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

Barbara Luke, Sc.D., M.P.H.,[a] Morton B. Brown, Ph.D.,[b] Ethan Wantman, M.B.A.,[c] Judy E. Stern, Ph.D.,[d] Valerie L. Baker, M.D.,[e] Eric Widra, M.D.,[f] Charles C. Coddington, III, M.D.,[g] William E. Gibbons, M.D.,[h] and G. David Ball, Ph.D.[i]

[a] Department of Obstetrics, Gynecology, and Reproductive Biology, Michigan State University, East Lansing, Michigan; [b] Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor, Michigan; [c] Redshift Technologies, New York, New York; [d] Department of Obstetrics and Gynecology, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire; [e] Department of Obstetrics and Gynecology, Stanford University, Palo Alto, California; [f] Shady Grove Fertility Center, Washington, District of Columbia; [g] Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minnesota; [h] Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, Texas; and [i] Seattle Reproductive Medicine, Seattle, Washington

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 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. (Fertil Steril® 2014;102:744–52. ©2014 by American Society for Reproductive Medicine.)
Key Words: Assisted reproductive technology, BMI, donor cycle, prediction model

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/lukeb-prediction-live-multiple-births-three-cycles/

Use your smartphone to scan this QR code and connect to the discussion forum for this article now.*

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

Received March 11, 2014; revised May 9, 2014; accepted May 12, 2014; published online June 14, 2014.
B.L. has received support from the Society for Reproductive Technologies (SART) and from National Institutes of Health (grant R01CA151973). M.B.B. has nothing to disclose. E.W. is under contract to the Society for Reproductive Technologies (SART) as a data vendor. J.E.S. has received grants from the National Institutes of Health and American Society for Reproductive Medicine (ASRM) and is a consultant for Cooley LLP. V.L.B. has nothing to disclose. E.W. has nothing to disclose. C.C.C. has nothing to disclose. W.E.G. has nothing to disclose. G.D.B. has nothing to disclose.
Supported by the Society for Reproductive Technologies (SART).
Presented at the 69th Annual Meeting of the American Society for Reproductive Medicine, Boston, Massachusetts, October 12–17, 2013.
Reprint requests: Barbara Luke, Sc.D., M.P.H., Department of Obstetrics and Gynecology, and Reproductive Biology, Michigan State University, 965 Fee Road, East Fee Hall, Room 628, East Lansing, Michigan 48824 (E-mail: lukeb@msu.edu).

Fertility and Sterility® Vol. 102, No. 3, September 2014 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2014.05.020

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 $\leq$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