

Cumulative live birth rates over multiple complete cycles of in vitro fertilisation cycles: ten-year cohort study of 20687 women following freeze-all strategy

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Abstract

Background

For patients embarking on in vitro fertilization (IVF) or Intracytoplasmic sperm injection (ICSI), one of the most concerned problems is their chance of a live-birth. The cumulative live birth rate (CLBR) after IVF has been reported in recent years; however these studies were all about conventional IVF strategy, the CLBRs following freeze-all strategy has not been reported.

Methods

This was a retrospective cohort study. A total of 20687 women undergoing their first and following IVF cycles during the period from January 1, 2007 through March 31, 2016 were included in this study. The primary Outcomes of the present study were presented in three types: the live birth rate per complete cycle, the conservative CLBR and the optimal CLBR.

Results

The CLBR increased from 50.74% for the first complete cycle to 64.41% after seven complete cycles, and varied by age category. The CLBR after five complete cycles declined from 77.11% for women younger than 31 years, to 8.63% for women older than 40 years. The predictors of live birth over multiple complete cycles for patients embarking on IVF following freeze-all strategy were women's age and causes of infertility. In the model constructed for patients finishing the first complete cycle, the number of oocyte retrieved at complete cycle one also played an important predictive role.

Conclusions

Among women undergoing IVF following freeze-all strategy, the CLBR after seven complete IVF cycles was 84.77% if there were no barriers to continue the IVF treatment, with variation by age. Two prediction models were developed to estimate their probability of having a baby over multiple complete IVF cycles with freeze-all strategy among patients before starting IVF and patients after the first complete cycle, which is critical for patients to make treatment decisions and preparations physically, emotionally and financially.

Background

Around the world, infertility and sterility will be the third most common disease after cancer and cardiovascular diseases in this century. The World Health Organization estimates 48.5 million couples worldwide are unable to have a live birth, whilst in China; one in eight couples suffer from infertility [1].

Most couples with continued unsolved fertility problems eventually choose in vitro fertilization (IVF) treatment, and one hundred thousand people are born as a result of IVF every year in China.

For patients embarking on IVF or Intracytoplasmic sperm injection (ICSI), one of the most concerned problems is their chance of a live-birth. The probability of success with IVF has traditionally been reported as the live birth rate per cycle, because of the simple calculation based on the cross-sectional statistic. However, this measure provides limited information for patients with a number of complete cycles, considering the difference in success between the patient in the first cycle and one who start a new cycle after failure in previous cycles. The cumulative live birth rate (CLBR) after IVF has been reported in many large national studies in recent years, which dealt with discontinuation of IVF by reporting the optimal cumulative live birth rate and the conservative cumulative live birth rate [2–4]. The rates estimated the cumulative probability of success per patient after one or more complete cycles of IVF treatment, which could be used in the counseling of patients about IVF treatment. Malizia et al. reported the CLBR after 6 cycles was 72% with the optimistic analysis and 51% with the conservative analysis among 6164 patients between 2000 and 2005 at one large center in Boston [2]. A prospective study conducting among 156947 UK women between 2003 and 2010 showed six cycles achieved CLBRs of 78.0% and 46.8% for the optimal and conservative estimates, respectively [4]. A retrospective study included 12869 patients who were registered in the Belgian national assisted reproductive technology (ART) registry between 2009 and 2011 revealed the optimal and conservative estimates of CLBRs after six cycles were 76.3% and 54.1% [5]. However, these studies were all about conventional IVF strategy, the CLBRs following freeze-all strategy has not been reported.

In recent years, the freeze-all strategy where all embryos are cryopreserved, and the frozen-thawed embryos are transferred in subsequent cycles, has been increasingly popular in ART practice [6–8]. The reasons for adopting this strategy are to eliminate the risk of ovarian hyperstimulation syndrome (OHSS), to increase pregnancy rates and live birth rates [9, 10]. With freeze-all strategy, patients can avoid exposure to the supraphysiological hormonal levels following controlled ovarian stimulation (COS), which can have detrimental effects on embryos and endometrium. In the previous study, we have reported the chance of having a child after the first complete IVF cycle was 50.74% with the freeze-all strategy [11]. According to this proportion, many patients have to undergo multiple complete cycles of IVF in order to have their first baby. For these patients, the CLBRs over multiple complete cycles is more meaningful, as they can make decisions about further treatment and preparations emotionally and financially. So in this study, we evaluated the CLBRs over multiple complete cycles of IVF based on data from 20687 patients following freeze-all strategy. In addition, as CLBRs could be affected by patients' age, infertility type, causes of infertility, and number of eggs collected, we developed a prediction model to estimate the chance of having a live birth over multiple complete cycles of IVF based on patient's characteristics and treatment characteristics at complete cycle one.

Methods

Study population

The study protocol was approved by the Ethics Committee (Institutional Review Board) of Shanghai Ninth People's Hospital affiliated to Jiao tong University School of Medicine.

The data used in this study was from the IVF database, which included all records about IVF treatments and outcomes in patients undergoing IVF treatments since 2007[11]. Details about the data collection method in this database have been described in our previous study [12]. In the database, the clinical outcomes of IVF were presented via a patient-anchored approach with all complete cycles were attached to the patient receiving IVF treatment. Records of all complete IVF cycles for women who underwent their first and following IVF cycles during the period from January 1, 2007 through March 31, 2016 were extracted. We excluded women who had treatment for the purpose of storage of eggs or embryos, as well as women receiving treatment with donor semen. In addition, patients were excluded from our study if they did not become pregnant but still had frozen embryos remaining. Women were censored from further analysis if they had an IVF live birth. One complete cycle was defined as all attempts at frozen-thawed embryo transfer resulting from one episode of ovarian stimulation [3, 4, and 13].

Treatment protocols

Women underwent standard ovarian stimulation, monitoring, oocyte retrieval, which has been described in previous study [14]. Oocytes were fertilized using IVF or ICSI. Embryos were graded on the third day according to the Cummins' criteria. All good-quality embryos (including grade 1 and grade 2 8-cell embryos) were frozen by vitrification on the third day after oocyte retrieval. The non-top-quality embryos were extendedly cultured and observed until they reached the blastocyst stage. At this stage, only good-morphology blastocysts were frozen on days 5 or 6. Frozen-thawed embryos were transferred in either the nature cycle or artificial cycle with endometrial preparation by exogenous estrogen and progesterone.

Baseline characteristics

Baseline characteristics of women included age (less than 31 years, 31 to 34 years, 35 to 37 years, 38 to 40 years and more than 40 years), infertility type (primary infertility and secondary infertility), causes of infertility (tubal infertility, ovulation disorders, endometriosis and male infertility). Treatment characteristics at the first complete cycle included type of cycle (IVF, ICSI, IVF + ICSI) and number of oocytes retrieved (1–5, 6–10, 11–15, 16–20, 21–25 and > 25).

Outcomes

The live birth in this study was defined as any birth event in which at least one infant was born alive. The primary Outcomes of the present study were presented in three types: the live birth rate per complete cycle, the conservative CLBR and the optimal CLBR. The CLBR was the total probability of live birth rate up to and including a given cycle. The conservative CLBR was calculated based on the assumption that women who did not return for the subsequent treatment had no chance of pregnancy and a live birth. The optimal estimates of the CLBR assumed that women who did not return for the subsequent treatment had the same chance of pregnancy and a live birth as those who did return.

Statistical analysis

All statistical analyses were performed using the statistical package Stata, Version 12.0. Patient characteristics and treatment characteristics of the first complete cycle were reported as the mean value \pm SD for continuous data and number of case/percentages for categorical data.

The conservative CLBR was equal to the total number of live births up to and including the specific cycle divided by the number of women who ever received IVF treatment during these cycles. The confidence intervals of live birth rates and conservative CLBRs were constructed by using the binomial distribution. The optimal estimates of CLBRs were calculated using the Kaplan-Meier method with Greenwood's approximation to compute confidence intervals.

We developed two models to calculate the cumulative probability of a live birth over consecutive complete cycles up to complete cycle seven using the discrete time regression. The model 1 was constructed using the patient characteristics to estimate the chance of a live birth over a maximum of seven consecutive complete cycles for patients ready to start IVF treatment. In the model 2, we using patient characteristics and treatment characteristics at first complete cycle to estimate the cumulative probability of a live birth after consecutive complete cycles, which could provide information about the further cycles for patients having finished first complete cycle. The complete cycle number was included in the two models as a discrete time variable. The potential predictors considered for analysis in this procedure were woman's age, infertility type, and causes of infertility and treatment characteristics (for model 2 only).

Results

Characteristics of the study population

After exclusions, the analysis cohort included 24648 women, with 32043 complete cycles and 13334 live births (Table 1). Live birth occurred in 41.61% of total cycles, and 64.46% of all women had a live birth. The proportion of women less than 31 years of age was 43.30%, 30.72% of the women were at the age between 31 and 34, and 6.16% were older than 40 years of age. More than half of women suffered from primary infertility and the main cause of infertility was tubal factor (67.97%). The majority (66.38%) of first complete cycles had IVF, 27.38% had ICSI and 6.24% had both IVF and ICSI. The median number of oocytes retrieved in the first complete cycle was 7 (inter-quartile-range 3–13). Stratified by the number of oocytes retrieved at first complete cycle, 39.83% of women had less than 6 oocytes, the proportion of women with 6–10 oocytes, 11–15 oocytes, 16–20 oocytes, 21–25 oocytes and more than 25 oocytes was 24.44%, 16.95%, 9.75%, 4.94% and 4.10%.

Table 1
 Characteristics of the analysis cohort of 20687 women commencing IVF
 treatment for infertility in China in 2007–2016

Characteristic	N (%)
The total number of women	20687(-)
Total number of women per complete cycle	
1	14382(69.52)
2	3739(18.07)
3	1402(6.78)
4	573(2.77)
5	270(1.31)
6	151(0.73)
7	78(0.38)
More than 7	92(0.44)
Number of complete cycles	32043(-)
The total number of Live-births(% , per complete cycle)	13334(41.61)
The number of Live-births at first cycle(% , per complete cycle)	10497(50.74)
Patient characteristics	
Women's age(mean \pm SD, yr)	31.83 \pm 0.03
\leq 30	8961(43.30)
31–34	6351(30.72)
35–37	2638(12.75)
38–40	1463(7.07)
\geq 41	1274(6.16)
Female infertility type	
Primary infertility	10601(51.24)
Secondary infertility	10086(48.76)
Causes of infertility(non-exclusive)	
Tubal	14324(67.97)
Ovulatory	2554(12.12)

Characteristic	N (%)
Endometriosis	2060(9.78)
Male cause	6701(31.80)
Treatment characteristics at complete cycle 1	
Type of cycle at complete cycle 1	
IVF	13732(66.38)
ICSI	5665(27.38)
IVF + ICSI	1290(6.24)
Number of oocytes retrieved at complete cycle 1 (mean ± SD)	
1–5	8239(39.83)
6–10	5055(24.44)
11–15	3507(16.95)
16–20	2017(9.75)
21–25	1021(4.94)
>25	848(4.10)

Live birth rates and cumulative live birth rates for consecutive complete cycles

Table 2 showed an overview of the calculation of the live birth rate, the conservative and optimal estimates of CLRBs for the whole cohort up to seven complete cycles. The live birth rates for the first and second complete cycle were respectively 50.74% (95%CI: 50.06, 51.42) and 30.72% (95%CI: 29.58, 31.87), and decreased to 15.26% (95%CI: 11.51, 19.67) for the sixth complete cycle and 8.23% (95%CI: 4.58, 13.43) for the seventh complete cycle. After the first complete cycle, 10190 (49.26% of the whole cohort) women did not have a live birth. Among these, 3885 (38.13%) women did not continue the next cycle, and 6305 (61.87%) women received more than one complete cycle of treatment.

Table 2

The live-birth rates and cumulative live-birth rates across complete cycles of IVF in 20687 women

Cycle number	Number of women	Number of Live births	Conditional-Live-birth rate %(95%CI)	Conservative-cumulative-live-birth rate %(95%CI)	Optimal-cumulative-live-birth rate %(95%CI)
1st	20687	10497	50.74(50.06,51.42)	50.74(50.06,51.42)	50.74(50.06,51.42)
2nd	6305	1937	30.72(29.58,31.87)	60.11(59.43,60.77)	65.87(65.14,66.61)
3rd	2566	574	22.37(20.77,24.03)	62.88(62.22,63.54)	73.51(72.71,74.30)
4th	1164	180	15.46(13.43,17.67)	63.75(63.09,64.41)	77.61(76.73,78.47)
5th	591	74	12.52(9.96,15.46)	64.11(63.45,64.76)	80.41(79.44,81.36)
6th	321	49	15.26(11.51,19.67)	64.34(63.69,65.00)	83.40(82.26,84.51)
7th	170	14	8.23(4.58,13.43)	64.41(63.76,65.07)	84.77(83.51,85.98)

The conservative estimates of CLBRs after three and seven complete cycles were 62.88% (95%CI: 62.22, 63.54) and 64.41% (95%CI: 63.76, 65.07), respectively, whereas these were 73.51% (95%CI: 72.71, 74.30) and 84.77% (95%CI: 83.51, 85.98) for the optimal estimates of CLBRs.

The live birth rate, the conservative and optimal estimates of CLBRs varied by age categories (Table 3 and Fig. 1). The live birth rates decreased with increasing age up to and including the fifth complete cycle, and the CLBRs decreased with increasing age by seven cycles. The live birth rate of the first complete cycle was 63.81% (95%CI:62.80,64.81) for women aged less than 31 years, 53.02% (95%CI:51.78,54.25) for women aged 31 to 34 years, 39.23% (95%CI:37.36,41.13) for women 35 to 37 years of age, 21.67% (95%CI:19.58,23.87) for women aged 38 to 40 years, and 4.71% (95%CI:3.61,6.02) for women older than 40 years. Seven complete cycles achieved the conservative CLBR of 77.37% (95%CI:76.49,78.23) for women aged less than 31 years, 68.75% (95%CI:67.59,69.88) for women aged 31 to 34 years, 54.02% (95%CI:52.09,55.93) for women 35 to 37 years of age, 33.29% (95%CI:30.87,35.77) for women aged 38 to 40 years, and 9.73% (95%CI:8.16,11.49) for women older than 40 years. The optimal estimate of CLBR after seven complete cycles was 95.81% (95%CI:94.31,97.02) for women younger than 31 years, 90.80% (95%CI:88.89,92.51) for women aged 31 to 34 years, 81.54% (95%CI:77.27,85.44) for women 35 to 37 years of age, 58.25%(95%CI:52.06,64.57) for women aged 38 to 40 years, and 19.45% (95%CI:14.11,26.47) for women older than 40 years. The optimal CLBRs across complete cycles were significantly different across age categories ($p < 0.001$).

Table 3

The live-birth rates and cumulative live-birth rate across complete cycles of IVF in 20687 women, stratified by age at first ovarian stimulation cycle.

Cycle number	N cycles	N Live-births	Conditional-Live-birth rate %(95%CI)	Conservative-cumulative-live-birth rate %(95%CI)	Optimal-cumulative-live-birth rate %(95%CI)
Aged less than 31 years					
1st	8961	5718	63.81(62.80,64.81)	63.81(62.80,64.81)	63.81(62.80,64.81)
2nd	2034	892	43.85(41.68,46.04)	73.76(72.84,74.67)	79.68(78.71,80.63)
3rd	620	233	37.58(33.75,41.52)	76.36(75.47,77.24)	87.32(86.32,88.28)
4th	226	51	22.57(17.29,28.58)	76.93(76.05,77.80)	90.18(89.12,91.17)
5th	96	16	16.67(9.83,25.65)	77.11(76.23,77.98)	91.82(90.64,92.89)
6th	52	18	34.62(21.97,49.09)	77.31(76.43,78.18)	94.65(93.26,95.84)
7th	23	5	21.74(7.46,43.70)	77.37(76.49,78.23)	95.81(94.31,97.02)
Aged 31 to 34 years					
1st	6351	3367	53.02(51.78,54.25)	53.02(51.78,54.25)	53.02(51.78,54.25)
2nd	1823	685	37.58(35.35,39.84)	63.80(62.61,64.98)	70.67(69.37,71.96)
3rd	688	192	27.91(24.58,31.42)	66.82(65.65,67.98)	78.86(77.48,80.20)
4th	294	71	24.15(19.37,29.46)	67.94(66.78,69.09)	83.96(82.47,85.39)
5th	149	35	23.49(16.94,31.12)	68.49(67.33,69.63)	87.73(86.12,89.24)
6th	72	14	19.44(11.06,30.47)	68.71(67.56,69.85)	90.11(88.35,91.72)
7th	29	2	6.90(0.85,22.77)	68.75(67.59,69.88)	90.80(88.89,92.51)
Aged 35 to 37 years					
1st	2638	1035	39.23(37.36,41.13)	39.23(37.36,41.13)	39.23(37.36,41.13)
2nd	978	239	24.44(21.77,27.26)	48.29(46.37,50.22)	54.08(51.94,56.26)
3rd	424	93	21.93(18.08,26.18)	51.82(49.89,53.74)	64.16(61.68,66.62)
4th	181	34	18.78(13.37,25.25)	53.11(51.18,55.03)	70.89(68.00,73.72)
5th	85	14	16.47(9.31,26.09)	53.64(51.71,55.56)	75.68(72.31,78.93)
6th	45	8	17.78(8.00,32.05)	53.94(52.02,55.86)	80.01(76.03,83.70)

Cycle number	N cycles	N Live-births	Conditional-Live-birth rate %(95%CI)	Conservative-cumulative-live-birth rate %(95%CI)	Optimal-cumulative-live-birth rate %(95%CI)
7th	26	2	7.69(0.46,25.13)	54.02(52.09,55.93)	81.54(77.27,85.44)
Aged 38 to 40 years					
1st	1463	317	21.67(19.58,23.87)	21.67(19.58,23.87)	21.67(19.58,23.87)
2nd	706	92	13.03(10.64,15.74)	27.96(25.67,30.33)	31.88(29.28,34.63)
3rd	363	43	11.85(8.71,15.62)	30.90(28.53,33.33)	39.95(36.76,43.30)
4th	197	17	8.63(5.11,13.46)	32.06(29.67,34.52)	45.13(41.42,49.02)
5th	100	8	8.00(3.52,15.16)	32.60(30.20,35.07)	49.52(45.06,54.16)
6th	63	8	12.70(5.65,23.50)	33.15(30.74,35.63)	55.93(50.28,61.74)
7th	38	2	5.26(0.64,17.75)	33.29(30.87,35.77)	58.25(52.06,64.57)
Aged more than 40 years					
1st	1274	60	4.71(3.61,6.02)	4.71(3.61,6.02)	4.71(3.61,6.02)
2nd	764	29	3.80(2.56,5.41)	6.99(5.65,8.53)	8.33(6.78,10.21)
3rd	471	13	2.76(1.48,4.67)	8.01(6.58,9.63)	10.86(8.90,13.21)
4th	266	7	2.63(1.06,5.35)	8.56(7.08,10.23)	13.20(10.74,16.17)
5th	161	1	0.62(0.02,3.41)	8.63(7.15,10.31)	13.74(11.12,16.92)
6th	89	1	1.12(0.03,6.10)	8.71(7.22,10.40)	14.71(11.63,18.51)
7th	54	3	5.56(1.16,15.39)	9.73(8.16,11.49)	19.45(14.11,26.47)

Predicting the live birth over multiple complete cycles

In model 1, the chance of having a baby decreased with the number of complete cycles up to complete cycle 5. For example, the chance of a live birth after complete cycle 3 was 65% less than that after complete cycle 1, and the chance after complete cycle 5 was 76% lower than after complete cycle 1 (Table 4). Increasing women's age reduced the chance of a live birth (≥ 41 years vs. ≤ 30 years; adjusted odds ratio 0.04, 95% confidence interval 0.03 to 0.05). In addition, women with a diagnosis of ovulatory infertility or endometriosis infertility had about a 15% reduced chance of a live birth.

Table 4

Predicting the live birth over multiple complete cycles of IVF adjusted for patient characteristics

Predictors	Model 1		Model 2	
	Odds ratio(95%CI)	P value	Odds ratio(95%CI)	P value
Number of complete cycles				
1(reference)	1		1	
2	0.45(0.41,0.49)	< 0.001	0.67(0.62,0.73)	< 0.001
3	0.35(0.31,0.39)	< 0.001	0.56(0.49,0.64)	< 0.001
4	0.25(0.21,0.31)	< 0.001	0.43(0.35,0.53)	< 0.001
5	0.24(0.18,0.32)	< 0.001	0.42(0.31,0.56)	< 0.001
6	0.29(0.20,0.42)	< 0.001	0.47(0.32,0.70)	< 0.001
7	0.15(0.08,0.27)	< 0.001	0.25(0.13,0.48)	< 0.001
Patient characteristic				
Women's age (year)				
≤ 30 (reference)	1		1	
31–34	0.68(0.63,0.73)	< 0.001	0.79(0.73,0.86)	< 0.001
35–37	0.38(0.34,0.42)	< 0.001	0.50(0.46,0.56)	< 0.001
38–40	0.17(0.15,0.20)	< 0.001	0.27(0.23,0.30)	< 0.001
≥ 41	0.04(0.03,0.05)	< 0.001	0.07(0.05,0.08)	< 0.001
Secondary infertility vs. Primary infertility	0.95(0.88,1.01)	0.105	0.94(0.88,1.01)	0.096
Tubal infertility, yes vs.no	1.07(0.99,1.15)	0.069	1.03(0.95,1.12)	0.421
Ovulatory infertility, yes vs.no	0.76(0.69,0.84)	< 0.001	0.85(0.76,0.94)	0.002
Endometriosis infertility, yes vs.no	0.75(0.67,0.83)	< 0.001	0.91(0.81,1.01)	0.082

Predictors	Model 1		Model 2	
	Odds ratio(95%CI)	P value	Odds ratio(95%CI)	P value
Male cause infertility, yes vs.no	1.05(0.98,1.12)	0.196	1.12(1.03,1.22)	0.008
Treatment characteristics at complete cycle 1				
Type of cycle at complete cycle 1				
IVF(reference)			1	
ICSI			0.79(0.72,0.87)	< 0.001
IVF + ICSI			1.07(0.95,1.22)	0.263
Number of oocytes retrieved at complete cycle 1				
1–5(reference)			1	
6–10			2.21(2.03,2.40)	< 0.001
11–15			3.38(3.05,3.76)	< 0.001
16–20			4.63(4.01,5.35)	< 0.001
21–25			6.81(5.45,8.51)	< 0.001
>25			9.59(7.20,12.77)	< 0.001

After the first complete cycle, the odds of a live birth decreased by 21% if the treatment was ICSI (Table 4, model 2). The chance of having a baby increased by more than eight times for women with over 25 oocytes at complete cycle 1, compared with women with 1 to 5 oocytes. Similar to results of model 1, the odds of a live birth decreased with increasing number of complete cycles and women's age.

Discussion

To our knowledge, this is the first study to report estimates of live birth rates and CIBRs across complete cycles among large sample population with freeze-all strategy during ten years. Although many studies about IVF have been reported, most of them were limited by small samples, conventional IVF strategy, and the use of pregnancy or live birth rate per cycle as the primary outcome [15, 16]. Few researches reported the cumulative live birth rate per patient among population using freeze-all strategy. This study conducting in 20687 patients reported the conservative and optimal estimates of CLBRs, which could

reflect the chance of success for patients undergoing IVF treatment with freeze-all strategy. In this study, we presented the clinical outcome of IVF in a patient-anchored approach and all cycles were attached to the patient receiving IVF treatment. Despite the live birth rate declined with the increasing number of cycles, the CLBRs increased up to and including the fifth cycle in the whole cohort. The conservative and optimal estimates of CLBRs in our population of more than 20000 patients undergoing up to five complete cycles of IVF treatment were 64.11% and 80.41%, respectively. As the CLBRs may be underestimated or overestimated by the conservative or optimal estimated, the 'realistic' CLBR for our population was probably between the two estimates.

CLBRs after IVF have been reported across nations. The CLBRs for the conservative and optimal estimates (51% and 72%) after six complete cycles reported by Malizia et al. from a large center in Boston were lower than these in our study (64.34% and 83.40%)[2]. Comparing with the conservative and optimal estimates of CLBRs after six complete cycles in the UK (43.90% and 75.50%) and Belgium (54.10% and 76.30), corresponding figures from our research were slightly higher[5, 17]. We speculate that the higher CLBRs in our study is related with our treatment protocol—freeze all strategy, which has been reported that could increase pregnancy rate and live birth rate by avoiding the potential deleterious effects of controlled ovarian stimulation on the endometrium. In addition, the differences in age structure, causes of infertility between our study population and previous study population may also contribute to the different CLBRs across nations. So randomized controlled trials are needed to verify the finding in future study.

As we all known, maternal age was an important factor affecting the fertility in the natural population. In our study, the CLBRs also declined with the increasing of the age. Leridon reported the final proportions of women ending in a live birth was 94% for women starting attempts to conceive at age 30 years, 86% for those starting age 35 years and 65% for those starting at age 40 years in the natural population[18]. Our optimal CLBRs after seven complete cycles for women younger than 31 years, aged 31 to 34 years, aged 35 to 37 years, and aged between 38 and 40 years were 95.81%, 90.80%, 81.54%, and 58.25%, respectively. These figures proved that IVF could reduce the gap in the probability of having a live birth for the infertility women no more than 40 years. However, the possibility of delivering a live baby was only 19.45% for women older than 40 years after seven complete courses of IVF treatment. This suggested that IVF could not completely compensate for the decrease of fertility among women older than 40 years. In addition, our age-stratified CLBRs also could provide individualized information about the chance of success for patients of any age.

In this study, we constructed two models to estimate the chances of a live birth over one or more complete cycles. For patients embarking on IVF following freeze-all strategy, model one could predict the probability of having a baby over multiple complete cycles using the patient's baseline characteristics, including age, infertility type and causes of infertility. But for patients finishing the first complete cycle, the treatment information at complete cycle one was available. So we developed model two by adding the treatment information to make the prediction more precise. In model one, age was an important predictor for the chance of live birth. In model two, besides age, the number of oocyte retrieved at

complete cycle one also played an important predictive role. The two models can be used by patients before starting IVF and patients after the first complete cycle to estimate their probability of having a baby for making treatment decisions.

Many studies have been conducted to predict the success of IVF. David predicted the cumulative chances of having a baby over a complete package of IVF, but this model only applied to population using the conventional IVF strategy [19]. R.K. Dhillon also made a prediction models for live birth following IVF, but this study included patients undergoing their first fresh cycle of IVF and was limited to use prior to first cycle only [20]. Our study is the first to estimate the probability of having a baby over multiple complete cycles of IVF for patients following strategy, which can be used as a guiding tool in making decisions about treatment with freeze-all protocol.

Our research has some limitations. First, we did not adjust factors such as body-mass-index, smoking and alcohol use in our model, as these variables were unavailable in our IVF database [21]. Second, this model is developed for freeze-all strategy, so patients undergoing IVF treatment with conventional IVF strategy could not estimate their chance of having a live birth using this model.

Conclusion

This study showed the CLBRs over one and more complete cycles of IVF with freeze-all strategy and its variation across age. In addition, two prediction models were developed to estimate their probability of having a baby over multiple complete IVF cycles with freeze-all strategy among patients before starting IVF and patients after the first complete cycle, which is critical for patients to make treatment decisions and preparations physically, emotionally and financially.

Abbreviations

AOR: Adjusted odds ratio; ART: Assisted reproductive technology; CLBR: Cumulative live birth rate; COS: Controlled ovarian stimulation; ICSI: Intracytoplasmic sperm injection; IVF: In vitro fertilization; OHSS: Ovarian hyperstimulation syndrome.

Declarations

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Author's contributions

YPK and HYG supervised the entire study, including procedures, conception, design, and completion. BW, JYL, MRY and YW were responsible for the collection of data. QQZ contributed the analysis data and

drafted the article. All authors have read and approved the final manuscript.

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Availability of data and materials

The transcripts from which this manuscript was developed are available on request from the corresponding author.

Ethics approval and consent to participate

This study was approved by the Ethics Committee (Institutional Review Board) of Shanghai Ninth People's Hospital. Participant consent was not required as only routinely collected and anonymized secondary data were used.

Consent for publication

Not applicable.

Declaration of Competing interests

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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Figures

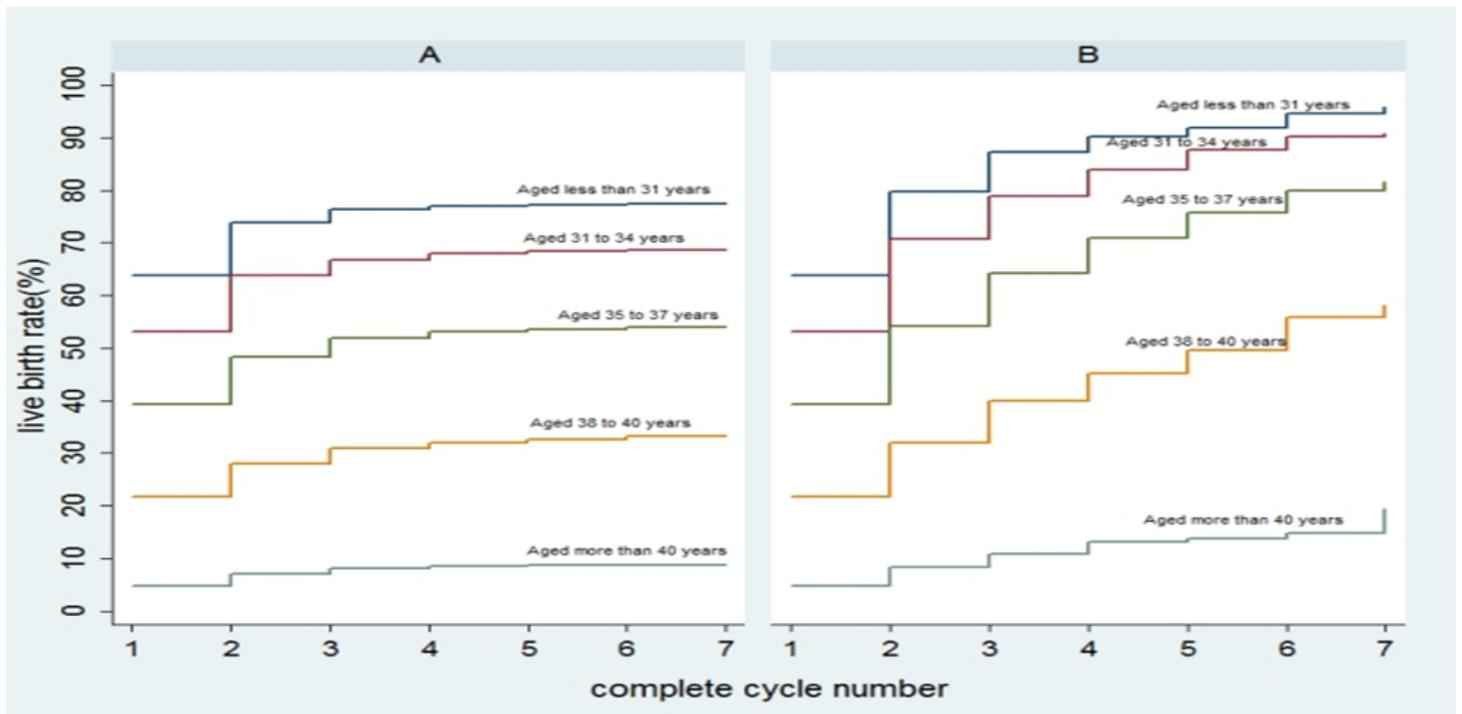


Figure 1

Cumulative live birth rates per women over complete cycles of IVF (A)conservative estimate (B) optimal estimate