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Trends and Outcomes of Fresh and Frozen Donor Oocyte Cycles in the United States

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Abstract

Objective: To examine trends, characteristics, and outcomes of donor oocyte embryo transfer cycles by original oocyte and resultant embryo state and determine whether oocyte state (fresh or frozen) is differentially associated with clinical pregnancy, live birth, and term, normal birthweight neonates among singleton live births.

Design: Retrospective cohort study

Subjects: Patients undergoing donor oocyte embryo transfer cycles in the United States reporting to National Assisted Reproductive Technology Surveillance System (NASS) from 2013–2020

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Attestation statements: Data were obtained from the National ART Surveillance System (NASS), which collects data on nearly all ART treatments performed in the United States. The results of this analysis have not been previously published. NASS data are protected by the Assurance of Confidentiality under the Public Health Act Section 308(d). Data will be made available to the editors of the journal for review or query upon request in accordance with these confidentiality protections https://www.cdc.gov/art/nass/index.html#data.

Trial Registration: Not applicable to this study.

Exposure: Original donor oocyte and resultant embryo state (fresh or frozen)

Main Outcome Measures: Annual numbers and proportions of total donor oocyte embryo transfer cycles stratified by oocyte and embryo state and single embryo transfer cycles resulting in live birth of term (≥37 weeks gestation), normal birthweight (≥2500g) singletons during 2013–2020. Rates of live birth and term, normal birthweight neonates among singleton live births for 2018–2020 are also reported. Relative risks (RR) examine associations between donor oocyte state and live birth and term, normal birthweight neonates among singleton live births resulting from donor oocyte embryo transfer cycles.

Results: From 2013–2020, there were 135,085 donor oocyte embryo transfer cycles, of which the proportions increased for frozen embryos (42.3% to 76.6%), fresh embryos using frozen donor oocytes (19.9% to 68.3%) and single embryo transfer (SET) (36.4% to 85.5%). During 2018–2020, there were 48,679 donor oocyte embryo transfer cycles. Rates of live birth were lower with frozen compared to fresh donor oocytes for both fresh (46.2%, 55.9%; aRR 0.83 [95% CI 0.79–0.87]) and frozen (41.3%, 45.8%; aRR 0.94 [95% CI 0.91–0.98]) embryo transfer cycles. Among singleton live births, rates of delivering a term, normal birthweight neonate were similar for frozen compared to fresh donor oocyte transfer cycles among fresh (77.3, 77.2%; aRR 1.01 [95% CI 0.98–1.03]) and frozen (75.6, 75.1%; aRR 1.02 [95% CI 0.99–1.04]) embryos.

Conclusion: In this national study of donor oocyte embryo transfer cycles, frozen embryo transfers, fresh embryo transfers using frozen oocytes, and SET increased. Although frozen compared to fresh oocytes were associated with a slightly reduced rate of live birth, rates of term, normal birthweight neonates among singleton live births were comparable between donor oocyte states.

Capsule:

Donor oocyte embryo transfers increasingly use frozen embryos, frozen oocytes, and single embryo transfer; while live births were higher among fresh oocytes, term, normal birthweight live births among singletons were comparable between donor oocyte states.

Keywords

donor oocyte; cryopreservation; frozen; live birth; pregnancy outcome

Introduction

Donor oocyte embryo transfer has increased in the United States since the first donor oocyte pregnancy in 1983 (1), with 7.4% of all IVF cycles in the United States using donor eggs or embryos in 2020 (2). Donor oocytes allow patients to have a successful pregnancy even when facing issues of their own oocyte quality or quantity, such as from a genetic condition, diminished ovarian reserve, or primary ovarian insufficiency (5).

Oocyte vitrification became standard practice in 2012, and since then, using frozen donor oocytes has become an option for patients considering donor oocyte embryo transfer (6). Cryopreservation may offer benefits to women using donor oocytes, such as improved convenience, shorter preparation time, and diversity of oocyte selection (7) as

well as decreased cost (8). Accordingly, frozen donor oocyte embryo transfer has grown increasingly common and is now available at most fertility clinics (2); however, evidence regarding outcomes of frozen compared to fresh donor oocytes remains limited. A prior study suggested donor oocyte state (frozen versus fresh) has no impact on implantation, pregnancy, or live birth rates among fresh embryo transfer cycles but did not investigate perinatal outcomes such as gestational age at delivery and birthweight (9). Another study investigating donor oocyte embryo transfer cycles found that the odds of live birth and good perinatal outcome, defined as a singleton live birth at ≥37 weeks with birthweight between 2,500g and 4,000g, were slightly lower for frozen compared to fresh donor oocytes among fresh embryo transfer cycles (10). This analysis did not assess transfer cycles using frozen embryos and incorporated transfer cycles not resulting in clinical pregnancy (10), which makes interpretation of the results challenging. To our knowledge, no studies have explored outcomes for frozen embryo transfer cycles using donor oocytes. Using national surveillance data, this study examines trends, characteristics, and outcomes of donor oocyte embryo transfer by original oocyte and resultant embryo state (fresh or frozen) in the setting of increased utilization of vitrification in the United States.

Materials and Methods

Data for this study were obtained from the National ART Surveillance System (NASS), a federally mandated surveillance system established under the Fertility Clinic Success Rate and Certification Act of 1992 and maintained by the Centers for Disease Control and Prevention (CDC) (2). NASS collects data on ART procedures performed in the United States, including patient demographics; obstetric and medical history; and details of ART procedures and their outcomes (2). NASS is estimated to cover 98% of all ART procedures in the United States with data validated annually (2).

The study population included all transfer cycles involving embryos derived from donor oocytes reported to NASS from 2013–2020. The primary exposure of interest in this study was the original state of the donor oocyte and the resultant embryo (fresh or frozen). Information on oocyte state was available in NASS for fresh embryo transfer cycles beginning in 2013 but was limited before 2018 for frozen embryo transfer cycles; therefore, some analyses were limited to cycles reported to NASS during 2018–2020 to stratify by oocyte and embryo state. Transfer cycles involving a combination of fresh and frozen embryos, gestational carriers, and donated embryos (embryos donated by another patient or couple who previously underwent ART treatment and had extra embryos available) were excluded.

We first examined the total annual number of ART transfer cycles as well as trends in numbers and proportions of donor oocyte embryo transfer cycles during 2013–2020, including the annual number of these cycles overall and stratified by embryo state. We examined the proportion of donor oocyte embryo transfer cycles using fresh embryos stratified by oocyte state and the percentage of all donor oocyte embryo transfer cycles involving single embryo transfer (SET) and resulting in live birth that were singleton, term (≥37 weeks of gestation), and normal birthweight (≥2500g) live births. Finally, among donor oocyte embryo transfer cycles using fresh embryos, we calculated the proportions of transfer

cycles that resulted in live births of term, normal birthweight singletons stratified by oocyte state.

We then described characteristics of donor oocyte embryo transfer cycles during 2018–2020 stratified by oocyte and embryo state, including donor and recipient demographics, egg retrieval characteristics, recipient obstetric history and treatment cycle characteristics. A multiple imputation approach was used to address missing data on recipient race and ethnicity in NASS (11).

Finally, we investigated cycle outcomes stratified by original oocyte and resultant embryo state for donor oocyte embryo transfer cycles during 2018–2020. NASS defines clinical pregnancy as an ultrasound-confirmed presence of one or more intrauterine gestational sacs with or without heartbeat and/or fetal pole or by documented birth (still or live), miscarriage, or induced abortion. This definition excludes transfer cycles resulting in biochemical pregnancy or ectopic pregnancy. Live birth was defined as delivery of one or more infants with at least one born alive at ≥20 weeks of gestation. Miscarriage was defined as loss of a clinical pregnancy occurring at <20 weeks of gestation. We calculated clinical pregnancy and live-birth rates among transfer cycles, miscarriage rates among clinical pregnancies, multiples rates among live births, and rates of term (≥37 weeks of gestation), normal birthweight (birthweight of ≥2500g) neonates among singleton live births. To assess whether each of these outcomes was differentially associated with donor oocyte state (fresh or frozen) prior to fertilization, predicted marginal proportions were calculated from logistic regression models to estimate unadjusted and adjusted relative risks comparing frozen to fresh oocytes for each outcome. Separate models were constructed for fresh and frozen embryo transfer cycles, controlling for the following covariates: recipient age, recipient race/ethnicity, recipient BMI, infertility diagnoses (diagnoses are not mutually exclusive and include diminished ovarian reserve, tubal factor, endometriosis, uterine factor, ovulation disorder including polycystic ovaries, male factor, unexplained infertility, and other), history of prior pre- and full-term births, number of prior spontaneous miscarriages, number of prior ART cycles, use of pre-implantation genetic testing, intracytoplasmic sperm injection (ICSI, included only for fresh embryo transfer cycles), and assisted hatching. A missing category was created for BMI to retain all observations in the multivariable models. Due to small sample size, recipient race/ethnicity for Non-Hispanic Native Hawaiian or other Pacific Islander, American Indian/Alaska Native, and two or more races were combined into one category. Oocyte donor age and embryo stage at transfer could not be included in the models due to significant missing data. We also conducted a sensitivity analysis for live birth and term, normal birthweight neonates among singleton live births limited to transfer cycles where only one embryo was transferred.

All analyses were conducted using SAS version 9.4 (SAS Institute) and SUDAAN 11.0.3 (RTI International). Epidemiological research using NASS data is approved by the Institutional Review Board at the CDC.

Results

Trends 2013–2020

From 2013–2020, there were 1,237,607 total ART transfer cycles in in the United States, and of these, 135,085 were donor oocyte embryo transfer cycles (Figure 1A). The annual number of donor oocyte embryo transfer cycles remained relatively stable from 2013 to 2019 (range: 17,021–17,484) but decreased to 14,511 in 2020; however, the percent of donor oocyte embryo transfers among all ART transfer cycles decreased in the same period from 12.4 to 8.8%. The absolute number and proportion of frozen embryo transfer cycles among all donor oocyte embryo transfer cycles increased from 7,208 (42.3%) in 2013 to 11,119 (76.6%) in 2020, while fresh embryo transfer cycles decreased from 9,829 (57.7%) to 3,384 (23.3%) (Figure 1B). Among fresh embryo transfer cycles during this period, the proportion using a frozen donor oocyte increased from 19.9% to 68.3%, while the proportion using a fresh oocyte decreased from 80.1% to 31.7% (Figure 1C).

While the proportion of all donor oocyte embryo transfer cycles utilizing SET increased from 36.4% in 2013 to 85.5% in 2020 (Figure 2A), the proportion of all donor oocyte SET cycles resulting in live birth of term, normal birthweight singletons remained relatively stable (32.5–34.6%) during the same period (Figure 2B). Furthermore, when examining these trends by original oocyte state (fresh or frozen) among fresh donor oocyte SET cycles, the proportions of fresh donor oocyte SET cycles resulting in live birth of term, normal birthweight singletons also remained relatively stable during 2013–2020 (ranging from 41.7–43.1% for fresh oocytes and from 33.3–36.8% for frozen oocytes) (Figure 2C).

Donor, Recipient, and Treatment Characteristics 2018–2020

There were 48,679 donor oocyte embryo transfer cycles during 2018–2020 in the United States (Table 1). Most donor oocyte embryo transfer cycles involved fresh oocyte/frozen embryos (53.0%), followed by frozen oocyte/frozen embryos (20.6%), frozen oocyte/fresh embryos (16.4%), and fresh oocyte/fresh embryos (10.0%).

The mean age of oocyte donors was 26.8 (SD = 3.9) years; however, donor age was missing for 35% of donor oocyte embryo transfer cycles (n = 16,979), a higher proportion of which were for embryos derived from frozen oocytes (56% versus 22% for embryos derived from fresh oocytes). Donor oocyte retrieval cycle characteristics were available for fresh oocyte/fresh embryo transfer cycles only. The mean number of oocytes retrieved per fresh oocyte/fresh embryo transfer cycle was 22.9 (SD = 11.6).

The mean age for oocyte recipients was 42.0 years (SD = 5.4). The majority of donor oocyte recipients were Non-Hispanic White (62.5%), followed by Non-Hispanic Asian (16.6%), Non-Hispanic Black (9.9%), and Hispanic (9.5%). Less than one percent were American Indian or Alaska Native, Non-Hispanic Native Hawaiian or other Pacific Islander, or two or more races. Three out of four donor oocyte recipients reported a diagnosis of diminished ovarian reserve (76.3%), and the majority had no prior births (61.2%) but had prior ART cycles (82.2%), 2.9 (SD = 3.1) prior ART cycles on average.

Among all donor oocyte embryo transfer cycles, pre-implantation genetic testing (PGT) was used in 32.0%; more specifically, PGT was used in 5.9% of fresh/fresh, 2.0% of frozen/fresh, 46.9% in fresh/frozen, and 31.4% of frozen/frozen donor oocyte embryo transfer cycles. More than one embryo was transferred in 18.9% of donor oocyte embryo transfer cycles. Among donor oocyte embryo transfer cycles for which embryo stage was known (22.2% missing stage), most embryos were transferred at days 5–7 (92.5%).

Outcomes 2018–2020

Among all donor oocyte embryo transfer cycles, fresh oocyte/fresh embryos had the highest rates of pregnancy (66.1%) and live birth (55.9%), though it is notable this was the least frequent category (Table 1), while frozen oocyte/frozen embryos had the lowest rates of pregnancy (51.4%) and live birth (41.3%) (Table 2). Among pregnancies, the miscarriage rate was lowest for fresh oocyte/fresh embryo (14.3%) and highest for frozen oocytes/frozen embryo (18.5%) transfer cycles. Among live births, the rate of multiple births was highest for fresh oocyte/fresh embryo transfer cycles (12.9%), followed by frozen oocyte/fresh embryo (8.9%), fresh oocyte/frozen embryo (7.8%), and frozen oocyte/frozen embryo (5.2%) transfer cycles. The proportion of singleton live births resulting in term, normal birthweight neonates was consistent by oocyte and embryo state (75.1%–77.3%).

Among donor oocyte embryo transfer cycles from 2018–2020, the rate of clinical pregnancy was significantly lower for frozen versus fresh oocytes among fresh embryo transfer cycles (aRR 0.85 [95%. CI 0.82–0.89]) and frozen embryo transfer cycles (aRR [0.95 [95% CI 0.93–0.98]) (Table 2). Similarly, the rate of live birth was significantly lower using frozen versus fresh oocytes among fresh embryo transfer cycles (aRR 0.83 [95% CI 0.79–0.87]) and frozen embryo transfer cycles (aRR 0.94 [95% CI 0.91–0.98]). Among all clinical pregnancies resulting from fresh embryo transfer cycles, the risk of miscarriage was significantly higher among cycles using frozen as compared with fresh donor oocytes (aRR 1.18 [95% CI 1.04–1.32]); however, among clinical pregnancies resulting from frozen embryo transfer cycles, risk of miscarriage did not differ by oocyte state after controlling for potential confounders (aRR 1.07 [95% CI 0.99–1.15]). Among cycles resulting in singleton live births, donor oocyte state was not associated with a difference in the adjusted relative rate of delivering a term, normal birthweight neonate among either fresh or frozen embryo transfer cycles (aRR 1.01 [95% CI 0.98–1.03] and aRR 1.02 [95% CI 0.99–1.04], respectively). In sensitivity analyses of cycles involving transfer of a single embryo (9,738 fresh embryo transfer cycles and 29,489 frozen embryo transfer cycles), donor oocyte state was not associated with adjusted relative risk of live birth for either fresh or frozen donor oocyte embryo transfer cycles. While the sensitivity analysis demonstrated a slightly lower rate of delivering a term, normal birthweight neonate for frozen versus fresh donor oocytes with fresh embryo transfer among singleton live births (aRR 0.95 [95% CI 0.92–0.99]), donor oocyte state was not associated with term, normal birthweight neonate among singleton live births resulting from frozen embryo transfer (aRR 1.00 [95% CI 0.97–1.03]).

Discussion

The absolute number of donor oocyte embryo transfers remained stable from 2013–2019 with a decrease in 2020 coinciding with the onset of the COVID-19 pandemic (12). During the same period, the proportion of donor oocyte embryo transfers using frozen embryos as well as the proportion of fresh donor embryo transfer cycles using frozen oocytes increased. These trends occurred alongside a rise in the proportion of single embryo transfers among all donor oocyte embryo transfer cycles. Although the rate of clinical pregnancy and live birth were slightly lower for frozen versus fresh donor oocytes for both fresh and frozen embryo transfers, term, normal birthweight neonates among the resultant singleton live births were comparable for fresh and frozen oocytes with either embryo state.

Because oocyte cryopreservation is no longer considered experimental and has become an option at 99% of clinics (2), patients may increasingly choose frozen donor oocyte embryo transfer when considering fertility options. The increasing use of SET reflects improved adherence to the American Society for Reproductive Medicine's (ASRM) recommendations (5, 13). The growing use of SET may also reflect limited embryo availability in the setting of an increased proportion of frozen oocyte use among fresh embryos 2013–2020; however, the data regarding frozen oocyte among frozen embryos is not available for this period due to missing oocyte state data among frozen embryos before 2018 in NASS.

Factors other than cryopreservation, such as embryo quality, may have influenced success rates of SET cycles. Among SET cycles from 2013–2020 using fresh embryos, frozen compared to fresh donor oocytes consistently yielded lower proportions of singleton live births resulting in term, normal birthweight neonates. During 2018–2020, the rate of multiple births among live births resulting from donor oocyte transfer cycles ranged from 5.2%–12.9%, notably lower than the twin birth rate of 37% among fresh embryo cycles using either fresh or frozen donor oocytes in 2010 described in a previous analysis, (14) though these rates may not be directly comparable. This trend likely also reflects increasing compliance with ASRM guidelines (5,13).

Nearly one-third (32.0%) of donor oocyte embryo transfer cycles in 2018–2020 used PGT. Patients and clinicians may choose PGT to improve chances of transferring a 'good' quality embryo; however, evidence does not support PGT as standard practice for embryos resulting from donor oocytes. The impact of PGT on donor oocyte cycles remains unknown (15) and has not been shown to be cost-effective for fresh donor oocytes (16) or improve the odds of a live birth for frozen donor oocytes (17). Additionally, oocyte donors falling within the ASRM recommended age range of 21–34 years (5) generally have a lower risk of aneuploidy (17) compared to oocytes from patients of advanced maternal age, who are frequently oocyte recipients. In the present study, the mean age of recipients in 2018–2020 was 42.0 years, only one year greater than the mean age of recipients reported in 2010 (14). Over one third of donor oocyte recipients were over the age of 45; however, only 0.6% of transfers occurred over the age of 55, which remains consistent with ASRM Ethics Committee Recommendations (19).

Our finding that term, normal birthweight neonates among singleton live births are similar between fresh and frozen oocytes for either state of embryo is consistent with a previous study among donor oocyte fresh embryo transfer cycles (10) but existing evidence regarding pregnancy outcomes is limited (9,10). We selected term, normal birthweight neonates among singleton live births as our primary outcome (10, 13, 14, 20). Although this analysis suggests that frozen compared to fresh donor oocyte state may be associated with a slightly lower chance of clinical pregnancy and live birth, factors other than oocyte cryopreservation may explain this finding, such as inability to control for embryo quality or the number of available donor oocytes, which is not collected in NASS. While the number of oocytes retrieved was greater than 10 in most fresh donor oocyte transfer cycles (Table 1), frozen donor oocytes are typically purchased in small batches of about six oocytes (7). As a result, patients choosing frozen donor oocyte embryo transfer may have limited oocyte and subsequent embryo options resulting in lower-quality embryos for transfer. Decreased embryo quality may also explain the increased rate of miscarriage among fresh embryo transfer cycles using frozen compared to fresh oocytes. Although previous work found that the rate of singleton live birth at ≥37 weeks with birthweight between 2,500g and 4,000g, was unaffected by the number of available oocytes (10), authors found a diminished proportion of high-quality embryos among those using frozen donor oocytes. Overall, selection bias due to reduced embryo quality among transfer cycles using frozen oocytes may have influenced outcomes.

This study has several limitations. First, describing trends among frozen embryos using donor oocytes was not possible since NASS only began capturing information regarding oocyte state for cryopreserved embryos in 2018. Second, as a retrospective cohort study, these analyses are limited by missing data. The age for a large proportion of oocyte donors was missing; however, since most oocyte donors are selected in accordance with the ASRM recommended age range of 21–34 years (5), missing values likely follow a similar pattern of selection. In this study, 96.3% of oocyte donors with known age were <35 years old. The larger proportion of missing age of donor data for transfer cycles using frozen compared to fresh oocytes may reflect the challenges of data sharing between clinics that performed donor oocyte retrieval and cryopreservation and recipient clinics that enter data in NASS. Other characteristics of oocyte donor cycles were restricted to transfer cycles using fresh donor oocytes or embryos. As a result of missing data, several covariates were either excluded from the multivariable analysis (e.g., donor age, embryo stage at transfer), retained with missing data (e.g., BMI), or included for only fresh embryo transfers (e.g., ICSI). In addition, previous efforts by Zhang et al. to multiply impute patient race and ethnicity in NASS allowed for inclusion of this information despite missing data for over 30% of patients (11). Third, we were unable to control for some additional variables such as oocyte availability and embryo quality because of large amounts of missing data. Finally, although we did not compare all four oocyte and embryo states simultaneously, we felt that potential unknown confounders were better addressed by comparing outcomes within one state of embryo and eliminated the problem of selecting a sole reference group.

The use of a national surveillance system including almost all ART procedures in the United States strengthens the generalizability of this study. Controlling for all confounding variables available in NASS for which there were sufficient data, as well as using a multiple

imputation approach for missing race and ethnicity, also improves the study validity. Restriction of the outcomes analysis to the years 2018–2020 reflects current practices regarding donor oocyte embryo transfer cycles. To our knowledge, our study is also the first to investigate transfer cycle outcomes by donor oocyte state for frozen embryos. Finally, our focus on patient-centered outcomes— live birth and the delivery of normal birthweight, term neonates among singleton live births— provides practical clinical insight that will aid patients and clinicians considering donor oocytes as a fertility treatment.

Conclusions

National IVF surveillance data through 2020 suggests that patients selecting donor oocytes increasingly utilize frozen versus fresh embryos among all embryo transfers, frozen versus fresh oocytes among fresh embryo transfers, and single embryo transfer. Although frozen compared to fresh donor oocyte state was associated with decreased likelihood of clinical pregnancy and live birth, singleton term normal weight births following donor oocyte embryo transfer appear similar regardless of the donor oocyte state.

The impact of oocyte state on cycle and pregnancy outcomes in addition to other factors such as cost, timing, and oocyte pool diversity can be considered. While the pregnancy and live birth rates may be impacted slightly by oocyte state with some benefit to fresh donor oocyte embryo transfer (likely due to the increased number of oocytes and resultant embryos, allowing for selection of the best quality embryo), the outcome of singleton term normal weight births appear similar regardless of the donor oocyte state. Physicians and patients can make an individualized, informed decision based on the patient's unique situation and goals.

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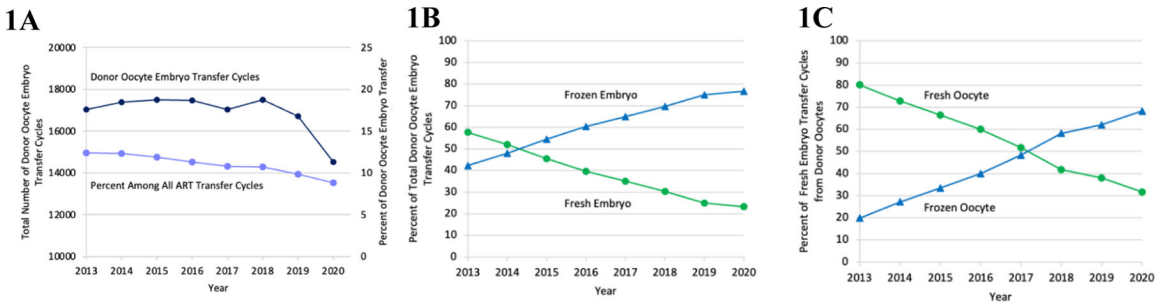

Figure 1. Trends in Donor Oocyte Embryo Transfer Cycles in the United States, 2013–2020

(A) Total Absolute Number of Donor Oocyte Embryo Transfer Cycles and Percent of Donor Oocyte Embryo Transfer Cycles Among All ART Transfer Cycles (B) Proportion of Donor Oocyte Embryo Transfer Cycles using Frozen versus Fresh Embryos (C) Proportion of Fresh Embryo Transfer Cycles using Frozen versus Fresh Donor Oocytes

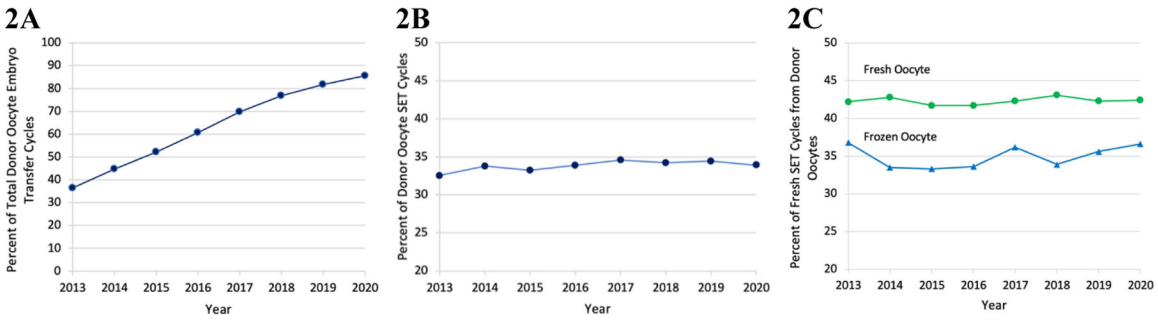

Figure 2. Trends in Single Embryo Transfer (SET) and Perinatal Outcomes Among Donor Oocyte Embryo Transfer Cycles in the United States, 2013–2020

(A) Proportion of Donor Oocyte Embryo Transfer Cycles Utilizing SET **(B)** Proportion of Donor Oocyte SET Cycles Resulting in Singleton Live Births at ≥37 Weeks and Birthweight of ≥2,500 g **(C)** Proportion of Fresh Donor Oocyte Embryo Transfer Cycles Utilizing SET Cycles Resulting in Singleton Live Births at ≥37 Weeks and Birthweight of ≥2,500 g for Fresh and Frozen Donor Oocytes

Table 1:

Characteristics of Embryo Transfer Cycles Derived from Donor Oocytes by Oocyte and Embryo State, 2018–2020

Characteristics	**Total Number (%)[a]**	**Fresh oocyte, Fresh embryo N (%)**	**Frozen oocyte, Fresh embryo N (%)**	**Fresh oocyte, Frozen embryo N (%)**	**Frozen oocyte, Frozen embryo N (%)**
	48679	4871 (10.0%)	7983 (16.4%)	25814 (53.0%)	10011 (20.6%)
Donor and Egg Retrieval Characteristics					
Oocyte donor age, years					
Mean (SD)	26.8 (3.9)	27.0 (3.7)	26.0 (3.3)	27.0 (4.0)	26.2 (3.6)
<30	25050 (79.0%)	3292 (77.5%)	3110 (85.3%)	15097 (77.1%)	3551 (84.1%)
30–34	5469 (17.3%)	810 (19.1%)	509 (14.0%)	3560 (18.2%)	590 (14.0%)
35–37	693 (2.2%)	95 (2.2%)	16 (0.4%)	545 (2.8%)	37 (0.9%)
38–40	332 (1.1%)	40 (0.9%)	8 (0.2%)	266 (1.4%)	18 (0.4%)
41–42	86 (0.3%)	8 (0.2%)	f	66 (0.3%)	f
43–44	23 (0.1%)	f	f	15 (0.1%)	f
≥45	47 (0.2%)	f	f	34 (0.2%)	12 (0.3%)
Missing	16979	624	4335	6231	5789
Stimulation protocol [b]					
Unstimulated		544 (11.3%)			
LH/HCG		322 (6.7%)			
FSH		3799 (78.6%)			
GnRH Agonist suppression		17 (0.4%)			
GnRH Agonist flare		7 (0.1%)			
GnRH Antagonist suppression		145 (3.0%)			
Missing		37			
Number of oocytes retrieved [b]					
Mean (SD)		22.9 (11.6)			
1–10		646 (13.3%)			
11–23		2187 (44.9%)			
≥24		2038 (41.8%)			
Recipient Characteristics					
Recipient age					
Mean (SD)	42.0 (5.4)	40.8 (5.6)	41.9 (5.1)	42.0 (5.5)	42.5 (5.1)
<35	4776 (9.8%)	702 (14.4%	691 (8.7%)	2638 (10.2%)	745 (7.4%)
35–37	4533 (9.3%)	528 (10.8%)	723 (9.1%)	2465 (9.6%)	817 (8.2%)
38–40	7275 (14.9%)	817 (16.8%)	1251 (15.7%)	3781 (14.6%)	1426 (14.2%)
41–42	7295 (15.0%)	759 (15.6%)	1380 (17.3%)	3588 (13.9%)	1568 (15.7%)
43–44	8528 (17.5%)	806 (16.6%)	1584 (19.8%)	4318 (16.7%)	1820 (18.2%)
45–54	15977 (32.8%)	1241 (25.4%)	2313 (29.0%)	8849 (34.3%)	3574 (35.7%)

Characteristics	**Total Number (%)[a]**	**Fresh oocyte, Fresh embryo N (%)**	**Frozen oocyte, Fresh embryo N (%)**	**Fresh oocyte, Frozen embryo N (%)**	**Frozen oocyte, Frozen embryo N (%)**
≥55	295 (0.6%)	18 (0.4%)	41 (0.5%)	175 (0.7%)	61 (0.6%)
Race/ethnicity					
Non-Hispanic White	30446 (62.6%)	3133 (64.3%)	5120 (64.1%)	16081 (62.3%)	6113 (61.1%)
Non-Hispanic Asian	8086 (16.6%)	674 (13.8%)	991 (12.4%)	4856 (18.8%)	1566 (15.6%)
Non-Hispanic Black	4805 (9.9%)	492 (10.1%)	962 (12.0%)	2171 (8.4%)	1180 (11.8%)
Hispanic	4646 (9.5%)	498 (10.2%)	806 (10.1%)	2341 (9.1%)	1000 (10.0%)
Two or more races	377 (0.8%)	39 (0.8%)	57 (0.7%)	211 (0.8%)	70 (0.7%)
American Indian, Alaska Native	160 (0.3%)	15 (0.3%)	23 (0.3%)	87 (0.3%)	36 (0.4%)
Non-Hispanic Native Hawaiian or other Pacific Islander	159 (0.3%)	20 (0.4%)	24 (0.3%)	68 (0.3%)	47 (0.5%)
Recipient BMI at transfer					
<18.5	777 (1.9%)	57 (1.4%)	104 (1.5%)	492 (2.3%)	124 (1.5%)
18.5–24.9	18680 (46.2%)	1823 (43.1%)	2910 (43.0%)	10346 (48.5%)	3601 (44.4%)
25.0–29.9	11152 (27.6%)	1268 (30.0%)	1989 (29.4%)	5645 (26.5%)	2250 (27.7%)
≥30	9824 (24.3%)	1079 (25.5%)	1771 (26.1%)	4838 (22.7%)	2136 (26.3%)
Missing	8246	644	1209	4493	1900
Infertility diagnosis [c]					
Tubal factor	3567 (7.3%)	404 (8.3%)	580 (7.3%)	1800 (7.0%)	783 (7.8%)
Endometriosis	2458 (5.1%)	273 (5.6%)	374 (4.7%)	1302 (5.0%)	509 (5.1%)
Uterine factor	3076 (6.3%)	214 (4.4%)	447 (5.6%)	1706 (6.6%)	709 (7.1%)
Ovulatory disorder	2856 (5.9%)	333 (6.8%)	448 (5.6%)	1558 (6.0%)	517 (5.2%)
Diminished ovarian reserve	37141 (76.3%)	3643 (74.8%)	6203 (77.7%)	19497 (75.5%)	7798 (77.9%)
Male factor	7822 (16.1%)	790 (16.2%)	1210 (15.1%)	4159 (16.1%)	1663 (16.6%)
Other	11720 (24.1%)	1007 (20.7%)	1439 (18.0%)	7087 (27.5%)	2187 (21.9%)
Unexplained	2073 (4.3%)	193 (4.0%)	383 (4.8%)	1002 (3.9%)	495 (4.9%)
Number of prior ART cycles					
Mean (SD)	2.9 (3.1)	1.9 (2.6)	2.0 (2.6)	3.4 (3.2)	3.1 (3.4)
0	8679 (17.8%)	2070 (42.5%)	2938 (36.8%)	2425 (9.4%)	1246 (12.5%)
1	10279 (21.1%)	788 (16.2%)	1409 (17.7%)	5817 (22.5%)	2265 (22.6%)
2–5	22181 (45.6%)	1595 (32.7%)	2884 (36.1%)	12802 (49.6%)	4900 (49.0%)
6–10	6349 (13.0%)	350 (7.2%)	633 (7.9%)	3998 (15.5%)	1368 (13.7%)
11+	1191 (2.5%)	68 (1.4%)	119 (1.5%)	772 (3.0%)	232 (2.3%)
Number of prior spontaneous miscarriages					
0	29792 (61.2%)	3286 (67.5%)	5118 (64.1%)	15542 (60.2%)	5846 (58.4%)
1	11335 (23.3%)	970 (19.9%)	1742 (21.8%)	6138 (23.8%)	2485 (24.8%)
≥2	7552 (15.5%)	615 (12.6%)	1123 (14.1%)	4134 (16.0%)	1680 (16.8%)
Number of prior births					
0	29790 (61.2%)	3624 (74.4%)	5472 (68.6%)	14784 (57.3%)	5910 (59.0%)

Characteristics	**Total Number (%)[a]**	**Fresh oocyte, Fresh embryo N (%)**	**Frozen oocyte, Fresh embryo N (%)**	**Fresh oocyte, Frozen embryo N (%)**	**Frozen oocyte, Frozen embryo N (%)**
≥1	18889 (38.8%)	1247 (25.6%)	2511 (31.4%)	11030 (42.7%)	4101 (41.0%)
Number of prior preterm births					
0	45774 (94.0%)	4730 (97.1%)	7672 (96.1%)	24017 (93.0%)	9355 (93.5%)
≥1	2905 (6.0%)	141 (2.9%)	311 (3.9%)	1797 (7.0%)	656 (6.5%)
Number of prior full-term births					
0	31732 (65.2%)	3718 (76.3%)	5663 (70.9%)	15993 (62.0%)	6358 (63.5%)
1	12145 (24.9%)	773 (15.9%)	1458 (18.3%)	7257 (28.1%)	2657 (26.5%)
≥2	4802 (9.9%)	380 (7.8%)	862 (10.8%)	2564 (9.9%)	996 (10.0%)
Treatment Cycle Characteristics					
Use of ICSI					
Yes	31691 (90.6%)	4204 (86.4%)	7902 (99.0%)	18346 (88.4%)	1239 (89.8%)
No	3292 (9.4%)	663 (13.6%)	78 (1.0%)	2410 (11.6%)	141 (10.2%)
Missing	13696	4	3	5058	8631
Use of assisted hatching					
Yes	47389 (97.6%)	4629 (95.4%)	7786 (98.1%)	25208 (97.9%)	9766 (97.7%)
No	1145 (2.4%)	222 (4.6%)	150 (1.9%)	541 (2.1%)	232 (2.3%)
Missing	145	20	47	65	13
Use of PGT					
Yes	15571 (32.0%)	287 (5.9%)	158 (2.0%)	11981 (46.4%)	3145 (31.4%)
No	32805 (67.4%)	4584 (94.1%)	7769 (97.3%)	13653 (52.9%)	6799 (67.9%)
Number of embryos transferred					
1	39488 (81.1%)	3593 (73.8%)	6195 (77.6%)	20977 (81.3%)	8723 (87.1%)
2	8912 (18.3%)	1246 (25.6%)	1737 (21.8%)	4701 (18.2%)	1228 (12.3%)
≥3	279 (0.6%)	32 (0.7%)	51 (0.6%)	136 (0.5%)	60 (0.6%)
Embryo stage at transfer [b]					
Days 2–4		283 (7.5%)			
Days 5–7		3503 (92.5%)			
Missing		1085			
Number of fetal heartbeats at first ultrasound					
0	2056 (7.8%)	196 (6.2%)	341 (7.6%)	1074 (7.6%)	445 (8.8%)
1	22470 (83.9%)	2561 (80.5%)	3708 (83.1%)	11841 (84.2%)	4360 (85.9%)
2	2200 (8.2%)	408 (12.8%)	401 (9.0%)	1124 (8.0%)	267 (5.3%)
≥3	64 (0.2%)	17 (0.5%)	12 (0.3%)	29 (0.2%)	6 (0.1%)
N/A[d]	21889	1689	3521	11746	4933
Plurality					

Characteristics	**Total Number (%)[a]**	**Fresh oocyte, Fresh embryo N (%)**	**Frozen oocyte, Fresh embryo N (%)**	**Fresh oocyte, Frozen embryo N (%)**	**Frozen oocyte, Frozen embryo N (%)**
1	20537 (91.9%)	2366 (87.1%)	3372 (91.2%)	10901 (92.3%)	3898 (94.8%)
2	1762 (7.8%)	341 (12.6%)	319 (8.6%)	891 (7.6%)	211 (5.1%)
3	37 (0.2%)	10 (0.4%)	7 (0.2%)	15 (0.1%)	5 (0.1%)
N/A[e]	26343	2154	4285	14007	5897

Note: Missing shown for all characteristics with >5% missing values but not included in the denominators; for remainder of characteristics <1% were missing.

Abbreviations: SD = standard deviation, LH/HCG = luteinizing hormone/human chorionic gonadotropin, FSH = follicle stimulating hormone, GnRH = gonadotropin-releasing hormone, BMI = body mass index, ART = assisted reproductive technology; ICSI = intracytoplasmic sperm injection; PGT = preimplantation genetic testing, N/A = not applicable.

[a]Percentages based on cycles with known information.

[b]Available for fresh oocyte/fresh embryo transfer cycles only.

[c]Infertility diagnosis categories are not mutually exclusive.

[d]Not applicable refers to transfer cycles that did not result in clinical pregnancy.

[e]Not applicable refers to transfer cycles that did not result in birth.

[f]To protect confidentiality, cells with values of 1–4 f are suppressed. Also suppressed are data that can be used to derive suppressed cell values. These values are included in totals.

Table 2:

Comparing Outcomes of Frozen Versus Fresh Donor Oocytes in Fresh and Frozen Embryo Transfer Cycles, 2018–2020

Outcome	FRESH EMBRYO TRANSFER CYCLES				FROZEN EMBRYO TRANSFER CYCLES			
	Oocyte State		Relative Risk [95% CI][a]		Oocyte State		Relative Risk [95% CI][a]	
	Frozen	Fresh			Frozen	Fresh		
	Number (%)		RR	aRR[b]	Number (%)		RR	aRR[b]
Among transfers								
Clinical pregnancy	4469 (56.3%)	3198 (66.1%)	0.85* (0.82–0.89)	0.85* (0.82–0.89)	5092 (51.4%)	14267 (55.6%)	0.92* (0.90–0.95)	0.95* (0.93–0.98)
Live birth	3666 (46.2%)	2702 (55.9%)	0.83* (0.79–0.87)	0.83* (0.79–0.87)	4087 (41.3%)	11732 (45.8%)	0.90* (0.87–0.94)	0.94* (0.91–0.98)
Among clinical pregnancies								
Miscarriage	740 (16.6%)	456 (14.3%)	1.16* (1.04–1.30)	1.18* (1.04–1.32)	940 (18.5%)	2347 (16.5%)	1.12* (1.04–1.22)	1.07 (0.99–1.15)
Among live births								
Multiples	325 (8.9%)	348 (12.9%)	0.69* (0.56–0.85)	0.73* (0.60–0.90)	213 (5.2%)	903 (7.8%)	0.68* (0.55–0.84)	0.63* (0.51–0.79)
Among singleton live births								
≥37 weeks gestation and birthweight ≥2500 grams	2583 (77.3%)	1816 (77.2%)	1.00 (0.98–1.03)	1.01 (0.98–1.03)	2929 (75.6%)	8135 (75.1%)	1.01 (0.98–1.03)	1.02 (0.99–1.04)

Abbreviations: CI = confidence interval, RR = relative risk, aRR = adjusted relative risk.

*Significant with $\alpha = 0.05$

[a]Reference groups are fresh donor oocytes for each state of embryo transfer cycle (i.e., comparing frozen to fresh oocytes among fresh embryo transfer cycles and comparing frozen to fresh oocytes among frozen embryo transfer cycles.)

[b]Covariates in the adjusted models include recipient age, recipient race/ethnicity, recipient BMI, infertility diagnoses, history of prior births, number of prior spontaneous miscarriages, number of prior ART cycles, and use of pre-implantation genetic testing, ICSI (included in model for fresh embryos only) or assisted hatching.