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# In Vitro Fertilization and the Law: How Legal and Regulatory Neglect Compromised a Medical Breakthrough

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# IN VITRO FERTILIZATION AND THE LAW: HOW LEGAL AND REGULATORY NEGLECT COMPROMISED A MEDICAL BREAKTHROUGH

Steve P. Calandrillo\* and Chryssa V. Deliganis\*\*

*The rise of assisted reproductive technology like in vitro fertilization (“IVF”) as a method of human reproduction represents a remarkable medical achievement. Live births and success rates have increased dramatically in the past decade, so much so that many fertility clinics now “guarantee” a baby to clients who sign up. But with successes come inevitable downsides. Everyone knows that the price tag is steep, but given the demand, relatively few individuals are deterred. More insidious are the increased birth-defect risks associated with reproductive technologies. For some time it was assumed that these risks were due to the fact that individuals attempting IVF were older and possessed greater risk factors themselves. Now, however, recent research is showing that it may be IVF itself, and, in particular, the dramatic rise of a new technique called intracytoplasmic sperm injection (“ICSI”), that is responsible for negative outcomes. IVF providers face little incentive to impress these risks on their customers, and operate in a largely unregulated environment in which cash is king and informed consent is optional. The incentive to report high live-birth rates dictated by the profit motive pushes some clinics to implant more embryos than necessary and to recommend technologies that may increase births despite the fact that they increase defect rates.*

*Sadly, law and regulation lag far behind the technology in this arena. While some industry groups have promulgated responsible guidelines for appropriate use of reproductive technology, they come with no viable enforcement or disciplinary mechanisms. Law’s absence has contributed to a “wild west” mentality in some fertility clinics, where anything goes if it will make money. It is past time that the*

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*law and medical regulators become involved in assessing the rapidly growing reproductive technologies available today in order to preserve their benefits while mitigating the risks that are largely unknown or ignored by most patients.*

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### INTRODUCTION

A remarkable transformation in human reproduction is underway in our society. For all of human history, there was but one tried-and-true method available to individuals who wished to be parents. Today, however, extraordinary pharmaceutical and technological innovation is fundamentally changing the way Americans have children. The technology continues to expand by leaps and bounds every year, while law and governmental regulation lag far behind. From fertility drugs, to intra-uterine insemination, to the advent of in vitro fertilization (“IVF”), and now intracytoplasmic sperm injection (“ICSI”), modern medicine has paved the way for millions of Americans to have children who were previously only the subject of their unrequited dreams.

Obviously, these transformational reproductive breakthroughs have provided immeasurable joy for new parents. Today, ten million children are alive who could not have been born just one generation ago.

However, these new innovations and technologies carry their own unique risks, from multiple births to low birth weight to severe birth defects. Yet these inherent dangers are often glossed over by a fertility industry now making billions of dollars per year. The perverse financial incentives, paired with the pressure for reproductive clinics to advertise better outcomes (i.e., live births), have led some to engage in practices that are not only questionable, but that are sometimes even quite dangerous for their patients.

Why are these risks and dangers becoming exponentially worse today? Quite candidly, it is the stunning absence of law and regulation in the medical reproductive arena. Technological advances have greatly outpaced the introduction of responsible laws and regulation. Politicians will not touch the controversial subject with a ten-foot pole, and federal funding of embryo research is explicitly banned. Not surprisingly, government regulators have therefore been largely uninvolved and ineffective in the field. Further, the reproductive professionals themselves resist all forms of outside interference, fearing that their skyrocketing profits might be in danger. They cry, “We can regulate ourselves—keep law out!” But we all know what happens when the fox guards the hen house.

Part I of this Article details the historical background of fertility treatments, ranging from pharmaceutical breakthroughs to intrauterine insemination to IVF and now ICSI. Part II explores the downsides of fertility treatments’ unparalleled “success,” and, in particular, examines the hidden dangers of fertility drugs, the risk of multiple births, birth defects, and the unique challenges posed by IVF and ICSI. The “wild west” mentality of the industry has even prompted the inventor of the latter technique to publicly criticize its dramatic overuse. Part III lays out the current legal and regulatory oversight scheme in the United States, paying attention to the enormous gaps in coverage, the lack of enforcement mechanisms, and the consequences for patients. Part IV offers normative recommendations for legal and public policy reform, including mandated disclosure of risks, mandatory certification of fertility clinics, and the explicit federal regulation of IVF and ICSI. Adopting these legal and regulatory approaches allows for the ability to maintain the benefits of these amazing new reproductive innovations, while also preventing future abuses.

In sum, it is past time for legislatures and regulators to address the unique benefits and challenges created by the rise of modern reproductive technologies. If we fail to muster the political will to do so today, thousands of future lives will suffer as a result.

## **I. THE REMARKABLE HISTORY OF ASSISTED REPRODUCTION**

For many people, starting a family is the most fulfilling and important task they will ever undertake—an intimate act central to realizing one’s life goals. However, biology is not always kind. For all of human history, countless millions of people have been unable to have children. Today, however, assisted reproductive technology has opened the doors of parenthood to millions for whom those doors were once firmly shut.

### A. Early Discoveries

Modern assisted reproductive technology (“ART”) is the culmination of over 100 years of research and experimentation. As early as 1878, researchers began attempts to fertilize mammalian eggs in vitro.<sup>1</sup> These early attempts were largely unsuccessful, and although the possibility that fertilization occurred in some cases has not been ruled out, most early claims of success were inadequately substantiated or based on misinterpreted results.<sup>2</sup> However, a major breakthrough in IVF experimentation came in 1951 with the discovery of sperm capacitation by Colin Russell Austin and Min Chueh Chang.<sup>3</sup> Capacitation refers to changes that sperm undergo prior to fertilization while residing in a female’s reproductive tract.<sup>4</sup> Within a few years of their discovery, researchers successfully fertilized rabbit eggs in vitro for the first time.<sup>5</sup> During the “golden age” of IVF research that followed, numerous experiments were conducted on a wide range of mammal species,<sup>6</sup> culminating in 1969 with the first convincing fertilization of human eggs in vitro.<sup>7</sup> The achievement was made possible by research done on hamster IVF that allowed for the proper modification of culture-medium protocols.<sup>8</sup> However, despite researchers’ success in fertilizing eggs in vitro, it would be nearly another decade before in vitro resulted in a live birth.<sup>9</sup>

In July 1978, Louise Brown became the first person born as a result of IVF.<sup>10</sup> Her mother, Lesley Brown, had enlisted the aid of Patrick Steptoe and

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1. Barry D. Bavister, *Early History of In Vitro Fertilization*, 124 REPROD. 181, 182 (2002) (In vitro essentially means in glass, or in other words, in the laboratory. This is contrasted with in vivo, which means inside a living organism).

2. *Id.* at 182–83.

3. *Id.* at 183 (“Both Austin and Chang postulated that the spermatozoa of some mammalian species need to reside for some time with the female reproductive tract before acquiring the capacity to penetrate eggs, and Austin (1951) coined the term ‘capacitation’ to refer to the change spermatozoa undergo during this time.”); see also C.R. Austin, *Observations on the Penetration of Sperm into the Mammalian Egg*, 4 AUSTL. J. SCI. RESEARCH SERIES B 581 (1951); M.C. Chang, *Fertilizing Capacity of Spermatozoa Deposited into the Fallopian Tubes*, 168 NATURE 697 (1951).

4. Bavister, *supra* note 1, at 183.

5. *Id.*

6. *Id.* at 183–84 (IVF research was performed with hamsters, mice, rats, sheep, pigs, and cats).

7. *Id.* at 184 (Fertilization of human eggs in vitro was first “convincingly achieved in 1969, as evidenced by sperm penetration, polar body emission and formation of pronuclei.” (citing B.D. Bavister et al., *Identification of the Midpiece and Tail of the Spermatozoon During Fertilisation of Human Eggs In Vitro*, 20 J. REPROD. & FERTILITY 159 (1969))).

8. *Id.* at 183–84 (“[I]t may be claimed that hamster IVF paved the way for human IVF.” (citing R. Yanagimachi & M.C. Chang, *Fertilisation of Hamster Eggs In Vitro*, 200 NATURE 281 (1963); R. Yanagimachi & M.C. Chang, *In Vitro Fertilisation of Golden Hamster Ova*, 156 J. EXPERIMENTAL ZOOLOGY 361 (1964))).

9. Bavister, *supra* note 1, at 184 (the first human birth from an IVF embryo occurred in 1978).

10. Jeff Wang & Mark V. Sauer, *In Vitro Fertilization (IVF): A Review of 3 Decades of Clinical Innovation and Technological Advancement*, 2 THERAPEUTICS &

Robert Edwards at Oldham General Hospital in England in an attempt to overcome her persistent infertility.<sup>11</sup> The successful procedure involved laparoscopic surgery to retrieve one of her eggs, which was then fertilized in a laboratory, and later transferred back into the uterus.<sup>12</sup> This original procedure did not utilize any fertility drugs.<sup>13</sup> Steptoe and Edwards went on not only to repeat this result successfully in future experiments, but also substantially improved their technique over the next several years.<sup>14</sup>

### ***B. Dramatic Explosion in ART Technology During the 1980s***

The 1980s witnessed dramatic growth and advancement in assisted reproductive technologies. Between 1980 and 1983, the widespread use of fertility drugs such as clomiphene<sup>15</sup> and leuporelin<sup>16</sup> in the IVF process drastically improved the pregnancy rate by 6%–30% per cycle.<sup>17</sup> By the mid-1980s, several alternative methods of assisted reproduction came to fruition, including gamete intrafallopian transfer (“GIFT”) and zygote intrafallopian transfer (“ZIFT”).<sup>18</sup> These procedures differed from IVF in a number of ways. GIFT involves fertilization in vivo—in other words, within the woman’s reproductive tract rather than in a laboratory.<sup>19</sup> ZIFT was similar to traditional IVF but also involved a

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CLINICAL RISK MGMT. 355, 356 (2006); *see also* P.C. Steptoe & R.G. Edwards, *Birth After Reimplantation of a Human Embryo*, 312 LANCET 366, 366 (1978).

11. Wang & Sauer, *supra* note 10.

12. *Id.* (citing Steptoe & Edwards, *supra* note 10).

13. *Id.* (noting that no medications were used to “stimulate the ovaries” of Lesley Brown prior to laparoscopic egg retrieval).

14. *Id.*

15. Commonly marketed as Clomid, clomiphene has been around since the 1960s and has long been used to treat ovulatory dysfunction in women desiring a pregnancy. In a clinical study of over 7,000 patients suffering from impediments to ovulation, administration of Clomid resulted in a roughly 30% pregnancy rate. Of those pregnancies, about 8% were multiple. *See Clomid FDA label*, U.S. FOOD & DRUG ADMIN. (Nov. 22, 2012), [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/016131s026lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/016131s026lbl.pdf).

16. Commonly marketed as Lupron, leuporelin is indicated to treat female fertility conditions such as Endometriosis and Uterine Leiomyomata. *See Lupron FDA Label*, U.S. FOOD & DRUG ADMIN. (Nov. 30, 2013), [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/016131s026lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/016131s026lbl.pdf). However, it should be noted that the drug is contraindicated for women who may become pregnant while using the drug due to potential harm to the fetus. *Id.* (“LUPRON DEPOT may cause fetal harm when administered to a pregnant woman.”).

17. *Id.*; *see also* R.G. Edwards & P.C. Steptoe, *Current Status of In-Vitro Fertilisation and Implantation of Human Embryos*, 2 LANCET 1265 (1983).

18. Wang & Sauer, *supra* note 10, at 357.

19. STEVE PARKER, *IN VITRO FERTILIZATION* 33 (2007) (“In this technique, eggs and sperm . . . are collected and checked as in a standard IVF procedure. But instead of placing the eggs and sperm into a culture medium, they are put back into the woman’s fallopian tube using a laparoscope. Fertilization then takes place in the fallopian tube, as happens in natural conceptions.”).

second laparoscopy to transfer the fertilized egg into the fallopian tube.<sup>20</sup> Both procedures offered advantages over the original IVF method developed by Steptoe and Edwards.

However, IVF soon returned to the forefront of reproductive technology due to major breakthroughs in ultrasound technology in the late 1980s. These improvements transformed the process of oocyte retrieval into the modern outpatient IVF procedure we know today. In 1987 the development of ultrasound-guided transvaginal follicle aspiration created numerous advances over its predecessor techniques, and quickly became the “procedure of choice.”<sup>21</sup> The innovation did away with the necessity of laparoscopy, and in turn decreased the time, expense, and risk involved in the oocyte retrieval process.<sup>22</sup> The improvement was so substantial that IVF procedures transitioned from one or two hours of hospital-based operating-room time to a mere 10 or 15 minute process that could be performed in an office setting.<sup>23</sup> The dramatic improvement in ultrasound technology marginalized GIFT and ZIFT, as those procedures continued to necessitate invasive surgery.<sup>24</sup> In contrast, IVF could now be performed without laparoscopy, and instead utilized less expensive and minimally invasive ultrasound-guided aspirations.<sup>25</sup> Thus, despite a lower pregnancy rate per procedure, by the early to mid-1990s IVF had become firmly ensconced as the preferred method of assisted reproduction and has remained so ever since.<sup>26</sup>

### C. Addressing Male Infertility: ICSI and IVF

While traditional IVF was often successful in treating female infertility, the overall effectiveness of the procedure was limited by its inability to adequately address male infertility.<sup>27</sup> However, the male end of the fertility equation was soon addressed. In 1992 researchers introduced a new procedure, known as ICSI,

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20. *Id.*; see also Wang & Sauer, *supra* note 10, at 357 (explaining that ZIFT allowed for the confirmation of fertilization while maintaining some of the theoretical benefits of GIFT but that the procedure required two laparoscopies to complete).

21. Wang & Sauer, *supra* note 10, at 358 (“First reported in 1987, this oocyte retrieval technique quickly became the procedure of choice due to better visualization, finer control, and less patient discomfort compared with other available methods.” (citing Matts Wikland et al., *Use of a Vaginal Transducer for Oocyte Retrieval in an IVF/ET Program*, 15 J. CLINICAL ULTRASOUND 245 (1987))).

22. *Id.*

23. *Id.*

24. *Id.*

25. *Id.*

26. *Id.* at 358–59 (“By 1995, Society for Assisted Reproductive Technology (SART) data noted that IVF, GIFT, and ZIFT consisted of 70%, 6%, and 2% of ART cycles respectively, despite pregnancy rates of 22.3%, 28.7%, and 30.3% for each procedure. . . . In 2003, GIFT and ZIFT were used in only 0.1% and 0.4% of ART cycles, while IVF represented the remaining 99.5% of cases.”); see also CTRS. FOR DISEASE CONTROL & PREVENTION, ASSISTED REPRODUCTIVE TECHNOLOGY REPORT: NATIONAL ART SUCCESS RATES (2003), [http://nccd.cdc.gov/DRH\\_ART/Apps/NationalSummaryReport.aspx](http://nccd.cdc.gov/DRH_ART/Apps/NationalSummaryReport.aspx) (select “2003” from the drop-down menu at the top of the page).

27. Wang & Sauer, *supra* note 10, at 359.

designed to address many of the challenges posed by male infertility.<sup>28</sup> ICSI differs from traditional IVF in that, instead of letting the sperm and eggs mingle freely in order to achieve conception, a single sperm is isolated and injected directly into the cytoplasm of the egg with a microneedle.<sup>29</sup> Because the procedure requires only a single healthy sperm, it is especially useful to treat infertility in a man who suffers from a low sperm count or the presence of abnormal sperm (e.g., those that cannot “swim” on their own).<sup>30</sup> The development of testicular sperm extraction (“TESE”) has allowed fertilization rates of up to 70%, despite using only a few poor-quality sperm.<sup>31</sup>

After its introduction, ICSI quickly gained popularity, rapidly transitioning into clinical practice and accounting for 11% of all IVF cycles by 1995.<sup>32</sup> Moreover, the popularity of ICSI has continued to expand rapidly—in 2011 the procedure accounted for a shocking 67% of all IVF cycles.<sup>33</sup> However, Jeff Wang and Mark Sauer note that there is still a significant debate on the propriety of “altering the process of natural selection” so drastically, since ICSI allows potentially poor-quality sperm to fertilize eggs that never would have had a chance before its invention.<sup>34</sup>

#### *D. Remarkable Outcomes (and Expenses)*

Today IVF is practiced in a majority of the world’s countries,<sup>35</sup> and since its inception, the procedure is estimated to be responsible for the birth of around ten million babies.<sup>36</sup> In the United States, roughly 10% of Americans suffer from some kind of fertility problem leading approximately one million people to seek fertility treatment annually.<sup>37</sup> The revenue generated by this market activity is immense—IVF is a costly procedure with a single cycle of treatment costing \$10,000–\$20,000.<sup>38</sup> What’s more, because IVF is not always successful in

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28. *Id.* (citing Gianpiero Palermo et al., *Pregnancies After Intracytoplasmic Injection of Single Spermatozoon into an Oocyte*, 340 LANCET 17, 17–18 (1992)).

29. *See* PARKER, *supra* note 19, at 32.

30. *Id.*

31. Wang & Sauer, *supra* note 10, at 359.

32. *Id.* (citing CTRS. FOR DISEASE CONTROL & PREVENTION, ASSISTED REPRODUCTIVE TECHNOLOGY SUCCESS RATES: NATIONAL SUMMARY AND FERTILITY CLINICS REPORT (1995)).

33. CTRS. FOR DISEASE CONTROL & PREVENTION, ASSISTED REPRODUCTIVE TECHNOLOGY REPORT: NATIONAL ART SUCCESS RATES 4 (2011), *available at* <http://www.cdc.gov/art/pdf/2011-report/national-summary/art-2011-national-summary-report.pdf> [hereinafter 2011 ART REPORT].

34. Wang & Sauer, *supra* note 10, at 359–60 (discussing inheritable causes of male infertility, their transmission via ICSI, and the potential for increased health problems in children conceived via ICSI); *see also* discussion *infra* Part II.

35. KAY ELDER & BRIAN DALE, IN-VITRO FERTILIZATION viii (3d ed. 2011).

36. *Id.*

37. NAOMI R. CAHN, TEST TUBE FAMILIES: WHY THE FERTILITY MARKET NEEDS LEGAL REGULATION 1 (2009).

38. CHARLES P. KINDREGAN JR. & MAUREEN MCBRIEN, ASSISTED REPRODUCTIVE TECHNOLOGY: A LAWYER’S GUIDE TO EMERGING LAW AND SCIENCE 95 (2d ed. 2011) (citing

producing a pregnancy, many patients have to undergo multiple procedures, significantly raising the overall cost and risk of treatment.<sup>39</sup> The fertility industry has grown to accommodate this demand—with nearly 500 clinics in existence nationwide, fertility drugs alone make up a \$3 billion per year industry.<sup>40</sup> In light of the incredible cost for what is essentially an elective procedure, it should not come as a surprise that insurance coverage for IVF is limited or nonexistent in most states.<sup>41</sup>

As the industry has grown, the use of artificial reproductive technology, including both IVF and pharmaceutical interventions, has steadily increased.<sup>42</sup> In 1996 there were nearly 65,000 ART cycles resulting in 14,507 live-birth deliveries for a total of 20,840 live-born infants.<sup>43</sup> By 2011 the number of ART cycles had more than doubled to over 150,000, resulting in 47,818 live births for a total of 61,610 live-born infants.<sup>44</sup> Moreover, as the usage of IVF has increased, so has the prevalence of ICSI—in 2011 ICSI accounted for 67% of all ART cycles.<sup>45</sup> This represents a dramatic increase in the use of a procedure that 16 years ago accounted for only 11% of all IVF procedures.<sup>46</sup> In fact, the percentage of IVF cycles utilizing ICSI has increased every single year from 1997 to 2011.<sup>47</sup>

The explosion in ICSI's popularity also tracks a dramatic uptick in the success rate of IVF. According to the Centers for Disease Control and Prevention ("CDC"), in 1997 30.7% of IVF cycles resulted in live births for mothers under the age of 35.<sup>48</sup> In that year, ICSI was used in only 35% of all IVF cycles.<sup>49</sup> In contrast, by 2010 41.5% of all IVF cycles resulted in live births for mothers under the age of 35—with ICSI being used in 66% of all IVF cycles.<sup>50</sup> The trend holds true for all of the surveyed age groups: as the percentage of IVF cycles utilizing

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Judith F. Darr, *Assessing Reproductive Technologies: Invisible Barriers, Indelible Harms*, 23 BERKELEY J. GENDER L. & JUST. 18, 36 n.64 (2008)).

39. *See id.*

40. CAHN, *supra* note 37.

41. KINDREGAN & MCBRIEN, *supra* note 38 (citing Judith F. Darr, *Assessing Reproductive Technologies: Invisible Barriers, Indelible Harms*, 23 BERKELEY J. GENDER L. & JUST. 18, 36 n.64 (2008)).

42. *See* CAHN, *supra* note 37.

43. CTRS. FOR DISEASE CONTROL & PREVENTION, ASSISTED REPRODUCTIVE TECHNOLOGY REPORT: NATIONAL SUMMARY AND FERTILITY CLINICS SUCCESS RATES (1996).

44. 2011 ART REPORT, *supra* note 33, at 3.

45. *Id.* at 4.

46. Wang & Sauer, *supra* note 10, at 359 (citing NAT'L CTR. FOR CHRONIC DISEASE PREVENTION & HEALTH PROMOTION, 2003 ASSISTED REPRODUCTIVE TECHNOLOGY SUCCESS RATES: NATIONAL SUMMARY AND FERTILITY CLINIC REPORTS (2005)).

47. *See* CTRS. FOR DISEASE CONTROL & PREVENTION, ASSISTED REPRODUCTIVE TECHNOLOGY REPORT: NATIONAL SUMMARY AND FERTILITY CLINICS SUCCESS RATES (1997), available at [http://nccd.cdc.gov/DRH\\_ART/Apps/NationalSummaryReport.aspx](http://nccd.cdc.gov/DRH_ART/Apps/NationalSummaryReport.aspx) [hereinafter 1997 ART REPORT]; CTRS. FOR DISEASE CONTROL & PREVENTION, ASSISTED REPRODUCTIVE TECHNOLOGY REPORT: NATIONAL SUMMARY AND FERTILITY CLINICS SUCCESS RATES (2010) [hereinafter 2010 ART REPORT], available at <http://www.cdc.gov/art/ART2010/#report1>.

48. 1997 ART REPORT, *supra* note 47.

49. *Id.*

50. 2010 ART REPORT, *supra* note 47.

ICSI has increased, so has the percentage of cycles resulting in live births.<sup>51</sup> This trend is particularly pronounced among older women. In 1997 only 7.6% of IVF cycles resulted in live births for women aged 41–42.<sup>52</sup> By 2010, the live-birth rate had risen to 12.4% for women in this age group—a 63% increase.<sup>53</sup>

The data shows several unmistakable trends over the last 15 years: (1) the percentage of IVF cycles utilizing ICSI increased dramatically; (2) the percentage of IVF cycles that led to live births increased almost every single year; and (3) the percentage of successful outcomes for older mothers increased substantially.<sup>54</sup> Many of the genetic factors that prohibited spontaneous reproduction in both sexes have now been overcome by traditional IVF and ICSI.<sup>55</sup> The inevitable tick of the biological clock is no longer the same barrier it once was to older women.<sup>56</sup> In the words of one commentator, “Creating a family, regardless of whether you are an infertile husband-and-wife couple, a same-sex couple, or a single person, now involves a deliberate choice.”<sup>57</sup>

However, it should be noted that all of the successes detailed above offer no glimpse into patient outcomes *after* a live birth has occurred. As with every pioneering technology, there are inevitable downsides, some of which may not be immediately apparent.

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51. See *supra* text accompanying note 47 (data from 1997–2011 shows consistent upward trend in success rates and usage of ICSI).

52. 1997 ART REPORT, *supra* note 47 (data from 1997 shows 6,691 IVF cycles performed on women aged 41–42 with a success rate of 7.6%).

53. 2010 ART REPORT, *supra* note 47 (data from 2010 shows 10,122 cycles performed on women aged 41–42 with a success rate of 12.4%).

54. See *supra* text accompanying note 47 (data is currently available from 1997–2011 allowing for the identification of trends within that range).

55. See Wang & Sauer, *supra* note 10, at 362. Moreover, emerging technologies such as preimplantation genetic diagnosis (“PGD”) have allowed couples suffering from some sex-linked diseases and other genetic disorders to have children free of those conditions. See CAHN, *supra* note 37, at 62. PGD is generally available to screen for several kinds of diseases: (1) testing to determine the sex of the embryo for sex-linked diseases like Duchenne muscular dystrophy; (2) diseases that result from a single gene defect such as cystic fibrosis; and (3) chromosomal disorders. Frances A. Flinter, *Preimplantation Genetic Diagnosis Needs to Be Tightly Regulated*, 322 BRIT. MED. J. 1008, 1008–09 (2001). PGD can also be used to screen for aneuploidy (e.g., Down’s Syndrome), though this is not allowed in some countries (e.g., the United Kingdom). *Id.* at 1009. However, for its many promising benefits, PGD also has risks. One study found that the procedure has the potential to lower the live-birth rate for older women. See Sebastian Mastenbroek et al., *Preimplantation Genetic Screening: A Systematic Review and Meta-Analysis of RCTs*, 17 HUM. REPROD. UPDATE 454, 454 (2011). Another suggested PGD might be responsible for increasing the perinatal death rate in multiple pregnancies. Inge Liebaers et al., *Report on a Consecutive Series of 581 Children Born After Blastomere Biopsy for Preimplantation Genetic Diagnosis*, 65 OBSTETRICAL & GYNECOLOGICAL SURV. 240, 240 (2010).

56. See CAHN, *supra* note 37 (noting that by the age of 40, 33% of couples are infertile and that 18% of women using ART technology were over the age of 40 in 2004).

57. *Id.* at 3.

## II. THE DOWNSIDE OF SUCCESS

While ART has provided millions of couples with the incredible opportunity to become parents, emerging research suggests that it comes with significant risks for the children produced. The profit motive leads some fertility clinics to prescribe drugs that may unnecessarily cause multiple births and associated negative health outcomes for both mothers and children. When IVF is the reproductive route of choice, some clinics have been known to harvest more eggs and implant more embryos than responsible medical providers should. Worse, the emerging new IVF technique of choice, ICSI, presents risks that many soon-to-be parents are wholly unaware of.

### *A. The Dangers of Assisted Reproduction: Fertility Drugs and the Risk of Multiples*

Assisted reproduction spans a wide range of procedures, each with its own benefits and risks. The most widely used “first option” in the assisted reproduction field is not IVF or ICSI; rather, fertility drugs—such as Clomid, Lupron, Repronex—form the foundation of most modern infertility treatments.<sup>58</sup> These drugs are generally used to stimulate ovulation and allow for the harvesting of multiple oocytes.<sup>59</sup> The rise of ovulation-stimulation drugs has contributed to a rapid increase in the number of high-order pregnancies involving three or more fetuses.<sup>60</sup> ART-related use of the drugs typically involves the removal of multiple eggs after stimulation and then fertilization via either IVF or ICSI.<sup>61</sup> In contrast, when used without ART, the ovulation drugs are typically used in conjunction with timed sexual intercourse, or some other form of assisted insemination such as intrauterine insemination (“IUI”).<sup>62</sup> Both uses are associated with extremely high incidences of multiple gestation and multiple births.<sup>63</sup> In fact, *roughly 44% of all*

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58. See Laura A. Schieve et al., *Estimation of the Contribution of Non-assisted Reproductive Technology Ovulation Stimulation Fertility Treatments to US Singleton and Multiple Births*, 170 AM. J. EPIDEMIOLOGY 1396 (2009) (concluding that roughly 4.6% of infants born in the U.S. in 2005 resulted from non-ART ovulation treatments, which is four times greater than the contribution of ART).

59. *Reproductive Health, Infertility FAQs*, CTRS. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/reproductivehealth/Infertility/index.htm> (last updated June 20, 2013) (discussing the use and purpose of common fertility drugs).

60. See Norbert Gleicher et al., *Reducing the Risk of High-Order Multiple Pregnancy After Ovarian Stimulation with Gonadotropins*, 343 NEW ENG. J. MED. 2 (2000); Schieve et al., *supra* note 58, at 1397.

61. See Schieve et al., *supra* note 58.

62. *Id.* Despite the success of IVF, intrauterine insemination remains relatively common, often making up the first step before couples resort to the more invasive—and expensive—IVF. IUI involves the placement of washed and concentrated sperm directly into a woman’s uterus around the time she releases one or more eggs. *Tests and Procedures: Intrauterine Insemination: Definition*, MAYO CLINIC (June 29, 2013), <http://www.mayoclinic.org/tests-procedures/intrauterine-insemination/basics/definition/prc-20018920>. The procedure is often undertaken with sperm from an anonymous donor or from a known male, often the husband.

63. Schieve et al., *supra* note 58.

ART procedures result in twins, and about 5% result in triplets or higher-order multiples.<sup>64</sup>

While some infertile parents are not overly deterred by the thought of having twins or triplets, they are often far less aware that multiple-order pregnancies are associated with a dramatically increased risk of substantial health problems. Compared to singletons, multiple-order pregnancies are subject to markedly higher risks of pregnancy complications, preterm delivery, infant death, and neurological impairments in the surviving babies.<sup>65</sup> Preterm delivery is especially common, as the length of pregnancy decreases significantly with each additional fetus. In fact, about 60% of twins, and more than 90% of higher-order multiples, are born premature.<sup>66</sup> Low birth weight is also common and often results from preterm delivery.<sup>67</sup> According to data gathered by the CDC, in 2005 97% of all triplets or higher-order multiples conceived through ART were born premature.<sup>68</sup> While advances in preterm care have brightened outlooks for these babies somewhat, the costs are extraordinary and the children are still at increased risk for early health problems and lasting disabilities like cerebral palsy, hearing loss, and intellectual disability.<sup>69</sup> Moreover, at least one study has found that opposite-sex twins born from non-IVF-controlled ovarian stimulation had a significantly higher incidence of very low birth weight and severe prematurity compared to opposite-sex twins that were conceived naturally.<sup>70</sup>

Singletons and mothers are not entirely immune from the dangers posed by ovulation treatments either. Some studies have suggested that singletons conceived with the aid of non-ART ovulation treatments may be at increased risk of pregnancy complications, low birth weight, preterm delivery, and other poor outcomes.<sup>71</sup> Mothers also face the risk of health problems associated with carrying twins, triplets, or higher-order multiples to term. Especially common is pre-eclampsia, a complication characterized by high blood pressure, swelling, and

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64. Victoria Clay Wright et al., *Assisted Reproductive Technology Surveillance—United States, 2005*, 57 MORBIDITY & MORTALITY WKLY. REP. SURVEILLANCE SUMMARIES 1, 8 (2008).

65. See Schieve et al., *supra* note 58; see also Wright et al., *supra* note 64, at 1.

66. See *Multiples: Twins, Triplets and Beyond*, MARCH OF DIMES (Dec. 2009), <http://www.marchofdimes.com/pregnancy/multiples-twins-triplets-and-beyond.aspx>.

67. *Id.* (“More than half of twins and almost all higher-order multiples are born with low birthweight (less than 5½ pounds or 2,500 grams). [Low birth weight] can result from premature birth and/or poor fetal growth. Both are common in multiple pregnancies.”).

68. See Wright et al., *supra* note 64, at 1.

69. *Id.* (discussing the health and disability challenges facing low birth weight babies).

70. Willem Ombelet et al., *Perinatal Outcome of 12,021 Singleton and 3,108 Twin Births After Non-IVF-Assisted Reproduction: A Cohort Study*, 21 HUMAN REPROD. 1025, 1030 (2006).

71. *Id.* (citing Marco Gaudoin et al., *Ovulation Induction/Intrauterine Insemination in Infertile Couples is Associated with Low-Birth-Weight Infants*, 188 AM. J. OBSTETRICS & GYNECOLOGY 611 (2003); Bengt Källén et al., *Neonatal Outcome in Pregnancies from Ovarian Stimulation*, 100 OBSTETRICS & GYNECOLOGY 414 (2002); Ombelet et al., *supra* note 70).

protein in the urine.<sup>72</sup> The condition can be dangerous, in some cases leading to seizures, kidney, or liver damage, and can potentially put both the mother's and child's lives at risk.<sup>73</sup> This complication is especially concerning because it may occur in as many as 40% of all triplet pregnancies.<sup>74</sup> Finally, for many high-order pregnancies, obstetricians strongly suggest "multifetal reduction"—i.e., aborting some fetuses to increase the chance of positive outcomes for the rest.<sup>75</sup> While the procedure generally poses little physical risk to the mother, the difficult decision it involves can cause severe emotional and family turmoil.<sup>76</sup> The decision may be most distressing for women carrying triplets, as triplets face an increased risk of poor outcomes, but not of the same obvious magnitude as higher-order pregnancies.<sup>77</sup>

Further, the radically increased medical cost associated with caring for twins, triplets, or higher-order pregnancies comes hand-in-hand with the health problems linked to multiple births. According to a recent study published in the *American Journal of Obstetrics and Gynecology*, pregnancies resulting in delivery of twins are about five times more expensive than a singleton pregnancy.<sup>78</sup> However, even more alarming is that higher-order pregnancies resulting in the delivery of triplets or more are 20 times more expensive than a singleton pregnancy.<sup>79</sup> By the numbers, a typical singleton pregnancy costs about \$21,000, a pregnancy resulting in twins costs \$105,000, and a pregnancy resulting in triplets or more costs a staggering \$400,000.<sup>80</sup> While expenses for singletons are largely maternal-related, costs for multiples skew heavily toward infant-related care.<sup>81</sup>

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72. *Multiples: Twins, Triplets and Beyond*, *supra* note 66 (citing AM. COLL. OF OBSTETRICIANS & GYNECOLOGISTS, ACOG PRACTICE BULL. NO. 56: MULTIPLE GESTATION: COMPLICATED TWIN, TRIPLET, AND HIGHER-ORDER MULTIFETAL PREGNANCY (2004)).

73. *See id.*; Roxanne Patel Shepelavy, *When Fertility Treatments Become Frightening*, SELF, April 2009, available at <http://www.self.com/health/2009/04/multifetal-reduction>.

74. *See* Shepelavy, *supra* note 73.

75. *See id.* ("A fairly simple procedure, reduction poses few risks to the mother and is usually recommended by high-risk obstetricians to avoid the dangers of multiples: potentially deadly blood pressure swings and a higher chance of gestational diabetes, anemia and kidney infections for the mom; prematurity, cerebral palsy or death shortly after birth for the babies.").

76. *See id.* (discussing the difficult decisions women pregnant with high-order multiples must make regarding multifetal reduction. On one side of the decision, a better chance at normal lives for the remaining fetuses, on the other, deciding to undergo an abortion procedure, often in violation of closely held family or religious beliefs.).

77. *See id.* (discussing the difficulty of counseling women carrying triplets on reduction, noting that many women know families with healthy triplets, introducing anecdotal evidence that may make weighing the risks more difficult).

78. Elkin V. Lemos et al., *Healthcare Expenses Associated with Multiple vs. Singleton Pregnancies in the United States*, 209 AM. J. OBSTETRICS & GYNECOLOGY 586.e1 (2013).

79. *Id.*

80. *Id.*

81. *Id.* at 586.e4 ("For singleton pregnancy, maternal expenses accounted for approximately 60% of overall cost, whereas, for twins or higher order multiple births,

Given the cost distribution, it comes as little surprise that multiples were considerably more likely than singletons to require admission to the neonatal intensive care unit (“NICU”) after delivery.<sup>82</sup> Overall, the increased costs resulted from a wide variety of factors including increased use of the NICU, heavy use of Caesarean section for delivery, and longer overall hospital stays for both the mother and infants.<sup>83</sup>

The data presented above has made it increasingly clear that fertility treatment of any kind increases the chance of a multiple—and especially high-order multiple—pregnancy. Currently, however, because ovulation stimulation is not recorded nationally, it is not possible to determine accurately what percentage of multiple births result from ovulation induction or ART.<sup>84</sup> Nonetheless, there is a general medical consensus that only about 20% of triplet or higher-order pregnancies result from natural conception.<sup>85</sup> Triplets are conceived naturally in only about 1 in 10,000 pregnancies.<sup>86</sup> Higher-order pregnancies are extremely rare in natural conception.<sup>87</sup> Thus, the unique and significant risks posed by carrying three, four, or even more babies to term can be almost exclusively attributed to the rise of ART.<sup>88</sup> While a responsible fertility clinic can mitigate some of the risks associated with multiple-pregnancy by transferring fewer embryos during IVF,<sup>89</sup> the risk of a high-order pregnancy is not so easily mitigated for patients using fertility drugs alone.<sup>90</sup> Moreover, not every clinic is responsible. Many choose to implant far more embryos than is recommended by the American Society for Reproductive Medicine, which, as a result, raises the likelihood of high-order multiple pregnancies.<sup>91</sup>

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expenses for infant care accounted for approximately 70% and 85% of total expenses, respectively.”).

82. *Id.* at 586.e3 (“Infants of twins or triplets or more were more likely to be admitted to NICU and had a higher mortality rate compared with infants of singletons (47.7% [triplets or more] vs 24.2% [twins] and 2.9% [singletons]; 2.0% [triplets or more] vs 0.5% [twins] and 0.06% [singletons]; all  $P < .0001$ .”).

83. *Id.* at 586.e4.

84. *Id.* at 586.e2.

85. *Id.* (citing Practice Committee of American Society for Reproductive Medicine, *Multiple Gestation Associated with Infertility Therapy: An American Society for Reproductive Medicine Practice Committee Opinion*, 97 J. FERTILITY & STERILITY 825 (2012)).

86. AM. SOC’Y FOR REPRODUCTIVE MED., MULTIPLE PREGNANCY AND BIRTH: TWINS, TRIPLETS, AND HIGH-ORDER MULTIPLES: A GUIDE FOR PATIENTS (2012), available at [http://www.asrm.org/BOOKLET\\_Multiple\\_Pregnancy\\_and\\_Birth/](http://www.asrm.org/BOOKLET_Multiple_Pregnancy_and_Birth/).

87. *Id.*

88. See Schieve et al., *supra* note 58 (“The striking increase in multiple births in the United States in recent decades is attributed primarily to infertility treatments that include ovulation stimulation medications.”).

89. See Shepelavy, *supra* note 73 (discussing the American Society for Reproductive Medicine’s guidelines that recommend implantation of one embryo for women under 30 and two for women 30–35).

90. See *id.* (discussing the difficulty in accurately determining the number of eggs released and fertilized after using ovulation stimulation drugs).

91. Naomi R. Cahn & Jennifer M. Collins, *Eight is Enough*, 103 NW. U. L. REV. COLLOQUY 501, 502–03 (2009) (discussing the case of the now-famous “Octomom,” Nadya

***B. The Dangers of IVF and ICSI: Birth Defects and Genetic Considerations***

IVF, and its subcategory ICSI, have come under increased scrutiny as recent studies show links between the procedures and higher risks of birth defects and other health problems in children.<sup>92</sup> Unfortunately, it can now be fairly concluded that children conceived in the laboratory are more likely to suffer from congenital birth defects and other health problems than those conceived naturally.<sup>93</sup> The defects can be severe. Canadian researchers concluded that children “conceived with use of IVF/ICSI have three times as high a risk of a congenital heart defect as naturally conceived infants.”<sup>94</sup> A recent study published in 2012 illustrates the scale of the risks and remaining uncertainty that surrounds ART. The study, a meta-analysis published by Juan Wen and colleagues in the *Journal of Fertility and Sterility*,<sup>95</sup> specifically examined epidemiological data that assessed the risk of birth defects after ART, and compared that data to the risk difference of birth defects after ICSI and IVF.<sup>96</sup> The results of the study suggest that “there is a significantly increased risk of birth defects in infants conceived by ART, but ICSI did not increase the risk compared with [traditional] IVF.”<sup>97</sup> However, the study focused only on birth defects, and did not evaluate the genetic concerns, particularly those unique to ICSI, such as the transmission of genetic mutations that cause male infertility.<sup>98</sup> Moreover, as a meta-study, it is not entirely clear to what extent the authors were able to adjust for risk factors such as maternal age. Regardless, the authors concluded that, compared to a spontaneous

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Suleman. Suleman was a 33-year-old unemployed woman, who at the time of undergoing fertility treatment was already caring for six children. Nonetheless, “[t]he fertility clinic that treated Suleman agreed to implant her with at least six embryos during an in vitro fertilization (IVF) procedure.” Suleman later gave birth to octuplets in early 2009 and has been a media sensation ever since).

92. See, e.g., Marilyn Marchione, *Birth Defect Risk Rises with Some Fertility Treatments*, TODAY (May 5, 2012, 11:42 AM), [http://www.today.com/id/47305522/ns/today-today\\_health/t/birth-defect-risk-rises-some-fertility-treatments/#.VOeQajofw6U](http://www.today.com/id/47305522/ns/today-today_health/t/birth-defect-risk-rises-some-fertility-treatments/#.VOeQajofw6U).

93. See Juan Wen et al., *Birth Defects in Children Conceived by In Vitro Fertilization and Intracytoplasmic Sperm Injection: A Meta-Analysis*, 97 FERTILITY & STERILITY 1331 (2012) (evaluating 56 previous studies and concluding that children conceived by IVF and ICSI are at “significantly increased risk for birth defects).

94. Shi Wu Wen et al., *A Comprehensive Assessment of Outcomes in Pregnancies Conceived by In Vitro Fertilization/Intracytoplasmic Sperm Injection*, 150 EUR. J. OBSTETRICS & GYNECOLOGY & REPROD. BIOLOGY 160, 161–62 (2010) (noting that heart defects were not minor and were not likely to be associated with prematurity).

95. See Juan Wen et al., *supra* note 93.

96. *Id.* at 1333.

97. See *id.*

98. See The Practice Comm. of the Am. Soc’y for Reproductive Med. & Practice Comm. of the Soc’y for Assisted Reproductive Tech., *Genetic Considerations Related to Intracytoplasmic Sperm Injection (ICSI)*, 86 FERTILITY & STERILITY Suppl. 4 (2006); Gozde Zorlu, *IVF Boys Have Shorter Fingers, May Have Fertility Problems*, BIONEWS (Feb. 15, 2010), [http://www.bionews.org.uk/page\\_54590.asp](http://www.bionews.org.uk/page_54590.asp).

conception, IVF and ICSI significantly increased the risk of birth defects in children.<sup>99</sup>

Studies increasingly show that the phenomenal explosion in ICSI may be primarily responsible for causing birth defects, though there remains some uncertainty as to what extent parental factors are to blame.<sup>100</sup> Since ICSI involves the direct injection of sperm into an egg—even though that sperm would have likely been too weak to fertilize the egg without medical intervention—some researchers understandably became concerned about the health risks of the procedure shortly after it was invented.<sup>101</sup> Despite these common-sense fears, there was no experimental phase of testing for the ICSI procedure before it was introduced for human use.<sup>102</sup> This was due, at least in part, to the immediate clinical success of the procedure in producing live births.<sup>103</sup> Additionally, some early studies generally did not show a significantly increased risk of birth defects with either IVF or ICSI.<sup>104</sup> Perhaps unsurprisingly, much of this early research was plagued by methodological problems including small sample sizes and inconsistent definitions for major birth defects.<sup>105</sup> As researchers Jennifer Kurinczuk and Carol Bower found, such deficiencies may have led to an underestimation of the relative prevalence of birth defects among infants conceived with assisted reproductive technology.<sup>106</sup>

A 2012 study by Michael Davies, published in the *New England Journal of Medicine*, found that only ICSI, and not traditional IVF, was associated with a

99. Juan Wen et al., *supra* note 93; *see also* Maryse Bonduelle et al., *A Multi-Centre Cohort Study of the Physical Health of Five-Year-Old Children Conceived After Intracytoplasmic Sperm Injection, In Vitro Fertilization and Natural Conception*, 20 HUM. REPROD. 413 (2004) (concluding that children conceived via ICSI, and to a lesser extent IVF, experienced more birth congenital malformations than naturally conceived children and were more likely to need healthcare resources); Michele Hansen et al., *The Risk of Major Birth Defects After Intracytoplasmic Sperm Injection and In Vitro Fertilization*, 346 NEW ENG. J. MED. 725 (2002) (“Infants conceived with use of intracytoplasmic sperm injection or in vitro fertilization have twice as high a risk for a major birth defect as naturally conceived infants.”).

100. Practice Comm. of the Am. Soc’y for Reproductive Med. & Practice Comm. of the Soc’y for Assisted Reproductive Tech., *supra* note 98.

101. *See* Jim M. Cummins & Anne M. Jequier, *Concerns and Recommendations for Intracytoplasmic Sperm Injection (ICSI) Treatment*, 10: Suppl. 1 HUM. REPROD. 138 (1995); Christopher J. de Jonge & Jessica Pierce, *Intracytoplasmic Sperm Injection—What Kind of Reproduction is Being Assisted?*, 10 HUM. REPROD. 2518 (1995).

102. *See* Anne Drapkin Lyerly, *Marking The Fine Line: Ethics and the Regulation of Innovative Technologies in Human Reproduction*, 11 MINN. J. L. SCI. & TECH. 685, 688 (2010) (citing Ryuzo Yanagimachi, *Is an Animal Model Needed for Intracytoplasmic Sperm Injection (ICSI) and Other Assisted Reproduction Technologies?*, 10 HUM. REPROD. 2525, 2526 (1995); Egbert R. te Velde et al., *Commentary, Concerns About Assisted Reproduction*, 351 LANCET 1524, 1524 (1998)).

103. *Id.*

104. *See* Hansen et al., *supra* note 99.

105. *Id.*

106. *Id.* (citing Jennifer J. Kurinczuk & Carol Bower, *Birth Defects in Infants Conceived by Intracytoplasmic Sperm Injection: An Alternative Interpretation*, 315 BMJ 1260 (1997)).

statistically significant increase in birth defects.<sup>107</sup> The study analyzed data from birth registries and clinics in southern Australia and utilized advanced statistical techniques to isolate the procedural risks associated with different forms of ART.<sup>108</sup> In contrast to the meta-analysis offered by Juan Wen, the *New England Journal of Medicine* study concluded that “the increased risk of birth defects associated with [traditional] IVF was no longer significant after adjustment for parental factors.”<sup>109</sup> So while the study suggested that both IVF and ICSI were associated with a higher risk of birth defects when compared to spontaneous conception, once the data was adjusted for maternal age and other parental risk factors, only the ICSI correlation remained.<sup>110</sup> The results suggest that increased risk of birth defects is plausibly linked to the ICSI procedure itself,<sup>111</sup> but that “differences in male infertility factors that lead to the use of ICSI may also underlie the association.”<sup>112</sup> Nonetheless, the magnitude of the risk appears to be substantial. The results of the *New England Journal of Medicine* study show that, before adjusting for factors such as maternal age, IVF was associated with a 26% increase in birth defects compared with spontaneous conception, while ICSI was associated with a staggering 77% increase.<sup>113</sup> After adjustment, the increased risk for traditional IVF largely disappeared, but ICSI was still associated with a roughly 57% increase in birth defects<sup>114</sup>—these numbers suggest that ICSI may be associated with a far greater birth-defect risk than what was previously believed. For example, an earlier German study found that before adjustment, ICSI was associated with only a roughly 44% increase in birth defects as compared to spontaneously conceived children.<sup>115</sup>

The *New England Journal of Medicine* study also revealed additional insight into the world of ART and the women who undertake it. The authors note that women who used ART were more likely to be older, white, affluent, and

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107. See Michael Davies et al., *Reproductive Technologies and the Risk of Birth Defects*, 366 NEW ENG. J. MED. 1803 (2012).

108. See *id.*

109. *Id.*

110. *Id.* at 1809 (“After multivariate adjustment, the association between IVF and the risk of any birth defect was no longer significant, whereas the increased risk of any birth defect associated with ICSI remained significant.”).

111. *Id.* (citing Bonduelle et al., *supra* note 99; Jennifer J. Kurinczuk, *Safety Issues in Assisted Reproduction Technology: From Theory to Reality – Just What Are the Data Telling Us About ICSI Offspring Health and Future Fertility and Should We Be Concerned?*, 18 HUM. REPROD. 925 (2003)).

112. *Id.*

113. *Id.* at 1803 (“The corresponding odds ratios [before and after adjustment for risk factors such as maternal age] with in vitro fertilization (IVF) (165 birth defects, 7.2%) were 1.26 (95% CI, 1.07 to 1.48) and 1.07 (95% CI, 0.90 to 1.26), and the odds ratios with intracytoplasmic sperm injection (ICSI) (139 defects, 9.9%) were 1.77 (95% CI, 1.47 to 2.12) and 1.57 (95% CI, 1.30 to 1.90).”).

114. *Id.* (“The increased risk of birth defects associated with IVF was no longer significant after adjustment for parental factors.”).

115. See Alexander Katalinic et al., *Pregnancy Course and Outcome After Intracytoplasmic Sperm Injection: A Controlled, Prospective Cohort Study*, 81 FERTILITY & STERILITY 1604 (2004) (finding a relative risk of 1.44 before adjustment for risk factors).

nulliparous than women who conceive spontaneously.<sup>116</sup> Moreover, their children were more likely to be stillborn, delivered by Cesarean section, and have a lower mean birth weight than naturally conceived children.<sup>117</sup> These observations are consistent with previous studies, which also found that pregnancies achieved after ICSI resulted in “a higher number of preterm and low birth weight children.”<sup>118</sup>

On a slightly unrelated note, one of the most interesting aspects of the study involved a comparison of outcomes between frozen embryos and fresh embryos in traditional IVF and ICSI.<sup>119</sup> For both IVF and ICSI, the researchers surprisingly “found a significant increase in the risk of birth defects associated with fresh-embryo cycles but not with frozen-embryo cycles.”<sup>120</sup> Although the study admittedly utilized a small sample size, the results suggest that using frozen embryos may be *safer* than using fresh ones in both IVF and ICSI.<sup>121</sup> The authors explored several possible explanations, including “a reduced likelihood that developmentally compromised embryos will survive the thawing process and the temporal separation of the developing embryo from exposure to hormonal stimulation drugs.”<sup>122</sup>

More importantly, the risk of ICSI is distinguished from that of traditional IVF by unique genetic considerations associated with the removal of natural selection from the fertilization process. Some of these genetic risks, especially those relating to passing down infertility, may not manifest themselves until later in life—and thus escape analysis in most studies of IVF outcomes.<sup>123</sup> A recent study of boys conceived through ICSI suggests that they may have shorter fingers than their peers, a metric that is commonly associated with fertility problems.<sup>124</sup> These revelations are particularly concerning given the rapid increase in the number of couples undergoing IVF,<sup>125</sup> and the proliferation of ICSI as the most popular method of IVF.<sup>126</sup> Recently, ICSI inventor Andre Van Steirteghem quite shockingly came out and publicly urged against ICSI’s widespread use, citing concerns that defective sperm may allow genetic disorders to be passed on to the

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116. See Davies et al., *supra* note 107, at 1805.

117. *Id.*

118. Katalinic et al., *supra* note 115.

119. *See id.*

120. See Davies et al., *supra* note 107, at 1810.

121. *Id.* (noting, however, that the risk of birth defects with fresh cycles of IVF was “significantly lower” than the risk with fresh cycles of ICSI).

122. *Id.* at 1811.

123. See David Derbyshire, *Infertility Time Bomb: IVF Children Have Higher Risk of Infertility, Obesity, and Diabetes*, DAILY MAIL (Feb. 22, 2010), <http://www.dailymail.co.uk/health/article-1252901/Infertility-time-bomb-IVF-children-higher-risk-infertility-obesity-diabetes.html> (noting that the increased number of multiples resulting from IVF pregnancies puts them at risk for problems later in life); Zorlu, *supra* note 98 (noting that the boys in the study were still too young to test for infertility directly).

124. *Id.*

125. See 2011 ART REPORT, *supra* note 33 (indicating that there were over 150,000 ART cycles performed in the United States during 2011).

126. *See id.* (ICSI made up 67% of all IVF procedures performed in the United States in 2011).

next generation.<sup>127</sup> Specifically, Professor Van Steirteghem warned that problems like diabetes, heart disease, and obesity could be passed on to future generations through defective sperm.<sup>128</sup> In his view, the ICSI procedure should be reserved for only those situations where more traditional methods of IVF have failed.<sup>129</sup>

However, responsible voices opposed to the proliferation of ICSI are at odds with powerful market forces behind its growth into the new mainstay procedure of a multibillion-dollar industry. Early studies suggested that ICSI was capable of higher fertilization rates than traditional IVF and that was all that mattered.<sup>130</sup> While there may be some truth in those results,<sup>131</sup> the modern consensus is that ICSI does not improve outcomes in cases of unexplained infertility or advanced maternal age, and that its routine use should be confined to treating male factor infertility.<sup>132</sup>

In the United States, the government tracks fertilization and live-birth rates for each individual ART clinic.<sup>133</sup> These statistics are public and permit direct comparison and competition between clinics, allowing patients to shop around for the clinic with the highest “success” rates. Given that IVF is only available to those in the United States who can pay for it privately,<sup>134</sup> clinics necessarily compete for a limited pool of patients. In this environment, posting a higher success rate than one’s competitors can have a significant impact on a clinic’s bottom line.<sup>135</sup> In light of these perverse incentives, perhaps most troubling is that

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127. Maren Urner, *IVF Technique Is Overused, Says Its Inventor*, BIONEWs (Mar. 1, 2010), [http://www.bionews.org.uk/page\\_55180.asp](http://www.bionews.org.uk/page_55180.asp) (speaking at this year’s conference for the Advancing Science Serving Society (ASSS), Professor van Steirteghem highlighted “the possibility that the direct injection of sperm into the egg, a technique known as ICSI . . . might enable fertilization with genetically defective sperm, raising the prospect that problems like diabetes, heart disease and obesity could be passed on to future generations.”).

128. *Id.* (referring to comments made by Professor Andre Van Steirteghem at the 2010 conference for ASSS).

129. *Id.*

130. See, e.g., Gloria Calderón et al., *Intracytoplasmic Sperm Injection Versus Conventional In-Vitro Fertilization: First Results*, 10 HUM. REPROD. 2835 (1995); Dianna Payne et al., *Successful Treatment of Severe Male Factor Infertility in 100 Consecutive Cycles Using Intracytoplasmic Sperm Injection*, 9 HUM. REPROD. 2051 (1994).

131. Practice Comms. of the Am. Soc’y for Reprod. Med. & Soc’y for Assisted Reprod. Tech., *Intracytoplasmic Sperm Injection (ICSI) for Non-Male Factor Infertility: A Committee Opinion*, 98 FERTILITY & STERILITY 1395, 1397 (2012) (conceding that “ICSI can increase fertilization rates when lower than expected or failed fertilization has previously occurred with conventional insemination”).

132. See *id.* (summarizing the conclusions of the Committee).

133. See 2011 ART REPORT, *supra* note 33 (presenting success rates by age group for each of 450 fertility clinics tracked in the United States).

134. See PARKER, *supra* note 19, at 50.

135. Patients seeking fertility treatments that often cost in excess of \$10,000 per attempt have strong incentives, both financial and emotional, to choose a clinic with a rate of successful births per cycle of treatment. Because the CDC makes these success rates public, they serve as a de facto ranking system for fertility clinics. See 2011 ART REPORT, *supra* note 33. Much as colleges and professional schools are ranked by *U.S. News & World Report*, so are clinics ranked by their success rates. Every clinic fights to post better

ICSI's rapid rise could reflect overuse of the procedure and inadequate disclosure of the procedure's risks to patients. But once the initial studies reported higher live-birth rates associated with ICSI, those other concerns were quickly swept under the rug by the fertility industry.

### III. CURRENT LEGAL AND REGULATORY OVERSIGHT OF ASSISTED REPRODUCTIVE TECHNOLOGY

#### A. Regulations Barely Exist and Voluntary Guidelines Do Not Work

Modern assisted reproduction is a multibillion dollar industry<sup>136</sup> that affects hundreds of thousands of people every year in the United States. However, despite its size and rapid growth, the fertility industry is subject only to very limited state and federal regulation.<sup>137</sup> While some industry groups have promulgated responsible guidelines for the use of assisted reproductive technologies, the absence of viable enforcement mechanisms leaves many clinics subject only to self-regulation or, in some cases, the enforcement of more general laws by the courts.<sup>138</sup> Moreover, a comparison of the American Society for Reproductive Medicine's United States guidelines to those issued by the organization's counterpart in the United Kingdom suggests that the United States guidelines are somewhat less stringent. ART's meteoric rise strongly suggests that it will play an increasingly important role in reproduction for future generations. Nonetheless, law has lagged far behind this groundbreaking technology in the United States. Today, for example, the IVF industry mostly operates as a free market and there is little that restricts or controls choices made by physicians, patients, or donors.<sup>139</sup>

ART exists largely outside the current reach of federal regulatory powers. Professor Anne Drapkin Lyerly concludes that this may partly be the result of the dissociation of innovation in reproductive medicine from experimentation.<sup>140</sup> Generally, federally funded medical researchers are subject to significant regulation and oversight by the Department of Health and Human Services ("DHHS").<sup>141</sup> However, the U.S. government's reluctance to fund research on embryos and reproductive medicine has seriously eroded any oversight or regulatory ability that DHHS could have had over ART.<sup>142</sup> In 1994, President

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numbers than its competitors, which may lead to shady reporting practices and a singular focus on inflating success rates. Without sufficient regulatory oversight, the profit motive takes over.

136. See *About Eggsploitation*, EGGSPLOITATION, [www.eggsploitation.com/about.htm](http://www.eggsploitation.com/about.htm) (last visited Feb. 22, 2015).

137. See CAHN, *supra* note 37, at 44 (discussing the limited state and federal oversight of participants in the fertility industry); Lyerly, *supra* note 102, at 698 (stating that "research and clinical treatment of infertility has been virtually unregulated").

138. See, e.g., Jesse Reynolds, *Preventing the Next Fertility Clinic Scandal*, BIOETHICS FORUM (Mar. 13, 2009, 9:43 AM), [www.thehastingscenter.org/Bioethicsforum/Post.aspx?id=3240](http://www.thehastingscenter.org/Bioethicsforum/Post.aspx?id=3240).

139. See KINDREGAN & MCBRIEN, *supra* note 38, at 96.

140. See Lyerly, *supra* note 102, at 698.

141. See, e.g., 45 C.F.R. § 46.101 (2014).

142. See Lyerly, *supra* note 102, at 698.

Clinton declared that federal funding should not be made available for research involving the creation or destruction of embryos.<sup>143</sup> Shortly thereafter in 1996, Congress began attaching a rider to DHHS appropriations bills that effectuated the presidential declaration.<sup>144</sup> Thus, Lyerly argues that the absence of federal funding in the field of assisted reproduction helps explain ICSI's "curious" evolution:

Because scientifically rigorous development and refinement of ICSI would have involved the creation, destruction, and discarding of embryos, research involving this technique would not have been eligible for federal funding. As such, the technology advanced rapidly with neither federal funding, nor the scientific scrutiny or human subjects' protections that accompany it.<sup>145</sup>

As the comment suggests, Congress's fear of political controversy created a vacuum of federal oversight, and in turn played a major role in ICSI's quick transition from experimental procedure to mainstay of the IVF industry.

Other federal agencies only possess limited regulatory oversight of the assisted reproduction industry. The Food and Drug Administration ("FDA") has largely steered clear of directly regulating assisted reproduction, and has only recently engaged in limited regulation surrounding cloning<sup>146</sup> and the classification of medical devices used in the assisted reproduction.<sup>147</sup> By contrast, the CDC has been at least somewhat involved in regulating ART and the fertility industry. The CDC has statutory authority to regulate pursuant to the Fertility Clinic Success Rate and Certification Act.<sup>148</sup> However, CDC regulation concerns only the certification of laboratories and the reporting of pregnancy success rates achieved by fertility clinics utilizing ART.<sup>149</sup> While the Fertility Clinic Success Rate and Certification Act provides some basic (but voluntary) reporting of clinics' advertising claims, thus far the federal government has not attempted to effectuate mandatory regulation of the fertility industry's use of ART in the United States.<sup>150</sup>

State regulation of ART is similarly undeveloped, providing little substance to fill the void left by the absence of federal legislation. Most states have

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143. *Id.* at 700.

144. *Id.* The rider states that "no funds [can] be appropriated for any project involving '1) the creation of a human embryo or embryos for research purposes; or 2) research in which a human embryo or embryos are destroyed, discarded or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 C.F.R. 46.208(a)(2) and section 498(b) of the Public Health Service Act (42 USC 289g(b)).'" *Id.* (citing 1 NAT'L BIOETHICS ADVISORY COMM'N, ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH 35 (1999)).

145. *Id.* at 701.

146. *See* KINDREGAN & MCBRIEN, *supra* note 38 at 220; *see also* Richard A. Merrill, *Human Tissues and Reproductive Cloning: New Technologies Challenge FDA*, 3 HOUS. J. HEALTH L. & POL'Y 1 (2002).

147. *See* FDA Obstetrical and Gynecological Devices, 21 C.F.R. § 884.1 (2014).

148. 42 U.S.C. § 263a (2012).

149. *See id.* (laying out the requirements for certification as a "laboratory"); 42 U.S.C. § 263a-1 (2012) (providing the standards for reporting pregnancy success rates to the CDC).

150. *See* KINDREGAN & MCBRIEN, *supra* note 38, at 97, 221.

not attempted to regulate the fertility industry's use of ART or its advertisement.<sup>151</sup> However, a few states have taken a more aggressive approach, enacting statutes that govern issues such as insurance coverage and disclosure requirements.<sup>152</sup> Virginia, for example, requires fertility clinics to disclose a variety of success metrics to patients before performing fertility treatments.<sup>153</sup> However, noticeably absent from the statute is any specific, mandatory disclosure of the health risks associated with fertility drugs, IVF, or ICSI.

Presumably, the general tort-law doctrine of informed consent would operate to require disclosures regarding risks, but it is far from obvious whether proper disclosures and truly informed consent occurs under the current relaxed regulatory regime. In 1996, a joint council of the American Medical Association ("AMA") issued a report that identified several serious ethical violations within the practice of assisted reproduction.<sup>154</sup> The report characterized these violations as "subtle deception," and noted "deceptive advertising and insufficient informed consent are probably the most common manifestations of this type of ethical violation."<sup>155</sup> The report recommended stricter adherence to ethical guidelines and increased self-regulation, but stopped short of calling for a legislative solution to the unethical practices plaguing the industry.<sup>156</sup> Nonetheless, despite the absence of legislation, some patients have been able to maintain causes of action against clinics that employ deceptive marketing under more general consumer-protection laws.<sup>157</sup>

In sum, legislation addressing the concerns raised by ART has not been forthcoming, and today the United States is unquestionably a "guideline" country. The majority of existing assisted-reproduction regulation takes the form of professional guidelines published by the American Society for Reproductive Medicine ("ASRM").<sup>158</sup> While the ASRM guidelines cover a variety of important issues relating to both sound clinical and ethical practice, they have nonetheless

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151. *Id.* at 217.

152. *Id.* at 98 (discussing a varied patchwork of state regulation regarding insurance, written parenthood agreements, and counseling requirements).

153. VA. CODE ANN. § 54.1-2971.1 (2014) (requiring disclosure of live birth success rates, pregnancies per completed cycle, total number of live births, and testing protocols for gamete providers).

154. AM. MED. ASS'N COUNCIL ON ETHICAL & JUDICIAL AFFAIRS & COUNCIL ON SCI. AFFAIRS, ISSUES OF ETHICAL CONDUCT IN ASSISTED REPRODUCTIVE TECHNOLOGY 2 (1996), available at <http://www.ama-assn.org/ama1/pub/upload/mm/369/70b.pdf>.

155. *Id.*

156. *See id.*

157. *See Karlin v. IVF America Inc.*, 712 N.E.2d 662 (N.Y. 1999). The advertising also plays on infertile parents' fear of "not doing everything they can" to have a baby of their dreams. For example, Seattle Reproductive Medicine regularly runs radio ads featuring a woman who is "partly" worried about bills and expenses, but "all" of whom desperately desires a baby. The spot concludes with an ominous-sounding male voice implicitly warning infertile individuals that despite their other valid concerns, they will live to regret a decision not to pursue assisted reproductive technology.

158. *See Practice Committee Documents*, AM. SOC'Y FOR REPROD. MED., [www.asrm.org/Guidelines/](http://www.asrm.org/Guidelines/) (last visited Dec. 18, 2013).

faced criticism from commentators.<sup>159</sup> Perhaps the most poignant criticism is that the guidelines have no teeth because the ASRM do not provide any approved protocols that must be followed—in fact, adherence to the guidelines is voluntary, subject to the discretion of the individual physician.<sup>160</sup> As such, the usefulness of ASRM guidelines to mitigate the negative effects of the profit motive is suspect at best.

The only real avenue of enforcement for ASRM guidelines is through a process of clinical certification. The United States Society for Assisted Reproduction (“SART”), a subsidiary of ASRM, operates a certificate program for clinics that adhere to ASRM minimum guidelines, maintain high ethical standards, and report annual data to SART.<sup>161</sup> However, there is no requirement that a clinic be SART certified to operate in the United States.<sup>162</sup> As a result, while SART can revoke its certification from a rogue clinic,<sup>163</sup> such a clinic may continue to operate and many customers would never notice the difference. Roughly 10% of all fertility clinics in the United States are not SART certified.<sup>164</sup> Thus, consider that, while the ASRM recommends that no more than two embryos be implanted in a woman younger than age 35,<sup>165</sup> there is no explicit mechanism to compel adherence to this guideline, and as a result it may be easily violated. This is hardly the robust “written commitment to ethical principles” that the 1996 AMA joint committee envisioned to be the optimal self-regulatory solution to ethical lapses in the practice of assisted reproduction.<sup>166</sup> Moreover, it highlights that the guidelines are an ineffective regulatory mechanism to protect patients. Finally, as one commentator points out, even if the guidelines were enforceable, they are directed toward the fertility profession, and unlike other regulated industries, they do not enjoy any input from the public or disciplines outside of law and medicine.<sup>167</sup>

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159. See Lyerly, *supra* note 102, at 702.

160. See *Practice Committee Documents*, *supra* note 158 (“These guidelines have been developed to assist physicians with clinical decisions regarding the care of their patients. They are not intended to be a protocol to be applied in all situations, and cannot substitute for the individual judgment of the treating physicians based on their knowledge of their patients and specific circumstances. The recommendations in these guidelines may not be the most appropriate approach for all patients.”).

161. See Howard W. Jones, Jr. et al., *International Federation of Fertility Societies Surveillance 2010* at 1 (2010), available at [https://www.infertilitynetwork.org/files/IFFS\\_Surveillance\\_2010.pdf](https://www.infertilitynetwork.org/files/IFFS_Surveillance_2010.pdf).

162. *Id.*

163. See *Oversight of Assisted Reproductive Technology*, AM. SOC’Y OF REPROD. MED. (2010), available at [http://www.asrm.org/uploadedFiles/Content/About\\_US/Media\\_and\\_Public\\_Affairs/OversiteOfART%20\(2\).pdf](http://www.asrm.org/uploadedFiles/Content/About_US/Media_and_Public_Affairs/OversiteOfART%20(2).pdf).

164. See *id.*

165. Practice Comm. for the Am. Soc’y of Reproductive Med. & Practice Comm. for the Soc’y of Assisted Reprod. Tech., *Criteria for the Number of Embryos to Transfer: A Committee Opinion*, 99 FERTILITY & STERILITY 44 (2013).

166. AM. MED. ASS’N COUNCIL ON ETHICAL & JUDICIAL AFFAIRS & COUNCIL ON SCI. AFFAIRS, *supra* note 154.

167. See Lyerly, *supra* note 102, at 702.

### *B. Foreign Approaches*

Many other countries have taken a much more aggressive approach in regulating ART. A 2010 survey conducted by the International Federation of Fertility Societies examined ART regulation in 107 countries and found that 42% employed legislative regulation of ART.<sup>168</sup> Previously, this proportion was larger, but the change was likely a result of the first-time inclusion of many developing countries in the 2010 survey.<sup>169</sup> Over 40 countries, including most of Europe, have enacted specific legislation that regulates the use of ART.<sup>170</sup> Twenty-six countries, including the United States, have only voluntary guidelines in place.<sup>171</sup> Two-thirds of the countries with enacted legislation have some version of a licensing requirement, and many are quite stringent.<sup>172</sup> For example, in Australia, the penalty for operating a non-accredited facility is up to ten years in prison, a far cry from the voluntary certification requirements imposed by SART in the United States.<sup>173</sup>

The United Kingdom has perhaps the most well-developed system of ART regulation and should be used as a model for what is necessary in America. The Human Fertilisation and Embryological Authority (“HFEA”) has several key responsibilities, including issuing licenses to IVF clinics and other establishments carrying out embryo research. It also regulates the storage of gametes and embryos, and implements the directives of the European Union relating to ART.<sup>174</sup> The HFEA requires that before a license will be issued, all clinics must demonstrate that they can comply with the “Code of Practice.”<sup>175</sup> The Code is frequently updated and covers “all details of the clinical and embryological practice associated with assisted reproductive technology.”<sup>176</sup> While at first glance this might seem similar to the U.S. guidelines system, it differs greatly because licensure is mandatory in the United Kingdom and clinics cannot operate “outside” the Code.<sup>177</sup> In addition to the independent HFEA, the National Institute for Health and Clinical Excellence (“NICE”), part of the National Health Service, publishes guidelines for providers to complement the regulations promulgated by the HFEA.<sup>178</sup>

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168. See Jones et al., *supra* note 161, at 512.

169. *Id.* (discussing the inclusion in the survey of developing countries, many of which had little or no regulation on the use of ART).

170. See *id.*

171. See *id.*

172. See *id.*

173. See *id.*

174. See *Who We Are and What We Do, Our Role as Regulator*, HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY (HFEA), <http://www.hfea.gov.uk/135.html> (last updated Dec. 5, 2013).

175. See Jones et al., *supra* note 161, at 510.

176. See *id.*

177. See *id.*

178. See NAT’L INST. FOR HEALTH & CLINICAL EXCELLENCE, FERTILITY: ASSESSMENT AND TREATMENT FOR PEOPLE WITH FERTILITY PROBLEMS, NICE CLINICAL GUIDELINE 156 (Feb. 2013), available at <http://guidance.nice.org.uk/cg156> (hereinafter NICE).

Comparison of the U.S.'s ASRM guidelines and the U.K.'s NICE guidelines reveals that the ASRM guidelines allow for the transfer of greater numbers of embryos to women undergoing IVF than their NICE counterparts. For a woman's first cycle, the ASRM recommends the transfer of one to two high-quality cleavage-stage embryos for women under 35, two for women 35–37, three for women 38–40, and five for women 41 and older.<sup>179</sup> If the patient has already gone through one unsuccessful cycle, the ASRM then recommends two embryos for women under 35, three for women 35–37, four for women 38–40, and five for women over 41.<sup>180</sup> This is in stark contrast to NICE's far more conservative approach. NICE recommends that in the first cycle of treatment, clinics transfer only one embryo for women under 37.<sup>181</sup> Even after an unsuccessful cycle (or two), the NICE guidelines strongly suggest transferring only a single high-quality embryo, and never more than two.<sup>182</sup> For older women, the NICE guidelines suggest that no more than two embryos be transferred.<sup>183</sup> This conservative approach to IVF is an explicit attempt by the British government to decrease the incidence of costly multiple births.<sup>184</sup> As multiple births are significantly more costly than singletons,<sup>185</sup> this is an issue of obvious importance in a socialized healthcare system. It is also especially relevant given that Europeans use ART services at twice the rate of Americans.<sup>186</sup> Some European countries, for instance Germany, set explicit legal maximums on the number of embryos that may be transferred in an IVF procedure and consider breach of the law a felony violation.<sup>187</sup>

Given the differences in legal and regulatory environment, it is not surprising that researchers have compared ART outcomes between Europe and the United States. In particular, a recent study published in the *Journal of Human Reproduction* explored why IVF patients in the United States have significantly higher rates of clinical pregnancy and delivery than European patients.<sup>188</sup> The study confirms that clinics in the United States transfer a greater number of

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179. Practice Comm. for the Am. Soc'y of Reproductive Med. & Practice Comm. for the Soc'y of Assisted Reprod. Tech., *supra* note 165, at 44–45.

180. *Id.* at 45.

181. *See* NICE, *supra* note 178, at 10.

182. *See id.*

183. *Id.* at 10–11.

184. *See* Bazian, *New NICE Guidelines for NHS Fertility Treatment*, NAT'L HEALTH SERV. (Feb. 20, 2013), <http://www.nhs.uk/news/2013/02February/Pages/New-NICE-guidelines-for-NHS-fertility-treatment.aspx> (“The NICE guidelines also include new recommendations on the number of fresh or frozen embryos that should be transferred to a woman's womb, these are designed to reduce the risk of multiple births following IVF.”).

185. *See supra* Part II.

186. *See* Norbert Gleicher et al., *A Formal Comparison of the Practice of Assisted Reproductive Technologies Between Europe and the USA*, 21 HUM. REPROD. 1945 (2006).

187. *Id.* at 1946 (citing Embryonenschutzgesetz [ESchG] [Act on the Protection of Embryos], Dec. 13, 1990, BGBL at 2746 (Ger.)).

188. Gleicher et al., *supra* note 186, at 1947 (finding that clinical pregnancy rates in the United States were 32.8% per cycle start and only 24.3% per cycle start in Europe).

embryos per ART cycle than their European counterparts.<sup>189</sup> Specifically, Europeans were far more likely to receive a single or double embryo transfer than patients in the United States; and Americans, by contrast, were nearly twice as likely as Europeans to receive three or four embryos.<sup>190</sup> Unsurprisingly, the study's data also shows that multiple pregnancies were also far more common in the United States.<sup>191</sup> However, the study's authors note that the increased number of embryos transferred does not alone explain the differences in clinical pregnancy rates between the two continents.<sup>192</sup> Nonetheless, the authors conclude there are substantial differences in the practice of ART between the continents, and "[t]hese differences appear primarily driven by greatly diverging regulatory environments on both sides of the Atlantic and, at least based on pregnancy rates, do not appear to benefit the European population."<sup>193</sup> However, some commentators have been critical of this conclusion, specifically noting that Europe's reduced rate of multiple pregnancies evidences the substantial benefits of increased regulation of ART.<sup>194</sup>

While the United States may never elect to regulate reproductive technology to the same extent as witnessed in Europe, the current regulatory void and lack of meaningful oversight has contributed to a "wild west" mentality at some American IVF clinics.<sup>195</sup> In this environment, the profit motive reigns supreme, breeding conflicts of interest between clinics and patients, institutionalizing practices of subtle deception, and contributing to the health crisis of multiple births. A well-functioning free market for ART services depends upon consumers having access to the best possible information in order both to make informed treatment decisions and to avoid negative outcomes. To the contrary, the current regulatory system in the United States has failed to ensure the integrity of the informed consent process, and has failed to adequately address the growing burden of multiple births. The existing patchwork of voluntary guidelines, state

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189. *Id.* at 1949 ("The study confirms that the US transfers more embryos than Europe (Table IV). Indeed, only 33.5% of U.S., and 63.7% of European, cycles received one or two embryos. In contrast, almost twice the number of patients had three or four embryos transferred (66.4%) in the US than in Europe (36.3%).").

190. *See id.*

191. *Id.* ("[M]ultiple pregnancies were significantly more frequent in the US (38.6%) than in Europe (25.5%).").

192. *Id.*

193. *Id.*

194. *See* Karl Nygren et al., Letter to the Editor, *On the Benefit of Assisted Reproduction Techniques, A Comparison of the USA and Europe*, 21 HUM. REPROD. 2194 (2006).

195. A recently filed federal case in the Western District of Texas, *Maher v. Vaughn, Silverberg & Assocs.*, quoted a previous SSRN version of this Article for the "wild west" proposition. In *Maher*, Plaintiff expressly required an Austin IVF clinic to use sperm from a donor that she specified, but the clinic used sperm from a different donor. Rather than acknowledge their error, the clinic initially claimed that Plaintiff consented to use of other sperm in order to increase her chance of pregnancy, a charge she vehemently denies. *See* Plaintiff's First Amended Complaint, *Maher v. Vaughn, Silverberg & Assocs.*, No. 1:13-CV-0543-SS, (W.D. Tex. Mar. 6, 2015), 2015 WL 1010512.

law, and limited federal oversight is not sufficient to ensure the fertility market remains free, fair, and safe for the twenty-first century.

#### IV. RECOMMENDATIONS FOR LAW AND POLICY REFORM

It is clear that the meteoric rise of ART has vastly outpaced the development of a cohesive legal framework governing its practice. The increasing use of IVF, ICSI, and other ART procedures raises important and often emotional issues that deserve considered legal and policy solutions. ART is here to stay, and it seems likely that the technology will play an increasingly important role in human reproduction in the future. As this groundbreaking technology continues to advance, the law must keep pace. The current relaxed self-regulation and patchwork state law is ineffective at mitigating the conflicts of interest created by profit motive in the ART industry. Conceiving a child is an emotional rollercoaster for infertile couples; as they look for hope in an otherwise bleak situation, they may be especially vulnerable to the “subtle deception” methods that sparked the AMA’s concern back in 1996.<sup>196</sup> But what can law accomplish, and, perhaps more importantly, what should new regulation of ART look like?

There are several distinct areas of ART that might benefit from increased oversight and regulation, but because the existing regulation in both has been insufficient to mitigate conflicts of interest in the profit-driven fertility industry, two issues deserve special attention: the complications raised by multiple births and the specific choice of ART method.

##### *A. Dealing with Complications Raised by Multiples*

First, we must address the oft-written-about problem of multifetal pregnancies as a result of ART. This topic has received much attention over the years from commentators, and is an area where many European countries have pursued expanded regulation.<sup>197</sup> Some commentators have called for increased regulation of ovulation-inducing fertility drugs and have even gone so far as to suggest their complete prohibition.<sup>198</sup> Another outside-the-box idea might be the implementation of a tradable “permit system” for multiple pregnancies. This permit system could be something akin to the cap-and-trade system used for pollutants, but would cap the number of multifetal pregnancies, and would allow clinics to purchase permits allowing them to provide treatments likely to result in multiple pregnancies.<sup>199</sup> This idea, Richard Hawkins suggests, would force

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196. See AM. MED. ASS’N COUNCIL ON ETHICAL & JUDICIAL AFFAIRS & COUNCIL ON SCI. AFFAIRS, *supra* note 154.

197. See *supra* Part III.B (discussing the more stringent regulatory environment in Europe and the continent’s propensity to employ measures to combat the increasing incidence of multiple pregnancies).

198. See Lars Noah, *Assisted Reproductive Technology and the Pitfalls of Unregulated Biomedical Innovation*, 55 FLA. L. REV. 603, 665 (2003) (“[A]n effort to further restrict or entirely prohibit the continued marketing of fertility drugs may offer a simpler and more effective (though no less controversial) approach to the problem of multifetal pregnancies.”).

199. See Richard J. Hawkins, *Assisted Reproductive Technology and the Externality of Multiple Births*, 2009 MICH. ST. L. REV. 719, 743–46 (2009) (describing the

interested parties to internalize the costs of their reproductive choices and, as a consequence, reduce the incidence of multiple births and their externalities to the healthcare system.<sup>200</sup> Still others have suggested a federal law codifying embryo-transfer limits in the provision of infertility care.<sup>201</sup> Such a law would likely resemble the mandatory embryo-transfer limits present in some foreign countries.<sup>202</sup> However, the true goal of any new regulation in this area must be to mitigate or displace the incentive structure that pushes for-profit clinics to produce pregnancies without considering the risks and costs of a multiple pregnancy.

### ***B. Influencing the Choice of ART Method***

The second major area deserving regulatory attention is the choice of reproductive technology to be utilized by a patient. This issue is of special importance given the meteoric rise of ICSI and the abundance of research that suggests the procedure may carry greater risks to future children than more traditional methods of IVF.<sup>203</sup> However, the issues deserving of attention here are even broader. Professor Lyerly has suggested a need for a significant reevaluation of how research is performed in the ART field. Lyerly notes that the challenges of regulating ART *innovation* are separate and distinct from those of regulating the *practice* of ART.<sup>204</sup> She proposes that the requirements for informed consent be both clarified and standardized, including explicit disclosure and separate requirements for participating in research versus standard clinical procedures.<sup>205</sup> A clear and standardized system for obtaining informed consent would significantly benefit clinical practice, and would go a long way to ameliorate the practices of subtle deception that undoubtedly still plague the profit-driven fertility industry. Any law that will standardize what must be disclosed to ART patients should also mandate full disclosure of: (1) the for-profit nature of the fertility clinic; and (2) the potential conflict of interest between the clinic (in its desire to post high pregnancy and birth rates) and the patient who desires a healthy singleton baby.

### ***C. A Measured Regulatory Response***

Finally, it should be noted that not all commentators agree that increased regulation of ART is desirable. In fact, Professor Kerry Lynn Macintosh has expressed significant reservations about restricting access to ART, warning that advocates of increased public oversight “have failed to recognize the eugenic

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structure and enforcement of the author’s proposed tradable permit system for multiple births).

200. *Id.* at 753.

201. *See* Judith Daar, *Federalizing Embryo Transfers: Taming the Wild West of Reproductive Medicine?*, 23 COLUM. J. GENDER & L. 257, 257 (2012).

202. *See* Jones, *supra* note 161.

203. *See supra* Part II.

204. *See* Lyerly, *supra* note 102, at 708 (“The challenges of regulating *innovation* in ARTs are distinct from those of regulating the *practice* of ART and need their own solutions.”).

205. *Id.* at 709 (“[R]equirements for informed consent should be both clarified and standardized. They should include guidance about the distinct differential requirements for consent to participating in research versus consent to participating in clinical practice that necessarily includes inadequately tested though standard procedures.”).

implications of acting to ‘protect’ children from their own existence.”<sup>206</sup> She worries that regulation of “conventional” technologies like IVF and ICSI could have serious eugenic implications, relegating an entire class of people to perpetual childlessness.<sup>207</sup>

#### *D. Mandated Disclosure and the Regulation of ICSI*

ICSI has transformed assisted reproduction by allowing infertile men the chance to reproduce. However, with great technological advances comes risk of misuse, and accordingly ICSI’s success at producing live births comes with downsides. That said, as ICSI becomes the mainstay of fertility clinics across the nation, it is imperative that clinics adequately counsel patients on the risks of the procedure, lest patients misconceive ICSI’s popularity for its safety.

Specifically, truly informed consent requires full and clear disclosure of recent research on ICSI’s risks compared to alternative treatment methods. While this life-giving advance has helped countless parents over the last 20 years, the increasing evidence of its dangers<sup>208</sup> should counsel prudence for both patients and doctors. Today, researchers agree that the full disclosure of ICSI’s risks—both for birth defects and for less obvious long-term genetic problems—should be fully disclosed to potential patients.<sup>209</sup>

However, ICSI’s rapid takeover of the assisted reproduction market raises the possibility that consumers may not currently be operating with full information, and raises the likelihood of inadequate informed consent. While the CDC’s most recent data from 2011 shows that 67% of IVF cycles involved ICSI in United States,<sup>210</sup> that number may be much higher in certain states or at individual clinics. For example, two-thirds of fertility clinics in Arizona utilize ICSI more than 90% of the time.<sup>211</sup> While it is not impossible that ICSI’s extensive use simply reflects consumer preferences, it seems more plausible that many consumers are

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206. See Kerry Lynn Macintosh, *Brave New Eugenics: Regulating Reproductive Technologies in the Name of Better Babies*, 2010 U. ILL. J.L. TECH. & POL’Y 257, 310 (2010).

207. *Id.* (“That public eugenics should reemerge in the twenty-first century, speaking solemnly about the welfare of children, should give us all serious pause. Whatever the dangers of ART may be, they are nothing compared to the power of the state to relegate a class of disabled persons to childlessness based on the prejudgment that the lives of their offspring are not worth living. Such discrimination betrays our core values and must not be tolerated.”).

208. See *supra* Part II.B.

209. See, e.g., Katalinic et al., *supra* note 115, at 1613 (discussing the need to counsel couples that there is an increased risk of complications in pregnancy course, pregnancy outcome, and a risk of major malformation); The Practice Comm. of the Am. Soc’y for Reproductive Med. & The Practice Comm. of the Soc’y for Assisted Reproductive Tech., *supra* note 98, at 183 (“Only those fully apprised of the risk for transmitting a genetic defect and its potential effect on their offspring should be offered ICSI.”); Davies et al., *supra* note 107, at 1812 (“[O]ur findings can help provide guidance in counseling patients who are considering treatment for infertility.”).

210. See 2011 ART REPORT, *supra* note 33, at 24.

211. See, e.g., *id.* at 32–41 (showing that six out of Arizona’s nine fertility clinics utilize ICSI in more than 90% of all IVF cycles).

simply unaware of the most recent research illustrating the unique risks associated with ICSI.

In light of the risks associated with ICSI, experts in the field—including ICSI's inventor—argue that the process should be reserved for use only when absolutely necessary.<sup>212</sup> In their view, ICSI should not be the first choice utilized to help infertile couples become parents. Thankfully, ICSI's overuse has not gone entirely unnoticed and has recently attracted the scrutiny of U.K. regulators.<sup>213</sup> According to the *Independent*, Lisa Jardine, chairperson of the U.K.'s HFEA, believes that some IVF clinics are using ICSI simply because it is “easier and has a lower chance of fertilization failure than standard IVF, rather than because it is in the best interests of patients.”<sup>214</sup> In Britain, data collected by the HFEA shows that 30% of ICSI cycles are not related to male infertility—even though male factor infertility was the driving force behind its invention. In addition, Allan Pacey, chairperson of the British Fertility Society, has confronted the procedure's overuse as well. Pacey suggests that, in light of ICSI's risks, it should be used only “when it's needed, and not as some kind of guarantee against fertilization failure, which is how some clinics approach it.”<sup>215</sup> In a similar vein, a group of researchers recently concluded that, not only are more stringent criteria desirable to combat ICSI's overuse, but that reserving the procedure for proven applications may not negatively affect pregnancy outcomes.<sup>216</sup> Regardless, infertility patients deserve full disclosure of the risks for the procedures they elect to undertake.

Jennifer Jurinczuk captured this sentiment succinctly in a 2003 piece for the *Journal of Human Reproduction*:

Pregnancy is something of a lottery for all couples. However, compared with couples who conceive spontaneously, for those who require IVF or ICSI the lottery is weighed more heavily against a successful outcome at every stage of the process, not just conception. This is the reality alongside the hope that must be conveyed at counselling to all couples contemplating treatment. Indeed this counselling must be sufficiently detailed to ensure that, whilst the ICSI procedure itself is regarded as a routine procedure in

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212. See Urner, *supra* note 127 (quoting Allan Pacey, IVF specialist at the University of Sheffield, as stating that ICSI should be used only when absolutely necessary); Brooke Hodes-Wertz et al., *Is Intracytoplasmic Sperm Injection Overused?*, 187 J. UROLOGY 602 (2012) (“[A]lthough intracytoplasmic sperm injection is one of the greatest advances in our field, it is overused and should only be done for clinically proven indications.”).

213. See Steve Connor, *Survival of the Unfittest: IVF Technique “Used Too Widely,” Watchdog Warns*, INDEP. (Nov. 3, 2013), <http://www.independent.co.uk/news/science/survival-of-the-unfittest-ivf-technique-used-too-widely-watchdog-warns-8919258.html>.

214. *Id.*

215. *Id.* (quoting Allan Pacey, chairman of the British Fertility Society).

216. Hodes-Wertz et al., *supra* note 212 (concluding that more stringent criteria for ICSI do not compromise clinical outcomes and as such ICSI should be reserved for proven applications).

most IVF clinics, prospective recipients do not equate routine with being completely safe and completely risk-free for their offspring.<sup>217</sup>

### *E. Moving Forward into the Future*

In sum, there is no silver bullet to combat infertility. IVF technology has come a very long way and provided an entire generation of adults with the chance to start a family, but it remains a risky endeavor. Regulations that mandate full disclosure of the multitude of risks associated with assisted reproduction are a critical starting point in bringing ART regulation into the twenty-first century and ensuring that patient consent is truly informed.

To start, significant reforms must be made to the current patchwork of laws governing the use of ART in the United States. ART has evolved at such a break-neck pace that it has far outgrown the system of voluntary self-regulation and reporting as it currently exists. Moreover, the inconsistent state laws regulating ART are far from sufficient and do not supplant the need for nationwide standards. Remedying the conflicts of interest that have become ensconced in the practice of ART will take a concerted effort by lawmakers and healthcare regulators, and cannot be expected to occur without some form of governmental intervention. While the exact form that governmental intervention should take remains a topic for discussion, the need for clear and ethical practice standards grows ever more pressing as ART business booms. But what will regulation of ART in the United States look like?

#### *1. Federal Oversight*

One possibility is that the threat of statutory regulation might be enough to coerce the fertility industry to self-regulate better. At least one commentator has suggested that the threat of federal legislation on embryo-transfer limits might prompt SART and ASRM to adopt “more stringent restrictions with greater consequences for noncompliance.”<sup>218</sup> In that situation, the option of direct regulation would always remain on the table if the threat alone did not lead to the desired outcome.<sup>219</sup> Such an approach could also be successful in other areas of ART regulation. For instance, the threat of explicit federal regulation of the informed consent process might prompt ASRM and SART both to standardize the informed consent system and to better police clinics’ disclosure practices. The threat of legislative action has proven effective in other countries, as it was this

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217. See Jennifer J. Kurinczuk, *Safety Issues in Assisted Reproduction Technology: From Theory to Reality – Just What are the Data Telling Us About ICSI Offspring Health and Future Fertility and Should We Be Concerned?*, 18 HUM. REPROD. 925 (2003).

218. Lyria Bennet Moses, *Understanding Legal Responses to Technological Change: The Example of In Vitro Fertilization*, 6 MINN. J.L. SCI. & TECH. 505, 617–18 (2005) (“To create stronger restrictions on multiple embryo transfer in the United States than exist at present, one could either regulate the practice directly or threaten such regulation, hoping to encourage ASRM and SART to adopt more stringent restrictions with greater consequences for non-compliance.”).

219. *Id.* at 618 (“Direct regulation will remain as an option if the threat proves to be ineffective.”).

sort of regulatory threat that led to the creation of the U.K.'s Voluntary Licensing Authority.<sup>220</sup>

Regardless, some form of increased federal oversight of the informed consent process is likely necessary to ensure that patients are able to make decisions about innovative procedures with full knowledge of the risks and benefits. Clinics should also be required to disclose to patients both their for-profit nature and the potential conflict of interest between the patient and a clinic seeking higher pregnancy and birth rates. Disclosure is of special importance with regard to novel procedures like ICSI. Despite its widespread use, a growing body of research strongly suggests ICSI carries increased risks for children as compared to traditional IVF.<sup>221</sup> Accordingly, any reform of the informed consent process should mandate full disclosure of these risks to prospective patients. Finally, while the ASRM guidelines pave the way for a strong self-regulatory regime, they need stronger federal enforcement mechanisms in order to mitigate successfully the perverse incentives created by the pursuit of profit.

## 2. Mandatory Clinic Certification

Requiring ART clinics to obtain SART certification would go a long way in ensuring compliance with ASRM's ethical and practice guidelines.<sup>222</sup> Such a move would protect a doctor's discretion for individual patients' treatment plans, but would also ensure that clinics do not systematically operate outside the industry's accepted ethical norms.

A strong and enforceable clinic certification system is perhaps the best option for addressing the conflicts of interest and ethical shortcomings that have long haunted the fertility industry. With mandatory certification come clear and enforceable rules that apply the ethical norms of the industry to *all* clinics. Eliminating the ability of IVF clinics to ignore ASRM embryo-transfer guidelines is a reasonable first step in addressing the rising costs of multiple births in the United States. Similarly, conditioning clinic certification on the implementation of a standardized and robust informed consent process would both protect patients and prevent clinics from sugar-coating the risks of ART procedures. Whether ASRM would be up to the task of significantly strengthening its current SART certification system remains to be seen, but mandatory certification of ART clinics, either through ASRM or through a federal agency, is a sensible way to start regulating ART in the twenty-first century.

While there are likely dozens of other possible details to work out, there is simply no denying that it is well past time for meaningful government intervention in the ART industry.

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220. *Id.* at 617 (citing MICHAEL MULKAY, *THE EMBRYO RESEARCH DEBATE: SCIENCE AND THE POLITICS OF REPRODUCTION* 57–58 (1997)).

221. *See* Marchione, *supra* note 92.

222. *See* Jones et al., *supra* note 161 (describing the SART certification process, enforcement of ASRM guidelines, and the ability of clinics to operate without SART approval).

### CONCLUSION

The drive to reproduce is at the center of human beings' survival on this planet. Sadly, not all individuals are born equally capable in this quest. For those who desperately desire children but cannot have them on their own, the remarkable growth of ART over the past few decades has been a transformative innovation. Some ten million babies now inhabit the earth because of unbelievable breakthroughs in reproductive technology.

However, pioneering advancements eventually create challenges, and can lead to potential abuses if left unchecked. Today, thousands of would-be parents are spending their life fortunes on ART without being adequately informed of the benefits and risks. The dramatic increase in the use of ICSI during IVF procedures is of particular concern, since modern medicine is now capable of fertilizing eggs with sperm that would have failed the natural selection process on their own. IVF providers face little incentive to impress these risks on their customers, and operate in a largely unregulated environment where cash is king. The incentive to report high live-birth rates dictated by the profit motive pushes clinics to both implant more embryos than necessary and recommend technologies that may increase births notwithstanding increased defect rates.

Law and regulation have lagged far behind technological advances in this arena. Their absence has contributed to a "wild west" mentality in some fertility clinics, where anything goes if it will make money. It is now past time we act to change that reality. At a minimum, stricter federal regulation of the fertility industry is necessary to preserve its benefits while mitigating its risks. Truly informed consent can only be achieved when patients know exactly what they are getting themselves into. Legislation or regulation mandating specific information disclosures is necessary because our current system of voluntary guidelines lacks teeth and viable enforcement mechanisms. Mandatory fertility clinic certification would also ensure that all enterprises are operating on a level playing field, and that patients receive standardized information regarding risks and outcomes.

We are living in a transformative time in the history of human reproduction. With common sense regulation to curb potential conflicts and abuses, we can ensure that the miracle of parenthood will be available to millions more would-be parents in generations to come.