ETHICS & MEDICS
April 2018 Volume 43, Number 4
A Commentary of The National Catholic Bioethics Center on Health Care and the Life Sciences

Also in this issue: "Embryo Mortality and In Vitro Fertilization" by Laura Elm

Understanding Social Science Studies on the Family

Carr J. Smith and Julia M. Smith

Opinions vary as to the relative importance of Roger Bacon's *Opus majus* composed in the 1200s, the invention of the printing press by Johannes Gutenberg around 1440, and Isaac Newton's 1687 work, *Mathematical Principles of Natural Philosophy*, but few would disagree that the scientific revolution ushered in by these and works by scores of other scientists, inventors, and engineers has transformed the world.[1] Material and intellectual progress has placed science on the highest pedestal of modern society. It is only natural that the social sciences would covet the credibility of the more objective experimental sciences.

Despite an almost limitless diversity of questions, the experimental sciences share a methodological foundation for studies involving human beings. Two basic designs can be employed. In the first case, research subjects are compared by some measurement(s) with matched control subjects who differ as little as possible from one another except in the variable being evaluated. In the second case, research subjects serve as their own control by providing a baseline measurement(s) at study time zero, and then some treatment (agent, action, conditionality, or inquiry) is applied and the same measurement(s) are taken again.[2] In both of these protocols, it is essential that the only significant difference between the samples is the variable under consideration. Following data collection, statistical analysis is conducted to determine if the results could have occurred by chance in more than one out of twenty experiments. Results not occurring by chance at this 95 percent confidence level are considered to be statistically, although not necessarily clinically, significant.

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Even with the two most statistically powerful and well-controlled protocols for human evaluation—the randomized, double-blind, placebo-controlled clinical trial and the prospective epidemiology study—a high degree of expertise and care is essential to avoid inadvertently introducing bias into the study design. Unfortunately, it is extremely difficult to avoid doing this in social science studies. Clinical epidemiology has extensively examined the sources of bias in human studies.[3]

Bias in Social Science Studies

Despite the confidence with which the results from social science studies are communicated to the public, it is a straightforward process to deconstruct some of their claims. Before considering the types of potential bias, it should be noted that even the results from much better controlled experiments suffer from low rates of reproducibility. For example, in 2012, researchers at Amgen were unable to reproduce the results in forty-seven of fifty-three landmark cancer papers.[4] In addition, there is a prevailing bias against publishing negative results[5] or those that contradict the prevailing paradigms in the field. Concomitantly, iconoclastic research is less likely to be funded in the first place.

Once a social science study has been published, how does one determine the credibility of its results? First, examine the sample size. A small number of research subjects or a homologous population can limit the generalizability of any conclusions. Critics have questioned the validity of Sigmund Freud's findings for both these reasons.[6] Second, determine the level of blinding used in the study. In a single-blind experiment, subjects do not know whether they received the intervention or a placebo. In a double-blind experiment, neither the subjects nor the researchers evaluating them know who received which. In an observational study, in which variables are observed but not manipulated, it is similarly important not to inform participants about the precise purpose of data collection. Margaret Mead's study of adolescence in Samoan girls illustrates the importance of this concept. The subjects were not blinded to the study hypothesis[7] and therefore told Mead what she wanted to hear.[8] This is an example of response bias.

Third, look for obvious sampling errors. Opinion polls can be skewed when the sample comes from a non-representative population, for example, one that includes too many members of one political party or residents of a geographic area in which there is a prevailing opinion on a particular issue. Fourth, consider the possible effect of recall bias, which can occur when subjects want to shift the blame

for a bad outcome. For example, substance abusers might over-report bad childhood experiences.

Social Science Studies on the Family

A particular focus of social science research since the mid-1800s has been the structure and role of the family in society.[9] The Progressive Era (1890–1920) introduced Americans to European intellectuals who were hostile to the family. The following quote by John Dewey is illustrative: "Hence the great task of the school is to counteract and transform those domestic and neighborhood tendencies that are still so strong, even in a nominally collectivist regime."[10] Later, the tumult of the 1960s and the resultant changes in education mainstreamed criticisms of the family, which are disseminated widely today through both print and electronic media. Many of these criticisms are based on social science research allegedly demonstrating that raising children in traditional families is unnecessary,[11] insufficient,[12] obsolete,[13] disadvantageous, or harmful.[14] This onslaught of negativity can be bewildering and has influenced public opinion.

Some investigators have used studies that examine the well-being of adopted children to demonstrate that nontraditional families are equivalent if not superior to traditional families. These studies employ a subtle form of bias, referred to as the problem of colinearity, which merits its own discussion.

Remember that the most basic assumption underlying any study is that the variables under consideration are the only significant differences between the sample groups. Adults who want to adopt have demonstrated a robust desire to care for a child and represent a highly self-selected subpopulation. It is not surprising that members of this group on average possess considerable socioeconomic advantages and motivation as compared with the general population.

However, one cannot consider only whether a child was adopted by a traditional or a nontraditional family, as many other variables influence a person's well-being. If researchers fail to control for all the variables that have a causal relationship with the outcome, they are likely to assign too much weight to an unimportant variable or infer that a relationship exists where one does not. Moreover, many of the variables that influence well-being are qualitative and therefore considerably more difficult to evaluate than quantitative variables like SAT scores, college graduation rates, and job success. Furthermore, the indices used to measure qualitative variables are necessarily less precise.

Veiled Criticisms of the Family

In his classic work *Man's Search for Meaning*, the great Austrian psychiatrist and Holocaust survivor Viktor Frankl makes the case that "the greatest task for any person is to find meaning in his or her life."[15] Many postmodern intellectuals find life most meaningful when denigrating the value of humanity in general and the family in particular.[16] The exuberance of this pursuit has been nothing if not persistent, as longshoreman-turned-philosopher Eric Hoffer described in 1959: "What puzzles me is the passionate blind effort by scientists, psychologists, historians, economists, businessmen, industrialists, revolutionaries, military men to hack away at man's uniqueness—to demonstrate that there is no basic difference between man and the rest of creation. It is a blind, concerted effort to downgrade man."[17] Scientifically veiled criticisms of the family will exist for the foreseeable future, so we should understand their limitations.

Notes

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16. See, for example, the ideas regarding the sanctity of life presented in Peter Singer, *Practical Ethics*, 3rd ed. (Cambridge, UK: Cambridge University Press, 2011).
17. Eric Hoffer, *Working and Thinking on the Waterfront* (Titusville, NJ: Hopewell Publications, 2009), 113.

Embryo Mortality and In Vitro Fertilization

Laura Elm

Since 1997, the Centers for Disease Control and Prevention (CDC) have published annual assisted reproductive technology success rate reports, including the *ART National Summary Report* and the *ART Fertility Clinic Success Rate Report*, which contain data on cycles performed two years prior and the associated pregnancy and birth outcomes. These documents provide the public with insight into utilization rates, trends, and outcomes at the 464 reporting fertility clinics in the United States. According to the Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA), clinics are required to report ART cycles to the CDC on an annual basis.[1]

The *2015 ART National Summary Report* (National Summary) was published in October 2017 and counted 231,936 ART cycles. Egg and embryo banking cycles (also know as "freeze-all cycles") (45,779) and cycles using previously frozen eggs (4,003) were not factored into success rates. Of the remaining 182,154 cycles, 54 percent used fresh embryos, and 46 percent used frozen embryos. Donor eggs were used in 7 percent and 17 percent of fresh and frozen cycles, respectively. Procedures started in 2015 resulted in 60,778 live-birth deliveries of 72,913 infants. In vitro fertilization (IVF) accounted for more than 99 percent of reported ART cycles.[2]

ART Outcomes: Patient Event or Embryo Mortality?

This essay hopes to convey the problematic framework of ART outcomes as they are published today, reframe the logic to focus on human embryo mortality, and quantify a population of human beings generally not accounted for in publicly available IVF data. Because this is one of the first attempts to estimate pre-transfer embryo mortality in IVF, this analysis focuses on fresh non-donor cycles only, that is, rounds of IVF treatment that include immediate transfer of at least one embryo and in which the embryos transferred were engendered using the recipient's own eggs. We hope to produce future analyses that include mortality rates for other ART cycle types. The following analysis was done using the CDC's 2015 National Summary data in conjunction with a retrospective study conducted by one of the nation's largest ART delivery systems.

The National Summary's outcomes analysis for fresh non-donor cycles consists of counts of patient procedures ("stages") performed and the resulting pregnancies and live births: 91,090 cycles, 80,644 retrievals, 59,336 transfers, 26,708 pregnancies, and 21,771 live births.[3]

The CDC's analysis is patient-centric and obscures the fact that one or several new stakeholders, that is, the living embryos, have been introduced into the procedure. To be able to assess embryonic population size and mortality rates, increased transparency of the IVF stages of fertilization and monitoring is necessary.

To reframe the outcomes so they reflect post-transfer embryo mortality, calculations were performed across the CDC's data to obtain the total number of embryos transferred in fresh non-donor cycles: 110,062. The number of live-born infants (26,822) was calculated and then subtracted from the total number of embryos transferred. The result is 83,240 embryos, who did not survive from transfer to birth. This equates to a mortality rate of seventy-six deaths per one hundred embryos transferred, or 3.1 post-transfer deaths for every one post-transfer survivor.

Uncounted Human Beings

Post-transfer mortality is one side of the story; embryos generated by ART fertilization may also pass away prior to transfer. Causes of pre-transfer death in fresh cycles include spontaneous arrest and intentional discard. While not the focus of this article, cryopreserved embryos may die during thaw prior to an intended frozen cycle or as a result of elective thaw and discard. Embryo remains are typically disposed of as medical waste.

To aid clinics in complying with FCSRCA requirements, the CDC created the National ART Surveillance System. NASS-reportable data elements include "2 pronuclei" and "embryos available for transfer."[4] CDC publication of this data, with an explanation that the term "2 pronuclei" is synonymous with "one-cell human embryo," could illuminate the IVF process and help people more thoroughly evaluate the decision to pursue ARTs.

Some may say that it is sufficient to account for only the embryos "good enough" to transfer. If pushed beyond erroneous statements that human embryos are anything other than unique, complete living human beings, they may support their position by arguing that aneuploid, poor-quality, or otherwise abnormal embryos are unlikely to survive the journey through the fallopian tube or implant in the uterus, whether they were engendered in vivo or in vitro. Therefore, one of the supposed benefits of IVF is that it removes the time and effort involved in waiting for nature to take its course with embryos that may never have survived in vivo in the first place. However, the assessment or presumption of viability is immaterial to the need for comprehensive, objective reporting of legally available medical procedures. In the absence of the CDC's analysis and publication of fertilization data, two other sources may offer clues that help estimate the number of embryos who

Laura Elm is the founder of Sacred Heart Guardians and Shelter in St. Paul, Minnesota, whose mission facilitates burial for the remains of human embryos who die in IVF laboratories and would otherwise be disposed of as medical waste. In the six months it has been reaching out to IVF clinics, the organization has yet to receive any remains for burial.

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ETHICS & MEDICS

VOLUME 43, NUMBER 4
APRIL 2018

are generated through fresh non-donor IVF cycles and do not survive to transfer or freezing.

In a retrospective review of autologous IVF cycles occurring between 2004 and 2008 at a large fertility practice, 110,939 embryos were conceived, 31,437 were transferred, and 12,845 were cryopreserved.[5] Simple math shows that 66,657 died in the laboratory, either spontaneously or as a result of selective discard. The data from this clinic's study allow us to calculate a ratio of postfertilization outcomes: 1.0 transferred to 0.4 cryopreserved to 2.1 pre-transfer death/discard.

By applying this ratio to the CDC data, reframed outcomes for fresh non-donor cycles is estimated to be 91,090 cycles, 80,644 retrievals, 385,215 embryos generated (231,129 pre-transfer die/discard and 44,025 cryopreserved), 110,062 embryos transferred, 26,708 pregnancies, 21,771 live births, and 26,822 infants born. Total embryo mortality is estimated at 314,369 (83,240 in utero and 231,129 pre-transfer death/discard), or eighty-two of one hundred embryos. Three-quarters of total embryo mortality occurred in the laboratory.

Patient Blogs

Infertility is a challenging diagnosis, and patients may look for support in online communities. These forums provide anecdotal data on pre-transfer embryo mortality:

> "They retrieved 26 eggs, all mature. 21 fertilized. But today I got the call that only 11 have made it to the 5-day blastocyst phase. We are having those 11 PGD'd [diagnosed before implantation] so I expect to lose a few more before all is said and done. . . . Is it normal to lose about 50% between Day 2 and Day 5?"
>
> "We retrieved 21 eggs, 17 fertilized, 8 made it to blast, 2 were transferred fresh and only 1 was of an excellent enough quality to freeze."
>
> "A grand total of ONE frozen embryo from 3 fresh cycles! . . . First cycle i got 3 fertilized eggs . . . transferred 2. . . . The other one couldnt freeze. 2nd cycle i got 4 fertilized eggs. . . . transferred 2. 3rd cycle had 5 fertilize . . . transferred 2 . . . and none to freeze!"[6]

In this conversation, twenty-nine of fifty IVF-generated embryos passed away in the laboratory. This online conversation and the many threads like it support a hypothesis that a substantial number of the embryos generated through IVF perish in the laboratory. It is also apparent that embryos are often discussed as a statistical means to a desired end.

Tallying Embryo Death

The gift of life is a wonder on which to reflect. The awesome fact that a new human being in a one-celled body has all the specifications, motivation, and energy to continuously drive the development of his or her material self is simply amazing. We talk often about serving the needs of those on the fringe of society. Today, this includes the human beings in culture dishes and cryotanks. It is imperative to know how many there are and advocate for the recognition of their humanity. It is highly desirable that the CDC provide transparent embryo mortality data and that medical professionals delivering IVF, in their role as trusted advisors and clinical experts, counsel patients that fertilized eggs are human embryos, that is, human beings, and that pre- and post-transfer embryo mortality not only occurs on a regular basis but represents a substantial loss of human life.

Notes

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