

# Initial experience with a risk-sharing in vitro fertilization–embryo transfer program with novel features

Jacques P. Stassart, M.D., Romaine B. Bayless, M.D., Colleen L. Casey, M.D., and William R. Phipps, M.D.

Reproductive Medicine and Infertility Associates, Woodbury, Minnesota

**Objective:** To describe outcomes of the first 100 consecutive infertility patients participating in a risk-sharing program with uncomplicated eligibility requirements. The program included the costs of FSH-containing gonadotropin preparations and provided a full payment refund if no birth occurred that resulted in a normal infant surviving to an age of 1 month.

**Design:** Retrospective cohort study.

**Setting:** Private IVF center.

**Patient(s):** Infertility patients <35 years of age, considered to be good autologous oocyte IVF candidates at time of program enrollment.

**Intervention(s):** Retrospective analysis of outcomes of fresh IVF-ET and frozen embryo transfer cycles involving conventional treatment protocols.

**Main Outcome Measure(s):** Cumulative successful pregnancy rate.

**Result(s):** Of the first 100 patients enrolled in the program, 82 have had a delivery of a normal infant surviving to an age of 1 month, and another 6 have undelivered ongoing pregnancies at 20+ weeks. Nine participants completed the program without completing a successful treatment cycle, and another three remain enrolled.

**Conclusion(s):** Infertility patients <35 years of age participating in a risk-sharing program with uncomplicated eligibility requirements are very likely to have a successful pregnancy. Other centers may wish to incorporate some of the described program's features into their own risk-sharing IVF programs. (Fertil Steril® 2010; ■: ■–■. ©2010 by American Society for Reproductive Medicine.)

**Key Words:** Assisted reproductive technology, cumulative live-birth rate, IVF utilization, risk-sharing IVF

Because of their expense, utilization of IVF-ET services is heavily influenced by insurance coverage, both in the United States (1, 2) and other countries (3). In the United States, especially in states without mandated IVF-ET coverage, the combination of high costs and uncertainty about outcome has given rise since the early 1990s to so-called “shared-risk” or “risk-sharing” programs (4). Such programs typically involve a fee substantially higher than that of a single fee-for-service IVF-ET cycle, but if no pregnancy results after a predetermined number of fresh and frozen embryo transfer (FET) cycles, most or all of the fee is returned.

Although many ethicists have concluded that they may ethically expand access to IVF services (5, 6), risk-sharing programs have been criticized as being at least potentially exploitative and misleading (4). Specific concerns raised by critics include the fact that program eligibility may require medically unnecessary pretreatment testing procedures or expensive adjunctive treatments that provide financial benefit to the provider (7). Additionally, risk-sharing programs generally do not include the costs of the medications involved. Thus, a patient completing a program without success may receive a refund but still bear the costs of the medications

involved, the most expensive of which by far are the FSH-containing gonadotropin preparations. Still another criticism has been that providers, given the adverse financial consequences for them of an unsuccessful cycle, may be biased toward overly aggressive ovarian stimulation protocols or the transfer of excessive numbers of embryos, placing the health of the patient and her fetuses at increased risk (7, 8).

Despite the fact that many IVF centers have long offered risk-sharing programs, and one early report (9), we are not aware of any recent reports in the literature describing outcomes of patients participating in such programs. Our center has for many years offered a variety of risk-sharing programs. In the fall of 2006, a new program was launched for patients considered to be good candidates for autologous oocyte IVF-ET, incorporating a novel set of features to address the concerns discussed above. This report describes outcomes for the first 100 consecutive patients enrolled in the program.

## MATERIALS AND METHODS

This retrospective study of the described risk-sharing program's first 100 participants involved secondary use of pre-existing data and was determined by the Chesapeake Institutional Review Board (IRB) to be exempt from IRB oversight.

## General Overview of Program

The program was structured to provide a patient considered to be a good autologous oocyte IVF-ET candidate the option of a full payment refund if, within 12 months of her first treatment cycle, she had failed to conceive a pregnancy that resulted in the birth of a normal infant alive 1 month after delivery. Before a repeat fresh cycle, the program required performance of

Received March 10, 2010; revised May 3, 2010; accepted May 15, 2010.  
J.P.S. has received research funding from and served as a consultant and speaker for Ferring Pharmaceuticals. R.B.B. has nothing to disclose.  
C.L.C. has nothing to disclose. W.R.P. has nothing to disclose.

Funding to initially promote the described program and for institutional review board services was provided by Ferring Pharmaceuticals.

Reprint requests: Jacques P. Stassart, M.D., Reproductive Medicine and Infertility Associates, 2101 Woodwinds Drive, Suite 100, Woodbury, MN 55125 (FAX: 651-222-6050; E-mail: [jstassart@rmia.com](mailto:jstassart@rmia.com)).

FETs of any cryopreserved embryos. The 12-month period could be extended by the program director (J.P.S.) in the event of unforeseen circumstances, such as a late pregnancy complication resulting in no live birth. A participant could exit the program and receive a full refund, for any reason and at any time, unless cryopreserved embryo(s) were available for an FET, in which case charges for services rendered during the cycle in which those embryos were obtained would be deducted from the refund amount. A participant could also be terminated during the program before 12 months at the discretion of the medical director, in which case she would be provided a full refund.

### Program Eligibility Requirements

Eligibility requirements included female age <35 years at time of agreement signing, body mass index >19 and <33 kg/m<sup>2</sup>, a maximal FSH level ≤ 10 IU/L (drawn on cycle day 2 or 3 in cycling women; Immulite 1000 chemiluminescent assay, Siemens Healthcare Diagnostics, Deerfield, IL), no prior unsuccessful IVF-ET cycles, documentation of a normal uterine cavity, performance of corrective surgery for known tubal disease (e.g., proximal tubal cauterization or salpingectomy for hydrosalpinx), and the presence of ≥ 500,000 viable sperm in an ejaculate or donor sperm specimen. Exclusion criteria included a prior poor follicular response to gonadotropins, current cigarette smoking by either partner, the use of medications known to adversely impact on IVF-ET, known chromosomal abnormalities (in either partner), and the need for preimplantation genetic diagnosis. These requirements could be waived on an individualized basis (e.g., in the case of a marginally elevated FSH level but a recent good response to gonadotropins).

### Program Services

The program fee of \$25,000 provided for trial transfer and saline sonohysterogram (performed routinely in the absence of a recent cavity evaluation), all monitoring services, all oocyte retrievals (including anesthesia) and ETs, all embryology services (including intracytoplasmic sperm injection [ICSI], assisted hatching [AHA], and embryo cryopreservation and storage for 12 months), and all FSH-containing gonadotropin preparations, comprising highly purified FSH and hMG (Bravelle and Menopur; Ferring Pharmaceuticals, Parsippany, NJ). At the start of the program, Ferring provided our center with 500 75-U vials of highly purified FSH, but otherwise all FSH preparations were purchased by the center from a mail-order pharmacy before being dispensed to patients. The fee did not cover other medications used in a fresh or FET cycle, such as oral contraceptives, leuprolide acetate, hCG, or estrogen and P preparations, or the cost of donor sperm if required. It also in general did not cover services that might be rendered for treatment-related complications, such as emergency ward services for ovarian hyperstimulation syndrome or postretrieval bleeding, although most patients had insurance coverage for such services.

### Ovarian Stimulation and Patient Procedures

During fresh cycles, participants were treated with individualized ovarian stimulation protocols involving either leuprolide acetate or a GnRH antagonist. When leading follicles reached a mean diameter of 18 mm, hCG was administered, followed 36 hours later by transvaginal oocyte retrieval, conducted under monitored anesthesia that involved propofol, fentanyl, and midazolam, administered by a nurse anesthetist. In general, all mature oocytes were subjected to ICSI and AHA performed according to standard criteria. Embryo transfer was performed on day 3 or 5 after retrieval, and suitable supernumerary embryos were frozen at the blastocyst stage on day 5 or 6. Before a repeat fresh cycle, FETs were performed in cycles involving conventional estrogen/P regimens. In both fresh and FET cycles the number of embryos transferred was based on American Society for Reproductive Medicine guidelines (10, 11).

### Statistical Methods

The modified Wald method was used to calculate 95% confidence interval (CI) values of a proportion. For categorical variables, comparisons among groups based on fresh cycle number or occurrence of a fresh cycle successful

pregnancy were made using Fisher's exact test or  $\chi^2$  test as appropriate, with statistical significance defined as  $P < .05$ .

### RESULTS

The first fresh treatment cycle of the first participant started in December 2006, and that of last of the first 100 consecutive participants in August 2009. Table 1 provides a summary of participant characteristics, which are consistent with their status as good IVF-ET candidates. Four participants, including three in cases that also involved a male factor, had marginally elevated FSH levels (up to 14.0 IU/L) but were accepted into the program because of recent acceptable responses to gonadotropins in non-IVF treatment cycles or other mitigating factors. Before entering the program, 80 of the participants had undergone IUIs in treatment cycles also involving clomiphene citrate, letrozole, and/or FSH-containing gonadotropin preparations.

Table 2 provides an overview of outcomes to date. Overall, as of April 2010, 88% (95% CI, 80%–93%) of the 100 participants have had a pregnancy from treatment considered to be successful for the purpose of this report (i.e., one resulting in a birth of a normal infant alive 30 days after delivery [82 pregnancies], or an ongoing undelivered pregnancy that has progressed beyond 20 weeks' gestation [6 pregnancies]). The live births listed in Table 2 do not include three that were followed by neonatal demise. However, in all three such cases, a delivery of a viable infant ensued, live births that are included in Table 2. One of these cases involved an FET pregnancy that was complicated by severe pre-eclampsia requiring cesarean delivery at 29 weeks and neonatal death at age 4 weeks. This patient's next fresh cycle involved a gestational carrier, a relative who served without financial compensation, with delivery of healthy twins at 35 weeks.

As indicated in Table 2, the cumulative successful pregnancy rate per single fresh cycle start (including immediately ensuing FET pregnancies) did not significantly differ according to cycle number. Overall, the 100 first fresh cycle starts resulted in 60 successful

**TABLE 1**

**Characteristics of program participants (n = 100).**

Characteristic	Value
Age (y) <sup>a</sup>	31.2 ± 3.0
Participants with previous pregnancy	44
Gravidity <sup>b</sup>	1.70 ± 1.47
Parity <sup>b</sup>	0.55 ± 0.73
Participants with no previous pregnancy	56
FSH (IU/L)	7.01 ± 2.03
Duration of infertility (y) <sup>a</sup>	3.33 ± 2.65
Initial infertility diagnosis	
Tubal factor	3
Ovulatory dysfunction	8
Diminished ovarian reserve	1
Endometriosis	5
Male factor	31
Other factor	2
Unknown factor (unexplained infertility)	8
Multiple factors	42
Female only	2
Female and male	40

Note: Values are number or mean ± SD.

<sup>a</sup> At time of first fresh cycle start.

<sup>b</sup> For participants with previous pregnancy only.

Stassart. Risk-sharing IVF-ET. Fertil Steril 2010.

**TABLE 2****Outcomes of program participants.**

Parameter	Fresh cycle number				Total
	1	2	3	4	
Participants starting fresh cycle	100	38	14	1	153
Fresh cycle pregnancies					
Live normal birth without neonatal demise	50	15	7	1	73
Undelivered, ongoing at 20+ wk	1	3	0	0	4
FET pregnancies					
Live normal birth without neonatal demise	8	1	0	0	9
Undelivered, ongoing at 20+ wk	1	1	0	0	2
No successful pregnancy after fresh cycle or ensuing FET(s)	40 (40) <sup>a</sup>	18 (47) <sup>a</sup>	7 (50) <sup>a</sup>	0 <sup>a</sup>	12 <sup>b</sup>

Note: Values in parentheses are percentages.

<sup>a</sup> Includes only participants starting indicated fresh cycle. All differences in the proportions of fresh cycle starts resulting in no successful pregnancy were not significant by Fisher's exact test.

<sup>b</sup> Includes all participants.

Stassart. Risk-sharing IVF-ET. Fertil Steril 2010.

pregnancies (60%), as compared with the subsequent 53 that resulted in 28 successful pregnancies (53%). Of the 88 successful pregnancies, 77 (88%) were a consequence of a fresh cycle, and 11 of an FET. Of the 12 participants whose treatment did not result in a successful pregnancy, 3 remain enrolled in the program, with repeat fresh cycle starts planned. The remaining nine participants have exited the program and received a refund, including two women who conceived without intervention while still enrolled in the program.

Table 3 summarizes data regarding the fresh cycles. There were no complications requiring hospital admission or an emergency ward visit. However, during one cycle no fresh ET was performed because of ovarian hyperstimulation syndrome. Instead, all suitable embryos were frozen at the blastocyst stage, and a single transvaginal ultrasound-guided paracentesis was performed. The only higher-order multiple gestation was a triplet pregnancy, following a day-3 transfer of two embryos, that included a set of

**TABLE 3****Fresh cycle characteristics.**

Parameter	Fresh cycle number				Total
	1	2	3	4	
Participants starting fresh cycle	100	38	14	1	153
Total gonadotropin dose (IU)	2,974 ± 1,033	3,456 ± 1,519	3,048 ± 1,125	4,350	3,109 ± 1,190
Retrievals performed	100	38	14	1	153
Total oocytes retrieved	11.5 ± 5.8	11.1 ± 5.6	12.2 ± 7.2	6	11.4 ± 5.8
Mature oocytes retrieved	8.5 ± 4.7	8.1 ± 4.6	9.6 ± 6.2	5	8.5 ± 4.8
Day-3 fresh ET	56	26	12	0	94
Day-5 fresh ET	39	10	2	1	52
No fresh ET	5	2	0	0	7
No. of embryos transferred					
1	8	5	0	0	13
2	87	27	9	1	124
3	0	4	5	0	9
Clinical pregnancy <sup>a</sup>	58	20	8	1	87
Live normal birth without neonatal demise or undelivered ongoing pregnancy at 20+ wk	51	18	7	1	77
Twin gestation <sup>b</sup>	16 <sup>c</sup>	6	2	1	25 <sup>c</sup>
Higher-order multiple gestation	1 <sup>d</sup>	0	0	0	1 <sup>d</sup>

Note: Values are number or mean ± SD.

<sup>a</sup> Intrauterine pregnancy sac with documented fetal cardiac activity.

<sup>b</sup> Excluding pregnancies with spontaneous "vanishing twin."

<sup>c</sup> Including one set of monozygotic diamniotic twins.

<sup>d</sup> Triplet pregnancy including set of monozygotic diamniotic twins (described in text).

Stassart. Risk-sharing IVF-ET. Fertil Steril 2010.

monozygotic diamniotic twins. This pregnancy was complicated by a severe case of twin-to-twin transfusion syndrome and ultimately resulted in the delivery of two living infants, only one of whom survived.

Figure 1 provides information regarding embryo cryopreservation for all participants and a summary of FET results for those not achieving a successful pregnancy in a fresh cycle. The proportion of fresh cycles with embryos frozen did not differ significantly according to whether a successful pregnancy occurred in the fresh cycle, either for first fresh cycles (29 of 51 [57%] vs. 26 of 49 [53%] for successful vs. unsuccessful, respectively) or for subsequent fresh cycles overall (12 of 26 [46%] vs. 8 of 27 [30%] for successful vs. unsuccessful, respectively). However, the proportion of fresh cycles with embryos frozen was marginally higher for first fresh cycles than for subsequent fresh cycles overall (55 of 100 [55%] vs. 20 of 53 [38%];  $P = 0.042$ ,  $\chi^2$  test).

In no case were cryopreserved embryos thawed without a resulting transfer. Overall, 37 FETs were performed in cases without a previously successful pregnancy, including 16 of a single embryo and 21 of two embryos. These resulted in 13 clinical pregnancies (35% of transfers) and 11 live births (30% of transfers), including two twin pregnancies, one of which was monozygotic diamniotic. Additionally many women with successful fresh cycle pregnancies had frozen embryos, including some who have undergone FETs resulting in ongoing pregnancies (data not shown).

## DISCUSSION

The results we describe suggest that women considered to be good candidates for IVF-ET can be well served by the option of a relatively straightforward risk-sharing program that requires minimal pretreatment testing. Assuming no late pregnancy losses or neonatal deaths in the six undelivered pregnant cases, and no additional pregnancies in the three nonpregnant women still enrolled in the

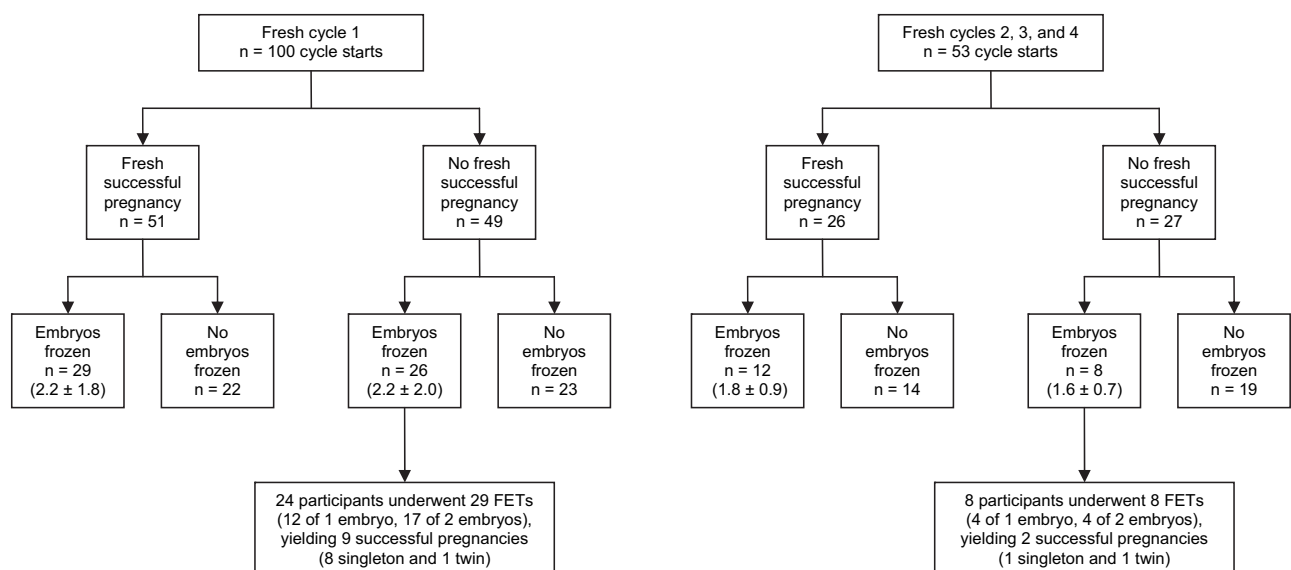
program, 88% (95% CI, 80%–93%) of participants will have had a live birth of a viable infant.

The figure of 88% is a realistic estimate of success for similar infertility patients in general undergoing IVF treatment over time, unlike cumulative pregnancy estimates based on per-cycle rates or life table analyses, which are prone to flawed assumptions regarding dropouts (12, 13). This high proportion is consistent with results of a recent large study from a state with mandated IVF coverage, conducted by Malizia et al. (14), who for patients aged <35 years undergoing up to six cycles found a cumulative live-birth rate of 86% using an “optimistic analysis,” and of 65% using a “conservative analysis.” Because program eligibility criteria were not only age-related, presumably on average our patients were more favorable treatment candidates than the entire group of women aged <35 years described by Malizia et al., but in any event we would agree with their conclusion that “IVF may largely overcome infertility in younger women.” In this regard, increased awareness of the high likelihood of success in such a population might make more acceptable mandated IVF-ET coverage, by which all purchasers of health insurance contribute to costs, at least for such favorable patient populations.

Given the well-documented increased risk for adverse perinatal outcomes in twin as opposed to singleton IVF pregnancies (15), the high proportion of program participants achieving a successful pregnancy perhaps occurred at the cost of what many (16, 17) although not all (18, 19) clinicians would consider to be an unacceptably high twin pregnancy rate. Including the initially ongoing triplet pregnancy that resulted in the birth of live twins as described above, the overall percentage of ongoing twin pregnancies was 32% (28 of 88), similar to the value of 33% for fresh cycles in women aged <35 years reported nationally in 2008 for all Society for Assisted Reproduction Technology member clinics (20). Overall, the mean number of embryos transferred in both fresh and FET cycles was 1.89, because the vast majority of

**FIGURE 1**

Overview of embryo cryopreservation for all participants and of FET results for participants without successful pregnancy during a fresh cycle. For cycles in which embryos were frozen, the mean number ( $\pm$ SD) is given in parentheses.



Stassart. Risk-sharing IVF-ET. Fertil Steril 2010.

participants did not desire an elective single embryo transfer (eSET). To address this issue, and in keeping with the most recent American Society for Reproductive Medicine guidelines (21), we have recently changed our center's protocol for the number of embryos routinely transferred on day 5 of fresh cycles or during blastocyst FETs, to increase the number of eSETs, using an approach similar to that described by Ryan et al. (22). We expect at most this will have only a modest effect on the fresh cycle live-birth rate, potentially offset by additional FET pregnancies.

One advantage of a risk-sharing program may in fact be the ability to persuade more patients to proceed with an eSET. From the perspective of society as a whole, or from that of third-party payers, IVF costs are clearly minimized when eSETs are routinely performed in women aged <35 years, but not from the perspective of patients paying out-of-pocket for IVF services on a fee-for-service basis (23). In contrast, from the standpoint of financial disincentives to proceed with an eSET, risk-sharing IVF patients should closely resemble patients in states with mandated IVF coverage, patients who are more inclined to transfers of fewer embryos in general, given the reported association of mandated coverage and tendencies to both lower numbers of embryos transferred and lower multiple birth rates (2, 24, 25).

A related advantage of risk-sharing programs is their intrinsic emphasis on the cumulative live-birth rate per single fresh cycle start, including births from cryopreserved embryos. Many investigators believe that such a cumulative measure is the best relevant standard of success in IVF (26–28). Risk-sharing programs similarly have as an intrinsic focus the cumulative live-birth rate for participants over the course of multiple treatment cycles, which for most couples considering a course of treatment is the most important endpoint of all (14, 29).

As for specific concerns raised by critics of risk-sharing programs, the program we describe required minimal testing to determine eligibility, and the most expensive component of the testing, an evaluation of the uterine cavity, was included if necessary. There were also no additional charges for potentially expensive services, such as ICSI or AHA, and the stimulation protocols used were no different from those for fee-for-service patients. The program differs from some risk-sharing programs that regard a clinical pregnancy as a successful outcome, and from most risk-sharing programs in that patients not having a successful outcome receive a full refund. These features, although serving to increase the fee charged, have the benefit to the patient of shifting the financial burden to the provider if a successful birth is not achieved. Also of note, although a few other programs now also include medication costs, when first launched in 2006 the program's inclusion of FSH-containing gonadotropins was unique. This inclusion also has the effect of shifting the financial burden away from the patient, not only in ultimately unsuccessful

cases but also in those requiring repeat fresh cycles for a successful outcome. Furthermore, this feature as well may minimize any temptation of providers to use higher-than-needed gonadotropin doses.

The fee of \$25,000 was based on our center's prior experience with patients meeting program eligibility requirements. It was anticipated to provide revenue essentially identical to that generated if all services had been provided on a fee-for-service basis, and corresponded to roughly double the amount borne by patients for a single fresh IVF cycle at our center, factoring in the possibility of ICSI, AHA, and cryopreservation-related procedures. In keeping with this basis, it was increased to \$26,000 in January 2010. For other centers using a similar approach, the fee would vary as a function of center-specific program component costs.

After the described program was introduced, our center continued to offer its other risk-sharing programs, programs more suitable for other patient populations, based on, for example, age or having insurance coverage for monitoring and/or medications. One specific goal of the new program, however, was to provide an incentive for women considered to be good autologous oocyte IVF candidates to undergo treatment sooner than later, with the end result of more desired pregnancies for less total cost.

For most patients, \$25,000 is a large sum of money and does not reflect the entire costs of participation in the program, because some testing done before program participation and medications other than the FSH-containing gonadotropin preparations required out-of-pocket payment if not covered by insurance. We chose not to include other medications in the program primarily because of the administrative complexity. Regardless, out-of-pocket costs were not exorbitant, and \$25,000 is substantially less than what the few studies to date that have addressed the issue have suggested an infertility patient would be willing to pay to become pregnant. One study, for example, found that 150 potential childbearers would be willing to pay \$17,730 for a 10% chance at having a child through IVF in the event of infertility (30).

Our results do not directly address the relative merits of IVF-ET and non-IVF treatment modalities for the group of patients studied. It is possible that especially women whose infertility is unexplained, or on the basis of a mild factor, would be best served by first undergoing treatment modalities involving IUIs, although most of our patients with such diagnoses had done so. Furthermore, two recent studies suggest that for such couples either deleting altogether or minimizing the number of IUI cycles before IVF-ET is preferable from the standpoint of cost-effectiveness (31, 32).

In summary, we describe an uncomplicated risk-sharing program. The program's relative simplicity and the results achieved in our experience are such that other centers may wish to incorporate some of its features into their own risk-sharing IVF programs.

## REFERENCES

- Hammoud AO, Gibson M, Stanford J, White G, Carrell DT, Peterson M. In vitro fertilization availability and utilization in the United States: a study of demographic, social, and economic factors. *Fertil Steril* 2009;91:1630–5.
- Omurtag KR, Styer AK, Session D, Toth TL. Economic implications of insurance coverage for in vitro fertilization in the United States. A review. *J Reprod Med* 2009;54:661–8.
- Chambers GM, Sullivan EA, Ishihara O, Chapman MG, Adamson GD. The economic impact of assisted reproductive technology: a review of selected developed countries. *Fertil Steril* 2009;91:2281–94.
- Ethics Committee of the American Society for Reproductive Medicine. Shared-risk or refund programs in assisted reproduction. *Fertil Steril* 2004;82(Suppl 1):S249–50.
- Robertson JA, Schneyer TJ. Professional self-regulation and shared-risk programs for in vitro fertilization. *J Law Med Ethics* 1997;25:283–91.
- Andereck WS, Thomasma DC, Goldworth A, Kushner T. The ethics of guaranteeing patient outcomes. *Fertil Steril* 1998;70:416–21.
- Scott RT Jr, Silverberg K. Ethics of guaranteeing patient outcomes: a complex issue whose time has not come. *Fertil Steril* 1998;70:422–4.
- Murray TH. Money-back guarantees for IVF: an ethical critique. *J Law Med Ethics* 1997;25:292–4.
- Levy MJ. Panel one: marketing strategies and informing the patient/consumer. A fertility center describes its shared-risk program. *Womens Health Issues* 1997;7:172–6; discussion 86–7.
- Practice Committee of the Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine. Guidelines on the number of embryos transferred. *Fertil Steril* 2004;82:773–4.

11. Practice Committee of the Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine. Guidelines on number of embryos transferred. *Fertil Steril* 2006;86: S51–2.
12. Daya S. Life table (survival) analysis to generate cumulative pregnancy rates in assisted reproduction: are we overestimating our success rates? *Hum Reprod* 2005;20:1135–43.
13. Verhagen TE, Dumoulin JC, Evers JL, Land JA. What is the most accurate estimate of pregnancy rates in IVF dropouts? *Hum Reprod* 2008;23:1793–9.
14. Malizia BA, Hacker MR, Penzias AS. Cumulative live-birth rates after in vitro fertilization. *N Engl J Med* 2009;360:236–43.
15. Boulet SL, Schieve LA, Nannini A, Ferre C, Devine O, Cohen B, et al. Perinatal outcomes of twin births conceived using assisted reproduction technology: a population-based study. *Hum Reprod* 2008;23:1941–8.
16. De Neubourg D, Gerris J. What about the remaining twins since single-embryo transfer? How far can (should) we go? *Hum Reprod* 2006;21:843–6.
17. Karlström PO, Bergh C. Reducing the number of embryos transferred in Sweden-impact on delivery and multiple birth rates. *Hum Reprod* 2007;22: 2202–7.
18. van Wely M, Twisk M, Mol BW, van der Veen F. Is twin pregnancy necessarily an adverse outcome of assisted reproductive technologies? *Hum Reprod* 2006;21:2736–8.
19. Gleicher N, Barad D. Twin pregnancy, contrary to consensus, is a desirable outcome in infertility. *Fertil Steril* 2009;91:2426–31.
20. Society for Assisted Reproductive Society. All SART member clinics, clinic report summary, 2008. Available at: [https://www.sartcorsonline.com/rptCSR\\_PublicMultYear.aspx?ClinicPKID=0](https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=0). Accessed March 8, 2010.
21. Practice Committee of the Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine. Guidelines on number of embryos transferred. *Fertil Steril* 2009;92:1518–9.
22. Ryan GL, Sparks AE, Sipe CS, Syrop CH, Dokras A, Van Voorhis BJ. A mandatory single blastocyst transfer policy with educational campaign in a United States IVF program reduces multiple gestation rates without sacrificing pregnancy rates. *Fertil Steril* 2007;88:354–60.
23. Little SE, Ratcliffe J, Caughey AB. Cost of transferring one through five embryos per in vitro fertilization cycle from various payor perspectives. *Obstet Gynecol* 2006;108:593–601.
24. Reynolds MA, Schieve LA, Jeng G, Peterson HB. Does insurance coverage decrease the risk for multiple births associated with assisted reproductive technology? *Fertil Steril* 2003;80:16–23.
25. Henne MB, Bundorf MK. Insurance mandates and trends in infertility treatments. *Fertil Steril* 2008;89: 66–73.
26. Tiitinen A, Hyden-Granskog C, Gissler M. What is the most relevant standard of success in assisted reproduction?: the value of cryopreservation on cumulative pregnancy rates per single oocyte retrieval should not be forgotten. *Hum Reprod* 2004;19:2439–41.
27. Germond M, Urner F, Chanson A, Primi MP, Wirthner D, Senn A. What is the most relevant standard of success in assisted reproduction?: the cumulated singleton/twin delivery rates per oocyte pick-up: the CUSIDERA and CUTWIDERA. *Hum Reprod* 2004;19:2442–4.
28. Thurin-Kjellberg A, Olivius C, Bergh C. Cumulative live-birth rates in a trial of single-embryo or double-embryo transfer. *N Engl J Med* 2009;361:1812–3.
29. Heijnen EM, Macklon NS, Fauser BC. What is the most relevant standard of success in assisted reproduction? The next step to improving outcomes of IVF: consider the whole treatment. *Hum Reprod* 2004;19:1936–8.
30. Neumann PJ, Johannesson M. The willingness to pay for in vitro fertilization: a pilot study using contingent valuation. *Med Care* 1994;32:686–99.
31. Pashayan N, Lyratzopoulos G, Mathur R. Cost-effectiveness of primary offer of IVF vs. primary offer of IUI followed by IVF (for IUI failures) in couples with unexplained or mild male factor subfertility. *BMC Health Serv Res* 2006;6:80.
32. Reindollar RH, Regan MM, Neumann PJ, Levine BS, Thornton KL, Alper MM, et al. A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial. *Fertil Steril*. In press.