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Judith F. Daar; Robert G. Brzyski

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analyses must be reworked substantially and possibly uncover more potentially negative effects of undersupply and oversupply. That dilemma cannot be solved unless the supply is known—further argument for more accurate measure of physician supply.

The study by Staiger et al¹ provides one of several options for testing and comparing physician supply; in this case, US Census statistics and a cohort aging model. The model assumes consistent cohort effects over time when there may in fact be substantial changes in participation in clinical practice depending on the birth cohort—that is, physicians in the age range of 45 to 54 years may practice substantially more hours today than a similarly aged group in 2020. The lag in retirement reporting may be addressed with more timely reporting of activity from licensing agencies or third-party payers. For instance, development of better data collection and reporting mechanisms at the state level from licensing boards could be used to regularly update a central registry overseen by the Federation of State Medical Boards. What is surprising is that all of these are not used in a robust combination to provide a more consensus estimate of current and future effective supply of physicians. The federal government does, from time to time, issue a projection of physician supply,¹⁰ but it usually provokes more contention than agreement. The effects of this federal report on policy debates are often attenuated because the projection is often too late to really provide much guidance.

The physician workforce is one of the most critical factors that must be considered in current health care reform

efforts and discussions. Having accurate estimates for determining not only the number of physicians, but also current and future physician workforce requirements and capabilities for delivering primary and specialty care, will be essential for achieving and sustaining effective health care reform.

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REFERENCES

1. Staiger DO, Auerbach DI, Buerhaus PJ. Comparison of physician workforce estimates and supply projections. *JAMA*. 2009;302(15):1674-1680.
2. US National Library of Medicine. AMA deceased physicians card file. <http://www.nlm.nih.gov/exhibition/genealogy/amabiopage.html>. Accessed September 9, 2009.
3. Theodore CN, Haug JN, Balfe BE, Roback GA, Franz EJ. *Reclassification of Physicians, 1968*. Chicago, IL: American Medical Association; 1971.
4. Steinbrook R. For sale: physicians' prescribing data. *N Engl J Med*. 2006;354(26):2745-2747.
5. Fox DM. From piety to platitudes to pork: the changing politics of health workforce policy. *J Health Polit Policy Law*. 1996;21(4):825-844.
6. Reinhardt UE. *Physicians Productivity and the Demand for Health Manpower: An Economic Analysis*. Cambridge, MA: Ballinger Publishing Co; 1975.
7. Cooper RA, Getzen T, Johns MM, Ross-Lee B, Sheldon GF, Whitcomb ME. *Physicians and Their Practice Under Health Care Reform*. Philadelphia, PA: The Physicians Foundation; 2009.
8. Medicare Payment Advisory Commission. *Report to Congress: Improving Incentives to the Medicare Program*. Washington, DC: Medicare Payment Advisory Commission; 2009.
9. Grumbach K. Fighting hand to hand over physician workforce policy. *Health Aff (Millwood)*. 2002;21(5):13-27.
10. Bureau of Health Professions. *Physician Supply and Demand*. Rockville, MD: Health Resources and Services Administration, US Dept of Health & Human Services; 2006.

Genetic Screening of Sperm and Oocyte Donors Ethical and Policy Implications

Judith F. Daar, JD

Robert G. Brzyski, MD, PhD

FAMILY FORMATION THROUGH THE USE OF ASSISTED reproductive technology (ART) has increased steadily since the introduction of in vitro fertilization in 1978. Worldwide, more than 3 million individuals can trace their conception to in vitro fertilization, with nearly 3 in every 100 births in the United States currently attributable to some form of assisted conception.¹⁻³ Concomitantly increasing are the numbers of births using third-party gamete donors—men and

women who contribute sperm and eggs to another individual's or couple's reproductive enterprise. Although inaptly called donors because gamete providers typically receive compensation for their services, these individuals are essential to prospective parents who are without partners, in same-sex relationships, cannot afford advanced reproductive techniques such as microsurgical sperm aspiration, in vitro fertilization, and intracytoplasmic sperm injection, or whose infertility is linked to poor gametic quality.

Author Affiliations: Whittier Law School, Costa Mesa, California, and College of Medicine, University of California at Irvine, Irvine (Ms Daar); and University of Texas Health Science Center at San Antonio (Dr Brzyski).

Corresponding Author: Robert G. Brzyski, MD, PhD, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Dr, MSC 7836, San Antonio, TX 78229 (brzyski@uthscsa.edu).

See also p 1681.

In this issue of *JAMA*, Maron et al⁴ report the case of a male donor who unwittingly transmitted hypertrophic cardiomyopathy, a hereditary and potentially lethal cardiac anomaly, to offspring whose parents obtained his donor sperm from a commercial sperm bank. While highlighting the potential public health risks associated with undetected genetic mutations in gamete donors, the authors also raise critical questions about the practicality of comprehensive genetic testing of donors. Cost, coupled with the large and increasing multitude of detectable genetically transmitted diseases, pose significant challenges for ART patients, clinicians, and other professionals.

Legitimate concerns regarding the transmission of genetic disorders prompted Maron et al⁴ to call for a 2-pronged approach, using proactive and reactive measures to address and prevent the introduction of donor-based mutations into the recipient parents' genetic line. First, the authors advocate enhanced donor screening protocols, using family history as well as genetic and diagnostic testing (such as electrocardiogram for hypertrophic cardiomyopathy) to more effectively identify diseases detectable by these methods. Second, the authors suggest recording donor information in a national searchable database to facilitate identification and notification of affected offspring should a genetic disorder arise anywhere in the donor's pedigree.

Mandating comprehensive genetic screening of gamete donors as well as establishing a national donor registry may strike law and policy makers as measured and appropriate responses to prevent multigenerational transmission of donor-based genetic disorders. Before any such legal schemes are established, it is essential to consider the potential effects on each stakeholder in the ART equation, namely gamete donors, intended parents who use donor gametes, commercial sperm banks and egg donor agencies, and the offspring born with the aid of third-party donors.

In the main, gamete donors are unmarried men and women in their 20s and early 30s who are not parents. Individuals in this demographic group typically do not contemplate their own genetic health, let alone that of their offspring, until faced with their own childbearing decisions. For this reason, pretest and posttest genetic counseling should be required elements of any genetic screening protocol. However, evidence from another system of mandatory screening, regional newborn screening programs, indicates these counseling elements are not uniformly met.⁵ Donors need to understand that discovery of genetic information has individual as well as intragenerational and intergenerational significance. To the extent that testing for predisposition to heritable adult-onset disorders such as Alzheimer disease, breast cancer, and colorectal cancer are available, donors must be given the opportunity to make an informed choice about whether they wish to learn the results.

Donor tracing, as a posthoc response once a genetic disorder manifests or is detected in offspring, has generated substantial public debate. Some individuals involved with

ART have suggested a mandatory national gamete donor registry.^{6,7} Others favor a voluntary registry to centralize, maintain, and disseminate genetic and other medical information about gamete donors. Interest in a national donor database coalesced around a 2008 symposium during which representatives from the sperm and egg donor industry, donor-conceived children and their parents, and ART clinicians reportedly showed support for a voluntary registry,⁸ but to date no such system has been implemented. Hurdles include establishing a consensus regarding content, access, privacy, and financial responsibility. Attempts to enact laws requiring gamete donors to be named on offspring birth certificates have garnered only weak support, reinforcing US norms that protect donor anonymity.⁹

The cost of enhanced genetic donor screening will no doubt pass to gamete recipients, affecting the ability of less wealthy individuals to access this form of third-party reproduction. Those who can proceed will likely welcome the larger pool of health-related information. Geneticists caution, however, that prospective parents should be counseled about the limitations of genetic testing and its relationship to long-term offspring health. Providing recipients a clean genetic bill of health about a chosen donor can lead to a false sense of confidence about the risk of illness their child might face. A significant proportion of some genetic conditions, such as neurofibromatosis, arise from de novo mutations.

Careful counseling is especially advised when donor test results are negative for cancer-susceptibility genetic mutations, such as those found in the early onset breast cancer 1 (*BRCA1*) and breast cancer 2 (*BRCA2*) genes. Understanding that the majority of breast and ovarian cancers are not linked to these genes will help parents develop a more realistic outlook on their child's overall cancer risk. Moreover, preconception counseling should make clear that genetic testing may reduce the risk for specific diseases but cannot eliminate the 3% to 4% risk for birth defects that exists in all live-born children.¹⁰

Current use of genetic screening by sperm and egg donor enterprises is best described as inconsistent, largely because no federal regulations standardize donor screening for genetic anomalies. US Food and Drug Administration guidelines on gamete donation focus primarily on infectious agents, with scant attention paid to genetic disorders.¹¹ Arguably, it is not clear that such a standard would be effective or efficient given that genetic disorders can arise de novo, as well as cluster around demographic features such as race, ethnicity, sex, and religion—thus obviating the need to screen in many populations. In fact, obtaining a detailed family medical history may be just as useful in detecting a donor's likelihood of transmitting certain genetic diseases.¹⁰

Gamete agencies that support screening donors are not without guidance. The American Society for Reproductive Medicine has published practice guidelines for gamete and embryo donation including specific recommendations on

genetic screening for gamete donors.¹² Compliance with its guidelines is voluntary, and data suggest the majority of sperm banks and egg donor agencies do not follow the established screening protocols. In the case of sperm banks, only half of all programs reported conducting a chromosome analysis on donor applicants, whereas a quarter of all egg donor agencies reported no screening for oocyte donors.^{10,13} Even in centers that did report testing, most did not fully follow the guidelines set forth by the American Society for Reproductive Medicine. While not insurmountable, shifting from an environment of no or low screening to a standard of robust activity will require a period of technical and cultural transition.

Preventing transmission of genetic disorders to donor offspring is vital to individual health, as well as the health of the burgeoning ART field. Incidence of transmission via gamete donors is rare compared with transmission in the general population, but penetrance in any child can be devastating. In addition to hypertrophic cardiomyopathy, gamete donors have been linked to transmission of several disorders including autosomal dominant polycystic kidney disease,¹⁴ cystic fibrosis,¹⁵ and severe congenital neutropenia.¹⁶ With each new case, calls for enhanced screening and mandatory registration of gamete donors understandably grow louder.¹⁷

Opponents of mandatory genetic screening of gamete donors cite cost and the impracticality and low yield associated with a comprehensive approach as a rationale for maintaining the current market-driven program-by-program system. Maron et al⁴ present a strong counterargument, which states that enhanced screening, as suggested by the American Society for Reproductive Medicine, and simple diagnostics such as electrocardiogram, are in the public's best interest. Adding baseline genetic screening to current US Food and Drug Administration regulations and establishing a voluntary registry of gamete donors are sensible enhancements to a field historically vigilant of offspring health and patient confidence.

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REFERENCES

1. European Society for Human Reproduction and Embryology. Three million babies have been born using assisted reproductive technologies. *Women's Health Law Weekly*. July 16, 2006. <http://www.newsrx.com/newsletters/Womens-Health-Law-Weekly/2006-07-16/071020063331228WH.html>.
2. Centers for Disease Control and Prevention; American Society for Reproductive Medicine, Society for Assisted Reproductive Technology. 2006 Assisted reproductive technology success rates: national summary and fertility clinic reports. Atlanta, GA: US Dept of Health and Human Services, Centers for Disease Control and Prevention; 2008. <http://www.cdc.gov/art/ART2006/508PDF/2006ARTCover-National.pdf>. Accessed September 4, 2009.
3. Institute for Science, Law and Technology Working Group. ART into science: regulation of fertility techniques. *Science*. 1998;281(5377):651-652.
4. Maron BJ, Lesser JR, Schiller NB, Harris KM, Brown C, Rehm HL. Implications of hypertrophic cardiomyopathy transmitted by sperm donation. *JAMA*. 2009;302(15):1681-1684.
5. Farrell M, Certain LK, Farrell P. Genetic counseling and risk communication services of newborn screening programs. *Arch Pediatr Adolesc Med*. 2001;155(2):120-126.
6. Graham J. When a disease is donated: mom's quest to warn daughter's offspring goes to the heart of a thorny debate on sperm, egg donors. *Chicago Tribune*. March 27, 2008:A1.
7. Cahn N. Necessary subjects: the need for a mandatory national donor gamete registry. *DePaul J Healthcare Law*. 2008;203-224. http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1120389. Accessed September 4, 2009.
8. Foohey P. Potential national voluntary gamete donor registry discussed at recent health law symposium. *J Law Med Ethics*. 2008;36(3):597-601.
9. HR 355, 95th Leg, 1st Sess (MO 2009).
10. Sims CA, Callum P, Ray M, Iger J, Falk RE. Genetic testing of sperm donors: survey of current practices [published online ahead of print March 31, 2009]. *Fertil Steril*. doi:10.1016/j.fertnstert.2009.01.139.
11. US Department of Health and Human Services; US Food and Drug Administration; Center for Biologics Evaluation and Research. Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS), August 27, 2007. <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm073964.htm>. Accessed September 4, 2009.
12. Practice Committee of American Society for Reproductive Medicine; Practice Committee of Society for Assisted Reproductive Technology. 2008 Guidelines for gamete and embryo donation: a practice committee report. *Fertil Steril*. 2008;Nov(90)(5 suppl):S30-S44.
13. Powis Z, Peters KP, Blatt S. Genetic screening of oocyte donors. *Fertil Steril*. 2004;82(suppl 2):S188. doi:10.1016/j.fertnstert.2004.07.496.
14. *Johnson v Superior Court*, 80 Cal App 4th 1050 (2000).
15. *Paretta v Medical Offices for Human Reproduction*, 760 NYS 2d 639 (2003).
16. Boxer LA, Stein S, Buckley D, Bolyard AA, Dale D. Strong evidence for autosomal dominant inheritance of severe congenital neutropenia associated with ELA2 mutations. *J Pediatr*. 2006;148(5):633-636.
17. Kramer W. The case for comprehensive medical testing of gamete donors. Donor Sibling Registry Web site. <http://donorsiblingregistry.com/bionews10.pdf>. Accessed September 24, 2009.