

Limiting Multiple Births from Assisted Reproductive Technology

Assisted reproductive technology (ART) is a category of fertility treatments in which both eggs and sperm are handled.¹ [Common forms of ART](#) include conventional in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Between 1996 and 2006, the number of ART procedures performed in the United States more than doubled, and the number of infants born using ART nearly tripled. While ART allows individuals to have children who might not otherwise be able to, it increases risk for adverse maternal and perinatal outcomes including multiple births and, consequently, low birth weight and prematurity. State legislation and healthcare practices can affect ART practices that increase risk of multiple births. State health agencies can play important roles by developing ART surveillance procedures and working with stakeholders to raise awareness about the risks of multiple births and recommended ART practices.

ART AND RISKS TO MATERNAL AND INFANT HEALTH

ART significantly increases the likelihood of multiple-gestation pregnancies. In fact, in 2011 nearly half of ART infants (45.6%) were born in multiple-birth deliveries, compared to just 3.4 percent of all infants.² Multiple-gestation pregnancies increase risk for poor birth outcomes including premature births, low birth weights, disabilities, deaths,³ and high C-section rates.⁴

Low birth weight (less than 2,500 grams) is a major contributor to neonatal and infant mortality. Low birth weight infants are at increased risk for a host of health problems from neurodevelopmental disabilities to respiratory disorders.⁵ Because many ART infants are multiples (for example, twins or triplets), they are more likely to have low birth weight than non-ART infants. In 2011, nearly one-third (31.0%) of ART infants—including both multiple-gestation and singleton infants—were low birth weight, compared with 8.1 percent of all infants.⁶

Preterm infants are also at increased risk for health problems, developmental issues, and death compared to full-term infants.⁷ ART infants are more likely to be born preterm than non-ART infants. In 2011, 36.2 percent of ART infants were born preterm, compared with 11.8 percent of all infants.⁸ Prematurity and multiple births also significantly impact healthcare costs. In 2010, a total of 21,638 ART infants in the U.S. were born preterm, resulting in a societal economic burden of \$1.34 billion.⁹ Between 2005 and 2010, the total all-cause health care cost of delivering twins (\$104,831) or triplets and higher order multiples (\$407,199) was significantly higher than the cost of delivering a singleton baby (\$21,458).¹⁰ In September 2011, ASTHO President David Lakey (TX) issued his [ASTHO President's Challenge: the Healthy Babies Initiative](#). His goal for the challenge is to improve birth outcomes by reducing infant mortality and prematurity by 8 percent by 2014.

Opportunities for State Health Agencies

- Establish state-based surveillance of ART-related maternal and infant health outcomes.
- Assess perceptions and address practices related to multiple embryo transfer during ART.

FACTORS INFLUENCING ART USE AND MULTIPLE BIRTHS

A number of policy and healthcare practice factors impact ART use.

STATE MANDATED HEALTH INSURANCE COVERAGE

The proportion of ART-conceived infants among all infants born varies significantly from state to state, from 0.1 percent in Guam to 4.8 percent in Massachusetts. Some of this variation may be explained by differences in state health insurance coverage for ART procedures. Currently, 15 states mandate insurance coverage for infertility treatment, although terms of coverage vary widely. For example, only eight of these states include coverage for ART, and just four of these states—Illinois, Massachusetts, New Jersey, and Rhode Island—have mandated comprehensive insurance coverage that covers at least four cycles of IVF. Each of these four states has ART usage rates higher than the national average. In fact, Illinois, Massachusetts, and New Jersey had rates more than 1.5 times the national rate.¹¹

EMBRYO TRANSFER PRACTICES

Multiple embryo transfer during an ART procedure significantly increases risk for multiple-gestation pregnancies. Expert panel opinion recommends transferring only single embryos to patients with a good prognosis to ensure singleton pregnancies and births.¹² While [elective single embryo transfer \(eSET\)](#) – transfer of only a single embryo when more than one embryo is available – is practiced most often, transferring two or more embryos continues to be common practice. This may be because ART can be expensive, so healthcare providers and their patients may try to maximize the chance of conception.¹³ In addition, couples undergoing infertility treatments may view multiple births as an acceptable or even desirable outcome, and may not be aware of the increased risks.¹⁴

ROLE OF STATE HEALTH AGENCIES

State health agencies can support efforts to improve ART use and reduce adverse outcomes in a number of ways.

ART SURVEILLANCE

The CDC Division of Reproductive Health (DRH) monitors all ART procedures performed in the United States using the National ART Surveillance System (NASS), a web-based ART reporting system.¹⁵ DRH also partners with state health agencies through the [States Monitoring Assisted Reproductive Technology \(SMART\) Collaborative](#)¹⁶ to strengthen the capacity of states to evaluate ART-related maternal and perinatal outcomes and programs through state-based public health surveillance systems, as an extension of national surveillance efforts. The SMART Collaborative links information from ART surveillance with birth records, infant and fetal death records, hospital discharge registries, birth defects registries, and cancer registries. The linked data set creates a population-based data registry of ART and non-ART births that can monitor and examine ART pregnancy outcomes. Currently, three states (Connecticut, Massachusetts, and Michigan) participate in the SMART Collaborative.

AWARENESS AND EDUCATION

State health agencies also can support efforts to raise awareness – among both healthcare providers and individuals undergoing fertility treatment – about the risks of multiple births and the impact of single embryo transfer on multiple birth rates. For example, the Connecticut Department of Public Health (CT DPH) is partnering with CDC, March of Dimes, and the Connecticut Department of Social Services to raise awareness about embryo transfer practices and encourage use of eSET when appropriate, through communications channels that includes a [factsheet](#). In addition, healthcare

providers can raise awareness among their patients undergoing fertility treatment about the risks of multiple embryo transfer and recommend single embryo transfer more widely.

STATE EXAMPLES

- **Florida** was a member of the SMART Collaborative from 2008-2014 and used linked data from vital statistics and NASS to examine characteristics of women who undergo ART procedures versus those who do not, as well as perinatal outcomes by method of conception. In addition, linked data were used to assess the relationship between pre-pregnancy body mass index, ART use, and preterm birth.¹⁷ Florida added five questions about infertility and ART to the [2012 Florida Behavioral Risk Factor Surveillance Survey \(BRFSS\)](#) and, together with Michigan, led the effort to standardize linked files, which resulted in significant improvement of data quality in Florida and other states.
- **Massachusetts** collects various data on birth certificates related to ART, including use of fertility medications, as well as data from hospitals and mothers, and plans to link the data to NASS. The [Massachusetts Pregnancy Risk Assessment Monitoring System \(PRAMS\)](#) also collects self-reported ART data. The Massachusetts Department of Public Health also partnered with the Society for Assisted Reproductive Technology, Boston University School of Public Health, and CDC to create the Massachusetts Outcomes Study of Assisted Reproductive Technology database. Massachusetts conducted careful assessment of the quality of ART information collected on birth certificates, which led to recommendations to improve data collection.¹⁸
- The **Michigan SMART Surveillance** project, guided by the Michigan Infertility Advisory Committee, aims to assess pregnancy and child health outcomes through the Michigan Infertility Surveillance Program, which uses data from the NASS/Michigan vital records linked files, Michigan hospital discharge files, birth defects and cancer registries, Michigan BRFSS, and Michigan PRAMS. The project also is developing a comprehensive [surveillance plan](#) to inform planning, implementation, evaluation, and policy development for improvement of ART and non-ART outcomes. In addition, the project provides epidemiological and research consultation for development of public health efforts related to ART, with a focus on underrepresented populations.¹⁹
- In **Connecticut**, CDC estimates that 10-15 percent of low birth weight babies are the result of ART. The CT DPH is partnering with CDC, March of Dimes, and the Connecticut Department of Social Services (Medicaid) to conduct surveillance on the impact of ART on adverse maternal and infant outcomes and to encourage consumers to choose eSET when appropriate. To date, vital records data have been matched to create longitudinal files that include delivery sets, birth, infant death, and fetal death records for 2002–2011. Next steps include linking this data to NASS; adding newborn hospitalization data; adding questions to the 2013 CT BRFSS related to reproductive health, family planning, and infertility; and engaging fertility clinics to explore how eSET can be more fully incorporated into clinical practice.

¹ CDC. "Assisted Reproductive Technology." Available at <http://www.cdc.gov/art/index.htm>. Accessed 5-19-2014.

² Sunderam S, Kissin D, Crawford S, et al. "Assisted Reproductive Technology Surveillance—United States, 2011." *Morbidity and Mortality Weekly Report*. 2014;63(10). Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6310a1.htm>. Accessed 12-12-2014.

³ *Ibid.*

⁴ Kissin D. "Assisted Reproductive Technology (ART): States Monitoring ART (SMART) Collaborative." 2012. Available at http://www.naphsis.org/mtg/Documents/KISSIN_NAPHSIS_SMART_Overview_June_6_2012.pdf. Accessed 5-19-14.

-
- ⁵ CDC. "Pediatric and Pregnancy Nutrition Surveillance System: Is Low Birthweight a Problem?" Available at http://www.cdc.gov/pednss/how_to/interpret_data/case_studies/low_birthweight/what.htm. Accessed 5-19-14.
- ⁶ Sunderam S, Kissin D, Crawford S, et al. "Assisted Reproductive Technology Surveillance—United States, 2011." *Morbidity and Mortality Weekly Report*. 2014;63(10). Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6310a1.htm>. Accessed 12-12-2014.
- ⁷ Behrman RE, Stith Butler A, eds. "Preterm birth: causes, consequences, and prevention." Washington, DC: National Academies Press; 2006.
- ⁸ Sunderam S, Kissin D, Crawford S, et al. "Assisted Reproductive Technology Surveillance—United States, 2011." *Morbidity and Mortality Weekly Report*. 2014;63(10). Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6310a1.htm>. Accessed 12-12-2014.
- ⁹ Kissin D, Jamieson D, Barfield W. "Monitoring Health Outcomes of Assisted Reproductive Technology." *N Engl J Med*. 2014. 371(1):91-93.
- ¹⁰ Lemos E, Zhang D, Van Voorhis B, et al. Healthcare expenses associated with multiple vs singleton pregnancies in the United States. *Am J Obstet Gynecol* 2013;209:586.e1-11.
- ¹¹ Sunderam S, Kissin D, Crawford S, et al. "Assisted Reproductive Technology Surveillance—United States, 2011." *Morbidity and Mortality Weekly Report*. 2014;63(10). Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6310a1.htm>. Accessed 12-12-2014.
- ¹² American Society for Reproductive Medicine. "Multiple Gestation Associated with Infertility Therapy: An ASRM Practice Committee Opinion, 2011." *Fertil Steril*. 2012. 97:825–34.
- ¹³ Bitler, M, Schmidt L. "Utilization of infertility treatments: the effects of insurance mandates." *Demography*. 2012. 49:125–49.
- ¹⁴ Sunderam S, Kissin D, Crawford S, et al. "Assisted Reproductive Technology Surveillance—United States, 2010." *Morbidity and Mortality Weekly Report*. 2013. 62(9). Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6209a1.htm>. Accessed 5-19-2014.
- ¹⁵ Kissin D. "Assisted Reproductive Technology (ART): States Monitoring ART (SMART) Collaborative." 2012. Available at http://www.naphsis.org/mtg/Documents/KISSIN_NAPHSIS_SMART_Overview_June_6_2012.pdf. Accessed 5-19-14.
- ¹⁶ Mneimneh AS, Boulet SL, Sunderam S, et al. States Monitoring Assisted Reproductive Technology (SMART) Collaborative: data collection, linkage, dissemination, and use. *J Womens Health (Larchmt)*. 2013 Jul;22(7):571-7.
- ¹⁷ Sauber-Schatz EK, Sappenfield W, Grigorescu V, et al. Obesity, assisted reproductive technology, and early preterm birth—Florida, 2004-2006. *Am J Epidemiol*. 2012 Nov 15;176(10):886-96.
- ¹⁸ Cohen B, Bernson D, Sappenfield W, et al. Accuracy of assisted reproductive technology information on birth certificates: Florida and Massachusetts, 2004-06. *Paediatr Perinat Epidemiol*. 2014 May;28(3):181-90.
- ¹⁹ Michigan Department of Community Health. "Michigan's Surveillance Plan for the States Monitoring Assisted Reproductive Technology (SMART) Collaborative." Available at http://www.michigan.gov/documents/mdch/MISMART_Surv_Plan_380274_7.pdf. Accessed 5-19-14.