Web Supplementary Material for 'Predicting the chances of having a baby after one or more complete cycles of in-vitro fertilisation: a population-based study of linked cycle data from 113,873 women'

Figure A1 Flow chart of exclusion criteria

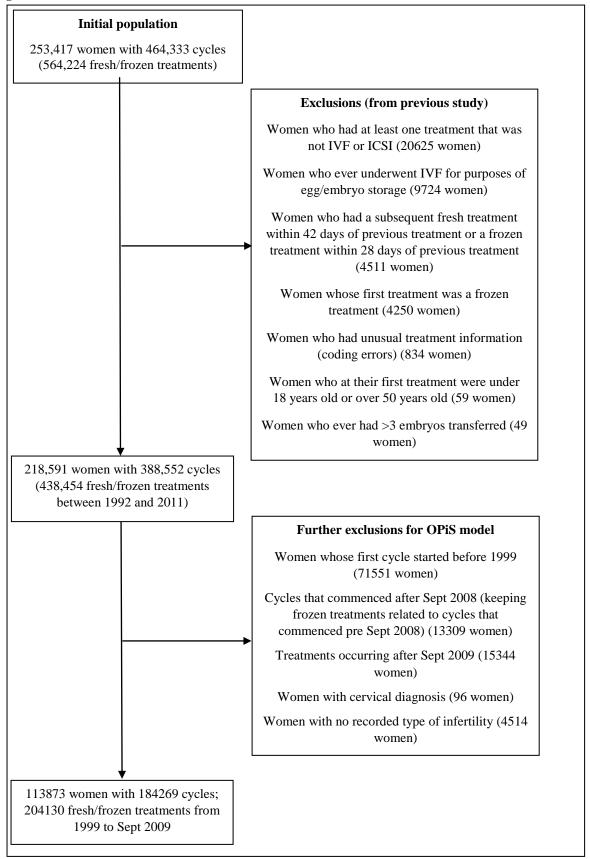


Table A1 Univariable relationship between patient characteristics and treatment information and livebirth over multiple complete cycles of IVF (adjusting for complete cycle number)

Predictors	OR (95% CI)	p-value
Cycle number		
2 v 1	0.77 (0.75 to 0.79)	< 0.001
3 v 1	0.64 (0.62 to 0.67)	< 0.001
4 v 1	0.56 (0.52 to 0.60)	< 0.001
5 v 1	0.48 (0.42 to 0.54)	< 0.001
6 v 1	0.42 (0.34 to 0.52)	< 0.001
Patient characteristics		
Female age to years	0.918 (0.916 to 0.920)	< 0.001
Female age to as interquartile odds ratio ¹	1.02 (1.01 to 1.03)	< 0.001
Duration to years	0.85 (0.81 to 0.89)	< 0.001
Previous pregnancy in couple to no v yes	1.50 (1.16 to 1.94)	0.002
Tubal infertility to yes	0.32 (0.20 to 0.50)	< 0.001
Anovulation	0.61 (0.59 to 0.63)	< 0.001
Male factor	0.960 (0.958 to 0.963)	< 0.001
Unexplained	1.02 (0.99 to 1.04)	0.16
Endometriosis	0.88 (0.86 to 0.90)	< 0.001
Year of first egg retrieval	0.97 (0.94 to 1.00)	0.04
Year of first egg retrieval to as interquartile odds ratio ¹	1.10 (1.08 to 1.13)	< 0.001
First complete cycle characteristics		
Number of eggs collected	1.08 (1.07 to 1.08)	< 0.001
Number of eggs collected to as interquartile odds ratio ¹	1.32 (1.29 to 1.34)	< 0.001
Treatment type to IVF v ICSI	0.52 (0.46 to 0.58)	< 0.001
Cryopreservation of embryos to yes v no	5.62 (3.51 to 9.01)	< 0.001
Number and stage of embryos transferred		< 0.001
No embryos transferred v Double cleavage stage	0.20 (0.19 to 0.21)	< 0.001
Single cleavage stage v Double cleavage stage	0.37 (0.35 to 0.39)	< 0.001
Single blastocyst v Double cleavage stage	1.61 (1.40 to 1.84)	< 0.001
Double blastocyst v Double cleavage stage	2.19 (2.05 to 2.34)	< 0.001
Triple cleavage stage v Double cleavage stage	0.61 (0.58 to 0.63)	< 0.001
Triple blastocyst v Double cleavage stage	0.78 (0.58 to 1.05)	0.10

The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile of the restricted cubic spline fit of the predictor and the odds of a live-birth for the 25th percentile of the restricted cubic spline fit of the predictor.

Table A2. Adequacy of each predictor from pre-treatment model

Rank	Predictor	Difference in -2*log likelihood ratio ¹	Adequacy statistic
1	Female age	7722.78	0.8463
2	Duration of infertility	714.57	0.0783
3	Treatment type (ICSI v IVF)	429.35	0.0471
4	Treatment year	293.67	0.0322
5	Tubal infertility	104.56	0.0115
6	Male factor infertility	83.96	0.0092
7	Unexplained infertility	9.38	0.0010
8	Anovulatory infertility	4.27	0.0005
9	Primary infertility	2.02	0.0002

¹Full model -2*log likelihood ratio = 9125.36

Table A3. Adequacy of each predictor from post-treatment model

Rank	Predictor	Difference in -2*log	Adequacy statistic
		likelihood ratio ¹	
1	Female age	6834.53	0.4350
2	Cryopreservation of embryos	6073.29	0.3866
3	Number of eggs	5932.47	0.3776
4	Number and stage of embryos transferred	1932.99	0.1230
5	Duration of infertility	568.58	0.0362
6	Treatment year	278.63	0.0177
7	Tubal infertility	102.18	0.0065
8	IVF versus ICSI	35.50	0.0023
9	Primary infertility	1.26	0.0001

¹Full model -2*log likelihood ratio = 15708.54

Table A4 The effect of each predictor on live-birth over multiple complete cycles of IVF adjusted for patient characteristics and treatment information at the first complete cycle in patients who had no eggs collected in the their first complete cycle (post-treatment model)

Predictors	Odds Ratio (95% CI)	p-value
Cycle number		
2 (Reference)	1	
3	0.87 (0.76 to 1.00)	0.06
4	0.83 (0.66 to 1.03)	0.10
5	0.80 (0.53 to 1.17)	0.27
6	0.56 (0.25 to 1.12)	0.13
Patient characteristics		
Female age, 37 versus 31 years ¹	0.45 (0.38 to 0.53)	< 0.001
Duration, years	0.96 (0.94 to 0.98)	< 0.001
Previous pregnancy in couple, no v yes	1.03 (0.89 to 1.19)	0.71
Male factor infertility, yes v no	1.18 (1.00 to 1.40)	0.05
Tubal infertility, yes v no	1.12 (0.93 to 1.35)	0.23
Unexplained infertility, yes v no	1.22 (1.00 to 1.48)	0.05
Anovulatory infertility, yes v no	1.08 (0.90 to 1.29)	0.39
Year first complete cycle started, 2006 v 2001 ¹	1.31 (1.16 to 1.47)	< 0.001
Treatment type, ICSI v IVF	0.67 (0.37 to 1.12)	0.14

 $^{^{1}}$ The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age and year of first egg retrieval. It is defined as the ratio of the odds of a live-birth for the 75^{th} percentile and the odds of a live-birth for the 25^{th} percentile of the predictor.

Table A5. Characteristics of patients and treatment in couples with complete data versus incomplete data

	Complete cases N (%), unless	Incomplete cases N (%), unless
Characteristics	otherwise stated	otherwise stated
Total number of women	93284 (81.92)	20589 (18.08)
Characteristics with complete data		,
Patient details		
Female Age, mean (SD)	34.11 (4.58)	34.31 (4.79)
Type of infertility		
Tubal	22048 (23.64)	4497 (21.84)
Anovulatory	13348 (14.31)	2594 (12.60)
Male factor	40212 (43.11)	9541 (46.34)
Unexplained	25953 (27.82)	6740 (32.74)
Endometriosis	6034 (6.47)	1556 (7.56)
Year of first egg retrieval 1999	6920 (7.21)	2600 (12.06)
2000	6820 (7.31) 9143 (9.80)	2688 (13.06) 537 (2.61)
2001	9693 (10.39)	570 (2.77)
2002	10567 (11.33)	755 (3.67)
2003	10594 (11.36)	716 (3.48)
2004	11078 (11.88)	762 (3.70)
2005	11636 (12.47)	856 (4.16)
2006	12691 (13.60)	1037 (5.04)
2007	11062 (11.86)	2406 (11.69)
2008	0 (0.00)	10262 (49.84)
Treatment characteristics at Cycle 1		
IVF	55841 (59.86)	11670 (56.68)
ICSI	37443 (40.14)	8919 (43.32)
Eggs collected, median (IQR)	8 (5, 13)	8 (4, 12)
Embryos created, median (IQR)	5 (2, 8)	4 (2, 7)
Cryopreservation of embryos	24252 (26.00)	4698 (22.82)
Number of frozen treatments	0.4452 (00.52)	10074 (02 (1)
0 1	84452 (90.53)	19274 (93.61)
2	7159 (7.67) 1388 (1.49)	1111 (5.40) 180 (0.87)
3	225 (0.24)	21 (0.10)
4	43 (0.05)	2 (0.01)
5	8 (0.01)	1 (0.00)
6	8 (0.01)	0 (0.00)
7	1 (0.00)	0 (0.00)
Characteristics with missing data		
Patient details	Patient details	Patient details
Duration (years), median (IQR)	4 (3, 6)	4 (3, 7)
Previous pregnancy in couple		540.4 (04.5°)
No	69107 (74.08)	6434 (31.25)
Missing ¹	0 (0.00)	10262 (49.84)
Treatment characteristics at Cycle 1 Number of embryos transferred, first fresh treatment		
No transfer	12570 (13.47)	2931 (14.24)
1	7759 (8.32)	2274 (11.04)
2	65525 (70.24)	13891 (67.47)
3	7430 (7.96)	1445 (7.02)
Missing Stage of embryo transfer, first fresh treatment	0 (0.00)	48 (0.23)
Cleavage	77982 (83.60)	15616 (75.85)
Blastocyst	2732 (2.93)	1020 (4.95)
Missing	0 (0.00)	1020 (4.95)

Table A6 Pre-treatment model adjusted for patient characteristics using couples with complete data only

Predictors	Parameter Estimate (95% CI)	OR (95% CI)	p-value
Intercept	-0.9563 (-1.3191 to -0.5946)	-	< 0.001
Cycle number			
1	0	1	
2	-0.2414 (-0.2689 to -0.2139)	0.79 (0.76 to 0.81)	< 0.001
3	-0.4219 (-0.4648 to -0.3793)	0.66 (0.63 to 0.68)	< 0.001
4	-0.5638 (-0.6372 to -0.4913)	0.57 (0.53 to 0.61)	< 0.001
5	-0.7204 (-0.8524 to -0.5919)	0.49 (0.43 to 0.55)	< 0.001
6	-0.8719 (-1.1065 to -0.6491)	0.42 (0.33 to 0.52)	< 0.001
Patient characteristics			
Female age as restricted cubic spline ¹			
Age	0.0255 (0.0142 to 0.0369)	-	< 0.001
Age1	-0.1790 (-0.2302 to -0.1279)	-	< 0.001
Age2	0.4589 (0.1785 to 0.7398)	-	0.001
Age3	-1.2062 (-1.7099 to -0.7037)	-	< 0.001
37 versus 31 years of age ²		0.60 (0.58 to 0.62)	< 0.001
Duration (years)	-0.0279 (-0.0314 to -0.0244)	0.97 (0.97 to 0.98)	< 0.001
Treatment type, ICSI	0.2076 (0.1766 to 0.2387)	1.23 (1.19 to 1.27)	< 0.001
IVF	0	1	
Male factor infertility, yes	-0.0908 (-0.1298 to -0.0518)	0.91 (0.88 to 0.95)	< 0.001
no			
Tubal infertility, yes	-0.1052 (-0.1433 to -0.0671)	0.90 (0.87 to 0.94)	< 0.001
no	0	1	
Unexplained infertility of couple, yes	0.0583 (0.0188 to 0.0978)	1.06 (1.02 to 1.10)	0.004
no	0	1	
Anovulatory infertility of couple, yes	0.0363 (-0.0022 to 0.0747)	1.04 (1.00 to 1.08)	0.06
no	0	1	
Previous pregnancy in couple, no	-0.0938 (-0.1218 to -0.0658)	0.91 (0.89 to 0.94)	< 0.001
yes	0	1	
Year of first egg retrieval, as restricted cubic spline ³			
Year	0.0297 (0.0074 to 0.0520)	1.03 (1.01 to 1.05)	0.01
Year1	-0.0211 (-0.0906 to 0.0484)	0.98 (0.91 to 1.05)	0.55
Year2	0.1641 (-0.0522 to 0.3805)	1.18 (0.95 to 1.46)	0.14
2006 v 2001 ²	,	1.21 (1.17 to 1.24)	< 0.001

 $^{^{1}} Age1=max((Age-26)/k,0)**3+(11*max((Age-41)/k,0)**3-(15)*max((Age-37)/k,0)**3)/4;\\ Age2=max((Age-31)/k,0)**3+(6*max((Age-41)/k,0)**3-(10)*max((Age-37)/k,0)**3)/4;\\ Age3=max((Age-34)/k,0)**3+(3*max((Age-41)/k,0)**3-(7)*max((Age-37)/k,0)**3)/4;\\ where k=15**(2/3).$

² The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year of first egg retrieval and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile and the odds of a live-birth for the 25th percentile of the predictor.

 $^{^3}$ Year1=max((Year+9)/k,0)**3+((6)*max((Year)/k,0)**3-(9)*max((Year+3)/k,0)**3)/(3); Year2=max((Year+6)/k,0)**3+((3)*max((Year)/k,0)**3-(6)*max((Year+3)/k,0)**3)/(3); where k= 9**(2/3).

Table A7 Post-treatment model adjusted for patient and treatment characteristics using couples with complete data only

-1.6093 (-1.9602 to -1.2596)		
-1.0073 (-1.7002 t0 -1.2390)		
0	1	
-0.1993 (-0.2289 to -0.1697)	0.82 (0.80 to 0.84)	< 0.001
-0.3687 (-0.4150 to -0.3228)	0.69 (0.66 to 0.72)	< 0.001
-0.5190 (-0.5986 to -0.4406)	0.60 (0.55 to 0.64)	< 0.001
-0.6899 (-0.8319 to -0.5518)	0.50 (0.44 to 0.58)	< 0.001
-0.8420 (-1.0914 to -0.6052)	0.43 (0.34 to 0.55)	< 0.001
,	,	
0.0236 (0.0116 to 0.0357)	_	< 0.001
	-	< 0.001
	_	0.02
	_	< 0.001
0.500=(0.005=00000000)	1.53 (1.48 to 1.58)	< 0.001
-0.0203 (-0.0240 to -0.0166)	-	< 0.001
,	1.06 (1.05 to 1.07)	< 0.001
-0.0601 (-0.0898 to -0.0304)	,	< 0.001
		< 0.001
	,	
	_	0.21
	_	< 0.001
0.0 150 (0.0220 to 0.00 12)	1.27 (1.23 to 1.30)	< 0.001
	(
0.0638 (0.0564 to 0.0711)	_	< 0.001
,	_	< 0.001
0.0170 (0.0201 to 0.0272)	1.30 (1.27 to 1.33)	< 0.001
-0.0875 (-0.1138 to -0.0613)		< 0.001
		< 0.001
0.0232 (0.3700 to 0.0330)	1.07 (1.02 to 1.52)	(0.001
0	1	
-	-	< 0.001
,	,	< 0.001
	,	0.04
,	,	< 0.001
		0.60
0.4049 (0.0265 to 0.7654)	1.50 (1.03 to 2.15)	0.03
	-0.1993 (-0.2289 to -0.1697) -0.3687 (-0.4150 to -0.3228) -0.5190 (-0.5986 to -0.4406) -0.6899 (-0.8319 to -0.5518) -0.8420 (-1.0914 to -0.6052) 0.0236 (0.0116 to 0.0357) -0.1456 (-0.1999 to -0.0914) 0.3468 (0.0492 to 0.6448) -0.9852 (-1.5192 to -0.4524) -0.0203 (-0.0240 to -0.0166) -0.0601 (-0.0898 to -0.0304) -0.2242 (-0.2553 to -0.1931) 0.0080 (-0.0044 to 0.0204) 0.0490 (0.0338 to 0.0643) 0.0638 (0.0564 to 0.0711) -0.0476 (-0.0561 to -0.0392) -0.0875 (-0.1138 to -0.0613) 0.6252 (0.5968 to 0.6536) 0 -0.9868 (-1.0595 to -0.9153) -0.5645 (-0.6200 to -0.5095) 0.1794 (0.0039 to 0.3540) 0.6007 (0.5228 to 0.6788) 0.0137 (-0.0371 to 0.0643)	-0.1993 (-0.2289 to -0.1697) -0.3687 (-0.4150 to -0.3228) -0.5190 (-0.5986 to -0.4406) -0.6899 (-0.8319 to -0.5518) -0.8420 (-1.0914 to -0.6052) 0.0236 (0.0116 to 0.0357) -0.1456 (-0.1999 to -0.0914) 0.3468 (0.0492 to 0.6448) -0.9852 (-1.5192 to -0.4524) -0.0203 (-0.0240 to -0.0166) -0.0242 (-0.2553 to -0.1931) 0.0080 (-0.0044 to 0.0204) -0.0490 (0.0338 to 0.0643) 0.0638 (0.0564 to 0.0711) -0.0476 (-0.0561 to -0.0392) -0.0875 (-0.1138 to -0.0613) 0.6252 (0.5968 to 0.6536) 10.036 (0.039 to 0.94) -0.9868 (-1.0595 to -0.9153) -0.5645 (-0.6200 to -0.5095) 0.1794 (0.0037 to 0.0543) 0.120 (1.00 to 1.42) 0.6007 (0.5228 to 0.6788) 0.0137 (-0.0371 to 0.0643) 1.82 (1.69 to 1.97) 1.01 (0.96 to 1.07)

 $^{^{1}} Age1 = max((Age-26)/k,0)**3 + (11*max((Age-41)/k,0)**3 - (15)*max((Age-37)/k,0)**3)/(4);$ Age2=max((Age -31)/k,0)**3+(6*max((Age -41)/k,0)**3-(10)*max((Age -37)/k,0)**3)/(4);Age3=max((Age -34)/k,0)**3+(3*max((Age -41)/k,0)**3-(7)*max((Age -37)/k,0)**3)/(4);where k=15**(2/3);

² The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year of first egg retrieval and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile and the odds of a live-birth for the 25^{th} percentile of the predictor. ³ Year1=max((Year+8)/k,0)**3+((4)*max((Year+1)/k,0)**3-(7)*max((Year+4)/k,0)**3)/(3);

where k = 7**(2/3);

 $^{^{4}}$ Eggs1=max((Eggs-3)/k,0)**3+((6)*max((Eggs-18)/k,0)**3-(15)*max((Eggs-9)/k,0)**3)/(9); where k = 15**(2/3);

Table A8 Parameter estimates and odds ratios (95% CI) for each of the predictors in the pre-treatment model, adjusted for patient characteristics and a random intercept for IVF centre

Predictors	Parameter Estimate (95% CI)	OR (95% CI)	p-value
Intercept	-1.0161 (-1.3551 to -0.6770)		< 0.001
Cycle number			
1 (Reference)	0	1	
2	-0.2341 (-0.2601 to -0.2081)	0.79 (0.77 to 0.81)	< 0.001
3	-0.4257 (-0.4668 to -0.3847)	0.65 (0.63 to 0.68)	< 0.001
4	-0.6030 (-0.6737 to -0.5324)	0.55 (0.51 to 0.59)	< 0.001
5	-0.7933 (-0.9186 to -0.6679)	0.45 (0.40 to 0.51)	< 0.001
6	-0.9220 (-1.1382 to -0.7057)	0.40 (0.32 to 0.49)	< 0.001
Patient characteristics			
Female age as restricted cubic spline ¹			
Age	0.0239 (0.0135 to 0.0342)	-	< 0.001
Age1	-0.1894 (-0.2365 to -0.1423)	-	< 0.001
Age2	0.5038 (0.2447 to 0.7630)	-	< 0.001
Age3	-1.3032 (-1.7678 to -0.8387)	-	< 0.001
37 versus 31 years of age ²		0.58 (0.56 to 0.60)	< 0.001
Duration, years	-0.0242 (-0.0274 to -0.0209)	0.98 (0.97 to 0.98)	< 0.001
Treatment type, ICSI v IVF	0.1872 (0.1584 to 0.2161)	1.21 (1.17 to 1.24)	< 0.001
Male factor infertility, yes v no	-0.1223 (-0.1574 to -0.0871)	0.88 (0.85 to 0.92)	< 0.001
Tubal infertility, yes v no	-0.1154 (-0.1505 to -0.0802)	0.89 (0.86 to 0.92)	< 0.001
Unexplained infertility, yes v no	0.0445 (0.0088 to 0.0803)	1.05 (1.01 to 1.08)	0.01
Anovulatory infertility, yes v no	0.0163 (-0.0198 to 0.0523)	1.02 (0.98 to 1.05)	0.38
Previous pregnancy in couple, no v yes	-0.0759 (-0.1013 to -0.0504)	0.93 (0.90 to 0.95)	< 0.001
Year of first egg retrieval, as restricted cubic			
spline ³			
Year	0.0249 (0.0049 to 0.0449)	-	0.01
Year1	-0.0264 (-0.0862 to 0.0334)	-	0.39
Year2	0.2001 (0.0262 to 0.3741)	-	0.02
2006 v 2001 ²		1.18 (1.15 to 1.22)	< 0.001

 $[\]begin{array}{l} ^{1} Age1=max((Age-26)/k,0)**3+(11*max((Age-41)/k,0)**3-(15)*max((Age-37)/k,0)**3)/4; \\ Age2=max((Age-31)/k,0)**3+(6*max((Age-41)/k,0)**3-(10)*max((Age-37)/k,0)**3)/4; \\ Age3=max((Age-34)/k,0)**3+(3*max((Age-41)/k,0)**3-(7)*max((Age-37)/k,0)**3)/4; \\ where k=15**(2/3); \end{array}$

² The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year of first egg retrieval and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile and the odds of a live-birth for the 25th percentile of the predictor.

³ Year1=max((Year+9)/k,0)**3+((6)*max((Year)/k,0)**3-(9)*max((Year+3)/k,0)**3)/(3); Year2=max((Year+6)/k,0)**3+((3)*max((Year)/k,0)**3-(6)*max((Year+3)/k,0)**3)/(3); where k=9**(2/3).

Table A9 Parameter estimates and odds ratios (95% CI) for each of the predictors in the post-treatment model, adjusted for patient characteristics and treatment information and a random intercept for IVF centre at the first complete cycle

Predictors	Parameter Estimate (95% CI)	OR (95% CI)	p-value
Intercept	-1.8010 (-2.1291 to -1.4730)		< 0.001
Cycle number			
1 (Reference)	0	1	
2	-0.1950 (-0.2229 to -0.1671)	0.82 (0.80 to 0.85)	< 0.001
3	-0.3732 (-0.4173 to -0.3292)	0.69 (0.66 to 0.72)	< 0.001
4	-0.5561 (-0.6321 to -0.4801)	0.57 (0.53 to 0.62)	< 0.001
5	-0.7468 (-0.8808 to -0.6128)	0.47 (0.41 to 0.54)	< 0.001
6	-0.8651 (-1.0933 to -0.6368)	0.42 (0.34 to 0.53)	< 0.001
Patient characteristics	,	,	
Female age as restricted cubic spline ¹			
Age	0.0244 (0.0134 to 0.0353)	-	< 0.001
Age1	-0.1607 (-0.2105 to -0.1109)	-	< 0.001
Age2	0.4069 (0.1331 to 0.6807)	-	0.004
Age3	-1.0666 (-1.5564 to -0.5769)	-	< 0.001
Interquartile odds ratio ²		1.57 (1.52 to 1.62)	< 0.001
Duration, years	-0.0178 (-0.0213 to -0.0144)	0.98 (0.98 to 0.99)	< 0.001
Previous pregnancy in couple, no v yes	-0.0497 (-0.0766 to -0.0228)	0.95 (0.93 to 0.98)	< 0.001
Tubal infertility, yes v no	-0.2241 (-0.2530 to -0.1953)	0.80 (0.78 to 0.82)	< 0.001
Year of first egg retrieval, as restricted cubic spline ³			
Year	-0.0066 (-0.0176 to 0.0044)	-	0.24
Year1	0.0710 (0.0588 to 0.0832)	-	< 0.001
37 versus 31 years of age ²		1.29 (1.26 to 1.32)	< 0.001
Treatment information at first complete cycle			
Number of eggs collected as restricted cubic spline ⁴			
Eggs	0.0612 (0.0545 to 0.0680)	-	< 0.001
Eggs1	-0.0451 (-0.0529 to -0.0373)	-	< 0.001
Number of eggs to 13 v 5 ¹²		1.29 (1.26 to 1.32)	< 0.001
Treatment type, IVF v ICSI	-0.1151 (-0.1397 to -0.0905)	0.89 (0.87 to 0.91)	< 0.001
Cryopreservation of embryos, yes v no	0.6674 (0.6396 to 0.6952)	1.95 (1.90 to 2.00)	< 0.001
Number and stage of embryos transferred			< 0.001
Double cleavage stage	0	1	
No embryos transferred	-1.0756 (-1.1440 to -1.0071)	0.34 (0.32 to 0.37)	< 0.001
Single cleavage stage	-0.5733 (-0.6231 to -0.5235)	0.56 (0.54 to 0.59)	< 0.001
Single blastocyst stage	-0.1094 (-0.2566 to 0.0377)	0.90 (0.77 to 1.04)	0.14
Double blastocyst stage	0.3628 (0.2887 to 0.4369)	1.44 (1.33 to 1.55)	< 0.001
Triple cleavage stage	-0.0191 (-0.0681 to 0.0299)	0.98 (0.93 to 1.03)	0.44
	0.2125 (-0.1047 to 0.5298)	1.24 (0.90 to 1.70)	0.19

 $^{^{1}} Age1=max((Age-26)/k,0)**3+(11*max((Age-41)/k,0)**3-(15)*max((Age-37)/k,0)**3)/(4);\\ Age2=max((Age-31)/k,0)**3+(6*max((Age-41)/k,0)**3-(10)*max((Age-37)/k,0)**3)/(4);\\ Age3=max((Age-34)/k,0)**3+(3*max((Age-41)/k,0)**3-(7)*max((Age-37)/k,0)**3)/(4);\\ where k=15**(2/3);$

² The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year of first egg retrieval and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile and the odds of a live-birth for the 25th percentile of the predictor.

 $^{^{3}}$ Year1=max((Year+8)/k,0)**3+((4)*max((Year+1)/k,0)**3-(7)*max((Year+4)/k,0)**3)/(3); where k= 7**(2/3):

where $k=7^{**}(2/3)$; 4 Eggs1=max((Eggs-3)/k,0)**3+((6)*max((Eggs-18)/k,0)**3-(15)*max((Eggs-9)/k,0)**3)/(9); where $k=15^{**}(2/3)$;

Text S1. Further detail on statistical methods

Missing data

Single imputation was performed to impute values for those predictors with missing information. The imputation was performed using a combination of the Markov Chain Monte Carlo method (to attain a monotone missing data pattern), predicted mean matching regression (to impute continuous predictors with missing data), logistic regression (to impute binary predictors), and the discriminant function method regression (to impute nominal categorical predictors). We used all predictors described above, last complete cycle number, and livebirth outcome information (such as live-birth occurrence, last complete cycle number, time from first to last cycle) informed the imputation process. The models were also developed only in those couples with complete data.

When the distribution of predictors was assessed by year of first treatment, the proportion of couples with no previous pregnancy was consistently between 65-70% until it dropped to 13% in 2008. This was assumed to be due to a data recording problem and therefore it was decided that this variable should be treated as missing for 2008. This resulted in 9% of women having a missing value for this predictor. Furthermore, 16% of women had missing duration of infertility, 0.9% had missing stage of embryo transfer, and 0.04% had no data on the number of embryos transferred. Overall 20589 (18.1%) women had at least one piece of missing information.

Single imputation was used to impute missing values in 18% of couples in order to increase statistical power and adjust for any biases caused by excluding women with missing information. Single rather than multiple imputation was used because methods to assess model performance such as discrimination and calibration are much more straightforward to calculate using the former. The database was very large and the amount of missing data was relatively low meaning that there was minimal risk of underestimation of the uncertainty associated with imputed values as can arise when using single imputation in small datasets.²

Internal validation

When developing a new statistical model it is important to assess for 'overfitting'. This occurs when there are too many predictors included in the model in relation to the number of observations such that its generalisation to new patients is too optimistic.² To assess overfit, an internal validation was carried out using bootstrapping to calculate the 'optimism', defined as the true performance of the model minus the apparent performance. Three hundred bootstrap samples, each containing the same number of patients, were generated with replacement. In each sample a stepwise selection process to derive the original model was applied. The calibration slope was calculated for each of the 300 sample derived models (apparent performance) and also for each of the 300 sample derived models applied to the original dataset (true performance). The difference between the two calibration slopes for each sample was averaged over the 300 samples. This reflected the optimism of the calibration slope in the original model.

Text S2. Predicting continuation of IVF after a failed first complete cycle

Methods

We conducted a further analysis to investigate the effect of patient characteristics and treatment information from the first complete cycle on continuing to a second complete IVF cycle. Women who had a live-birth in their first complete cycle were excluded from the analysis. A Cox regression model was used to predict the hazard of continuation of IVF after a failed first complete cycle. The start time was date of last treatment (fresh or frozen-thawed transfer attempt) in the first complete cycle and the end date was either the date of egg collection in the second complete cycle or the end of follow-up (30th September 2009), whichever came first. Patients were censored if they did not start a second complete cycle during follow-up. The same patient and treatment predictors were used in this model as was used in the post-treatment discrete time model.

Results

Younger female age and shorter duration of infertility were associated with an increased chance of continuing treatment (see table below). Women who never had a previous pregnancy were 28% more likely to continue than women who had a previous pregnancy. Tubal and anovulation infertility resulted in a decreased chance of continuing treatment. Women who had a single fresh cleavage stage embryo transfer in their first complete cycle had a decreased chance of continuing compared to those who had a double cleavage stage transfer. Those who had no fresh embryos transferred in their first complete cycle had a 8% increased chance of continuing compared to those who had a double cleavage stage transfer.

The chances of continuing reduced by 25% in those who had cryopreserved embryos in their first complete cycle. This may be because the patient did not have them all transferred by the end of follow-up.

Table showing the effect of patient and treatment characteristics on continuing IVF to complete cycle 2 in patients who did not have a live-birth in complete cycle 1.

Parameter	Hazard Ratio (95% CI)	p-value
Previous pregnancy in couple, no v yes	1.28 (1.25 to 1.31)	< 0.001
Tubal infertility, yes v no	0.93 (0.90 to 0.96)	< 0.001
Anovulatory infertility, yes v no	0.88 (0.85 to 0.90)	< 0.001
Male factor infertility, yes v no	1.05 (1.01 to 1.08)	0.005
Unexplained infertility, yes v no	1.03 (0.99 to 1.06)	0.13
Endometriosis, yes v no	0.97 (0.93 to 1.01)	0.19
Treatment type, ICSI v IVF	0.94 (0.92 to 0.97)	< 0.001
Cryopreservation of embryos, yes v no	0.75 (0.73 to 0.77)	< 0.001
Stage of embryos transferred		
Double cleavage stage	1	
No embryos transferred	1.08 (1.04 to 1.11)	< 0.001
Single cleavage stage	0.91 (0.87 to 0.94)	< 0.001
Single blastocyst stage	0.92 (0.77 to 1.09)	0.32
Double blastocyst stage	0.93 (0.86 to 1.01)	0.09
Triple cleavage stage	1.02 (0.99 to 1.06)	0.22
Triple blastocyst stage	0.99 (0.75 to 1.30)	0.93
Year first complete cycle started, 2001 v 2006	1.28 (1.25 to 1.30)	< 0.001
Female age, 31 versus 38 years ¹	1.15 (1.13 to 1.17)	< 0.001
Duration, 3 v 7 years	1.18 (1.17 to 1.19)	< 0.001
Number of eggs collected, 12 v 4	1.05 (1.03 to 1.07)	< 0.001

Text S3. Formula to calculate the predicted probability of a live-birth over a maximum of six complete cycles of IVF

Calculating probabilities from the pre-treatment model

Variable names (and range of possible values)

Age - Female age (18 to 50 years)

Duration - How long have you been trying to conceive? (0 to 21 years)

Previous - Have you been pregnant before? (1=No; 0=Yes)

Tubal - Do you have a problem with your tubes? (1=Yes; 0=No)

Anovulation – Do you have an ovulation problem? (1=Yes; 0=No)

MaleFactor – Do you have a male factor fertility problem? (1=Yes; 0=No)

Unexplained – Do you have an unexplained fertility problem? (1=Yes; 0=No)

Treatment – Which fertility treatment are you planning on having? (1=ICSI; 0=IVF)

Table showing parameter estimates (95% CI) for each of the predictors in the pre-treatment model, adjusted for patient characteristics

Predictors	Parameter Estimate (95% CI)	p-value
Intercept	-0.9948 (-1.3204 to -0.6701)	< 0.001
Cycle number		
1 (Reference)	0	
2	-0.2394 (-0.2652 to -0.2136)	< 0.001
3	-0.4110 (-0.4518 to -0.3705)	< 0.001
4	-0.5628 (-0.6333 to -0.4933)	< 0.001
5	-0.7189 (-0.8448 to -0.5962)	< 0.001
6	-0.8138 (-1.0333 to -0.6044)	< 0.001
Patient characteristics		
Female age as restricted cubic spline ¹		
Age	0.0275 (0.0172 to 0.0378)	< 0.001
Age1	-0.1805 (-0.2273 to -0.1338)	< 0.001
Age2	0.4553 (0.1981 to 0.7127)	< 0.001
Age3	-1.1990 (-1.6606 to -0.7383)	< 0.001
Duration, years	-0.0295 (-0.0327 to -0.0263)	< 0.001
Treatment type, ICSI v IVF	0.2155 (0.1874 to 0.2435)	< 0.001
Male factor infertility, yes v no	-0.1005 (-0.1352 to -0.0659)	< 0.001
Tubal infertility, yes v no	-0.0957 (-0.1304 to -0.0611)	< 0.001
Unexplained infertility, yes v no	0.0602 (0.0250 to 0.0954)	< 0.001
Anovulatory infertility, yes v no	0.0492 (0.0138 to 0.0845)	0.01
Previous pregnancy in couple, no v yes	-0.0772 (-0.1024 to -0.0520)	< 0.001
Year of first egg retrieval, as restricted cubic spline ³		
Year	0.0334 (0.0138 to 0.0531)	< 0.001
Year1	-0.0370 (-0.0961 to 0.0222)	0.22
Year2	0.2173 (0.0452 to 0.3894)	0.01

 $^{^{1}} Age1=max((Age-26)/k,0)**3+(11*max((Age-41)/k,0)**3-(15)*max((Age-37)/k,0)**3)/4;\\ Age2=max((Age-31)/k,0)**3+(6*max((Age-41)/k,0)**3-(10)*max((Age-37)/k,0)**3)/4;\\ Age3=max((Age-34)/k,0)**3+(3*max((Age-41)/k,0)**3-(7)*max((Age-37)/k,0)**3)/4;\\ where k=15**(2/3);$

Using the information from the above table, the model formula is calculated as follows:

1. The following Age1 to Age3 equations are first calculated using the female age and then feed into the XB equation below in point 3:

```
\label{eq:age-26} Age1=max((Age-26)/k,0)**3+(11*max((Age-41)/k,0)**3-(15)*max((Age-37)/k,0)**3)/4;\\ Age2=max((Age-31)/k,0)**3+(6*max((Age-41)/k,0)**3-(10)*max((Age-37)/k,0)**3)/4;\\ Age3=max((Age-34)/k,0)**3+(3*max((Age-41)/k,0)**3-(7)*max((Age-37)/k,0)**3)/4;\\ where k=15**(2/3), **means 'to the power of'
```

² The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year of first egg retrieval and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile and the odds of a live-birth for the 25th percentile of the predictor.

³ Year1=max((Year+9)/k,0)**3+((6)*max((Year)/k,0)**3-(9)*max((Year+3)/k,0)**3)/(3); Year2=max((Year+6)/k,0)**3+((3)*max((Year)/k,0)**3-(6)*max((Year+3)/k,0)**3)/(3); where k=9**(2/3).

2. Calculate the following Year1 and Year2 equations. Use the value Year=0 for the most up to date predictions and then feed into the XB equation below in point 3:

```
\label{eq:Year1} Year1=max((Year+9)/k,0)**3+((6)*max((Year)/k,0)**3-(9)*max((Year+3)/k,0)**3)/(3); \\ Year2=max((Year+6)/k,0)**3+((3)*max((Year)/k,0)**3-(6)*max((Year+3)/k,0)**3)/(3); \\ where k=9**(2/3).
```

3. Calculate XB

```
\label{eq:XB} \begin{split} XB &= -0.9948 + 0.0362^a + (0.0275*Age) + (-0.1805*Age1) + (0.4553*Age2) + (-1.1990*Age3) + \\ (-0.0295*Duration) + (-0.0772*Previous) + (-0.0957*Tubal) + (0.0492*Anovulation) + \\ (-0.1005*MaleFactor) + (0.0602*Unexplained) + (0.2155*Treatment) + (0.0334*Year) + \\ (-0.0370*Year1) + (0.2173*Year2). \end{split}
```

4. For each couple we want to calculate their probability of live-birth after the first, second,, sixth cycle of IVF:

```
PCycle1 = exp(XB)/(1+exp(XB))

PCycle2 = exp(XB - 0.2394)/(1+exp(XB - 0.2394))

PCycle3 = exp(XB - 0.4110)/(1+exp(XB - 0.4110))

PCycle4 = exp(XB - 0.5628)/(1+exp(XB - 0.5628))

PCycle5 = exp(XB - 0.7189)/(1+exp(XB - 0.7189))

PCycle6 = exp(XB - 0.8138)/(1+exp(XB - 0.8138))
```

5. We then calculate the cumulative probability of a live-birth after 1, 2, 3,...., 6 cycles:

```
\begin{split} & \text{CumPCycle1} = 1\text{-}(1\text{-}p1) \\ & \text{CumPCycle2} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)) \\ & \text{CumPCycle3} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)) \\ & \text{CumPCycle4} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)\text{*}(1\text{-}p4)) \\ & \text{CumPCycle5} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)\text{*}(1\text{-}p4)\text{*}(1\text{-}p5)) \\ & \text{CumPCycle6} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)\text{*}(1\text{-}p4)\text{*}(1\text{-}p5)\text{*}(1\text{-}p6)) \\ \end{split}
```

Calculating probabilities from the post-treatment model

Variable names (and range of possible values)

```
Age - Female age (18 to 50 years)

Duration - How long have you been trying to conceive? (0 to 21)

Previous - Have you been pregnant before? (1=No; 0=Yes)

Tubal - Do you have a problem with your tubes? (1=Yes; 0=No)

Eggs - How many eggs were collected on your first IVF cycle? (1 to 28)

Treat - Was your first cycle IVF or ICSI? (1= ICSI; 0= IVF)

Cryo - In your first cycle did you have embryos frozen? (1=Yes; 0=No)
```

Stage – What type of embryo transfer did you have in your first fresh embryo transfer? (Double cleavage stage; No embryos transferred; Single cleavage stage; Single blastocyst stage; Double blastocyst stage; Triple cleavage stage; Triple blastocyst stage)

^aTo inflate predictions to 2013 we must add an additional 0.0362

Table showing the parameter estimates (95% CI) for each of the predictors in the post-treatment model, adjusted for patient characteristics and treatment information at the first complete cycle

Predictors	Parameter Estimate (95% CI)	p-value
Intercept	-1.7612 (-2.0781 to -1.4453)	< 0.001
Cycle number		
1 (Reference)	0	
2	-0.1934 (-0.2212 to -0.1658)	< 0.001
3	-0.3539 (-0.3977 to -0.3103)	< 0.001
4	-0.5124 (-0.5883 to -0.4375)	< 0.001
5	-0.6790 (-0.8139 to -0.5476)	< 0.001
6	-0.7665 (-0.9987 to -0.5451)	< 0.001
Patient characteristics		
Female age as restricted cubic spline ¹		
Age	0.0271 (0.0162 to 0.0380)	< 0.001
Age1	-0.1556 (-0.2052 to -0.1061)	< 0.001
Age2	0.3816 (0.1095 to 0.6541)	0.01
Age3	-1.0187 (-1.5064 to -0.5321)	< 0.001
Duration, years	-0.0208 (-0.0242 to -0.0174)	< 0.001
Previous pregnancy in couple, no v yes	-0.0504 (-0.0770 to -0.0237)	< 0.001
Tubal infertility, yes v no	-0.2207 (-0.2493 to -0.1921)	< 0.001
Year of first egg retrieval, as restricted cubic spline ³		
Year	0.0018 (-0.0090 to 0.0125)	0.75
Year1	0.0619 (0.0499 to 0.0738)	< 0.001
Treatment information at first complete cycle		
Number of eggs collected as restricted cubic spline ⁴		
Eggs	0.0642 (0.0576 to 0.0707)	< 0.001
Eggs1	-0.0499 (-0.0573 to -0.0425)	< 0.001
Cryopreservation of embryos, yes v no	0.6497 (0.6235 to 0.6760)	< 0.001
Number and stage of embryos transferred		< 0.001
Double cleavage stage	0	
No embryos transferred	-1.0833 (-1.1519 to -1.0157)	< 0.001
Single cleavage stage	-0.5662 (-0.6157 to -0.5171)	< 0.001
Single blastocyst stage	0.0694 (-0.0749 to 0.2132)	0.35
Double blastocyst stage	0.5817 (0.5126 to 0.6507)	< 0.001
Triple cleavage stage	0.0217 (-0.0252 to 0.0684)	0.36
Triple blastocyst stage	0.4559 (0.1376 to 0.7623)	0.004
Treatment type, ICSI v IVF	-0.0968 (-0.1209 to -0.0728)	< 0.001

 $^{^{1}} Age1= \overline{\max((Age-26)/k,0)}**3+(11*\max((Age-41)/k,0)**3-(15)*\max((Age-37)/k,0)**3)/4; \\ Age2= \max((Age-31)/k,0)**3+(6*\max((Age-41)/k,0)**3-(10)*\max((Age-37)/k,0)**3)/4; \\ Age3= \max((Age-34)/k,0)**3+(3*\max((Age-41)/k,0)**3-(7)*\max((Age-37)/k,0)**3)/4; \\ where k=15**(2/3);$

Model formula:

1. The following Age1 to Age3 equations are first calculated using the female age and then feed into the XB equation below in point 4:

```
\label{eq:age-age} Age1=max((Age-26)/k,0)**3+(11*max((Age-41)/k,0)**3-(15)*max((Age-37)/k,0)**3)/4;\\ Age2=max((Age-31)/k,0)**3+(6*max((Age-41)/k,0)**3-(10)*max((Age-37)/k,0)**3)/4;\\ Age3=max((Age-34)/k,0)**3+(3*max((Age-41)/k,0)**3-(7)*max((Age-37)/k,0)**3)/4;\\ where k=15**(2/3), **means 'to the power of'
```

2. Calculate the following Year1 equation. Use the value Year=0 for the latest year of data to predict future patients' probability of live-birth:

```
Year1=max((Year+8)/k,0)**3+((4)*max((Year+1)/k,0)**3-(7)*max((Year+4)/k,0)**3)/(3); where \ k=7**(2/3).
```

² The interquartile odds ratio was calculated to aid interpretation of the restricted cubic spline effects of age, year of first egg retrieval and eggs collected. It is defined as the ratio of the odds of a live-birth for the 75th percentile and the odds of a live-birth for the 25th percentile of the predictor.

 $^{^{3}}$ Year1=max((Year+8)/k,0)**3+((4)*max((Year+1)/k,0)**3-(7)*max((Year+4)/k,0)**3)/(3); where k= 7**(2/3);

 $^{^{4}}$ Eggs1=max((Eggs-3)/k,0)**3+((6)*max((Eggs-18)/k,0)**3-(15)*max((Eggs-9)/k,0)**3)/(9); where k= 15**(2/3);

```
3. The following Eggs1 equation is first calculated using the number of eggs and then feeds into the XB
equation below:
Eggs1=max((Eggs-3)/k,0)**3+((6)*max((Eggs-18)/k,0)**3-(15)*max((Eggs-9)/k,0)**3)/(9);
where k = 15**(2/3).
4. Calculate XB
XB = -1.7564 + 0.0362^{a} + (0.0272*Age) + (-0.1556*Age1) + (0.3812*Age2) + (-1.0184*Age3) + (-1.0184*Age3
(-0.0208*Duration) + (-0.0504*Previous) + (-0.2207*Tubal) + (0.0018*Year) + (0.0619*Year1) + (0.0619*Year1
(0.0630*Eggs) + (-0.0479*Eggs1) + (-0.0968*Treat) + (0.6490*Cryo) + Stage
<sup>a</sup>To inflate predictions to 2013 we must add an additional 0.0362
where Stage equals the following values depending on group chosen:
If Double cleavage stage then Stage=0:
If No embryos transferred then Stage= -1.0842:
If Single cleavage stage then Stage= -0.5675;
If Single blastocyst stage then Stage= 0.0684;
If Double blastocyst stage then Stage= 0.5802;
If Triple cleavage stage then Stage= 0.0218;
If Triple blastocyst stage then Stage= 0.4547.
5. For each couple we want to calculate their probability of live-birth after the first, second, ...., sixth cycle of
PCycle1 = exp(XB)/(1+exp(XB))
PCycle2 = exp(XB - 0.1933)/(1 + exp(XB - 0.1933))
PCycle3 = exp(XB - 0.3537)/(1+exp(XB - 0.3537))
PCycle4 = exp(XB - 0.5122)/(1+exp(XB - 0.5122))
PCycle5 = exp(XB - 0.6788)/(1+exp(XB - 0.6788))
PCycle6 = exp(XB - 0.7666)/(1 + exp(XB - 0.7666))
6. We then calculate the cumulative probability of a live-birth after 1, 2, 3, ...., 6 cycles:
CumPCycle1 = 1-(1-p1)
CumPCycle2 = 1-((1-p1)*(1-p2))
CumPCvcle3 = 1-((1-p1)*(1-p2)*(1-p3))
CumPCycle4 = 1-((1-p1)*(1-p2)*(1-p3)*(1-p4))
CumPCycle5 = 1-((1-p1)*(1-p2)*(1-p3)*(1-p4)*(1-p5))
CumPCycle6 = 1-((1-p1)*(1-p2)*(1-p3)*(1-p4)*(1-p5)*(1-p6))
The following model must be used for patients with ZERO eggs collected:
Variable names (and range of possible values)
```

```
Age - Female age (18 to 50 years)

Duration - How long have you been trying to conceive? (0 to 21)

Previous - Have you been pregnant before? (1=No; 0=Yes)

Tubal - Do you have a problem with your tubes? (1=Yes; 0=No)

Anovulation - Do you have an ovulation problem? (1=Yes; 0=No)

MaleFactor - Do you have a male factor fertility problem? (1=Yes; 0=No)

Unexplained - Do you have an unexplained fertility problem? (1=Yes; 0=No)

Treatment - Which fertility treatment are you planning on having? (1=ICSI; 0=IVF)
```

Model formula:

1. The following Age1 to Age3 equations are first calculated using the female age and then feed into the XB equation below in point 4:

2. Please calculate the following Year1 equation using the value Year=0 and then feed into the XB equation below. The reason Year is fixed to 0 is because we want to always use the latest year of data to predict future patients' probability of live-birth:

```
Year1=max((Year+8)/k,0)**3+((4)*max((Year+1)/k,0)**3-(7)*max((Year+4)/k,0)**3)/(3); where k=7**(2/3).
```

3. Calculate XB

```
\label{eq:XB} \begin{split} XB &= -1.9379 + 0.0362^a + (0.0392*Age) + (-0.2921*Age1) + (0.7076*Age2) + (-1.1876*Age3) + \\ & (-0.0424*Duration) + (0.0271*Previous) + (0.1139*Tubal) + (0.0787*Anovulation) + \\ & (0.1680*MaleFactor) + (0.1950*Unexplained) + (0.0369*Year) + (0.0205*Year1) + (-0.4042*Treat) \end{split}
```

^aTo inflate predictions to 2013 we must add an additional 0.0362

4. For each couple we want to calculate their probability of live-birth after the first, second, ..., sixth cycle of IVF:

```
\begin{split} & PCycle1 = 0 \\ & PCycle2 = exp(XB)/(1+exp(XB)) \\ & PCycle3 = exp(XB - 0.1364)/(1+exp(XB - 0.1364)) \\ & PCycle4 = exp(XB - 0.1846)/(1+exp(XB - 0.1846)) \\ & PCycle5 = exp(XB - 0.2207)/(1+exp(XB - 0.2207)) \\ & PCycle6 = exp(XB - 0.5796)/(1+exp(XB - 0.5796)) \end{split}
```

5. We then calculate the cumulative probability of a live-birth after 1, 2, 3,, 6 cycles:

```
\begin{split} & \text{CumPCycle1} = 1\text{-}(1\text{-}p1) \\ & \text{CumPCycle2} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)) \\ & \text{CumPCycle3} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)) \\ & \text{CumPCycle4} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)\text{*}(1\text{-}p4)) \\ & \text{CumPCycle5} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)\text{*}(1\text{-}p4)\text{*}(1\text{-}p5)) \\ & \text{CumPCycle6} = 1\text{-}((1\text{-}p1)\text{*}(1\text{-}p2)\text{*}(1\text{-}p3)\text{*}(1\text{-}p4)\text{*}(1\text{-}p5)\text{*}(1\text{-}p6)) \\ \end{split}
```

References

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- 2. Steyerberg EW. Clinical prediction models: a practical approach to development, validation, and updating. New York: *Springer*, 2009.