# Elective single embryo transfer trends and predictors of a good perinatal outcome—United States, 1999 to 2010

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**Objective:** To assess trends in elective single ET and identify factors associated with a good perinatal outcome.
**Design:** Retrospective cohort study.
**Setting:** Clinic-based data.
**Patient(s):** A total of 886,686 fresh, nondonor cycles reported to the National Assisted Reproductive Technology Surveillance System during 1999–2010, of which 17,166 met criteria for elective single ET.
**Intervention(s):** None.
**Main Outcome Measure(s):** Rates of elective single ET and good perinatal outcome (term, singleton infant with normal birth weight).
**Result(s):** In 2010, elective single ET comprised 5.6% of all fresh transfers, representing an eightfold increase since publication of first guidelines in 2004 recommending elective single ET. Compared with other ETs, elective single ETs were nearly twice as likely to result in a good perinatal outcome (37.1% vs. 18.9%, respectively). Among women using elective single ET, those aged <35 and 35–37 years had a good perinatal outcome (40.2% and 32.5%, respectively). In multivariable, log-binomial analyses, factors positively associated with a good perinatal outcome included male factor infertility, day 5 ET, and having ≥3 supernumerary embryos for cryopreservation.
**Conclusion(s):** Between 1999 and 2010, national rates of elective single ET increased. Given the frequency of good perinatal outcomes among women aged 35–37 years, guidelines for elective single ET could be expanded to include patients in this age group with favorable prognoses. (Fertil Steril® 2013;99:1937–43. ©2013 by American Society for Reproductive Medicine.)
**Key Words:** Elective single ET, single ET, in vitro fertilization, singleton pregnancy, good perinatal outcome

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Multiple gestations, and their associated complications, remain the most common adverse outcome associated with assisted reproductive technology (ART). The most effective method for reducing the risk of multiple births after ART is to limit the number of embryos transferred. Evolving practice guidelines from the American Society for Reproductive Medicine (ASRM) and the Society of Assisted Reproductive Technologies (SART) have led to a steady decline in the frequency of higher order (≥3) ETs during the past decade (1). This downward trend has caused an increased number of double ETs, resulting in an unchanged, or even slightly increased, rate of twin gestation resulting from ART (1). Elective single ET, defined as the transfer of only one embryo when more than one high-quality embryo is available, has been proposed as the only means of avoiding multiple gestations after IVF (2).

As observed in several studies (3–9), elective single ET successfully reduces the risk of multiple gestations, without significantly compromising

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live birth rates. However, in prior studies, the population had been restricted to select subsets of patients with the most "favorable prognosis," thereby limiting the generalizability of the findings (3–9). In a study of unselected patients (10), use of elective single ET effectively eliminated multiple gestations, but nearly halved pregnancy rates (PRs), compared with double ETs. Due to low rates of elective single ET in the United States, there has only been one small, single center analysis evaluating factors associated with birth outcomes after fresh elective single ET (11). An analysis of national data would add to this study, which found that younger maternal age and blastocyst expansion were positively associated with clinical pregnancy and live birth among patients with favorable prognosis.

Given the limited information on use of elective single ET in the United States, we analyzed data from the Centers for Disease Control and Prevention National ART Surveillance System (NASS) to estimate national trends in elective single ET from 1999 through 2010. Furthermore, because the motivation behind promoting elective single ET is to increase the rate of healthy, singleton infants after ART, we sought to identify characteristics associated with a good perinatal outcome after elective single ET.

## MATERIALS AND METHODS

The data used for this analysis were obtained from NASS, which was established after the enactment of the Fertility Clinic Success Rate and Certification Act of 1992. This law mandates that ART clinics report data annually to the Centers for Disease Control and Prevention for all cycles initiated during that year (12). The data include patient demographics, medical and obstetric history, infertility diagnosis, and information regarding resultant pregnancies and births. Approximately 6.5% of ART clinics did not provide data to Centers for Disease Control and Prevention in 2010 (13). Because most nonreporting clinics are small, we estimate that NASS contains information on more than 97% of all ART cycles performed in the United States (13). The study was reviewed and approved by the Institutional Review Board of the Centers for Disease Control and Prevention.

The elective single ET study population was defined as fresh, nondonor cycles in which a single embryo was transferred and at least one supernumerary embryo was available for cryopreservation. The comparison group consisted of all other fresh, nondonor cycles. These included cycles in which only one embryo was available for transfer (single ET without additional embryos available for cryopreservation), as well as transfers of more than one embryo.

The characteristics assessed included maternal age, race/ethnicity, infertility diagnosis, number of prior pregnancies, number of prior spontaneous abortions, number of prior live births, number of prior ART cycles, year of cycle treatment, insurance mandate status for state of residence, number of oocytes retrieved, use of intracytoplasmic sperm injection (ICSI) (± male factor infertility), use of assisted hatching, use of preimplantation genetic diagnosis (for years 2004 and later), embryo stage at transfer, number of embryos transferred, and number of supernumerary embryos cryopreserved. Because race/ethnicity was unknown or missing in nearly 40% of the study population, an unknown/missing category was included to allow evaluation of these data in multivariable analyses. Also, as patients may have had more than one infertility diagnosis, these diagnoses were not mutually exclusive. To assess potential temporal differences in elective single ET practices, we compared transfers performed in 2005–2010 with those performed in 1999–2004, as the first ASRM/SART guidelines recommending elective single ET were published in September 2004 (14). With regard to embryo stage at transfer, we chose to restrict our analysis to the two most common days for embryo transfer (day 3 for cleavage stage and day 5 for blastocyst stage), which together represented 82.5% of all transfers.

A "good perinatal outcome" was defined as the live birth of a singleton infant born at term (≥37 completed weeks of gestation) and at a normal birth weight (≥2,500 g) (15). Gestational age was calculated by subtracting the date of oocyte retrieval from the date of delivery, then adding 14 days to adjust for the theoretical date of the last menstrual period.

We used SAS statistical software version 9.3 (SAS Institute) to conduct all analyses. For all transfers and selected maternal age strata, we calculated the percentage of all ETs meeting elective single ET criteria for each year. We used Mantel-Haenszel statistics to assess trends in the proportion of elective single ET during the study period, and two-tailed $\chi^2$ tests to compare the distribution of maternal and cycle characteristics for the elective single ET group with all other fresh, nondonor transfers during the study period.

To evaluate factors associated with good perinatal outcome among the cycles with elective single ET, we calculated the frequency of good outcomes for each of these maternal and cycle characteristics. Log-binomial models were used to calculate unadjusted and adjusted risk ratios (RR) for the association between maternal and cycle characteristics and a good perinatal outcome after elective single ET. The number of previous pregnancies was not included as a predictor in the adjusted models because it represented the sum of number of previous abortions and number of previous live births, two variables that were already included in the model. Preimplantation genetic diagnosis was also excluded from the models because this information was not ascertained for all study years. We also conducted stratified analyses to examine potential effect modification by maternal age using a variety of different maternal age groupings; no differential effects were noted thus stratified results were not presented. Due to the high proportion of missing or unknown race data, we compared the findings for adjusted models with and without the race variable. Because differences between the two models were nominal, we retained race in the final model.

## RESULTS

During the study years 1999–2010, a total of 1,541,825 ART cycles were included in NASS. Of the 1,111,766 cycles using fresh, nondonor oocytes, 886,686 (79.8%) proceeded to transfer at least 1 embryo, and 17,166 (1.9%) met elective single ET criteria.

Until 2004, less than 1% of all transfers in the United States were elective single ET (Fig. 1). Since that time, there has been