ORIGINAL ARTICLE

Cumulative Live-Birth Rates after In Vitro Fertilization

Beth A. Malizia, M.D., Michele R. Hacker, Sc.D., M.S.P.H., and Alan S. Penzias, M.D.

ABSTRACT

BACKGROUND

Outcomes of in vitro fertilization (IVF) treatment are traditionally reported as pregnancies per IVF cycle. However, a couple's primary concern is the chance of a live birth over an entire treatment course.

METHODS

We estimated cumulative live-birth rates among patients undergoing their first fresh-embryo, nondonor IVF cycle between 2000 and 2005 at one large center. Couples were followed until either discontinuation of treatment or delivery of a live-born infant. Analyses were stratified according to maternal age and performed with the use of both optimistic and conservative methods. Optimistic methods assumed that patients who did not return for subsequent IVF cycles would have the same chance of a pregnancy resulting in a live birth as patients who continued treatment; conservative methods assumed no live births among patients who did not return.

RESULTS

Among 6164 patients undergoing 14,248 cycles, the cumulative live-birth rate after 6 cycles was 72% (95% confidence interval [CI], 70 to 74) with the optimistic analysis and 51% (95% CI, 49 to 52) with the conservative analysis. Among patients who were younger than 35 years of age, the corresponding rates after six cycles were 86% (95% CI, 83 to 88) and 65% (95% CI, 64 to 67). Among patients who were 40 years of age or older, the corresponding rates were 42% (95% CI, 37 to 47) and 23% (95% CI, 21 to 25). The cumulative live-birth rate decreased with increasing age, and the age-stratified curves (<35 vs. ≥40 years) were significantly different from one another ($P<0.001$).

CONCLUSIONS

Our results indicate that IVF may largely overcome infertility in younger women, but it does not reverse the age-dependent decline in fertility.

From Boston IVF, Waltham, MA (B.A.M., A.S.P.); and the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center and Harvard Medical School — both in Boston (B.A.M., M.R.H., A.S.P.). Address reprint requests to Dr. Penzias at Boston IVF, 130 Second Ave., Waltham, MA 02451, or at apenzias@bidmc.harvard.edu.

N Engl J Med 2009;360:236-43.

When a couple presents to a physician for a fertility evaluation and requires in vitro fertilization (IVF), their main question is whether this treatment will result in a baby. The statistic commonly quoted to couples is the outcome per cycle according to maternal age. The primary reason for the frequent use of this cross-sectional statistic is the simplicity with which it can be calculated. The national reporting systems in North America, Europe, the Middle East, Australia, and New Zealand are cross-sectional and list IVF outcomes as pregnancies per cycle. However, this statistic has limited value for individual patients because it does not account for the potential need for multiple IVF cycles and the likely difference in success between the first-time patient and one who did not become pregnant in previous attempts. In contrast to cross-sectional reporting, longitudinal analysis makes use of repeated observations from a cohort over time and provides a better estimate of a woman's history over multiple IVF cycles. The cumulative live-birth rate is used to estimate the outcome of the entire course of treatment.

Studies reported in the literature that estimate the cumulative live-birth rate have many limitations, including small samples[1-8] and inconsistent inclusion criteria and outcome measures. Previous studies have not included IVF cycles that involve the transfer of frozen embryos[1,6,9,10] and have not reported live-birth rates,[7,9] including multiple deliveries,[1,3,5,11] as the primary outcome. Some studies have calculated cumulative success rates over IVF cycles simply by summing the rates from all cycles[2,12,13] or only with the standard Kaplan–Meier method.[14] However, the cumulative live-birth rate may be overestimated with the use of these methods.[1,3,4,7,9]

We conducted this study to provide accurate, evidence-based estimates of the likelihood that a couple presenting for IVF will have a pregnancy resulting in a live birth. We report the cumulative live-birth rates among more than 6000 patients undergoing multiple IVF cycles (both fresh and frozen) in a single large center.

METHODS

PATIENTS

We performed a retrospective cohort study including all patients undergoing their first fresh-embryo, nondonor IVF cycle during the period from 2000 through 2005 at Boston IVF (Waltham, MA). Patients were followed during treatment at our center for at least 1 year until either discontinuation of treatment or delivery of a live infant. The primary outcome was delivery of one or more live infants in up to six IVF cycles. We believe this represents a reasonable range of cycles, since many patients in Massachusetts have insurance benefits for up to six cycles. Furthermore, there is a marked reduction in success after four to six cycles,[1,10] and after six cycles the number of patients treated decreases significantly.

All patients without a live birth in an IVF cycle were eligible for the subsequent cycle, including patients with cancelled cycles and those with a pregnancy that did not result in a live birth. The group that did not return for treatment included women who transferred to another IVF center, used oocyte donation or a gestational carrier, or discontinued treatment for any reason.

The study was approved by the institutional review board at Beth Israel Deaconess Medical Center, and the approval allowed for retrospective chart review and anonymous results reporting without informed consent.

FRESH-EMBRYO TRANSFER

Patients underwent protocols for ovarian stimulation, monitoring, and oocyte retrieval as previously described.[15] Intracytoplasmic sperm injection is the direct injection of sperm into the oocyte to enhance fertilization. Assisted hatching involves the disruption of the zona pellucida before the embryo transfer to potentially enhance implantation.[16] In general, the embryo transfer took place 3 days after the oocyte retrieval. The number of embryos transferred reflected national guidelines, with some variation according to individual patient needs. Cryopreservation was generally performed 3 days after oocyte retrieval and included only embryos that were deemed viable according to morphologic criteria.

FROZEN-EMBRYO TRANSFER

IVF cycles with the use of cryopreserved embryos were performed after priming the uterus with exogenous estradiol (Vivelle-Dot, Novartis, or Estrace, Bristol-Myers Squibb) with or without the downregulation of gonadotropin-releasing hormone. Luteal-phase support with progesterone was provided as it was in fresh-embryo IVF cycles.[15] Thawed embryos were deemed viable for placement if more

Table 1. Characteristics of the 6164 Women at the Start of Cycle 1.*

Characteristic	Value
Age	
Mean — yr	35.8±4.7
<35 yr — no. (%)	2678 (43.4)
35 to <38 yr — no. (%)	1360 (22.1)
38 to <40 yr — no. (%)	836 (13.6)
≥40 yr — no. (%)	1290 (20.9)
Body-mass index†	25.1±4.9
Gravidity — no. (%)	
0	3077 (49.9)
1	1499 (24.3)
≥2	1456 (23.6)
Unknown	132 (2.1)
Parity — no. (%)	
0	4466 (72.5)
1	1137 (18.4)
≥2	334 (5.4)
Unknown	227 (3.7)
FSH, day 3 of menstrual cycle — mIU/liter‡	7.1±3.4

* Plus–minus values are means ±SD. Percentages may not sum to 100 because of rounding.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ The follicle-stimulating hormone (FSH) level on day 3 of the menstrual cycle is a marker of ovarian reserve.

than 50% of the blastomeres and the zona pellucida survived intact. Frozen-embryo–transfer cycles were analyzed as unique treatment events.

DATA COLLECTION

Baseline information included characteristics of the patients and details of each IVF cycle and outcome. Ovarian reserve was assessed by measurement of the follicle-stimulating hormone (FSH) level on day 3 of the menstrual cycle. Pregnancies were confirmed on the basis of increasing levels of β-human chorionic gonadotropin and fetal heartbeat on transvaginal ultrasonography. All pregnancies were followed, and the primary outcome was delivery of one or more live infants, confirmed on the basis of medical records.

STATISTICAL ANALYSIS

All analyses were conducted with the use of SAS software, version 9.1.3 (SAS Institute). The cumulative probability of the first live birth during the study period was estimated with the Kaplan–Meier method, according to the IVF cycle number. When data were stratified, the log-rank test was used to compare survival curves.

We used the Kaplan–Meier method, which censors data for patients who do not return for treatment, to estimate the cumulative live-birth rate and 95% confidence intervals. This method assumes that women who did not return for subsequent IVF cycles had the same chance of a pregnancy resulting in a live birth as those who did return for treatment; we refer to this as the "optimistic" cumulative live-birth rate. Since many women will not return after a poor response to IVF treatment, this method may overestimate the cumulative live-birth rate.[14] Therefore, we also present the "conservative" cumulative live-birth rate, calculated with the assumption that patients who did not return for subsequent IVF treatment had no chance of a pregnancy resulting in a live birth. Our population's cumulative live-birth rate probably lies between these estimates.

To evaluate the potential fertility of women who did not return for treatment, we used a t-test or the Mann–Whitney U test, as appropriate, to compare the characteristics of these women with the characteristics of those who returned for treatment. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

For the Kaplan–Meier analysis of data stratified according to age, cohorts were constructed according to the following maternal age groups at the start of cycle 1: younger than 35 years, 35 to younger than 38 years, 38 to younger than 40 years, and 40 years or older. These age strata are similar to those used by the Centers for Disease Control and Prevention and the Society for Assisted Reproductive Technology.[17]

RESULTS

CHARACTERISTICS OF THE PATIENTS

Our cohort included 6164 patients who underwent a total of 14,248 IVF cycles during the study period. Baseline characteristics of the patients at the start of cycle 1 are summarized in Table 1. Clinical characteristics according to the cycle are shown in Table 2. The patients underwent a maximum of 10 cycles and a mean (±SD) of 2.3±1.5 cycles; however, we limited our analysis to 6 IVF cycles.

Table 2 also shows the percentage of cycles that involved intracytoplasmic sperm injection, assisted

Table 2. Clinical Characteristics According to IVF Cycle.*

Characteristic	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Overall cohort — no./total no. (%)†	6164/6164 (100.0)	3837/4653 (82.5)	2228/3053 (73.0)	1170/1753 (66.7)	573/949 (60.4)	276/474 (58.2)
Type of cycle — %						
Fresh-embryo	100.0	83.2	84.9	86.5	85.9	84.1
ICSI‡	23.4	34.4	36.5	39.4	39.4	44.4
AH‡	2.6	8.2	16.5	30.8	34.6	40.5
Total dose of gonadotropin — IU‡	2762±1497	3447±1738	3595±1736	3821±1808	4047±1840	3735±1974
Peak estradiol level — pg/ml‡	1408±1105	1229±966	1271±1015	1330±1155	1256±1042	1236±1008
Oocytes retrieved — no.‡	9.9±6.2	9.0±5.4	9.4±5.7	9.6±5.9	9.5±5.9	9.5±6.2
Embryos cryopreserved — no.‡	1.3±2.4	0.8±1.8	0.8±1.8	0.8±1.9	0.8±2.1	0.5±1.2
Embryos transferred — no.§	2.3±1.1	2.4±1.2	2.6±1.3	2.7±1.4	2.7±1.5	2.8±1.6

* Plus–minus values are means ±SD. AH denotes assisted hatching of embryos before transfer, and ICSI intracytoplasmic sperm injection. To convert the values for estradiol to picomoles per liter, multiply by 3.671.
† The denominator is the number of women eligible to return for that IVF cycle (the number of women in the previous cycle minus the number of women with a pregnancy resulting in a live birth).
‡ These data were calculated only for fresh-embryo IVF cycles.
§ These data were calculated for all IVF cycles (both fresh-embryo and frozen-embryo cycles).

hatching, and fresh-embryo rather than frozen-embryo transfer. The use of intracytoplasmic sperm injection and assisted hatching increased with subsequent cycles, whereas the percentage of cycles involving frozen-embryo transfer remained stable.

CYCLE OUTCOME

Table 3 shows the number of women undergoing oocyte retrieval and embryo transfer, as well as pregnancy and live-birth rates, among the 6164 women presenting for their first fresh-embryo IVF cycle. The data for subsequent cycles are reported for patients who returned to our center. Table 3 also shows the singleton, twin, and triplet deliveries in our population. Of the 3126 live births in our cohort, 70.9% involved singletons, 27.3% twins, and 1.7% triplets. There were no multiple births beyond triplets in this population. Of the eight patients who had four fetal heartbeats (quadruplets) on the first prenatal ultrasound study, seven delivered twins and one lost the pregnancy.

OVERALL CUMULATIVE LIVE-BIRTH RATE

Figure 1 shows the optimistic and conservative cumulative live-birth rates. After three IVF cycles, the conservative cumulative live-birth rate was 45% (95% confidence interval [CI], 44 to 46) and the optimistic rate was 53% (95% CI, 51 to 54). After six cycles, the conservative and optimistic cumulative live-birth rates were 51% (95% CI, 49 to 52) and 72% (95% CI, 70 to 74), respectively.

CUMULATIVE LIVE-BIRTH RATE ACCORDING TO AGE

The optimistic and conservative cumulative live-birth rates calculated according to maternal age at the start of cycle 1 are shown in Figure 2. Among patients younger than 35 years of age, the optimistic cumulative live-birth rate after six IVF cycles was 86% (95% CI, 83 to 88) and the conservative estimate was 65% (95% CI, 64 to 67). Both the optimistic and conservative cumulative live-birth rates decreased with increasing age, and the age-specific rates were significantly different from one another ($P<0.001$).

PATIENTS WHO DID NOT RETURN FOR TREATMENT

To assess the validity of our estimates, we compared patients who did not return for the next IVF cycle with patients who did. Women who did not return for cycles 2 through 4 tended to have poorer potential for fertility due to their older age, higher levels of FSH on day 3 of the menstrual cycle and higher gonadotropin doses received, lower peak estradiol levels, and fewer oocytes retrieved and embryos frozen, as compared with the women who did return for a subsequent cycle. On average, women who did not return for treatment had had

Table 3. Cycle Outcomes.*

Cycle	No. in Cohort	Patients Who Did Not Return for Treatment†	Oocyte-Retrieval Procedures‡	Embryo-Transfer Procedures‡	Pregnancies‡	Live Births‡	Deliveries§		
							Singleton	Twin	Triplet
		no./total no. (%)				*no. (%)*			
1	6164	NA	5360 (87.0)	4825 (78.3)	2025 (32.9)	1511 (24.5)	1046 (69.2)	439 (29.1)	26 (1.7)
2	3837	816/4653 (17.5)	3450 (89.9)	3142 (81.9)	1115 (29.1)	784 (20.4)	563 (71.8)	207 (26.4)	14 (1.8)
3	2228	825/3053 (27.0)	2019 (90.6)	1839 (82.5)	673 (30.2)	475 (21.3)	343 (72.2)	125 (26.3)	7 (1.5)
4	1170	583/1753 (33.3)	1078 (92.1)	993 (84.9)	337 (28.8)	221 (18.9)	160 (72.4)	55 (24.9)	6 (2.7)
5	573	376/949 (39.6)	527 (92.0)	483 (84.3)	157 (27.4)	99 (17.3)	78 (78.8)	19 (19.2)	2 (2.0)
6	276	198/474 (41.8)	255 (92.4)	235 (85.1)	58 (21.0)	36 (13.0)	27 (75.0)	9 (25.0)	0

* NA denotes not applicable.
† The denominator is the number of women eligible to return for that IVF cycle (calculated as the number of women in the previous cycle minus the number of women with a pregnancy resulting in a live birth).
‡ The denominator is the number of women in the cycle cohort.
§ The denominator is the number of live births in the cycle.

more pregnancies and had more children before their first IVF cycle. For cycles 2, 3, and 4, all these differences were significant ($P<0.05$), with the exception of the FSH level in cycle 4 ($P=0.17$). (See the table in the Supplementary Appendix, available with the full text of this article at NEJM.org.) The population of women who did not return for treatment included patients who pursued treatment with the use of donor oocytes or a gestational carrier. Seven percent of our population proceeded to this form of treatment at our center.

DISCUSSION

The cumulative live-birth rate in our population of more than 6000 patients undergoing up to six cycles of IVF was between 51% and 72%. The higher (optimistic) estimate of the cumulative live-birth rate, which assumed that women who did not return for subsequent IVF cycles had the same chance of a pregnancy resulting in a live birth as those who remained in treatment, was probably an overestimate. Like other investigators, we found that women who did not return for treatment had a poorer prognosis than those who did return.[2,7,18] However, the conservative estimate, which assumed that the live-birth rate in the population of women who did not return for treatment was zero, was probably overly pessimistic. Even with a poorer prognosis, patients may have become pregnant without IVF treatment, at another IVF center, or with the use of donor oocytes, or they may have had a child with a gestational carrier. Thus, the true cumulative live-birth rate in our population was probably between the conservative and optimistic estimates.

There is a natural decline in fertility with age, both in the general population[19] and in the population with decreased fertility,[17] and our age-stratified cumulative live-birth rates decreased with increasing age. Our cumulative live-birth rates among women 39 years of age or younger who were treated with up to six cycles of IVF appeared to be similar to or higher than those reported in the general population[20-22]; this suggests that IVF overcomes infertility in younger women. However, women 40 years of age or older should be informed that IVF does not completely reverse the age-dependent decrease in fertility.

Age is an important factor to consider in counseling women before IVF treatment; however, the available literature is limited to studies that have not reported age[2] or have reported outcomes only for a subgroup of the population.[1,3,4,6,9] In the few studies that report results stratified according to age, the numbers are too small in the subgroups of older women and those with multiple IVF cycles to draw meaningful conclusions.[3,10] In our study, there was a large number of patients in each age group through six IVF cycles, and we report specific cumulative live-birth rates that can be used to counsel patients of any age.

Previous studies have also been limited by small samples,[1-8] the use of pregnancy (rather than live birth) as the primary outcome,[5-7,9,13] and the failure to report multiple births.[1,3,5,11] In addition,

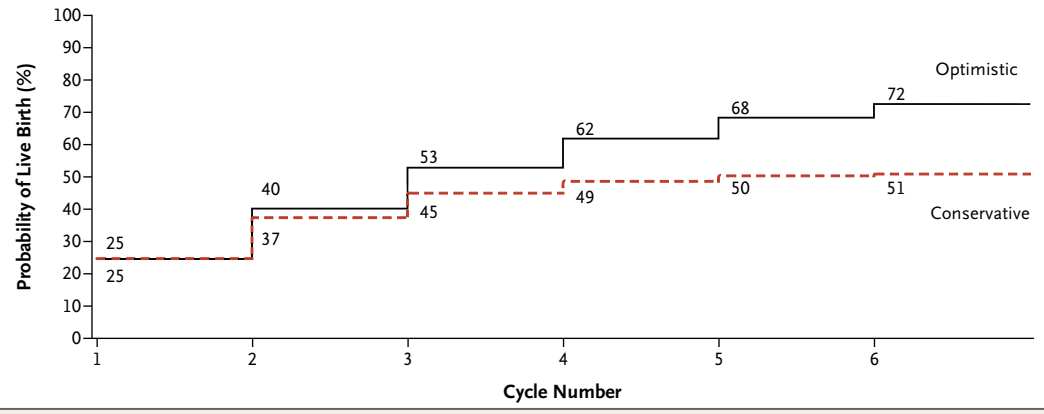

Figure 1. Kaplan–Meier Curves for Optimistic and Conservative Cumulative Live-Birth Rates among 6164 Women.

The optimistic cumulative live-birth rate is based on the assumption that patients who did not return for treatment had the same chance of a pregnancy resulting in a live birth as those who remained in treatment. The conservative cumulative live-birth rate assumes that patients who did not return for treatment did not have a pregnancy resulting in a live birth. These two curves show the best-case and worst-case estimates of the cumulative live-birth rate in the study population.

since some studies have been performed outside the United States, the findings may not reflect the chance of success in a U.S. population.[17,23] The earliest studies to report cumulative live-birth rates were performed more than a decade ago and reflect outcomes before the widespread use of intracytoplasmic sperm injection.[5,11,13,24] The previous studies used life-table analysis to calculate the cumulative live-birth rate without taking into account the possibility that live-birth rates were lower among patients who discontinued treatment than among those who remained in treatment; thus, they probably overestimated this rate.[10,18,24]

Several investigators have sought to account for this potential overestimation.[1,3,7] A recent study[9] reported rates of realized and potential pregnancy; however, the authors did not evaluate live-birth rates and did not include frozen-embryo–transfer cycles. Two studies reported optimistic, realistic, and pessimistic cumulative rates,[3,7] yet neither study defined the patient groups or the estimated pregnancy or live-birth rate used in the analysis. Although we observed that patients who discontinued treatment at our center had a poorer prognosis than those who continued treatment, we lacked information to make valid assumptions about their live-birth rate. We therefore report the optimistic and conservative curves to allow physicians to accurately present the best-case and worst-case cumulative live-birth rates to patients.

Although our focus is cumulative rates, per-cycle comparisons with 2005 national data indicate that the average patient age and percentage of fresh-embryo cycles in our study are similar to the national average, whereas our rates of pregnancy and live births per cycle are slightly lower. Approximately one quarter of IVF deliveries at our center result in twins, and we have a very low percentage of triplet births; our rate of multiple deliveries is lower than both the national average[17] and the results of the study conducted by Witsenburg et al., which, to our knowledge, is the only other study to report multiple cumulative live-birth rates.[2] Our lower pregnancy, live-birth, and multiple-delivery rates per cycle may have been influenced by insurance coverage for infertility care in Massachusetts; this coverage encourages the transfer of fewer embryos.[25,26] The number of embryos transferred has decreased both over the period of our study and since the 2005 national statistics were published.[12,25] Furthermore, single-embryo transfer, highlighted in the most recent national guidelines,[27] may reduce the rate of multiple live births without compromising the cumulative live-birth rate when consecutive fresh and frozen single-embryo transfer is used.[28]

Previous studies have either excluded frozen-embryo–transfer cycles from the cumulative live-birth rate[1,6,9,10] or included the outcome with the corresponding fresh-embryo cycle.[2,3] With advances in embryo cryopreservation, live-birth rates associated with frozen-embryo cycles have nearly doubled over the past decade.[17] Although a frozen-embryo–transfer cycle does not involve intensive

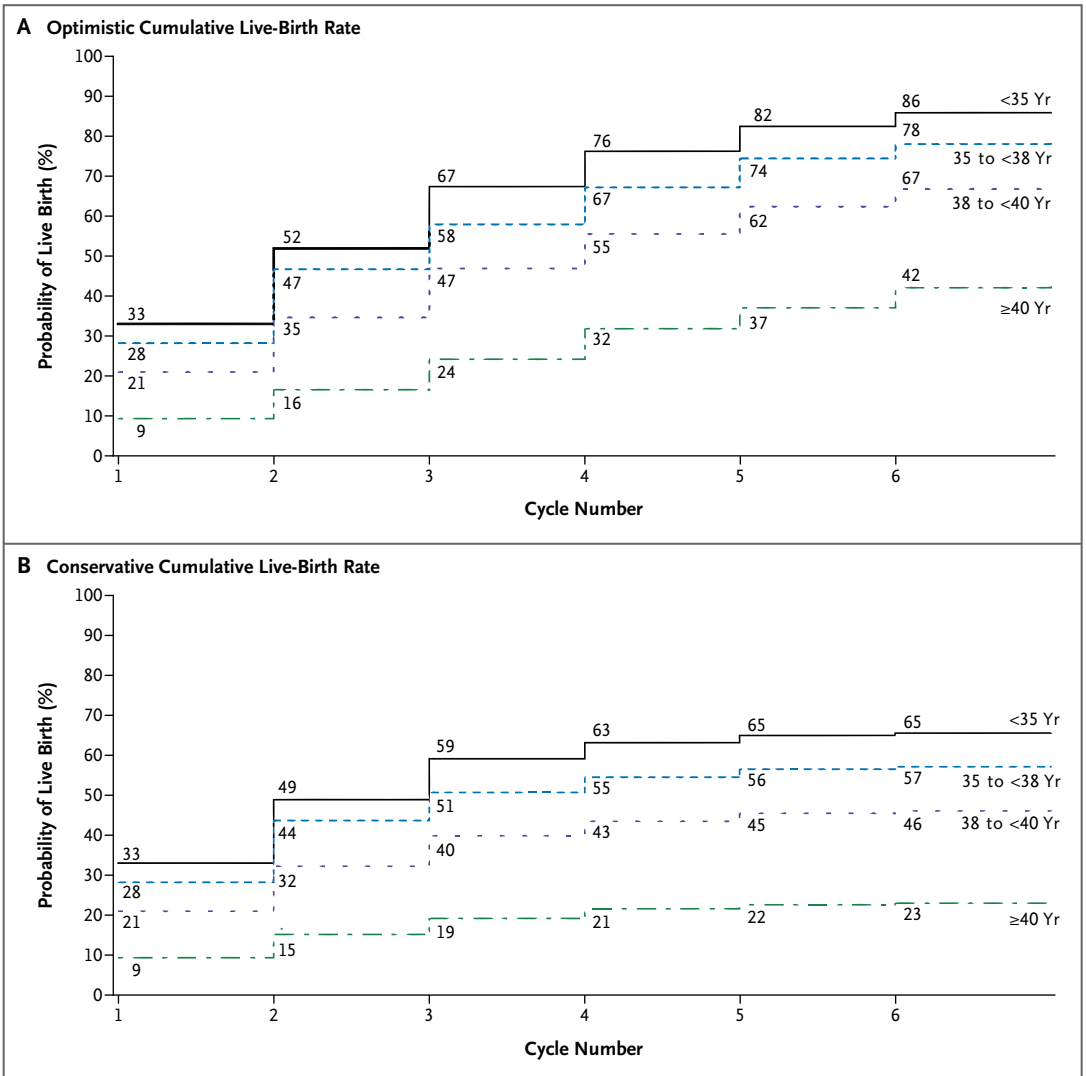

Figure 2. Cumulative Live-Birth Rates Stratified According to Maternal Age at the Start of Cycle 1.

Panel A shows the optimistic cumulative live-birth rates stratified according to age. These rates are based on the assumption that patients who did not return for treatment had the same chance of a pregnancy resulting in a live birth as those who remained in treatment. Panel B shows the conservative cumulative live-birth rates stratified according to age. These rates are based on the assumption that patients who did not return for subsequent IVF cycles had no chance of a pregnancy resulting in a live birth. In both panels, the age-stratified curves are significantly different from one another (P<0.001). These optimistic and conservative rates reflect the best-case and worst-case estimates, respectively, of the cumulative live-birth rate for each age group in the population.

hormonal treatment or oocyte retrieval, as in a fresh-embryo IVF cycle, it still involves a substantial commitment from the patient's perspective. Therefore, frozen-embryo–transfer cycles warrant inclusion as well as separate consideration in estimating cumulative live-birth rates.

Among the women who did not become pregnant or who had a pregnancy that did not result in a live birth, less than 10% returned to our center for six IVF cycles. This rate is similar to the high dropout rate reported elsewhere[1,6] and highlights the physical, emotional, and financial strain of IVF.[2,3,18] Financial constraints were probably mitigated in our study, since it was performed in Massachusetts, where most patients with health insurance have fertility benefits.[29] In states with full insurance coverage of infertility treatment, as in Massachusetts, the use of IVF is greater than it is in states without such coverage.[26] Our results may more accurately reflect the potential effec-

tiveness of IVF treatment for patients whose decisions are influenced by factors other than financial limitations.

We did not classify patients according to the cause or causes of infertility; however, other studies have shown that the cumulative live-birth rate does not vary substantively with the indication for IVF.[2,3,7] We also did not exclude women on the basis of age, results of ovarian-reserve testing, or other prognostic factors. The inclusion of all patients presenting for their first IVF cycle and undergoing all combinations of treatment increases the generalizability of our results.

Our goal was to calculate a meaningful cumulative live-birth rate to answer a couple's primary question — what is the chance that IVF will result in a baby? These age-specific optimistic and conservative cumulative live-birth rates can facilitate individualized counseling in a large population of patients considering IVF treatment.

Dr. Malizia reports receiving an educational grant from Ferring Pharmaceuticals for work unrelated to this study, and Dr. Penzias, receiving consulting and lecture fees and grant support (to Boston IVF) from Ferring Pharmaceuticals and grant support (to Boston IVF) from EMD Serono, Organon, and Repromedix. No other potential conflict of interest relevant to this article was reported.

We thank Benjamin B. Taylor, M.D., M.P.H., for his assistance with revisions of an earlier version of the manuscript, Emily B. Levitan, Sc.D., for her statistical review, and the many nurses, assistants, scientists, and physicians at Boston IVF for their care of the patients in this study.

REFERENCES

1. Elizur SE, Lerner-Geva L, Levron J, Shulman A, Bider D, Dor J. Cumulative live birth rate following in vitro fertilization: study of 5,310 cycles. Gynecol Endocrinol 2006;22:25-30.
2. Witsenburg C, Dieben S, Van der Westerlaken L, Verburg H, Naaktgeboren N. Cumulative live birth rates in cohorts of patients treated with in vitro fertilization or intracytoplasmic sperm injection. Fertil Steril 2005;84:99-107.
3. Olivius K, Friden B, Lundin K, Bergh C. Cumulative probability of live birth after three in vitro fertilization/intracytoplasmic sperm injection cycles. Fertil Steril 2002; 77:505-10.
4. van Disseldorp J, Eijkemans MJ, Klinkert ER, te Velde ER, Fauser BC, Broekmans FJ. Cumulative live birth rates following IVF in 41- to 43-year-old women presenting with favourable ovarian reserve characteristics. Reprod Biomed Online 2007;14:455-63.
5. Engmann L, Maconochie N, Bekir JS, Jacobs HS, Tan SL. Cumulative probability of clinical pregnancy and live birth after a multiple cycle IVF package: a more realistic assessment of overall and age-specific success rates? Br J Obstet Gynaecol 1999; 106:165-70.
6. Klipstein S, Regan M, Ryley DA, Goldman MB, Alper MM, Reindollar RH. One last chance for pregnancy: a review of 2,705 in vitro fertilization cycles initiated in women age 40 years and above. Fertil Steril 2005;84:435-45.
7. Stolwijk AM, Wetzels AM, Braat DD. Cumulative probability of achieving an ongoing pregnancy after in-vitro fertilization and intracytoplasmic sperm injection according to a woman's age, subfertility diagnosis and primary or secondary subfertility. Hum Reprod 2000;15:203-9.
8. Hull MG, Eddowes HA, Fahy U, et al. Expectations of assisted conception for infertility. BMJ 1992;304:1465-9.
9. Lintsen AM, Eijkemans MJ, Hunault CC, et al. Predicting ongoing pregnancy chances after IVF and ICSI: a national prospective study. Hum Reprod 2007;22: 2455-62.
10. Fukuda J, Kumagai J, Kodama H, Murata M, Kawamura K, Tanaka T. Upper limit of the number of IVF-ET treatment cycles in different age groups, predicted by cumulative take-home baby rate. Acta Obstet Gynecol Scand 2001;80:71-3.
11. Tan SL, Maconochie N, Doyle P, et al. Cumulative conception and live-birth rates after in vitro fertilization with and without the use of long, short, and ultrashort regimens of the gonadotropin-releasing hormone agonist buserelin. Am J Obstet Gynecol 1994;171:513-20.
12. Dickey RP, Taylor SN, Lu PY, Sartor BM, Rye PH, Pyrzak R. Effect of diagnosis, age, sperm quality, and number of preovulatory follicles on the outcome of multiple cycles of clomiphene citrate-intrauterine insemination. Fertil Steril 2002;78:1088-95.
13. Guzick DS, Wilkes C, Jones HW Jr. Cumulative pregnancy rates for in vitro fertilization. Fertil Steril 1986;46:663-7.
14. Bland JM, Altman DG. Survival probabilities (the Kaplan-Meier method). BMJ 1998;317:1572.
15. Eaton JL, Hacker MR, Harris D, Thornton KL, Penzias AS. Assessment of day-3 morphology and euploidy for individual chromosomes in embryos that develop to the blastocyst stage. Fertil Steril 2008 April 26 (Epub ahead of print).
16. Seif MM, Edi-Osagie EC, Farquhar C, Hooper L, Blake D, McGinlay P. Assisted hatching on assisted conception (IVF & ICSI). Cochrane Database Syst Rev 2006;1: CD001894.
17. American Society for Reproductive Medicine, Society for Assisted Reproductive Technology. 2005 Assisted reproductive technology success rates: national summary and fertility clinic reports. Atlanta: Centers for Disease Control and Prevention, 2007.
18. Land JA, Courtar DA, Evers JL. Patient dropout in an assisted reproductive technology program: implications for pregnancy rates. Fertil Steril 1997;68:278-81.
19. Tietze C. Reproductive span and rate of reproduction among Hutterite women. Fertil Steril 1957;8:89-97.
20. Guttmacher AF. Factors affecting normal expectancy of conception. JAMA 1956; 161:855-60.
21. Zinaman MJ, Clegg ED, Brown CC, O'Connor J, Selevan SG. Estimates of human fertility and pregnancy loss. Fertil Steril 1996;65:503-9.
22. Gnoth C, Godehardt D, Godehardt E, Frank-Herrmann P, Freundl G. Time to pregnancy: results of the German prospective study and impact on the management of infertility. Hum Reprod 2003;18: 1959-66.
23. Andersen AN, Goossens V, Ferraretti AP, et al. Assisted reproductive technology in Europe, 2004: results generated from European registers by ESHRE. Hum Reprod 2008;23:756-71.
24. Tan SL, Royston P, Campbell S, et al. Cumulative conception and livebirth rates after in-vitro fertilisation. Lancet 1992;339: 1390-4.
25. Stern JE, Cedars MI, Jain T, et al. Assisted reproductive technology practice patterns and the impact of embryo transfer guidelines in the United States. Fertil Steril 2007;88:275-82.
26. Jain T, Harlow BL, Hornstein MD. Insurance coverage and outcomes of in vitro fertilization. N Engl J Med 2002;347:661-6.
27. Guidelines on number of embryos transferred. Fertil Steril 2006;86:5 Suppl: S51-S52.
28. Pandian Z, Templeton A, Serour G, Bhattacharya S. Number of embryos for transfer after IVF and ICSI: a Cochrane review. Hum Reprod 2005;20:2681-7.
29. Jain T, Hornstein MD. Disparities in access to infertility services in a state with mandated insurance coverage. Fertil Steril 2005;84:221-3.