# Health of Children Born after ICSI


*Basil C. Tarlatzis, MD, PhD*

*Professor of Obstetrics – Gynaecology*
*and Reproductive Medicine*
*Aristotle University of Thessaloniki, Greece*

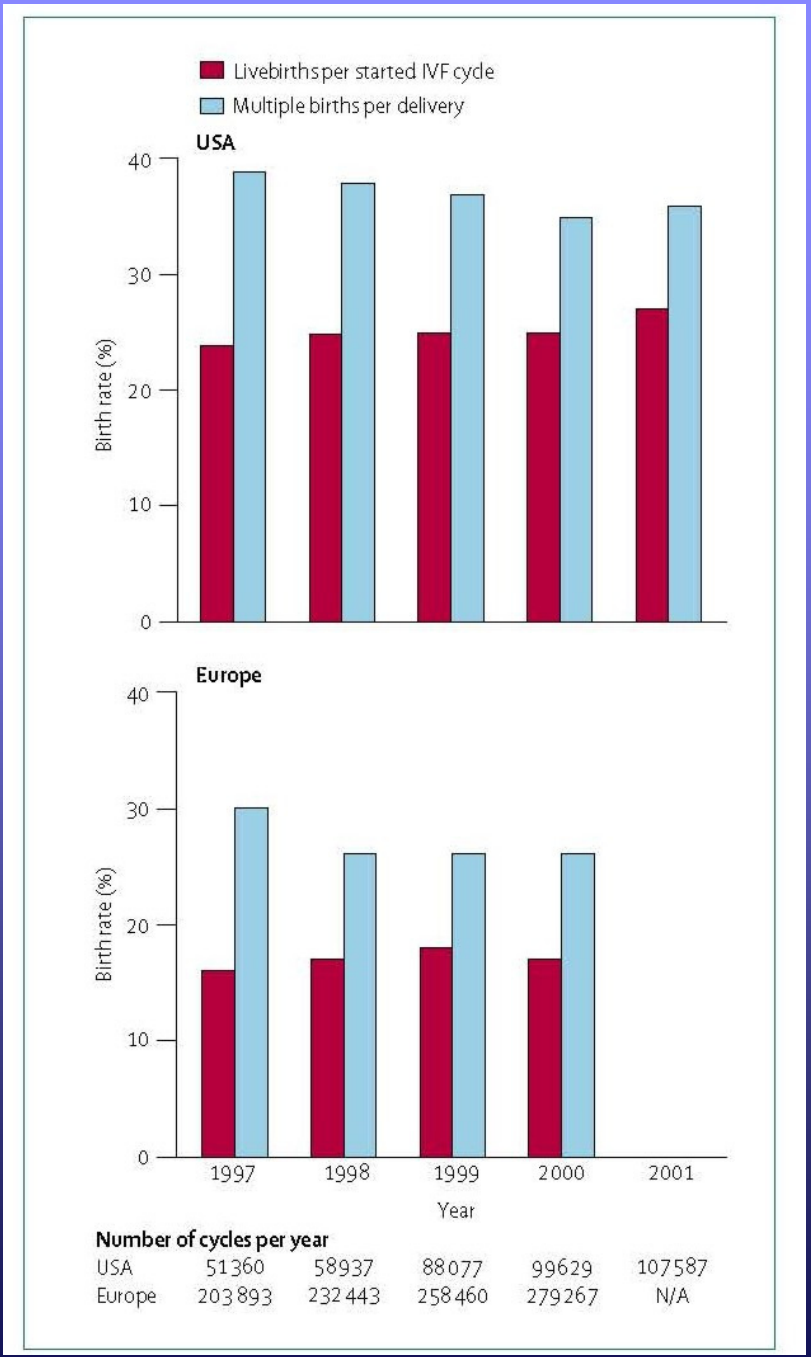

# ART Children

- 1978: IVF, Louise Brown *(R.Edwards, P.Steptoe)*
- 1990 : ICSI *(Palermo, Van Steirteghem, Devroey)*
- 2005 : World

  *More than* 3 million children (200 000 per year )

  Approx. half from multiple pregnancies

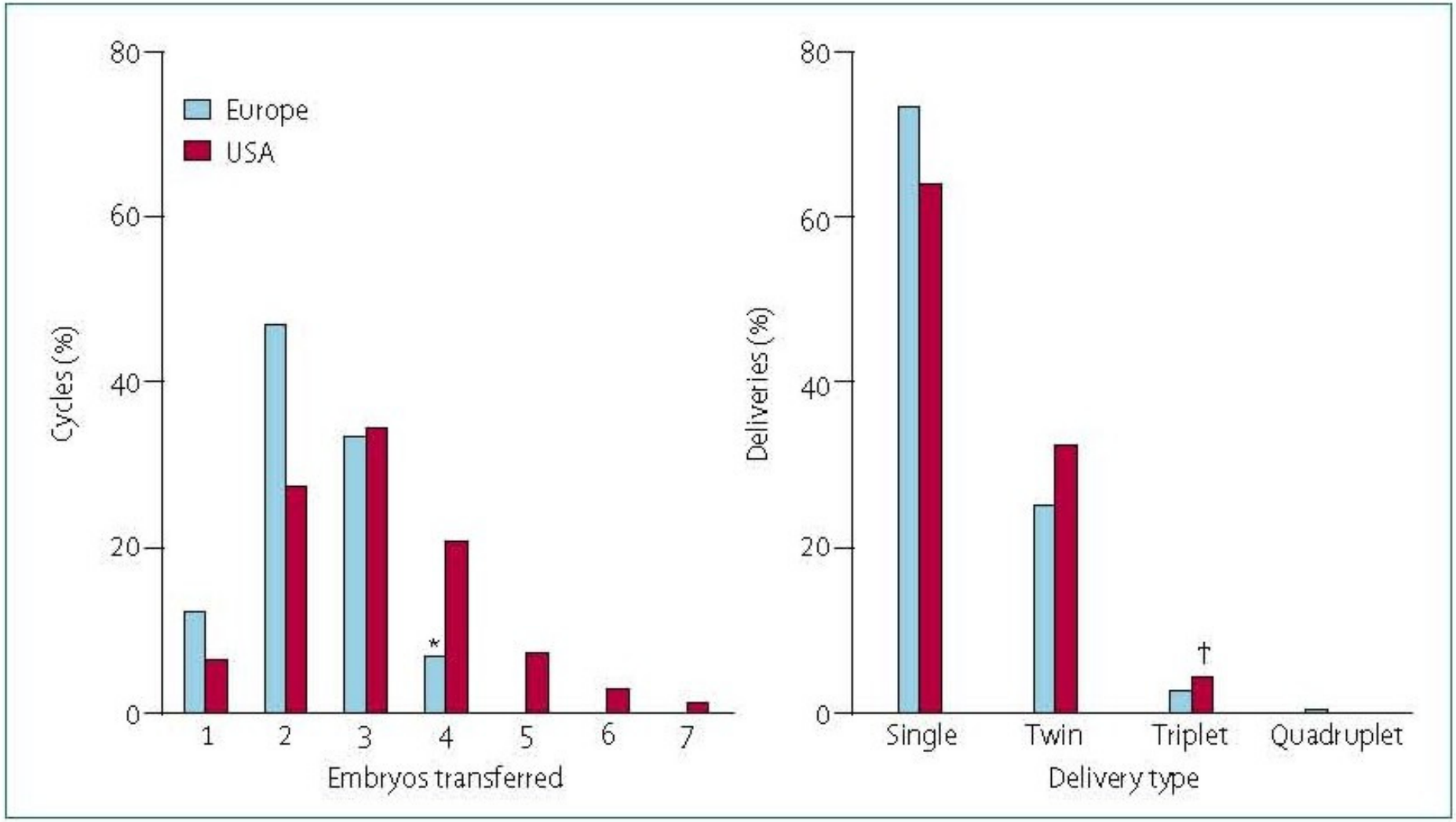
# The Problem of Multiple Pregnancies




**Number of cycles per year**

| | | | | | |
|---|---|---|---|---|---|
| USA | 51360 | 58937 | 88077 | 99629 | 107587 |
| Europe | 203893 | 232443 | 258460 | 279267 | N/A |

***Fauser et al, Lancet 365, 1807, 2005***




*Fauser et al, Lancet 365, 1807, 2005*

# Multiplicity and Pregnancy Complications

| | Singleton | Twin | Triplet | P |
|---|---|---|---|---|
| Pre-eclampsia | 1.2 | 2.9 | 5.6 | 0.001 |
| Preterm labour | 7.1 | 19.7 | 40.4 | 0.001 |
| PROM | 2.8 | 7.8 | 13.6 | 0.001 |

*FIVNAT, 1998*

# CHILDREN BORN AFTER ASSISTED REPRODUCTION TECHNIQUES

- Perinatal Outcome
- Congenital Malformations
- Chromosomal Abnormalities
- Psychomotor development
- Genomic Imprinting Defects
- Cancer

# Coding systems

- **Classification by system**
  - ICD international coding system
- **National registers**
  - British Pediatric Classification adds additional numbers to the ICD code
  - guidelines for coding
- **Eurocat**
  - surveillance of congenital anomalies
- **MC Kusick**

*Bonduelle et al., 2002*

# Major Malformations in IVF, ICSI and Naturally Conceived Children

**Table II.** Odds Ratio From a Meta-Analysis in Subgroups and Overall

| | OR | 95% CI | | Number of studies |
|---|---|---|---|---|
| | | Lower | Upper | |
| IVF Single | 1.51 | 0.85 | 2.7 | 8 |
| IVF Multiple | 0.92 | 0.75 | 1.12 | 7 |
| ICSI Single | 1.33 | 0.90 | 1.95 | 6 |
| ICSI Multiple | 1.18 | 0.60 | 2.37 | 4 |
| IVF All | 1.28 | 0.93 | 1.75 | 16 |
| ICSI All | 1.23 | 0.80 | 1.88 | 7 |
| IVF/ICSI[a] | 1.29 | 1.01 | 1.67 | 19 |

[a] Using a single OR for each publication all statistical significance tests for heterogeneity were $P < .0001$ and random effects model was used.

*Rimm et al, J Ass Repr Gen, 21, 437, 2004*

**Table 2.** Analysis of sub-cohorts in a meta-analysis on the risk of major malformations after IVF and ICSI. Data according to Hansen *et al.* (2005).

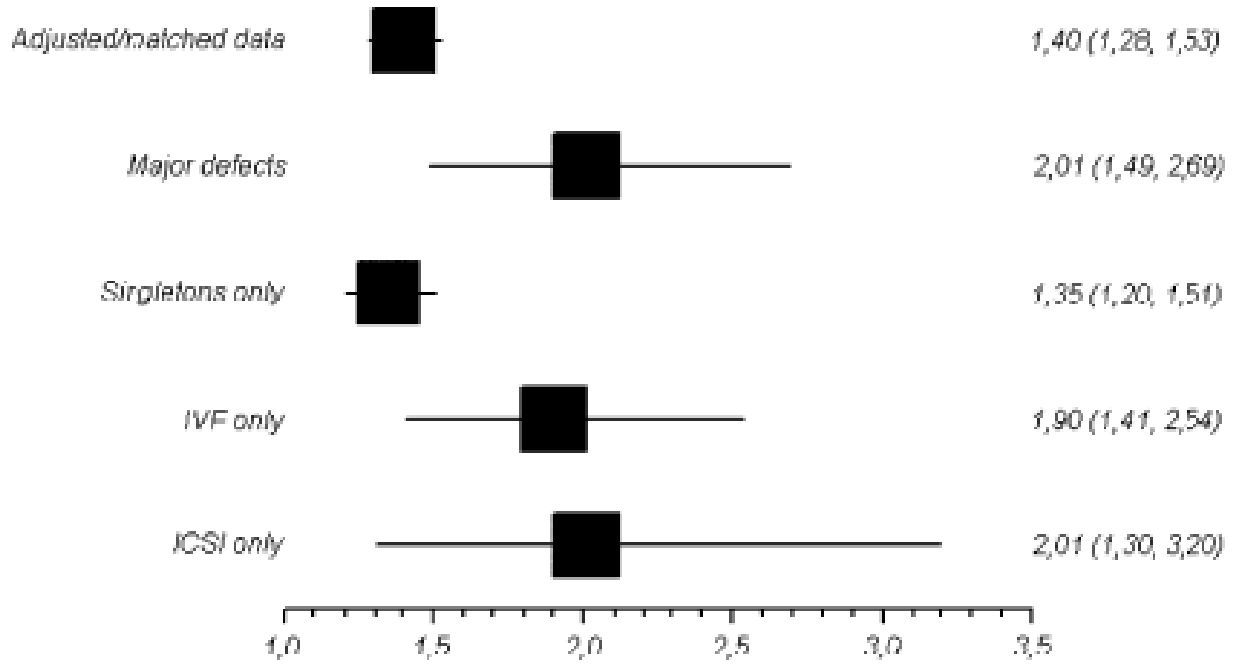
| | *No. studies* | *Pooled OR* | *95% CI* |
|---|---|---|---|
| Major birth defects | 15 | 1.32 | 1.20–1.45 |
| All infants (singletons and multiples) | 17 | 1.36 | 1.28–1.45 |
| Singletons only | 15 | 1.31 | 1.17–1.46 |
| IVF only | 12 | 1.94 | 1.50–2.50 |
| ICSI only | 5 | 1.28 | 1.14–1.43 |

ICSI = intracytoplasmic sperm injection; OR = odds ratio; CI = confidence interval.

*Ludwig, RBM Online 10, suppl 3, 83, 2005*

# FIGURE 2

Estimates of congenital malformation risk (pooled odds ratios) in children born after ART. Published by Hansen et al. 2005.




*Ceelen. Growth and development of children born after IVF. Fertil Steril 2008.*

***Ceelen et al, Fertil Steril, 2008***

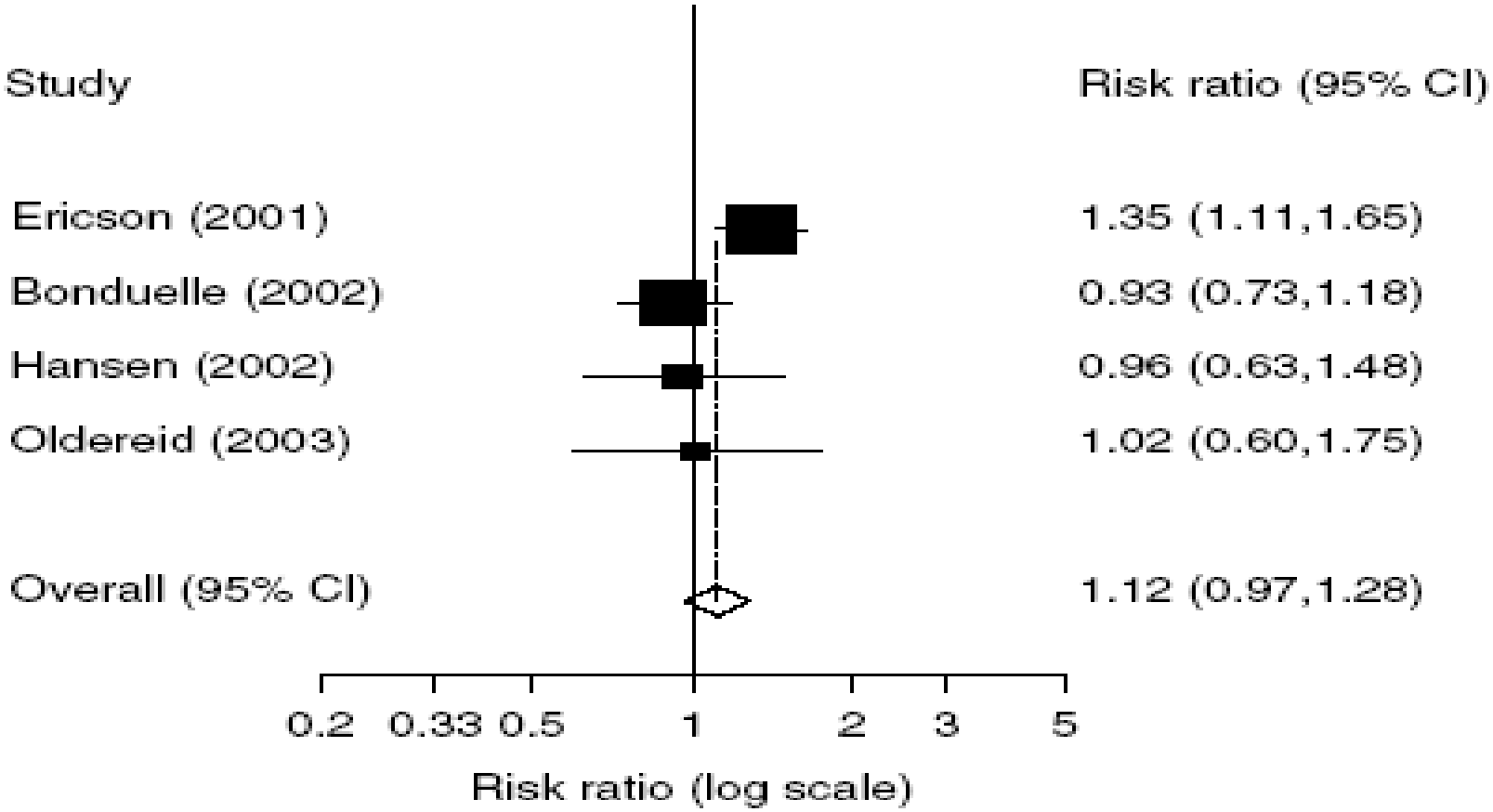
## Risk for Congenital Malformations in ART Children *(Sweden)*

### Congenital Malformations among Infants Born after IVF Compared with All Infants*

| | All[a] | | "Weeded"[b] | |
|---|---|---|---|---|
| Adjustments | OR | 95% CI | OR | 95% CI |
| Year of birth | 1.42 | 1.32–1.52 | 1.52 | 1.29–1.66 |
| Year of birth and maternal age | 1.40 | 1.30–1.60 | 1.48 | 1.30–1.62 |
| Year of birth and parity | 1.39 | 1.29–1.49 | 1.50 | 1.28–1.64 |
| Year of birth, maternal age, and parity | 1.33 | 1.24–1.43 | 1.44 | 1.32–1.57 |
| Singletons | 1.30 | 1.20–1.41 | 1.39 | 1.26–1.53 |
| Multiple births | 1.02 | 0.91–1.15 | 0.96 | 0.76–1.21 |
| Also years of known childlessness | 1.05 | 0.95–1.16 | 1.12 | 0.99–1.28 |
| Also maternal smoking | 1.04 | 0.93–1.16 | 1.12 | 0.98–1.27 |
| Singletons | 1.07 | 0.95–1.21 | 1.11 | 0.95–1.29 |
| Multiple births | 0.86 | 0.70–1.05 | 0.94 | 0.73–1.19 |

*Kallen et al, Birth Def Res, 73, 162, 2005*

# Meta-analysis of Major Birth Defects in IVF and ICSI Children




*Lie et al, Intern J Epidemiol, 34, 696, 2005*

# Risk for Congenital Malformations in ART Children *(Sweden)*

Distribution of All Infants with a Congenital Malformation (Irrespective of Source) According to IVF Method Used*

| Method | Number of infants: Malformed | Number of infants: Total | Percent | 95% CI | OR | 95% CI |
|---|---|---|---|---|---|---|
| Standard IVF | | | | | | |
| Fresh stimulated | 829 | 10116 | 8.2 | 7.7–8.7 | 1.00 | Reference |
| Fresh unstimulated | 3 | 112 | 2.7 | 0.6–7.6 | 0.30 | 0.10–0.88 |
| Frozen | 81 | 1055 | 7.7 | 6.1–9.5 | 0.94 | 0.74–1.21 |
| ICSI | | | | | | |
| Ejaculated sperm | 371 | 4248 | 8.7 | 7.9–9.6 | 1.08 | 0.94–1.25 |
| Epididymal sperm | 10 | 135 | 7.4 | 3.6–13.2 | 0.95 | 0.49–1.87 |
| Testicular sperm | 11 | 147 | 7.5 | 6.8–13.0 | 0.93 | 0.49–1.75 |
| Frozen ejaculated sperm | 28 | 343 | 8.2 | 5.5–11.6 | 0.99 | 0.66–1.49 |
| Frozen other sperm | 3 | 33 | 9.1 | 1.9–24.3 | 0.98 | 0.38–4.11 |
| Frozen unspecified | 5 | 43 | 9.1 | 3.9–25.1 | 1.30 | 0.50–3.36 |
| Other or unspecified | 3 | 48 | 6.3 | 1.3–17.2 | 0.76 | 0.24–2.40 |
| All ICSI vs. all standard IVF | | | | | | |
| Standard IVF | 913 | 11283 | 8.1 | 7.6–8.6 | 1.00 | Reference |
| ICSI | 428 | 4949 | 8.6 | 7.9–9.5 | 1.00 | 0.74–1.36 |

*Numbers and odds ratio (OR) with 95% confidence interval (95% CI) for any malformation according to IVF method. Adjustment for year of birth, maternal age, and number of infants in birth.

*Birth Defects Research (Part A) 73:162–169 (2005)*

# ICSI-CFO Study (supported by EU)
# Members of Steering Committee

M. Bonduelle

I. Ponjaert

BELGIUM

A. Sutcliffe

J. Barnes

UNITED KINGDOM

A. Loft

DENMARK

U-B Wennerholm

SWEDEN

B. Tarlatzis

GREECE

# ICSI-CFO Study (supported by EU)

- Study of 1515 ICSI, IVF and spontaneously conceived children at the age of 5 years and their families

# ICSI CFO Study: Major malformations at 5 years

| | ICSI<br>n 540 | IVF<br>n 437 | Control<br>n 538 | p-value |
|---|---|---|---|---|
| Neonatal | 3.3% | 2.1% | 1.9% | ns |
| Childhood | **3.0%[1]** | 2.3% | 0.4%[1] | [1]0.001 |
| Total major malformation | **6.3%[2]** | 4.3% | 2.2%[2] | [2]0.001 |

*Bonduelle et al, Hum Reprod, 20, 413, 2004*

# Prevalence of Major Malformations

- ICSI vs control: OR 2.85 (CI 1.46-5.59)
- IVF vs control: OR 1.82 (CI 0.86-3.85)
  - After adjustment for maternal age, educational level, social class, smoking and drinking, OR slightly attenuated
  - ICSI vs control: OR 2.54 (CI 1.13-5.71)
  - IVF vs control: OR 1.67 (CI 0.70-3.98)

***Bonduelle et al, Hum Reprod, 20, 413, 2004***

# Uro-genital Major Malformations in ICSI (n=20)

Hypospadias (3)

Congenital malformations of male genital organs

Hydrocoele (3)

Undescended testicle, unilateral (4)

Duplication of ureter

Urethral stenosis (3)

Congenital vesico-ureteric junction obstruction (2)

Congenital vesico-uretero-renal reflux (3)

*Bonduelle et al, Hum Reprod, 20, 413, 2004*

# Major Malformations in ICSI Children vs Controls

| Procedure | Total boys MAJ % | Total girls MAJ % | Boys and girls % |
|---|---|---|---|
| ICSI *vs* Control | 8.2%<br>RR 2.60<br>CI: 1.2 – 5.5 | 3.6%<br>RR = 1.44<br>CI: 0.99 - 2.09 | 6.3%<br>RR = 2.58<br>CI: 1.37 - 4.84 |

***Bonduelle et al, Hum Reprod, 20, 413, 2004***

# Malformations in ICSI Children by Sperm Origin

| Sperm origin | Major % | Abnormal / total |
|---|---|---|
| Ejaculate | 4.2%[1,2] | 32 / 758 |
| Epididymal | 9.1%[1] | 2 / 22 |
| Testicular | 12.5%[2] | 2 / 16 |
| | [1,2] FE n.s. | |

*Bonduelle et al, Hum Reprod, 20, 413, 2004*

# Prevalence of Major Malformations

- Increase in ICSI children
  - Not detected at birth
  - Partially due to increased defects in
    - uro-genital system
  - Higher malformation rate in ICSI
    - Boys 8.2% > girls 3.6%

***Bonduelle et al, Hum Reprod, 20, 413, 2004***

# Subfertility as a risk factor

- *Buck Louis (2005)* highlighted major drawback of all studies, ie one group is fertile, the other one is subfertile.
- Optimal study design would be:
  1. Comparison spontaneous and ART conceptions in subfertile population
  2. Comparison spontaneous and ART conceptions in fertile population

## Subfertility and Risk for Major Malformations

- Spontaneous conception in subfertile couples in Sweden (1983 – 1986)

  *Ghazi et al, 1991*

**Table 3.** Risk of premature birth (a) and major malformations (b) depending on the time to pregnancy (Ghazi *et al.*, 1991).

| *Time to pregnancy (years)* | *Odds ratio* | *95% Confidence interval* |
|---|---|---|
| (a) | | |
| 1 | 1.03 | 1.01–1.26 |
| 2 | 1.13 | 1.01–1.26 |
| 3 | 1.16 | 1.00–1.35 |
| 4 | 1.29 | 1.07–1.55 |
| ≥5 | 1.60 | 1.44–1.77 |
| (b) | | |
| 1 | 0.97 | 0.85–1.10 |
| 2 | 1.00 | 0.87–1.16 |
| 3 | 1.01 | 0.83–1.24 |
| 4 | 1.14 | 0.90–1.45 |
| ≥5 | 1.18 | 1.01–1.37 |
| 1–3 | 0.99 | 0.90–1.08 |
| ≥4 | 1.17 | 1.03–1.33 |

***Ludwig, RBM Online 10, suppl 3, 83, 2005***

# CHILDREN BORN AFTER ASSISTED REPRODUCTION TECHNIQUES

- Perinatal Outcome
- Congenital Malformations
- Chromosomal Abnormalities
- Psychomotor development
- Genomic Imprinting Defects
- Cancer

## Chromosomal Abnormalities in ART Babies

- No systematic data in conventional IVF
- Limited data in ICSI fetuses
- Data from VUB
  - 1586 fetal karyotypes
  - Initially in almost all pregnancies - now in < 50%

# PREVALENCE OF INHERITED AND DE NOVO ABERRATIONS

## PREVALENCE IN VUB ICSI FOETUSSES

- **TOTAL:** 47/1586 = 2.96% = x 3
- **DE NOVO:** 25/1586 = 1.58% = x 3
- **INHERITED:** 22/1586 = 1.39% = x 3

*Bonduelle M L, ICSI-Related Risk for the Children, PhD Thesis, April 2003*

# PREVALENCE OF INHERITED AND DE NOVO ABERRATIONS

## INHERITED CHROMOSOMAL ANOMALIES

- PATERNAL TRANSMISSION : 17/22
- MATERNAL TRANSMISSION : 5/22

---

- BALANCED : 21/22
- UNBALANCED : 1/22

*Bonduelle M L, ICSI-Related Risk for the Children, PhD Thesis, April 2003*

# Prenatal Diagnosis in 1586 ICSI Fetuses in VUB

| Abnormal results | n | % | Confidence Interval | % normal population [1, 2, 3] |
|---|---|---|---|---|
| ■ *De novo* | 25 | **1.6%*** | 1.02 - 2.32 % | 0.45 - 0.87% |
| Sex chrom | 10 | **0.6%*** | 0.30 - 1.16 % | 0.19 - 0.27% |
| Autosomal | 15 | 0.9% | 0.53 - 1.56 % | 0.26 - 0.60% |
| Numerical | 8 | 0.5% | 0.22 - 0.99 % | 0.14 - 0.33% |
| Structural | 7 | 0.4% | 0.18 - 0.91 % | 0.11 - 0.22% |
| ■ Inherited | 22 | **1.4%*** | 0.87 - 2.09 % | 0.47 - 0.37% |
| Total | 47 | 3.0% | 2.19 - 3.92 % | 0.92% |

[1] ***Jacobs et al., 1992 on 34 910 newborns***
[2] ***Ferguson-Smith et al., 1984 on 52 965 prenatal samples***
[3] ***Hook et al., 1982; 1982***

*** significant**

# NUMBER OF CHROMOSOMAL ABERRATIONS IN AZOOSPERMIC MALES

| References | n | Klinefelter XXY (%) | Other sex chromosome abnormalities (%) | Autosomal aberrations (%) |
|---|---|---|---|---|
| Hendry 1976 | 54 | 3 (5.6) | - | 2 (3.0) |
| Micic 1984 | 356 | 26 (7.3) | 2 (0.6) | 2 (0.6) |
| Retief 1984 | 106 | 12 (11.3) | 6 (0.6) | - |
| Bourrouillou 1985 | 383 | 49 (12.8) | 5 (1.5) | 5 (1.3) |
| Rivas 1987 | 163 | 31 (19.0) | 5 (3.0) | 2 (1.2) |
| Matsuda 1989 | 84 | 3 (3.4) | 2 (2.2) | 2(2.2) |
| | 1151 | 124 (11.0) | 20 (1.7) | 13 (1.1) |

# Prevalence of De Novo Chromosomal Anomalies

| | Sex | Auto | Total |
|---|---|---|---|
| Bonduelle et al., 2002 | 10 (0.63%) | 15 (0.95%) | 25/586 (1.6%) |
| Aboulghar et al., 2001 | 7 (1.63%) | 8 (1.86%) | 15/430 (3.4%) |

*Bonduelle et al., 2002*

# De Novo Chromosomal Anomalies and Sperm Parameters / Origin

- ***Sperm count***

  $< 20.10^6$ / ml $\Rightarrow$ 2.1 %* chromosomal abnormalities

  Fisher's Exact 2 tailed test $p < 0.05$
- ***Sperm motility***

  < 50 % normal motility $\Rightarrow$ more chromosomal abnormalities

  Fisher's Exact 2 tailed test $p < 0.05$
- ***Sperm origin*** $\Rightarrow$ no influence

# Chromosomal Abnormalities in ICSI Embryos Using OTA or TESE Spermatozoa

| | OTA | TESE | P Value |
|---|---|---|---|
| Embryos (N) | 830 | 100 | |
| Normal (%) | 347 (41.8) | 22 (22.0) | <0.001 |
| Aneuploid (%) | 218 (26.2) | 17 (17.0) | NS |
| Mosaic (%) | 220 (26.5) | 53 (53.0) | <0.001 |

*Silber et al, Fertil Steril, 79, 30, 2004*

# Chromosomal Abnormalities in Sperm from Azoospermic Men

| Semen Origin | Sperm Analyzed (N) | Nullisomy (%) | Autosom Disomy (%) | Sex Chr Disomy (%) | Diploidy (%) |
|---|---|---|---|---|---|
| Testicular | 490 | 18 (3.7)[a] | 10 (2.0)[b] | 21 (4.3)[c] | 7 (1.4)[d] |
| Epididym | 6675 | 29 (0.43)[a] | 34 (0.51)[b] | 41 (0.61)[c] | 16 (0.24)[d] |
| Ejaculated | 25150 | 67 (0.27)[a] | 128 (0.51)[b] | 113 (0.45)[c] | 82 (0.33)[d] |

*[a,b,c,d] p<0.01*

*Palermo et al, Hum Reprod, 17, 570, 2002*

# Chromosomal Abnormalities in Sperm from Infertile and Fertile Men

| | Chromosomal Abnormalities (%) | P Value |
|---|---|---|
| Nonobstructive Azoospermia | 19.6 | <0.001 |
| Obstructive Azoospermia | 8.2 | <0.001 |
| Severe OTA | 13.0 | <0.001 |
| Semen Donors | 1.6 | |

*Levron et al, Fertil Steril, 63, 479, 2001*

# Genetic Risks in ICSI Children

- Risk due to higher maternal age (31%)
- More (5.3%) parental (paternal) abnormal karyotypes
- More (6%) risk for monogenic diseases
  - Infertility is part of disease CF/CBAVD, Steinert
  - Genetic abnormality causes infertility: Yq11 (micro) deletions
- More multifactorial disorders in infertilie patients?

$\Rightarrow$ Genetic counselling needed in high risk situations

# CHILDREN BORN AFTER ASSISTED REPRODUCTION TECHNIQUES

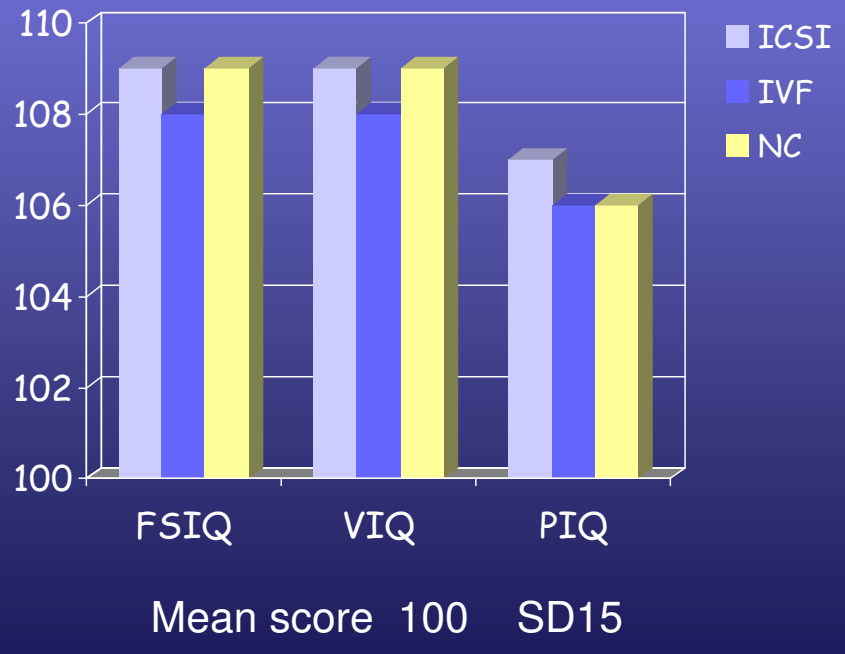
- Perinatal Outcome
- Congenital Malformations
- Chromosomal Abnormalities
- Psychomotor development
- Genomic Imprinting Defects
- Cancer

# Cognitive Development at 5 Years

Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R): FSIQ, VIQ, PIQ

- NO differences between ICSI, IVF and NC children on FSIQ, VIQ and PIQ
- Gender effect

  Girls obtain higher scores than boys on FSIQ, VIQ and PIQ



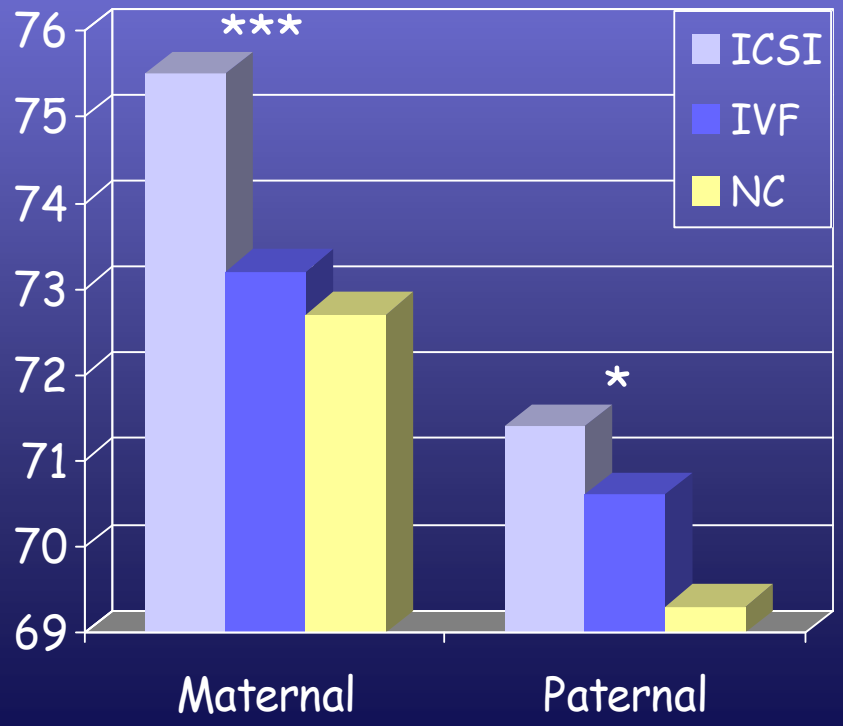

***Ponjaert-Christoferson et al, Pediatr, 115, 283, 2005***

# Socio-emotional Development & Family Relationships

## Results

- No evidence of increased child behavioural problems (CBCL)
- No evidence of more stress in families who have used ICSI or IVF (PSI)
- Greater investment in parenting associated with ICSI, and less in work (Greenberger)

Maternal and paternal commitment to parenting (Greenberger)




*Barnes et al, Hum Repr, 19, 1480, 2004*

# Sperm Concentration and Cognitive Development

- No significant difference in total intelligence quotient (IQ) – performance or verbal IQ- between ICSI and IVF children depending on sperm origin (testicular, epididymal or ejaculated) or sperm concentration (<1, 1-5, 5-20 or >20x$10^6$ / ml).

*Wennerholm et al, Hum Reprod, 2006*

# Laterality in ICSI and IVF versus Naturally Conceived Children

Table 1. Observed left handedness (for drawing and writing) in five-year-old children in assisted reproduction treatment groups compared with naturally conceived (NC) controls.

| Conception groups ($n$) | Percent left handed | $\chi^2$ *vs* NC control | Significance ($P$) |
|---|---|---|---|
| NC control girls (250) | 12.4 | – | – |
| IVF girls (198) | 8.6 | 1.68 | n.s. |
| ICSI girls (243) | 7.0 | 4.10 | <0.05 |
| NC control boys (273) | 13.9 | – | – |
| IVF boys (227) | 11.5 | 0.68 | n.s. |
| ICSI boys (282) | 13.8 | 0.01 | n.s. |

*Sutcliffe et al, Br J Obstet Gynaec, 112, 1, 2005*

**Human Reproduction Update**, Vol.14, No.3 pp. 219–231, 2008
Advance Access publication March 26, 2008

doi:10.1093/humupd/dmn005

# Neuromotor, cognitive, language and behavioural outcome in children born following IVF or ICSI–a systematic review

**K.J. Middelburg[1,5], M.J. Heineman[2,3], A.F. Bos[4] and M. Hadders-Algra[1]**

*[1]Department of Paediatrics, Division of Developmental Neurology, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands; [2]Department of Obstetrics and Gynaecology, University Medical Center Groningen, Groningen, The Netherlands; [3]Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, The Netherlands; [4]Department of Paediatrics, Division of Neonatology, University Medical Center Groningen, Groningen, The Netherlands*

# Neuromotor and Mental Development of ICSI Children at 5.5 Years (Germany)

**TABLE 3**

**Test results of the Kaufman Assessment Battery for Children.**

| | ICSI group (n = 276) | Control group (n = 273) | *P* value to reject nonequivalence[a] |
|---|---|---|---|
| Sequential processing | 101.90 ± 11.53 | 101.71 ± 11.72 | >.01 |
| Simultaneous processing | 104.57 ± 11.03 | 104.59 ± 10.91 | >.01 |
| Learning ability/intelligence | 102.87 ± 9.19 | 102.78 ± 9.04 | >.01 |
| Planning ability | 102.97 ± 11.32 | 101.60 ± 11.25 | >.01 |

*Note:* Complete test results were available for 271 ICSI children and 268 control children.

[a] Null hypothesis for equivalence: $\mu$ (control) − $\mu$ (ICSI) > 4 units.

*Ludwig et al, Fertil Steril, 2009*

# CHILDREN BORN AFTER ASSISTED REPRODUCTION TECHNIQUES

- Perinatal Outcome
- Congenital Malformations
- Chromosomal Abnormalities
- Psychomotor development
- Genomic Imprinting Defects
- Cancer

# Genomic Imprinting Defects

**Angelmann's syndrome** ***(neurogenetic disease)***

***Cox et al, 2002:*** **2 cases after ICSI**

**Beckwith-Wiedemann syndrome** ***(human large baby syndrome)***

***Sutcliffe et al,1995:*** **1 case after cryopreserved ET**

***Olivennes et al, 2001:*** **1 case after IVF**

***DeBaun et al, 2002:*** **2 cases after IVF**

**4 cases after ICSI (ejacul. sperm)**

**1 case after ICSI (testic. sperm)**

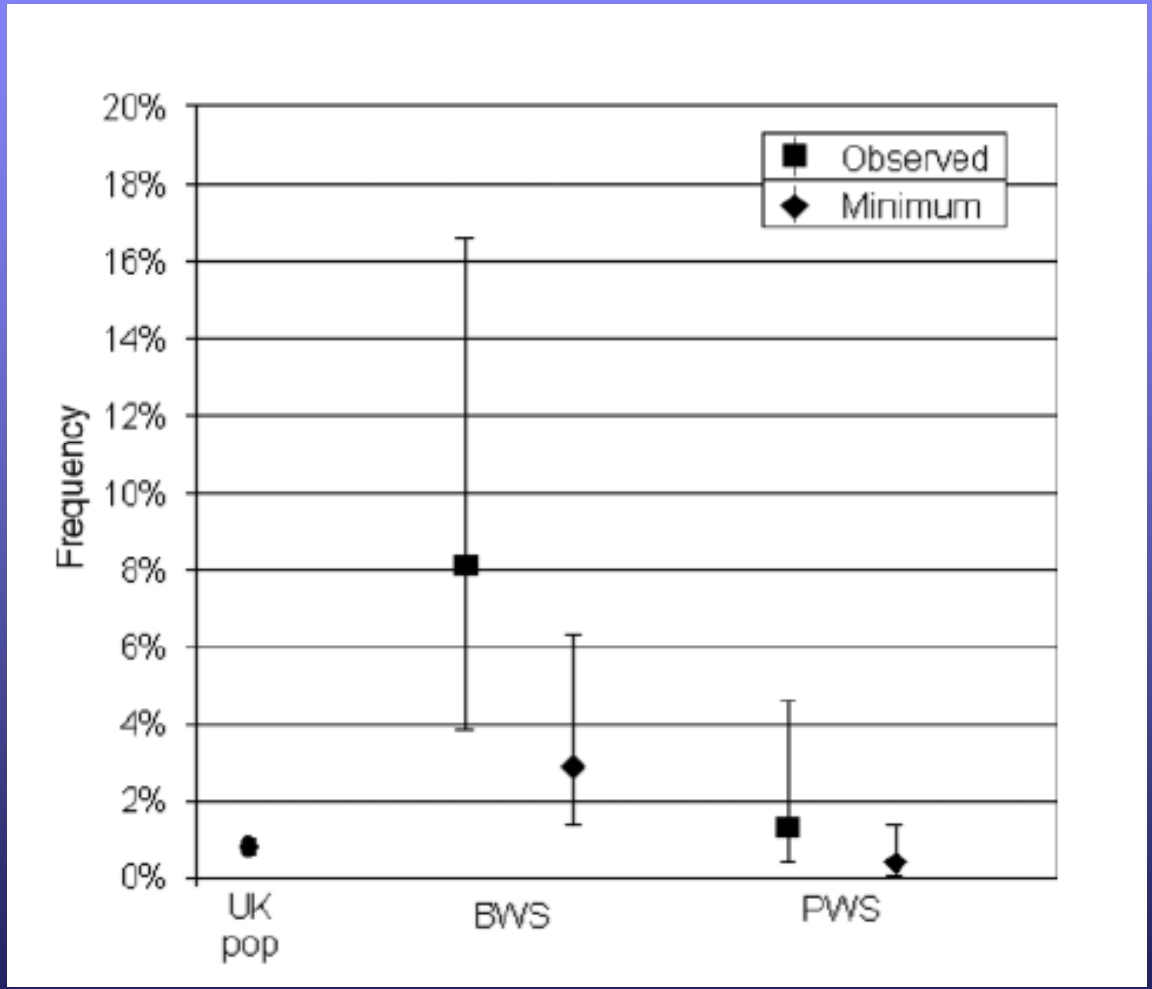
***Maher et al, 2003:*** **3 cases after IVF**

**3 cases after ICSI**

**Retinoblastoma**

***Moll et al, 2003:*** **5 cases after IVF**

# Beckwith-Wiedemann and Prader-Willi Syndromes in IVF/ICSI Children and the UK Population




*Sutcliffe et al, Hum Reprod, 2006*

# CHILDREN BORN AFTER ASSISTED REPRODUCTION TECHNIQUES

- Perinatal Outcome
- Congenital Malformations
- Chromosomal Abnormalities
- Psychomotor development
- Genomic Imprinting Defects
- Cancer

# INCIDENCE OF CANCER IN CHILDREN CONCEIVED BY ART

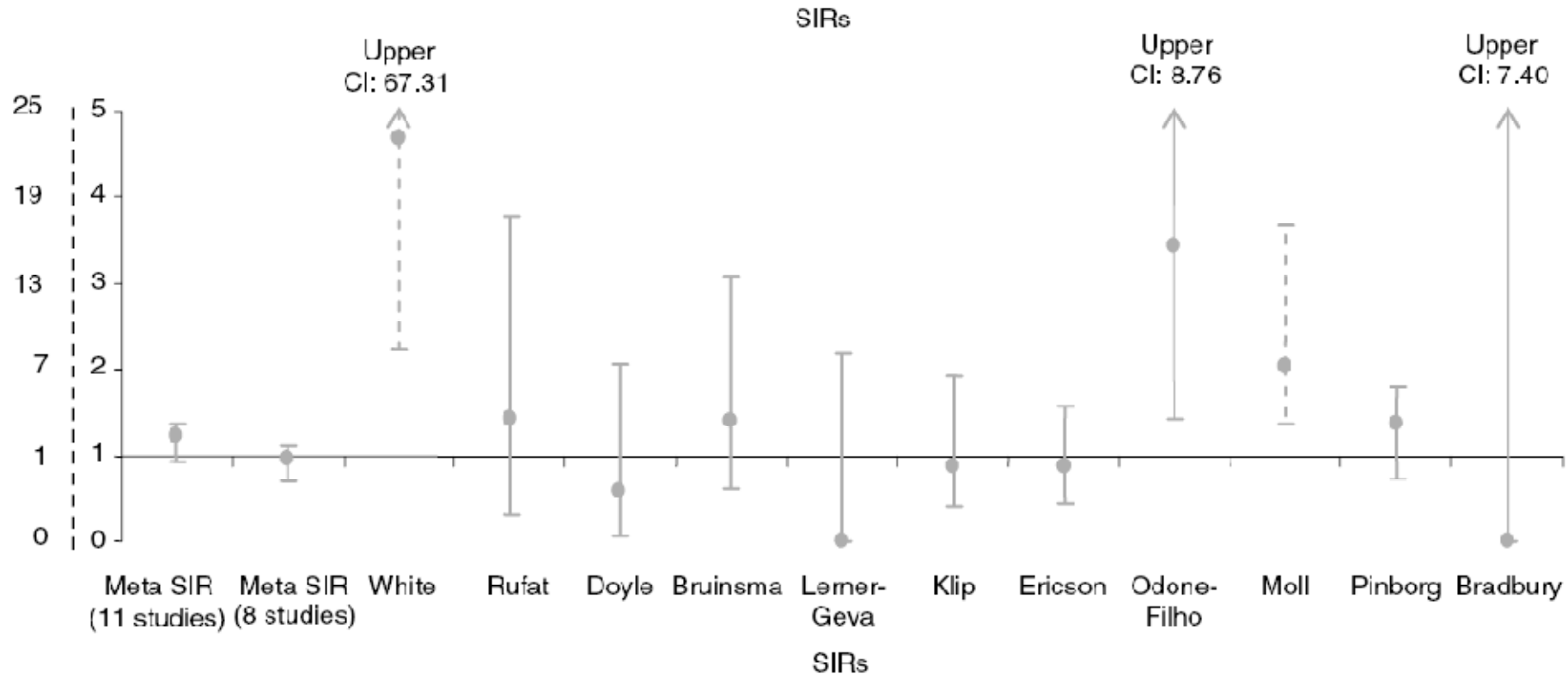
| | Country | Mean follow-up (years) | Total cohort size (n) | Total cases (n) | Comparison group | SIR | 95% CI |
|---|---|---|---|---|---|---|---|
| Doyle et al (1998)[97] | UK | 8·6 | 2507 | 2 | General population | 0·57 | 0·7–2·06 |
| Bruinsma et al (2000)[98] | Australia | 3·9 | 5249 | 6 | General population | 1·39 | 0·62–3·09 |
| Lerner-Geva et al (2000)[99] | Israel | 4·3 | 332 | 0 | General population | | |
| Brinton et al (2004)[100] | Denmark | 20 | 30 364 | 51 | General population | 1·14 | 0·8–1·5 |

SIR=standardised incidence ratios.

*Table 3*: Risk of childhood cancer after ART

*Sutcliffe and Ludwig, Lancet, 2007*

# INCIDENCE OF CANCER IN CHILDREN CONCEIVED BY ART




*Raimondi et al, Br J Cancer, 2005*

# Fertility

# Fertility of ART Children

- Louise Brown and her sister gave birth to healthy children
- These represents the first, second generation children after IVF.

# Pregnancy and Children Outcome after ART: *Is there a Reason for Concern?*

- Multiple pregnancies remain an important risk factor
- Slightly higher risk of perinatal complications (prematurity, low birth weight), even in singletons, probably related to infertility
- Slightly higher risk of inherited chromosomal anomalies in relation to parental chromosomes and of de novo anomalies related to sperm quality

# Pregnancy and Children Outcome after ART: *Is there a Reason for Concern?*

- Slightly higher risk of major malformations mostly in relation to maternal age, infertility and underlying parental disease
- Psycho-motor development is normal but the neuro-developmental outcome might be influenced by neonatal problems

# Pregnancy and Children Outcome after ART: *Is there a Reason for Concern?*

- Based on the available data, no reason for major concern
- Proper counselling of the couples on existing risks
- Larger studies are necessary to assess the health risks associated with ART but also infertility per se

***Thank you!***