OOCYTE CRYOPRESERVATION: A SOCIO-DEMOGRAPHIC VIEWPOINT

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Introduction

Fertility trends in rich countries have been dominated by a shift towards later age at childbearing. This *fertility postponement* has been fuelled by multiple factors, in particular by the expansion of university education, massive rise in women's labour participation, higher partnership instability, economic uncertainty and unemployment in young adulthood, as well as a diffusion of values and lifestyles not compatible with parenthood (Sobotka 2010; Mills et al. 2011; Adsera 2005; Lesthaeghe 2010; Goldin 2006; Ní Bhrolcháin and Beaujouan 2012). A spread of efficient contraception, especially the pill and, in most countries, widening access to legal abortion, were of paramount importance in facilitating this shift to later timing of parenthood: many young adults nowadays enjoy prolonged period of sexual relations without much fear of unintended pregnancy (Goldin and Katz 2002). Mean age of mothers at first birth has reached 28-30 years in most European countries; in Spain and Switzerland it has already surpassed this threshold (VID 2012).

The rising age at childbearing has accentuated a conflict between biological and health rationale to have children at young reproductive ages and the economic and social rationale, which makes it advantageous for most couples to have children much later in life (Sobotka 2010; Schmidt et al. 2012). Specifically, late parenthood has been associated with numerous advantages for the parents (and some for their children), including lower income loss and less severe career interruption for mothers (Miller 2009), more stable partnerships (Sobotka 2010), better financial and housing situation, a stronger sense of "being ready" for parenthood (Mills et al. 2011), and even higher happiness level among the parents (Myrskylä and Margolis 2012). But the *postponement transition* (Kohler et al. 2002) cannot continue indefinitely: many more women than in the past have postponed family formation past age 35 when rising infertility may endanger the realisation of their plans to have children (Leridon 2008; te Velde et al. 2012).

On this background, assisted reproduction (ART) can be expected to play an increasing role for couples in higher reproductive ages. New reproductive technologies may help women with poor oocyte quality achieving a pregnancy. Whereas in vitro fertilisation using fresh oocytes has shown low success rates among women at higher reproductive ages (Stolwijk et al. 2000; Leridon 2004; Leridon and Slama 2008, Sullivan et al. 2008; CDC 2012a) oocyte cryopreservation (or "egg freezing") for non-medical reasons appears to be particularly promising and it may partly erode the boundaries of reproductive age. As N. Hass (2011) noted in the *Vogue*, "stopping the biological clock through egg freezing has long been the ultimate feminist fantasy." Media and general public have shown enthusiasm and interest in

this rapidly developing technology: Google search of the term “egg freezing” gave 431,000 hits as of December 2012.

This paper discusses the potential role of oocyte cryopreservation (OC) from a socio-demographic viewpoint. I focus on its non-medical or “social” aspect linked to its potential to fulfil fertility plans among the couples who plan to have children later in life. I leave aside the discussion on oocyte cryopreservation for patients with cancer and other medical conditions, including premature menopause, where the OC use is clearly justified and does not raise any ethical issues (Dondorp and Wert 2009).

The paper is structured as follows. Next section gives summarises major trends in the long-term increase of the number women who chose to have children at advanced reproductive ages. Then I analyse the potential demand for oocyte cryopreservation for non-medical reasons, looking at both the number of women who might eventually use IVF treatment with OC as well as the number of women who may consider OC as a precautionary “safety measure” when deciding for later childbearing. Thereafter I discuss the limitations and drawbacks of OC that will limit its use well below its estimated potential. Final section provides concluding discussion on short-term and long-term prospects on social oocyte cryopreservation.

The rising importance of childbearing at late reproductive ages: intentions, birth rates, and use of assisted reproduction

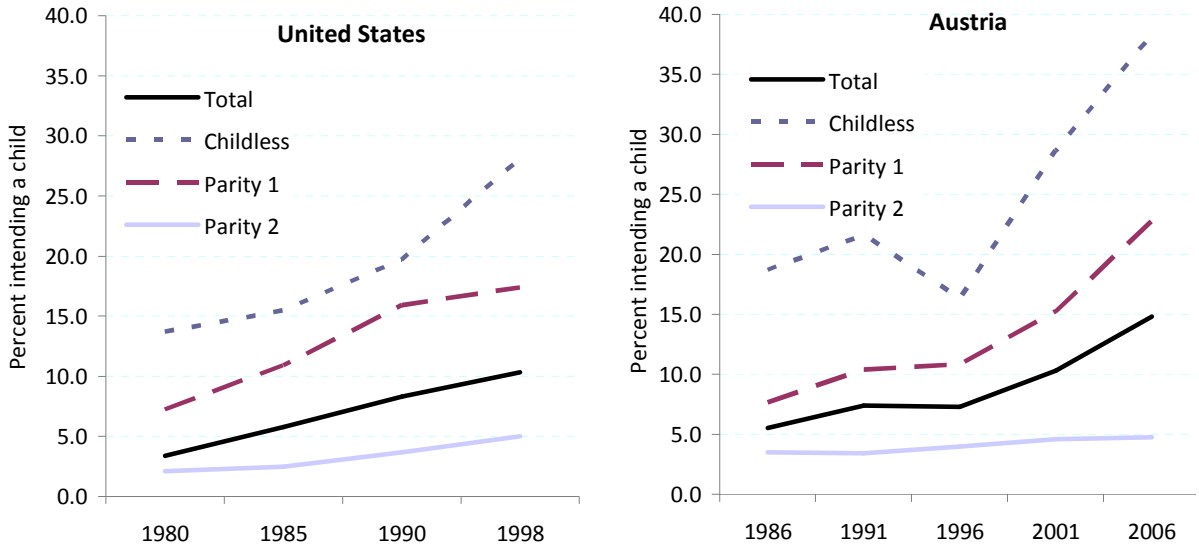
Many different indicators clearly show that childbearing has been on the rise among women past age 35, in particular among those still remaining childless or having only one child, and among the group with university education (e.g., Sobotka 2010, Lappegård and Rønsen 2005). After about a century of declining childbearing rates at higher ages, accompanying the shift to a small family size, birth rates at advanced reproductive ages reached a trough and then started rising steadily across most rich countries during the 1980s-1990s. This reversal has been studied in detail for women aged 40 and older and has also been documented for women at ‘extreme’ childbearing ages of 50 and older (Sobotka et al. 2007; Billari et al. 2007). This study uses selected data for eight rich countries with diverse social policies and institutional backgrounds (Austria, the Czech Republic, the Netherlands, Spain, Sweden, Japan, and the United States) to illustrate trends in childbearing intentions, birth rates and rates of assisted reproduction at ages 35 and older.

Childbearing intentions among women past age 35

There are rich sets of period and cohort data on birth rates by age and other characteristics of the mother. However, considerably less comprehensive evidence exists about reproductive plans of women and men. Typically, surveys of reproductive intentions are not carried out regularly and they often rely on different questions about short-term (next 1-4 years) and ‘lifetime’ reproductive plans that are not compatible between countries. I provide an illustration for Austria and the United States, where repeated surveys asked identical questions about future childbearing intentions among women of reproductive age. These data reveal parallel trends in both countries (Figure 1). At age 35-39, when infertility and sterility start increasing rapidly, an ever higher share of women indicate they intend to have a child in the future. In the United States, their share has tripled from 3% to 10% between 1980 and 1998, while in Austria their share almost tripled from 6% to 15% between 1986 and 2006 (excluding uncertain respondents). There are sharp and rising differences in intending a birth

at later reproductive ages among women of different parities; among the childless, the declared intentions rose particularly steeply, reaching 28% in the U.S. in 1998 and even 38% in Austria in 2006. Only a few women with two children intend to have another one—a clear indication of a strong orientation towards a two-child family. At the same time, the share of women who are still childless in their late 30s has also risen continually. For instance, in Spain only one out of ten women born in 1945 was childless when reaching age 35; this share then climbed rapidly for the women born in the 1950s and 1960s and reached over one third for the cohort born in 1973.

Figure 1: Percentage of women aged 35-39 who intend to have another child in the future: United States (1980-1998) and Austria (1986-2006)



Sources: United States: Current Population Survey (published in Hagewen and Morgan 2005, Table 1); Austria: Microcensus survey, author's computations. Graph excludes responses of uncertain respondents (see also Sobotka 2009).

Trends in birth rates at ages above 35

For numerous reasons, only a fraction of reproductive intentions get realised; frequent changes in reproductive intentions have been observed across the life course (Quesnel-Vallée and Morgan 2003; Liefbroer 2009). At higher reproductive ages, the reasons for non-realisation of childbearing plans include infertility, poor health, difficult employment and economic circumstances, partnership dissolution, partner's disagreement, not having a right partner, inadequate housing, as well as competing careers and incompatible lifestyles (Leridon 2008; Régnier-Loilier and Vignoli 2011; Rosina and Testa 2009; Philipov et al. 2009; NIPSSR 2011). In addition, considerable number of respondents express uncertainty about their desires and intentions or state that they are fine with both possible outcomes, having or not having another child (McQuillan et al. 2011; Ní Bhrolcháin and Beaujouan 2011).

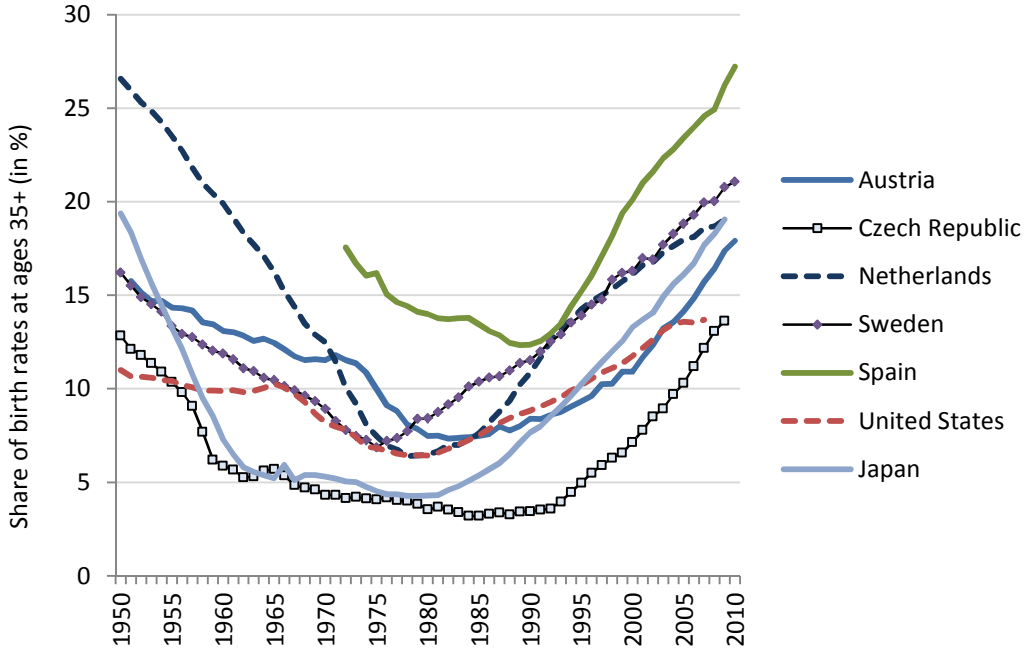
Although childbearing intentions change, trends in birth rates at advanced reproductive ages point at the same direction. Sharp increase has been recorded in births rates above age 35, in particular among the childless women. Some of the key trends are summarised for selected European countries, United States and Japan in Figure 2. Between 1950 and 2010, a U-shaped pattern in the share of birth rates at ages above 35 is visible in most countries, with a lowest share reached in the late 1970s and 1980s (Figure 2a). Since then the share of birth rates realised at higher reproductive ages has doubled in Austria, Spain and the United States,

trebled in the Netherlands, Sweden and Japan and quadrupled in the Czech Republic. In Spain, birth rates of women aged 35+ account for more than a quarter of the total fertility rate since 2009, in the other analysed countries it reached between 14% (the Czech Republic) and 21% (Sweden). Yet sharper relative rise in childbearing at higher reproductive ages has been observed for first birth rates. In the past, "late" childbearing has been typical of women having larger families, whereas recently it has increasingly become characteristic of women who have delayed their first or second birth (Sobotka et al. 2007). Consequently, the share of first birth rates at later ages has risen by a factor of 4-6 since reaching the minimum in the 1970s-1980s; this rise has been particularly steep in Spain where almost one out of five first births now occurs at ages 35+ (Figure 2b). Sharp increases have also taken place among women approaching the menopause. At ages 45+, childbearing still remains relatively rare; in most countries there is less than one first birth per thousand women at these ages. Although very low, these birth rates have risen exceptionally fast, especially in Austria, Sweden, and the United States where they jumped by a factor of 10 or more between the mid-1980s and 2007-2010 (Figure 2c). This trend has been in part driven by increasing frequency of ART using oocyte donation (see also below).

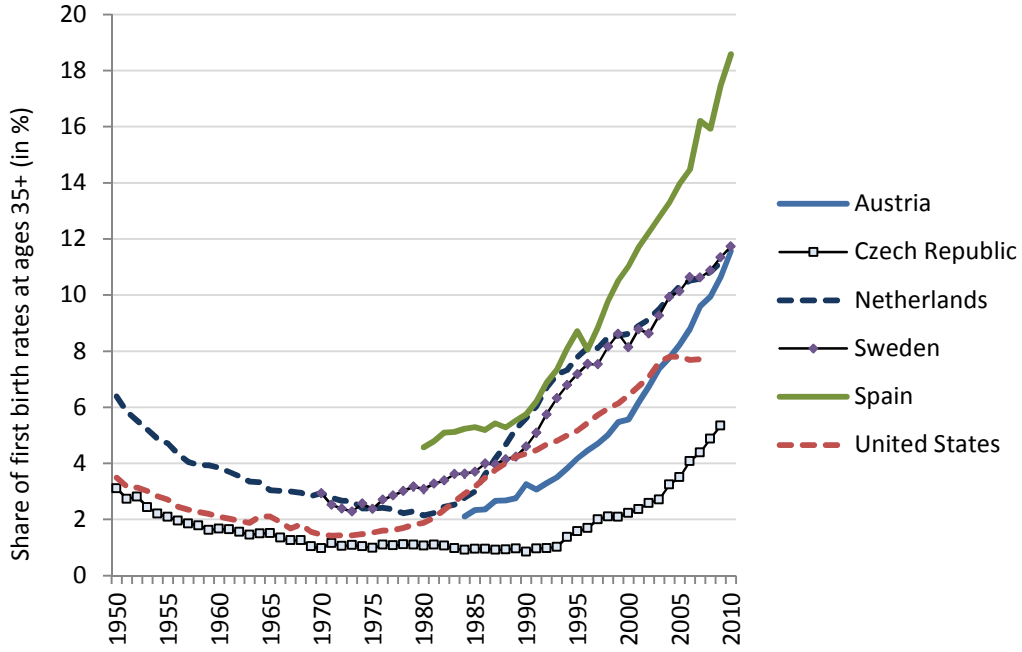
Figure 2d further highlights the rising likelihood of first births at advanced reproductive ages. In the early 1980s a woman still childless at age 35 typically had a likelihood of 10-15% that she would become a mother before reaching the end of her reproductive period (measured either at age 50 or 55, depending on data availability). Most recently, in 2007-10 this likelihood has risen in five analysed countries to a range from around 30% (Austria, Czech Republic) up to 45-47% (Spain, Sweden). In addition to that, the share of women remaining childless into their mid- to late- 30s also increased rapidly. This shift has been most pronounced among women with university education, who need many years to complete their studies and to get a foothold on the labour market (Lappegård and Rønsen 2005, Martin 2000, Ekert-Jaffé et al. 2002, Rendall et al. 2005).

Figure 2: Selected indicators of birth rates and first birth rates among women aged 35+ in five European countries, United States and Japan

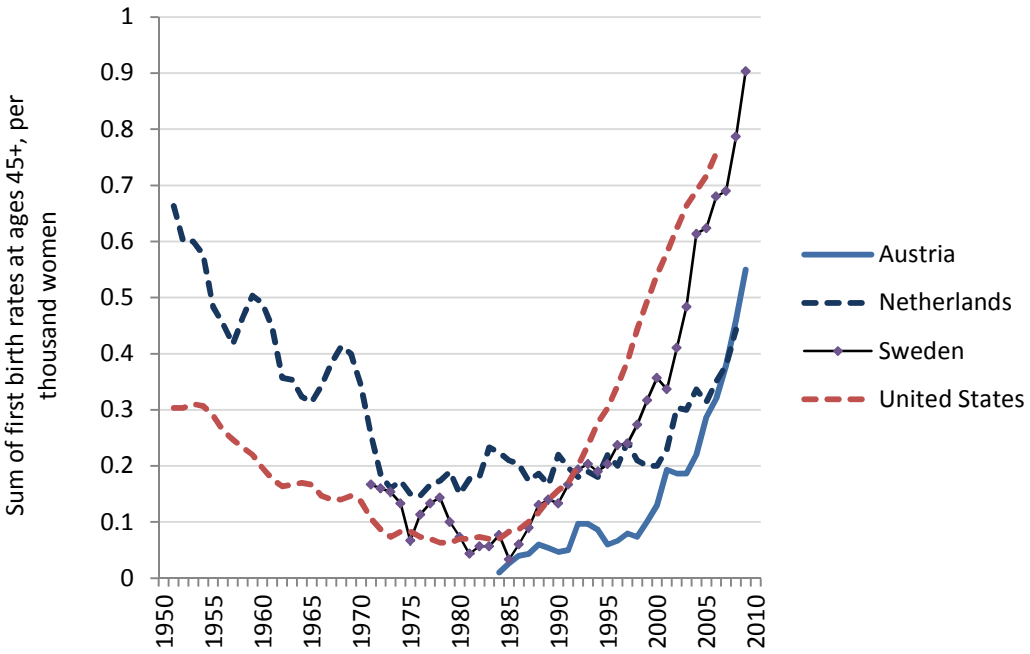
a. Share of birth rates among women aged 35+ on the total fertility rate, in %, 1950-2010



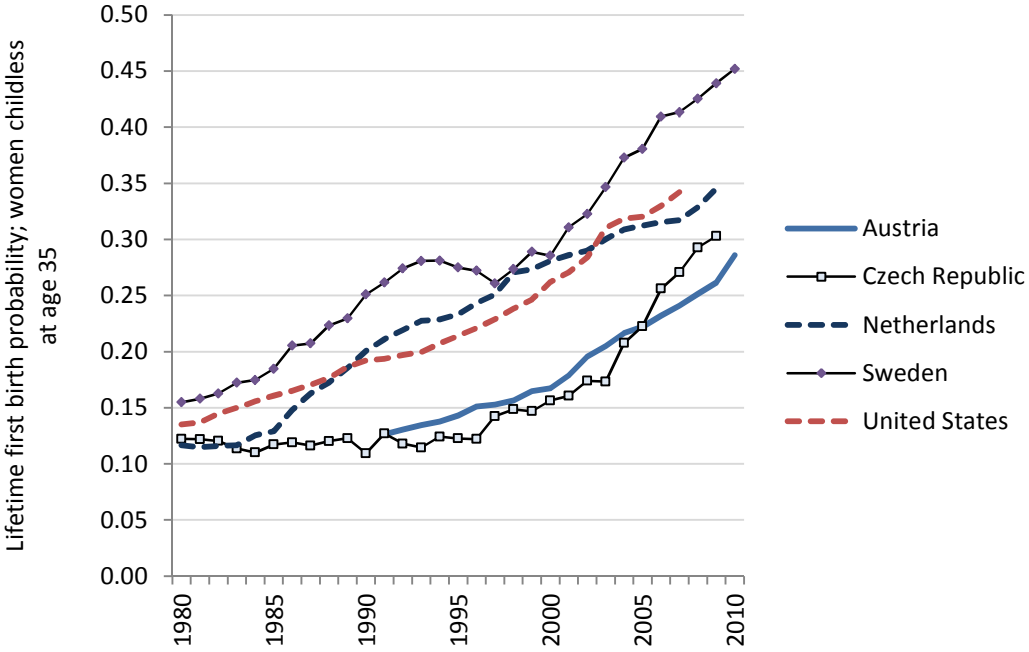
b. Share of first birth rates among women aged 35+ on the total fertility rate for first births, in %, 1950-2010



c. Sum of first birth rates at ages 45+, per thousand women (smoothed, using 3-year moving averages), 1950-2010



d. Lifetime probability of giving birth to a first child among women still childless when reaching age 35, 1980-2010



Sources: All countries except Spain: Computations based on the Human Fertility Database (2012). Spain: Computations based on Eurostat (2011) and INE (2012).

Infertility, sterility and ART use at advanced reproductive ages

As ever higher share of births has been shifted into ages when infertility becomes common many women have to make considerable effort to become pregnant and to get a desired child. Many studies have demonstrated that infertility, sterility, the frequency of miscarriages, and pregnancy complications increase gradually among women around age 35 and then skyrocket at ages above 40. Leridon (2008) estimated that by age 40 almost 17% of women are permanently sterile (unable to conceive), while as many as 35% of women will remain childless if starting their pregnancy effort at that age. Different measures based on the National Survey of Family Growth carried out regularly in the United States further illustrate the extent of infertility at ages 35+. In 2006-10 a quarter of currently married childless women aged 35-39 and 30% of those aged 40-44 have been estimated as infertile (CDC 2012b). Almost a quarter of married childless women aged 40-44 have ever received any infertility service, including advice, tests, ovulation drugs, or artificial insemination. The share of married childless women with *impaired fecundity* (this includes inability or difficulty of getting pregnant or of carrying pregnancy to term) reached 39% at age 35-39 and 47% at age 40-44. This statistics also suggests that rapidly rising birth rates at ages 35+ mask an equally impressive rise in the number of women and couples who cannot get pregnant at those ages and who may potentially seek infertility treatment. These couples also have considerable potential demand for oocyte cryopreservation (see below).

Some evidence on the rising demand for infertility treatment linked to postponed childbearing is provided by the available reports on ART use at higher reproductive ages. Age 40 can be seen as a boundary where the IVF treatments using women's own oocytes show low success rates due to a combination of a low pregnancy rate cycle as well as a high rate of pregnancy loss, especially due to miscarriage. In the United States only 20% of ART cycles at age 41-42

using non-donor eggs in 2009 resulted in pregnancy and 12% resulted in live birth (CDC 2012a). In effect, ART use at advanced reproductive ages can be very costly when costs are measured per successful delivery or live birth (Sullivan et al. 2008). In Europe, ART use above age 40 depends in part on legislation regulating access to ART and its reimbursement (ESHRE 2008). Nevertheless, both number of ART cycles initiated to women aged 40+ and live births to these women have had a rising tendency. Given low success rates of assisted reproduction at higher ages with fresh non-donor oocytes, the use of donor oocytes (OD) has become common among women of advanced reproductive ages. Remarkably stable success rates of ART using OD with age imply that this technique has also been used among women past the usual age of menopause (e.g., Grossman et al. 2012), shifting the limits of childbearing age and leading to a rapid rise in the number of births among women aged 50+, although from very low initial values (Sobotka et al 2007, Billari et al. 2007, Salihu et al. 2003).

To illustrate the rising relevance of ART at late reproductive ages I review ART trends among women past age 40 in Spain and the United States. Comparability of these data across countries and over time is hindered by a number of factors: lack of comprehensive data collection and reporting, incomplete coverage of ART cycles and, yet more common, of ART pregnancies, live births and deliveries. Furthermore, age-specific data on ART treatments are often not published or different age categories are used in different countries and for different types of ART. Moreover, the data from the national registers are affected by *reproductive tourism*: they frequently also include women from other countries receiving treatment in national ART clinics, while they exclude treatments their residents receive abroad. Therefore, the data below should be taken as rough illustrations of general trends. In Spain, the number of ART treatments among women aged 40+ skyrocketed between 2002 and 2006, when the number of OD cycles exceeded the use of IVF/ICSI with non-donor fresh oocytes (Figure 3a). The total number of all registered treatments at high reproductive ages, including intrauterine insemination, more than doubled from 5.0 thousand in 2002 to 11.4 thousand in 2010 (this can be compared with 24.5 thousand births to women aged 40+). The estimated number of live births following ART treatment, adjusted for pregnancies that were lost to observation, more than tripled from about 850 in 2002 to around 2,900 in 2010; this fast rise reflects in part an increasing rate of deliveries per ART cycle, achieved especially by a higher use of donor oocytes (Figure 3b). When these numbers of ART births are related to all births among Spanish mothers aged 40 and older, ART turns out to have a sizeable contribution. One out of eight births and one out of five first births at advanced reproductive ages in Spain could be attributed to ART, especially to the use of donor oocytes (assuming that first births make up 60% of all ART births).

Figure 3a: Estimated number of ART cycles in Spain among women aged 40+

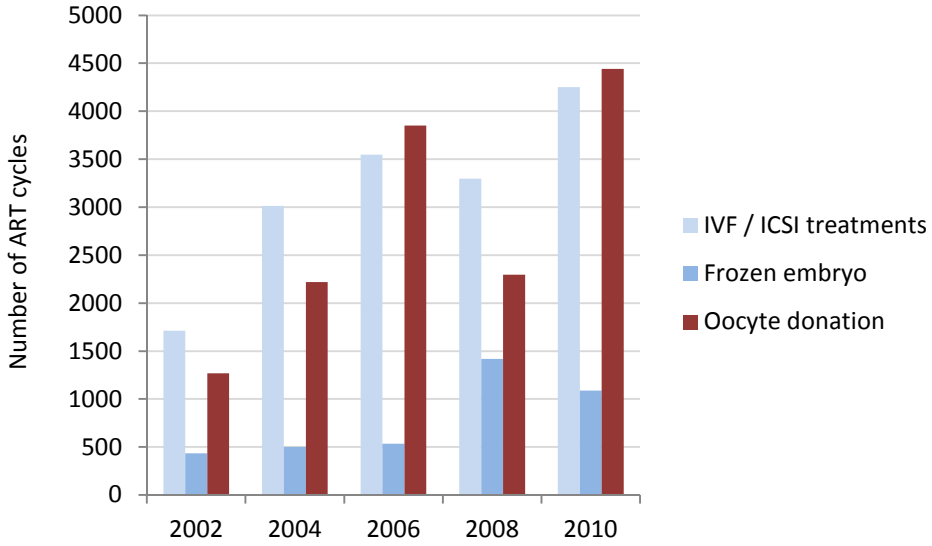
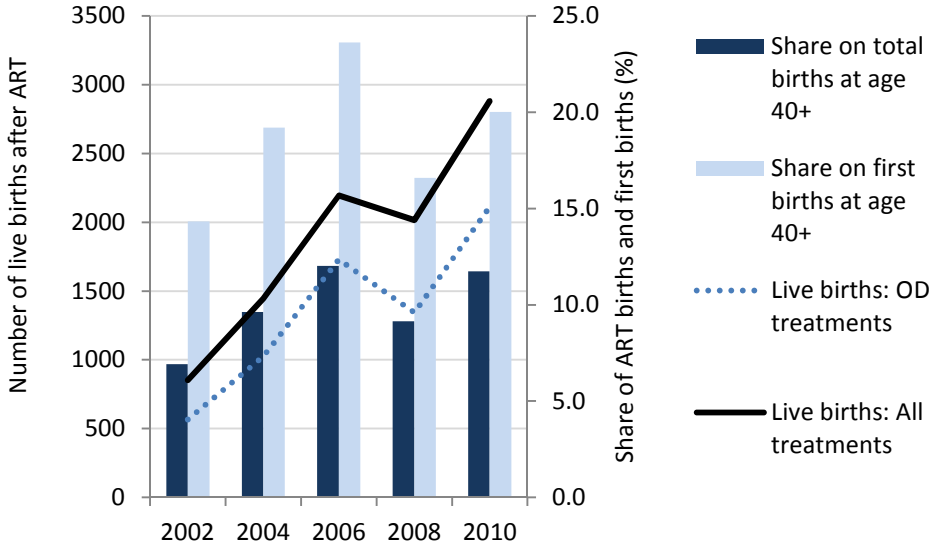


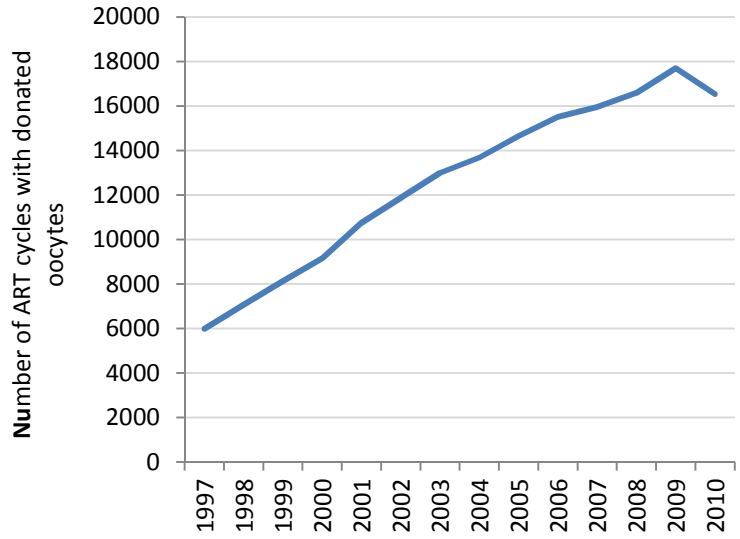
Figure 3b: Estimated number of births resulting from ART and the share of ART births on total and first births; Spanish mothers aged 40+



Sources: Computations and estimates based on Registro SEF reports for the years 2002, 2004, 2006, 2008 and 2010, ESHRE 2012, Eurostat (2011) and INE (2012)

Similar trends have been observed in the United States, where comparable time series of ART data are assembled by the Centers for Disease Control and Prevention (CDC 2012a). Between 1997 and 2009 the number of ART cycles using donor oocytes tripled to 17.7 thousand thousand, before falling in 2010, possibly as a part of a general slight decline in ART during economic recession. Donor oocytes in the U.S. are used predominantly at advanced reproductive ages when many women have no viable oocytes left. After age 45, ART-OD represents a large majority of ART cycles in the United States (CDC 2012a, Figure 46). Table 1 compares ART use and ART live births in 1997 and 2009 in the United States at advanced reproductive ages (41 years and older except for donor oocytes where all cycles are included). Over this period, the overall number of ART cycles to women aged 41+ rose from 13.4 to 36.3 thousand and the estimated number of ART births in this category reached 9.3 thousand. This represented one out of nine births and three out of ten first births to women at ages above 40.

Figure 4: Number of ART cycles using donor oocytes in the United States, 1997-2010 (women of all ages)



Sources: CDC 2012c, national summaries for years 1997-2010 available at http://apps.nccd.cdc.gov/art/Apps/NationalSummaryReport.aspx

Table 1: ART use and ART births in the United States among women aged 41+, 1997 and 2009[3]

	Cycles & treatments at ages 41+		Estimated live births resulting from ART	
	1997	2009	1997	2009
IVF + ICSI	6691	16090	762	1737
Frozen embryos (FE)	774	2561	140	569
Donor oocytes (OD, all ages)	5980	17697	3307	6994
Total	13445	36348	4209	9300
Estimated share on total live births at ages 41+ (%)			8	11
Estimated share on first births at ages 41+ (%)			22	30

Sources: Computations and estimates based on CDC 2012a, 2012b, Human Fertility Database 2012 (data on live births in 1997) and NCHS 2011.
Note: Share of ART births on total first births at ages 41+ is estimated assuming that 60% of ART births at those ages are first births. Note that no separate statistics by age is published on the use of donor oocytes; therefore, all OD treatments are included in the table.

"Social egg freezing": Potential demand and use

Delayed childbearing implies considerable risk of infertility and involuntary childlessness (te Velde et al. 2012), which can only partly be offset by the IVF using non-donor oocytes (Leridon 2004; Habbema et al. 2009). In this context, oocyte cryopreservation appears to be a potential "win-win" strategy, which could expand women's reproductive lives without presenting them with stark choices between ineffective natural reproduction, IVF/ICSI treatment with own oocytes, ART with donor oocytes, or adopting a child. Unlike biological reproduction and IVF treatment with non-donor oocytes, oocytes preserved early in life—ideally before age 30—and then used at advanced reproductive ages are likely to offer high success rates similar to those for donor oocytes. As of now, OC is still in an early phase to

allow a serious analysis of its use. Rather, I estimate its hypothetical use under ideal conditions and then provide a critical appraisal of different forces that will limit its use and potential.

Under ideal (and purely hypothetical) conditions social OC would offer a smooth procedure with high success rates, would be widely available at little or no cost to the users (e.g., as a part of health insurance coverage), would raise few ethical objections, and would be widely accepted by the public. If such conditions are fulfilled, how many women should be "storing their eggs" for the future? How many women would eventually use IVF with their cryopreserved oocytes? This thought exercise allows estimating the potential limits of OC use. For that purpose, I work with the data on birth rates and ART treatments in Spain, which has progressed far in the transition to late parenthood and currently has, alongside Switzerland, the highest age at first birth globally (VID 2012, Schmidt et al. 2012).

First I estimate the potential IVF use with cryopreserved oocytes, assuming that all women who need to undergo assisted reproduction have enlisted in OC earlier in life. Next, I provide estimates of the number of women who might consider OC as a safety strategy because their plan to have children later in life puts them at a high risk of impaired fecundity. To estimate the potential of OC use I present a series of alternative scenarios based on different thresholds for its use, starting from the most restrictive definition (IVF with OC use replacing only the ART with donor oocytes among women past age 40) up to the widest definition, including all women considering having first birth after age 35 or any birth after age 40 (Table 2). These different scenarios give a wide range of numerical estimates of the share of women who might chose OC and who might eventually use IVF with their preserved oocytes.[1]

If all women planning to have a child later in life had "stored" their oocytes at younger ages, how many may actually use them for assisted reproduction? If we start from the narrowest and most obvious option—an IVF with women's own cryopreserved oocytes replacing the use of donor oocytes at ages 40+—the share would amount to 0.7% in each birth cohort. If all ART treatments (including artificial insemination which also has a very low success rate at ages 40+) were replaced by IVF using OC, 1.4% women would make use of the procedure. If all childless women who ever try getting pregnant after age 40 would use it, their share would amount to 0.8-2.4%, depending on whether only those definitely sterile would turn to IVF, or also those with infertility or impaired fecundity. Including all women who are trying to get

[1] These scenarios combine diverse demographic and biomedical data. Birth rates and first birth rates by single years of age among women aged 35 and older are based on the data for Spain in 2010 (own computations from the data of INE 2012 and EUROSTAT 2011). Recent ART use by age and by ART method as well as the estimates of the number of ART births by age are computed from registered data for Spain in 2008 and adjusted for pregnancies lost to observation (computations based on Registro SEF report for 2008 and ESHRE 2012; see also Figures 3a and 3b). The estimated share of women intending to have children after ages 35 and 40 is estimated separately by parity and is based on Austrian data (the 2006 *Microcensus* survey analysed in Figure 1). The estimates of permanent sterility (inability to conceive) by single year of age are based on Leridon (2008, Table 2). Data on infertility and impaired fecundity (which includes difficulties in carrying pregnancy to term) by age (5-year age groups) are based on a sample of married childless US women surveyed in 2002-2006 in the National Survey of Family Growth (CDC 2012b). A number of additional assumptions have been applied in these scenarios, including the split of ART births into first births and higher-order births; 65% of ART births at ages 35-39 and 60% of ART births at ages 40+ are assumed to be first births. Additional assumptions have also been made about the number of women ever undergoing ART treatment after age 40, as this figure cannot be directly estimated from the statistics on total treatments (ART cycles) or on the number of successful treatments (deliveries, live births). Further details about the OC use scenarios and the underlying data and assumptions can be provided by the author upon request.

pregnant (also those who already have a child), the share would range from 2.7% to 3.7%. Finally, including also childless women aged 35-39 who are infertile or assuming that the trend of postponing childbearing will further continue provides the highest share of women who may eventually use IVF with OC, between 4.0% and 7.6% in each cohort.

To achieve any of these rates of IVF-OC use, women would first need to use the option of oocyte cryopreservation at younger ages. How many women might potentially consider using the technology? Again, I present a range of scenarios depending on whether this "hedging strategy" is used only by childless women or by all who plan to have a child, whether the age threshold is 35 or 40, and also depending on different estimates of pregnancy attempts and reproductive intentions later in life. When only childless women past age 40 are included, the potential demand for oocyte cryopreservation reaches from 2.4% to 4.5% with current age-specific first birth rates in Spain and 3.7%-7.5% if parenthood is further shifted to later ages. If all women attempting to become pregnant after age 40 are included, the potential demand for OC reaches between 7.8% and 11.6% with current birth rates and 11.7%-12.5% with additional shifts in childbearing age ("shifting age model" in Table 3). Finally, if also all women planning to become mothers after age 35 are included, the share of potential OC users skyrockets to 16.6%-22.8% in each cohort and 20.8%-28.2% if additional shifts in childbearing age take place.

Table 2: Percentage of women who would use IVF with own cryopreserved oocytes according to different scenarios

Model / assumption	**Share of the female birth cohort (%)**	
	Current pattern	**Shifting age model (+50%)**
1. Replacement of donor oocytes	0.67	..
2. Replacement of all other ART treatments after age 40	1.37	..
3. All women who intend to have a child and cannot conceive / carry pregnancy to term after age 39		
Childless women:		
Sterility model	0.83	1.24
Infertility model	1.12	1.68
Impaired fecundity model	2.37	3.55
All women:		
Sterility model	2.68	4.03
Infertility model	3.66	5.48
Infertility model, including childless women after age 35	5.04	7.56

Table 3: Percentage of women who might consider oocyte cryopreservation as a back-up option (women potentially at risk of impaired fecundity due to postponed childbearing)

Model / assumption	Share of the female birth cohort, in %	
	Current pattern	Shifting age model
1. Childless women aiming to get pregnant after age 40		
Observed birth rates model	2.4-3.5	3.7-5.2
Intention-based model	4.5	7.5
2. All women aiming to get pregnant after age 40		
Observed birth rates model	7.8-8.3	11.7-12.5
Intention-based model	11.6	..
3. Childless women aiming to get pregnant after age 35 and all women aiming to get pregnant after age 40		
Observed birth rates model	16.6-23.9	20.8-29.9
Intention-based model	22.8	28.2

Notes and data sources for tables 2 and 3: See footnote 1 for methods, assumptions and data sources.

The "real world": forces that will limit the expansion of oocyte cryopreservation

The scenarios presented in the previous section are hypothetical estimates based on the assumption that all women fulfilling a given set of conditions would opt for an OC at younger ages or would later use IVF with OC when facing infertility at advanced reproductive ages. This exercise should be seen as mapping the potential use of the new technology (or, defining the potential set of "consumers"), while in reality a number of factors will limit the actual use of OC to considerably lower levels. At present, the OC is too recent to appreciate its risks, costs, effectiveness, acceptance, and advantages and this discussion will rather give an overview of different factors affecting its future use rather than a more precise quantitative estimate on the impact of each individual force.

Uncertainty about long-term success rates, potential pregnancy complications, and health risks for mother and child. While OC has been spreading rapidly in the last years and the number of births resulting from the transfer of cryopreserved oocytes has risen exponentially (Noyes et al. 2009), it will take another decade or so before sufficient amount of data accumulates to study long-term success rates of IVF-OC for long periods of time and identify all the potential pregnancy complications and health risks for mothers and their children. As IVF using OC is still in its "experimental" phase (although this has been debated, see Noyes et al. 2010), there are many reasons to be careful about embracing or recommending its use for social reasons (Dondorp and Wert 2009).

Costs. Choosing an OC and, eventually, using it in order to achieve pregnancy later in life is a costly strategy, involving payment for oocyte retrieval, regular payments for storing the oocytes and, eventually, also all the costs of IVF treatments. Cost assessment is tricky and two studies using widely different assumptions arrived at diverging cost estimates, putting a price tag of one live-born child after IVF-OC at 24,600 US Dollars (van Loendersloot et al. 2011) vs. 135,520 US Dollars (Hirshfeld-Cytron et al. 2012a; see also the discussion in Hirshfeld-Cytron et al. 2012b). The main difference between these studies was that the model users in Hirshfeld-Cytron et al. 2012a tried first to achieve natural conception before turning

to IVF, while the model users in van Loendersloot et al. 2011 were first pursuing an IVF use, before eventually attempting to achieve natural pregnancy. The potential OC users should weight these high costs against the likelihood that they may achieve spontaneous pregnancy or that the ART use may not result in the delivery of live birth. The spread of OC will also depend on who will be paying most of the costs of OC for social reasons. If governments or health insurance companies were to subsidise the technology, the annual costs may reach hundreds of millions EUR in a country such as Spain.

Success not guaranteed. As is the case of any ART treatment, the success of OC is far from being guaranteed. Research so far suggests IVF-OC success rates comparable to IVF using fresh oocytes (Dondorp et al. 2012). Among older women, its success rate in terms of the number of live-birth deliveries per one IVF cycle might eventually approach success rates of ART with donor oocytes (there are not yet enough data to support this conjecture). In the model by van Loendersloot et al. 2011, IVF-OC users aged 40 achieve a cumulative live birth rate of 73.7% after four cycles of IVF with frozen and then thawed oocytes and another 10.7% through natural conception following unsuccessful IVF. Even this high success rate implies that one out of six women postponing childbearing until age 40 would never achieve live birth despite putting considerable effort (and money) into preserving their oocytes.

Stress surrounding OC and IVF. Oocyte retrieval and IVF treatments, especially when repeated or unsuccessful are stressful experiences, physically and psychologically taxing. Many women may prefer avoiding such experience.

Early decision necessary for successful outcome planned much later in life. To achieve highest success rate with IVF using oocyte cryopreservation the oocytes should be collected relatively early in life, preferably until age 30, as ART cycles performed with more mature oocytes display a gradual decline in success rates with age (e.g., CDC 2012a, Figure 47). This implies that women should make a decision to preserve their oocytes at an age when they are often uncertain about their reproductive plans or when their future plans seem to be too distant to act on them and commit considerable resources into OC. Many women will tend, in economic terminology, to “discount the future”, and to ignore the future threat of infertility and involuntary childlessness in a similar way as young smokers often ignore the abstract threat of getting cancer later in life. Moreover, many women are not well aware of the pace of age-related increase of infertility (Mac Dougall et al. 2012). Women may also not be able to envision their partnership, career and health later in life, risking that they will make use of their preserved oocytes if they face unforeseen and difficult life circumstances.

Acceptance. As any other advanced medical technology related to reproduction, oocyte cryopreservation may not be universally accepted for religious, ethical, cultural and other reasons, or simply because of fear of possible side effects or of trying an unfamiliar procedure. An online survey of Belgian respondents aged 21-40 found only a low proportion (3.1%) declaring they would consider freezing oocytes for social reasons, with a much higher share (28.4%) responding “maybe” and more than a half saying “no” (Stoop et al. 2011). This rather low acceptance may change, however, as the new OC technology matures, spreads, becomes more effective and more familiar to wider public.

Ethical concerns. A number of ethical concerns regarding OC for social reasons can be voiced. One is potentially unequal access. Due to high costs involved in OC, women with lower income and disadvantaged social background may not be able to cover the costs necessary for OC and, eventually, IVF using OC. Second are possible risks from having

children late in life. While using IVF with OC may limit some of the risks of late motherhood associated with natural reproduction or with the IVF using fresh non-donor oocytes, some risks remain and need to be better monitored. Older mothers are likely to have children with older fathers and higher paternal age (>40) has been associated with pregnancy complications and selected adverse outcomes in children (Sartorius and Nieschlag 2009). Very old parents (>50) may also have physical difficulties in coping with childrearing demands and risk experiencing poor health, cognitive decline and other age-related adverse outcomes well before their children reach adulthood. However, no consistent evidence exists on the adverse outcomes of very late parenthood on psychological and physical outcomes and wellbeing of children (e.g., Schmidt et al. 2012). Third concern pertains to the possible effect of OC on fuelling further postponement of childbearing and contributing to infertility and childlessness. Many women erroneously believe that ART is highly effective in giving women a chance of achieving pregnancy at late reproductive (or even post-reproductive) ages (Maheshwari et al. 2008, Wyndham et al. 2012). The same misperception may be stimulated by a spread of oocyte cryopreservation: many women will falsely believe that the new technology will allow them to have child at any age. This believe may lead to an additional shift in childbearing age, both among the women choosing OC as well as among other women not making an advantage of this new technology.

Discussion and conclusions

As the length of human life has continually expanded during the last century (Oeppen and Vaupel 2002) and many markers of the life course such as finishing studies, entering labour market, or starting a family have been delayed (Lee and Goldstein 2003), the boundaries of reproductive age, marked by menopause, remained remarkably stable. Many couples have to seek a careful balance between economic, cultural, and social rationale of having children later in life and a biological rationale of reproducing at younger ages. Remarkable percentage of childless women in their late 30s still intend to have a child later in life and many will not be able to achieve this goal via natural conception.

Will “social egg freezing” revolutionise assisted reproduction and blur the boundaries of reproductive span? Will *eggsurance* become a routine exercise and motherhood beyond age 50 an accepted matter of choice, just another lifestyle on offer in the post-modern variety of living arrangements and family relations? Only the future will tell. For now, oocyte cryopreservation represents a rapidly evolving technology with considerable potential, but also many practical and ethical repercussions. It may soon move from an “experimental” stage to a fully recognised ART option (Noyes et al. 2010). On the positive side, women and couples who are in difficult life situation or are not simply ready to have children in their thirties may choose a “safe strategy” of preserving their oocytes for a possible use later in life. This should give them some extra “breathing space” (Dondorp et al. 2012). This strategy is likely to yield high success rate and, for the first time, offer women at ages above 40 with impaired fecundity, a high chance of having a child of their own, rather than deciding between involuntary childlessness, ART use with donor oocytes, and an adoption. In addition, oocyte cryopreservation is less objectionable practice for the Catholic Church than embryo cryopreservation, which may lead to its faster adoption in some countries, especially when they enacted legal restrictions on embryo cryopreservation, as was the case in Italy (Noyes et al. 2010).

On the negative side, OC requires considerable resources, its long-term success rates and potential negative effects are still unknown, and there are many psychological and practical

barriers to its use. Most of all, if oocyte cryopreservation is to become successful and relatively common, many women would have to make an important decision to "freeze and store their eggs" early in life, without knowing whether they will eventually make any use of their preserved oocytes at higher ages, whether they will still intend to have children, whether they will still be able to get naturally pregnant or will have to use IVF, or, indeed, if they turn to IVF use, whether it will help them achieving live birth. Therefore, OC is a long-term investment with uncertain outcome. It potentially provides a significant, but only partial protection against reproductive aging and involuntary childlessness.

This study has demonstrated that in light of the progressing postponement of parenthood to higher reproductive ages, OC has a considerable potential. Assisted reproduction already contributes significantly to the observed number of births and birth rates among women past age 40, despite low success rates of fresh non-donor IVF cycles or the need to give up the idea of "reproducing own genes" in the ART with donor oocytes. In vitro fertilisation with cryopreserved oocytes appears to be a more effective option offering higher pregnancy rates achieved with non-donor oocytes. Therefore, it should soon start replacing some of these "traditional" ART methods among women at advanced reproductive ages. In the long-term, the potential share of women who may make use of IVF with cryopreserved oocytes has been estimated in the range of up to 5% (or even 7.6% if the postponement of childbearing further continues) and the share of women who may potentially consider oocyte cryopreservation ranged from 2.4% to 29.9%, depending on models, assumptions and data used. This is a potential demand, which will not be fully realised; nevertheless it points out at potentially huge and rapidly expanding opportunities for health professionals and IVF clinics offering OC. Tests of ovarian reserve will allow women to obtain individual assessment of their ovarian reserve which will in turn help them to make informed decision about OC, in part independently of their age. As the cryopreservation of oocytes spreads, more research should accumulate on its long-term risks and advantages. As soon as possible, proper monitoring of OC use, IVF-OC cycles and their outcomes should be established across Europe and in other countries in order to effectively evaluate this technology as it rapidly evolves. Also, a debate should ensue about most effective regulation of oocyte cryopreservation for non-medical reasons, especially with regard to its ethical aspects, age limits, access rules, and possible cost coverage for economically disadvantaged women.

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