

# The pros and cons of the requirement by the Society for Assisted Reproductive Technology (SART) for their members who perform in vitro fertilization and related procedures to report their pregnancy rates to the center for disease control

J.H. Check<sup>1,2</sup>

<sup>1</sup>Cooper Medical School of Rowan University, Camden, NJ; <sup>2</sup>Cooper Institute for Reproductive and Hormonal Disorders, P.C., Mt. Laurel, NJ (USA)

## Summary

**Purpose:** To present pros and cons of the requirement of in vitro fertilization (IVF) centers, to record their statistics, and make them public. **Materials and Methods:** Various tricks are presented as to how some IVF centers can “pad” their pregnancy rates. **Results:** Some of these “tricks” include not trying as hard with the patients’ own oocytes but steering them into donor oocyte programs because, though they could eventually get pregnant with their own eggs, it could be at the detriment of the given IVF center’s pregnancy rates, which in turn, could be “bad for business”. **Conclusions:** Published statistics help a patient to choose an experienced center with a good pregnancy rate, but the consumer should not necessarily equate the IVF center with the highest pregnancy rates as the best center for their problem.

**Key words:** Diminished oocyte reserve; Blastocysts transfer; Pre-implantation genetic diagnosis; Embryo stockpiling; Donor oocyte.

## Pros

In vitro fertilization with embryo transfer (IVF-ET) is a very expensive procedure. The obvious new advantage of the availability of pregnancy rates by consumers (i.e., the infertile couple or woman) is to “get the best bang for their buck”. These published statistics can also aid the woman’s gynecologist to make the proper referral recommendation to a woman seeking her gynecologists’ opinion as to which IVF center to consult.

Another benefit of publishing data from a large reporting entity is that the large power advantage from an extremely large data set can help physicians to improve the efficacy of the IVF procedure. For example, we concluded from our own patient population that the technique of performing intracytoplasmic sperm injection (ICSI) can cause a mild decrease in pregnancy rate per embryo transferred [1-4]. Despite these publications there is a good chance that most practicing reproductive endocrinologists would not have read these studies [1-4]. Even if some infertility specialists read these data, they may state that so many studies seem to indicate one conclusion only to be followed by other studies seemingly refuting these claims. Thus, some infertility specialists even reading these publications may not change their policy on “ICSI for everyone” until another study from another IVF center corroborates these

data, or a group of small studies are performed, and the meta-analysis confirms these conclusions, or a large randomized multi-center prospective study corroborates these conclusions. However, because most IVF centers are a member of Society for Assisted Reproductive Technology (SART), and large multi-center studies can be performed, quick data can be accrued to compare pregnancy rates with conventional vs. ICSI method of fertilization for cases not involving obvious male factor. Indeed the data from SART concluded that the use of ICSI can lower the potential of a given embryo to successfully implant, thus confirming our data.

It is much more likely though that the published data from SART, which not only includes individual data, but large conglomerates, would have a far greater influence on the infertility specialist to use conventional insemination rather than ICSI. Many of these IVF centers used the ICSI therapy to prevent the rare failure of fertilization with the new realization that ICSI may lower the chance of a successful outcome. Furthermore, public knowledge could help the infertile couple question the suggested use of ICSI by the infertility specialist, thus saving the couple a considerable amount of money and possibly improving their odds of a pregnancy. Unfortunately, some infertility specialists will perform ICSI to gain more remuneration per IVF-ET cycle, and published data from a large data set

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could allow the consumer to question the wisdom of ICSI vs. conventional oocyte insemination.

## Cons

Though one would like to believe that the sole objective for most physicians is to heal the patient, and their own financial compensation comes in at a distant second or not at all, unfortunately this would be a naïve concept. Total dedication to the patients' needs and not to the physician's needs is not a policy of many physicians.

Reproductive endocrinologists who perform IVF-ET generally receive far more remuneration than their medical endocrinologist colleagues and are in the top salary percentage of all physicians. The high salary is directly related to the generally high price of IVF-ET.

Fierce competition can be a positive thing with all given IVF centers trying their best to use the best equipment, have the best personnel, including the most experienced physicians and embryologists. However, the fact that pregnancy rates become public knowledge can lead to practices that are not always directed toward the best interest for the patient in order to maintain their high pregnancy rates. Below are listed some of the practices by certain IVF-ET centers that are not always in the best interest of patients:

*1) Try to convince patient whose prognosis following IVF-ET is reduced to not try with their own oocytes but, instead, use donated oocytes.*

This policy can apply to women with diminished oocyte reserve or couples that have had several previous failures with IVF-ET. Our patient population desiring IVF are predominantly women who were either denied IVF because of poor prognosis, or women who failed to conceive despite IVF. So the statements that I will be making in this editorial come from a vast personal experience, and frequently includes patients who have first sought help from some of the most well known, and seemingly highly successful, IVF centers.

There have been several previous publications suggesting a very poor prognosis for IVF-ET, even in young women, is diminished oocyte reserve [5-7]. However, it has been made very clear in subsequent publications in major peer reviewed journals that the poor prognosis is mostly related to the use of high dosage FSH stimulation leading to aneuploidy of the embryos (related mostly to creating meiosis II errors from down-regulating FSH receptors to a key molecule important for chromosome separation during meiosis II) [8, 9].

There have been several publications over the years showing that using mild FSH stimulation protocols can provide reasonable pregnancy rates per transfer in women with diminished oocyte reserve though somewhat reduced [10-12]. The younger the women, the less adverse effect of diminished oocyte reserve on pregnancy rates [13].

In an updated study, we found a live delivered pregnancy rate of 42.2% in women aged  $\leq 35$  with normal oocyte reserve but success rates were only about 20%, less at 33.5% in women with diminished oocyte reserve [14]. For women aged 36-39 the live delivered pregnancy rates were 33.0% vs. 22.2% (about 33% less) and for 40-42 more than 50% less (20.9% vs. 9.1%) [14].

Possibly there are some infertility specialists that are not aware that mild stimulation protocols can yield these type of results in women with diminished oocyte reserve. However, it would be naïve to believe that some of these highly sophisticated IVF centers would not be aware that decent but "reduced" pregnancy rates can be achieved in these couples. It thus seems likely that the risk of lowering their highly touted pregnancy rates, which will be recorded and known to referring physicians and patients alike, influences their decisions to deny the woman IVF with their own oocytes and steer them in the direction of donor oocytes. I have personally witnessed women with decreased oocyte reserve denied IVF with their own oocytes for problems that required IVF (e.g., tubal and severe male factor) whose insurance would pay for the IVF as long as her own oocytes were used, but yet were advised that only donor oocytes would work (at a huge expense since the insurance did not pay for donor oocyte program). Many of these women conceived with their own oocytes with IVF in our practice using mild ovarian hyperstimulation [13].

*2) Minimum number of dominant follicles or oocytes so retrieval is cancelled, trick*

Some IVF centers, with the hopeful intention of not actually going through with the ET, will give the woman a chance with IVF with their own oocyte, but convince them it would have to be cancelled if there are not a minimum amount of dominant follicles sufficient for retrieval (I have seen five follicles as a frequent requirement). This way the center keeps the couple in their fold, receives some remuneration for follicular monitoring, does not lower their published pregnancy rates per transfer, and then collects the big financial prize of a lucrative donor oocyte cycle. It should be noted that with women aged  $\leq 39$  with such significant oocyte depletion that only one embryo could be transferred that for the 65% that had a six, seven, or eight cell embryos, the live delivered pregnancy rates were 31%, 25%, and 36.4%, respectively [15].

*3) Grow the embryos to blastocyst stage, trick*

In the aforementioned study of single ET in women with diminished oocyte reserve, those 35% of the women with a four-cell or five-cell embryo had a live delivered pregnancy rate of 3.8% and 9.5%, respectively [15]. Thus, the majority of these women with four- or five-cell embryos would probably not make it to blastocysts stage. Thus, one way to receive remuneration for an IVF cycle, keep the couple still in the fold for donor oocytes, yet not

lower the published pregnancy rates, is to advise taking the embryos to blastocyst stage. Without a transfer there is no decrease in the pregnancy rate per transfer, but this is at the expense of the couple having a markedly reduced, but still possible pregnancy if the transfer was performed on day 3. In fact, the blastocyst transfer can be used to increase pregnancy rates per transfer. This would apply to women, who despite having normal oocyte reserve, have poor quality embryos on day 3. By allowing the embryo to grow to blastocyst, the hope for the IVF center is that none will get to day 5 for transfer. Frequently, when embryos make it to day 5, but are not good expanded blastocysts, the fertility specialist may advise not to transfer the embryo because it will not lead to a pregnancy. Obviously the couple would have nothing to lose to transfer the poor quality embryos (and sometimes successful pregnancy ensues), but with the threat of a reduction in published pregnancy rate per transfer, the fertility specialist will make a decision in the best interest of the IVF center but not the patient.

#### 4. *Stockpile the embryos, trick*

The less oocytes retrieved, the lower the chance of having a good number of high quality day 3 embryos (blastomere number, lack of fragmentation, and symmetry) and thus the lower the chance of pregnancy per transfer. One of the limiting factors in achieving a pregnancy following ET is whether there is a chromosomally normal embryo.

Supposing out of four oocyte retrievals, a normal oocyte was present only in the first retrieval, and there were only two embryos formed. The physician may convince the couple to freeze the embryos and stockpile them and perform another or multiple IVF cycles to attain more embryos. By having more embryos, the given IVF center has better odds that more embryos will allow the development of some higher quality embryos that will lead to a higher pregnancy rate per transfer for that IVF center. However, for the consumer, the couple may have paid for three or four IVF cycles to achieve a pregnancy when the chromosomally normal embryo was in the first IVF cycle. Thus they paid for four cycles when one would have sufficed. Furthermore, the freezing and subsequent thaw of normal embryos may reduce pregnancy rates vs. fresh ET in some IVF centers.

#### 5) *Limit the number of ET cycles.*

Some women seem to have a lower chance of conception with IVF-ET despite the apparent transfer of good quality embryos. These women may eventually conceive but it may take possibly five or six cycles to conceive. However, there may be some who will not conceive. Many IVF centers will refuse to do more IVF cycles after a certain number of failures even if that is the couples' wishes to have more IVF attempts even if the success rate is reduced, but certainly not impossible.

6) *Selecting only chromosomally normal embryos by encouraging pre-implantation genetic diagnosis (PGD) or pre-implantation genetic sampling (PGS).*

The pervading thought had been that by transferring only a chromosomally normal embryo, the pregnancy rates would improve. Unfortunately day 3 embryo biopsies proved detrimental to the embryos and thus negated the benefit of transferring chromosomally normal embryos. Recently, however, the hope is that trophectoderm biopsy will provide minimal damage to the embryo. It remains to be seen whether this proves cost-effective or not. Again, those IVF centers performing this procedure will have the benefit of spuriously higher pregnancy rates by not transferring any embryos if none are normal.

If a good prognosis patient aged  $\leq 35$  has at least a 50% live delivery rate per transfer then these 50% may have paid 4,000 USD more for their IVF cycle by adding PGS. To properly evaluate these newer techniques of trying to identify the best embryos to transfer (and thus improve the statistic of pregnancy rate per transfer), one has to be sure that it is not to the detriment of the pregnancy rate per oocyte retrieval where all embryos are eventually transferred after freezing them. For example, some embryos that could have resulted in a pregnancy had they been transferred on day 3, may not make it to blastocyst stage. It still remains to be seen what, if any, decrease in pregnancy rates may occur from the trophectoderm biopsy when data from many centers are reported. Even if the procedure proves detrimental, by not transferring any aneuploid embryos, a given IVF center may increase the statistics of pregnancy rate per transfer at the patient's financial expense (even if eventually it is shown to reduce a woman's chance of a live delivery from a given oocyte retrieval). One of the IVF centers in our state advertises that they have the highest live delivery pregnancy rates per transfer at 67% in women aged  $\leq 35$ . This is accomplished by having a great deal of experience, the best equipment and personnel, but also this IVF center also practices all of the techniques mentioned above that can spuriously pad the pregnancy rates per transfer.

By comparing our statistics for women  $\leq 35$  with normal oocyte reserve, we show a live delivered pregnancy rate per transfer of only 42.2% [14]. However, we use none of the tricks mentioned above, and in fact, even our group with normal oocyte reserve are generally of poorer prognosis frequently representing women who failed IVF previously or had thin endometria, or made poor quality embryos [14]. However, if one looks at the live delivered pregnancy rate per retrieval, i.e., the pregnancy rate with all of the embryos fresh or frozen transferred (unless pregnancy occurred first), the live delivered pregnancy rate was 67% [14]. These pregnancy rates were achieved "without tricks" in a relatively poor prognosis population.

## Conclusion

There are definite benefits of the requirement of publishing of a given IVF center's statistics. Most importantly, it allows the infertile couple, and the referring physician alike, to determine the expertise and success rate of a given IVF center. However, to make a choice, it is important for the consumer to consider all factors including cost, location, and whether the patient is the right "type of patient" for that IVF center. More importantly the public needs to be aware that some IVF centers will give advice that is more beneficial to the IVF center than the patient. They need to be aware that the quest for publishing higher pregnancy rates, which are good for business, can sometimes influence a given IVF center to render an opinion without giving 100% consideration for the patient's desire. Thus patients receiving an opinion that is not in keeping with their hopes and desires should consider getting a second opinion.

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Corresponding Author:  
J.H. CHECK, M.D., PH.D.  
7447 Old York Road  
Melrose Park, PA 19027 (USA)  
e-mail: laurie@ccivf.com