

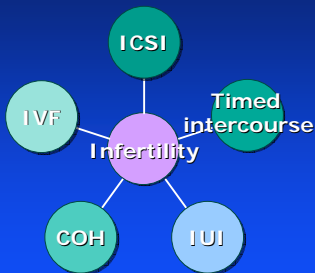
Prematurity, LBW and associated health risks: Results in Flanders between 1993 and 2004

W Ombelet ^o, G Martens ^{*}

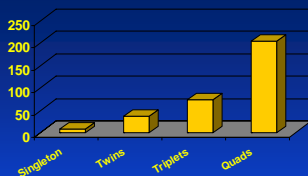
^o Genk Institute for Fertility Technology, Belgium
^{*} Study Centre for Perinatal Epidemiology (SPE), Brussels, Belgium

Eshre Campus Workshop, Luebeck, 18-01-08

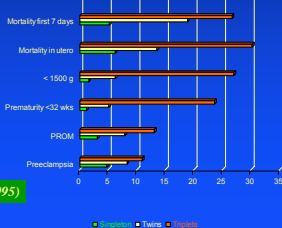
The Spectrum of Care

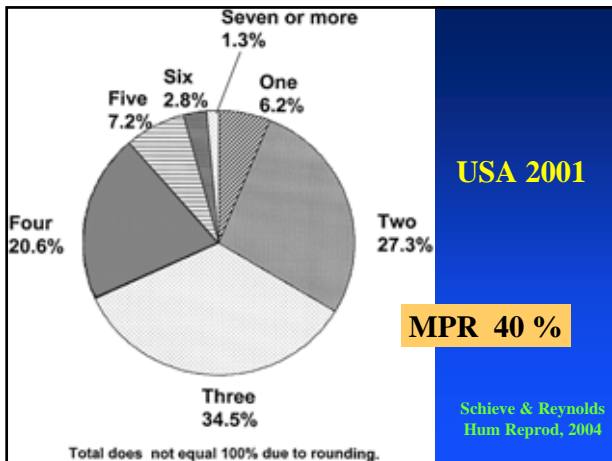


Population of England and Wales 1992



French IVF results 1986-1993 (FIVNAT 1995)





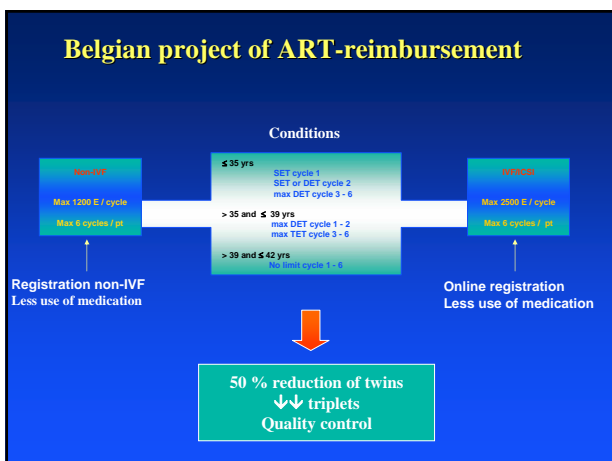
The Wall Street Journal, October 7, 2005

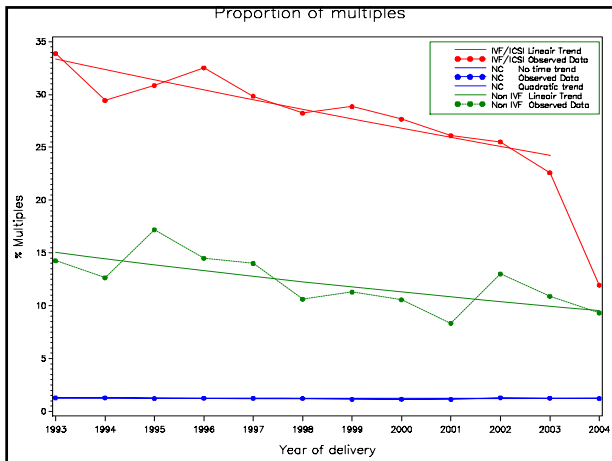
Human Reproduction Update, Vol.11, No.1 pp.3-14, 2005
Advance Access publication November 4, 2004

Multiple gestation and infertility treatment: registration, reflection and reaction—the Belgian project

Willem Ombelet^{1,4}, Petra De Sutter², Josiane Van der Elst² and Guy Martens³

¹Geek Institute for Fertility Technology, Department of Obstetrics and Gynaecology, Geel, Fertility Centre, Ghent University Hospital, Ghent and ²SPE (Studiecentrum voor Perinatale Epidemiologie), Brussels, Belgium





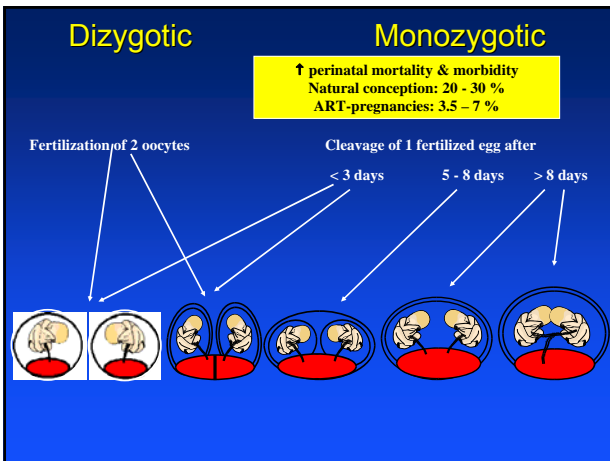
**Pregnancy following ART
a risk pregnancy is born !!
also for singletons**

ESHRE-meeting Den Haag 1992
Poster 336a
Ombelet et al., Hum Reprod 7 (Suppl 2), 181, 1992

**Perinatal outcome
of singletons and twins after ART**
Helmerhorst et al., BMJ, 2004

- Systematic review of controlled studies
- Period: 1985 – 2002
- 17 matched studies
- 8 non-matched studies

	ART	NC	OR
Singletons			
< 32 w	2.0	0.8	3.48 (2.16-5.66)
< 37 w	11.4	6.1	2.04 (1.80-2.32)
PNM	1.24	0.8	1.68 (1.11-2.55)
Twins			
< 32 w	6.8	7.1	NS
< 37 w	50.0	45.6	1.07 (1.02-1.13)
PNM	2.30	4.33	0.58 (0.44-0.77)



Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis
Jackson et al., *Obstet & Gynecol*, 2004

- Period: 1978 – 2002
 - ◆ Medline, Biosis, PhD's, bibliographies, conference proceedings
- IVF-singletons // matched for parity & female age
- 15 studies
- 12 283 IVF-cycles versus 1.9 million NC singletons

IVF vs spt pregnancies	OR
< 2500 gr (LBW)	1.8 (1.4 - 2.2)
< 1500 gr (VLBW)	2.7 (2.3 - 3.1)
SGA	1.6 (1.3 - 2.0)
< 37 w	2.0 (1.7 - 2.2)
PNM	2.2 (1.6 - 3.0)

Non-IVF
Obstetric and perinatal outcome

- lack of registration
- Only three studies (IUI):

Nuojua-Huttunen et al, *HR*, 14, 2110, 1999
Identical perinatal outcome compared to IVF & natural conception

Gaudoin et al, *AJOG*, 188, 611, 2003
Increased risk of prematurity & LBW compared to natural conception

Non-IVF Obstetric and perinatal outcome

- Wang et al., HR, 17, 945, 2002
- Cohort-study - Australia

1015 AIH (730) + DI (285)
1019 IVF-ICSI-GIFT
1019 matched controls (NC)

Multivariate regression analysis

Increased risk for prematurity

IVF > AIH-DI > NC

SPE registration Flanders

All hospital deliveries in Flanders
> 21 wks - ≥ 500 gr

Questionnaire
Obstetricians

Data obstetric
events

Questionnaire
Paediatricians

Data perinatal
events

Data Coordinator - Review errors

GLOBAL YEARLY REPORT

SPE registration : parameters

General data

- Gestational age
- Parity
- Birth weight
- Maternal age
- Fetal sex

Obstetric data

- Caesarean section rate
- Epidural analgesia
- Presentation at delivery
- Induction of labour

Perinatal data

- Apgar score 1' & 5'
- Birth weight
- Duration pregnancy
- Congen. Malformations
- Transfer to NIC
- Perinatal mortality
- Intubation
- IC-bleeding
- RDS
- convulsions

SPE – results 1993-2003

Number of births : 631 449

	Spontaneous	ART (%)	Total
Singleton	587 181	19 824 (3.2)	607 005
Twins	14 479	8 926 (38.1)	23 405
Triplet	213	826 (79.4)	1 039

29 576 (4.7%)

SPE – results 1993-2002 perinatal risks

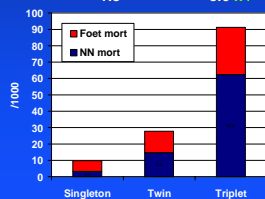
Birth weight at delivery

grams	singl.(%) (n=17.761)	twins(%) (n=8.096)	triplets(%) (n=799)
500-999	0.7	3.1 (x7)	10.0 (x14)
1000-1499	0.8	4.8 (x6)	19.0 (x23)
1500-2499	6.1	48.2	63.8
≥ 2500	92.4	43.8	7.1

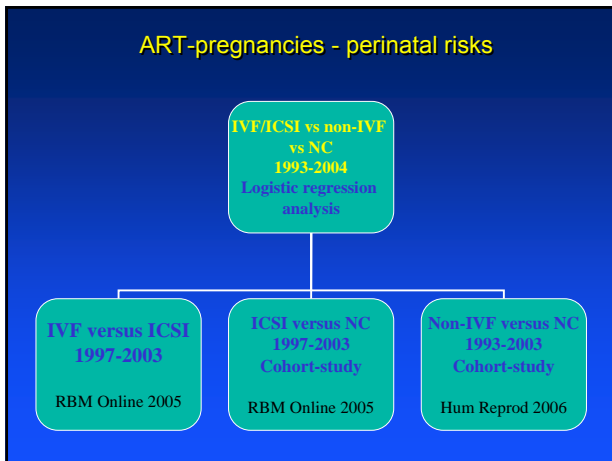
SPE – results 1993-2002 perinatal risks

Neonatal interventions & complications

	singletons(%)	twins(%)	triplets(%)
Endotracheal ventilation	1.8	7.5 x4	22.1 x12
Intracranial bleeding	0.5	1.9 x4	5.6 x11
Convulsions	0.2	0.4 x2	1.5 x7
Lung disease	1.8	8.0 x4	20.4 x11



ART-pregnancies - perinatal risks



Study 1

Obstetric and perinatal outcome of 1655 ICSI and 3974 IVF singleton and 1102 ICSI and 2901 IVF twin births: a comparative analysis



Willem Ombeki started his career in infertility and IVF in 1984 in Pretoria, South Africa. Since 1987 he has been working in the Department of Obstetrics and Gynaecology in the St. Jans Hospital of Leuven, Belgium. He is the founder of the Leuven Institute for Fertility Technology and Chairman of four 'Andrology in the Nineties' meetings. In 1998 he obtained his PhD degree at the University of Leuven. His thesis was entitled 'The value of sperm morphology and other semen parameters in diagnosis and treatment of human subfertility'. In 1999 he became Head of the Department, and from 2001 to 2004 he was the President of the Flemish Society of Obstetrics and Gynaecology.

Dr Willem Ombeki

Willem Ombeki^{1,2,3}, Isabelle Cadron², Jan Gerrits², Petra De Sutter⁴, Eugene Bosmans⁵, Guy Martens⁶, Gunther Buyssens⁷, Paul Debrant^{7,8}, Geert Molenberghs⁹, Wilfried Gynaesiers⁷

Reprod Biomed Online. 2005 Jul;11(1):76-85

Risks of ICSI

Damage to internal structure oocyte

Bypassing natural selection process of zona pellucida

Delayed replication of the male genome

Different synchrony of fertilisation events

Microinjection of
- sperm-associated foreign DNA
- biochemical contaminants

Microinjection of:
- immature sperm
- sperm carrying genetic defects

-- Procedure-dependent risks

-- Procedure-independent risks

Singletons: ICSI = 1655 & IVF = 3974

	ICSI (%)	IVF (%)	OR
< 1500 gr	1.9	2.0	0.95 (0.63-1.43)
< 32 w	1.6	1.9	0.87 (0.56-1.36)
< 37 w	9.2	12.4	0.58 (0.47-0.71)
PNM	1.2	1.1	1.09 (0.62-1.91)
Transfer NIC	19.5	21.6	0.88 (0.76-1.02)
Intubation	1.7	2.5	0.71 (0.46-1.07)
IC bleeding	0.4	0.7	0.51 (0.21-1.24)
Convulsions	0.2	0.3	0.69 (0.23-2.08)
Cong. Malform	2.1	2.1	0.96 (0.65-1.42)

Twins: ICSI = 1102 & IVF = 2901

	ICSI (%)	IVF (%)	OR
< 1500 gr	9.0	8.5	1.06 (0.83-1.35)
< 32 w	8.8	8.5	1.02 (0.73-1.43)
< 37 w	58.2	57.0	1.05 (0.86-1.29)
PNM	3.1	2.4	1.29 (0.83-1.99)
Stillbirth	2.1	1.0	2.04 (1.14-3.64)
Transfer NIC	67.4	69.8	0.90 (0.77-1.04)
Intubation	7.7	7.4	1.04 (0.79-1.36)
IC bleeding	1.8	2.3	0.77 (0.47-1.27)
Convulsions	0.5	0.3	1.76 (0.56-5.40)
Cong. Malform	5.7	5.3	1.07 (0.79-1.36)

Stillbirths: IVF vs ICSI

IVF (30/2901 = 1.03 %)

Cervic.incomp + PPROM: 7
 Cervic.incomp: 4
 PPROM: 5
 PIH +/- IUGR: 4 (13.3%)
 Solutio placentae: 2
 Cong. Malformation: 2
 Unknown: 6

ICSI (23/1102 = 2.08 %)

Cervic.incomp + PPROM: 7
 PPROM: 4
 PIH +/- IUGR: 8 (34.8%)
 Unknown: 2

Immunologic factor ??

Study 2

Perinatal outcome of ICSI pregnancies compared with a matched group of natural conception pregnancies in Flanders (Belgium): a cohort study



When Ombesi started his career in infertility and IVF in 1984 in Pretoria, South Africa. Since 1987 he has been working in the Department of Obstetrics and Gynaecology in the St. Jans Hospital of Ghent, Belgium. He is the founder of the Ghent Institute for Fertility Technology and Chairman of the 'Andrology in the Newborn' meetings. In 1988 he obtained his PhD degree at the University of Leuven. His thesis was entitled 'The value of sperm morphology and other semen parameters in diagnosis and treatment of human subfertility'. In 1999 he became Head of the Department, and from 2001 to 2004 he was the President of the Flemish Society of Obstetrics and Gynaecology.

Dr Willem Ombesi

Willem Ombesi^{1,2}, Karen Poossee¹, Petra De Sutter¹, Jan Gerris¹, Eugène Boonans¹, Guy Maréchal¹, Gustaf Ruysschock¹, Paul Debuysse¹, Geert Molenberghs¹, Wilfried Ouytsaers¹

Reprod Biomed Online. 2005 Aug;11(2):244-53.

ICSI // matched control study

ICSI singletons: 1655
Control population: 430 565

ICSI twins: 1102
Control population: 430 565



Matched for parity, fetal sex, female age,
year of delivery, place of delivery
For each case two controls

Singletons
Cases: 1655
Controls: 3278

Twins
Cases: 1102
Controls: 2163

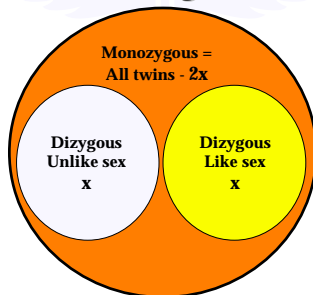
Singletons: ICSI = 1655 & NC = 3278

	ICSI (%)	Controls (%)	OR
< 1500 gr	1.9	1.5	1.25 (0.78-1.99)
< 32 w	1.6	1.5	1.05 (0.64-1.72)
< 37 w	9.2	7.9	1.17 (0.95-1.46)
PNM	1.2	0.7	1.73 (0.91-3.28)
Transfer NIC	19.5	18.8	1.05 (0.90-1.22)
Intubation	1.7	1.8	0.97 (0.62-1.52)
IC bleeding	0.4	0.5	0.70 (0.27-1.77)
Convulsions	0.2	0.4	0.66 (0.21-2.50)
Cong. Malform	2.1	2.1	1.02 (0.67-1.56)

Twins: ICSI = 1102 & NC = 2163

	ICSI (%)	Ctr (%)	OR
< 1500 gr	8.8	10.1	0.86 (0.67-1.11)
< 32 w	8.6	10.1	0.84 (0.65-1.08)
< 37 w	58.5	57.2	1.06 (0.91-1.23)
PNM	3.1	2.7	1.16 (0.74-1.81)
Stillbirth	2.1	1.4	1.52 (0.88-2.62)
Transfer NIC	67.4	70.3	0.88 (0.75-1.02)
Intubation	7.6	8.7	0.86 (0.66-1.13)
IC bleeding	1.8	2.6	0.70 (0.41-1.16)
Convulsions	0.5	0.8	0.69 (0.27-1.75)
Cong. Malform	3.2	3.0	1.06 (0.68-1.64)

Weinberg Rule



**Unlike-sex Twins:
ICSI = 470 & NC = 907**

	ICSI (%)	Ctr (%)	OR
< 1500 gr	7.6	9.0	0.83 (0.55-1.25)
< 32 w	8.5	9.0	0.93 (0.63-1.39)
< 37 w	61.7	53.8	1.38 (1.10-1.75)
PNM	3.8	1.4	2.74 (1.26-5.98)
Stillbirth	2.1	0.8	2.80 (1.06-7.39)
Transfer NIC	70.8	70.9	0.99 (0.78-1.28)
Intubation	7.4	7.6	0.98 (0.64-1.49)
IC bleeding	1.1	2.1	0.50 (0.18-1.35)
Convulsions	0.6	0.5	1.16 (0.22-1.35)
Cong. Malform	3.2	2.3	1.39 (0.67-2.85)

Study 3

Perinatal Outcome of 12.021 singleton and 3.108 twin births after non-IVF assisted reproduction: a cohort study. *Hum Reprod* 21:1025-1032, 2006

Perinatal outcome of 12 021 singleton and 3108 twin births after non-IVF-assisted reproduction: a cohort study

Willem Ombelet^{1,2,3}, Guy Martens³, Petra De Sutter¹, Jan Gerrits¹, Eugene Boumans², Gunther Ruysinck³, Paul Defoort^{1,3}, Geert Molenberghs⁴ and Wilfried Gyselaers²

¹Scientific Board of the Flemish Society of Obstetrics and Gynaecology, St Niklaas, ²Department of Obstetrics and Gynaecology, Ghent Institute for Fertility Technology, Ghent, ³FPE (Instituut voor Perinatale Epidemiologie), Brussels and ⁴Centre for Statistics, Limburgs Universitair Centrum, Diepenbeek, Belgium

To whom correspondence should be addressed at: ZIK, Schepse Bos 6, 3000 Ghent, Belgium. E-mail: w.ombel@pandora.be

Non-IVF // matched control study

Non-IVF singletons: 12 021
Control population: 587 181

Non-IVF twins: 3 108
Control population: 14 479

Matched for parity, fetal sex, female age, year of delivery
For each case one control

Singletons
Cases: 12 021
Controls: 12 021

Twins
Cases: 3108
Controls: 3108

Non-IVF vs matched controls Singletons: non-IVF = 12021 = Controls

	non-IVF (%)	Ctr (%)	OR
< 1500 gr	1.3	0.9	1.47 (1.14-1.90)
< 32 w	1.3	0.9	1.45 (1.12-1.88)
< 37 w	7.8	6.0	1.30 (1.18-1.44)
PNM	0.7	0.5	1.14 (1.00-1.97)
Stillbirth	0.5	0.3	1.66 (1.07-2.58)
Transfer NIC	18.2	15.8	1.19 (1.11-1.27)
Intubation	1.5	1.4	1.04 (0.84-1.29)
IC bleeding	0.4	0.3	1.37 (0.85-2.19)
Convulsions	0.1	0.2	0.73 (0.40-1.32)
Cong. Malform	1.8	1.7	1.05 (0.86-1.26)

Non-IVF vs matched controls
Twins: non-IVF = 3108 = Controls

	non-IVF (%)	Ctr (%)	OR
< 1500 gr	8.5	7.3	1.19 (0.98-1.44)
< 32 w	7.9	6.6	1.20 (0.99-1.46)
< 37 w	53.7	50.9	1.11 (1.01-1.23)
PNM	3.1	2.5	1.28 (0.94-1.75)
Stillbirth	1.4	1.5	0.94 (0.71-1.31)
Neonatal death	1.7	0.9	1.84 (1.14-2.98)
Transfer NIC	67.9	67.8	1.00 (0.90-1.12)
Intubation	7.9	6.2	1.25 (1.03-1.53)
IC bleeding	1.9	1.5	1.28 (0.86-1.90)
Convulsions	0.3	0.4	0.75 (0.32-1.78)
Cong. Malform	2.6	2.7	0.96 (0.71-1.31)

Non-IVF vs matched controls
DZ-twins: non-IVF = 1320 = Controls

	non-IVF (%)	Ctr (%)	OR
< 1500 gr	9.0	6.8	1.61 (1.21-2.14)
< 32 w	8.6	6.4	1.37 (1.02-1.86)
< 37 w	54.5	46.6	1.96 (1.67-2.31)
PNM	3.4	2.2	1.57 (0.96-2.59)
Stillbirth	1.6	0.9	1.76 (0.82-3.82)
Transfer NIC	67.7	67.0	1.03 (0.87-1.22)
Intubation	7.4	7.0	1.04 (0.79-1.36)
IC bleeding	1.8	2.3	1.06 (0.78-1.44)
Convulsions	0.2	0.7	0.22 (0.05-1.03)
Cong. Malform	6.2	5.5	1.13 (0.81-1.59)

SPE – results 1993 - 2003
Conclusion Study 3

Non-IVF versus matched controls

- Singl: ↑ PNM, stillbirth
- Twins: ↑ prematurity (<37w), neonatal death
- DZ-twins: ↑ prematurity (< 32 w, < 37w) & VLBW

non-IVF pregnancies (singl & twins)
 are to be considered as
 “risk pregnancies”

Study 4

Results in Flanders between 1993 and 2004

- Total number of births: 750751
- 59523: Mode of conception unknown (7.9 %)
- number of births investigated: 691228
- Number of singleton births: 664803
- Number of twin births: 25313

Twins
 Spt: 15846
 IVF-ICSI: 6118
 Non-IVF: 3349

Singletons
 Spt: 642613
 IVF-ICSI: 8995
 Non-IVF: 13195

Study 4

Results in Flanders between 1993 and 2004

- Logistic regression analysis
 - ◆ IVF/ICSI versus NC versus non-IVF
 - ◆ Singletons – twins - Unlike-sex twins

Logistic regression analysis including mode of conception, female age, fetal sex, parity & year of delivery

SPE – results 1993-2004 singleton births

Totaal	IVF/ICSI	non-IVF	NC
664803	8995	13195	642613
	%	%	%
< 1500 gr	2.2	1.3	0.8
< 2500 gr	9.4	6.6	4.9
< 32 w	2.0	1.3	0.8
< 37 w	11.3	7.8	5.8
PNM	1.21	0.74	0.64
NIC-transfer	21.2	18.3	15.0
Congen. Malf	2.5	1.8	1.6
Intubation	7.9	5.8	5.3
IC bleeding	2.2	1.5	1.2

**SPE – results 1993-2004
singleton births**

	IVF/ICSI %	NC %	OR
< 1500 gr	2.2	0.8	2.51 (2.16-2.90)
< 2500 gr	9.4	4.9	1.76 (1.64-1.90)
< 32 w	2.0	0.8	2.34 (2.00-2.73)
< 37 w	11.3	5.8	1.92 (1.79-2.05)
PNM	1.21	0.64	1.90 (1.57-2.30)
NIC-transfer	21.2	15.0	1.34 (1.27-1.41)
Congen. Malf	2.5	1.6	1.55 (1.35-1.78)
Intubation	7.9	5.3	1.45 (1.27-1.72)
IC bleeding	1.5	1.2	1.64 (1.24-2.16)

**SPE – results 1993-2004
singleton births**

	non-IVF %	Spt %	OR
< 1500 gr	1.3	0.8	1.53 (1.31-1.79)
< 2500 gr	6.6	4.9	1.24 (1.16-1.33)
< 32 w	1.3	0.8	1.52 (1.30-1.77)
< 37 w	7.8	5.8	1.31 (1.23-1.40)
PNM	0.74	0.64	1.12 (0.91-1.37)
NIC-transfer	18.3	15.0	1.17 (1.12-1.23)
Congen. Malf	1.8	1.6	1.13 (0.99-1.28)
Intubation	5.8	5.3	1.10 (0.95-1.67)
IC bleeding	1.5	1.2	1.26 (0.95-1.67)

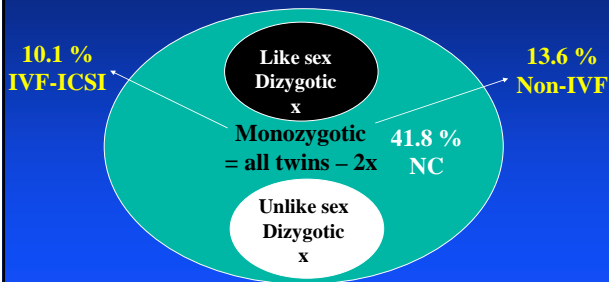
**SPE – results 1993-2004
singleton births**

	non-IVF %	IVF/ICSI %	OR
< 1500 gr	1.3	2.2	0.61 (0.50-0.75)
< 2500 gr	6.6	9.4	0.71 (0.64-0.78)
< 32 w	1.3	2.0	0.65 (0.52-0.80)
< 37 w	7.8	11.3	0.68 (0.62-0.75)
PNM	0.74	1.21	0.59 (0.45-0.78)
NIC-transfer	18.3	21.2	0.88 (0.82-0.94)
Congen. Malf	1.8	2.5	0.73 (0.60-0.78)
Intubation	5.8	7.9	0.75 (0.61-0.92)
IC bleeding	1.5	2.2	0.77 (0.70-1.24)

SPE – results 1993-2004 twin births

Totaal	IVF/ICSI	non-IVF	NC
25313	6118	3349	15846
	%	%	%
< 1500 gr	8.0	8.7	8.7
< 2500 gr	56.9	56.9	54.3
< 32 w	8.2	8.0	8.5
< 37 w	55.4	55.8	52.1
PNM	2.65	3.17	2.93
NIC-transfer	69.3	68.7	67.8
Congen. Malf	3.3	2.7	3.1
Intubation	11.4	12.2	12.6
IC bleeding	3.4	3.1	3.4

Weinberg Rule



SPE – results 1993-2004 unlike-sex twin births

	non-IVF	NC	OR
	%	%	
< 1500 gr	9.3	7.0	1.18 (0.90-1.53)
< 2500 gr	58.1	50.2	1.22 (1.05-1.41)
< 32 w	9.1	6.8	1.01 (0.99-1.09)
< 37 w	55.8	47.8	1.07 (0.98-1.17)
PNM	3.55	2.04	1.59 (1.04-2.42)
NIC-transfer	68.5	65.5	1.04 (0.89-1.23)
Congen. Malf	2.5	2.4	1.03 (0.69-1.53)
Intubation	11.7	10.8	1.06 (0.79-1.41)
IC bleeding	2.9	3.1	0.94 (0.55-1.60)

SPE – results 1993-2004
unlike-sex twin births

	IVF/ICSI %	non-IVF %	OR
< 1500 gr	8.0	9.3	1.15 (0.86-1.53)
< 2500 gr	57.1	58.1	1.03 (0.88-1.21)
< 32 w	8.9	9.1	0.99 (0.94-1.04)
< 37 w	54.0	55.9	1.12 (0.88-1.44)
PNM	2.84	3.55	1.25 (0.80-1.94)
NIC-transfer	69.3	68.5	0.95 (0.79-1.13)
Congen. Malf	3.0	2.5	0.88 (0.59-1.13)
Intubation	10.7	11.7	1.00 (0.73-1.37)
IC bleeding	3.0	2.9	0.89 (0.49-1.60)

Conclusion

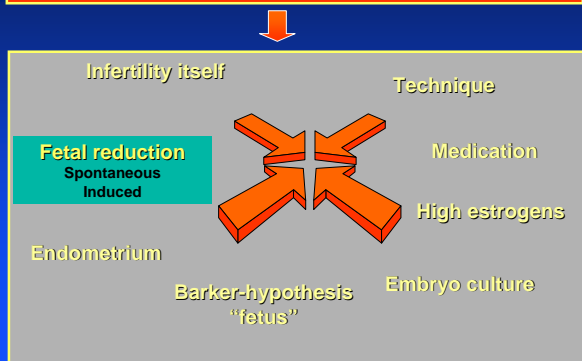
Perinatal mortality & morbidity

Singletons: IVF/ICSI > non-IVF > NC

Twins: IVF/ICSI = non-IVF = NC

Unlike-sex twins: non-IVF (>)= IVF/ICSI > NC

Why are ART-pregnancies at risk ?



Consequences of vanishing twins in IVF/ICSI pregnancies

Pinborg et al., Hum Reprod 2005, 20:2821-9.
10 % of IVF singletons originates from a twin gestation
Sptn reductions > 8 week = Obstetrical & perinatal risk

Shebl et al., Fertil Steril 2007
case-control study
↑ risk for LBW and SGA

De Sutter et al., Hum Reprod 2006, 21:2633-7.
Birthweight of SET vs DET singletons
SET: ↑ birthweight

A comparison of the outcomes between twin and reduced twin pregnancies produced through ART

Cheang et al., F & S, 2007

The fetal reduction group (n = 353) was associated with a higher incidence of extreme prematurity, prematurity, and lower birth weight than the nonreduced group (n = 389).

These findings were more pronounced among patients with a higher initial number of fetuses

Hypothesis

Fetal reduction (to singletons or twins)
Spontaneous reduction of multiples

Increased risk for prematurity & LBW
More often in non-IVF group
Non-IVF: more often high-order multiples

Data fetal reduction → twin: 1993-2004			
	Non-IVF	IVF/ICSI	NC
SPE: 12669 twins	1673 (13.2 %)	3060 (24.1 %)	7936 (62.6 %)

Data fetal reduction → twin: 1993-2004			
	Non-IVF	IVF/ICSI	NC
High-order → twin: 85	67 78.8 %	16 18.8 %	2 2.3 %
Triplet → twin: 390	169 43.3 %	196 50.2 %	25 6.4 %
Total MPR: 475	236 49.6 %	212 44.6 %	27 5.7 %
SPE: 12669 twins	1673 (13.2 %)	3060 (24.1 %)	7936 (62.6 %)

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475/12669 = 3.7 %	236/1673 = 14.1 %	212/3060 = 6.9 %	27/7936 = 0.3 %

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	Non-IVF	IVF/ICSI	NC
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475/12669 = 3.7 %	236/1673 = 14.1 %	212/3060 = 6.9 %	27/7936 = 0.3%
High-order → twin	4.0 %	0.5 %	0.02 %

**With special thanks to all midwives,
gynaecologists and paediatricians of Flanders
and to the co-workers of the SPE who made
this presentation possible !**