Chapter 6
The Profile of a Pioneer Cohort of Women Opting for Oocyte Cryopreservation for Non-medical Reasons

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Introduction

Since 2009 the Centre for Reproductive Medicine of the UZ Brussel offers the possibility to women in anticipation of gamete exhaustion (AGE) [1] to cryopreserve their oocytes. The onset took place in an era of societal and political debate (e.g. The Netherlands) and warnings by the main professional organizations in the area of reproductive medicine [2, 3] especially about the non-medical use of oocyte cryopreservation. For instance, the American Society of Reproductive Medicine [2] stated that oocyte cryopreservation is an "experimental procedure" that should not be offered or marketed as a means to defer reproductive aging. The British Fertility Society (BFS) agrees that oocyte cryopreservation should not be portrayed as a means to counteract age related fertility decline [3].

What was initially offered to women faced with illness or medical treatment resulting in infertility is nowadays a treatment that is (luckily) more often used for non-medical indications leading many ethicists in the area of reproduction to examine the benefits and pitfalls of this application. Objections formulated against AGE-banking are that; the whole process of reproduction becomes medicalized and perhaps even commercialized undermining rather than expanding women's reproductive autonomy [4]. Moreover, healthy women have to undergo a stress-inducing high technological fertility treatment without having an actual fertility problem and little is known about the welfare of the children born after the use of cryopreserved oocytes. One also assumes that women will deliberately postpone motherhood until the time of their choosing, that women will give priority to their careers and that oocyte cryopreservation will offer a false sense of security that one is optimizing her chances of motherhood [4].

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In contrast, those in favour of AGE-banking for non-medical reasons stress the possible benefits for women and their right to ascertain reproductive autonomy after comprehensive counselling. More precisely, personal reproductive decisions should be free from interference unless they will cause serious harm to others. Another argument in favour of AGE-banking for non-medical reasons is that it alleviates gender inequality by allowing women to extend their reproductive years just as men are able to do already for many decades. As such, women should also gain access to this technology that will offer them this possibility to preserve their fertility [5]. Furthermore, this practice might be beneficial to the future child since it will be conceived when women feel ready, have a stable relationship and are financially secure but most importantly, the child will have a biological bond with his mother. Another advantage of oocyte cryopreservation instead of embryo cryopreservation is that it empowers women because it makes them less dependent of their partner and it allows her to have a child with a partner of her choosing [5].

Regardless of the societal and political debate oocyte cryopreservation seems only to elicit interest in a small niche of the female population. In a large survey (n > 1000), [6] only 3% of the women stated they were going to freeze oocytes. There was another 28.5% who was interested and considered oocyte freezing. This added up to 31.5% 'potential freezers'. In another study [7] only 4% of the women who inquire by phone at the Extend Fertility centre, Boston, USA about the fertility preservation treatment go on to use the technique. Ter Keurst et al. [8] who investigated the intentions of childless women aged between 28 and 35 years to use fertility preservation stated that 85% had thought about fertility preservation but only 4.6% had actually made a decision about it. Authors conclude that in general women have a low intention to use fertility preservation despite being childless, having a desire for a (genetically related) child, being in the age range when fertility starts to decline and having reasonable fertility knowledge. They relate these low intentions to three main issues; 'lack of perceived susceptibility to infertility' and 'defining overly optimistic parenthood goals' by giving themselves around 3 years to have two children (from 34.4 to 37.6 years). 'Failure to consider the use of fertility preservation' is the third issue. To explain this third factor they point to the work of Rogers [9] of 1962 about the diffusion of innovations. According to him the first stage of diffusion happens when individuals know about the technology but have not been inspired to get more precise information. So knowing that fertility preservation exists women tend not to find out more about it (e.g. take contact with a fertility centre). Another way to define this failure is the fact that women might rely on ART with fresh oocytes to overcome fertility problems. However, older women felt more susceptible to infertility and had higher intentions to use fertility preservation.

Besides the fact that only a small niche of the female population seems to be interested it is also striking that when women actually candidate to become an AGE banker they do this at a suboptimal age—in their late 30s—when oocyte reserve and quality strongly diminished and pregnancy rates drop significantly [10]. According to Ter Keurst et al. [8], the knowledge of the candidate AGE-banker on fertility issues is reasonable but may lack precision about fertility decline and the success of fertility preservation. Women might only feel susceptible to infertility at this age while not realising that at that time fertility preservation rates are not optimal which is reflected in the lack of a feasible parenthood plan. The main preventive measure these authors propose is for health care professionals and policy makers to increase fertility aware-

ness and support women in creating a realistic plan to achieve parenthood goals via educational campaigns or family planning consultations. Mertes and Pennings [10] discern three different steps to make the current practice of oocyte cryopreservation more clinically and ethically sound: creating public awareness; offering individualized, age-specific information and counselling; and offering predictive tests such as anti-Müllerian hormone measurements and antral follicle count. The main objective of these measures is to convince those women who are most likely to benefit from banking in AGE to present themselves before age 35 and to discourage fertility clinics from specifically targeting women who have already surpassed the age at which good results can be expected all this not to install false hope in reproductively older women.

Studies examining the actual AGE-banker and her motivation(s) to opt for this procedure could challenge the speculations and assumptions made about this specific population but are still scarce anno 2017. A study [11] reported on a small number of women (n = 20) wanting to cryopreserve their oocytes for non-medical reasons. These women were on average 38.6 years old and often they were single and had a high educational level. Wanting to take advantage of all possible reproductive opportunities feeling pressured by their biological clock and wanting an 'insurance policy' against future age-related infertility were the main reasons for opting for oocyte cryopreservation. The pivotal events to apply for the treatment were the recent awareness of the existence of the technique; their advanced reproductive age and not wanting to single parent a child. Another study [12] also reported on a small group of women (n = 23) who froze their oocytes. On average they were 36.7 years old, mostly university educated, 87% was single and 88% was prepared to donate there eggs for research or to women in need of donor eggs in case they would not use there eggs. Their motivation to cryopreserve oocytes was very similar to the motivations reported in the Gold-study but 1/5 also saw it as a preventive measure against age related fertility decline or other medical issues that would make them infertile (e.g. cancer treatment).

Hodes-Wertz [13] described the largest cohort of women post oocyte cryopreservation. One hundred and eighty three patients out of 478 (38%) participated in a survey follow-study. At the time of oocyte cryopreservation more than 80% was aged 35 years or older. Women were aware of the age related infertility and wished they had undergone the procedure at an earlier age. Unawareness of the technology and/or readily availability followed by not being ready and not being concerned about their reproductive future or unable to afford it were the reasons they gave for not acting sooner. They also felled that the popular media falsely portrayed the upper age limit for natural conception and 19% of the respondents added that workplace inflexibility contributed to their reproductive dilemma. However, "having no partner at the time to conceive with" was the main reason to pursue oocyte cryopreservation.

Counselling AGE-Bankers

In order to get acquainted with the candidates for AGE-banking (for non-medical reasons) these women were systematically counselled in accordance with the recommendations by the main professional bodies (ASRM and BFS and later ESHRE [14]). Counselling was performed by a gynaecologist and a psychologist in a

non-directive manner with respect for reproductive autonomy making sure that realistic expectations are being created and that well-informed decisions can be made about oocyte cryopreservation an whether to proceed with the treatment or not.

All candidates underwent a semi-structured interview performed by a psychologist in which the following topics were addressed: socio-demographics, mental health, relationships and child desire, discovery of the possibility to cryopreserve oocytes, initial motives to opt for this treatment and/or alternatives, openness about this project towards family, friends and the received support, the possible disadvantages, risks and limitations of the treatment and the use of the cryopreserved oocytes.

A minor medical assessment was performed by a gynaecologist and blood samples were taken in order to evaluate hormone levels (FSH and AMH) and an antral follicle count was performed.

Between July 2009 and December 2012, 243 women contacted the Centre for Reproductive Medicine with the intention to freeze their oocytes. Not all of them had already made the decision to actually freeze oocytes and for many of them it was unsure whether it would medically/physically feasible and responsible to perform this treatment because of their advanced reproductive age. About half of the women (n = 124 or 51%) went through with the treatment although for four candidates (1.6%) oocyte pick-up had to be cancelled because of a low response.

One hundred and nineteen candidates (49%) did not start treatment; 21 candidates were refused for treatment usually because they were over 40 years old, 14 candidates hormones levels were unfavourable to start treatment, 20 candidates stated at the intake that they were still undecided whether they would start the treatment, for 22 candidates it remained unclear why they did not take upon treatment and 33 (13.6%) candidates did not go through with the treatment for ‘other reasons’ (e.g. 4 became pregnant spontaneously, 9 found a partner, 9 made a switch to another treatment, 6 found it too expensive, 5 mentioned other reasons not to perform treatment). On average these patients underwent 1.83 (±1.06) oocyte pick-ups and have 15.96 (±9.8) oocytes in the freezer.

Counselling these women also allowed us to document on the profile of this population. Data are presented from women who did not only apply for treatment but who also actually went through with the treatment (n = 124).

Socio-Demographics

Women were of an advanced reproductive age, on average 36.74 (±2.59) years old, highly educated (70.2% university degree, 28.2% degree) full time employed (79.8%) and mostly Dutch speaking (73.4%) according to their Dutch (57.3%) or Belgian (18.5%) nationality.

Mental Health and Relationships

Almost all women (97.6%) had had relationships in the past and at the time of the intake the majority (82.3%) was single. About 38.1% experienced a relationship break-up the past year and 16.1% women had one or more abortions in the past while none of the women already had a child. 20.2% did follow some form of therapy (psychotherapy or psychotropic medication or a combination) usually in the context of relational suffering e.g. to deal with a (recent) break-up, to reflect on why they had such a hard time finding the right partner.

Desire for a Child Versus Desire for a Partner

At present, 19.5% of the women did not feel a very outspoken desire for a child, 39.9% felt this desire only since a few years and 40.7% stated they always had pictured themselves as future mothers. So, not surprisingly more than one third (42.7%) of the women felt at this moment in time a stronger desire for a partner than that they felt the need to fulfil their desire for a child (5.6%). However, for one-third (34.7%) both desires were strongly connected. The main explanatory factor as to why they did not have children yet was the fact they did not find the right partner yet to have children with (62.9%). Only 4% stated they gave full priority to their career, 5.6% was undecided about whether they wanted to have children or not, in other cases the (ex-) partner did not have a desire for a child (anymore) or a combination of the above factors were mentioned as the reason why they did not have children yet.

Discovery of the Possibility and Motives to Cryopreserve Oocytes

One third of the women (36.6%) had discovered the possibility to freeze oocytes because the topic appeared in the media or by searching on the internet (11.4%). Age bankers started to network as well, through the internet but also in the waiting room of the fertility clinic and many of the women who candidate today for age banking know somebody who also had this treatment or is interested in having it. For 22% the possibility to cryopreserve oocytes was pointed out to them by friends, colleagues or relatives.

The main reasons to candidate for this treatment were: assurance against future age-related infertility (55.6%), buying more time to find that right partner (37.9%) and taking the pressure of the search for a suitable partner (29%). Another 28.2% of the women also saw the benefits of this treatment in the light of new or future relationships. By cryopreserving their oocytes they stated they could give their relationships

more time to blossom before bringing up the subject of child-desire, hereby avoiding putting pressure on their partner and/or relationship. A less important reason to perform oocyte cryopreservation was the idea of having tried everything by taking advantage of all possible (reproductive) opportunities to preserve their fertility (26.6%).

Alternatives

Before the possibility of oocyte cryopreservation was discovered; adoption or staying childless were considered as alternatives by respectively 16.9% and 10.5% of the women. Becoming a single mother with the use of either anonymous or known donor sperm was a more popular alternative, considered by approximately one third (33.1%) of the women but rather as a last resort at a very advanced reproductive age. Only 1.6% would consider conception after a one-night stand and 4.8% stated they have no alternatives in mind if they could not freeze their oocytes. However, clearly for most women (84.7%) actively keep on searching for 'mister right' was the only valuable option in order to avoid single parenthood and the need for donor eggs at an older reproductive age. 65.3% also actively engaged in the search for a partner by visiting dating sites, consulting dating agencies and by addressing their social network (19.2%). 17.7% already has a relationship at the moment of intake (early or established >6 months) while 16.9% is not actively engaging in finding a suitable partner.

Attitudes and Concerns

None of the women who cryopreserved oocytes formulated any moral, religious or ethical objections about oocyte cryopreservation for non-medical reasons and the majority stated they had no problem with the fact they had to undergo a fertility treatment while being considered healthy and/or fertile and they accepted that at present little information is available on the well-being of the children born after oocyte cryopreservation.

Disadvantages of the Oocyte Cryopreservation

The use of hormones (44.4%) and the financial costs (21%) were considered as the main disadvantages of the treatment. Less mentioned disadvantages were: the concern that the treatment will be a physical or a psychological burden (8.1%), the fact that one has to undergo a fertility treatment (4%), the fact that the treatment does not offer any guarantees on childbearing (7.3%), the practical arrangements that need to

be made (16.9%) and some personal fears that had to be overcome before engaging in this treatment (e.g. fear of stigmatization, gynaecological examination, fear that their oocytes would be switched with those of other patients).

Openness and Support from the Social Network

The overall majority of the women (98.4%) had shared their intentions to cryopreserve oocytes with at least one person in their entourage and none of them felt discouraged to undergo this treatment. Reactions were positive (82%) or mixed (18%) as some people showed some concern about the fact that their daughter/relative/friend was about to undergo a treatment. However, 22.6% did not tell their parents about their plans to cryopreserve their oocytes and in 13.7% of the cases the father was not informed. Because they did not want to worry them, they were undecided at intake about continuing this treatment or they wanted first to make sure they got the permission of the centre to freeze oocytes. In contrast, two patients stated they were embarrassed to tell their parents because they believed their parents would prefer them to have children the traditional way by first finding a suitable partner, getting married and have children the natural way. By cryopreserving their oocytes it felt as if they were failing in the eyes of their parents. About 8.1% stated they would have no support during treatment -amongst which a few women who actually preferred 'to do this on their own' (n = 6). All of the others stated they would get support from their entourage during treatment. With this support they meant they would find someone that would accompany them to the clinic (73.4%) the day of oocyte retrieval and 17.7%, will not only be accompanied to the clinic but will also get financial support. In case women have a partner, 77.2% tells the partner about the plans to undergo a treatment. In our sample 22 women had an ongoing relationship and 17 partners knew about the plans of their partner.

Treatment Aspects

76.6% stated they could afford different treatment cycles, which cost about 2500 euro per cycle including medication, oocyte pick-up and 10 years of oocyte cryopreservation.

However, the other 23.4% stated it would not be possible to pay for a second treatment cycle. On average they wanted to repeat the treatment 1.83 times (±1.06) and the average age women thought of using their oocytes was 42.73 years with a SD of 2.51 years.

However, the actual decision to repeat the treatment would depend on how the first treatment was experienced and on the number of oocytes cryopreserved after the first treatment cycle.

Use of the Cryopreserved Oocytes

If they would find a suitable partner most of them would want to try to become pregnant spontaneously, than perform IVF with fresh collected material and in last instance, perform IVF with their cryopreserved oocytes (86.3%). 3.2% would because of their age at present immediately use the vitrified oocytes and 8.9% would first ask doctor's advice before deciding what to do. If they would no longer need their oocytes 22% was unsure about their destination at the time of intake or 4.9% was sure that they would certainly not let them get destroyed, 33.3% would donate them for scientific research, 15.4% would let them get destroyed and 19.6% stated they would donate them anonymously or known to a woman with fertility problems.

The Profile of the Pioneer Cohort of Women Opting for Oocyte Cryopreservation

When we summarize the results obtained from this group of women we may state that women who bank oocytes in anticipation of gamete exhaustion (AGE) are highly educated single women of an older reproductive age, struggling with relationships but having a strong desire for a partner that momentarily beats their desire for a child. They want to fond a family with this suitable partner and raise a child in the presence of a father. Although most women are highly educated and have a career only a very small percentage attributes the fact that they do not have children yet to the deliberate postponement of the realization of their desire for a child in function of a career. A recent break-up, advanced reproductive age, awareness of the possibility were the pivotal events to candidate for treatment. Well aware of the importance not to solely relay on this possibility to attain their reproductive goal, the majority of the women actively or more passively engaged in finding a suitable partner. By cryopreserving their oocytes they wanted to buy more time to find that partner, relieve the pressure of the search for a partner and take an insurance against future age-related infertility. In general women seemed to be well aware of the risks and limitations of the treatment but were not stressed out about them or did not feel discouraged. Most of the time able to afford different treatment cycles the financial cost was one of the main disadvantages of the treatment besides the need to use hormones. These financial and physical efforts they have to make might contribute to the fact that cryopreserved oocytes are considered as precious goods that will only be used in last instance, after having tried to become pregnant spontaneously and/or having performed a fresh IVF cycle. Moreover, these vitrified oocytes are also considered to be very personal goods. In case they do not need them, the majority would prefer to donate them for scientific research or let them get destroyed rather than to donate them anonymously (or known) to women in need of donor eggs.

Discussion

The assessed cohort of women represents a very homogenous group possibly related to the descriptive nature of the study and to the pioneer population involved. The population of women opting the cryopreserve oocytes may become more diverse as the indication for oocyte cryopreservation would become more common. In the general population of women of a reproductive age, women were found to be concerned about financial costs, health risks for themselves and a future child, the impact of hormones and success rates linked to oocyte cryopreservation making them more reluctant towards the possibility [15]. The actual age-banker in our cohort seems to be much less worried about those aspects and wants to grasp the opportunity to prevail (what is left of) her fertility. Possibly, only a very specific niche of the female population might benefit from this treatment and is interested in having it.

It is clear that the profile of these women needs to be considered preliminary and further follow-up is needed. This pioneer cohort of women seems to be functioning well on a cognitive level according to their educational levels and engagement in employment. Although all these women are highly educated and have a career, it is confirmed that women attribute their childlessness to 'not having met a suitable partner' rather than to 'prioritisation of career achievements'. At the relational/emotional level more instability and suffering is noticed. Starting a relationship is not a problem for this cohort, it is the long-term establishment that seems not to be evident; partners do not live up to their expectations, often it is stated that the partners in the past were "not ideal" to have a child with, regularly a discrepancy is mentioned in the desire for a child between them and the past or current partner and also a reproach of a lack of engagement of the (ex-) partner is frequently reported. Women often seek psychotherapy in order to address these relational issues.

The profile of the women in our cohort seems to be very similar to those described by other authors [11–13]. Unfortunately, the women in our cohort also cryopreserved oocytes at a suboptimal reproductive age (mean 36.95 years). Concurrently, to offering women the possibility to cryopreserve oocytes, efforts to promote change in social and political structures in order to eliminate discriminatory features of society should be made. Mertes and Pennings [10] promote; creating public awareness; having children at a younger reproductive age and offering individualized, age-specific information and counselling and predictive tests (anti-Müllerian hormone measurements or antral follicle count) in order to help women to create realistic expectations and to make well-informed decisions. As a result from counselling, women may have a realistic view on the treatment aspects (pitfalls and limitation) however, they may (still) have unrealistic expectations about partners and relationships. Wanting to cryopreserve oocytes in their late 30s, still hoping for prince charming to come along and only willing to accomplish the desire for a child with this "perfect" partner may not be very realistic. What are the chances of finding this partner in the coming 5 years when they have not met him over the past 20 years? For some women age banking at an older reproductive age also means they will be

flirting with the legal age limit in Belgium for embryo transfer, which is set at age 47. The question remains how many women will be able to benefit from age banking and use it for what they intend to use it, namely, buying time to find the right partner and to fond a family. On the other hand, a significant amount of women—usually the reproductively speaking, older women—in our cohort (aged 38, 39) also consider the possibility of becoming a single parent, hereby showing a more realistic perspective on their reproductive options.

Continued follow-up of this cohort is necessary in order to have a better view on the trajectory of these women and to refine counselling at intake. More research exploring the personality features of these women is needed for a better understanding of this population. Moreover, results need to be analysed in relation to the societal, financial, educational demands and changes in Western society, making it hard for women to achieve important life goals (establish a career, finding a partner, having children) within a short timeframe, between the age of 30 and 40 when fertility has already declined.

Key Points Women who cryopreserve oocytes:

1. Are often single and do not have children (yet) because they did not meet the right partner to have children with not because they prioritise their career achievements
2. Have the desire to start a family rather than to single parent a child
3. Function well professionally and are financially independent but experience more relational suffering
4. Should be counselled prior to treatment preferably by a psychologist in a non-directive manner with respect for reproductive autonomy and a gynaecologist who provides individualized, age-specific information, in order to make sure that realistic expectations are being created and that well-informed decisions can be made by the candidate about oocyte cryopreservation and whether to proceed with the treatment or not
5. Do this at an advanced reproductive age when fertility has already declined and in a context of Western society where there is a limited timeframe to accomplish important life goals. The general population of women and potential age bankers in specific would benefit from campaigns creating more awareness on age related fertility decline and possible ways to counteract.

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