

Social freezing in Switzerland and worldwide – a blessing for women today?

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Summary

This is a critical review of the medical, ethical, judicial and financial aspects of the so called “social freezing”, the cryopreservation of a woman’s oocytes for non-medical purposes. The possibility of storing the eggs of fertile women in order to prevent age-related fertility decline is being widely promoted by fertility centres and the lay press throughout the world.

Research data has shown that social freezing should ideally be performed on women around 25 years of age in order to increase their chances of a future pregnancy. In reality, it is mostly performed after the age of 35.

Unfortunately, social freezing is in general not a solution for the underlying societal problems to fit in with professionally active women and having children. It only delays the existing problems. Furthermore, it creates a lot of potential new problems. A great deal more should be undertaken to offer real solutions to the underlying societal problems which are in part: pre-school education, care in the event of childhood illness, and the many weeks of school holidays, acceptance of professionally active women having children, and more job offers with a workload <100%). Furthermore, society should be informed about the decreasing chances of pregnancy with increasing maternal (and paternal) age as well as the increasing risks of miscarriage and obstetric/neonatal complications.

Detailed information for woman considering social freezing is crucial. Every doctor, proposing social freezing to his patients, should be up to date with all these details. Follow-up studies on the outcome of these children are needed.

Key words: *IVF-ICSI; fertility preservation; non-medical reasons; social freezing; oocyte freezing; oocyte vitrification; ethics*

Introduction

Egg freezing for social reasons means the cryopreservation of a woman’s oocytes for non-medical purposes, i.e. as prevention for age-related fertility decline. To be more precise, social freezing means egg storing of a healthy, fertile woman (one or more in-vitro fertilisation (IVF)-stimulation cycles), in order to have a pregnancy after her career, i.e. at the age of 45 to 50.

For about 10 years, in parallel with the technical improvement of oocyte freezing, the possibility of egg storing for non-medical purposes is more extensively discussed and more commonly accepted by the general population and expert committees; not only in the United States, but also in Europe. Likewise, in Switzerland, more emphasis is focussed on the promotion of social freezing. Articles in the lay press are publicising the theme and lectures are regularly organised for lay people, by centres which offer this practice. In addition, beautiful advertising brochures are sent to gynaecologists in order to promote social freezing to their patients. Information is widespread on the internet. Here are examples of messages conveyed from the different brochures: “I choose the right moment”; “You choose your personal best”; “Art, literature, fashion, children – too much at once? You’d like to enjoy every day of your life and spend your life in your own way. Take advantage of your new freedom to act!”; “Develop your business plan! You’ve got innovative ideas and want to realise your full potential. Besides, you want to have children – some day. Oocyte preservation offers you fertility freedom!” By the same token, it is proposed to audiences at Swiss congress lectures, to offer her one or more cycles of “Social Freezing” as a birthday present to, for example, a daughter studying medicine.

It is a fact that the peak of reproductive performance for women is 25 years. After that reproductive aging begins and pregnancy rates decline relatively fast from 35 years. Conversely miscarriage rates rise exponentially. After the age of 43 years, chances of becoming pregnant are extremely low. It is also a fact that combining career and motherhood, at the same time, is a very difficult challenge for women. Social freezing is advertised to harmonise these incompatibilities. But is it really the solution to the problem? Or could it also create other problems?

Neonatal and maternal risks of primiparity at an advanced maternal age (≥40 years)

Maternal risks

With increasing age, pre-pregnancy chronic medical conditions and with that obstetrical risks and adverse birth outcomes rise [1–4]. Consequently, pregnancy complications

are very elevated (84.7%) compared to younger women, i.e. gestational hypertension (45% vs 6.4%), pre-eclampsia (18.3% vs 3%–4%), gestational diabetes (42.7% vs 6.1%), cerclage (9.2%), preterm delivery (33.8%), hospitalisation during pregnancy (48.1%), caesarean sections (93.9% vs 25%) [5]. Age is also an independent risk factor for placenta praevia, placental abruption, perinatal mortality and especially foetal death [6]. Primiparity may be a specific risk factor [7], as preeclampsia is regarded as a disease of nulliparous women [8, 9]. Even though maternal mortality rates are very low in Europe, they are increasing with increasing age [10].

Moreover, postnatal depression is significantly elevated with increasing maternal age, (OR = 0.96, p-value = 0.019), and this, independent of socioeconomic and reproductive characteristics, conjugal status or substance consumption [11].

Neonatal risks

Due to advanced maternal age and pregnancy complications, neonatal complications are also increased, comprising prematurity (33.8% vs 7% in younger women) and lower mean birth weights among infants of women ≥ 50 years old ($p = 0.0003$; $p = 0.01$ for singletons and $p = 0.04$ for multiples) compared with younger women [5]. The incidence of low birth weight (LBW) also rises with increasing maternal age. Among women aged 50–65 years, 68.5% of the infants have a LBW [5]. LBW and its resulting consequences are one of the main causes for perinatal morbidity and mortality. It has to be mentioned that intrauterine growth restriction, which is correlated with increasing maternal age, was found to alter foetal programming and can lead to lifelong health implications, i.e. cardiovascular disease, type 2 diabetes mellitus and obesity [12].

Conversely, it seems that children of 40 year old mothers have fewer hospital admissions and unintentional injuries, better language development and fewer social and emotional difficulties [13]. In addition, other data show that older parents can provide advantages, such as: relational stability, parent-child interactions and financial situation compared to younger parents [14].

Risks and adverse effects of IVF-intracytoplasmic sperm injection (ICSI) treatments

Perinatal outcome after ART

The main risk of IVF-ICSI is multiple pregnancies (essentially twins, but also triplets). It is very well known and does not require explanation that risks of perinatal morbidity and mortality are extremely increased in multiples compared to singletons.

However, after ART, even among singletons a heightened risk of adverse perinatal outcomes has been observed as compared to spontaneous conception, including low and very low birth weight [15–19]. Three meta-analyses [20–22] have supported these data and a consensus statement of the National Institute of Health suggests informing and warning patients concerning these risks [23]. A recent meta-analysis has shown an elevated risk for preterm birth

even in singletons after elective single embryo transfer, compared to spontaneously conceived singletons [24]. The reasons for these adverse perinatal outcomes are not yet elucidated; infertility itself, ovarian stimulation and in-vitro manipulations are taken into consideration.

And yet another unresolved concern is the potential risk of epigenetic changes and imprinting defects after in-vitro cultures, especially after extended culture of embryos (blastocyst stage) [25].

Malformation rate in children conceived after IVF-ICSI

Since the delivery of the first IVF baby, Louise Brown in 1978, a vast number of follow-up studies have been undertaken. While initially no differences between malformation rates after spontaneous conception and IVF-ICSI were found [26, 27], subsequently data showed significant elevated malformation rates in children conceived after IVF-ICSI [28–31].

The reasons for this are not clear today; paternal and maternal socio-demographic and anamnestic risk factors as well as infertility, ovarian stimulation and in-vitro manipulations are under discussion. Accordingly, it is unclear today if IVF in patients without infertility would lead to the same elevated malformation rate in children or if it would be different because there is no inherent infertility factor.

Malformation rate in children conceived after freezing-thawing of unfertilised oocytes and consecutive ICSI

Research data available in the literature is minimal. A review on 58 articles (23 case reports and 35 case series), including 308 children after slow freezing and 289 after vitrification, showed no elevation of malformation rate (1.3%) [32]. Further outcome studies are essential in order to have conclusive data.

Outcome of children after vitrification

Because of the formation of ice crystals in the oocyte (which can destroy the skeleton of the cell), cryoprotectants are added. However, fertilisation and pregnancy rates with the conventional slow freezing method of oocytes are limited.

Vitrification is a newer technique with an ultra rapid cooling of the oocytes in order to avoid ice crystals. The first baby after vitrification was born in 1999, a healthy girl. The only existing follow-up study, including 200 children, is reassuring [33]. However, meaningful data are lacking. Besides, there is no data available on the long-term follow-up of these children.

Long term health effects in children conceived after IVF-ICSI

The risk of long term health effects in children conceived after IVF-ICSI cannot be specified yet. Study results have shown an increased cardiovascular and cardio metabolic risk in healthy children after IVF-ICSI [34–36]. However, the clinical impact of these findings and the clinical long term consequences are not yet clear. The oldest IVF children are in their thirties and the oldest ICSI children are just around twenty years of age. There is a need to investigate

the long term health of IVF-ICSI-children and their risk of diseases later in life in epidemiologic follow-up studies.

Risks of failure (respectively chances of success)

In Switzerland, mean pregnancy rates per transfer (of 2 embryos) are 19.5% after freezing and thawing of the (pre-) embryos [37].

These numbers cannot be adopted for women who perform social freezing because this comprises freezing and thawing of already fertilised oocytes (pre-embryos) which are known to have a better implantation potential after thawing compared to non-fertilised frozen oocytes, even though cryopreservation techniques (i.e. vitrification) nowadays have made substantial progress.

Recent data show that survival and fertilisation rates of unfertilised oocytes after vitrification are significantly higher compared to those after slow freezing (78.9% vs 57.9% and 72.8% vs 64.6%) [38].

According to the results of a meta-analysis, the implantation potential of one metaphase-II oocyte that has survived the freezing-thawing process is estimated to be 7% (95%CI: 4.3–11.2) after slow-freezing and 7.7% (95%CI: 5.3–11) after vitrification [39]. Other data show that the implantation rate per thawed oocyte after vitrification can be as high as per fresh oocyte (around 12.9%) [40]. At the same time, slow freezing protocols are much more efficacious nowadays and can reach 11.8% per thawed oocyte in some centres, according to some authors [41]. (Implantation rate is defined as the probability of a single embryo to implant after transfer and it is calculated as the number of gestational sacs per 100 transferred embryos. It has to be stressed that the implantation potential of an embryo is, among other factors, dependent on maternal age.)

However, there are no concrete data in literature concerning the “baby take home rate” per thawed unfertilised oocyte.

The chances of becoming pregnant after preservation of oocytes depend on the one hand, on the number of the cryopreserved oocytes, but on the other hand, on the biological age with its impact on spindle configuration and chromosomal arrangement. Both decrease dramatically with age. Women, considering social freezing, are unfortunately very often around 38 years of age, which leads to a very low cost-efficiency.

Risks of ovarian hyperstimulation syndrome

According to the literature, the risk of women having ovarian hyperstimulation syndrome lies between 1% and 10%. In this special collective, the risk of relevant hyperstimulation syndrome is estimated to be lower (around 1%), because no transfer is performed in these women and special prevention measures (i.e. antagonist protocols with ovulation induction by agonists) can be applied.

Risks of oocyte pick-up

The risk of women incurring complications due to the oocyte pick-up (bleeding, infection, injury to other organs or complications due to anaesthesia) is very low (1/1000).

Legal issues of fertility preservation in Switzerland

The Swiss law of assisted reproductive technologies came into effect 01 January 2001 [42]. Different aspects of IVF-ICSI are regulated, namely what is allowed to be cryopreserved and how long: oocytes/ovarian tissue, sperm/testicular tissue and pre-embryos can be frozen for up to 5 years (article 15). In the case of medical treatment of an illness, such as cancer which could cause infertility, gametes can be cryopreserved longer (article 15). It is forbidden by law to freeze embryos (article 17.3).

In the context of the Swiss law, social freezing in Switzerland makes no sense. Ideally, the woman should be around 25 years to do a social freezing. But the “Career problem” is generally not solved within 5 years, and rarely nowadays by the age of 30. On the other hand, a cryopreservation at the age of 35 in order to plan a pregnancy at the age of 40 is too late because of the biological aging of the oocytes.

Nonetheless, social freezing is proposed and performed in Swiss fertility centres. Patients still have the possibility to transfer their oocytes in fertility centres abroad, where other legal regulations exist.

Another unsolved juridical issue of the Swiss law is that IVF-treatments are only allowed in the case of infertility, which is not at all the case of young career women who are drawn to social freezing. But as always in legal issues, there exist different judicial interpretations. According to those, stimulation and freezing of oocytes have to be completely separated from the process of IVF-ICSI-fertilisation. As fertilisation would only be undertaken when the woman has become infertile due to age, social freezing would be legal in Switzerland according to this interpretation of the law.

Ethical issues

Reproductive autonomy versus well-being of the child

An ethical principle is the respect for the autonomy of people. People can decide whether to have children, with whom, how many etc. Advocates of social freezing extrapolate that persons should also have the right to decide the moment to reproduce, according to their priorities (child-bearing in relation to other life plans).

At the opposite end of the spectrum is the well-being of the child. According to Swiss law, the well-being of the future child is the first and supreme principle. In keeping with this, elevated risk of potential medical complications for the future child should be avoided. Besides that, it is primordial for the child's well-being to have young and vigorous (or healthy) parents. Consequently, situations such as, 65–70 years and older mothers/parents with fully pubescent children should be averted.

Another ethical issue is that social freezing is the embodiment of the trend in society to accept less and less the finiteness and unavailability of the human life.

Other concerns are the possibility to create high (and potentially false) hopes and introducing medical processes to primary fertile women.

Financial issues

Social freezing is a very expensive procedure and the cost is entirely assumed by the woman/couple in Switzerland. Cost of only one cycle of IVF-stimulation (with oocyte pick-up and -freezing) can vary between CHF 3,000 and CHF 5,300. Several IVF-stimulation cycles are promoted in order to increase the chances of a pregnancy.

Additionally, annually storage costs have to be added (between CHF 200 and CHF 300 per year).

And last but not least, costs for one thawing cycle (including fertilisation with the partner's sperm) are in addition (between CHF 2,500 and CHF 3,500). In general, several thawing cycles are necessary to get an ongoing pregnancy. A cost-based decision analysis on the cost efficiency of fertility preservation for social indications has come to the conclusion that neither oocyte cryopreservation nor ovarian tissue cryopreservations are cost-effective for otherwise healthy women planning delayed childbearing [43].

Arguments for social freezing

Arguments for social freezing are that the ethically delicate oocyte donation as well as the burden of ineffective fertility treatments and chromosomal abnormalities, at an older age, could be avoided. Social freezing "promises" women to practice their reproductive autonomy and simultaneously to increase their chances of genetic motherhood.

Social freezing can give some hope to women who have not had the chance to meet a partner. To the present-day, unfortunately, many intelligent and well educated women are confronted with the phenomenon of staying single.

Advocates of social freezing consider age related fertility decline to be a medical problem which should be prevented by this relatively new technology. In Israel for example, women between 30 to 41 years of age are allowed to undergo four retrieval cycles or the retrieval of 20 oocytes if they fear a decline of fertility; thawed fertilised eggs can be implanted until the age of 54 [44]. Costs are generally taken over by various Israeli health funds.

Arguments against social freezing

Every medical intervention has its inherent risks. As mentioned above, even today, there exists for the future child (and also for the mother) many health risks due to the IVF-ICSI treatment, especially in woman over 45 years of age. Beyond that, there are many unresolved questions concerning the health and the outcome/follow-up of IVF-ICSI children. In general, these risks are considered to be relatively low and IVF-ICSI treatment in the case of infertility is regarded as acceptable. But, it is open to question whether to expose healthy women without inherent infertility factors and their future children, unnecessarily, to adverse physical outcomes (not to mention the psychological problems of the children whose mothers could be taken for their grandmothers and all the other ethical issues).

In addition, it has to be considered that pregnancy, delivery and raising children does not ever really fit into a woman's career plan, independently of age. There is no "ideal time" and it is always complicated to organise child care

whatever the age of the mother, e.g. before and after school, in the case of childhood illness, during the weeks and months of school holidays and so on. Energy and force of human beings decrease slowly but surely with age. A woman of around 35 years can cope with concomitant short nights and the stress of performing during the day, whereas for women of 45–50 this is generally a much more difficult task.

It has also to be considered that grand-parents, who nowadays help a lot in looking after their grandchildren during the school holidays or in the case of illness, would be in the case of delayed motherhood (after social freezing) either in a state of health incompatible compared to the energy of the children, or deceased. It has also to be mentioned that later on, these old parents will for the same reasons not be able to look after their grandchildren. And it has also not to be forgotten that the resulting children could be very ashamed to have parents who could be perceived as their grand-parents, possibly leading to psychological problems.

Social freezing does not solve one problem; it only delays the time of the multiple problems to be confronted, especially in Switzerland with its rigid structures and the paternalistic view of the role of the woman in society.

Finally, even with 20 stored oocytes, there is no a guarantee of getting pregnant after social freezing. Moreover, the risk of reaching 45 or 50 years of age without becoming pregnant, despite of a lot of physical and psychological stress (not to mention the financial issues) is not negligible.

Future strategies

Unfortunately, reports in the lay press on more or less famous women giving birth to a child at around the age of 50 are presenting a distorted picture of reality. Studies around the world have shown that young people are not aware of the natural limits of human fertility [45, 46]. Consequently, school-children should be informed of the decreasing chances of pregnancy with increasing maternal age as well as the increasing risks of miscarriage and obstetrical/neonatal complications.

Moreover, substantial changes in social structures, i.e. crèches, day nurseries, day schools, child care during the long holiday periods and care of ill children are needed. Additionally, major rethinking of the perception of ideals and traditional gender roles is urgently required, especially in the quite paternally orientated country of Switzerland. Currently, women who have children are often not considered suitable for leadership, fearing that their performance could be diminished. This thinking is probably even more pronounced in the German speaking part of Switzerland compared to the Romandie.

Significant efforts have to be made in order to counteract these problems. Politicians of different parties, supported by medical societies, e.g., for example, the Swiss Society of Gynaecology and Obstetrics, should urgently work hand in hand in order to solve the aforementioned problematic issues.

Conclusion

Social freezing should be performed around the age of 25 years in order to improve chances of becoming pregnant. It could give some hope for women who unfortunately do not find a partner in their thirties.

Social freezing is regrettably not a realistic solution for women seeking compatibility with their professional and family life. On the contrary, it creates a lot of potentially new problems.

A lot of efforts should be made to solve the underlying societal problems (preschool, child care in case of illness and during the months of school holidays, acceptance of professionally active women having children, job offers with a workload <100%, job sharing possibilities etc.).

Furthermore, society should be informed about the decreasing chances of pregnancy with increasing maternal (and paternal) age as well as the increased risks of miscarriage and obstetric/neonatal complications.

Although social freezing is not a solution for the underlying problems, nonetheless it can be beneficial in specific situations. Detailed information on the (limited) possibility of health risks for the future child (especially in the case of delayed motherhood), the yet unsolved questions about the outcome of IVF-ICSI children and of the relatively new technique of vitrification, information on the risk of failure, the judicial, ethical and psychological issues and last but not least on the high costs is crucial. Every doctor, proposing social freezing to his patients, should be familiar with up to date and all the above mentioned data.

Follow-up studies on the outcome of the children after vitrification and particularly after social freezing are urgently needed.

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