Chapter 2

eSET

ANTICIPATING NEW SUCCESS AND RE-NETWORKING IVF

"Who's afraid of single embryo transfer?" In 1998, two Belgian doctors posted this question on the debate forum of *Human Reproduction*, the official journal of the European Society of Human Reproduction and Embryology (ESHRE) (Coetsier and Dhont 1998). Single embryo transfer (SET) sounds straightforward: transferring only one embryo can only result in a singleton birth, thus reducing if not eliminating multiple pregnancy created by IVF. Chapter 1 has explained the "number policy" that started in the late 1980s with "three"—transferring no more than three embryos—and then moved to "two," the so-called double embryo transfer (DET), to reduce the chances of triplet or quadruplet pregnancy. Starting in the late 1990s, however, some policymakers and members of the medical community noticed that DET was inadequate. The triplet rate declined with DET, but the percentage of twins remained high or even higher. The laboratory and clinic practices continued to improve, so as the pregnancy rate increased, so did the twin rate. For example, the European data in 1998 show that, among more than thirty thousand deliveries after IVF and ICSI (intracytoplasmic sperm injection), the multiple birth rate was 26.3 percent, including 23.9 percent twin deliveries, 2.3 percent triplets, and 0.1 percent quadruplets (Nygren, Nyboe Andersen, and EIM 2001). If counting number of babies rather than number of deliveries, some global data show that almost 50 percent of IVF kids are born from multiple birth (ESHRE Task Force on Ethics and Law 2003). Test-tube babies used to betoken miracles; now they foretell multiples.

Single embryo transfer was proposed to handle the overwhelmingly high percentages of multiple pregnancy and birth. SET has different faces. The "natural cycle" used in the case of the first "test-tube baby," Louise Brown (see chapter 1), entailed single embryo transfer. Without egg stimulation drugs, women usually produce one egg per month for retrieval and therefore have at most one embryo in the lab for transfer. Even when an egg stimulation drug is used, it is likely that only one embryo will be available for transfer. This is called "compulsory SET," or cSET (Gerris et al. 2009: 56–57). cSET often means a poor result from egg stimulation, retrieval, or fertilization, which leads to the making of only one embryo in the lab—an unwelcome result for both practitioners and patients. Since the late 1990s, what IVF experts have promoted as the best risk-prevention policy is neither the natural cycle nor cSET but "elective single-embryo transfer" (eSET). The US Society for Assisted Reproductive Technology (SART) defines eSET as "an embryo transfer in which more than one high-quality embryo exists but it was decided to transfer only one embryo" (Practice Committee of ASRM and the Practice Committee of SART 2012). It refers to the practice of choosing a single embryo for transfer—hopefully the best one—among several available candidates.

Who is afraid of eSET? The provocative question asked in 1998 indicates the fear about what could happen if single embryo transfer became real:

> We … need to consider an individualized embryo transfer policy: *elective transfer of a single embryo* in patients at risk for multiple gestation and a more liberal attitude for those with a less good prognosis. Would this *reduce significantly the number of multiple pregnancies without dramatic fall in overall success rates*? Can we in fact *anticipate the effect* of such a strategy on our IVF results, in terms of the overall pregnancy rate and multiple pregnancy rate? (Coetsier and Dhont 1998: 2663, emphasis added)

A new anticipation arose. The desired future was not only to achieve pregnancy and live birth but also to avoid the risk of multiple pregnancy. It is clear that the promotion of eSET was meant to further reduce the risk of multiple pregnancy, yet the leading concern was a decline in the "success rate." The balance between risk and success, as shown in chapter 1, continued. Implanting just one embryo even though several were available was indeed a "never-before zone" in the world of IVF. In 1998, only around 10 percent of IVF cycles in Europe were SET (Nygren, Nyboe Andersen, and EIM 2001), and most of these were probably cSET, not the ideal eSET.

In this chapter, I present the anticipatory practices of eSET. What has been done to make eSET work? How can eSET become a new routine of IVF? Who are the leaders to make eSET possible? I start with the useful framework of "anticipatory work" articulated by Adele Clarke (2016): hope work, abduction, and simplification (see the introduction to this book). I illustrate what kind of anticipatory work is needed for implementing eSET. I argue that practicing eSET entails re-networking IVF, both globally and locally. While the international IVF epistemic community does build an important foundation for eSET, national contexts matter. The state, medical societies, and civic groups intertwine in different ways to shift eSET from an experimental to a routine practice.

New Hope Work: Redefining Success

IVF has been promoted as a hope technology (Inhorn 2020). The hope is to enable infertile couples, and sometimes single women and same-sex couples, to have genetically related children. The chance of fulfilling that hope is often measured by the "success rate." Multiple embryo transfer (MET) was part of hope work by IVF experts to increase the success rate. The multiple births resulting from MET are sometimes celebrated as an unexpected blessing. However, if the mother and babies suffer complications and even death, the miracle can become a nightmare. If the babies are in critical condition, this can hardly be regarded as hope being fulfilled.

In light of the risk associated with IVF, various stakeholders started to develop a new hope work focused on redefining success. The ideal goal is not to become pregnant or "take a baby home" but to "take a *healthy* baby home." To reach this best possible future that IVF can bring, it was necessary to clarify what the future should be and how to reach that ideal. This new hope work is therefore composed of two aspects: identifying false hope and advocating a new ideal future. I will show how IVF scientists, medical societies, and policymakers have been working to articulate the new hope of IVF and justify the need for eSET.

Identifying False Hope

Challenging the mainstream definition of "success" was the first step in identifying false hope. As chapter 1 shows, "success rate" is the primary criterion for evaluating the effectiveness of IVF. In the early period of IVF, success was defined as chemical pregnancy and the clinical pregnancy rate. This meant that a positive pregnancy test or an ultrasound showing a fetus counted as success, regardless of whether miscarriage or stillbirth occurred later. Pennings (2000: 2466) has paraphrased the old saying about surgical operations ("The operation was a success. Regrettably, the patient died") to point out the irony of "success" in multiple pregnancy by IVF: "The establishment of the pregnancy was successful. Regrettably, the children are handicapped and the mother suffers from depression." Clearly, success needed to be redefined.

Thus we can see that, even though clinicians and medical societies may prefer to reveal the pregnancy rate from IVF because it is higher than the live birth rate, this creates false hope. Leaders of the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) observed that in the early period "both national and international reports have focused on *markers of efficacy*, while issues of access to treatment and *safety* have not been addressed" (Adamson et al. 2001a: 1284, emphasis added). What to report reflects the central value of the monitoring system—namely, what we should care about: success (markers of efficacy) or risk (safety). The typical way to identify "false hope" was to present the adverse outcomes along with "success" rates.

The independent regulatory body in the UK, the Human Fertilisation and Embryology Authority (HFEA), does this in its annual reports, which began in 1991. The very first table in each report shows the live birth and multiple birth rates for IVF, ICSI, and donor insemination. For example, the table published in 1998 presents the multiple birth rates (around 27 percent) right next to the live birth rates (around 15 percent). This indicates the shadow (multiple birth) that casts a pall over the goal (live birth). In addition, the number of embryos is cross-tabulated with live birth rates, multiple birth rates, and stillbirth and neonatal birth rates. Although live birth rates increased with number of embryos transferred (NET), adverse outcomes also did so. The juxtaposition of the success of live births with the tragedy of deaths and complications yielded an important warning. The HFEA's data reporting illustrates what the research has shown: "Success, however, has come *at the expense* of an increased incidence of multiple gestations, along with their inherent maternal, neonatal, and pediatric complications" (Stern et al. 2007: 275, emphasis added).

International medical organizations often include safety as an important part of hope. They present multiple birth rates across countries to compare the degree of false hope. In 1997, the ESHRE began to present the data reported by European countries, with multiple births being presented after the pregnancy/delivery rates (Nygren and Nyboe Andersen 2001). This revealed that the overall multiple birth rate of 29.6 percent in Europe was lower than the 37 percent in the US and Canada. Moreover, it highlighted that Sweden and Denmark had reduced their triplet rate to 0.4 percent, whereas the UK still had 3.3 percent and Spain 11.9 percent. Similarly, the ICMART yields data on safety and presents the global trend. The International Working Group for Registers on Assisted Reproduction (IWGRAR, later transformed into the ICMART) showed in its first world report that Taiwan had the highest number of embryos transferred during IVF, followed by the US and South Korea (Adamson et al. 2001b). In presenting the data collected in 2000, the ICMART quickly realized the serious consequences of multiple birth in the US, Middle East, and Latin America. Singleton babies became minorities: the figures show that "in Latin America, only 48.7 percent, and in the Middle East, only 44.1 percent, of the newborns [from IVF] were singleton babies" (Adamson et al. 2006: 1606). Some regions still transferred four or more embryos. The ICMART's annual reports have shown that Taiwan and South Korea *continue* to have some of the highest NET, leading to the highest multiple birth rates, while Japan has the lowest rates in East Asia (Dyer et al. 2016).

Reporting the neonatal outcomes of IVF works directly to highlight the false hope it can offer. The ESHRE has listed stillbirths and miscarriages from the beginning but has not included detailed data on birth rates and prematurity. Such follow-up data require a stronger monitoring system. Taiwan is one of the few countries that has reported low birthweights from the very beginning of the ART registry in 1998 (Wu, Ha, and Tsuge 2020). The earliest report, based on the state-run registry, showed a high prevalence of premature babies among those of low birthweight, with triplets suffering the most. The warning sign of low birthweight is also included in the annual report, but the official report failed to point out that this is a serious health problem and thus did not link it to a call for action. I discuss below how to translate data related to the new hope work, so as to prompt changes in IVF practices.

Representing the Real Hope: "Taking a Healthy Baby Home"

In addition to revealing the false hope for a healthy baby that could result from IVF, the medical community struggled to present the real hope. In 2001, the ESHRE convened a special task force to address the complications of IVF and listed ten points to explain why the problem of multiple pregnancy in IVF had not yet been solved (ESHRE Campus Course Report 2001). Two of the ten points are about the definition and presentation of "success":

- The success of IVF is too often expressed in terms of pregnancies instead of healthy newborn children per cycle.
- There is a lack of enforcement by journal editors to express results in terms of singleton pregnancies and healthy children. (ibid.: 791)

Both these points challenge the traditional calculation of success rates, which did not accurately represent the real hope: taking a healthy baby home. And both points propose a new way to measure success: counting the healthy singletons. Johannes L. H. Evers (2002: 158), the chair of the ESHRE, reviewed the benefit and risk of IVF and declared in *The Lancet*, "The most appropriate outcome variable of all assisted reproduction procedures … is not pregnancy rate, but singleton livebirth rate per cycle started." The leading journals on assisted conception also agreed to require standardized terminology in reporting success in clinical studies (Barlow 2004).

Some doctors and scholars have similarly called for new indicators to peg the quality of ART. To reach the standard of "taking a healthy baby home," some propose that efficacy should focus on "singleton delivery" (Adamson et al. 2001a) or "delivery rate of singleton, normal weight and live birth" (Min et al. 2004) as the success rate. Such data are not easy to collect. A division of labor exists: IVF experts aim to make women pregnant, obstetricians are in charge of maternal care, and pediatricians care for the test-tube babies. As a result, IVF experts may not see the full outcomes of birth. Women may not give birth in the IVF clinics, so tracing IVF outcomes requires additional efforts. What is more, the ESHRE Campus Course report (2001) points out that IVF experts tend to pursue the pregnancy rate without viewing the adverse outcomes that multiple embryo transfer brings, and thus they fail to feel responsible. Therefore, counting the live birth rate itself involves strongly mandating the reporting system. When a national registry system is built, "live birth rate" and "singleton birth rate" must become the routine calculation of success rates.

The most challenging new hope work is to prioritize the outcome of "taking a healthy baby home." This outcome takes into account not only a successful live birth but also the health condition of the newborn baby. Some innovative terms were therefore created. The IVF center at Monash University in Melbourne proposed the measure of "the singleton, term gestation, live birth rate per cycle initiated," dubbing it BESST (Birth Emphasizing a Successful Singleton at Term) statistics (Min et al. 2004). Not only does the numerator in this measure reflect the value of taking a healthy baby home but the denominator counts the start of treatment, rather than the date of embryo transfer, to recognize the length of the process that aspiring parents may undergo. Jason Min and colleagues presented their clinical outcomes with the BESST calculation. This report is believed to be the first to valorize the new hope of "taking a healthy baby home." The success rates decreased progressively from preclinical pregnancies (24.8 percent) to viable pregnancies (19.6 percent) to live deliveries (17.0 percent) to live singleton deliveries (12.4 percent) to term gestation (11.1 percent). This meant that at the Monash IVF center, the aspiring parents' "prospect of a singleton, term gestation, live birth of a baby per cycle begun was 11.1 percent" (Min et al. 2004: 7). Even though 11.1 percent is much lower than the conventional success rates, the team claimed that "this is precisely what a subfertile couple wishes to know" (ibid.: 6).

The US is probably the only country that stipulated a law specifically on success rates. The Fertility Clinic Success Rate and Certification Act was enacted in 1992. Since then, the Centers for Disease Control (CDC) and the SART have required each ART clinic to report its performance data and have published those data annually by clinic. In 2013, a new success rate came forth: the "term, normal weight & singleton live births" rate. This new item highlights the births of singletons born no sooner than thirty-seven full weeks and weighing at least twenty-five hundred grams (five pounds eight ounces). This "term, normal weight & singleton live births" rate is calculated per transfer cycle rather than per treatment cycle as advocated by the Monash IVF team. Still, this rate is lower than the "singleton live birth" rate, "live birth rate," and "pregnancy rate." For example, in the 2013 report (CDC, ASRM, & SART 2015), for women who were between thirty-five and thirty-seven years old with fresh embryos from nondonor eggs, the rate of taking a healthy singleton baby home was 19.6 percent—much lower than the live birth rate (31.6 percent) and almost half of the pregnancy rate (38 percent). This low rate may not be what clinicians would like to present, but the state mandates that the data be presented on what the couple is hoping for.

Incorporating adverse health outcomes and innovative indicators in national registries is not an easy task. Different stakeholders (physicians, counselors, policymakers, and patients) may place emphasis on different indicators (Dancet et al. 2013; Thompson 2016). Establishing better indicators also requires that demanding infrastructure changes be made. Tracking health outcomes of babies is challenging work because women may go to different clinics for ART and for childbirth. To account for whether single embryo transfer leads to better health outcomes, cycle-based data for individual patients are needed rather than clinic-based data, which are aggregates. A shift to care-centered data reporting requires information technology reform, new regulatory requirements, and sometimes consensus mobilization (Wu, Ha, and Tsuge 2020). IVF clinic websites also became a new challenge for presenting success. Some countries like Australia and the UK started offering guidelines on how to present success rates on clinics' websites and social media.[1]

Abduction: Testing eSET

How do we achieve the new hope—namely, "take a healthy baby home"? The answer involves abduction work. Adele Clarke (2016: 90–91) defines abduction as "tacking back and forth multiple times between the empirical information collected … and new theorizings about that data to generate new conceptualization—and adding a future-orientedness to its utility." In the late 1990s, several new trials began to test ways to fulfill the new hope of healthy singleton babies. A prestigious evidence-based Cochrane review provided the answer in 2005.

The Cochrane review produced a recommendation on number of embryos transferred after IVF and ICSI. The principle was to find the balance: "While the most effective way to minimize multiple pregnancy is to limit the number of embryos transferred, such a policy has to be balanced against the risk of reducing the overall pregnancy rates in IVF" (Pandian et al. 2005). We have seen this pattern repeatedly: success rates cannot be compromised. eSET was assessed as to whether or not it was meeting this principle. The authors of this Cochrane review combined four studies, from Belgium, Finland, the Netherlands, and Sweden, to compare the results of single and double embryo transfer. They were all randomized controlled trials, viewed as the highest standard of evidence. The review concludes that "a single embryo transfer policy involving a fresh followed by a frozen embryo transfer *reduces the risk of multiples while achieving a live birth rate* comparable with that achieved by transforming two fresh embryos" (Pandian et al. 2005: 2682, emphasis added). The evaluation equally weights both the success (live birth rate) and the risk (multiple pregnancy rate). Evidence-based medicine recommends that implanting one embryo each time for two times could reach the same live birth rate as implanting two embryos at one time, while significantly reducing the multiple pregnancy rate. One plus one equals two, and the risk would be reduced too.

The Cochrane review pointed to a new course of action for IVF clinicians. The data collected for testing eSET yields "probabilistic anticipations of the future that in turn demand action in the present" (Adams, Murphy, and Clarke 2009: 255). One Cochrane review did not change the whole IVF world. Its authors suggested that to make the policy work, it must identify women who have higher chances of twin pregnancy, such as those who are younger than thirty-five and have some good embryos for future use. The authors also admit that this is only clinically effective, and also needs to consider cost-effectiveness and acceptability (Pandian et al. 2005: 2686). Even the clinical effectiveness needs a lot of new refinement, particularly about how to select the embryos.

Abduction continues on how to make eSET feasible. One new invention is the "cumulative success rate." Like what the Cochrane review shows, the success rates of two "eSET" equal those of one "DET." This requires a new conceptualization of calculating success. The traditional method of calculating success rate "per cycle" would *not* reflect the efficacy of eSET. "Cumulative live birth rate" takes two or more transfer cycles to present the outcomes. The Cochrane review counts one fresh eSET and one frozen eSET embryo as the denominator. This usually leads to an equal or even better live birth rate than that rate produced by one DET. Due to the maturity of cryopreservation, clinicians tend to choose the best embryos in early cycles and then freeze surplus embryos (and sometimes eggs) for future use. This also reduces the need to do additional intrusive egg-retrieval procedures, thus lowering women's health risk. Therefore, the egg retrieval cycle can count as one cycle for the new success rate.[2]

eSET starts with selecting the "best" embryo, but what is the best? The question of how to select the best embryo has opened up a new wave of research. The "how" question therefore moves from balancing success and risk to pursuing best quality. Abduction expands. The IVF community has often reflected on its inadequacy in judging embryo quality. The ESHRE team on reducing multiple birth of IVF (ESHRE Campus Course Report 2001: 790–91) listed the three major technical limitations:

- Lack of efficiency of IVF, necessitating the transfer of more than one embryo.
- Poor predictability of embryo survival and implantation potential.
- Overall poor results of cryopreservation programmes.

The IVF medical community is aware that to make eSET feasible, it needs to develop various techniques. For instance, it needs to know how to select a good prognosis group for practicing eSET; it needs to improve the lab technique to decide whether to implant day three embryos or those that will develop to the blastocyst stage (day five or six); and it needs to stabilize cryopreservation so that frozen embryos can be safely used in later transfer cycles (also see Gerris et al. 2009).[3]

New techniques continue to evolve and be subject to deliberate debate. Time-lapse imaging has been used to record the development of embryos within the embryo incubator, seeking to provide better visual information to embryologists when selecting and deselecting candidates for embryo transfer (Herrero and Mesequer 2013). Embryologists' observation has been shown to vary greatly, so artificial intelligence (AI) is now used to increase the accuracy of embryo assessment (e.g., Bormann et al. 2020). Preimplantation genetic testing (PGT), used for monogenic diseases, began to be applied to embryo selection in the mid-2000s. Aneuploidy, the most common type of chromosome abnormality, has been regarded as the leading cause of implantation failure and miscarriage for IVF. Therefore, PGT for aneuploidies (PGT-A) is used to select embryos based on their genetic composition, hoping to improve implantation and reduce miscarriage, and thus enhance eSET (Lee et al. 2015). However, opponents remain. Since the error rate of PGT-A is not zero, PGT-A can risk wasting a good embryo. If counting by the cumulative success rate, "survival of the fittest" may achieve good outcomes as well as "no embryo left behind" (Munne et al. 2016). According to the latest survey by the International Federation of Fertility Societies (IFFS), more and more countries regard PGT-A as an established medical practice, but some, including Japan, still list it as experimental (IFFS 2019). IFFS and ASRM statements all ask for more research to test its efficacy (IFFS 2019; Practice Committee of ASRM and Practice Committee of SART 2018; for the difficulty of building evidence-based medicine for these "add-ons" to IVF, see Perrotta and Geampana 2021). Abduction continues.

Simplification: SET Guidelines

Setting a guideline for eSET is the simplification work needed to anticipate "taking a healthy baby home." As Clarke (2016: 96) argues, "Simplification is necessary because of TMI (too much information)—the increasingly common situation in which there is too much information, too much data to manage—or too much affect." Embryo selection and patient selection both involve complicated conditions. To effectively implement policy to reduce the risk of multiple births, some medical societies and national/regional regulatory agencies have offered either voluntary or legally mandatory guidelines on the number of embryos transferred for IVF practices. Although the content of these guidelines varies, simply transferring *one* embryo is usually the major statement.

The first guideline mandating single embryo transfer came from Sweden. The complete registry data in Sweden made the agenda evident. Sweden started its registry in 1982, the year the country's first IVF baby was born. A group of scholars revealed the striking increases in multiple births, congenital malformations, and low-birthweight/high-risk babies that IVF created and published these findings in *The Lancet* (Bergh et al. 1999). The Swedish doctors recognized that eSET was the major strategy to reduce the risk (Hazekamp et al. 2000). To prevent adverse outcomes, double embryo transfer (DET) has been promoted in Sweden since the 1990s. In 2001, 81.6 percent of cycles were DET, the highest in Europe (Nyboe Andersen et al. 2005). However, twin pregnancy remains high—23.3 percent in 2001, for example. In 2002, the South Swedish Health Care Region required that all IVF cycles offered in public hospitals must adopt SET, except under circumstances that justified the use of DET (Saldeen and Sundstrom 2005). IVF is included in the public healthcare in Sweden, and risk prevention and cost management are important parts of this agenda. The regulatory agency in Sweden is regional, so the reform started in local districts. The local policy soon led to the national mandate requirement. In 2003, the Swedish

National Board of Health and Welfare issued a new guideline stating that, except when the risk of twinning is low, all public-health-supported IVF treatments must be SET.

Sweden's innovative policy is straightforward. The major rationale is to reduce health risks and lower the costs of neonatal care (Bhalotra et al. 2019). The confidence to issue the guideline came from research findings confirming that the cumulative success rates of SET do not differ from those of DET. Data from several pioneering research studies in other Nordic countries also confirmed the feasibility of practicing SET. The abduction work continued. The mandatory SET policy in Sweden was evaluated, showing promising outcomes: the SET rate increased from 25 percent one year before to 73 percent one year after; the multiple pregnancy rate decreased from 23 percent to 6 percent; and the clinical pregnancy rate remained unchanged (Saldeen and Sundstrom 2005). Risk decreased and success remained. The Swedish team announced that the SET policy is "the most reasonable way to solve the problem of the high incidence of multiples after IVF" (ibid.: 7).

Although the Swedish policy reform has been well reported in the global IVF community, it has not traveled easily to other countries. By 2007, the IFFS reported the "resistance to eSET" (Jones et al. 2007: S19). Among the twenty-six countries that have some legal regulation or guideline on number of embryos transferred (NET), most still had three embryos as the maximum, and a few had two as the rule. The magic number of only one embryo transferred became part of law only in Sweden and Belgium. Finland claimed that SET was the norm in practice without any law or guideline. Some countries, such as Australia and the US, included "one" in their guideline only for specific conditions, such as young maternal age and high embryo quality. Howard Jones and Jean Cohen claim that for the 2007 IFFS report, "the most striking finding is the great diversity in these laws and guidelines" (ibid.: S5). This certainly is true of the regulation of NET.

The anticipatory work shown so far—new hope work to redefine success, and abduction work to test various clinical skills—is often shared globally, through journal publications, international medical societies' recommendations, and evidence-based medicine. However, the practice of simplification—issuing a guideline to implant only one embryo in most circumstances—varies greatly among nations. To fully grasp the implementation of SET requires that we turn our attention to the national contexts. Which contexts?

Promissory Capital and Redistributing Cost

Why do some countries demand eSET while others ignore it? The IVF community is keenly aware that many factors are involved (Jones et al. 2007: S19–S22; Adamson 2009; Maheshwari, Griffiths, and Bhattacharya 2011; Ezugwu and Van der Burg 2015; Adamson and Norman 2020). They argue that the capacity for embryo selection and cryopreservation varies among labs, and that having the expertise to reach a certain pregnancy rate is the precondition for trying eSET, especially when the competition among clinics is aggressive. Some also argue that patients may prefer twins, or even triplets, because they are more efficient, so that they hesitate to accept eSET. Among the different explanations for resistance to eSET, however, the financial factor is the usually the crucial one.

The way IVF is financially organized shapes the dimensions of anticipation. In chapter 1, I presented the multiple dimensions of anticipation that are framed by specific stakeholders: for example, feminist groups highlight the risks of IVF, whereas pioneering scientists focus on the opportunities for successful birth. The never-before-clinical practice of eSET intended to reduce risk without compromising success rate. The public health sector has the strongest sense of the need to act on the foreseeable risk, precisely because the health of mothers and infants is endangered by multiple birth and the cost of care is increasing. Thus, when IVF is incorporated as part of public healthcare, the high multiple birth rate tends to ring a warning bell and solicit action to change more urgently in the public health sector than in other sectors.

Some note that the early pattern shows that an eSET policy is only feasible in Europe, where a few countries offer a subsidy program for IVF (Pandian et al. 2005). For example, the UK's National Health Services (NHS) fund some IVF cycles, and most neonatal care services receive public financing. The increasing multiple births from IVF have therefore increased the burden on NHS resources for neonatal care. The HFEA, the monitoring agency for IVF in the UK, started the eSET policy in 2007 with the slogan "One at a Time." In 2009, the guideline became of part of the licensing requirement, but this was later removed due to a legal challenge arguing that eSET reduced success rates and increased patients' emotional burdens.[4] Still, due to the continuous efforts from the medical societies of embryologists and IVF doctors, eSET has been encouraged. The rate of multiple birth in the UK decreased from 26.6 percent in 2009 to

16.3 percent in 2013, but remained far from the goal of lower than 10 percent. Both the HFEA and the medical societies continued to promote "One at a Time" clinical practices and provide the best possible clinical evidence for embryo selection, patient selection, data reporting, and public communication to achieve eSET (Harbottle et al. 2015). The 10 percent multiple birth target for all age groups was first reached in 2018 (HFEA 2020).

For most other countries, where IVF is highly privatized and *not* integrated into the public healthcare system or covered by national health insurance, eSET needs subsidy programs if it is to be implemented. As mentioned earlier, aspiring parents pursue quick success to save money, so clinicians pursue high success rates, often with the tacit promise of multiple embryo transfer to attract clients. The competitive environment of the IVF business, combined with the emotional and financial burdens that IVF users face, therefore make transferring more embryos for a higher success rate sound rational.

This IVF market follows the "logics of capital" in anticipation (Adams, Murphy, and Clarke 2009: 260). IVF promises a new family with kid(s), as long as you invest money to start the treatment. What Charis Thompson (2005: 258) calls "promissory capital" in the IVF enterprise is raised with the expectation of "something that unfolds over time in the future." Presenting a high success rate is a major predictive guarantee that renders the investment less speculative. eSET threatens the promise if it decreases the success rate or requires more cycles to reach the same cumulative success rate as that of multiple embryo transfer (MET). It is worth noting that the expectation in IVF differs from other expectations in the promissory bioeconomy. For example, commercial umbilical cord blood banks also operate within the promissory economy, encouraging parents to store their newborns' cord blood for its stem cells, thus securing a "what if" in the future (Martin et al. 2008). Even if the investment is never put into use for regenerative therapy, parents may still feel thankful because this means their child is healthy. IVF is different. Not reaching the goal of having a baby means loss of expectation. Even if the failure could be attributed to the patients themselves being too old, too fragile, or coming to the clinics too late, never seeing a positive sign on the pregnancy test is still viewed as a bad investment.

To implement eSET, the new agenda is to provide public financing for privately paid IVF—in other words, to redistribute the cost, and hopefully reassemble IVF. In most countries IVF is paid for out of pocket, whether fully or partially. Whether IVF should receive

Table 2.1. Guidelines on Number of Embryos Transferred (NET) for Countries with and without Public Financing for In Vitro Fertilization (IVF). Sources: Keane et al. 2017; IFFS 2019. © Chia-Ling Wu

Countries		NET		Total	Guideline for Women < 35 Years Old				
		Yes	No		One embryo	Two embryos	Three embryos	Four embryos	Average (N)
Public Financing for IVF	Yes	27 (84%)	5 (16%)	32 (100%)	7	10	10	0	2.11 (27)
	No	16 (53%)	14 (47%)	30 (100%)	1	7	6	2	2.56 (16)
Total		43	19	62	8	17	16	2	43

public funds involves complicated debates, with the rationales ranging from equal access and reduction of health risk to pronatalism (Neumann 1997; Mladovsky and Sorenson 2010; Keane et al. 2017; Wu et al. 2020). Not all countries with public financing bind subsidies to SET, but almost all that do practice SET do so with public financial support. Table 2.1 shows that, among those countries with public financing, 84 percent have required limiting the number of embryos. And among them, seven countries ask for SET for women under thirty-five years old. In contrast, for those who do not provide any public financing for IVF, only one country—Colombia—requires SET for young women.

In the US, even when scientists proposed eSET to lower the risk of multiple pregnancy, "improved insurance coverage" was often mentioned as the broader context to support the clinical procedure (Davis 2004: 2442). But little has been done.[5] For example, in the ASRM guideline recommended in 2004, only women under thirty-five years old with embryos of cleavage stage were recommended for NET of one to two embryos. Studies show that such a guideline was far from an ideal eSET policy and that it did not reduce multiple birth (Stern et al. 2007).

Next, I present two cases to illustrate how redistributing the cost of IVF can work for practicing eSET: the well-known Belgian Project, and the less known JSOG Project. The two cases shed light on how anticipatory work needs to reassemble the money, but in diverse ways. Most studies of promissory capital or bioeconomy focus on how the market is built (e.g., Waldby and Mitchell 2006;

Petersen and Krisjansen 2015; Krolokke 2018). Here I present ways the twenty-year-old IVF market may be able to change.

The Belgian Project: Anticipating with Cost-Effective Rationing

On 1 July 2003, Belgium started to finance IVF with a strict limit on the number of embryos transferred (NET) during IVF. As table 2.2 shows, Belgium reimburses up to six IVF cycles in exchange for restriction of NET. For younger women to receive the reimbursement, the guideline requires that the first cycle be SET and the second be eSET. Bundling SET with financial support became a model solution for reducing multiple pregnancy. Willem Ombelet, the president of the Flemish Society of Obstetrics and Gynecology (VVOG) from 2001 until 2004, proudly called this "The Belgian Project." How did it start?

The reshaping of the financial allocation began in 2001. The Belgian government wanted to change the reimbursement of IVF and asked for the policy design. IVF in Belgium had been regulated by the state, first with a data-reporting system in 1993 and then with standard requirements and quality control of IVF hospitals and clinics. The state also appointed members of the College of Physicians in Reproductive Medicine to monitor ART. The state has been involved in all aspects of IVF regulation. Its reform to reduce multiple birth was carried out by the country's two major medical societies: the government-appointed Belgian College of Physicians in Reproductive Medicine and the Belgian Society for Reproductive Medicine.

The path toward "doing something" was also paved by academic research. To begin with, Belgian IVF specialists had actively experimented with eSET since the late 1990s (Coetsier and Dhont 1998; Gerris et al. 1999). Research teams from Ghent and Antwerp reported a series of studies showing that eSET could reach the same success rate as DET for young women. "It took a lot of clinical courage to launch the study altogether," the Antwerp team claimed, because it involved extending the use of eSET to women up to thirty-seven years old (ESHRE Campus Course Report 2001: 797). The Belgian doctors attempted to prove that as long as there were embryos of good quality to transfer, eSET could result in the same, or even better, pregnancy rate and live birth rate as DET. The myth that two embryos are a better guarantee than one was dismissed by these pioneers. These doctors also worked actively to transform their

TABLE 2.2. The Belgian Regulation on Number of Embryos Transferred (NET) in In Vitro Fertilization (IVF) in 2003. © Chia-Ling Wu

Age	Number of Embryos Transferred (NET)		
	Cycle 1	Cycle 2	Cycles 3–6
<36	1	1 or 2*	Maximum 2
36–39	Maximum 2	Maximum 2	Maximum 3
40–42	No restriction.		

*Two embryos are allowed if embryo quality is not sufficient.

scientific findings into clinical practices, asking colleagues to take eSET as "the ideal to which we should strive, taking into account the many objectives and subjective variables that give our work its human depth" (ESHRE Campus Course Report 2001: 799).

The anticipated outcomes included money saving. By the time the financial reform started, the Belgian National Health Care system already covered 50–70 percent of medication, clinic visits, and treatment monitoring. What was not covered included laboratory costs, for which couples needed to pay 1,000–1,250 euros. The proposal to the government bundled clinical practices with money: namely, reimbursement for up to six cycles of IVF and ICSI in exchange for a strict guideline on NET, with the goal of reducing twin pregnancies by 50 percent. The reimbursement did not cover women over forty-three years old, showing that the agenda was focused more on cost-effectiveness than on fairness.

The medical societies presented a simple "before and after" graph, highlighting the gain through the cost reduction (Ombelet et al. 2005: 10). The evidence-based policymaking mobilized both the experiment data (to show the efficacy of eSET) and the registry data (to calculate health outcomes and cost). The calculation was based on Belgium's registry of IVF since 1991 and the perinatal data on all births in Flanders since 1988. In terms of "short-term benefit," it shows that in 1997, with 28 percent of IVF births as twins and 5 percent as triplets, the care cost of the neonatal ICU was 11.875 million euros. With implementation of the new reimbursement and new guideline, it was estimated that by 2003 twin deliveries would decrease by half (to 14 percent) and triplets would be only 0.5 percent, so that the money needed for healthcare of premature

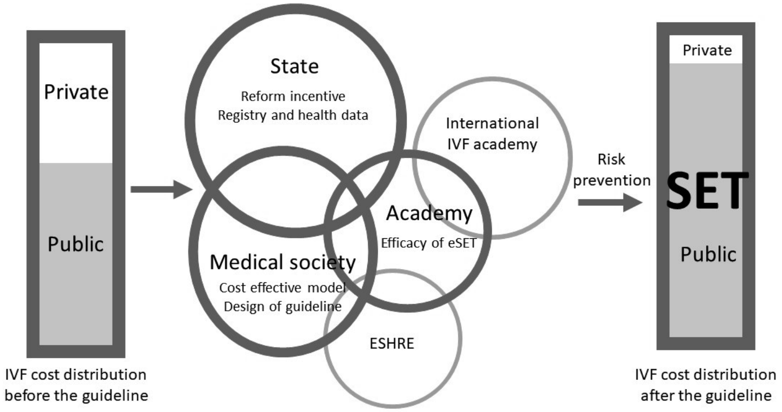


FIGURE 2.1. Anticipatory Governance of In Vitro Fertilization (IVF): The Belgian Project (SET = single embryo transfer; eSET = elective single-embryo transfer). © Chia-Ling Wu

babies would be 7.25 million euros—close to the amount needed to reimburse the cost of seven thousand IVF cycles. The public money spent on IVF would therefore be the same, but the need for neonatal care would be reduced significantly.

In terms of "long-term benefit," the money saved on the lifetime costs of caring for severely handicapped children due to multiple birth could be as much as 52.5–70 million Euros. Never before had the financial cost of the creation of lives (IVF) and the care of lives (neonatal care) been so simply and clearly presented. Taking reproduction as a continuous process (e.g., Almeling 2015), the redistribution of cost can lead to a win-win-win situation: the state budget might be decreased, the financial burden on the family could be relieved, and the health of mothers and babies would improve. To carry out the anticipatory work of implementing eSET, Belgium therefore employed an integrated triple helix of the state, the academy, and the medical society. The promissory capital was transferred into public funding, with scientific calculation to optimize the outcomes in terms of healthcare cost. Figure 2.1 shows my conceptualization of the Belgian model.

The effect of the new regulation was immediate and obvious—namely, a "sharp decrease in multiple pregnancy rate" (Van Landuyt et al. 2006). In just fifteen months, the multiple pregnancy rate for women less than thirty-six years old decreased from 28.9 percent to

6.2 percent. And for all the patients, the rate decreased from 29.1 percent to 9.5 percent. The practices of SET became the model practices, from around 15 percent in early 2000 to around 50 percent since 2004 (De Neubourg et al. 2013). All the research shows that the overall pregnancy rate did not change much (Gordts et al. 2005; Van Landuyt et al. 2006; De Neubourg et al. 2013). For the cost, a study analyzing hospital bills showed that after three years of the SET guideline, the multiple birth rate had decreased by half and the health cost was reduced by 13 percent (Peeraer et al. 2017).

This model is a distinguished way to reduce the health risk of multiple birth by reallocating public money. In retrospect, the Belgian leader of IVF gave the credit to the reimbursement program:

> Although Belgian infertility specialists were aware of the twin epidemic and knew about the possible advantages of single embryo transfer (SET) many years before the reimbursement policy was launched in 2003, a significant drop of twins could only be observed from 2004 on, which means that *only a financial incentive made the difference*. (Ombelet 2016: 190, emphasis added)

While noting the importance of financial support as the crucial aspect, the Belgian expert singled out Japan as an exception:

> One of the exceptions is Japan. In this country ART practices seem to be regulated by *the rules and moral policy* of a society without any stringent regulation. It is surprising that Japan obtained 86 percent of SET in 2012, compared with 59.6 percent in Belgium. (Ibid., emphasis added)

What rules? What moral policy? Compared with the "Belgian Project," the "Japanese Project" is seldom presented in the English literature. Since the primary agent to promote SET in Japan is the Japan Society of Obstetrics and Gynecology (JSOG), I will call it the JSOG Project here. The JSOG Project utilizes a different re-networking model, in which the three elements of registry-finance-guideline were reorganized to pave the road to SET in Japan.

The JSOG Project: Anticipating with Avoidance of Controversy

Japan announced its SET guideline in April 2008, the strictest in East Asia. Unlike Sweden and Belgium, where the local and national governments issued the regulation, it was the medical society, the

JSOG, that recommended the new practice. The JSOG's guideline states that single embryo transfer (SET) is the primary principle. Double embryo transfer (DET) can be considered only for women thirty-five years or older for whom the first two SET cycles fail (table 2.3). The voluntary guideline in Japan is stricter than the legal regulation in Belgium, where there is no limitation on NET for older women. As shown below, with its guideline Japan has one of the highest SET rates and one of the lowest multiple birth rates for its IVF practices.

The case of Japan illustrates another social context of the anticipatory work to implement eSET. In what follows, I argue that the SET guideline is shaped by each country's sociopolitical context and by the national "sociotechnical imaginary," which Jasanoff and Kim (2009: 120) define as "collectively imagined forms of social life and social order reflected in the design and fulfillment of nation-specific scientific and/or technological projects." In other words, the eSET network building in Japan (aka the JSOG Project) needs to be understood through two waves of controversy: the social concerns over IVF in Japan in the early years, and the interprofessional conflict between Japanese IVF doctors and neonatologists.

Social Concerns over IVF

Beginning in the late 1970s, worries about IVF triggered the Japanese medical community to actively govern the newly developed technology (Wu, Ha, and Tsuge, 2020). During the early period, several surveys of patients seeking fertility treatment showed that fear of having a child with a malformation was one of the common reasons for refusing to undergo IVF (Iwaki et al. 1979; Iwaki, Tachibana, and Ogura 1983; Suzuki 1983). Some Japanese ob-gyns expressed feeling in the early years that IVF "is not natural" (Tsuge 1999). Some leading doctors and governmental officials voiced strong anxiety about the possibility of producing a "deformed child" (*kikei-ji*) through IVF, or about the high level of compensation that could be involved if this occurred, while noting medical professionals' responsibility for the health of babies (Yamaguchi et al. 2005; Mori 2010). Although similar worries surfaced elsewhere, in Japan they remained loud and strong. The discourse of doubt around Japan's IVF development was related to other highly publicized controversies on topics of technology and health, such as Minamata disease (linked to environmental pollution) and Wada heart transplants (leading to debates on brain death). The technological optimism that had accompanied Japan's economic miracle faced new challenges

Table 2.3. The JSOG Opinion on Number of Embryos Transferred (NET) in In Vitro Fertilization (IVF) in 2008. © Chia-Ling Wu

Age	Number of Embryos Transferred (NET)		
	Cycle 1	Cycle 2	Cycles 3–
<35	1 as the principle		
≥35	1	1	Maximum 2

in dealing with these widely reported controversies, lawsuits, and requests for high-fee compensation.

To reduce the worries about the new technology, not only from the public but also from their medical colleagues, three university-based IVF teams adopted the strategy of self-regulation along with their experimental practice (Suzuki 2014; Tanaka 2015; Yui 2016). This included establishing a new nationwide medical society on ART and setting up ethics committees at the university level to codify ethical guidelines. These decentralized ethical institutions helped individual medical teams demonstrate their capacity for self-regulation in order to gain social trust.

Moving from self-monitoring of individual medical teams to national health surveillance, the various ethical measures were eventually combined at the old JSOG, which had existed since 1949. In the early 1980s, with leaders from the three major universities holding important positions in the society, the JSOG announced its guidelines on IVF, started the clinic registration system, and initiated Japan's voluntary registry. The JSOG has maintained its autonomy of ART governance ever since, with only some governmental interference through ART subsidy programs after the mid-2000s (Tsuge 2016). Without a national law to regulate ART in Japan, the governance of IVF largely remains under the JSOG's jurisdiction.

Risk prevention to avoid controversy has been a major agenda item. For example, in the early reports of registry data, "risk" was the main theme. The reports emphasized the high miscarriage rate, high multiple pregnancy rate, and the possibilities of abnormalities in the newborns, and presented these as important factors in the evaluation of ART. The reports also made comparisons with "normal reproduction," where the miscarriage rate and multiple pregnancy rate are much lower. Although not using the exact term "taking a healthy baby home," the very first report strongly emphasized the same goal and tied it to the very action of collecting data:

> The higher incidence of miscarriage and *multiple pregnancy* for ART than for natural conception means there is risk for both mothers and babies. We need to deal with the problems of the high-risk pregnancy …, the abnormal newborns, and the follow-up of children's health. The main goal of this technology is not pregnancy only, but the birth of a healthy baby. For this purpose, we need to collect better and richer data in the future. (JSOG Science Committee 1990: 397; emphasis added)

"Better and richer data" meant following up on the health of infants. The abnormal cases soon became a routine list in the annual report. The JSOG advocated improving data quality so as to better evaluate the prevalence and causes of risks and thereby ensure the care quality of IVF.

The controversy over fetal reduction strengthened the concerns about ART. Fetal reduction was first practiced in Japan in 1986 to deal with the problem of a quadruplet pregnancy caused by ovary-stimulating drugs. Dr. Yahiro Netsu performed the fetal reduction to reduce the four fetuses to two, leading to the birth of healthy twins (Netsu 1998). The experiment came from a painful lesson he had learned. In 1982, a woman pregnant with quadruplets due to the egg stimulation drug came to him for advice. Multiple pregnancy due to the infertility treatment had increased in Japan since the 1970s, and the media often reported on it with curiosity and joy. At that time, people had no choice but to abort all the fetuses if they wanted to avoid multiple pregnancy. The woman decided not to do this, and started a tough journey. With intensive prenatal care, she gave birth to three healthy babies and a fourth baby with cerebral palsy (CP). When Dr. Netsu later encountered a similar case, he decided to experiment with fetal reduction surgery, which resulted in a successful story.

However, the event led to a series of attacks from the Japan Association of Obstetrics and Gynecology for Maternal Protection (JAOGMP), which was in charge of abortion practices among doctors. Abortion had been legalized in 1948, but fetal reduction raised questions about what does and does not constitute "ethical boundary-work" (Wainwright et al. 2006). The JAOGMP and other opponents mobilized some contents of the law to claim that Dr. Netsu might have violated the abortion regulation. Although the case was eventually settled, media zeal made it a public issue or, as it was often phrased, "a scandal."

The JSOG started conducting a series of surveys to better understand the practices of fetal reduction. The earliest survey was done by Dr. Takumi Yanaihara (1998), who worked for the ethics committee of the JSOG and criticized Dr. Netsu's practice seriously. The survey found that, of the 197 institutions for infertility treatment, 15 practiced fetal reduction, which had resulted in 87 cases in 1996. For cases of women pregnant with three or more fetuses, 30.3 percent adopted fetal reduction to reduce the fetuses to two or one. Among the 69.5 percent who continued the multiple pregnancy, 10.9 percent had health problems. The need to prevent the incidence of multiple pregnancy became more urgent.

In 1996, the JSOG announced the first code of ethics to prevent multiple pregnancy. It instructed its members in the careful use of ovary-stimulating drugs and limited the number of embryos transferred to three or fewer—the first such restriction in East Asia. The 1996 guideline reduced the incidence of quadruplets and triplets, but the registry data show that the prevalence of twins remained high. The registry data helped identify ovary-stimulating drugs as the cause of half of the higher-order pregnancies, followed by multiple embryo transfer (MET) (Irahara 2002). In addition, JSOG leaders surveyed international trends and recognized that limiting MET further would be the more effective measure to reduce multiple pregnancy (Irahara and Kuwahara 2003).

It is worth noting that Japan's feminists became an important pressure group to monitor IVF. The Japanese branch of the international feminist organization FINRRAGE was established in Tokyo in 1991. It started from a small reading group of feminist literature on ARTs, and expanded to thousands of members in its heyday in the late 1990s. This became an important source of critical voices representing women's experiences. In 2000, the group published *New Report on Infertility: The Survey of Real Experiences of Infertility Treatment and Reproductive Technologies* to voice the women's worries about the health risk, safety, and financial burden of seeking ARTs (FINRRAGE no kai 2000). In addition, feminist scholars such as Azumi Tsuge (1999) have published research to challenge the medical model of treating infertility since the 1990s. The JSOG and related medical societies sometimes invited FINRRAGE leaders and feminist scholars to their forums to incorporate diverse voices when discussing ethical issues, enhancing their capacity to be engaged with public debates.

However, the direct impetus to make the JSOG take further action came from other medical professionals.

Interprofessional Conflict

Almost all the Japanese doctors I interviewed agreed that it was pressure from pediatricians/neonatologists that made ob-gyns change their ART practices. One of the JSOG leaders vividly described how neonatologists urged the organization to take action:

> [Around 2002 to 2004] we met very strong criticisms from the neonatologists, many times and at many conferences, because at that time Japan's health care system did not have enough personnel in the neonatal intensive care to handle the situation. … They asked us to make a big change to reduce the pre-term labor and low birthweight, or they could not continue the neonatal intensive care unit. … As representatives of JSOG, we were invited to attend the symposium held by the society of prenatal care. They always accused us. *But it was not my fault. We were just collecting data. That is the direct reason we established the cycle-based data of the registry.* Because we did not know enough about the reasons causing the high rate of multiple pregnancy. (Dr. J-K interview, Taipei, April 2018, emphasis added)

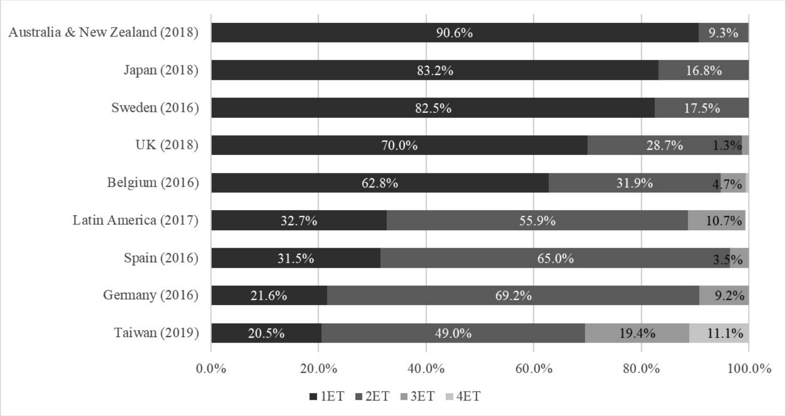
The JSOG's registry data, which did not include information such as the percentage of low-birthweight IVF babies, were not adequate to reveal these problems. The government did not associate the data on neonatal outcomes with the development of IVF. Therefore, the neonatologists' face-to-face pressure and strong emotion were required to convince JSOG leaders to take further measures to reduce the health risks to newborns.

The interprofessional conflict between those who transfer embryos to make women pregnant and those who care for fragile premature babies is not about the jurisdiction of medical expertise or professional autonomy (Abbott 1988) but about the unacceptable burden created by the division of labor. The 2001 ESHRE report points out why multiple pregnancy was less recognized by IVF experts: "Infertility specialists are frequently not involved in obstetric care and hence have no direct feedback from the obstetric outcome of their treatment successes" (ESHRE Campus Course Report 2001: 791). When neonatal care units face personnel shortages, such as occurred in Japan, confrontation may arise.

These JSOG leaders worked on both the registry and the ethics committees, which helped them translate the neonatologists' anger into new codes of practice. The first step was to change the registry system from site-based to cycle-based in order to provide evidence with which to evaluate IVF practices.[6] The second step was to build a new guideline. In 2008, after discussion and evaluation, the JSOG announced its recommendation of single embryo transfer (SET) for women under thirty-five years old to solve the problem of multiple pregnancy. By that time, Sweden and Belgium had built the SET guideline, and Japan became the first in Asia to follow. The acceptance of the SET guideline in Japan involved many factors, including improvements in the technical process of embryo selection, the refinement of data reporting for policy evaluation, and the partial subsidy program initiated in Japan in 2004 to boost the low fertility rate.

Unlike Sweden, Japan did not make IVF part of the public healthcare system. When the first test-tube baby was born in 1982 in Japan, comprehensive health insurance had already been established, but the Japanese government did not include IVF due to its low success rate (Semba 2005). Unlike Belgium, Japan did not initiate a subsidy program aiming to reduce health risk. The financial subsidy of IVF was initiated by the Japanese government as a pronatalist policy. In 2002, when the total fertility rate reached the record low of 1.3, some local governments began to offer a subsidy program to promote a higher birth rate. The national policy started in 2004 for couples under a certain economic threshold, and only 15 percent of IVF cycles received a subsidy. The subsidy was later extended, partially due to strong lobbying from the Fertility Information Network (FINE), an NGO aiming to relieve the financial burden for infertile couples to receive medical treatment.[7] By 2016, a new age limit—up to forty-three years old—was established, and resources were increased to cover 32 percent of cycles for about 39 percent of the cost (Maeda 2019).

Thus it was the JSOG, not the government, that set up the SET guideline. In doing so, JSOG leaders utilized the opportunity created by the government subsidy program to increase the birth rate in ways that support SET. With strong agreement among JSOG members, the SET guideline has reached almost full compliance. Data show that the use of SET increased rapidly after the JSOG's 2008 guideline, from 46.5 percent in 2007 to 82.2 percent in 2018—close to the rates in Sweden, Australia, and New Zealand, and much higher than those in Belgium and the UK, not to mention in those countries without a strict SET policy, such as Taiwan (graph 2.1). And in Japan, all the perinatal health risks, such as stillbirth, cesarean section, preterm birth, and low birthweight, decreased significantly (Takeshima et



Graph 2.1. Number of Embryos Transferred (NET) by Selected Countries. (1ET = one embryo transferred; 2ET = two embryos transferred; etc.) Sources: HFEA 2019; JSOG Science Committee 2020; Newman, Paul, and Chambers 2020; ROC Ministry of Health and Welfare 2020; Wyns et al. 2020; and Zegers-Hochschild et al. 2020. © Chia-Ling Wu and Wei-Hong Chen

al. 2016). Osamu Ishihara—the key person who promoted upgrading the registry in the JSOG and a devoted representative in the International Committee for Monitoring ART (ICMART)—has successfully used Japan's high-quality data to present Japan's approach in international comparative studies (e.g., Chambers et al. 2014). Japan has been singled out in ICMART reports as a successful case of practicing SET (e.g., Adamson et al. 2018).

Unlike the integrated triple helix of the state, academy, and medical society in Belgium, the JSOG was the reform engine that did the main anticipatory work to implement eSET in Japan. Although the Japanese government's subsidy program was intended to boost the birth rate, the JSOG recognized it as a timely tool for reducing the financial burden of practicing SET for practitioners and patients alike. The JSOG allied with the international IVF academy to provide research findings on eSET, and with international IVF societies such as the ICMART for guidance on reducing risk through data reporting. The JSOG Project also shows that redistributing cost was only part of the momentum driving SET as a routine practice (figure 2.2). I argue that it was the waves of controversy—from (a) the early social concerns about IVF to (b) the intraprofessional disputes among IVF pioneers about fetal reduction to (c) the interprofessional conflict between IVF doctors and neonatologists about neonatal care—that

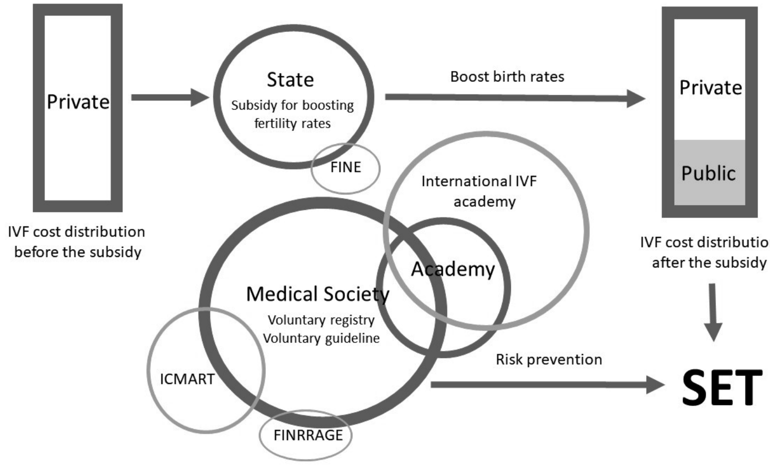


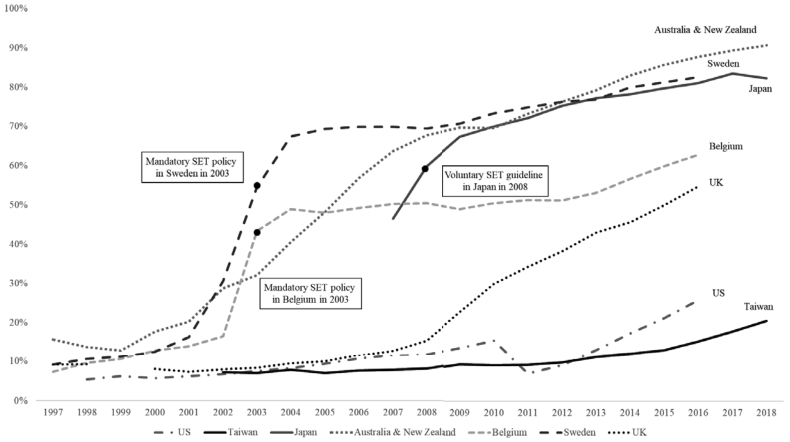
FIGURE 2.2. The Japanese Society of Obstetrics and Gynecology (JSOG) Project. (FINE = Fertility Information Network; FINRRAGE = Feminist International Network for Resistance to Reproductive and Genetic Engineering; ICMART = International Committee for Monitoring Assisted Reproductive Technologies; IVF = in vitro fertilization; SET = single embryo transfer.) © Chia-Ling Wu

step-by-step intensified the ethical responsibility of JSOG leaders and members to act on preventing the risk posed by multiple birth.

Conclusion: Building an eSET Network

This chapter has analyzed the intensive anticipatory work required for the routine practice of eSET to reduce multiple pregnancy/birth in IVF. The "hope work" involved centers on redefining success. The international IVF community has promoted the use of the live birth rate, and the singleton full-term live birth rate, to present the value of "taking a healthy baby home." The abduction needed to test the efficacy of eSET involves much biomedical innovation, from calculating cumulative success rates to improving embryo selection accuracy, thus building the foundation for eSET practice. SET has started to work as a simple and straightforward guideline in some countries. Hope work, abduction, and simplification altogether make eSET desirable and feasible.

Anticipatory work enacts eSET only in some countries. Graph 2.2 shows that Sweden, Belgium, and Japan all had a sharp rise



Graph 2.2. Percentage of Single Embryo Transfer (SET) in All In Vitro Fertilization (IVF) Cycles for Selected Countries. Sources: *Australia and New Zealand*: Lancaster et al. 1995, 1997; Hurst et al. 1997, 1999, 2001a, 2001b; Dean and Sullivan 2003; Bryant, Sullivan, and Dean 2004; Waters, Dean, and Sullivan 2006; Wang et al. 2006, 2007, 2008, 2009, 2010, 2011; Macaldowie et al. 2012, 2013, 2014, 2015; Harris et al. 2016; Fitzgerald et al. 2017, 2018; Newman et al. 2019, 2020; *Belgium, Sweden, and UK*: Nygren, Nyboe Andersen, and EIM 2001, 2002; Nyboe Andersen et al. 2004, 2005, 2006, 2007, 2008, 2009; Mouzon et al. 2010, 2012; Ferraretti et al. 2012, 2013; Kupka et al. 2014; EIM for ESHRE et al. 2016a, 2016b, 2017, 2018, 2020a, 2020b; *Japan*: Saito et al. 2017; Ishihara et al. 2018, 2019, 2021; *US*: CDC, ASRM, SART, and RESOLVE 2000–2002; CDC, ASRM, and SART 2003–18; and *Taiwan*: ROC Ministry of Health and Welfare 2021a. © Chia-Ling Wu and Wei-Hong Chen

in practicing SET in the years they issued their SET guidelines. The contrast is seen in the low percentages of SET practiced in the US and Taiwan, where there is no strong recommendation on, or regulation of, SET. SET policies work in different ways. Most countries that establish a SET guideline combine the guideline with public financing, as in the Belgian Project. The international IVF community has repeatedly contended that reorganizing promissory capital is essential for the routine use of SET (Pandian et al. 2005; Davis 2004). However, Japan stands out as a different case, in which sociotechnical imaginaries of IVF have been infused with concerns and conflicts. This shaped the framing of anticipatory work in Japan primarily in terms of risk prevention. The result is that, with reflexive leaders of Japan's medical society to articulate the diverse anticipatory work needed, SET has become routine in Japan even without much public financing from the government.

Comparative analysis of the Belgian Project and the JSOG Project demonstrates the different national formations of eSET. The new invention of calculating success, the evidence shown in Cochrane reviews (Pandian et al. 2005; Glujovsky et al. 2016), and the recommendations by the ICMART and the IFFS are important resources and are shared globally. Yet, locally, it is the state (Sweden), dual cooperation of the state and medical societies (Belgium), or the medical society (Japan), depending on the IVF governance, that designs the different programs for implementing eSET. The anticipated crisis of IVF—the increasing adverse outcomes due to multiple pregnancy/birth—has prompted a variety of responses. I have shown, via the actions of the JSOG Project, that the sociotechnical imaginaries of IVF guide the direction of anticipation. In the case of Japan, avoidance of controversy led to adoption of eSET. In chapter 3, I present the different sociotechnical imaginaries of IVF in Taiwan, which direct an anticipatory regime that still welcomes multiples today.

Notes

1. The Reproductive Technology Accreditation Committee of Australia published a guideline in 2017, titled "Public Information, Communication and Advertising: Australian Clinics," on how to present success rates on websites and social media. Even though the guideline recommends that clinics report "per cycle started" as the denominator of success rates, none of the thirty surveyed clinics did so (Goodman et al. 2020).
2. For example, ten eggs may be retrieved from a single procedure, resulting in eight embryos for future use. The doctor would choose a "best" fresh embryo to transfer. If it does not lead to pregnancy, then the available frozen embryo is used for the next transfer. As long as the woman reaches pregnancy and live birth with one of these first two transfers, or within transfers of her eight other embryos, the process counts as a success. In other words, if the woman becomes pregnant from the third attempt at implantation, this counts as success (1/1), whereas in the old calculation, the first two cycles would be counted as failures (1/3). In addition, for those clinics promoting natural-cycle IVF, cumulative success rates are preferred in presenting the results. For example, the famous Kato clinic in Japan shows that the cumulative live birth rate for women thirty-five to thirty-seven years old is 51 percent by the completion of four cycles, compared to 17 percent after the first cycle (Bodri et al. 2014).

3. Take the assessment of embryos as an example. The so-called grading system of embryos has transformed greatly but does not always reach consensus. Much research explores how to grade and score embryos (see the review of Van Blerkom 2009; Harbottle et al. 2015). Traditional scoring relies on morphological assessment, including the development and appearance of embryos. However, there have been no national or international efforts to reach a consensus, so "numerous grading schemes evolved which varied in both complexity and efficacy" (Bolton et al. 2015: 157). The blastocyst stage of embryo development, five or six days after the insemination of sperm into eggs in the lab, once met the standard for high-quality embryos in the guideline of the ASRM (Practice Committee of ASRM and Practice Committee of SART 2013) but also raised new concerns because couples could lose all the embryos for use (Harbottle et al. 2015). A Cochrane review of twenty-eight randomized control trials showed no difference in cumulative pregnancy rates between blastocyst transfer groups and cleavage-stage (days 2–3) transfer groups (Glujovsky et al. 2016).
4. For the UK debates on implementing eSET, see "The UK Human Fertilisation and Embryology Authority's 'One at a Time' Campaign," Centre for Public Impact, 7 January 2019, retrieved 17 February 2021 from https://www.centreforpublicimpact.org/case-study/uk-human-fertilisation-embryology-authoritys-one-time-campaign.
5. Historically, IVF has not been on the healthcare priority list in the US. For example, in the famous 1991 Oregon priority-setting list, IVF was listed as number 701 out of 714 conditions (Dixon and Welch 1991). Low birthweight (defined as 750–999 grams in this program) was ranked 123 out of 714, in the top 20 percent, whereas extremely low birthweight (< 500 grams) was ranked 713, the lowest in the priority ranking. This implies that the general public is willing to spend public resources on neonatal care, but not on improving IVF so that it no longer increases the need for neonatal care. When the Clinton administration in the US proposed the Health Security Act in 1993, IVF was among the medical packages that were explicitly excluded from the standard coverage list (Neumann 1997). Groups of infertile couples were the major force lobbying for coverage of infertility treatment in the US, but reducing health risk was not the major concern (King and Meyer 1997).
6. The early data came from the clinics' report of their annual aggregate data: the total number of cycles; distribution of NET; total cases of miscarriage, live birth, and stillbirth; and so on. This type of data cannot reveal how NET is associated with twin and triplet births. The cycle-based reporting system, in contrast, requires that clinics report every single case to a new online reporting system. This yields data for evaluation of clinical practices. In addition, the new registry data add the new items: the neonatal health outcomes. Every cycle needs to

report the newborn's sex, length of term, birthweight, and abnormal outcomes, and it must also follow the situation to twenty-eight days after the birth. Some IVF clinics told us that the new registry system requires one or several full-time staff to make the records and do the follow-up work.

7. The feminist group FINRRAGE in Japan collected infertile women's opinions and found that financial burden was the major obstacle infertile couples faced during treatment. However, the major action of FINRRAGE in Japan was to challenge unnecessary treatment rather than ask for a public financing program.