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ORIGINAL RESEARCH

Deciding how many embryos to transfer: ongoing challenges and dilemmas

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Abstract Despite the risks associated with twin and higher-order multiple births, and calls in many countries for single-embryo transfer as the standard of care for good-prognosis patients, providers frequently transfer additional embryos, raising critical questions as to why this is the case and what can be done about it. In-depth interviews of approximately 1 h each were conducted with 27 IVF providers (17 physicians and 10 other healthcare providers) and 10 patients. Professional guidelines often contain flexibility and ambiguities or are unenforced. Thus, both providers and patients frequently wrestle with several dilemmas. Decisions about the number of embryos to transfer emerge as dyadic, dynamic and affected by several factors (e.g., providers' type of institution, and personal and professional experiences and perceptions of the data), leading to differences in whether, how and with what effectiveness clinicians address these issues with patients. Many clinicians feel that the evidence concerning the apparent increased risk associated with a twin birth is not 'compelling', and patients frequently minimize the hazards. These data, the first to explore several critical aspects of how providers and patients view and make decisions about the number of embryos to transfer, thus highlight tensions, uncertainties and challenges that providers and patients confront, and have key implications for future practice, research, policy and education.



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Despite the risks associated with twin and other higher-order multiple births, and subsequent calls for single-embryo transfer (SET) as the standard of care for good-prognosis patients, most providers transfer additional embryos, raising critical questions as to why this is the case. As a consequence

of assisted reproduction via IVF, rates of twin and other higher-order multiple births have increased over recent years, essentially doubling between the mid-1970s and 2011 in many developed countries, including the UK, France, Germany, the USA and South Korea ([Osterman et al., 2015](#);

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Pison et al., 2015). Critics have decried an 'epidemic' of multiple births (Muir, 2001), and the case of 'Octomom' in the USA – in which a woman on federal assistance gave birth to octuplets following treatment with artificial reproductive technologies – brought world-wide attention to this issue (Davidson, 2010).

When transferring more than one embryo, the rate of complications increases. Among infants born to mothers through IVF, twins are 12 times more likely than singletons to be born prematurely, 16 times more likely to have low birth weight, and about five times more likely to have respiratory complications or jaundice (Sazonova et al., 2013). Mothers of twins are about two and a half times more likely than those of singletons to have pre-eclampsia, over eight times more likely to have premature pre-term rupture of membranes, and four times more likely to require a Caesarean section (Sazonova et al., 2013). Although some providers and patients may see twins as a means of saving money, the overall cost per live birth (for both mothers and infants) for one double-embryo transfer (DET), rather than two SET, until 6 months of age, are roughly equal, given neo-natal intensive-care unit (NICU) and other expenses (Thurin-Kjellberg et al., 2006). Over time, twins can cost even more, given the associated long-term complications (Collins, 2007; Wølner-Hanssen and Rydhstroem, 1998).

Opponents of establishing SET as the standard of care for good-prognosis patients argue that twins are desirable, and that the reported risks are exaggerated (Gleicher and Barad, 2009). A meta-analysis of studies published from 1995–2008 (Baruffi et al., 2009) found that DET had about twice the pregnancy and birth rate of SET. Yet over the past decade, since many of these studies were conducted, SET success has increased substantially, while higher complications with DET continue. A more recent meta-analysis (McLernon et al., 2010) found that the birth rate from a fresh SET followed by a frozen SET was not significantly different than that of one fresh DET (38% versus 42%), and that the risks of a preterm birth were five times higher for DET than for SET. One Italian centre recently suggested that twin pregnancies compared with singleton pregnancies had 31.8 times the rate of perinatal complications (La Sala et al., 2016). Other data show that for women over 40, transferring three, rather than two embryos does not increase the live birth rate (Lawlor and Nelson, 2012).

Therefore, as SET success rates continue to rise, commentators have increasingly argued that SET should become the standard of care (Kissin et al., 2015), and that this may be achievable through altering insurance reimbursement, providing appropriate educational materials and including patients' partners in discussions of risk (Griffin et al., 2012; Hope and Rombauts, 2010; Leese and Denton, 2010).

In recent years, guidelines in various countries have thus sought to reduce the number of embryos transferred, including the UK (HFEA, 2013), Australia/New Zealand (Norman, 2016), and Canada (Canadian Fertility and Andrology Society, 2006). The number of countries that limit the number of embryos to be transferred has been steadily increasing, and in 2013 was around 17 (Stillman et al., 2013). In the UK, the Human Fertilization and Embryology Authority (HFEA) has progressively lowered the maximum multiple birth rate from 24% in 2009/2010, to 15% in

2010 and 10% in 2012 (HFEA, 2013). Belgium coupled reimbursement for assisted reproductive technologies to a restriction in the number of embryos transferred and reduced the multiple pregnancy rate from 27% in 2003 to 11% in 2010 (De Neubourg et al., 2014). However, many countries still allow considerable room for physician discretion. The American Society of Reproductive Medicine (ASRM), for instance, states that 'physicians should be encouraged to counsel good-prognosis patients to accept' SET; and highlights the importance of clinical judgement in selecting the best candidates (The Practice Committee of the ASRM, 2012). For patients <35 years of age with a favourable prognosis, 'providers should only transfer a single embryo, and not more than two embryos' (The Practice Committee of the ASRM and the Practice Committee of the SART, 2013). For patients aged 38-40, and 41-42, ASRM states that no more than three and five cleavage-stage embryos, respectively, should be transferred. Patients, who have failed two or more IVF cycles or have a less favourable prognosis, can receive an additional embryo. For patients aged over 43, there is no limit (The Practice Committee of the ASRM and the Practice Committee of the SART, 2013).

Since 1998, the rate of twin and multiple births have begun to decrease – as providers have begun to transfer three or more embryos less frequently (Kulkarni et al., 2013) – but remain higher in numerous countries than many observers argue is optimal. Thus, 17% of all Canadian births were twins in 2013 (Canadian Fertility and Andrology Society, 2006), and multiples accounted for approximately 17% of British pregnancies (HFEA, 2013) and 19.4% of all births in Europe in 2011 (Kupka et al., 2016). Among cycles using IVF and intra-cytoplasmic sperm injection (ICSI), transfers of three and four embryos accounted, respectively, for 14.5% and 1.3% in Europe as a whole, including 49.4% and 9.9% in Greece, 34.6% and 4.5% in Italy, 26.2% and 3.1% in Hungary, and 40.7% and 7.9% in Bulgaria (Kupka et al., 2016). Twin and triplet deliveries accounted for 18.6% and 0.6% of assisted reproductive technology births using IVF and ICSI in Europe as a whole, including, 41.5% and 3.5% in Greece, 28.2% and 1.7% in Romania, 22.0% and 6.5% in Moldova, and 26.5% and 5% in Serbia (Kupka et al., 2016). The most recent summary data available from the Society for Assisted Reproductive Technologies (SART) from 2013, suggests that among all transfers using fresh non-donor eggs or embryos, 76.4% involved one or more embryos and 20.7% involved three or more embryos; and the average number of fresh and thawed embryos from non-donor eggs transferred in women under 35 was 1.8% and 1.7%, respectively (Centers for Disease Control and Prevention, 2013). Among live births from fresh embryos, for mothers under 35 and aged 35-37, respectively, 28.3% and 25.5% of US births were twins and approximately 1% were triplets or higher-order multiples. *The SART Clinic Summary Report (2016)* lists the percentage of cycles, retrievals and transfers resulting in live births, but does not separate these data by the number of embryos transferred (1 versus 2 or more). The success rates would presumably be lower for singletons (versus twins).

A few studies have suggested that physicians may fail to follow SET because of patient requests. A literature review revealed that most patients prefer twins rather than singletons (Leese and Denton, 2010). In one study, 52% of

clinicians were found to deviate from ASRM's guidelines concerning embryo transfers due to patients' requests, 51% deviated when using frozen embryos, and 70% did so when patients had failed prior IVF, and only 34% routinely discussed with all patients SET (Jungheim et al., 2010). In certain developing, as well as in developed countries, most patients prefer transfer of at least two embryos, and providers often comply with these requests (Balasubramanyam, 2010).

Though some commentators have argued that patients' preference for twins results from limitations in insurance coverage of assisted reproductive technology, the data concerning this claim are mixed. In the USA, states that mandate some IVF insurance coverage have slightly lower rates of twins (26% versus 28%) and triplets (3.4% versus 3.9%), though the absolute differences are not high (2% and 0.5%, respectively) (Martin et al., 2011). Twins and other multiple births are also far more common in the USA than in several other countries, possibly due to differences in insurance coverage (Chambers et al., 2014). However, in a study in Denmark, where two embryo transfers and three IVF cycles were reimbursed, 59% of patients nonetheless preferred twins because of desires for siblings and reduction of physical and psychological stresses from undergoing IVF – not because of economics (Højgaard et al., 2007). Yet in this study, though all subjects had received counselling with a nurse concerning the risks of twin pregnancies, 58.4% of participants stated that they had not received oral counselling on the advantages and disadvantages of twin pregnancies; and of those who said they had received such counselling, 32.3% said they needed additional information. Among the 58.4% who said they had not received counselling, 70.6% said they needed additional information on twin pregnancies. Hence, most of these subjects who preferred twins may not have understood or appreciated the risks involved. Murray et al. (2004) also found that most patients preferred DET, even if receiving an extra leaflet or 10-minute conversation with a nurse about the issues involved. Critical questions thus arise of exactly how patients and providers communicate and interact regarding these issues – how providers discuss these issues with patients, why most patients fail to recall these conversations, and how patients view and understand these potential risks.

Same-sex male couples may also often prefer twins so that each will have a biological child (Greenfeld and Seli, 2011). Moreover, Jungheim et al. (2010) found that clinics where fewer than half of all IVF cycles were self-financed were much less likely to limit the number of embryos transferred due to patient requests than did clinics where more than half of all IVF cycles were self-financed. Additionally, the amount of insurance held had no effect on deviations due to previous failed IVF cycles, or use of frozen embryos. Jungheim et al. (2010) suggested that patients with insurance may want to take aggressive approaches after IVF failure; but presumably patients without insurance would want to do so as well. These researchers suggested, too, that clinics with a higher number of insured patients had less SET because of more competition from other IVF clinics. Yet research has shown that as competition increases between assisted reproductive technology clinics in a city, higher-order multiple

pregnancies (triplets or more) using non-donor eggs decreases slightly (from 8.43% to 8.24%) (Steiner et al., 2005). Whether competition decreases rates of twins is unknown.

Other factors may thus be involved in patients' opposition to SET. Patients, surveyed in 1999–2000, overestimated rates of premature, low birth weight and death of low-birth neo-nates, yet 68% still felt that a twin pregnancy was desirable. Only 58%, however, remembered being counselled about the risks of multiple births, and the median length of the counselling, they recalled, was only 5 min (Kalra et al., 2003). In a study of college students, persuasive communication strategies and highlighting the risks involved led respondents to prefer SET (van den Akker and Purewal, 2011).

Though some observers have argued that to decrease the rate of twins, insurance coverage for IVF should be increased (Johnston et al., 2015), this proposed policy change may be more likely in countries with a nationalized, single-payer health system (e.g., Belgium), as opposed to a more privatized system, such as in the USA, where several obstacles arise. Infertility, since it does not increase mortality, may be seen as being less of a public health priority than lethal disorders (e.g., cancer and heart disease). In many countries, increasing insurance to cover unlimited fertility treatment for all those who seek it (heterosexual couples, single men and women and same-sex couples) would be extremely costly. Hence, it remains unclear whether sufficient political will exists in many countries to mandate that insurance companies cover IVF for everyone, whether this change will occur, and if so, where, when and by how much. Opponents may argue, too, that multiple births can be avoided easily by physicians simply transferring fewer embryos.

Research is urgently needed to examine factors that shape patients' and physicians' attitudes about the number of embryos transferred, particularly concerning acceptance of using more than one IVF cycle (ASRM, 2012); yet such research remains scant. No further studies of assisted reproductive technology providers' practices or attitudes concerning these issues have been published since Jungheim's 2010 survey, which raised many unexamined questions, for example, why most physicians deviate from guidelines in various situations. Extensive literature searches have found no other studies of how providers view these issues – why they have not fully followed recommendations to transfer fewer embryos, and what challenges, if any, they face.

Crucial questions thus remain of why professional organizations in many countries and many IVF providers continue to allow twin births, despite the risks. How do providers and patients perceive, understand and negotiate these tensions and make these decisions? What do providers do and why? How do they decide what to do when patients prefer twins, do conflicts persist, and if so, how do providers address these? Given that obstacles will be likely to impede significant increases of insurance coverage for assisted reproductive technology in many countries, it is vital to explore these questions, to grasp what other approaches, if any, might help reduce the number of twin births.

Thus, as part of a study of how providers and patients view and make decisions concerning several key aspects of IVF use, these issues were examined.

Materials and methods

In brief, as summarized in [Table 1](#), and described elsewhere ([Klitzman, 2016](#)) 37 in-depth semi-structured interviews of approximately 1 h each were conducted in the USA with 27 assisted reproductive technology providers – 17 physicians and 10 other providers (seven mental health providers, two nurses and one other) – and 10 patients. One physician and three other providers were also themselves patients. Patients and providers were recruited through electronic mailing lists (listservs), direct emails and word of mouth. Providers were also recruited through national ASRM meetings (e.g., preimplantation genetic disorders [PGD] and mental health provider interest group meetings). Attendees were approached to ascertain if they might be interested in participating in an interview study, and if so, information was subsequently emailed to them about it. Most of those asked agreed to participate and did so. A mental-health listserv was used, which is received by approximately 60 members (not all of whom are active), of whom 15 responded, and eight were then interviewed. Additional interviews were conducted as background, for informational purposes, with eight physicians, nine mental health providers and 14 patients, and informed (but were not included in) the final formal data analysis. Interviews for the formal data analyses were conducted with each group until ‘saturation’ was reached (i.e. ‘the point at which no new information or themes are observed in the data’; [Guest et al., 2006](#)). Interviewees were from across the USA.

Interviews explored participants’ views and decisions regarding ethical issues concerning several aspects of assisted reproductive technology, and were systematically analysed to obtain detailed descriptions of these issues. Providers described various patients they had treated, and interactions with colleagues; and patients often described interactions with various providers and other patients. From a theoretical standpoint, [Geertz \(1973\)](#) has advocated studying aspects of individuals’ lives, decisions and social situations not by imposing theoretical structures, but by trying to understand the individuals’ own experiences, drawing on their own words and perspectives to obtain a ‘thick description’. The methodology adapted elements from *Grounded Theory* ([Strauss and Corbin, 1990](#)) and was thus informed by techniques of ‘constant comparison’ with data from different contexts compared for similarities and

differences, to see if they suggest hypotheses. This technique generates new analytic categories and questions, and checks them for reasonableness. These methods have been used in several other studies examining key aspects of health behaviour and doctor-patient relationships and communications in genetics and other areas ([Klitzman, 2012, 2013](#); [Klitzman and Daya, 2005](#); [Klitzman et al., 2007, 2013](#)).

The questionnaire (see [Appendix](#) for sample questions) was drafted, drawing on prior literature. Transcriptions and initial analyses of interviews occurred during the period in which the interviews were being conducted, enhancing validity, and helped shape subsequent interviews. Interviews were conducted via phone. The Columbia University Department of Psychiatry Institutional Review Board approved the study, and all participants gave informed consent.

Once the full set of interviews was completed, subsequent analyses were conducted in two phases, primarily by a trained research assistant and the Principal Investigator. In phase I, they independently examined a subset of interviews to assess factors that shaped participants’ experiences, identifying categories of recurrent themes and issues that were subsequently given codes. The Principal Investigator and research assistant read each interview, systematically coding blocks of text to assign ‘core’ codes or categories (e.g., issues concerning whether and why to transfer more than one embryo, and who decides). While reading the interviews, a topic name (or code) was inserted beside each excerpt of the interview to indicate the themes being discussed. The Principal Investigator and research assistant then worked together to integrate these independently developed coding schemes into a single scheme. Next, they prepared a coding manual, defining each code and examining areas of disagreement until reaching consensus. New themes that did not fit into the original coding framework were discussed, and modifications made in the manual when deemed appropriate.

The research assistant and the Principal Investigator then independently content-analysed the data to identify the principal subcategories and ranges of variation within each of the core codes. The sub-themes identified by each coder were reconciled into a single set of ‘secondary’ codes and an elaborated set of core codes. These codes assess subcategories and other situational and social factors, including subcategories such as the desire to transfer more than one embryo because of lower costs, or a belief that the data on twins having more complications than singletons were not compelling; and decisions being made by patients versus providers versus a committee.

Codes and sub-codes were then used in analysis of all of the interviews. To ensure coding reliability, two coders analysed all interviews. Where necessary, multiple codes were used. Similarities and differences between participants were assessed, examining categories that emerged, ranges of variation within categories and variables that may be involved.

Areas of disagreement were examined through closer analysis until a consensus was reached through discussion. Consistency and accuracy in ratings were checked regularly by comparing earlier and later coded excerpts.

To ensure that the coding schemes established for the core codes and secondary codes were both valid (i.e. well grounded in the data and supportable) and reliable (i.e. consistent in meaning), they were systematically developed

Table 1 Characteristics of interviewees.

	Male	Female	Total
Physicians	14	3	17
Physicians who are also patients	0	1	1
Type of practice			
University affiliated	5	1	6
Private practice	9	2	11
OTHER assisted reproductive technology providers (e.g., mental health providers, nurses)	1	9	10
Other providers who are also patients	0	3	3
Patients	1	9	10
TOTAL	16	21	37

and well-documented. Data were also examined in the context of issues in the literature, posing questions and collecting sufficient details to substantiate points that arose.

Given the ASRM's recommendations that providers develop policies, the scant data that exist on how providers view these issues, and the absence of prior research on key aspects of clinicians' views and practices concerning these issues (e.g., the processes by which they decide how many embryos to transfer), this paper focuses on provider attitudes and practices, rather than those of patients.

Results

Overall, as seen in Fig. 1, providers and patients alike wrestle with issues surrounding the number of embryos to transfer. Although clinics tend to follow ASRM guidelines, these allow a degree of flexibility, and contain ambiguities. Decisions about how many embryos to transfer emerge as dyadic and dynamic, and affected by several factors, fostering differences in whether, how, and with what effectiveness clinicians address these issues with patients.

Given the increasing success rate of IVF and concomitant increase in multiple births, several – but by no means all –

providers have decreased to a certain degree the number of embryos they transfer. Although several clinicians felt that the need to transfer only one embryo, rather than two, was clear ('Even twins are dicey.' [Other provider-patient #10]), in general providers appeared to end up transferring additional embryos, due to both the patients' and the providers' views and goals.

Patients' perspectives as they affect providers' practice

Medical factors: low and uncertain odds of success

Given that the odds of success are uncertain and less than 50%, many prospective parents, especially those who have failed to get pregnant previously, are eager simply to have a baby, and thus ignore or discount the risks involved. One 41-year old patient said:

I never feared multiple pregnancies, because we just wanted a baby. We should have been thinking – but weren't – 'what are we gonna do with two or three?' We thought, 'Whatever it will be, will be.' [Patient #9]

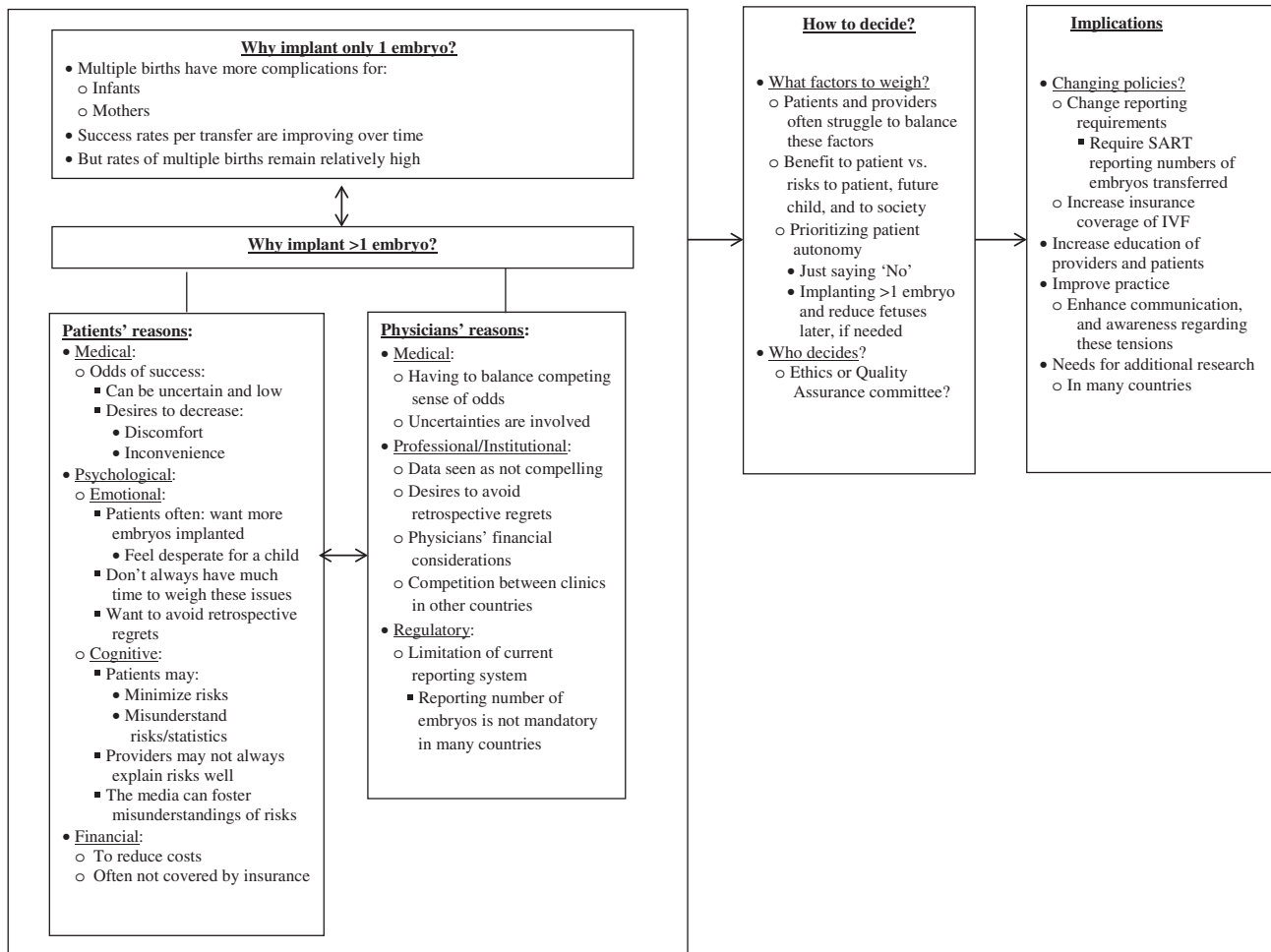


Fig. 1 Issues concerning the number of embryos to implant

Patients often struggle with these questions, aware of the conflicting pros and cons and feel unsure how to proceed. Patients may therefore opt to transfer an additional embryo when a single one might suffice. As one patient said:

I struggled with: Do we put two in because one might not make it? What if both take? What if we put in one and it doesn't work, and we then have to do it all over again? And how do you choose which one to put in? If we do another cycle and have two, I would transfer only one, because I know now for sure that I carry very well. My problem is getting healthy eggs, not necessarily carrying them. If your problem is carrying them, I would be more inclined to put in two. But if this was my first cycle, and we had two, I don't know what we would have done. [Patient #4]

The vagaries involved can make decisions about how many embryos to transfer very difficult for patients.

Questions also arise concerning when providers do and should discuss these issues with patients. Given the uncertainties involved, clinics may not know in advance the number of viable embryos available, and thus offer patients scant time to make these decisions:

Our clinic doesn't actually tell you how many eggs or embryos you have until you are ready to do the transfer. The doctors said they'd call us that morning. But they don't tell us the actual number until we're on the gurney and ready to go. So you don't have time to really think how many you want to put in or freeze. If you have three, is it worth freezing just one, or freezing two in and putting one in? [Patient #4]

Psychological factors

Patients may dismiss, minimize or deny the risks and possible harm to themselves and children born as multiple births, and may seek to rationalize their decisions:

Most patients are pretty much in denial: 'It won't happen to me'. By now everybody should know somebody who's had twins who ended up in a NICU. But they don't care. They think it won't happen to them. [Other provider-patient #9]

Partly, patients may have competing needs, desires, anxieties and stresses. 'Patients are very fickle because they're desperate, looking for magic guarantees.' [Other provider #5]. Consequently, patients may not fully grasp the dangers involved, and focus only on the potential benefit – having a child ('Most women don't understand the risks. A lot of women want to get it over with.' [Other provider-patient #9]). In fact, the statistics are not straightforward, and patients may therefore miscomprehend or be misled by them:

Most people don't understand the statistics. Some patients look at pregnancy statistics as opposed to take-home baby statistics. Statistics can also be moved around. Statistics on live births are inflated by the number of multiple pregnancies. Patients don't really understand the numbers, unless they're a researcher. [Other provider #5]

Misunderstandings partly reflect insufficient education about these complications among patients and the public at large:

40% of women say they would rather have quadruplets than have nothing. Because the public has no idea how devastating prematurity is. In part, the popular press is not reporting the problem of multiple births well. [Physician #10]

Media reports can also promote inaccurate understandings of the odds and dangers involved. Cases such as 'Octomom' can lack important detail and follow-up:

The media isn't quite getting multiple pregnancies. Even with the octuplets, six are doing fine, breathing and having blood pressure. The press doesn't talk about what they're going to look like later. [Physician #10]

Providers may also not necessarily communicate with patients adequately about these risks, because of competing goals. Doctors themselves may want to increase their success rates, and thus not fully inform patients of the potential dangers. As one mental health professional said:

The amount of information given to patients is woefully inadequate. Clinics want to keep up their numbers. Most patients are not informed of the risks of having twins. The only therapy patient I've had who was fully informed of those risks was herself a doctor, and she agonized for a long time about what would happen if both of the transferred embryos took. The field is moving toward SET. But I'm not sure if patients are adequately counselled about the success rate of those treatments. [Other provider-patient #9]

Burdens on patients

Patients may also want twins, rather than two separate pregnancies, to reduce financial as well as physical and psychological stresses and burdens involved with each cycle. Providers are often acutely aware of the financial pressures on patients. 'Patients should have insurance that would help us provide care to everybody. Then, we would have greater ability to do single-embryo transfers.' [Physician #7]. Patients confront both financial and non-financial burdens:

A 35-year-old friend had IVF, and had twins and had to pay 100% out of pocket. If I were in her place, I would be more likely to transfer two. I wouldn't want to have to go through this all over again, and lay out more money. [Patient #4]

Individual patients face not only improved odds of a take-home baby, but lower expenses, which physicians in other areas of medicine, generally covered by insurance, may not normally consider. 'It's hard to argue against people wanting to transfer two because of cost.' [Physician #1]

Physician perspectives

Medical factors

In trying to estimate the odds of success per embryo for any one patient, providers balance several competing sets of

statistics, including their own overall experience and effectiveness with past patients:

When we transfer two, usually only one takes. So we transfer two. We have less than 20% twins. If our rate of twins was higher, we probably would go to SET. Transferring three? Extremely rare. We might consider it on frozen embryos: if the couple has gotten to the end of the frozen ones, and three are left, we'll probably transfer three. If we had a lot of recipients get pregnant with twins, the doctors would feel more comfortable doing single-embryo transfers. [Other provider #7]

Still, questions arise as to what rate of twins would be high enough to prompt SET.

Professional and institutional factors

The data 'aren't compelling'

Importantly, not all providers feel the data are sufficiently compelling regarding the risks involved in multiple births. One physician said about the risks involved when a patient, pregnant with triplets, refuses to reduce the number of fetuses, 'Triplets are a little grey. Quadruplets not grey at all. Twins are really not grey.' [Physician #7].

Concerning a patient who ultimately refused to reduce from three fetuses, this physician added:

If the data were compelling – if she had quadruplets – I'd say, 'You really do need to get this done.' But I think that for triplets, the data are not compelling enough for me to say that. [Physician #7]

Providers may thus weigh their views of the data, especially in the face of strong patient desires to have more than one child. Yet many commentators have strongly disagreed that the evidence is insufficient, given the relatively high rate of complications faced by twins and triplets. Questions thus arise of exactly how compelling the evidence would need to be to alter more providers' practices.

Providers who have seen close-up the physical harm of multiple births may perhaps be more convinced. Providers' concerns may in part reflect their own experiences:

I have seen first-hand what could happen: I know people who went through IVF, and ended up with extremely premature infants in the NICU, born at 25 weeks. Another set of twins are now 15, but one's extremely disabled. [Other provider-patient #9]

Yet physicians who feel that the data are insufficient may consequently mention or discuss these risks with patients, little, if at all:

Some physicians in our programme just tell the patient, 'You have two blastocoels', put back two, and don't even talk to them about one. Maybe twins isn't bad; we're over-exaggerating it. But it's still an admirable goal to try to cut down the amount of twins. [Physician #10]

The marginal increased risks may be low for each individual patient, but become of concern from a broader public health perspective; yet providers may only factor

these larger social costs when they have themselves witnessed or experienced them.

Doctors and patients may also transfer more embryos than needed to avoid later retrospective regret, frustration and anger. 'If we put two in a 37-year-old and she doesn't get pregnant, then you say, 'Maybe I should have put in three instead.' [Physician #11].

Benefits to physicians

Providers may support patients' desires for twins partly because doing so can help doctors with their own success rates or profit, given competition for patients. Physicians may agree to additional embryo transfers in order to increase their published success statistics:

Part of the motivation for some physicians is to get their numbers up of take-home babies per cycle. Other doctors want patients to get pregnant, and know that a slightly better way is to put in two embryos, in spite of all the recent evidence that if you're under 35, one embryo would pretty much work as well as two. [Other provider-patient #9]

Providers may also seek to satisfy and thereby keep their patients, which can further prompt transfer of two or more embryos. 'People are moving toward SET, but not so quickly – it is very competitive. Big money.' [Other provider #5]. One physician transfers just single embryos, but feels able to do so only because of a lack of competition – no other clinic exists within hundreds of miles:

More clinics don't transfer only one – because of competition. The other nearest IVF centre is three or four hours away from us. In contrast, if you have a clinic down the hall, and you say, 'No I'm not going to do that,' patients say, 'Fine,' and go *there*. It's monetarily and competition driven. [Physician #1]

The number of clinics in a particular geographic area may thus affect clinic policies.

Regulatory

Effects of current reporting requirements

Providers may also be very motivated by the need to report success rates per cycle ('It's hard to find a private practitioner who is not intently aware of the statistics.' [Physician # 11]). Many physicians want to improve their statistics; and the current data-reporting rules require that providers list pregnancy rates (but not implantation rates), further motivating transfer of extra embryos:

The reporting system disincentivizes transferring fewer embryos. We look mostly at pregnancy rates, rather than implantation rates. So in many programmes, if a patient doesn't want to put only one embryo back, nobody will argue with them. If the guidelines say one, a lot of patients want to put back two. Doctors say, 'Fine.' But if we were looking at implantation rates rather than pregnancy rates, your implantation rates can be better if you put back one, and you might be a little bit more persuasive with your patients who are trying to decide between one and two. [Physician #10]

Altering reporting requirements can reduce the number of embryos transferred, but significant obstacles can impede such changes:

I've been pushing for change for years. Implantation rates are very down in the depths of the reporting system. I'm kind of radical: you shouldn't report pregnancy rates at all because people are going to look at pregnancy rates because they understand it. If you reported implantation rates without pregnancy rates, they'd have to look at that. You can explain what it is, and they'd be able to judge a programme better, because implantation rate is a better judge. But I don't think that's going to come to be. [Physician #10]

Reporting is in fact optional rather than mandatory for physicians in many other countries, where the doctors do not all list their success rates, perpetuating problems. Concerning the so-called 'Octodoc', for instance, one physician said:

On his success rates page, there are no success rates...He doesn't report SART. He doesn't have to. You can choose not to. Transferring double embryos skews success rate data, but does not necessarily mean that those clinics are more successful. That's double-speak right there. It just means that their patients have a 13%-33% chance of twins versus our 8% of twins. [Physician #9]

In various ways, doctors may also manipulate the data they provide. Physicians felt that to get good rates, some colleagues carefully selected or rejected certain patients, or only treated patients with very high-quality embryos:

A little bit 'icky' are doctors who do minimal IVF stimulations. It's supposed to be minimal stimulation, but I saw a patient who was on about 300 gonadotrophins. He won't do a transfer unless you make a nice blast[ocyst]. So she underwent five stimulations – five egg retrievals for a cumulative of 10 eggs retrieved and she had only one embryo transferred. He's playing with his rates, only transferring high-quality blasts. Other patients don't get a transfer, so he can report that he has a good pregnancy rate per transfer. He tells people what they want to hear. He doesn't talk about the fact that she still had five surgeries and five retrievals! Minimal stimulation is great, but really the risk of IVF is the egg retrieval, not the stimulation. That has a very high 'ick factor' for me because it's a snake-charmer practice: 'You don't want to take drugs? You don't have to take drugs. We can do just as good: Look at our rates!' But, the right answer is somewhere in between the European model of stimulating less and our model of stimulating more. Pregnancy rates in the US are easily 30%, if not 50% better than Europe. Yes, we have more multiples, but that's because we have a much higher implantation rate. [Physician #9]

Providers may also 'game' the statistics and produce twins to improve their reported rates, though still following the guidelines, broadly speaking:

People are choosing patients based on the FSH or their ovarian reserve, cherry-picking the best patients to try to have their best results. So they're transferring more embryos than they should. [Physician #11]

Yet gaming the statistics can produce problems – most egregiously with Octomom:

Octomom was a terrible outcome. To try to improve pregnancy rates, the doctors were putting back more and more embryos, and in one case got burned. [Physician #1]

Clinics may manipulate reported rates in other ways as well – e.g., by having separate, non-reported, 'research' protocols:

We all believe that one particular institution has two protocols, a research protocol, where they put through their high FSH patients, and don't do anyone else with a FSH greater than 10. [Physician #9]

But often, providers are still not entirely sure of these colleagues' practices.

To boost their reported success rates, providers may also select or refuse to treat patients in various ways, and reject certain patients whom other physicians might accept:

Doctors differ somewhat in turning away patients who have a reduced prognosis for pregnancy. We get patients who have been turned away elsewhere for things like elevated FSH. The other provider doesn't want to treat them. I feel, depending on their prognosis, that for patients with a 10% likelihood of pregnancy, as long as they're adequately counselled, treatment may not be unreasonable. [Physician #7]

Questions therefore arise, too, of whether to treat patients with low odds of success, and if so when, in what way and how to decide.

The quality of reported data can also vary widely – the completeness, accuracy and validity of diagnoses or outcomes. Consequently, data from Europe may not always be fully comparable:

The more data you get, the less accurate it is. Those of us who are academic and/or involved with SART are very gung-ho about getting the data, and putting it in appropriately. But a lot of programmes see it as another task to do, and just put in whatever data are the fastest to put in. The more you do that, the more problems you're going to have. You end up with numbers, but they may not be accurate, particularly with diagnosis. How do you diagnose male factor in an IVF cycle? Doctors handle ovulatory factor and endometriosis differently. Or ovarian reserve – half the time people forget that that even exists in the diagnostic codes. So when you start getting too much data, people are not interested in putting the information in; or the numbers are subjective. You get the numbers, but what do they mean? [Physician #10]

Processes of decision-making: how to decide

Prioritizing patient autonomy versus other factors

Clinicians may face conflicts with patients' desires and then have to decide how to proceed. Patients may push to have additional embryos transferred, prompting difficulties or contentious discussions – whether, depending on

the patients' age and prognosis, simply to follow patient autonomy:

In the 'how-many-embryos-to-transfer?' conversation with a 42-year-old who wants six because she gets the math, you say, 'I don't want to do six,' or, 'No, I won't do that.' They say, 'They're my embryos!' I say, 'Well, I have to follow our professional society guidelines and I won't deviate from: no more than five.' [Physician #9]

When patients request additional transfers to increase their odds of success and decrease their out-of-pocket costs, providers may have difficulty weighing the clashing considerations involved. Clinicians vary in whether to yield to these requests, and if so, when:

With our single-embryo transfer policy, we wrestle with the competing ethical areas of patient autonomy versus the physician's social responsibility to do what's right for society. The patient says, 'I want two embryos because I want twins.' You say, 'Well, twins are not a good outcome. They have premature delivery and use up resources more rapidly. It's very expensive, and we can't avoid it.' 'Well, I want them anyway.' [Physician #1]

Providers vary in how they then proceed – whether effectively to let the patient decide, reflecting in part rising patient consumerism:

Who makes those decisions? Doctors used to make all the calls: this is the way we do it. Patients were accepting. Lately, it seems that the patient gets whatever she wants. Doctors throw up their hands and say, 'Well, that's what she wanted.' That's ridiculous! It shouldn't remove the responsibility from the physician. At what point should a physician say, where excessive healthcare costs are involved, 'No, we're not doing that'? Healthcare costs are increasing hugely because of the attitude: we can do it. We get paid to do it. But no one asks *should* we do it. [Physician #1]

Providers frequently see these dilemmas as fundamentally ethical, recognizing underlying tensions of how to balance individual patients' desires against broader health costs to society as a whole. These attitudes may also be changing over time.

Who decides: the physician versus ethics or QA committees?

Physicians face questions of whether they should make these decisions on their own or in conjunction with other professionals. Providers differ, too, in whether they consult with a Quality Assurance (QA) or other type of committee. A physician in a private practice said:

If anything looks exceptional, we bring it to QA for all of us to discuss. Our patients sign a consent form about how many embryos to transfer. It hurts our pregnancy rates, but we don't treat our pregnancy rate. We treat our patients. We are very proud of American pregnancy rates, but we need to get our twin and triplet rates down. If you freeze them and do one, and then another one in another cycle, you're almost as good as if you were to transfer two at one time. [Physician #13]

The type of clinic can shape these decision-making processes. Providers who work within academic medical contexts or hospitals can face additional implicit and explicit pressures:

My hospital had a meeting of the medical executive directors with 500 people, and they had me talk with a maternal-fetal specialist about the impact of IVF on the hospital. I thought it was going to be a lynching. I'm independent, but on staff at the hospital. I'm not there very often; I do outpatient things and am not tied by the hospital or run by them. You'd be amazed at the cost for twins or occasionally triplets. From a cost point of view, you want to have singletons because the complications otherwise are difficult. I have patients who lose twins at 23 weeks. Some complicated twin pregnancies are in bed for six months. It's a risk and a cost issue. I have competitors in my region with pretty terrible records: triplets, quads. [Physician #11]

Hospital environments, in which physicians periodically have to present their work to others outside assisted reproductive technology, can thus act as a form of oversight or social control.

Implications: changing guidelines or policies?

The fact that relatively high rates of both twin and higher-order multiple births continue poses critical questions concerning the need for possible additional guidelines, or for regulations. Competing potential risks and benefits of such additional policies need to be weighed against each other. These clinicians opposed rules (rather than guidelines), or stricter mandates that would diminish their autonomy – stressing that clinical judgment can play an important role in these decisions. 'Unfortunately, some doctors don't exercise appropriate judgment, or follow the guidelines, and act like cowboys and cowgirls, and make the rest of us look bad.' [Physician #7]. This physician acknowledges potential limitations of the approach of simply following patients' autonomy – physicians may not all use their ethical judgment to follow an alternative course. Yet even though providers may not all follow certain guidelines, they tended to oppose more stringent approaches, feeling that current guidelines, rather than tighter regulations, suffice:

The question becomes: What exactly is a guideline? Should doctors be punished for not adhering? Should there be rules, rather than guidelines? No! We're taking care of individual patients. [Physician #7]

Yet, while preferring suggested guidelines – rather than regulations – this doctor nonetheless queries their scope, meaning and implications. A broad continuum exists of levels and types of guidelines, based on several characteristics (e.g., whether violators will be disciplined) and their implementation and enforcement.

Providers may feel that changes to the reporting policies are needed, but will be elusive due to the complex federal bureaucratic structures and processes involved. While changes in reporting requirements may have helped decrease the rates

of births of three or more infants at a time, reduction in the frequency of twins may be harder:

The CDC [Centers for Disease Control], to change, goes through a huge bureaucracy – the OMB [Office of Management and Budget]. So SART says: ‘We don’t want to do it because people will go to the CDC more – because they’ll understand the pregnancy rates better than they’ll understand implantation rates.’ SART is probably going to make changes and push to the top line percentage of retrievals that end up with a single baby, because that’s in there too, but buried. I think there’s some movement to at least push that into the top, which would be almost as good as implantation rates. Because that has to be the incentive. The CDC basically says, ‘We want you to report pregnancy rates and decrease the multiple pregnancy rates,’ but these two goals conflict with each other. It’s very hard to change it. They are very interested, but there is that conflict. They have to push it through. They’re not a free agent, but have to go through the OMB. Eventually, they’re starting to see that that report is not going to minimize the twin deliveries. We’ve done very well minimizing triplets. [Physician #10]

Physicians may therefore also be somewhat ambivalent about maximizing individual patient versus broader public health benefits.

Despite possible needs for improvement in implementation and enforcement of policies, many providers feel that SART is simply limited in its regulatory power, and that the threat of losing one’s membership insufficiently motivates physicians to follow guidelines:

The problem is that the only thing SART has to threaten doctors with is non-membership, which some doctors would probably welcome because then they wouldn’t have to pay or register their results. By law, you’d still have to register with the CDC. But that’s our dilemma: until we can create brand-name recognition that a ‘SART-approved clinic’ is in fact superior, and that clinics don’t become a member simply just by paying dues, no one really cares – there’s not a whole lot of bite in being removed from membership. [Physician #1]

These clinicians generally favour increasing professional self-regulatory mechanisms first, before initiating government regulations:

SART wants to set up guidelines for very stringent monitoring of clinic performance, and ask clinics with poor performance to change, taking steps from there. It should start with self-regulation. There have been improvements over time. If there isn’t continued improvement, it’s time for more regulation – as in Scandinavian and other European countries. [Physician #1]

The threat of government regulation, if models of professional self-regulation fail, could potentially enhance adherence, though it has not yet proven sufficient.

Government regulations could potentially mandate transfer of only one embryo at a time, but given patients’ financial constraints, may face opposition from patients, unless costs are more fully covered. To reduce the incidences of twins and other multiple births, other government

policies, concerning insurance coverage, may also then be needed:

If the government would mandate that insurance companies pay for IVF, I would be the first to say: only do elective SET. I see the result of twins and triplets, and the maternal complications for ovarian stimulation – people hospitalized during an IVF cycle. But patients and doctors are willing to do it, and try to transfer more, and not be so cautious, because the patient is paying for it. Different states have IVF mandates, and I would totally support SET, or support PGD only for medical reasons. [Other provider #1]

Conclusions

These data, the first to explore several critical aspects of how providers view and make decisions about how many embryos to transfer, highlight how professional recommendations and guidelines in this area can contain flexibility and ambiguities, and lack enforcement, raising challenges, tensions and dilemmas that providers and patients therefore confront. While Højgaard et al. (2007) found that Danish patients faced challenges (having to weigh their preferences for twins against risks to the unborn children), the current data shed important added light on why these challenges persist, and examine for the first time how providers and patients respond to these challenges. Specifically, while Højgaard et al. (2007) found that most patients in a Danish clinic preferred DET, the present data suggest that for various reasons, both patients and providers often minimize the risks of twins. Though the previous prior literature has focused largely on limitations in insurance coverage as contributing to high rates of twins, the present data suggest how other, non-economic factors – social, psychological, cognitive, medical, logistical and professional – can play critical roles as well. Though, as found in Denmark, patients may still prefer twins, even in countries that provide insurance, the present data probe how providers and patients then confront and respond to ensuing tensions, given professional recommendations favouring SET.

The present data also suggest possible strategies that have not been previously reported for addressing these problems, and several directions for future research. Specifically, eight findings that have not been presented in the literature have key implications for future research, practice, education and guidelines. Firstly, while the past literature has focused on either patient or provider views and decisions, the present data highlight how these decisions can in fact be highly dyadic and dynamic, involving both providers’ and patients’ attitudes and perceptions concerning the risks.

Secondly, while Jungheim et al. (2010) found that 99% of clinics routinely discuss with patients the number of embryos to transfer, and 37% discuss SET with all patients, the present data suggest how clinicians may in fact vary widely in the quality of these discussions. These data extend and build substantially on prior findings that the median length of time of consulting about these issues with providers was 5 min (Kalra et al., 2003), and that a 10-minute consultation with a nurse did not increase acceptability of SET to patients (Murray et al., 2004). The present data add considerably to the past literature, in suggesting that providers differ considerably in what they actually say, how thoroughly they discuss these issues; whether they communicate the risks

involved, and if so which risks, how effectively and when (e.g., on the day of the transfer versus before). These data suggest that providers may not fully explain or convey these risks, and may even minimize them; and that patients may also then minimize these dangers, or feel that these odds do not apply to them.

Thirdly, while recommendations in certain countries (e.g., the USA) suggest that transferring additional embryos for women who seek them is justified if patients are informed about the risks involved, the present data suggest that patients may commonly misunderstand, minimize or deny these risks. Patients may feel they don't need to worry about these dangers since the odds of each risk occurring is <50% (i.e. 53.3% of twins are not born premature and 61.2% have normal birth weight) (Sazonova et al., 2013). These data suggest that patients may seek rationalizations for why these risks will not apply to them: for example because they exercise and are healthy. Patients in other areas of medicine commonly minimize or deny possible risks to themselves (Rabinowitz and Peirson, 2006), and do so here, too. Yet past research on patients' perceptions of SET have viewed these attitudes as fixed entities, and has not explored the degree to which patients may misunderstand the risks involved in any treatment. Physicians must obtain informed consent, and patients thus need to understand the risks and benefits involved, but the present data suggest that that may not always occur. While Jungheim found that most clinics deviated from guidelines, due to patient requests, the current data suggest that patient requests themselves may vary widely in how informed and firm they are. Therefore, the present data suggest clinicians should not always simply follow patient requests, but instead should ascertain how fully informed and strong these requests are. Guidelines should, arguably, also specify that providers should carefully discuss specific relevant details with patients (e.g., risks, estimated success rates, etc.), and the cumulative odds for at least one of these risks occurring. Studies in other areas of medicine show that patients may benefit most from being told not either absolute or relative rates alone, but rather both, along with proportions (e.g., 'one out of ten,' rather than '10%' of patients) (Lloyd, 2001; Peters et al., 2011).

Fourthly, these data suggest that physicians may fail to follow SET due to not only their views of 'patient autonomy', but due to their belief that the data on the risks faced by twins are 'not compelling', thereby undermining efforts to increase SET. These data also suggest, for the first time, several reasons for these perceptions of the data as insufficient. For any one patient, the odds of success with twins are relatively good (i.e. 50% of twins will be healthy); and individual clinicians may not consider the high costs that hospitals and the health care system as a whole encounter, partly because these providers do not observe or bear these costs. Rather, paediatricians, not reproductive endocrinology and infertility (REI) specialists, are responsible for, and have experienced difficulties in, treating harmful outcomes that twins face, for example in the NICU. Generally, in assessing risks and benefits, individuals tend to have cognitive 'biases due to the retrievability of instances', outweighing their own personal experience of bad events (Tversky and Kahneman, 1974). The risks may thus be easy for REI specialists and prospective patients to discount. The costs generated by these risks also accrue not to these

REI specialists, but to society and the eventual parents. Individual patients may downplay the odds for themselves, and providers may go along with these patients' views and desires, proceeding to fulfil patients' requests and transfer additional embryos, rather than discouraging patients.

Fifthly, these data suggest that providers may at times transfer additional embryos due to their own competing motives and pressures – desires, in many countries, to increase their reported rates of success. Physicians may therefore not always adequately communicate these dangers to patients, and may be biased in arguing that patient autonomy should readily trump all other considerations.

Sixthly, these data suggest that physicians may be over prioritizing patient autonomy and ignoring or undervaluing other ethical considerations – the rights of the unborn child, beneficence toward these future offspring, non-maleficence and social justice. In focusing on patient autonomy, physicians may be downplaying their ethical responsibilities concerning the future child, public health burdens to society as a whole and the need to avoid harm to the mother and future children. Arguably, at a certain point, wider social and public health costs and risks to the mother and future offspring may at times outweigh the autonomy of an individual patient. Dilemmas surface of precisely how much obligation providers have to follow these other principles; yet clinicians should at least seriously consider these other ethical concerns, especially given both potential patient misunderstandings of risks, and possibilities of physicians having conflicting motives.

Seventhly, while research has indicated that providers may differ in how many embryos they transfer, the present data suggest that clinicians also vary in how they make these decisions: whether they do so informally or formally (through an ethics or QA committee that may include not only assisted reproductive technology providers). These data suggest, too, that providers vary in these decisions due to several factors, such as the type of institution in which they work, and their own personal or professional experiences and perceptions of the persuasiveness of the risk data.

Finally, while the prior literature has examined provider and patient views dichotomously as either for or against SET (versus DET), the present data also suggest how providers and patients have difficulties because they in fact wrestle with multiple sets of questions, comparisons and pros and cons, including competing statistics regarding a patient's prior pregnancy success – weighing the relative risks and benefits of SET against not just DET, but against having no baby. Providers and patients may see SET as having advantages over DET, but perceive DET as having advantages over no child – thus focusing only on the outcome (to have a baby) rather than on the risks as well. While SET can produce either one or no baby, DET can yield two, one or zero offspring. Since the patient's overwhelming goal is to avoid zero, DET may seem, on balance, a better bet statistically. Yet patients may misunderstand and/or be unsure how to weigh these multiple comparisons. Thus, provider and patient education should focus on not just SET versus DET, but on these more complex considerations as well, for example DET versus IVF failure.

These findings have several important implications for further practice, policy, education and research. Though a few commentators have suggested increasing insurance coverage, doing so poses challenges: for example, the cost of providing sufficient infertility care to everyone who wants

it may be prohibitive. Rather, these data suggest that several other approaches (e.g., improving provider-patient communication about these complexities) can help. Attention and consensus are also needed on several key questions, such as when a clinic's rate of twins is too high, such that the clinic should change its practices.

The success that a few countries, such as Belgium, have had in lowering rates of twin births appears to result largely from the fact that these countries' national health services cover a substantial part of the cost of IVF, and can therefore more effectively mandate restrictions on its use. Governments can thus forcefully limit numbers of embryos transferred as part of payments. In contrast, in many other countries, where IVF is reimbursed much less or not at all, recommendations to limit the numbers of embryos transferred face additional hurdles, and may have considerably less success. Hence, countries can vary widely in use of SET due to the presence of a single insurance payer. Given competing economic and political priorities that can impede the adoption of such policies, pursuing other potential ways to increase SET use is thus critical.

Professional organizations and/or governments in many countries should consequently develop additional guidelines, and further encourage providers to decrease the number of embryos transferred. For instance, current guidelines in the USA, stating that for patients under 35 years of age 'providers should only transfer a single embryo, and not more than 2 embryos', gives mixed messages, sanctioning transfer of two embryos, and fuelling the continued epidemic of twins and could be changed to state that physicians should 'discourage' DET in healthy young women, for example.

Improvements in clinics' reporting requirements could potentially help. In only 11 of 27 EU countries was public access to data from individual clinics available in 2011 (Kupka et al., 2016). Reporting by clinics was voluntary in 14 EU countries, including Ireland, Spain and the Netherlands in 2006 – the most recent year for which such information is available on the website for the European Society for Human Reproduction and Embryology (ESHRE) (ESHRE, 2009). Increasing public access to individual clinic data, and requiring reporting by clinics may therefore be helpful as well. Professional organizations and/or government agencies could all explicitly collect and publish the success rates of SET versus DET. In many countries, current reporting requirements disincentivize providers from transferring fewer embryos. For instance, between 2005 and 2010, the proportion of cycles that US IVF programmes failed to report increased from 3.3% to 7.4%. Of these clinics, 3.8% performed 50% of these excluded cycles, which totalled 37% of these Centers' entire cycles (Kushnir et al., 2013), and these clinics consequently reported much better pregnancy rates, and increased their share of US assisted reproductive technology cycles by 19.9%. The researchers analysing these data therefore found lessened transparency of reporting, and recommended prospective reporting of each initiated cycle by all clinics. Williams et al. (2015), reviewing subsequent debates about additional data reporting to SART, concluded that several changes are needed: reporting not only all cycle initiations prospectively, but cycle outcomes on an embryo transfer basis, perinatal assisted reproductive technology outcomes, assisted reproductive technology outcomes adjusted for risks (e.g., age, body mass index, duration of

fertility), and clinics' concordance with the ASRM's recommended limits for number of embryos transferred, and increased comprehensibility of these data by patients (Williams et al., 2015). Proponents of SET have emphasized the need for increased insurance coverage for assisted reproductive technology and improved education of patients (Kissin et al., 2015); yet the present data suggest that changing reporting requirements may help as well.

Such alterations in reporting requirements will likely encounter resistance (Gleicher, 2004), but the present data add further support to efforts to expand reporting in these ways, highlighting how current reporting is limited, fuels misunderstanding and may be self-serving. Better, fuller reporting would provide more transparency, and perhaps implicit strategies of 'naming and shaming' non-adherent clinics. Moreover, SART, for instance, currently cautions viewers of its reports that the data should not be used for comparing clinics. Yet for patients, who are eager to find a clinic, the publication of each participating clinic's rates on one site inevitably invites such comparisons. Hence, helping patients to make such comparisons, for example by publishing additional data (such as each clinic's sociodemographic and prior obstetrical or medical data), may be helpful.

These findings also underscore needs to enhance professional, patient and public education about the risks of twins and other multiple births. Patients may think, for instance, that since, on average, only 50% of embryos will succeed, transferring two should lead to a successful pregnancy. Yet many patients will still then end up with twins, while other prospective parents remain childless. Clinicians, especially if they are transferring extra embryos, should proceed with care, and rigorously ensure that patients fully grasp these risks. The data also suggest a need to develop decision-making tools for patients, to help them grasp the relative risks, benefits and costs to them. Given ongoing media reports of celebrities and others having twins, education of journalists about the risks involved can also be beneficial.

These data suggest several avenues for future research. Quantitative studies of patient attitudes have assessed preferences for DET versus SET (Leese and Denton, 2010; Murray et al., 2004), but only one study has explored the strength of those preferences – specifically, examining how desirability of twins on a 1 to 6 scale correlated with recent high, low or medium risk information (Newton et al., 2007) – and no studies have examined patients' understanding, misunderstanding and acceptance or minimization of these risks (i.e. perceptions of how applicable these risks are), or how differences within a couple get negotiated. The present data underscore the need to examine exactly what risks providers convey to patients; how much time clinicians spend doing so, and how effectively; how often patients seeking DET minimize the risks; how often providers using DET feel the risk data about twins are insufficiently compelling; what they feel the risks in fact are; what odds they feel would be compelling enough to switch to SET; and how they weigh these risks against other considerations.

Some providers have begun to use SET with single blastocyst transfer after pre-implantation genetic screening. However, data are lacking on how frequently providers in various countries are adopting this practice. Moreover, for the reasons described here, many patients will presumably still prefer to have twins, rather than singletons.

These data have several potential limitations. The sample size is sufficient for qualitative research designed to elucidate the issues and themes that emerge; however, future studies using larger samples are needed to analyse statistically how various groups may differ (e.g., physicians versus patients). This study was also designed to shed light on the range of providers' and patients' experiences, views and interactions concerning these issues, rather than to quantify the percentages of different types of respondents who adopted each of these attitudes and behaviours. However, future studies can measure the rates at which these phenomena occur in larger samples in multiple countries. As the first data to probe these issues, inter-rater reliability was not calculated statistically; however, future studies, using larger samples can do so. Moreover, these data appear to have a certain face validity, illuminating challenges that many patients and providers confront. These interviewees worked in the USA; yet extensive literature searches indicate a lack of data addressing these questions in other countries, and arguably, similar challenges and tensions exist in many other countries as well. These interviews were also conducted at one point in time. Future studies can thus examine providers' and patients' attitudes and practices in other countries, and whether these shift over time, and if so, how. Yet, enrolment of physicians and other providers is also difficult. Healthcare providers are increasingly difficult to recruit for surveys, as indicated by response rates declining over time (Cho et al., 2013; Cull et al., 2005).

In summary, these data, the first to explore several critical aspects of decisions concerning how many embryos physicians should transfer following IVF, have vital implications for future practice, research, policy and education.

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Appendix A. Sample questions for providers

What challenges do you face in your work as an assisted reproductive technology provider?

How do you address the challenges?

Have you faced challenges concerning the number of embryos to transfer to a patient? If so, when? What was difficult about the situation? What did you do? How did you make these decisions?

How do you view these issues?

How have your patients viewed these issues?

What additional thoughts do you have about these issues?

References

- Balasubramanyam, S., 2010. Knowledge and attitudes of women towards multiple embryo transfer, fetal reduction and multiple pregnancy. *Int. J. Infertility Fetal Med.* 1 (1), 31–34.
- Baruffi, R.L., Mauri, A.L., Petersen, C.G., Nicoletti, A., Pontes, A., Oliveira, J.B., et al., 2009. Single-embryo transfer reduces clinical pregnancy rates and live births in fresh IVF and Intracytoplasmic Sperm Injection (ICSI) cycles: a meta-analysis. *Reprod. Biol. Endocrinol.* 7, 36.
- Canadian Fertility and Andrology Society, 2006. Guidelines for the number of embryos to transfer following in vitro fertilization. *J. Obstet. Gynaecol. Can.* 799–813. <http://sogc.org/wp-content/uploads/2013/01/182E-CPG-Septembre20061>.
- Centers for Disease Control and Prevention, 2013. Assisted Reproductive Technology (ART) Data. http://nccd.cdc.gov/drh_art/rdPage.aspx?rdReport=DRH_ART.ClinicInfo&ClinicId=9999&ShowNational=1 (Accessed June 24, 2016).
- Chambers, G.M., Hoang, V.P., Sullivan, E.A., Chapman, M.G., Ishihara, O., Zegers-Hochschild, F., et al., 2014. The impact of consumer affordability on access to assisted reproductive technologies and embryo transfer practices: an international analysis. *Fertil. Steril.* 101 (1), 191–198. <http://dx.doi.org/10.1016/j.fertnstert.2013.09.005>.
- Cho, Y.I., Johnson, T.P., Vangeest, J.B., 2013. Enhancing surveys of health care professionals: a meta-analysis of techniques to improve response. *Eval. Health Prof.* 36 (3), 382–407.
- Collins, J., 2007. Cost efficiency of reducing multiple births. *Reprod. Biomed. Online* 15 (Suppl. 3), 35–39.
- Cull, W.L., O'Connor, K.G., Sharp, S., Tang, S.F., 2005. Response rates and response bias for 50 surveys of pediatricians. *Health Serv. Res.* 40 (1), 213–226.
- Davidson, C.M., 2010. Octomom and multi-fetal pregnancies: why federal legislation should require insurers to cover in vitro fertilization. *William Mary J. Women Law* 17, 135.
- De Neubourg, D., Peeraer, K., Debrock, S., D'Hooghe, T., 2014. Belgium model of coupling reimbursement of ART costs to restriction in number of embryos transferred. *BMJ* 348g1559. <http://dx.doi.org/10.1136/bmj.g1559> (No abstract available, 2014 Feb 19).
- European Society of Human Reproduction and Embryology, 2009. Comparative Analysis of Medically Assisted Reproduction in the EU: Regulation and Technologies - Final Report. Available at: <https://www.eshre.eu/Guidelines-and-Legal/Legislation-for-MAR-treatments.aspx>. (Accessed: June 29, 2016).
- Geertz, C., 1973. *Interpretation of Cultures: Selected Essays*. Basic Books, New York. https://monoskop.org/images/5/54/Geertz_Clifford_The_Interpretation_of_Cultures_Selected_Essays.pdf.
- Gleicher, N., 2004. Is it time to limit IVF transfers to one embryo? *Contemporary OB/GYN*. <http://contemporaryobgyn.modernmedicine.com/contemporary-obgyn/content/tags/elective-single-embryo-transfer/some-infertility-patients-twins-are-?page=0,0> (Accessed June 24, 2016).
- Gleicher, N., Barad, D., 2009. Twin pregnancy, contrary to consensus, is a desirable outcome in infertility. *Fertil. Steril.* 91 (6), 2426–2431.
- Greenfeld, D.A., Seli, E., 2011. Gay men choosing parenthood through assisted reproduction: medical and psychosocial considerations. *Fertil. Steril.* 95 (1), 225–229.
- Griffin, D., Brown, L., Feinn, R., Jacob, M.C., Scranton, V., Egan, J., et al., 2012. Impact of an educational intervention and insurance coverage on patients' preferences to transfer multiple embryos. *Reprod. Biomed. Online* 25, 204–208.
- Guest, G., Bunce, A., Johnson, L., 2006. How many interviews are enough? An experiment with data saturation and variability. *Field Methods* 18 (1), 59–82.
- Højgaard, A., Ottosen, L.D., Kesmodel, U., Ingerslev, H.J., 2007. Patient attitudes towards twin pregnancies and single embryo transfer – a questionnaire study. *Hum. Reprod.* 22 (10), 2673–2678. <http://humrep.oxfordjournals.org/content/22/10/2673.full.pdf+html>.
- Hope, N., Rombauts, L., 2010. Can an educational DVD improve the acceptability of elective single embryo transfer? A randomized controlled study. *Fertil. Steril.* 94 (2), 489–495.

- Human Fertilization and Embryology Authority (HFEA), 2013. Fertility treatment in 2013: Trends and Figures. Available at: <http://www.hfea.gov.uk/9463.html>. (Accessed October 11, 2016).
- Johnston, J., Gusmano, M.K., Patrizio, P., 2015. Reducing rate of fertility multiples requires policy changes. *JAMA Pediatr.* 169 (3), 287.
- Jungheim, E.S., Ryan, G.L., Levens, E.D., Cunningham, A.F., Macones, G.A., Carson, K.R., et al., 2010. Embryo transfer practices in the United States: a survey of clinics registered with the Society for Assisted Reproductive Technology. *Fertil. Steril.* 94 (4), 1432–1436.
- Kalra, S.K., Milad, M.P., Klock, S.C., Grobman, W.A., 2003. Infertility patients and their partners: differences in the desire for twin gestations. *Obstet. Gynecol.* 102 (1), 152–155.
- Kissin, D.M., Boulet, S.L., Adashi, E.Y., 2015. Yes, elective single-embryo transfer Should be the standard of care. In: Carrell, D.T., Schlegel, P.N., Racowsky, C., Gianaroli, L. (Eds.), *Biennial Review of Infertility*. vol. 4, Part 4. Springer International Publishing, Switzerland, pp. 177–187.
- Klitzman, R., 2012. Institutional review board community members: who are they, what do they do, and whom do they represent? *Acad. Med.* 87 (7), 975–981.
- Klitzman, R., 2013. How good does the science have to be in proposals submitted to institutional review boards? An interview study of institutional review board personnel. *Clin. Trials* 10 (5), 761–766.
- Klitzman, R., 2016. How old is too old? Challenges faced by clinicians concerning age cutoffs for patients undergoing in vitro fertilization. *Fertil. Steril.* 106 (1), 216–224.
- Klitzman, R., Daya, S., 2005. Challenges and changes in spirituality among doctors who become patients. *Soc. Sci. Med.* 61 (11), 2396–2406.
- Klitzman, R., Thorne, D., Williamson, J., Chung, W., Marder, K., 2007. Disclosures of Huntington Disease risk within families: patterns of decision-making and implications. *Am. J. Med. Genet.* 143A (16), 1835–1849.
- Klitzman, R., Appelbaum, P.S., Fyer, A., Martinez, J., Buquez, B., Wynn, J., et al., 2013. Researchers' views on return of incidental genomic research results: qualitative and quantitative findings. *Genet. Med.* 15 (11), 888–895.
- Kulkarni, A.D., Jamieson, D.J., Jones Jr., H.W., Kissin, D.M., Gallo, M.F., Macaluso, M., et al., 2013. Fertility treatments and multiple births in the United States. *N. Engl. J. Med.* 369 (23), 2218–2225.
- Kupka, M.S., D'Hooghe, T., Ferraretti, A.P., de Mouzon, J., Erb, K., Castilla, J.A., et al., 2016. Assisted Reproductive Technology in Europe, 2011: results generated from European registers by ESHRE. *Hum. Reprod.* 31 (2), 233–248. <http://humrep.oxfordjournals.org/content/31/2/233.full.pdf+html>.
- Kushnir, V.A., Vidali, A., Barad, D.H., Gleicher, N., 2013. The status of public reporting of clinical outcomes in assisted reproductive technology. *Fertil. Steril.* 100 (3), 736–741.
- La Sala, G.B., Morini, D., Gizzo, S., Nicoli, A., Palomba, S., 2016. Two consecutive singleton pregnancies versus one twins pregnancy as preferred outcome of in vitro fertilization for mothers and infants: a retrospective case-control study. *Curr. Med. Res. Opin.* 28, 1–6. <http://www.tandfonline.com/doi/pdf/10.1185/03007995.2015.1136602> ([Epub ahead of print]).
- Lawlor, D.A., Nelson, S.M., 2012. Effect of age on decisions about the numbers of embryos to transfer in assisted conception: a prospective study. *Lancet* 379, 521–527.
- Leese, B., Denton, J., 2010. Attitudes towards single embryo transfer, twin and higher order pregnancies in patients undergoing infertility treatment: a review. *Hum. Fertil.* 13 (1). <http://www.tandfonline.com/doi/abs/10.3109/14647270903586364> (Published online 08 Feb 2010).
- Lloyd, A.J., 2001. The extent of patients' understanding of the risk of treatments. *Qual. Health Care* 10 (Suppl. 1), i14–i18. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1765734/pdf/v010p00i14.pdf>.
- Martin, J.R., Bromer, J.G., Sakkas, D., Patrizio, P., 2011. Insurance coverage and in vitro fertilization outcomes: a US perspective. *Fertil. Steril.* 95 (3), 964–969.
- McLernon, D.J., Harrild, K., Bergh, C., Davies, M.J., de Neubourg, D., Dumoulin, J.C., et al., 2010. Clinical effectiveness of elective single versus double embryo transfer: meta-analysis of individual patient data from randomised trials. *BMJ* 341, c6945. <http://dx.doi.org/10.1136/bmj.c6945>.
- Muir, H., 2001. 'World faces 'epidemic' of twins'. *New Scientist*. July 16. <https://www.newscientist.com/article/dn1001-world-faces-epidemic-of-twins/> (Accessed June 24, 2016).
- Murray, S., Shetty, A., Rattray, A., Taylor, V., Bhattacharya, S., 2004. A randomized comparison of alternative methods of information provision on the acceptability of elective single embryo transfer. *Hum. Reprod.* 19 (4), 911–916.
- Newton, C.R., McBride, J., Feyles, V., Tekpetey, F., Power, S., 2007. Factors affecting patients' attitudes toward single- and multiple-embryo transfer. *Fertil. Steril.* 87 (2), 269–278.
- Norman, R.J., 2016. Singular success: ART in Australia and New Zealand. *O&G Magazine* 18 (1), 34–36.
- Osterman, M.J.K., Kochanek, K.D., MacDorman, M.F., Strobino, D.M., Guyer, B., 2015. Annual summary of vital statistics: 2012–2013. *Pediatrics* 135 (6), 1115–1125.
- Peters, E., Hart, P.S., Fraenkel, L., 2011. Informing patients: the influence of numeracy, framing, and format of side effect information on risk perceptions. *Med. Decis. Mak.* 31 (3), 432–436.
- Pison, G., Monden, C., Smits, J., 2015. Twinning rates in developed countries: trends and explanations. *Popul. Dev. Rev.* 41 (4), 629–649.
- Rabinowitz, T., Peirson, R., 2006. 'Nothing is wrong, doctor': understanding and managing denial in patients with cancer. *Cancer Invest.* 24 (1), 68–76.
- SART CORS Clinic Summary Report: All SART Member Clinics, 2016. Available at: https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=0 Accessed June 24.
- Sazonova, A., Källen, K., Thurin-Kjellberg, A., Wennerholm, U.B., Bergh, C., 2013. Neonatal and maternal outcomes comparing women undergoing two in vitro fertilization (IVF) singleton pregnancies and women undergoing one IVF twin pregnancy. *Fertil. Steril.* 99 (3), 731–737.
- Steiner, A.Z., Paulson, R.J., Hartmann, K.E., 2005. Effects of competition among fertility centers on pregnancy and high order multiple gestation rates. *Fertil. Steril.* 83 (5), 1429–1434.
- Stillman, R.J., Richter, K.S., Jones Jr., H.W., 2013. Refuting a misguided campaign against the goal of single-embryo transfer and singleton birth in assisted reproduction. *Hum. Reprod.* 28 (10), 2599–2607. <http://dx.doi.org/10.1093/humrep/det317> (Epub 2013 Jul 30).
- Strauss, A., Corbin, J., 1990. *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. Sage Publications, Newbury Park, CA.
- The Practice Committee of the American Society for Reproductive Medicine, 2012c. Multiple gestation associated with infertility therapy: an American Society for Reproductive Medicine Practice Committee opinion. *Fertil. Steril.* 97 (4), 825–834.
- The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology, 2013c. Criteria for number of embryos to transfer: a committee opinion. *Fertil. Steril.* 99 (1), 44–46.
- Thurin-Kjellberg, A., Carlsson, P., Bergh, C., 2006. Randomized single versus double embryo transfer: Obstetric and paediatric outcome and a cost-effectiveness analysis. *Hum. Reprod.* 21 (1), 210–216.

- Tversky, A., Kahneman, D., 1974. Judgment under uncertainty: heuristics and biases. *Science* 185 (4157), 1124-31.
- van den Akker, O.B., Purewal, S., 2011. Elective single-embryo transfer: Persuasive communication strategies can affect choice in a young British population. *Reprod. Biomed. Online* 23 (7), 838–850.
- Williams, R.S., Doody, K.J., Schattman, G.L., Adashi, E.Y., 2015. Public reporting of assisted reproductive technology outcomes: past, present, and future. *Am. J. Obstet. Gynecol.* 212 (2), 157–162.
- Wølner-Hanssen, P., Rydhstroem, H., 1998. Cost-effectiveness analysis of in-vitro fertilization: estimated costs per successful pregnancy after transfer of one or two embryos. *Hum. Reprod.* 13 (1), 88–94.

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