

ART and the Neonate

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Letters to the Editor

BIRTH AFTER THE REIMPLANTATION OF A HUMAN EMBRYO

SIR,—We wish to report that one of our patients, a 30-year-old nulliparous married woman, was safely delivered by caesarean section on July 25, 1978, of a normal healthy infant girl weighing 2700 g. The patient had been referred to one of us (P.C.S.) in 1976 with a history of 9 years' infertility, tubal occlusions, and unsuccessful salpingostomies done in 1970 with excision of the ampullæ of both oviducts followed by persistent tubal blockages. Laparoscopy in February, 1977, revealed grossly distorted tubal remnants with occlusion and peritubal and ovarian adhesions. Laparotomy in August, 1977, was done with excision of the remains of both tubes, adhesolysis, and suspension of the ovaries in good position for oocyte recovery.

Pregnancy was established after laparoscopic recovery of an oocyte on Nov. 10, 1977, in-vitro fertilisation and normal cleavage in culture media, and the reimplantation of the 8-cell embryo into the uterus 2½ days later. Amniocentesis at 16 weeks' pregnancy revealed normal α -fetoprotein levels, with no chromosome abnormalities in a 46 XX fetus. On the day of delivery the mother was 38 weeks and 5 days by dates from her last menstrual period, and she had pre-eclamptic toxæmia. Blood-pressure was fluctuating around 140/95, œdema involved both legs up to knee level together with the abdomen, back, hands, and face; the blood-uric-acid was 390 μ mol/l, and albumin 0.5 g/l of urine. Ultrasonic scanning and radiographic appearances showed that the fetus had grown slowly for several weeks from week 30. Blood-œstriols and human placental lactogen levels also dropped below the normal levels during this period. However, the fetus grew considerably during the last 10 days before delivery while placental function improved greatly. On the day of delivery the biparietal diameter had reached 9.6 cm, and 5 ml of amniotic fluid was removed safely under sonic control. The lecithin: sphingomyelin ratio was 3.9:1, indicative of maturity and a low risk of the respiratory-distress syndrome.

We hope to publish further medical and scientific details in your columns at a later date.

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P. C. STEPTOE

R. G. EDWARDS



Dr Robert Edwards with photos of IVF babies at the Bourn Hall Clinic, Cambridgeshire, in 1989

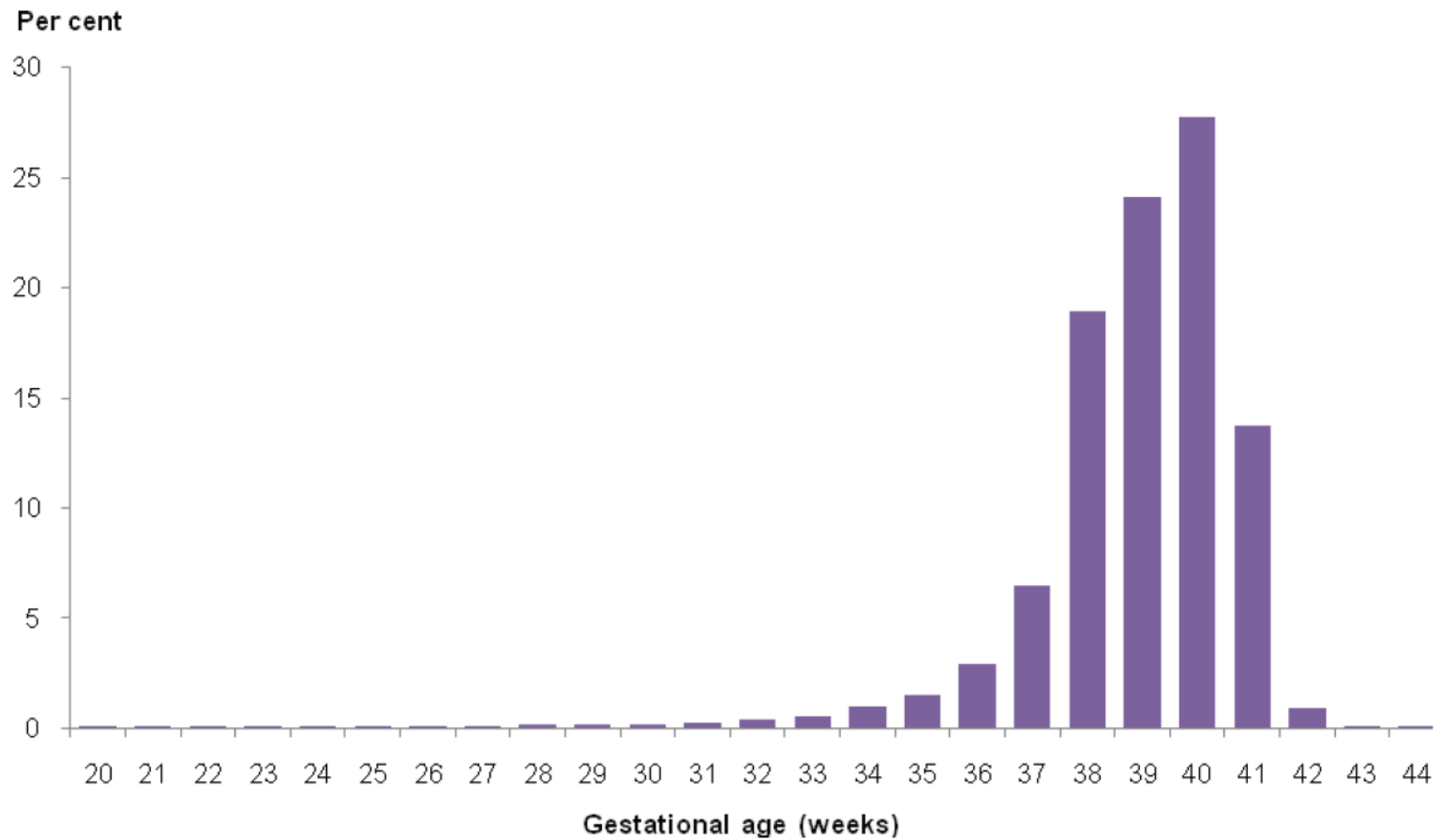
IVF pioneer Robert Edwards wins Nobel prize for medicine

Women who gave birth by whether pregnancy was the result of assisted reproduction technology (ART) and state and territory, 2007

	NSW	Vic	Qld	WA	SA	Tas	ACT	NT	Total
Number									
ART	n.a.	1,979	2,145	n.a.	n.a.	230	74	n.a.	4,428
Not ART	n.a.	69,209	57,080	n.a.	n.a.	5,986	5,342	n.a.	137,617
Not stated	n.a.	1	3	n.a.	n.a.	—	3	n.a.	7
Total	n.a.	71,189	59,228	n.a.	n.a.	6,216	5,419	n.a.	142,052
Per cent									
ART	n.a.	2.8	3.6	n.a.	n.a.	3.7	1.4	n.a.	3.1
Not ART	n.a.	97.2	96.4	n.a.	n.a.	96.3	98.6	n.a.	96.9
Not stated	n.a.	0.0	0.0	n.a.	n.a.	—	0.1	n.a.	0.0
Total	n.a.	100.0	100.0	n.a.	n.a.	100.0	100.0	n.a.	100.0

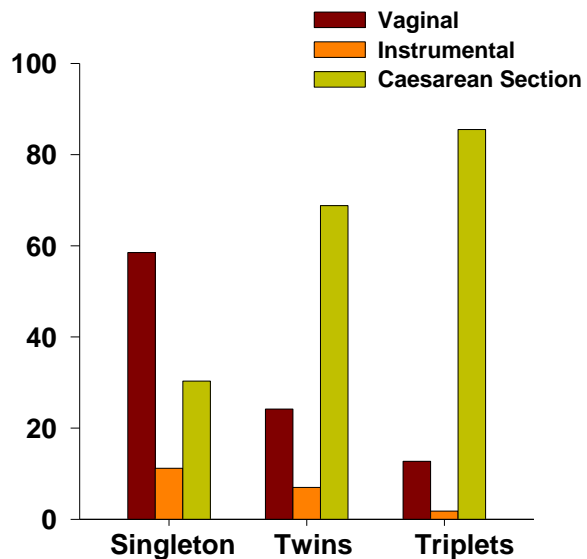
n.a. Data not available.

The average age of women who received ART was 34.1 years. This was higher than the average age of women who did not receive ART treatment (29.8 years). In 2007, 62.7% of mothers who received ART treatment were having their first baby and 37.3% had given birth previously.

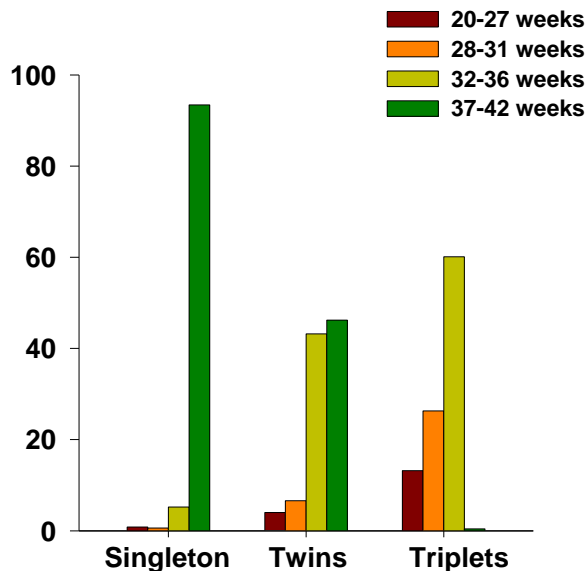


Distribution of gestational age, 2007 (per cent)

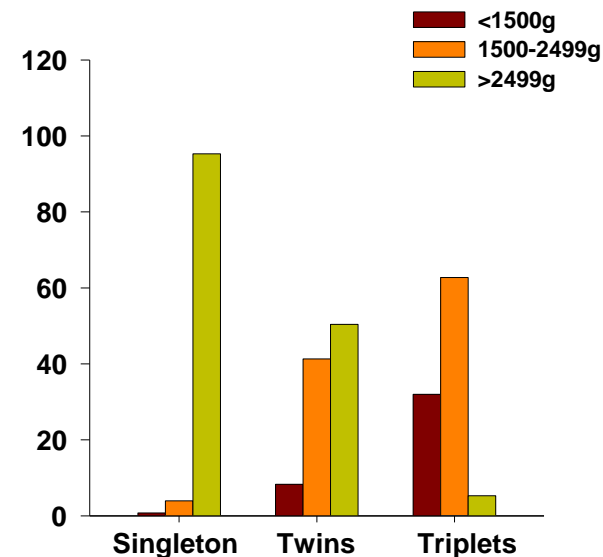
Delivery Mode



Gestational Age



Birth Weight

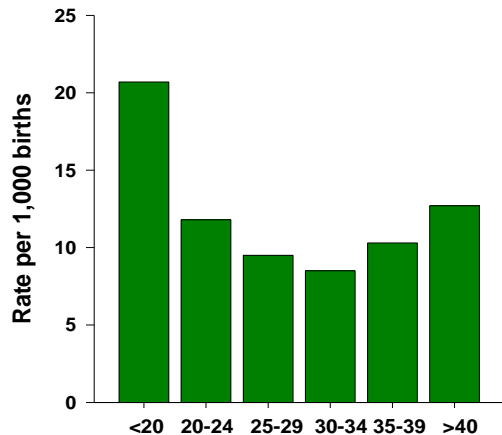


Gestational age (weeks)	Singletons		Twins		Triplets		Total	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Total	284,862	100.0	9,115	100.0	228	100.0	294,205	100.0
20-36	18,827	6.6	4,899	53.7	227	99.6	23,953	8.1
Mean (weeks)	38.9		35.3		31.3		38.8	

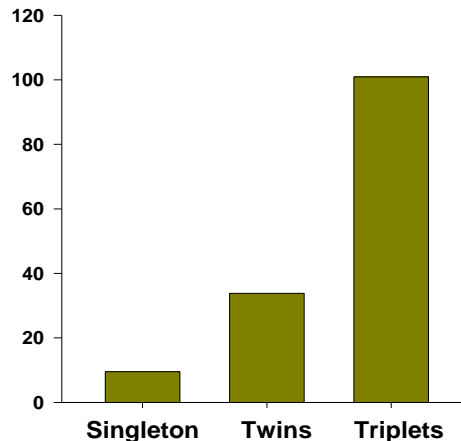
Birthweight (g)	Singletons		Twins		Triplets		Total	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Total	282,887	100.0	8,931	100.0	209	100.0	292,027	100.0
Less than 1,500	2,149	0.8	740	8.3	67	32.1	2,956	1.0
Less than 2,500	13,346	4.7	4,432	49.6	198	94.7	17,976	6.2
Mean (g)	3,406		2,413		1,701		3,374	



Maternal Age

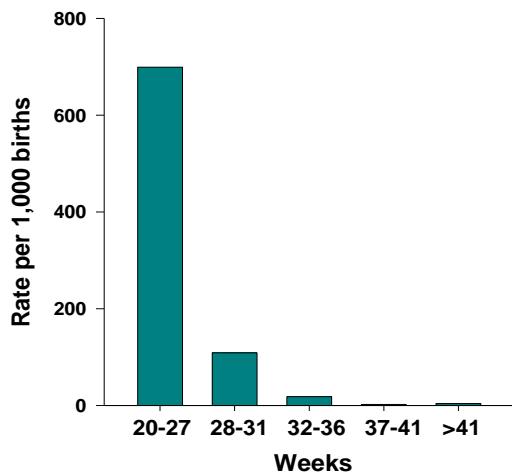


Plurality

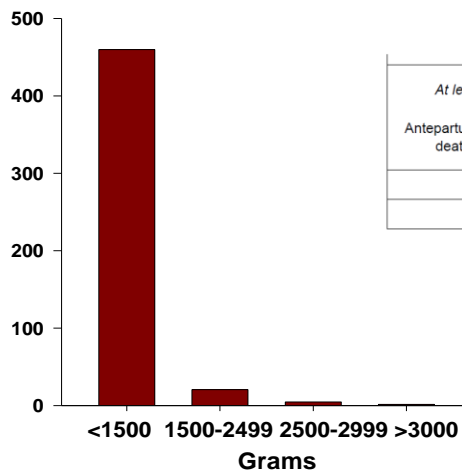


Perinatal mortality

Gestational Age



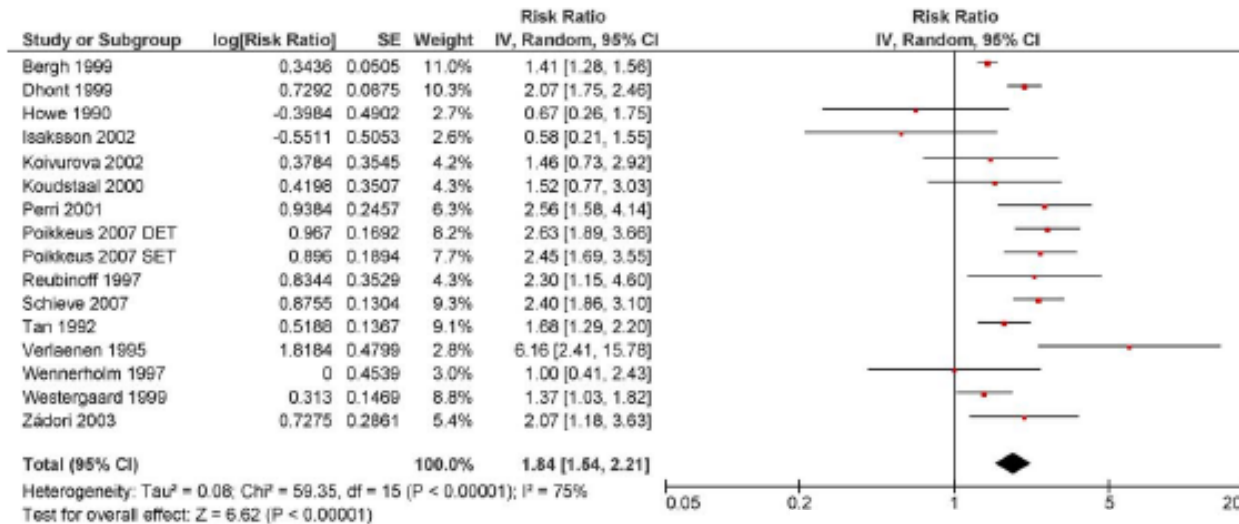
Birth Weight



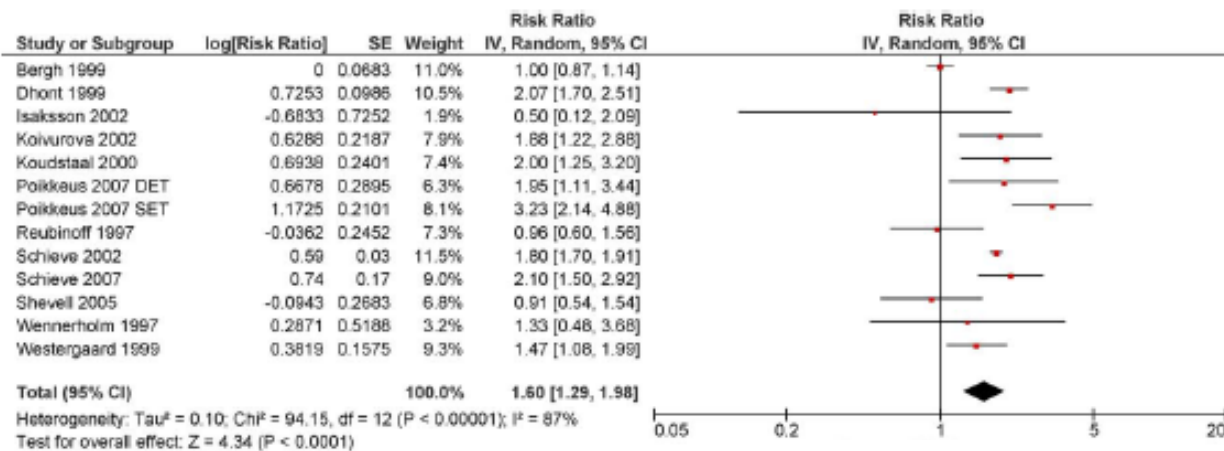
Labour		Birth		7 days	28 days	1 year
At least 20 weeks or 400 grams		0-6 days		7-27 days	28 days-<1 year	
Antepartum fetal deaths	Intrapartum fetal deaths	Early neonatal deaths		Late neonatal deaths	Postneonatal deaths	
Fetal deaths		Neonatal deaths				
Perinatal deaths						
Infant deaths						



Preterm birth and low birth weight among *in vitro* fertilisation singletons

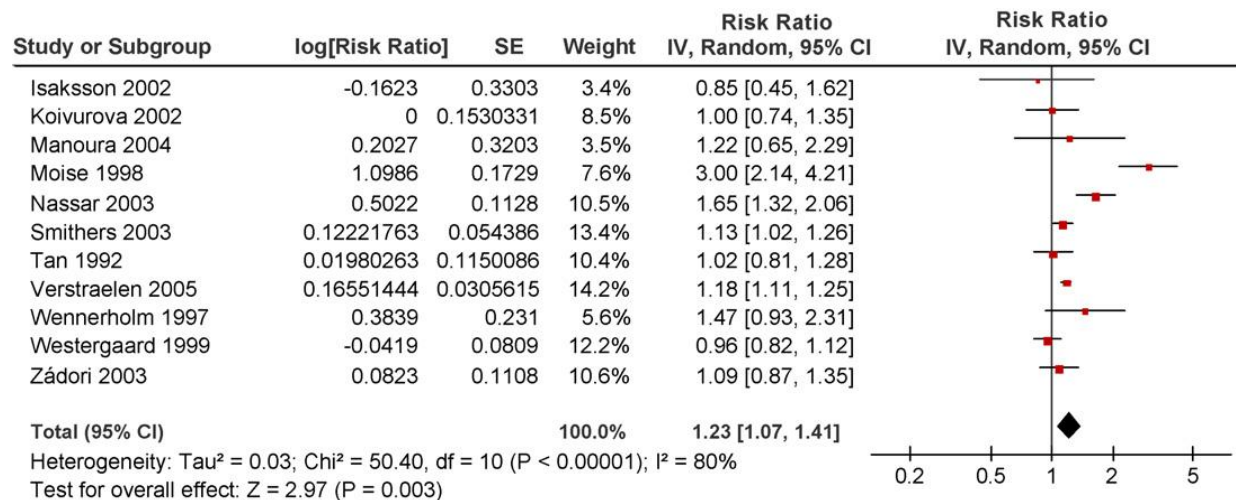


Preterm Birth

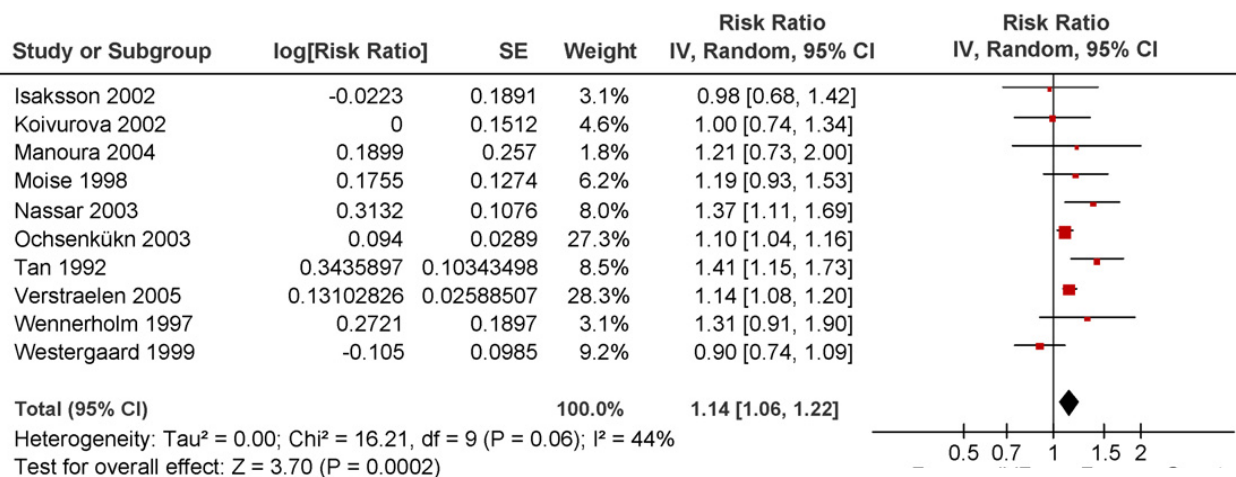


Low Birth Weight

Preterm birth and low birth weight among *in vitro* fertilisation twins

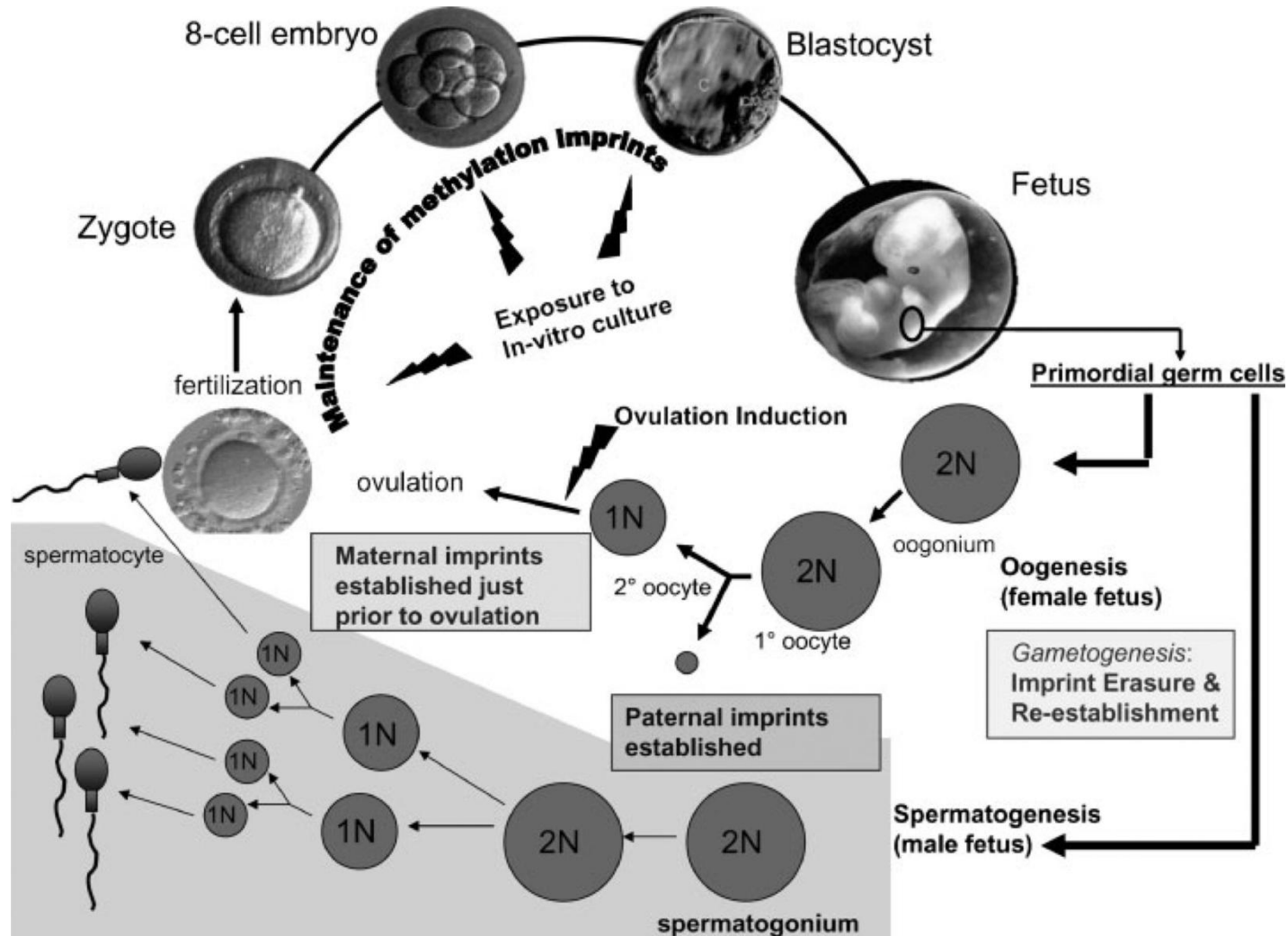


Preterm Birth



Low Birth Weight

Why?



An overview of studies on early development, cognition, and psychological well-being in children born after ART

Table 1. Studies on the Early Mental and Psychomotor Development of Children Born After In Vitro Fertilization

Ref. (Year/Country)	Sample Size	Control Group(s)	Age of Children	Method	Outcome
Mushin et al ^{11,12} (1986/1985/Australia)	33 IVF singletons/twins	—	12–37 mo	Bayley Scales of Infant Development, Denver Development Screening Test	Overall scores within the normal range
Yovich et al ¹³ (1986/Australia)	20 IVF	—	1st birthday	Griffith Developmental Scales	Scores within the normal range; only one infant under the general quotient
Morin et al ¹⁴ (1989/United States)	83 IVF	93 NC	13–30 mo	Bayley Scales of Infant Development	Scores within the normal range (mental scale IVF-NC: 115 vs 111; motor scale IVF-NC: 114 vs 108). High score for IVF explained by high socioeconomic status and “wantedness”
Gershoni-Baruch et al ¹⁵ (1991/Israel)	33 IVF (HFTVS) 45 IVF (non-HFTVS) singletons/twins	33 NC (HFTVS) 45 NC (non-HFTVS) singletons/twins	12–30 mo	Bayley Scales of Infant Development	Scores within the normal range and no differences between groups; twins lower mental indices than singletons
Brandes et al ¹⁶ (1992/Israel)	116 IVF singletons/twins/triplets	116 NC singletons/twins/triplets	12–45 mo	Bayley Scales of Infant Development, Stanford-Binet Scales	Scores of IVF within normal range and no differences with NC. Twins lower mental indices compared with singletons
Raoul-Duval et al ^{19,36} (1994/1993/France)	33 IVF singletons	33 NC, 33 OI	9, 18, 36 mo	Brunet-Lezine test	Psychomotor development is satisfactory, no differences with control groups
Ron-El et al ¹⁷ (1994/Israel)	26 IVF singletons	29 NC	≥28 mo	McCarthy Scales of Children’s Abilities	No differences between groups on General Cognitive Index (IVF-NC: 102 vs 106) and on verbal, perception, motor, and memory indexes
Gibson et al ¹⁸ (1998/Australia)	65 IVF singletons	62 NC	1 yr	Bayley Scales of Infant Development	Scores within normal range, no group differences (mental scale IVF-NC: 102 vs 103; motor scale IVF-NC: 90 vs 89)
Koivurova et al ²⁰ (2003/Finland)	299 IVF singletons/multiples	558 NC	0–3 yr	Developmental Milestone Test modified after Bayley Scales	No differences in psychomotor development at different age periods
Sutcliffe et al ^{21,22} (1995/United Kingdom)	91 IVF cryopreserved embryos; singletons/twins/triplets	83 NC	IVF: 25.08 mo NC: 29.19 months	Griffith Scales of Mental Development	Mean Griffith quotient in both groups in normal range and above 100 (IVF-NC: 105.69 vs 108.18); no similar age at testing
Wennerholm et al ²³ (1998/Sweden)	255 IVF cryopreserved embryos; singletons/twins	225 IVF, fresh embryos 252 NC	0–18 mo	Information about delayed psychomotor development recorded from Child Health Centers	No differences between the groups for delay in psychomotor development
Pinborg et al ²⁴ (2003/Denmark)	472 IVF/ICSI twins	634 IVF/ICSI singletons 1132 NC twins	3–4 yr	Speech development and motor function by questionnaire by the mother	No differences between twin groups. Poorer speech development in twins than singletons. No differences for motor function

IVF, in vitro fertilization; NC, naturally conceived children; HFTVS, high-frequency transvaginal ultrasonography; OI, ovulation induction without IVF; ICSI, intracytoplasmic sperm injection.

Comparable longer-term cognitive outcomes

Table 2. Studies on the Cognition and School Performance of Children Born After In Vitro Fertilization

Ref. (Year/ Country)	Sample Size	Control Groups	Age of Children	Method	Outcome
Cederblad et al ²⁷ (1996/Sweden)	99 IVF singletons/ twins/triplets	Swedish population	2.9–7 yr; mean age, 5.2 yr	Griffith Scales of Mental Development	Cognitive development of IVF above mean of Swedish population, but IVF parents from higher socioeconomic class
Levy-Shiff et al ²⁸ (1998/Israel)	51 IVF	51 NC	9–10 yr	Wechsler Intelligence Scale for Children, Bender Visual Motor Gestalt Test, Benton Visual Retention Test, Reading Comprehension Test, Rating Scale for School Adjustment	No differences in intelligence (IQ), visuomotor coordination, visual memory, and verbal comprehension
Olivennes et al ²⁹ (1997/France)	422 IVF	—	6–13 yr	Questionnaire (via mail or telephone) by parents to obtain information about school performance: rank in class, advanced, average or delayed according to age	92.2% at least average achievement, 3.8% low achievement, 3.8% a year or more delayed, and 0.2% attending special education classes
Olivennes et al ³⁰ (1996/France)	82 IVF frozen embryos	—	1–9 yr	See Olivennes et al ²⁹	No pathological features in scholastic performance: only one child with low achievement, no children delayed or attending special education

Achievement test performance in children conceived by IVF

L. Mains¹, M. Zimmerman², J. Blaine¹, B. Stegmann¹, A. Sparks¹,
T. Ansley³, and B. Van Voorhis^{1,*}

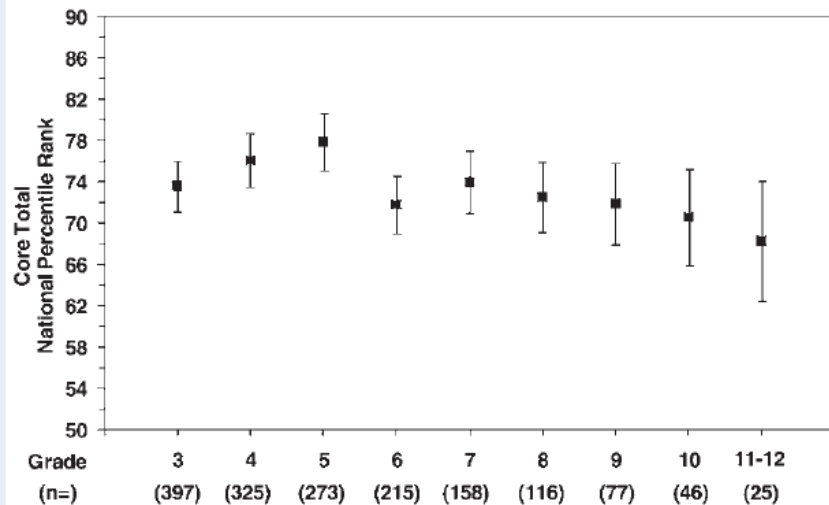


Figure 1 CT NPR by grade, for children conceived by IVF. NPR 50th percentile represents the national average.

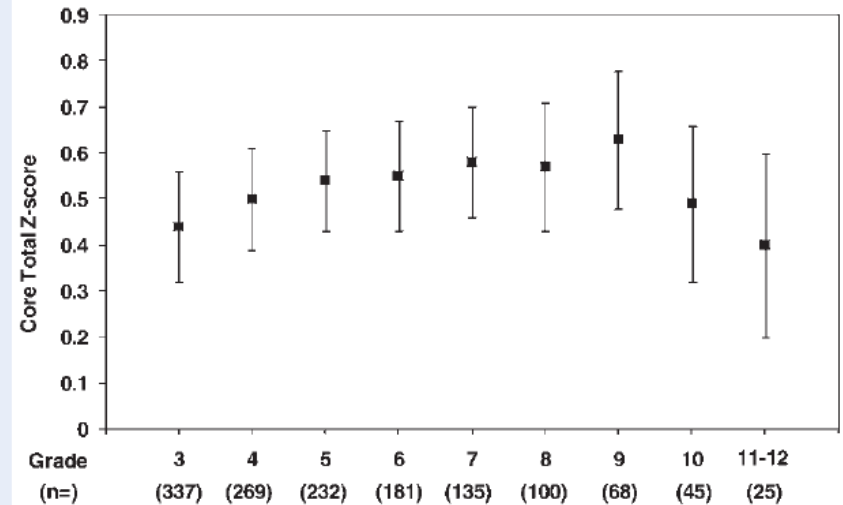


Figure 2 Normalized CT z-scores by grade. A z-score of zero indicates IVF children scored identical to their matched peers.



