

Multiple pregnancy and eSET

ESHRE WORKSHOP ON RISKS AND
COMPLICATIONS OF ART

Lübeck, Germany, January 18th 2008

22/01/2008 Jan Gerris - Fertility Centre - University Hospital Ghent 1

Overview of the lecture

- Epidemiology and biology of multiple pregnancies
- Epidemiology of induced multiple pregnancies
- Monozygotic twinning after infertility treatment
- Twins – perinatal consequences
- How to limit COS/AI and ART-twinning
- Conclusion

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Biological Factors in Twinning

Monozygotic twinning (~30%)
spontaneously stable in 1 /250 births
higher with ovarian stimulation and ART
higher with day 5 transfer
by and large remains constant

Dizygotic twinning (~70%)
race
genetic factors
maternal age
ovarian stimulation and ART
sharp and huge increase

22/01/2008 Hankins & Saade 2005. Paediatr Perinat Epidemiol 19 Suppl 1:8-9. 3

Twin placentation

Fig. 1-11 (continued)
 (a) Relationship between zygosity and chorionicity per 100 monozygotic twinned twin pairs.
 (b) A fused DC placenta, an MZ/DC placenta and an MZ/DC placenta.

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Relationships between zygosity and chorionicity

Figure 1-4 Relationship between zygosity and chorionicity:
 (a) Fused DC (upper), PIC/DA (middle) and PIC/MA (lower). DC twins may be DZ or MZ. The DC septum prevents vascular communication (red). PIC/DA and PIC/MA placentas are always MZ and usually have vascular anastomoses.
 (b) All PIC twins are MZ, but not all MZ twins are PIC. Likewise, all DZ twins are DC, but not all DC twins are DZ, as one-third of MZ twins are DC.

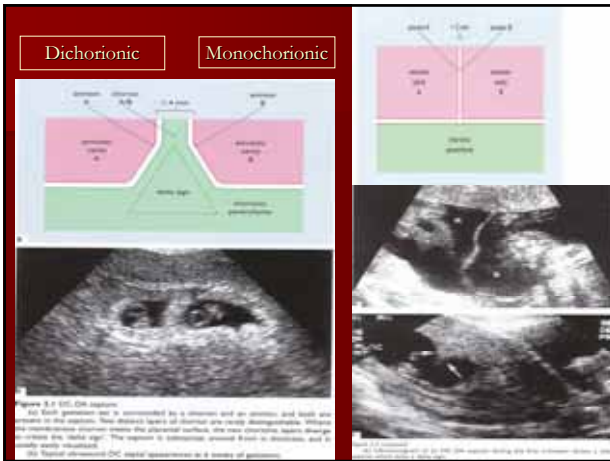
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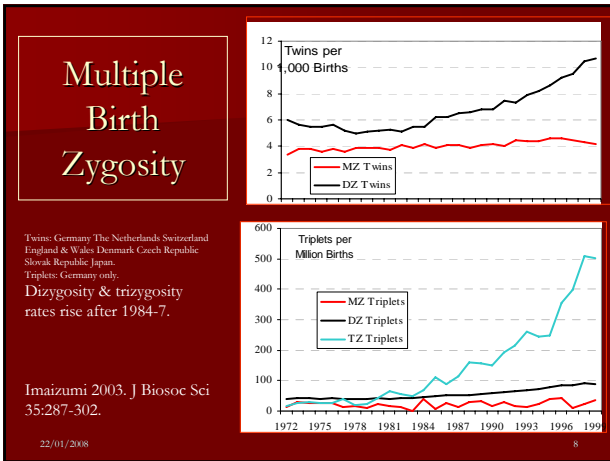
Time sensitive placental development in monozygotic twins

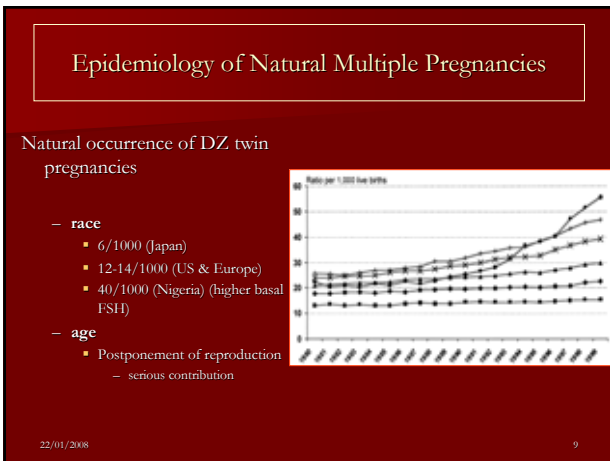
Days

- 0: 2 Chorions, 2 Amnions
- 4: 1 Chorion, 2 Amnions
- 8: 1 Chorion, 1 Amnion
- 12: 1 Chorion, 1 Amnion

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Age and Dizygotic Twinning

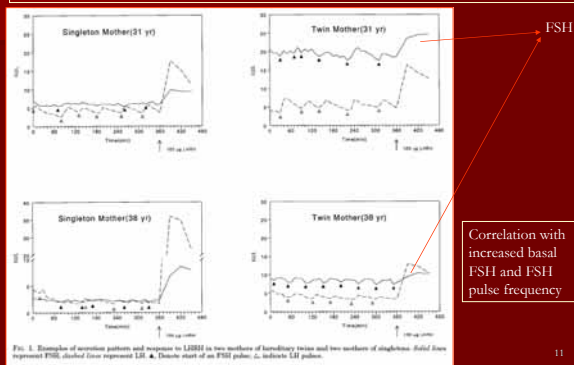
- Frequency increases from puberty up to age 37
- Correlates with maximal hormonal stimulation as determined by FSH levels
- Age accounts for (only) 25% to 30% of the increase in multiple births from 1980 to 2000

Hankins & Saade 2005. Paediatr Perinat Epidemiol 19 Suppl 1:8-9.

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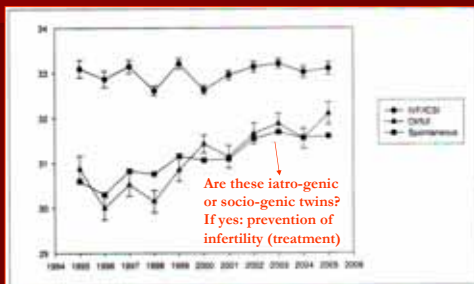
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The contribution of maternal age in the risk of twinning (Lambalk 1998)



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Evolution of maternal age in dizygotic twins in The Netherlands 1995 - 2006

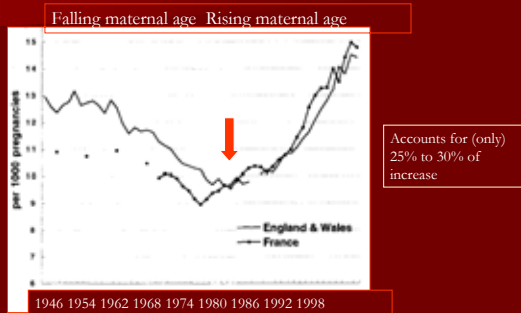


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Lambalk, VU Amsterdam 2007

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Impact of Maternal Age on Multiple Births



22/01/2008 Blondel & Kaminski 2002. Semin Perinatol 26:239-49.

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Genetic Factors in Dizygotic Twinning

Dizygotic twins

No risk factors	1 / 107 births
Mother a dizygotic twin	1 / 58 births
Father a dizygotic twin	1 / 116 births

22/01/2008 Hankins & Saade 2005. Paediatr Perinat Epidemiol 19 Suppl 1:8-9. 14

Parity and Dizygotic Twinning

	Primigravid	Multigravid
	Twins (%)	
Sweden	1.3	2.7
Nigeria	2	7

22/01/2008 Hankins & Saade 2005. Paediatr Perinat Epidemiol 19 Suppl 1:8-9. 15

Spontaneous DZ twinning: marker of high fecundity?

Natural dizygotic twinning involves:

- multiple ovulations
- successful fertilization of two ova
- multiple implantations
- maintenance of a multiple pregnancy

Zhu 2007:

Increasing TTP is associated with decreasing DZ twinning prevalence

Axmon 2005, Ferrari 2007:

MPs tend to have shorter TTP than singleton pregnancies

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Multiples after non-IVF: Size of the problem (in Belgium)

1993-2002: SPE-data
N deliveries : 574.197

	singletons	twins	triplets
Spontaneous	96.8%	61.9%	20.3%
IVF / ICSI	1.2%	24.6%	41.5%
Non-IVF	2.0%	13.5%	38.2%

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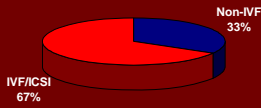
(courtesy W. Ombetel and SPE)

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Pregnancies after ART : n = 26.656

IVF / ICSI 46.5%
Non - IVF 53.5%

Multiples after ART: n = 8.895 (33.4%)

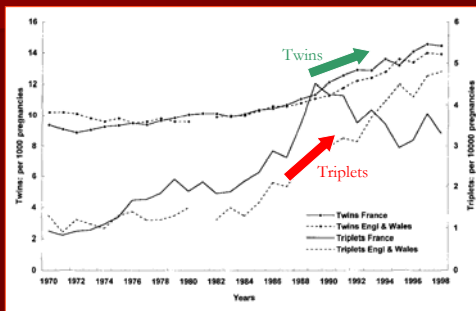


COH / TC 23.8%
AIH / AID 9.5%
IVF / ICSI 66.7%

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Twins and Triplets: England and Wales and France 1970-1998

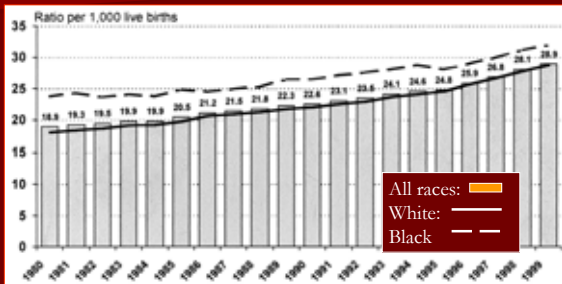


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Blondel & Kaminski 2002, Semin Perinatol 26:239-49.

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Twin Births: United States



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Source: National Center for Health Statistics.
Russell et al 2003. Obstet Gynecol 101:129-36.

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IATROGENIC MULTIPLE PREGNANCIES

Factors involved in the increase

- Rising age at childbirth (25 to 30%)
- Ovarian stimulation and ART
 - 40% of triplets originates from ART
 - 80% of triplets originates from infertility treatments
 - ART: 2% of twins in USA; 10% in France; 13% in Sweden, 30% in East Flanders (reflects access to treatment)
- Infertility treatments are more frequent in older women
- Twinning is a much larger problem than triplets

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IVF in Europe (1997 vs. 2002) Results from national registries collected by ESHRE

	TWINS		TRIPLETS	
	1997	2002	1997	2002
Denmark	24,2	23,1	0,4	0,3
Finland	26,3	15,2	1,1	0,2
France	23,7	21,0	1,9	0,7
Italy	20,3	24,1	5,1	4,1
Norway	28,2	28,9	1,2	0,3
Spain	32,7	27,7	11,7	3,4
Sweden	25,4	19,2	0,4	0,2
Germany	22,3	25,2	5,3	1,2
UK	25,9	21,8	3,3	0,6

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Underreporting of triplet reductions Hum Reprod 2006

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Multiple pregnancies (ART)

influence of stimulation protocol

- Natural cycle (TC, IUI): 1 - 2 %
- Clomiphene citrate (TC, IUI): 5 - 7 %
- hMG / rec FSH (TC, IUI): 15 - 25 %
- IVF / ICSI: 25 - 35 %

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Results of IUI with more or less aggressive stimulation protocols (17 studies)

<i>Type of stimulation</i>	<i>N cycles</i>	<i>Monthly Conc rate</i>	<i>% Multiples</i>	<i>% triplets</i>
CC/hMG	593	0.09	5	0.0
150 IU hMG	1528	0.12	19	3.2
150-225 IU hMG	1500	0.18	21	4.5
Analogue/hMG	259	0.20	31	8.5

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Take home message

Controlled ovarian hyperstimulation is at present uncontrolled and is bound to cause an epidemic in undesired multiple pregnancies

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Increased monozygotic twinning frequency after ovulation induction / IVF?

Spontaneous ovulation 0.3-0.4%
Ned 0.25% (www.cbs.nl)

Edwards <i>et al</i> , 1986	IVF	1.0%
Derom <i>et al</i> , 1993	ovulation induction	1.2%
Wenstrom <i>et al</i> , 1993	IVF/GIFT	3.2%
Slotnick <i>et al</i> , 1996	IVF	2.2%
Bergh <i>et al</i> , 1999	IVF/ICSI	3.4%

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Monozygotic twinning following assisted conception: an analysis of 81 consecutive cases

Mina Alikani^{1,2}, Natalie A.Cekleniak¹, Eurof Walters² and Jacques Cohen¹ Hum Reprod 2003

Table I. Overall incidence of MZ twinning

Cycle type	Non-MZ twin pregnancies	MZ twin pregnancies	Total	Incidence of MZ twinning (%)
Regular	3185	64	3249	1.97
Recipient	537	8	545	1.47
Thaw	502	9	511	1.76
Total	4224	81	4305	1.88

Table III. Clinical profiles of non-ovocyte donation fresh embryo transfer pregnancies (values are mean (± SEM))

Pregnancy group ^a	No. patients	Maternal age (years)	Paternal age (years)	Total no. treatments ^b	No. drug ampoules	No. days of Gn	Peak E ₂ (pg/ml)	Peak progesterone (ng/ml)	No. oocytes retrieved	No. embryos replaced
Group A	64	35.3 (0.49)	37.8 (0.73)	2.44 (0.25)	42.2 (1.85)	8.71 (0.20)	1954 (131)	1.42 (0.22)	16.5 (0.96)	3.22 (0.13)
Group B	1391	34.5 (0.09)	33.0 (0.15)	1.97 (0.04)	42.4 (0.37)	8.85 (0.04)	1912 (24)	1.51 (0.05)	16.9 (0.21)	3.36 (0.02)
Group C	1794	35.9 (0.29)	37.7 (0.14)	2.35 (0.04)	44.1 (0.34)	9.00 (0.04)	1909 (23)	1.40 (0.05)	15.8 (0.19)	3.15 (0.02)
A versus B ^c		NS	NS	P < 0.01	NS	NS	NS	NS	NS	NS

Gn = gonadotrophin; NS = not significant.
Group A includes MZ twin multiple pregnancies; group B includes non-MZ twin multiple pregnancies; and group C includes singleton pregnancies.

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Role of zona pellucida?
Extended in vitro culture?

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Monozygotic twinning associated with day 5 embryo transfer in pregnancies conceived after IVF

Victoria Wright^{1,2}, Laura A.Schieve¹, Anjel Vahratian¹ and Meredith A.Reynolds¹ Hum Reprod 2004

226 MZ pregnancies

vs.

23,880 singletons
15,092 other MP

Table I. Cases of MZ multiple pregnancies by number of embryos transferred and number of fetal hearts on ultrasound

Difference between embryos transferred and fetal hearts	No. of embryos transferred	No. of fetal hearts on ultrasound	No. of cases with this pattern	Total no. of cases
1	1	2	30	218
	2	3	117	
	3	4	60	
	4	5	6	
	5	6	0	
	6	7	2	
2	1	3	1	10
	2	4	6	
	3	5	1	
	4	6	1	
	5	7	1	
3	2	5	1	1

Table II. Relationship between day of transfer and pregnancy, multiple gestation and MZ multiple gestation

Day of transfer	No. of cycles (%)	Mean no. of embryos transferred	No. of pregnancies	Pregnancy (%) (pregnancies/transfer)	Multiple gestation (%) (multiple gestations/pregnancy)	At least one MZ multiple gestation (%) (MZ multiple gestation/pregnancy)
2	6679 (6.2)	3.33	2337	35.0 ^a	39.1	0.2
3	77,256 (71.3)	3.32	29,144	37.7	38.9	0.4
4	3169 (2.9)	3.22	1010	31.9 ^b	37.1	0.4
5	17,828 (16.3)	2.50	7921	44.5 ^b	40.0 ^b	1.2 ^b
6	3604 (3.3)	2.39	1122	31.1 ^b	31.8 ^b	0.9 ^b
Total	108,336 (100.0)	3.15	41,534	38.3	39.1	0.6

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Mortality and Morbidity in Multiple Pregnancy

- Zygosity, chorionicity and amnionicity are important factors in twin pregnancy
- Perinatal morbidity in twins:
 - all twins: 14%
 - dichorionic: 9%
 - monochorionic: 26%
 - monoamniotic: 50%

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TWINS

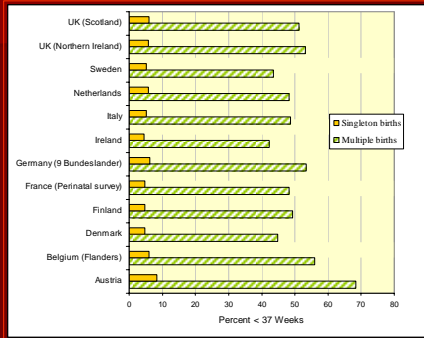
- « A nice chance to have 2 babies at once ! »
- « ...to make up for lost time »

- Maternal mortality X 2 or 3
- Transfer in ICU X 15.5
- Severe prematurity X 4
- SFGA X 4
- Infant mortality X 5
- Cerebral Palsy X 5 to 10

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Multiple Pregnancy and Prematurity

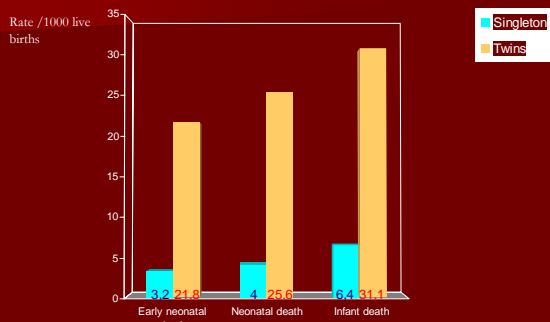


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Blondel et al 2006. BJOG 113:528-35.

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Neonatal & Infant Mortality Singleton & Twin Live Births USA, 1995-98

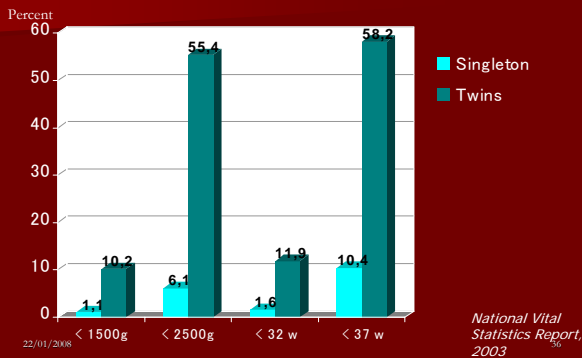


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Alexander & Salihu, Multiple Pregnancy, 2005

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Birth Weight & Gestational Age Characteristics Singletons & Twins: USA, 2002



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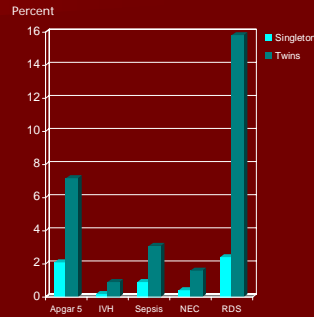
National Vital Statistics Report, 2003

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Neonatal Morbidity in Singleton & Twins

Twins vs singletons

	RR (95% CI)
Apgar ⁵ <7	3.4 (2.7-4.4)
IVH (gr 3 & 4)	5.2 (2.5-10.8)
Sepsis	3.3 (2.2-5.0)
NEC	4.5 (2.5-7.9)
RDS	6.4 (5.4-7.7)



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Gardner et al, *Obstet Gynecol*, 1995 37

Cerebral Palsy in Twins vs Singletons Meta-analysis



Twins vs singletons:

CP: 195/22,578 vs 2,007/1,047,230

RR 4.5 (3.9-5.2)

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Grather et al, 2000

Maternal Morbidity

Multiple (n=44,674) vs singleton pregnancy (n=165,188)

	RR (95% CI)
Pre-eclampsia	2.8 (2.7-2.9)
Gestational diabetes	1.1 (1.9-1.2)
Myocardial infarction	3.7 (2.3-5.8)
Heart failure	12.9 (2.7-62.3)
Venous thromboembolism	2.7 (2.0-3.5)
Pulmonary oedema	7.1 (4.5-11.3)
Post partum haemorrhage	1.9 (1.8-1.9)
Caesarean delivery	2.2 (2.1-2.2)
Hysterectomy	2.3 (1.7-3.2)

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Walker et al, *BJOG*, 2004

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The clinical tools ...

in IVF SET

- Judicious single embryo transfer
- Both for near-elimination of triplets and for drastic reduction of twins



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in non-IVF SOFT

- Judicious use of gonadotropins for single ovarian follicle treatment



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Randomized trials comparing eSET with eDET

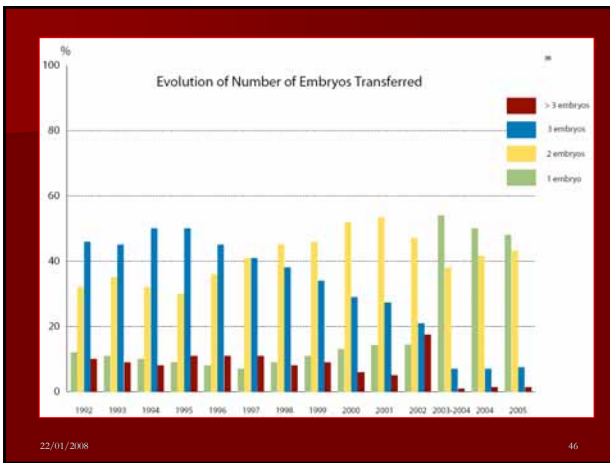
Study	n	eSET		DET	
		PR (%)	Twins (%)	PR (%)	Twins (%)
Geris, 1999	53	10/26 (38.5)	1/10	20/27 (74.0)	6/20
Martikainen, 2001	144	24/74 (32.4)	1/24	33/70 (47.1)	11/28
Gardner, 2004	48	14/23 (60.9)	0	19/25 (76.0)	9/19
Thurin, 2004	661	94/330 (28.5)	1/91	146/331 (44.1)	47/142
Lukassen, 2005	107	20/54 (37.0)	0	25/53 (47.2)	7/19
Total	1013	162/507 (31.9)	3 (1.8)	243/506 (48.0)	80/238 (33.6)

OR = 1.50 (99% CI = 1.22 – 1.85)

- Meta-analysis inappropriate because different study designs
- Conclusion: eDET > eSET (efficacy)

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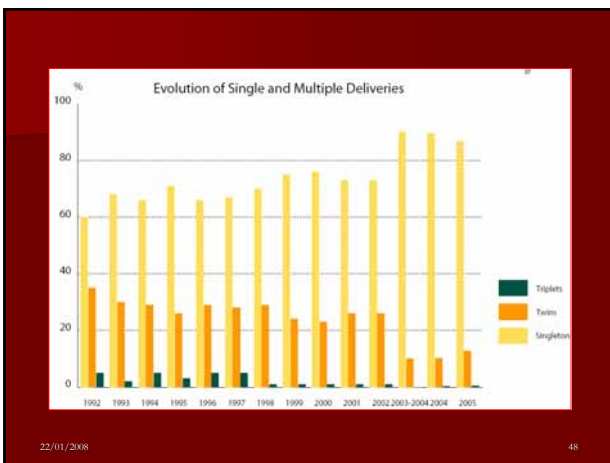
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Comparison of outcomes between period 1 and period 2

	Period 1 = 2002				Period 2 = 010703 - 300604			
	<36	36-40	>40	All	<36	36-40	>40	All
N ongoing pregnancies (%)								
1 heart beat	806 (71.2)	158	38	1002 (70.6)	1812 (92.1)	324	104	2240 (90.7)
2 heart beats	315 (27.8)	66	20	401 (28.2)	151 (7.7)	53	14	218 (8.8)
3 heart beats	11 (1.0)	5	1	17 (1.2)	4 (0.2)	6	2	12 (0.5)
IR (%)	18.4	13.6	7.4		24.7	14.7	7.2	

22/11/2008 Optimized embryo selection 47



Birthweight of singletons after assisted reproduction is higher after single- than after double-embryo transfer

Hum Reprod, 2006

Petra De Sutter^{1,3*}, Ilse Delbaere^{1*}, Jan Gerris¹, Hans Verstraeten¹, Sylvie Goetgeck², Josiane Van der Elst¹, Marleen Temmerman³ and Marc Dhont¹

Table II. Outcome parameters of SET and DET singleton pregnancies (gestational age, birthweight, preterm birth and

	SET (n = 404)	DET (n = 431)	Adjusted P-value	Crude OR (CI)
Gestational age (days)	276.2 (±10.5)	273.4 (±15.0)	<0.01	
Birthweight (grams)	3324.6 (±1509.7)	3204.3 (±1617.5)	<0.01	
Preterm birth	6.2%	10.4%		1.77 (1.06-2.94)
Low birthweight	4.2%	11.6%		2.99 (1.69-5.27) (<25

CI, confidence interval; DET, double-embryo transfer; OD, odds ratio; SET, single-embryo transfer. Parameters adjusted for maternal age, parity, cycle rank number, indication for assisted reproduction, assisted reproduction embryo quality, compulsion to apply SET/DET and sex of the child.

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First-trimester bleeding and pregnancy outcome in singletons after assisted reproduction

Petra De Sutter¹, Julie Bontneck, Valerie Schutysers, Josiane Van der Elst, Jan Gerris and Marc Dhont

Hum Reprod 21; 1907-11, 2006

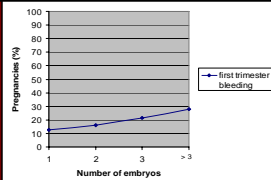
Infertility Centre, University Hospital Gent, Gent, Belgium

Patients	253 with bleeding	1179 without bleeding	
% 2 nd T bleeding	12.3%	3.0%	4.56 (CI 2.76-7.56)
% 3 rd T bleeding	5.1%	1.9%	2.85 (CI 1.42-5.73)
% P-PROM	7.6%	3.2%	2.44 (CI 1.83-4.31)
% Preterm contractions	13.9%	6.7%	2.27 (CI 1.48-3.47)
% IUGR	3.2%	5.5%	0.57 (CI 0.270-1.21)
% intrauterine death	0.8%	1.0%	0.78 (CI 0.17-3.48)
% Caesarean section	19%	19.4%	0.98 (CI 0.69-1.39)
Duration of pregnancy	272±17	275±14	P= 0.0092
% Preterm births	11.6%	7.4%	1.64 (CI 1.05-2.55)
% Very preterm births	2.4%	0.8%	3.05 (CI 1.12-8.31)
Birth weight (g)	3157±607	3272±559	P=0.0038
% low birth weight	8.8%	7.2%	1.24 (CI 0.76-2.02)
% very low birth weight	2.4%	0.7%	3.56 (CI 1.28-9.90)
% 1 min Apgar score <7	8.1%	8.0%	1.02 (CI 0.61-1.71)
% 5 min Apgar score <7	2.1%	2.6%	0.80 (CI 0.32-2.03)
% NICU admission	17.9%	11%	1.75 (CI 1.21-2.54)
% perinatal deaths	1.2%	1.4%	0.87 (CI 0.25-3.02)



Linear correlation between incidence 1st trimester bleeding and number of embryos transferred

Not only does eSET cause less twin-related morbidity and mortality but also healthier singletons



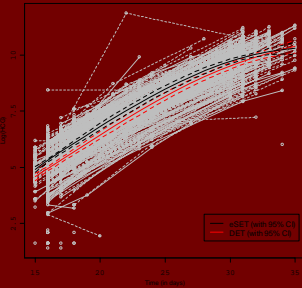
Embryos	Total Pregnant	1 st trim. bleeding	Controls
1	208	26 (12.5%)	182 (87.5%)
2	795	129 (16.2%)	666 (83.8%)
3	347	75 (21.6%)	272 (78.4%)
> 3	82	23 (28.0%)	59 (72%)

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HCG levels in early IVF/ICSI pregnancies are higher in singletons after SET compared with singletons after DET

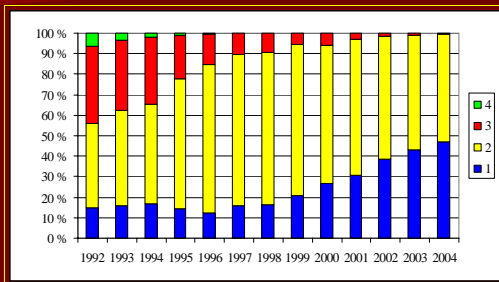
Delbaere et al., 2008 (PhD)



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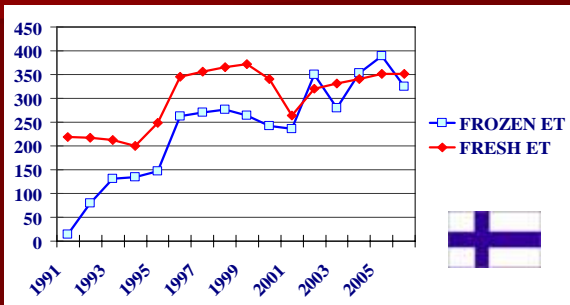
The number of transferred embryos in IVF+ICSI in Finland 1992-2004



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Aila Tiitinen, NFS meeting, Helsinki, August 2006

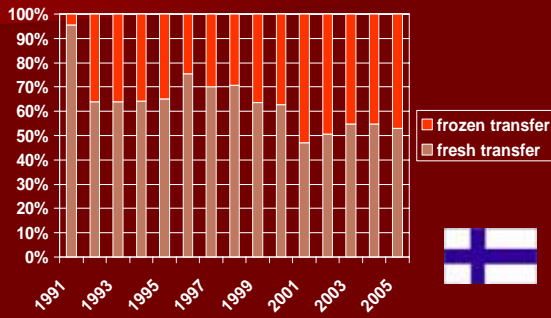
The number of embryo transfers at Helsinki University Hospital 1991 - 2006



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The proportion of children born after fresh or frozen embryo transfer



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Swedish Experience: 1 + 1 cryo = 2

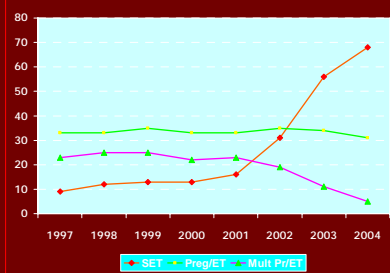
Thurin et al., N Engl J Med 2004; 351: 2440-2442.
Academic Hospital Göteborg and 10 other Scandinavian centres RCT

• Fresh DET:

- * 42.9% live birth rate
- * 33% twins

• Fresh SET + 1 cryo-SET:

- * 28.5%
- * + cryo: 38.8%



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% SET in Sweden

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Dutch experience: 2 x 1 = 1 x 2


Lukassen et al., Hum Reprod 2005; 20: 702-708 - UMC Nijmegen

Table II. The cumulative outcome of fresh embryo transfers

Variable	SET (n = 54)			DET (n = 53)
	1st cycle	2nd cycle	Cumulative	
No. of subjects	54	40	54	53
No. of transfers	54	35 ^a	89	88
Clinical pregnancy [n (%)]	20 (37)	10 (25)	30 (56)	31 (47)
Miscarriage [n (%)]	6 (11)	2 (5)	8 (15)	7 (11)
Ectopic pregnancy [n (%)]	0	0	0	0
Live birth [n (%)]	14 (26)	8 (20)	22 (41)	23 (36)
Singleton [n (% of live births)]	14 (100)	8 (100)	22 (100)	23 (100)
Twin [n (% of live births)]	0	0	0	0 (37)
Perinatal death (n)	0	0	0	1
Preterm birth < 37 weeks [n (%)]	2 (14)	0	2 ^b (10)	5 ^d (20)
Low birthweight infants (<2500 g) [n (%)]	1 (7)	0	1 ^c (5)	10 ^e (40)

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 **USA: Elective Single Embryo Transfer (eSET) vs. 2 Blastocyst ET @ SGFC 2006**

	IVF using Own Eggs		IVF using Donor Eggs	
	Blast eSET	2 Blast ET	Blast eSET	2 Blast ET
# Cycles	180	698	68	160
% Pregn / ET	68%	61%	67%	67%
% Multiples	1.6%	50%	0.0%	63%

22/01/2008 (Stillman R. et al.) 58

Australia **Elective transfer of single fresh blastocysts and later transfer of cryostored blastocysts reduces the twin pregnancy rate and can improve the in vitro fertilization live birth rate in younger women**


Michael Henman, M.Med.Sc., James W. Catt, Ph.D., Tina Wood, B.Sc.(Agr.), Mark C. Bowman, MB, Ph.D., C.R.E.I., Kylie A. de Boer, Ph.D., and Robert P. S. Jansen, M.D., C.R.E.I. Sydney IVF, Sydney, New South Wales, Australia

TABLE 1
Immediate clinical results from the fresh blastocyst transfers, comparing eSET with elective two-embryo transfer.

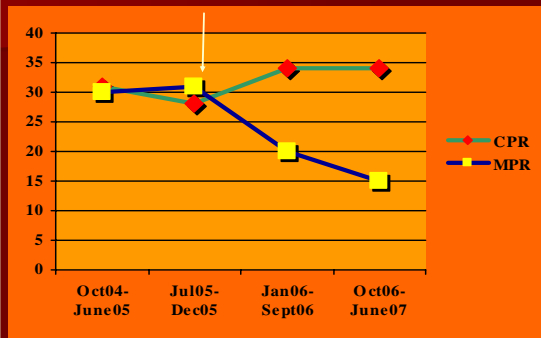
	One fresh blastocyst (eSET)	Two fresh blastocysts	χ^2
Transfer procedures	121	285	
Gestational sac-positive pregnancies	58 (48)	173 (61)	5.1 ($P < .025$)
Fetal heart-positive pregnancies	54 (45)	163 (57)	4.9 ($P < .03$)
Twin fetal hearts	1 (2)	72 (44)	
Fetal heart-positive implantations	55 (45)	236 (42)	ns
Fetal heart-positive fetal losses	4 (7.3)	27 (11.4)	0.43 (ns)
Loss of all fetuses before delivery	4 (7.4)	11 (6.8)	0.02 (ns)
Babies born alive	51	209	
Pregnancies ending with live birth	50	152	
Couples still without a baby	71 (59)	133 (47)	4.4 ($P = .035$)
Blastocysts in cryostorage	574	872	

Note: Numbers in parentheses are percentages.
ns = nonsignificant.

Henman. Elective single blastocyst transfer. Fertil Steril 2005.

 **UK: Braude et al., 2007**

Introduction of SET policy



Period	CPR (%)	MPR (%)
Oct04-June05	~30	~30
Jul105-Dec05	~28	~28
Jan06-Sept06	~35	~20
Oct06-June07	~34	~15

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Five pillars for eSET



- Creating awareness
- International agreement on patient and embryo characteristics prior to SET
- Marketing the idea
- In-depth counseling
- Appropriate funding



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(1) Creating awareness ...

- ...with physicians, midwives, nurses, mental health practitioners, clinical embryologists, laboratory technicians, insurers, politicians, ethicists
- ...with patients
- ...with all (in)directly involved in promoting good clinical outcome after ART

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(2) International agreement on patient and embryo characteristics prior to eSET...

- ...which can be used in all routine clinical IVF units in the world
- ...the development of sophisticated methods of embryo selection for eSET is to be welcomed ...
- ... but, to make eSET work on a large scale, the focus is on easy, cheap and reproducible methods, which at present rely on light microscopic observation of cleavage rate and morphology

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(3) Marketing the idea...

... in order to maintain pressure on the kettle

organizing meetings on the outcome of ART

stressing safety and quality in meetings and written material

...through the network of scientific societies (ESHRE, ASRM, ...)

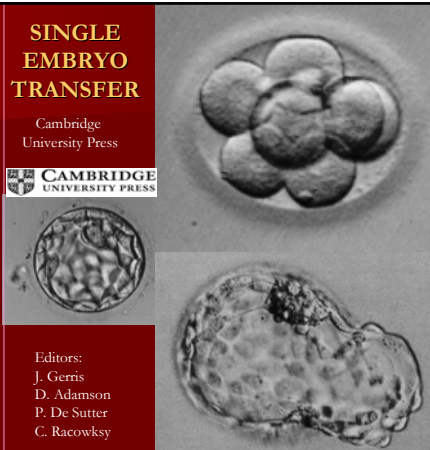
...through the lay press

22/01/2008

SINGLE EMBRYO TRANSFER

Cambridge University Press

CAMBRIDGE UNIVERSITY PRESS



Editors:
J. Gerris
D. Adamson
P. De Sutter
C. Racowksy

(4) In-depth counseling...

- ... by understanding, in a cross-cultural way, factors
 - that determine the perception of multiple pregnancies all over the world,
 - factors that impede eSET,
- ... by applying effective methods to inform patients orally and in written regarding the risks and complications of multiple pregnancies

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(5) Appropriate funding...

- ... through any mechanism compatible with national health care policies and systems
- striking the balance between reasonable access to treatment for all who need it and an acceptable percentage of complications
- taking into account a reasonable remuneration of all working in ART

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Overview of the lecture

- Epidemiology and biology of multiple pregnancies
- Epidemiology of induced multiple pregnancies
- Monozygotic twinning after infertility treatment
- Twins – perinatal consequences
- How to limit COS/AI and ART-twinning
- Conclusion

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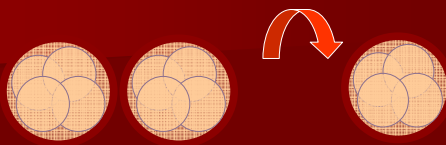
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- MPs are the major drawback of ART
- Twins represent, in absolute numbers, the major provider of complications
- DZ twins are the major problem but a stable biological phenomenon like MZ twinning is influenced both by non-ART and ART
- Multiples can, in the majority of IVF/ICSI cycles, be prevented by reducing the number of embryos transferred
- The goal of ART should be to give **ONE HEALTHY** baby to couples

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Reducing the number of twin births



Single embryo transfer in selected cases

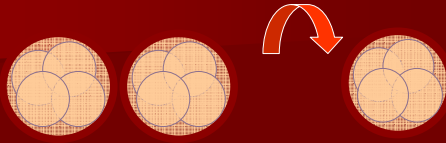
Twin-prone
patient selection

Embryo
selection

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Reducing the number of twin births



Single embryo transfer in all cases except



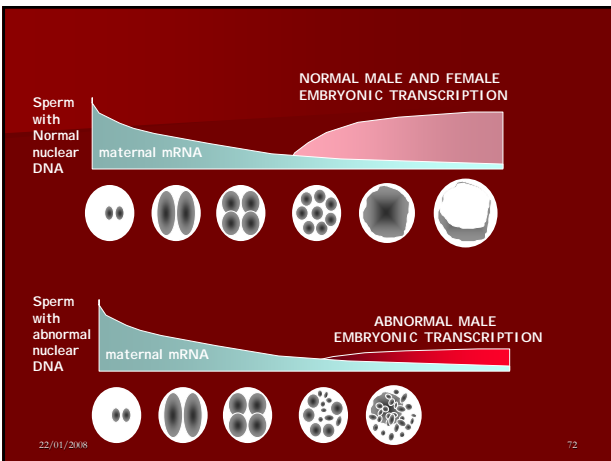
In patients with poor prognosis

If only poor quality embryos are available

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