

voor Thomas, Milo, Quinten en Lenah.

It is never too late to be what you might have been.

George Eliot

Promotor Prof. dr. Guido Pennings
 Vakgroep Wijsbegeerte en Moraalwetenschap

Decaan Prof. dr. Marc Boone
Rector Prof. dr. Anne De Paepe

Nederlandse vertaling:

Het invriezen van eicellen in anticipatie op leeftijdsgerelateerde onvruchtbaarheid. Baat het niet dan schaadt het niet?

Alle rechten voorbehouden. Niets uit deze uitgave mag worden verveelvoudigd, opgeslagen in een geautomatiseerd gegevensbestand, of openbaar gemaakt, in enige vorm of op enige wijze, hetzij elektronisch, mechanisch, door fotokopieën, opnamen, of enige andere manier, zonder voorafgaande toestemming van de uitgever.

Egg banking in anticipation of age-related fertility decline

Using medical technology for better, not for worse

Heidi Mertes

Proefschrift voorgelegd tot het behalen van de graad van doctor in de wijsbegeerte

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Preface and acknowledgements

This dissertation bundles research that was conducted on grants from Ghent University and the Research Foundation - Flanders (Fonds voor Wetenschappelijk Onderzoek Vlaanderen) between 2009 and 2014. These grants were for research into ethical issues surrounding fertility preservation in general, so not only egg banking in the context of aging, but also in the context of oncofertility; not only oocyte banking, but also ovarian and testicular tissue banking; not only fertility preservation for adults, but also for children. However, the articles that were selected for this dissertation are limited to the topic of egg banking in anticipation of age-related fertility decline. In total, five international peer reviewed articles are included, of which four are published in journals indexed in the Web of Science. Also, parts of a forthcoming book chapter are included to fill up a 'gap' not covered by the publications. The necessary changes have been made to these different publications in order to reflect the most recent state-of-the-art and to avoid repetition in the dissertation.

I am first and foremost indebted to Guido Pennings, promotor of this thesis, without whom this thesis would never have been made. Guido, thank you for your continuing support throughout my (young) career, continuous belief in my abilities, for being a continuous source of inspiration and critical reflection and for your continuous insistence that I should attempt to obtain a PhD in Philosophy next to my PhD in Moral Sciences. You were right: it was feasible! (Veerle: go for it, girl!)

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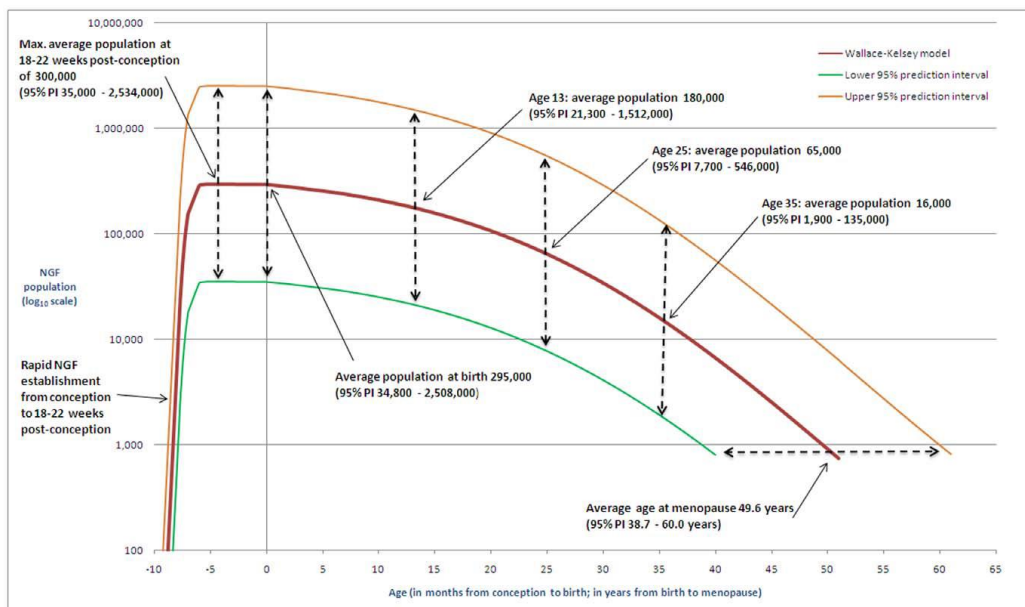
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Introduction

Setting the scene

Human egg cells, or oocytes, are exceptional in both their trajectory throughout a woman's life and in their properties. According to the famous Wallace-Kelsey model of ovarian reserve throughout life, thousands to millions of non-growing follicles are produced in the ovaries of developing female foetuses in the first half of the pregnancy. This number remains relatively stable throughout the second half of the pregnancy and girls are born with an average of 295,000 follicles (with a very wide range, from 35,000 to 2,500,000). After birth, the number of follicles (or 'ovarian reserve') immediately starts a steep decline (note that the Y-axis of the graph below is exponential).



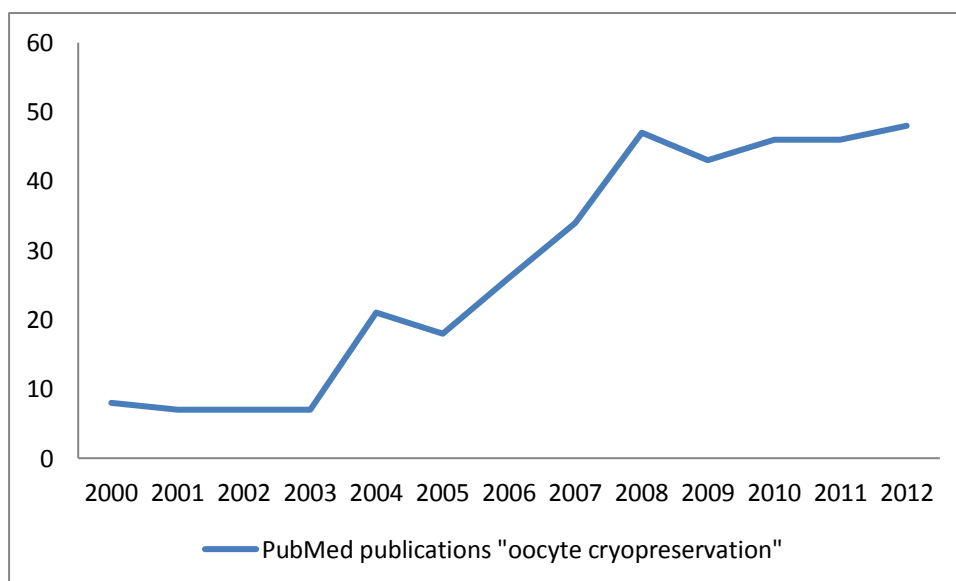
Illustrative example of non-growing follicle populations predicted by the Wallace-Kelsey model, @ 2010, Wallace, Kelsey

Even before puberty starts, most follicles are lost. At age 25, women are estimated to have an average of 65,000 follicles left, at age 35 16,000. At age 40, only 3% of the original

ovarian reserve remains. Women enter menopause at the average age of 50 years, again with a very wide range (Wallace and Kelsey, 2010).

The end of fertility, however, does not coincide with the complete depletion of the ovarian reserve. Most women are subfertile or infertile at least a decade before entering into menopause. The main cause for age-related subfertility is not the decline in the quantity of germ cells, but rather a decline in the quality of these cells due to oocyte aging, leading to decreased fertilization rates, polyspermy, digyny, parthenogenesis, chromosomal abnormalities, apoptosis, structural alteration and hardening of the zona pellucida, epigenetic changes and others (Miao et al, 2009). As illustrated by the high rates of healthy live births after egg donation, aging of the uterus is not a major contributor to age-related subfertility.

As oocyte quality and – in second instance – oocyte quantity are to blame for age-related subfertility, the obvious ‘solution’ would be to store young, healthy oocytes early in life, in case a woman would want to reproduce after the end of her natural reproductive lifespan. However, this is where the exceptional properties of human egg cells surface. Mature oocytes have a diameter of about 0,1 mm and contain a large amount of fluid, making them notoriously difficult to freeze (or cryopreserve). Although the first healthy live birth from a frozen human egg cell dates back to 1986, egg freezing has long been so inefficient that it was hardly considered a valid treatment option (Gook, 2011). From 2004 onwards, however, there is a clear explosion in research directed at oocyte cryopreservation (OC), as illustrated by the sharp increase in published studies on this subject.



This research effort led to improvements in both the method known as slow freezing and in vitrification or ultra-rapid freezing, in which the oocyte acquires a glass-like state. This

increase in research efforts (unsurprisingly) coincides with the introduction of the very restrictive and controversial Italian law 40/2004, regulating assisted reproduction in Italy. This law stipulated that IVF embryos could no longer be cryopreserved and that all created embryos (with a maximum of three) should be transferred in the first cycle (Boggio, 2005). Much is to be said about this law, but here it suffices to say that Italian practitioners in the field of ART had to resort to the experimental technique of oocyte freezing in order to ‘rescue’ the oocytes that could not be used in the first, fresh cycle and avoid repeated hormonal treatments and laparoscopies (Manna & Nardo, 2005). This undoubtedly contributed to a fast development and adoption of new cryopreservation techniques.

With improvements in both the slow freezing technique and ultra-rapid cooling by vitrification, oocyte cryopreservation has, since a couple of years, become an efficient procedure with high survival rates after thawing and with reassuring preliminary data on the health of the resulting offspring (Cobo et al, 2008; Noyes et al, 2009; Noyes et al, 2010; Almodin et al., 2010; Grifo and Noyes, 2010; Rienzi et al., 2010; Trokoudes et al., 2011; Cobo et al, 2014; De Munck et al, 2015). These advancements have given a boost to the field of oncofertility, providing fertility preservation for oncology patients. If their treatment permits it, women who are at risk of losing their fertility due to cancer, cancer treatment or other grave illnesses are now given the option of storing oocytes (rather than embryos) before starting cancer treatment.

However, not only cancer patients are at risk of losing their fertility, but all women in their late thirties are and many of them still have a desire for parenthood. When looking at the first world countries, there has been a steady increase of women’s age at first childbirth in the last five decades. The introduction of effective contraception, an increase in women’s education and labour marked participation, value changes, gender equity, partnership changes, housing conditions, economic uncertainty and the absence of supportive family policies have been identified as causes for this trend (Mills et al, 2011). This ‘postponement’ of motherhood is linked to a higher rate of involuntary childlessness and smaller family sizes than desired due to increased infertility and fetal death with higher age (Smith et al, 2012). Also, the number of women faced with age-related infertility who rely on donor oocytes to conceive is rising steadily (Stoop et al, 2014a). Therefore, also for healthy women who desire to have children, but who fear to be faced with age related subfertility by the time they want to conceive a child, OC could be beneficial. However, whereas the introduction of OC – even with the experimental technique of vitrification – for oncofertility was met with much enthusiasm and optimism, the expansion of the option of OC for ‘medical reasons’ to OC for ‘non-medical reasons’, ‘social reasons’ or ‘anticipated gamete exhaustion’ (AGE-banking) (Stoop et al, 2014b) did not incite the same reactions. In 2008, the American Society for Reproductive Medicine (ASRM) stated that:

“Oocyte cryopreservation is an experimental procedure that should not be offered or marketed as a means to defer reproductive aging, primarily because data relating to clinical outcomes are limited. [...] However, unlike healthy women, [women with cancer or other illnesses requiring immediate treatments that seriously threaten their future fertility] may have no viable options and therefore may be appropriate candidates for such treatment despite its experimental status” (ASRM, 2008, p. S134).

The European Society for Human Reproduction and Embryology (ESHRE) took a similar stand:

“In view of the lack of success and clinical applications in the case of ovarian tissue, this application should not be offered to women as a means to preserve their fertility potential when there is no immediate threat to their fertility. According to similar reasoning, oocyte freezing for fertility preservation without a medical indication should not be encouraged.” (ESHRE, 2004, p. 461).

Given the rapid developments in the years that followed, several authors have called directly upon ASRM and ESHRE for a less restrictive attitude (Homburg et al. 2009; Rybak and Lieman 2009). This resulted in a revision of the ESHRE-guidelines in 2012, now stating that:

“[i]n the light of new scientific developments, and after considering relevant ethical arguments [...] oocyte cryopreservation to improve prospects of future child bearing should also be available for non-medical reasons” (ESHRE, 2012, p. 1231).

The ASRM, however, despite lifting the ‘experimental’ label from OC for medical purposes in 2012, maintained its stance that OC should not be offered for non-medical reasons due to a lack of data for this specific indication and due to the fact that:

“[m]arketing this technology for the purpose of deferring childbearing may give women false hope and encourage women to delay childbearing” (ASRM, 2012, p. 41).

An Israeli study from 2011, surveying both ‘experts’ in ART and in bioethics and laypersons about their attitudes towards AGE banking found a significant discrepancy in acceptance. Whereas 80% of experts reported that they feel OC should be allowed for ‘personal (non-medical) reasons’, only 56% of medical students and 40% of the general population had a similar attitude (Brezis et al, 2011). Regardless of acceptance rates, demand for AGE banking is rising steadily. Cobo et al (2016), for example, report a fivefold increase in demand in the past 8 years.

Central questions and structure of this thesis

This thesis presents critical ethical reflection on the practice of oocyte cryopreservation for healthy women. It tackles the following four normative questions:

- Should we freeze the eggs of women who fear that age-related fertility decline will interfere with their reproductive plans? (chapters 1 and 2)
- How should we freeze eggs for these women? (chapter 3)
- Who should pay the bill? (chapters 4 and 5)
- Can egg banking also be considered as a solution to ethical problems in the context of egg donation? (chapter 6)

To frame the first question, an analysis is made of how different stereotypes influence the different responses that have been given. Keeping the dangers of these stereotypes in mind, an inventory is then made of arguments for and against egg freezing for healthy women, resulting in the conclusion that there are no *prima facie* reasons to prohibit the offer of OC to healthy women.

However, a cautious approach is advocated. Even though the introduction of OC for healthy women in the clinic is not necessarily ethically problematic, it can result in unethical practices. The second part of this thesis therefore sets out guidelines for a proper introduction.

One aspect that is discussed separately in the third part is the issue of financing. Depending on how OC for healthy women is conceptualised (self-donation, prevention, social egg freezing, ...), it is either self-evident or counterintuitive to treat it in the same way as other interventions in reproductive medicine. In the first chapter of part III the options and rationales for and against public funding are discussed. In the second chapter, the issue of companies offering OC to their employees as a healthcare benefit is discussed. The final chapter looks at the future impact of OC for/by healthy women. It is to be expected that many women will not use their stored oocytes and might consider donating them to people who are subfertile. Also, 'freeze and share' agreements may be possible in which a women's oocytes are retrieved both for future autologous use and for donation. Important elements in the 'traditional' ethical deliberations regarding oocyte donation are the fact that healthy women are subjected to potentially harmful procedures and the issue of reimbursement. Both these issues become very different when the primary objective of oocyte retrieval is (also) beneficial for the donor.

Methodology

My *modus operandi* was not the same for each of the articles in this thesis, but in general, there are seven steps that have led up to the ethical analyses in this dissertation: (1) identification of a moral concern; (2) study of the facts necessary to understand the concern; (3) inventarisation of the arguments used to support or reject positions in regard to the moral concern involved; (4) extension of this inventory with possible additional arguments which are relevant from a moral perspective, but have not yet been voiced; (5) critical analysis of the arguments presented in (3) and (4), focussing on consistency with scientific facts, internal consistency, consistency with related practices and on argumentative flaws; (6) a conclusion bringing the strongest arguments together and (7) when appropriate, the formulation of recommendations about possible 'solutions' or preferred courses of action.

This methodology can be labelled as a version of critical applied ethics, an approach described by Molewijk et al (2004) and further elaborated by Leget, Borry and De Vries (2009), which integrates empirical research with normative research and considers "the empirical and the normative as two independent focuses of the ellipse that is called bioethics" (Leget et al, p.231). The method as described by the latter authors involves five stages:

(a) *the determination of the problem*. In my case, the first starting point was the observation that a distinction was made between the application of oocyte cryopreservation for (so-called) medical reasons and for (so-called) social reasons, linked to a different value judgement.

(b) *the description of the problem*. This includes a critical look at the vocabulary used and of the claims made, which was very much needed in my research, as 'social egg freezing', 'fertility preservation', 'fertility insurance', 'lifestyle choices' and related terms are not value-free. Also the incorporation of empirical data on the profiles of the women who are interested in oocyte cryopreservation (for example to determine whether these profiles match the portrayals of these women) is an illustration of this step.

(c) *effects and alternatives*. Especially for this phase empirical data are of central importance to my analyses (the odds of achieving a pregnancy after egg freezing, risks of ovarian stimulation, psychological impact of egg freezing etc), although for some issues hypothetical effects and alternatives were also discussed, for example in chapters 4 (What are the alternative funding options and which impact *might* they have?) and 6 (Which impact *might* company-sponsored egg freezing have on the women?).

(d) *the normative weighing*. As Leget et al mention, this is where "we enter the very heart of normative ethics" (Leget et al, 2009; blz 233). Although I rely heavily on empirical research, this dissertation itself is not empirical, but normative.

(e) *evaluation of the effects of a decision...* because “bioethics is a never-ending process of evaluation and re-evaluation” (Leget et al, 2009; p 233).

Two important clarifications are needed in regard to my position towards critical applied ethics. First, I do not generate empirical data myself, but rely on empirical data that are present in the literature. Literature from different disciplines was gathered: medical research dealing with, for example, the technical aspects of slow freezing and vitrification or with the chances of conception at different ages; demographic research about, for example, the age at first childbirth; sociological research about the profile of women who present themselves for oocyte cryopreservation or about the impact of employment situations on fertility, psychological research about the impact of childlessness, et cetera. These empirical sources were supplemented by a great deal of literature concerning bioethical and philosophical issues such as reproductive liberty, autonomy, distributive justice, justice in healthcare, resource allocation, et cetera. Next to academic literature, also statements issued by regulators and professional societies were picked up, as were media reports. This last category was very important for chapter 1, in which I aimed to investigate the validity of the different discourses regarding healthy women cryopreserving their eggs.

Second, the method of critical applied ethics as described by Leget et al (2009) focuses on integration of the empirical with ethical theories. In my case, this should be interpreted to also include integration with ethical principles and other, more straightforward cases. This means that I incorporate principlism and arguing by analogy, supplemented with a focus on sound argumentation, that is, devoid from argumentative flaws and focussed on consistency (Mertes & Pennings, 2011). The most convincing description of my methodology is therefore the wide reflective equilibrium (Daniels, 1996). The method of reflective equilibrium consists in working back and forth among our considered judgments (or “intuitions”) about particular instances or cases, the principles or rules that we believe govern them, and the theoretical considerations that we believe bear on accepting these considered judgments, principles, or rules, revising any of these elements wherever necessary in order to achieve an acceptable coherence among them. This model is especially suitable for the normative evaluation of an on-going field of research – such as oocyte cryopreservation – as the reflective equilibrium that is achieved can be constantly challenged by new advances in science and may be modified as new elements arise in our thinking (Schroeter, 2004). Although the method of reflective equilibrium is thus not a method of achieving some kind of normative ‘truth’, it does provide an important tool for justification (Daniels, 2011). Moreover, this method acknowledges that normative conclusions are always provisional.

Terminology

In the debate regarding oocyte cryopreservation in anticipation of age related fertility decline, several terms have been used to describe the procedure. Unfortunately most of these terms also have a normative connotation and/or incorporate presuppositions that are not necessarily well founded. As the choice of words is not innocent in ethical debates, I will go over the most important ones and indicate why I have chosen to use ‘AGE banking’ in this dissertation.

Fertility preservation is a general term referring to all measures that are taken to enable people to reproduce after losing their ability to reproduce naturally. It is not used exclusively in anticipation of fertility decline due to aging, but more frequently in the context of premature subfertility and infertility after a disease or medical treatment (with the field of oncofertility focussing specifically on cancer). Fertility preservation measures include storage of egg cells and sperm cells, but also of embryos, ovarian and testicular tissue, or the transposition of ovaries during irradiation therapy. This term can be criticised on the basis of the fact that fertility is only potentially and partly ‘preserved’, as there is no guarantee that the intervention will eventually lead to a healthy live birth. At the same time, fertility preservation measures can make the crucial difference between having no chance whatsoever to reproduce, and still having ‘a’ chance of reproducing, even if fertility is in much worse shape than it would have been, had the person not had a disease, undergone a treatment or aged.

Social egg freezing is a widely used term, both in the academic literature and in the popular media. It is usually used in a dichotomy with ‘medical egg freezing’, to indicate that the reason for cryopreserving oocytes is not a disease or medical treatment, but rather a set of social circumstances. It oftentimes has a pejorative connotation, in the sense that social reasons for egg freezing are seen as less legitimate than medical reasons. It – deliberately or not – resonates the argument that we should not use medical interventions to solve social problems (see below in chapters 1 and 2). As will be discussed in the coming chapters, the dichotomy between medical and social indications for egg freezing is arbitrary and this term reflects stereotypes that are not representative for the actual practice.

Non-medical egg freezing is less judgemental than social egg freezing, but it still departs from a clear distinction between medical and non-medical indications. Note that we do not call other age-related health problems (e.g. osteoporosis, bad eyesight, hearing problems) non-medical problems. The fact that this term is used here (while we do not say that our grandmother wears eyeglasses for non-medical reasons), hints at a normative difference between medical and non-medical egg freezing, which I would like to problematize, rather than adopt.

Elective egg freezing steps away from the dichotomy between medical and non-medical/social egg freezing, but implies that whereas for healthy women it is a deliberate choice to store eggs, an option they choose between a number of other options, this would not be the case for women freezing their eggs in the context of oncofertility (presuming that in this case it is a necessity, their only choice). In both cases, however, egg banking is not a part of some bigger life plan, it is rather a plan B to save any reproductive potential that can be saved given the suboptimal position a woman is in. As will be discussed in the coming chapters (especially chapters 1, 2 and 3), egg banking in order to purposefully 'postpone' childbearing is rare.

Egg banking in anticipation of age-related fertility decline is my preferred terminology, but unfortunately not very practical to use. This however describes best which group of women I am referring to in this dissertation.

AGE banking, whereby AGE is an acronym for 'anticipated gamete exhaustion' is the term that I will use throughout this dissertation. It was coined and extensively explained by Stoop et al in 2014 and refers to several relevant elements: the anticipation of infertility, aging and banking/storing eggs. I am aware that the 'banking' metaphor is not devoid of normativity. On the one hand it makes clear that egg banking is about temporarily putting them in a repository, where they can later be collected by the same person who deposited them. On the other hand, a bank may lead to connotations of money and trade, which is not what I would want to reinforce. I hope it will be clear to the readers that 'banking' should be read as synonymous for 'storing' and that the connotation with trade and commercialisation is unintended.

Importance

According to ethicists Hayry and Takala "it is the job of philosophers to provide conceptual analyses of arguments, views, decisions, doctrines, policies, and, in general, of anything related to values, norms, duties, virtues, rights, liberties, and any number of entities and notions referred to or employed in moral and political discussions." (2014). When I published the first articles from this dissertation in 2011, there was hardly any literature in the field of bioethics focussing on the topic of oocyte cryopreservation for healthy women. Although it was already technically possible, the introduction in the clinic was not yet widespread and many centres for reproductive medicine were struggling with the question whether or not to limit the offer of oocyte cryopreservation to cancer patients and other patients whose fertility was threatened by illness or medical treatments. The first responses to oocyte cryopreservation as a preventive measure for healthy women, whose fertility was 'merely' threatened by aging, were rather negative.

At the time, both slow freezing and vitrification were experimental procedures of which not even short term outcome data were available. This instigated reluctance of introducing it into the clinic, which is in principle a desirable attitude. Yet, the fact that the safety of the procedure was not established, cannot be a reason to offer it to one group of patients, but not the other. One can even argue that a less vulnerable group of participants in the first clinical trials would be more appropriate than a more vulnerable group, also taking into account that cancer treatment was sometimes delayed because of the time needed for ovarian stimulation and that there was a lot of uncertainty over the effects of ovarian stimulation on several malignancies. Thus, ethical reflection was called for. I am optimistic that my work has had a valued impact on the field. The five articles that are included in this manuscript (published between 2011 and 2013) have at present been cited almost 120 times, of which 49 times in articles indexed in the Web of Science.

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Should we freeze healthy women's eggs?

Pros and cons in arguments and narratives

Chapter 1

The portrayal of healthy women requesting oocyte cryopreservation

Abstract:

The possibility to cryopreserve oocytes to be used in IVF treatment later in life has not only enlarged the reproductive options of cancer patients who are faced with gonadotoxic treatments, but also holds the promise of enlarging the reproductive options of healthy women whose personal circumstances (most often the absence of a partner) do not allow them to reproduce in their most fertile years. Opinions for and against this application of the cryopreservation technology are often based on different portrayals of the women who might use it. Three different portrayals can be discerned in the debate about the ethics of so-called 'social egg freezing' or 'non medical egg freezing'. First, these women have been portrayed as selfish career-pursuing women. Second, healthy women who might benefit from oocyte cryopreservation have been portrayed as victims of a male-oriented society that makes it difficult for women to combine motherhood with a good education or professional responsibilities. Third, healthy women opting to cryopreserve oocytes have been portrayed as wise, proactive women who will not have to depend on oocyte donors should they suffer from age-related infertility by the time they are ready to reproduce. Each of these three portrayals has its own shortcomings that one should be wary of, as they lead to an oversimplification of the ethical debate.

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1.1 Introduction

Although the first report of a live birth from a frozen oocyte dates back to 1986 (Chen, 1986), oocytes have long been notoriously difficult to cryopreserve. However, following advancements in slow freezing and especially since the introduction of vitrification, the survival rates of oocytes after thawing have risen significantly. In combination with ICSI, good fertilization rates are achieved, making oocyte cryopreservation an efficient procedure (Rienzi, 2010). As safety data are also reassuring (although long term follow-up data are not yet available), it is now considered both safe and efficient enough for routine clinical application by many (Cobo et al, 2010; Noyes, 2010; Rienzi et al, 2010; Rienzi et al, 2012; Cobo et al, 2014; De Munck et al, 2015).

The possibility to cryopreserve oocytes to be used in IVF treatment later in life has enlarged the reproductive options of cancer patients who are faced with gonadotoxic treatments. It also holds the promise of expanding the reproductive options of healthy women whose personal circumstances (most often the absence of a partner) do not allow them to reproduce in their most fertile years. However, this latter possibility has been criticized by many and also professional bodies such as the ASRM and ESHRE were initially reluctant to support this particular application (ASRM, 2007; ESHRE, 2004). Objections that were voiced included the experimental status of vitrification, the fact that expanding the reproductive lifespan is unnatural and represents an unwarranted medicalization of reproduction and that it would lead to an unwelcome increase in the age of mothers (Jones, 2009; Martin, 2010; Mc Cullough, 2004; Shkedi-Rafid and Hashiloni-Dolev, 2011). These concerns will be addressed in chapter 2.

However, part of the debate was not based on fundamental objections, but rather on more emotionally charged arguments and prejudices, led by stereotyping of the healthy women who might request oocyte cryopreservation. Three different portrayals can be discerned in the debate about the ethics of so-called ‘social egg freezing’ or ‘non medical egg freezing’ (Martin, 2010). First, these women have been portrayed as selfish career-pursuing women, which leads to a position that does not support oocyte cryopreservation by healthy women. Second, healthy women who might benefit from oocyte cryopreservation have been portrayed as victims of a male-oriented society that makes it difficult for women to combine motherhood with a good education or professional responsibilities. Third, healthy women opting to cryopreserve oocytes have been portrayed as wise, proactive women who will not have to depend on oocyte donors should they suffer from age-related infertility by the time they are ready to reproduce. As these portrayals are quite prominent in the lay media and shape public opinion, it is important to have an insight in the extent to which they are truthful and in what their shortcomings are.

1.2 Selfish, career-pursuing women

When the phenomenon of egg freezing for so-called 'social reasons' first hit the headlines, the portrayal of the women who might request this new technology was largely judgmental and negative:

The popular media conjured up visions of selfish, self-absorbed career women deliberately avoiding motherhood in their 20s and 30s whilst relying on cryobiology to produce their own genetic babies for them in their 40s and 50s. (Lockwood, 2003; p.152)

Social egg freezing generally arises because a woman chooses to delay bearing children. This could be because they wish to further their career before parenthood. (Catt, 2009)

[Professor Ledger] believes that it is ethically questionable for women to freeze their eggs purely for 'lifestyle reasons'. (Fletcher, 2009)

In contrast with women who are faced with the prospect of infertility due to cancer treatment, these women were seen as facing infertility due to their own 'life style choices' and thus due to their own *fault*. In this case the reasoning goes that women who postpone motherhood to pursue a career until the point where they suffer from age-related fertility decline, are themselves accountable for this misfortune as they misplaced their priorities.

Available data (although limited) on the profile of women requesting AGE banking show that most of these women are indeed highly educated, which appears to support the first narrative (Nekkebroeck et al, 2010; Hodes-Wertz et al, 2013; Baldwin et al, 2015; Cobo et al, 2016). However, most of these women do not request egg freezing at a young age with the intent of putting motherhood on hold in order to pursue their careers. Rather, the large majority of women consider the procedure to be a back-up plan in case natural reproduction fails (Hodes-Wertz et al, 2013). Oftentimes, they present themselves when they are approaching their forties and are faced with the fact that although they want to be parents, they have not found the right partner yet (which, granted, may be due in part to investing a lot of time in their education and careers) (Cobo et al, 2016). Thus, these women did not necessarily choose to delay parenthood, but their personal situation did not allow them to have children earlier in life. For these women, oocyte cryopreservation is a way of clinging onto the last straw of hope they have for ever establishing a family at a moment when their ovarian reserve has already diminished substantially.

The question then is: was it wrong for these women to invest in their education and career at the expense of their fertility? Would it be better if women paid more attention to

childbearing than to career building at the time when they are most fertile (between the ages of 20 and 30)? Several studies have found that women find it increasingly important to first complete their education, have financial security, good housing and a stable relationship before taking on the responsibility of parenthood (Lampic et al., 2006; Maheshwari et al., 2008; Tough et al, 2007). These are not selfish concerns, but considerations that are made in the best interest of their future children. Bonneux et al. (2008) have argued that the rising age of women at first childbirth is a trend that increases overall wellbeing and that should not be regretted in itself, even if it is regrettable that the peak of natural female fertility does not coincide with this age period. They even go as far as to say that having children before the age of 23 is not to be encouraged, given the heightened risk of social deprivation. This means that the ‘perfect’ time for reproducing – not too early for reasons of wellbeing, not too late for medical reasons – is between the ages of 25 and 35. As previously argued by Lockwood (2011, p. 338), “[b]oth women and men, especially if they have received a tertiary-level education and have good employment prospects, are simply unprepared to cope with the consequences of the very narrow window of opportunity for parenthood that exists in the decade between realization of educational, career and economic goals and the onset of, at best, a reduced family size compared with their ideal and, at worst, involuntary childlessness.”

This brings us to the second narrative: if it is in fact not the educated women’s fault that they cannot reproduce at the optimal age, can we then put the blame on society?

1.3 Victims of a male-oriented society

The premise of this second narrative is that society, and most notably the way the labor market is structured, makes it difficult for women to combine motherhood with a good education or professional responsibilities. The labor market is seen as leaving little room for family responsibilities, which was workable years ago with an all-male labor force and women as primary caregivers, but is not adapted to today’s typical family with two working partners.

This second narrative can be invoked to support oocyte cryopreservation by healthy women as an intervention that women are entitled to, given the expectations of today’s society:

It seems unfair that society at large, which creates the economic, educational, and professional conditions that encourages deferred maternity, discourages women

from using technology to bypass a biological inequity—the early loss of fecundity. (Gosden et al, 2000)

[W]omen face reductions in earning capacity and potentially serious financial implications that men do not. In fact, they may have very few choices at all. (Savulescu & Goold, 2008)

[W]e are disturbed by the implied judgment that our society, having failed to sufficiently safeguard the ability of many women in their twenties and thirties to establish families without jeopardizing career advancement, cannot withstand the challenges posed by elective deferral of childbearing. (Rybak & Lieman, 2009).

Alternatively, the idea that society forces women to postpone parenthood can be invoked to oppose oocyte cryopreservation. In this case, it is argued that although accepting oocyte cryopreservation as a ‘quick fix’ for social inequalities can heal the problem of age-onset infertility, it does not tackle the root of the problem, which ought to be remedied by taking measures that make it easier for women to have their children earlier in life:

[O]ne might ask whether we actually help women [...] by taking for granted their bad employment situation and offering them egg freezing to deal with it. (Goold & Savulescu, 2008; p. 50)

[T]echnological solutions to social problems may result in a greater degree of repression rather than liberation [...] Would it not be likely [...] that women, who already feel that they are expected by employers to postpone (or give up) motherhood, would now be expected to freeze their eggs if they pursue a career? [...] the best way to overcome society’s restrictive influence on the individual’s ability to act autonomously is to change the societal norms that give rise to this oppression, rather than encouraging individuals [...] to adapt to these norms. (Shkedi-Rafid and Hashiloni-Dolev, 2012; p. 156-157)

The reproductive technology of egg freezing [...] cannot escape the serious feminist worry about potentially reinforcing patriarchy and leaving the problematic social structures largely intact. (Petropanagos, 2010; p. 233)

[E]gg freezing may leave the hard work of moving society toward greater sexual equality untouched [...] technological solutions to social problems are inadequate and often result in the further oppression of disadvantaged groups. (Harwood, 2009; p.46)

Fertility preservation for social reasons is then a type of unnecessary medicalization of society that can be avoided by creating a better social climate for working mothers. In a study by Hodes-Wertz et al (surveying AGE bankers from a clinic in New York), nineteen percent of women opting for AGE banking indicate that workplace inflexibility

contributed to a delay in their parental project (Hodes-Wertz et al, 2013). This indicates that much work remains to be done in order to achieve a better balance between professional and private responsibilities. However, it also indicates that such efforts would not make the demand for AGE banking disappear. Moreover, symptoms and root causes are best treated simultaneously in order to obtain the fastest results. Dondorp and de Wert (2009) have pointed out that women “cannot afford to wait until society has been changed in a way that would allow them to have it all at the right time” (p. 1781). Few people would argue that the individual medical treatment of obesity should be halted because the distribution of obesity over socioeconomic classes shows that social inequality or poverty is the underlying problem. Medical treatment and societal change are not mutually exclusive and thus there is no reason to abandon one to pursue the other.

Also, whether societal change will have any impact on the age of first-time mothers, and if such an impact is even desirable to start with, is debatable. In this context it is both amusing and remarkable that a 1969 study from Maxwell and Montgomery found that at that time, there was societal pressure towards early parenthood “although this is opposed to the desire of young couples for delayed parenthood” (Maxwell & Montgomery, 1969, p. 340). This presents us with the question: has this situation reversed itself in the last 50 years and is there currently societal pressure to delay parenthood – a claim that is supported by young mothers who report that “society [sees] them as “bad mothers” simply because they [are] young” (Benzies et al., 2006, p. 629) – while women would prefer to have children at a younger age? Or have women’s preferences stayed the same while they are now finally liberated of the societal pressure to reproduce as young as possible? A study by Tough et al. (2007) in a Canadian population shows that most consider the ideal age to begin parenting to be somewhere between the ages of 25 and 35. This is in line with the previously mentioned findings that women prefer to complete their education, have financial security, good housing and a stable relationship before starting a family. Thus, it is very unlikely that socio-economical measures to stimulate having children before these goals have been met will have a great impact, nor that such measures are desirable. Hakim (2003) makes the same prediction that family-friendly adaptations to employment policies – although welcomed by parents (male and female) seeking to better combine parental and professional obligations – will not automatically lead to more children and/or younger parents. She bases herself on a preference theory with the underlying idea that such measures would benefit people who are ‘home-centered’ to start with (mainly women), which is the same group that would be willing to cut back on their career to have children anyhow. At the same time, such measures are unlikely to affect people who are ‘work-centered’. This theory is also confirmed by data from Van Balen (2005), indicating that a strong desire to have children overrides motivations to postpone motherhood.

Another way to look at the trend to delay parenthood is to consider it in regard to an increased acceptance of voluntarily childless couples and an increased awareness that a life without children is not inferior in terms of overall wellbeing to a life with children and may indeed be more rewarding. Childfree couples remain a minority but their numbers have been growing steadily and are already estimated to be higher than involuntarily childless couples (Agrillo & Nelini, 2008). Delaying parenthood can then be seen as a conscious decision aimed at enjoying the best of both worlds (first without and then with children), rather than being some kind of second-best option. In other words, it is too simple to claim that women are forced by a male-oriented society to delay childbearing and that changing employment policies to render them more women-friendly is all it takes to lower the age of first-time mothers. Rather, many women prefer to delay motherhood and have good reasons to do so, even in a world where having children would not have an impact on career opportunities.

1.4 Wise, proactive women

This brings us to the starting point of the last narrative: neither women, nor society at large (nor men for that matter) should be scolded for a shift in the age of primigravid women. Societal and personal factors make it a smart choice for women and men to delay parenthood, despite the risk of remaining childless all together. Also, an abundance of dating websites cannot guarantee that every woman will meet her ‘mister right’ in her early twenties, nor that he will agree to have children at that age. So does a woman in her early thirties who wants to have children but not in her current condition have other options besides storing her oocytes until the circumstances are better? Sure, she does: she can either wait it out and risk remaining childless or having to rely on donor oocytes, or she can rush into having children without having a stable relationship or a stable financial situation. However, these are not necessarily better options, neither for her nor her future offspring, than to store her oocytes (even with a limited chance of success). Reproducing as fast as possible can be a great strategy from a gynecological point of view, but it may be a very bad choice from many other points of view.

The third narrative therefore takes the fact that many women attempt to reproduce in their late thirties – after their most fertile period – as a given, rather than as a variable that ought to change. According to this third narrative, the right way to present ‘elective egg freezing’ is not to see it as an alternative to reproducing earlier in life – as this is often simply not an option or not a good one – but as a back-up plan in case natural reproduction fails and as an alternative to relying on donor oocytes. It can be seen as a

form of self-donation whereby the younger version of a woman donates eggs to her older version so that she is able to reproduce at an older age while keeping the genetic link between parent and child and while using younger oocytes with less risks of complications (Rybak & Lieman, 2009; Knopman et al, 2010; Hodes-Wertz et al, 2013). Rather than representing unnecessary medicalization of reproduction, elective egg freezing then becomes a form of preventive medicine (Stoop, 2010; Lockwood, 2011):

Many women end up childless as a result of postponing childbearing. Some want to plan ahead and try to prevent this outcome. As long as these women are fully informed and able to make rational decisions about their fertility, we should allow them to make their own financial decisions. (Goold & Savulescu, 2009; p. 57)

[W]hat if some women do want to freeze their eggs at 30, to 'use' at 45 and achieve what is genetically their own baby? Is that decision somehow less moral than using IVF at 45 with a 5% chance of a pregnancy and a 70% chance of a miscarriage, or using the precious, scarce resource of donor eggs and settling for 'someone else's' baby as preferable to no baby at all? (Lockwood, 2003, p. 153)

While this third narrative is all too easily embraced by commercial enterprises that offer egg freezing services, it is unfortunately not unproblematic. If women would deliberately delay childbearing until their forties, they could proactively freeze their eggs around their 30th birthday and achieve good success rates. However, this is not how things usually go in practice. As discussed earlier, women usually do not plan to have their children in their late thirties or forties, but they postpone childbearing bit by bit by lack of a partner, a demanding job, financial insecurity, etc. (a phenomenon also known as 'perpetual postponing') and before they know it their reproductive years have passed (Lockwood, 2011). Women are not inclined to undergo the demanding and costly procedure of ovarian stimulation and oocyte retrieval at the peak of their fertility. At that moment they are either not yet thinking about starting a family or they expect to find a partner in due time. Several studies have indicated that women underestimate the speed at which female fertility declines and that the possibilities of overturning age-related infertility through IVF are highly overestimated (Hammarberg & Clarke, 2005; Lampic et al., 2006; Maheshwari et al., 2008; Bretherick et al., 2010). Moreover, cryopreserving oocytes requires a substantial financial investment that women are only willing to make when there is a substantial possibility that they will ever 'cash in' on this investment. It is only when their time is running out, when approaching the symbolic age of forty, that most women start to worry about remaining childless and resort to oocyte cryopreservation. The oocytes that are preserved at that point already have a decreased potential to result in a successful pregnancy. Moreover, when lack of a partner is the problem, this problem may persist so that frozen oocytes remain unused. Thus, although egg freezing is potentially a wise and proactive measure for women in today's society, in

practice it is often a desperate measure with a low utility (Mertes and Pennings, 2011, see chapter 3).

However, this last narrative can serve as an ideal to be pursued. One can only hope that through public education on declining fertility with age, a reduction in costs and awareness about the possibility to store oocytes at a young age, the women cryopreserving their oocytes will one day resemble the ideal of smart, proactive women rather than the image of desperate singles...

1.5 Conclusion

The ethical debate regarding oocyte cryopreservation for healthy women has often been reduced to putting the women on trial who might benefit from it. Who are these women who want to defy nature and do they deserve this new expansion of their reproductive liberty? Three different narratives can be discerned: women interested in elective egg freezing are either portrayed as selfishly prioritizing their career over motherhood, as being forced by society to postpone motherhood or as smart, proactive women who have discovered a new means to make their career compatible with motherhood. The first narrative is probably the furthest away from reality, as the age at which healthy women currently request oocyte cryopreservation indicates that 'postponement' of childbearing is seldom planned at a young age and thus that freezing oocytes is rather an emergency intervention than part of a well designed life plan to 'have it all'. However, it is argued here that also the other two narratives are misrepresentations to a certain extent. Just as it is inaccurate to state that women choose to delay childbearing in order to advance their careers, it is also inaccurate to say that they have no other option but to delay childbearing. When people have their children depends on an interplay between contextual factors and personal values and neither one will completely override the other. Finally, the image of smart, proactive women is rather an idealistic picture of who the best candidates would be than an accurate depiction of those who actually come forward.

In conclusion, it may be interesting to learn who the candidates for elective oocyte cryopreservation are, what their motives are and how they got into a situation in which they need to or want to delay childbearing until after their reproductive years. However, a judgmental approach will not offer a clear answer to the question whether elective egg freezing is good or bad medical practice. The central question should not be whether or not women are deserving of oocyte cryopreservation, but whether or not oocyte cryopreservation for this particular indication does more good than harm. This

evaluation will depend a lot on the utility rate, that is, on the number of women who actually return to use their frozen oocytes and on the success rates for these women. As argued elsewhere (Mertes and Pennings, 2011, see chapter 3), if the only candidates for AGE banking are women whose ovarian reserve is already at a critical threshold, then the utility of this procedure will be very low and women will be buying false hope at a high price. However, if women become more aware of the effect of aging on their fertility, of the possibility to store oocytes in their fertile years (preferably before age 35) and of the limits of the procedure (especially when they are already over the age of 35), oocyte cryopreservation may be a welcome intervention for women who long to preserve their fertility longer than they naturally could.

1.6 References

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Chapter 2

Arguments for and against

Abstract:

In this chapter, the different arguments pro and con oocyte cryopreservation to counter age-related fertility decline will be presented and critically assessed. The arguments that we should not try to circumvent natural boundaries, solve societal problems with medical solutions or that AGE banking will have a negative impact on society are found wanting or only partially convincing. On the other side of the debate, the argument that we should allow AGE banking to combat gender inequality in terms of the maximal age at childbirth is dismissed, but the argument that women's reproductive autonomy should be respected, that this technology may not only clinically, but also psychologically benefit patients and that it is inconsistent to support egg donation by others, but not autologous egg donation appear to carry some weight.

Based on:

Mertes H. Ethical aspects of AGE banking. In D. Stoop (ed.) The prevention of age related fertility loss. Springer, forthcoming.

2.1 Introduction

In this second chapter, the focus is shifted from the portrayals of the women who (might) request oocyte cryopreservation (OC) in response to age-related fertility decline – or anticipated gamete exhaustion (AGE) – to the procedure itself. First, arguments will be presented that lead to a fundamental objection against, or a fundamental support for ‘AGE banking’. The main arguments against AGE banking are that it is unnatural, that it amounts to unwarranted medicalization and that it has a negative impact on society. The main arguments for AGE banking are that it leads to more gender equality and reproductive autonomy, that it generates psychological benefits and diminishes the need for third party reproduction. In chapter 3, these fundamental objections will be complemented with concerns about the practical implementation strategies that may be followed.

2.2 Fundamental objections against AGE banking

2.2.1 The argument from nature

A first set of fundamental objections against AGE-banking relate to the idea that this technology pushes the boundaries of nature. The age at which the average woman becomes infertile is then not merely labelled as a biological fact, as the age at which women can no longer have children, but rather as the age at which women should no longer have children. In ethical theory, this phenomenon is known as the is-ought fallacy. Unless if one starts from the religious belief that everything was created for a clear purpose and that we live in the best of all possible worlds, the (average) natural state of things does not teach us anything about how things ought to be. This also implies that there is no obvious reason why medical interventions should be limited to preserving or restoring the natural state of things – as is done in ‘medical’ egg freezing – and should not be used to counter natural phenomena that have a negative impact on our wellbeing. It should be remarked that many illnesses are age-related, just as the decline in female fertility, and that many medical interventions are performed to solve inconveniences that may be considered ‘normal’ if they occur at a certain age. In fact, not much of modern day medicine would remain, if we were to cancel all interventions for age-related health problems. Yet, nobody seems to be opposed to the treatment of Alzheimer’s disease or osteoporosis. The distinction between medical and non-medical egg freezing based on the idea that aging is not a medical problem is therefore problematic. If we have good reasons

to counteract infertility for women with a desire for parenthood, then it matters little what the cause of the pending infertility is.

Also, besides the fact that the distinction between medical and non-medical OC is irrelevant, it is also a false distinction in the sense that there is a grey area in between these two applications (Stoop et al, 2014). For instance, should women who request OC due to a prognosis of unexplained premature ovarian insufficiency be regarded as freezing for medical or non-medical reasons? Even for cancer patients, certain regimens of radiation or chemotherapy will lead to immediate sterility in (reproductively speaking) older women, but not in younger women. If the former decide to store their oocytes, this decision will be both disease-related and age-related.

2.2.2 Medicalization

A related objection against AGE-banking is that it provides a medical solution for a problem that in essence is not a medical problem, but a societal one, namely the steady rise in women's age at first childbirth, now on average between 25 and 35 years old (Lemoine & Ravitsky, 2014). This can then be attributed either to the woman herself or to the way the labour market is structured, as was discussed in the previous chapter.

If women are held accountable for 'delaying' childbearing due to 'lifestyle choices', the non-medical alternative to OC is obvious and simple: women should reproduce earlier. This reasoning was reflected in the ASRM's statement from 2007, which implied that women who want to bank eggs for age-related fertility decline "have other options", whereas, for example, cancer patients do not (ASRM, 2007). This is however easier said than done as the most important reason for banking eggs in healthy women is the lack of a partner (Nekkebroeck et al, 2010; Hodes-Wertz et al., 2013; Baldwin et al, 2015; Stoop et al, 2015; De Groot et al, 2016). Should we thus encourage women to become single mothers? Should we advise them not to wait for Mr. Right, but go for Mr. Good Enough? As mentioned earlier, the desire to postpone parenthood until a secure and stable personal situation is established cannot be easily pushed aside.

Alternatively, rather than holding women accountable for the rising age at first childbirth, society might be blamed, in the sense that many women experience difficulties in starting a parental project during their reproductive lifespan due to professional obligations. While fertility preservation can offer a solution to this problem once it presents itself, it does not tackle the root cause. Fertility preservation for social reasons is then a type of unnecessary medicalization of society that can be avoided by creating a better social climate for working mothers. However, societal change takes time. While we might attempt to tackle the (hypothetical) root cause of delayed

childbearing by making it easier for young parents (both women and men) to combine personal and professional responsibilities, this is unfortunately not a solution for women who are in their late thirties and involuntarily childless today. Therefore, long term solutions to the benefit of future generations should not prevent us from offering practical solutions to the present generation (Dondorp & de Wert, 2009; see chapter 1). Moreover, keeping in mind that lack of a partner is the primary reason to request AGE banking, we should be sceptical that reforms in the labour market will reduce the demand for AGE banking. At the same time, we should remain vigilant that the option of AGE banking is not invoked as an excuse to invest less in reforms in the labour market that enable a better combination of professional and parental obligations.

2.2.3 A negative impact on society

Related to the argument that women's employment situation does not allow them to reproduce at a young age, there is a concern that the offer of AGE banking will increase the pressure on women to invest in their careers while they are young at the expense of pursuing parenthood. This concern became especially convincing when Facebook and Apple announced that they would start offering OC to their female employees. As will be argued in chapter 5, even if AGE banking in itself may not be ethically problematic, the offer by employers is. For such a policy to be implemented with respect for women's reproductive autonomy, a substantial number of conditions need to be fulfilled, which can be reduced to three categories: (1) women should understand the benefits, risks and limitations, (2) women should feel no pressure to take up the offer; (3) the offer should have no negative effect on other family-friendly policies and should in fact be accompanied by such policies. Fulfilling these conditions may turn out to be impossible. Thus, regardless of companies' possible good intentions, women's reproductive autonomy is not well served by offering them company-sponsored AGE banking (this claim will be further elaborated on in chapter 5).

Another concern is that the offer of AGE-banking may cause an increase in the average age at which women become mothers. Although this effect is possible, there are various reasons why it is unlikely that this effect would be significant. First, the number of women opting to bank oocytes is likely to remain a small fraction of all women desiring to become mothers, as the procedure requires a substantial physical and financial effort. Second, it is wrong to assume that these women make a choice between reproducing 'now' or reproducing a couple of years later. For many of the women opting for AGE banking, reproducing at the moment of freezing is not an option (due to lack of a partner, as mentioned). The more likely alternatives are thus either not reproducing at all, or reproducing via donor oocytes at the same age as they would reproduce with their own, cryopreserved oocytes. Third, the overwhelming majority of women who bank oocytes

do so in their late thirties and on average consider the maximum age to use the oocytes below 44 years (Stoop et al, 2015). This means that even for the small fraction of women who would consider a pregnancy at the time of freezing if AGE banking were not available (for example as a single mother through donor conception in countries where this is available for single women), motherhood is only ‘postponed’ for about 5 years. Preliminary results from egg banking programs reported on by Cobo et al, even suggest a shorter average time between the time eggs are banked and women return to use them (Cobo et al, 2016). In conclusion, the most likely effect of offering fertility preservation to healthy women is not a decline in the number of young mothers but a small incline in the number of older mothers. Whether this is a positive or negative evolution is debatable. Studies focusing on the physical risks associated with pregnancy and childbirth after 40 – which are elevated but not necessarily problematic – would consider this a negative evolution. As previously pointed out by several authors, however, this is a very one-dimensional perspective, as there are also substantial benefits to late parenthood, for example psychologically and economically (Bernstein and Wiesemann, 2014; Ekberg, 2014). Therefore, even if AGE banking would result in a slight increase in the average age at first childbirth, this is not necessarily a negative evolution.

2.3 Fundamental arguments for AGE banking

2.3.1 Gender equality

An argument in favour of AGE banking is that this intervention is emancipatory in nature as it can fix the factual discrimination between men and women in regard to their reproductive lifespan: if men are able to conceive children at an advanced age, then women should have the same liberty. This is again an example of the is-ought-fallacy. The mere biological fact that a 70-year old man is capable of conceiving children, says nothing about the morality of doing so. However, as reproductive freedom is highly valued in our society, we do not impose forced sterilization on men above a certain age. Reproduction at an advanced age is thus a liberty right, but that does not mean that it is also a claim right. That means that if an infertile senior citizen (male or female) applies for IVF treatment, it may not be granted based on considerations regarding the welfare of the future child. Given the fact that pregnancy complications are an additional concern in the case of women, a lower cut-off age in ART for women than for men may be justified.

2.3.2 Reproductive autonomy

The main argument for AGE banking is that it increases reproductive autonomy. This claim is not uncontroversial. As mentioned above and as will be discussed in chapters 3 and 5, depending on how egg banking is marketed and offered to women, it can either reinforce reproductive liberty or put it under pressure. This is not typical for egg banking, but for many innovations and practices in reproductive medicine (e.g. surrogacy or egg donation). In this context Widdows has argued that “[f]eminists should deny the prevailing assumption that to prevent exploitation, all that is necessary is to ensure that the woman gives her fully informed consent to whatever act is in question. This assumption rests on the philosophical and political premise that if the individual freely consents – to seemingly any act – then it is not possible to consider her exploited. But it is, and she is” (Widdows, 2009, p. 21). On the other side of the debate, Robertson has argued that “there is no reason to think that women do not end up with more rather than less reproductive freedom as a result of technological innovation. If so, procreative liberty is an important bulwark that helps women achieve the greater freedom that reproductive advances make possible. [...] Although procreative liberty gives little protection from family or internal pressures to procreate or from lack of resources, it does prevent arbitrary, moralistic, or speculative governmental impositions on a woman’s procreative choice”, adding also that social policy does need to protect women from private sector coercion, which will also be discussed in chapters 3 and 5 (Robertson, 1994, p. 231).

Thus, starting from the premise that due care is taken in the provision of egg banking, going beyond merely requiring informed consent, we can say that due to this new technology, women are theoretically able to extend their reproductive lifespan and are thus less dependent on donor oocytes if they wish to reproduce at an age at which their ovarian reserves are depleted (see below). As mentioned above, the age at which women desire to have children rises and not all women succeed in finding a partner with whom to share parenthood before the decline of their fertility. When single, childless women reach their late thirties and still want to become mothers, they – unlike men – are under pressure to find a partner fast and embark on parenthood with that new partner fast, or resort to single parenthood. AGE banking can relieve women of this pressure by offering them a couple more years to find a suitable partner, thus allowing for more autonomous choices (De Groot et al, 2016). Research by Hodes-Wertz et al. (2013) and by Stoop et al (2015) shows that a large majority of women opting for AGE banking feels empowered by the procedure. This is also confirmed by anecdotal reports, such as those by Richards (2015). Caveats are that only a limited number of oocytes can be banked, so that a pregnancy – let alone a live birth – can certainly not be guaranteed and that women still face legal restrictions on the age until which they can use their banked oocytes to (try to)

establish a pregnancy. As Robertson noted in this regard, “\$50,000 for egg freezing at 37 is an expensive and probably ineffective way to quiet the ticking fertility clock. If a woman is listening carefully, this move will only lessen the thrum, not quiet it altogether” (Robertson, 2014, p 122). Also, as will be discussed in chapter 5, if women experience pressure to bank their oocytes (for example as a way of showing that they take their careers seriously), their reproductive autonomy will be limited, rather than increased.

Absolute prerequisites for AGE banking to positively influence reproductive autonomy are therefore that absence of outside pressure and the procurement of correct information about the possibilities and limitations. The overly optimistic portrayal of AGE banking as ‘insurance against infertility’ or as a means to defer childbearing while retaining fertility misguides women about the limitations. If a woman with a very strong desire for parenthood would defer childbearing relying on banked oocytes and subsequently fails to achieve a pregnancy with those banked oocytes, her reproductive autonomy was very ill-served by AGE banking.

2.3.3 Psychological benefit

Linked to reproductive autonomy and the pressure on finding a suitable partner when a woman approaches the end of her reproductive lifespan is the observation that women may not only derive a clinical benefit (the chance of conceiving a child), but also a psychological benefit from knowing that there is still ‘a chance’ for her to have children, regardless of whether she ever actually uses her stored eggs. Research by Stoop et al (2015) shows that even women who have banked oocytes but have never used them or no longer envisage using them do not regret their decision to bank and would do so again in similar circumstances. Also, some women decide a couple of years after banking that they will embark on single parenthood although their preferential life plan involved building a family with a partner. Banking then allowed them some extra time to consider the option of single parenthood without Damocles’ sword hanging above their heads. Also, even if women eventually remain childless, the fact that they banked their eggs gives them the impression that they ‘tried everything they could’ (De Groot et al, 2016). This is an important element in coping with involuntary childlessness, as was previously described by Daniluk (2001).

2.3.4 Self-donation

A strong argument for allowing AGE banking is that it is in fact a form of oocyte donation which does not involve a third party (Knopman et al., 2010; Rybak and Lieman, 2009). If a woman is currently unable to conceive due to a depletion of her ovarian reserve, she can

establish a pregnancy with donor oocytes, but there are some drawbacks to this option. First, the resulting child will not have a genetic connection with the mother. Although this is not necessarily problematic, it is a suboptimal option for many people, either because they identify parenthood with genetic parenthood (or at least presuppose that one is 'more' of a parent when there is a genetic connection) or because they fear a disruption of their family unit if the donor would claim a role or if the child would regard the donor as the 'real' mother (Wyverkens et al, 2015). Second, oocyte donation requires that a healthy woman is subjected to ovarian stimulation and oocyte retrieval. These are unpleasant and time-consuming procedures with (limited) risks involved, which hold no benefit for the woman who is subjected to these risks. Both donor anonymity and open identity donation are potentially problematic for the donor, in the former case because she might want to know the person resulting from her donation, in the latter case because she might not want to be contacted by that person. As we currently allow donor conception despite these drawbacks, it would be inconsistent not to allow a woman to donate oocytes to her future self. In this case the genetic link is maintained and the person subjected to the risks of ovarian stimulation is the same person as the one who reaps the benefit of (potential) parenthood. The only dissimilarity that might be invoked to justify a different approach is that in the case of 'regular' oocyte donation, the need for a donor oocyte is present, whereas when a woman decides to bank oocytes for future use, she can never be certain that there will ever be an actual need. Therefore, the effort might be in vain.

2.4 Conclusion

Despite the original opposition against AGE banking for healthy women, AGE banking has found its way to the clinic rather fast. One reason for this evolution may be that a number of the initial ethical objections to oocyte freezing for so-called 'social' or 'non-medical' reasons were not very convincing, especially given the contrast with the warm welcome oocyte banking received in the field of oncofertility. The arguments that we should not try to circumvent natural boundaries, solve societal problems with medical solutions or that AGE banking will have a negative impact on society are either flawed or only partially convincing. On the other side of the debate, the argument that we should allow AGE banking to combat gender inequality in terms of the maximal age at childbirth was dismissed, but the argument that women's reproductive autonomy should be respected, that this technology may not only clinically, but also psychologically benefit patients and that it is inconsistent to support egg donation by others, but not autologous egg donation appear to carry some weight.

However, even if there are good arguments to bring AGE banking to the clinic, a cautious approach is warranted. First of all, the utility of the procedure may be low and women may be overly optimistic about their chances of conceiving after AGE banking. They should therefore be properly counselled and sufficiently informed about their personal chances of success. Misleading information by commercial companies and coercive offers from companies to their female employees are to be avoided and finally, reflection is needed on access to the technology and on the extent in which reimbursement by public healthcare is desirable. These issues will be discussed in the following chapters.

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How should we freeze healthy women's eggs?

Recommendations for a responsible introduction into the clinic

Chapter 3

AGE banking for better, not for worse

Abstract:

The possibility for healthy women to cryopreserve their oocytes in order to counter future infertility has gained momentum in recent years. However, women tend to cryopreserve oocytes at an age that is suboptimal from a clinical point of view - in their late thirties - when both oocyte quantity and quality have already considerably diminished and success rates for eventually establishing a pregnancy are thus limited. This also gives rise to ethical concerns, as the procedure is seen as giving false hope to (reproductively speaking) older women. We evaluate which measures can be taken to turn AGE banking into a procedure that is both clinically and ethically better than the current practice. The main objective of these measures is to convince those women who are most likely to (want to) reproduce at an above average age to cryopreserve their oocytes at a time when this intervention is still likely to lead to a life birth and to discourage fertility clinics from specifically targeting women who have already surpassed the age at which good results can be expected.

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3.1 Introduction

Women and their reproductive choices are always a welcome subject for ethical concern. Whether voluntary prostitution, surrogacy or oocyte donation are concerned, one of the recurring questions is always this: should women be allowed to engage in practices that may cause them physical or psychological harm, or should these practices be prohibited in the name of women's wellbeing and the moral high ground? The latest issue to feed the traditional standoff between respecting women's autonomous decisions and (paternalistically) protecting them from exploitation is the possibility for healthy women to cryopreserve their oocytes, just in case they have no (good) oocytes left by the time they are ready to reproduce. While the option for cancer patients to freeze oocytes in the face of treatments that may render them infertile is met with enthusiasm, offering the same option to healthy women is met with a lot more suspicion and reluctance, both by practitioners and policy-makers (ASRM, 2007; Jones, 2009; Martin, 2010; McCullough, 2004; Shkedi-Rafid and Hashiloni-Dolev, 2011). First, there are a number of 'fundamental' objections, as discussed in chapter 2.

Second, there are a number of more emotionally charged objections. Not only is the yuck-factor at play but there is also an ambiguous depiction of women who seek to store their oocytes for 'non-medical reasons'. As was discussed in chapter 1, opponents of AGE banking oftentimes depict these women either as selfish career women (and thus undeserving of help) or as victims of a male-oriented society that neglects young mothers and of an unscrupulous fertility industry that is ready to cash in on their fear for infertility (and thus in need of protection). (Martin, 2010) But why should these women be either perpetrators or victims? Instead of casting a moral verdict, we start from the simple observation that more and more women postpone motherhood and we grant that those who consider to go through the burdensome procedure of cryopreserving oocytes, most likely have very good reasons for postponing motherhood.

While the success rates of IVF with oocytes that have been subjected to slow freezing are significantly lower than those with fresh oocytes (Borini et al., 2010; Magli et al., 2010), cryopreservation with the vitrification technique offers success rates similar to those with fresh oocytes (Almodin et al., 2010; Grifo and Noyes, 2010; Kim et al., 2010; Rienzi et al., 2010; Trokoudes et al., 2011; Potdar et al 2014; Rienzi et al, 2017; Crawford et al, 2017). However, just as for fresh oocytes, the outcomes of IVF with vitrified oocytes are – unsurprisingly – highly dependent on maternal age at the time of freezing (Rienzi et al, 2010). According to the data of the ASRM of all the SART member clinics for 2009, for women younger than 35, 41,4% of regular (fresh embryo) IVF cycles result in a live birth, women aged between 35 and 37 can expect a live birth rate per cycle of 31,7%, women aged between 38 and 40 a rate of 22,3% and women aged 41-42 a rate of 12,6% (ASRM Office

of Public Affairs, 2010). If only 40-year old women resort to egg freezing in a desperate attempt to 'save' their fertility, it will hardly produce any positive results and we believe that it is this image that has sparked the narrative of social egg freezers as women vulnerable to exploitation (Martin, 2010). However, by banning AGE banking, women who would stand to benefit from it and would not be exploited but helped by having a number of eggs in storage, will also lose out. If long term follow-up shows that vitrification is safe for the offspring and if correct information is supplied to candidate-freezers about the decline in their fertility, about pregnancy complications related to maternal age and about their individual chances of conceiving with their frozen eggs, a large part of the women who decide to cryopreserve their oocytes might actually be making a very rational and justified choice.

The biggest challenge, however, is to assure that the procedure is used by those women who are most likely to benefit from it, namely women whose oocytes have not already considerably aged. In order to reach this goal, a double approach is needed. First, women need to be informed that they should store their oocytes before age 35 and second, the centres that offer elective oocyte cryopreservation should refrain from specifically targeting those women who are most desperate, namely those approaching their forties. In this way, AGE banking is used for better, but not for worse.

3.2 The divergence between the best case scenario and the worst case scenario

The best case scenario of elective freezing is the following. A woman in her late twenties or early thirties realizes that, although she has a strong desire to become a mother, she is unlikely to be in a good position to have children in the coming years (for example because she is single). She knows that by the time she will be ready to reproduce, her oocytes will have aged considerably (leading to low implantation rates and a higher risk of chromosomal abnormalities) or her ovarian reserve will be completely depleted so that she will remain childless or will have to use donor oocytes. This woman therefore proactively turns to an alternative option, namely to cryopreserve the young oocytes she has today, and use them to establish a pregnancy at a later point in her life.

Since 2012, the ASRM no longer considers oocyte vitrification to be an experimental procedure (ASRM, 2012). Currently available data are very encouraging, both concerning the health of the resulting offspring, (especially for vitrification) concerning oocyte survival after freezing and thawing and concerning the subsequent success rates which

are comparable to those of fresh oocytes (Almodin et al., 2010; Grifo and Noyes, 2010; Kim et al., 2010; Rienzi et al., 2010; Trokoudes et al., 2011; Cobo et al, 2014; Potdar et al 2014; Rienzi et al, 2017; Crawford et al, 2017). Long term follow-up data on children born from vitrified oocytes are not yet available due to the novelty of the technique and thus the possibility remains that oocyte freezing may affect the long term health of the offspring. However, while it is currently uncertain if such risks are involved in oocyte cryopreservation, they are certain to exist in aged oocytes. This means that even in this innovative phase, freezing eggs for future use can reasonably be expected to increase the overall health of future offspring for those women who have already decided to postpone motherhood. One might argue that relying on young donor oocytes is still safer, but this is not a valid alternative option for many women as donor oocytes are in short supply and worries exist about the physical and psychological welfare of donors. Moreover, without wanting to over-estimate the importance of a genetic link between parents and children or the psychological damage suffered by donor-conceived children, we believe it is fair to say that, when given the option, parents strongly prefer to have a genetic link with their children (Ravin et al., 1997). Oocyte cryopreservation can therefore – in principle – be applauded as another step in offering women more reproductive freedom.

The worst case scenario, is that a woman only becomes aware of – or pays attention to – a decline in her fertility when she approaches or passes the symbolic age of 40 while lacking a stable relationship, then desperately seeks to hang on to whatever is left of her ovarian reserve and resorts to oocyte cryopreservation. In this scenario, a woman will either be irresponsive to ovarian stimulation all together or she will need multiple ovarian stimulation cycles to harvest a limited number of oocytes that are likely to give her a fairly small chance of conceiving when she is finally ready to reproduce. As Sage et al. (2008) have reported, “[t]he likelihood of retrieving an adequate number of mature oocytes decreases dramatically with age”. Moreover, the odds are considerable that a woman who is not ready to reproduce at 40 is no more ready a few years later and will thus never even return to use her frozen eggs. In this scenario, oocyte cryopreservation for healthy women appears to be a waste of medical resources and a source of unnecessary health risks.

At present, women who opt for elective cryopreservation tend to lean more towards the worst case scenario than to the best case scenario, as the average reported age of women freezing their eggs is 37-38 (Gold et al., 2006; Klein et al., 2006; Sage et al., 2008; Nekkebroeck et al., 2010; Vallejo et al, 2013; Garcia-Velasco et al., 2013; Baldwin et al, 2015; Stoop et al, 2015; Cobo et al, 2016; De Groot et al, 2016). Moreover, the number of women who have so far actually frozen their oocytes might even represent the ‘best’ fraction of those who present themselves, as many women need to be turned down when preliminary tests indicate a diminished ovarian reserve. Of those women who do start the stimulation protocol, Klein et al. (2006) report a 24% cancellation rate due to suboptimal

response and of those cycles that they completed, only 58% yielded more than 10 oocytes, while standard stimulation was employed.

There are several ways to deal with this situation: we can opt for a status quo, in which AGE banking will bring about more heartache than happiness, we can ‘pull the plug’ on AGE banking and label it ‘unethical’, whereby women will not be dragged into the worst case scenario, but only at the expense of those in the best case scenario or – preferably – we can try to promote oocyte cryopreservation for those women who are most likely to benefit from it and discourage or refuse those women who are the least likely to benefit from using the procedure. As female fertility starts to decline steeply from age 35 onwards, the optimal timing for elective freezing would be between 30 and 35. Freezing at a younger age would be more favourable from a clinical point of view, but it would result in low usage rates, as the chances are considerable that these women will find a partner and reproduce naturally before their ovarian reserve is depleted. Freezing at an older age would significantly reduce the success rates (Cil et al, 2013; Cobo et al, 2016). Freezing above 43 years old is futile (with pregnancy rates per cycle of 2% and lower) and should not be offered at present (Hourvitz et al., 2009).

3.3 Public awareness

As mentioned, the average reported age of non-medical patients freezing their oocytes is 37-38 years (Gold et al., 2006; Klein et al., 2006; Sage et al., 2008; Nekkebroeck et al., 2010; Vallejo et al, 2013; Garcia-Velasco et al, 2013; Baldwin et al, 2015; Stoop et al, 2015; Cobo et al, 2016; De Groot et al, 2016). However, both Gold et al and Stoop et al report that women indicate that if they had been aware of the possibility to freeze earlier, they would have done so earlier. Creating more public awareness is therefore a key factor in lowering the average age of social freezers. What exactly should women know in order to make an informed decision regarding elective oocyte cryopreservation? Merely informing them about the technical possibility to freeze eggs is not enough. Public awareness should be created on several fronts:

- First, women need to be made aware that their fertility starts to decline long before the onset of menopause and that the age of 35 is a crucial turning point, rather than the age of 40.
- Second, they need to know that this means that not only their chances of conceiving naturally, but also their chances of conceiving through IVF (with their own – aged – oocytes) plummet at that point. This is important, as several studies have indicated that women not only underestimate the speed at which female

fertility declines but also overestimate the possibilities of overturning age-related infertility through IVF (Bretherick et al., 2009; Lampic et al., 2006; Maheshwari et al., 2008).

- Next, women should be informed that if they want children, but can foresee that they will not be ready to reproduce at 35, they can increase their chances of establishing a pregnancy and of having a healthy baby after that age if they cryopreserve their eggs at a younger age.
- Finally, women above 35 need to understand that if they still want to cryopreserve oocytes, they are less likely to benefit from the procedure than their younger counterparts. Not only will the quality of their oocytes already have diminished, but they will also need to undergo more stimulation cycles to obtain the same number of oocytes. In other words: while they will need more oocytes, less will be harvested per stimulation cycle, rendering the whole procedure much more burdensome and less efficient.

The most straightforward way to create public awareness is by launching awareness campaigns as is done for example to stimulate breast cancer screening or to reduce smoking. In the past, several countries have organized campaigns to make women aware of a decline in fertility with age, but the objective was to stimulate women to have children at a younger age. If a similar effort was launched at present, we would expect the message to be at least twofold: women should have their children 'on time' or freeze their eggs on time (Dondorp and de Wert, 2009). Women have not always been very receptive towards the message of fertility decline and in fact, there is no significant difference in fertility awareness between women who intend to have their first child before or after their 30th birthday, which indicates that fertility awareness has little or no impact on the average planned age at first birth (Lampic et al., 2006). This does not mean, however, that women will be equally unreceptive to the message that oocyte cryopreservation is available for them, quite on the contrary. The fact that a better knowledge about fertility decline with age does not lead to women reproducing at a younger age can be attributed to the fact that family planning is very dependent on personal circumstances, as mentioned above. Thus, a decline in fertility is only one of many factors that women take into account when balancing the pro's and con's of reproducing earlier or later in life and only for those women who have a very strong child wish will it be a factor that outweighs the others. For other women, the message that they should reproduce at a young age will come across as intrusive and pedantic (Williams, 2005). By adding the possibility to cryopreserve oocytes to the message of fertility decline, women may feel helped rather than lectured.

Not everyone will agree that information campaigns to inform women about the possibility to cryopreserve oocytes are warranted, either because the problem (infertility due to age) is not grave enough, or simply because one can expect an automatic increase

in awareness as private cryobanks will start to offer AGE banking and will advertise their services. Private cryobanks have a financial benefit in informing women about a decline in their fertility with age and about the option of oocyte cryopreservation as more 'customers' will generate more revenue. Many fertility clinic websites offer correct information and are upfront about what their potential customers can expect. However, in some cases commercial interests can also taint the information that is conveyed and lead to an overly optimistic representation of AGE banking. Women browsing the internet in search for information on egg freezing will find claims such as "Egg freezing effectively suspends the ever-present ticking of the reproductive biological clock" (http://uscfertility.org/fertility_options/egg_freezing/) and "There are now safe, successful techniques to preserve a woman's fertility indefinitely" (<http://www.infertile.com/infertility-treatments/preserving-your-fertility.htm>). Even the use of terms such as 'fertility preservation' may create the impression that by freezing oocytes, a status quo is offered as far as a woman's reproductive options are concerned. However, this is far from true. Every preserved oocyte represents one single chance to conceive, not a conception, let alone a baby. For example, Rienzi et al report an ongoing implantation rate per warmed oocyte of 12,9% in women with a mean age of 35,5 (Rienzi et al., 2010). Cil et al report a 14,1% and a 16,1% live birth rate after vitrification when respectively 2 or 6 oocytes are thawed which were banked at age 37 (Cil et al, 2013). In this perspective, a lottery ticket would be a better metaphor for a cryopreserved oocyte than an insurance policy, especially for women freezing in their late thirties or later. A minimum requirement for websites that seek to inform women honestly is that success rates are stratified by age. A study by Abusief et al. (2007) shows that in the US, only 52% of private fertility clinics and 33% of academic fertility clinics publish success rates based on age on their websites. Moreover, only 35% of the former and 22% of the latter clarify their definition of success rates.

A crucial question is to what extent women will be equally receptive to information offering them little hope as to information offering them much more hope of a successful pregnancy. Chances are that they will deem the centres that present the highest success rates and the most optimistic message to be the most competent ones. As Cutting et al. (2009) have previously mentioned, "the request for treatment [...] and the circumstances around it carry emotional and life issues which can impede the ability of patients to hear and process the information around oocyte cryopreservation".

All things considered, cryobanks will play a large part in creating public awareness in the years to come, but to make sure that women have easy access to unbiased information, it is preferable that independent health care workers such as general physicians and especially gynaecologists who are not connected to centres that offer oocyte cryopreservation either actively inform their patients around age 30 when they come for check-ups and/or place flyers in their waiting rooms. If gynaecologists discuss the issue

of declining fertility and the option of elective freezing with their patients before they start to browse the internet for answers, women's expectations are more likely to be realistic and they can be guided in the interpretation of success rates that they will find.

3.4 Specific data to be offered to candidate-freezers

After handing them the necessary unbiased information about the procedure, physicians or gynaecologists can refer women who express interest in AGE banking to specialized fertility centres. It is crucial that these centres present some specific information to candidate-freezers and provide individual and independent counselling. In line with the suggestions of Cutting et al. (2009), subjects that need to be discussed include the following.

First, rather than 'overall' success rates, success rates should be given for the specific age of the candidate (at the time of freezing), especially when she is over 35. Hourvitz et al. (2009) report clinical pregnancy rates (for regular IVF) of 7,7%, 5,4%, 1,9% and 0% and delivery rates of 4,2%, 3,3%, 0,6% and 0% per cycle for women aged 42, 43, 44 and 45, respectively. This means that presenting a 44 year old woman with statistics from 42 year old women – which seems like a minor age difference – gives her a fourfold overestimation of her chances to achieve a clinical pregnancy and an even greater overestimation of her chances of a live birth, which illustrates the importance of precision in this area.

Even if ages are specified, success rates in IVF treatment in general are all but unambiguous. Statistics can be given on fertilization rates, cleavage rates, implantation rates, clinical pregnancy rates, biochemical pregnancy rates, live birth rates, (term) singleton live birth rates, per patient, per stimulation cycle, per retrieved oocyte, per fresh embryo, per embryo surviving thawing, per embryo transferred or per transfer cycle. For a woman to be well informed, she should not be drowned in irrelevant information obscuring the rates that actually matter to her personally. A broad discussion on this topic has already taken place. For regular IVF, a good standard appears to be the term singleton live birth rate per initiated ART cycle (Min et al., 2004) or alternatively the live birth rate per ovarian stimulation started (Griesinger et al., 2004), whereby the percentage of multiple pregnancies is specified.

In the specific context of elective oocyte cryopreservation, however, it may be better to focus on cumulative birth rates. Unlike 'standard' IVF-patients, a social freezer cannot take it 'one cycle at a time'. What a social freezer wants to know is this: "If I freeze 10 (or

15, 20, 25,...) oocytes, what are my chances of eventually having a child/children?" Once this question is answered, she can move on to the next question: "How many stimulation cycles will I (likely) need to obtain the number of oocytes that I want?" Cil et al have made calculations regarding the probability of live-birth (singleton+multiple) stratified by age and based on either the number of thawed oocytes, the number of injected oocytes and the number of embryos transferred (Cil et al, 2013). The minimal acceptable chance of a live birth and the maximum number of cycles should essentially be defined by the woman herself. The fact that not all IVF patients complete the maximum number of covered cycles even when they remain childless, while others take out loans to finance extra cycles, illustrates that not all people go to the same lengths to fulfil their child wish. However, valuable information can be provided by the fertility clinic on the preferable number of oocytes to bank. For example, whereas reproductively speaking older women need to bank more oocytes than younger women to obtain the same success rate, a recent study by Cobo et al calculated that for women aged 36 or older, banking more than 11 oocytes no longer increases their chances of success, whereas for women aged 35 or younger, the chance of success continues to rise until the 15th oocyte banked (Cobo et al, 2016). The cumulative live birth rates achieved in their sample with 5, 8 and 15 oocytes in the younger group were 15,4%, 40,8% and 85,2%. The cumulative live birth rates achieved with 5, 8 and 11 oocytes in the older group were 5,1%, 19,9% and 35,6%. These data can help patients make informed choices on whether to bank eggs and on how many stimulation cycles to choose for. Although respect for the reproductive decision making of the women presenting themselves for AGE banking is of paramount importance, this does not mean that reproductive clinics do not have the right to refuse treatment for those women whose chances of success are minimal. The exclusion of women above a certain age limit can be justified even when women are not deceived about their chances of success, as assisting these women would represent a waste of medical resources. A study by Rudick et al. (2009) shows that from those centres in the USA that offer AGE banking, all programs accept women under the age of 35, half of them accept women aged 40 and about a third of them is willing to go beyond 40.

3.5 Specific tests to be offered to candidate-freezers

In estimating ovarian response and thus the successful aspiration of oocytes and the number of cycles needed, predictive tests such as antral follicle count and/or antimullerian hormone (AMH) measurements should be offered (Jayaprakasan et al., 2010). It has been suggested that such tests can also be used to inform women about their chances of conceiving – either naturally or by IVF – and about the expected time of onset

of infertility and menopause. If they were indeed able to do so, this would be an important tool in counselling women who want to cryopreserve their oocytes about how long they can 'wait and see' and when they should start considering freezing. However, at present, data on this subject are inconclusive and further research needs to be conducted to determine under which circumstances these tests can be useful. Relying on the currently available data, it appears that while they are good indicators of ovarian reserve, these tests offer less – if any – insight into the quality of the remaining oocytes as also women with undetectable levels of AMH still have a chance of achieving a pregnancy (Broer et al., 2009; Guerif, 2009; La Marca, 2010; Riggs et al, 2011; Broer et al, 2013; Gomez et al, 2016; Tokura et al, 2013). For women under 35, they are therefore poor predictors of pregnancy rates. That being said, at least one study indicates that AMH testing is indicative of pregnancy rates in women of advanced age, which is of course of particular importance for social freezers (Lee et al., 2009). At present, the best way to counsel candidate freezers about their reproductive options is probably to take into consideration a number of variables such as age, family history of premature ovarian failure and ovarian reserve as measured by antral follicle count or AMH testing.

3.6 Conclusion

Given the increased efficiency of oocyte freezing by vitrification and given the reassuring data on the health of resulting offspring, the possibility for women to store their oocytes theoretically expands their reproductive options and allows them to overcome the increasing gap between the optimal age to reproduce from a gynaecological point of view and the optimal age to reproduce from a socio-economic point of view. However, the average age of women who are currently opting to cryopreserve their oocytes (37 years) is too high to achieve a good balance between costs and benefits. If these women believe that they are insured against childlessness, they are more often wrong than right. Ideally, women in their early thirties who plan to postpone childbearing until their late thirties or forties should be informed about the possibility to freeze their eggs. Women whose oocytes have already significantly aged and are thus unlikely to benefit from elective oocyte cryopreservation should be honestly informed about their success rates and should not be specifically targeted.

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Who pays the bill?

Who should, who can and who should definitely not pay for egg banking?

Chapter 4

Public funding

Abstract:

Despite the initial reactions of disapproval, more and more fertility clinics are now offering oocyte cryopreservation to healthy women in order to extend their reproductive options. However, so-called 'social freezing' or AGE banking is not placed on equal footing as 'regular' IVF treatments when public funding is concerned. In those countries or states where IVF patients receive a number of free cycles, we argue that at least the fertilization and transfer cycles of women who proactively cryopreserved their oocytes should be covered. Moreover, when the argument of justice is consistently applied, coverage should also include the expenses of ovarian stimulation, oocyte retrieval and storage. Different modalities are possible: full coverage from the onset, reimbursement in cash or reimbursement in kind, by offering more free transfer cycles.

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4.1 Introduction

While acknowledging that the ethical debate on whether AGE banking should be offered in the first place is not yet settled in many places, this chapter starts from the observation that fertility clinics in several countries, among which the United States, the United Kingdom, Belgium, The Netherlands and Israel, now offer AGE banking to women – usually highly educated, in their late thirties and single – who have a strong desire to have children, have few fertile years ahead of them but are not ready to embark on parenthood just yet. This evolution has led to another morally contentious question, namely: who should pay for elective oocyte cryopreservation?

AGE banking is currently only available for women who are affluent enough to pay for the ovarian stimulation drugs, medical procedures, vitrification or slow freezing procedure and storage fees. In a small sample (n=29) of women who inquired about oocyte banking but eventually decided not to store their eggs, almost half indicate that they would have, had the procedure been considerably less expensive (Stoop et al, 2015). Although the right to reproduce is widely recognized as a liberty-right, it is generally not regarded as a claim-right (Shanner, 1995). In the context of AGE banking, this means that while women should have the liberty to cryopreserve their oocytes if they so wish, they cannot make claims on society to financially support their efforts to ward off infertility. However, many western countries have a healthcare system that covers a certain number of IVF-cycles to assure equal access to IVF technology for those who cannot reproduce naturally and several US states mandate infertility insurance coverage. This indicates that, at least in those jurisdictions, the right to reasonable healthcare is extended to fertility treatment (ESHRE Task Force on Ethics and Law, 2008).

4.2 Should countries with publicly funded IVF extend coverage to AGE banking?

If oocyte cryopreservation is an accepted procedure to counter infertility and if fertility treatment is covered by public healthcare, should the logical consequence then be that AGE banking is also covered by public healthcare (or mandated insurance coverage) or is there a relevant distinction between ‘regular’ IVF and IVF with previously stored oocytes? Interestingly, a study by Brezis et al (2011) showed that although laypersons are less open to the idea of AGE banking than experts in the field (ART practitioners and bioethicists), they are more in favour of including it in insurance coverage than ‘experts’. Also De Groot

et al. report that a large proportion of Dutch women who are on a waiting list for AGE banking argue that it should be at least partially reimbursed as they believe it will improve equal access, will be cost-effective and is justified by the fact that the delay in reproduction is at least partially due to societal structures (De Groot et al, 2016).

For the matter of reimbursement or healthcare coverage, two steps of the AGE banking procedure should be considered separately: first, ovarian stimulation, oocyte retrieval, cryopreservation and storage and second (several years later), thawing and fertilisation of the cryopreserved oocytes. At the time of the first step, women who request AGE banking are healthy persons who ask for a procedure that results in stored oocytes that may or may not be used, depending on the further course of their lives. At the time of the second step, they are patients asking for a medical intervention.

A woman presenting at the fertility clinic asking for elective oocyte cryopreservation thus differs indeed from other IVF patients in a crucial manner: she is not infertile, which is in most countries a requirement to receive free IVF cycles. The term 'elective freezing' puts the focus on the idea that oocyte cryopreservation by healthy women resembles other instances of elective medical interventions – such as cosmetic surgery – that generally have no therapeutic benefit (unless psychologically). This sparks the sentiment that there is no reason why society should finance such 'whims' of women who want to have it all (cf chapter 1). However, while the line between medical and social interventions may serve as a general criterion to reimburse or not, there are many exceptions especially in the field of reproduction. Elective abortion, contraception and pregnancy care are prime examples (Harwood, 2009). Pregnancy is not a disease but we still consider abortion and pregnancy care as medical interventions worthy of coverage. Also in the field of medically assisted reproduction, numerous instances (lesbian couples, single women, gamete donation etc.) are hard to fit in a definition of 'medical'. Moreover, AGE banking is not a procedure that is devoid of therapeutic benefits. Although it does not provide an instant remedy to a medical problem or prevent medical problems from occurring (as for vaccination, for example), it can be described as 'anticipatory' medicine: women anticipate on possible future problems by storing eggs. There is a possible therapeutic benefit, but instead of being instant, it is located in the future. A possible analogy is the preventive measure of providing iodine pills to people living near a nuclear facility to substantially diminish the risk of thyroid cancer in case of a nuclear incident. No-one would argue that these pills should not be provided because the persons involved are not yet ill or under imminent threat, as when the risk does present itself, it will be too late to take the necessary measures (such as distributing iodine pills or banking oocytes).

When a woman presents herself at the fertility clinic years after the initial egg banking, requesting IVF-treatment with her previously stored oocytes, the context shifts from a preventive to a curative one. She does not differ from other IVF patients in any crucial

manner. For those countries that provide women who are infertile due to advanced age with a number of free IVF-cycles paid for by the health care system, it would seem straightforward that if these women's cycles are covered when they use their own fresh – but old – oocytes or donor oocytes, they should also be covered when they use their own cryopreserved oocytes. This does not only follow from the consistency requirement. At the time of use, the patient's own previously frozen oocytes have practical and ethical advantages compared to anonymous donor oocytes or the patient's 'fresh' oocytes, and their use should be encouraged. Compared with donor oocytes, there are no concerns over the welfare of the donor and the donor-conceived children. Compared with fresh but aged oocytes, the success rates and health prospects for the resulting babies are most likely better, as most complications in children from (reproductively speaking) older mothers are related to the age of the oocyte, rather than to the age of the mother herself. If the two-tiered procedure of elective cryopreservation and IVF treatment is regarded as a whole, these arguments lead to the conclusion that it should be reimbursed according to the same standards as 'regular' IVF treatment. However, as both steps are distinct in time and as step one (storage) does not necessarily lead to step two (treatment), a more nuanced policy may be needed. We will consider the option of offering full coverage, but also the alternative options of offering a refund for the first step of the procedure on the condition that a woman returns for the second step, either in cash or in kind.

4.3 Full coverage

A first option would be to cover AGE banking from the onset, merely setting restrictions on factors such as the number of cycles and the woman's age (in light of a reasonable chance of pregnancy), similar to restrictions for regular IVF. This would lower the threshold for women to cryopreserve, make the option available to women with lower incomes and thus increase fair access. However, an implementation of this strategy would mean that the legal requirement in some countries of an infertility diagnosis prior to ovarian stimulation cannot be maintained.

A likely objection to full coverage is that this could be a suboptimal allocation of scarce funds. Health care budgets are strained and several countries are already struggling to accommodate the present IVF-demand. One would expect that the added costs would not be overwhelming. Ovarian stimulation and oocyte retrieval are uncomfortable procedures that women will only undertake if they are convinced that they will actually benefit from the procedure. Moreover, if all women who have their oocytes frozen would use them later on, there would actually be a net benefit if one considers the costs per live

birth. The reason behind this is that the live birth rate will be higher when (frozen-thawed) 'younger' eggs are used compared to 'older' eggs of subfertile women (Kim et al., 2010), the miscarriage rate will be lower (Van Loendersloot et al., 2010) and younger oocytes will lead to less chromosomal abnormalities in the offspring. Also, women opting for AGE banking will need fewer stimulation cycles at a younger age than they will need for regular IVF at an older age and there will be no need for stimulation of third party donors. 'Losses' are only made when cycles are performed for women who do not return for treatment and do not donate their oocytes to others. However, three cost-effectiveness studies, conducted by Van Loendersloot et al. (2011), Hirshfeld-Cytron et al (2012a) and by Devine et al (2015) resulted in conflicting results. The (US-based) study of Hirshfeld-Cytron et al concludes that AGE banking would result in an additional cost of 135,520 USD per live birth (and increase the cumulative live birth rate from 72% to 79%), the European study of Van Loendersloot et al concluded that if 61% of women return to use their oocytes, OC is cost effective at an additional 24 600 USD per live birth (increase in live birth rate from 65% to 84%) and (US-based) Devine et al conclude that AGE banking decreases the cost per live birth with approximately 15,000 USD (with an increased live birth rate from 42% to 62%). As the authors of the first two studies have clarified themselves, these differences can be explained by the differences in the scenarios they used and differences in costs (Hirshfeld-Cytron et al, 2012b).

A key factor in establishing cost-effectiveness is to attract the category of women that is most likely to benefit from the procedure, meaning those who have a high chance of actually returning for treatment and whose oocytes are frozen at a point when they are still likely to lead to good fertilization rates. As argued in chapter 3, women who request cryopreservation of their oocytes between ages 30 and 35 are most likely to meet these criteria. In light of the lower success rates for 'older' women, a policy might be envisaged that offers full coverage to women younger than, for example, 36. This is the age at which Cil et al found the highest discrimination capability for success versus failure (Cil et al, 2013). However, currently most women who want to cryopreserve their oocytes present themselves at a later age. In Hodes-Wertz et al's sample, 84% of AGE bankers were 36 or older (Hodes-Wertz et al, 2013). It is also interesting to note that in a follow-up study by Stoop et al of women who banked oocytes (on average) two years prior to the study, only half of the women think that they will even use them (Stoop et al, 2015).

Besides the cost-objection to full coverage, another objection might be that full coverage would lead to an increase of women opting for egg banking and to more women postponing motherhood. Whether the possibility of oocyte cryopreservation will cause a postponement of motherhood is debatable and will only be confirmed or refuted if and when elective freezing becomes widely available. One should always keep in mind, however, that when women choose to store oocytes and postpone motherhood, they do this because in their eyes, the circumstances for raising a child may or will be better at a

later point in their lives than at the present (as discussed in previous chapters). Thus, the possibility that more women will postpone motherhood is not a valid argument against public funding, unless one starts from the premise that children are always better off being born to a young mother than to an older one, regardless of the circumstances. This is not a plausible premise. Again, most women who opt for AGE banking postpone motherhood for lack of a partner (Nekkebroeck et al., 2010; Hodes-Wertz et al, 2013; Stoop et al, 2015; Cobo et al, 2016). It is not particularly convincing to argue that it is better for these women to become single mothers at age 35 than sharing parenthood with a partner at age 40.

The fact that more women would be inclined to cryopreserve their oocytes at a young age can in contrast also be regarded as a desirable evolution in the sense that a greater number of the women who postpone motherhood will have young oocytes available to them and thus fewer will have to rely on donor oocytes. Another positive consequence on a societal level is that more donor oocytes will become available for those women who did not freeze proactively, as there will always be a certain percentage of women who store their oocytes but eventually do not return for IVF treatment. Moreover, this new source of donor oocytes would have fewer ethical objections attached to them, as one can be sure that the donor voluntarily underwent the ovarian stimulation and oocyte retrieval procedure (see chapter 6). In fact, women who have taken the step to cryopreserve oocytes at one point, but have ultimately decided to remain childless or whose child wish has been fulfilled, have a perfect donor profile in yet another sense, as they realize how important a child wish can be, but at the same time no longer have an interest in using their oocytes themselves. Of course, it is important that women who want to donate when their cryostorage ends are properly counselled about this important decision and are warned that they may later be confronted with their genetic offspring. This, however, also applies to egg sharers and current oocyte donors.

4.4 Partial coverage

Another option is to cover only the second step of the procedure. In this scenario, the retrieval and storage of oocytes would be paid for by the woman herself, as she requests an elective procedure without immediate necessity. Oocyte thawing, fertilization and transfer cycles would be covered by the same principles of 'regular' IVF since the woman is at that point indiscernible from other IVF-patients. The logic of this scheme is that health insurance only kicks in when a 'medical' problem (infertility) presents itself, and at that time the best treatment option is chosen: either IVF with fresh oocytes from the

patient, IVF with donor oocytes, or IVF with previously frozen oocytes from the patient. If the data on the health of children resulting from cryopreserved oocytes continues to be reassuring, the latter option is most likely to be the best option. When cryopreserved oocytes are already available, the patient does not require ovarian stimulation, she does not need to rely on donor oocytes and there is a smaller chance of chromosomal abnormalities in the offspring.

Although this solution is in line with current practice and appears to be logical, it is not fair towards the women who decide to freeze their oocytes. In hindsight, a woman who did not cryopreserve eggs at a younger age will be covered for both steps of the procedure, while a woman who was more foreseeing and decided to freeze her eggs beforehand is only covered for the second – and cheapest – step. Moreover, the former's procedure is likely to involve more risks for the resulting children and is less cost-effective.

4.5 Cash back

This unfairness could be corrected either by offering women a refund for the first step of their IVF-treatment provided that they also undergo the second step and thus complete the procedure. As noted by Stoop (2010), “it would be illogic not to reimburse these women when using their vitrified oocytes once they are faced with infertility while women of the same age get fresh IVF treatments fully covered.” The refund could either only cover ovarian stimulation and oocyte retrieval, or also include the costs related to storage.

This cash back system appears to be the most fair, but there are also some downsides to this approach. As the moment when a woman first pays for the retrieval and storage of her oocytes and the moment when she would be refunded are several years apart, the refund of several thousands of Euros/dollars will be experienced as a considerable financial ‘bonus’. Whereas now, women only turn to IVF after trying to conceive naturally, they may be tempted to request IVF treatment with their previously cryopreserved oocytes (rather than trying to achieve a natural conception) for reasons of financial gain. At first sight, this appears to be a case of ‘overuse’ of medical resources. Demanding an infertility diagnosis before women can undergo covered IVF-cycles and claim the refund is not a guarantee to prevent this. Infertility is not a disease that is easily diagnosed and often remains unexplained and clinically undetectable. The common definition of infertility is the absence of pregnancy after a year of regular unprotected intercourse, but it is impossible for a physician to check this criterion.

One can however argue about whether or not giving preference to the previously stored oocytes really is a case of problematic use of medical resources. Offering (frozen oocyte) replacement cycles to a 40-year woman whose ovarian reserve is not yet depleted can also be considered as less ethically challenging than pushing her to reproduce naturally with higher chances of miscarriage and chromosomal abnormalities in the resulting child while she has ‘young’ oocytes in storage. Which is the best scenario (using the banked oocytes as a first line treatment or as a last resort) will depend on patient specific characteristics, such as the status of her ovarian reserve once she returns and on the number of children she desires to have. For most patients, the ideal scenario, however, would be attempting natural conception first, then ‘regular’ IVF and as a final step IVF with banked oocytes, as this sequence maximises the overall chances of achieving parenthood (Stoop et al, 2016).

4.6 More free transfer cycles

A final strategy might be not to offer a refund in cash for women who request IVF treatment with previously frozen oocytes, but to offer them a refund in kind, more specifically a number of additional transfer cycles. The cost of thawing, fertilization and transfer of the embryo is considerably lower than the cost of a full IVF cycle and thus many more replacement cycles can be offered for the same price. In this kind of arrangement, women are not financially motivated to undergo IVF while they are still fertile. A practical disadvantage of this scheme is that coverage is generally calculated per stimulation cycle, not per transfer cycle. One would need to compare the total cost of an IVF cycle (which usually includes several replacement cycles for fresh and thawed oocytes or embryos) to the cost of thawing, fertilization and replacement in order to determine how many transfer cycles would equal the price of an average full IVF cycle.

In countries that already cover several IVF cycles, this arrangement loses a lot of its appeal as women who opt for elective freezing are unlikely to need these ‘extra’ transfer cycles. Still, although there is no perfect equality of both groups (IVF patients of advanced age with or without previously cryopreserved oocytes), there is at least an attempt to limit the inequality.

4.7 Which strategy is most sound?

Of the four strategies that we discussed, the one that presents the biggest challenge to the values of justice and equality is partial funding, which is in fact common practice at present. From the proposed alternatives, the cash back-system is expected to be the most appealing one as it is cost-effective, no public money is 'wasted' on unnecessary medical procedures, it is compatible with the widespread legal requirement that IVF cycles are only covered when there is a diagnose of infertility and it is fair when comparing women faced with age-related infertility who did previously cryopreserve their oocytes to those who did not. However, it is not a fair system when one compares women who freeze and return for treatment to those who do not return. We might imagine two single women who freeze their eggs at age 34, hoping to find their Mister Right soon without being forced to have children with the first man that comes along. One finds a partner to share parenthood with and returns for treatment at age 38, while the other remains single, does not want to be a single mother and therefore does not return for treatment. Only the first woman will be reimbursed, although there is no morally relevant reason that sets her apart from the second, other than that she was more lucky. As such, the second woman actually suffers a 'double loss'.

Whether the fourth strategy (extra transfer cycles) offers an actual advantage or not will depend largely on the local context. In Belgium, for example, six IVF cycles are covered by public health insurance. Taking into consideration that each of these six started cycles represents several transfer cycles, it is very unlikely that patients would benefit from extra cycles. In places where only one or two cycles are free of charge, however, extra free replacement cycles will often be useful.

Also the appeal of the first strategy – full coverage – will depend on local factors. While it is a fair system that would improve the live birth rate for women treated for age-onset infertility, the public healthcare system probably will not want to add women who request AGE banking to the waiting lists of women who are already subfertile and who are sure to want IVF treatment. In countries where there are no waiting lists, however, full coverage up to a certain age would send a clear message that those who want to bank their oocytes better do it when their chances of success are still reasonably high.

On a policy level, a systematic analysis of these local legal and contextual factors should be undertaken in order to determine which strategy is the most 'fair' for all parties involved, given the local context. Even a combination of several policies might be envisaged. For example, for a country such as Belgium, we could imagine a system in which women who cryopreserve their oocytes before age 36 are covered in full, while women who cryopreserve their oocytes at a higher age would only be covered for

fertilization and transfer. Such a policy may be justified based on a trade-off between considerations regarding equity of access, cost-effectiveness and public education (namely: that oocyte freezing is best done before age 36). In the UK, by contrast, a system that offers more free transfer cycles might be the better choice when there are already many infertile couples on the waiting lists.

4.8 Conclusion

Although elective oocyte cryopreservation is being offered by an increasing number of fertility clinics, it is far from clear what its place is – or should be – within systems that offer a number of free IVF cycles. If women who have proactively cryopreserved their oocytes return for treatment at a point when they can no longer conceive naturally and have not reached the maximum age limit for embryo transfer, they should be treated on equal terms as other IVF patients and also receive free treatment. It is less straightforward, however, whether or not the covered cycles should include the first step of the procedure, namely the costs related to ovarian stimulation, oocyte retrieval, oocyte freezing (/vitrification) and storage. Although paying for elective procedures is counterintuitive, there may be good reasons to argue for full coverage from the onset in specific contexts. Alternatively, a cash back system or more free transfer cycles could be considered. The preferred strategy will often depend on local legal and contextual factors.

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Chapter 5

Company benefit

Abstract:

Purpose - A critical ethical analysis of the initiative of several companies to cover the costs of oocyte cryopreservation for their healthy employees. The main research question is whether such policies promote or confine women's reproductive autonomy.

Results - A distinction needs to be made between the ethics of AGE banking in itself and the ethics of employers offering it to their employees. Although the utility of the former is expected to be low, there are few persuasive arguments to deny access to oocyte cryopreservation to women who are well informed about the procedure and the success rates. However, it does not automatically follow that it would be ethically unproblematic for employers to offer egg banking to their employees.

Conclusions - For these policies to be truly 'liberating', a substantial number of conditions need to be fulfilled, which can be reduced to three categories: (1) women should understand the benefits, risks and limitations, (2) women should feel no pressure to take up the offer; (3) the offer should have no negative effect on other family-friendly policies and should in fact be accompanied by such policies. Fulfilling these conditions may turn out to be impossible. Thus, regardless of companies' possible good intentions, women's reproductive autonomy is not well served by offering them company-sponsored AGE banking.

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5.1 Introduction

In October 2014, the media reported that Facebook and Apple are including oocyte cryopreservation in their employee benefit package (up to 20,000 USD) and that women had started taking up this opportunity (Friedman, 2014). Other companies have since voiced their intentions to follow suit or introduced the same policy, for example Citigroup, JP Morgan Chase, Google and law firms (Bennett, 2014; Robertson, 2014). The most important reasons why employers typically offer perks and (health) benefits to their employees is to attract and retain good employees and to make sure they remain healthy (and thus productive). In this case, although the offer is healthcare-related, the former motive is said to apply to the case of egg freezing. In Silicon Valley, competition for talent is extremely high, resulting in tremendous efforts of the different companies to go above and beyond when perks and benefits are concerned. Knowing that it is difficult for educated women to combine their career and family plans – not to mention the wage penalty that young mothers face (Buckles, 2008) – the rationale is that young promising women will be charmed by the option of putting their fertility ‘on ice’ and thus choose for those employers that include egg freezing in their benefit package. However, these new policies were ill received by many and the intentions of Facebook and Apple were widely questioned. The most common reproach is that the offer is actually not intended to be a benefit for the employee, but rather for the employer, as childless employees have more time available to invest in their jobs. This chapter does not aim to uncover the ‘true intentions’ of employers offering egg freezing, but does aim to make a critical ethical analysis of the pros and cons of this new (alleged) benefit in terms of women’s reproductive liberty.

5.2 Preceding debate on ‘social egg freezing’ or AGE banking

It is important to highlight that even outside the context of employment, oocyte cryopreservation for healthy women is still controversial, despite its wide availability. As was argued in previous chapters, reasons to principally oppose the possibility for healthy women to bank their oocytes are lacking and are particularly unconvincing as cancer patients are actively encouraged to preserve their fertility. Whether one’s fertility is threatened by disease, therapy or age is irrelevant, if women want to take proactive measures to preserve their fertility, they should be able to do so regardless of the cause of the perceived threat to their fertility. However, that does not mean that there are no reasons for concern regarding how the procedure might be marketed to women and

regarding the information and counseling that is available to the women who express their interest in egg freezing (see chapter 3). Women of advanced reproductive age should be honestly informed about the (low) success rates they can expect and young women should be informed that postponing childbearing will always reduce their chances of becoming parents, even if their oocytes are banked. Although the ASRM has outlined clear guidelines regarding the information that should be provided to candidate egg bankers (ASRM, 2008), the information that is made available on fertility clinics' websites has been reported to be deplorable (Avraham et al, 2014).

While banking oocytes for AGE-banking promises to increase women's reproductive autonomy, reduce the incidence of involuntary childlessness and reduce the need for donor oocytes, an important limitation is that these benefits are difficult to predict in individual cases. Some women will bank their eggs without ever needing them, some will bank their eggs but will not succeed in establishing a pregnancy, some will not bank and wish they had later on. Increasing the utility is difficult. High utility requires that good quality eggs are banked and that many women return to thaw and fertilize them. However, these two factors are inversely correlated. In order to bank good quality oocytes with high chances of a live birth, women should ideally bank eggs at the peak of their fertility. However, women who bank eggs at a young age are not very likely to need them as they still have a lot of time ahead of them to reproduce naturally. Women in their late thirties have a lot less fertile years ahead of them and are thus more likely to face a depletion of their ovarian reserve once they attempt to establish a pregnancy. However, the quality of their oocytes has already diminished. This means that – merely based on utility – there is only a very small fragment of the population that we ought not to discourage from banking their oocytes, somewhere between the ages of 30 and 35. Moreover, even for this population, the previous remark that postponing always reduces the chances of a successful pregnancy (with or without banked oocytes) remains valid. Thus, for women who have a strong desire for parenthood and who have found the partner they want to share parenthood with, egg banking is never the preferred option. This very small category of women who may potentially benefit from egg banking contrasts sharply with the way egg banking is marketed as the next big step in women's reproductive liberty and as the ultimate road to 'having it all' (that is, a family and a career). Egg freezing cocktail parties and flyers reading "Working, shopping, egg freezing?" seem to suggest that virtually all women, but especially those with higher education, should take up the opportunity of egg banking, either as a deliberate life plan, or as an insurance policy 'just in case'.

Fertility clinics are therefore accused of misrepresenting the costs and benefits and of offering this expensive procedure with a low utility merely with their own financial interests in mind, rather than the best interests of their patients/clients. This idea is reinforced by the fact that most women who bank their eggs today do not match the

stereotype of the wise, proactive women banking good quality oocytes, but rather of the (reproductively speaking) older single women desperately trying to hold on to the last couple of (reduced quality) oocytes they have left so that they can be fertilized if and when Mr Right comes along (see chapter 1). However, there is an important remark to be made here. Both personal stories in popular media (Richards, 2013; McCarthy, 2015) and a study by Stoop et al (2015) suggest that an aspect of AGE-banking that has not received its fair share of attention is the psychological effect it has on women. More specifically, a recurring story is that – unlike men – women in their thirties feel substantial pressure to find their significant other before the end of their fertility and some report being faced with the dilemma of either ‘settling’ for a partner despite having doubts about the relationship or continue looking for the perfect match while risking remaining childless (Waldby, 2015). In the Belgian study, 32% of the respondents indicated that they banked their oocytes because they wanted to take away the pressure to find a partner and 49% indicated that they wanted to give themselves more time to find a partner (Stoop et al, 2015). Another psychological effect that has previously been described in the setting of ART is the phenomenon of anticipated decision regret (Tymstra, 2007). Women want to have the idea that they ‘tried everything’ in order not to feel regrets later (Daniluk, 2001; De Groot et al, 2016). This is also a major reason for resorting to egg banking (Stoop et al, 2015). These psychological factors also explain why – both in the setting of egg banking and in the ART-setting in general – even those for whom the treatment was not clinically successful (that is: did not result in a healthy live birth) seldom regret having undergone the procedure (Stoop et al, 2015; Daniluk, 2001), despite the significant cost and efforts.

5.3 Pros of company-sponsored egg freezing

How does the offer of employers to cover the costs of AGE-banking affect this debate?

First, it counters the concern for exploitation. If not a woman herself, but rather her employer or (work related) health insurer would pay for the procedure, one cannot say that vulnerable women at the verge of losing their fertility are being exploited in the sense that they are tricked into paying a large sum of money to buy a false sense of security.

Second, it counters the reproach that the average woman opting for AGE-banking is too old. We can expect the average age of women who would bank their eggs through their health insurance or employer to be lower than the age at which women are banking today. Most women delay the significant financial investment until the moment they are relatively sure they will eventually ‘cash in’ on it (that is: use their banked oocytes), which

is per definition not at the peak of their fertility. The younger a woman is, however, the more optimistic she will be about being able to start building a family before she loses her fertility and thus the less inclined she will be to invest a large sum of money into egg banking. If the cost of the investment is no longer an element to be taken into consideration, even women who are less worried about finding a partner 'in time' may become interested in banking, which will lower the average age and thus raise the quality of the banked eggs. This is not to say that we should expect a massive uptake and thus an overconsumption of medical services, as the procedure remains physically burdensome and is thus not something that women will undergo on a whim.

Another effect could be that the profile of banking women may change on a different level than age alone (although this remains a hypothesis). At present, virtually all women who are cryopreserving their oocytes are single and lack of a suitable partner has repeatedly been identified as the main reason for egg freezing (Baldwin et al, 2014). If companies start covering it, more women may consider AGE banking in combination with the deliberate postponement of parenthood as a means to achieve their professional aspirations. If this shift would occur based on company policies, several conclusions can be drawn, of which at least two speak in favor of company-sponsored egg banking. First, in terms of utility one might consider this to be a positive evolution, as this would provide a cohort of egg bankers who freeze young but have no intention of trying to establish a pregnancy naturally in their fertile years and are thus more likely to return to use their banked oocytes after their reproductive lifespan. Second, in terms of justice, one might argue that if women dedicate their most fertile years to their careers, it is only fair that their employer – who benefits from the delay to parenthood – bears the costs of their attempt to safeguard their fertility for the future.

Last but not least, we should mention on the pro-side of the debate that in principle, the possibility for women to bank eggs regardless of their financial situation can be said to expand their reproductive autonomy. Stoop et al (2015) documented that financial considerations are a barrier to AGE banking for a significant portion of the women who inquired about the procedure but eventually decided against banking. In their study, 13 out of 29 women would have banked had the procedure been significantly less expensive. From this perspective, external financing would bring an additional reproductive option within reach for a larger number of women. Many women will have no need for this benefit, but for others it may be a welcome alternative for rushing into parenthood under suboptimal circumstances (lack of a stable relationship, financial instability, demanding job responsibilities,...). This need not necessarily be framed in terms of reproductive autonomy, but in terms of autonomy 'tout court', as it may have a significant effect on many aspects of a woman's life. This idea fits nicely into a branch of feminism that has been labeled neoliberal feminism, faux feminism or 'lean in feminism'. This last term refers to a bestselling book by Sheryl Sandberg, the current COO of... Facebook (Sandberg,

2014). Sandberg's aim is to inspire young women to become leaders in today's society and in aspiring to lead, they should not be deterred by the seeming incompatibility between family and career. Although she does not specifically address the topic of egg banking, it is not hard to see how egg banking fits in this rhetoric. Also feminist scholar Marcia Inhorn called upon young female academics to consider freezing their eggs so that they can postpone motherhood until after they have landed their first tenure-track job (Inhorn, 2013).

5.4 Cons of company-sponsored egg freezing

Not all feminists are convinced that egg banking has a liberating effect on women though, quite to the contrary, radical feminists tend to be diametrically opposed to Sandberg's new feminist ideology (Petropanagos, 2010; Catapan et al, 2014; Baylis, 2015). As Françoise Baylis wrote, "oocyte cryopreservation as an employee benefit is not only counterproductive but offensive. It not only fails to empower young women, it actually disempowers them by overtly entrenching the otherwise subtle message that women who have babies are not serious about their careers" (Baylis, 2015). Next, she calls on those companies that offer egg banking to exchange this measure for an employee benefit package that is 'truly family-friendly'.

The accusation that Facebook and Apple are not family-friendly companies is not entirely appropriate, as many of the leading companies in silicon valley and Facebook in particular are exemplary in this regard, despite the fact that they are under no legal obligation to provide even a single day of paid maternity leave. However, as other companies start copying Facebook in offering egg banking, it is very doubtful that they will be as eager to copy Facebook's 4 months of paid maternity and paternity leave (also for same-sex couples and adoptive parents), financial assistance in IVF and adoption procedures, designated breast-feeding rooms or the 4000 USD 'baby cash' when their fulltime employees become parents. As long as the company supports both having children and delaying childbirth, one might argue that they are not pushing their employees in a certain direction. However when the investment in egg banking is not accompanied by child-friendly policies or is even introduced at the expense of such policies, there is a clear message that the employer prefers the employee to defer childbearing. The worry that is expressed by Baylis and others that women will be disempowered may therefore indeed be a legitimate concern.

Ideally, the benefits and perks that are offered in the sphere of family building should remove constraints and thus offer employees a greater liberty in choosing the path in life

that they desire. IVF coverage is a good example. It makes IVF accessible to people who might not be able to afford it otherwise but there is no reason to believe that IVF coverage would push employees towards IVF against their will. Employees thus only stand to gain from such a policy. This is less straightforward when it comes to coverage for egg banking. In this case, the offer may cause women to defer childbearing against their better judgment for a short term gain, namely to buy credit from their employer in the hope to land a promotion. At the end of the day, however, these women may find themselves in a situation in which they have in fact sacrificed, rather than safeguarded their fertility by banking their eggs if none of their banked eggs leads to a healthy live birth or if they do not have enough oocytes in storage to reach the desired family size. Those who bank eggs as a last resort have nothing to lose, but those – such as young employees in a stable relationship – who deliberately adjust their life plans relying on their frozen fertility do, as egg banking may give them a false sense of security.

Even without the offer of egg banking, the labor market is not always well organized to cope with mothers (and dedicated fathers) on the work floor, let alone in the board room. At the same time, few human desires are so little questioned and so widely respected as the desire to become a parent – not to say that even in Western societies, choosing not to become a mother is still oftentimes frowned upon, rather than the other way around (Ashburn-Nardo, 2017). Thus, up until recently, although the pregnancies of women in their thirties may have been impractical for their employers, they had a valid ‘excuse’ to become pregnant: it was now or never. Furthermore, employers had an incentive to make life as comfortable as possible for parenting employees, for example in allowing flexible working hours or support in daycare, in order not to lose them. With the availability of egg banking, the ‘now or never’-excuse is no longer valid as it presents another additional option for perpetual postponers (Berrington, 2004). While it might have been ‘not done’ to ask of employees to forego parenthood in light of their professional obligations, it appears more acceptable to ask of employees to merely postpone parenthood. As age limits apply in most countries for embryo transfer, and as women banking their eggs indicate themselves that they (on average) intend to establish a pregnancy before their 43rd birthday (Stoop et al, 2015), women will not postpone motherhood until after their retirement though. Also, these ‘older’ mothers in the workforce may be even less dispensable than their younger counterparts. These two factors indicate that family-friendly policies would still be needed and might still be implemented. However, this optimism has limits. If the average age at first childbirth should rise in companies offering egg banking, they will end up with a smaller segment of employees who are parents and smaller groups are less likely to be catered to. It is thus not far-fetched to suggest that the offer of egg banking may turn out to be at the expense of family-friendly policies. What the impact will be of company-sponsored egg banking on postponement is, however, uncertain at present. Somewhat reassuring studies in this regard are those by Hakim

(2003) and Van Balen (2005), both indicating that a strong desire to have children overrides motivations to postpone motherhood. However, for the large group of women who have a less urgent desire for parenthood, the offer of egg banking 'free of charge' may influence their decision to postpone conceiving a child.

This brings us to another possible problem when egg banking is offered by employers, namely neutral provision of the necessary information and non-directive counseling. Just to give one example, it would be very relevant that the employee knows that she will need ICSI (with the associated cost) to fertilize her stored eggs a couple of years down the road and whether or not this will also be covered by her employer/health care provider or not. This and other information about the technicalities, success rates and possible risks need to be provided by a neutral person who is not affiliated with the company paying for the procedure. Information provision by the employer involves a conflict of interest that is to be avoided.

A final ethical con against company-sponsored egg freezing is that this benefit might result in a situation in which employees become indebted to their company and that their company holds a certain power over them in a very private way. Much will depend on the specifics of the agreement, for example on whether or not a woman is required to reimburse her employer if she leaves the company the day after banking her eggs and whether or not the employer is aware of which employees have or have not taken up the opportunity of banking. Also, certain expectations will be present towards the women who bank eggs, in particular the expectation that they will not become pregnant immediately after banking. Also here, the specific practical details are determining. If the employer does not have any access to the medical records of the employees, even for those procedures that are covered by the company's health insurance, these expectation will not be present.

5.5 Conclusion

What are we to conclude after analyzing the pros and cons of companies offering AGE banking to their employees? Is it the final step in female liberation now that the women working for these companies not only have the theoretical possibility of putting their fertility on ice, but also the practical means? Or does it increase the (potentially internalized) oppression of women by increasing the likelihood that they will not only be free to postpone parenthood, but pushed to do so against their better judgment? There is no clear answer to these questions as a lot will depend on the practical details of the

agreement between employer and employee and on the personal circumstances of each separate individual.

What is clear, however, is that for these policies to be truly ‘liberating’, a substantial number of conditions need to be fulfilled, which can be reduced to three categories. Company-sponsored egg freezing would be liberating if and only if (1) women understand the benefits, risks and – perhaps most importantly amidst the hype – limitations (cf. the SART/ASRM guidelines), (2) women feel no pressure to take up the offer (whether or not a woman banks her eggs should thus not have any influence on her career opportunities); (3) the offer has no negative effect on other family-friendly policies and is in fact accompanied by such policies. These conditions should lead to a situation in which (1) (on a personal level) only those women bank their eggs for whom – all things considered – this is their best available option of achieving the life goals that are most important to them personally (which should be very few women) and (2) (on a societal level) women remain free to have their children while they are young, without suffering serious professional setbacks. If companies take these requirements seriously, they will have to invest a lot of time and effort in fulfilling them and many will argue that they are impossible to fulfill. Thus, regardless of companies’ possible good intentions, women’s reproductive autonomy is more often than not ill-served by offering them company-sponsored AGE banking.

But, to all sincerely feminist companies, there is also an easy way to comply: do not include egg banking in your benefit package, but use the funds to make it easier for women to balance professional and parental obligations and make sure your female employees earn enough money so that those who want to, can finance egg banking themselves and can deliberate on its merits in private.

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Egg banker today, egg donor tomorrow?

Chapter 6

Implications of oocyte cryostorage for the practice of oocyte donation

Abstract:

As the efficiency of oocyte cryopreservation increased rapidly in recent years, oocytes are currently being stored either in the course of IVF-treatments, or as a fertility preservation measure. These practices may have an impact on the number of available donor oocytes due to two different dynamics: first, a certain percentage of women for whom oocytes were cryopreserved will eventually not use their eggs and may decide to donate them to others; second, especially in the practice of AGE banking, women may opt to donate a part of the retrieved oocytes in 'freeze and share' schemes in order to reduce the costs. In this article, we aim to sketch the ethical implications of such developments in general and the issue of payment to oocyte donors in particular.

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6.1 Introduction

Oocytes may be cryopreserved in a number of circumstances: during the course of an IVF-treatment, at the request of women whose fertility is threatened by diseases or aggressive medical treatments (so-called 'medical freezing'), at the request of women who fear infertility due to aging (AGE banking) or in the context of egg banks for fertility treatment. These practices may have an impact on the number of available donor oocytes due to different dynamics. First, donor egg banking allows the oocytes of one donor (or one stimulation cycle) to be distributed between different recipients in smaller batches, which results in a more efficient allocation and a lower cost for the recipients (Robertson, 2014). Second, a certain percentage of women for whom oocytes were cryopreserved with the intent of autologous use will eventually not use their eggs and may decide to donate them to others. Third, especially in the practice of AGE banking, women may opt to donate a part of the retrieved oocytes in 'freeze and share' schemes in order to reduce the costs. For the purpose of this dissertation, I will not look into this first dynamic, which was already discussed by Robertson (2014), but rather the second and third, which is relevant for women who resort to AGE banking. The ethical implications of these developments in general and the issue of payment to oocyte donors in particular will be discussed. I will start by sketching the situation for donation for reproductive purposes and look into donation for research purposes at the end of the chapter.

As a preliminary remark, it must be pointed out that the implications of this potential new source of donor oocytes on the practice of oocyte donation will be more pronounced for those countries where patients are currently faced with waiting lists for IVF treatment with donor oocytes as more oocytes will shorten those waiting lists. In, amongst others, the US, Spain, and some East European countries, this is not an issue. However, as we will show, even in such countries, there still may be a significant impact on certain aspects of the practice of oocyte donation, including the price of oocyte donation cycles.

6.2 Oocytes cryopreserved during IVF treatment

In the course of IVF treatments, it is common practice to harvest more oocytes than can be fertilised and replaced in one cycle. Currently, most fertility centres opt to fertilise all the available oocytes and cryopreserve the high quality embryos that are not transferred in the first cycle. However, as these embryos 'belong' to two individuals, disagreements may arise over their disposition. Now that the efficiency of oocyte cryopreservation

(through vitrification) equals that of embryo cryopreservation, it may thus be wiser to freeze oocytes instead of embryos (although this practice will probably be less cost-effective as a certain percentage of oocytes will be frozen, but will eventually fail to fertilize). Other reasons for freezing oocytes rather than embryos include legal restrictions on the storage of embryos (such as in Italy), religious/ethical objections of the patients or the inability of the male partner to produce semen at the time of oocyte retrieval. In recent years, many clinics are also starting to adopt a freeze-all strategy (with an hCG-free protocol) in order to avoid ovarian hyperstimulation syndrome and increase IVF success rates (Evans et al, 2014; Roque, 2015). In such a protocol both embryos or oocytes can be cryopreserved, both with its own benefits and drawbacks (Devroey et al, 2011; Mertes and Pennings, 2011).

6.3 Deciding to donate

Regardless of the reason why oocytes are frozen during the course of IVF treatment, a number of these oocytes will remain unused due to a myriad of reasons and will thus become surplus or spare oocytes. In the years after egg storage, women may have completed their family through natural conception or IVF with other oocytes, pass away, break up with their partner or abandon their desire to have children. The same disposition options should be offered for these spare oocytes as for spare embryos after IVF treatment: prolonged storage, disposal, donation to other couples or donation to research.

We expect less reluctance to donate oocytes to other IVF patients when spare eggs are already in storage than when a woman has to undergo the stimulation and retrieval procedures specifically for the purpose of donation or when donation implies a decrease in the woman's own chance of conceiving (such as in egg sharing). At present, few women are keen to come forward as donors unless when directed (or cross-) donation to a friend or family member is concerned, or when donors receive a personal benefit, either in cash or in kind (in egg sharing schemes). Potential donors need to overcome a double threshold: the first regards the physically demanding procedures of ovarian stimulation and oocyte retrieval, the second regards the psychological burden of becoming the genetic parent of a child that one does not know.

For women who already have spare oocytes in storage, the first threshold is removed. In this case the decision to donate does not imply any extra physical hardship. Some additional testing for infectious or hereditary diseases may be requested, but the effort will be minimal compared to the oocyte stimulation and retrieval procedure itself.

However, the psychological threshold remains largely intact. Many – if not most – women find the idea of having a genetic child grow up in an unknown family emotionally troubling, and therefore, even if the physical burden is lifted, it is unlikely that large numbers of women with spare oocytes will be donating them for reproductive purposes. Nevertheless, the percentage of women who choose donation may be higher for spare oocytes than for spare embryos. First, the donation of oocytes appears to be less emotionally troubling due to the different narratives that, for example, link eggs to cells and embryos to children (Kirkman, 2003; de Lacey, 2005). Whether this distinction is rational (as both donated oocytes and donated embryos have the potential to become genetic children of the donor) is disputable, but that does not change the observation that the experience for donors is different. Second, one of the reasons why couples do not donate their embryos to other IVF patients is that they are a symbol of their partnership (Provoost et al, 2009). This objection to donation does not arise for oocytes.

If there is a trend to cryopreserve oocytes rather than embryos, even a small percentage of donations might be sufficient to meet the current demand. As a general indication, in 2010 25,187 egg donation cycles were reported to the ESHRE registry (representing 991 clinics in 31 European countries) and there were 15,504 donor oocyte transfer cycles (with an average of 2 embryos per transfer) in the US (SART, 2012; Kupka et al, 2014). Practical advantages of using oocytes that are already in storage, rather than relying on fresh oocytes are, for example, that there is no need to synchronise the cycles of donor and recipient, that the number of available oocytes is known beforehand so that oocytes of one donor can be directed to several recipients and that donors can be tested for infectious diseases after the window period. An ethical advantage is that healthy women do not need to be subjected to the procedures of ovarian stimulation and oocyte retrieval, which are not beneficial for their own health, and which may – in seldom cases – even be harmful to them. These advantages also hold true in places where there is no donor oocyte shortage, meaning that even in those places the availability of spare frozen oocytes may have an impact on the practice of oocyte donation.

A practical disadvantage of relying on IVF patients as egg donors is that most egg donor programs maintain an upper age limit of 35. In the UK, only 41,6% of cycles (fresh and thawed combined) were performed in women below 35 years of age in 2010 (HFEA, 2012). For the same year, only one third of fresh embryo cycles were performed in women under 35 in the US (SART, 2012). However, on average, more oocytes are harvested from younger women, which means that they are more likely to have spare oocytes compared to their older counterparts, which is for example reflected in the fact that in thawed embryo cycles the number of women below 35 rises to 50% (for the US). Also, the younger the patient is, the more likely she is to conceive on her first attempt (SART, 2012; HFEA, 2012), which again makes it a plausible assumption that women below 35 are more likely to have spare oocytes left at the end of their treatment than IVF patients above 35. Nevertheless,

in countries where paid donation is the norm, the average age of current – paid – donors is likely to be significantly lower than the expected average age at which spare oocyte donors will have had their oocytes harvested, which makes paid donors more attractive candidates for recipients, as the recipients will have a better chance of conceiving with younger eggs. A trade-off will thus need to be made between the practical and ethical advantages of using spare oocytes on the one hand and better success rates when recruiting healthy young donors on the other hand. An additional factor to be considered will undoubtedly be the cost. As we will discuss below, spare oocytes are likely to be the cheaper option, which will make it attractive even in those places where there is no shortage. The future will tell if this will lead to a shift from fresh to frozen spare embryos or if this will lead to an increase in the demand, as it may open up the option of donor conception for a range of patients who are currently unable to afford the costs involved in donor recruitment and donor compensation.

6.4 Reimbursement

Whether or not donors should receive financial compensation for anything other than out-of-pocket expenses has been a much debated issue for several years (Dickenson, 2009; ESHRE Task Force on Ethics and Law, 2007; Ethics Committee of the ASRM, 2007; Flower, 2010; Gazvani et al, 1997; Hyun, 2006; Johnston, 2006; Levine, 2010; Mertes and Pennings, 2007; Steinbock, 2004; Thompson, 2007). Although most donors indicate altruism as their prime motivation to donate oocytes, it cannot be denied that the offer of money to offset physical discomfort and time investment or the price cut for patients in egg sharing programs (which accounted for half of the total number of donated oocytes in 2010 in the UK) serve as important incentives (Lindheim et al, 2001; Pennings and Devroey, 2006; Purewal and van den Akker, 2009; HFEA, 2012). Some authors have argued that one should steer clear of such incentives, fearing that they might lead to commodification of oocytes, undue inducement and/or exploitation of financially deprived women (Dickenson, 2009). Although we have previously questioned the validity of these objections and defended limited reimbursements, it is interesting to consider whether the prospect of spare oocytes becoming available for donation might render this debate superfluous all together (Mertes and Pennings, 2007). In this regard, it is interesting to compare the donation of spare oocytes to the donation of spare embryos by former IVF patients who have decided they no longer need those embryos for themselves. To our knowledge, these donors are not retrospectively compensated for the financial or physical investment in the creation of their embryos and this custom goes unquestioned. There are several possible explanations for this.

First, as the time when the investments are made and the time of the donation are usually several years apart, even a partial reimbursement at the time of donation would make the embryo donation look more like an embryo sale (Robertson, 1995). Even though an offer of compensation might be inspired by laudable principles such as reciprocity or a just distribution of the costs by all the beneficiaries, it may still be perceived by the donors as offensive and of actually devaluing their gift.

Second, when someone gives something away that she no longer needs, it is not obvious in common social practice that the receiver of the gift ought to compensate the cost or efforts that were originally invested in creating or obtaining the gift. Of course, it is not immoral to ask money for a second hand car, especially if it was never used by the original owner, but note that that is a case in which an item is sold, meaning that an amount of money is offered that equals the financial value of the car (as determined by supply and demand). Embryos fall outside this economic realm and cannot be exchanged for money. Therefore, the only possible justification for compensation of embryo donors would have to be based on establishing a just, proportional distribution of the costs (both financial and in terms of time and effort) and benefits. This is the rationale that also underlies egg sharing programs, in which a woman shares her oocytes with another woman, who in turn contributes to the costs of the donor's IVF treatment (and thus the ovarian stimulation and oocyte pickup of which she also profits). However, this paradigm is not applicable for embryo donation as the original intention is a morally relevant difference between the two cases. We can use the analogies of hitchhiking and carpooling to demonstrate this claim and to answer the question of reimbursement. In the context of hitchhiking, a person takes her car to go to a certain destination. During the trip, she picks up another person who has the same destination. It is part of the practice of hitchhiking that the car driver does not ask for money. Gratitude is a constitutive rule of hitchhiking. Carpooling is essentially different. Here two people want to go to the same destination but they make an agreement beforehand that the person who drives will receive compensation for the costs that she makes (the gasoline bill will for example be split in half). The rules make perfect sense within the practices. The hitchhiker is not willing or unable to pay for the trip and accepts the uncertainty about whether being picked up, timing etc. The car driver is free to decide whether or not to go and when, to pick up the hitchhiker or not, depending on whether she wants company or whatever. The car-pooling passenger, however, knows when and how she will travel but she has to pay a certain amount for that certainty. The driving party in the carpooling commits herself to driving at a certain time etc. An IVF patient who underwent the treatment for herself, without making any commitments to future candidate-recipients of a possible surplus, and then asks for reimbursement at the end would make the same mistake as a car driver who picks up a hitchhiker and asks for a contribution. These patients want to

have all the advantages of the uncommitted car driver and the advantages of cost sharing in a carpooling-system.

Egg sharing or other existing forms of fresh oocyte donation follow the car-pooling scenario, the donor and the receiver set out on a joint project together and decide beforehand that they will share the costs and benefits (or that the receiver will offset the investments made by the donor by a financial compensation). When spare embryos are donated, the donors originally made their investments only to their own benefit. We could argue that it would be nice if recipients of a donor embryo would show their gratitude, and many infertile patients might be willing to sacrifice a great deal of money for the chance of carrying a baby to term, but this does not imply that the donors have a legitimate claim to demand a compensation for the time and effort they have invested in the creation of the donated embryo. A more complicated situation would arise in a scenario in which the donors are still paying off the debt they incurred in pursuing IVF treatment at the time when they donate their spare embryos. If the embryo recipients would propose to help them settle this debt, we might be more inclined to look upon this as not merely a nice gesture, but as a fair distribution of the costs, as in this case the financial investment is still ongoing. Also, in this case there would be less ambiguity about whether the receiver is reimbursing expenses or purchasing an embryo.

However, as a general rule, we can state that embryo donors are not compensated for the investments that were necessary to create their embryos, due to concerns over commodification of embryos and the fact that it is not common social practice to compensate people for the investments that they made for their own benefit when they allow a third person to share the benefits. When the donation of spare oocytes is concerned, the same considerations come into play. If enough women come forward as spare oocyte donors (and in this case one can be sure that the donation is 'truly' altruistic), there would no longer be a need to attract donors by means of financial incentives and thus the ongoing ethical debate about this issue can potentially come to an end. An important reservation that needs to be made is that in those countries where donor compensation is currently common practice and especially where donor compensations vary significantly depending on donor characteristics, a market for paid donation will persist for those patients who are only willing to accept fresh oocytes, or oocytes from donors with specific traits. In countries where donor compensation is not the norm and that currently rely on egg sharing programs, these programs are likely to become less appealing as using spare frozen oocytes will become a cheaper, less burdensome and less controversial alternative. On a negative note, this also implies that the women who are now only able to afford IVF treatment thanks to these egg sharing programs, will no longer be able to fulfil their child wish.

6.5 Oocytes cryopreserved in anticipation of age related fertility decline

Let us now turn our attention to the women opting for AGE banking as potential oocyte donors. Nekkebroeck et al. (2010) reported that in their clinic, from the women who opt for oocyte cryopreservation for non-medical reasons, 13,3% have the intention to donate them to another woman if they would not need their oocytes themselves, an additional 26,7% was undecided. Hodes-Wertz et al report that 11% of the women they surveyed would be willing to donate their oocytes for infertility treatment (Hodes-Wertz et al, 2013). While there are no data yet on whether these women actually follow through on their intentions and while the group of women cryopreserving oocytes for age related fertility decline is still small, we should also take this group into consideration as potential spare oocyte donors. Currently, as already mentioned, the average age of women resorting to AGE banking is 37-38 years. Considering that most oocyte donation programs have an upper age limit for the donor of 35, a number of the spare oocytes from this source will either not be eligible for donation, or will only be accepted if there is a substantial donor oocyte shortage. However, as far as oocytes younger than 35 years old are concerned, the donation of these oocytes would have the same practical advantages as donation by (former) IVF patients and would be largely uncontroversial.

As for IVF patients, we argue that these women should not be compensated for the time and effort invested in obtaining and storing their oocytes, as this was done for self-interested reasons, not on the receiver's behalf. However, both public opinion and the donors themselves may be more open to the offer of compensation for the actual costs that were incurred to obtain and store these oocytes in the context of AGE banking than in the context of 'regular' IVF. Women who freeze eggs in anticipation of future infertility but who eventually do not use them themselves, may not look upon them as a surplus that remains unused, but rather as a (bad) investment. This is somewhat different for IVF patients, who are more likely to perceive the costs they made as the price for fertility treatment as a whole and the spare oocytes as a by-product of that undertaking. The former will perceive the costs as the price they paid to generate these eggs and will feel that they did not get a return on their investment, making them more open to the option of recuperating some of their expenses. This perception may be flawed to a certain extent. When one buys an insurance policy against hurricane damage during a 10 year period and no damage is suffered in that time frame, one might say that there was no return on the investment made. However, during those 10 years, those who bought the insurance had a certain 'peace of mind' that those without the insurance did not have and they did not have to put other investments on hold in order to be able to cope with the costs that a hurricane might inflict. One cannot sufficiently point out that oocyte cryopreservation –

unlike insurance coverage – is an investment that is not even guaranteed to pay off if disaster (in this case infertility) does strike, but nevertheless, women who resort to AGE banking can be said to benefit from a similar peace of mind, not in the sense that they are certain to have children in the future, but rather in the sense that the option of parenthood is not yet completely gone. Also taking away the pressure of finding a partner to reproduce with fast is reported by many women as a reason to resort to AGE banking (Stoop et al, 2015) At the time when a woman makes the investment to cryopreserve her eggs, she knows that there is only a chance that she will eventually establish a pregnancy using these eggs, not a guarantee, and yet she esteems at that point that the price is not too high for the gamble that she is taking.

In short, a women who stores oocytes for autologous use and decides to donate them later on cannot make a legitimate claim on the recipients of her oocytes to offset the financial investment that she made to obtain and store them. At the time when the investment was made, this was done for self-interested reasons and the decision to make the investment was not influenced by the future recipients. Nevertheless, we acknowledge that there may be a greater margin for acceptance of compensation for these donors rather than for IVF patients who donate spare oocytes. Although the donor cannot claim compensation, the offer of compensation is not immoral as it can be grounded in principles of reciprocity, just distribution of costs and benefits, or gratitude. An exception to this rule would be women who donate spare oocytes the collection of which they did not finance themselves. This might occur in the case of company-sponsored egg banking, egg banking covered by health insurance or when a combination is made of donation to others and egg banking for autologous use, whereby the donor did not contribute in the costs.

6.6 Freeze and share

This brings us to another way in which an overlap is created between the practice of AGE banking and oocyte donation in countries faced with a donor oocyte shortage. Rather than donating oocytes that were frozen for self-use, but that remain in storage due to circumstances, oocytes can also be donated immediately at the time of freezing in a new form of egg sharing, making extra oocytes available today, rather than in a few years time. The idea of ‘freeze and share’ arrangements was developed at the London Bridge Fertility, Gynaecology and Genetics Centre and offers a way for women to offset the costs of retrieval and storage. Women are eligible to participate in the freeze and share program if they are “fit, healthy and under 35” and if they are likely to respond to relatively low

doses of fertility drugs. They undergo three treatment cycles over a 12 month period and the mature eggs of suitable quality that are obtained are equally divided between the donor and the recipient. The donor does not need to pay for the cost of oocyte retrieval and gets free storage for 5 years (Atalla, 2008). At first sight this is a win-win-situation. First, women who cannot afford to pay for the oocyte cryopreservation procedure are now able to benefit from this new technology. Second, in areas faced with an oocyte shortage, more oocyte will become available so that more women will be able to receive donor oocytes.

However, this arrangement is not commended by everyone: “In the ‘freeze and share’ scheme, vulnerable women as they approach their mid-30s are being encouraged to put their faith in a storage technique with as yet unproven efficacy in the hand of a clinic offering storage in exchange for eggs to donate to other women. These women may then delay childbearing, become infertile, not conceive with their own stored eggs and know that a woman or women conceived with the fresh eggs they donated some years previously” (Parsons, 2008). This concern for the psychological ramifications for women entering into a freeze and share agreement have also been voiced in the context of egg sharing by IVF patients in order to get free or discounted treatment. As the system implies that women donate before they know whether they will eventually become mothers themselves, they should receive counselling about possible feelings of regret if it turns out that the recipients became mothers while they may not. However, in the egg sharing context, it has been shown that this is a concern for a minority of the women (Ahuja et al, 1998), and most patients perceive the arrangements as a win-win procedure (Blyth, 2004).

Other objections to egg sharing are that the donors’ consent is not free from outside pressure as their options are often limited by financial considerations (Englert, 1996), that egg sharing might lead to “a general erosion of social altruism” and that it represents a de facto commercialisation of human gametes (Johnson, 1999). Freeze and share programs are likely to be challenged with those same objections. All these objections can be brought back to the fact that a large percentage of egg sharers are indeed motivated by the benefit in kind that they receive, rather than by altruism. A report by the Nuffield Council on Bioethics (2011) stresses that the reward of egg sharing should not be perceived as payment, but as ‘the opportunity to bear a child’, but the fact remains that the decision to enter into an egg sharing scheme is often contingent upon the (lack of) financial resources of the IVF patient. A study by Pennings and Devroey (2006) shows that in Belgium, the number of egg sharers decreased with 70% after full reimbursement for 6 IVF cycles was installed. This indicates that the success of egg sharing is to a large extent a consequence of unequal access to healthcare services, which is ethically troubling. However, while this is a strong argument to plead for public funding of IVF, we believe it is not a strong argument to ban the practice of egg sharing in places where public IVF-

funding is not available. The fact that a number of – admittedly financially deprived – women opt for egg sharing, means that for them, in their particular situation, this is the best option. Taking this option away does not empower them, but limits their freedom even further.

For freeze and share, the objection that the scheme takes advantage of the precarious situation of women who desperately want IVF, is less convincing than for ‘traditional’ egg sharing, as there is less urgency in this case. Egg sharers need ART treatment and they need it now, while ‘egg freezers’ are storing eggs for possible future use. In other words, the pressure on women who want to freeze eggs is less strong and they will be in a better position to think through all the pro’s and con’s. For these women, sharing eggs will be less of ‘an offer they can’t refuse’ than for infertility patients. However, the peculiar position that these women are in, does require an extra effort on the level of counselling. Women who consider to participate in a freeze and share program not only need to be informed about the practical aspects of the oocyte retrieval procedure, but also about the psychological impact of egg donation, the effect on their own chances of conceiving and about the limitations of oocyte cryostorage as a fertility preservation measure in general.

6.7 Donating for research

A number of the difficulties that were outlined for both IVF patients and AGE bankers do not apply if oocytes are donated for research purposes. First and most importantly, as the oocytes donated to research do not result in offspring, the psychological burden is largely absent. One cannot be confronted with an unknown child in search of its genetic mother and neither does one have to wonder about who this unknown child may be and under which circumstances it will grow up. If both this psychological barrier to donate oocytes and the physical barrier of having to undergo ovarian stimulation and oocyte retrieval do not apply (as the oocytes are already in storage), we would expect a large number of women to donate their unused oocytes to research when given the option. This expectation is reinforced by empirical data showing that donation for research is the preferred disposition option for spare embryos (Lyerly and Faden, 2007; Provoost et al, 2012), which is explained by the observation that IVF patients in general do not want their embryos (and the efforts involved in creating them) to go to waste, but at the same time have difficulties with the idea of having a genetic child growing up in a different family (Provoost et al, 2009). As a general indication, Nekkebroeck et al (2010) and Hodes-Wertz et al (2013) report that respectively 46,7% and 63% of AGE bankers would be willing to donate ‘leftover’ oocytes to research. This new source of human oocytes for research

would not only be easily accessible for researchers, it would also stir much less commotion in the general population and in regulatory bodies than the use of oocytes from donors who would have to go through hormone stimulation and oocyte pick-up for the purpose of donation. Until now, the recruitment of research donors has been very difficult and ethical concerns have been repeatedly voiced (Mertes & Pennings, 2007). The procedure of oocyte donation is deemed to be disproportionately burdensome in comparison to the possible scientific benefits, there are concerns about the fact that those who donate do not represent the part of society that is most likely to benefit from the research and there are concerns about informed consent (Beeson and Lippman, 2006; George, 2007; Magnus and Cho, 2005). While financial incentives to donate have been accepted in some jurisdictions, they have been outlawed by others. In the scenario where spare oocytes are donated (from either of the three sources described above), there is no longer a causal tie between the decision to donate and the hardship involved in the oocyte retrieval procedure, which renders most of the objections to research donation superfluous. Moreover, in this scenario, chances of recruiting a sufficient number of donors without offering financial compensation are much higher than in the current situation.

Finally, some of the concerns related to the freeze and share program would not apply if the oocytes donated under such a scheme are donated for research instead of infertility treatments. For instance, the concern regarding the psychological burden on women who remain childless in the knowledge that another woman may have a child resulting from her oocytes, would not apply. An egg sharing program in which IVF patients agree to donate half of their oocytes for research in return for a 50% discount on their IVF treatment was approved in 2006 for the UK's Newcastle University and is not considered as exploitative by the participants (Newcastle University Press Office, 2006; Haines et al, 2012). A similar program for women who want to store eggs for future use (instead of access to IVF treatment) is probably even less controversial as these women are in a less precarious situation. Whether the costs of a 'freeze and research' scheme should be divided 50/50 between donor and recipient, as in the Newcastle University's egg sharing scheme (for IVF patients and researchers) or if the researcher should pay the full cost, as in the Bridge Centre's freeze and share scheme (for social freezers and IVF patients) is debatable. However, this question may be irrelevant in practice if our hypothesis that spare oocytes will become available at no added cost for research institutes holds true, as in this case, there will be no need to rely on egg sharing schemes.

On a critical note, we must concede that some researchers may not be too keen on using oocytes that have been subjected to vitrification or slow freezing, as these manipulations may constitute a confounding factor in their research data. However, this may not be an issue for all types of research.

6.8 Conclusion

In conclusion, as a side-effect of the ability to freeze oocytes in a safe and effective way, we anticipate that more oocytes will become available for donation from a variety of sources. Oocytes may be frozen for different reasons and as the years pass by, a part of them will remain unused by the woman for whom they were originally stored. It is reasonable to expect that if the option is presented, many of these oocytes will be directed to research and these new kinds of donations will put an end to most – if not all – of the practical hurdles and ethical concerns regarding oocyte donation for research purposes, even the issue of financial reimbursement. Thus, the ongoing ethical debate surrounding 'research donation' may finally be quelled.

Although the effect may be less prominent, there will probably also be a positive effect on the number of oocytes donated to IVF patients. While some particular scenarios require special attention, the donation of spare oocytes for third party reproduction offers more benefits than problems. The most controversial development are the freeze and share arrangements, whereby women who donate oocytes to IVF patients get free storage of half of the retrieved number of eggs for (future) autologous use. If, as a result of the donation of spare oocytes, there is a sufficient increase in donor oocytes to accommodate the present demand, these arrangements are likely to be abandoned again. Nonetheless, in countries where egg sharing between IVF patients is currently allowed, freeze and share agreements – if accompanied by careful counselling – should also be allowed.

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Conclusion

This dissertation set out to answer four normative questions, or at least to shed a light on the main ethical issues associated with each of them:

- Should we freeze the eggs of women who fear that age-related fertility decline will interfere with their reproductive plans? (chapters 1 and 2)
- How should we freeze eggs for these women? (chapter 3)
- Who should pay the bill? (chapters 4 and 5)
- Can egg banking also be considered as a solution to ethical problems in the context of egg donation? (chapter 6)

So how far have we come in answering them?

Should we freeze healthy women's eggs?

The original opposition to egg banking for healthy women – as opposed to the prototype case of egg banking by women faced with gonadotoxic cancer treatment – was largely based on bad arguments (e.g. “we should respect the natural limits of female fertility”, “reproduction should not be medicalized”, “the experimental status of oocyte vitrification is a reason to withhold it from healthy women, but not from diseased women”), false premises (e.g. “women want to freeze their eggs to advance their careers”, “egg banking will have a detrimental effect on society”) and stereotyping (e.g. “women who want to postpone motherhood are selfish”, “women who want to postpone motherhood are victims of a male-oriented society”). Moreover, the dichotomy between ‘medical egg freezing’ and ‘non-medical’ or ‘social egg freezing’ is not straightforward at all, which is why I have attempted to avoid this terminology as much as possible in this dissertation. For example, in which category would we place a woman with a family history of early menopause? Or a woman who has undergone cancer treatment 20 years earlier and now wants to bank eggs, fearing premature ovarian failure? It is not the case that woman faced with gonadotoxic treatment will be sterile the day after treatment, whereas ‘AGE bankers’ remain fertile for years to come. In fact, in many instances the former will have more fertile years ahead of them than the latter (see also Mertes, 2015). Taking this into account, the ASRM’s statement that women whose fertility is threatened

by disease or medical treatments have no other options besides freezing their eggs, while healthy women do have other options is misleading (ASRM, 2007). It appears that there are few morally significant differences left between women whose fertility is threatened by disease and women whose fertility is threatened by aging which would permit a differential treatment. As a basic rule, like cases should be treated alike. Therefore, it is inconsistent to allow egg banking in the context of oncofertility, but not in the context of AGE banking.

One might still conclude, however, that equal treatment of both cases means that egg banking in the context of oncofertility should be abolished. However, given the advances made in the efficiency and safety of oocyte vitrification (at least until further notice, as long term follow-up still needs to be gathered), I conclude that there is no principled reason why women should be denied access to egg banking. Nevertheless, there are some legitimate ethical concerns linked to AGE banking, which brings us to the second question.

How should we offer AGE banking?

It is important to make AGE banking available to those women who have the highest chance of benefiting from it, while discouraging its use by women who are unlikely to benefit. The ideal candidate for AGE banking would be a 34 year old woman who is not in a (stable) relationship, or in a relationship in which parenthood is not (yet) an option and who has a conditional desire for parenthood (that is, parenthood is desired within certain side constraints such as a dedicated partner, financial stability etc.). Moreover, this woman would have to be well-informed about the limitations of the possibilities of establishing a pregnancy and reaching a healthy live birth, about the efforts, discomforts and risks involved and about the costs associated with obtaining a sufficient number of oocytes, storing them and using them afterwards. Also, she should be free from outside pressure (for example from her employer). In the ideal scenario, AGE banking should be considered as a plan B in case future attempts at natural conception fail: a plan B that has a chance of success, but that is not a guarantee for success. Women who inquire about AGE banking at a very young age, arguing that they will postpone parenthood to build a successful career first, should be stimulated to consider whether there will be more or less room for raising children ten or fifteen years down the road once they have landed that perfect job they are now aiming for and whether or not they are willing to gamble their odds of being able to establish a family. Finally, women who inquire about AGE banking at a point when they are very close to being infertile should be counselled properly about their individual chances of success. For many of those women, AGE banking will be a desperate measure with a very small chance of success, rather than a plan B with a reasonable chance of success. It is important to be aware of the fact that many women have reported to be happy about their decision to bank eggs, even if they think that the chances that they will ever use them are slim. For many women the loss of

their fertility may come very suddenly, and egg banking may give them the time to come to terms with that new reality. At the same time, the psychological argument only goes that far. If in a couple of years from now, it would turn out that very few women come back to use their banked oocytes, psychological support and counselling might be the preferential treatment option for women at the verge of losing their fertility, rather than AGE banking. As always, one option does not exclude the other.

Who should pay the bill?

Different conceptions of distributive justice and different conceptions of the goals and duties of public healthcare lead to different answers to this question. In my analysis of this issue, I have started from current practice in healthcare coverage of fertility treatment and argued for consistency. Starting from a context in which several cycles of IVF treatment are covered by public healthcare, also when the cause of infertility is reproductive aging, at least the second part of the intervention – thawing and fertilising the oocytes and replacing the resulting embryos – ought to be covered by public healthcare. This is not a controversial claim: these women would be equally subfertile or infertile than other IVF patients by then but rather than being treated with their own aged oocytes or donor oocytes they could be treated with their own young oocytes. The counterargument that these women purposefully delayed parenthood and are therefore accountable for their misfortune is not convincing, as was extensively discussed in this dissertation.

A more difficult question then, is whether or not the first part of the intervention – the collection and storage of oocytes – should be publicly funded or become part of standard healthcare insurance policies covering fertility treatment. In terms of resource allocation, it is important to know whether this approach would be more or less cost-effective than current practice, that is: treating reproductively speaking older women with their own oocytes with low chances of success and/or with donor oocytes with better chances of success (oftentimes in successive order). The cost-effectiveness studies that are currently available provide conflicting information. Also, such an analysis is never value-free, as one will also have to decide which investment is acceptable for each additional live birth. The most problematic unknown factor, however, is how many women will return to use their eggs. For AGE banking to be a sound investment of the healthcare budget, many women will have to return or donate their eggs to other women. Follow-up of the women who have banked their eggs in recent years will shed a light on this in the years to come. The flipside of not incorporating AGE banking in public healthcare or standard insurance packages, is that it remain inaccessible for large groups of women. Rather than giving a definite advise for or against public funding, I concluded that the local context is decisive in determining which approach is most consistent with current policies regarding reproductive health.

Another option is that employers offer egg banking to their female employees as a perk or (health) benefit. I argued that for these policies to be truly empowering (which they are claimed to be), a substantial number of conditions would have to be fulfilled, which are however difficult to fulfil. Women would have to be properly informed about the benefits, risks and limitations, feel no pressure to take up the offer (whether or not a woman banks her eggs should thus not have any influence on her career opportunities) and the offer should be accompanied by family-friendly policies. As the offer itself may already be considered to be a form of pressure, it is wiser not to offer egg banking to employees.

Can egg banking also be considered as a solution to ethical problems in the context of egg donation? In the final part of the dissertation, I hypothesized how egg banking may not only incite, but also solve ethical concerns, namely in the context of oocyte donation. Egg donation is controversial because it separates genetic from gestational and social motherhood and because it incites concerns over the wellbeing of the egg donors. If women would be willing to donate their banked eggs (either for research or for fertility treatment) after deciding they no longer need them for their own reproductive purposes, then this would be a less controversial source of egg cells than current forms of egg donation in which a woman's ovaries are stimulated with the sole intent of donating and in which women are oftentimes paid for their donation, which raises concern over exploitation and commodification of body material. Women may also decide to combine egg donation and egg banking for autologous use in a system similar to egg sharing agreements between IVF patients. In this case, original concerns over pressure to donate remain largely intact.

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Appendix 1: English summary

Should we freeze healthy women's eggs?

Chapter 1: The portrayal of healthy women requesting oocyte cryopreservation

The possibility to cryopreserve oocytes to be used in IVF treatment later in life has not only enlarged the reproductive options of cancer patients who are faced with gonadotoxic treatments, but also holds the promise of enlarging the reproductive options of healthy women whose personal circumstances (most often the absence of a partner) do not allow them to reproduce in their most fertile years. Opinions for and against this application of the cryopreservation technology are often based on different portrayals of the women who might use it. Three different portrayals can be discerned in the debate about the ethics of so-called 'social egg freezing' or 'non medical egg freezing'. First, these women have been portrayed as selfish career-pursuing women. Second, healthy women who might benefit from oocyte cryopreservation have been portrayed as victims of a male-oriented society that makes it difficult for women to combine motherhood with a good education or professional responsibilities. Third, healthy women opting to cryopreserve oocytes have been portrayed as wise, proactive women who will not have to depend on oocyte donors should they suffer from age-related infertility by the time they are ready to reproduce. Each of these three portrayals has its own shortcomings that one should be wary of, as they lead to an oversimplification of the ethical debate.

The first narrative is probably the furthest away from reality, as the age at which healthy women currently request oocyte cryopreservation indicates that 'postponement' of childbearing is seldom planned at a young age and thus that freezing oocytes is rather an emergency intervention than part of a well designed life plan to 'have it all'. However, also the other two narratives are misrepresentations to a certain extent. Just as it is inaccurate to state that women choose to delay childbearing in order to advance their

careers, it is also inaccurate to say that they have no other option but to delay childbearing due to socio-economic conditions. When people have their children depends on an interplay between contextual factors and personal values and neither one will completely override the other. Finally, the image of smart, proactive women is rather an idealistic picture of who the best candidates would be than an accurate depiction of those who actually come forward.

Chapter 2: Arguments for and against

Despite the original opposition against AGE banking for healthy women, AGE banking has found its way to the clinic rather fast. One reason for this evolution may be that a number of the initial ethical objections to oocyte freezing for so-called ‘social’ or ‘non-medical’ reasons were not very convincing, especially given the contrast with the warm welcome oocyte banking received in the field of oncofertility. The arguments that we should not try to circumvent natural boundaries, solve societal problems with medical solutions or that AGE banking will have a negative impact on society are either flawed or only partially convincing. On the other side of the debate, the argument that we should allow AGE banking to combat gender inequality in terms of the maximal age at childbirth was dismissed, but the argument that women’s reproductive autonomy should be respected, that this technology may not only clinically, but also psychologically benefit patients and that it is inconsistent to support egg donation by others, but not autologous egg donation appear to carry some weight.

How should we freeze healthy women’s eggs?

Chapter 3: AGE banking for better, not for worse

However, even if there are good arguments to bring AGE banking to the clinic, a cautious approach is warranted. The utility of the procedure may be low and women may be overly optimistic about their chances of conceiving after AGE banking. If the only candidates for AGE banking are women whose ovarian reserve is already at a critical threshold, then the utility of this procedure will be very low and women will be buying false hope at a high price. However, if women become more aware of the effect of aging on their fertility, of the possibility to store oocytes in their fertile years (preferably before age 35), of the limits of the procedure (especially when they are already over the age of 35) and of their

personal chances of success, oocyte cryopreservation may be a welcome intervention for women who long to preserve their fertility longer than they naturally could.

Who pays the bill?

Chapter 4: Public funding

Although elective oocyte cryopreservation is being offered by an increasing number of fertility clinics, it is far from clear what its place is – or should be – within systems that offer a number of free IVF cycles. If women who have proactively cryopreserved their oocytes return for treatment at a point when they can no longer conceive naturally and have not reached the maximum age limit for embryo transfer, they should be treated on equal terms as other IVF patients and also receive free treatment. It is less straightforward, however, whether or not the covered cycles should include the first step of the procedure, namely the costs related to ovarian stimulation, oocyte retrieval, oocyte freezing (/vitrification) and storage. Although paying for elective procedures is counterintuitive, there may be good reasons to argue for full coverage from the onset in specific contexts. Alternatively, a cash back system or more free transfer cycles could be considered. The preferred strategy will often depend on local legal and contextual factors.

Chapter 5: Company benefit

Several companies have decided to offer egg banking to their employees. It is however unclear whether this will lead to more or less reproductive autonomy. For these policies to be truly empowering, a substantial number of conditions need to be fulfilled, which can be reduced to three categories. Company-sponsored egg freezing would be liberating if and only if (1) women understand the benefits, risks and – perhaps most importantly amidst the hype – limitations, (2) women feel no pressure to take up the offer (whether or not a woman banks her eggs should thus not have any influence on her career opportunities); (3) the offer has no negative effect on other family-friendly policies and is in fact accompanied by such policies. These conditions should lead to a situation in which (1) (on a personal level) only those women bank their eggs for whom – all things considered – this is their best available option of achieving the life goals that are most important to them personally (which should be very few women) and (2) (on a societal level) women remain free to have their children while they are young, without suffering serious professional setbacks. If companies take these requirements seriously, they will

have to invest a lot of time and effort in fulfilling them and many will argue that they are impossible to fulfil. Thus, regardless of companies' possible good intentions, women's reproductive autonomy is more often than not ill-served by offering them company-sponsored AGE banking.

Egg banker today, egg donor tomorrow?

Chapter 6: Implications of oocyte cryostorage for the practice of oocyte donation

In conclusion, as a side-effect of the ability to freeze oocytes in a safe and effective way, we anticipate that more oocytes will become available for donation from a variety of sources. Oocytes may be frozen for different reasons and as the years pass by, a part of them will remain unused by the woman for whom they were originally stored. It is reasonable to expect that if the option is presented, many of these oocytes will be directed to research and these new kinds of donations will put an end to most – if not all – of the practical hurdles and ethical concerns regarding oocyte donation for research purposes, even the issue of financial reimbursement. Thus, the ongoing ethical debate surrounding 'research donation' may finally be quelled.

Although the effect may be less prominent, there will probably also be a positive effect on the number of oocytes donated to IVF patients. While some particular scenarios require special attention, the donation of spare oocytes for third party reproduction offers more benefits than problems. The most controversial development are the freeze and share arrangements, whereby women who donate oocytes to IVF patients get free storage of half of the retrieved number of eggs for (future) autologous use. If, as a result of the donation of spare oocytes, there is a sufficient increase in donor oocytes to accommodate the present demand, these arrangements are likely to be abandoned again. Nonetheless, in countries where egg sharing between IVF patients is currently allowed, freeze and share agreements – if accompanied by careful counselling – should also be allowed.

Appendix 2: Nederlandstalige samenvatting

Moeten we eicellen van gezonde vrouwen invriezen?

Hoofdstuk 1: De portrettering van gezonde vrouwen die hun eicellen wensen in te banken

De mogelijkheid om eicellen in te vriezen om op een later moment te gebruiken in een IVF-behandeling opent perspectieven voor patiënten die worden geconfronteerd met een ziekte die hun vruchtbaarheid bedreigt of die gonadotoxische behandelingen dienen te ondergaan. Het opent echter evenzeer perspectieven voor vrouwen met een kinderwens die met lede ogen aanzien hoe ze het einde van hun vruchtbare jaren naderen terwijl ze niet in de juiste omstandigheden verkeren om zich aan het ouderschap te wagen (b.v. doordat ze nog geen geschikte levenspartner gevonden hebben). Meningingen voor en tegen deze toepassing zijn vaak gebaseerd op verschillende portrettingen van de vrouwen die er mogelijk beroep op zouden doen. Men kan drie verschillende stereotypen onderscheiden: (1) egoïstische carrièrevrouwen, (2) slachtoffers van een door mannen gedomineerde maatschappij die het moeilijk maakt voor vrouwen om het moederschap te combineren met een degelijke opleiding en/of professionele verantwoordelijkheden, (3) verstandige, proactieve vrouwen die niet zullen moeten vertrouwen op donoreicellen wanneer ze geconfronteerd worden met leeftijdsgerelateerde onvruchtbaarheid op het moment waarop ze kinderen willen. Elk van deze stereotypen heeft tekortkomingen die leiden tot een verarming van het ethisch debat.

Het eerste stereotype is wellicht het verst verwijderd van de werkelijkheid, vermits de leeftijd waarop vrouwen momenteel hun eicellen inbanken aangeeft dat het zelden gaat om een gepland uitstel van de kinderwens op jonge leeftijd. Integendeel, het inbanken van eicellen is eerder een paniecreactie dan een onderdeel van een minutieus uitgedacht plan om 'alles te hebben'. De andere twee stereotypen stroken echter ook niet met de werkelijkheid. Net zoals het inaccuraat is te stellen dat vrouwen het krijgen van kinderen uitstellen om voorrang te geven aan hun carrière, is het ook inaccuraat te stellen dat ze geen andere optie zouden hebben door de socio-economische realiteit waarin ze leven. Het moment waarop mensen kinderen krijgen hangt af van een samenspel tussen verschillende contextuele factoren en persoonlijke waarden. Het beeld van de verstandige, proactieve vrouw is tenslotte een eerder idealistisch beeld van wie de beste

kandidate zou zijn om eicellen in te banken dan een waarheidsgetrouwe afspiegeling van degenen die er momenteel interesse in tonen.

Hoofdstuk 2: Argumenten voor en tegen

Ondanks de aanvankelijke tegenstand tegen het inbankenen van eicellen voor gezonde vrouwen, heeft deze toepassing toch snel de weg naar de kliniek gevonden. Een mogelijke reden voor deze evolutie is dat een aantal van de oorspronkelijke ethische bezwaren die het zogenaamde 'social egg freezing' contrasteerden met het inbankenen van eicellen (wat wel met open armen werd ontvangen) bij nader toezien niet overtuigend zijn gebleken. De argumenten dat we niet mogen ingaan tegen natuurlijke grenzen, dat maatschappelijke problemen niet aangepakt mogen worden met medische interventies of dat het inbankenen van eicellen voor gezonde vrouwen een negatieve impact zou hebben op de maatschappij zijn weinig overtuigend gebleken. Aan de andere zijde van het debat houdt ook het argument dat het inbankenen van eicellen genderongelijkheid tegengaat (in de zin dat de maximumleeftijd waarop mannen en vrouwen kinderen kunnen krijgen dichter bij elkaar zou komen te liggen) weinig steek, maar het argument dat de reproductieve autonomie van vrouwen gerespecteerd dient te worden, dat er niet enkel een klinisch, maar ook een psychologisch voordeel verbonden is aan het inbankenen van eicellen en dat het inconsistent is eiceldonatie aan derden toe te staan, maar niet aan de toekomstige zelf, kunnen niet zo gemakkelijk aan de kant worden geschoven.

Hoe moeten we eicellen van gezonde vrouwen invriezen?

Hoofdstuk 3: Eicellen inbankenen voor de toekomst: baat het niet dan schaadt het niet?

Het feit dat er goede argumenten zijn om het inbankenen van eicellen voor gezonde vrouwen toe te staan, neemt echter niet weg dat er aan bepaalde randvoorwaarden voldaan moet zijn om tot een ethisch verantwoorde klinische praktijk te komen. Het uiteindelijke nut van de procedure is mogelijk laag en vrouwen kunnen hun kansen op een kind na het inbankenen van eicellen overschatten. Als de enige kandidates voor het inbankenen van eicellen vrouwen zijn waarvan de ovariële reserve reeds zeer klein is, dan zal ook de kans op succes zeer klein zijn en kopen vrouwen valse hoop aan een hoge prijs. Als vrouwen in de toekomst echter beter geïnformeerd zouden worden over het effect van veroudering op hun vruchtbaarheid, over de mogelijkheid om eicellen in te banken

tijdens hun vruchtbare jaren (bij voorkeur voor de leeftijd van 35 jaar), over de limieten van de procedure (voornamelijk wanneer ze reeds ouder zijn dan 35) en over hun persoonlijke kans op succes, dan kan het inbankenen van eicellen wel een dankbare interventie zijn voor vrouwen die een noodoplossing zoeken om hun vruchtbaarheid zo lang mogelijk te bewaren.

Wie betaalt de rekening?

Hoofdstuk 4: Publieke gezondheidszorg

Hoewel een toenemend aantal vruchtbaarheidsklinieken het invriezen van eicellen aanbiedt, is het niet duidelijk wat de plaats er van is – of zou moeten zijn – binnen een systeem waarin de ziektekostenverzekering de kosten van verscheidene IVF-cycli op zich neemt. Wanneer vrouwen die eerder proactief eicellen hebben bewaard zich aanmelden voor een IVF-behandeling op het moment waarop ze niet langer vruchtbaar zijn (en nog niet de leeftijdsgrens voor IVF hebben bereikt), dan dienen ze op dezelfde manier behandeld te worden als andere IVF-patiënten en dient de ziektekostenverzekering eveneens de kost van de transfercycli op zich te nemen. Het is echter minder vanzelfsprekend of ook de eerste stap van de procedure, namelijk de kosten verbonden aan de ovariële stimulatie, pick-up, invriezen en bewaren van de eicellen, gedekt zou moeten worden door de gezondheidszorg. Er kunnen zowel voor als tegen dit idee goede argumenten naar voren worden gebracht. Mogelijke alternatieven zijn een cashback-systeem of het aanbieden van extra transfercycli. Lokale wettelijke en contextuele factoren zijn bepalend voor welke aanpak het meest wenselijk is.

Hoofdstuk 5: Bedrijfsvoordeel

Verscheidene bedrijven hebben beslist om het inbankenen van eicellen aan te bieden aan hun werknemers. Het is echter onduidelijk of dit tot meer, dan wel minder reproductieve autonomie zal leiden. Opdat dit aanbod de reproductieve vrijheid werkelijk zou verhogen, moet aan een aantal voorwaarden voldaan zijn. Ten eerste moeten geïnteresseerde werknemers de voordelen, risico's en vooral de beperkingen van de ingreep begrijpen. Ten tweede mogen vrouwen onder geen beding druk ervaren om het aanbod op te nemen (het al dan niet inbankenen van eicellen mag dus geen repercussies hebben voor haar carrièrekansen binnen het bedrijf). Ten derde mag het aanbod geen negatief effect hebben op andere gezinsvriendelijke maatregelen en moet het er zelfs

door geflankeerd worden. Deze voorwaarden zouden moeten leiden tot een situatie waarin (1) (op een persoonlijk vlak) enkel die vrouwen eicellen invriezen waarvoor – alles in beschouwing genomen – dit hun beste beschikbare optie om de levensdoelen te bereiken die voor hen persoonlijk het meest belangrijk zijn (wat in principe zeer weinig vrouwen zouden moeten zijn) en (2) (op een maatschappelijk niveau) vrouwen de vrijheid behouden om kinderen te krijgen op relatief jonge leeftijd zonder daarvan ernstige professionele nadelen te ondervinden. Als het al mogelijk is om aan deze voorwaarden te voldoen, dan zullen ze alleszins grote investeringen vergen van bedrijven. Ongeacht de goede intenties van sommige bedrijven, zal het aanbod om eicellen in te vriezen in de meerderheid van de gevallen geen positieve impact hebben op de reproductieve autonomie van de werkneemsters.

De donoren van morgen

Hoofdstuk 6: Implicaties van het invriezen van eicellen voor de huidige praktijk van eiceldonatie

Als een neveneffect van de mogelijkheid om eicellen op een veilige en efficiënte manier in te vriezen, kan men vermoeden dat er meer eicellen beschikbaar zullen worden voor donatie uit verschillende bronnen. Eicellen kunnen om verschillende redenen worden ingebankt en met het verstrijken van de jaren, zullen een heel aantal ervan niet worden gebruikt door de vrouwen die ze hebben ingevroren. Wanneer deze vrouwen de optie krijgen om hun eicellen te doneren voor wetenschappelijke of reproductieve doeleinden, dan is de kans groot dat velen onder hen hiertoe bereid zullen zijn. Vooral op het gebied van onderzoek zou dit een bron van eicellen zijn zonder de praktische en ethische problemen die vandaag verbonden zijn aan eiceldonatie, met inbegrip van het probleem van de financiële vergoeding.

Hoewel het meest waarschijnlijke scenario is dat minder vrouwen zullen doneren voor reproductie dan voor onderzoek, kunnen we toch ook positief effect verwachten op de beschikbaarheid van donoreicellen voor fertiliteitsbehandelingen. Ook in deze context zijn er minder ethische bezorgdheden verbonden aan de donatie van ‘overgebleven’ eicellen dan aan de huidige praktijk van eiceldonatie. De meest controversiële ontwikkeling zijn de ‘freeze and share’ constructies, waarbij vrouwen die eicellen doneren aan IVF patiënten als tegenprestatie ook de helft van de verkregen eicellen voor eigen gebruik kunnen inbanken. Het is mogelijk dat wanneer binnen enkele jaren ingevroren eicellen beginnen vrijkomen (bv van vrouwen die de wettelijke leeftijdslimiet

voor een IVF-behandeling hebben overschreden), er geen nood meer zal zijn aan 'freeze and share' overeenkomsten. Dit neemt echter niet weg dat er geen reden is om dit soort contracten niet toe te staan in landen waar momenteel ook 'egg sharing' tussen IVF-patiënten wordt toegestaan, hoewel dit steeds in combinatie moet gebeuren met voldoende counseling.

