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A prediction model for live birth and multiple births within the first three cycles of assisted reproductive technology

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Abstract

Objective—To develop a model predictive of live-birth rates (LBR) and multiple birth rates (MBR) for an individual considering assisted reproduction technology (ART) using linked cycles from Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) for 2004–2011.

Design—Longitudinal cohort.

Setting—Clinic-based data.

Patient(s)—288,161 women with an initial autologous cycle, of whom 89,855 did not become pregnant and had a second autologous cycle and 39,334 did not become pregnant in the first and

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second cycles and had a third autologous cycle, with an additional 33,598 women who had a cycle using donor oocytes (first donor cycle).

Intervention(s)—None.

Main Outcome Measure(s)—LBRs and MBRs modeled by woman's age, body mass index, gravidity, prior full-term births, infertility diagnoses by oocyte source, fresh embryos transferred, and cycle, using backward-stepping logistic regression with results presented as adjusted odds ratios (AORs) and 95% confidence intervals.

Result(s)—The LBRs increased in all models with prior full-term births, number of embryos transferred; in autologous cycles also with gravidity, diagnoses of male factor, and ovulation disorders; and in donor cycles also with the diagnosis of diminished ovarian reserve. The MBR increased in all models with number of embryos transferred and in donor cycles also with prior full-term births. For both autologous and donor cycles, transferring two versus one embryo greatly increased the probability of a multiple birth (AOR 27.25 and 38.90, respectively).

Conclusion(s)—This validated predictive model will be implemented on the Society for Assisted Reproductive Technology Web site (www.sart.org) so that patients considering initiating a course of ART can input their data on the Web site to generate their expected outcomes.

Keywords

Assisted reproductive technology; BMI; donor cycle; prediction model

Over the last quarter of a century assisted reproduction technology (ART) has become more integrated into U.S. society to the point that more than 1% of births annually are achieved by this method (1). During this time, there have been major developments in techniques and progressive improvements in pregnancy outcomes (2). Providers of ART are required by U.S. law to report annual success rates to the Centers for Disease Control and Prevention (CDC) (3). The benefit of these data being collected for U.S. families is that it has resulted in a large, contemporary database with sufficient detail to permit estimation of probabilities of a live birth. Generating realistic probabilities over the course of several cycles based on individualized factors may be the deciding factor for many patients considering treatment. For clinicians, the ability to weigh the relative effects of individual factors before starting treatment may facilitate planning a more accurate course of therapy. Several prediction models have been proposed, each with exclusions and limitations (4–6). The purpose of this analysis is to develop a model predictive of live birth and multiple births within the first three fresh autologous cycles and first fresh donor cycle using a contemporary U.S. national database and to implement this model on the on the Society for Assisted Reproductive Technology (SART) Web site (www.sart.org).

MATERIALS AND METHODS

The data source for this study was the SART Clinic Outcome Reporting System (SART CORS), which contains comprehensive data from more than 90% of all clinics performing ART in the United States. Data were collected and verified by SART and reported to the CDC in compliance with the Fertility Clinic Success Rate and Certification Act of 1992

(Public Law 102–493). The data in the SART CORS are validated annually (7, 8) with some clinics having on-site visits for chart review based on an algorithm for clinic selection. During each visit, data reported by the clinic were compared with information recorded in patients' charts. In 2010, records for 2,070 cycles at 35 clinics were randomly selected for full validation, along with 135 embryo-banking cycles (7). The full validation included review of 1,352 cycles for which a pregnancy was reported, of which 446 were multiple-fetus pregnancies. Nine out of 10 data fields selected for validation were found to have discrepancy rates of ≤5%. The exception was the diagnosis field, which had a discrepancy rate of 18%. For approximately 20% of the discrepancies, a single wrong diagnosis was reported, mainly the diagnoses of "other" or "unexplained," instead of a specific cause. For another 50% of the discrepancies, multiple causes of infertility were found in the medical record, but only a single cause was reported. The study was approved by the Committees for the Protection of Human Subjects at Dartmouth College, and Michigan State University, respectively, and was analyzed using SAS 9.2 software (Cary, NC).

Linking Cycles to Individual Women

Women whose first treatment cycle was initiated between January 1, 2004, and December 31, 2011, and reported to the SART CORS database were included. Cycles were linked by woman's date of birth, last name, first name, and social security number (when present); linkages across clinics also included partner's name and sequence of ART outcomes, as needed. Cycles were linked in a series of steps that involved matching the cycles with exact name and date of birth first (step "E" for exact) followed by matches that were progressively less certain due to variations in spelling or format of names, changes in names over time, or data entry error (steps Number 1 to Number 5). Programmed steps were checked for accuracy by reviewing a portion of the records by hand. The first match step (E, exact) was for exact matches. The majority of these were repeat cycles within a single clinic, but when a patient attended more than one clinic and when name, date of birth, and social security number matched between clinics, this was also considered an exact match.

The second match step (Number 1) involved coding names using Soundex software (Soundex SQL Server 2000) to facilitate phonetic matches in names entered differently across clinics (e.g., Frazier and Frasier; O'Neill and O'Neal). These matches were accepted if the date of birth and/or social security numbers matched. At the Number-2 level, cycles were matched that differed as the result of the presence of special characters or hyphenated names. Cycles were sorted first by date of birth and then by last name and first name. Social security numbers and partner name were used to adjudicate uncertain matches. The Number-3 level checked for those patients with the same first and last name and date of birth that agreed by month but differed by plus or minus 1 year. At the Number-4 level we checked those patients with the same first and last name and a date of birth containing the same month and day but a different year. At the Number-5 level we reviewed patients with the same date of birth and first name but whose last names differed, which might occur due to marriage or divorce. At steps Number 3 to Number 5, all close matches were again adjudicated by social security numbers or partner name.

We excluded from these analyses women for whom there was a reported history in the first cycle of a prior ART cycle and women whose first cycle used a frozen embryo (which indicated previous ART treatment). Cycles were also excluded from analyses if designated as research, embryo banking, or using a gestational carriers (surrogates); in such cases, all subsequent cycles were also excluded. Cycles up to and including the first live birth were used; that is, cycles were censored after a live birth. Included were the first three fresh autologous cycles and the first fresh donor cycle. When estimating the live-birth rate at the second or third cycle, the latter cycle (second or third, respectively) must have occurred by December 31, 2011.

Selection of Factors

The objective of developing these models was to provide estimates of the probability of a live birth and a multiple birth to an individual considering ART treatment for the first time. Based on prior research (9–13), the relevant factors for the model included age, body mass index (BMI, kg/m^2), diagnosis of the cause of the infertility, and prior birth history. We considered including race/ethnic origin because it has been shown to affect the live-birth rate (9, 11, 12, 14, 15), but race is a heterogeneous factor. For example, women from the People's Republic of China, the Indian subcontinent, and the Philippines would all be classified as Asian but have very different racial origins; women classified as Black may be multigeneration Americans or recent immigrants from Africa. Even the classification white does not refer to a homogeneous racial group but to all the groups not classified elsewhere. There is little reason to assume that these diverse groups within a single racial classification have similar birth rates. It is also not known the primary reason for the differences that have been reported: they may be due to physiological, cultural, or sociological reasons that are or are not modifiable. Inclusion of race would add a patina of accuracy to the model that cannot be justified by the heterogeneity of the classification. Therefore, we believe that it is best to add the following caveat to the estimates: "These estimates are based on data from all cases in the SART database. They do not take into account all the possible factors that may influence the probability of a live birth. A reproductive endocrinologist at the fertility clinic will be able to advise you whether or not these estimates apply in your case." For the 3-year cumulative estimates, there should be an additional caveat: "It may be that during treatment your physician may determine that you have a condition that reduces the expectation of a successful live birth in a future cycle. If so, these cumulative estimates will no longer apply."

Live-birth Rates

Live births were limited to those reported as a live birth with length of gestation of at least 22 weeks and birth weights of at least 300 g. The models were developed to answer two different questions. Q-1: At the first cycle, what is the live-birth rate when either one or two embryos are transferred, and what is the probability of a multiple birth for each condition? These results enable the user to weigh the desirability of a higher success rate versus the likelihood of a multiple birth. Q-2: Because treatment at the first cycle is not always successful, what is the cumulative probability of a live birth when more than one cycle is performed? In this analysis, there is no limitation on the number of embryos transferred because the clinic may adjust the number based on treatment factors not considered in the

model. The cumulative live-birth rate over two or three cycles assumes that women who did not return for a subsequent cycle would have the same success rates as those who did return. The study population for cycle 2 included all women who failed cycle 1; the study population for cycle 3 included all women who failed cycle 1 and cycle 2. Assume:

$$\begin{aligned} P_1 &= LB_1, \\ P_2 &= LB_2 @ \text{cycle } 2, \\ P_3 &= LB_3 @ \text{cycle } 3 \end{aligned}$$

Then the cumulative probability of a live birth by cycle 2 is

$$PROB_2 = P_1 + P_2(1 - P_1),$$

and the cumulative probability of a live birth by cycle 3 is

$$PROB_3 = PROB_2 + P_3(1 - PROB_2).$$

Both models were developed for autologous cycles using data from the specified cycle. Only the first model was developed for donor cycles using data from the first cycle with fresh donor oocytes, which may have occurred after the first ART cycle.

Logistic regression modeling was performed using a backward-stepping algorithm, eliminating variables until those remaining were all statistically significant at $P<.05$. Women's age at cycle start was categorized as 18–29, 30–34, 35–37, 38–39, 40–44, and 45–59 years; BMI was categorized as ≤18.4, 18.5–24.9, 25.0–29.9, 30.0–34.9, 35.0–39.9, 40.0–44.9, 45.0–49.9, and ≥50.0 kg/m^2. The reproductive variables included the number of prior full-term births (0, 1, ≥2), number of infertility diagnoses (1, >1), infertility diagnosis (male factor, endometriosis, ovulation disorders, diminished ovarian reserve, tubal ligation, tubal hydrosalpinx, tubal other, uterine factor, other factor, and unexplained), and number of embryos transferred (1, 2, or unrestricted). Models were developed separately for autologous cycles and for the first donor cycle.

Multiple Birth Rates

The prediction models for a multiple birth at the first cycle with one or two embryos transferred were generated separately by oocyte source (autologous, donor).

Validation of the Model

To validate the model, the data set was randomly divided into 20 groups using a random number generator. Then, in turn, 20 models were estimated, each from all the data excluding one of these 20 groups (i.e., each from approximately 95% of the data). This model was then applied to the data from the excluded group, and the live-birth rate (or rate of multiples) was calculated. The results over all 20 analyses were summarized by the observed live-birth rate and its standard error, the predicted live-birth rate, the difference between the observed and

predicted live-birth rates, the expected standard error of the difference, and the observed standard error of the difference. A good model will have a small difference and an observed standard error of the difference similar to the expected standard error. For all the main effects, the difference between the observed and expected live-birth rates was less than 0.5% with most less than 0.1%. For some interactions, larger differences were observed, but primarily when the sample size was very small. The observed standard error was similar to the expected standard error except for very small sample sizes.

RESULTS

The final data set for analysis included 288,161 women with an initial autologous cycle (cycle 1); of these, 89,855 did not become pregnant and had a second autologous cycle (cycle 2), and 39,334 did not become pregnant in the first or second cycles and had a third autologous cycle (cycle 3). Additionally, we included 33,598 women who had a cycle using donor oocytes (first donor cycle).

The live-birth rate with autologous oocytes was 32.1% in cycle 1, 24.5% in cycle 2, and 23.0% in cycle 3; with donor oocytes, the live-birth rate was 49.3% in the first donor cycle (Table 1). The characteristics of the study population are presented in Table 1.

Table 2 (autologous) and Table 3 (donor) present the factors in the final models. For ease of interpretation, the adjusted odds ratio (AOR) is specified; this can be converted into coefficients of the model by a natural log transformation that gives the difference between the level of the factor presented in the table and the reference group (AOR = 1) in the logistic regression model; that is, AOR > 1 is associated with positive coefficients in the model and AORs < 1 with negative coefficients.

With autologous oocytes, the probability of a live birth in cycle 1 with one or two embryos transferred declined from an AOR 0.82–0.92 at ages 30–34 years to an AOR 0.03 at age ≥45 years (Table 2, left panel). The use of donor oocytes attenuated the effect of age, with an AOR ranging from 1.21 for ages 30–34 years to AOR 0.99 at ages ≥45 years (Table 3, left panel). Increasing BMI was associated with a progressive decline in the probability of a live birth, from AOR 0.91–0.96 at BMI 25.0–29.9 to AOR 0.20–0.59 at BMI of ≥50.0; the use of donor oocytes did not modify this effect. The models for cycles 2 and 3 did not differ significantly in their factors (i.e., were parallel) and thus only needed a single factor (cycle number) to differentiate between them (Table 2, right panel).

Prior gravidity had a positive effect in autologous cycles 2 and 3, improving the probability of a live birth by 14%–19%. History of prior full-term birth was also a positive factor influencing the probability of a subsequent live birth, more so with the history of one prior birth than with two; this effect was similar for both autologous and donor cycles.

The diagnosis of male factor infertility or ovulation disorder was associated with an increased probability of live birth in autologous cycles (AOR 1.05–1.15 and 1.09–1.45, respectively). The diagnosis of diminished ovarian reserve was associated with a decreased probability of live birth in autologous cycles (AOR 0.66–0.77) but a statistically significantly increased probability in the donor cycle (AOR 1.13). The infertility diagnoses

of tubal factors (tubal ligation, tubal hydrosalpinx, and tubal other) and uterine factor were associated with a decreased probability of a live birth for both autologous and donor cycles. The presence of two versus one infertility diagnoses was associated with a decreased probability of a live birth (AOR 0.82–0.97) in autologous cycles.

The probability of a multiple birth in cycle 1 declined with age in both autologous and donor cycles, and additionally with higher BMIs in autologous cycles; it varied by infertility diagnosis in autologous cycles (increased with ovulation disorders and tubal ligation, and decreased with diminished ovarian reserve) and increased with prior full-term births in donor cycles. For both autologous and donor cycles, transferring two versus one embryo greatly increased the probability of a multiple birth (AOR 27.25 and 38.90, respectively) (Tables 2 and 3, panels labeled multiples).

Examples of Live-birth Rates and Multiple Birth Rates by BMI, Age, and Diagnosis

Three examples are given in Table 4 of live-birth rates and multiple birth rates for cycle 1 with one or two embryos transferred for autologous and donor cycles, and the cumulative live-birth rate over three cycles for autologous cycles, based on having a single infertility diagnosis and a gravidity of zero. The first example shows the effect of BMI for a woman age 35–37 years with the diagnosis of endometriosis. The live-birth rate in cycle 1 with two embryos transferred decreased across BMI groups from 46% to 26% in autologous cycles and from 59% to 30% with donor cycles; the multiple birth rate decreased from 32% to 21% for autologous cycles and was constant at 43% for donor cycles. The cumulative live-birth rate for autologous cycles by cycle 3 across BMI groups decreased from 66% to 45%.

The second example shows the effect of maternal age on the live-birth rate and the multiple birth rate for a woman with a normal BMI (18.5–24.9) and the diagnosis of an ovulation disorder. The live-birth rate in cycle 1 with two embryos transferred decreased across age groups from 57% to 4% in autologous cycles and 58%–56% with donor cycles; the multiple birth rate decreased from 43% to 10% for autologous cycles and 46%–39% for donor cycles. The cumulative live-birth rate for autologous cycles by cycle 3 across age groups decreased from 82% to 10%.

The third example shows the effect of maternal diagnosis on the live-birth rate and multiple birth rate for a woman aged 35 to 37 years with a normal BMI (18.5–24.9). The live-birth rate in autologous cycle 1 with two embryos transferred ranged from 39% to 40% (diminished ovarian reserve, uterine factor, tubal hydrosalpinx) to 43%–46% (endometriosis, tubal ligation, tubal other, and other), to 47%–48% (male factor infertility, ovulation disorders, and unexplained); the cumulative rate by cycle 3 ranged from 55% to 61%, 64%–66%, and 69%–71%, respectively, for these diagnoses. The live-birth rate for donor cycles with two embryos transferred for these diagnosis groups ranged from 54% to 62%, 54%–59%, and 59%–63%, respectively. The multiple birth rate in cycle 1 with two embryos transferred ranged from 28% to 34% for autologous cycles and was constant at 43% for donor cycles.

DISCUSSION

This analysis, developing a model predictive of live birth and multiple births based on U.S. national data, extends our prior studies of cumulative live-birth rates with ART treatment (12, 13, 16–18). The prediction model presented here is intended for an individual considering ART and provides the probability of success over the course of the first three fresh autologous cycles and the first fresh donor cycle, as well as the effect of transferring one versus two embryos on the live-birth rate and the multiple birth rate. This validated predictive model will be implemented on the SART Web site (www.sart.org) so that patients considering initiating a course of ART can input their data on the Web site to generate their expected outcomes.

The strengths of this model include the use of contemporary national data, linking a woman's individual cycles, and model validation. We considered seven factors in this prediction model: patient age, body mass index, history of prior full-term births, number of diagnoses and specific diagnoses, oocyte source, and number of embryos transferred. Cycles using donor oocytes consistently had higher live-birth rates than those using autologous oocytes. Live-birth rates declined with patient age when autologous oocytes were used, but not when donor oocytes were used. Increasing BMI was associated with a progressive decline in the live-birth rate in both autologous and donor cycles. The number of embryos transferred modestly increased the live-birth rate but greatly increased the multiple birth rates for both autologous and donor cycles. Because of the high rates of multiple births attributable to ART, estimated to account for 36% of twin births and 77% of triplet and higher-order births in the United States in 2011 (19), we included the probabilities for this outcome, as well as a live birth, to facilitate a comparison of the risk versus benefit in transferring more than one embryo. Nationally and internationally, the goal of contemporary ART is a healthy singleton born at term (20–22).

This model is subject to several limitations. As described in the *Materials and Methods* section, validation studies conducted by the CDC and SART indicate that there is some error in the entry of diagnosis, most often the overuse of the categories of "other" and "unexplained" (7, 8). Another limitation is the validity of the outcome data because it is reported by the ART patient or the obstetric provider. We have recently demonstrated very high rates of agreement between the SART CORS outcome data and vital records in Massachusetts (23), including plurality of the live birth (99.5%), live-birth/fetal death status (99.9%), birth date within 1 day (94.9%), and birthweight within 100 g (89.6%). Another potential limitation is the assumption that women who did not return for subsequent cycles had live-birth rates similar to those who chose to continue. This assumption may not be appropriate for all women who have a negative prognosis at any time during ART treatment.

CONCLUSION

These validated predictive models of live birth and multiple births should be useful in helping women who are considering starting a course of ART. The models include factors that significantly affect both live birth and multiple birth rates and the magnitude of those factors, and will be available on the SART Web site (www.sart.org).

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TABLE 1

Description of study population.

	Cycle number							
	Autologous					Donor		
Source of oocytes	**First**	**Second**	**Third**	**First**	**First**	**First**	**First**	**First**
No. of embryos transferred[a]	–	–	–	1	2	–	1	2
Factor								
Women and cycles (N)	288,161	89,855	39,334	30,523	135,522	33,598	3,414	22,438
Live births (N)	92,471	22,032	9,052	8,705	61,654	16,570	1,647	12,820
Live-birth rate (%)	32.1	24.5	23.0	28.5	45.5	49.3	48.2	57.1
Age, mean y (SD)	35.0 (4.8)	36.4 (4.7)	36.9 (4.6)	34.8 (4.9)	33.4 (4.3)	41.4 (5.3)	42.0 (5.2)	41.3 (5.2)
18–29 (%)	16.1	9.8	7.8	16.8	22.2	3.5	3.2	3.6
30–34 (%)	33.2	27.2	25.6	35.8	42.1	8.8	7.4	9.0
35–37 (%)	21.4	22.1	22.4	19.9	21.1	10.2	7.6	10.3
38–40 (%)	17.8	23.1	23.6	15.1	10.6	17.3	15.2	17.6
41–43 (%)	9.5	14.7	16.5	9.8	3.3	26.6	27.2	26.9
44–59 (%)	2.0	3.2	4.1	2.7	0.6	33.5	39.4	32.6
Race and ethnicity								
(%) Non-Hispanic white	69.6	70.5	71.7	68.5	72.0	73.2	73.9	74.4
Hispanic	8.3	7.0	5.9	6.8	8.0	6.8	4.9	6.4
Asian	11.0	11.7	11.9	13.8	10.1	9.9	11.3	9.9
Black	8.4	8.2	8.0	8.0	7.5	7.0	6.6	6.5
Mixed	2.1	2.0	1.9	2.4	1.8	2.5	2.8	2.4
Other	0.7	0.6	0.6	0.6	0.6	0.5	0.5	0.5
Unknown	35.3	37.2	39.4	37.2	35.0	36.0	37.2	36.9
BMI, mean kg/m^2 (SD)	25.6 (5.8)	25.7 (5.8)	25.5 (5.7)	25.0 (5.6)	25.6 (5.7)	25.2 (5.3)	24.4 (4.8)	25.3 (5.3)
≤18.4 (%)	2.7	2.7	2.8	3.4	2.7	2.6	3.4	2.5
18.5–24.9 (%)	54.3	54.2	54.8	58.5	54.4	56.4	62.2	55.6
25.0–29.9 (%)	24.1	23.7	23.6	22.1	24.1	25.4	22.9	25.7
30.0–34.9 (%)	11.0	11.2	11.1	9.3	11.1	9.8	7.2	10.3
35.0–39.9 (%)	5.2	5.3	5.1	4.6	5.2	3.9	3.0	4.0

	Cycle number							
	Autologous					Donor		
Source of oocytes	**First**	**Second**	**Third**	**First**	**First**	**First**	**First**	**First**
40.0–44.9 (%)	1.8	2.0	1.9	1.4	1.7	1.4	0.9	1.4
45.0–49.9 (%)	0.6	0.6	0.5	0.4	0.5	0.4	0.3	0.3
≥50.0 (%)	0.2	0.2	0.2	0.3	0.2	0.2	0.0	0.2
Missing	52.6	50.5	47.8	43.8	49.1	56.8	36.5	56.3
Gravidity (%)								
0	55.4	49.0	43.2	53.7	59.0	48.3	45.5	48.7
1	20.6	25.3	28.3	20.6	20.0	20.8	22.2	20.9
≥2	24.0	25.7	28.5	25.7	21.1	31.0	32.3	30.4
Prior full-term births (%)								
0	78.4	79.9	81.4	75.2	80.5	77.6	74.8	78.5
1	13.5	13.3	12.9	15.7	12.4	13.0	18.0	12.4
≥2	8.1	6.7	5.7	9.1	7.1	9.4	7.2	9.0
No. of infertility diagnoses								
1 (%)	73.4	69.3	68.7	74.3	75.5	69.7	75.0	69.6
>1 (%)	26.6	30.7	31.3	25.7	24.5	30.3	25.0	30.4
Infertility diagnosis (%)								
Male factor	39.6	39.1	38.7	37.4	43.1	18.2	14.8	18.2
Endometriosis	10.5	10.6	10.4	8.7	11.1	5.1	4.1	5.2
Ovulation disorders	12.5	10.8	10.8	12.4	14.8	4.3	3.3	4.3
Diminished ovarian reserve	17.8	25.8	27.5	19.2	10.0	75.1	77.4	75.6
Tubal ligation	4.0	3.0	2.4	3.2	4.0	2.1	1.2	2.0
Tubal hydrosalpinx	1.7	1.6	1.8	1.5	1.7	0.5	0.2	0.5
Tubal other	14.6	14.4	14.3	12.8	15.2	5.5	4.4	5.4
Uterine factor	4.3	4.9	5.2	5.0	3.6	4.1	3.7	4.0
Other factor	13.3	14.4	14.3	16.6	11.0	18.8	18.3	18.2
Unexplained	12.2	11.8	11.9	12.9	13.2	3.1	2.8	3.2
No. of embryos transferred, mean (SD)	1.8 (1.2)	2.0 (1.4)	2.2 (1.5)	1 (0)	2 (0)	1.9 (0.8)	1 (0)	2 (0)
None (%)	18.7	20.5	19.7			9.3		
1 (%)	10.6	9.6	9.0	100.0		10.2	100.0	

	Cycle number							
	Autologous					Donor		
Source of oocytes	First	Second	Third	First	First	First	First	First
2 (%)	47.0	34.8	30.5		100.0	66.8		100.0
3 (%)	17.0	22.3	24.6			11.7		
4 (%)	4.9	8.6	10.5			1.6		
≥5 (%)	1.7	4.2	5.7			0.5		

[a]When not specified, the number of embryos transferred was as specified in the database and not limited to 1 or 2.

TABLE 2

Prediction models for autologous cycles.

	Cycle 1 Live birth						Cycle 1 Multiples			Cycle 1 Live birth			Cycles 2 and 3 Live birth		
Characteristics and outcomes	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**
No. of embryos transferred[a]		1			2			1 or 2		–	–	–	–	–	–
Cycles (N)		30,523			135,522			70,359			288,161			129,189	
Age (y)															
18–29	1.00	Reference	< .0001	1.00	Reference	< .0001	1.00	Reference	< .0001	1.00	Reference	< .0001	1.00	Reference	< .0001
30–34	0.82	0.77, 0.88		0.92	0.89, 0.95		0.87	0.84, 0.91		0.90	0.88, 0.92		0.90	0.86, 0.94	
35–37	0.53	0.49, 0.58		0.70	0.68, 0.73		0.68	0.65, 0.71		0.67	0.65, 0.69		0.67	0.64, 0.70	
38–40	0.24	0.21, 0.26		0.42	0.41, 0.44		0.43	0.40, 0.47		0.42	0.41, 0.43		0.46	0.44, 0.49	
41–43	0.12	0.11, 0.15		0.15	0.13, 0.10		0.27	0.21, 0.35		0.18	0.18, 0.19		0.22	0.21, 0.24	
44–59	0.03	0.02, 0.06		0.03	0.02, 0.05		0.15	0.04, 0.66		0.04	0.03, 0.04		0.05	0.04, 0.06	
BMI (kg/m^2)															
≤18.4	0.93	0.77, 1.12	< .0001	0.90	0.82, 0.99	< .0001	0.95	0.82, 1.09	.004	0.88	0.82, 0.95	< .0001	0.91	0.82, 1.02	< .0001
18.5–24.9	1.00	Reference		1.00	Reference		1.00	Reference		1.00	Reference		1.00	Reference	
25.0–29.9	0.91	0.83, 0.98		0.96	0.92, 1.00		0.99	0.94, 1.05		0.96	0.94, 0.99		0.95	0.91, 0.99	
30.0–34.9	0.70	0.62, 0.80		0.83	0.79, 0.87		0.98	0.91, 1.06		0.83	0.79, 0.86		0.82	0.77, 0.87	
35.0–39.9	0.69	0.58, 0.82		0.69	0.64, 0.74		0.94	0.83, 1.05		0.72	0.68, 0.76		0.75	0.69, 0.82	
40.0–44.9	0.38[b]	0.28, 0.52		0.58[b]	0.52, 0.65		0.89[b]	0.75, 1.07		0.61[b]	0.56, 0.66		0.66[b]	0.58, 0.74	
45.0–49.9	0.38[b]	0.28, 0.52		0.58[b]	0.52, 0.65		0.89[b]	0.75, 1.07		0.61[b]	0.56, 0.66		0.66[b]	0.58, 0.74	
≥50.0	0.20	0.07, 0.58		0.42	0.29, 0.61		0.59	0.29, 1.22		0.42	0.31, 0.56		0.57	0.37, 0.87	
Gravidity															
0	–	–		–	–		–	–		–	–		1.00	Reference	< .0001
1	–	–		–	–		–	–		–	–		1.19	1.15, 1.23	
≥2	–	–		–	–		–	–		–	–		1.14	1.10, 1.19	
Prior full-term births															
0	1.00	Reference	< .0001	1.00	Reference	< .0001				1.00	Reference	< .0001	1.00	Reference	.01
1	1.19	1.10, 1.28		1.13	1.09, 1.17		–	–		1.12	1.09, 1.15		1.01	0.96, 1.05	
≥2	1.08	0.98, 1.20		1.10	1.04, 1.16		–	–		1.05	1.02, 1.08		0.91	0.85, 0.97	

	Cycle 1 Live birth						Cycle 1 Multiples			Cycle 1 Live birth			Cycles 2 and 3 Live birth		
Characteristics and outcomes	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**
Diagnosis															
Male factor	1.15	1.08, 1.23	< .0001	1.05	1.02, 1.08	.002	–	–		1.09	1.06, 1.12	< .0001	1.09	1.06, 1.12	< .0001
Endometriosis	–	–		–	–		–	–		–	–		0.92	0.88, 0.96	< .0001
Ovulation disorders	1.45	1.33, 1.57	< .0001	1.08	1.04, 1.12	< .0001	1.09	1.04, 1.14	.001	1.09	1.05, 1.12	< .0001	1.14	1.09, 1.18	< .0001
Diminished ovarian reserve	0.75	0.68, 0.83	< .0001	0.77	0.73, 0.81	< .0001	0.84	0.78, 0.91	< .0001	0.66	0.64, 0.68	< .0001	0.67	0.67, 0.70	< .0001
Tubal ligation	–	–		0.93	0.86, 0.99	.03	1.12	1.03, 1.22	.01	–	–		–	–	
Tubal hydrosalpinx	–	–		0.77	0.71, 0.84	< .0001	–	–		0.81	0.76, 0.86	< .0001	0.76	0.68, 0.85	< .0001
Tubal other	–	–		0.89	0.85, 0.92	< .0001	–	–		0.92	0.90, 0.95	< .0001	0.88	0.84, 0.91	< .0001
Uterine factor	–	–		0.79	0.74, 0.84	< .0001	–	–		0.81	0.78, 0.85	< .0001	0.81	0.76, 0.87	< .0001
Other factor	1.09	1.01, 1.19	.04	–	–		–	–		0.86	0.84, 0.89	< .0001	–	–	
Unexplained	1.17	1.08, 1.28	.0003	1.06	1.02, 1.10	.007	–	–		1.09	1.05, 1.12	< .0001	0.89	0.85, 0.92	< .0001
No. of diagnoses															
2 vs. 1	0.82	0.76, 0.88	< .0001	0.95	0.92, 0.99	.006	–	–		0.97	0.94, 0.99	.02	–	–	
No. of embryos transferred															
2 vs. 1	–	–		–	–		27.25	23.40, 31.74	< .0001						
Cycle															
3 vs. 2													0.95	0.92, 0.98	.0004

Note: – = Factor not present in final model.

[a] When not specified, the number of embryos transferred was as specified in the database, and not limited to 1 or 2.

[b] Body mass index (BMI) categories were combined into one group (40.0–49.9) because of small numbers, so the adjusted odds ratio (AOR) and 95% confidence interval (CI) are the same for both 40.0–44.9 and 45.0–49.9.

TABLE 3

Prediction models for donor cycles.

		First cycle Live birth			First cycle Multiples	
Characteristics	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**
No. of embryos transferred		1–2			1–2	
Cycles (N)		25,852			14,467	
Age (y)						
18–29	1.00	Reference	<.0001	1.00	Reference	.005
30–34	1.21	1.03, 1.41		0.87	0.70, 1.08	
35–37	1.07[a]	0.93, 1.22		0.88	0.71, 1.09	
38–40	1.07[a]	0.93, 1.22		0.87	0.71, 1.06	
41–43	1.07[a]	0.93, 1.22		0.80	0.65, 0.97	
44–59	0.92	0.80, 1.06		0.75	0.62, 0.92	
BMI (kg/m^2)						
≤18.4	0.87	0.69, 1.09	<.0001	–	–	
18.5–24.9	1.00	Reference		–	–	
25.0–29.9	0.84	0.77, 0.92		–	–	
30.0–34.9	0.76	0.67, 0.86		–	–	
35.0–39.9	0.71	0.59, 0.86		–	–	
40.0–44.9	0.63[a]	0.46, 0.87		–	–	
45.0–49.9	0.63[a]	0.34, 1.16		–	–	
≥50.0	0.30	0.12, 0.79		–	–	
Prior full-term births						
0	1.00	Reference	.0004	1.00	Reference	.003
1	1.11	1.03, 1.20		1.19	1.07, 1.32	
≥2	0.89	0.81, 0.98		1.11	0.98, 1.26	
Cause of infertility						
Diminished ovarian reserve	1.13	1.06, 1.20	<.0001	–	–	
Tubal ligation	0.77	0.64, 0.94	.008	–	–	
Tubal other	0.80	0.71, 0.89	<.0001	–	–	

	First cycle Live birth			First cycle Multiples		
Characteristics	**AOR**	**95% CI**	***P* value**	**AOR**	**95% CI**	***P* value**
Uterine factor	0.79	0.70, 0.90	.0003	–	–	
Unexplained	1.19	1.02, 1.38	.03	–	–	
No. of embryos transferred						
2 vs. 1	1.46	1.36, 1.58	<.0001	38.9	27.05, 55.89	<.0001

Note: – = Factor not present in final model.

[a] Age categories (35–43 years) were combined because of small numbers, so the adjusted odds ratios (AOR) and 95% confidence intervals (CI) are the same for all levels within these combined categories.

TABLE 4

Examples of live-birth rates (%) and multiples (%) by women's characteristics and cycle parameters.

		Autologous							Donor			
Example	**Woman's characteristics**	**Cumulative LBR**			**LBR**		**Multiples**		**LBR**		**Multiples**	
	No. of embryos transferred	LBR			1	2	1	2	1	2	1	2
	Cycle number	1	2	3	1	1	1	1	1	1	1	1
1. Effect of BMI	BMI (kg/m^2)											
Age: 35–37 y	<18.4	33	50	63	28	43	1.6	31	46	56	1.9	43
Diagnosis: endometriosis	18.5–24.9	36	54	66	29	46	1.7	32	50	59	1.9	43
	25.0–29.9	35	52	65	27	45	1.7	31	46	55	1.9	43
	30.0–34.9	32	48	60	23	41	1.6	31	43	52	1.9	43
	35.0–39.9	29	45	57	22	37	1.6	30	41	51	1.9	43
	40.0–49.9	26	46	61	14	33	1.7	32	50	59	1.9	43
	50.0–69.0	19	34	45	8	26	1.0	21	23	30	1.9	43
2. Effect of age	Age (y)											
BMI: 18.5–24.9	18–29	48	70	82	53	57	2.7	43	48	58	2.1	46
Diagnosis: ovulation disorders	30–34	45	67	79	48	54	2.3	39	53	62	1.9	43
	35–37	38	58	71	37	48	1.8	34	50	59	1.9	43
	38–40	28	46	59	21	36	1.2	24	50	59	1.9	43
	41–43	14	26	36	12	16	0.7	17	50	59	1.7	40
	44–59	3	7	10	4	4	0.4	10	46	56	1.6	39
3. Effect of diagnosis	Diagnosis											
Age: 35–37 y	Male factor	38	57	70	32	47	1.7	32	50	59	1.9	43
BMI: 18.5–24.9	Endometriosis	36	54	66	29	46	1.7	32	50	59	1.9	43
	Ovulation disorders	38	58	71	37	48	1.8	34	50	59	1.9	43
	DOR	27	43	55	24	39	1.4	28	53	62	1.9	43
	Uterine factor	31	49	61	29	40	1.7	32	44	54	1.9	43
	Tubal ligation	36	55	68	29	44	1.9	34	43	53	1.9	43
	Tubal hydrosalpinx	31	48	60	29	39	1.7	32	50	59	1.9	43
	Tubal other	34	52	64	29	43	1.7	32	44	54	1.9	43
	Other	33	51	64	31	46	1.7	32	50	59	1.9	43

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		Autologous						Donor			
Example	**Woman's characteristics**	**Cumulative**			**LBR**		**Multiples**	**LBR**		**Multiples**	
	Unexplained	38	56	69	33	47	1.7	32	54	63	1.9	43

Note: These examples are all based on having a single infertility diagnosis and gravidity of zero. BMI = body mass index; DOR = diminished ovarian reserver; LBR = live-birth rate.