The dangers of multiple pregnancy and elective single embryo transfer

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Disclosure

Institutional research and/or traveling grants have been received in 2009 and 2010 by the following companies :

- Merck-Serono
- Ferring
- Cook

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Learning objectives

After this lecture, participants should be able to

- Understand the risks and complications of multiple pregnancies
- Describe the patients who are twin prone and candidates for elective SET
- Understand the conclusions from randomized trials comparing SET with DET
- Have an idea of the worldwide application of the SET strategy to date
- Compare SET with DET from a health-economic perspective

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Slide 4

Multiple embryo transfer to increase the chance for *a* (successful?) pregnancy

Table 1. Embryo number at transfer relative to multiple implantation, pregnancy rate, embryonic implantation, and abnormality rate

No. of embryos	No. of cycles	Single gestation (No.)	Twin gestation (No.)	Triplet gestation (No.)	Quadruple gestation (No.)	Pregnancy rate per embryo transfer (%)	Multiple pregnancy rate (%)	Embryo implant.	Infants with abnormalities No.	%
1	227	22	0	0	0	9.7*	*	9.7†	0	0.0
2	402	97	17	0	0	28.4‡	15	16.3	5	2.3
3	661	164	74	10	0	37.3	34	17.2	6	1.8
4	832	207	84	32	6	39.5	56	14.9	15	2.7
5	47	15	5	1	0	40.4	42	11.1	2	7.6
6	4	1	1	0	0	50.0	50	12.5	0	0.0
Total	2173	504	181	43	6	35.8	42.3	15.4	24	2.4

*p < 0.00001, significantly lower than all other embryo transfer groups.
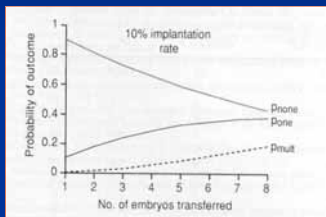‡p < 0.005, significantly lower than three, four, five, and six embryo transfer groups.
†p < 0.05, significantly lower than two, three, and four embryo transfer groups.

Elsner et al., Hum Reprod 1997

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Slide 5

Trade-off of the probability of no pregnancy versus a multiple pregnancy as the number of embryos transferred increases,

assuming a 10% implantation rate

1 embryo transferred:
* P_{one} = 10%
* P_{mult} = 0%
* P_{none} = 90%

3 embryos transferred:
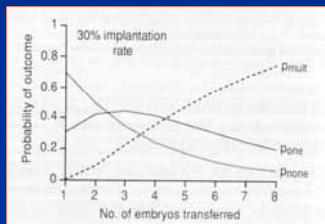* P_{one} = 27.5%
* P_{mult} = 2.5%
* P_{none} = 70%

Martin and Welch, FS 1998

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Trade-off of the probability of no pregnancy versus a multiple pregnancy as the number of embryos transferred increases, assuming a 30% implantation rate

1 embryo transferred:
* P_{one} = 30%
* P_{mult} = 0%
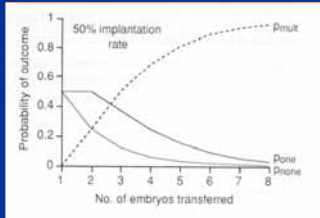* P_{none} = 70%

3 embryos transferred:
* P_{one} = 44%
* P_{mult} = 22%
* P_{none} = 34%

Martin and Welch, FS 1998

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Slide 7

Trade-off of the probability of no pregnancy versus a multiple pregnancy as the number of embryos transferred increases,
assuming a 50% implantation rate

1 embryo transferred:
* P_{one} = 50%
* P_{mult} = 0%
* P_{none} = 50%

2 embryos transferred:
* P_{one} = 50%
* P_{mult} = 25%
* P_{none} = 25%

Martin and Welch, FS 1998

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	IR(%)	n embr	P_{one}	P_{mult}	P_{none}
	5	19	0.38	0.25	0.38
	10	9	0.39	0.23	0.39
	15	6	0.40	0.22	0.38
	20	4	0.41	0.18	0.41
	25	3	0.42	0.16	0.42
	30	3	0.44	0.22	0.34
	35	2	0.46	0.12	0.42
	40	2	0.48	0.16	0.36
One TQE	40	1	0.40	0.00	0.60
	45	2	0.50	0.20	0.30
	50	1	0.50	0.00	0.50

Pregnancy outcomes at various implantation rates if the number of embryos transferred is selected to maximize the P (singl. pregn.)

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The dangers of multiple pregnancy

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%
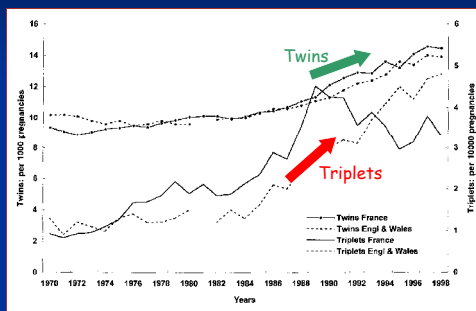 - monochorionic: 26%
  - monoamniotic: 50%

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

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

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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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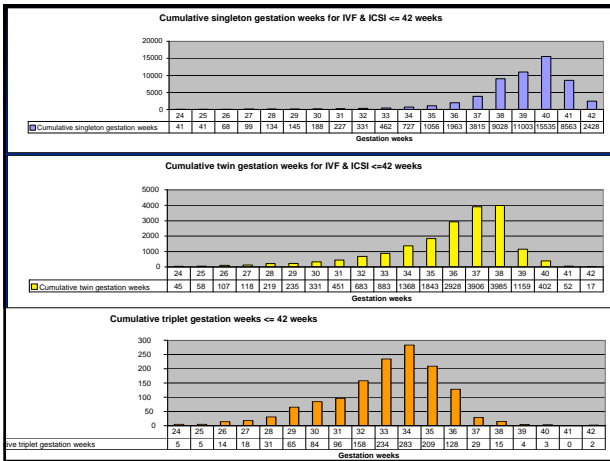## Cumulative singleton gestation weeks for IVF & ICSI <= 42 weeks

	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
Cumulative singleton gestation weeks	41	41	68	99	134	145	188	227	331	462	727	1056	1963	3815	9028	11003	15535	8563	2428

Gestation weeks

Cumulative twin gestation weeks for IVF & ICSI <=42 weeks

	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
Cumulative twin gestation weeks	45	58	107	118	219	235	331	451	683	883	1368	1843	2928	3906	3985	1159	402	52	17

Gestation weeks

Cumulative triplet gestation weeks <= 42 weeks

	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
live triplet gestation weeks	5	5	14	18	31	65	84	96	158	234	283	209	128	29	15	4	3	0	2

Gestation weeks

Multiple Pregnancy and Prematurity

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

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

Alexander & Salihu, Multiple Pregnancy, 2005

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

Percent

- Singleton
- Twins

60
50
40
30
20
10
0

55,4
58,2
10,2
6,1
1,1
1,6
14,9
10,4

< 1500g   < 2500g   < 32 w   < 37 w

National Vital Statistics Report, 2003

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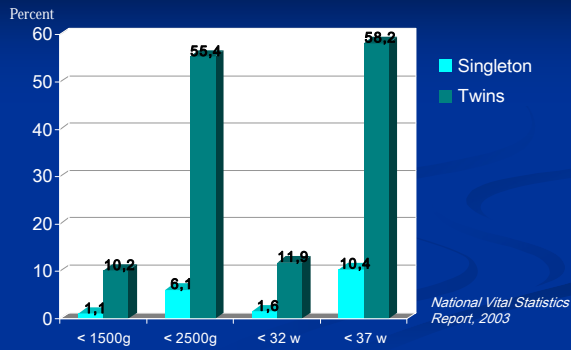
Neonatal Morbidity in Singleton & Twins

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)

Percent

- Singleton
- Twins

16
14
12
10
8
6
4
2
0

Apgar 5   IVH   Sepsis   NEC   RDS
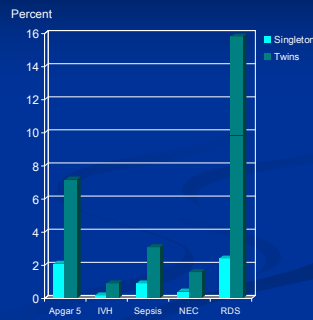
Gardner et al, Obstet Gynecol, 1995

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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)

Grether et al, 2000

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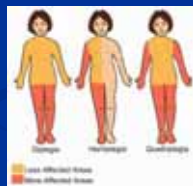
Maternal Morbidity

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)

Walker et al, BJOG, 2004

Risks of miscarriage and early preterm birth in trichorionic triplet pregnancies with embryo reduction versus expectant management: new data and systematic review

A.T.Papageorghiou, K.Avgidou, V.Bakoulas, N.J.Sebire and K.H.Nicolaides[1]

Cochrane plots (random effects model) for miscarriage (top) and early preterm birth (bottom) in triplet pregnancies, following embryo reduction (ER) versus expectant management.

MISCARRIAGE: x2

PRETERM BIRTH: 1/3

Independent from ethical considerations, embryo reduction is an emergency measure not a solution

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Elective single embryo transfer

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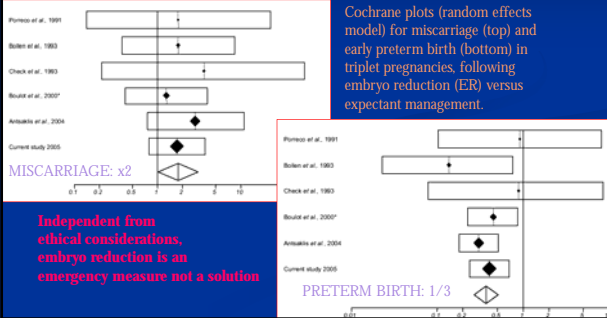
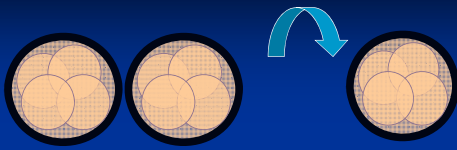**Reducing the number of twin births**

Single embryo transfer in <u>selected</u> cases

Twin-prone
patient selection

Embryo
selection

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The pioneers

- Coetsier T, Dhont M. (Ghent) Avoiding multiple pregnancies in in-vitro fertilization: who's afraid of single embryo transfer? Hum Reprod 1998;13:2663-4. **<u>The concept</u>**

- Vilska S, Tiitinen A, Hydèn-Granskog C, Hovatta O. (Helsinki) Elective transfer of one embryo results in an acceptable pregnancy rate and eliminates the risk of multiple birth. Hum Reprod 1999;14:2392-5.

- In women with medical contraindications for MP (hemi-uterus, isthmic insufficiency, IDDM,…) **<u>The first clinical data</u>**

  <u>Pregnancy rate</u>

- 74 elective SET   29.7% + FER = 47.3%
- 94 non-elective SET   20.2%
- 742 two-embryo transfers   29.4%   24% twins

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Patient selection

Multivariate analysis of >2000 cycles: robot photo of SET-suitable patient

- **Female age**   < 35-37 years of age
- **IVF cycle number**   1st and 2nd
- **No. of good quality embryos available** ≥ 2
- **Tubal factor infertility**   (absent)

(Strandell et al., Hum Reprod, 2000)

Univariate and multivariate analysis of 661 cycles

+
- IVF as method of fertilization
- No of 4-cell embryos on day 2
- FSH per oocyte retrieved

(Thurin et al., Hum Reprod, 2005)

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RCT: SET versus DET
in pts. <34y, 1st trial, at least two TQEs

Group	SET	DET
N cycles (transfers)	29	36
N postive HCG	18	28
N clinical pregnancies	14	26
N ongoing pregnancies	11	26
N multiplepregnancies	1 MZ	6
Conception rate (%)	18/29 (62.1%)	28/36 (77.8%)
CPR (%)	14/29 (48.3%)	26/36 (72.2%)
OPR (%)	11/29 (37.9%)	24/36 (66.7%)
MPR (%)	1/11 (9.1%)	6/24 (25%)
OIR (%)	11/29 (37.9%)	30.73 (41.7%)

Gerris J et al. Prevention of twin pregnancy after in-vitro fertilization
or intracytoplasmic sperm injection based on strict embryo criteria:
a prospective randomized clinical trial. Hum Reprod 1999;14:2581-7.

Fragment.	N bl D2	N bl D3	Implanted fraction (%)	N embryos
2	4	10	50.0	10
1	4	8	44.2	547
2	4	9	41.7	24
2	4	8	40.4	193
1	4	9	37.5	40
1	5	10	36.4	22
2	5	10	35.7	14
1	5	8	32.4	34
1	5	9	31.1	45
1	2	7	29.4	17
1	2	8	29.2	24
1	2	6	28.6	14
2	5	9	28.6	42
1	6	10	27.3	11
2	2	8	27.3	11
1	4	7	24.8	101
2	5	7	23.8	21
2	4	7	20.7	58
1	3	7	20.0	10
1	4	10	20.0	25

Embryo characterisation: Ranking of implantation potential of embryos with 1-to-1 documented outcome on the basis of day 2/3 morphology

The implantation potential of human embryos is not a categorical variable (top versus non-top = a useful simplification) but a continuous variable ranging between 0-50% for the "best" (= "least bad") embryos.

JUDICIOUS eSET IS LINKED TO RIGID EMBRYO SELECTION

Total: 1704 SETs of embryos, all without MNB's, at least 10 embryos in each group

Clinical results and the Belgian model

BELGIAN FUNDING REGULATION

- Six IVF/ICSI cycles (= oocyte harvests) funded in a life-time
- 1250 € per cycle for laboratory costs (gamete procurement and handling)
- Including cryocycles
- Up to the age of 43 years

Linked to a rational transfer strategy

≤ 36 years

1st attempt ever or 1st trial after previous IVF/ICSI-delivery: always one embryo;

2nd attempt: one embryo if of sufficient quality; two if of insufficient quality;

≥3rd attempt: max 2 embryos.

>36 – ≤39 years

1st and 2nd attempt: maximum 2 embryos;

≥3rd attempt: max 3 embryos.

> 39 years

No maximum number of embryos to transfer is dictated

CRYOCYCLES: 1 or 2 embryos

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

Petra De Sutter[1,3*], Ilse Delbaere[1*], Jan Gerris[1], Hans Verstraelen[1], Sylvie Goetgeluk[2], Josiane Van der Elst[1], Marleen Temmerman[1] and Marc Dhont[1]   Hum Reprod, 2006

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 (±509.7)	3204.3 (±617.5)	<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

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Obstetric and neonatal outcome after single embryo transfer

P.Poikkeus[1,3], M.Gissler[2], L.Unkila-Kallio[1], C.Hyden-Granskog[1] and A.Tiitinen[1]

[1]Department of Obstetrics and Gynaecology, Helsinki University Central Hospital and [2]National Research and Development Centre for Welfare and Health (STAKES), Helsinki, Finland and

[3]To whom correspondence should be addressed at HYKS-instituutti huone 3009/Terkko, Haartmaninkatu 4, 00290 Helsinki, Finland. Tel: +358-50-3646 534, fax: +358-9-4717 5550; E-mail: piia.poikkeus@hus.fi

BACKGROUND: Single embryo transfer (SET) pregnancies practically lack vanishing twins and may be associated with improved neonatal outcome. Our objective was to compare the obstetric and neonatal outcome of SET singletons with the outcome of singletons following double embryo transfer (DET) and spontaneous conception. METHODS: A 7-year (1997–2003) cohort of fresh SET ($n = 269$) and DET ($n = 230$, including 25 vanishing twins) cycles resulting in singleton birth at Helsinki University Central Hospital, Finland, was linked to the Finnish Medical Birth Register and the obstetric and neonatal outcome data compared with that from 15,037 spontaneously conceived singleton pregnancies. RESULTS: The obstetric and neonatal outcome of the SET group was comparable to that in the DET group. Compared with the comparison cohort, gestational hypertension ($P = 0.005$), placenta praevia ($P < 0.001$), preterm contractions ($P = 0.01$) and maternal hospitalization ($P < 0.001$) was more typical of women in the SET group. After adjusting for age, parity and socio-economic status the SET pregnancies showed increased risks of Caesarean section [odds ratio (OR) 1.54 with 95% confidence interval (CI) 1.18–2.00], preterm birth (OR 2.85; 95% CI 1.96–4.16) and low birthweight (OR 2.01; 95% CI 1.19–3.99) compared with the comparison cohort. CONCLUSIONS: Our results indicate that subject- and infertility-related mechanisms other than the number of transferred embryos influence the neonatal outcome of singleton IVF pregnancies.

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

Petra De Sutter[1], Julie Bontinck, Valerie Schutysers, Josiane Van der Elst, Jan Gerris and Marc Dhont

Infertility Centre, University Hospital Gent, Gent, Belgium

Hum Reprod 21; 1907–11, 2006

Patients	253 with bleeding	1179 without bleeding	
% 2nd T bleeding	12.3%	3.0%	4.56 (CI 2.76-7,56)
% 3rd 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	1st 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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Results of SET versus DET - Finland

Type of transfer	Transfers	CPR/ET	DR/ET	TPR/D
	N	n (%)	n (%)	n (%)
2 embryos	517	203 (40.0)	160 (30.9)	42/160 (26.2)
compulsory SET	94	17 (18.1)	13 (13.8)	1/13 (7.7)
elective SET	127	49 (38.6)	34 (26.8)	1/34 (2.9)

Tiitinen et al., Hum Reprod 2001; 16: 1140-1144   34

Cryo-augmentation effect after eSET

Type of ET	Transfers	PR	DR	Twins
	n	n (%)	n (%)	n (%)
Fresh ET	127	49 (38.6)	34 (26.8)	1 (2.9)
Frozen ET	129	39 (30.2)	32 (24.8)	4 (12.5)
1 embryo	46	8 (17.4)	5 (10.9)	0
2 embryos	83	31 (37.3)	27 (32.5)	4 (14.8)
CPR/patient		78 (62.4)	66 (52.8)	5 (7.6)

Tiitinen et al., Hum Reprod 2001; 16: 1140-1144   35

Cryopreservation

- When more eSET is performed, more embryos are available for cryopreservation
- Optimal standard of success = the cumulative OPR per oocyte harvest = fresh + frozen/thawed attempts
- The more eSET the better a centre
- The more cryocycles the better the centre

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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%
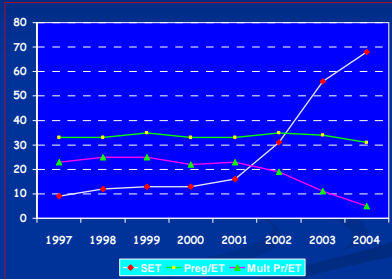
% SET in Sweden

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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	
Clinical pregnancy [n (%)]	20 (37)	10 (25)	(56)	(47)
Miscarriage [n (%)]	6 (11)	2 (5)	8	
Ectopic pregnancy [n (%)]	0	0	0	1
Live birth [n (%)]	14 (26)	8 (20)	(41)	(36)
Singleton [n (%) of live births]	14 (100)	8 (100)	22	
Twin [n (%) of live births]	0	0	0	(37)
Perinatal death (n)	0	0	0	1
Preterm birth < 37 weeks [n (%)]	2 (14)	0	2[c] (10)	5[d] (20)
Low birthweight infants (<2500 g) [n (%)]	1 (7)	0	1[e] (5)	10[f] (40)

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doi:10.1093/humrep/dem099

eSET irrespective of the availability of a good-quality embryo in the first cycle only is not effective in reducing overall twin pregnancy rates

Aafke P.A.van Montfoort[1,5], Audrey A.A.Fiddelers[2], Jolande A. Land[1,4], Carmen D.Dirksen[2], Johan L.Severens[2], Joep P.M.Geraedts[3], Johannes L.H.Evers[1] and John C.M.Dumoulin[1]

INTRODUCTION: In several clinics, elective single-embryo transfer (eSET) is applied in a selected group of patients based on age and the availability of a good-quality embryo. Whether or not eSET can be applied irrespective of the presence of a good-quality embryo in the first cycle, to further reduce the twin pregnancy rate, remains to be elucidated. METHODS: In patients <38 years two transfer strategies were compared, which differed in the first cycle only: group A (n = 141) received eSET irrespective of the availability of a good-quality embryo, and group B (n = 174) received eSET when a good-quality embryo was available while otherwise they received double embryo transfer (DET; referred to as eSET/DET transfer policy). In any subsequent cycle, in both groups the eSET/DET transfer policy was applied. RESULTS: After completion of their IVF treatment (including a maximum of three fresh cycles and the transfer of frozen-thawed embryos), comparable cumulative live birth rates (62.4% in group A and 62.6% in group B) and twin pregnancy rates (10.1 versus 13.4%) were found. However, patients in group A required significantly more fresh (2.0 versus 1.8) and frozen (0.8 versus 0.5) cycles. CONCLUSIONS: The transfer of one embryo in the first cycle, irrespective of the availability of a good-quality embryo, in all patients <38 years, is not an effective transfer policy for reducing the overall twin pregnancy rate.

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eSET irrespective of the availability of a good-quality embryo in the first cycle only is not effective in reducing overall twin pregnancy rates **?**

Aafke P.A.van Montfoort[1,5], Audrey A.A.Fiddelers[2], Jolande A. Land[1,4], Carmen D.Dirksen[2], Johan L.Severens[2], Joep P.M.Geraedts[3], Johannes L.H.Evers[1] and John C.M.Dumoulin[1]

INTRODUCTION: In several clinics, elective single-embryo transfer (eSET) is applied in a selected group of patients based on age and the availability of a good-quality embryo. Whether or not eSET can be applied irrespective of the presence of a good-quality embryo in the first cycle, to further reduce the twin pregnancy rate, remains to be elucidated. METHODS: In patients <38 years two transfer strategies were compared, which differed in the first cycle only: group A (n = 141) received eSET irrespective of the availability of a good-quality embryo, and group B (n = 174) received eSET when a good-quality embryo was available while otherwise they received double embryo transfer (DET; referred to as eSET/DET transfer policy). In any subsequent cycle, in both groups the eSET/DET transfer policy was applied. RESULTS: After completion of their IVF treatment (including a maximum of three fresh cycles and the transfer of frozen–thawed embryos), comparable cumulative live birth rates (62.4% in group A and 62.6% in group B) and twin pregnancy rates (10.1 versus 13.4%) were found. However, patients in group A required significantly more fresh (2.0 versus 1.8) and frozen (0.8 versus 0.5) cycles. CONCLUSIONS: The transfer of one embryo in the first cycle, irrespective of the availability of a good-quality embryo, in all patients <38 years, is not an effective transfer policy for reducing the overall twin pregnancy rate.

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Trente-neuvième Journée thématique de la SFEF (Paris, 22 mai 2008)

Transfert monoembryonnaire : expérience du CHU de Rennes

Single-embryo transfer: Rennes' Hospital experience

D. Le Lannou *, M.-C. Laurent, J.-F. Griveau, E. Véron, F. Jaffré, G. Jouve,
A. Gueho, K. Morcel

Transfert de deux embryons versus deux transferts d'un embryon chez des patientes de pronostic différent

	Moins bon pronostic (n = 63)		Très bon pronostic (n = 67)	
	1 embryon	2 embryons	1 embryon	2 embryons
Transfert frais	15 G (23 %)	20 G (32 %)	21 G (31 %)	27 G (40 %)
Transfert congelé	6 G (13,6 %)	–	7G (17 %)	–
Total	21 G (33 %)	20 G (32 %)	28 G (42 %)	27 G (40 %)

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Trente-neuvième Journée thématique de la SFEF (

Transfert monoembryonnaire : expé

Single-embryo transfer: R

D. Le Lannou *, M.-C. La

Gynécologie Obstétrique & Fertilité 35 (2007) 474-479

DÉBAT

Contre l'obligation du transfert monoembryonnaire

Against the obligation of single embryo transfer

P. Merviel *, E. Lourdel, R. Cabry, N. Grenier, P. Sanguinet, L. Henry, F. Brasseur, H. Copin

Transfert de deux embryons versus deux transferts d'un embryon chez des

			pronostic (67)	
			1 embryon	2 embryons
Transfert		G (32 %)	21 G (31 %)	27 G (40 %)
Transfert			7G (17 %)	–
Total		(33 %)	20 G (32 %)	28 G (42 %)	27 G (40 %)

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Elective single blastocyst transfer reduces twin rates without compromising pregnancy rates — USA (Criniti et al., Fertil Steril 2005;84:1613-9)

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 — Australia (Henman et al., Fertil Steril 2005)

UK: Braude et al., 2007
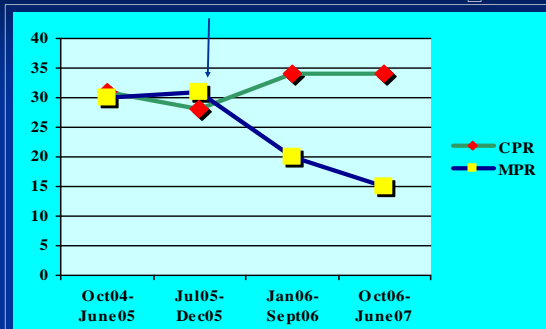
Prerequisites for a particular centre to implement esET

- 1. Excellent results (the better the centre, the higher % of eSET)
- 2. Willingness to decrease a very high MP rate
- 3. Willingness to invest in optimization of a freeze/thaw programme
- 4. eSET must be compatible with specific societal circumstances in which the centre works

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Health-economic aspects of SET

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A real-life prospective health economic study of elective single embryo transfer versus two-embryo transfer in first IVF/ICSI cycles

J.Gerris[1,5], P.De Sutter[2], D.De Neubourg[1], E.Van Royen[1], J.Vander Elst[2], K.Mangelschots[1], M.Vercruyssen[1], P.Kok[2], M.Elseviers[3], L.Annemans[4], P.Pauwels[1] and M.Dhont[2]

- Prospective non-randomized multicenter study, comparing SET with DET in good prognosis patients
- 408 cycles - 367 transfers

	eSET	DET
N of transfers	201 (56%)	158 (44%)
Clinical pregn rate	83/206 (40.3%)	65/161 (40.4%)
Live births	77/206 (37.4%)	59/161 (36.6%)
Singletons	77 (100%)	39 (66%)
Twins	-	20 (34%)

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Real-life health-economic study

This prospective health economic study shows that eSET is equally effective as but ~50% cheaper than double embryo transfer in first IVF/ICSI cycles.

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Health economic comparison SET/DET and singletons/twins in DET
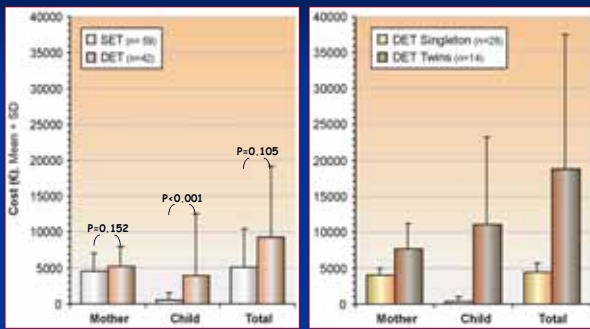
Only cases with complete data included

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De Sutter, P., Gerris, J. and Dhont, M. (2002) A health-economic decision-analytic model comparing double with single embryo transfer in IVF/ICSI. *Hum. Reprod.*, **17**, 2891–2896.

A health-economic decision-analytic model comparing double with single embryo transfer in IVF/ICSI: a sensitivity analysis
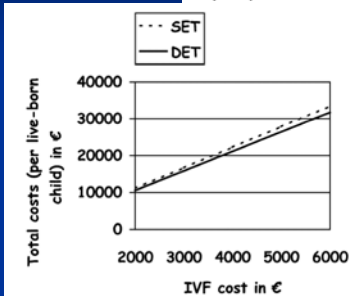
Figure 2. Correlation between IVF costs and total cost per live-born child for SET and DET, taking into account increases in neonatal care expenses, proportionally to IVF costs.

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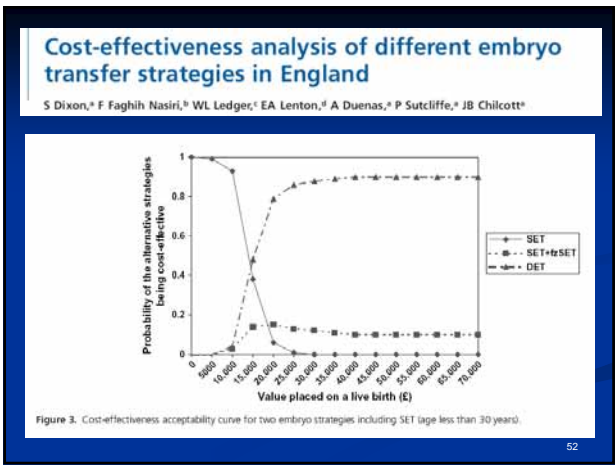
Cost-effectiveness analysis of different embryo transfer strategies in England

S Dixon,[a] F Faghih Nasiri,[b] WL Ledger,[c] EA Lenton,[d] A Duenas,[a] P Sutcliffe,[a] JB Chilcott[a]

Figure 3. Cost-effectiveness acceptability curve for two embryo strategies including SET (age less than 30 years).

Economic evaluations of single- versus double-embryo transfer in IVF

A.A.A.Fiddelers[1,5], J.L.Severens[1,2], C.D.Dirksen[1], J.C.M.Dumoulin[3], J.A.Land[4] and J.L.H.Evers[2]

		Costs (€)	Effects (%)	Costs per effect (€)	ICER (DET versus eSET)
Gerris et al. (2004)	eSET (one cycle)	7126	37.4	NR[a]	
	DET (one cycle)	11 039	36.6	NR[a]	NR[a]
Lukassen et al. (2005)	eSET (two cycles)	NR[a]	40.7	13 438	
	DET (one cycle)	NR[a]	35.8	13 680	NR[a]
Thurin et al. 2006[b]	eSET (one cycle)	9309	38.8	23 984	
	DET (one cycle)	12 318	42.9	28 712	71 940
Thurin et al. 2006[c]	eSET (one cycle)	10 905	38.8	NR[a]	
	DET (one cycle)	14 676	42.9	NR[a]	91 722
Fiddelers et al. (2006)	eSET (one cycle)	7334	20.8	35 260	
	DET (one cycle)	10 924	39.6	27 586	19 096

It can be concluded that DET is the most expensive strategy. DET is also most effective if performed in one fresh cycle. eSET is only preferred from a cost-effectiveness point of view when performed in good prognosis patients and when frozen/thawed cycles are included. If frozen/thawed cycles are excluded, the choice between eSET and DET depends on how much society is willing to pay for one extra successful pregnancy.

Conclusion: SET in whom and when?

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Perceived barriers to elective single embryo transfer among IVF professionals: a national survey

Thank you !