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Trends and Correlates of Good Perinatal Outcomes in Assisted Reproductive Technology

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Abstract

OBJECTIVE—To estimate trends in good perinatal outcomes (singleton live births at term with birthweight more than 2,500 g) among live births after assisted reproductive technology in the United States from 2000 to 2008, and associated factors among singletons in 2008.

METHODS—Using retrospective cohort data from the National Assisted Reproductive Technology Surveillance System from 2000 to 2008, we calculated relative change and χ^2 tests for trend in the proportion of good perinatal outcomes among assisted reproductive technology live births (n=444,909) and liveborn singletons (n=222,500). We conducted univariable analyses followed by multiple logistic regression to estimate the effects of various characteristics on the outcome among singletons born in 2008 after fresh, nondonor assisted reproductive technology cycles (n=20,780).

RESULTS—The proportion of good perinatal outcomes among all liveborn neonates increased from 38.6% in 2000 to 42.5% in 2008, whereas it declined marginally among singletons from 83.6% to 83.4%. One previous birth, transfer of fewer than three embryos, and the presence of fewer than three fetal hearts on 6-week ultrasound examination were associated with good perinatal outcome among singletons. Non-Hispanic black race, tubal factor infertility, uterine factor infertility, ovulatory disorder, and 5-day embryo culture were associated with reduced odds for a good outcome. The strongest association was the presence of one fetal heart compared with more than two (adjusted odds ratio 2.43, 95% confidence interval 1.73–3.42).

CONCLUSION—From 2000 to 2008, good perinatal outcomes increased among assisted reproductive technology live births. Among singleton live births, odds for good outcome were greatest with the presence of a single fetal heart and lowest in women of non-Hispanic black race.

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Assisted reproductive technology, fertility treatment that involves oocyte retrieval, laboratory handling of gametes, and the transfer of embryos or gametes into the fallopian tubes or uterus, has become increasingly utilized since its inception in 1978. In 2008, there were 61,430 neonates born after assisted reproductive technology, representing more than 1% of all United States births.¹ Although pregnancy and live birth rates after assisted reproductive technology continue to increase, those born after assisted reproductive technology have increased risks of preterm delivery, low birthweight, and perinatal mortality.^{2–5}

Although a portion of the increased risk of adverse pregnancy outcomes is attributable to the increased incidence of multiple gestations with assisted reproductive technology, studies have consistently demonstrated elevated risks of preterm delivery and low birthweight in singletons conceived after assisted reproductive technology in comparison with those in the general population.^{6–13} Some studies conclude that adverse outcomes result from an assisted reproductive technology treatment effect.^{14–17} Others suggest that underlying infertility, older age, chronic illness, primiparity, and other characteristics unique to women undergoing assisted reproductive technology play a significant role.^{13,18–24} Moreover, some studies are inconclusive or suggest that underlying characteristics of women undergoing assisted reproductive technology and treatment factors affect outcomes to a similar degree.^{25–28}

American Society for Reproductive Medicine guidelines regarding embryo transfer as well as numerous research studies, commentaries, and developments in the field have changed the practice of assisted reproductive technology over the past decade, leading physicians to transfer fewer embryos when appropriate. We conducted analyses of the Centers for Disease Control and Prevention National Assisted Reproductive Technology Surveillance System to estimate how the proportion of good perinatal outcomes has changed among the United States assisted reproductive technology birth cohort from 2000 to 2008. To identify possible predictors of good perinatal outcomes after assisted reproductive technology, we further analyzed a subset of births from the most recent year, 2008.

MATERIALS AND METHODS

Data used in this study were obtained from National Assisted Reproductive Technology Surveillance System, which collects information about assisted reproductive technology cycles performed at United States fertility assisted reproductive technology clinics, as mandated by law (Fertility Clinic Success Rate and Certification Act of 1992, Public Law No. 102-493, October 24, 1992). Assisted reproductive technology procedures include those involving the laboratory handling of gametes, namely in vitro fertilization (IVF) transcervical embryo transfer, gamete intrafallopian transfer, and zygote intrafallopian transfer. National Assisted Reproductive Technology Surveillance System data include patient demographics, patient obstetrical and medical history, parental infertility diagnosis, clinical parameters of the assisted reproductive technology procedure, and information regarding resultant pregnancies and births. Approximately 5–12% of assisted reproductive technology clinics did not report data to Centers for Disease Control and Prevention during 2000–2008. Because most nonreporting clinics are small, we estimate that National Assisted

Reproductive Technology Surveillance System contains information about more than 95% of all assisted reproductive technology cycles performed in the United States.

In vitro fertilization transcervical embryo transfer can be categorized further into the following groups: 1) fresh, donor; 2) fresh, nondonor; 3) frozen, donor; and 4) frozen, nondonor. Cycles involving fresh embryos are defined as those in which embryos were transferred after embryo culture. Cycles involving frozen embryos are defined as those in which thawed, previously frozen embryos were transferred. Donor embryo transfer refers to the transfer of donor embryos, whereas nondonor embryo transfer refers to the transfer of the patient's own embryos.

We used data on all live births resulting from assisted reproductive technology cycles performed between 2000 and 2008 for the analysis of trends in good perinatal outcomes among all assisted reproductive technology live births (n=444,909) and among the subset of assisted reproductive technology liveborn singletons (n=222,500). Because we wanted to estimate the effects of factors other than multiple births on perinatal outcomes, we limited our analyses to singleton live births resulting from fresh, nondonor IVF transcervical embryo transfer cycles performed in 2008 (n=21,451), thereby ensuring homogeneity of the study population. We excluded 483 neonates for whom data were unavailable on birthweight or gestational age and 188 neonates born to gestational carriers. Our final study population for this analysis consisted of 20,780 neonates.

We defined a "good perinatal outcome" to be the live birth of a singleton neonate born at term (37 or more completed weeks of gestation) weighing 2,500 g or more. For fresh embryo transfers, we calculated gestational age by subtracting the date of oocyte retrieval from the date of birth and adding 14 days to adjust for theoretical last menstrual period. For assisted reproductive technology cycles involving transfer of previously frozen embryos, and in cases in which the date of oocyte retrieval was missing, we calculated gestational age by subtracting the date of embryo transfer from the date of birth and adding 17 days to adjust for theoretical last menstrual period and days in embryo culture.

All statistical analyses were performed using SAS statistical software 9.2. We estimated trends in proportion of good perinatal outcomes among all assisted reproductive technology live births and assisted reproductive technology singleton live births from 2000 to 2008 using χ^2 test for trend among the following cycle groups: fresh, nondonor; fresh, donor; frozen, nondonor; and frozen, donor. For each of these groups, we calculated the relative change in proportion of good perinatal outcomes from 2000 to 2008 and computed a χ^2 test for trend.

We examined the distribution of maternal and treatment characteristics for liveborn singletons and for all liveborn neonates after fresh, nondonor assisted reproductive technology cycles initiated in 2008. For singletons, univariable analyses were conducted to evaluate associations with good perinatal outcome with the χ^2 test for differences in proportions for the following characteristics: maternal age; gravidity; previous births; race or ethnicity; parental infertility diagnosis; use of intracytoplasmic sperm injection; use of assisted hatching; availability of supernumerary embryos for freezing; number of embryos

transferred; number of fetal hearts on 6-week ultrasound examination; number of days of embryo culture; history of spontaneous abortion; and history of assisted reproductive technology cycles. Race or ethnicity data were missing for more than 30% of all assisted reproductive technology births. To allow use of data for these births, we created a category of “unknown” for those with missing data for the race or ethnicity variable. Because patients may have had more than one infertility diagnosis, the presence or absence of each diagnosis was handled as an individual variable.

Factors that were determined to be significant based on univariable analysis ($P < .05$) were included in a logistic regression model to describe predictors of good perinatal outcome. We used stepwise multiple logistic regression and included only those variables that had a two-tailed $P < .05$ in the final model. We calculated the adjusted odds ratios (ORs) and accompanying 95% confidence intervals (CIs) for each term. We also calculated a χ^2 statistic for goodness-of-fit on the final model, which indicated an adequate fit.

We conducted sensitivity analyses using multiple logistic regression in the manner described, limiting the original sample of 2008 liveborn singletons after fresh, nondonor assisted reproductive technology to those with: 1) one fetal heart on 6-week ultrasound examination ($n=17,289$); 2) one embryo transferred ($n=2,128$); and 3) nonmissing data ($n=13,613$) for the race or ethnicity variable. Additionally, we repeated univariable analysis for tubal factor infertility, limiting this group to those solely with tubal factor infertility diagnosed ($n=3,376$) compared with all others ($n=17,404$).

Last, to assess the validity of our results among the population of assisted reproductive technology live births, we conducted separate analyses to assess associations with good outcomes among the population of all live births after 2008 fresh, nondonor assisted reproductive technology cycles ($n=40,288$). We used univariable analyses for the factors described and defined good perinatal outcomes as live births at 37 completed weeks or more, with birth-weights of at least 2,500 g. In addition to these factors, we tested singleton compared with nonsingleton live birth for association with the outcome. Factors determined to be significant were included in a stepwise logistic regression model controlling for clustering effects of mothers with multiple birth outcomes by incorporating a random effects model. This study was approved by the Institutional Review Board of the Centers for Disease Control and Prevention.

RESULTS

The total number of liveborn neonates conceived after assisted reproductive technology increased 76%, from 34,861 in 2000 to 61,430 in 2008 (Table 1). Similarly, the number of liveborn singleton neonates conceived after assisted reproductive technology increased 95% during the same time period. The percentage of good perinatal outcomes among all assisted reproductive technology liveborn neonates increased from 38.6% in 2000 to 42.5% in 2008 ($P < .05$). An increase in good perinatal outcomes among all assisted reproductive technology live births was observed in all assisted reproductive technology cycle groups, with a significant trend ($P < .05$) for all with the exception of frozen, donor cycles. The percentage of good perinatal outcomes among all singleton live births, however, declined slightly from

83.6% in 2000 to 83.4% in 2008. In addition, there was a small decline in good perinatal outcomes among liveborn singletons in the fresh, nondonor cycle group from 84.1% to 83.9%. A decline also was observed in the frozen, nondonor cycle group, although a significant trend was not detected ($P=0.13$). Some year-to-year variation was seen for the other cycle types, but overall the percentages of births with good perinatal outcomes changed little, with no significant trend detected.

The study population chosen to investigate factors associated with good perinatal outcomes—singleton neonates born after fresh, nondonor IVF transcervical embryo transfer in 2008 ($n=20,780$)—was similar in most characteristics to all liveborn neonates after fresh, nondonor IVF transcervical embryo transfer from the same year (Table 2), but was substantially different with respect to the frequency of good perinatal outcomes. The greatest differences between the two groups were observed in the proportion of neonates born at or after 37 weeks of gestation (87% of singletons and 62% of all liveborn neonates) and with a birthweight of at least 2,500 g (90% of singletons and 66% of all liveborn neonates). For both groups, most neonates were born to women 30–39 years of age and to women with no previous births. Approximately half of the neonates in both groups were born to women with one or more previous pregnancies. Although more than 30% of reported assisted reproductive technology cycles did not contain data for the race or ethnicity variable, most neonates for whom maternal race was reported were born to women of non-Hispanic white race. The most common infertility diagnosis in both groups was male factor, and uterine factor was the least common diagnosis. For both groups, in most procedures, intracytoplasmic sperm injection was used and use of assisted hatching was less common. Availability of supernumerary embryos for cryopreservation after assisted reproductive technology cycles was somewhat less common among singleton neonates (44%) than for all liveborn neonates (49%). Ten percent of singleton live births, and 6% of all live births, resulted from the transfer of a single embryo. Two or more fetal hearts were observed much less commonly in the assisted reproductive technology singleton group, and the assisted reproductive technology singleton group had a smaller proportion of embryos transferred on day 5 (at blastocyst stage). The groups were similar in terms of number of previous spontaneous abortions and number of previous assisted reproductive technology cycles.

Results of univariable analyses indicated that one previous birth, the transfer of one or two embryos compared with more than two, and the presence of one or two fetal hearts on 6-week ultrasound examination compared with more than two hearts were associated with good perinatal outcomes (Table 3). All of these associations remained significant in the final multiple logistic regression model. Non-Hispanic black race, tubal factor infertility, uterine factor infertility, ovulatory disorder, and 5 days of embryo culture were inversely associated with good perinatal outcomes in the final model. The strongest positive association with good perinatal outcome was estimated for the presence of one fetal heart on 6-week ultrasound examination as compared with more than two fetal hearts (adjusted OR 2.4, 95% CI 1.7–3.4), and the strongest negative association was estimated for non-Hispanic black as compared with non-Hispanic white race (adjusted OR 0.5, 95% CI 0.4–0.6). Limiting the sample to those with one heart on 6-week ultrasound examination ($n=17,289$) did not change the other associations retained in the final model to any appreciable extent (results not

shown). When we limited the sample to those with one embryo transferred (n=2,128), most of the associations were in the same direction as observed in the original analysis, although not significant (results not shown). However, the transfer of blastocyst stage embryos was not associated with the outcome (adjusted OR 1.0, CI 0.8–1.4) in this additional analysis.

To assess the effect of the missing race or ethnicity data on our results, we limited the sample to those with nonmissing data (n=13,613). Most of the observed associations were retained in the final model (results not shown), with effect estimates more than 1.0 observed for one previous birth, the presence of fewer fetal hearts on 6-week ultrasound examination, and the transfer of one embryo; the effect estimate for tubal factor infertility remained less than 1.0. Most notably, one fetal heart on 6-week ultrasound examination remained the strongest predictor of good outcomes (adjusted OR 1.7, 95% CI 1.1–2.7) and non-Hispanic black race remained the strongest negative predictor (adjusted OR 0.5, 95% CI 0.4–0.6).

Because we did not expect tubal factor infertility to be inversely associated with good outcomes, we investigated this in greater detail. Because the groups of fertility diagnosis were not mutually exclusive, we repeated univariable analysis, comparing those solely diagnosed with tubal factor infertility (n=3,376) with all others (n=17,404), and association with the outcome was retained (results not shown).

Last, we tested for associations with good outcomes among all assisted reproductive technology live births in 2008 after fresh, nondonor assisted reproductive technology and found that most observed associations were retained in the final model, with effect estimates more than 1.0 for one previous birth, the presence of fewer fetal hearts on 6-week ultrasound examination, and the transfer of one embryo; the effect estimates for non-Hispanic black race, tubal factor infertility, ovarian disorder, and transfer of blastocyst stage embryo were less than 1.0. The presence of one fetal heart had the strongest association with good outcomes (adjusted OR 48.0, 95% CI 40.9–56.3) and non-Hispanic black race remained the strongest negative predictor (adjusted OR 0.6, 95% CI 0.5–0.7). Additionally, maternal age older than 30 was associated with good outcomes in this analysis. We also found that there were fewer multiple births in older women despite increased numbers of embryos being transferred.

DISCUSSION

Traditionally, success in assisted reproductive technology has been viewed as clinical live birth. More recently, it has been suggested that success should be defined as the birth of a healthy singleton.²⁹ We report an increase in good perinatal outcomes among all assisted reproductive technology live births from 2000 to 2008, a finding that likely reflects changes in the practice of assisted reproductive technology in the United States. After the first publication of American Society for Reproductive Medicine guidelines regarding embryo transfer in 1998 and 1999, the numbers of embryos transferred decreased sharply in the subsequent years.³⁰ Between 2000 and 2008, the percentage of fresh, nondonor IVF cycles that involved the transfer of a single embryo increased from less than 1% to 10%.¹ Although techniques and practices may have changed, singletons born after assisted reproductive technology remain at risk for adverse outcomes.

In our analysis, the strongest predictor of good outcomes was the presence of a single fetal heart. This finding is consistent with a recent analysis that demonstrated that spontaneous losses increase the odds for preterm birth and low birthweight in singletons.³¹ Furthermore, we found that transferring fewer embryos resulted in better outcomes.

Race was also an important predictor of perinatal outcomes. A recent large analysis regarding racial disparities in assisted reproductive technology with respect to birth outcomes reported increased risks for low birthweight and preterm delivery among singletons born to non-Hispanic black women.³² Although the reasons for racial disparity in assisted reproductive technology remain unclear, we found non-Hispanic black race to be strongly associated with a lower likelihood of good perinatal outcomes.

Uterine factor infertility, ovulatory disorders, tubal factor infertility, and embryo transfer after 5 days of embryo culture were inversely associated with good perinatal outcome. Tubal disease may alter the intrauterine environment during pregnancy. In a study of patients using donor oocytes, hydrosalpinges in the recipient were associated with higher miscarriage and ectopic pregnancy rates,³³ and a larger meta-analysis demonstrated that early pregnancy loss was more common in assisted reproductive technology patients with hydrosalpinx among those with tubal factor infertility.³⁴

Our analysis of national surveillance data should be considered in light of its strengths and limitations. The use of nationwide surveillance data provides increased statistical power and the restriction of our analysis to data from 1 year decreases the chances that our results are affected by changes in assisted reproductive technology.

Our findings regarding race should be interpreted with caution given that more than 30% of data regarding maternal race were missing. However, the similarity in the effect estimates for the unknown and the non-Hispanic white race or ethnicity groups, the lack of a change in our finding for non-Hispanic black race on restriction of the analyses to nonmissing data, and the fact that most women who undergo assisted reproductive technology are of non-Hispanic white race suggest that those for whom race or ethnicity data were missing were mostly non-Hispanic white women. Sufficient data were unavailable to examine the effects of body mass index, chronic disease, socioeconomic status, and behavioral or lifestyle characteristics on outcomes. Last, our study describes factors associated with outcomes among singleton live births and should be interpreted with this in mind.

These results demonstrate that good perinatal outcomes among singleton births after fresh, nondonor IVF are predicted by multiple factors. Single embryo transfer was associated with superior outcomes, whereas non-Hispanic black race was associated with less favorable outcomes. Future work is needed to investigate the mechanisms behind these effects and to identify reasons for racial disparities to improve outcomes.

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References

1. Centers for Disease Control and Prevention, American Society for Reproductive Medicine, Society for Assisted Reproductive Technology. Assisted reproductive technology success rates: national summary and fertility clinic reports. Atlanta (GA): United States Department of Health and Human Services; 2010.
2. Tan SL, Doyle P, Campbell S, Beral V, Rizk B, Brinsden P, et al. Obstetric outcome of in vitro fertilization pregnancies compared with normally conceived pregnancies. *Am J Obstet Gynecol.* 1992; 167:778–84. [PubMed: 1530039]
3. Dhont M, De Sutter P, Ruysinck G, Martens G, Bekaert A. Perinatal outcome of pregnancies after assisted reproduction: a case-control study. *Am J Obstet Gynecol.* 1999; 181:688–95. [PubMed: 10486485]
4. Bergh T, Ericson A, Hillensjo T, Nygren KG, Wennerholm UB. Deliveries and children born after in-vitro fertilisation in Sweden 1982–95: a retrospective cohort study. *Lancet.* 1999; 354:1579–85. [PubMed: 10560671]
5. Koivuova S, Hartikainen AL, Gissler M, Hemminki E, Sovio U, Jarvelin MR. Neonatal outcome and congenital malformations in children born after in-vitro fertilization. *Hum Reprod.* 2002; 17:1391–8. [PubMed: 11980770]
6. Perri T, Chen R, Yoeli R, Merlob P, Orvieto R, Shalev Y, et al. Are singleton assisted reproductive technology pregnancies at risk of prematurity? *J Assist Reprod Genet.* 2001; 18:245–9. [PubMed: 11464574]
7. Schieve LA, Meikle SF, Ferre C, Peterson HB, Jeng G, Wilcox LS. Low and very low birth weight in infants conceived with use of assisted reproductive technology. *N Engl J Med.* 2002; 346:731–7. [PubMed: 11882728]
8. Helmerhorst FM, Perquin DA, Donker D, Keirse MJ. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. *BMJ.* 2004; 328:261. [PubMed: 14742347]
9. Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. *Obstet Gynecol.* 2004; 103:551–63. [PubMed: 14990421]
10. Schieve LA, Ferre C, Peterson HB, Macaluso M, Reynolds MA, Wright VC. Perinatal outcome among singleton infants conceived through assisted reproductive technology in the United States. *Obstet Gynecol.* 2004; 103:1144–53. [PubMed: 15172846]
11. McGovern PG, Llorens AJ, Skurnick JH, Weiss G, Goldsmith LT. Increased risk of preterm birth in singleton pregnancies resulting from in vitro fertilization-embryo transfer or gamete intrafallopian transfer: a meta-analysis. *Fertil Steril.* 2004; 82:1514–20. [PubMed: 15589852]
12. McDonald SD, Murphy K, Beyene J, Ohlsson A. Perinatal outcomes of singleton pregnancies achieved by in vitro fertilization: a systematic review and meta-analysis. *J Obstet Gynaecol Can.* 2005; 27:449–59. [PubMed: 16100639]
13. Schieve LA, Cohen B, Nannini A, Ferre C, Reynolds MA, Zhang Z, et al. A population-based study of maternal and perinatal outcomes associated with assisted reproductive technology in Massachusetts. *Matern Child Health J.* 2007; 11:517–25. [PubMed: 17345154]
14. Ombelet W, Martens G, De Sutter P, Gerris J, Bosmans E, Ruysinck G, et al. Perinatal outcome of 12,021 singleton and 3108 twin births after non-IVF-assisted reproduction: a cohort study. *Hum Reprod.* 2006; 21:1025–32. [PubMed: 16339165]
15. Shih W, Rushford DD, Bourne H, Garrett C, McBain JC, Healy DL, et al. Factors affecting low birthweight after assisted reproduction technology: difference between transfer of fresh and cryopreserved embryos suggests an adverse effect of oocyte collection. *Hum Reprod.* 2008; 23:1644–53. [PubMed: 18442997]
16. Henningsen AK, Pinborg A, Lidegaard O, Vestergaard C, Forman JL, Andersen AN. Perinatal outcome of singleton siblings born after assisted reproductive technology and spontaneous conception: Danish national sibling-cohort study. *Fertil Steril.* 2011; 95:959–63. [PubMed: 20813359]

17. D'Angelo DV, Whitehead N, Helms K, Barfield W, Ahluwalia IB. Birth outcomes of intended pregnancies among women who used assisted reproductive technology, ovulation stimulation, or no treatment. *Fertil Steril*. 2011; 96:314–20. e2. [PubMed: 21718990]
18. Kallen B, Olausson PO, Nygren KG. Neonatal outcome in pregnancies from ovarian stimulation. *Obstet Gynecol*. 2002; 100:414–9. [PubMed: 12220758]
19. Gaudoin M, Dobbie R, Finlayson A, Chalmers J, Cameron IT, Fleming R. Ovulation induction/intrauterine insemination in infertile couples is associated with low-birth-weight infants. *Am J Obstet Gynecol*. 2003; 188:611–6. [PubMed: 12634629]
20. Basso O, Baird DD. Infertility and preterm delivery, birth-weight, and Caesarean section: a study within the Danish National Birth Cohort. *Hum Reprod*. 2003; 18:2478–84. [PubMed: 14585905]
21. Wang YA, Sullivan EA, Black D, Dean J, Bryant J, Chapman M. Preterm birth and low birth weight after assisted reproductive technology-related pregnancy in Australia between 1996 and 2000. *Fertil Steril*. 2005; 83:1650–8. [PubMed: 15950632]
22. Romundstad LB, Romundstad PR, Sunde A, von Doring V, Skjaerven R, Gunnell D, et al. Effects of technology or maternal factors on perinatal outcome after assisted fertilisation: a population-based cohort study. *Lancet*. 2008; 372:737–43. [PubMed: 18674812]
23. Pelinck MJ, Keizer MH, Hoek A, Simons AH, Schelling K, Middelburg K, et al. Perinatal outcome in singletons after modified natural cycle IVF and standard IVF with ovarian stimulation. *Eur J Obstet Gynecol Reprod Biol*. 2010; 148:56–61. [PubMed: 19850400]
24. Jaques AM, Amor DJ, Baker HW, Healy DL, Ukoumunne OC, Breheny S, et al. Adverse obstetric and perinatal outcomes in subfertile women conceiving without assisted reproductive technologies. *Fertil Steril*. 2010; 94:2674–9. [PubMed: 20381039]
25. Isaksson R, Gissler M, Tiitinen A. Obstetric outcome among women with unexplained infertility after IVF: a matched case-control study. *Hum Reprod*. 2002; 17:1755–61. [PubMed: 12093835]
26. Kapiteijn K, de Bruijn CS, de Boer E, de Craen AJ, Burger CW, van Leeuwen FE, et al. Does subfertility explain the risk of poor perinatal outcome after IVF and ovarian hyperstimulation? *Hum Reprod*. 2006; 21:3228–34. [PubMed: 17023490]
27. Chung K, Coutifaris C, Chalian R, Lin K, Ratcliffe SJ, Castelbaum AJ, et al. Factors influencing adverse perinatal outcomes in pregnancies achieved through use of in vitro fertilization. *Fertil Steril*. 2006; 86:1634–41. [PubMed: 17074345]
28. Tepper NK, Farr SL, Cohen BB, Nannini A, Zhang Z, Anderson JE, et al. Singleton Preterm Birth: Risk Factors and Association with Assisted Reproductive Technology. *Matern Child Health J*. 2012; 16:807–813. [PubMed: 21516300]
29. Min JK, Breheny SA, MacLachlan V, Healy DL. What is the most relevant standard of success in assisted reproduction? The singleton, term gestation, live birth rate per cycle initiated: the BESST endpoint for assisted reproduction. *Hum Reprod*. 2004; 19:3–7. [PubMed: 14688149]
30. Stern JE, Cedars MI, Jain T, Klein NA, Beaird CM, Grainger DA, et al. Assisted reproductive technology practice patterns and the impact of embryo transfer guidelines in the United States. *Fertil Steril*. 2007; 88:275–82. [PubMed: 17445805]
31. Luke B, Brown MB, Grainger DA, Stern JE, Klein N, Cedars MI. The effect of early fetal losses on singleton assisted-conception pregnancy outcomes. *Fertil Steril*. 2009; 91:2578–85. [PubMed: 18565521]
32. Fujimoto VY, Luke B, Brown MB, Jain T, Armstrong A, Grainger DA, et al. Racial and ethnic disparities in assisted reproductive technology outcomes in the United States. *Fertil Steril*. 2010; 93:382–90. [PubMed: 19081561]
33. Cohen MA, Lindheim SR, Sauer MV. Hydrosalpinges adversely affect implantation in donor oocyte cycles. *Hum Reprod*. 1999; 14:1087–9. [PubMed: 10221245]
34. Camus E, Poncelet C, Goffinet F, Wainer B, Merlet F, Nisand I, et al. Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies. *Hum Reprod*. 1999; 14:1243–9. [PubMed: 10325271]

Trends Among Liveborn Neonates After Assisted Reproduction in the United States, 2000–2008

Table 1

	2000	2001	2002	2003	2004	2005	2006	2007	2008	Relative Change, 2000–2008 (%)	P for Trend
No. of liveborn neonates conceived after ART	34,861	40,608	45,765	48,748	49,320	51,968	54,638	57,571	61,430	76.2	
No. of liveborn singleton neonates conceived after ART	16,350	18,896	21,614	23,710	24,893	26,559	28,652	29,938	31,888	95.0	
% of ART births born as singletons at term with weight more than 2,500 g among all ART live births, total	38.6	38.9	39.4	40.5	41.4	41.5	42.7	42.3	42.5	10.1	<.01
Fresh, nondonor	38.4	38.7	39.1	40.1	41.2	41.5	43.0	42.3	42.2	9.9	<.01
Fresh, donor	32.5	32.3	31.8	33.5	33.7	32.6	34.1	33.2	33.8	3.9	.01
Frozen, nondonor	47.5	47.7	50.4	50.0	50.0	50.9	49.7	50.0	50.9	7.3	<.01
Frozen, donor	41.7	43.6	44.3	46.6	44.7	43.0	46.0	46.7	44.8	7.5	.09
% of singletons born at term with weight more than 2,500 g among all ART liveborn singletons, total	83.6	84.1	83.9	83.9	83.5	82.9	83.3	83.3	83.4	-0.2	<.01
Fresh, nondonor	84.1	84.6	84.4	84.3	83.9	83.6	84.0	83.8	83.9	-0.2	.04
Fresh, donor	81.1	81.3	80.6	81.1	81.3	79.7	81.0	80.4	81.1	0.0	.67
Frozen, nondonor	84.3	84.5	85.3	85.6	84.4	83.6	83.6	84.6	83.9	-0.5	.13
Frozen, donor	78.9	79.0	80.3	80.3	78.6	78.2	78.7	79.3	78.9	0.0	.62

ART, assisted reproductive technology.

Table 2

Distribution of 2008 Liveborn Neonates After Fresh, Nondonor In Vitro Fertilization Transcervical Embryo Transfer by Characteristics

Characteristic	Liveborn Singletons After Fresh, Nondonor IVF Transcervical Embryo Transfer	Liveborn Neonates After Fresh, Nondonor IVF Transcervical Embryo Transfer
Total	20,780	40,228
Birthweight (g)		
Less than 2,500	2,017 (9.7)	13,501 (33.6)
At least 2,500	18,763 (90.3)	26,727 (66.4)
Gestational age at delivery (wk)		
At least 37	18,071 (87.0)	24,997 (62.1)
Less than 37	2,709 (13.0)	15,231 (37.9)
Maternal age (y)		
Younger than 30	3,372 (16.2)	7,277 (18.0)
30–34	7,815 (37.6)	16,239 (40.4)
35–39	7,531 (36.2)	13,679 (34.0)
40–44	2,048 (9.9)	3,010 (7.5)
45 or older	14 (0.1)	23 (0.1)
No. of previous pregnancies		
0	9,877 (47.6)	19,472 (48.5)
1	5,442 (26.3)	10,493 (26.1)
2 or more	5,420 (26.1)	10,192 (25.4)
No. of previous births		
0	14,735 (71.5)	28,756 (69.8)
1	4,437 (21.5)	8,391 (22.7)
2 or more	1,446 (7.0)	2,781 (7.5)
Race or ethnicity		
Unknown	7,617 (36.7)	14,584 (36.3)
Non-Hispanic white	10,143 (48.8)	19,861 (49.4)
Non-Hispanic black	674 (3.2)	1,306 (3.2)
Hispanic	994 (4.8)	2,057 (5.1)
Asian or Pacific Islander	1,352 (6.5)	2,420 (6.0)
Infertility diagnosis*		
Tubal factor	3,376 (16.3)	6,686 (16.6)
Endometriosis	2,614 (12.6)	5,320 (13.2)
Uterine factor	734 (3.5)	1,376 (3.4)
Ovulatory disorder	3,489 (16.8)	7,196 (17.9)
Diminished ovarian reserve	2,864 (13.8)	4,756 (11.8)
Male factor	8,263 (39.8)	16,317 (40.6)
Use of ICSI [†]		
Yes	15,047 (72.5)	28,898 (71.9)
No	5,720 (27.5)	11,303 (28.1)

Characteristic	Liveborn Singletons After Fresh, Nondonor IVF Transcervical Embryo Transfer	Liveborn Neonates After Fresh, Nondonor IVF Transcervical Embryo Transfer
Use of assisted hatching [‡]		
Yes	7,536 (36.3)	13,674 (34.0)
No	13,244 (63.7)	26,554 (66.0)
No. of supernumerary embryos cryopreserved		
Unknown	102 (0.5)	165 (0.4)
0	11,623 (56.2)	20,428 (51.0)
1 or more	9,055 (43.8)	19,635 (49.0)
No. of embryos transferred		
1	2,128 (10.2)	2,211 (5.5)
2	11,856 (57.1)	24,288 (60.4)
3 or more	6,796 (32.7)	13,729 (34.1)
No. of fetal hearts on 6-wk ultrasound scan		
1	18,914 (91.4)	18,996 (47.9)
2	1,618 (7.8)	18,364 (46.3)
3 or more	174 (0.8)	2,278 (5.8)
No. of days of embryo culture		
Unknown and all others	1,592 (7.7)	2,875 (7.2)
5	8,621 (41.5)	18,241 (45.3)
3	10,567 (50.9)	19,112 (47.5)
No. of previous spontaneous abortions		
0	14,723 (70.9)	28,817 (71.6)
1 or more	6,057 (29.2)	11,411 (28.4)
No. of previous ART cycles		
0	12,923 (62.2)	25,456 (63.3)
1	3,791 (18.2)	7,080 (17.6)
2 or more	4,066 (19.6)	7,688 (19.1)

IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; ART, assisted reproductive technology.

Data are n or n (%).

* Percentages do not add up to 100 because the groups are not mutually exclusive (one patient may have multiple diagnoses).

[†] Refers to the direct injection of sperm into an oocyte for the purpose of improving chances of fertilization.

[‡] Refers to treatments in which a minor defect is created in the zona pellucida for the purpose of improving chances of implantation.

Table 3

Predictors of Good Perinatal Outcomes Among 2008 Singleton Live Births Resulting From Fresh, Nondonor In Vitro Fertilization Intracervical Embryo Transfer

Characteristic	% Liveborn Singletons With Good Perinatal Outcome	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio* (95% CI)	P*
Total	84.2			
Maternal age (y)				
Younger than 30	83.3	1.00		
30–34	84.4	1.09 (0.98–1.21)		
35–39	84.5	1.09 (0.98–1.22)		
40–44	84.0	1.05 (0.90–1.22)		
45 or older	92.9	2.61 (0.34–19.97)		
No. of previous pregnancies				
0	84.2	1.00		
1	85.0	1.06 (0.97–1.17)		
2 or more	83.4	0.95 (0.87–1.04)		
No. of previous births				
0	83.8	1.00	1.00	
1	86.0	1.19 (1.09–1.31)	1.19 (1.08–1.32)	<.01
2 or more	82.6	0.92 (0.80–1.06)	0.95 (0.81–1.10)	
Race or ethnicity				
Non-Hispanic black	73.7	0.49 (0.41–0.59)	0.53 (0.43–0.64)	<.01
Hispanic	82.2	0.81 (0.68–0.96)	0.86 (0.72–1.05)	
Asian or Pacific Islander	82.9	0.85 (0.73–0.99)	0.89 (0.74–1.04)	
Unknown	84.4	0.95 (0.87–1.03)	0.93 (0.85–1.01)	
Non-Hispanic white	85.1	1.00	1.00	
Infertility diagnosis				
Tubal factor	81.8	0.81 (0.74–0.89)	0.82 (0.74–0.92)	<.01
No tubal factor	84.7	1.00	1.00	
Endometriosis	84.8	1.05 (0.94–1.18)		
No endometriosis	84.1	1.00		
Uterine factor	79.7	0.73 (0.60–0.87)	0.77 (0.64–0.94)	
No uterine factor	84.4	1.00	1.00	
Ovulatory disorder	81.1	0.77 (0.70–0.84)	0.73 (0.66–0.81)	
No ovulatory disorder	84.8	1.00	1.00	
Diminished ovarian reserve	84.0	0.98 (0.88–1.10)		
No diminished ovarian reserve	84.3	1.00		
Male factor	84.7	1.07 (0.99–1.15)		
No male factor	83.9	1.00		
Use of ICSI [†]				
Yes	84.3	1.01 (0.93–1.10)		
No	84.1	1.00		

Characteristic	% Liveborn Singletons With Good Perinatal Outcome	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio* (95% CI)	P*
Use of assisted hatching [‡]				
Yes	84.3	1.01 (0.94–1.09)		
No	84.2	1.00		
No. of supernumerary embryos cryopreserved				
0	84.6	1.00		
1 or more	83.7	0.93 (0.86–1.00)		
No. of embryos transferred				
1	85.8	1.20 (1.04–1.37)	1.27 (1.09–1.48)	<.01
2	84.4	1.08 (0.99–1.17)	1.18 (1.08–1.29)	
3 or more	83.4	1.00	1.00	
No. of fetal hearts on 6-wk ultrasound scan				
1	84.9	2.27 (1.63–3.16)	2.43 (1.73–3.42)	<.01
2	77.5	1.39 (0.98–1.97)	1.49 (1.04–2.13)	
3 or more	71.3	1.00	1.00	
No. of days of embryo culture				
5	83.2	0.88 (0.82–0.95)	0.86 (0.79–0.94)	<.01
3	85.0	1.00	1.00	
No. of previous spontaneous abortions				
0	84.5	1.00		
1 or more	83.4	0.92 (0.85–1.00)		
No. of previous ART cycles				
0	84.4	1.00		
1	83.8	0.96 (0.87–1.06)		
2 or more	84.2	0.99 (0.90–1.09)		

CI, confidence interval; ICSI intracytoplasmic sperm injection; ART, assisted reproductive technology.

* For those variables included in the final model.

[†] Refers to the direct injection of sperm into an oocyte for the purpose of improving chances of fertilization.

[‡] Refers to treatments in which a minor defect is created in the zona pellucida for the purpose of improving chances of implantation.