction of hormonal contraceptives in the early 1960s, women have gradually pursued educational, personal and professional goals and have become financially less dependent on their parents and partners, which has given rise to the phase of 'emerging adulthood' (Arnett, 2000). This phase, from the age of 18 years to the late 20s, is characterized by a sense of instability, 'falling in between' and opportunities (Harrison et al., 2011). Several decisions must be made within a short time frame: whether to get married, whether and when to have children and whether egg freezing should be considered.

Furthermore, male as well as female 'emerging adults' have specific preconditions that they want to see fulfilled before parenting. These preconditions include the search for the ideal partner with whom to have a long-standing relationship, experiencing relational happiness and the acquisition of the right economic context and good healthcare provision, at least if they have needed medical care in the previous year (Boivin et al., 2018; Inhorn et al., 2018). An absence of these preconditions may potentially jeopardize the goal of parenthood (Harrison et al., 2011). All this is embedded in a societal context in which the media gives the impression that motherhood after the age of 40 years is a matter of course. Nevertheless, the pursuit of a professional career and the overall lack of workplace flexibility have contributed to women's reproductive dilemma. In this context, delayed childbearing resulting in a reduced functional reproductive lifespan is a consequence of contemporary western society.

The technology of vitrification has markedly improved the efficacy of oocyte cryopreservation in terms of oocyte survival and pregnancy rates, and has boosted women's options for fertility preservation (Arav and Natan, 2013; Rienzi et al., 2016). Since 2012, oocyte vitrification in women at risk of declining fertility has no longer been considered experimental according to the American Society for Reproductive Medicine (ASRM) *The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive*

Technology, 2013). Fertility preservation in the context of oncological diseases (De Vos et al., 2014), gynaecological disorders (e.g. endometriosis or ovarian surgery Cobo et al., 2020; Streuli et al., 2018) or genetic conditions with a known impact on ovarian reserve (e.g. fragile-X syndrome or Turner syndrome Avraham et al., 2017; Vergier et al., 2019) is widely accepted by general society and the medical community, and hundreds of children have been born after oocyte cryopreservation (Cobo et al., 2018).

Elective egg freezing (EEF) is offered to women who need or want to postpone motherhood, as a strategy to mitigate the risk of age-related infertility. The increasing uptake of EEF has instigated a multidisciplinary debate on the current role and future perspectives of the procedure, and the concept of EEF remains controversial for several reasons. To describe the pros and cons of EEF and to start a focused discussion regarding the biological, technological, societal and ethical aspects related to the procedure, the authors decided to conduct an analysis of the strengths, weaknesses, opportunities and threats (SWOT analysis) of EEF and to incorporate the available evidence and expert opinions from the different disciplines involved, including ethicists, psychologists, embryologists and fertility doctors.

STRENGTHS: STRENGTHS ARE THE INTERNAL ATTRIBUTES OF THE ISSUE THAT ARE CONSIDERED HELPFUL TO ACHIEVE AN OBJECTIVE

Technical advances in cryobiology

The vitrification technique is considered one of the most important developments in human reproductive medicine, and the process has largely demonstrated safety and efficiency. Compared with oocytes cryopreserved using slow freezing, vitrified oocytes have a significantly higher survival rate after warming, because vitrification avoids ice-crystal formation, which impairs cell survival (De Munck and Vajta, 2017). Hence, one vitrified oocyte has a pregnancy likelihood of approximately 8%, versus around 2% after slow oocyte freezing (Rienzi et al., 2016). Sibling oocyte studies in an autologous oocyte IVF programme (Chamayou et al., 2006) and in an oocyte donation programme (Cobo et al., 2010) have shown that the

reproductive efficacy of vitrified oocytes (fertilization, embryo development, implantation and clinical pregnancy rates) is comparable to that of fresh oocytes (Cobo and Diaz, 2011). Results from centres of expertise (Cobo and Diaz, 2011) show survival rates of more than 95%, 92% and 85% in women who had oocytes vitrified at the age of <36 years, 36–38 years and >38 years, respectively. Oocytes from women of advanced age were more likely to be dysmorphic at the vitrification and warming timepoints (Coello et al., 2019).

Safety of oocyte vitrification

From the start of the clinical application of oocyte vitrification a decade ago, thousands of children have been born using the technique, a large subset of them after vitrified-egg donation. Data on obstetric and perinatal health are reassuring (Cobo et al., 2014). No increase in aneuploidy rates has been demonstrated after trophoctoderm biopsy (Chang et al., 2019; Forman et al., 2012) and no epigenetic modifications with a clinical impact have been suggested after oocyte vitrification, although published data from epigenetic studies in human oocytes are scarce (Di Pietro et al., 2010).

Safety data related to obstetric and neonatal outcomes after IVF with vitrified-warmed oocytes are predominantly derived from studies in oocyte donation programmes, and no differences in adverse outcomes have been reported when comparing fresh versus vitrified oocytes (Cobo et al., 2010).

New paradigms in stimulation protocols

As endometrial receptivity does not have to be considered when ovarian stimulation is performed in the context of EEF, random start protocols and consecutive rounds of ovarian stimulation can be used if there are time constraints, with equivalent results when compared with conventional-start ovarian stimulation protocols (Ortega et al., 2018). Oral progestins instead of injectable gonadotrophin-releasing hormone (GnRH) analogues to prevent the LH surge may reduce the cost of ovarian stimulation (la Marca and Capuzzo, 2019) while the number of mature oocytes and embryo quality are not affected. Obstetric and neonatal outcomes are also comparable to those

when using GnRH-analogue protocols (Wang *et al.*, 2018).

High chance of success

Based on studies in oocyte donors, but also in women who return to use their vitrified oocytes, it appears that when EEF is performed at a young age, roughly before the age of 36 years, high live birth rates can be achieved, depending on the number of vitrified metaphase II (MII) oocytes, with 20–25 eggs corresponding to an 80–85% chance of having a baby (Blakemore *et al.*, 2021; Hoyos *et al.*, 2020). According to the literature, oocyte quality and ploidy are affected by age (Fransiasik *et al.*, 2014; Rubio *et al.*, 2017); when oocytes are vitrified at a younger age (<35–36 years), EEF could be considered a valuable tool to mitigate age-related fertility impairment. When fertility preservation is performed in women in their late 20s or early 30s, live birth rates will summit and reach levels that may be comparable with those of oocyte donation programmes (Blakemore *et al.*, 2021); oocyte vitrification at a young age would help to reduce the need for future oocyte donation and could avoid a substantial number of very low prognosis IVF cycles at an advanced age. In spite of this, according to a theoretical model developed to calculate the cost-effectiveness of EEF, oocyte cryopreservation was not cost-effective in young women aged 25–30 years, because of the low utilization rate, and was most cost-effective at age 37 years (Mesen *et al.*, 2015), which was also the mean age of women who had EEF in two large studies from Spain and Australia (Cobo and García-Velasco, 2016; Hammarberg *et al.*, 2017).

The potential to complete the family plan

The typical aim of fertility treatment has been to obtain one healthy baby. However, the objective could be more ambitious, and EEF holds the potential to increase the chances of reaching the desired family size. Women who conceive their first child naturally at a more advanced age may struggle to achieve a pregnancy with a second child. Many of these women could boost their prospects of having more than one child with autologous oocytes if they had their oocytes cryopreserved at a relatively young age, although there are no studies that have investigated the expectations regarding family size among women who undergo EEF.

OPPORTUNITIES: OPPORTUNITIES ARE EXTERNAL CONDITIONS CONSIDERED AS HELPFUL TO ACHIEVE THE OBJECTIVE

Patient safety

Women are often anxious about how EEF could affect their future fertility and gynaecological and sexual health. Nevertheless, published evidence is reassuring regarding the impact on future fertility and the risk of breast cancer or gynaecological cancer (Beebejaun *et al.*, 2021).

Even if the incidence of severe ovarian hyperstimulation syndrome (OHSS) has been eliminated since the overall adoption of a single injection of a GnRH agonist instead of human chorionic gonadotrophin (HCG) for triggering final oocyte maturation, there may still be a risk of mild or even moderate OHSS in hyper-responders (Feinberg, 2016; Pennings, 2020). The aim of an optimal ovarian response has to be balanced against the incidence of these side effects. However, the strong arguments to avoid a hyper-response that have been advocated in the setting of altruistic oocyte donation programmes (Pennings, 2020; Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology, 2020) have not yet transpired in relation to EEF, and the question of whether a hyper-response should be avoided in the context of EEF should be a subject for debate. Although the GnRH agonist trigger strategy is of paramount importance, other strategies have been described to prevent the syndrome (la Marca and Capuzzo, 2019).

The real need for global fertility education: identifying the optimal moment for EEF

In the fertility clinic, fertility doctors often see patients who express their frustration with the low success rates of IVF treatment at an advanced age. A very common concern with these women is the lack of publicly available information about the age-related fertility decline.

Most women report that they received information about EEF from friends, relatives, social media and non-specialized webpages (Hodes-Wertz *et al.*, 2013). Nevertheless, although most gynaecologists currently inform

women about the age-related fertility decline, and knowledge of this issue in the general practitioner setting is growing, there is room for improvement in the communication of this information from health providers to the public (Yee *et al.*, 2021). This information is crucial, but it is countered by inflated hope and false optimism about the capacity of assisted reproductive technology (ART) capacity to revert the age effect (Yu *et al.*, 2015). This is an important consideration when developing fertility education platforms: while the optimal age for oocyte cryopreservation is before 36 years, the average age at which women are currently accessing these services is 38 years (Harper *et al.*, 2017), an age at which the efficiency of the procedure is already reduced. However, there is a tendency in several countries towards developing platforms for fertility awareness raising and fertility education for adolescents and young adults (Harper *et al.*, 2021).

On a similar note, information about the age-related fertility decline is increasingly available on social media, and health providers have liaised with celebrities and influencers to enhance the reach and impact of this information (Kudesia *et al.*, 2017). In the end, it is the health professionals' duty to inform, and to advocate EEF in a timely manner as an opportunity for women to counteract the impact of delayed motherhood on the chances of having a baby, thereby pointing out the pros, cons and limitations of the approach. In the authors' opinion, oocyte cryopreservation should only be recommended if there is a reasonable prospective chance of success, and should therefore be discouraged in women above the age of 40 years.

Reducing fertility pressure

Oocyte cryopreservation is usually considered as a 'back-up' procedure, and women resort to EEF 'just in case it should be necessary' (Stoop *et al.*, 2015), because one of the main objectives of EEF is to reduce the fertility pressure that arises in women in their mid-30s and that stems from the decline in reproductive potential with increasing age.

The main reported reason for women to have their oocytes cryopreserved is the lack of a partner or, by extension, the feeling that 'Mr Right' has not yet arrived, or the fear of engaging with a wrong

person whom they deem unsuitable to co-parent or father their future children. On a similar note, these women want to avoid 'panic partnering'. Contrary to popular belief, these reasons are more frequent than the ambition to develop a career, or the increased time required for academic and professional pursuits and economic pressures (*Carroll and Kroløkke, 2018; Hodes-Wertz et al., 2013*). Indeed, women embark on EEF procedures because they strive to have a stable loving relationship and offspring genetically related to themselves (*Carroll and Kroløkke, 2018*).

Doing whatever is possible to achieve one's objectives produces confidence and satisfaction; in this respect, oocyte freezing would provide women with a 'plan B' in case the 'right' partner turns up at a moment when fertility is already significantly reduced. Several surveys have been conducted to gauge women's attitudes to EEF, with results that varied depending on the participants' knowledge; according to a cross-sectional survey study of 663 women from the general population in Ireland, most women who were aware of the effect of age on fertility considered freezing their oocytes, and 60% of respondents argued that postponing maternity is a female right (*O'Brien et al., 2017*). In a survey among women who had their oocytes frozen, the main reason was the sense of a lack of time to create a family, the absence of a partner and to prevent future regrets, although some had non-oncological medical reasons (*Baldwin et al., 2019*).

Minimize the need for oocyte donation in the future

The utilization of cryopreserved oocytes after EEF in women with age-related infertility could be considered as autologous oocyte donation. Indeed, advanced female age is the major medical indication for prospective oocyte recipients (*De Geyter et al., 2020*). Hence, the need for oocyte donation could be lower on a large scale if the uptake of EEF were substantially higher.

On the other hand, oocytes harvested for EEF that are left unused by the women themselves could eventually be donated to other women who request ART using egg donation: according to a recent study among Australian women, most of the women who had EEF would consider donating their oocytes if they

did not need them (*Polyakov and Rozen, 2021*). This option could at least partly resolve the controversy surrounding EEF, would mitigate the lack of oocyte donors and improve both cost-effectiveness and utilization rates. The stored oocytes would ultimately be used to produce a child and therefore the cost for an extra birth would decrease substantially (*Baldwin et al., 2015; Mertes, 2015*). However, for this to be a realistic option, the mean age of EEF would have to go down considerably, as most countries have a maximum age limit of 35 years for oocyte donors; altruistic donation of oocytes vitrified at older ages is not feasible in view of the reduced chances of success and the increased risk of early pregnancy loss.

Empowering women

There is a shift towards the accomplishment of important life goals within a relatively short time frame between the ages of 30 and 40 years. Because of the pressure to achieve several life goals within a 10-year period, including obtaining a qualification, starting a career, finding the right partner, finding a home and having children, women may be rushed into unstable relationships, single motherhood or unwanted childlessness (*Goold and Savulescu, 2009*). Involuntary childlessness is associated with not only higher rates of self-esteem loss, depression and partner separation, but also higher rates of mortality and feelings of loss, guilt, loneliness and shame (*Fritz and Jindal, 2018*). In those societies with religious/social prejudices, women face challenging decisions, but it seems that they can reconcile thoughts and find a solution while trying to conform to traditional reproductive roles to they can undergo EEF (*Kiliç and Göçmen, 2018*).

EEF could result in an improvement and enhancement of women's reproductive autonomy; fertility preservation could alleviate the pressure and bridge the gap between the desire to have children and the feeling of being ready to have children with the right partner, and might also promote social and gender equity (*Alteri et al., 2019*). Women who have had their oocytes cryopreserved have more time to accomplish their family project while avoiding the pressure of the biological clock and may be more likely to establish a situation that is compatible from a psychosocial point of view with raising children (*Greenwood et al.,*

2018). Elective oocyte cryopreservation meets the current demand of women to gain more control of their reproductive potential, in a similar fashion to how contraception has.

WEAKNESSES: WEAKNESSES ARE THE ATTRIBUTES CONSIDERED DETRIMENTAL FOR THE CURRENT PURPOSE

Costs

In the majority of countries non-medical fertility preservation is not covered by public health systems. The crucial question here is whether EEF should be part of the basic healthcare package. Especially in countries that have a reimbursement of IVF costs, an argument can be made that EEF should also (at least partially) be reimbursed (*Baldwin et al., 2015*). However, the uptake of EEF is largely concentrated in the group of well-educated and high-earning women. This means that public reimbursement of EEF would imply that even more highly educated and wealthy women would have access. This seems to increase injustice because it would divert funds away from other, more equally distributed, fertility problems. Moreover, considering the low usage rate of these oocytes, no public health system could afford a universal plan for preservation (*Pennings, 2021*).

In the first decade of the 21st century, big companies such as Apple and Facebook started offering EEF to their female employees as part of those companies' health coverage. In 2016, almost 5% of big companies in the USA offered this option to their female workers over the age of 30 years. In the beginning, the suggestion was welcomed by society in general, but very soon critical voices were raised. This kind of offer would be an attempt for paternalistic control over female employees and their right to decide whether and when to have children. A sharp social debate started in which some groups have considered this as the furthest step of extreme capitalism. Most critical lobbies have claimed measures for better work and family balance to avoid delaying maternity solely for work incompatibilities, and have demanded to keep the option of EEF a private decision (*Rebar, 2016*).

The inconsistency of the concept

Some authors consider these treatments to be aberrant, because women who preserve oocytes for non-medical reasons

do not have a medical condition, and the generalization of fertility preservation might drive society to an excessive and unnecessary medicalization of fertility (Mertes, 2015; Myers and Martin, 2021; van de Wiel, 2020). However, it is very difficult to circumscribe what constitutes a medical reason. Ageing is not a disease in itself but it increases the prevalence of medical conditions in most systems, including the reproductive system (Myers and Martin, 2021).

The term 'social' is associated with a wish or a desire more than a need. Non-medical fertility preservation should be considered as a wish because there is another option: to have children now. If the main reason to delay childbearing is the lack of a suitable partner (Hodes-Wertz et al., 2013; van de Wiel, 2020), there would be an easy solution for that: use donor spermatozoa and avoid delaying motherhood (Shkedi-Rafid and Hashiloni-Dolev, 2011). To avoid these considerations, specialists have suggested renaming these treatments 'anticipated gamete exhaustion banking' (Pennings, 2013) or, as an even more accurate concept that includes the decline of quantity and quality of oocytes with female age, as well as the non-emergency nature: 'planned oocyte cryopreservation (planned OC)' (Stoop et al., 2014).

Women have always felt the pressure to make decisions about whether and when to have children, and some authors believe that EEF may pressurize women even more, especially those women who cannot afford the procedure or those with low ovarian reserve and who do not accomplish their expectations after the procedure (Daar et al., 2018; Pennings, 2021; van de Wiel, 2020).

The lack of biomarkers and predictive tests

Some professionals have advocated ovarian reserve screening in the general female population by means of anti-Müllerian hormone serum analysis and antral follicle count, in an effort to prevent unintended childlessness and infertility in the future (Gunnala and Schattman, 2017). Sadly, biomarker screening of functional ovarian reserve predicts neither the real reproductive lifespan, nor the actual level of fertility (Tal and Seifer, 2017). Ovarian reserve does not reflect natural fertility potential and findings showing a low ovarian reserve can cause stress and anxiety

in women who are not in a social and financial position to perform EEF or to have a child at the moment of diagnosis (ACOG, 2019). Moreover, normal ovarian reserve tests might be falsely interpreted as normal fertility and might encourage women to deliberately delay pregnancy, which is the opposite of the intended objective.

As there are currently no reliable markers of oocyte quality, only the number of vitrified MII oocytes and the age at vitrification are predictive of success in case of oocyte warming (Blakemore et al., 2021). In the future, it may become possible to score oocytes using a biochemical and molecular analysis of follicular fluid (Razi et al., 2021; Zhang et al., 2021) or cumulus gene expression (Adriaenssens et al., 2019; Van Vaerenbergh et al., 2021) to predict the possibility of good embryo quality.

False hope of fertility hope

Cryopreservation of oocytes does not reverse the natural age-related decline in fertility and should not be viewed as a guarantee of a future pregnancy. A 100% success rate does not exist due to unknown causes of infertility, but the oocyte efficiency rate is mainly dependent on the age at preservation (Cobo et al., 2018). Undergoing non-medical preservation between 35 and 37 years of age will optimize live birth rates as well as cost-effectiveness according to mathematical models (Ben-Rafael, 2018). Although there are some tools based on artificial intelligence to calculate how many oocytes would be necessary to achieve one, two or three children, many biases have been described. According to the literature, there is no evidence about the required number of oocytes, and it is not yet possible to counsel women on when to stop vitrifying (Esteves et al., 2020).

Several international reproductive societies (the European Society for Human Reproduction and Embryology, ASRM, Society for Assisted Reproductive Technology, American College of Obstetricians and Gynecologists, Canadian Fertility and Andrology Society and Royal College of Obstetricians and Gynaecologists) have published their guidelines to help patients and health counsellors. All of them insist on not creating false expectations (Argyle et al., 2016; Dondorp et al., 2012; The Practice Committee of the American Society

for Reproductive Medicine, 2021; The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology, 2013).

Low-return usage rate: low cost-effectiveness

According to the largest series on non-medical fertility preservation, published by Cobo and colleagues, only 12.1% of women returned to use their oocytes, at an average age of 39.2 years, after waiting for 2.1 years after cryopreservation (Cobo et al., 2018). Other groups, with smaller series of participants, have reported an even lower return rate (6.5%) (Blakemore et al., 2021). Women did not use their cryopreserved oocytes because they conceived naturally, because they did not want to be a single mother or because of their social, personal or professional situation (ACOG, 2014). A very low return rate makes the cost-effectiveness of the technique very uncertain (Ben-Rafael, 2018; Fuchs Weizman et al., 2021) and, depending on the cost of EEF per cycle and the return rate, the calculated societal cost per live birth could amount to several hundreds of thousands of euros (Ben-Rafael, 2018).

It is obvious that the earlier the oocytes are cryopreserved, the lower the utilization rate will be. If EEF is performed at a later age, the return rate will be higher, but the success rate will decline, in both cases affecting cost-effectiveness (Ben-Rafael, 2018; Mesen et al., 2015). It is an extremely difficult challenge to find the balance between age, return rate and cost-effectiveness of EEF. According to the published literature, the technique would only be cost-effective if almost 60% of women, vitrifying before they were 38 years old, recovered their stored oocytes (Fuchs Weizman et al., 2021), which is very far from current data.

Minimal but real risks of the technique

Although ovarian stimulation protocols have nowadays become less burdensome, medical risks should not be ignored. Interested women are usually afraid of the risks and express anxiety, false beliefs and fears about possible unwanted medical events (Daniluk and Koert, 2016). Women who plan to preserve their fertility are usually healthy and, although complications are mostly minor and rare, the risk of a significant complication is approximately

4 per 1000 procedures (0.4%), with 1 in 1000 women requiring further surgical intervention (*Levi-Setti et al., 2018*). OHSS and related complications in susceptible misdiagnosed patients, as well as other complications of surgery, are infrequent (*Levi-Setti et al., 2018*), but all of them have been described and ought to be carefully explained to women who consider EEF.

Unknown oocyte quality and future results

Predictors of future success are not only ovarian response, appropriate follicle growth and number of retrieved oocytes or mature oocytes. It is very important to clarify that embryo quality cannot be predicted at the stage of MII vitrified oocytes, and doctors should be sure that women have understood that a baby is not guaranteed, even if everything goes well from oocyte warming to implantation.

As explained before, at the present time, the main predictive factors for future success after oocyte warming are age at vitrification and the number of cryopreserved MII oocytes (*Blakemore et al., 2021; Cobo et al., 2018*). Nevertheless, although oocyte freezing has the potential to mitigate the sense of pressure, decisional regret can occur after vitrifying. Regret seems to be strongly linked to a disappointingly low number of retrieved eggs, a perceived lack of information prior to freezing, a lack of emotional support during the procedure and an overestimation of the probability of achieving a pregnancy (*Greenwood et al., 2018*); however, a recent Turkish study showed that EEF in women with diminished ovarian reserve was not associated with regret about their decision unless women had a lack of confidence in the efficacy of EEF (*Gurbuz et al., 2021*).

THREATS: THREATS ARE EXTERNAL CONDITIONS THAT COULD BE DETRIMENTAL TO THE OBJECTIVE

Late maternity

Women can carry pregnancies at almost any age, but studies indicate that both maternal and neonatal complications increase with the age of the pregnant woman. The main criticism of non-medical fertility preservation is related to the deliberate decision to delay maternity. Late motherhood involves

medical risks for mother and babies, such as pre-eclampsia, gestational diabetes, preterm birth, small-for-gestational-age babies or intrauterine growth restriction and other serious obstetric syndromes, including maternal or fetal deaths (*Pinheiro et al., 2019*). The derived expenses of these risks are huge and should also be considered. When fertility preservation is performed to delay pregnancy, these complications, if pregnancy occurred, could appear and should be discussed with the woman.

Legal restrictions

Legislation and professional codes differ among countries, limiting some women's direct access to fertility preservation. In some countries, oocyte storage is only allowed if there are genuine medical reasons such as severe disease or a risk of premature decline of fertility. For example, in France, ART was until recently restricted to medical conditions, so non-medical fertility preservation was strictly forbidden (*Alteri et al., 2019*). This situation has encouraged French women to go abroad to access these treatments and others.

Beside the matter of access, the maximum storage time has been a source of debate. Indeed, a short maximum storage time limits the utility and effectiveness of EEF and may force women to ship their oocytes to overseas fertility clinics or to have the oocytes fertilized with donor spermatozoa and stored as embryos (*Bowen-Simpkins et al., 2018*). In the UK, for instance, the government has recently agreed to change the maximum storage time from 10 years to a maximum of 55 years, after years of campaigning by several stakeholders.

Lack of control on laboratories with suboptimal results and their consequences

Virtually any fertility clinic can claim that they can freeze women's oocytes for a couple of thousand euros. There is very little legal regulation of the egg freezing practice (*Gürtin and Tiemann, 2021*). In the current authors' opinion, laboratories ought to be subject to audits to control their quality standards and to check their procedures and results, and caution is needed to prevent laboratories with low oocyte survival rates and poor success rates from advertising themselves while their 'clients' may be unaware of the poor performance.

Lack of a partner and the reversed educational gender gap

As explained before, contrary to general belief, all studies among elective egg freezers show that the main reason for women to freeze their eggs is the lack of a partner or the right partner (*Baldwin et al., 2019; Brown and Patrick, 2018; Carroll and Kroløkke, 2018; Inhorn et al., 2018*). These women are buying time in order to find this partner. However, highly educated women will find it very difficult to meet the right partner because women traditionally engage a partner with the same or a higher status than themselves. Due to women's emancipation, women who have attained higher education (and the related social status) outnumber the number of men with a higher education, and this reversed educational gender gap is increasing worldwide (*Inhorn et al., 2018*). The result is that EEF may increase the reproductive autonomy of individual women at a certain point in their life, but it does not solve the real problem for the group of highly educated women (*Pennings, 2021*). Unless they change their partner preferences, many of them will have to choose between becoming a single mother or looking for another life goal besides parenthood.

SUMMARY AND CONCLUSION

EEF has become a potential game changer for women in their 30s worldwide (*IFFS, 2019*) and is expected to expand even more, although several limitations, inconsistencies and uncertainties still need to be thoroughly analysed by professionals, by the relevant authorities and policy makers, and by society in general. There are certain arguments to recommend EEF widely, but the negative implications of EEF may affect health, efficiency, ethic balance, health, efficiency of the technique and mental health status of the women who use the procedure.

According to 2019 Eurostat data (www.ec.europa.eu), the mean age for women in the European Union to have their first child was 30.9 years, and this age has tended to increase (being 30.4 years in 2014), although there are geographical differences. Starting a family at a more advanced age has resulted in a reduction of the fertility rate (a mean of 1.53 children per woman in Europe, 1.14 in Malta and the Ukraine, and 1.23 in Spain), which has an impact on population



FIGURE 1 Summary of the strengths, weaknesses, opportunities and threats analysis of elective egg freezing (EEF).

replacement levels ("[\). The postponement of motherhood and the associated age-related fertility decline have provoked a gradual increase in fertility treatments, especially in women over 35 years \(Gleicher et al., 2016\).](https://ec.europa.eu/eurostat/databrowser/view/tps00017/default,)

The uptake of EEF is on the rise and may give women who are not in the position to attempt pregnancy, mostly because of the lack of a stable partner, the opportunity to have their own genetic children while mitigating the impact of the natural fertility decline. The costs of EEF are an important concern for a large subset of women who consider EEF, not just for those who have a limited income, but also for women who have a low ovarian reserve and who would need several rounds of EEF to obtain the number of oocytes they desire. Integrating research findings from sociological studies on EEF into the policy-making process is a key challenge for authorities but should eventually result in an appropriate balance between the pros and cons of EEF for a growing group of women worldwide. Finally, fertility clinics should adapt their services to current needs, tailored to the individual who requests reproductive

healthcare, including single women considering EEF (Inhorn et al., 2018). The findings of this SWOT analysis are summarized in FIGURE 1.

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