Evidence-based outcomes after oocyte cryopreservation for donor oocyte in vitro fertilization and planned oocyte cryopreservation: a guideline

The Practice Committee of the American Society for Reproductive Medicine

The American Society for Reproductive Medicine, Birmingham, Alabama

Objective: To provide evidence-based recommendations to practicing physicians and others regarding the efficacy of oocyte cryopreservation (OC) for donor oocyte in vitro fertilization and planned OC.
Methods: The American Society for Reproductive Medicine conducted a literature search, which included systematic reviews, meta-analyses, randomized controlled trials, and prospective and retrospective comparative observational studies published from 1986 to 2018. The American Society for Reproductive Medicine Practice Committee and a task force of experts used available evidence and through consensus developed evidence-based guideline recommendations.
Main Outcome Measure(s): Outcomes of interest included live birth rate, clinical pregnancy rate, obstetrical and neonatal outcomes, and factors predicting reproductive outcomes.
Result(s): The literature search identified 30 relevant studies to inform the evidence base for this guideline.
Recommendation(s): Evidence-based recommendations were developed for predicting the likelihood of live births after planned OC, autologous OC in infertile women, and donor OC, as well as factors that may impact live birth rates. Recommendations were developed regarding neonatal outcomes after using fresh vs. cryopreserved oocytes in cases of autologous or donor oocytes.
Conclusion(s): There is insufficient evidence to predict live birth rates after planned OC. On the basis of limited data, ongoing and live birth rates appear to be improved for women who undergo planned OC at a younger vs. older age. Although there are no significant differences in per transfer pregnancy rates with cryopreserved vs. fresh donor oocytes, there is insufficient evidence that the live birth rate is the same with vitrified vs. fresh donor oocytes. Neonatal outcomes appear similar with cryopreserved oocytes compared with fresh oocytes. Future studies that compare cumulative live birth rates are needed. (Fertil Steril® 2021;116:36–47. ©2021 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Planned oocyte cryopreservation, donor oocyte IVF, neonatal outcomes

Although oocyte cryopreservation (OC) has existed for decades, the technology has improved in recent years resulting in widespread clinical use. The first human pregnancy from a previously cryopreserved oocyte was reported in 1986 (1). In the past 20 years, rapid cooling (known as vitrification) has become a standard protocol for OC because intracellular ice crystal formation is minimized compared to slow cooling, resulting in improved post-warming oocyte survival. Oocyte cryopreservation was limited to investigational protocols until 2013, at which point the American Society for Reproductive Medicine (ASRM) Practice Committee stated that oocyte freezing is not "experimental" and allowed for its routine use in postmenarchal women facing gonadotoxic therapies (2). However, at that time, the ASRM Practice Committee document did not recommend OC "for the sole purpose of circumventing reproductive aging in healthy women' on the basis of limited data on safety, efficacy, ethics, emotional risks, and cost-effectiveness" (2). In recent years, the use of OC has greatly expanded not only for women facing gonadotoxic treatments but also for other indications, such as delaying childbearing, as well as for the purpose of oocyte donation. The Ethics Committee of the ASRM has

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suggested that the appropriate terminology for OC for these other indications should be designated as "planned OC."

The purpose of this guideline is to provide a systematic review of success rates (live birth rates and clinical pregnancy rates), factors that may impact success rates (e.g., age, ovarian reserve testing), and obstetrical and neonatal outcomes in scenarios of planned OC and cryopreserved donor oocytes. Given the limited published data regarding outcomes after planned OC, this document also reviews outcomes after in vitro vertilization (IVF) with cryopreserved oocytes from infertile women. Reasons include a desire to limit the number of oocytes inseminated at the time of a fresh IVF cycle by women who wish to preserve supernumerary oocytes for future use, or unplanned unavailability of spermatozoa at the time of oocyte retrieval. This document does not address outcomes in cases of OC for women facing gonadotoxic treatments or transgender care (2).

LIMITATIONS OF THE LITERATURE

Multiple challenges exist in interpreting the literature related to the effectiveness and safety of OC. Studies that evaluate outcomes after planned OC often are limited by lack of an untreated or control group. The technology has changed and improved over time, making it difficult to extrapolate success rates from oocytes that were cryopreserved many years ago to predict outcomes from those that have been cryopreserved more recently. Many older studies report on OC outcomes using slow cooling techniques. This document only includes studies of oocytes that were cryopreserved with vitrification. Many studies present data on intermediate outcomes, such as survival postwarming, fertilization, or blastulation rates. Studies may have different protocols for embryo transfer (e.g., cleavage vs. blastocyst embryos, number to transfer, and so forth), making it challenging to study blastulation rates and embryo quality. Although modeling studies have attempted to predict outcomes, they generally are extrapolated from published data and do not provide data from actual patient outcomes. Modeling studies are not included in this document because of methodologic parameters for guidelines. Published studies generally are from high-volume centers, and it is uncertain if findings from these investigations will be generalizable to lower-volume centers. Given the limited amount of prospective data regarding neonatal outcomes after using cryopreserved oocytes, this guideline includes data from retrospective case series.

METHODS

For a complete description of the methodologic process, including search strategy, assessment of the literature, and review, please see Appendix I.

PLANNED OC

What are Expected Live Birth Rates for Women Who Undergo Planned OC?

The use of OC is increasing among women seeking to preserve their fertility. Only a small proportion of women with cryopreserved oocytes have returned to use these oocytes to attempt pregnancy. A critical question is whether lifetime autologous live birth rates differ between women who have cryopreserve oocytes and those who do not. As of the date of publication, there are no randomized controlled trials that answer this question. Another important question is whether, in a nondonor oocyte population, live birth rates differ between fresh vs. cryopreserved oocytes. Included in this guideline is one intermediate-quality cohort study (3) and two low-quality observational studies (4, 5) that attempt to address these questions.

Doyle et al. (3) identified all autologous IVF embryo transfer cycles of warmed, vitrified oocytes performed at their center between 2009 and January 2015 (n = 128 cycles). Although most patients were infertile and had vitrified oocytes because of the unavailability of sperm on the day of retrieval or requests for limited insemination of retrieved oocytes, 32 warming cycles were included among 31 women who had undergone planned OC. IVF cycles using vitrified/warmed oocytes were compared with IVF outcomes from all 2963 fresh autologous intracytoplasmic sperm injection (ICSI) cycles performed at their center in 2013. The vitrified/warmed vs. fresh oocyte group was similar in mean age at retrieval (34.9 years vs. 35.5 years, $P>.05$). The authors note that the subgroup of women who had undergone planned OC were older than the infertile women who vitrified for other indications. The number of MII oocytes inseminated was lower in the vitrified oocyte group (8.0 vs. 10.1, $P=.0002$), but the fertilization rate with ICSI was comparable between groups (69.5% vs. 71.7%, $P>.05$). Significantly fewer cycles resulted in blastocyst-stage embryo transfer when comparing vitrified vs. fresh oocytes (50.9% vs. 66.1%, $P<.001$). Despite lower rates of blastocyst progression among vitrified oocytes, there was no difference in percentage of cycles without embryo transfer between fresh and vitrified (4.2 vs. 4.7%, $P>.05$). Adjusted implantation rates and clinical pregnancy rates were significantly greater among embryos derived from vitrified oocytes, and pregnancy loss per clinical pregnancy (adjusted) was greater among vitrified oocytes. Ongoing pregnancy per transfer was equivalent between autologous cryopreserved and fresh oocytes (38.6% vs. 36%, respectively $P>.05$). Without providing the specific data, the authors comment that there was no difference in live birth rates among the 31 women who had undergone planned OC vs. those who were infertile and cryopreserved oocytes for other reasons. They were not likely powered to detect a difference between these groups.

There were 2 smaller observational studies (4, 5) that retrospectively assessed outcomes of women who had undergone planned OC. Both investigations did not include a control group. Garcia-Velasco et al. (4) reported an ongoing pregnancy rate of 30.7% after 24 embryo transfers performed for women who had undergone planned OC (mean age 36.7 ± 4.2 years). Nagy et al. (5) reported a live birth rate of 17.4% after autologous oocyte vitrification and warming among 46 women who had undergone planned OC at a mean age of 33.9 ± 3.9 (range 25–43) years.

Summary statement. There is extremely limited evidence to predict the likelihood of live birth in women who undergo

planned OC. A cohort study from a single institution reported similar ongoing clinical pregnancy per transfer rates in women undergoing IVF with fresh compared to previously cryopreserved oocytes.

Recommendation. There is insufficient evidence to counsel women about the likelihood of live birth after planned OC.

What are Live Birth Rates for Infertile Women Who use Autologous Cryopreserved Oocytes for Indications Other Than Planned OC?

Included in this section are 11 intermediate-quality studies addressing the question of live birth rates among infertile women using autologous cryopreserved oocytes for nonelective indications: 1 randomized controlled trial (6), 7 cohort studies (3, 7–12), and 3 systematic reviews/meta-analyses (13–15).

Rienzi et al. (6) performed an intermediate-quality study in which infertile patients undergoing IVF/ICSI with >6 MII oocytes underwent randomization of their MII oocytes to fresh ICSI insemination or vitrification/warming/ICSI. Oocyte warming was performed when pregnancy did not occur after fresh embryo transfer. A total of 124 cycles (n = 124 patients) met inclusion criteria and 54 (43.2%) conceived with a fresh embryo transfer. Forty patients with a mean age of 35.5 years subsequently underwent a warming cycle during the study period. No significant difference was observed between groups of sibling oocytes in the fresh vs. vitrified groups in terms of fertilization rate, embryo development, or percentage of excellent-quality embryos, but embryos were not cultured past day 2. Among the vitrification group, the clinical pregnancy rate per embryo transfer was 38.5% and ongoing pregnancy rate per embryo transfer was 30.8%. Interpretation is limited, as pregnancy outcomes cannot be compared between fresh and vitrified oocytes given the study design.

Doyle et al. (3) identified all autologous IVF cycles performed at their center using vitrified warmed oocytes (n = 128 cycles) between 2009 and 2015. Live birth and ongoing pregnancy rates per transfer cycle were equivalent between autologous cryopreserved and fresh oocytes (38.6% vs. 36%, respectively $P>.05$).

Almodin et al. (7) compared 79 cycles in which patients underwent fresh IVF to 46 cycles among patients who failed fresh IVF and subsequently used supernumerary vitrified oocytes. The pregnancy rate per transfer was similar between fresh vs. cryopreserved/warmed groups (51.9% compared with 45.6%, not significant), but the investigators do not explicitly report live birth rates. Almodin et al. (8) described the vitrification of supernumerary oocytes after fresh IVF cycles and the outcomes of future warming cycles. Among 100 patients using cryopreserved oocytes in the first vitrified warming cycle, 32 (32%) had a live birth. Among 20 unsuccessful patients who opted for a second vitrified warming cycle, 6 (20%) had a term live birth. Rates of clinical pregnancy per transfer, miscarriage, and live birth per transfer were comparable between embryos derived from fresh or cryopreserved oocytes. In both studies by Almodin et al. (7, 8), appropriate comparisons are limited given the inherent heterogeneity between groups who conceived during their fresh transfer compared with those requiring the use of vitrified oocytes for a second or third cycle.

Crawford et al. (9) performed a cohort study analyzing 105,517 fresh embryo cycles in 2013 from the National ART Surveillance System with embryos derived from fresh and cryopreserved oocytes including autologous and donor oocytes. There were 422 cycles analyzed involving autologous cryopreserved oocytes with no evidence of differences in rates of cancellation, implantation, pregnancy, miscarriage, or live birth rate between autologous fresh and cryopreserved oocyte cycles (live birth rate 37.4% vs. 30.6%, absolute risk reduction 1.05, 95% confidence interval [CI] 0.86–1.30). Having at least 1 embryo cryopreserved, an indicator that multiple good-quality embryos were available, was the only factor associated with live birth for autologous cryopreserved oocyte cycles. This study was limited by a relatively small sample size in the autologous OC group and a lack of information about the reason for OC. Data were unavailable for stage of embryo transfer, embryo quality, method of cryopreservation, endometrial preparation, and age of patient cryopreserving oocytes.

Another cohort study describes outcomes after the accumulation of vitrified oocytes over multiple ovarian stimulation cycles among patients seeking to increase the number of embryos available for preimplantation genetic testing. In this study, 69 couples (female age 29–42.3 years, mean age 36.6) underwent multiple cycles of ovarian stimulation with cryopreservation of oocytes during the first 1 or 2 cycles, followed by ICSI with fresh and cryopreserved oocytes during the final cycle. Clinical outcomes were comparable between fresh and cryopreserved oocytes, with no differences in fertilization rate, clinical pregnancies per embryo transfer, and implantation rate (14/25 (56%) among euploid blastocysts from vitrified/warmed oocytes, and 28/46 (6.9%) among euploid blastocysts from fresh oocytes, $P>.05$). The authors do not report outcomes on the basis of maternal age or live birth rates (12).

Two cohort studies assessed outcomes after oocyte vitrification in women at risk for ovarian hyperstimulation syndrome (10, 11). One study retrospectively analyzed outcomes of 248 patients at risk of ovarian hyperstimulation syndrome, 152 of whom were coasted and 96 of whom underwent oocyte vitrification followed by warming and ICSI with embryo transfer in a subsequent natural cycle (10). A total of 1,026 vitrified MII oocytes were rewarmed during the study period. Clinical outcomes were compared between the vitrified oocyte and coasted groups, and implantation rate (sacs/embryos transferred) was higher in the vitrified oocyte group (32.1% vs. 19.2%, $P<.05$), as was clinical pregnancy rate (50% vs. 29.5%, $P<.005$). Live birth rates were not reported, and clinical outcomes were limited by the heterogeneous comparison of embryos transferred during a stimulated (coasted) cycle and a natural cycle. A second study identified 96 women requiring delayed embryo transfer because of ovarian hyperstimulation syndrome risk and allocated them to vitrification of oocytes or embryos (11). The fertilization rate and the number of "useful embryos" was significantly lower in the oocyte vitrification group compared with the embryo vitrification group. The cumulative live birth rate per

transferred embryo was calculated after 3 embryo transfers and was similar in the OC (n = 50) and embryo vitrification (n = 46) groups (26.9% vs. 27.1%, $P>.05$), although this study was not powered to detect a difference in live birth rates between the groups.

Three intermediate-quality systematic review/meta-analyses are included. Cobo et al. (6) identified and analyzed randomized controlled trials to assess the efficacy of oocyte vitrification. Five eligible studies (3 with autologous and 2 with donor oocytes) were identified, but only 1 study applies to the question of outcomes using autologous vitrified oocytes. Cil et al. (14) performed a meta-analysis of original data from 10 studies including 2265 OC cycles from 1805 patients. Slow cooling and vitrification were included, and all studies involved cryopreservation of surplus oocytes after an IVF cycle because embryo freezing was illegal or patients did not wish to freeze embryos. All embryo transfers were performed on day 2 or day 3, and the mean age of patients at freezing vitrified oocytes was 34.1 ± 4.7 (20–51) years. Overall survival and fertilization rates were higher with vitrification (85% and 79%) than slow cooling (65% and 74%; $P<.001$). Implantation rate was higher after vitrification than slow cooling, and the implantation rate was 13.2% per oocyte vitrified at 30 years compared with 8.6% for oocytes vitrified at 40 years. Potdar et al. (15) analyzed 21 articles comparing fertility outcomes using vitrified and fresh oocytes with a mix of donor and autologous oocyte sources. A proportional meta-analysis pooled results for 17 studies using the random-effects model. No significant difference was seen between vitrified and fresh oocytes in fertilization, cleavage, and clinical pregnancy rates. However, the ongoing pregnancy rate (defined as pregnancy progressing >20 weeks) per warmed oocyte was lower in the vitrified group (199/4358, 4.6%) compared with fresh (317/5938, 5.3%; odds ratio [OR] 0.74, 95% CI 0.61–0.89). Sensitivity analysis showed that this reduction in ongoing pregnancy rate was observed in nonrandomized control trials (non-RCTs) but not in RCTs. Live birth rate per warmed oocyte could not be assessed because of differences between studies in reporting ongoing pregnancy and live birth rate. Interpretation is limited by significant heterogeneity between studies.

Summary statement. Ongoing pregnancy rates per transfer appear similar in women who use oocytes vitrified for nonelective reasons compared with those who use fresh oocytes.

Recommendation. It is recommended that OC be offered as an option for women in situations where there is an unanticipated lack of sperm the day of retrieval, or a desire to limit the number of fertilized embryos. (Strength of Evidence: B; Strength of Recommendation: Moderate)

Among Women Who Undergo Planned OC, How Does Age at the Time of Oocyte Retrieval Modify Outcomes? Does Age at the Time of Oocyte Retrieval Help Identify an Optimal Candidate?

Age is known to be a critical factor predicting live birth rates among women with infertility undergoing in vitro fertilization. Female age at the time of OC would similarly be expected to influence live birth rates, but there currently are no randomized controlled trials that address how age modifies outcomes for planned OC. Included in this section are 1 intermediate-quality cohort study (3) and 1 low-quality observational study (5).

Doyle et al. (3) concluded that the clearest threshold between better and worse outcomes using autologous cryopreserved oocytes (n = 128 women) was <38 years vs. ≥38 years at the time of OC. The clinical pregnancy rate for patients <38 years was 60.2% compared with 43.9% for patients ≥38 years. The authors estimated live birth efficiency per warmed oocyte by age group and found that oocyte efficiency decreased with increasing age (7.4% for women <30 years, 7.0% for women 30–34 years, 6.5% for women 35–37 years, 5.2% for women ≥38 years). The efficiency among women 41–42 years was 6.8%, but this number was unreliable because of a very small sample size. Note that the study combined data for women who underwent planned OC, as well as infertile women with OC for another indication.

Nagy et al. (5) created a registry to evaluate cryopreservation techniques and oocyte source and found that live birth rates among women who underwent planned OC at <35 years (n = 24) were significantly greater than among those who cryopreserved oocytes at ≥35 years (n = 26, 23.8% vs. 12.0%, $P<.05$) (5). The study had a number of limitations including selection bias because of the inclusion of nonsequential patients, missing data and lack of data verification, changes in cryopreservation techniques after the initiation of the registry, and small sample size.

Summary statement. On the basis of limited data, ongoing and live birth rates appear to be improved for women who undergo planned OC at a younger vs. older age.

Recommendation.

- It is recommended to counsel women that live birth rates per embryo transfer are improved when OC is performed in younger as compared to older women. (Strength of Evidence: C; Strength of Recommendation: Weak).
- There are insufficient data to advise women on the optimal age to undergo planned OC.

Among Women Cryopreserving Oocytes for Any Indication, Planned or Unplanned, Do Baseline Demographic Characteristics or Comorbidities at the Time of Freezing, Independent of Age, (e.g., body mass index [BMI], Smoking, Ethnicity) Impact Outcomes? Are There Factors at the Time of Warming that Impact Outcomes (BMI, Smoking)? Are There Ways (e.g., Smoking Cessation, Weight Loss, and so forth) to Optimize the Cycle Outcome?

There are no randomized trials evaluating baseline demographic characteristics or comorbidities at the time of OC independent of age (e.g., BMI, smoking, ethnicity). There are no studies included in this guideline evaluating the impact of demographic characteristics or comorbidities on outcomes at

the time of oocyte warming, and no evidence of interventions to optimize cycle outcomes.

Recommendation.

- There is insufficient evidence to recommend that demographic characteristics or comorbidities, independent of age, affect the outcome of planned OC.
- There is insufficient evidence to recommend interventions to optimize outcomes after planned OC.

Do Ovarian Reserve Tests Independently Predict Live Birth Rate after Oocyte Freezing, Independent of Age?

There are no randomized trials or observational studies that evaluate the impact of ovarian reserve on live birth rate after OC, independent of age. In the IVF literature, ovarian reserve testing predicts the number of oocytes produced per cycle (16).

Recommendation. There is insufficient evidence to recommend ovarian reserve testing to predict live birth rates after planned OC for any indication, independent of age.

Among Women Pursuing OC, How Many Mature Oocytes Should be Cryopreserved to Achieve a Reasonable Chance of Live Birth?

To maximize the likelihood of future pregnancy(ies) with warmed oocytes, patients and physicians need guidance regarding the optimal number of oocytes to cryopreserve. There are no randomized controlled trials to address the number of oocytes needed to achieve a reasonable chance of live birth. Included in this section are 1 intermediate-quality cohort study (3) and 1 low-quality observational study (5). Although modeling studies have attempted to predict outcomes on the basis of numbers of oocytes cryopreserved, they generally are extrapolated from published data, and do not provide data from actual patient outcomes. Modeling studies are not included in this document because of methodologic parameters for guidelines.

Doyle et al. (3) analyzed 128 autologous IVF treatment cycles, in which 1283 vitrified oocytes were warmed. They analyzed live birth efficiency per warmed oocyte by age group and found that oocyte efficiency decreased with increasing age. When adjusted for age, calculated efficiencies were not significantly associated with number of oocytes warmed per cycle or total number of oocytes retrieved in the originating cycle. The authors estimate that to achieve a 70% chance of 1 live birth, women 30–34 years would need to cryopreserve 14 mature oocytes, women 35–37 years 15 mature oocytes, and women aged 38–40 years 26 mature oocytes.

Nagy et al. (5) analyzed data from 193 patients from 16 centers who had used cryopreserved (slow-cooled and vitrified) oocytes in autologous and donor IVF treatment cycles (5). Indications for autologous OC included medical, proof of concept, and planned OC (vitrification n = 36, slow-cooled n = 7). They calculated the efficiency of warmed oocytes by age group and found that among women <35 years each warmed oocyte produced a 2.6% chance of live birth compared with 1.3% among women ≥35 years. They calculated that among women <35 years, 38.8 oocytes are needed for a live birth compared with 77 oocytes among women ≥35 years. This study was limited by heterogeneity including donor and elective cycles, the inclusion of slow-cooled and vitrification, the inclusion of nonelective indications for cryopreservation, a small sample size for planned OC cycles, and conclusions on the basis of calculated value as opposed to actual data (n = 43).

Summary statement. Oocyte efficiency decreases with increasing age, but there are limited data to specify the optimal number of oocytes needed with planned OC.

Recommendation. There is insufficient evidence to counsel women of various ages on the absolute number of oocytes necessary to achieve a reasonable probability of a live birth after planned OC.

What are the Rates of Neonatal Complications (Obstetrical Outcomes, Birth Defects) for Women who Cryopreserved Oocytes for Autologous Use?

This guideline includes 1 low-quality cohort study that reported perinatal/neonatal outcomes with use of autologous oocytes for women who had undergone planned OC (4). There are five additional studies that examined neonatal outcomes of children born from infertile women having used their own previously cryopreserved oocytes, including four cohort studies of intermediate-quality (12, 17–19) and one case series of low-quality (20).

A small cohort study reported perinatal/neonatal outcomes with use of autologous oocytes for 560 women who had undergone planned OC (4). Twenty-six women returned to use their cryopreserved oocytes to attempt pregnancy. Five live births and 8 ongoing pregnancies were reported at the time of publication. Neonatal outcome information was limited to reporting a normal range of mean live birth weight (3150 g) and gender. This study reported very small numbers of live births and provided no relevant obstetric and neonatal information.

A retrospective cohort study by Cobo et al. (13) compared neonatal health outcomes in a large number of children born after the use of vitrified oocytes (n = 1027 children) and control group of fresh oocytes (n = 1224 children). The vitrified oocyte group was stratified further by autologous (n = 119 children) vs. donor (n = 908 children) cycles. This study did not include women using planned OC. No differences were found between the vitrified and fresh oocyte groups in the rate of obstetric problems (including diabetes, pregnancy-induced hypertension, preterm birth, anemia, and cholestasis), gestational age at delivery, birth weight, Apgar scores, birth defects, admission to neonatal intensive care unit, perinatal mortality, and puerperal problems. No differences in neonatal health outcomes were detected between use of autologous and donor cryopreserved oocytes. Limitations of the study are the small sample size of births (119 children) from cryopreserved autologous oocytes and that they only

analyzed births at or beyond 24 weeks possibly omitting adverse pregnancy outcomes that may occur before 24 weeks.

Four intermediate-quality retrospective cohort studies observed neonatal outcomes from previously cryopreserved oocytes. Anzola et al. (17) reported that maternal characteristics, obstetric outcomes, and perinatal outcomes were similar in vitrified/warmed oocyte/ICSI (50 infants) and fresh oocytes/ICSI (364 infants) groups. Chamayou et al. (12) conducted a retrospective cohort comparison of the first 50 babies born after autologous oocyte vitrification/warming cycles to a control group of 364 children conceived by fresh oocytes with IVF between 2011 and 2015. Results showed no statistical difference in risk of low birth weight, large for gestational age, birth defects, and cesarean section. Siano et al. (19) conducted a pilot study in which 14 infertile women underwent IVF therapy in which their oocytes were vitrified from 20 minutes to 1 hour before warming, and insemination by ICSI and embryo transfer. Neonatal health outcomes of the 7 pregnancies resulting in 6 deliveries were compared with 639 age-matched controls undergoing fresh oocyte IVF. There was no significant difference in obstetric, perinatal, and neonatal health outcomes between the 2 groups. Study group sample size was a major limitation of this study.

A case series reported on 936 live births from previously cryopreserved oocytes, of which 1.3% (n = 12) had congenital anomalies (20). The investigators concluded that there was no difference in adverse neonatal outcomes between their review of previously cryopreserved oocyte source and national public health reported data of naturally conceived infants. Some major limitations of this study are inclusion of case and series reports, not all reported births were subjected to peer review, and not all neonatal health information was available for every reported pregnancy and birth.

Summary statement. Based on a small number of studies with very small cohorts, there is limited evidence to conclude that neonatal outcomes are similar for oocytes previously cryopreserved for autologous use in infertile women compared with fresh oocytes.

Recommendation. Infertile women should be counseled that, based on a small number of births, neonatal outcomes appear similar after using their own previously cryopreserved oocytes compared with outcomes after the use of fresh oocytes. (Strength of Evidence: C; Strength of Recommendation: Weak)

What is the Proportion of Women Who Will use Their Electively Cryopreserved Oocytes?

There are no randomized trials or observational studies included in this guideline that evaluate the long-term rate of women using their oocytes that were cryopreserved for planned OC. Current studies only report use over a short term after cryopreservation.

Recommendation. There is insufficient evidence to counsel patients regarding the likelihood of the long-term use of oocytes cryopreserved for planned OC.

OC AND DONOR OOCYTE IVF

What are Clinical Pregnancy Rates and Live Birth Rates for Women Who Use Cryopreserved Vs. Fresh Donor Oocytes?

To evaluate pregnancy rates, this guideline refers to one high-quality randomized controlled trial (21), four intermediate-quality cohort studies (22–25) and one intermediate-quality meta-analysis (15). There currently are no randomized controlled trials that address the question of live birth rates using fresh vs. cryopreserved donor oocytes. To evaluate live birth rates using cryopreserved oocytes, this guideline includes two intermediate-quality cohort studies (26, 27).

To evaluate pregnancy rates between fresh and vitrified oocytes, Cobo et al. (21) performed a trial of approximated 600 recipients randomized to receive fresh (n = 289) vs. cryopreserved (n = 295) donor oocytes and they did not identify a statistically significant difference in ongoing pregnancy rates (43% vs. 41%, $P>.05$) (21). Of note, in the fresh and cryopreserved groups, all oocytes from one donor were allotted to a single recipient. Four cohort studies found no significant difference in ongoing pregnancy rates comparing fresh vs. previously vitrified oocytes (Table 1) (22–25). Two of these studies did note that the average age of the donors was lower in the vitrified group (22, 23) and that the mean number of oocytes collected in the vitrified group was significantly higher (22), which could have affected their results.

In addition to evaluating pregnancy rates per recipient, another consideration is to identify the ongoing pregnancy rate per warmed oocyte. A meta-analysis included 21 studies (seven RCTs [two donor studies], seven NRCT [two donor studies] and seven prospective cohort studies [two donor studies]). Limiting the analysis to the donor studies, the authors calculated an ongoing pregnancy rate with warmed donor oocytes of 8%. In comparing vitrified with fresh donor oocytes, the authors did not observe a difference in clinical pregnancy rates per warmed oocyte (fresh 512/6511, 7.9% vs. vitrified 330/5140, 6.4% OR 0.87, 95% CI 0.76–1.01) (15).

Given the increased emphasis on cumulative pregnancy rates and frozen embryo transfers, one study assessed the effect of double vitrification on pregnancy rate (i.e., transfer of a cryopreserved embryo that was either derived from a vitrified oocyte [group 1, n = 414] or a fresh oocyte [group 2, n = 1315]). The delivery rates were not significantly different for either day 3 frozen embryo transfers (33.2% and 30.4%) or blastocyst transfers (31.5% and 32.4%) (28) between the two groups.

To evaluate live birth rates, Trokoudes et al. (26) (Table 2) published a small prospective cohort study matching each donor with one to two recipients of fresh oocytes and one recipient of previously cryopreserved oocytes (the oocytes were vitrified 1 to 3 months before subsequent transfer). Outcomes were compared between recipients of fresh (n = 41) or previously cryopreserved (n = 36) oocytes. Advantages to this design included the ability to control donor characteristics between recipients as they were matched, as well as standardizing the mean number of oocytes (6.0 vs. 5.8, $P = .11$) received per recipient and mean number of embryos

TABLE 1

Summary of pregnancy rate data.

Citation	Pregnancy rate per recipient using fresh donor oocytes (n) (mean No. of embryos transferred)	Pregnancy rate per recipient using cryopreserved donor oocytes (n) (mean No. of embryos transferred)[a]
Cobo et al. (21)	49.8% (n = 289 recipients) (1.7)	50.2% (n = 295 recipients) (1.7)
Dominigues et al. (22)	60.9% (n = 78 recipients) (2.3)	59.0% (n = 426 recipients) (2.1)
Garcia et al. (23)	60.0% (n = 85 recipients) (1.98)	61.8% (n = 34 recipients) (1.94)
Kalugina et al (24)[b]	(n = 115 recipients)	(n = 221 recipients)
Wang et al. (25)	60% (n = 12/20) (1.9)	63.2% (n = 12/19) (1.9)

[a] *P* value was not significant for all studies.
[b] Actual pregnancy rates are not able to be extracted from the study.

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transferred (2.09 vs. 2.25, $P=.23$) on day 3. These authors did not identify a significant difference in live birth rates between groups (41.5% fresh oocytes and 47.2% vitrified oocytes, $P=.61$) (26).

In contrast, a retrospective analysis of the Society for Assisted Reproductive Technology data from 2013–2015 identified a significantly higher live birth rate with fresh vs. cryopreserved oocytes per recipient cycle start (51.1% vs. 39.7%, $P<.0001$) and per embryo transfer (56.4% vs. 45.3%, $P<.0001$). There was a significant increase in cycle cancellations using cryopreserved oocytes over time (15% cycle cancellation rate in 2015 in comparison to 8.5% cycle cancellation rate in 2013, $P<.0001$). This study raises important questions about tracking the success rates of these two modalities for pursuing birth through oocyte donation. Some major drawbacks to this study are that these results were based on aggregate outcome data, which did not allow for control of confounding variables, such as the number of oocytes allotted to recipients and method of OC (27).

Summary statement. In studies evaluating pregnancy rates, there is moderate evidence that pregnancy rates per transfer between fresh and previously vitrified donor oocytes are not significantly different. Further studies that assess live birth rates are needed.

Recommendation. It is recommended to tell recipients that previously cryopreserved donor oocytes are a reasonable option compared with fresh donor oocytes, given that there is good evidence that there are no significant differences in per transfer pregnancy rates compared with fresh donor oocytes. (Strength of Evidence: B; Strength of Recommendation: Moderate).

Are There Factors About the Donors (Age, Ovarian Reserve, and So Forth) that Would Potentially be Reflected in Outcomes with Cryopreserved Donor Oocytes? Are There Recipient Characteristics that are Related to Outcomes?

The ability to identify prospective characteristics of potential donors of vitrified oocytes and recipients to predict clinical success would provide significant advantages to achieving a live birth. However, few studies have evaluated characteristics linked to successful outcomes from previously vitrified oocytes and many studies are designed to try to control for as many of these variables as possible (i.e., inclusion/exclusion criteria for entry into a study). This guideline includes four intermediate-quality cohort studies that attempt to assess factors that predict success with cryopreserved donor oocytes (24, 26, 29, 30).

A large cohort study of 2140 donors over 6 years identified donor characteristics associated with survival of oocytes and attempted to develop a prediction model (29). In their models, the authors included donor age, storage duration, number of oocytes vitrified/warmed, donor's BMI, stimulation duration, total doses of gonadotropins, donor's peak estradiol and progesterone level on the day of human chorionic gonadotropin and ovarian stimulation protocols. However, none of these variables was predictive of a higher pregnancy rate. In regression models evaluating oocyte survival rates, the only variables that were statistically significant were donor age, number of oocytes vitrified, and total human menopausal gonadotropin dose. However, the differences accounted for using these variables were quite small (<1%) (29).

TABLE 2

Summary of live birth rate data.

Citation	Live birth rate per recipient using fresh donor oocytes (mean No. of embryos transferred)	Live birth rate per recipient using cryopresereved donor oocytes (mean No. of embryos transferred)	*P* value
Trokoudes et al. (26)	41.5% (n = 17/41) (2.09)	47.2% (n = 17/36) (2.25)	NS
Kushnir et al. (27)	51.1% (n = 11,156/21,832) (1.63)	39.7% (n = 3,306/8,328) (1.6)	<.001

Note: NS = not significant.

*The Practice Committee of the American Society for Reproductive Medicine*asrm@asrm.org. Oocyte cryopreservation. Fertil Steril 2021.*

Other factors that cohort studies have examined and have not found significant differences in terms of success rates include the type of stimulation protocol used for ovarian stimulation (24) and the duration of oocyte storage (up to 60 months with no significant decline in quality identified) (29). One factor that has been associated with cumulative live birth rates is the number of oocytes used (with a plateau being reached as the number of oocytes used reaches 40 oocytes) (29).

The uterine environment and preparation of the endometrium may have a role in success rates. One cohort study evaluated a shared oocyte donor program where a portion of the oocytes was cryopreserved for recipients (n = 425) and a portion was used in autologous cycles (n = 425). They reported higher implantation rates in the recipient cycles (43%) and the autologous frozen embryo transfer (FET) cycles (67%), in comparison with autologous fresh transfer cycles (37%, $P<.001$) (30).

Another small cohort study from an oocyte sharing program, where donors were matched with recipients to receive either fresh (n = 41) or previously cryopreserved oocytes (n = 36), demonstrated that there was a significant correlation in live birth rates using previously vitrified oocytes when stratified by the live birth rate of the recipient of the fresh oocytes. From donors where the recipient had a live birth after the fresh cycle donation, 60% of the recipients of the vitrified oocytes had a live birth. From donors where the recipient did not have a live birth on the fresh cycle, only 18.2% of recipients had a live birth on the cycle of oocyte warming ($P<.05$) (26). There were no statistically significant differences seen in embryo morphology between groups, but there was a wide range of donor ages in this study (22–35 years) and the authors did not indicate if higher live birth rates were achieved in recipients receiving oocytes from younger donors.

Summary statement. Factors associated with an improved live birth rate include the number of donor oocytes warmed and the delivery of a live birth in a prior donor cycle.

Recommendation.

- Recipients can be counseled that as the number of donor oocytes warmed increases, there is an associated increase in cumulative live birth rate (Strength of Evidence B, Strength of Recommendation: Moderate).
- Recipients can be counseled that live birth rates may be greater from vitrified oocytes that derive from donors who had a prior successful outcome after a fresh cycle of oocyte donation (Strength of Evidence C, Strength of Recommendation: Weak).
- Recipients can be counseled that the length of time oocytes have been cryopreserved is not associated with differences in oocyte survival or pregnancy rates (Strength of Evidence B, Strength of Recommendation: Moderate).
- There is insufficient evidence to recommend a particular stimulation protocol for oocyte donors or certain donor characteristics in terms of embryo quality or success rates.

What are the Rates of Neonatal Complications (Obstetrical Outcomes, Birth Defects) for Women who use Cryopreserved Vs. Fresh Donor Oocytes?

Obstetrical outcomes and health of the offspring remain a concern after the implementation of new technologies in assisted reproduction. The number of studies addressing this question in cryopreserved donor oocytes is limited. This guideline reviews the evidence evaluating obstetrical outcomes and neonatal complications after the use of cryopreserved donor oocytes and includes two intermediate-quality cohort studies (18, 29).

One retrospective cohort study (18) examined obstetrical and neonatal outcomes of singleton and multiple pregnancies conceived with the use of fresh and vitrified donor oocytes. This study comprised all birth outcomes over a period of approximately 5 years. Differences in pregnancy (including cholestasis, gestational diabetes, bleeding, preterm rupture of membranes, pregnancy-induced hypertension), delivery (including gestational age, prematurity, cesarean section), and neonatal outcomes (including birth weight, Apgar, birth defects, admission to neonatal intensive care unit, perinatal mortality) of 516 singleton and 160 multiple pregnancies conceived with fresh donor oocytes and 503 singleton and 201 multiple pregnancies conceived with vitrified donor oocytes were compared. No significant differences were found except for an increased risk of chorionic villus sampling or amniocentesis, although without any abnormal results, among singleton pregnancies conceived with vitrified compared to fresh donor oocytes (82/503 [16.3%] vs. 43/516 [8.3%]; OR 2.14; 95% CI [1.45–3.17], $P<.001$). This was attributed to a lesser amount of experience with oocyte vitrification. In addition, there were more female neonates born among multiple pregnancies conceived from vitrified compared to fresh donor oocytes (211/405 [52.1%] vs. 135/320 [42.2%]; OR 1.49; CI [1.11–2.04], $P<.02$). The strengths of this study include its large sample size, as well as the independent comparison of singleton and multiple pregnancies. However, it is limited by its single center nature, the fact that it only analyzed births at or beyond 24 weeks of gestation, and that its statistical power was limited to detect minor increases in the incidence of rare adverse outcomes.

A retrospective case series study (29), without a control group, reported neonatal outcomes for pregnancies conceived with vitrified donor oocytes from their 6-year experience of 1674 delivered neonates. They found a mortality rate of 0.2% (3/1674), one case of trigonocephaly, two unilateral renal hypoplasias, one Kawasaki syndrome, and one West syndrome.

Summary statement. In studies evaluating neonatal outcomes with cryopreserved vs. fresh donor oocytes, there does not appear to be a significant difference in the health of the babies. To date, there are a limited number of published studies reporting on neonatal outcomes.

Recommendation. Recipients can be counseled that, based on limited evidence, neonatal outcomes appear similar between vitrified and fresh donor oocytes (Strength of Evidence: C; Strength of Recommendation: Weak).

CONCLUSION

Although the use of planned OC has grown exponentially in the past 5 years, there are still a relatively limited number of studies providing age-related success rates. There has been a relatively short time interval between emergence of this new technology and its clinical use. More time in years is needed for women to complete their deferment of family building and use their cryopreserved oocytes to allow for more evaluation of clinical outcomes. Women considering planned OC should be fully informed of the limited published data about future pregnancy rates and neonatal outcomes. There is a risk of false belief that future childbearing is "guaranteed" and women will delay childbearing attempts beyond the point where autologous conception is an option. Data about pregnancy rates with cryopreserved donor oocytes seem reassuring, but larger studies are needed confirm that live birth rates and neonatal outcomes are not compromised compared to fresh oocytes. More data are needed about cumulative live birth rates with cryopreserved donor oocytes, especially given the common strategy of providing recipients a limited number of eggs.

UNANSWERED QUESTIONS

- Future investigations should provide more information about success rates and neonatal outcomes after planned OC. Larger cohorts will hopefully guide women about how many oocytes to freeze to provide reasonable reassurance of a future live birth and the best age to cryopreserve oocytes.
- Future studies should provide outcome data from clinics with high and low volumes of OC.
- Future studies should evaluate if there are factors in addition to age, such as ovarian reserve testing or lifestyle characteristics, that can aid in predicting future live birth rates with planned OC.
- Evidence-based counseling tools are needed for educating patients considering OC.
- More data are needed about cumulative live birth rates with cryopreserved donor oocytes.

RECOMMENDATIONS FOR PLANNED OC

- There is insufficient evidence to counsel women about the likelihood of live birth after planned OC.
- It is recommended that OC be offered as an option for to women in situations where there is an unanticipated lack of sperm the day of retrieval, or a desire to limit the number of fertilized embryos (Strength of Evidence: B; Strength of Recommendation: Moderate).
- It is recommended to counsel women that live birth rates per embryo transfer are improved when OC is performed in younger women as compared to older women (Strength of Evidence: C; Strength of Recommendation: Weak).
- There are insufficient data to advise women on the optimal age to undergo planned OC.
- There is insufficient evidence to recommend that demographic characteristics or comorbidities independent of age affect the outcome of planned OC.
- There is insufficient evidence to recommend interventions to optimize outcomes after planned OC.
- There is insufficient evidence to recommend ovarian reserve testing to predict live birth rates after planned OC for any indication, independent of age.
- There is insufficient evidence to counsel women of various ages on the absolute number of oocytes necessary to achieve live birth after planned OC.
- Infertile women should be counseled that, based on a small number of births, neonatal outcomes appear similar after using their own previously cryopreserved oocytes compared with outcomes after the use of fresh oocytes (Strength of Evidence: C; Strength of Recommendation: Weak).
- There is insufficient evidence to counsel patients regarding the likelihood of the long-term use of oocytes cryopreserved for planned OC.

RECOMMENDATIONS FOR DONOR OC

- It is recommended to tell recipients that previously cryopreserved donor oocytes are a reasonable option compared with fresh donor oocytes, given that there is good evidence that there are no significant differences in per transfer pregnancy rates compared with those with fresh donor oocytes (Strength of Evidence: B; Strength of Recommendation: Moderate).
- Recipients can be counseled that as the number of donor oocytes warmed increases, there is an associated increase in cumulative live birth rate (Strength of Evidence B, Strength of Recommendation: Moderate).
- Recipients can be counseled that live birth rates may be greater from vitrified oocytes that derive from donors who had prior successful outcome after a fresh cycle of oocyte donation (Strength of Evidence C, Strength of Recommendation: Weak).
- Recipients can be counseled that the length of time that oocytes have been stored is not associated with differences in oocyte survival or pregnancy rates (Strength of Evidence B, Strength of Recommendation: Moderate).

- There is insufficient evidence to recommend a particular stimulation protocol for oocyte donors or certain donor characteristics in terms of embryo quality or success rates.
- Recipients can be counseled that, based on limited evidence, neonatal outcomes appear similar between vitrified and fresh donor oocytes (Strength of Evidence: C; Strength of Recommendation: Weak).

SUMMARY RECOMMENDATIONS AND FUTURE DIRECTIONS

- There is insufficient evidence to predict live birth rates after planned OC.
- On the basis of limited data, ongoing and live birth rates appear to be higher for women who undergo planned OC at a younger vs. older ages.
- Ovarian reserve tests can be used to estimate the anticipated oocyte yield.
- There are no significant differences in per transfer pregnancy rates with cryopreserved vs. fresh donor oocytes.
- Neonatal outcomes appear similar with cryopreserved oocytes.
- There is a pressing need for additional data about long-term outcomes and cumulative live birth rates with cryopreserved oocytes, after planned OC and use of cryopreserved donor eggs.

Acknowledgments: This report was developed under the direction of the Practice Committee of the ASRM as a service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Practice Committee and the Board of Directors of ASRM have approved this report. This document was reviewed by ASRM members and their input was considered in the preparation of the final document. The following members of the ASRM Practice Committee participated in the development of this document: Alan Penzias, M.D.; Ricardo Azziz, M.D., M.P.H., M.B.A.; Kristin Bendikson, M.D.; Tommaso Falcone, M.D.; Jessica Goldstein, R.N.; Karl Hansen, M.D., Ph.D.; Micah Hill, D.O.; Sangita Jindal, Ph.D.; Suleena Kalra, M.D., M.S.C.E.; Zac Knight, Ph.D.; Jennifer Mersereau, M.D.; Richard Reindollar, M.D.; Chevis N. Shannon, Dr.P.H., M.P.H., M.B.A.; Anne Steiner, M.D., M.P.H.: Cigdem Tanrikut, M.D.; Hugh Taylor, M.D.; and Belinda Yauger, M.D. The Practice Committee acknowledges the special contribution of Jennifer Mersereau, M.D.; Luis Hoyos, M.D.; Kathryn Go, Ph.D.; Kara Goldman, M.D.; Christine Skiadas, M.D.; and Michael Mersol-Barg, M.D. in the development of this document. Per ASRM policy, all members of ASRM task forces and the Practice Committee disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients for the preceding 12 months. Committee members were reminded to update potential disclosures annually and if new potential conflicts arose during their appointments. Before live discussions or meetings, Committee members were reminded verbally and in writing to disclose any new or previously undisclosed relationships. Disclosures were reviewed for conflicts by the ASRM Chief Medical Officer and the Chair of the Practice Committee. Task force members for whom conflicts were identified were excused from this project. Members of the Practice Committee who were found to have conflicts of interest based on the relationships disclosed did not participate in the discussion or development of the document.

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Panel: This evidence-based guideline with recommendations for clinicians was developed by a multidisciplinary group, comprised of the ASRM Practice Committee and a task force of medical experts, which included specialists in obstetrics and gynecology, reproductive endocrinology and infertility, fertility preservation, reproductive surgery, endometriosis, uterine anomalies, fibroids, assisted reproductive technology, in vitro fertilization, and epidemiology/biostatistics. Members of the task force for this clinical practice guideline consisted of medical professionals at various levels of training, including fellows and senior experts, as well as experts with less than 10 years of posttraining, Clinical Reproductive Scientist Training Program scholars, a clinical epidemiologist who is also a reproductive medicine subspecialist, and a methodologic specialist. In addition, a select group of patients participated in document scoping and review.

Review Process: The Practice Committee, a multidisciplinary body, reviewed this document at various stages of development. After thorough review of the final draft by the task force for this guideline as well as the Practice Committee, this document was reviewed by ASRM executive leadership. The document then proceeded to a 15-day period of open review by ASRM members, which includes patient advocates, genetic counselors, mental health professionals, nursing professionals, legal professionals, laboratory personnel, research scientists, and physicians boarded in one or more specialties. The ASRM Board of Directors also reviewed the document over a period of 15 days. The input of all was considered in the preparation of the final document.

Patient/Public Perspective: To incorporate perspectives of those who might be affected most by the recommendations in this guideline, a group of patient volunteers and lay stakeholders in reproductive medicine who were not involved in the scoping or development of this guideline reviewed the document. Their feedback was considered in the preparation of the final document.

Updating Policy: Document expiration: October 2024

ASRM reviews and updates or retires its evidence-based guidelines every 5 years or after significant scientific developments or change in public policy as determined by the ASRM Practice Committee.

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Resultados basados en la evidencia después de la criopreservación de ovocitos para la fecundación in vitro de ovocitos de donantes y la criopreservación planificada de ovocitos: una guía.

Objetivo: Proporcionar recomendaciones basadas en la evidencia a los médicos y otras personas relacionadas con respecto a la eficacia de la criopreservación de ovocitos (CO) para la fecundación in vitro de ovocitos de donantes y la CO planificada.

Métodos: La Sociedad Estadounidense de Medicina Reproductiva realizó una búsqueda bibliográfica, que incluyó revisiones sistemáticas, metaanálisis, ensayos controlados aleatorios y estudios observacionales comparativos prospectivos y retrospectivos publicados desde 1986 a 2018. El Comité de Práctica de la Sociedad Estadounidense de Medicina Reproductiva y un grupo de trabajo de los expertos utilizaron la evidencia disponible y, mediante consenso, desarrollaron recomendaciones de guías basadas en la evidencia.

Principales medidas de resultado: Los resultados de interés incluyeron la tasa de nacidos vivos, la tasa de embarazo clínico, los resultados obstétricos y neonatales y los factores que predicen los resultados reproductivos.

Resultado(s): La búsqueda bibliográfica identificó 30 estudios relevantes para formar la base de evidencia para esta guía.

Recomendación(es): Se desarrollaron recomendaciones basadas en la evidencia para predecir la probabilidad de nacidos vivos después de la CO planificada, la CO autóloga en mujeres infértiles y la CO de donante, así como los factores que pueden afectar las tasas de nacidos vivos. Se desarrollaron recomendaciones con respecto a los resultados neonatales después de usar ovocitos frescos versus criopreservados en casos de ovocitos autólogos o de donantes.

Conclusión (es): No hay evidencia suficiente para predecir las tasas de nacidos vivos después de la CO planificada. Sobre la base de datos limitados, las tasas de nacidos vivos y en curso parecen mejorar para las mujeres que se someten a un AO planificado a una edad más joven que a una edad mayor. Aunque no hay diferencias significativas en las tasas de embarazo por transferencia con ovocitos de donantes criopreservados versus frescos, no hay evidencia suficiente de que la tasa de nacidos vivos sea la misma con ovocitos vitrificados versus frescos de donantes. Los resultados neonatales parecen similares con los ovocitos criopreservados en comparación con los ovocitos frescos. Se necesitan estudios futuros que comparen las tasas acumuladas de nacidos vivos.