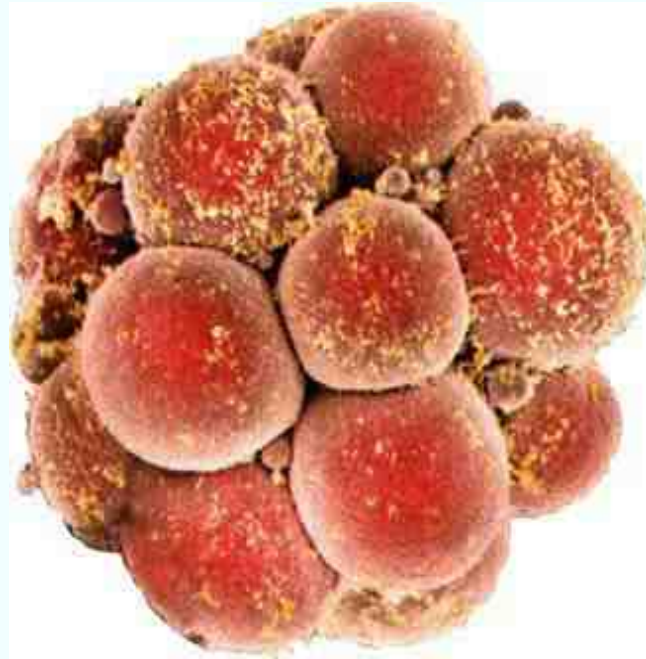


Current Status of PGD / PGS



Joep Geraedts

Maastricht, The Netherlands

Antalya

PGD and PGS

PGD: ART used for genetic reasons to detect a suspected abnormality

PGS: Genetic screening used to select the embryos with the highest developmental potential to improve ART results

Different aims

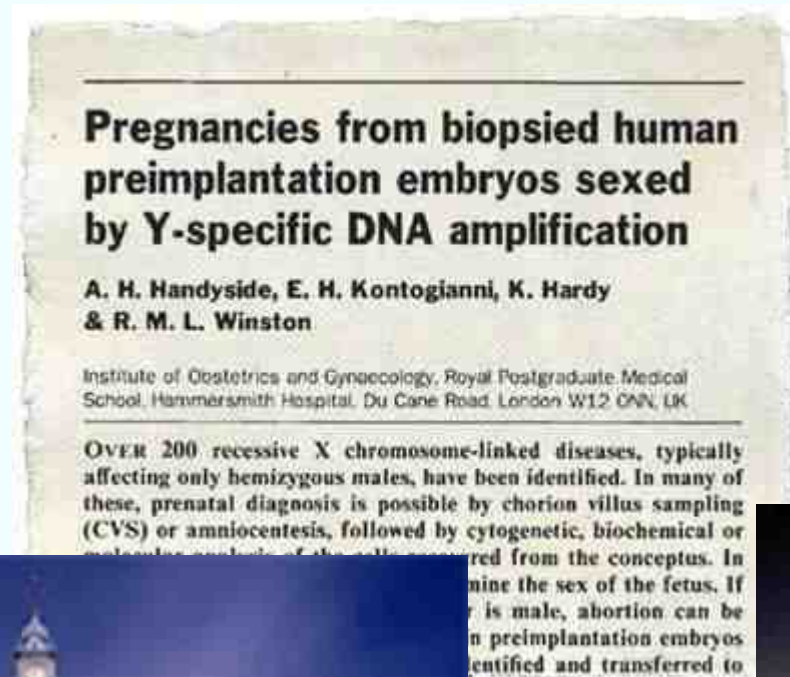
- **PGD aims at having a healthy child**
- **ART and PGS aim at having a child**

Alternatives for couples with increased genetic risk

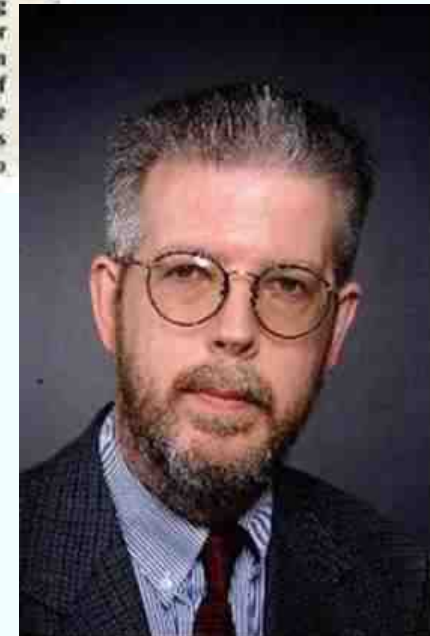
- **To accept the risk**
- **Refrain from having children**
- **Adoption**
- **Donation of sperm or oocytes**
- **Prenatal diagnosis (PND)**
- **Preimplantation genetic diagnosis (PGD)**

PGD

Celebration first published cases: 25 years



Hammersmith Hospital London



Prof. Alan Handyside

ESHRE PGD Consortium



Steering Committee 1997



Steering Committee 2014-2016

The PGD Consortium data collections

Data collections are an extremely valuable resource for monitoring accuracy, reliability, effectiveness and safety of PGD/PGS

The PGD Consortium data collections

Documents

Citations

Sort on: [Date \(newest\)](#) [Citation count \(descending\)](#) [...](#)

[Date \(newest\)](#) [Citation count \(descending\)](#) [...](#)

		<2011	2011	2012	2013	2014	2015	Subtotal	>2015	Total
	Total	679	100	99	71	77	13	360	0	1039
1	ESHRE PGD Consortium data collection XII: Cycles from Januar...	2014	Loading...			6	2	8		8
2	ESHRE PGD Consortium data collection XI: Cycles from January...	2012			18	15	3	36		36
3	The ESHRE PGD consortium: 10 years of data collection	2012			13	18	30	5	66	66
4	ESHRE PGD consortium data collection X: Cycles from January ...	2010	1	24	37	15	7	1	84	85
5	ESHRE PGD Consortium data collection IX: Cycles from January...	2009	33	33	12	9	3	57		90
6	ESHRE PGD Consortium data collection VIII: Cycles from Janua...	2008	45	10	5	1	1	17		62
7	ESHRE PGD consortium data collection VII: Cycles from Januar...	2008	40	7	6	3	2	1	19	59
8	ESHRE PGD consortium data collection VI: Cycles from January...	2007	69	5	7	2	3	17		86
9	ESHRE PGD Consortium data collection V: Cycles from January ...	2006	68	6	3	1	2	12		80
10	ESHRE PGD Consortium data collection IV: May-December 2001	2005	67	2	4	1	1	8		75
11	ESHRE Preimplantation Genetic Diagnosis Consortium: Data col...	2002	171	4	7	2	3	1	17	188
12	ESHRE Preimplantation Genetic Diagnosis (PGD) Consortium: Da...	2000	100	5	2	1	1	9		109
13	ESHRE Preimplantation Genetic Diagnosis (PGD) Consortium: Pr...	1999	85	4	3		3	10		95

Display 25 results

Page 1 / 1

Consortium members by country

(June 2015)

Total number of centres: 124

NORTH- AND SOUTH-AMERICA



number of centres: 11

Europe



number of centres: 86

AFRICA, ASIA, AUSTRALIA and RUSSIA



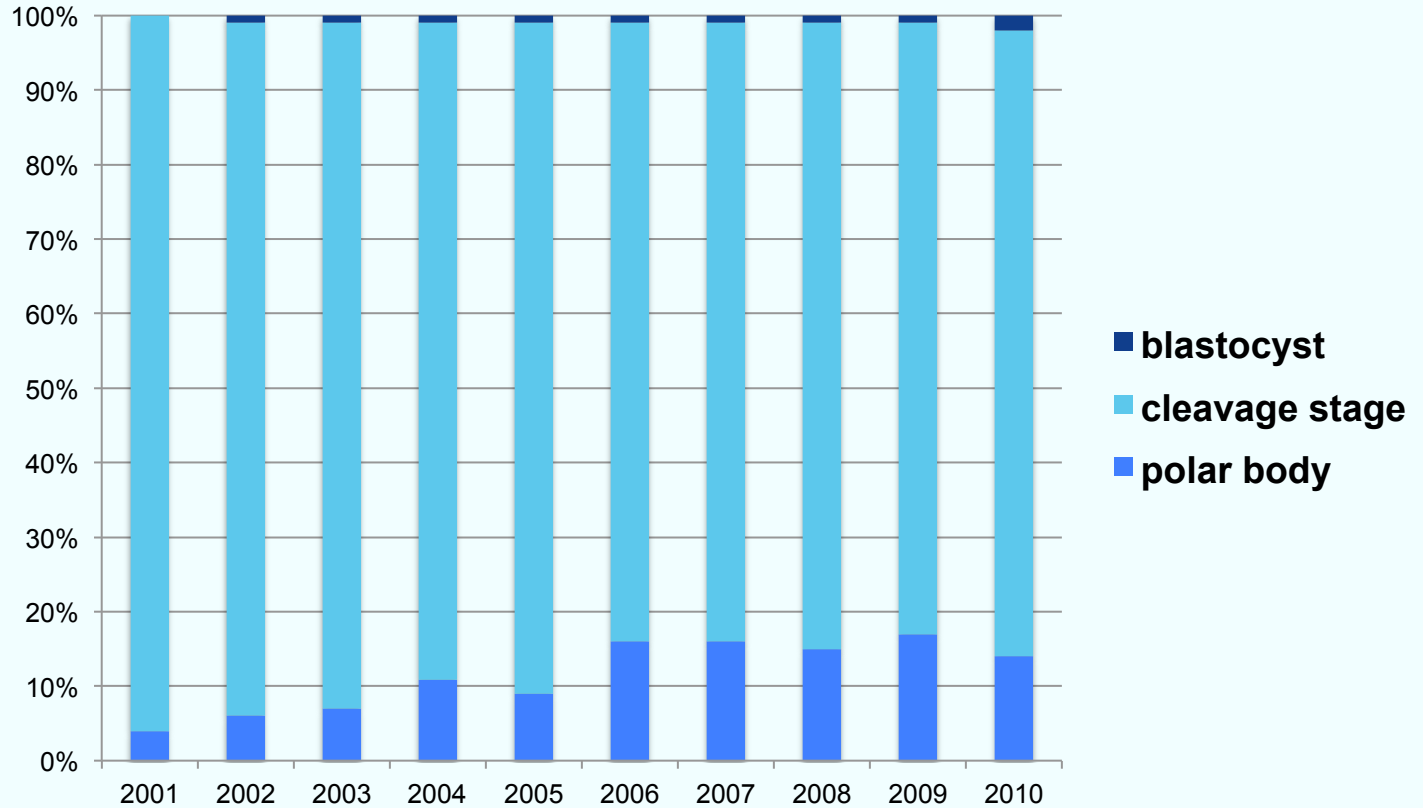
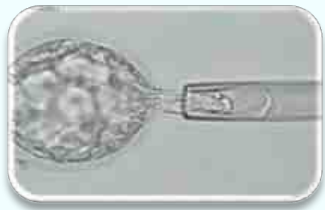
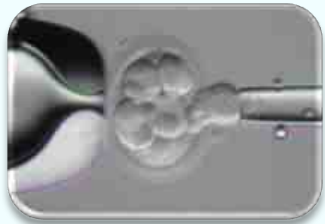
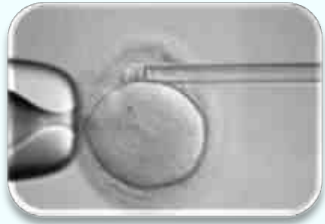
number of centres: 27

Trends in PGD

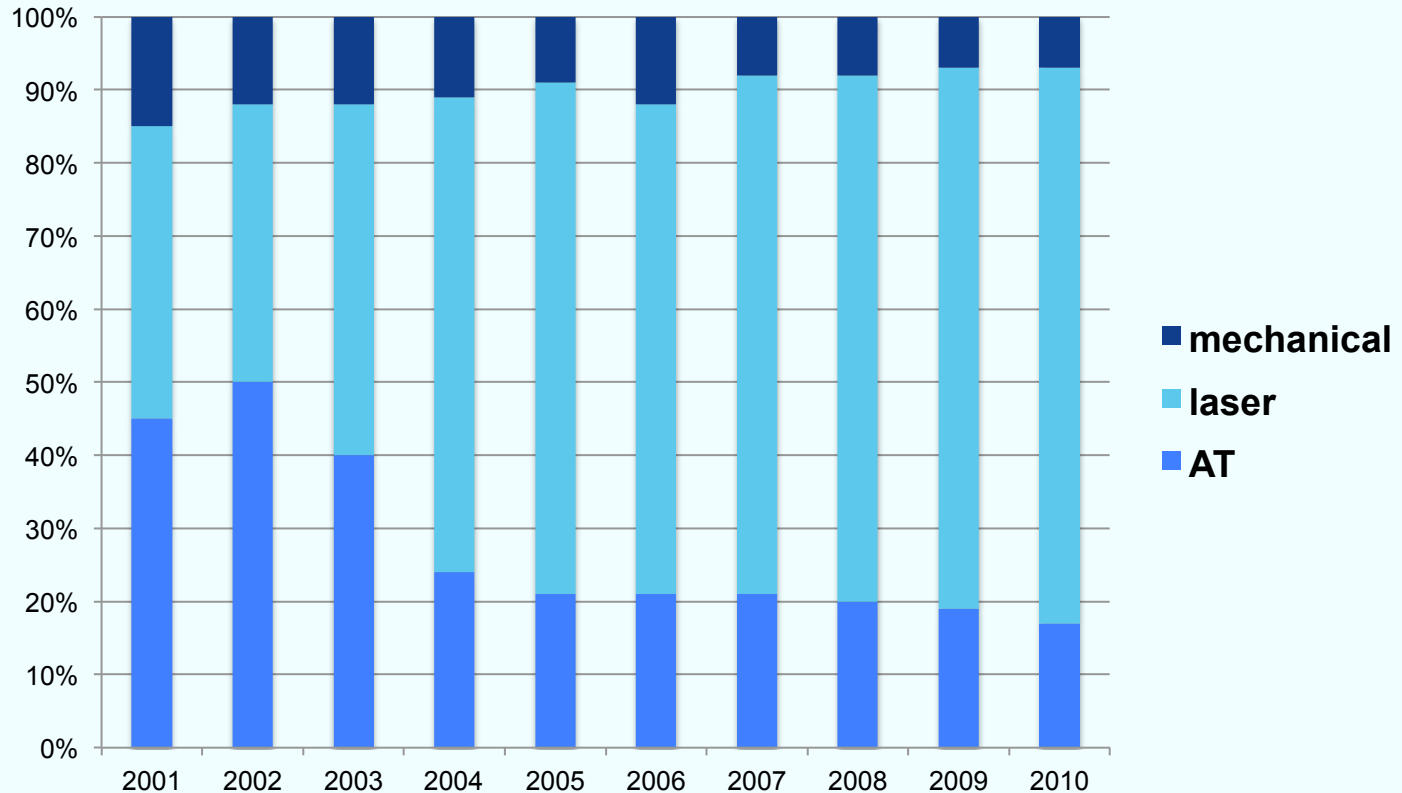
ESHRE PGD DATA I - XV

Dr. Edith Coonen, Maastricht

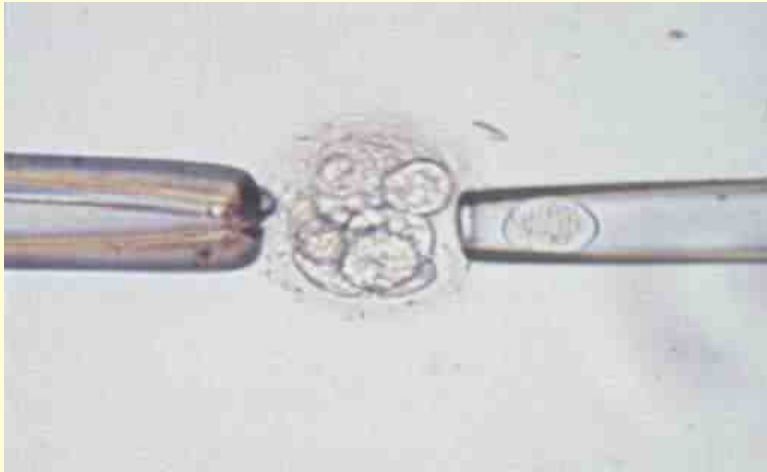
Type of biopsy



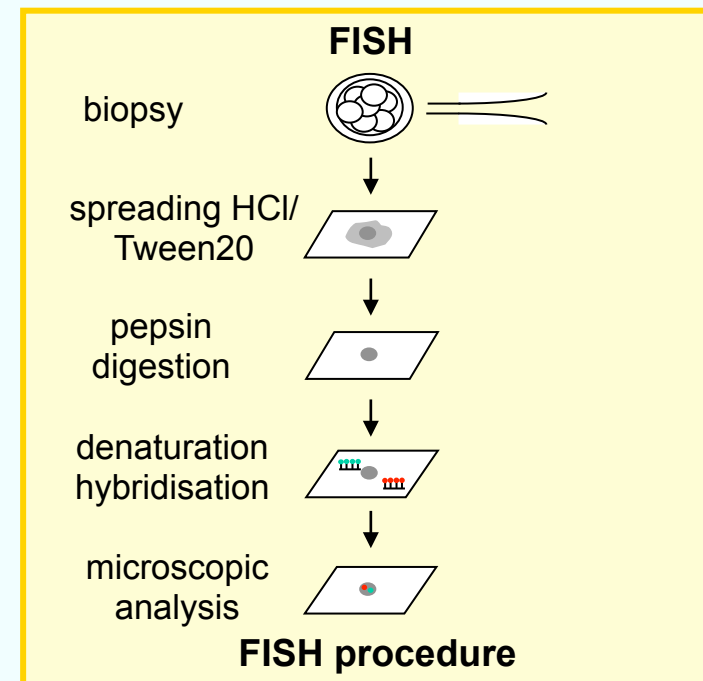
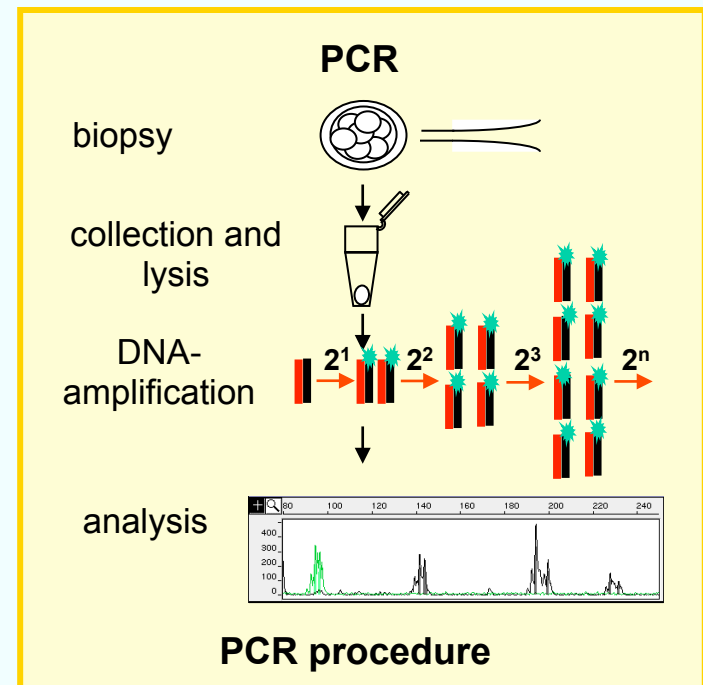
Method of biopsy



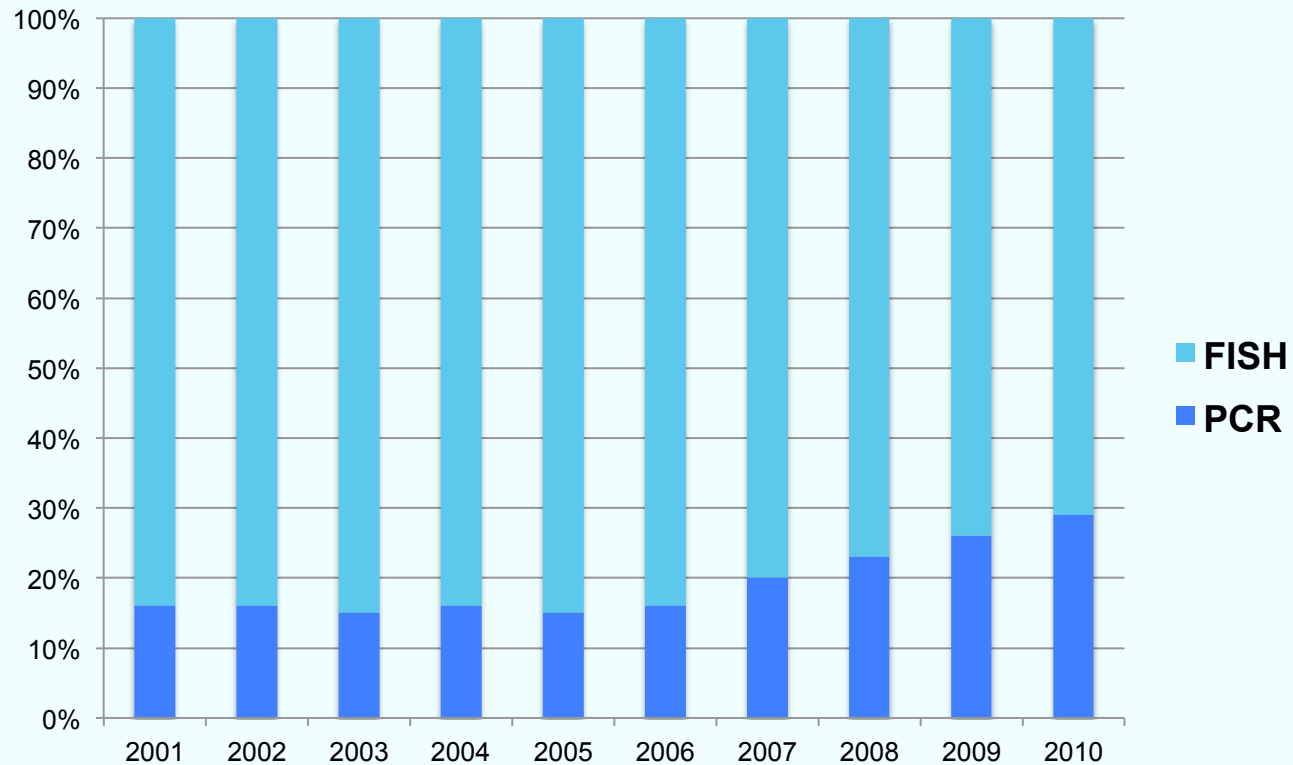
Diagnostic procedures



- Sex determination (FISH)
- Structural chromosome abnormalities (FISH)
- Aneuploidy screening (FISH)
- Monogenic diseases (PCR)
 - HLA typing (PCR)



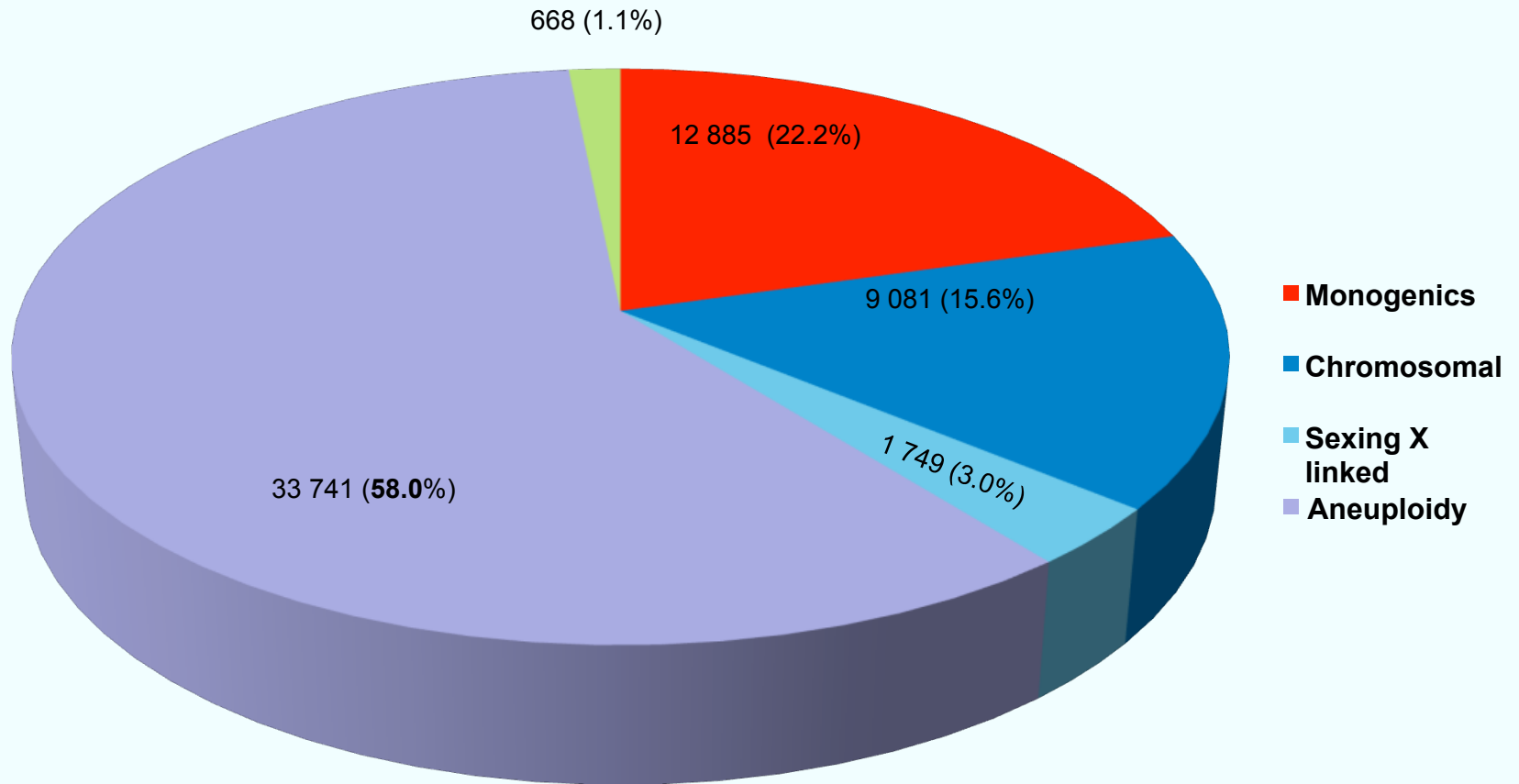
Method of analysis



Numbers

	Data I	Data XV
Centers	16	63
Cycles	366	6782
Pregnancies	82	1394
Deliveries	63	1158

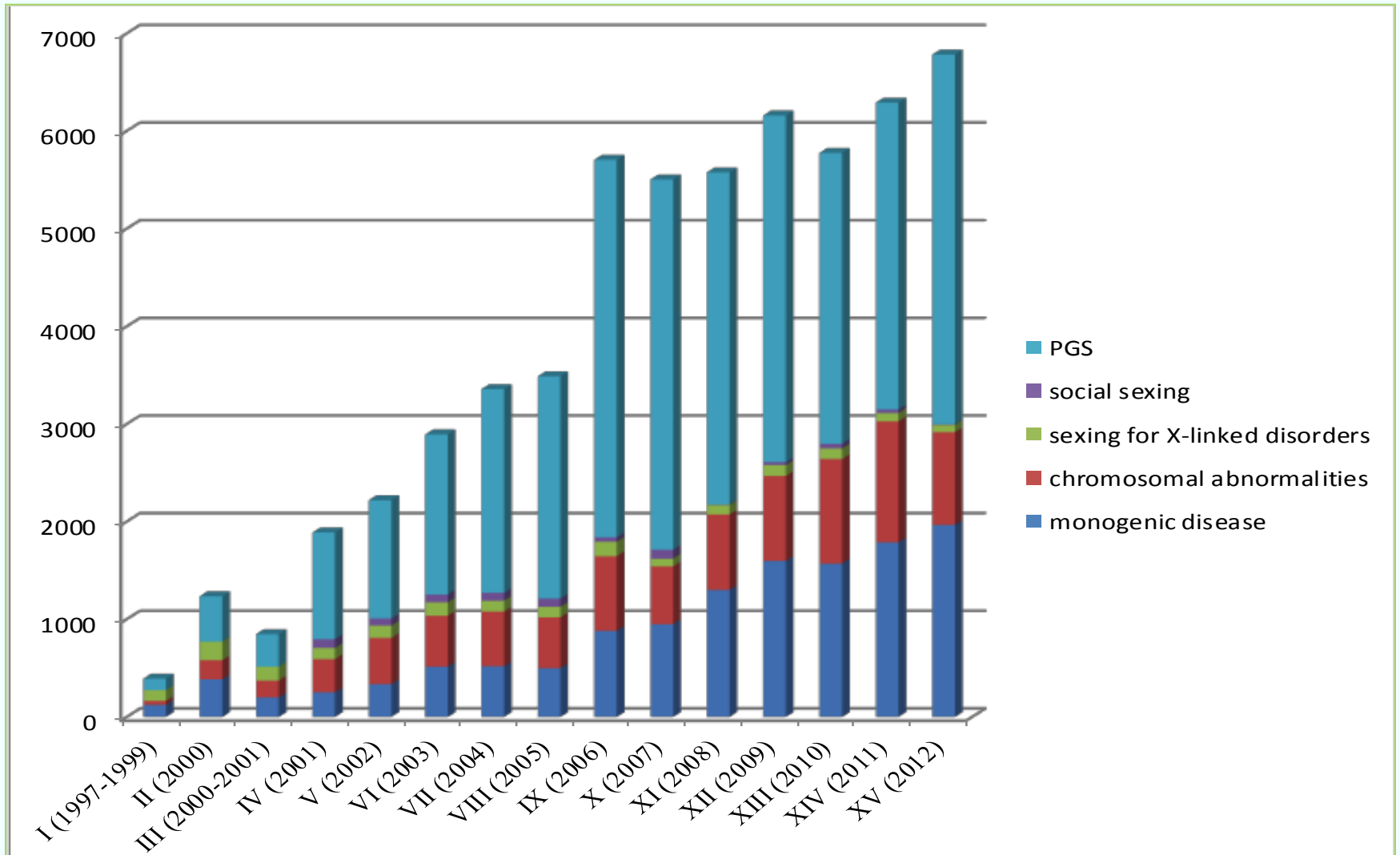
Cycles to OR cumulative data I-XV



Indications

	Data I	Data XV
Monogenic disorders	33%	29%
Chromosomal disorders	10%	14%
Sexing only	25%	1%
Social sexing	0%	0.1%
PGS	32%	56%

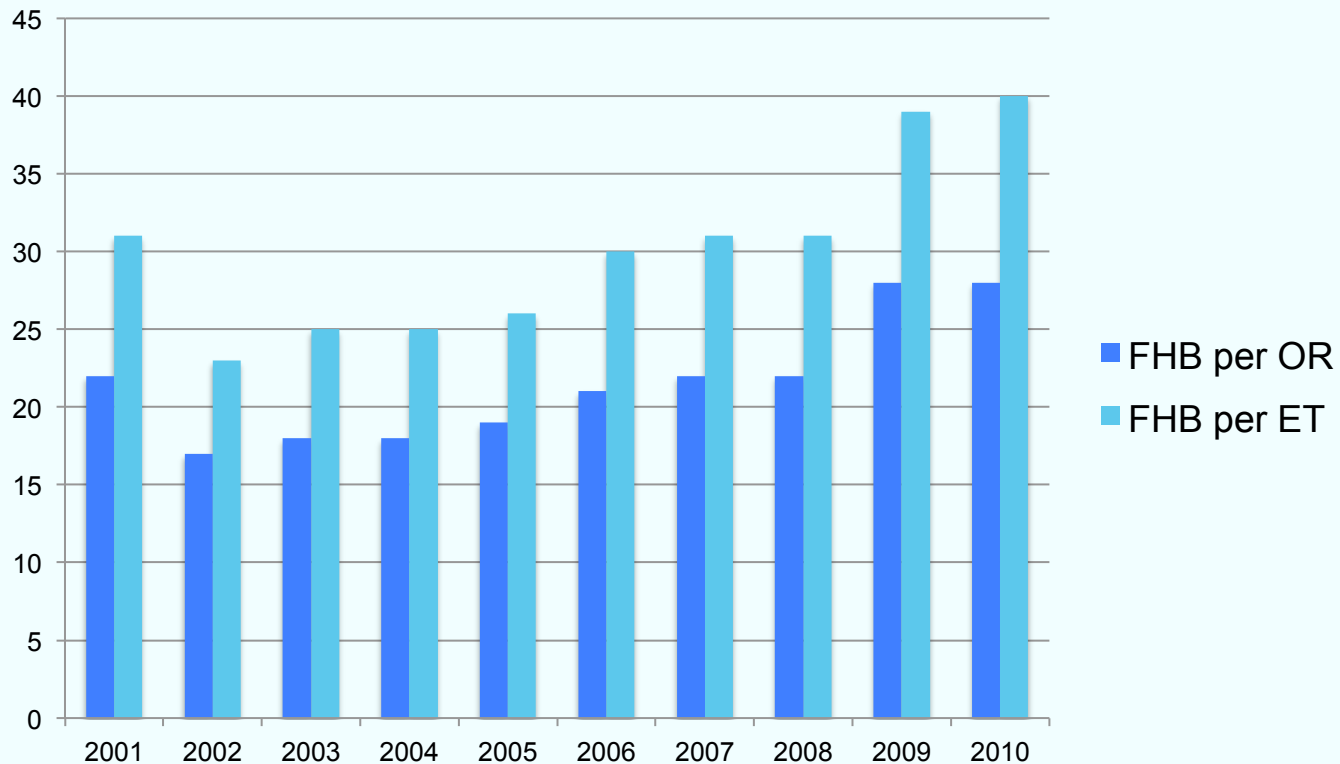
Indications



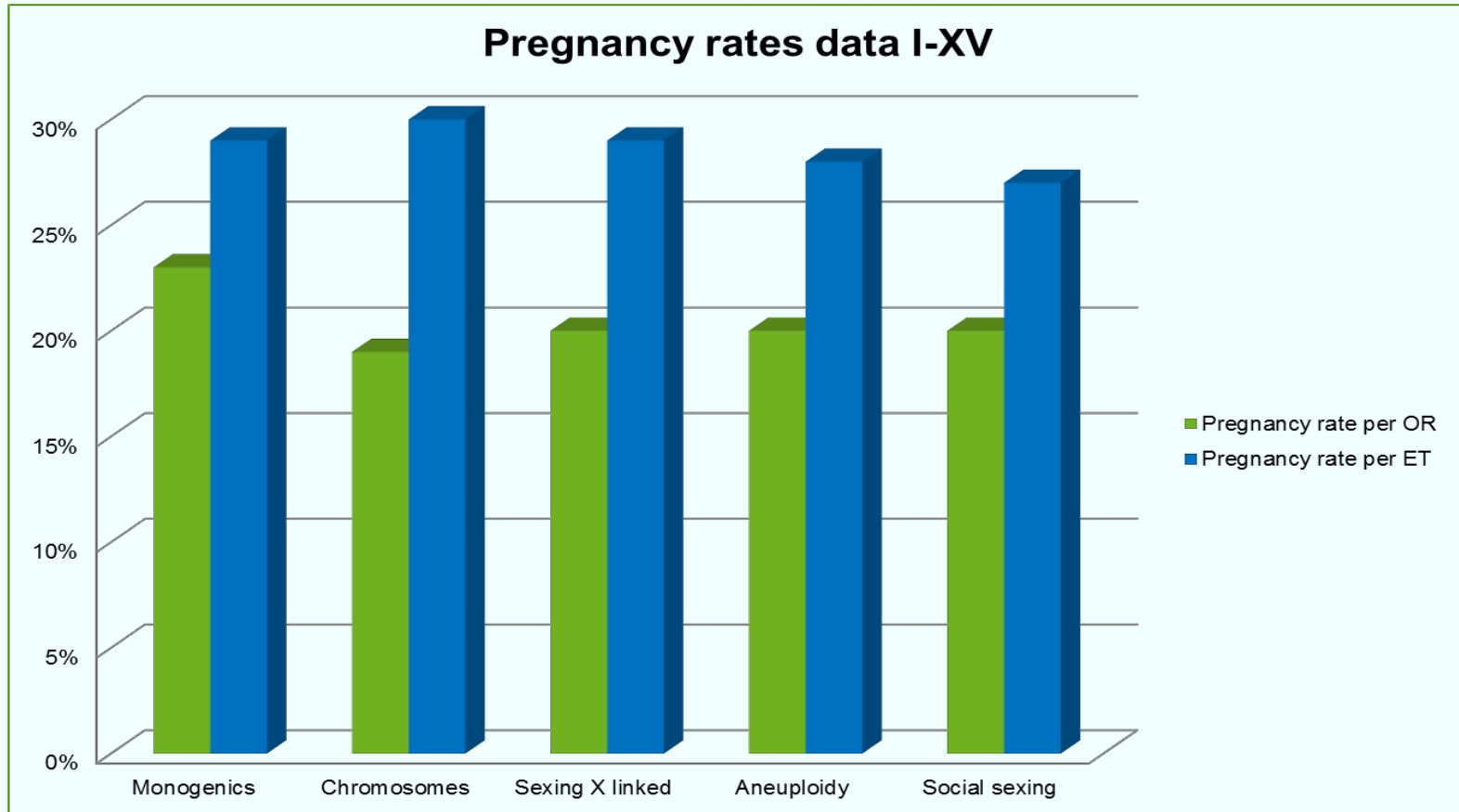
Top 10 PGD diseases in Data XIII

- **Dominant**
 - Huntington's disease 158
 - Myotonic dystrophy 114
 - BRCA 1 or 2 50
- **Recessive**
 - Cystic fibrosis 150
 - Beta Thalassemia 81
 - Spinal muscular atrophy 44
 - Beta Thalassemia + HLA 36
- **X-linked (specific diagnosis)**
 - Fragile X syndrome 124
 - Duchenne muscular dystrophy 42
 - Haemophilia A or B 16

Pregnancy rates

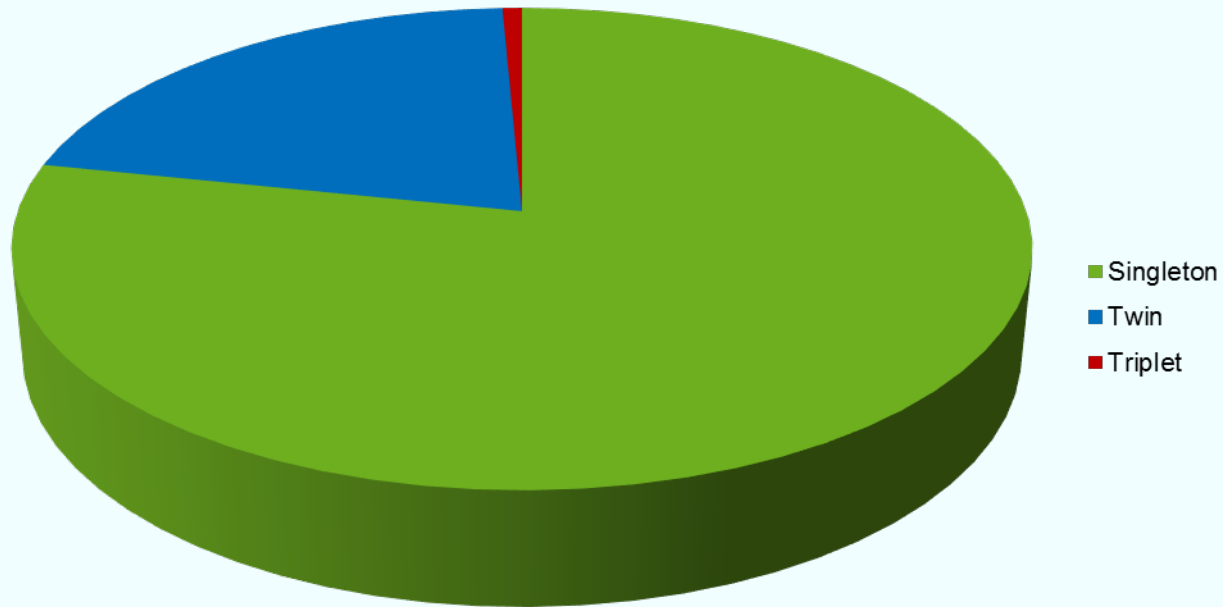


Pregnancy rates data I-XV



Cumulative data on deliveries (I-XV)

9012 deliveries



A typical PGD cycle (data XV)

- **12 - 13 oocytes at OR**
- **6 - 7 oocytes fertilised after ICSI (50-60%)**
- **5 - 6 embryos biopsied (80-90%)**
- **5 - 6 embryos diagnosed ($\approx 95\%$)**
- **2 transferable embryos ($\approx 35\%$)**
- **1 – 2 embryos transferred ($\approx 65\%$)**

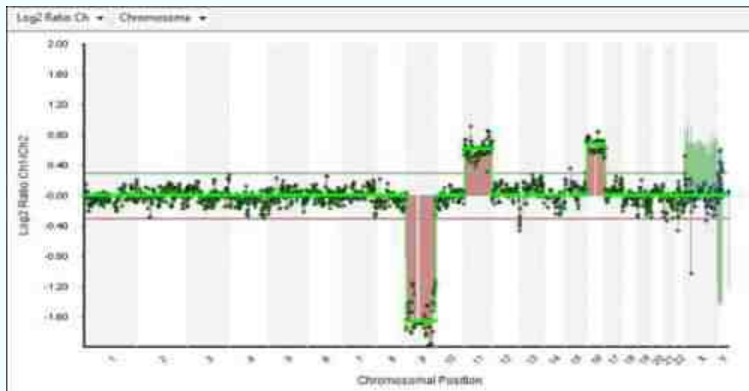
Causes of misdiagnosis

- **Confusion of embryo and cell number**
- **Transfer of the wrong embryo**
- **Maternal or paternal contamination**
- **Allele dropout**
- **Use of incorrect and inappropriate probes or primers**
- **Probe or primer failure and**
- **Chromosomal mosaicism.**

The majority of these causes can be prevented by using robust diagnostic methods within laboratories working to appropriate quality standards.

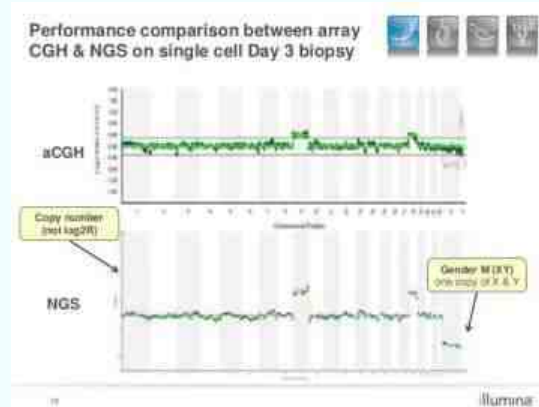
Developments in genome analysis

Array-CGH

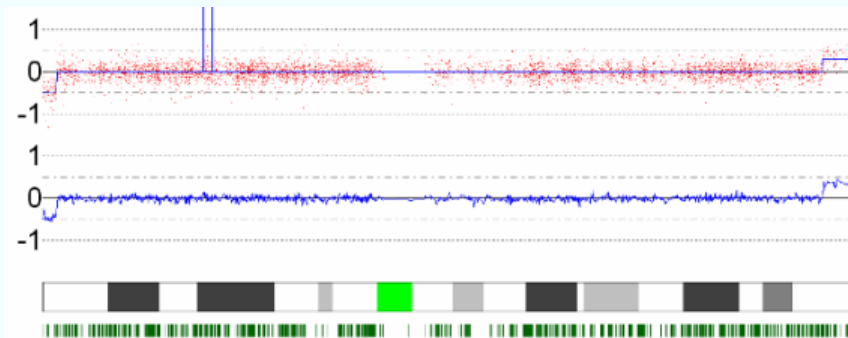


LOW

NGS

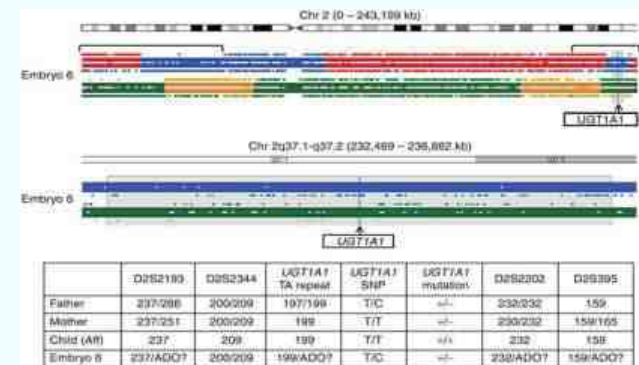


SNP-arrays



HIGH

Karyomapping



Trends in genetic analysis – PGD Consortium survey

**Data collected by
Dr. Martine De Rycke, Brussels**

PGD for chromosomal indications (n=757)

- **FISH** **71%**
- **aCGH** **27%**
- **CGH/PCR/qPCR/SNP/NGS** **2%**

PGS (n=2725)

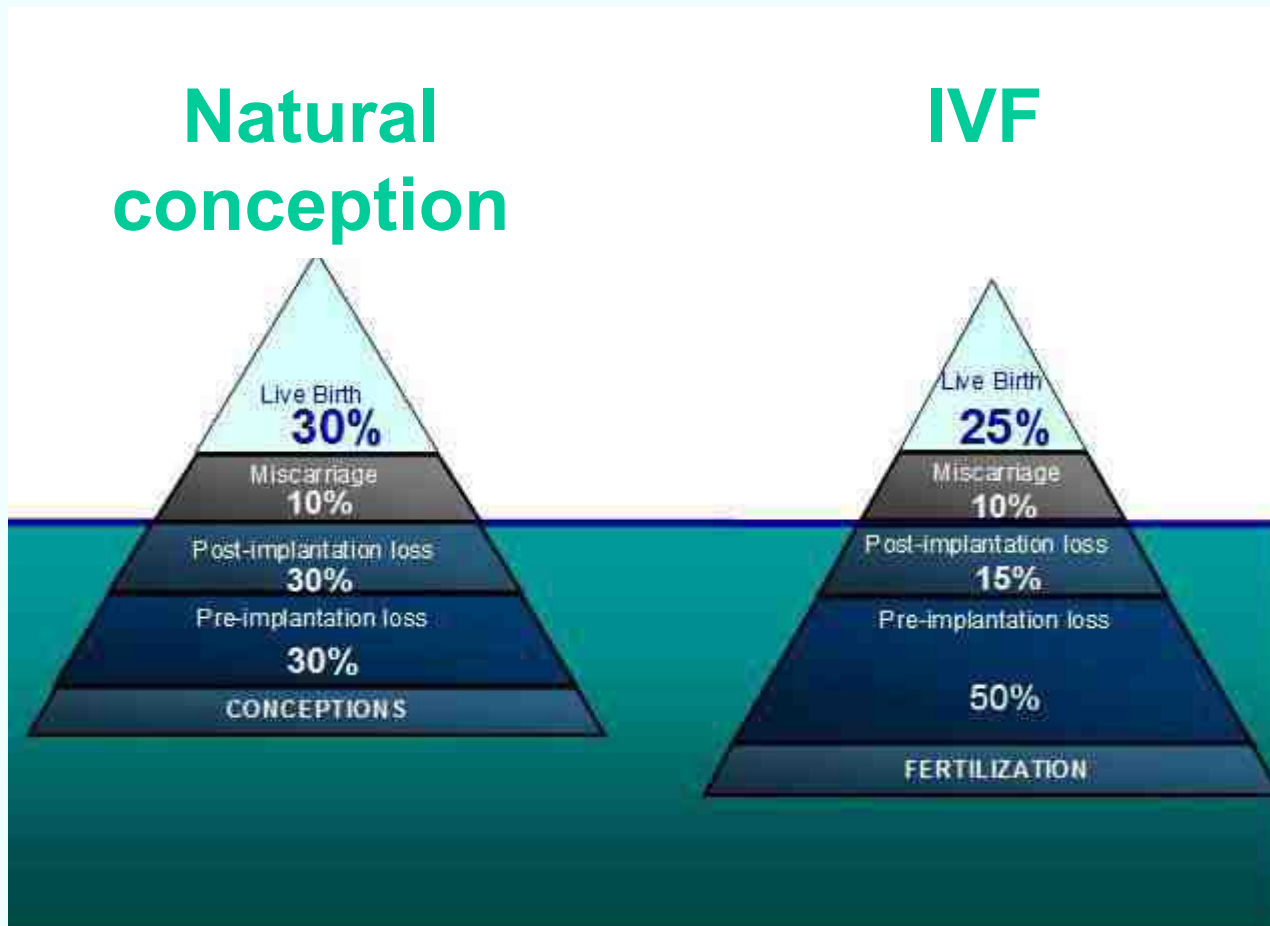
- **FISH** 17%
- **aCGH** 76%
- **SNP** 2%
- **qPCR** 4%
- **NGS** <<1%

PGD for monogenic disease (n=1068)

- **PCR-STR** **85%**
- **WGA-PCR** **15%**
- **NGS** **<<1%**

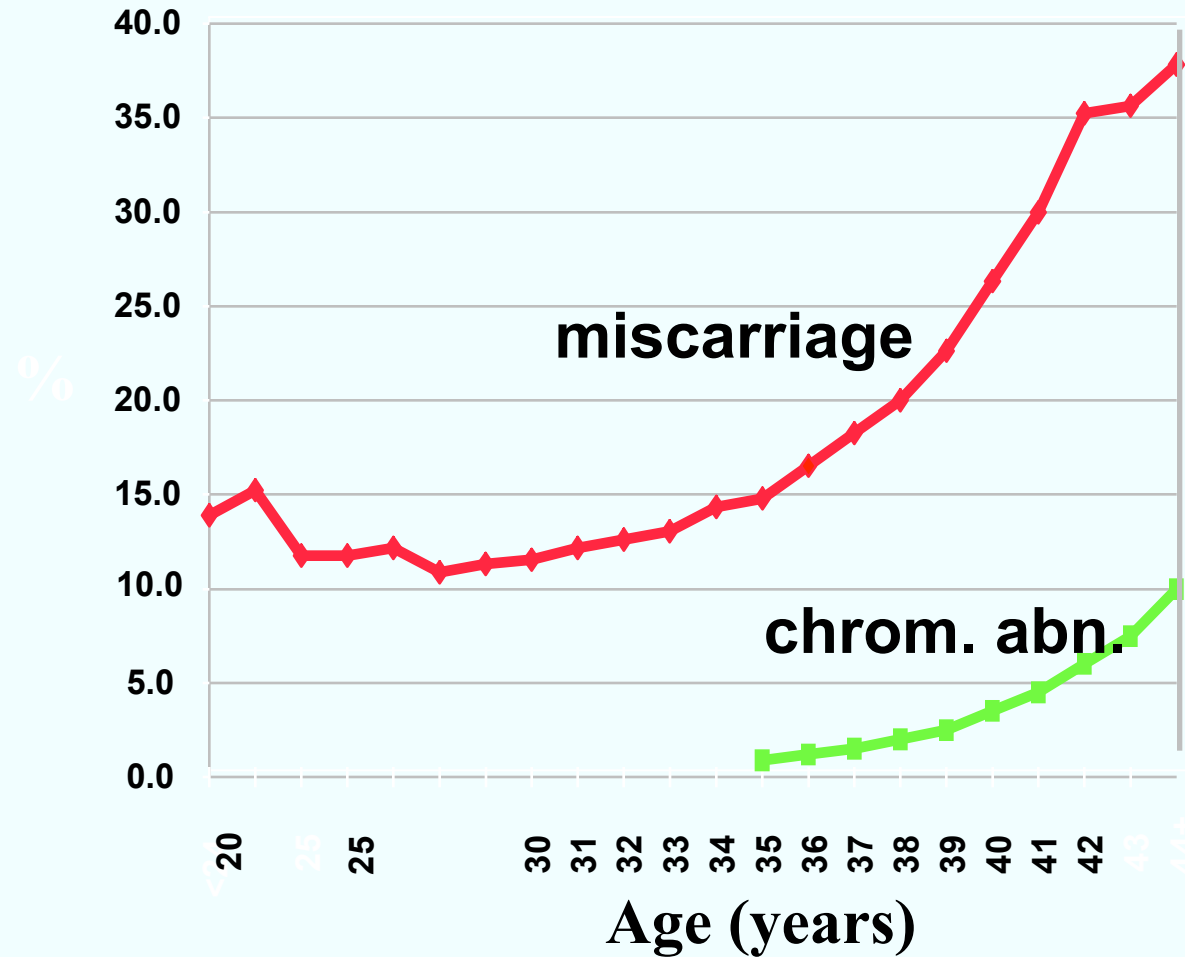
PGS

Why PGS??



Macklon et al., 2002 & Boomsma et al., 2009

Maternal age specific risks



*Gardner &
Sutherland, 1996*

Aneuploidy can cause

- **Preimplantation growth arrest and death**
- **Failed implantation**
- **Implantation of an abnormal conceptus**
- **Early miscarriage**
- **(Induced) late abortion**
- **Delivery of an affected child with a trisomy or monosomy**

PGS 1.0

In 1993 PGS was started on the basis of the hypothesis that selection of euploid oocytes and embryos during assisted reproduction would improve results.

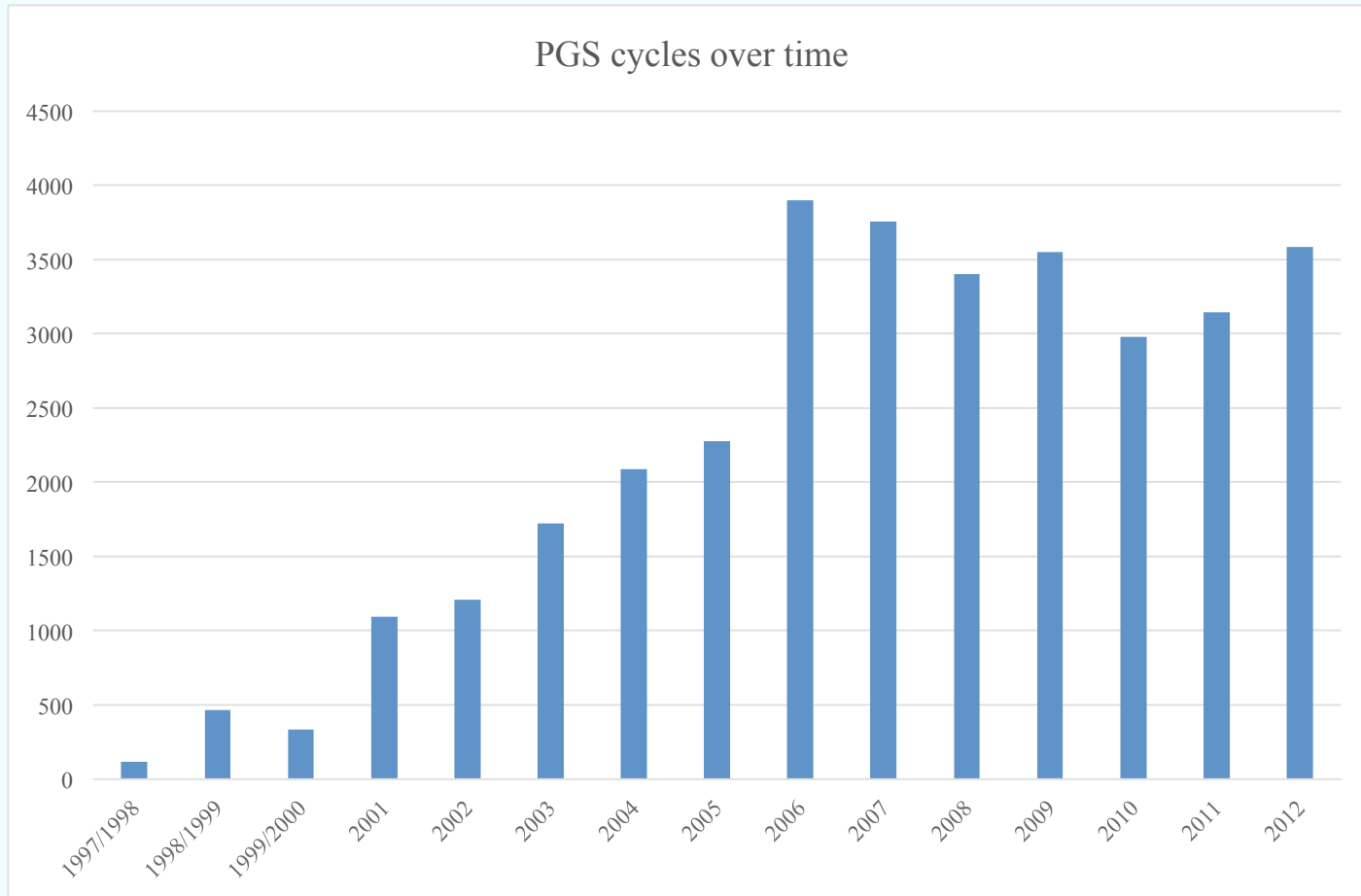
However, after about 15 years it was shown that PGS 1.0 was ineffective in improving IVF pregnancy rates and in reducing miscarriage rates.

PGS 1.0

The main reasons for this were threefold:

- **Damage of the preimplantation embryo during cleavage stage.**
- **Incomplete assessment of chromosomal status using FISH.**
- **Mosaicism of the day-3 embryo due to mitotic errors.**

Number PGS cycles



PGS 2.0

In comparison to PGS 2.0 is characterized by:

- 1. Polar body biopsy or trophectoderm biopsy in place of day-3 embryo biopsy.**
- 2. Aneuploidy assessments of all 24 chromosome pairs instead of FISH of a limited set of chromosomes.**

Polar body biopsy

- **Does not touch the future embryo**
- **More time for analysis**
- **No mosaicism**
- **Compatible with legal situation in some countries**
- **No paternal errors detected**
- **No diagnosis of postzygotic abnormalities**

Trophectoderm biopsy

- **Maternal and paternal errors detected**
- **Does not touch the future embryo**
- **Less embryos need to be analysed**
- **Multiple cells give more material for analysis**
- **Compatible with legal situation in some countries**
- **Trophectoderm might not be representative for the inner cell mass (mosaicism)**
- **Longer in vitro culture: might give more epigenetic effects**



Blastocentesis: a source of DNA for preimplantation genetic testing. Results from a pilot study

Luca Gianaroli, M.D., M. Cristina Magli, M.Sc., Alessandra Pomante, Ph.D., Anna M. Crivello, B.Sc., Giulia Cafueri, B.Sc., Marzia Valerio, B.Sc., and Anna P. Ferraretti, M.D.

Reproductive Medicine Unit, Società Italiana Studi di Medicina della Riproduzione, Bologna, Italy

Patient selection / Indication groups PGS 2.0

- **Maternal age (advanced)**
- **Infertility or PGD patient**
- **Repeated implantation failure**
- **Recurrent miscarriage**
- **Severe male factor infertility**
- **Selection of best embryo for SET**

Aims PGS 2.0

- **To improve time to pregnancy**
- **To assess the prediction value of having no euploid oocytes/embryos in future ART cycles.**
- **To aid in single embryo transfer strategies**

Impact of blastocyst biopsy and comprehensive chromosome screening technology on preimplantation genetic screening: a systematic review of randomized controlled trials.

- **Three trials have been published comparing PGS 2.0 and routine IVF care.**
- **PGS 2.0 is associated with higher clinical implantation rates, and higher ongoing pregnancy rates when the same number of embryos is transferred in both PGS and control groups.**
- **Additionally, PGS 2.0 improves embryo selection in eSET practice, maintaining the same ongoing pregnancy rates between PGS and control groups, while sharply decreasing multiple pregnancy rates.**
- **These results stem from good-prognosis patients undergoing IVF.**
- **Whether these findings can be extrapolated to poor-prognosis patients with decreased ovarian reserve remains to be determined.**

Thank you



joep.geraedts@mumc.nl