Why are multiple pregnancy rates and single embryo transfer rates so different globally, and what do we do about it?

G. David Adamson, M.D.[a] and Robert J. Norman, M.D.[b]

[a] Equal3 Fertility, Cupertino, California; and [b] Robinson Research Institute, University of Adelaide, Adelaide, Australia

In the early years of in vitro fertilization, overall pregnancy rates were low, and it was considered necessary to transfer more than one embryo to increase the chances of pregnancy. It was not until advances in assisted reproductive technologies resulting in increased pregnancy rates that the concept of transferring just one embryo was considered possible. A consequence of improvements in implantation rates was also an increase in multiple pregnancies when more than one embryo was transferred. Although some countries have reduced the number of embryos transferred, international data show that in many parts of the world high twin and higher order multiple pregnancy rates still exist. Even in developed countries these problems persist depending on clinical practice, funding of health services, and patient demands. Perinatal and other outcomes are significantly worse with twins compared with singleton pregnancies and there is an urgent need to reduce multiple pregnancy rates to at least 10%. This has been achieved in several countries and clinics by introducing single embryo transfer but there are many barriers to the introduction of this technique in most clinics worldwide. We discuss the background to the high multiple rate in assisted reproduction and the factors that contribute to its persistence even in excellent clinics and in high-quality health services. Practices that may promote single embryo transfer are discussed. (Fertil Steril® 2020;114:680–9. ©2020 by American Society for Reproductive Medicine.)

Key Words: Multiple pregnancy, twins, single embryo transfer, IVF, assisted reproduction

Discuss: You can discuss this article with its authors and other readers at https://www.fertstertdialog.com/posts/31344

The birth of Louise Brown in 1978 resulted after 102 failed embryo transfers–a live birth rate (LBR) per cycle start of <1% (1). Since then, in vitro fertilization (IVF) has come a long way with LBRs globally in 2015 of 19.2% per oocyte retrieval with fresh embryo transfer and 24.8% with frozen embryo transfer (FET) (2). In 2017 the cumulative LBR per intended oocyte retrieval following all embryo transfers for women younger than age 35 in the United States was 54.7% (3). This increased pregnancy rate resulted from many scientific, technological, and clinical advancements in assisted reproductive technology (ART) practice (4). However, the increased implantation rate associated with this significant progress resulted in an epidemic of multiple births associated with IVF, which in turn has led to poorer outcomes for mothers, babies, and society and challenged the dictum *primum non nocere* (5–7).

In vitro fertilization practitioners should be compelled to ask the following questions: "Why do higher multiple rates occur with ART?", "Why is there so much variability globally?", and "What can we do about it?" Because all progress starts by examining the facts and telling the truth, it is constructive to review the global data on multiple birth and single embryo transfer (SET) rates to understand the available data with respect to multiple birth rates and SET and how we can learn from each other (8). Importantly, data collected in registries globally do not allow for differentiation between elective SET (eSET) and obligatory SET so in this article SET refers to both (9, 10). We will address these questions by doing the following: reviewing the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) global data on ART since the year 2000, and specifically multiple births; assessing changes in twin rates over time; identifying reasons for the wide variability in different countries and regions; noting reasons for increased ART twin birth rates compared with natural occurrence; evaluating the role of SET; considering how the optimal twin rate should be determined and who should decide; and recommending actions that can be taken now to reduce multiple rates in ART (11–20).

Received September 2, 2020; accepted September 2, 2020.
G.D.A. is CEO of ARC Fertility and Consultant for Abbott and LabCorp. R.J.N. has nothing to disclose.
Reprint requests: G. David Adamson, M.D., Equal3 Fertility, 20195 Stevens Creek Boulevard, Suite 100, Cupertino, California, USA 95014 (E-mail: gdadamson@arcfertility.com).

Fertility and Sterility® Vol. 114, No. 4, October 2020 0015-0282/$36.00

https://doi.org/10.1016/j.fertnstert.2020.09.003

To simplify discussion, the focus will be primarily on twin multiple births because they are much more common and because triplet and higher order multiple rates will decrease if the twin rate decreases. This is not intended in any way to understate the greatly increased morbidity and mortality associated with higher order multiple pregnancy for both mothers and babies.

ART, MULTIPLE PREGNANCY, AND POORER OUTCOMES

Indisputable data confirm increased maternal, neonatal, and childhood morbidity and mortality in ART pregnancies, both singleton and multiple (21, 22). This results in poorer clinical outcomes, more immediate cost to society and individuals, and increased lifetime costs and emotional distress for families and society. The issue of poorer outcomes after ART is complex because there are many confounding variables, including the following: population characteristics of those undergoing ART; impact of ART ovarian stimulation and clinical protocols; and influence of laboratory procedures manipulating gametes, embryo culture, and cryopreservation. However, the most important reason for poorer outcomes is the increased rate of multiple pregnancy with ART compared with non-ART pregnancies and that is the issue that will be addressed in this article.

Natural and ART twin pregnancies have differences in outcomes also, although ART pregnancies are not always worse (23, 24). However, both have significantly poorer outcomes as multiples than singleton non-ART and ART pregnancies. Therefore, we maintain that lowering ART twin rates would benefit patients, professionals, and society.

GLOBAL MULTIPLE BIRTH AND SET RATES

The major factor determining multiple pregnancy rate (MPR) in ART is the lack of eSET, defined as the transfer of one (a single) embryo selected from a larger cohort of available embryos (25). The clinical decision to perform eSET can be complex (26). The ICMART has published reports in peer-reviewed journals since 2000 (11–20). The last published reports were for 2011 and 2012. Manuscripts accepted for publication and in preparation for 2013 and 2014 and data collected by ICMART for 2015 and 2016 have similar findings (9). There are wide variations in outcomes across the participating countries as reported to ICMART. The most important observations are the wide variation in LBRs per oocyte retrieval, twin delivery rate per delivery, SET rate per embryo transfer, and overall average number of embryos transferred (Table 1). With fresh embryo transfer, the delivery rate per oocyte retrieval was almost three times as high in the highest region compared with the lowest, the twin delivery rate almost four times higher, the SET rate over six times higher, and the average number of embryos transferred more than twice as high. For countries the differences were even greater. With FET the range of differences for similar metrics was also startling and similar in pattern to fresh embryo transfer (Table 2). However, although the delivery rate was 7% higher with FET compared with fresh transfers, the twin delivery rate was only 57% that of fresh transfers, the SET rate 64% higher, and the average number of embryos transferred was 17% lower. More recent data from the first registry report from China for 2016 showed a twin rate with IVF, intracytoplasmic sperm injection (ICSI), and FET of 27.9%, 27.2%, and 24.2%, respectively (27). For Latin America in 2017 the IVF/ICSI twin rate was 17.3% with a SET rate of 26.9%, and for FET the twin rate was 16.1% and the SET rate 38.1% (28). The highest twin rate from fresh nondonor IVF and ICSI with at least 100 embryo transfers was Taiwan at 35.4% and the lowest was Japan at 4.2%. For frozen nondonor with at least 100 embryo transfer cycles the highest twin rate was in Romania at 26.7% and the lowest was in Japan at 4.2%.

A retrospective analysis of the accumulated ICMART world ART registry between 2003 and 2014 was presented using ICMART data at the virtual European Society of Human

TABLE 1

Global delivery, twin and single embryo transfer rates, and number of embryos transferred for fresh nondonor in vitro fertilization and intracytoplasmic sperm injection cycles.

Fresh nondonor IVF and ICSI cycles	Delivery rate/retrieval	Twin deliveries/delivery	SET/embryo transfer	Average no. embryos transferred, n
Global average	20.0	19.6	31.4	1.91
Region				
Asia	11.1	16.7	49.7	1.78
Australia/New Zealand	19.8	6.9	68.4	1.33
Europe	20.6	18.5	27.5	1.90
Latin America	23.1	21.1	13.9	2.22
Middle East	27.8	25.3	10.6	2.59
Middle East (Israel)	15.9	NA	NA	NA
North America	32.3	26.7	18.9	2.21
Sub-Saharan Africa	22.7	23.1	13.9	2.83
Country				
Highest[a]	59.4	35.4	74.8	3.15
Lowest[a]	7.9	4.2	6.1	1.25

Note: Data is presented as percent, unless stated otherwise. Adapted from Adamson et al. ICMART World Report 2011 (19). ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; NA = not available; SET = single embryo transfer.
[a] Only countries with >100 cycles included.

Adamson. Addressing multiple pregnancy in assisted reproduction. Fertil Steril 2020.

TABLE 2

Global delivery, twin and single embryo transfer rates, and number of embryos transferred for frozen embryo nondonor post-in vitro fertilization and intracytoplasmic sperm injection cycles.

FET nondonor cycles	Delivery rate/embryo transfer	Twin deliveries/delivery	SET/embryo transfer	Average no. embryos transferred, n
Global average	21.4	11.1	51.6	1.59
Region				
Asia	24.0	5.0	69.8	1.39
Australia/New Zealand	20.9	6.6	80.0	1.20
Europe	15.9	12.7	37.9	1.72
Latin America	23.6	17.8	14.8	2.18
Middle East	14.5	18.5	10.9	2.59
Middle East (Israel)	NA	NA	NA	NA
North America	32.9	21.1	32.5	1.86
Sub-Saharan Africa	16.4	15.4	25.0	2.25
Country				
Highest[a]	35.2	26.7	89.0	2.74
Lowest[a]	5.6	4.2	5.4	1.11

Note: Data is presented as percent, unless stated otherwise. Adapted from Adamson et al., ICMART World Report 2011 (19). ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; NA = not available; SET = single embryo transfer.
[a] Only countries with >100 cycles included.

Adamson. Addressing multiple pregnancy in assisted reproduction. Fertil Steril 2020.

Reproduction and Embryology (ESHRE) meeting in 2020 (29). From 2003 to 2014 the global MPR after fresh embryo transfer decreased from 26.8% to 16.7% and with FET from 17.8% to 10.3%. The global SET rate increased with fresh embryo transfer from 14.7% to 40.0% and for FET from 23.4% to 61.6%. These data, and ICMART data in the annual publications, demonstrate the strong correlation between MPR and SET (30) (Figure 1). However, the data also show wide variations with some countries performing well at the beginning and throughout the time interval, others improving significantly, and some having high MPRs that did not change much during the period studied (30) (Figure 1). Of note, global LBRs have remained stable over this interval in many countries but also have decreased in some countries that have moved to a large majority of SET cycles (11–20). The ICMART reports LBR per fresh nondonor IVF and ICSI cycle with an egg retrieval only for cycles in which an embryo transfer is performed. Cycles in which all embryos are frozen are not included in the calculation, so the reduction in global LBR per egg retrieval is likely a real trend. However, it must be noted that this likely is due to transfer of fewer fresh embryos, which, of course, means more embryos are available for subsequent FET. Therefore, the small decrease in LBRs from fresh transfers does not mean that the cumulative LBR is decreasing. Indeed, although more recent data are needed to analyze current trends, it is likely that cumulative LBRs are steady or increasing while twin delivery rates are decreasing.

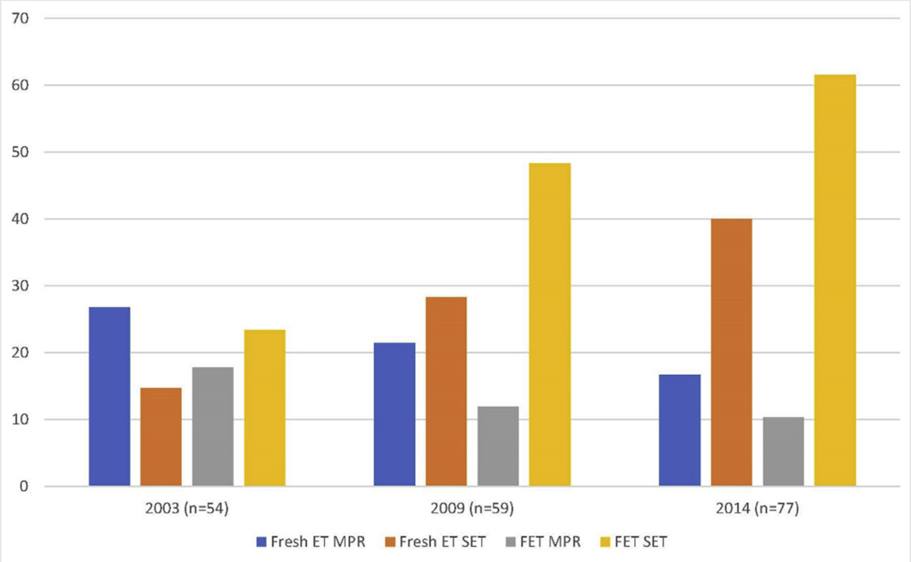
CAUSES OF HIGHER MPRs WITH ART?

Multiple birth following ART is primarily the result of transfer of more than one embryo, emphasizing the ideal of moving to a SET every time regardless of embryo quality and maternal age (31). However, numerous factors affect the decision regarding the use of eSET and why this ideal is far from being achieved.

Female age is the most important demographic factor determining the number of embryos transferred because of the rapidly reducing pregnancy rates with oocytes from older women (32, 33). There is also the time pressure on older women to have their family and multiples are often initially welcomed as a way to complete rapidly a family in the shortest time. A longer duration of infertility and previous unsuccessful cycles increase the number of embryos transferred because of patient and physician pressure to obtain success with rates decreasing with increasing duration of infertility (32, 34). Patients and physicians face different kinds of pressures too regarding number of embryos to transfer and these pressures are not always aligned in the same direction (26).

The number and quality of embryos available for transfer is the most important biological factor determining the number of embryos transferred. The perceived quality of the embryo(s), historically based on morphology, is a very important metric, despite its well-documented limitations (35). Increasingly, assessment with time-lapse morphology sometimes assisted by algorithms and artificial intelligence, preimplantation genetic testing for aneuploidy (PGT-A) with biopsy or noninvasive PGT-A, and metabolic assessment of the culture media are used by some but not all developed countries (36–39). The day of transfer affects the number transferred because implantation rates increase as embryos survive longer in culture. More day 3 cleavage stage embryos are transferred than day 5 or 6 blastocyst stage (40). Laboratory procedures, such as ICSI and assisted hatching (AH), may affect decisions regarding number of embryos to transfer. Even with the transfer of a single euploid embryo, other factors, such as age, affect LBRs (41, 42). Therefore, it can be acceptable in some patients, especially older patients, to transfer more than one embryo because MPRs are much lower than in younger patients. The improved culture conditions in modern embryology and greater use of blastocyst transfer undoubtedly have played a major role in encouraging the

FIGURE 1



Global multiple pregnancy and single embryo transfer rates for fresh embryo transfer and frozen embryo transfer in 2003, 2009, and 2014. Fresh ET MPR = fresh embryo transfer multiple pregnancy rate; Fresh ET SET = fresh embryo transfer single embryo transfer rate; FET MPR = frozen embryo transfer multiple pregnancy rate; FET SET = frozen embryo transfer single embryo transfer rate.

Adamson. Addressing multiple pregnancy in assisted reproduction. Fertil Steril 2020.

use of SET in clinics that have pioneered SET; belief and practice in the value of PGT-A has encouraged the increased use in countries such as the United States. Historically, a greater number of frozen/thawed embryos were used per transfer because of lower success rates. This is no longer true since cryopreservation with vitrification technology has improved in the past decade and there is some evidence that the endometrium is more receptive in a FET than fresh embryo transfer because hormone levels are more physiological (43). However, globally, variability in the quality and outcomes with cryopreservation creates differences in confidence and use of cryopreserved embryos (44).

Multiple studies have demonstrated that financial issues are the primary driver of ART use (45, 46). There is nowhere globally where the cost of ART is so low that the societal need can be met without subsidies of some type, be they national health plans, private insurance, or other means of financing. The subsidy level is affected by the structure of the ART delivery system within the general health system (i.e., private/public and legislation regarding funding). The issue is not one of cost but of affordability (45). This study included 30 high and upper middle income countries selected because needed data could be collected to evaluate and quantify the impact of consumer cost, health care system characteristics, and sociodemographic factors on access to ART and embryo transfer practices. Affordability is defined as the mean net cost of a standard IVF cycle (after subsidy) as a percentage of disposable income. Data show a moderate correlation between more affordability and use, fewer number of embryos transferred, higher percentage of eSET, and lower percentage of cycles with three or more embryos transferred. The association between affordability and embryo transfer practices was strongest in countries with relatively low numbers of embryos already being transferred per cycle. Higher numbers of embryos are transferred in jurisdictions with relatively expensive ART. However, models indicate that jurisdictions that currently transfer high numbers of embryos would be relatively resistant to transferring fewer embryos even when incentivized by lower costs to consumers. These findings are consistent with findings in the United States showing that states with insurance mandates transfer lower numbers of embryos (46–49). Other studies have shown the correlation between affordability, use, and SET (50, 51).The conclusion is simple but well established—when ART is more affordable more patients have ART treatments, more SET is performed, and the twin rate is lower.

The environment in which ART centers function affects how ART is practiced. Almost uniquely within the United States, the publication of outcomes either through mandatory reporting or self-publicity has resulted in a highly competitive marketplace for more than a quarter century. Although consumer understanding has improved with respect to the many factors influencing a clinic's success rate and although the Society for Assisted Reproductive Technology has emphasized that clinics cannot be compared directly on outcome rates, clinics still feel compelled to report the best possible pregnancy rates (52). This situation of mandatory reporting and publication of clinic-specific outcomes unintentionally can lead practices to strive for maximum pregnancy rates but at the expense of higher twin rates, and this changes behavior. The incentive to attract patients can be greater than that for conservative embryo transfer practices. In the

United States the overriding competitive nature of the marketplace limits the impact of lower patient costs in states where funding of some portion of the IVF cycle is mandated by law (45). In many other countries individual clinic outcome rates are not reported and so this pressure is not present.

Another significant factor that determines clinic practice is the way in which outcomes are reported (53). Clinics will tend to change practice patterns to optimize the metrics emphasized in outcomes (e.g., pregnancy rates per egg retrieval, per patient, cumulative per egg retrieval, fresh vs. frozen transfers, and twin and high order MPRs). In countries in which effectiveness is emphasized, more attention is focused on obtaining high pregnancy rates and less on avoiding multiples, whereas the opposite is true in countries in which low MPRs are the standard and pregnancy rates, per se, are less emphasized. Two countries exemplifying these two different approaches are the United States and Japan (19, 29). This limits the value of international data comparisons; nevertheless, while challenges remain with data collection and the application of ART registry data, they have provided high value to ART practitioners seeking to understand global trends (54, 55).

Commercialization of ART centers is a major influencer of MPRs because the economic model of the business drives provider behaviors, including those that affect MPR (56). Commercialization of IVF clinics is increasing globally as regulatory conditions, business complexity, competition, and need for capital drive both horizontal and vertical consolidation. This can bring benefits with capital, business expertise, and standards of excellence. However, models that base business profit and provider remuneration on high volume of patients, expensive add-ons primarily for profit, or advertisement of high pregnancy rates can influence indirectly and directly provider behavior and lead to less than optimal clinical outcomes, including high MPRs. Properly aligned, they also can promote high-quality care for patients and positive working environments for health care professionals. Many of the issues with commercialization are yet to be defined adequately and managed. Some specific concerns with competition include the use of unnecessary "add-ons" that increase IVF cost but have not been proven to be cost-effective and may even cause harm (57, 58). Some argue commercialization and commoditization of ART services are but one of several causes that have led to a worldwide decrease of IVF birth rates per fresh embryo transfer over the past decade (59).

ECONOMIC AND SOCIOLOGICAL/CULTURAL/ RELIGIOUS FACTORS CONTRIBUTING TO HIGH MBR

As noted previously economic factors that affect affordability are major drivers of access to care, utilization, SET, and MPR (60–62). Affordability is the major driver of access to care, utilization, SET, and MPR, and is based on cost of the IVF, availability of subsidies, per capita income, net spendable income after necessities, and availability of alternative financing sources (45, 60–62). This topic is covered by Chambers et al in this edition.

Sociological and cultural factors are more important than generally recognized in driving use of ART services and the types of services provided (62, 63). These factors result in wide differences among countries and sometimes even regions of countries (e.g., the United States and the United Kingdom) with respect to the type of health system, regulations, and guidelines (64). This complex situation is compounded further by societal and personal values placed on motherhood, women in society, gender equity, desired baby girls versus boys, and value of twins (65–69).

Other factors that affect MPR are societal differences of individual versus social good (i.e., the desire for a pregnancy for self despite the potential costs to society), the perception of risk in different countries and cultures, and the perspective and expectations around informed consent. All these can create significant ethical issues (70–74).

Although often intertwined but sometimes distinct from societal cultural norms are religious and social mores regarding human reproductive rights (e.g., the right to have a baby, the right to control one's reproductive situation with birth control or abortion, and access to reproductive services). The greater the difficulty in obtaining care the more likely women are to take chances to achieve their reproductive goals. In IVF this translates into the transfer of more embryos than is optimal to increase the chances of a live birth. A significant moral and ethical issue with multiple births involves the fact that health care for complications of pregnancy, premature delivery, and twin neonates is less likely available and places a higher burden on individuals and society in lower/ middle income countries (75).

WHAT IS THE OPTIMAL TWIN RATE?

The optimal twin rate is difficult to determine, but if a goal is not set it cannot be achieved. It seems reasonable to start with the natural twin rate, while recognizing it is not possible to achieve that because the twin rate is higher in patients undergoing ART even with SET due to monozygosity.

Many issues must be considered, and they are difficult because clinicians, scientists, and ethicists of good standing and intention have different opinions regarding how to balance effectiveness versus safety. Some believe that because twins have proven poorer outcomes than singletons, the only appropriate approach is SET for all, which would approach but not reach the natural twin rate and would be <5%, but the LBR could be decreased significantly in some, especially poor prognosis patients. Others believe that, although twin pregnancy is more complicated for the mother, has poorer outcomes for the babies, and has higher lifetime cost, there are mitigating factors because there are two babies rather than one and the goal is to have any baby at all so protocols that maximize pregnancy rates, although associated with higher multiple birth rates, are appropriate (59).

Today, almost all clinicians would agree that SET is the goal. However, many believe the specific clinical situation (e.g., age, failed cycles, patient desires) can affect this clinical decision (76). Increasingly, cost-effectiveness of treatment and outcomes is being measured (76–81). Most studies show that mandatory SET will reduce the twin rate to <5% but with a possible one-third reduction in LBR per transfer compared with double embryo transfer (DET) (76–78). However, data from Australia and New Zealand show increasing LBRs, particularly with frozen cycles, and also continually increasing SET rates that are now approximately 80% (29). As clinical and laboratory practice improve, the case for SET becomes stronger. Modelling of data from a population found that selection of patients based on prognostic indicators might mitigate about half of the expected fewer live births associated with SET on the first embryo transfer while achieving a twin rate of approximately 10% or less. However, if all good-quality embryos are replaced as SET over multiple FETs, there is a compelling case that SET has the potential to produce an equivalent number of live births than repeated DET with a potential increased cost of one more embryo transfer per egg retrieval (31). Interviews and focus groups with patients suggest that many patients still prefer DET because the potential for twins is seen as positive and the additional transfer procedures can be emotionally, physically, and financially draining (78). However, a SET versus DET randomized trial in Australia was abandoned two decades ago when patients reading the information sheet refused to be randomized to DET, so setting the scene for the highly successful voluntary inception of SET in Australia and New Zealand (82).

IS THERE AN ECONOMIC ARGUMENT FOR DET?

Some of the stated economic benefits of DET are the increased LBR on the first embryo transfer compared with SET, the saving of time because pregnancy occurs earlier for the woman, and the avoidance of costs of the second embryo transfer (59, 60). One of the difficulties of ART research in this regard is that the additional cost of IVF maternal, neonatal, and child health care is often calculated, but the value of multiple births is not (60). When two babies are born there may be economic benefits: the economic productive value of an additional human being to society; the value of taxes paid to governments; and the nonfinancial value to family and friends (60, 77). On a strictly financial calculation, it is easy to show that the additional baby in a twin delivery more than economically pays the health care system and society back for the additional cost they have incurred (59, 76). Some calculations show that DET is more cost-effective than SET with an 18-year horizon used to consider live births, life-years, and quality-adjusted life years (77). This calculus is supported by the following: in 2011, the Environmental Protection Agency set the value of a human life at $9.1 million, the Food and Drug Administration at $7.9 million, and the Department of Transportation at $6 million—clearly all many multiples of the additional cost of having twins even if statistically there are additional maternal, neonatal, and childhood costs (83). Additionally, the great majority of twin pregnancies have outcomes within normal limits, so not all twin pregnancies turn out badly (5). Although well over 95% of singleton pregnancies have outcomes within normal limits, not all singletons turn out well. The optimal twin outcome needs to be determined based on multiple complex societal and personal health, economic, societal, and religious factors. Although it is good to strive for a global standard that can be considered as a place to start, individual countries, physicians, and patients undoubtedly will adapt their goals to meet their own perceived needs. These decisions are related intrinsically to deep cultural values to which we must be sensitive while striving for optimal clinical outcomes. Nevertheless, the most cost-effective outcomes are achieved by sequential SET that both maximizes the cumulative number of healthy singletons born and minimizes the cost and poorer outcomes of twins.

WHO SHOULD DETERMINE THE OPTIMAL TWIN RATE IN ART CYCLES?

Government, representing society values and economic involvement in both costs and benefits, often decides through regulation and subsidies while other interested parties, whether religious, legal, or ethics based, will have input. Professional societies can set standards, individual providers and embryologists providing care bring clinical expertise, and staff commit to the individual patient. These entities should function based on principles of beneficence, nonmaleficence, social justice, and patient autonomy. Because patients are those most affected, it could be argued they should have the greatest influence because the right to reproductive autonomy is extremely important and the right to found a family is part of the United Nations Charter of Rights (6, 84). This could be considered a hierarchy of interest in the outcome of reproductive care, with the general framework of care decided by society and other stakeholders and within that framework individual decisions made by the patient with her physician. All stakeholders, including patients and their physicians, face the challenge to balance beneficence and harm as well as social justice and patient autonomy. Individual clinics also will choose a different emphasis within the bounds of the legal and ethical frameworks of their communities. Every country and even regions within countries will do this differently.

WHERE DO WE START TO LOWER TWIN RATE?

We can start with knowledge of the worldwide statistics on outcomes of ART. The good news is that the MPR is decreasing, and the SET rate is increasing. However, the variation among countries is very wide. As a generalization, it is also true that developed countries with the lowest MPRs have, with significant exceptions, the lowest LBRs. Increasingly, however, countries have MPRs in the 10% range and acceptable pregnancy rates.

Countries that have the lowest MPR generally have mandated or have voluntary or professional guidelines that ensure the great majority of patients undergo SET. Mandates are not always necessary, for example, Japan, Australia, and New Zealand have very high SET rates based on professional guidelines. There are many perspectives on the issue of regulations versus guidelines, and each country needs to create an environment over time that works in their societal, professional, and patient culture (85–88). However, guidelines on number of embryos to transfer need frequent updating because of technology advances and change in practice. Furthermore, they are not always complied with (89–91). Adherence to evidence-based standards is clearly the best way to lower MPR and the goal should be to perform SET in almost all patients, and especially those younger than age 38 (92). Many would argue that SET should be performed essentially always in women younger than age 40 and in all women of any age with a known euploid embryo as a result of PGT-A. Importantly, most but not all countries with low MPR have substantial subsidies to increase access to care and to decrease the perceived pressure to get pregnant regardless of the risk. Continued efforts to increase coverage for infertility care is a high priority.

Countries that have not lowered their MPR generally have more private ART services with challenges and environments creating lower technological standards and are poorly subsidized. This leads to higher number of embryos transferred and often unnecessary unproven additional therapies (57–59). Such countries would benefit from mandates and/or guidelines and subsidies for patients. Where subsidies are not provided or inadequate, some clinics have introduced packaged treatment cycles that encourage SET by reducing financial pressures (92). The public, policy makers, other professionals, fertility specialists and their staffs, and patients also need more education about the risks of twins and how the optimal cumulative LBR can be obtained while maintaining a low MPR (93, 94). It has been shown that patient education and more comprehensive informed consent will increase the use of SET (73, 89, 94). SET may not be the best approach for every patient, but it clearly is for the great majority of patients.

An important aspect of this education is the reporting of outcomes. Although many different metrics have been used to assess IVF, it can be argued strongly that the metric that matters most to the patient is healthy singleton term baby per intention to treat. This translates into cumulative LBR of a healthy singleton per patient who wants a baby. This is the metric that the Society for Assisted Reproductive Technology and other registries are now implementing and should be used in counseling patients (95). Many other metrics are important for assessing different aspects of patient, clinical, surgical, and laboratory care (96–100). Continued scientific progress with clinical and laboratory application will improve implantation rates and increase confidence in SET.

Much progress has been made in performing SET, which depends on optimizing individual protocols for the patient, executing the protocol without error, carrying out the minimum necessary but not unneeded laboratory services, choosing the best embryo for transfer, and performing a flawless embryo transfer. All these steps can be focused both on maximizing healthy singleton LBR and minimizing the MPR. Today, there is much research pertaining to all these areas of ART. None is more important than determining which embryo to choose for embryo transfer. Despite wide acclaim the promise of PGT-A has yet to be realized and newer technologies such as AI are yet to be validated (40, 101–103). It clearly is possible to choose a single embryo for SET at cleavage or blastocyst stage without doing PGT-A, which is a technology that has not become the standard of care globally and is not necessary for SET (30, 64). However, further research on other embryological technologies and endometrial receptivity almost certainly will increase implantation rates and so encourage the greater use of SET (104, 105).

CONCLUSION

The ART community has made incredible progress over 42 years since Louise Brown was born. Our challenge now is to decrease the MPR and to increase the cumulative number of healthy singleton babies for each patient who presents wanting a baby. Single embryo transfer is the most immediate step to achieve the reduction of multiple pregnancies. Excellent ART treatment with cryopreservation and subsequent SET will maximize the cumulative LBRs. Advocacy for societal subsidies for patients will reduce pressure on patients and providers. This will result from promotion of SET and education of the public and policy makers regarding reproductive rights, gender equity, diversity and inclusion, and increased access to fertility and IVF care (106). Appropriate reporting will help all stakeholders assess progress and determine the best way forward. Professional societies need to take the lead collaborating with international organizations such as the World Health Organization, governments, the public, providers, and patients. National and international standards with validation and certification of programs for all aspects of ART will improve quality of care and increase LBRs. Additional information through research to enhance clinical and laboratory excellence, improve our assessment of the embryo with imaging, metabolomics, genetics, artificial intelligence, and other technologies to prioritize embryos for replacement will further our progress. Today, the goal for all countries should be a twin pregnancy rate of not more than 10% with maintenance and even improvement of current healthy singleton LBRs. This target should be adjusted downward toward a 5% twin rate as progress is made in the coming years. The fact that some countries and many individual clinics have already achieved these goals points the way to a bright future.

REFERENCES

1. Brindsen P. The Story of Patrick Steptoe, Robert Edwards, Jean Purdy and Bourn Hall Clinic. In: Kovacs G, Brinsden P, DeCherney A, editors. The History of IVF. Cambridge: Cambridge University Press; 2019:28–36.
2. Adamson GD, Dyer S, Chambers G, Ishihara O, Mansour R, Banker M, et al. for International Committee for Monitoring ART. International Committee for Monitoring Assisted Reproductive Technologies (ICMART) Preliminary World Report on ART, 2015. Session 40. O-144. European and global ART monitoring. ESHRE Annual Meeting, 2019.
3. Society for Assisted Reproductive Technology. National Summary Report 2017. Available at: https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?reportingYear=2017. Accessed August 13, 2020.
4. Niederberger C, Pellicer A, Cohen J, Gardner DK, Palermo GD, O'Neill CL, et al. Forty years of IVF. Fertil Steril 2018;110:185–324.
5. Practice Committee of the American Society for Reproductive Medicine. Multiple gestation associated with infertility therapy: an American Society for Reproductive Medicine Practice Committee opinion. Fertil Steril 2012; 97:825–34.
6. Adamson GD, Baker VL. Multiple births from assisted reproductive technologies: a challenge that must be met. Fertil Steril 2004;81:517–22.
7. Oxford Reference. Quick Reference. Available at: https://www.oxfordreference.com/view/10.1093/oi/authority.20110803100345841#:

~:text=Quick%20Reference,its%20source%20is%20not%20known. Accessed August 15, 2020.
8. Sullivan D. Resources. Strategic Coach. Dan Sullivan's Best Career Advice: 10 Secrets To Success For Today's Entrepreneur. Available at: https://resources.strategiccoach.com/the-multiplier-mindset-blog/dan-sullivan-s-best-career-advice-10-secrets-to-success-for-today-s-entrepreneur. Accessed August 15, 2020.
9. International Committee for Monitoring Assisted Reproductive Technologies (ICMART). ICMART website. Available at: www.icmartivf.org. Accessed August 19, 2020.
10. Gerris J, de Sutter P, Racowsky C, Adamson GD, editors. Elective single embryo transfer. Cambridge: Cambridge Press; 2009.
11. Adamson GD, de Mouzon J, Lancaster P, Nygren KG, Sullivan E, Zegers-Hochschild F. International Committee Monitoring Assisted Reproductive Technology World Collaborative Report on In Vitro Fertilization, 2000. Fertil Steril 2006;85:1586–622.
12. de Mouzon J, Lancaster P, Nygren K, Sullivan E, Zegers-Hochschild F, Mansour R, et al. International Committee Monitoring Assisted Reproductive Technology World Collaborative Report on Assisted Reproductive Technology, 2002. Hum Reprod 2009;24:2310–20.
13. Nygren KG, Sullivan E, Zegers-Hochschild F, Mansour R, Ishihara O, Adamson GD, et al. International Committee for Monitoring Assisted Reproductive Technology (ICMART) World Report on Assisted Reproductive Technology, 2003. Fertil Steril 2011;95:2209–22.
14. Sullivan E, Zegers-Hochschild F, Mansour R, Ishihara O, de Mouzon J, Nygren KG, et al. International Committee for Monitoring Assisted Reproductive Technology (ICMART) World Report on Assisted Reproductive Technology, 2004. Hum Reprod 2013;28:1375–90.
15. Zegers-Hochschild F, Mansour R, Ishihara O, Adamson GD, de Mouzon J, Nygren KG, et al. International Committee for Monitoring Assisted Reproductive Technologies (ICMART) World Report on Assisted Reproductive Technology, 2005. Fertil Steril 2014;101:366–78.
16. Mansour R, Ishihara O, Adamson GD, de Mouzon J, Sullivan E, Zegers-Hochschild R. International Committee for Monitoring Assisted Reproductive Technology (ICMART) World Report on Assisted Reproductive Technology, 2006. Hum Reprod 2014;29:1536–51.
17. Ishihara O, Adamson GD, de Mouzon J, Sullivan E, Zegers-Hochschild R, Mansour R. International Committee for Monitoring Assisted Reproductive Technologies: world report on assisted reproductive technologies, 2007. Fertil Steril 2015;103:402–13.
18. Dyer S, Chambers GM, de Mouzon J, Nygren KG, Zegers-Hochschild F, Mansour R, et al. International Committee for Monitoring Assisted Reproductive Technologies world report: Assisted Reproductive Technology 2008, 2009 and 2010. Hum Reprod 2016;31:1588–609.
19. Adamson GD, de Mouzon J, Chambers G, Zegers-Hochschild F, Mansour R, Ishihara O, et al. International Committee for Monitoring Assisted Reproductive Technology: world report on assisted reproductive technology, 2011. Fertil Steril 2018;110:1067–80.
20. Mouzon J, Chambers GM, Zegers-Hochschild F, Mansour R, Ishihara O, Banker M, et al. International Committee for Monitoring Assisted Reproductive Technologies. World Report: on Assisted Reproductive Technologies, 2012. Hum Reprod 2020;35:1900–13.
21. Palomba S, Homburg R, Santagni S, Battista La Sala G, Orvieto R. Risk of adverse pregnancy and perinatal outcomes after high technology infertility treatment: a comprehensive systematic review. Reprod Biol Endocrinol 2016;14:76.
22. Multiple gestation pregnancy. The ESHRE Capri Workshop Group. Hum Reprod 2000;15:1856–64.
23. Andrijasevic S, Dotlic J, Aksam S, Micic J, Terzic M. Impact of conception method on twin pregnancy course and outcome. Geburtshilfe Frauenheilkd 2014;74:933–9.
24. Baxi A, Kaushal M. Outcome of twin pregnancies conceived after assisted reproductive techniques. J Hum Reprod Sci 2008;1:25–8.
25. Zegers FZ, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, et al. The International Glossary on Infertility and Fertility Care, 2017: Led by ICMART in Partnership with ASRM, ESHRE, IFFS, March of Dimes, AFS, GIERAF, ASPIRE, MEFS, REDLARA, FIGO. Fertil Steril 2017;108:393–406.
26. Glujovsky D, Sueldo CE, Coscia A, Carvalho P, Lancuba S, Martinez G, et al. Physicians and patients' motivations to perform elective single or double-embryo transfers: a nationwide survey. Patient Educ Couns 2018;101:945–50.
27. Bai F, Wang DY, Fan YJ, Qiu J, Wang L, Dai Y, et al. Assisted reproductive technology service availability, efficacy and safety in mainland China: 2016. Hum Reprod 2020;35:446–52.
28. Zegers-Hochschild F, Crosby JA, Musri C, Masoli D, Posada N. on behalf of the Latin American Network of Assisted Reproduction. Assisted reproductive technology in Latin America: the Latin American Registry, 2017. RBMO 2020;41:44–54.
29. Ishihara O, Zegers-Hochschild F, de Mouzon J, Dyer S, Mansour R, Banker M, et al. SET in a global perspective. Regional similarities and differences. ESHRE Annual Meeting (Virtual). O-158. 2020:i69.
30. International Committee for Monitoring Assisted Reproductive Technologies (ICMART). ICMART Reports and Publications. Available at: https://www.icmartivf.org/reports-publications/. Accessed August 20, 2020.
31. Kamath MS, Mascarenhas M, Kirubakaran R, Bhattacharya S. Number of embryos for transfer following in vitro fertilisation or intra-cytoplasmic sperm injection. Cochrane Database of Systematic Reviews 2020:CD003416. Accessed August 21, 2020.
32. McLernon DJ, Steyerberg EW, te Velde ER, Lee AJ, Bhattacharya S. Predicting the chances of a live birth after one or more complete cycles of in vitro fertilisation: population based study of linked cycle data from 113 873 women. BMJ 2016;355:i5735.
33. American College of Obstetricians and Gynecologists Committee on Gynecologic Practice and The Practice Committee of the American Society for Reproductive Medicine. Female age-related fertility decline. Fertil Steril 2014;101:633–4.
34. Klitzman R. Deciding how many embryos to transfer: ongoing challenges and dilemmas. Reprod Biomed Soc Online 2016;3:1–15.
35. Nasiri N, Eftekhari-Yazdi P. An overview of the available methods for morphological scoring of pre-implantation embryos in in vitro fertilization. Cell J 2015;16:392–405.
36. Armstrong S, Bhide P, Jordan V, Pacey A, Marjoribanks J, Farquhar C. Time-lapse systems for embryo incubation and assessment in assisted reproduction (Review). Cochrane Database of Systematic Reviews 2019:CD011320. Accessed May 25, 2018.
37. Khosravi P, Kazemi E, Zhan Q, Malmsten JE, Toschi M, Zisimopoulos P, et al. Deep learning enables robust assessment and selection of human blastocysts after in vitro fertilization. npj Digital Medicine 2019;2.
38. Bracewell-Milnes T, Saso S, Abdalla H, Nikolau D, Norman-Taylor J, Johnson M, et al. Metabolomics as a tool to identify biomarkers to predict and improve outcomes in reproductive medicine: a systematic review. Hum Reprod Update 2017;23:723–36.
39. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. The use of preimplantation genetic testing for aneuploidy (PGT-A): a committee opinion. Fertil Steril 2018;109:429–36.
40. Practice Committee of the American Society for Reproductive Medicine and Practice Committee of the Society for Assisted Reproductive Technology. Blastocyst culture and transfer in clinically assisted reproduction: a committee opinion. Fertil Steril 2018;110:1246–52.
41. Bergh C, Kamath MS, Wang R, Lensen S. Strategies to reduce multiple pregnancies during medically assisted reproduction. Fertil Steril 2020;114:673–9.
42. Mersereau J, Stanhiser J, Coddington C, Jones J, Luke B, Brown MB. Patient and cycle characteristics predicting high pregnancy rates with single-embryo transfer: an analysis of the Society for Assisted Reproductive Technology outcomes between 2004 and 2013. Fertil Steril 2017;108:750–6.
43. Wong KM, van Wely M, Mol F, Repping S, Mastenbroek S. Fresh versus frozen embryo transfers in assisted reproduction. Cochrane Database of Systematic Reviews 2017:CD011184. Accessed March 28, 2017.
44. Bosch E, De Vos M, Humaiden P. The future of cryopreservation in assisted reproductive technologies. Front Endocrinol (Lausanne) 2020;11:67.
45. Chambers G, Phuong Hoang V, Sullivan E, Chapman M, Ishihara O, Zegers Hochschild F, et al. The impact of consumer affordability on access to

assisted reproductive technologies and embryo transfer practices: an international analysis. Fertil Steril 2014;101:191–8.
46. Hamilton BH, McManus B. The effects of insurance mandates on choices and outcomes in infertility treatment markets. Health Econ 2012;21:994–1016.
47. Jain T, Harlow BL, Hornstein MD. Insurance coverage and outcome of in vitro fertilization. N Engl J Med 2002;347:661–6.
48. Martin JR, Bromer JG, Sakkas D, Patrizio P. Insurance coverage and in vitro fertilization outcomes: a US perspective. Fertil Steril 2011;95:964–9.
49. Reynolds MA, Schieve LA, Jeng G, Peterson HB. Does insurance coverage decrease the risk for multiple births associated with assisted reproductive technology? Fertil Steril 2003;80:16–23.
50. Lee AM, Connell MT, Csokmay JM, Styer AK. Elective single embryo transfer- the power of one. Contracept Reprod Med 2016;1:11.
51. Connolly MP, Griesinger G, Ledger W, Postma MJ. The impact of introducing patient co-payments in Germany on the use of IVF and ICSI: a price-elasticity of demand assessment. Hum Reprod 2009;24:2796–800.
52. Society for Assisted Reproductive Technology. Clinic Summary Report 2017. Palo Alto Medical Foundation. Available at: https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=2070. Accessed August 22, 2020.
53. Gunderson S, Jungheim ES, Kallen CB, Omurtag K. Public reporting of IVF outcomes influences medical decision-making and physician training. Fertil Res Practice 2020;6:1–6.
54. Adamson GD. A success story: impact of the United States in vitro fertilization data registry on advancing fertility care. Fertil Steril 2019;111:457–8.
55. Zegers FZ, Adamson GD. Monitoring ART outcomes: the registries. Vol. 5. Encyclopedia of reproduction. 2nd ed. Reference Module in Biomedical Research. New York: Elsevier, 2018.
56. Adamson GD, Rutherford A. Commercialization of IVF. In: Kovacs G, Brinsden P, editors. Alan Decherney A. In vitro fertilization: the pioneers' history. Cambridge: Cambridge University Press; 2018:240–8.
57. Balen A, Regan L, Avery S, Braude P, Cooke I, Dugdale G, et al. Lack of evidence for interventions offered in UK fertility centres. BMJ 2016;355:i6295.
58. Wilkinson J, Malpas P, Hammarberg K, Jackson E, Harper J, Mol BW. Do à la carte menus serve infertility patients? The ethics and regulation of in vitro fertility add-ons. Views Reviews 2019;112:973–7.
59. Gleicher N, Kushnir VA, Barad DH. Worldwide decline of IVF birth rates and its probable causes. Hum Reprod Open 2019:1–7.
60. Adamson GD. Economics in the development of embryo transfer policies. IFFS Trilogies. IFFS/ASRM Conjoint Meeting, 2013.
61. Chambers G, Adamson GD, Eijkemans M. Acceptable cost for the patient and society. Fertil Steril 2013;100:319–27.
62. Adamson GD. Global cultural and socioeconomic factors that influence access to ART. Women's Health 2009;5:351–8.
63. Prag P, Mills MC. Cultural determinants influence assisted reproduction usage in Europe more than economic and demographic factors. Hum Reprod 2017;32:2305–14.
64. International Federation of Fertility Societies' Surveillance (IFFS) 2019: Global Trends in Reproductive Policy and Practice, 8th ed. Global Reproductive Health 2019;4:e29.
65. Institute for Family Studies. More Gender Equality, Lower Fertility? Available at: https://ifstudies.org/blog/more-gender-equality-lower-fertility. Accessed August 22, 2020.
66. Nargund G. Helping women with their fertility should be part of the agenda for gender equality. FVV Ob Gyn 2014;6:50.
67. Fraser M. In: Gender inequality in in vitro fertilization: controlling women's reproductive autonomy. City University of New York Law Review 1998;2:183-210.
68. Mendoza R, Jáuregui T, Diaz-Nuñez M, de la Sota M, Hidalgo A, Ferrando M, et al. Infertile couples prefer twins: analysis of their reasons and clinical characteristics related to this preference. J Reprod Infertil 2018;19:167–73.
69. Leese B, Denton J. Attitudes towards single embryo transfer, twin and higher order pregnancies in patients undergoing infertility treatment: a review. Hum Fertil 2010;13:28–34.
70. Santos HC, Varnum MEW, Grossmann I. Global increases in individualism. Psychological Sci 2017;28:1228–39.
71. Vredembirgh AG, Cohen HH. Does culture affect risk perception? Proceedings of the Human Factors and Ergonomics Society Annual Meeting; 1995.
72. Bontempo R, Bottom WP, Weber EU. Cross-cultural differences in risk perception: a model-based approach. Risk Analysis 1997;17:479–88.
73. Dokras A, Van Voorhis BJ, Ryan G, Sparks AET, Sipe CS, Syrop CH. A mandatory single blastocyst transfer policy with educational campaign in a United States IVF program reduces multiple gestation rates without sacrificing pregnancy rates. Fertil Steril 2007;88:354–60.
74. Ethics Committee of the American Society for Reproductive Medicine. Disparities in access to effective treatment for infertility in the United States: an Ethics Committee opinion. Fertil Steril 2015;104:1104–10.
75. Ombelet W. Global access to infertility care in developing countries: a case of human rights, equity and social justice. Facts Views Vis Obgyn 2011;3:257–66.
76. Scotland GS, McLernon D, Kurinczuk JJ, McNamee P, Harrild K, Lyall H, et al. Minimising twins in in vitro fertilization: a modelling study assessing the costs, consequences and cost-utility of elective single versus double embryo transfer over a 20-year time horizon. BJOG 2011;118:1073–83.
77. van Heesch MMJ, van Asselt ADI, Evers JLH, van der Hoeven MAHBM, Dumoulin JCM, van Beijsterveldt CEM, et al. Cost effectiveness of embryo transfer strategies: a decision analytic model using long-term costs and consequences of singletons and multiples born as a consequence of IVF. Hum Reprod 2016;31:2527–40.
78. Practice Committee of the Society for Assisted Reproductive Technology and Practice Committee of the American Society for Reproductive Medicine. Elective single-embryo transfer. Fertil Steril 2012;97:835–42.
79. Medical Advisory Secretariat. In vitro fertilization and multiple pregnancies: an evidence-based analysis. Ont Health Technol Assess Ser 2006;6:1–63.
80. Chambers GM, Sullivan E, Ishihara O, Adamson GD. The economic impact of ART: a review of selected developed countries. Fertil Steril 2009;91:2281–94.
81. Roberts S, McGowan L, Hirst W, Brison D, Vail A, Lieberman B. Towards single embryo transfer? Modelling clinical outcomes of potential treatment choices using multiple data sources: predictive models and patient perspectives. Health Technol Asses 2010;14:1–237.
82. de Lacey S, Davies M, Homan G, Briggs N, Norman RJ. Factors and perceptions that influence women's decisions to have a single embryo transferred. Reprod Biomed Online 2007;15:526–31.
83. The Globalist. The Cost of a Human Life, Statistically Speaking. Available at: https://www.theglobalist.com/the-cost-of-a-human-life-statistically-speaking/#:~:text=As%20of%202011%2C%20the%20Environmental,of%20these%20the%20right%20answer%3F. Accessed August 22, 2020.
84. United Nations. Universal Declaration of Human Rights. Article 16. Available at: https://www.un.org/en/udhrbook/pdf/udhr_booklet_en_web.pdf. Article 16. Accessed August 22, 2020.
85. Busardò FP, Gulino M, Napoletano S, Zaami S, Frati P. The evolution of legislation in the field of medically assisted reproduction and embryo stem cell research in European union members. Biomed Res Int 2014;2014:307160.
86. Adamson GD. Regulation of the assisted reproductive technologies in the United States. Fertil Steril 2002;78:932–42.
87. Adamson D. IVF: tight regulation may not be suitable for all cultures. Nature 2008;454:938.
88. Adamson GD. Does self-regulation work for implementation of single embryo transfer. In: Gerris J, de Sutter P, Racowsky C, Adamson GD, editors. Single embryo transfer. Cambridge: Cambridge Press; 2009:249–68.
89. Practice Committee of the American Society for Reproductive Medicine, and the Practice Committee of the Society for Assisted Reproductive Technology American Society for Reproductive Medicine; and Society for Assisted Reproductive Technology, Birmingham, Alabama. Guidance on the limits to the number of embryos to transfer: a committee opinion. Fertil Steril 2017;107:901–3.
90. Keyhan S, Accharya KS, Acharya CR, Yeh JS, Provost MP, Goldfarb J, et al. How compliant are in vitro fertilization member clinics in following embryo

transfer guidelines? An analysis of 59,689 fresh first in vitro fertilization autologous cycles from 2011 to 2012. Fertil Steril 2016;106:645–52.e1.
91. Kim HH, Matevossian K. Are two better than one? Two sequential transfers of a single embryo may be better than a double-embryo transfer. Fertil Steril 2020;114:267–8.
92. Ethics Committee of the American Society for Reproductive Medicine. Financial ''risk-sharing'' or refund programs in assisted reproduction: an Ethics Committee opinion. Fertil Steril 2016;106:e8–11.
93. Human Fertilisation and Embryology Authority. Fertility treatment 2017: trends and figures. Available at: https://www.hfea.gov.uk/media/2894/fertility-treatment-2017-trends-and-figures-may-2019.pdf. Accessed August 22, 2020.
94. Adamson GD, Collura B. Challenges to patient choice of elective single embryo transfer (eSET) versus multiple embryo transfer (MET). Fertil Steril 2015;103:e9.
95. Society for Assisted Reproductive Technology. National Summary Report 2018. Available at: https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?reportingYear=2018. Accessed August 22, 2020.
96. Scott RT Jr, de Ziegler D. Introduction: key performance indicators in assisted reproductive technologies. Fertil Steril 2020;114:4–5.
97. Fischer C, Scott RT Jr. Three simple metrics to define in vitro fertilization success rates. Fertil Steril 2020;114:6–8.
98. Fabozzi G, Cimadomo D, Maggiulli R, Vaiarelli A, Ubaldi FM, Rienzi L. Which key performance indicators are most effective in evaluating and managing an in vitro fertilization laboratory? Fertil Steril 2020;114:9–15.
99. Jalas C, Seli E, Scott RT Jr. Key metrics and processes for validating embryo diagnostics. Fertil Steril 2020;114:16–23.
100. Pirtea P, de Ziegler D, Poulain M, Ayoubi JM. Which key performance indicators are optimal to assess clinical management of assisted reproduction cycles? Fertil Steril 2020;114:24–30.
101. Practice Committee and Genetic Counseling Professional Group (GCPG) of the American Society for Reproductive Medicine. Clinical management of mosaic results from preimplantation genetic testing for aneuploidy (PGT-A) of blastocysts: a committee opinion. Fertil Steril 2020;114:246–54.
102. Rosenwaks Z, Handyside AH, Fiorentino F, Gleicher N, Paulson RJ, Schattman GL, et al. The pros and cons of preimplantation genetic testing for aneuploidy: clinical and laboratory perspectives. Fertil Steril 2018;110:353–61.
103. Paulson RJ. Preimplantation genetic screening: what is the clinical efficiency? Fertil Steril 2017;108:228–30.
104. Boynukalin FK, Gultomruk M, Cavkaytar S, Turgut E, Findikli N, Serdarogullari M, et al. Parameters impacting the live birth rate per transfer after frozen single euploid blastocyst transfer. PLoS One 2020;15:e0227619.
105. Ishihara O, Araki R, Kuwahara A, Itakura A, Saito H, Adamson GD. The impact of frozen-thawed single blastocyst transfer on maternal and neonatal outcome: an analysis of 277,042 single embryo transfer cycles between 2008 and 2010 in Japan. Fertil Steril 2014;101:128–33.
106. Dyer S, Chambers G, Adamson D, Banker M, de Mouzon J, Ishihara O, et al. ART utilization: an indicator of access to infertility care. RBMO 2020;41:6–9.