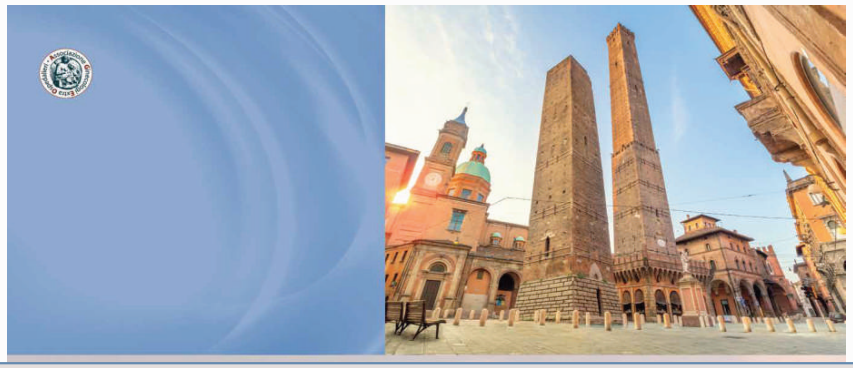


# PMA
# Implicazioni cliniche della diagnosi pre-impianto


*Anna Pia Ferraretti*

*Luca Gianaroli*

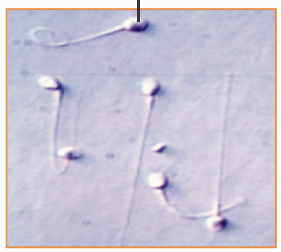
*Carla Tabanelli*

*M.Cristina Magli*

S.I.S.Me.R. Reproductive Mdicine Unit, Bologna, Italy

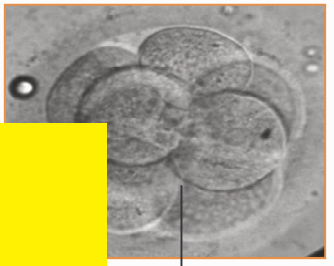
# Percorso convenzionale PMA



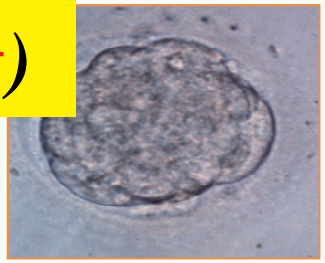






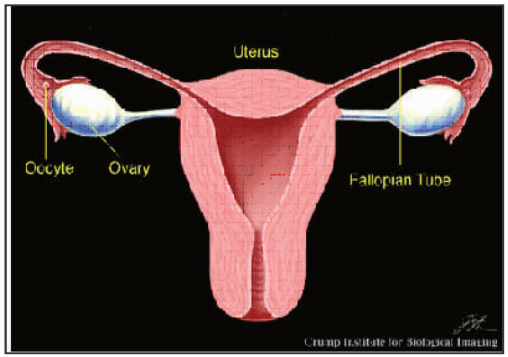






**Indagini per identificare anormalità genetiche prima del trasferimento in utero (dal 1990)**

***PGT : Pre-implantation Genetic Testing)***



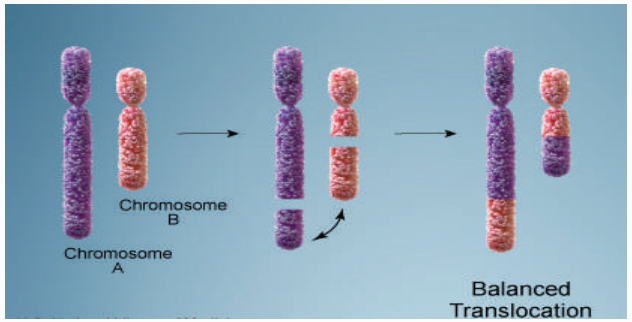
# Diagnosi pre-impianto
# PGT

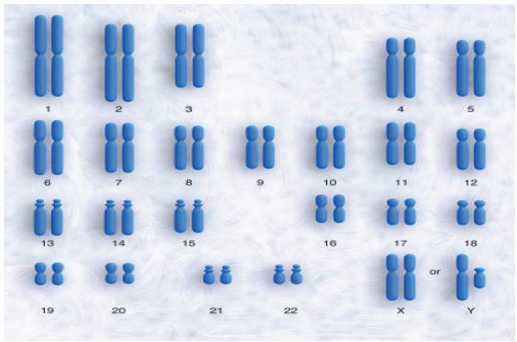
**DIAGNOSI DI MALATTIE MONOGENICHE**

**ANALISI DI RIARRANGIAMENTI STRUTTURALI**

**SCREENING DELLE ANEUPLOIDIE**



**PGT-M** *( PGD)*

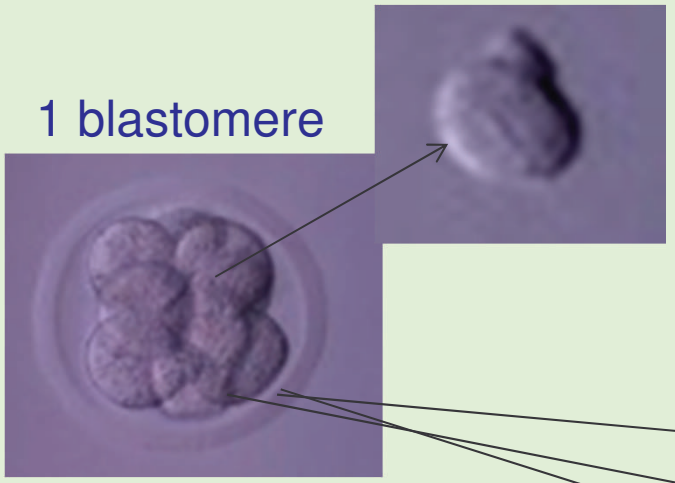
**PGT-SR** *(PGD)*

**PGT-A** *(PGS)*

# EVOLUTION of PGT SOURCE OF DNA

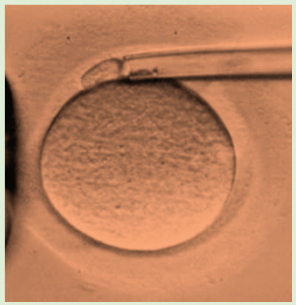
BIOPSY

1 blastomere



Handyside et al., 1990

PB1

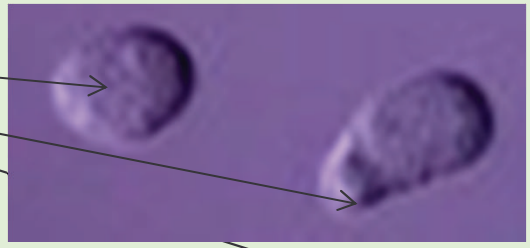


PB1+PB2



Verlinsky et al., 1990; 1995

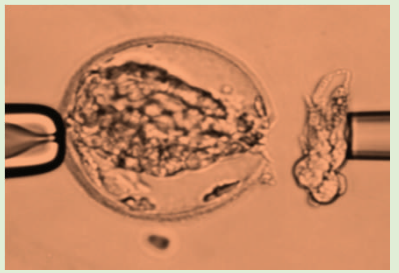
2 blastomeres



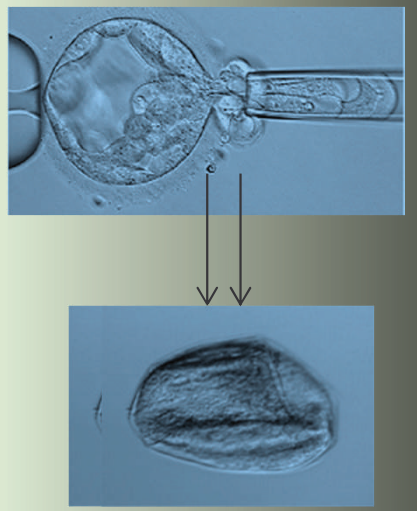
Decreased embryo implantation

De Vos et al., 2009

Trophectoderm cells



McArthur et al., 2005

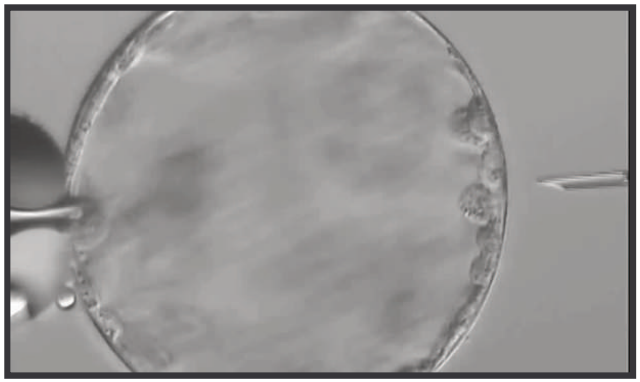


Schoolcraft et al., 2011

1990 1995 2000 2005 2010

# Evolution of the PGT technique : Future

## Collection of blastocoel fluid (Blastocentesis)



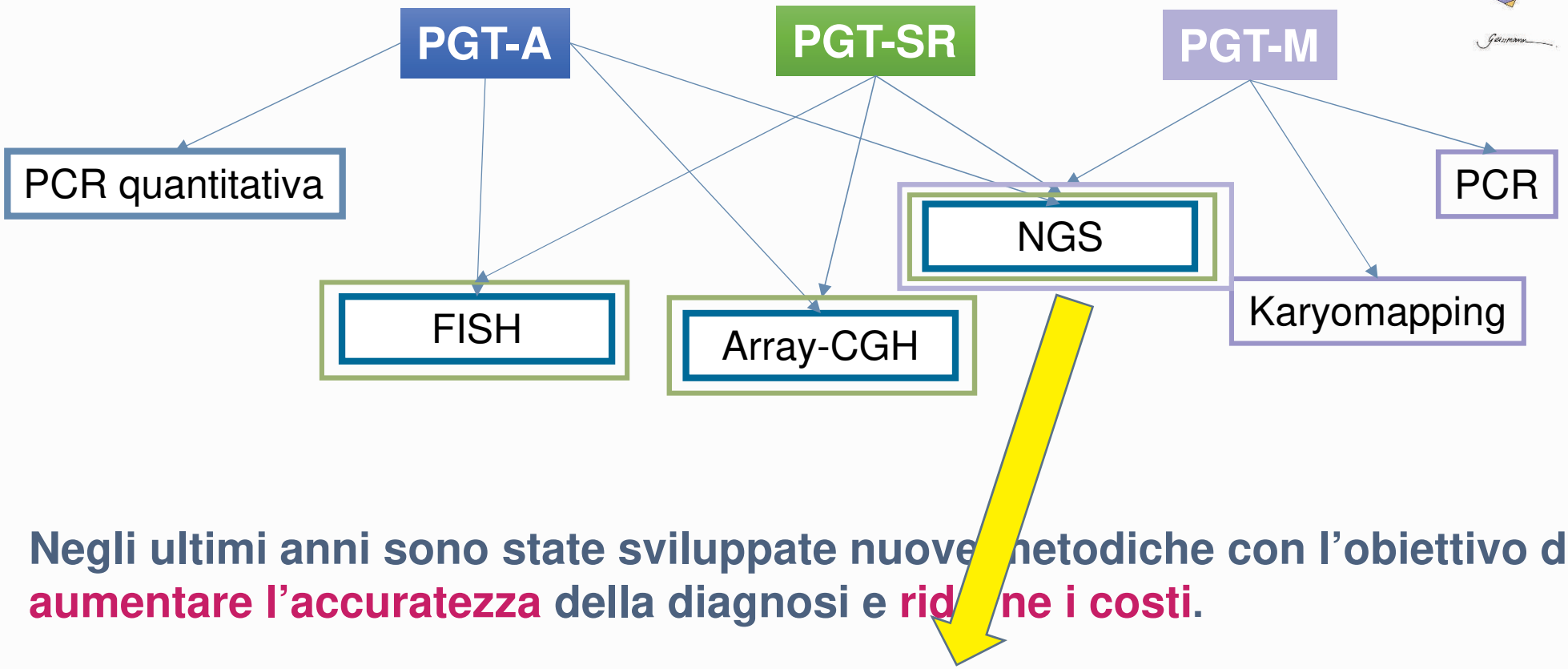
**Blastocentesis: a source of DNA for preimplantation genetic testing. Results from a pilot study**

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

# TECNICHE DI ANALISI MOLECOLARE

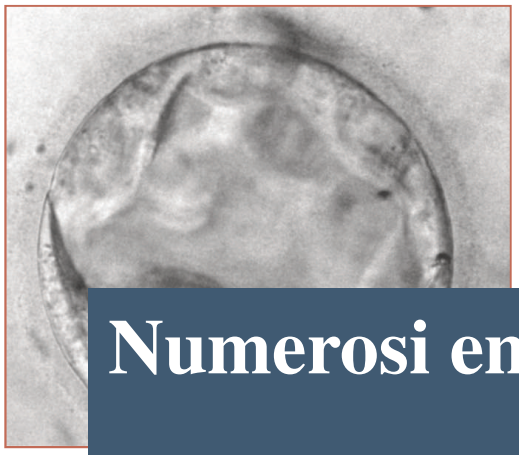





**Negli ultimi anni sono state sviluppate nuove metodiche con l'obiettivo di aumentare l'accuratezza della diagnosi e ridurne i costi.**

**Le tecniche di analisi molecolare di nuova generazione consentono l'analisi simultanea dell'assetto cromosomico e delle patologie monogeniche**

# DNA dalla blastocisti



**Vitrificazione di tutte le blastocisti biopsizzate in attesa di risposta**

**Numerosi embrioni conservati nelle crio-banche**

***- affetti da malattie***
***-aneuploidi***
***- con traslocazioni sbilanciate***

**ti**

**Efficienza della PGT** ( ***possibilità di avere embrioni idonei al trasferimento dopo la indagine)***
**è influenzata da tutte le variabili della PMA**

**Numero di ovociti prelevati** ( ***riserva ovarica***)
**Qualità del liquido seminale**
**Numero di embrioni da analizzare**



**Una rilevante percentuale di coppie non ha embrioni idonei per il trasferimento**

**Efficienza della PGT** ( ***possibilità di avere embrioni idonei al trasferimento dopo la indagine)***
**è influenzata da tutte le variabili della PMA**

**Numero di ovociti prelevati** ( ***riserva ovarica***)
**Qualità del liquido seminale**
**Numero di embrioni da analizzare**

**In caso di un numero ridotto di embrioni , si può procedere con una seconda stimolazione ovarica prima della indagine genetica**
***(accumulo)***

**Efficacia**
***Percentuale di gravidanze a termine dopo PGT***
***Costi-benefici***

# Diagnosi pre-impianto

**Tecnica applicata dal 1990**

**Dati del PGD Consortium (71 centri in tutto il mondo) :**

**Reports pubblicati dal 1997 ( ultimo report del 2012*) ( tot 56.800 cicli)***

**Dati SISMER dal 1996 (*1.540* cicli)**

**EBM ( dati da *studi prospettici randomizzati*, quando applicabili)**

# Safety of babies born after 20 yrs of collection ( PGD Consortium)

**Data from > 6.500 babies born seems do not expose babies to higher risks compared to others ART's procedure**

**Misdiagnosis : 34 *(< 1%)***

***Recommandations :***

**Couples have to be informed about "potential unknown" long-term consequences**

**The follow up of the babies born is still an ethical need**

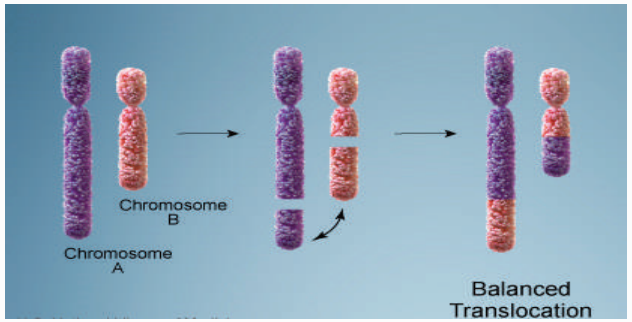
# Diagnosi pre-impianto

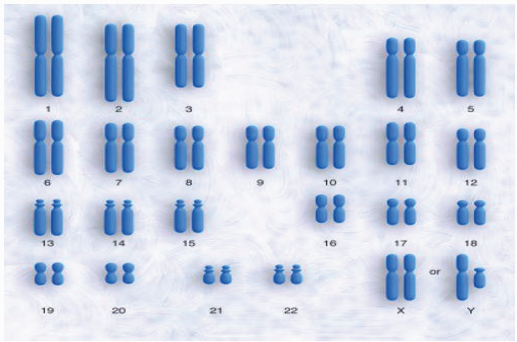
**DIAGNOSI DI MALATTIE MONOGENICHE**

**ANALISI DI RIARRANGIAMENTI STRUTTURALI**

**SCREENING DELLE ANEUPLOIDIE**



**PGT-M** *( PGD)*

**PGT-SR**

**PGT-A** *(PGS)*

# PGT-M

**Coppie portatrici di malattie genetiche ( fertili o infertili)**



**Fase preliminare**

- ***consulenza genetica per malattia specifica***
- ***consulenza PMA/PGD***
- ***fase pre-clinica***

**Obiettivo clinico**

**"Evitare l'impianto di embrioni malati ed evitare alla madre la decisione di una interruzione terapeutica della gravidanza**

**Alternativa alla diagnosi pre-natale?**

# PGT-M CLINICAL APPLICATION

**PGT-M can be carried out for any disorder in which the disease causing gene has been mapped.**

| Autosomal Recessive | Autosomal Dominant | X-linked | Triplet repeats expansion |
|---|---|---|---|
| • Cystic Fibrosis<br>• Beta Thalassemia<br>• Sickle Cell Anemia<br>• Spinal Muscular Atrophy (SMA)<br>• Adrogenital Syndrome (SAG)<br>• Congenital Adrenal Hyperplasia (CAH)<br>• Fanconi Anemia<br>• MCAD<br>• Tay Sachs disease<br>• Alpha-1-Antutripsin<br>• Epidermolysis Bull. | • Retinoblastoma<br>• Neurofibromatosis<br>• Li Fraumeni syndrome<br>• Familial Adenomatous polyposis<br>• Acondro-Hypocrondroplasia<br>• Multiple Endocrine Neoplasy 2<br>• Marfan Syndrome<br>• Osteogenesis Imperfecta<br>• Tuberous Sclerosis<br>• Retinitis Pigmentosa | • Duchenne/ Becker Muscular Dystrophy<br>• Hemophilia A-B | • Fragile X<br>• Myotonic Dystrophy<br>• Huntington |

# Risultati - Dati del PGD Consortium (dal 1997 al 2012)

| | |
|---|---|
| Cicli per PGT-M | 12.712 |
| Coppie fertili | 88% |
| Embrioni con diagnosi | 69.400 |
| Embrioni non affetti dalla malattia e trasferibili | 29784 (43%) |
| Cicli trasferiti | 9.944 |
| Gravidanze con BCF(% per ET) | 3.036 (31%) |
| Miscarriage rate | 10% |
| Errate diagnosi | 15 (<1%) |

# Risultati - Dati del PGD Consortium (dal 1997 al 2012)

| | |
|---|---|
| Cicli per PGT-M | 12.712 |
| Coppie fertili | 88% |
| Embrioni con diagnosi | 69.400 |
| Embrioni non affetti dalla malattia e trasferibili | 29.784 (43%) |
| Cicli trasferiti | 9.944 (78%) |
| Gravidanze con BCF/ET | 3.036 (31%) |
| Miscarriage rate | 10% |
| Errate diagnosi | 15 (<1%) |

# Risultati - Dati del PGD Consortium (dal 1997 al 2012)

| | |
|---|---|
| Cicli per PGT-M | 12.712 |
| Coppie fertili | 88% |
| Embrioni con diagnosi | 69.400 |
| Embrioni non affetti dalla malattia e trasferibili | 29784 (43%) |
| Cicli trasferiti | 9.944 |
| Gravidanze con BCF per singolo ET | 3.036 (31%) |
| Miscarriage rate | 10% |
| Errate diagnosi | 15 (<1%) |

# 202 coppie afferenti al SISMER per PGT-M

**Reproductive history**

- **16 infertile**
- **81 not proven fertility**
- **105 fertile** → **78 TOP affected fetus**; **57 affected children born** → **12 deceased children**

1 dead at the age of 2 years - Wiskott-Aldrich
1 dead at the age of 3 years - SSCP
1 dead at the age of 14 months – spinal-muscolar atrophy
1 dead 6 hrs after birth –type II glicogenosis
1 dead at the age of 7 months - spinal-muscolar atrophy
1 dead 5 hrs after birth - Potter 1
1 dead a the age of 6 years - Wiskott-Aldrich
1 dead after 12 hrs - 21 hydroxylase deficiency
1 dead at the age of 2 yrs – Menkes
1 dead at the age of 2 yrs – type II glycogenosis
1 dead at the age of 9 months – spinal-musclar atrophy

# Diagnosi pre-impianto per malattie genetiche ( S.I.S.Me.R)

| | 1996-2004 | 2005-2008 Legge 40 | 2009-2017 | TOTAL |
|---|---|---|---|---|
| No. patients | 28 | 0 | 74 | 104 |
| No. Cycles | 45 | | 92 ( 129 PU) | 137 (1.3 per patient) |
| Female age | 34.5 ± 3.3 | | 35.4 ± 3.7 | 35.1 ± 3.6 |
| No. oocytes | 569 | | 1191 | 1760 |
| (M±S) | (12.6 ± 6.2) | | (12.9 ± 5.7) | (12.8 ±5.8) |

# Patologie nelle 104 pazienti trattate

| Pathology | patients | Pathology | patients |
|---|---|---|---|
| CF | 32* | Aicardi Goutieres | 1 |
| Thalassemia | 23 | ATRX | 1 |
| Myotonic dystrophy | 5 | Citrullinemia | 1 |
| DMD | 5 | Fascioscapulohumeral dystrophy | 1 |
| Huntington | 5 | G6PD deficiency | 1 |
| Haemophilia | 4 | Holt-Oram | 1 |
| Neurofibromatosis 1 | 2 | LeschNyhan | 1 |
| Spastic paraparesis | 2 | Methylmalonic aciduria | 1 |
| Fragile X | 4 | Muscular dystrophy merosin deficient | 1 |
| | | Mucopolisacc | 1 |
| | | Optic atrophy | 1 |
| | | Paramyotonia congenita | 1 |
| | | Polycystic syndrome | 1 |
| | | Pompe syndrome | 1 |
| | | Primary dystonia | 1 |
| | | Retinitis pigmentosa | 1 |
| | | Retinoblastoma | 1 |
| | | SCIDX1 | 1 |
| | | Sclerosis tuberous | 1 |
| | | Simpson-Golabi-Behmel | 1 |
| | | Von Hippel-Lindau | 1 |
| | | Osteogenis Imperfecta | 1 |

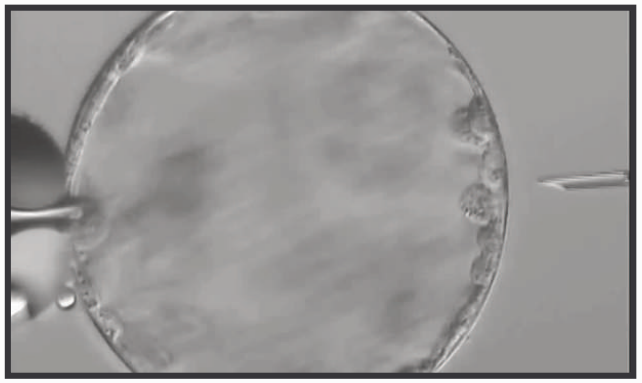
# Diagnosi pre-impianto per malattie genetiche ( S.I.S.Me.R)

| 1997 – 2017* | 1996-2005 | 2009-2017* | TOTAL |
|---|---|---|---|
| No. patients | 28 | 74 | 104 |
| No.cycles | 45 | 92 | 137 (1.3) |
| No. normal // carrier | 163/235=69% | 269 / 450=59.7% | 432/685=63% |
| No. cycles transferred ( fresh + frozen) | 40 | 130 | 170 |
| No. clinical pregnancies (% per ET) | 12 (30%) | 43 (33.0%) | 55 (32.3%) |
| Abortions | 3 | 7 | 10 |
| Term pregnancies | 9 | 36 | 45 |
| LBR per patient | 32 % | 49% | 43% |

# Evolution of the PGT-M technique : Future

**Next Generation Sequencing (NGS)**



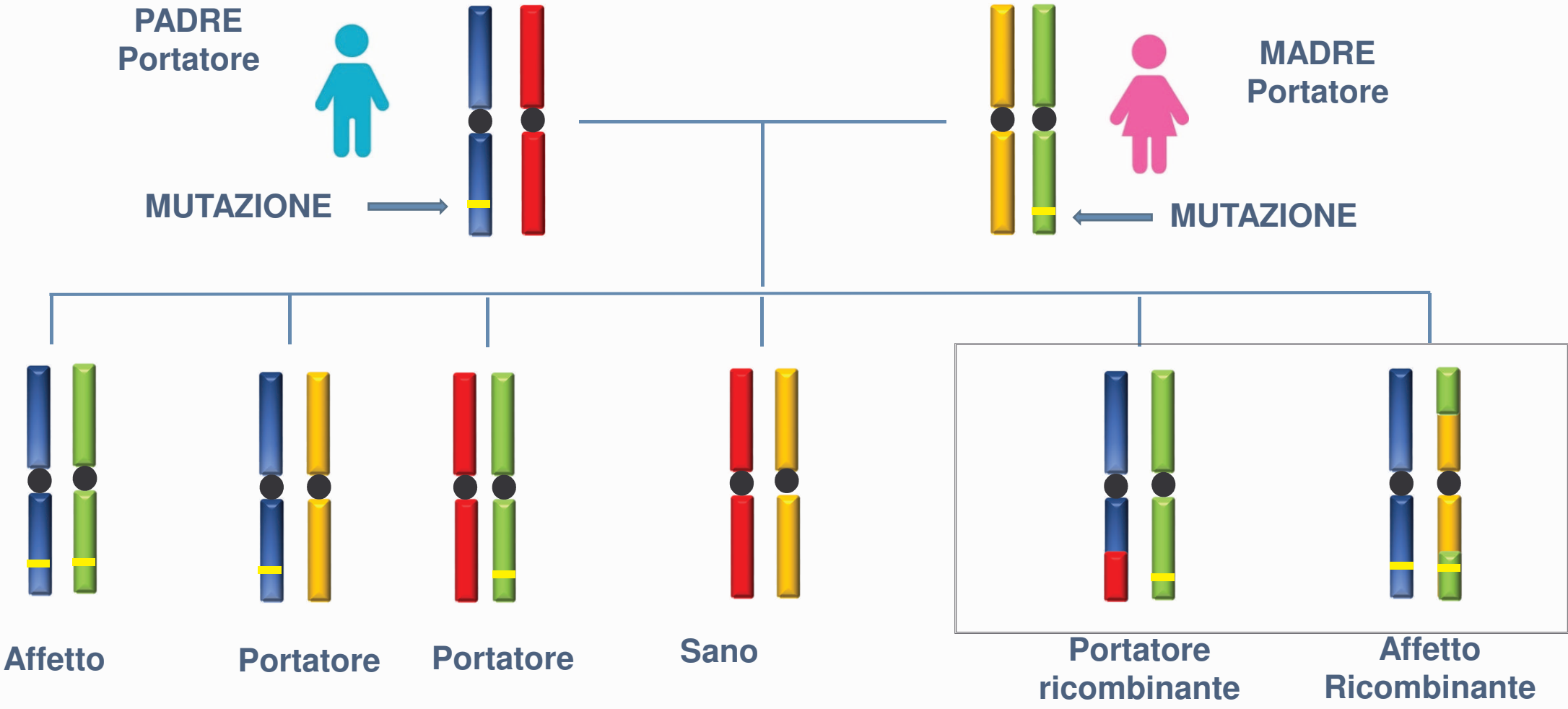


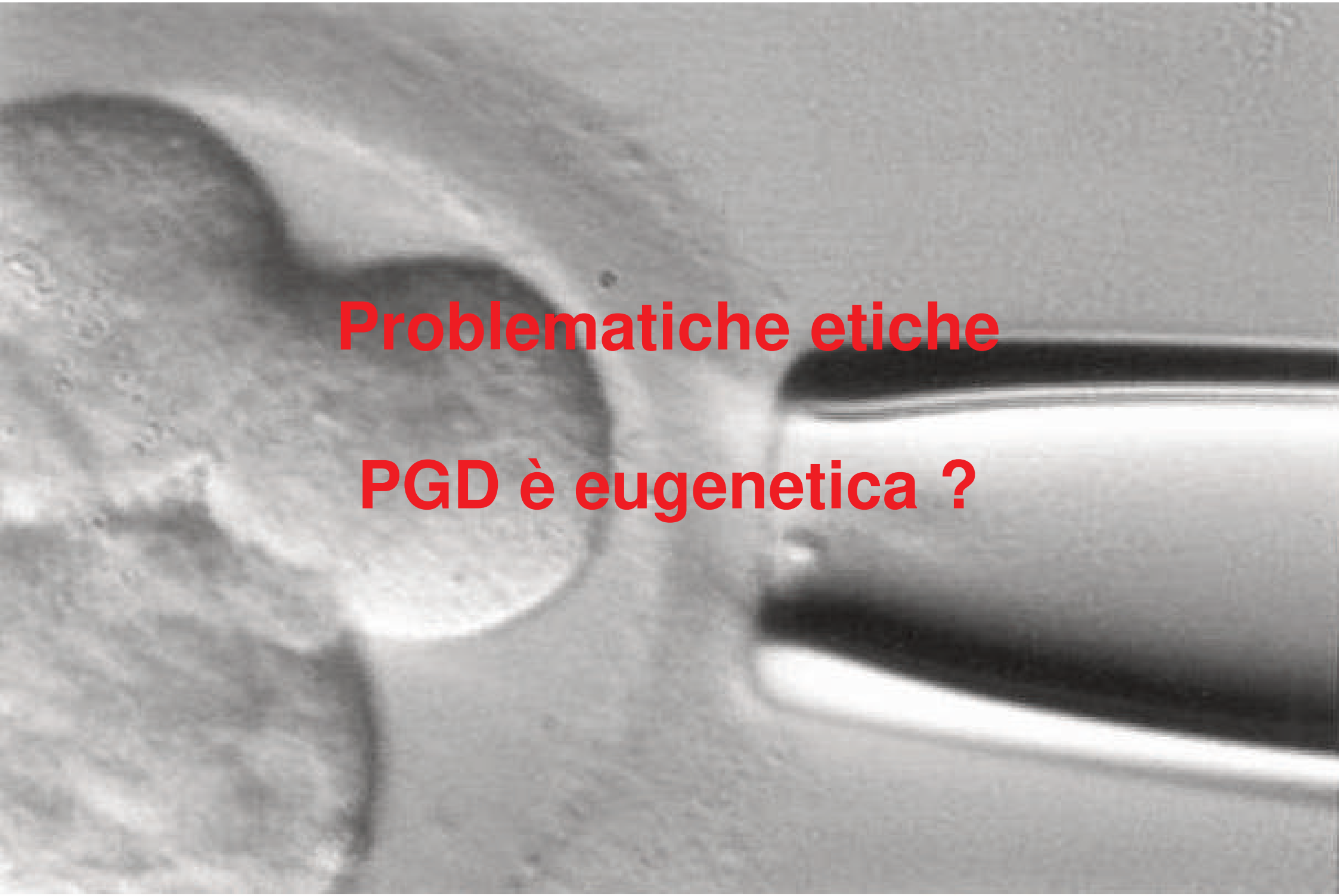
***Simultaneous testing of - genetic defect and chromosome anomalies of embryos at the same time.***

**Goldman et al 2016 :**
***~ 40% of unaffected embryos were aneuploid ( age 32.4 yrs)***

# KARYOMAPPING Set up semplificato

**Permette di individuare l'origine (materna o paterna) di ogni cromosoma**





# Problematiche etiche

# PGD è eugenetica ?

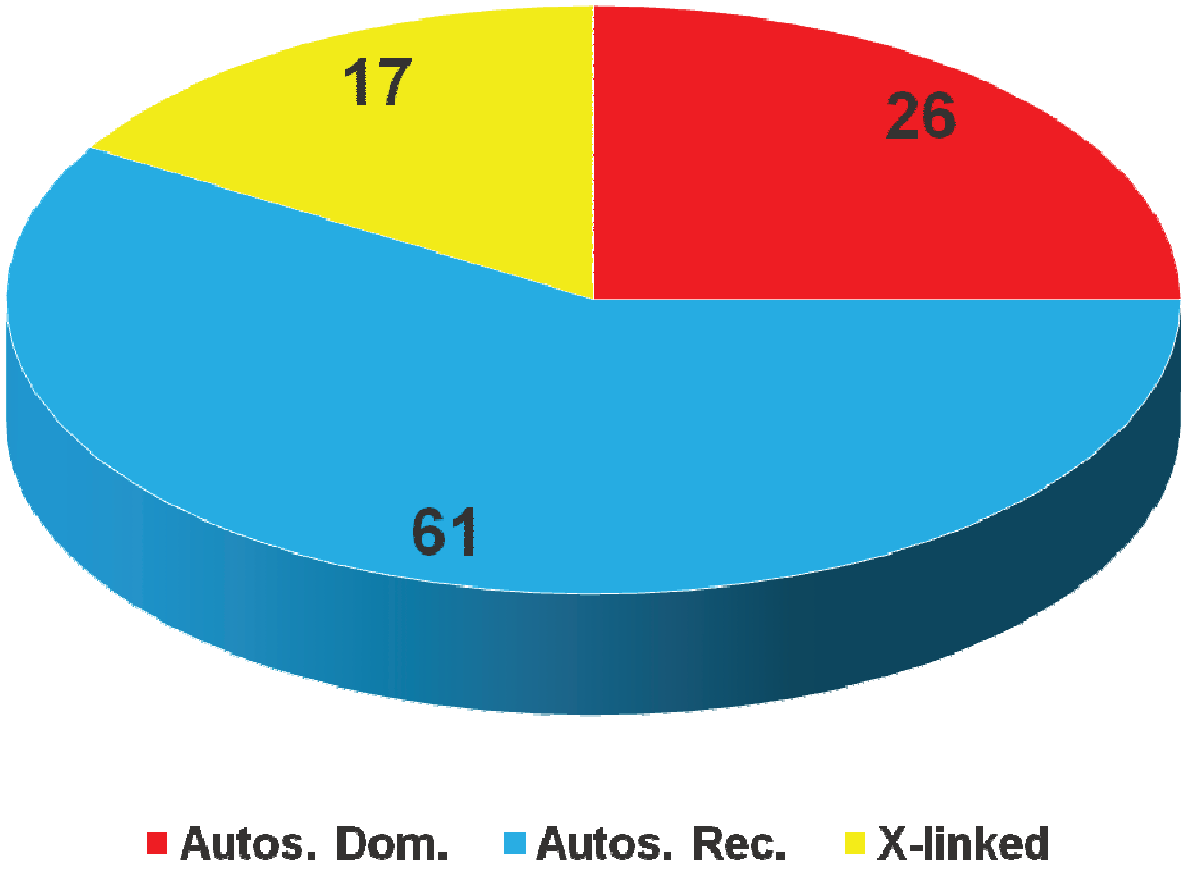
# ESHRE - ASRM - OMS

- **La PGD ( PGT-M) è una *tecnica consolidata ed efficace* nel ridurre il rischio di trasmissione di malattie genetiche alla prole come alternativa alla diagnosi pre-natale. Nel rispetto dei diritti fondamentali dei cittadini ( diritto alla libera scelta e diritto alla salute) *deve essere resa disponibile* a chi lo desidera.**

- **Per le sue importanti implicazioni medico-sociali e le controversie etiche, deve essere eseguita in *centri specializzati* ( ed autorizzati) e deve essere *regolamentata* per controllarne lo sviluppo scientifico e le applicazioni cliniche come espressione del massimo consenso pubblico raggiungibile**

- ***L'uso inappropriato* della tecnica deve essere disincentivato per evitare che una tecnica utile a finalità mediche diventi "impopolare"**

# Tipo trasmissione patologie nelle 104 pazienti trattate



# Diagnosi pre-impianto per malattie genetiche

**Dati del PGD Consortium : raccolti e pubblicati dal 1997 ( ultimo report dati del 2012*),* *12.712 cicli***

**Dati SISMER : dal 1996, *137 cicli in 104 pazienti***

**EBM : studi prospettici randomizzati non applicabili**

# Diagnosi pre-impianto

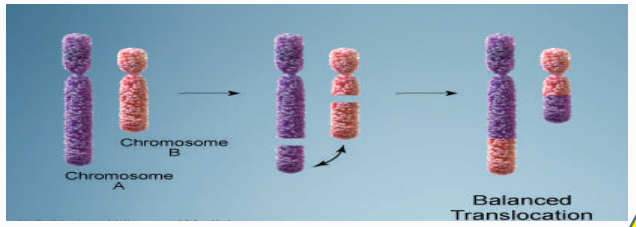
***Coppie con traslocazioni***

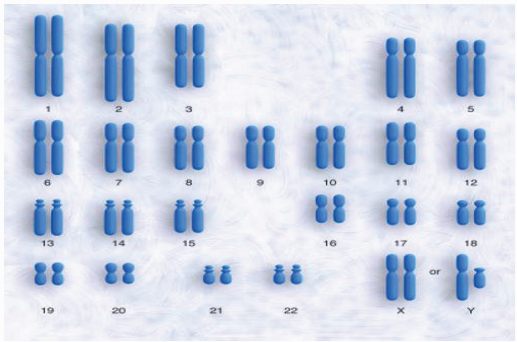
**DIAGNOSI DI MALATTIE MONOGENICHE**

**ANALISI DI RIARRANGIAMENTI STRUTTURALI (PGT-SR)**

**SCREENING DELLE ANEUPLOIDIE**



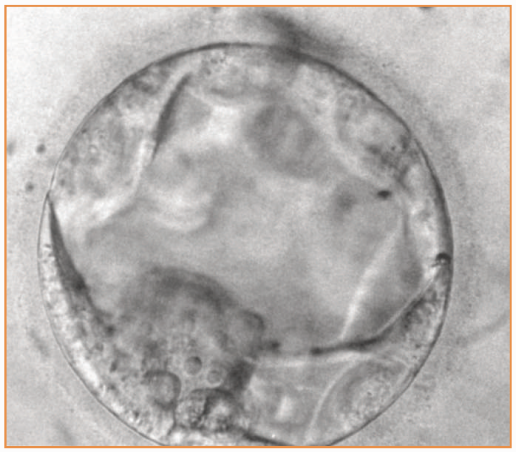



**PGT-M** *( PGD)*

**PGT-SR** *(PGD)*

**PGT-A** *(PGS)*

# PGT-SR +A



**Normale per la traslocazione**

**Alterato per aneuploidie**

**“Interchromosomal effect”** :

***più frequente per le traslocazioni Robersoniane rispetto le Reciproche e se il portatore della traslocazione è il partner maschile***

**Gianaroli et al. Possible interchromosomal effect in embryos generated by gemete from translocation carriers. Hum Reprod 2002;17:3201-3207.**

# Diagnosi pre-impianto per traslocazioni

**Dati del PGD Consortium : raccolti e pubblicati dal 1997 ( ultimo report dati del 2012*),* *8.921 cicli***

**Dati SISMER : dal 1996**

**EBM : studi prospettici randomizzati difficilmente applicabili**

# STORIA CLINICA DELLE COPPIE CON TRASLOCAZIONE

**311 COPPIE**
(1997-2017)

**205**
**TRASLOCAZIONE RECIPROCA**

**111 coppie gravidanza spontanea (n=270)**

**106**
**TRASLOCAZIONE ROBERTSONIANA**

**41 coppie gravidanza spontanea (n=88)**

**152 coppie hanno eseguito 213 cicli per PGT-SR**



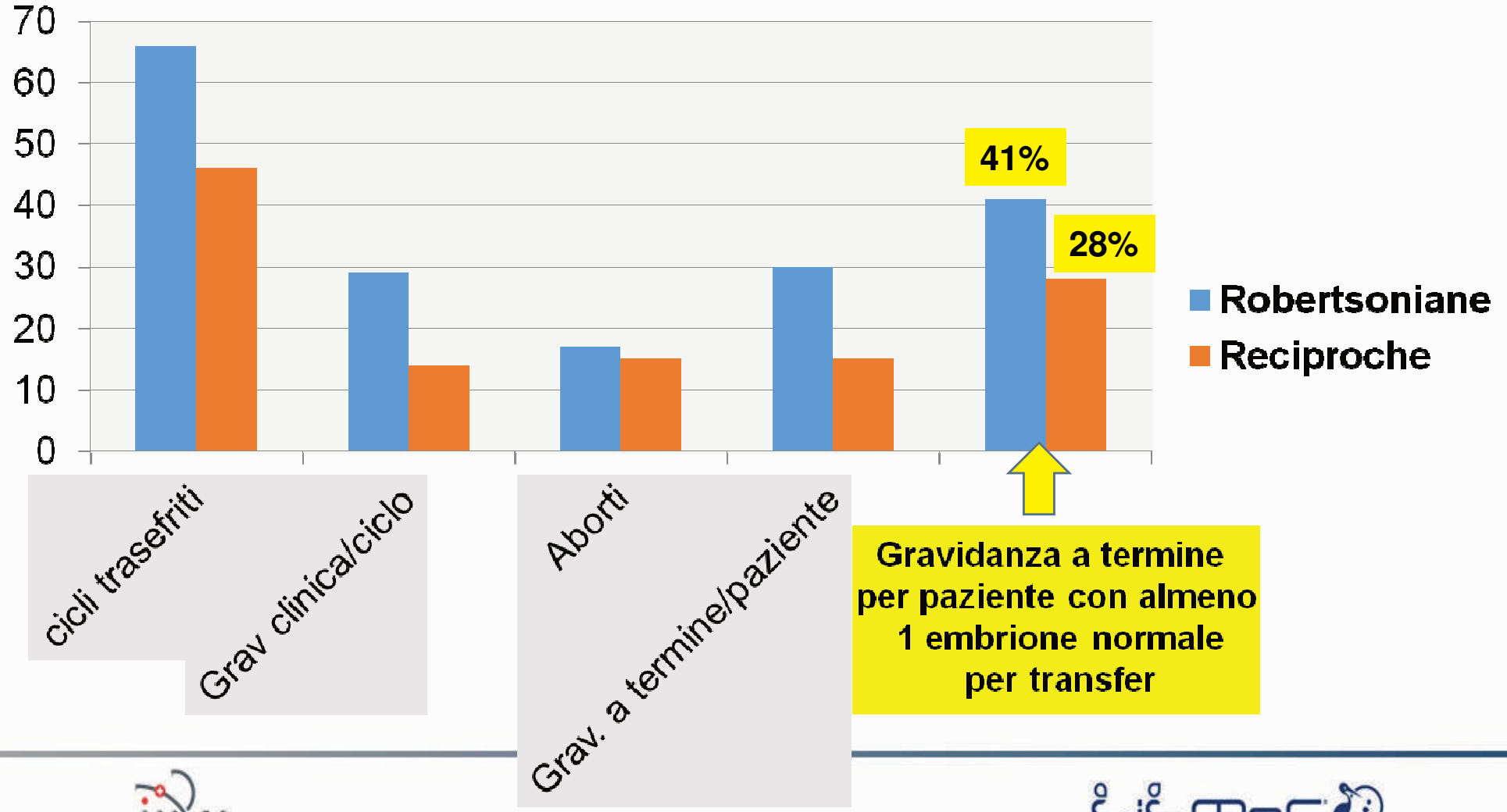

**5 normali**
**6 portatori**
**0.4% SANI**
9 gravi malformazioni

**6 normali**
**2 portatori**
**9% SANI**
2 gravi malformazioni

# Diagnosi pre-impianto per Traslocazioni
## *Stato cromosomico degli embrioni*

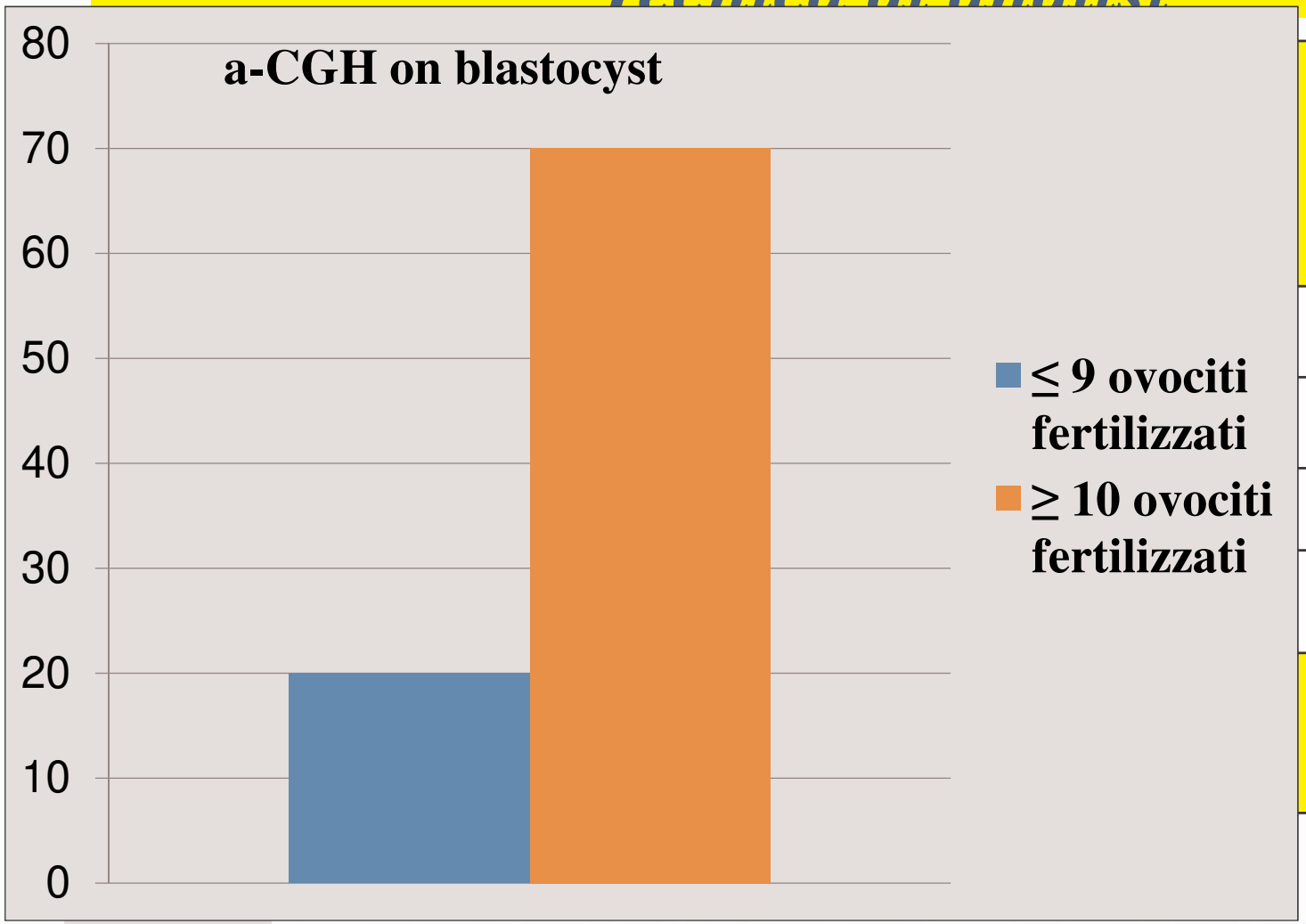
| 1996 – 2017<br>FISH and array-CGH | TRANSLOCATIONS | |
|---|---|---|
| | **Robertsonian** | **Reciprocal** |
| Cycles analysis /patients | 96/68 | 117/84 |
| Female age | 35.8 ± 4.5 | 35.8 ± 4.6 |
| Oocytes collected | 946 | 1287 |
| Mean/PU | 9.8 ± 5 | 11 ± 5.1 |
| Analysed | 442 | 627 |
| Normal/balanced + euploid (%) | 118 (26.7%) | 90 (14.3%) |

# Diagnosi pre-impianto per Traslocazioni ( S.I.S.Me.R)- *Risultati*



# Diagnosi pre-impianto per Traslocazioni ( S.I.S.Me.R)

## *Tecnica di analisi*




| The present *( a-CGH on blastocysts)* |
|---|
| 50 / 39 |
| 36 ± 4.5 |
| 25 (48) |
| 30 |
| 14/24 (58.3%) |

# Risultati - Dati del PGD Consortium (dal 1997 al 2012)

| Cicli | 8.921 |
|---|---|
| Embrioni con diagnosi | 49.475 |
| Embrioni trasferibili | 12.767 (26%) |
| Cicli trasferiti | 5.646 (63%) |
| Gravidanze con BCF ( % per ET) | 1.605 ( 28%) |
| Miscarriage rate | 12% |

# Diagnosi pre-impianto per traslocazioni

**Dati del PGD Consortium : raccolti e pubblicati dal 1997 ( ultimo report dati del 2012*),* *8.921 cicli***

**Dati SISMER : dal 1996**

**EBM : studi prospettici randomizzati difficilmente applicabili**

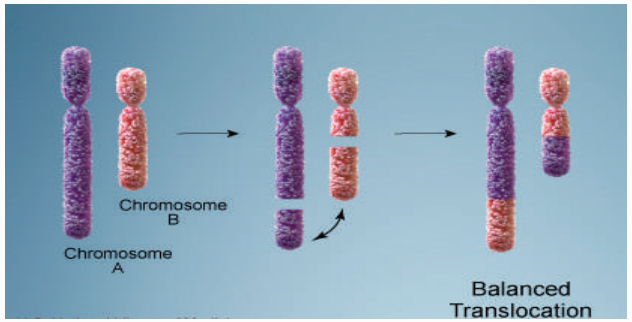
# Diagnosi pre-impianto

**DIAGNOSI DI MALATTIE MONOGENICHE**



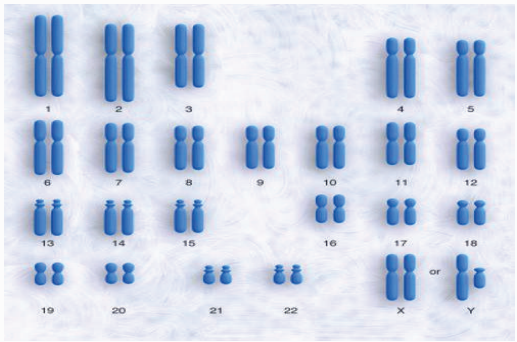

**PGT-M** *( PGD)*

**ANALISI DI RIARRANGIAMENTI STRUTTURALI**




**PGT-SR**

**SCREENING DELLE ANEUPLOIDIE**



**PGT-A** *(PGS)*

# Diagnosi pre-impianto

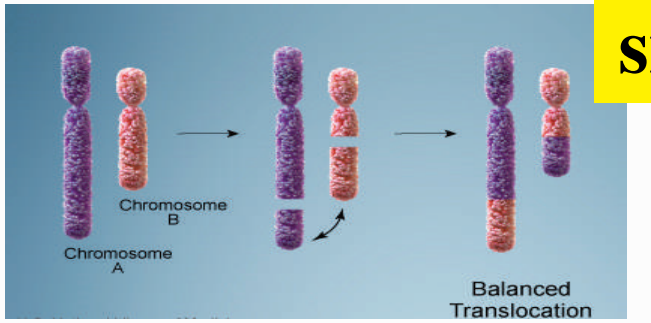
**DIAGNOSI DI MALATTIE MONOGENICHE**

**ANALISI DI RIARRANGIAMENTI STRUTTURALI**

**SCREENING DELLE ANEUPLOIDIE**

**In coppie infertili che si sottopongono a PMA**



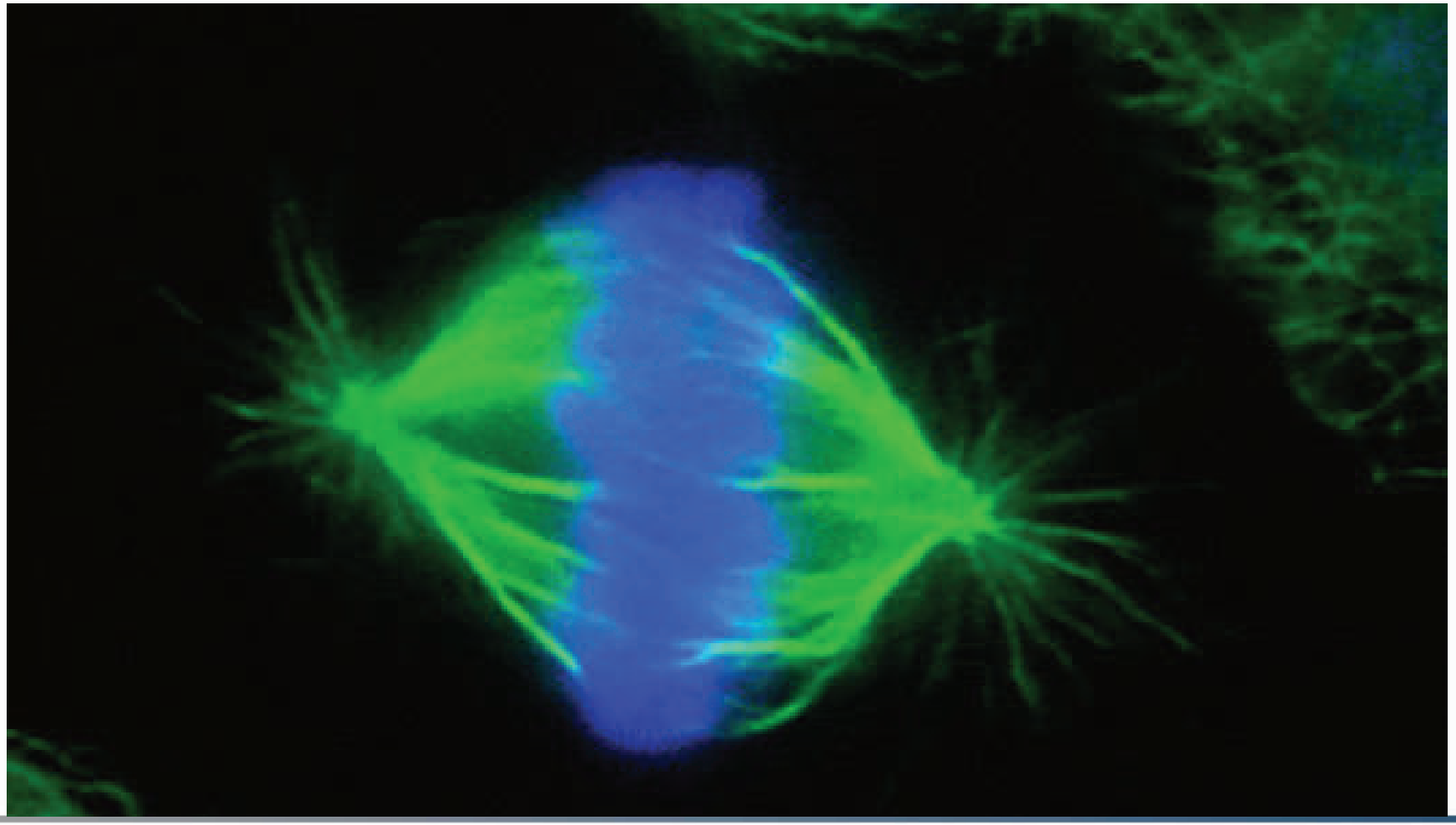



**PGT-M** *( PGD)*

**PGT-SR**

**PGT-A** *(PGS)*

# TO ERR (MEIOTICALLY) IS HUMAN



**IVF population includes couples at higher risk to produce aneuploid embryos**

***Advanced maternal age ( AMA)***

***Recurrent idiopathic miscarriage (RM)***

***Recurrent implantation failure (RIF)***

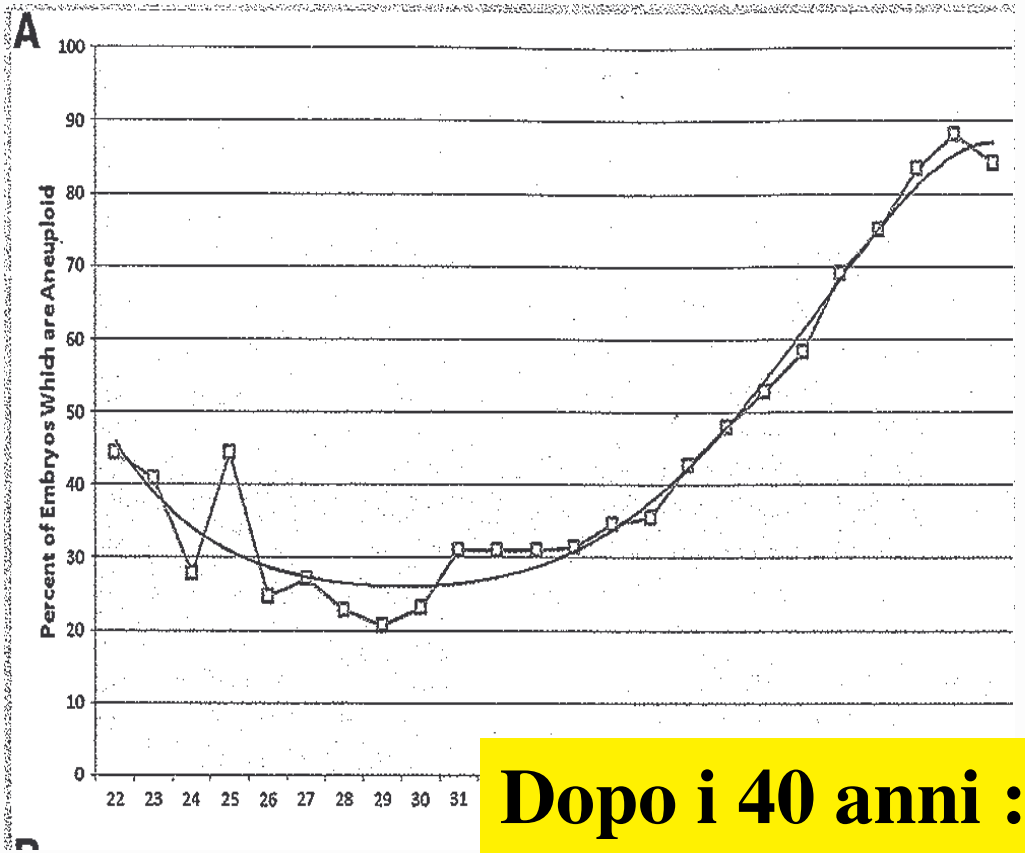
**Stato cromosomico degli ovociti/embrioni di questa popolazione**

# Incidenza delle aneuplidie nelle "poor prognosis couples"

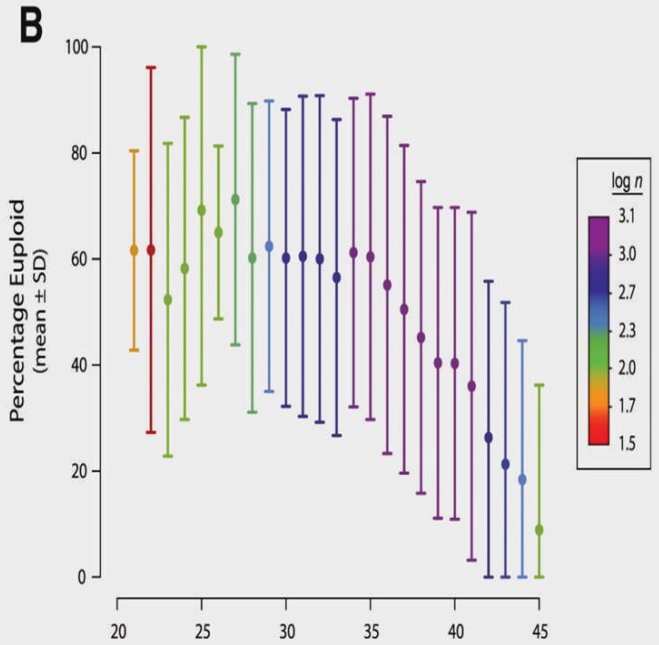
*Dati del PGD Consortium*
*(dal 1997 al 2012)*

| | |
|---|---|
| **Cicli PGT-A** | **32.832** |
| **Embrioni con diagnosi** | **169.268** |
| **Embrioni aneuploidi** | **117.089 (69%)** |

**15,169 consecutive biopsies on blastocysts**
**Aneuploid rate**




**46,439 (day 3 and day 5) embryos analyzed by aCGH**
**Euploid rate**

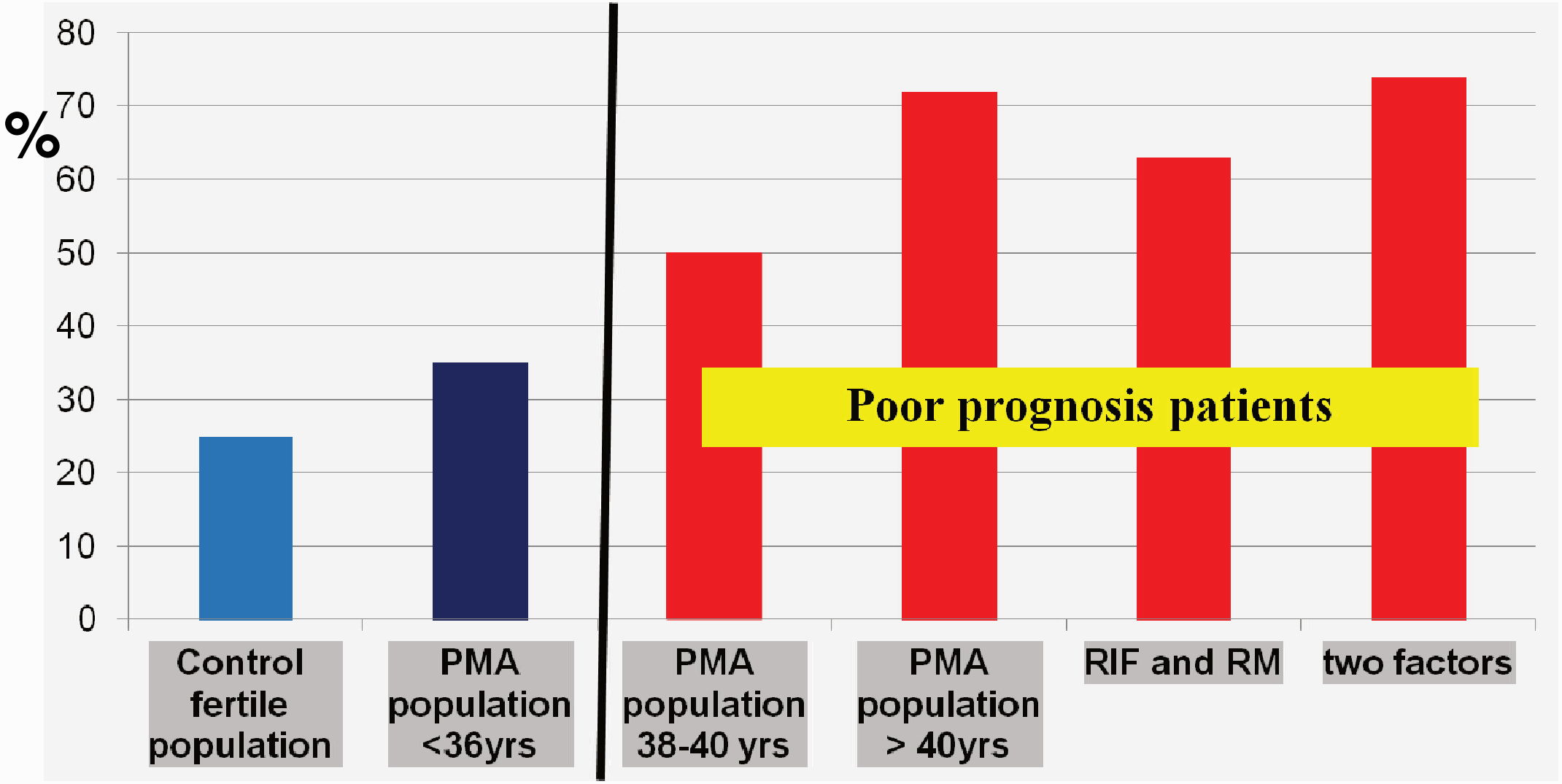



**Dopo i 40 anni :≥ 80 % aneuploidi**

*Franasiak et al, Fertil Steril 2013*

*Demko et al, Fertil Steril 2016*

# Aneuploidy rates




*Fragouli et al,2009, Kilani et al, 2014,Verpoest et al 2008, Kuliev et al 2008, Gianaroli et al 2011*

**IVF population includes couples at higher risk to produce aneuploid embryos**

- ***advanced maternal age ( AMA)***
- ***recurrent idiopathic miscarriage (RM)***
- ***recurrent implantation failure (RIF)***

***The biological rationale to select euploid embryos does sound very logical to increase the performance of ART***

ASRM
Annual Congress 2006

S.I.S.ME.R.
VISION 2000

# Good management of poor prognosis couples

- **To expose them to the highest probability of pregnancy they have with ART in the shortest time**
- **Do not expose them to unnecessary transfers**
- **To reduce the number of embryos transferred *( to reduce the risk of multiple pregnancies)***

# Azem et al. Fertil Steril 2005

**"transfer of six or more embryos improves the success rate in patients with repeated IVF failures"**



S.I.S.ME.R.
VISION 2000

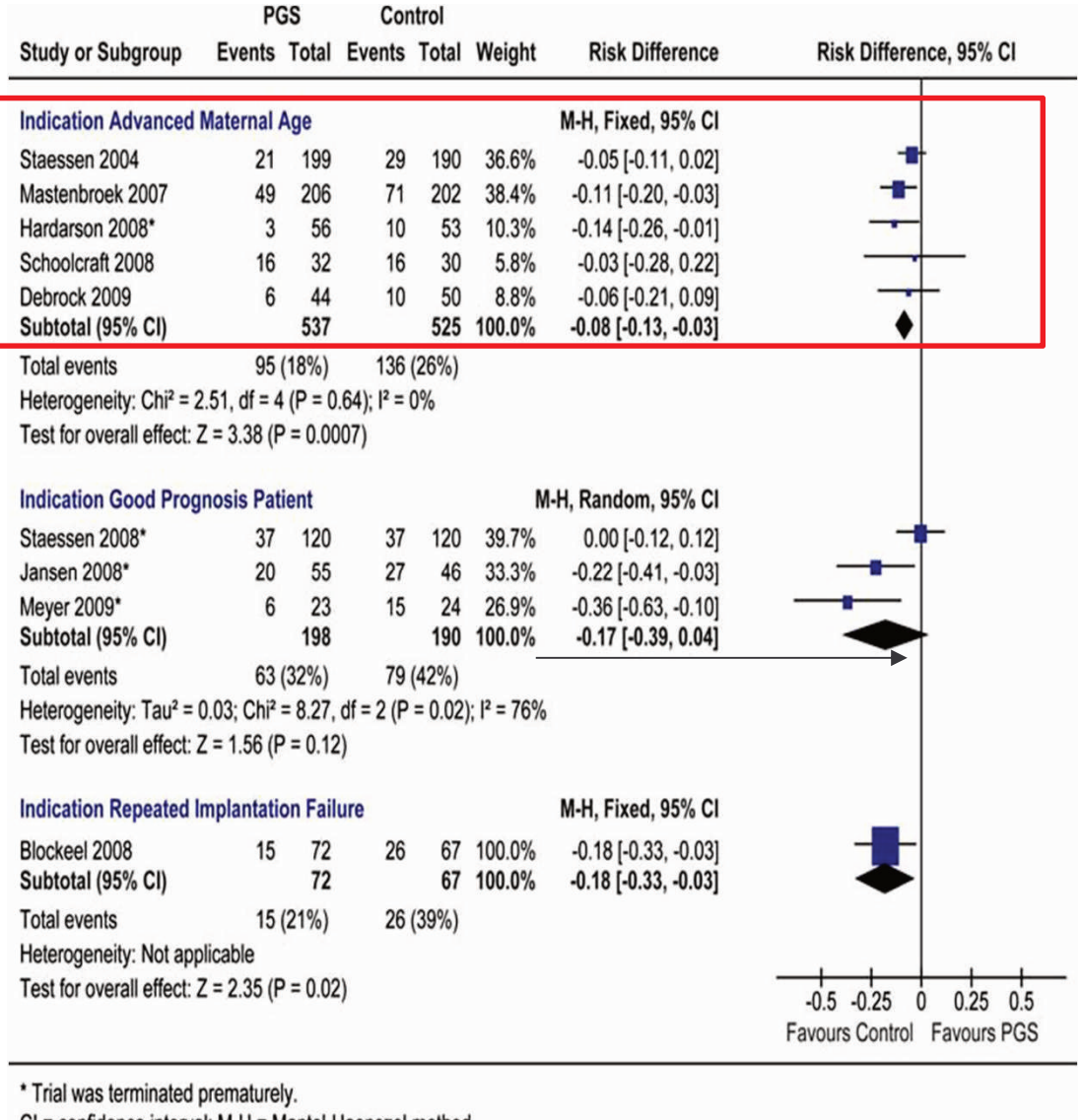
# Diagnosi pre-impianto per screening delle aneuploidie in coppie infertili che si sottopongono a PMA

**Dati del PGD Consortium : raccolti e pubblicati dal 1997 ( ultimo report dati del 2012*) :* *32.793 cicli***

**Dati SISMER : dal 1996 : *1190 cicli***

**EBM (CRT applicabili) : dati molto controversi**

# FISH for PGS: Randomized clinical trials ( 2004-2009)




* Trial was terminated prematurely.

CI = confidence interval; M-H = Mantel-Haenszel method

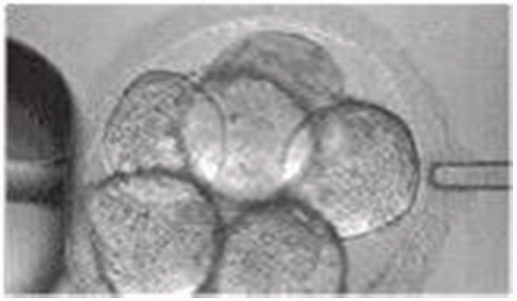
**Lower LBR/women with PGS**

**Mastenbroek et al., Preimplantation genetic screening: a systematic review and meta-analysis of RCTs. Hum Reprod Update 2011;17:454–466.**

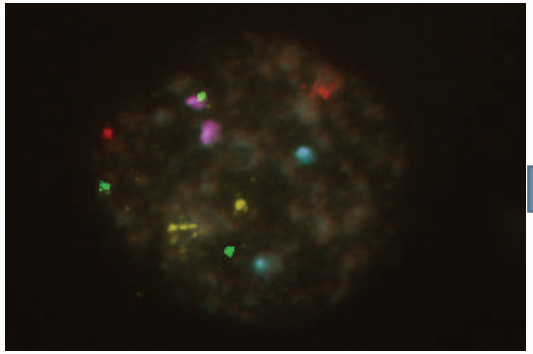
# Clinical impact of PGT-A in ART ?

## The Past

**First generation PGS (FISH on day 3 embryos)**



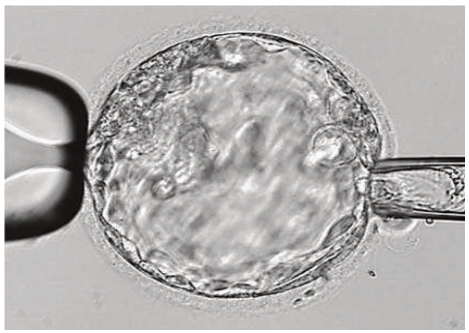
**Reduced embryo viability**



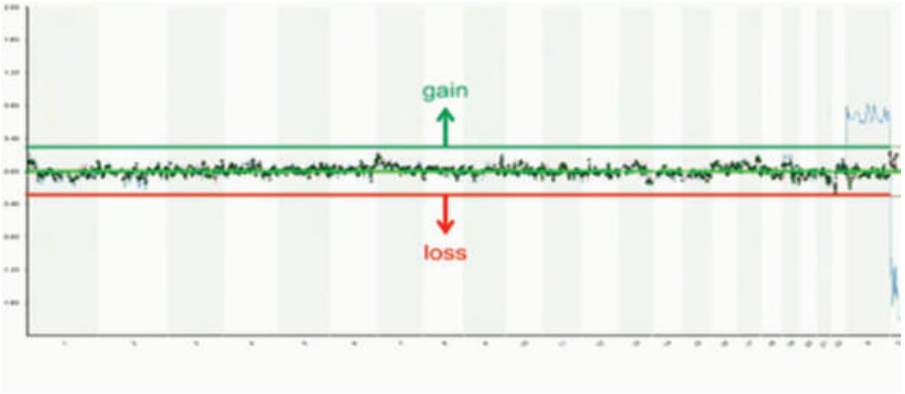
**Max 9 chromosomes analyzed**

# Clinical impact of PGT-A

**The present**



**arrayCGH**
**Full**
**Karyotiping**

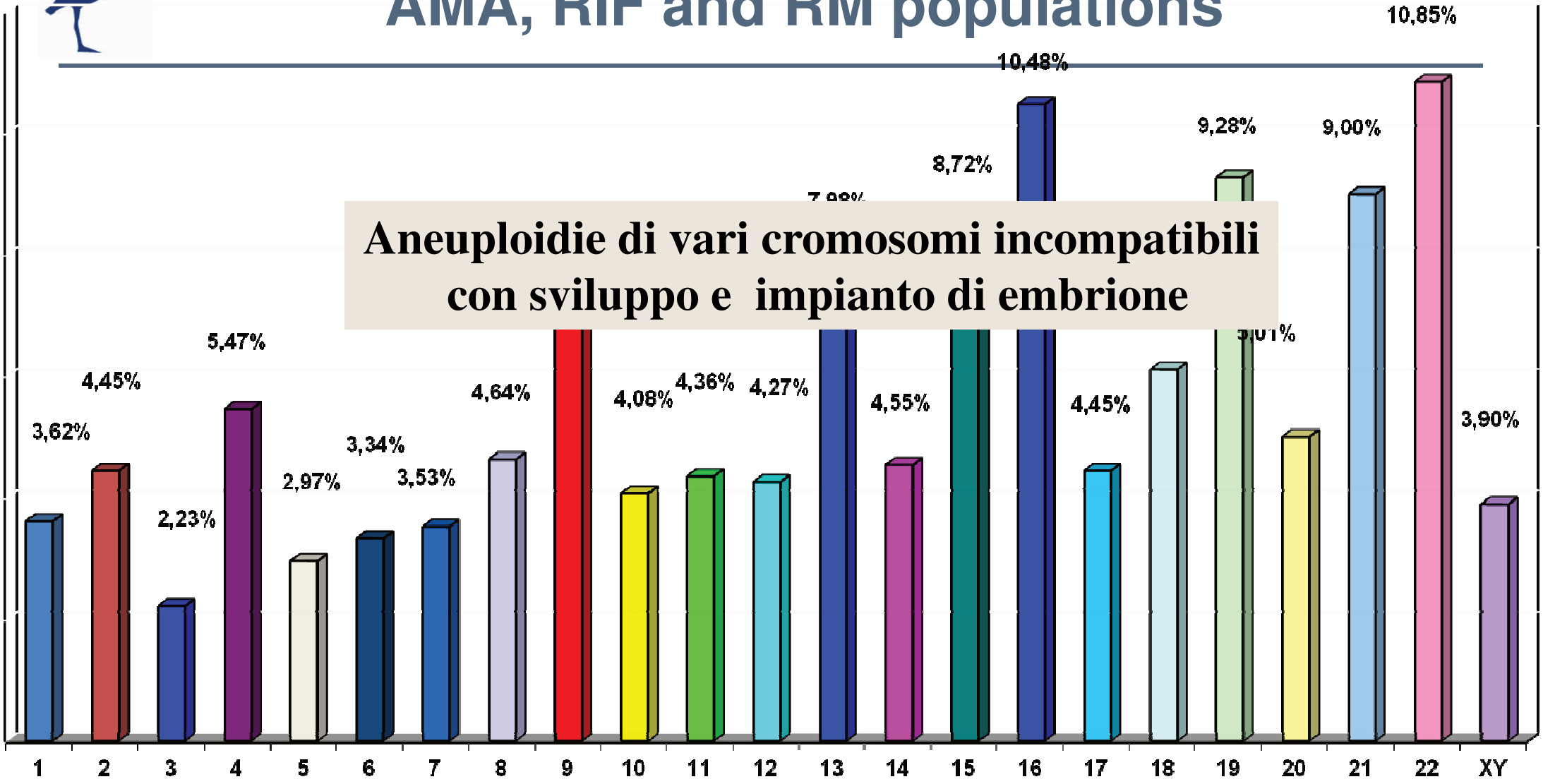



**More DNA: less no results**

**Reduced ( no) impact on embryo viability**

**Less mosaicism**

# CGH on polar bodies ( SISMER) in AMA, RIF and RM populations



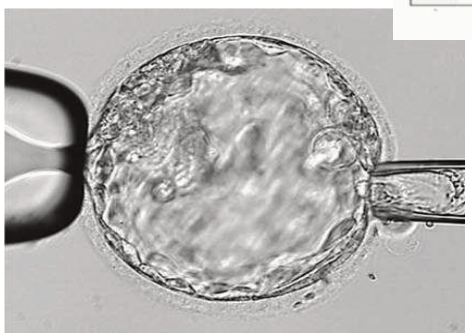

*Gianaroli et al 2013*

# Clinical impact of PGT-A in ART

**The present**



**arrayCGH**
**Full**
**Karyotiping**



**More DNA: less no results**

**Less mosaicism**

**Reduced ( no) impact on embryo implantation**

**Higher potential effect but the clinical value by EBM still need to be produced**

**Cost-effectiveness should be addressed**

**“ Lavori in corso “**

# NEW generation PGT-A

*in classical indications*

*( poor prognosis patients)*

- *advanced  maternal age ( AMA)*
- *recurrent idiopathic miscarriage (RM)*
- *recurrent implantation failure (RIF)*

# In vitro fertilization with preimplantation genetic diagnosis for aneuploidies in advanced maternal age : a randomized, controlled study

( ***Rubio et al,*** *Fertil Steril. 2017 May)*

**Patients 38-41 yrs at the first attempt**

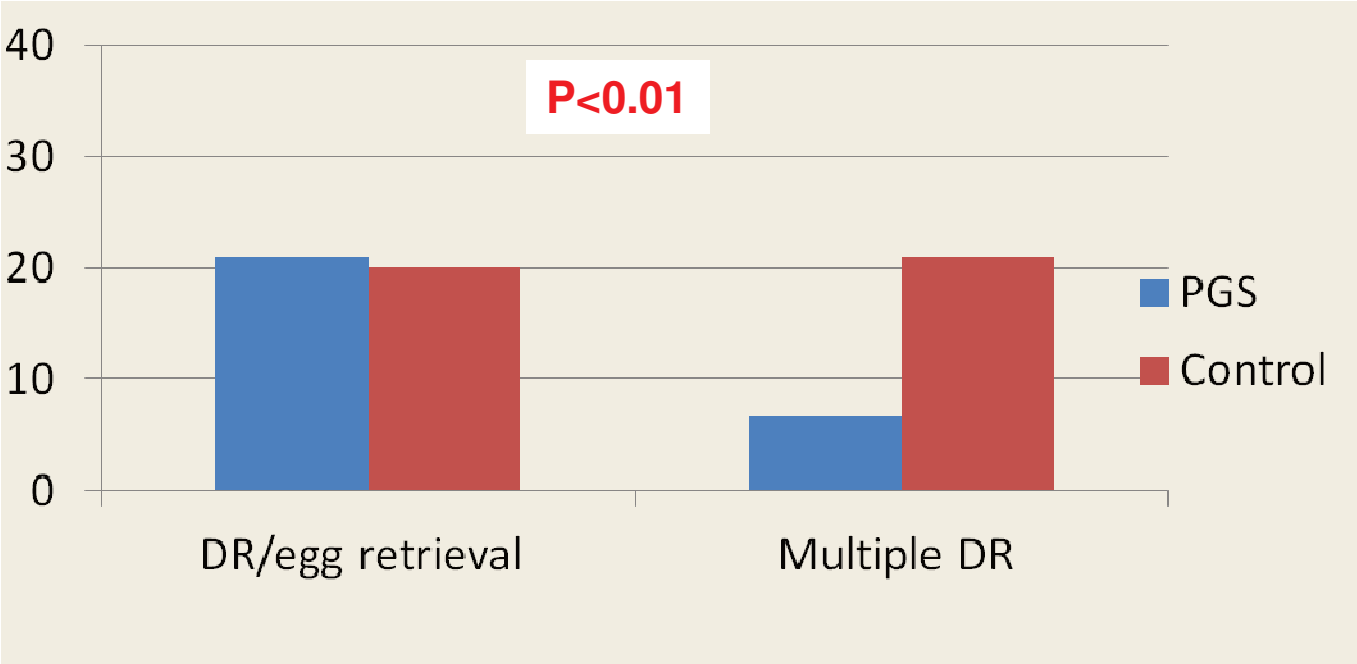
| | PGT-A | Non PGT-A | |
|---|---|---|---|
| Cycles | 100 | 105 | |
| Transfers | 68 (68%) | 95 (91%) | |
| Clinical pregnancies ( % per Patient) | 37 (37%) | 41 (39%) | ns |
| Miscarriages | 1 | 18 | P<0.007 |
| LBR per transfer | 54% (36/68) | 24% (23/95) | P<0.01 |
| LBR per patient | 36% (36/100) | 22% (23/105) | P<0.01 |
| Time to pregnancy resulting in live birth | 7.7 weeks | 14.9 weeks | |

# PGT-A in patients > 35 yrs
# Retrospective studies by CGH on blastocysts

Ubaldi et al 2015

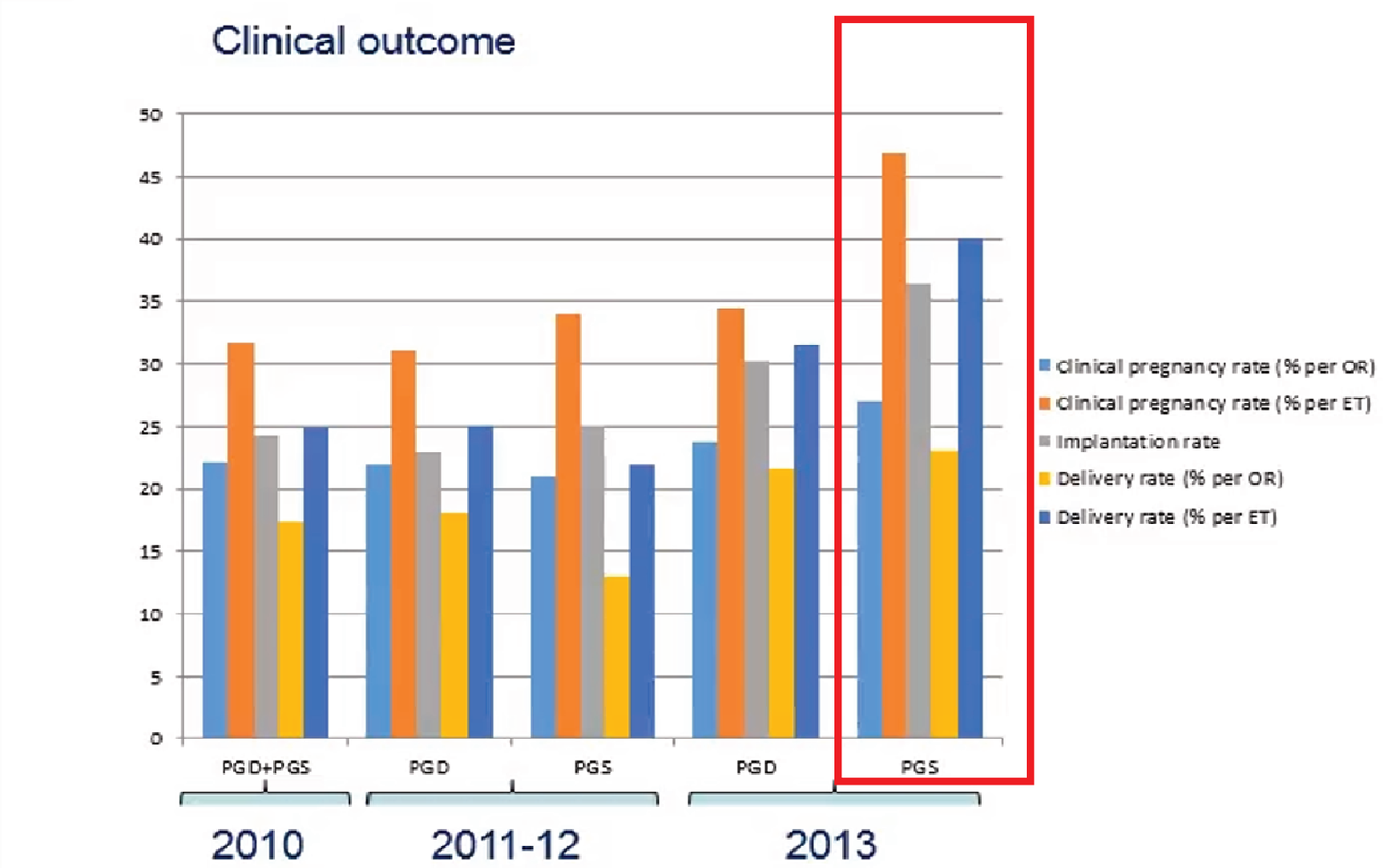
**eSET after PGS vs conventional transfer (2.9±1 blastocysts)**

**Reduction of the multiple pregnancy rate**



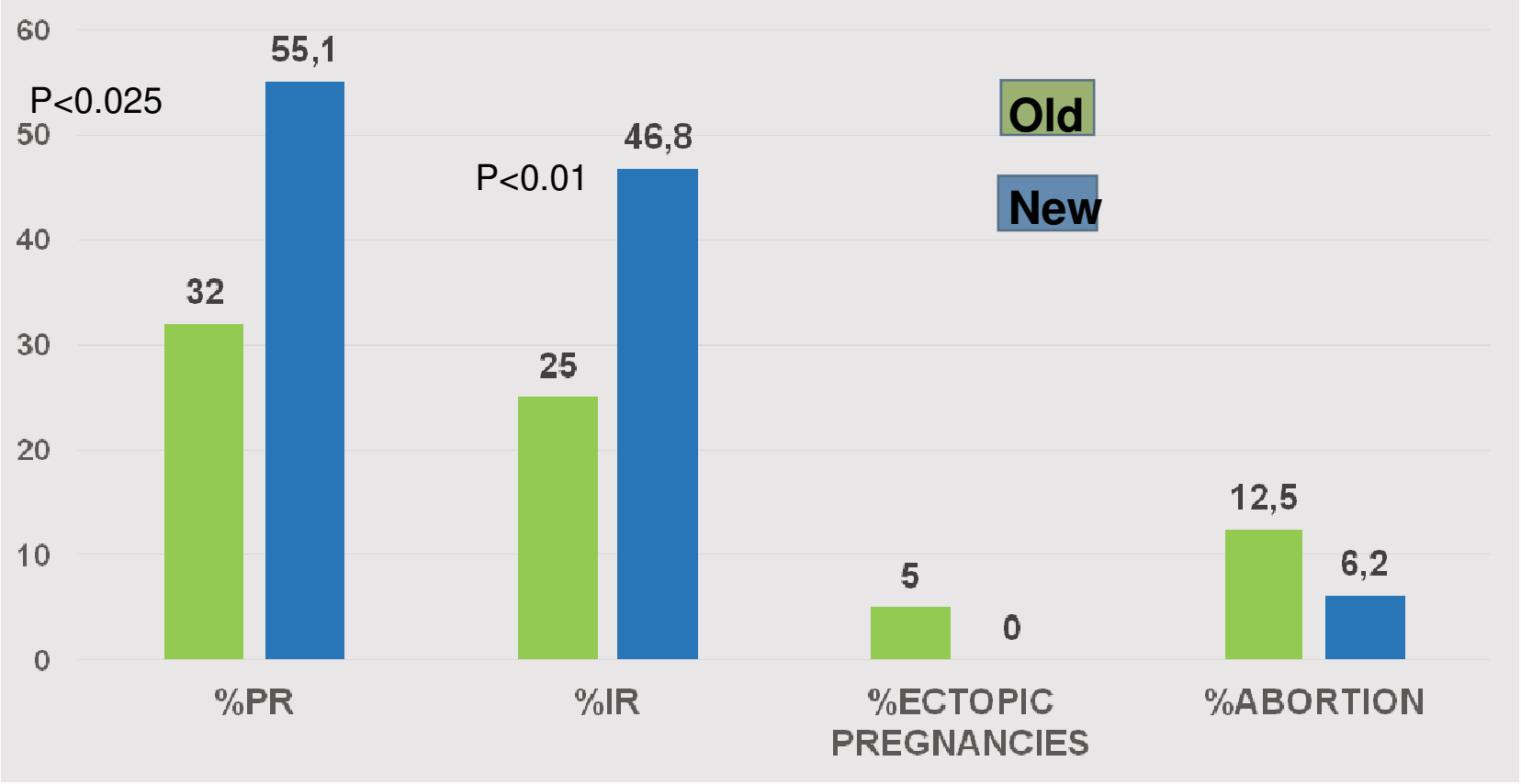
# PGD CONSORTIUM DATA 2010-2013
# PGT-A in poor prognosis patients

**Improvement of clininical PR/ET and Delivery Rate/ET**

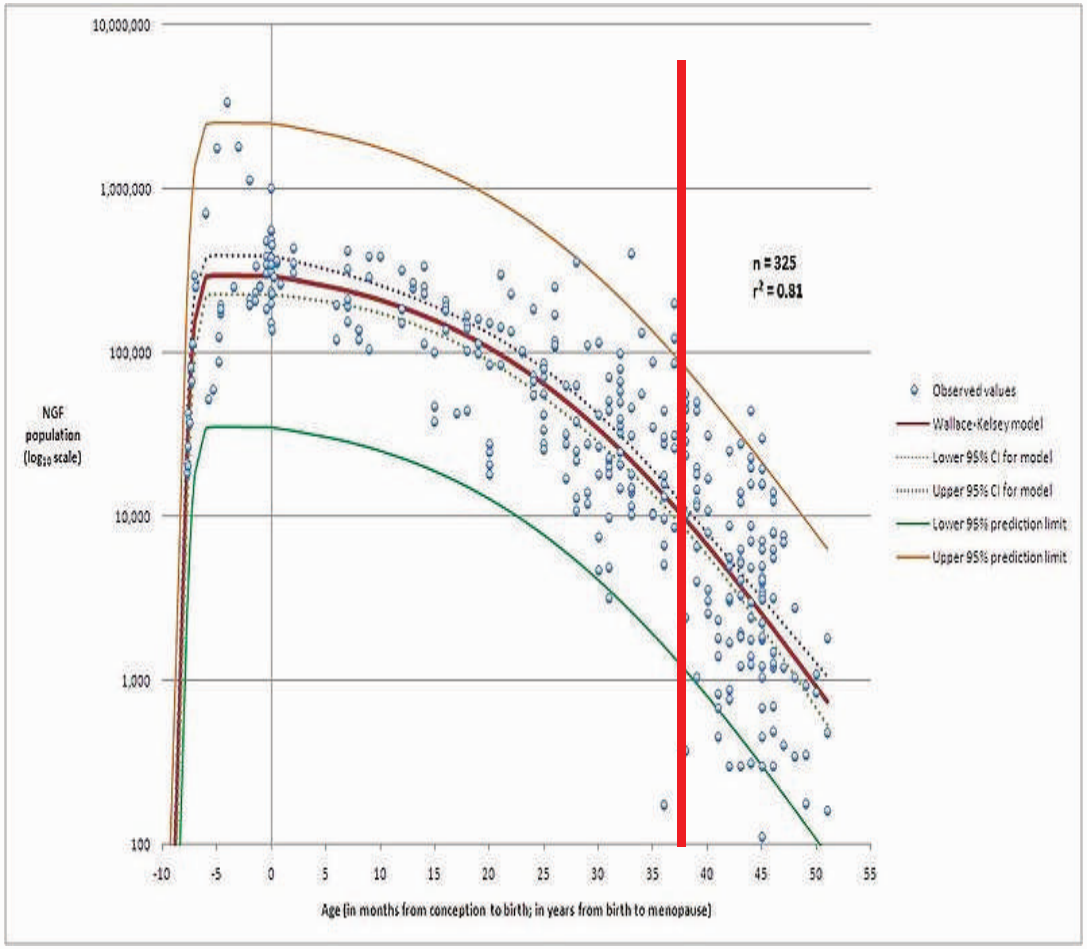


# PGT-A in poor prognosis patients Old vs new generation technique ( S.I.S.Me.R)

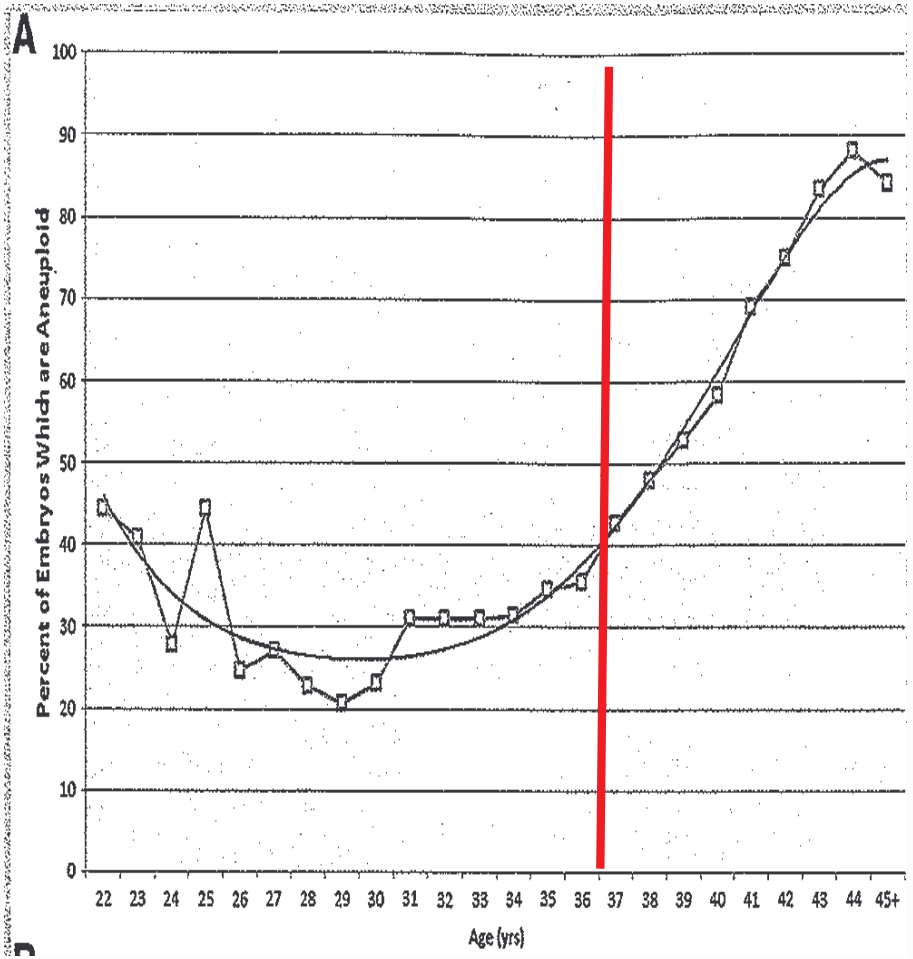
**Improvement of clininical PR/ET and reduction of the miscarriage rate**



# OVARIAN RESERVE




# ANEUPLOIDY RATE




Wallace and Kelsey. Human Ovarian Reserve from Conception to the Menopause PLoS One. 2010; 5(1): e8772.

## Cumulative number of blastocyst needed to produce at least one euploid blastocyst

### % of patients with normal blastocysts

| # of embryos | egg donors | <35 years | 35-37 years | 38-40 years | 41-42 years | >42 years |
|---|---|---|---|---|---|---|
| 1-3 | 83% | 80% | 71% | 57% | 36% | 22% |
| 4-6 | 97% | 95% | 92% | 82% | 59% | 43% |
| 7-10 | 99% | 98% | 96% | 89% | 74% | 50% |
| 10-17 | 100% | 99% | 99% | 97% | 88% | 64% |
| >17 | 100% | 100% | 100% | 99% | 97% | 87% |

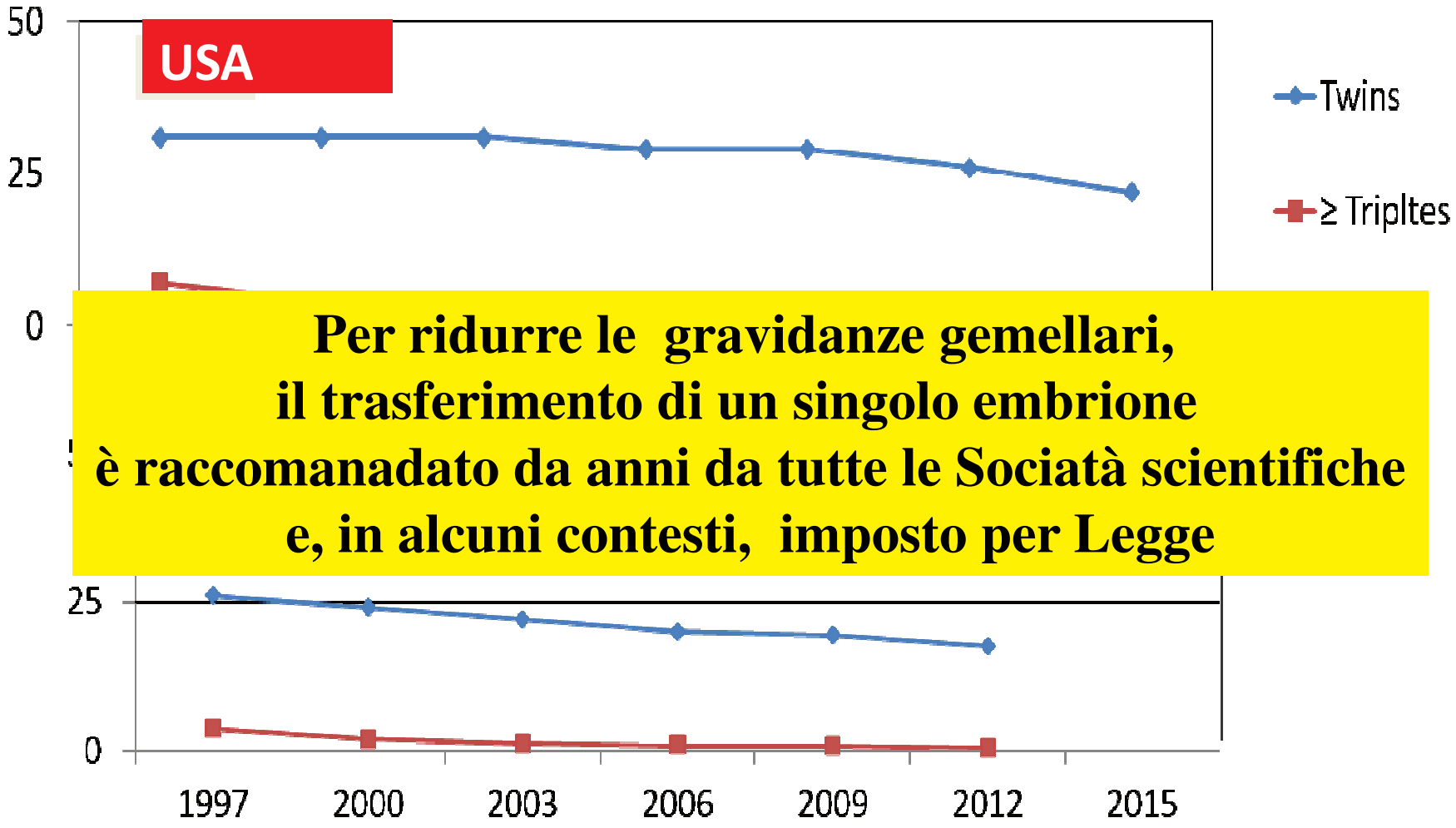
**Conclusions:**

- In women 35 and older more than 50% of embryos are chromosomally abnormal
- Women 41 and older need 18 or more embryos to secure one euploid one
- Of those with no euploid embryos in the first cycle, 38% (41-42 years old) and 25% (> 42 yeas old), those that produced 17 embryos produced euploid embryos in successive cycles.

Munné et al., ASRM 2015

# New scenario : PGT-A to increase the performance of eSET

**La gravidanza multipla è da anni considerata una delle complicanze maggiori della PMA**




**Per ridurre le gravidanze gemellari,**
**il trasferimento di un singolo embrione**
**è raccomanadato da anni da tutte le Sociatà scientifiche**
**e, in alcuni contesti, imposto per Legge**

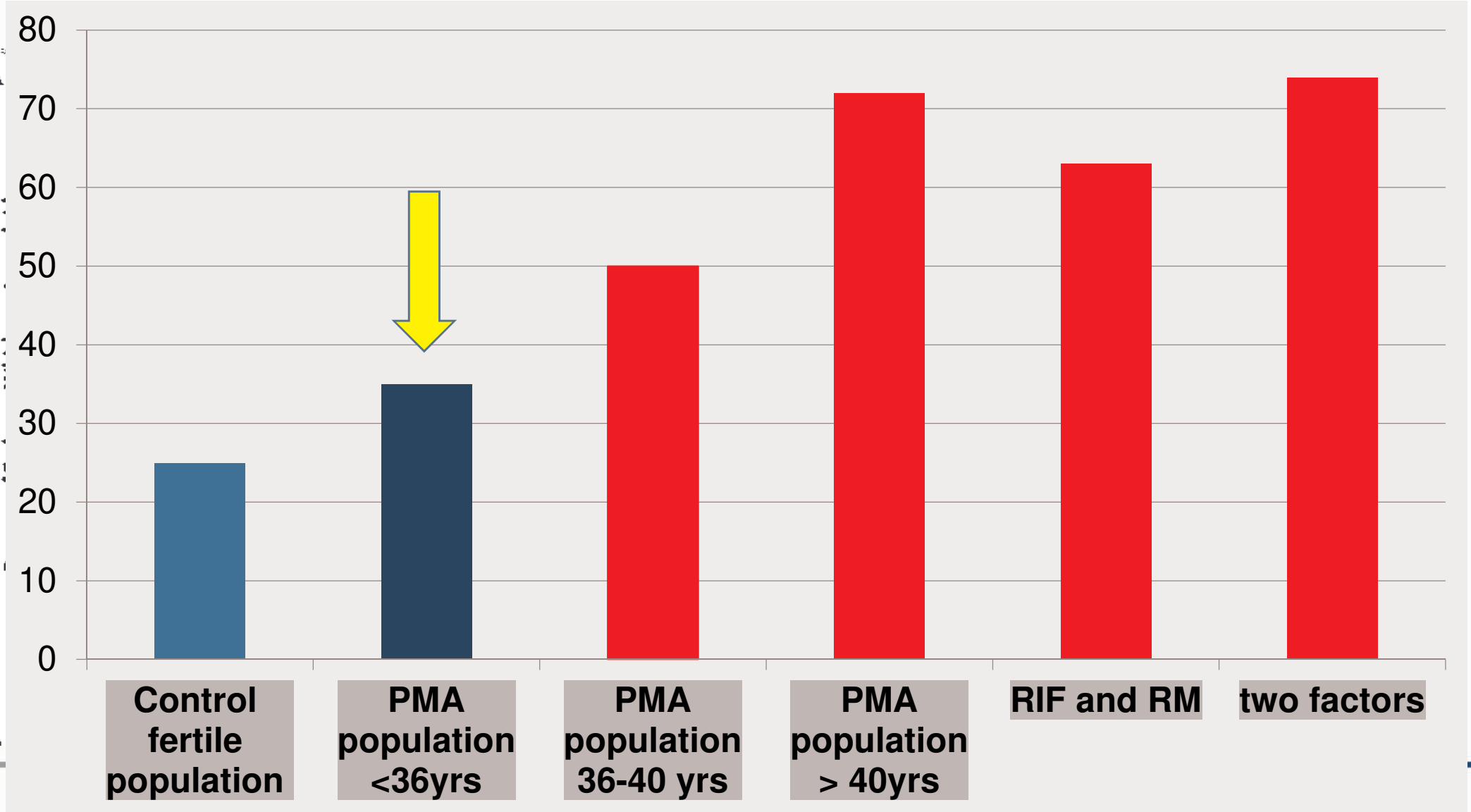
*Ferraretti et al HROpen 2017*

**"Acceptable costs for the patient and society"**
***Chambers et al, Fertil Steril 2013,100.319***

**"Under some circumstances, ART represents good values of money from a social perspective : the monetary values of providing ART treatments can be far covered by the revenue of ART children"**

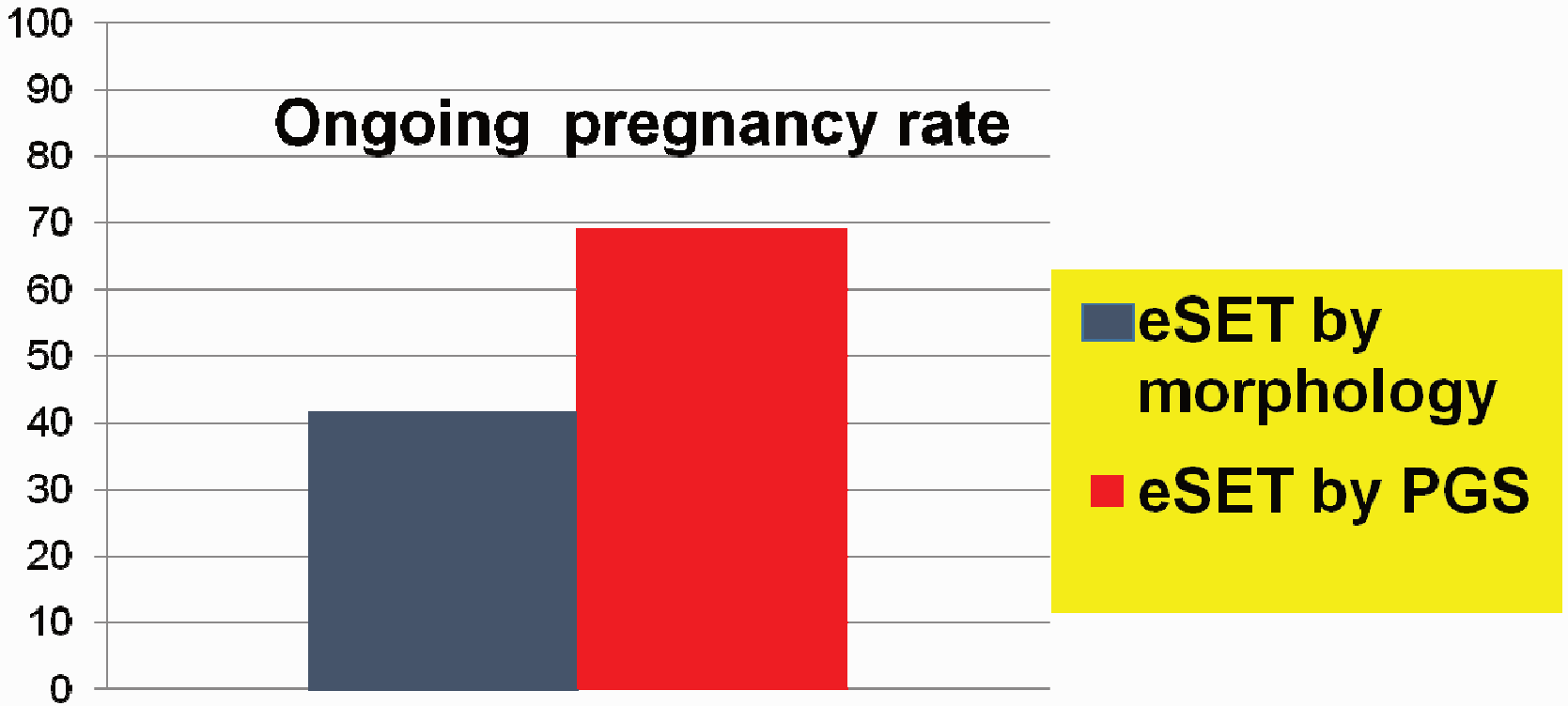
**"These clinical circumstances are true if babies born as singleton"**

# PGT-A in young patient



# Selection of single blastocysts for fresh transfer via standard morphology or with aCGH for good prognosis patients : a randomized pilot study on 100 patients

**103 women - Age < 35**




Young et al, Mol Cytogenetics 2012

# Comprehensive chromosome screening improves embryo selection: a meta-analysis

Elias M. Dahdouh, M.D., M.Sc.,[a,b,c] Jacques Balayla, M.D.,[c] and Juan Antonio García-Velasco, M.D., Ph.D.[d]

[a] Assisted Reproduction Center, CHU Sainte-Justine, University of Montreal, Montreal, Quebec, Canada; [b] PROCREA Clinics, Montreal, Canada; [c] Department of Obstetrics and Gynecology, University of Montreal, Montreal, Canada; and [d] Instituto Valenciano de Infertilidad (IVI) Madrid and Rey Juan Carlos University, Madrid, Spain

**Tre studi prospettici**

**Fertility and Sterility, December 2015**

# PGT-A : the future

**To increase safety**
**To increase accuracy**
**To reduce costs**

**Good prognosis patients**

**Euploid eSET**

**The highest probability of the birth of a single ( healthy) baby**

**Poor prognosis patients**

**To avoid unsuccessful transfers**
**To reduce the rate of miscarriages**
**To shorten the time to delivery**
**To reduce the risk of multiple pregnancies**