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4.22.2020

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**The effect of donor and recipient race on outcomes of assisted reproduction using data
from a vitrified donor oocyte bank**

By

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Master of Public Health

Epidemiology

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By

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B.S

Beijing University of Chemical Technology

2018

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Abstract

The effect of donor and recipient race on outcomes of assisted reproduction using data from a vitrified donor oocyte bank

By Yijun Liu

Study question: Does the race of female oocyte donors and recipients affect live birth rates and pregnancy outcomes following vitrified donor oocyte ART?

What is known already: A growing literature suggest that minority races- particularly Black women- have lower probability of live birth and worse pregnancy outcomes after autologous ART; however, questions still remain as to whether these racial disparities are due to differences in oocyte/embryo quality, an impaired uterine environment, or a combination of the two. Oocyte donation ART represents a unique approach to examine this question.

Study design, size, duration: This was a retrospective study conducted at a private fertility clinic that included 327 oocyte donors and 899 oocyte recipients who underwent a total of 1601 embryo transfer cycles between 2008 and 2015. All embryo transfer cycles included in this study used oocytes that were cryopreserved via vitrification for an oocyte bank and later thawed for recipients' use.

Participants/materials, setting, methods: Self-reported race of the donor and recipient and clinical endpoints were abstracted from medical records. The primary outcome was live birth, which was defined as the delivery of at least one live born neonate in a given embryo transfer cycle. We used multivariable cluster weighted generalized estimating equations with binomial distribution and log link function to evaluate the association between donor and recipient race on ART outcomes adjusted for donor age and BMI, recipient age and BMI, tubal and uterine factor infertility, and year.

Main results and the role of chance: Women who received oocytes from Hispanic donors had significantly higher probability of positive pregnancy test (RR 1.10, 95% CI 1.01, 1.20) and live birth (RR 1.20, 95% CI 1.05, 1.36) compared with women who received oocytes from White donors. Embryo transfer cycles with oocytes from Black donors (RR 0.86, 95% CI 0.72, 1.03) and Black recipients (RR 0.84, 95% CI 0.71, 0.99) had a lower probability of live birth compared to their White counterparts. There was no significant difference in the probability of live birth among Hispanic, Asian, and Other race recipients compared with White recipients.

Keywords: oocyte donor, oocyte recipient, race, ethnicity, in vitro fertilization, pregnancy, live birth.

Length: 340 words

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**The effect of donor and recipient race on outcomes of assisted reproduction using data
from a vitrified donor oocyte bank**

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Introduction

The use of assisted reproductive technology (ART) has become increasingly prevalent in the United States. From 2007 to 2016, the number of initiated ART cycles increased 39%, from 142,435 cycles to 197,737 cycles; ART pregnancies now account for 2% of all infants born in the United States (Centers for Disease Control and Prevention, 2018; Sunderam et al., 2019). Using national data from the Society for Assisted Reproductive Technology (SART) Clinical Outcome Reporting System (CORS), multiple studies have documented the existence of racial disparities in live birth rates and pregnancy outcomes among women undergoing autologous ART (Wellons et al., 2012). Across all of these analyses, White women consistently had the highest probability of live birth, followed by Hispanic, Asian, and Black women (Baker et al., 2010; Fujimoto et al., 2010; Luke et al., 2011; Seifer, Frazier, & Grainger, 2008; Seifer, Zackula, & Grainger, 2010). While the ability to leverage this large nation-wide database is a clear strength of the SART based studies, firm conclusions on racial disparities in ART outcomes are challenging to make since over 35% of cycles lack data on race/ethnicity. In agreement with the SART findings, however, are several clinic-specific studies which have also documented that race, most often Black race, may be a strong predictor of poor autologous oocyte ART outcomes, potentially attributable to differences in infertility diagnoses and obesity rates. (Feinberg, Larsen, Catherino, Zhang, & Armstrong, 2006; McQueen, Schufreider, Lee, Feinberg, & Uhler, 2015; Sharara & McClamrock, 2000).

Although a growing body of evidence suggests that race might have impacts on fertility and obstetric outcomes, questions still remain as to whether these racial disparities are due to differences in oocyte/embryo quality, an impaired uterine environment, or a combination of the two. Oocyte donation IVF represents a unique approach to examine this question. Research on the effect of race on ART outcomes in the context of oocyte donation is sparse. A matched cohort study performed at a private infertility clinic in Spain from 2003-2008 found that Black recipients (n = 280) had a lower probability of achieving an ongoing pregnancy after oocyte donation compared to matched White recipients but there were no significant difference in outcomes between South-East Asians and White recipients (Bodri,

Guillén, López, Vernaev, & Coll, 2010). In an analysis of 17,030 third party ART cycles from SART CORS from 2004-2013, non-Hispanic Black recipients had significantly lower live birth rates following oocyte donation compared to non-Hispanic White recipients. Asian/Pacific Islander and Hispanic recipients also had slightly lower live birth rates compared to White recipients, which was largely explained by a higher rate of spontaneous abortion in these two groups. The authors were not able to adjust for potential confounding and, similar to the SART studies in autologous IVF, they had to exclude 36.9% of studies that did not have race information (Shapiro et al., 2017). Neither of these previous studies had information on the oocyte donor's race. Only one small study (n=46) compared ovarian function parameters in White and Asian oocyte donors and found a higher rate of premature ovarian aging in Asian donors regardless of age (Gleicher, Weghofer, Li, & Barad, 2007).

To date, no large study has evaluated the effects of oocyte donor's race on the recipients' pregnancy outcomes in a racially diverse cohort. This study is intended to provide new insights to the knowledge on racial disparities in ART outcomes by utilizing a unique cohort of oocyte donors and recipients where the impact of race on oocyte quality and uterine environment can be better delineated. Our aim was to evaluate how the race of oocyte donors and recipients independently affect and interact with each other to influence ART outcomes using data from a large, racially diverse vitrified donor oocyte bank.

Materials and Methods

Study Design and Inclusion Criteria

This is a retrospective study using data from a national oocyte bank in Georgia (Reproductive Biology Associates) from 2008-2015. The project was approved through the institutional review board of Emory University (Protocol #: IRB00080463). Cycles included in this study were those in which oocytes were cryopreserved via vitrification for use in an oocyte bank and later thawed for recipients' use. We excluded cycles where: 1) no embryos were transferred, 2) Agonist protocols used for ovarian stimulation,

3) information on race was missing for either the donor or recipient, 4) gestational carriers were used, or 5) pregnancy outcome was missing. After exclusions, there were 327 oocyte donors who underwent 515 oocyte retrievals and 899 oocyte recipients who underwent 1601 embryo transfer cycles included in this study.

Exposure and Covariate Assessment

At the patient's initial visit, data is collected on age, self-identified race/ethnicity (i.e. White, Black, Asian, Hispanic, South Asian/Southeast Asian, American Indian, or Other), and reproductive history (including gravidity/parity). Height and weight are measured using standardized procedures to calculate body mass index (BMI). The antagonist protocol was employed for the oocyte donors' ovarian stimulation and, approximately 39-40 hours after trigger injection, mature oocytes were cryopreserved using minimum volume vitrification (Zsolt P. Nagy et al., 2009). For each retrieval, ovarian reserve data (e.g. bilateral antral follicle count and anti-Müllerian hormone) and ovarian stimulation data (e.g. total gonadotropin dose, number of days of stimulation, number of large follicles (>14mm) at time of trigger shot, peak estradiol levels, and trigger type) were recorded.

Recipient Preparation and Outcome Assessment

Oocyte recipients were administered leuprolide acetate, estrogen, and progesterone for endometrial preparation. Recipients received a cohort of vitrified oocytes (most commonly in batches of 6-8) and, 2-3 hours after warming, the oocytes were fertilized with sperm from a male partner or a sperm donor using intracytoplasmic sperm injection (ICSI) (Z.P. Nagy et al., 1995). The resulting embryo(s) were then cultured in the lab to cleavage stage (day 3) or blastocyst stage (day 5/6). In standard fashion, the highest quality embryo(s) were transferred into the recipient's uterus first, and the rest of the embryos were cryopreserved for potential future use. Some recipients subsequently underwent multiple frozen embryo transfers using these cryopreserved embryos.

Our main outcome of interest was live birth, which was defined as the delivery of at least one live born neonate in a given embryo transfer cycle. Secondary outcomes included a positive pregnancy test, which was defined as a serum β - human chorionic gonadotropin (hCG) level >6 mIU/mL, and pregnancy loss, which was defined as the loss of a pregnancy before 20 weeks. Additional outcomes included 1) the proportion of oocytes that survived warming, 2) the proportion of warmed oocytes that fertilized, and 3) the proportion of warmed oocytes that developed into usable embryos, which was calculated by adding the number of embryos transferred and the number cryopreserved. The delivery date and birthweight were recorded among all live born infants. Gestational age in days was calculated using the American College of Obstetricians and Gynecologists guidelines: (delivery date – transfer date) + 14 + cycle day of transfer. Preterm delivery was defined as a birth prior to 37 weeks gestation and low birthweight was defined as the birth of a neonate $<2,500$ grams.

Statistical Analysis

Among the oocyte donors, we compared demographic, reproductive, and ovarian stimulation parameters at their first retrieval across categories of donor race/ethnicity. In addition, we also compared characteristics of the oocyte recipients at the time of their first embryo transfer by categories of their race/ethnicity. Chi-square tests or Fisher's Exact test were used to compute the differences across categories.

To estimate the association between donor race, recipient race, as well as the joint effect of donor-recipient race and the probability of live birth among all embryo transfer cycles, we used cluster weighted generalized estimating equations (Wheeler, Maxson, Truong, & Swamy) with binomial distribution and log link function. These models account for the correlation between multiple embryo transfer cycles within a woman and non-ignorable cluster size. Our weight was equal to the inverse of the cluster size (number of embryo transfer cycles), which helped down-weight the women with more severe infertility who tended to undergo a greater number of embryo transfer cycles. We calculated the risk ratios (RRs) of live birth comparing the risk in a specific race category (e.g. Black, Hispanic, Asian, and

Other) with the risk in the reference race category (e.g. White). We also obtained the covariate-adjusted marginal mean probability of live birth for each race/ethnicity category at the mean level of continuous covariates and most common level of categorical covariates. For the outcomes of positive pregnancy test and miscarriage we used the same analytic approach (i.e. cluster weighted GEE with binomial distribution and log link function); however, for miscarriage, the analysis was restricted to only cycles that resulted in a positive pregnancy test. Sensitivity analyses were conducted stratifying on the number of embryos transferred (1 vs. 2-3) and restricting the analyses to only blastocyst transfers, only first embryo transfers, and only recipients without uterine factor infertility.

Only singleton live births with known gestational age at delivery were considered for the analyses of birth outcomes (e.g. gestational age and birthweight). The association between the length of gestation and oocyte donor and recipient race was analyzed using a cluster weighted Cox proportional hazard model with a robust sandwich covariance estimate. For the outcome of pre-term birth, we used cluster weighted GEE with binomial distribution and log link to calculate the RRs and 95% CI. The association between donor and recipient race/ethnicity and birthweight were computed using cluster weight GEE with normal distribution and identity link function. To obtain the ORs and 95% CIs for low birthweight, a cluster weighted GEE with binomial distribution and logit link function was used. For our additional outcomes following oocyte warming (e.g. % survived, % fertilized, % usable embryos) were analyzed the associations using GEE with binomial distribution and logit link function. Data are presented as back transformed marginal percentages at the mean level of continuous covariates and most common level of categorical covariates.

Confounding was evaluated based on prior knowledge and descriptive statistics from our cohort via the use of directed acyclic graphs. We adjusted for donor age, donor BMI, recipient age, recipient BMI, tubal factor infertility, uterine factor infertility, and the year of the retrieval in our final model. All tests of statistical significance were two-sided and a significance-level of 0.05 was used. All data were analyzed using SAS 9.4 (SAS Institute Inc, Cary, NC).

Results

Our 327 oocyte donors were, on average, young (mean age of 25 years) and slim (mean BMI of 22.3 kg/m²) and were most commonly White (75%) and nulliparous (78%) (**Supplemental Table 1**). The peak estradiol was significantly higher among Black, Hispanic, Asian and Other races compared with White women. There were also slight differences in year of retrieval, BMI, parity, and total gonadotropic dose across race categories; however, all other characteristics of the donors were similar. Among our 899 donor oocyte recipients, the mean age and BMI was 42 years and 23.4 kg/m², respectively (**Supplemental Table 2**). The majority of the recipients were White (73%) and nulliparous (72%). On average, the recipients who were Black, Hispanic, and of Other races tended to be older compared with White women while Asian oocyte recipients tended to be younger. Recipient BMI also varied across races, being significantly higher for Black recipients and lower for Asian recipients compared with White recipients. Concerning infertility diagnoses, uterine and tubal factor infertility were more common among Black recipients compared with other race groups. All other characteristics were similar across recipient race categories.

The mean (standard deviation) number of oocytes received and warmed among recipients was 6.3 (1.7) and this was similar across races. The adjusted percentage of oocytes that survived warming was significantly higher for donors of Asian (94.7%) and Other races (94.9%) compared with White donors (91.4%), although differences were small (**Table 1**). There were no differences in the percentage of oocytes that fertilized across donor race categories. The proportion of warmed oocytes that developed into usable embryos was significantly higher for Black (56.9%) and Hispanic (64.5%) donors in comparison with White donors (40.9%).

Donor oocyte recipients underwent a total of 1 (56.2%), 2 (27.9%), 3 (10.3%), or 4+ (5.6%) embryo transfer cycles throughout follow-up. Most often these transfers contained a single embryo (61%) at the blastocyst stage (90%). There was a high concordance of race between oocyte donors and recipients (**Supplemental Table 3**). For instance, 96% of White recipients received oocytes from White donors, 73% of Black recipients received oocytes from Black donors, and 62% of Asian recipients received

oocytes from Asian donors. There was less concordance among Hispanic donors and recipients (32%). Among the 1601 embryo transfer cycles, 1119 (70%) resulted in a positive pregnancy test (PPT) and 777 (49%) resulted in a live birth.

After multivariable adjustment, cycles with oocytes from Hispanic donors had a significantly higher probability of PPT (RR 1.10, 95% CI 1.01, 1.20) and live birth (RR 1.20, 95% CI 1.05, 1.36) compared with White donors (**Table 2**). Among Hispanic recipients, however, there was no significant difference in probability of PPT or live birth compared with White recipients. Cycles with oocytes from Black donors (RR 0.85, 95% CI 0.75, 0.96) and Black recipients (RR 0.85, 95% CI 0.77, 0.95) had a significantly lower probability of PPT compared to their White counterparts. While there was also a suggestion of a lower probability of live birth if the donor was Black (RR 0.86, 95% CI 0.72, 1.03) these results failed to reach conventional levels of statistical significance. On the other hand, cycles in which the recipient was Black had 0.84 (95% CI 0.71, 0.99) times the probability of live birth compared with cycles where the recipient was White. There was no statistically significant difference in the probability of live birth among Hispanic, Asian, and Other races recipients compared with White recipients. Results were similar after stratifying on the number of embryos transferred (1 vs. 2-3) and restricting the analyses to only blastocyst transfers, only first embryo transfers, and only recipients without uterine factor infertility (**Supplemental Table 4**).

To further isolate the independent effect of donor and recipient race on ART outcomes, we analyzed the joint effect of donor-recipient race on live birth, with a particular focus on donor-recipient pairs that were discordant on race (**Table 3**). Recipients who used oocytes from Hispanic donors had higher probability of live birth and this effect was similar in Hispanic (RR 1.19 95% CI 0.99, 1.43) and non-Hispanic recipients (RR 1.17 95% CI 0.99, 1.38) compared to White recipients using oocytes from White donors. On the other hand, Hispanic recipients who received oocytes from non-Hispanic donors did not have a higher risk of live birth compared to White recipients using oocytes from White donors. Black recipients had a lower probability of live birth compared to White recipients using oocytes from White donors regardless of whether their oocyte donor was Black (RR 0.86 95% CI 0.72, 1.02) or non-Black

(RR 0.79 95% CI 0.56, 1.11). Although numbers were small (n=21 transfer cycles), the lowest live birth rates were observed for non-Asian recipients who utilized oocytes from Asian donors (RR 0.54 95% CI 0.34, 0.87).

Finally, we evaluated the association between donor and recipient race and birth outcomes among the 640 singleton live births in our cohort (**Table 4**). Overall, there were no associations between donor or recipient race and gestational age although many of the effect estimates were imprecise. Singleton live births resulting from Asian donors and from Asian recipients had lower birthweights compared to White donors and recipients. All other comparisons with regard to birthweight were non-statistically significant.

Discussion

Among our large cohort of oocyte donors and recipients at a vitrified donor oocyte bank, we found that the highest probability of live birth was among recipients utilizing oocytes from Hispanic donors while Black recipients had the lowest probability of live birth regardless of oocyte donor race. To our knowledge, our study was the first to evaluate the joint effect of oocyte donor and recipient race on ART outcomes following oocyte donation. Our results add to the evidence from autologous ART cycles documenting racial disparities in ART outcomes between Black and White women even after adjusting for demographic and clinical characteristics.

While Black donors in our study had a significantly higher percentage of usable embryos following oocyte warming and fertilization, they had a lower probability of positive pregnancy test and live birth following transfer compared to ART cycles using oocytes from White donors. However, virtually all of the oocytes from Black donors included in our analysis went to Black recipients, making it impossible for us to determine how oocytes from Black donors would fare in non-Black recipients. Similar to findings from previous autologous and third party ART studies, Black recipients in our study had consistently lower risk of PPT and live birth (Bodri, et al., 2010; Humphries, Chang, Humm, Sakkas, & Hacker, 2016; Sharara & McClamrock, 2000). Moreover, this lower success with oocyte donation ART persisted whether Black recipients used oocytes from Black donors (73% of transfer cycles) or oocytes

from non-Black donors (27% of embryo transfer cycles). The lower pregnancy and live birth rates among Black recipients could be due to a significantly higher prevalence of tubal diseases (47.5%) as well as uterine factor infertility (44.1%) among Black recipients, which has been documented in multiple studies (Baker, et al., 2010; Fujimoto, et al., 2010; Kawwass et al., 2013). Some studies have also suggested that increased BMI in Black recipients might contribute to the less favorable IVF outcomes (Bendikson, Cramer, Vitonis, & Hornstein, 2005; Nichols, Higdon, Crane, & Boone, 2001; Sharara & McClamrock, 2000). Yet in our study, the association between Black race and lower probability of live birth persisted after statistical adjustment for these variables, suggesting alternate pathways. While our study was not designed to evaluate potential biological mechanisms underlying these racial disparities several hypotheses have been proposed. For instance, women of African descent tend to carry more frequent genetic mutations which can impact androgen metabolism, especially the conversion of dehydroepiandrosterone to testosterone (Shapiro, et al., 2017). Black women may also experience higher levels of psychosocial stress from both perceived (e.g. sexism and racism) and tangible pressures (e.g. food scarcity or homelessness) across the life-course (Wheeler, et al., 2018), which may be associated with adverse reproductive and pregnancy outcomes (Almeida, Bécares, Erbetta, Bettegowda, & Ahluwalia, 2018; Wheeler, et al., 2018). Clearly additional research is warranted to explore mechanisms that may be mediating this association.

Although we did not observe any significant differences in ART outcomes for Asian donors and recipients compared to White women, due to low numbers we cannot rule out small, clinically meaningful effects. For example, previous studies utilizing the SART database found that Asian women have significantly lower live birth rates following autologous ART compared to White women with effect estimates similar in magnitude to ours (Fujimoto, et al., 2010; Shapiro, et al., 2017). In concordance with our findings is a previous study which compared anonymous Asian and White donors and found no differences in pregnancy rates between the two (Huddleston et al., 2010). Our finding that singleton live births resulting from Asian donors and recipients had lower birthweights is in line with previous research from both spontaneous conceptions (Crawford et al., 2017; Wen, Kramer, & Usher, 1995) and autologous

ART cycles (Crawford, et al., 2017). An unexpected finding was that non-Asian recipients who received oocytes from Asian donors had the lowest probability of live birth in our study. While this analysis was severely limited by sample size, it is worthy of further study in other donor oocyte populations.

Contrary to findings from prior published work in autologous (Bodri, et al., 2010; Fujimoto, et al., 2010) and third party ART cycles (Shapiro, et al., 2017), Hispanic recipients in our study did not have lower success with ART. In fact, embryo transfer cycles in our study that used oocytes from Hispanic donors were found to have higher positive pregnancy and live birth rates independent of recipient race. We also found that Hispanic oocytes resulted in a larger percentage of useable embryos, which indicates that superior gamete quality could be mediating this association. No other previous studies have compared ART outcomes among Hispanic and White donors. Yet, if our finding of greater success rates among cycles utilizing Hispanic oocytes is true, it could extend the Hispanic/Latina paradox, a common finding that Latina mothers, particularly of Mexican origin (McGlade, Saha, & Dahlstrom, 2004), tend to have better pregnancy outcomes despite their social disadvantages (Fleuriet & Sunil, 2018; Hessol & Fuentes-Afflick, 2000; McGlade, et al., 2004), to earlier reproductive outcomes. To date, the prevailing hypothesis underlying the Hispanic paradox is that Latino women have stronger community networks of family and friends, which helps create a protective environment and results in healthier births (Fleuriet & Sunil, 2018; McGlade, et al., 2004). Whether this same rationale underlies the association with better quality oocytes is unclear.

Our study was strengthened by the relatively large sample size and the higher proportion of Black women represented among donors (11%) and recipients (13%) relative to national averages. Moreover, race was known on virtually all of our oocyte donors (97%) and recipients (94%), which decreased the likelihood of selection bias. The present study was also strengthened by the fact that all of our cycles came from an anonymous, vitrified donor oocyte bank, which ensured that none of our donors and recipients were biologically related and all patients were treated with a similar protocol. Our findings were subject to several limitations. Because this was a retrospective cohort based on data from the medical record, information on lifestyle and socioeconomic factors were not uniformly collected, which

likely resulted in unmeasured confounding. Of note, even though proxies of socioeconomic status were not collected, it is reasonable to speculate that the socioeconomic status of recipients was controlled for by design due to the high cost of ART procedures in a state without mandated fertility coverage. However, there may still be substantial variation among oocyte donors. While one of our primary interests was evaluating ART outcomes among race-discordant oocyte donor/recipient pairs, these analyses were often limited by sample size. Small numbers were also the reason why we combined all Asian races into one category; however, there still may be interesting regional differences to explore. We also had limited information on Hispanic origin and acculturation which could play an important role in the observed associations as suggested by other papers exploring the Hispanic paradox and birth outcomes (McGlade, et al., 2004). Finally, we did not collect information on cultural factors that might also contribute to the less favorable ART outcomes among minority women. For instance, there is evidence that Black women tend to wait longer before seeking help getting pregnant (Humphries, et al., 2016) due to concerns about the social stigma of infertility, stress and disappointment from spouse and family, and utilization of science or technology to conceive (Humphries, et al., 2016). While we adjusted for differences in recipient age, we could not account for these other factors.

In conclusion, our study corroborates and extends previous literature showing that Black women tend to have less favorable ART outcomes even when using healthy oocytes from oocyte donors. In contrast, women who utilized Hispanic oocytes tended to have better ART outcomes regardless of recipient race. Further research- particularly prospective cohort studies with targeted recruitment of minorities from a larger geographic catchment- is needed to confirm our findings and explore the potential mechanisms which may underlie these racial disparities in ART outcomes.

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Tables

Table 1: Association between donor race and early outcomes following oocyte warming and fertilization (among 327 donors and 899 recipients).

	Adjusted Percentage (95% CI)		
	Surviving Oocytes	Fertilized Oocytes	Usable Embryos
Donor Race			
White	91.4 (89.9, 92.7)	77.0 (75.1, 78.7)	49.8 (47.6, 52.1)
Black	93.8 (91.5, 95.6)	78.8 (73.0, 83.6)	56.9 (51.4, 62.3)*
Hispanic	95.0 (86.2, 98.3)	84.3 (73.3, 91.3)	64.5 (51.0, 76.1)*
Asian	94.7 (92.7, 96.1)*	80.3 (75.1, 84.6)	54.2 (48.1, 60.2)
Other	94.9 (92.1, 96.7)*	79.2 (75.4, 82.6)	52.6 (45.4, 59.6)

The denominator for all percentages is the number of oocytes that were warmed. The association between donor race and % oocytes surviving warm, % fertilized oocytes, and % usable embryos were analyzed using generalized estimating equations with binomial distribution and log link function. Models are adjusted for donor age, donor BMI and the year of the retrieval.

*P-value for comparison with reference group (White) is <0.05

Table 2: Association between donor and recipient race and probability of positive pregnancy test, live birth, and miscarriage (among 327 donors and 899 recipients who had a total of 1601 embryo transfer cycles).

	Positive Pregnancy Test (PPT)		Live Birth		Miscarriage	
	PPT/Transfer Cycles (%)	Adjusted Risk Ratio (95% CI)*	Live Births/Transfer Cycles (%)	Adjusted Risk Ratio (95% CI)*	Miscarriages/PPTs (%)	Adjusted Risk Ratio (95% CI)*
Donor Race						
White	874/1213 (72.1)	Reference	611/1213 (50.4)	Reference	253/874 (29.0)	Reference
Black	96/167 (57.5)	0.85 (0.75, 0.96)	67/167 (40.1)	0.86 (0.72, 1.03)	27/96 (28.1)	1.02 (0.62, 1.70)
Hispanic	32/44 (72.7)	1.10 (1.01, 1.20)	24/44 (54.6)	1.20 (1.05, 1.36)	7/32 (21.9)	0.72 (0.34, 1.50)
Asian	63/95 (66.3)	0.91 (0.82, 1.02)	43/95 (45.3)	0.92 (0.81, 1.06)	18/63 (28.6)	1.00 (0.70, 1.43)
Other	54/82 (65.9)	0.93 (0.82, 1.06)	32/82 (39.0)	0.88 (0.69, 1.11)	22/54 (40.7)	1.41 (0.87, 2.28)
Recipient Race						
White	840/1168 (71.9)	Reference	591/1168 (50.6)	Reference	240/840 (28.6)	Reference
Black	135/226 (59.7)	0.85 (0.77, 0.95)	90/226 (39.8)	0.84 (0.71, 0.99)	42/135 (31.1)	1.12 (0.71, 1.76)
Hispanic	43/59 (72.9)	1.07 (0.97, 1.17)	29/59 (49.2)	1.07 (0.90, 1.26)	13/43 (30.2)	1.05 (0.59, 1.86)
Asian	83/120 (69.2)	0.95 (0.86, 1.04)	55/120 (45.8)	0.94 (0.80, 1.10)	26/83 (31.3)	1.09 (0.72, 1.65)
Other	18/28 (64.3)	0.88 (0.69, 1.14)	12/28 (42.9)	0.88 (0.63, 1.24)	6/18 (33.3)	1.11 (0.54, 2.26)

Cluster weighted generalized estimating equations with binomial distribution and log link function were used to analyze the association between donor/recipient race and probability of PPT, miscarriage, and live birth. The weight was equal to the inverse of the number of embryo transfer cycles.

*Adjusted for donor age, donor BMI, recipient age, recipient BMI, tubal factor infertility, uterine factor infertility, and the year of the retrieval.

Table 3: Joint association between donor and recipient race and live birth (among 327 donors and 899 recipients who had a total of 1601 embryo transfer cycles).

Race Categories		Live Birth	
		Live Births/Transfer Cycles (%)	Adjusted Risk Ratio (95% CI)*
Donor	Recipient		
White	White	577/1123 (51.4)	Reference
White	Non-White	34/90 (37.8)	0.80 (0.62, 1.02)
Black	Black	67/166 (40.4)	0.85 (0.72, 1.02)
Black	Non-Black	0/1 (0.0)	N/A
Hispanic	Hispanic	11/19 (57.9)	1.19 (0.99, 1.43)
Hispanic	Non-Hispanic	13/25 (52.0)	1.17 (0.99, 1.38)
Asian	Asian	38/74 (51.4)	0.98 (0.83, 1.16)
Asian	Non-Asian	5/21 (23.8)	0.54 (0.34, 0.87)
Recipient	Donor		
White	White	577/1123 (51.4)	Reference
White	Non-White	14/45 (31.1)	0.75 (0.53, 1.05)
Black	Black	67/166 (40.4)	0.86 (0.72, 1.02)
Black	Non-Black	23/60 (38.3)	0.79 (0.56, 1.11)
Hispanic	Hispanic	11/19 (57.9)	1.20 (1.01, 1.43)
Hispanic	Non-Hispanic	18/40 (45.0)	0.99 (0.78, 1.25)
Asian	Asian	38/74 (51.4)	0.98 (0.82, 1.17)
Asian	Non-Asian	17/46 (37.0)	0.83 (0.61, 1.12)

Cluster weighted generalized estimating equations (GEE) with binomial distribution and log link function were used to analyze the association between donor/recipient race and probability of live birth. The weight was equal to the inverse of the number of embryo transfer cycles.

*Adjusted for donor age, donor BMI, recipient age, recipient BMI, tubal factor infertility, uterine factor infertility, and the year of the retrieval.

Table 4. Association between donor and recipient race/ethnicity and length of gestation and birthweight among donor-egg recipient singleton live births (N=640).

	Number of Live Births	Length of Gestation			Birthweight		
		Mean Weeks/ % <37 wks	Adjusted HR (95% CI)*	Adjusted RR of Pre-term (95% CI)*	Mean Grams/ % <2500g	Adjusted β (95% CI)	Adjusted OR of Low Birthweight (95% CI)*
Donor Race							
White	504	38.5 / 14.2	Reference	Reference	3325.1 / 8.4	Reference	Reference
Black	54	38.4 / 9.3	0.92 (0.71, 1.21)	0.45 (0.17, 1.20)	3142.9 / 7.4	-163.6 (-370.7, 43.6)	0.71 (0.26, 1.95)
Hispanic	17	37.7 / 23.5	1.36 (0.96, 1.92)	1.16 (0.49, 2.76)	3066.0 / 11.8	-215.3 (-489.8, 59.3)	0.97 (0.19, 5.09)
Asian	37	38.0 / 23.0	1.15 (0.82, 1.63)	1.26 (0.58, 2.74)	2988.4 / 24.3	-266.5 (-472.3, -60.6)	2.25 (0.92, 5.48)
Other	28	37.5 / 21.4	1.12 (0.61, 2.05)	0.94 (0.34, 2.55)	3076.8 / 11.1	-138.8 (-342.7, 65.1)	0.37 (0.08, 1.70)
Recipient Race							
White	486	38.5 / 13.5	Reference	Reference	3330.6 / 7.7	Reference	Reference
Black	75	38.0 / 14.7	0.98 (0.76, 1.26)	0.85 (0.41, 1.77)	3152.3 / 9.5	-112.4 (-284.6, 59.7)	0.63 (0.26, 1.52)
Hispanic	24	38.1 / 20.8	1.01 (0.77, 1.32)	0.73 (0.27, 2.01)	3103.3 / 20.8	-147.1 (-399.4, 105.3)	1.45 (0.44, 4.84)
Asian	48	37.9 / 29.2	1.01 (0.67, 1.51)	1.70 (0.94, 3.09)	2998.7 / 20.8	-259.6 (-433.9, -85.2)	1.89 (0.78, 4.56)
Other	7	38.0 / 14.3	0.74 (0.48, 1.16)	0.47 (0.08, 2.69)	2994.4 / 14.3	-203.6 (-603.3, 196.2)	0.80 (0.10, 6.50)

Analyses for gestational length were conducted using cluster weighted Cox proportional hazard and a robust sandwich covariance estimate. Analyses for pre-term birth and low birthweight were conducted using cluster weighted generalized estimating equations with binomial distribution and logit link function. Analyses for birthweight were conducted using cluster weighted generalized estimating equations with normal distribution and identity link function. Each observation was weighted inversely to the number of live births they contributed to the analysis.

*Adjusted for donor age, donor BMI, recipient age, recipient BMI, tubal factor infertility, uterine factor infertility, and the year of the retrieval.

Supplemental Table 1: Characteristics of Oocyte Donors by Race, 2008-2015

	Donor Race Categories						p-value*
	Total	White	Black	Hispanic	Asian	Other	
Number of women	327	245 (74.9)	36 (11.0)	12 (3.7)	21 (6.4)	13 (4.0)	
Age at first retrieval (Conley, #6)	25.0 (5.0)	26.0 (5.0)	26.5 (5.5)	26.0 (3.5)	23.0 (3.0)	25.0 (3.0)	0.12
Year of retrieval							0.07
2008-2009	83 (25.4)	56 (22.9)	13 (36.1)	5 (41.7)	4 (19.1)	5 (38.5)	
2010-2011	103 (31.5)	86 (35.1)	8 (22.2)	0 (0.0)	8 (38.1)	1 (7.7)	
2012-2013	101 (30.9)	69 (28.2)	14 (38.9)	5 (41.7)	7 (33.3)	6 (46.2)	
2014-2015	40 (12.2)	34 (13.9)	1 (2.8)	2 (16.7)	2 (9.5)	1 (7.7)	
BMI (kg/m²)	22.3 (3.4)	22.3 (3.3)	23.2 (4.1)	22.2 (4.0)	20.9 (3.4)	22.5 (2.6)	0.12
Number of prior births							0.07
0	225 (78.0)	188 (76.7)	32 (88.9)	8 (66.7)	20 (95.2)	7 (53.9)	
1	35 (10.7)	25 (10.2)	3 (8.3)	3 (25.0)	1 (4.8)	3 (23.1)	
≥2	37 (11.3)	32 (13.1)	1 (2.8)	1 (8.3)	0 (0.0)	3 (23.1)	
Anti-mullerian hormone (ng/mL)	4.4 (3.6)	4.2 (3.0)	3.1 (4.4)	6.1 (3.7)	4.9 (4.8)	6.5 (4.2)	0.29
Antral follicle count	32.0 (17.0)	32.0 (15.0)	35.0 (19.0)	40.0 (17.0)	32.0 (21.0)	30.0 (14.0)	0.29
Gonadotropin total dose (IU)	2400.0 (900.0)	2475.0 (900.0)	2287.5 (900.0)	2175.0 (787.5)	2025.0 (950.0)	2362.0 (450.0)	0.08
Days of stimulation							0.93
8-9	83 (25.4)	60 (24.5)	8 (22.2)	4 (33.3)	7 (33.3)	4 (30.8)	
10-11	201 (61.5)	152 (62.0)	22 (61.1)	7 (58.3)	13 (61.9)	7 (53.9)	
12-13	43 (13.2)	33 (13.5)	6 (16.7)	1 (8.3)	1 (4.8)	2 (15.4)	
No. of follicles >14mm	20.0 (9.0)	21.0 (10.0)	18.0 (5.5)	20.0 (9.5)	20.0 (11.0)	19.0 (7.0)	0.31
Peak estradiol (pg/mL)	2877.0 (2662.0)	2637.0 (2332.0)	3901.0 (2358.5)	4169.0 (2828.0)	4095.0 (2249.0)	3619.0 (3245.0)	0.001
Maturation trigger type							0.55
hCG/Ovidrel	121 (37.1)	94 (38.5)	14 (38.9)	5 (41.7)	5 (23.8)	3 (23.1)	
GnRH Agonist (Lupron)	205 (62.9)	150 (61.5)	22 (61.1)	7 (58.3)	16 (76.2)	10 (76.9)	

Data are presented as mean (standard deviation) or n (%) unless otherwise noted. The amount of women with missing data are as follows: 194 for anti-mullerian hormone, 2 for antral follicle count, and 1 for maturation trigger type.

*p-values for differences across donor race categories were calculated using Chi-Square tests for categorical variables and Kruskal-Wallis tests for continuous variables.

Supplemental Table 2: Characteristics of Oocyte Recipients by Race, 2008-2015

	Recipient Race Categories						p-value*
	Total	White	Black	Hispanic	Asian	Other	
Number of Women	899	659 (73.3)	118 (13.1)	32 (3.6)	70 (7.8)	20 (2.2)	
Age (years)	42.0 (6.0)	41.0 (6.0)	43.0 (6.0)	42.5 (6.0)	40.0 (6.0)	42.5 (4.0)	0.01
Year of Embryo Transfer							0.90
2008-2009	106 (11.8)	80 (12.1)	13 (11.0)	4 (12.5)	6 (8.6)	3 (15.0)	
2010-2011	302 (33.6)	220 (33.4)	41 (34.8)	9 (28.1)	24 (34.3)	8 (40.0)	
2012-2013	367 (40.8)	275 (41.7)	47 (39.8)	14 (43.8)	26 (37.1)	5 (25.0)	
2014-2015	124 (13.8)	84 (12.8)	17 (14.4)	5 (15.6)	14 (20.0)	4 (20.0)	
BMI (kg/m²)	23.4 (5.4)	23.1 (5.5)	26.1 (6.3)	22.9 (3.2)	21.9 (4.5)	22.7 (4.9)	<0.0001
Recent tobacco use	27 (3.0)	20 (3.0)	3 (2.5)	2 (6.3)	1 (1.4)	1 (5.0)	0.71*
Number of prior births							0.23
0	650 (72.3)	472 (71.6)	88 (74.6)	18 (56.3)	56 (80.0)	16 (80.0)	
1	177 (19.7)	137 (20.8)	19 (16.1)	8 (25.0)	10 (14.3)	3 (15.0)	
≥2	72 (8.0)	50 (7.6)	11 (9.3)	6 (18.8)	4 (5.7)	1 (5.0)	
Prior autologous IVF transfers							0.36
0	467 (52.1)	337 (51.3)	72 (61.0)	17 (54.8)	34 (48.6)	7 (35.0)	
1	168 (18.8)	123 (18.7)	19 (16.1)	8 (25.8)	13 (18.6)	5 (25.0)	
2	108 (12.0)	87 (13.2)	6 (5.1)	2 (6.5)	9 (12.9)	4 (20.0)	
≥3	153 (17.1)	110 (16.7)	21 (17.8)	4 (12.9)	14 (20.0)	4 (20.0)	
Prior donor IVF transfers							0.19
0	751 (83.8)	546 (83.2)	102 (86.4)	24 (75.0)	61 (87.1)	18 (90.0)	
1	92 (10.3)	74 (11.3)	5 (4.2)	6 (18.8)	6 (8.6)	1 (5.0)	
≥2	53 (5.9)	36 (5.5)	11 (9.3)	2 (6.3)	3 (4.3)	1 (5.0)	
Uterine factor infertility	142 (15.8)	69 (10.5)	52 (44.1)	5 (15.6)	11 (15.7)	5 (25.0)	<0.0001
Recurrent pregnancy loss	58 (6.5)	43 (6.5)	5 (4.2)	1 (3.1)	6 (8.6)	3 (15.0)	0.34
Tubal factor infertility	166 (18.5)	84 (12.8)	56 (47.5)	10 (31.3)	12 (17.1)	4 (20.0)	<0.0001
PCOS or other ovulatory dysfunction	27 (3.0)	24 (3.6)	1 (0.9)	0 (0.0)	2 (2.9)	0 (0.0)	0.35
Number of oocytes thawed							0.19
≤5	148 (16.5)	112 (17.0)	19 (14.1)	6 (18.8)	8 (11.4)	3 (15.0)	
6	537 (59.7)	383 (58.1)	77 (65.3)	24 (75.0)	40 (57.1)	13 (65.0)	
≥7	214 (23.8)	164 (24.9)	22 (18.6)	2 (6.3)	22 (31.4)	4 (20.0)	
Number embryos transferred							0.59
1	551 (61.3)	410 (62.2)	67 (56.8)	21 (65.6)	43 (61.4)	10 (50.0)	
2	338 (37.7)	242 (36.7)	50 (42.4)	11 (34.4)	27 (38.6)	9 (45.0)	

3	9 (1.0)	7 (1.1)	1 (0.9)	0 (0.0)	0 (0.0)	1 (5.0)	
Embryo stage at transfer							0.64
Day 3	92 (10.2)	68 (10.3)	10 (8.5)	3 (9.4)	7 (10.0)	4 (20.0)	
Day 5	807 (89.8)	591 (89.7)	108 (91.5)	29 (90.6)	63 (90.0)	16 (80.0)	

Data are presented as mean (standard deviation) or n (%) unless otherwise noted. Amount of women with missing data are as follows: 1 for BMI, 3 for number of prior births, and 3 for prior donor IVF transfers

*p-values for differences across donor race categories were calculated using Chi-Square tests for categorical variables and Kruskal-Wallis tests for continuous variables.

Supplemental Table 3: Overlap between donor and recipient race categories among the 1601 embryo transfer cycles.

# of embryo transfer cycles		Recipient Race					
		White	Black	Hispanic	Asian	Other	Total
Donor Race	White	1123	22	34	23	11	1213
	Black	0	166	0	0	1	167
	Hispanic	15	1	19	4	5	44
	Asian	6	7	0	74	8	95
	Other	24	30	6	19	3	82
	Total	1168	226	59	120	28	

Supplemental Table 4: Association between donor and recipient race and probability of live birth stratified by number of embryos transferred and restricted to only blastocyst transfers, only first embryo transfers, and only recipients without uterine factor infertility.

	Adjusted Risk Ratio of Live Birth (95% CI)*				
	1 Embryo Transferred (N= 983 cycles)	2-3 Embryos Transferred (N=618 cycles)	Only Blastocyst Transfers (N=1475 cycles)	Only First Embryo Transfer (N=899 cycles)	Only Recipients without Uterine Factor (N= 1331 cycles)
Donor Race					
White	Reference	Reference	Reference	Reference	Reference
Black	0.94 (0.74, 1.20)	0.79 (0.60, 1.03)	0.86 (0.72, 1.02)	0.88 (0.69, 1.11)	0.99 (0.83, 1.19)
Hispanic	1.28 (1.06, 1.56)	1.12 (0.91, 1.37)	1.15 (1.01, 1.32)	1.21 (0.98, 1.50)	1.22 (1.06, 1.41)
Asian	0.99 (0.84, 1.16)	0.84 (0.63, 1.11)	0.95 (0.84, 1.07)	0.84 (0.69, 1.03)	0.88 (0.74, 1.03)
Other	0.95 (0.74, 1.22)	0.75 (0.54, 1.05)	0.89 (0.72, 1.11)	0.78 (0.57, 1.07)	0.89 (0.70, 1.14)
Recipient Race					
White	Reference	Reference	Reference	Reference	Reference
Black	0.87 (0.70, 1.10)	0.81 (0.65, 1.02)	0.85 (0.72, 0.99)	0.83 (0.67, 1.03)	0.93 (0.78, 1.10)
Hispanic	1.12 (0.90, 1.39)	1.05 (0.82, 1.33)	1.07 (0.91, 1.27)	1.02 (0.78, 1.34)	1.08 (0.91, 1.29)
Asian	1.04 (0.87, 1.25)	0.79 (0.58, 1.07)	0.97 (0.83, 1.12)	0.85 (0.68, 1.06)	0.91 (0.76, 1.08)
Other	1.04 (0.64, 1.67)	0.75 (0.44, 1.28)	1.00 (0.73, 1.38)	0.86 (0.58, 1.28)	0.88 (0.58, 1.33)

Cluster weighted generalized estimating equations (GEE) with binomial distribution and log link function were used to analyze the association between donor and recipient race and probability of live birth. The weight was equal to the inverse of the number of embryo transfer cycles.

*Adjusted for donor age, donor BMI, recipient age, recipient BMI, tubal factor infertility, uterine factor infertility, and the year of the retrieval.