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Centro de Referencia Perinatal Oriente

Facultad de Medicina, Universidad de Chile

Pruebas genéticas preimplantacionales

Joaquín López G.

Becado PTE Genética Clínica

Tutora: Dra. Catherine Diaz

Definición

Pruebas genéticas preimplantacionales (PGT):
Pruebas moleculares orientadas al análisis de ADN de ovocitos o embriones para tipificado HLA o determinación de anomalías genéticas

Zegers-Hochschild, F. et al. (2017). The International Glossary on Infertility and Fertility Care, 2017. *Human reproduction (Oxford, England)*, *32*(9), 1786–1801

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PCR

NGS

FISH

aCGH

Table 1 Timeline and history of PGT

Year	Landmark	Reference
1944	Harvard physician John Rock published the first report claiming successful IVF and cleavage of a human oocyte	[8]
1955	Shettles repeated Rock's work and reported successful culture to the morula stage in vitro of a human embryo	[9]
1976	Achievement of first pregnancy but ectopic pregnancy	[10]
1978	Delivery of the first IVF baby	[11]
1983	First pregnancy which used embryo cryopreservation	[12]
1984	Egg donation became publicly available	[13]
1986	First pregnancy which used oocyte cryopreservation	[14]
1989	PGD was pioneered by American embryologist to test for the presence of the gene defects that cause cystic fibrosis, and PCR was carried out to detect X-linked diseases	[4]
1990	Use of the first polar body biopsy to check for a maternal unaffected gene	[15]
1992	First baby was created using ICSI	[16]
1993	Use of fluorescence in situ hybridization (FISH) technique in PGD	[17]
1999	Researchers demonstrated the use of Comparative Genomic Hybridization (CGH) technology on human blastomeres to check for aneuploidies of all chromosomes	[18, 19]
2001	First successful PGD with human leukocyte antigen matching for a sib with Fanconi anemia by haplotype analysis was introduced	[20]
2007	First controlled trial to compare three cycles of IVF with and without Preimplantation Genetic Screening (PGS) in women in the age group of 35–41 years	[21]
2008	Use of microarray and CGH platforms for the detection of aneuploidy of all 23 chromosome pairs	[22]
2010	Concept of Karyomapping was introduced	[23]
2011	First births reported after Preimplantation Genetic Diagnosis of structural chromosome abnormalities using array CGH (aCGH)	[24]
2013	Successful use of NGS technology for PGT-A	[25]
2017	Recommendations by the Practice Committee of the American Society for Reproductive Medicine (ASRM) and the Practice Committee of the Society for ART (SART) issued for transferring single euploid cleavage stage or blastocyst embryo irrespective of the age group	[26]
2018	Comparison of aCGH versus NGS for PGT-A showed marginally improved results with NGS with eSET	[27]
2018	Researchers showed that the extent of mosaicism influences the success rate of IVF	[28]
2020	Use of scRNA-seq to look into the factors that might affect the development of 8-cell human embryos	[29, 30]

Tian, Y. et al. (2024). Preimplantation genetic testing in the current era, a review. *Archives of gynecology and obstetrics*, *309*(5), 1787–1799.

Tipos de PGT

- Antes separados en “preimplantation genetic diagnosis” (PGD) y “preimplantation genetic screening” (PGS)

- PGT-A: evaluación de aneuploidías
- PGT-M: evaluación de anomalías monogénicas específicas (usualmente severas, también HLA)
- PGT-SR: rearreglos estructurales

Zegers-Hochschild, F. et al. (2017). The International Glossary on Infertility and Fertility Care, 2017. *Human reproduction (Oxford, England)*, *32*(9), 1786–1801

Indicaciones de PGT

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Table 2 Preimplantation genetic testing (PGT) indications summary

Type of PGT	Indications
PGT-A (Aneuploidy screening)	Advanced maternal age (typically over 35 years) Repeated implantation failure History of recurrent miscarriages Previous pregnancy with chromosomal abnormalities Severe male-factor infertility Couples desiring to increase the chance of a successful pregnancy
PGT-M (Monogenic/Single gene disorders)	One or both partners are known carriers of a genetic disorder Family history of a specific genetic disorder Previous child with a genetic disorder Couples at risk of transmitting a heritable genetic condition
PGT-SR (Structural rearrangements)	One or both partners have a known chromosomal rearrangement (e.g., translocations, inversions) Previous pregnancy with structural chromosome anomalies Recurrent miscarriages with suspected chromosomal cause Infertility with suspected chromosomal cause

Tian, Y. et al. (2024). Preimplantation genetic testing in the current era, a review. *Archives of gynecology and obstetrics*, *309*(5), 1787–1799

Contraindications for PGT

PGT should not be offered under the following conditions:

Without a definitive genetic disease diagnosis or positioning information for the disease-causing locus.

Selection of non-disease traits, such as appearance, height, and skin color.

Other circumstances where PGT is restricted under local laws, regulations, or ethics.

Some special considerations

Certain numerical aberrations of the sex chromosomes, such as 47,XYY, 47,XXX, have a low risk of transmission; therefore, PGT is not recommended for these conditions. However, the risk of chromosomal abnormalities increases in the offspring of parents with 47,XXY[13]. Therefore, the implementation of PGT may be considered appropriate in these cases.

PGT is not recommended for common chromosomal polymorphisms such as lqh+, 9qh+, inv(9)(p12q13), inv(Y)(p11q11), and Yqh+.

Xu et al. (2023). Preimplantation genetic testing guidelines of International Society of Reproductive Genetics . Reproductive and Developmental Medicine Vol. 07 Issue 01 Pages 3-11

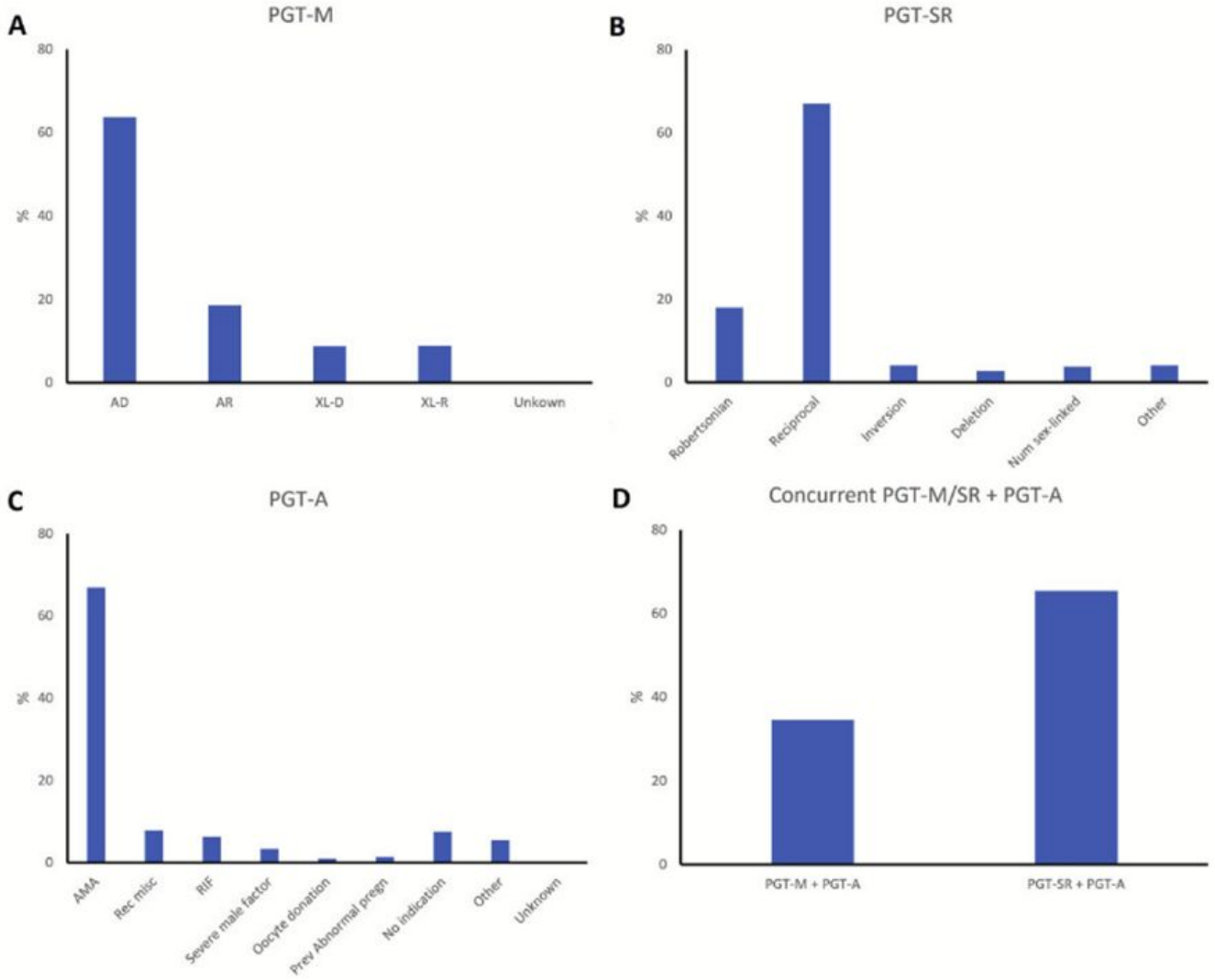

Figure 1. Distribution of PGT indications in 2018. (**A**) Preimplantation genetic testing for monogenic/single gene defects (PGT-M), (**B**) PGT for chromosomal structural rearrangements (PGT-SR), (**C**) PGT for aneuploidies (PGT-A), and (**D**) concurrent PGT-M/SR with PGT-A. AD, autosomal dominant; AR, autosomal recessive; XL-D, X-linked dominant; XL-R, X-linked recessive; AMA, advanced maternal age; Rec misc, recurrent miscarriage; RIF, repeated implantation failure; Prev abnormal pregn, previous abnormal pregnancy.

Spinella, F. et al. (2023). ESHRE PGT Consortium data collection XXI: PGT analyses in 2018. *Human reproduction open*, *2023*(2)

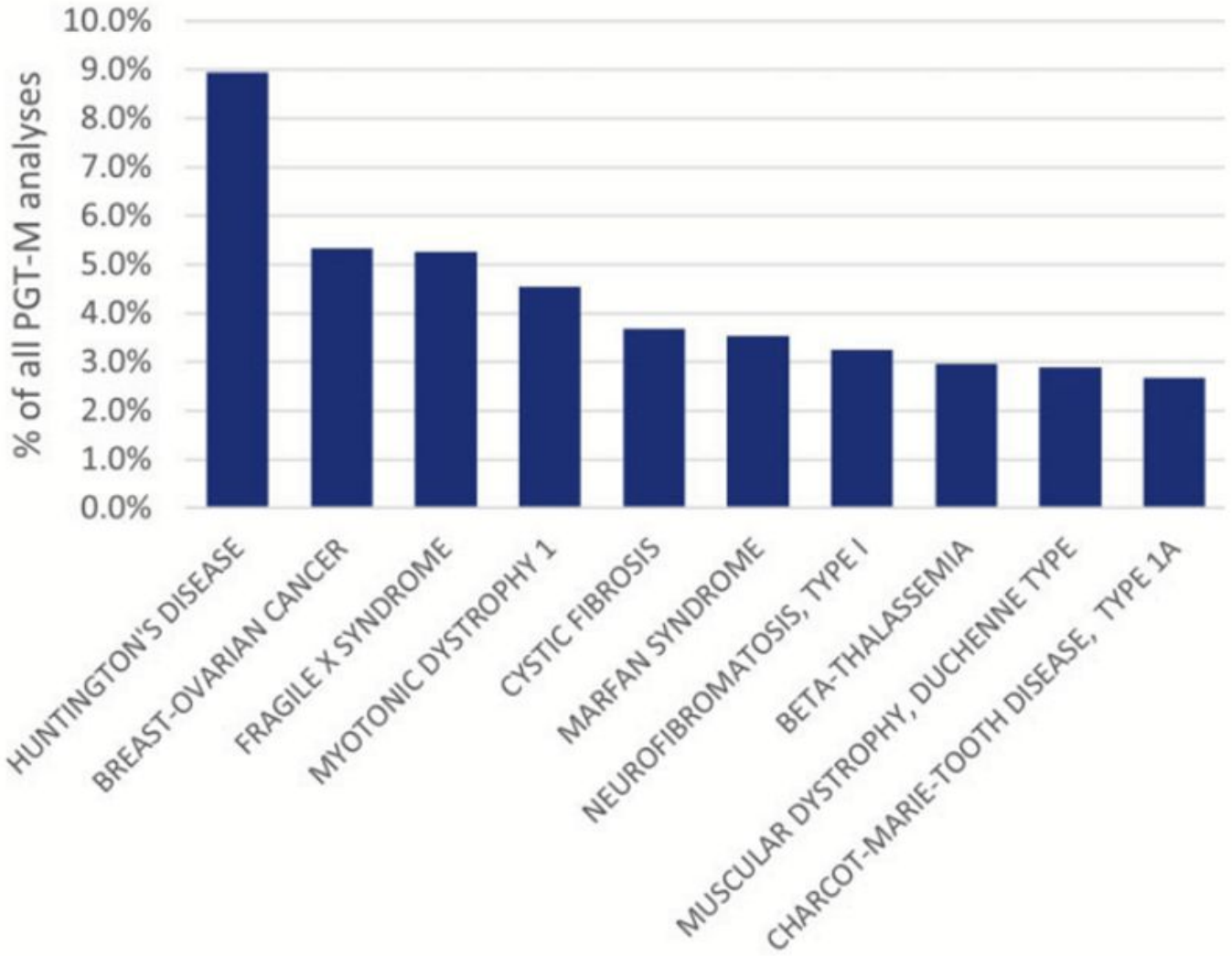

Figure 2. Top 10 of the indications for which PGT-M was applied in 2018. PGT-M: preimplantation genetic testing for monogenic/single gene defects.

Spinella, F. et al. (2023). ESHRE PGT Consortium data collection XXI: PGT analyses in 2018. *Human reproduction open*, *2023*(2)

Técnicas de biopsia

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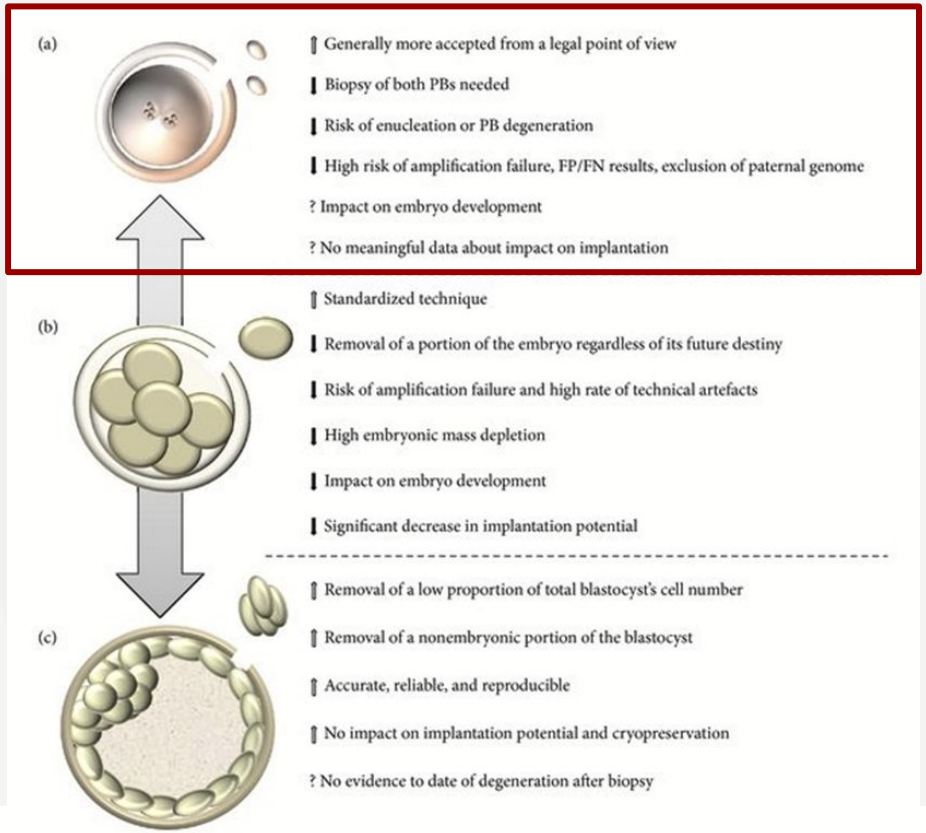
Biopsia de cuerpo polar

- Ambos en simultáneo o diferido (semana 16)
- Mínimamente invasivo
- Limitaciones: intensivo en trabajo y tiempo, no C-E, no evalúa componente paterno, no considera errores postcigóticos



Técnicas de biopsia

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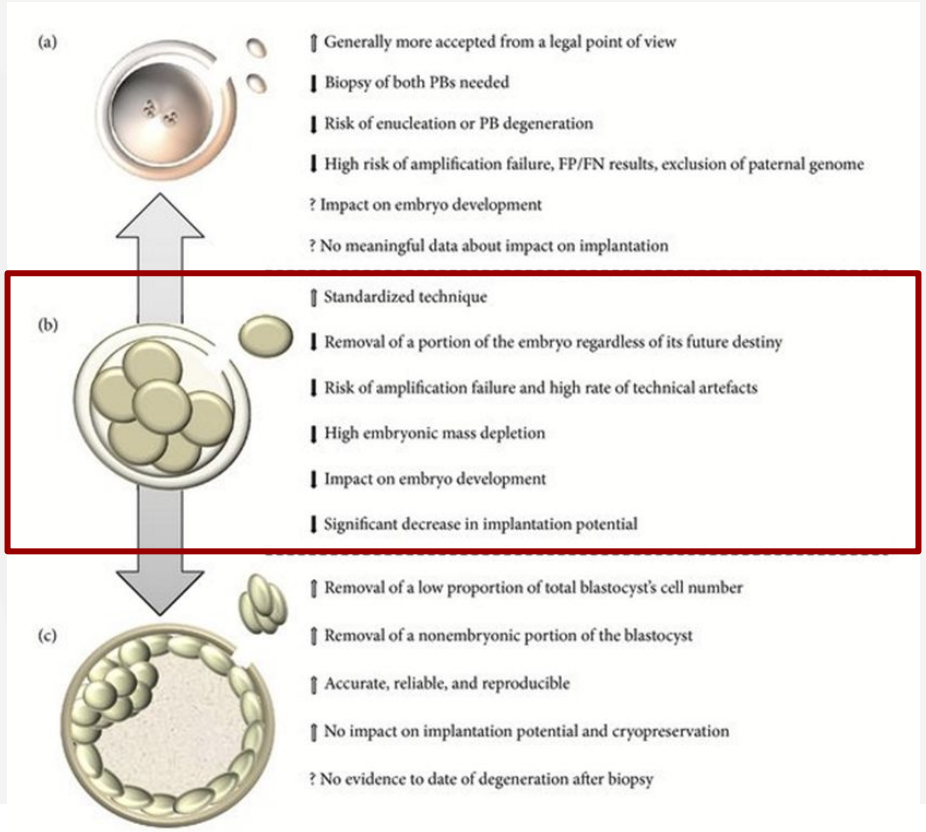
Biopsia de blastómero

- Día 3, extracción unicelular
- Evalúa componente materno y paterno
- Limitaciones: *Allele dropout*, amplificación preferencial, formación de ADN quimérico, altas tasas de fallo de amplificación



Técnicas de biopsia

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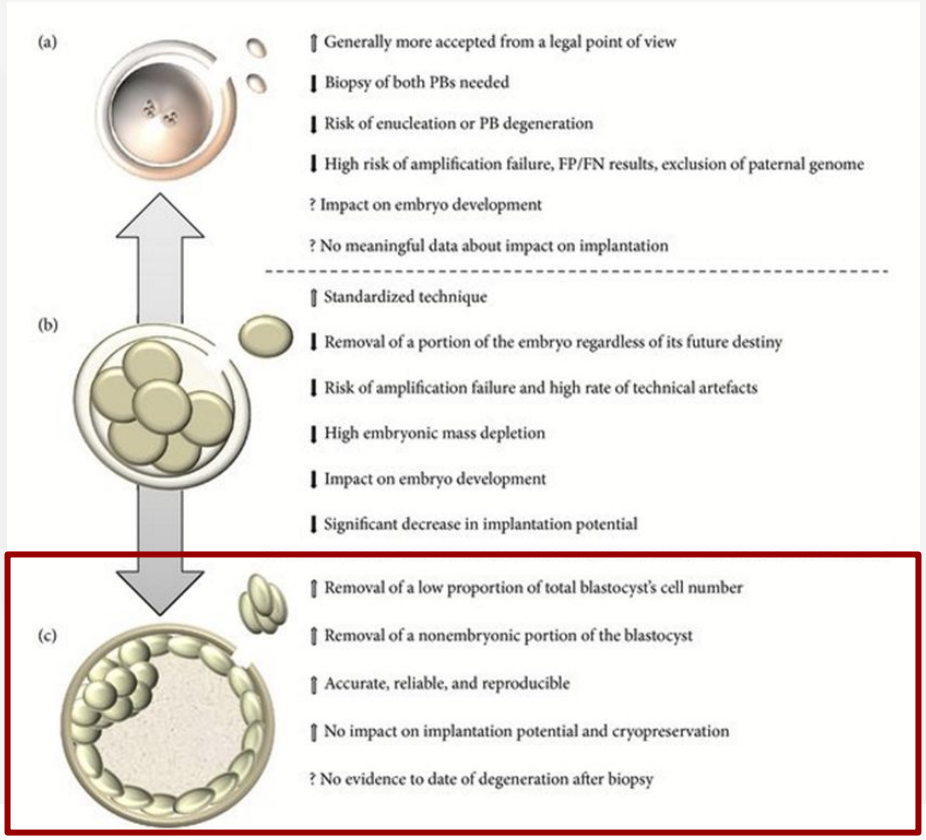
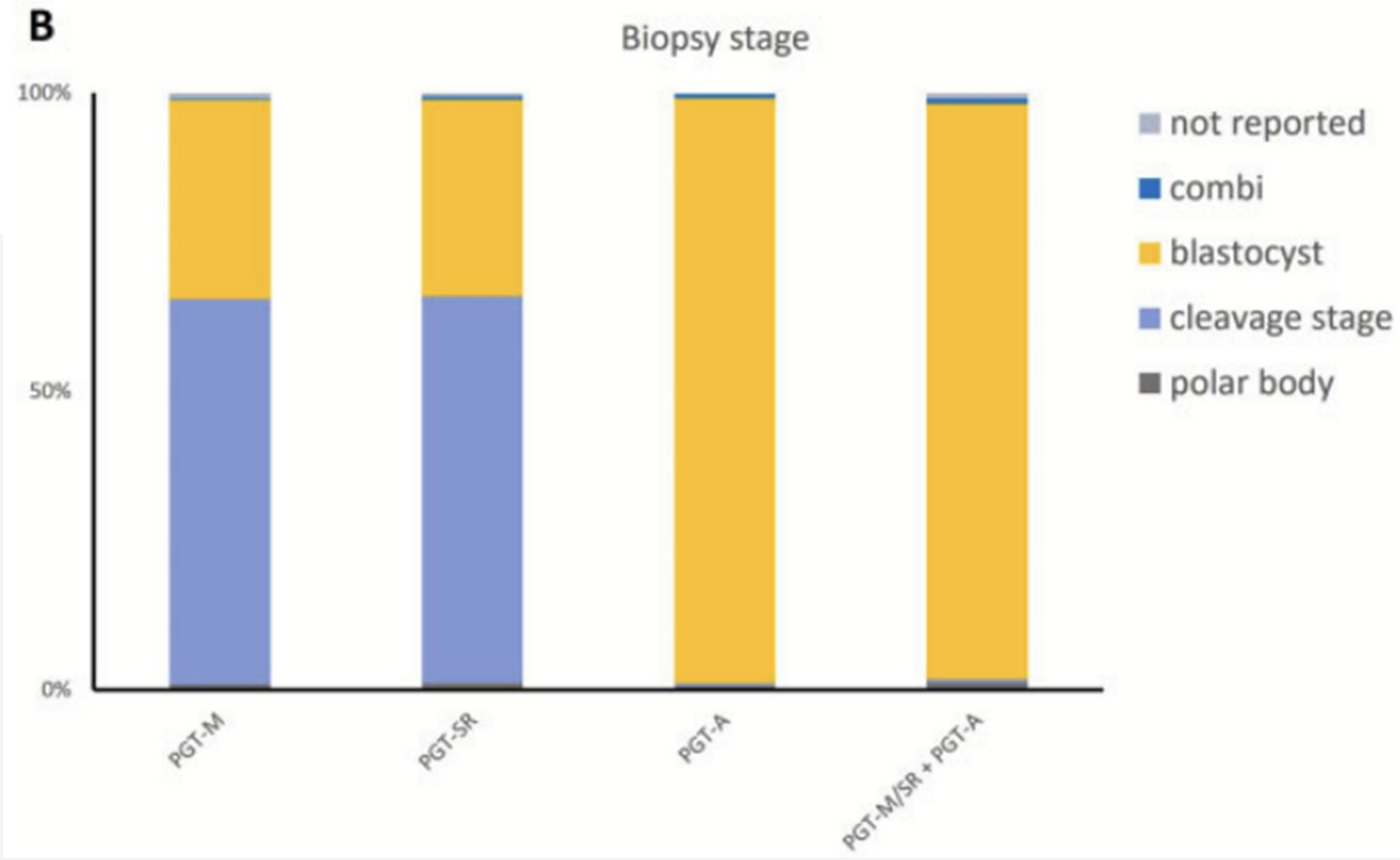
Biopsia de trofoectodermo

- Etapa de blastocisto, 5 – 10 células
- Técnicas:
  - Taladrado de zona (día 3, biopsia a los 5) con herniación de TE
  - Apertura de zona y aspiración (día 5): mayor cantidad de células, menor interferencia
  - Punción de zona (día 5): Técnica más fácil





Spinella, F. et al. (2023). ESHRE PGT Consortium data collection XXI: PGT analyses in 2018. *Human reproduction open*, *2023*(2)

ORIGINAL ARTICLE · Volume 104, Issue 2, P418-425, August 2015 Download Full Issue

Blastocoel fluid from differentiated blastocysts harbors embryonic genomic material capable of a whole-genome deoxyribonucleic acid amplification and comprehensive chromosome microarray analysis

Kyle J. Tobler, M.D. [a,b] · Yulian Zhao, Ph.D., M.D., M.B.A. [a] · Ric Ross, M.S. [c] · ... · Kim Thrift, B.S. [a] · Paul R. Brezina, M.D., M.B.A. [e,f,g] · William G. Kearns, Ph.D. [a,d] ... Show more

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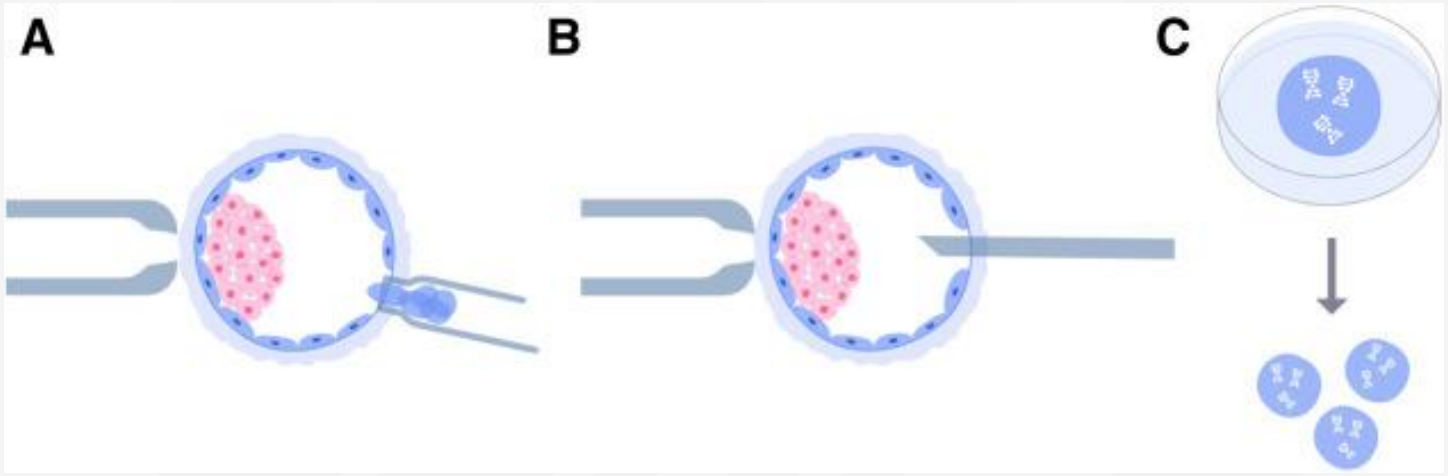

Cinnioglu, C. et al. (2023). A systematic review of noninvasive preimplantation genetic testing for aneuploidy. *Fertility and sterility*, *120*(2), 235–239.

Tobler, K. et al. (2015). Blastocoel fluid from differentiated blastocysts harbors embryonic genomic material capable of a whole-genome deoxyribonucleic acid amplification and comprehensive chromosome microarray analysis. *Fertility and sterility*, *104*(2), 418–425

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Variable	Data
Concordant karyotypes	48% (29/60)
Discordant karyotypes	52% (31/60)
Sensitivity	0.88 (95% CI: 0.62–0.98)
Specificity	0.55 (95% CI: 0.39–0.70)
Positive predictive value	0.41 (95% CI: 0.25–0.60)
Negative predictive value	0.92 (95% CI: 0.75–0.99)

Tobler, K. et al. (2015). Blastocoel fluid from differentiated blastocysts harbors embryonic genomic material capable of a whole-genome deoxyribonucleic acid amplification and comprehensive chromosome microarray analysis. *Fertility and sterility*, *104*(2), 418–425

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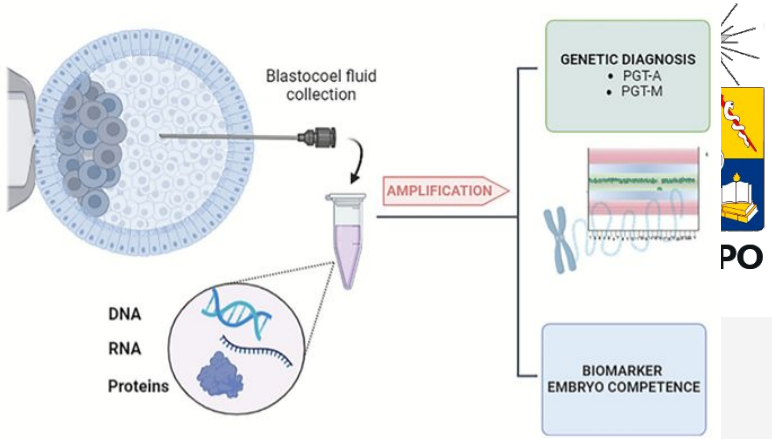
	TE		BF		SBM	
Probes	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
All	405		347		378	
Amplification failure	0/405	0.0 (0.0–9.1)	252/347	72.6 (67.6–77.3)	39/378	10.3 (7.4–13.8)
Concordant genotype	404/405	99.8 (98.6–99.9)	46/347	13.3 (9.9–17.3)	225/378	59.5 (54.4–64.5)
Discordant genotype	1/405	0.25 (0.01–1.4)	49/347	14.1 (10.6–18.2)	114/378	30.2 (25.6–35.1)

REVIEW

Blastocoel fluid as an alternative source of DNA for minimally invasive PGT and biomarker of embryo competence



Concordancia con biopsia de trofoectodermo varía entre publicaciones

TABLE 1 BLASTOCOEL FLUID DNA AMPLIFICATION RATES AND CONCORDANCE WITH PREIMPLANTATION GENETIC TESTING INFERRED FROM TROPHECTODERM BIOPSY

	PGT	Embryos	Fresh/frozen	Day	Volume	Amplification (%)	Concordance TE (%)
Palini et al., 2013	PGT-A	5	Fresh	5	0.3–0.5 nl	80	–
Perloe et al., 2013	PGT-A	32	9 fresh 23 frozen	-	-	28.10	33.3
Gianaroli et al., 2014	PGT-A	51	Fresh	-	1 μl	76.5	82
Tobler et al., 2015	PGT-A	96	Frozen	-	1 μl	63	48
Galluzi et al., 2015	PGT-M	9	Fresh	5–6	-	44	100 (one sample)
Magli et al., 2016	PGT-A	116	Fresh	5–6	10 nl	82	81
Zhang et al., 2016	PGT-M	11	Fresh	5–7	-	73	100 (one sample)
Shangguan et al., 2017	PGT-M	7	Fresh	5	1–2 nl	42.9–72.4	100 (six samples)
Tsuiko et al., 2018	PGT-A	16	Frozen	-	10 nl	87.50	40
Capalbo et al., 2018	PGT-A	23	Fresh	5–7	-	34.80	37.5
Capalbo et al., 2018	PGT-M	69	Fresh	5–7	-	27	2.9
Magli et al., 2019	PGT-A	256	Fresh	-	1 μl	71	66.3

PGT, preimplantation genetic testing; PGT-A, preimplantation genetic testing for aneuploidy; PGT-M, preimplantation genetic testing for monogenic disorders; TE, trophectoderm.

Campos, G. et al. (2024). Blastocoel fluid as an alternative source of DNA for minimally invasive PGT and biomarker of embryo competence. *Reproductive biomedicine online*

Diagnostic efficacy of blastocoel fluid and spent media as sources of DNA for preimplantation genetic testing in standard clinical conditions

Antonio Capalbo, Ph.D.,[a,b] Valeria Romanelli, Ph.D.,[a] Cristina Patassini, M.Sc.,[a] Maurizio Poli, D.Phil.,[a,c] Laura Girardi, M.Sc.,[a] Adriano Giancani, M.Sc.,[d] Marta Stoppa, M.Sc.,[d] Danilo Cimadomo, Ph.D.,[d] Filippo Maria Ubaldi, M.D.,[d] and Laura Rienzi, M.Sc.[d]

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Preimplantation genetic testing for monogenic diseases results in trophectoderm (TE), blastocoel fluid (BF), and spent blastocyst media (SBM) samples.

	TE		BF		SBM	
Probes	**N**	**% (95% CI)**	**N**	**% (95% CI)**	**N**	**% (95% CI)**
All	405		347		378	
Amplification failure	0/405	0.0 (0.0–9.1)	252/347	72.6 (67.6–77.3)	39/378	10.3 (7.4–13.8)
Concordant genotype	404/405	99.8 (98.6–99.9)	46/347	13.3 (9.9–17.3)	225/378	59.5 (54.4–64.5)
Discordant genotype	1/405	0.25 (0.01–1.4)	49/347	14.1 (10.6–18.2)	114/378	30.2 (25.6–35.1)
ADO	1/405	0.25 (0.01–1.4)	44/347	12.7 (9.4–16.7)	76/378	20.1 (16.2–24.5)
Materna	1/1	100.0 (2.5–100.0)	14/44	31.8 (19.9–46.6)	28/76	36.8 (26.1–48.7)
Paternal	0/1	0.0 (0.0–97.5)	30/44	68.2 (52.4–81.4)	48/76	63.2 (51.3–73.9)
Artifact	0/405	0.0 (0.0–9.1)	5/347	1.4 (0.5–3.3)	38/378	10.1 (7.2–13.5)
Mutation-specific only	76		65		69	
Amplification failure	0/76	0.0 (0.0–4.7)	49/65	75.4 (63.1–85.2)	11/69	15.9 (8.2–26.7)
Concordant genotype	75/76	98.7 (92.9–100.0)	8/65	12.3 (5.5–22.8)	40/69	58.0 (45.5–69.8)
Discordant genotype	1/76	1.3 (0.03–7.1)	8/65	12.3 (5.5–22.8)	18/69	26.1 (16.3–38.1)
ADO	1/76	1.3 (0.03–7.1)	8/65	12.3 (5.5–22.8)	12/69	17.4 (9.3–28.4)
Maternal	1/1	100.0 (2.5–100.0)	0/8	0.0 (0.0–36.9)	5/12	41.7 (15.2–72.3)
Paternal	0/1	0.0 (0.0–97.5)	8/8	100.0 (63.1–100.0)	7/12	58.3 (27.7–84.8)
Artifact	0/76	0.0 (0.0–4.7)	0/65	0.0 (0.0–5.5)	6/69	8.7 (3.3–18.0)

Note: The results are shown for all the probes analyzed and only for mutation-specific ones. ADO = allele dropout; CI = confidence interval.

Capalbo. Noninvasive embryo genetic testing. Fertil Steril 2018.

Baja concordancia tanto con fluido de blastocele como con medio usado

Capalbo, A. et al. (2018). Diagnostic efficacy of blastocoel fluid and spent media as sources of DNA for preimplantation genetic testing in standard clinical conditions. *Fertility and sterility*, *110*(5), 870–879.e5.

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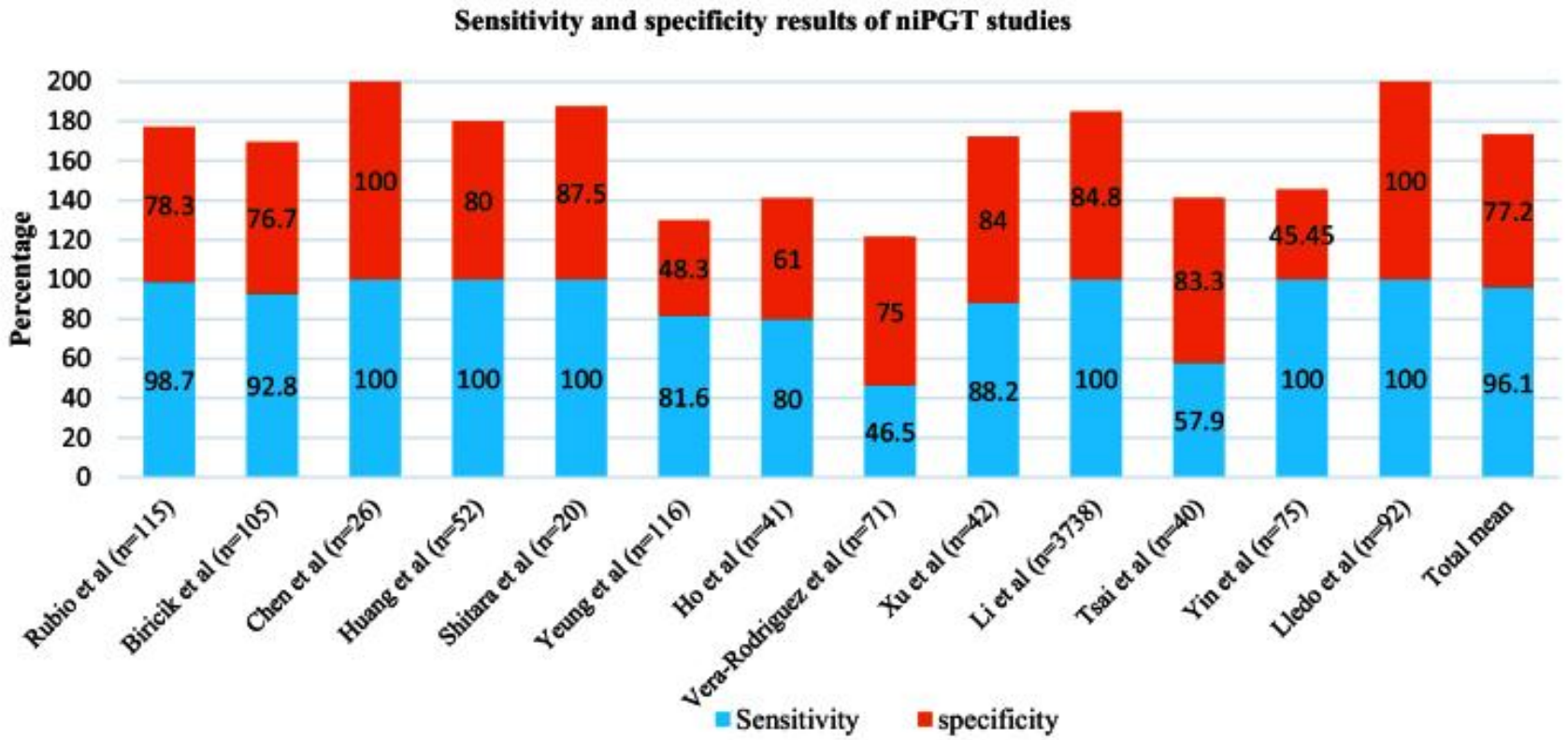

Karami, N. et al. (2024). Comparing the advantages, disadvantages and diagnostic power of different non-invasive pre-implantation genetic testing: A literature review. *International journal of reproductive biomedicine*, *22*(3), 177–190.

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Técnicas de estudio molecular

Técnicas de estudio molecular

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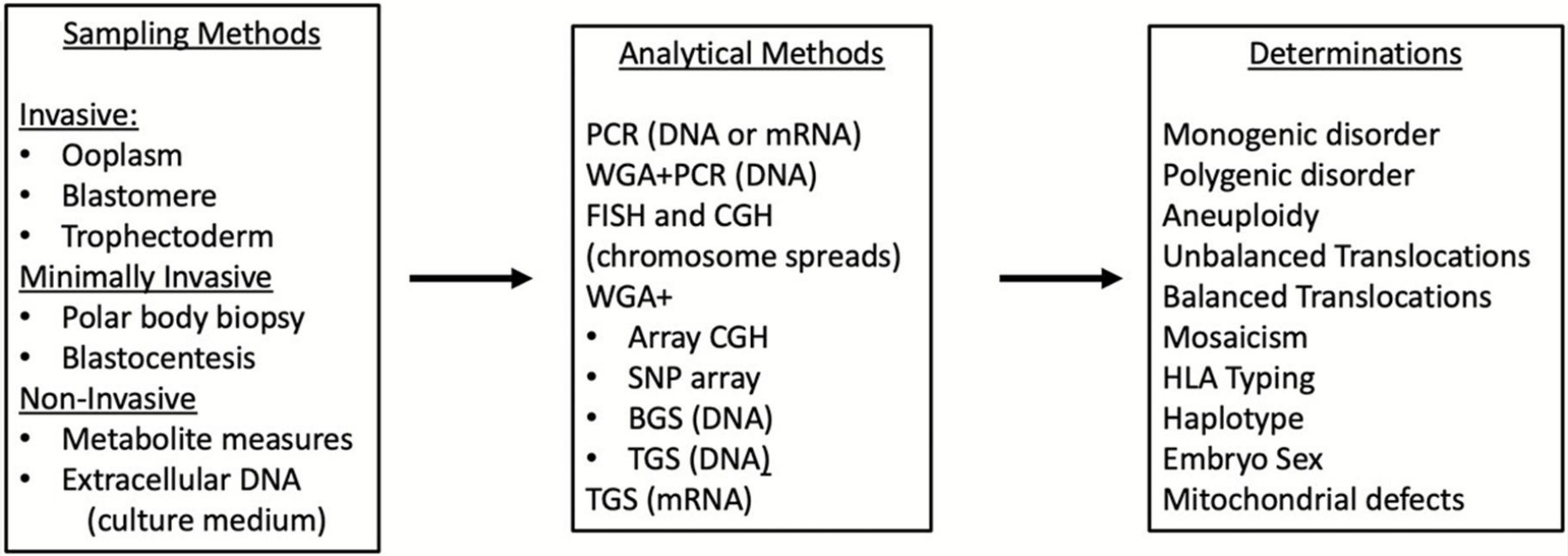

Latham K. E. (2024). Preimplantation genetic testing: A remarkable history of pioneering, technical challenges, innovations, and ethical considerations. *Molecular reproduction and development*, *91*(1), e23727

PCR

- Primera técnica, evaluación de regiones de interés
- Luego regiones polimórficas, CNVs y aneuplodías con amplificación de genoma completo
- Limitaciones por contaminación, sesgo de amplificación, allele dropout
- PCR multiplex

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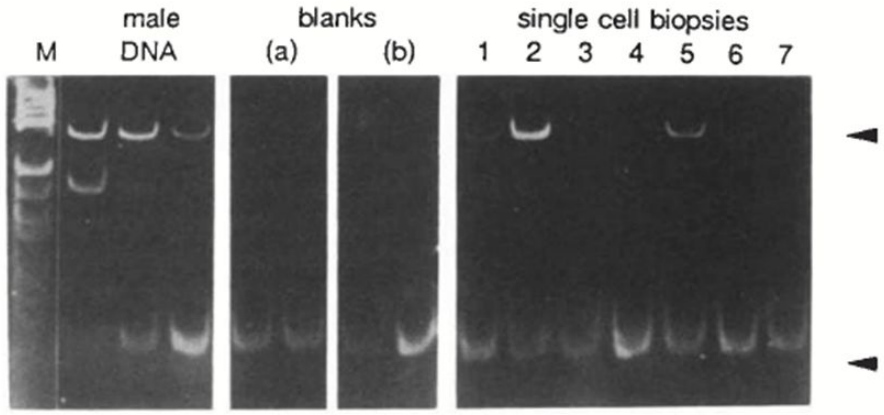
Letter | Published: 19 April 1990

Pregnancies from biopsied human preimplantation embryos sexed by Y-specific DNA amplification

A. H. Handyside, E. H. Kontogianni, K. Hardy & R. M. L. Winston



Handyside, A. H. et al. (1990). Pregnancies from biopsied human preimplantation embryos sexed by Y-specific DNA amplification. *Nature*, *344*(6268), 768–770

Hum Reprod. 1993 Feb;8(2):296-301. doi: 10.1093/oxfordjournals.humrep.a138040.

Preimplantation diagnosis of aneuploidy using fluorescent in-situ hybridization: evaluation using a chromosome 18-specific probe

B M Schrurs [1], R M Winston, A H Handyside

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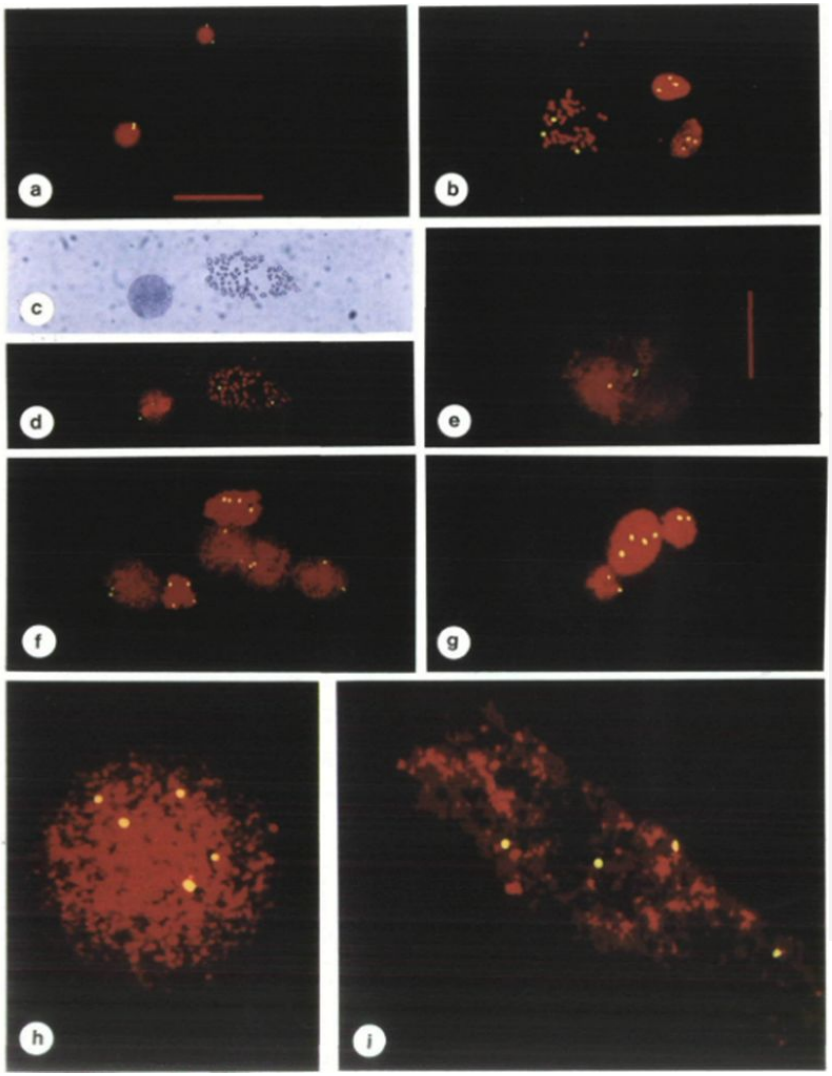
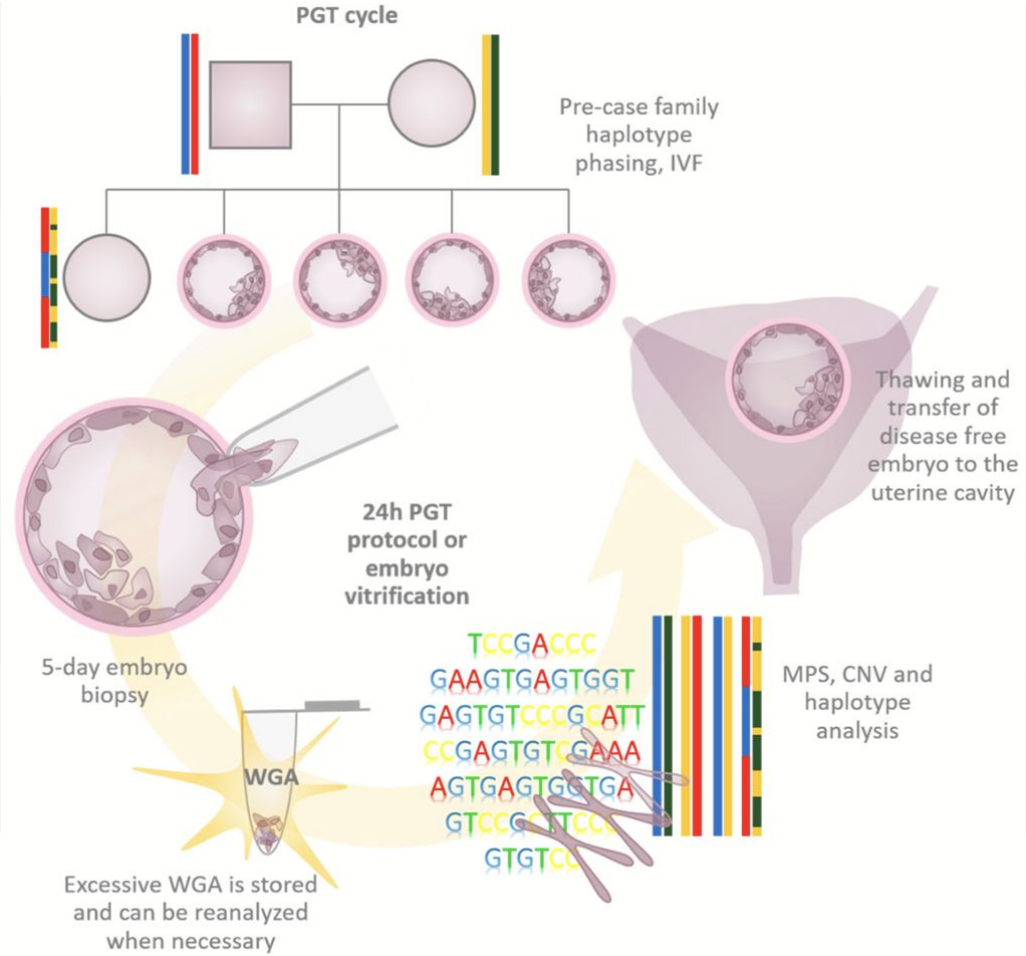


Schrurs, B. M. et al. (1993). Preimplantation diagnosis of aneuploidy using fluorescent in-situ hybridization: evaluation using a chromosome 18-specific probe. *Human reproduction (Oxford, England)*, *8*(2), 296–301.

Amplificación de genoma completo (WGA)

Técnica de preamplificación orientada a sintetizar suficiente ADN para usos río abajo



Volozonoka, L. et al. (2022). Whole Genome Amplification in Preimplantation Genetic Testing in the Era of Massively Parallel Sequencing. *International journal of molecular sciences*, *23*(9), 4819

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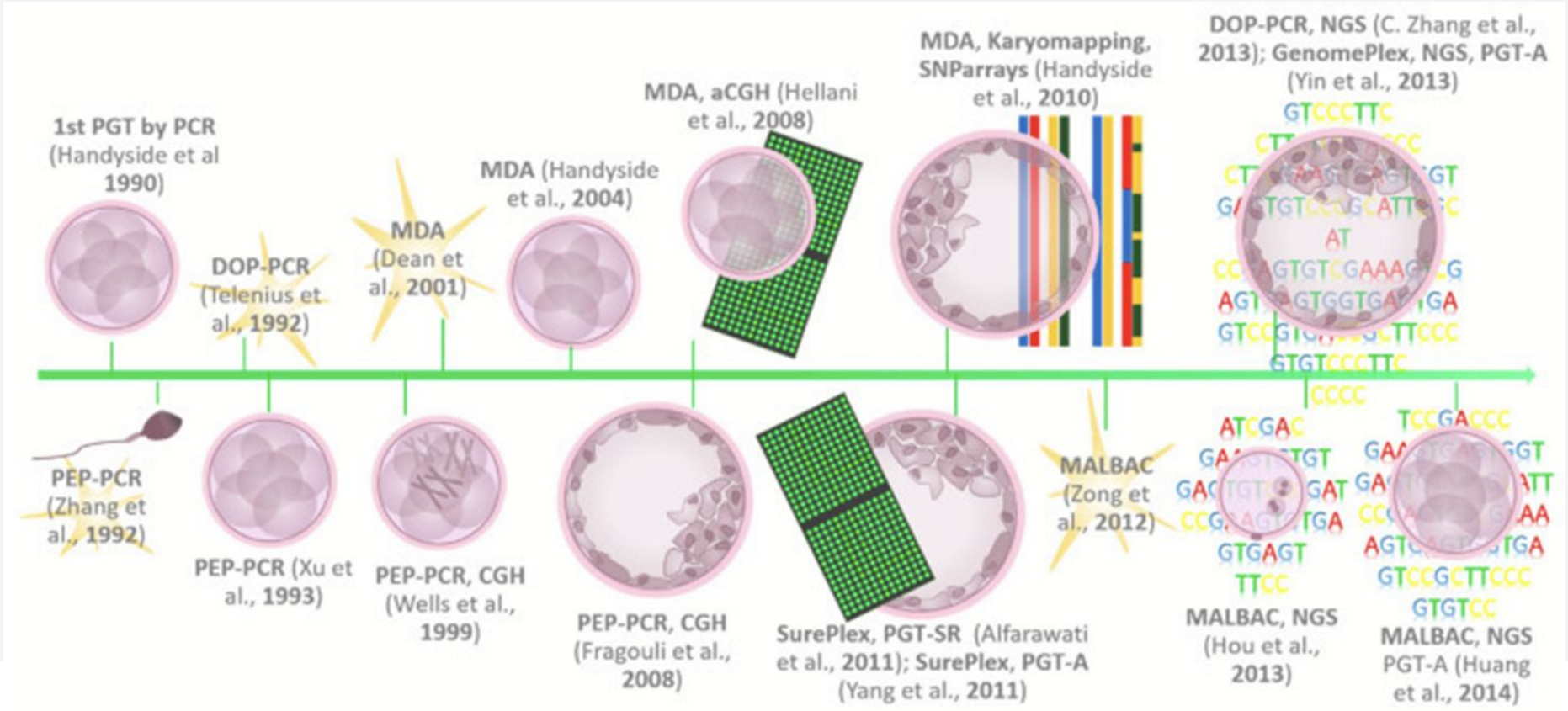

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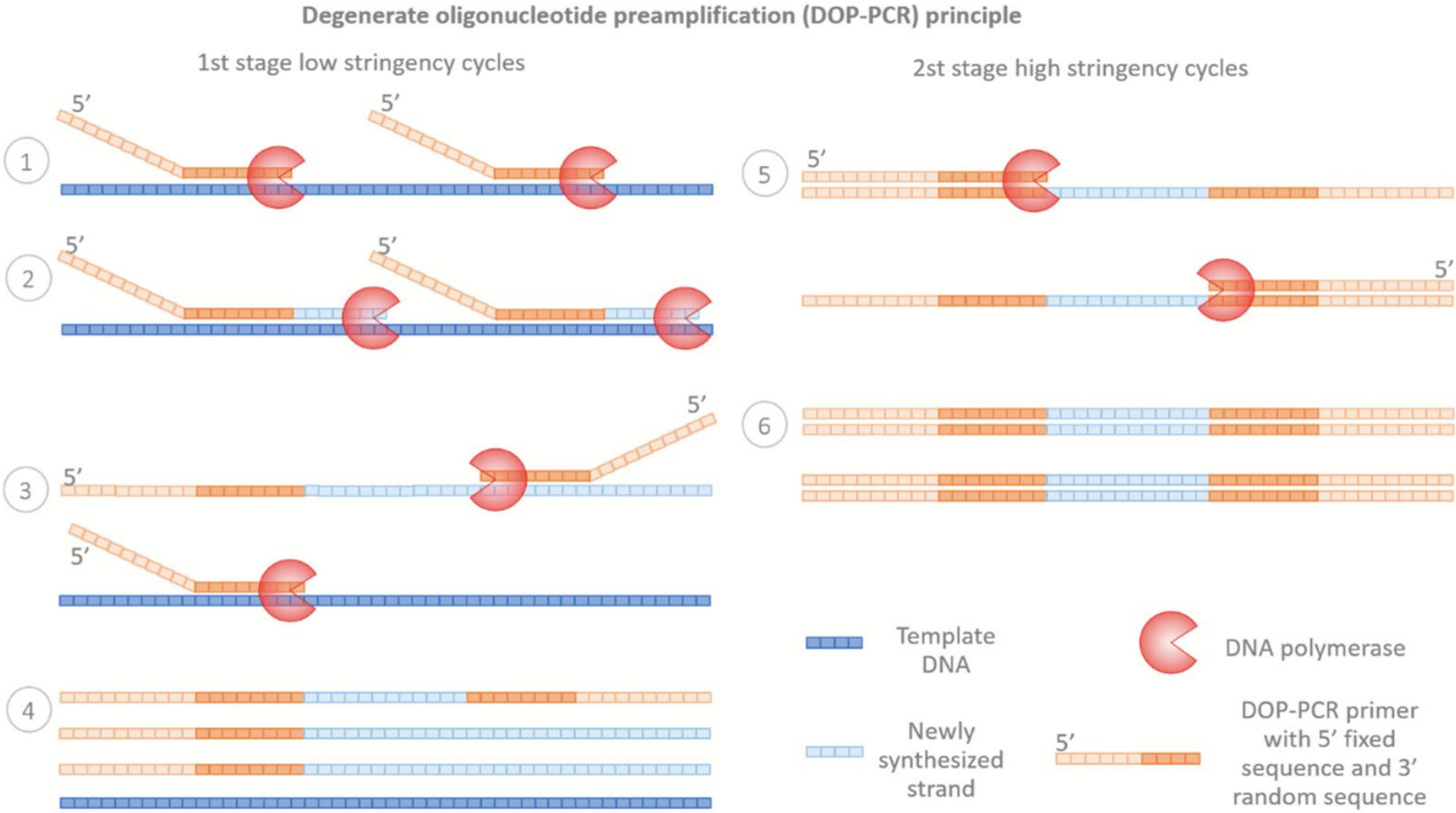

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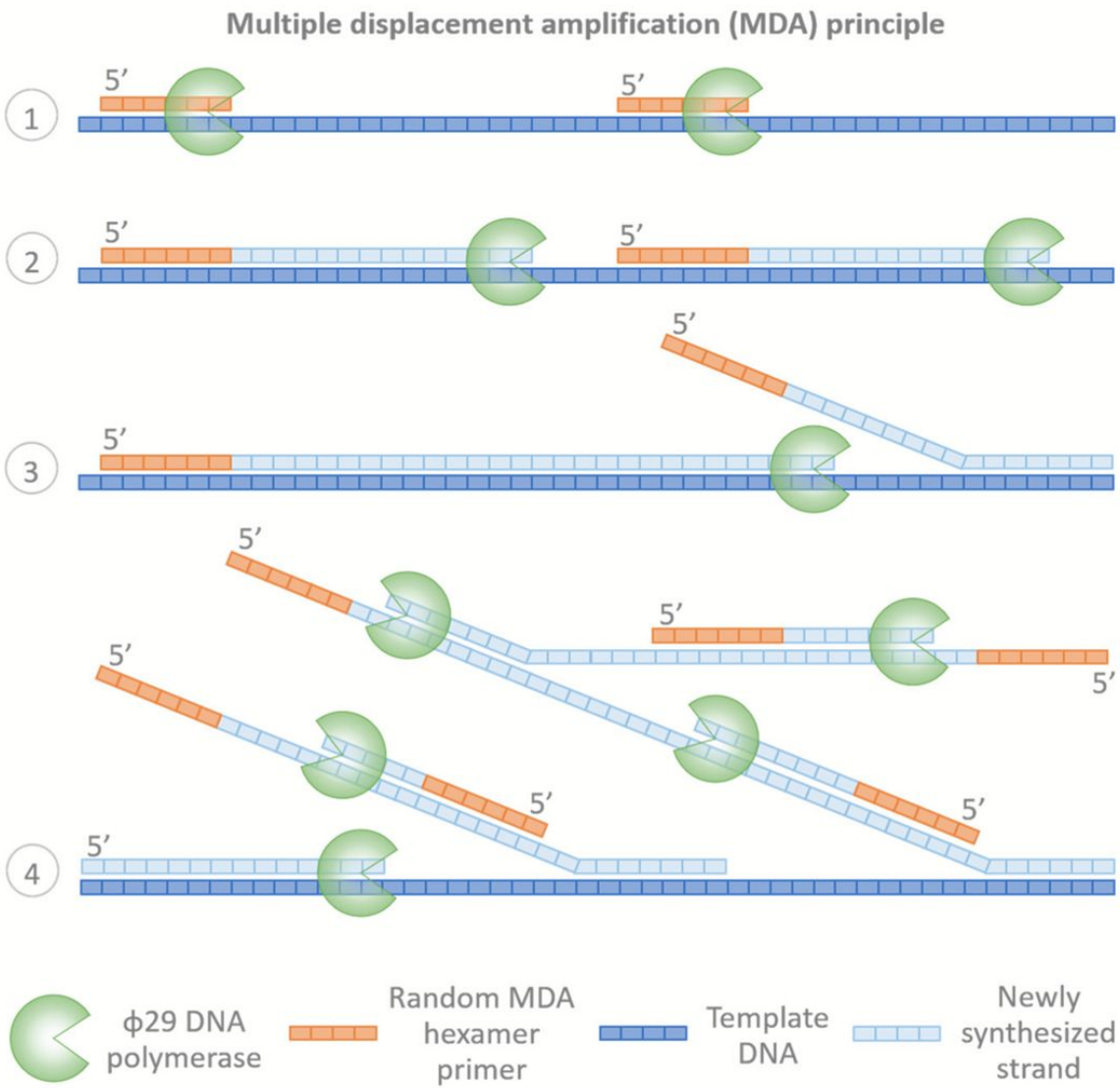

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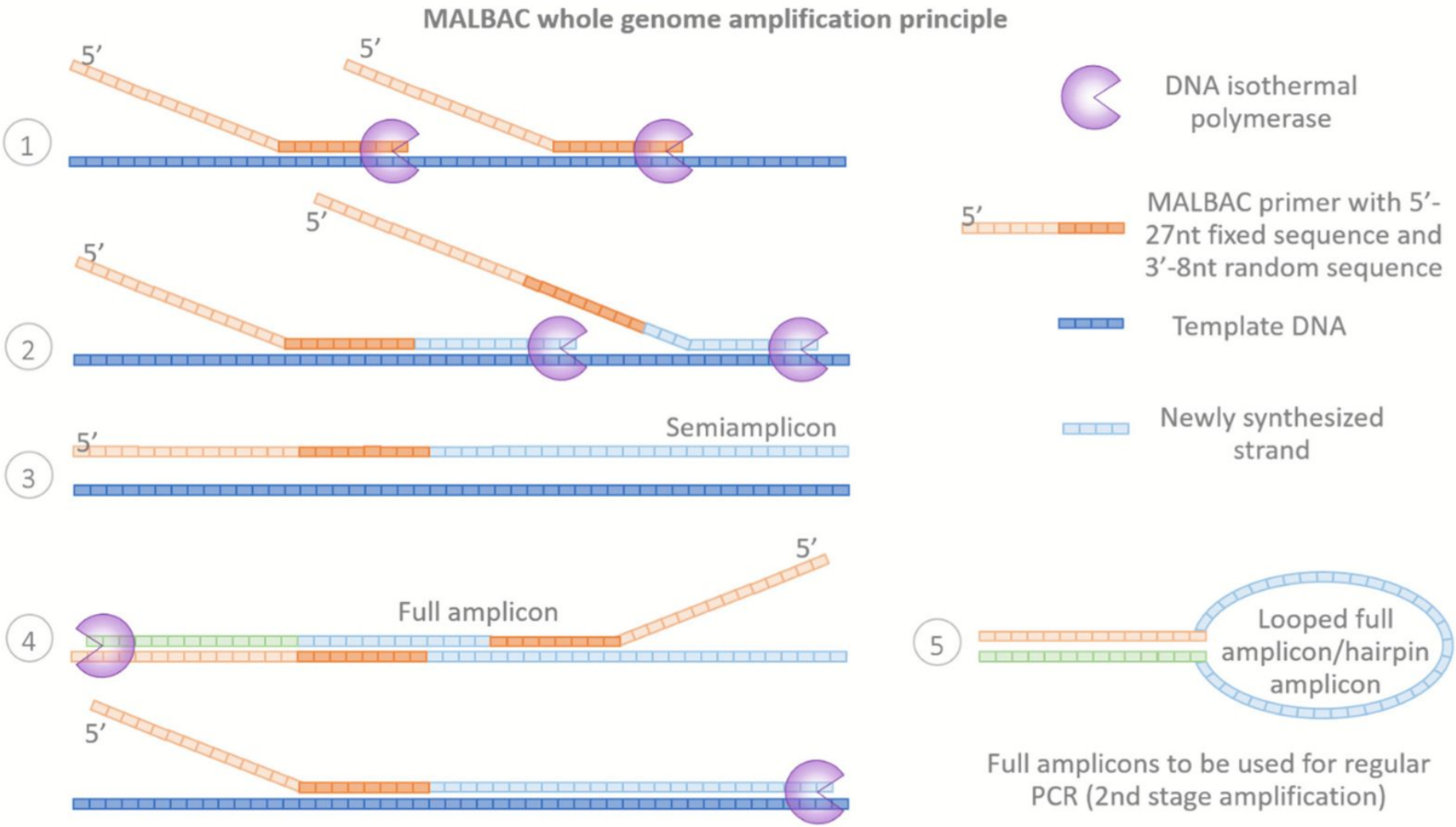

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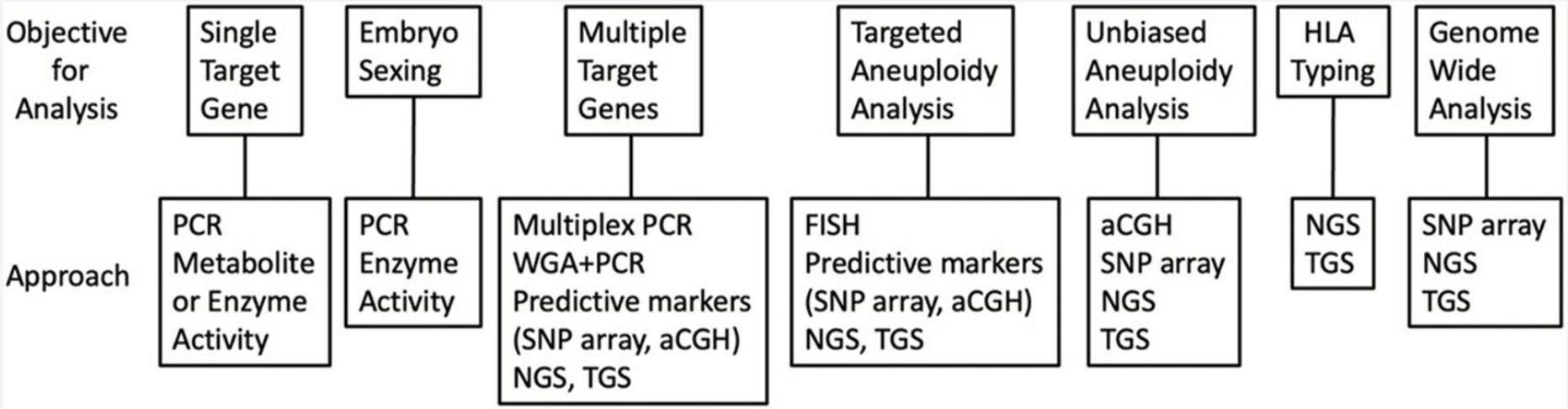

Latham K. E. (2024). Preimplantation genetic testing: A remarkable history of pioneering, technical challenges, innovations, and ethical considerations. *Molecular reproduction and development*, *91*(1), e23727

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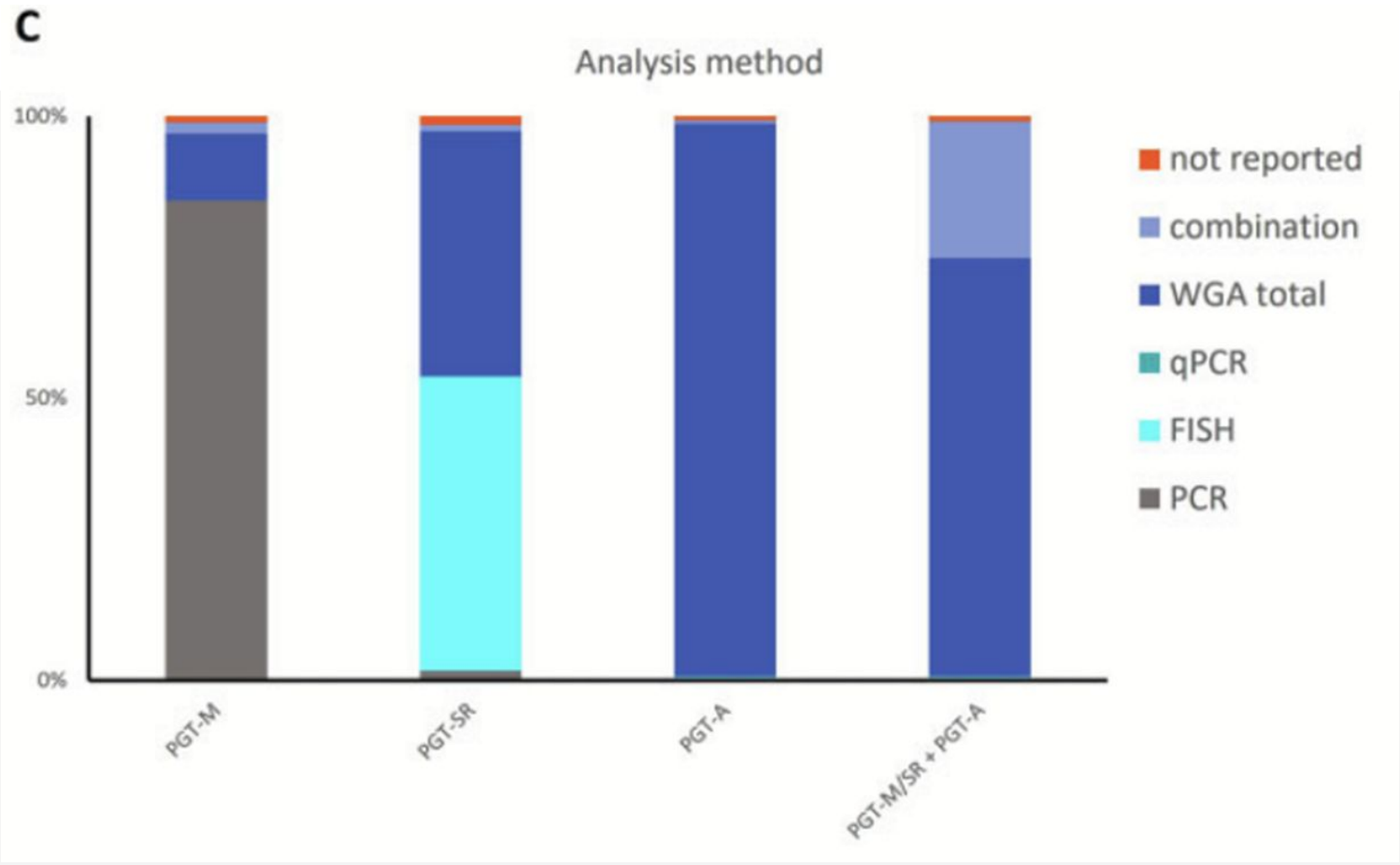
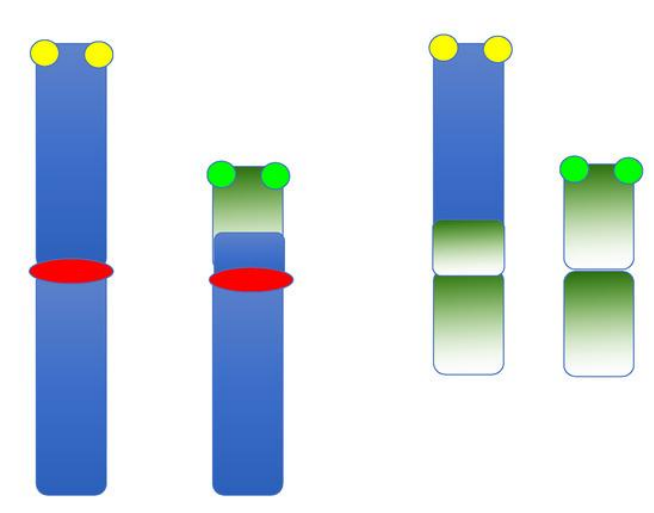


Spinella, F. et al. (2023). ESHRE PGT Consortium data collection XXI: PGT analyses in 2018. *Human reproduction open*, *2023*(2)

PGT-SR



FISH fue primera técnica usada

Intensiva en labor y limitada a regiones de interés

PGT-SR

STR-typing: PCR con primers flanqueando puntos de corte

- Puede detectar contaminación/disomía uniparental
- Laborioso, caso-específico, no escalable

aCGH

- Detecta imbalances de dosaje, no detecta balanceados

PGT-SR

CERPO

SNP array/karyomapping:

- Mayor resolución que aCGH
- Detecta haplotipos parentales, puede distinguir balanceados de no balanceados
- Requiere usualmente muestra de afectado y SNPs informativos cerca de punto de corte

NGS

- Gold standard actual, facilita estudio combinado (A, M, SR)
- No detecta portadores balanceados

Limitaciones

- Muestra puede no representar al embrión completo (mosaicismo con relevancia clínica incierta)
- WGA: riesgos de allele dropout, coverage disparejo o errores de amplificación
  - Sensibilidad limitada para CNVs, rearreglos balanceados o heteroplasmia de mtDNA
- Variabilidad interlaboratorio en reporte de mosaicismo

Kakourou, G et al. (2024). The current clinical applications of preimplantation genetic testing (PGT): acknowledging the limitations of biology and technology. *Expert review of molecular diagnostics*, *24*(9), 767–775.

Limitaciones

- Interpretación compleja de VUS y niveles de heteroplasmia de mtDNA
- Limitaciones biológicas inherentes:
  - Alta prevalencia de mosaicismo en embriones tempranos que resuelve espontáneamente
  - Epigenética asociada a FIV/PGT desconocida

Kakourou, G et al. (2024). The current clinical applications of preimplantation genetic testing (PGT): acknowledging the limitations of biology and technology. *Expert review of molecular diagnostics*, *24*(9), 767–775.

Limitaciones

Outcome studies after transfer of embryos with mosaic results.

Study	Embryos with mosaic results included, n[a]	Outcome: OP and LB	Outcome: SAB and biochemical pregnancies
Prospective			
Greco et al. 2015 (11)	18	6 of 18 (33.3%) LB rate; confirmed normal chromosomes by CV karyotype.	2 of 18 (11.1%) biochemical pregnancy rate; 0 of 6 (0%) SAB rate.
Munné et al. 2017 (6)	143	58 of 143 (40.6%) OP rate; no LB or karyotype confirmation data.	18 of 76 (23.7%) SAB rate per clinical pregnancy with GS.
Spinella et al. 2018 (21)	78	24 of 78 (30.8%) LB rate; no karyotype confirmation data.	6 of 30 (20.0%) SAB rate per clinical pregnancy with GS.
Victor et al. 2019 (22)	100	30 of 100 (30.0%) combined OP and LB rate per embryo transferred; 8 of 11 amniocenteses with confirmed normal chromosomes; 3 of 11 with chromosomal abnormalities of unspecified clinical significance.	7 of 37 (18.9%) SAB rate per clinical pregnancy with GS.
Retrospective[b]			
Maxwell et al. 2016 (23)	18	6 of 38 (15.8%) LB from aCGH embryos deemed euploid retroactively found to be mosaic by NGS.	12 of 38 (31.6%) of SAB from aCGH embryos deemed euploid retroactively found to be mosaic by NGS.
Fragouli et al. 2017 (24)	44	12 of 44 (27.3%) LB rate.	5 of 17 (29.4%) SAB rate per clinical pregnancy.
Lledó et al. 2017 (25)	52	13 of 52 (25.0%) combined OP and LB rate, 10 LB reported to be healthy.	1 of 14 (7.1%) SAB rate.
Zhang et al. 2019 (10)	102	48 of 102 (47%) LB rate; 3 of 3 amniocenteses with confirmed normal chromosomes. "All infants were found to be healthy after a detailed physical examination performed by a local pediatrician after delivery."	8 of 67 (11.9%) biochemical pregnancy rate; 12 of 59 (20.3%) SAB rate per clinical pregnancy.

Note: aCGH = array comparative genomic hybridization; CV = chorionic villi; GS = gestational sac; LB = live birth; NGS = next-generation sequencing; OP = ongoing pregnancy; SAB = spontaneous abortion.

Practice Committee and Genetic Counseling Professional Group (GCPG) of the American Society for Reproductive Medicine. Electronic address: asrm@asrm.org (2020). Clinical management of mosaic results from preimplantation genetic testing for aneuploidy (PGT-A) of blastocysts: a committee opinion. *Fertility and sterility*, *114*(2), 246–254.

Classifications and considerations for PGT-A mosaic results.

Category	Theory	Considerations
Percentage of mosaicism	A lower level of mosaicism (i.e., fewer aneuploid cells in a trophectoderm biopsy) is likely associated with a better outcome.	Data regarding clinical outcomes associated with higher vs. lower proportion of aneuploid cells in a trophectoderm biopsy have been inconsistent. Some studies have found that lower-level mosaicism is associated with improved ongoing pregnancy rates (21); while others have not found a statistically significant difference (6, 22, 27). Data do not support an equal distribution of mosaicism throughout the trophectoderm (28), suggesting that mosaicism levels may be highly dependent on the site of biopsy. Prenatal and postnatal data do not support an association between the level of mosaicism and phenotypic outcome (18).
Specific chromosome(s) involved	Mosaicism involving certain chromosomes is more likely to: Result in a viable, ongoing pregnancy despite a persisting aneuploid cell line in the fetus. Pose a risk for UPD syndromes. Pose a risk for fetal growth restriction if aneuploid cells persist in the placenta.	While there are data regarding mosaicism identified prenatally or postnatally and associated risks/outcomes depending on the specific chromosome number involved (16), it is not known whether this mosaicism is mechanistically related to embryonic mosaicism nor how well such data can be extrapolated to potential risks of transfer of an embryo with mosaic results. Mosaic aneuploidies involving most chromosomes have been reported in pregnancies or live births with abnormal phenotypes (18, 19).
Monosomy vs. trisomy	Monosomies of most chromosomes are not viable.	Current PGT-A methodologies cannot distinguish a pure monosomy or trisomy cell line from mixed reciprocal monosomy/trisomy cell lines present in the same biopsy (8). No difference in pregnancy or SAB rates has been seen when comparing embryos mosaic for monosomies vs. trisomies (6, 22). While pure non-mosaic monosomies are not viable (with the exception of 45,X), live births with mosaic autosomal monosomies have been reported in the literature (29).
Full chromosome vs. partial chromosome	Aneuploidies involving a full chromosome may have different chances of viability compared to those involving a chromosomal segment (deletion or duplication).	Data regarding clinical outcomes from embryos mosaic for full vs. partial aneuploidies have been inconsistent. Some studies have found a higher ongoing pregnancy rate for partial chromosome mosaics (10, 22, 24); while others have not found a difference (6). There are currently no data supporting an increased chance of viability with persisting fetal mosaicism of a partial chromosome aneuploidy compared to a full chromosome aneuploidy. Data suggest that mosaicism reported for partial chromosome aneuploidies are more likely to represent false-positive results due to test artifact (1), suggesting that these embryos may have better implantation potential. Prenatal and postnatal literature suggests that, in general, the smaller the chromosome segment, the more likely it is to be compatible with life with an abnormal phenotype (30). Due to the limited resolution of PGT-A platforms, it is essential to recognize that deletions and duplications detected by PGT-A are generally much larger than those detected in ongoing pregnancies or live births.
No. of chromosomes involved	Embryos diagnosed as mosaic for multiple chromosome aneuploidies may have lower chances of ongoing pregnancy.	There are some data indicating reduced pregnancy potential of embryos diagnosed as mosaic for three or more chromosomes (6) or segmental mosaic for two or more chromosomes (22); however, other studies did not find a significant difference between mosaicism involving one vs. two chromosomes (6, 25).

Note: PGT-A = preimplantation genetic testing for aneuploidy; SAB = spontaneous abortion; UPD = uniparental disomy.

ASRM. Clinical management of mosaic results. Fertil Steril 2020.

Practice Committee and Genetic Counseling Professional Group (GCPG) of the American Society for Reproductive Medicine. Electronic address: asrm@asrm.org (2020). Clinical management of mosaic results from preimplantation genetic testing for aneuploidy (PGT-A) of blastocysts: a committee opinion. *Fertility and sterility*, *114*(2), 246–254.

J Mol Diagn. 2021 Jun;23(6):710-718. doi: 10.1016/j.jmoldx.2021.02.011. Epub 2021 Mar 26.

Next-Generation Sequencing Is More Efficient at Detecting Mosaic Embryos and Improving Pregnancy Outcomes than Single-Nucleotide Polymorphism Array Analysis

Min Xiao [1], Cai-Xia Lei [2], Yan-Ping Xi [2], Yu-Lin Lu [3], Jun-Ping Wu [2], Xiao-Yu Li [3], Shuo Zhang [1], Sai-Juan Zhu [2], Jing Zhou [2], Xiong Li [2], Yue-Ping Zhang [2], Xiao-Xi Sun [4]

Table 2 Frequency of Euploid, Aneuploid, or Mosaicism in TE with Either NGS-Based PGT or SNP Array–Based PGT

Characteristics	SNP array (n = 3131)	NGS (n = 3296)	P value
Euploid	48.6 (1521/3131)	41.6 (1372/3296)	<0.001
Aneuploid	46.5 (1457/3131)	43.5 (1433/3296)	0.0148
Mosaicism	7.7 (240/3131)	23.3 (767/3296)	<0.001
Euploid and mosaicism (only mosaicism)	4.9 (153/3131)	14.9 (491/3296)	<0.001
Aneuploidy and mosaicism	2.8 (87/3131)	8.4 (276/3296)	<0.001

Data are given as percentage (number/total). Mosaicism includes whole-chromosome and copy number variation–level mosaicism.
NGS, next-generation sequencing; PGT, preimplantation genetic testing; SNP, single-nucleotide polymorphism; TE, trophectoderm.

Table 3 Pregnancy Outcomes for Patients Undergoing Frozen-Thawed Embryo Transfer with Either NGS-Based PGT or SNP Array–Based PGT with Adjusted Values after Multiple Logistic Regression Analysis

Characteristics	SNP array–based PGT (n = 596)	NGS-based PGT (n = 458)	P value
PHCG	60.57 (361/596)	59.39 (272/458)	0.7453
IR	51.34 (306/596)	49.56 (227/458)	0.6097
FHB	47.82 (285/596)	45.85 (210/458)	0.5673
BPR	9.56 (57/596)	10.48 (48/458)	0.6974
SAB	10.07 (60/596)	6.33 (29/458)	**0.0403**
OP/LBR	42.28 (252/596)	44.1 (202/458)	0.5963

Data are given as percentage (number/total). Significant P values are boldfaced.
BPR, biochemical pregnancy rate; FHB, fetal heartbeat; IR, implantation rate; NGS, next-generation sequencing; OP/LBR, ongoing pregnancy/live birth rate; PGT, preimplantation genetic testing; PHCG, positive human chorionic gonadotropin; SAB, spontaneous abortion; SNP, single-nucleotide polymorphism.

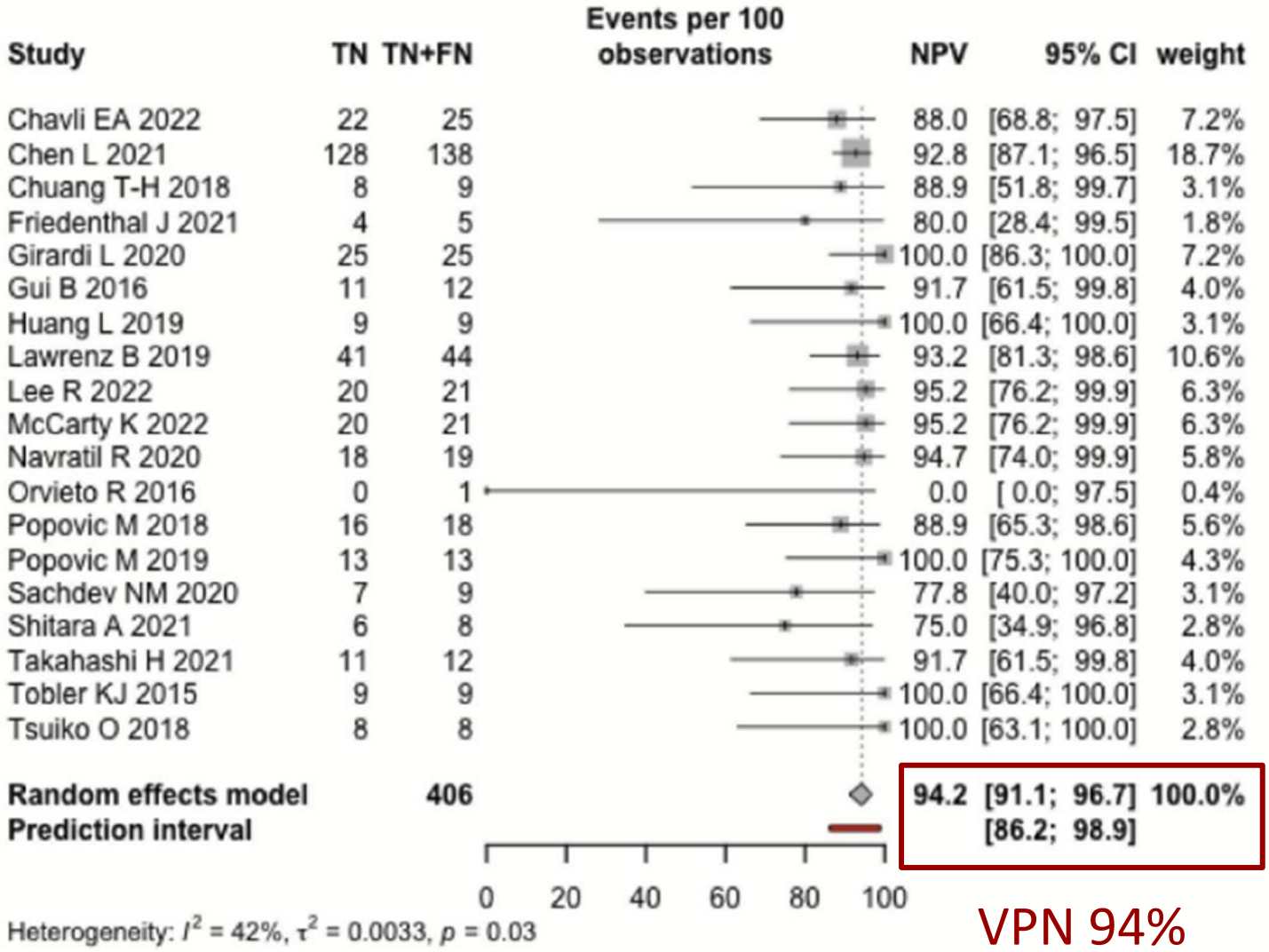
NGS tendría mayor rendimiento que array SNP para detección de mosaicismo

Xiao, M. et al. (2021). Next-Generation Sequencing Is More Efficient at Detecting Mosaic Embryos and Improving Pregnancy Outcomes than Single-Nucleotide Polymorphism Array Analysis. *The Journal of molecular diagnostics : JMD*, *23*(6), 710–718

Rendimientos

PGT-A

a. Negative predictive value of euploid embryos



VPN 94%

Bacal, V. et al. (2025). A systematic review and meta-analysis of the diagnostic accuracy after preimplantation genetic testing for aneuploidy. *PloS one*, *20*(5), e0321859.

PGT-A

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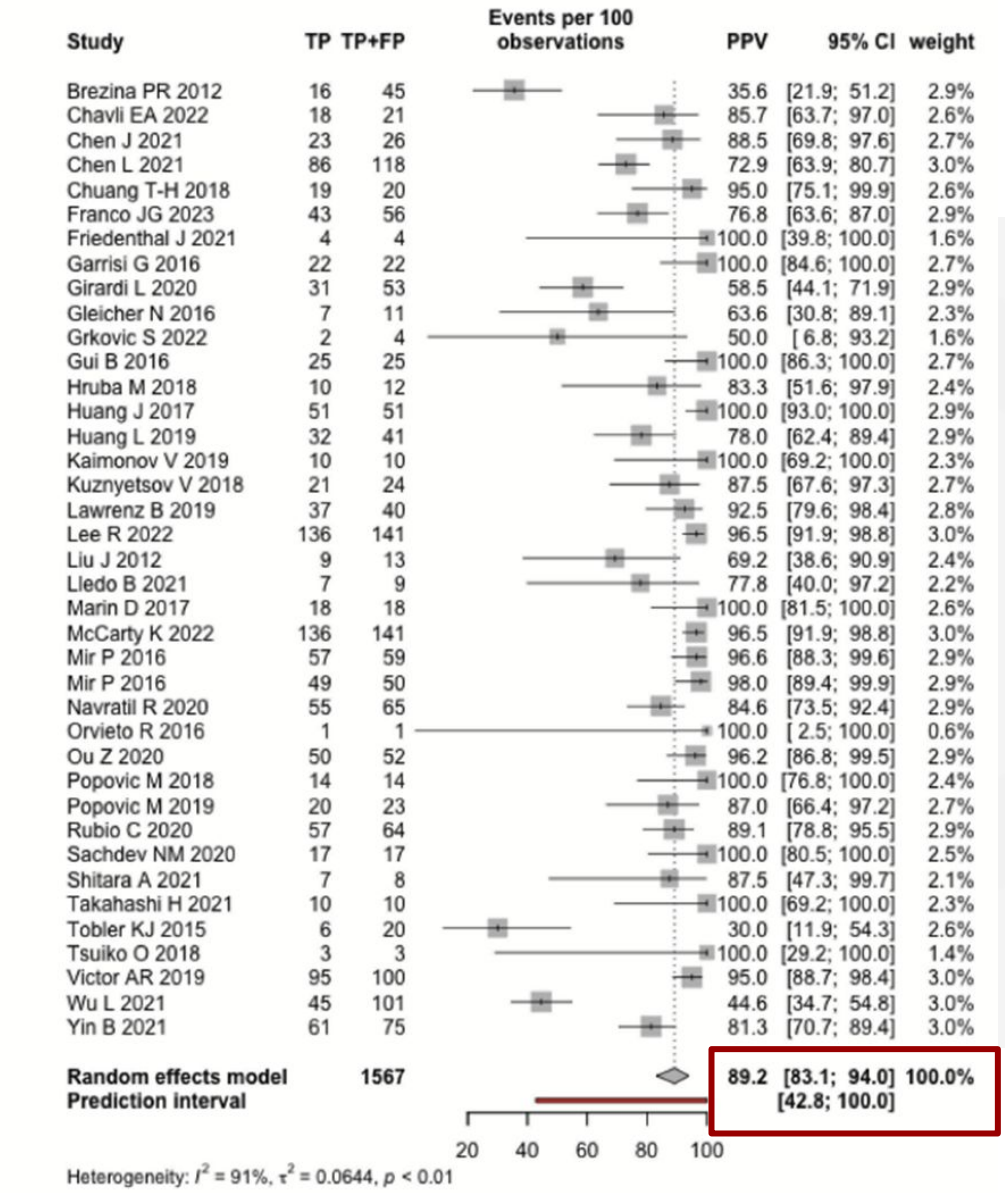
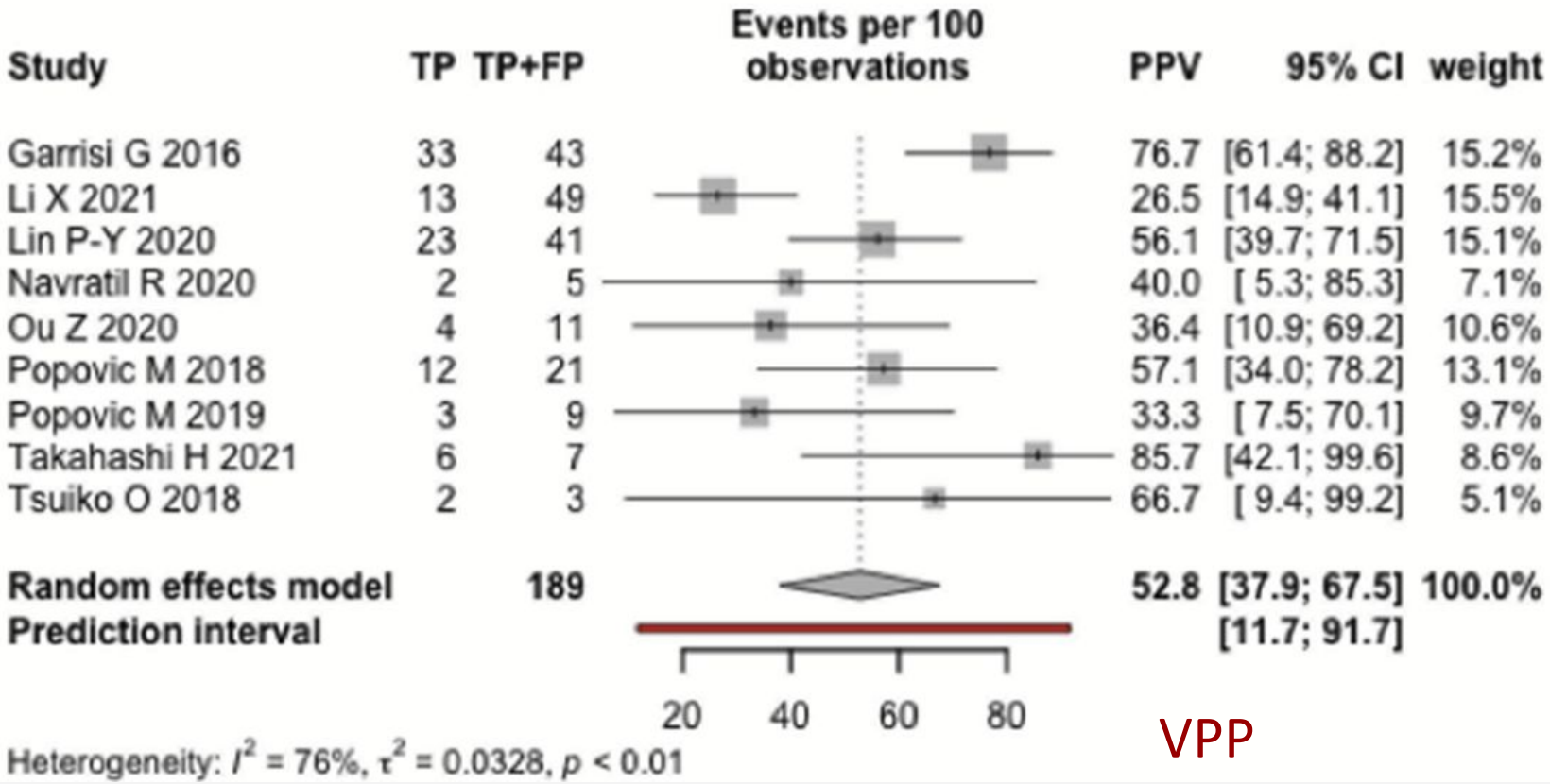
b. Positive predictive value of aneuploid embryos



VPP 89%

Bacal, V. et al. (2025). A systematic review and meta-analysis of the diagnostic accuracy after preimplantation genetic testing for aneuploidy. *PloS one*, *20*(5), e0321859.

c. Positive predictive value of mosaic embryos



VPP mosaicismo

Bacal, V. et al. (2025). A systematic review and meta-analysis of the diagnostic accuracy after preimplantation genetic testing for aneuploidy. *PloS one*, *20*(5), e0321859.

a. Euploid embryo transfer

PGT-A

Study	Misdiagnosed	Embryos Transferred	Events per 100 observations	rate	95% CI	weight
Chamayou S 2015	0	7		0.0	[0.0; 41.0]	0.7%
Chen D 2020	0	16		0.0	[0.0; 20.6]	1.5%
Daina G 2015	0	11		0.0	[0.0; 28.5]	1.1%
Friedenthal J 2020	19	1997		1.0	[0.6; 1.5]	6.9%
Hu X 2024	0	19		0.0	[0.0; 17.6]	1.7%
Huang C 2022	0	3		0.0	[0.0; 70.8]	0.3%
Huang J 2015	0	7		0.0	[0.0; 41.0]	0.7%
Katz-Jaffe M 2023	22	3992		0.6	[0.3; 0.8]	7.0%
Kim JG 2021	39	6671		0.6	[0.4; 0.8]	7.0%
Ma GC 2016	0	30		0.0	[0.0; 11.6]	2.3%
Ma X 2021	0	215		0.0	[0.0; 1.7]	5.5%
Maxwell SM 2016	4	76		5.3	[1.5; 12.9]	3.9%
Ou Z 2022	0	29		0.0	[0.0; 11.9]	2.3%
Ruttanajit T 2016	0	12		0.0	[0.0; 26.5]	1.2%
Scott RT 2012	0	133		0.0	[0.0; 2.7]	4.9%
Tan Y 2014	0	406		0.0	[0.0; 0.9]	6.2%
Tao X 2020	11	120		9.2	[4.7; 15.8]	4.7%
Tiegs AW 2016	5	579		0.9	[0.3; 2.0]	6.4%
Tiegs AW 2021	0	312		0.0	[0.0; 1.2]	5.9%
Treff NR 2011	0	20		0.0	[0.0; 16.8]	1.8%
Volozonoka L 2018	0	6		0.0	[0.0; 45.9]	0.6%
Wang J 2018	0	10		0.0	[0.0; 30.8]	1.0%
Wang Y 2021	0	8		0.0	[0.0; 36.9]	0.8%
Wang Y 2023	0	6		0.0	[0.0; 45.9]	0.6%
Wells D 2009	0	42		0.0	[0.0; 8.4]	2.9%
Werner MD 2014	10	4974		0.2	[0.1; 0.4]	7.0%
Yang J 2021	0	9		0.0	[0.0; 33.6]	0.9%
Zhai F 2022	0	73		0.0	[0.0; 4.9]	3.9%
Zhang L 2019	0	370		0.0	[0.0; 1.0]	6.1%
Zhang S 2017	0	13		0.0	[0.0; 24.7]	1.2%
Zhang S 2019	0	6		0.0	[0.0; 45.9]	0.6%
Zhang S 2021	0	12		0.0	[0.0; 26.5]	1.2%
Zhou Z 2018	0	12		0.0	[0.0; 26.5]	1.2%
Random effects model		20196		0.2	[0.0; 0.7]	100.0%
Prediction interval					[0.0; 3.4]	

0 10 20 30 40 50 60 70

Heterogeneity: $I^2 = 65\%$, $\tau^2 = 0.0041$, $p < 0.01$

Fig 3. Forest plots for pregnancy outcomes: misdiagnosis rate. a. Euploid embryo transfer. b. Aneuploid embryo transfer. c. Non-selection embryo transfer. d. Mosaic embryo transfer.

Tasa de error diagnóstico mínima en transferencia de embrión euploide

Bacal, V. et al. (2025). A systematic review and meta-analysis of the diagnostic accuracy after preimplantation genetic testing for aneuploidy. *PloS one*, *20*(5), e0321859.

PGT-A

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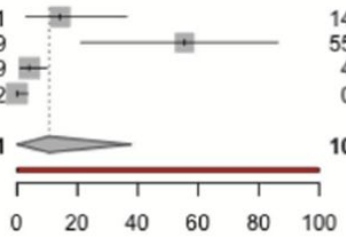
b. Aneuploid embryo transfer

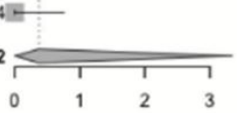
Study	Misdiagnosed	Embryos Transferred	Events per 100 observations	rate	95% CI	weight
Barad DH 2022	3	21		14.3	[3.0; 36.3]	24.7%
Gleicher N 2016	5	9		55.6	[21.2; 86.3]	21.7%
Scott RT 2012	4	99		4.0	[1.1; 10.0]	26.8%
Tiegs AW 2021	0	102		0.0	[0.0; 3.6]	26.8%
Random effects model		**231**		**10.6**	**[0.0; 38.1]**	**100.0%**
Prediction interval					**[0.0; 100.0]**	



Heterogeneity: $I^2 = 91\%$, $\tau^2 = 0.1049$, $p < 0.01$

c. Non-selection embryo transfer

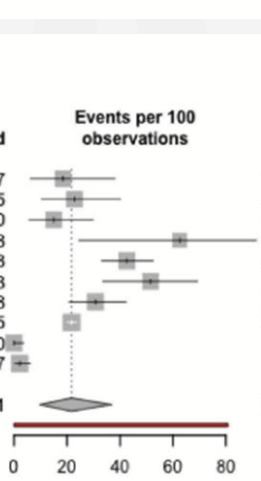
Study	Misdiagnosed	Embryos Transferred	Events per 100 observations	rate	95% CI	weight
Scott RT 2012	4	255		1.6	[0.4; 4.0]	48.5%
Shen X 2019	.	33				0.0%
Tiegs AW 2021	0	484		0.0	[0.0; 0.8]	51.5%
Random effects model		**772**		**0.4**	**[0.0; 3.3]**	**100.0%**



Heterogeneity: $I^2 = 91\%$, $\tau^2 = 0.0071$, $p < 0.01$

d. Mosaic embryo transfer

Study	Misdiagnosed	Embryos Transferred	Events per 100 observations	rate	95% CI	weight
Aharon D 2022	5	27		18.5	[6.3; 38.1]	9.6%
Barad DH 2022	8	35		22.9	[10.4; 40.1]	9.9%
Besser AG 2019	6	40		15.0	[5.7; 29.8]	10.0%
Fernandez Sanguino A 2022	5	8		62.5	[24.5; 91.5]	7.5%
Lin P-Y 2020	46	108		42.6	[33.1; 52.5]	10.6%
Rubino P 2018	17	33		51.5	[33.5; 69.2]	9.8%
Spinella F 2018	24	78		30.8	[20.8; 42.2]	10.4%
Spinella F 2023	445	2045		21.8	[20.0; 23.6]	10.9%
Victor AR 2019	0	100		0.0	[0.0; 3.6]	10.5%
Zhang YX 2020	3	137		2.2	[0.5; 6.3]	10.7%
Random effects model		**2611**		**21.7**	**[9.6; 36.9]**	**100.0%**
Prediction interval					**[0.0; 80.8]**	



Heterogeneity: $I^2 = 95\%$, $\tau^2 = 0.0678$, $p < 0.01$

20% de embriones transferidos con PGT mosaico no serían mosaico

Bacal, V. et al. (2025). A systematic review and meta-analysis of the diagnostic accuracy after preimplantation genetic testing for aneuploidy. *PloS one*, *20*(5), e0321859.

PGT-M

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Table 4 Factors affecting the diagnostic accuracy of PGD; Results from simple and multiple logistic regression by using centre as a cluster factor ($N = 923$[a])

	Crude OR (95% CI)	*Adjusted OR (95% CI)*
No. of cells used in PGD		
One cell	Ref	Ref
Two cells	**2.66 (1.35–5.24)**	**2.64 (1.71–4.06)**
Disease category		
AR	Ref	Ref
AD	**2.40 (1.77–3.26)**	**2.51 (1.50–4.20)**
XL-R	2.58 (0.87–7.69)	2.48 (0.85–7.26)
XL-D	**6.53 (2.90–14.72)**	**7.92 (4.54–13.80)**
PCR-PGD protocol		
Multiplex	Ref	Ref
Singleplex	0.84 (0.52–1.35)	**0.50 (0.27–0.92)**
Embryo morphology		
Class 1	Ref	Not included[b]
Class 4	1.30 (0.30–5.74)	
Combined biopsy-PGD-PCR strategies		
Singleplex one cell	Ref	Not included[c]
Singleplex two cells	**2.96 (1.77–4.94)**	
Multiplex one cell	1.47 (0.63–3.41)	
Multiplex two cells	**4.18 (2.20–7.90)**	

Bold reflects statistically significant results.

Tipo de herencia de enfermedad parece afectar la precisión diagnóstica del PGT-M

Dreesen, J. et al. (2014). Evaluation of PCR-based preimplantation genetic diagnosis applied to monogenic diseases: a collaborative ESHRE PGD consortium study. *European journal of human genetics : EJHG*, *22*(8), 1012–1018

PGT-M

CERPO

Table 5 Validity of PCR-PGD analysis compared with embryo reanalysis ($n = 808$ embryos, excluding aberrant)

	No. of subjects				Validity		
	TP	*FN*	*TN*	*FP*	*Se (95% CI)*	*Sp (95% CI)*	*Accuracy (95% CI)*
Overall	556	2	229	21	99.6% (98.7–99.9%)	91.6% (87.4–94.7%)	97.2% (95.8–98.2%)
Disease category							
AR	97	1	96	12	98.9% (94.4–99.9%)	88.9% (81.4–94.1%)	93.7% (89.4–96.6%)[a]
AD	382	0	104	7	100% (99.0–100%)	93.7% (87.4–97.4%)	98.6% (97.1–99.4%)[a]
XL-R	41	1	20	1	97.6% (87.4–99.9%)	95.2% (76.2–99.9%)	96.8% (89.0–99.9%)
XL-D	36	0	9	1	100% (90.2–100%)	90.0% (55.5–99.7%)	97.8% (88.5–99.9%)

Dreesen, J. et al. (2014). Evaluation of PCR-based preimplantation genetic diagnosis applied to monogenic diseases: a collaborative ESHRE PGD consortium study. *European journal of human genetics : EJHG*, *22*(8), 1012–1018

JOURNAL ARTICLE

Validation of preimplantation genetic diagnosis by PCR analysis: genotype comparison of the blastomere and corresponding embryo, implications for clinical practice

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J. Dreesen, M. Drüsedau, H. Smeets, C. de Die-Smulders, E. Coonen, J. Dumoulin, M. Gielen, J. Evers, J. Herbergs, J. Geraedts

Molecular Human Reproduction, Volume 14, Issue 10, October 2008, Pages 573–579,

PGT-M

Table III. Conversion of genotype outcome to diagnostic outcome for the different blastomere/embryo genotypes outcome groups.

Genotype outcome groups		Blastomeres/embryos compared (*N*)	Diagnostic outcome groups			
			T−D−	T−D+	T+D+	T+D−
Concordant		367	167	0	200	0
Discordant	ADO explained	32	5	0	8	19
	Contaminated	4	0	0	3	1
	Not confirmed	19	2	7	7	3
	Total	422	174	7	218	23

Table IV. Validation of the PGD–PCR analysis.

	Validity and diagnostic value of the PGD–PCR analysis		
	Total group	Class 1 group	Class 1 excluded
Sensitivity	96.9% (218/225)	82.9% (29/35)*	99.5% (189/190)*
False negative	3.1% (7/225)	17.1% (6/35)*	0.5% (1/190)*
Specificity	88.3% (174/197)	93.1% (27/29)	87.5% (147/168)
False positive	11.7% (23/197)	6.9% (2/29)	12.5% (21/168)
Accuracy	92.9% (392/422)	87.5% (56/64)	93.9% (336/358)
Misdiagnosis	7.1% (30/422)	12.5% (8/64)	6.1% (22/358)
LR (positive test)	8.30	12.01	8.00
LR (negative test)	0.04	0.18	0.006
Negative predictive value	96.1% (174/181)	81.8% (27/33)*	99.3% (147/148)*
Positive predictive value	90.5% (218/241)	93.6% (29/31)	90.0% (189/210)

*Significant different when Class 1 group compared with Class 1 excluded group; $P < 0.001$.

VPN sobre 99%

Dreesen, J. et al.. (2008). Validation of preimplantation genetic diagnosis by PCR analysis: genotype comparison of the blastomere and corresponding embryo, implications for clinical practice. *Molecular human reproduction*, *14*(10), 573–579

Clinical utility of combined preimplantation genetic testing methods in couples at risk of passing on beta thalassemia/ hemoglobin E disease: A retrospective review from a single center

Chonthicha Satirapod, Matchuporn Sukprasert, Bhakbhoom Panthan, Angkana Charoenyingwattana, Pawares Chitayanan, Wasun Chantratita, Wicharn Choktanasiri, Objoon Trachoo, Suradej Hongeng

PGT-M

CERPO

Total IVF cycles (n)	22
Embryos tested for thalassemia PGT-M [n (%)]	106 (100)
• Wild type	25 (23.58)
• Disease affected	43 (40.57)
• Carriers	28 (26.42)
• Inconclusive	4 (3.77)
• Failed whole genome amplification	6 (5.66)
Allele drop-out rate (%)	3.89
Number of couples obtaining successful genetic testing within the first 2 cycles [n (%)]	15 (100)
• Satisfactory embryo outcome	12 (80)
• Unsatisfactory embryo outcome (unable to transfer)	3 (20)
Implantation rate after embryo transfer [n (%)]	14 (100)
• Successful implantation	9 (64.29)
• Unsuccessful implantation	5 (35.71)
Accuracy of PGT by prenatal and postnatal confirmation (%)	100
Successful pregnancy after the first cycle of treatment (%)	40
Overall clinical outcome within the first 2 cycles of 15 families [n (%)]	15 (100)
• Successful pregnancy with live birth	8 (53.33)
• Successful pregnancy with first trimester miscarriage	1 (6.67)
• Failed implantation in both cycles	1 (6.67)
• Failed implantation in the first cycle and subsequent treatment cessation	2 (13.33)
• Unable to transfer in both cycles	1 (6.67)
• Unable to transfer in the first cycle and subsequent treatment cessation	2 (13.33)
Average IVF cycle number in nine women with successful pregnancy (mean ± SD)	1.33 ± 0.50

Satirapod, C. et al. (2019). Clinical utility of combined preimplantation genetic testing methods in couples at risk of passing on beta thalassemia/hemoglobin E disease: A retrospective review from a single center. *PloS one*, *14*(11), e0225457

Preimplantation genetic testing for structural rearrangements by genome-wide SNP genotyping and haplotype analysis: a prospective multicenter clinical study

PGT-SR

CERPO

Shuo Zhang,[a,b,c,aa] Yuan Gao,[d,e,f,g,h,i,aa] Xiaohong Wang,[j,aa] Qing Li,[k,aa] Jichun Tan,[l,m,aa] Bo Liang,[n,aa] Ming Gao,[d,e,f,g,h,i,aa] Junping Wu,[a,b,c] Xiufeng Ling,[o] Jiayin Liu,[p] Xiaoming Teng,[q] Hong Li,[r] Yun Sun,[s,t] Weidong Huang,[u] Xianhong Tong,[v] Caixia Lei,[a] Hongchang Li,[d,e,f,g,h,i] Jun Wang,[j] Shaoying Li,[k] Xiaoyan Xu,[l,m] Junqiang Zhang,[o] Wei Wu,[p] Shanshan Liang,[q] Jian Ou,[r] Qiongzhen Zhao,[u] Rentao Jin,[v] Yueping Zhang,[a,s] Chenming Xu,[a,w] Daru Lu,[x,y] Junhao Yan,[d,e,f,g,h,i] Xiaoxi Sun,[a,b,c] Kwong Wai Choy,[z] Congjian Xu,[a,b,c,w,*] and Zi-Jiang Chen[d,e,f,g,h,i,s,t,**]

Rearrangement type	Unbalanced rearrangements	De novo aneuploidies[a]	Complex abnormalities[b]	Non-carrier embryos	Carrier embryos	Total embryos
Reciprocal translocation	2657 (41.52%)	881 (13.77%)	882 (13.78%)	1029 (16.08%)	951 (14.86%)	6400
Robertsonian translocation	209 (18.25%)	249 (21.75%)	94 (8.21%)	289 (25.24%)	304 (26.55%)	1145
Inversion	17 (11.64%)	56 (38.36%)	4 (2.74%)	35 (23.97%)	34 (23.29%)	146
Insertion translocation[c]	9 (15.25%)	9 (15.25%)	7 (11.86%)	14 (23.73%)	20 (33.90%)	59
Total	2892 (37.32%)	1195 (15.42%)	987 (12.74%)	1367 (17.64%)	1309 (16.89%)	**7750**

[a]These de novo aneuploidies included 401 mosaic embryos with whole or segmental chromosomes. [b]The complex abnormalities result was defined as a combination of unbalanced rearrangements and one or more of the following features: monosomy, trisomy, segmental aneuploidy, or chromosomal mosaic. [c]For the small sample size in insert translocation subgroup, bias of carrier and non-carrier distribution was inevitable compared to the theoretical 50:50.

***Table 2:* The PGT-SR results of tested blastocysts.**

Zhang, S. et al. (2025). Preimplantation genetic testing for structural rearrangements by genome-wide SNP genotyping and haplotype analysis: a prospective multicenter clinical study. *EBioMedicine*, *111*, 105514.

Outcomes

J Assist Reprod Genet. 2021 Aug;38(8):1939-1957. doi: 10.1007/s10815-021-02227-9. Epub 2021 May 25.

PGT-A: who and when? A systematic review and network meta-analysis of RCTs

Outcomes asociados a PGT-A

CERPO

Live Birth per patient outcome

RN vivo por outcome

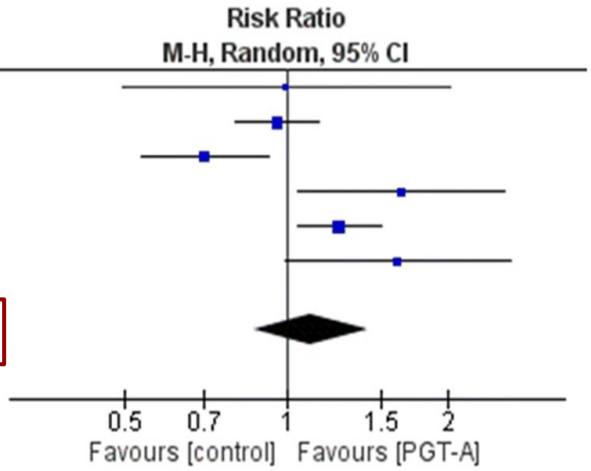
A

Study or Subgroup	PGT-A Events	PGT-A Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Fiorentino 2013	10	31	11	34	8.3%	1.00 [0.49, 2.02]
Munne 2019	137	330	143	331	22.7%	0.96 [0.80, 1.15]
Ozgur 2019	45	109	65	111	19.5%	0.71 [0.54, 0.93]
Rubio 2017	36	100	23	105	14.0%	1.64 [1.05, 2.57]
Scott 2013a	61	72	56	83	22.6%	1.26 [1.05, 1.50]
Sui 2020	32	103	20	104	12.8%	1.62 [0.99, 2.63]
Total (95% CI)		**745**		**768**	**100.0%**	**1.11 [0.87, 1.42]**
Total events	321		318			

Heterogeneity: Tau² = 0.06; Chi² = 19.88, df = 5 (P = 0.001); I² = 75%

Test for overall effect: Z = 0.83 (P = 0.41)

Cualquier edad



B

Study or Subgroup	PGT-A Events	PGT-A Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
3.1.1 ≤35						
Munne 2019	75	179	89	177	19.7%	0.83 [0.66, 1.04]
Ozgur 2019	45	109	65	111	18.7%	0.71 [0.54, 0.93]
Sui 2020	15	45	6	45	7.5%	2.50 [1.07, 5.86]
Subtotal (95% CI)		**333**		**333**	**45.9%**	**0.92 [0.62, 1.39]**
Total events	135		160			

Heterogeneity: Tau² = 0.09; Chi² = 7.92, df = 2 (P = 0.02); I² = 75%

Test for overall effect: Z = 0.38 (P = 0.71)

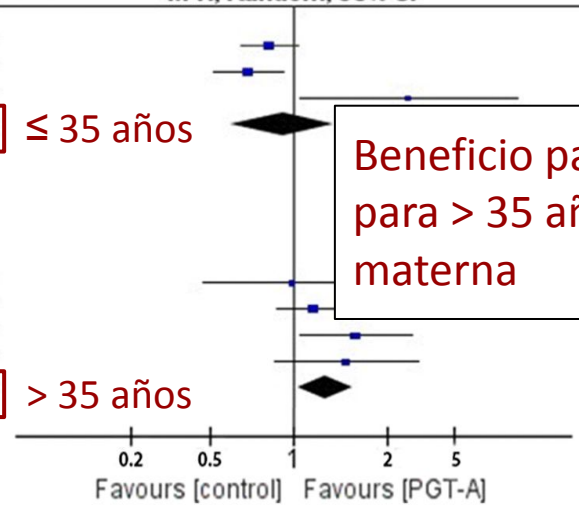
3.1.2 >35						
Fiorentino 2013	10	31	11	34	9.5%	1.00 [0.49, 2.02]
Munne 2019	62	151	54	154	18.3%	1.17 [0.88, 1.56]
Rubio 2017	36	100	23	105	14.5%	1.64 [1.05, 2.57]
Sui 2020	21	58	14	59	11.8%	1.53 [0.86, 2.70]
Subtotal (95% CI)		**340**		**352**	**54.1%**	**1.29 [1.05, 1.60]**
Total events	129		102			

Heterogeneity: Tau² = 0.00; Chi² = 2.43, df = 3 (P = 0.49); I² = 0%

Test for overall effect: Z = 2.37 (P = 0.02)

≤ 35 años

> 35 años



Beneficio parece existir para > 35 años de edad materna

Simopoulou M, et al. PGT-A: who and when? A systematic review and network meta-analysis of RCTs. J Assist Reprod Genet. 2021;38:1939–57

J Assist Reprod Genet. 2021 Aug;38(8):1939-1957. doi: 10.1007/s10815-021-02227-9. Epub 2021 May 25.

PGT-A: who and when? A systematic review and network meta-analysis of RCTs

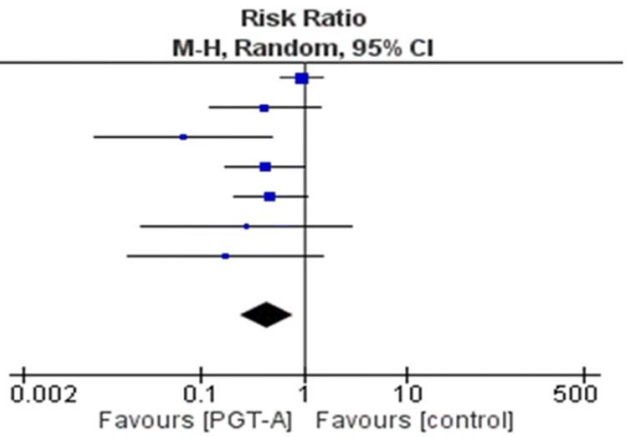
Outcomes asociados a PGT-A

Miscarriage per clinical pregnancy outcome

A

Study or Subgroup	PGT-A Events	PGT-A Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Munne 2019	27	165	30	175	28.0%	0.95 [0.59, 1.53]
Ozgur 2019	3	49	11	76	13.7%	0.42 [0.12, 1.44]
Rubio 2017	1	37	16	41	7.0%	0.07 [0.01, 0.50]
Scott 2013a	6	67	15	71	19.2%	0.42 [0.17, 1.03]
Sui 2020	7	39	12	32	20.8%	0.48 [0.21, 1.07]
Yang 2013	1	39	2	22	5.3%	0.28 [0.03, 2.94]
Yang 2017	1	58	4	41	6.1%	0.18 [0.02, 1.52]
Total (95% CI)		**454**		**458**	**100.0%**	**0.45 [0.25, 0.80]**
Total events	46		90			

Heterogeneity: Tau² = 0.26; Chi² = 11.73, df = 6 (P = 0.07); I² = 49%
Test for overall effect: Z = 2.71 (P = 0.007)

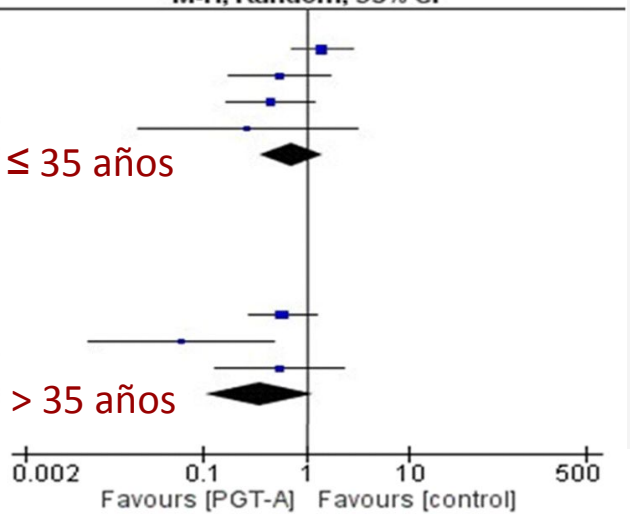


B

Study or Subgroup	PGT-A Events	PGT-A Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
3.3.1 ≤35						
Munne 2019	17	92	14	105	23.0%	1.39 [0.72, 2.65]
Ozgur 2019	4	49	11	76	15.0%	0.56 [0.19, 1.67]
Sui 2020	4	15	8	14	17.2%	0.47 [0.18, 1.21]
Yang 2013	1	39	2	22	5.1%	0.28 [0.03, 2.94]
Subtotal (95% CI)		**195**		**217**	**60.2%**	**0.73 [0.37, 1.44]**
Total events	26		35			
Heterogeneity: Tau² = 0.19; Chi² = 5.09, df = 3 (P = 0.17); I² = 41%						
Test for overall effect: Z = 0.91 (P = 0.36)						
3.3.2 >35						
Munne 2019	10	73	16	70	21.5%	0.60 [0.29, 1.23]
Rubio 2017	1	37	16	41	6.7%	0.07 [0.01, 0.50]
Sui 2020	3	24	4	18	11.5%	0.56 [0.14, 2.21]
Subtotal (95% CI)		**134**		**129**	**39.8%**	**0.37 [0.12, 1.17]**
Total events	14		36			
Heterogeneity: Tau² = 0.60; Chi² = 4.84, df = 2 (P = 0.09); I² = 59%						
Test for overall effect: Z = 1.69 (P = 0.09)						

≤ 35 años

> 35 años



RR de aborto por outcome clínico

Simopoulou M, et al. PGT-A: who and when? A systematic review and network meta-analysis of RCTs. J Assist Reprod Genet. 2021;38:1939–57

Outcomes asociados a PGT-A

CERPO

Comparison: Morphological or morphokinetic evaluation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect(95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk for control group	Corresponding risk for the PGT-A group			
Live-Birth	414 per 1000	431 per 1000 (360 to 588)	RR: 1.11 (0.87 to 1.42)	1513 (6)	⊕⊖⊖⊖very low [a,b]
`Live Birth - ≤35 years old	481 per 1000	405 per 1000 (298 to 669)	RR: 0.92(0.62-1.39)	666 (3)	⊕⊖⊖⊖very low [a,b]
Live Birth - >35 years old	290 per 1000	379 per 1000 (305 to 464)	RR: 1.29(1.05-1.60)	692 (4)	⊕⊕⊕⊖moderate [c]
Ongoing Pregnancy	432 per 1000	474 per 1000 (389 to 825)	RR: 1.31 (0.90-1.91)	933 (3)	⊕⊖⊖⊖very low [a,b]
Miscarriage	197 per 1000	101 per 1000 (49 to 158)	RR: 0.36 (0.17-0.73)	912 (7)	⊕⊕⊖⊖low [a]
Miscarriage - ≤35 years old	161 per 1000	133 per 1000 (60 to 232)	RR: 0.73 (0.37 to 1.44)	383 (3)	⊕⊕⊖⊖low [a]
Miscarriage - >35 years old	279 per 1000	104 per 1000 (33 to 326)	RR: 0.37 (0.12 to 1.17)	221(2)	⊕⊕⊕⊖moderate [d]
Clinical Pregnancy	521 per 1000	546 per 1000 (495 to 714)	RR: 1.14 (0.95 to 1.37)	1824 (9)	⊕⊖⊖⊖very low [a,b]
Clinical Pregnancy - ≤35 years old	570 per 1000	503 per 1000 (388 to 770)	RR 0.96 (0.68 to 1.35)	679 (3)	⊕⊖⊖⊖very low [a,b]
Clinical Pregnancy - >35 years old	406 per 1000	434 per 1000 (361 to 520)	RR 1.07 (0.89 to 1.28)	510 (2)	⊕⊕⊕⊕high
Cumulative Live Birth	368 per 1000	512 per 1000 (416 to 604)	RR 1.36 (1.13 to 1.64)	580 (4)	⊕⊖⊖⊖very low [b,e]

Evidencia de mejores resultados en RNV para > 35 años y tasa de aborto general

Simopoulou M, et al. PGT-A: who and when? A systematic review and network meta-analysis of RCTs. J Assist Reprod Genet. 2021;38:1939–57

ORIGINAL ARTICLE

Live Birth with or without Preimplantation Genetic Testing for Aneuploidy

Authors: Junhao Yan, M.D., Ph.D., Yingying Qin, M.D., Ph.D., Han Zhao, M.D., Ph.D., Yun Sun, M.D., Ph.D., Fei Gong, M.D., Ph.D., Rong Li, M.D., Xiaoxi Sun, M.D., Ph.D., +25 , and Zi-Jiang Chen, M.D., Ph.D. Author Info & Affiliations

Published November 24, 2021 | N Engl J Med 2021;385:2047-2058 | DOI: 10.1056/NEJMoa2103613

CERPO

Outcome	PGT-A Group (N=606)	Conventional-IVF Group (N=606)	Absolute Difference (95% CI)	Rate Ratio (95% CI)
Primary outcome				
Cumulative live-birth rate — no. (%)†	468 (77.2)	496 (81.8)	−4.6 (−9.2 to −0.0)	0.94 (0.89 to 1.00)
Singleton	462 (76.2)	478 (78.9)	−2.6 (−7.3 to 2.1)	0.97 (0.91 to 1.03)
Twin	6 (1.0)	18 (3.0)	−2.0 (−3.5 to −0.4)	0.33 (0.13 to 0.83)
Secondary outcomes				
Cumulative biochemical pregnancy — no. (%)	526 (86.8)	571 (94.2)	−7.4 (−10.7 to −4.2)	0.92 (0.89 to 0.96)
Cumulative clinical pregnancy — no. (%)	505 (83.3)	556 (91.7)	−8.4 (−12.1 to −4.7)	0.91 (0.87 to 0.95)
Cumulative ongoing pregnancy — no. (%)	479 (79.0)	514 (84.8)	−5.8 (−10.1 to −1.5)	0.93 (0.88 to 0.98)

Yan, J. et al. (2021). Live Birth with or without Preimplantation Genetic Testing for Aneuploidy. *The New England journal of medicine*, *385*(22), 2047–2058.

Systematic Reviews

Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies

Alice Poulton, MGenCouns; Melody Menezes, PhD; Tristan Hardy, PhD; Sharon Lewis, PhD; Lisa Hui, PhD

Outcomes asociados a PGT-M

TABLE 1
Inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Population	Individuals undergoing preimplantation genetic testing for a monogenic condition (PGT-M)	Individuals undergoing preimplantation genetic testing for structural rearrangements (PGT-SR), aneuploidy (PGT-A), or sex selection (PGT-SS) or reported the use of PGT-M for human leukocyte antigen typing for unaffected donor siblings.
Technique	Biopsy: blastomere or trophectoderm biopsy	Biopsy: polar body
	Insemination method: intracytoplasmic sperm injection	Insemination: not intracytoplasmic sperm injection
	Molecular analyses: polymerase chain reaction (PCR)-based approaches and genome-wide haplotyping methods	Molecular analyses: not PCR-based or karyomapping approaches
Outcomes	Clinical outcomes of PGT-M cycles (including number of oocytes retrieved per cycle, embryos suitable for biopsy per cycle, embryos suitable for transfer per cycle, clinical pregnancy rate per cycle, live birth rate per cycle)	Papers that did not report clinical pregnancy rate and live birth rate per cycle
Study	Quantitative data audit, observational studies, case series (>3 cases).	Reviews, letters, opinions, and case reports

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

Systematic Reviews

Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies

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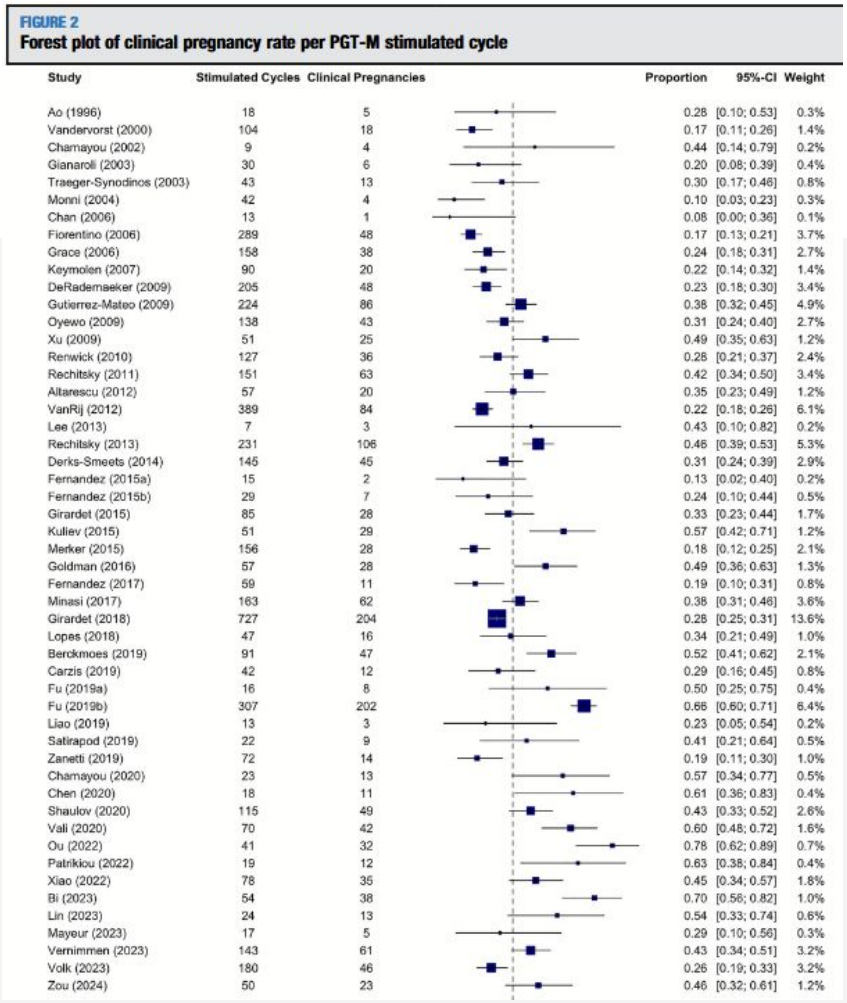
CERPO

FIGURE 2
Forest plot of clinical pregnancy rate per PGT-M stimulated cycle



Study	Stimulated Cycles	Clinical Pregnancies	Proportion	95%-CI	Weight
Ao (1996)	18	5	0.28	[0.10; 0.53]	0.3%
Vandervorst (2000)	104	18	0.17	[0.11; 0.26]	1.4%
Chamayou (2002)	9	4	0.44	[0.14; 0.79]	0.2%
Gianaroli (2003)	30	6	0.20	[0.08; 0.39]	0.4%
Traeger-Synodinos (2003)	43	13	0.30	[0.17; 0.46]	0.8%
Monni (2004)	42	4	0.10	[0.03; 0.23]	0.3%
Chan (2006)	13	1	0.08	[0.00; 0.36]	0.1%
Fiorentino (2006)	289	48	0.17	[0.13; 0.21]	3.7%
Grace (2006)	158	38	0.24	[0.18; 0.31]	2.7%
Keymolen (2007)	90	20	0.22	[0.14; 0.32]	1.4%
DeRademaeker (2009)	205	48	0.23	[0.18; 0.30]	3.4%
Gutierrez-Mateo (2009)	224	86	0.38	[0.32; 0.45]	4.9%
Oyewo (2009)	138	43	0.31	[0.24; 0.40]	2.7%
Xu (2009)	51	25	0.49	[0.35; 0.63]	1.2%
Renwick (2010)	127	36	0.28	[0.21; 0.37]	2.4%
Rechitsky (2011)	151	63	0.42	[0.34; 0.50]	3.4%
Altarescu (2012)	57	20	0.35	[0.23; 0.49]	1.2%
VanRij (2012)	389	84	0.22	[0.18; 0.26]	6.1%
Lee (2013)	7	3	0.43	[0.10; 0.82]	0.2%
Rechitsky (2013)	231	106	0.46	[0.39; 0.53]	5.3%
Derks-Smeets (2014)	145	45	0.31	[0.24; 0.39]	2.9%
Fernandez (2015a)	15	2	0.13	[0.02; 0.40]	0.2%
Fernandez (2015b)	29	7	0.24	[0.10; 0.44]	0.5%
Girardet (2015)	85	28	0.33	[0.23; 0.44]	1.7%
Kuliev (2015)	51	29	0.57	[0.42; 0.71]	1.2%
Merker (2015)	156	28	0.18	[0.12; 0.25]	2.1%
Goldman (2016)	57	28	0.49	[0.36; 0.63]	1.3%
Fernandez (2017)	59	11	0.19	[0.10; 0.31]	0.8%
Minasi (2017)	163	62	0.38	[0.31; 0.46]	3.6%
Girardet (2018)	727	204	0.28	[0.25; 0.31]	13.6%
Lopes (2018)	47	16	0.34	[0.21; 0.49]	1.0%
Berckmoes (2019)	91	47	0.52	[0.41; 0.62]	2.1%
Carzis (2019)	42	12	0.29	[0.16; 0.45]	0.8%
Fu (2019a)	16	8	0.50	[0.25; 0.75]	0.4%
Fu (2019b)	307	202	0.66	[0.60; 0.71]	6.4%
Liao (2019)	13	3	0.23	[0.05; 0.54]	0.2%
Satirapod (2019)	22	9	0.41	[0.21; 0.64]	0.5%
Zanetti (2019)	72	14	0.19	[0.11; 0.30]	1.0%
Chamayou (2020)	23	13	0.57	[0.34; 0.77]	0.5%
Chen (2020)	18	11	0.61	[0.36; 0.83]	0.4%
Shaulov (2020)	115	49	0.43	[0.33; 0.52]	2.6%
Vali (2020)	70	42	0.60	[0.48; 0.72]	1.6%
Ou (2022)	41	32	0.78	[0.62; 0.89]	0.7%
Patrikiou (2022)	19	12	0.63	[0.38; 0.84]	0.4%
Xiao (2022)	78	35	0.45	[0.34; 0.57]	1.8%
Bi (2023)	54	38	0.70	[0.56; 0.82]	1.0%
Lin (2023)	24	13	0.54	[0.33; 0.74]	0.6%
Mayeur (2023)	17	5	0.29	[0.10; 0.56]	0.3%
Vernimmen (2023)	143	61	0.43	[0.34; 0.51]	3.2%
Volk (2023)	180	46	0.26	[0.19; 0.33]	3.2%
Zou (2024)	50	23	0.46	[0.32; 0.61]	1.2%

Tasa de embarazo clínico por ciclo con PGT-M (general, no comparativo)

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies

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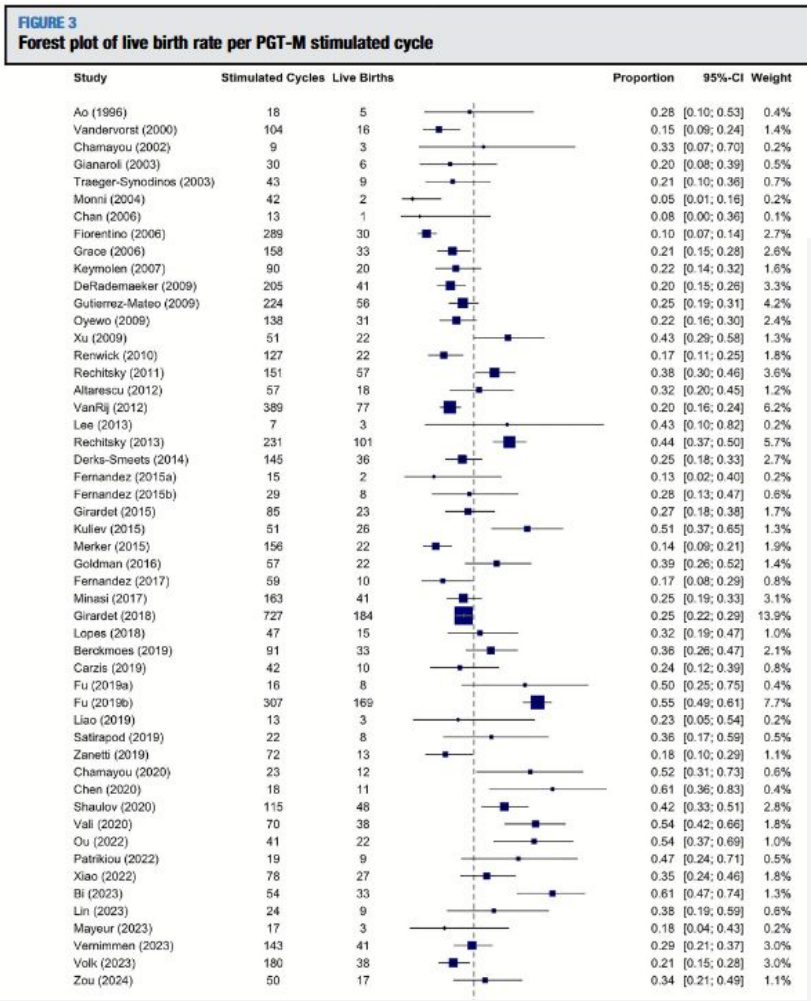
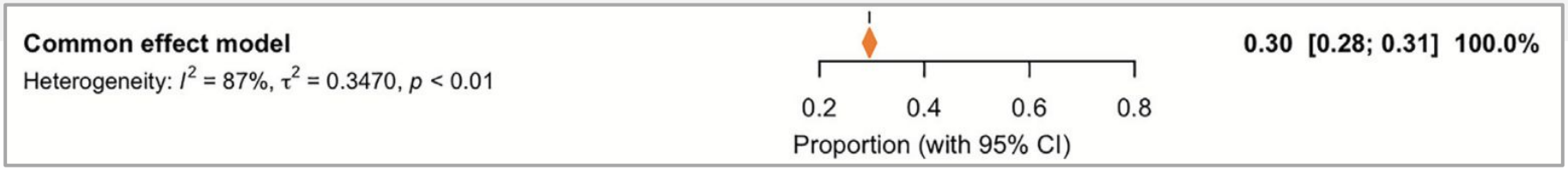
CERPO

FIGURE 3
Forest plot of live birth rate per PGT-M stimulated cycle



Tasa de nacido vivo por ciclo con PGT-M



Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

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TABLE 3
Quantitative analysis of PGT-M clinical outcome data: clinical pregnancy rates

Clinical outcome measure	Clinical pregnancy rate	
	n/N	% [95% CI]
Per stimulated cycle	1806/5305	34.0% [32.8%–35.33%]
Per embryos transferred[a]	1296/5229	24.8% [23.6%–26.0%]
Per embryo transfer cycle[b]	1499/3829	38.2% [37.6%–40.7%]

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

33% de embarazo clínico por ciclo con PGT-M

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

TABLE 4

Quantitative analysis of PGT-M clinical outcome data: live birth and ongoing pregnancy rates

Clinical outcome measure	Live birth and ongoing pregnancy rate	
	n/N	% [95% CI]
Per stimulated cycle	1577/5305	29.7% [28.5%–31.0%]
Per embryos transferred[a]	1146/5229	21.9% [20.8%–23.1%]
Per embryo transfer cycle[b]	1321/3829	34.5% [33.0%–36.0%]

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

TABLE 5

Quantitative analysis of PGT-M clinical outcome data: live birth rates (excluding ongoing pregnancies)

Clinical outcome measure	Live birth rate (excluding ongoing pregnancies)	
	n/N	% [95% CI]
Per stimulated cycle	1494/5305	28.2% [27.0%–29.4%]
Per embryos transferred[a]	1078/5229	20.6% [19.5%–21.7%]
Per embryo transfer cycle[b]	1239/3829	32.4% [30.9%–33.9%]

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

TABLE 6
Clinical outcomes according to inheritance pattern of the monogenic indication—recessive inheritance

	Clinical pregnancy rate		Live birth rate (excluding ongoing pregnancies)		Live birth and ongoing pregnancy rate	
Clinical outcome measure	n/N	% [95% CI]	n/N	% [95% CI]	n/N	% [95% CI]
Per stimulated cycle	578/1313	44.0% [41.4%–46.7%]	503/1313	38.3% [35.7%–41.0%]	514/1313	39.2% [36.5%–41.8%]
Per embryos transferred[a]	308/1201	25.6% [23.2%–28.2%]	273/1201	22.7% [20.4%–25.2%]	284/1201	23.7% [21.3%–26.2%]
Per embryo transfer cycle[b]	371/817	45.4% [42.0%]	329/817	40.3% [36.9%–43.7%]	340/817	41.6% [38.2%–45.1%]

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

TABLE 7
Clinical outcomes according to inheritance pattern of the monogenic indication—dominant inheritance

	Clinical pregnancy rate		Live birth rate (excluding ongoing pregnancies)		Live birth and ongoing pregnancy rate	
Clinical outcome measure	n/N	% [95% CI]	n/N	% [95% CI]	n/N	% [95% CI]
Per stimulated cycle	310/1076	28.8% [26.2%–31.6%]	248/1076	23.1% [20.6%–25.7%]	252/1076	23.4% [21.0%–26.0%]
Per embryos transferred[a]	237/945	25.1% [22.4%–28.0%]	190/945	20.1% [17.7%–22.8%]	194/945	20.5% [18.1%–23.2%]
Per embryo transfer cycle[b]	310/742	41.8% [38.3%–45.4%]	248/742	33.4% [30.1%–36.9%]	252/742	34.0% [30.7%–37.4%]

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

TABLE 8
Clinical outcomes according to inheritance pattern of the monogenic indication—mixed inheritance

	Clinical pregnancy rate		Live birth rate (excluding ongoing pregnancies)		Live birth and ongoing pregnancy rate	
Clinical outcome measure	n/N	% [95% CI]	n/N	% [95% CI]	n/N	% [95% CI]
Per stimulated cycle	927/2963	31.3% [29.6%–33.0%]	751/2963	25.4% [23.8%–26.9%]	819/2963	27.6% [26.1%–29.3%]
Per embryos transferred[a]	760/3116	24.4% [22.9%–25.9%]	623/3116	20.0% [18.6%–21.4%]	676/3116	21.7% [20.3%–23.2%]
Per embryo transfer cycle[b]	852/2308	36.9% [35.0%–38.9%]	692/2308	30.0% [28.2%–31.9%]	759/2308	32.9% [31.0%–34.8%]

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

Outcomes son distintos según patrón de herencia de enfermedad

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

¿PGT-M con PGT-A?

TABLE 9
Comparison of clinical outcomes between universally applied and no PGT-A groups—per stimulated cycle

Clinical outcome measure	Universally applied PGT-A n/N	Universally applied PGT-A %	No PGT-A n/N	No PGT-A %	*P* value[a]
Clinical pregnancy rate per stimulated cycle	406/938	43.3% [40.2%–46.5%]	1097/3371	32.5% [31.0%–34.1%]	<.0001
Live birth rate per stimulated cycle (excluding ongoing pregnancies)	299/938	31.9% [28.7%–34.9%]	938/3371	27.8% [26.3%–29.4%]	.0141
Live birth and ongoing pregnancy rate per stimulated cycle	353/938	37.6% [34.6%–40.8%]	948/3371	28.1% [26.6%–29.7%]	<.0001

PGT-A, preimplantation genetic testing for aneuploidy.

[a] Significance level of 0.05.

TABLE 10
Comparison of clinical outcomes between universally applied and no PGT-A groups—per embryo transferred

Clinical outcome measure	Universally applied PGT-A n/N	Universally applied PGT-A %	No PGT-A n/N	No PGT-A %	*P* value[a]
Clinical pregnancy rate per embryos transferred[b]	332/896	37.0% [33.9%–40.3%%]	689/3256	21.2% [19.8%–22.6%]	<.0001
Live birth rate per embryos transferred[b] (excluding ongoing pregnancies)	244/896	27.2% [24.3%–30.3%]	599/3256	18.4% [17.1%–19.8%]	<.0001
Live birth and ongoing pregnancy rate per embryos transferred	285/896	31.8% [28.8%–35.0%]	607/3256	18.6% [17.3%–20.0%]	<.0001

PGT-A, preimplantation genetic testing for aneuploidy.

[a] Significance level of 0.05; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred.

Mayor tasa de embarazo clínico y nacido vivo combinado vs PGT-M sin PGT-A

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

¿PGT-M con PGT-A?

TABLE 12

N-1 chi square comparison of clinical outcomes between universally applied and no PGT-A groups by inheritance pattern

Clinical outcome measure	Recessive *P* value[a]	Dominant *P* value[a]	Mixed *P* value[a]
Clinical pregnancy rate per stimulated cycle	.0106	.0112	<.0001
Live birth and ongoing pregnancy rate per stimulated cycle	.0583	.0041	<.0001
Live birth rate per stimulated cycle (excluding ongoing pregnancies)	.0405	.1354	.0428
Clinical pregnancy rate per embryos transferred[a]	<.0001	<.0001	<.0001
Live birth and ongoing pregnancy rate per embryos transferred[a]	<.0001	<.0001	<.0001
Live birth rate per embryos transferred[a] (excluding ongoing pregnancies)	<.0001	.007	.0033
Clinical pregnancy rate per embryo transfer cycle[b]	<.0001	.0113	<.0001
Live birth and ongoing pregnancy rate per embryo transfer cycle[b]	<.0001	.0046	<.0001
Live birth rate per embryo transfer cycle[b] (excluding ongoing pregnancies)	<.0001	.1704	.0002

[a] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryos transferred; [b] Outcomes, including clinical pregnancies and live births, only reported for studies recording number of embryo transfer cycles.

Poulton, A. et al. (2025). Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. *American journal of obstetrics and gynecology*, *232*(2), 150–163.

Outcomes a largo plazo

Chromosomal, gestational, and neonatal outcomes of embryos classified as a mosaic by preimplantation genetic testing for aneuploidy

Manuel Viotti, Ph.D.,[a,b] Ermanno Greco, M.D.,[c] James A. Grifo, M.D., Ph.D.,[d] Mitko Madjunkov, M.D.,[e,f] Clifford Librach, M.D.,[e,f,g] Murat Cetinkaya, M.D., Ph.D.,[h] Semra Kahraman, M.D.,[h] Pavel Yakovlev, M.D., Ph.D.,[i] Nikolay Kornilov, M.D.,[i,j] Laura Corti, M.Sc.,[k] Anil Biricik, Ph.D.,[l] En-Hui Cheng, Ph.D.,[m] Ching-Ya Su, M.S.,[m] Maw-Sheng Lee, M.D., Ph.D.,[m,n] Michael D. Bonifacio, M.Sc.,[o] Amber R. Cooper, M.D.,[b] Darren K. Griffin, D.Sc.,[p] Diane Y. Tran, B.S.,[q] Purvi Kaur, B.A.,[q] Frank L. Barnes, Ph.D.,[a,q] Christo G. Zouves, M.D.,[a,q] Andrea R. Victor, Ph.D.,[p,q,r] Andria G. Besser, M.S.,[d] Svetlana Madjunkova, M.D., Ph.D.,[e,f,s] and Francesca Spinella, Ph.D.[l]

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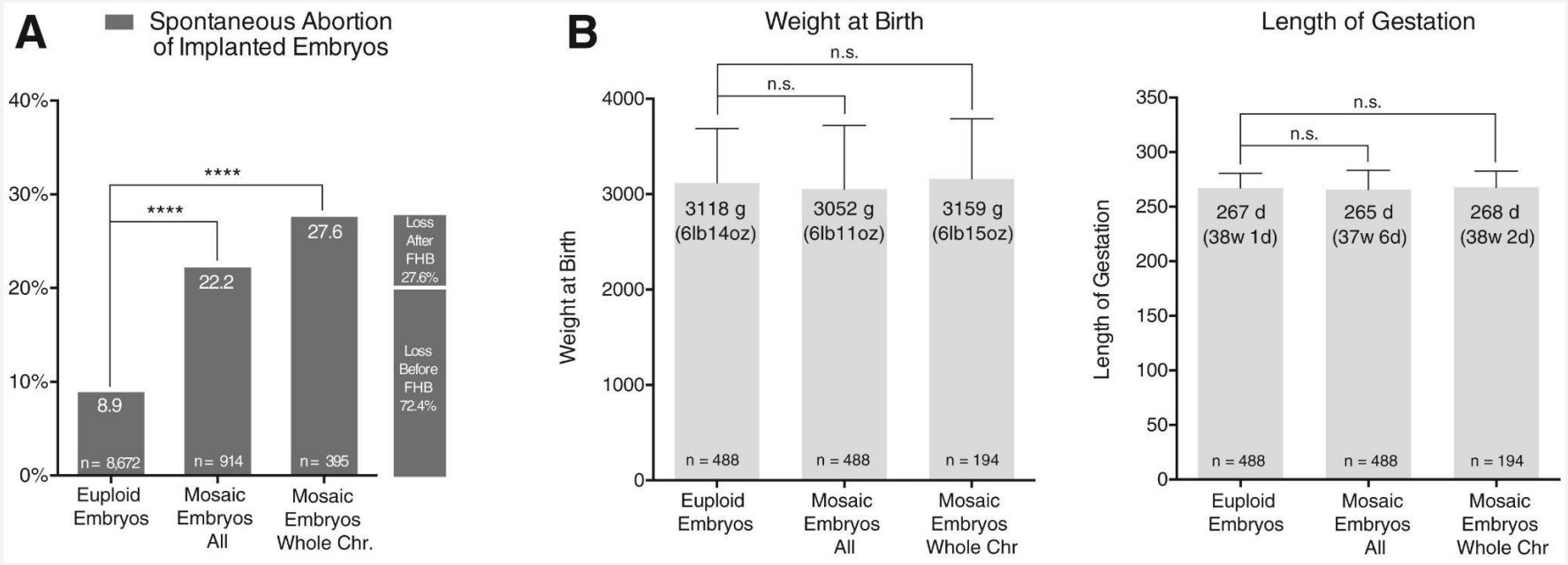

Mayor tasa de abortos en embriones mosaico

Viotti, M. et al. (2023). Chromosomal, gestational, and neonatal outcomes of embryos classified as a mosaic by preimplantation genetic testing for aneuploidy. *Fertility and sterility*, *120*(5), 957–966.

Details of abnormal results of prenatal tests performed in pregnancies from mosaic embryo transfers.

PGT-A result	Abnormal prenatal and POC test	Clinical outcome
mos(-10p) [20%]	Amnio microarray (1 Mb duplication of unknown significance in a different chromosome)	Birth
mos(+13q) [31%]	Amnio microarray (duplication of unknown significance in a different chromosome below the resolution of NGS PGT-A, maternally inherited)	Birth
mos(+5p) [36%]	Amnio microarray (likely benign duplication in different chromosomes below the resolution of NGS PGT-A, maternally inherited)	Birth
mos(-5p) [37%]	Amnio microarray (likely benign unrelated deletion in a different chromosome below the resolution of NGS PGT-A, maternally inherited)	Birth
mos (-2, -8) [30%]	Amnio microarray (interstitial microdeletion Chr2q13, 84.11 Kb)	Birth
mos(-17) [30%]	Amnio microarray (translocation; 46, XY, t (1:16) (p32-p13.3))	Birth
mos(+16p) [30%]	Amnio microarray (unrelated microdeletion in XX fetus, below the resolution of NGS PGT-A)	Birth
mos(+1p) [20%–40%]	Amnio microarray (likely benign CNV, below the resolution of NGS PGT-A)	Birth
mos(+18p) [40%]	POC cytogenetic karyotype (tetraploidy 92, XXXX) approximately 8 wk into pregnancy)	Spontaneous abortion
mos(-2) [22%]	POC Microarray (mos[+2, +14,+X]), confirmed no maternal contamination	Spontaneous abortion
mos(-14q) [29%]	Amnio microarray (mosaicism and UPD of a different chromosome)	Terminated
mos (+1q, -7, -8,+9,-19, -20, +21) [40%]	CVS karyotype G-banding (mos+21, 80%), CVS array (mos+21), Amnio karyotype and FISH (mos+21, 16%)	Terminated
mos(-1p36.33p31.1) [40%]	Amnio FISH: 15% of cells with a deletion in 1p36 POC FISH: 1.5% of analyzed brain cells with a deletion in 1p36, no abnormal cells found in villous tissue, or myocardium	Terminated
mos(+4q32.2q34.3, -Xq27.3-q28) [40%]	CVS microarray (mos+4q32.2q34.3, 60%)	Birth

Note: "PGT-A result" indicates the original call produced from PGT-A at the blastocyst stage. Square brackets indicate the level of mosaicism. "Abnormal test" indicates the nature of the prenatal test performed and details of the abnormality detected. "Clinical outcome" indicates the clinical outcome of the associated pregnancy. CNV = copy-number variation; CVS = chorionic villus sample; FISH = fluorescence in situ hybridization; NGS = next-generation sequencing; PGT-A preimplantation genetic testing for aneuploidy; POC = products of conception; UPD = uniparental disomy.

Viotti. Outcomes of mosaic embryos. Fertil Steril 2023.

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Poca correlación aparente PGT - pruebas invasivas prenatales

Viotti, M. et al. (2023). Chromosomal, gestational, and neonatal outcomes of embryos classified as a mosaic by preimplantation genetic testing for aneuploidy. *Fertility and sterility*, *120*(5), 957–966.

Preimplantation genetic testing and disorders of placental implantation: a systematic review and meta-analysis

Isaac J Chamani [1 2], Lauren L Taylor [3], Hailie Ciomperlik [3], Timothy Dunn [3], Anna C Reynolds [3], Beatriz Varman [4], Karin A Fox [5], Laura Detti [3]

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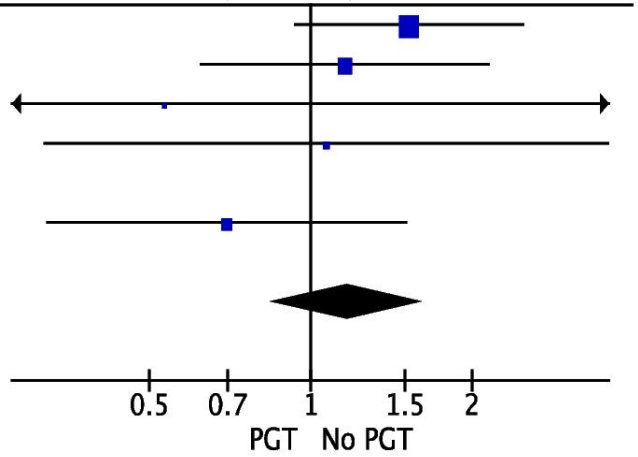
Study or Subgroup	PGT Events	PGT Total	No PGT Events	No PGT Total	Weight	Odds Ratio M-H, Random, 95% CI
Bay 2016	19	126	3173	30418	44.7%	1.52 [0.93, 2.49]
Gulersen 2021	22	496	20	519	28.0%	1.16 [0.62, 2.15]
Hasson 2017	1	51	3	83	2.0%	0.53 [0.05, 5.27]
Makjijani 2020	4	241	8	515	7.3%	1.07 [0.32, 3.59]
Sites 2021	68	585	189	2191	0.0%	1.39 [1.04, 1.87]
Zhang 2019	12	177	17	180	18.0%	0.70 [0.32, 1.51]
Total (95% CI)		**1091**		**31715**	**100.0%**	**1.17 [0.84, 1.62]**
Total events	58		3221			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.35$, df = 4 (P = 0.50); $I^2 = 0\%$

Test for overall effect: Z = 0.94 (P = 0.35)



Aparentemente sin correlación con desórdenes de implantación placentaria

Chamani, I. J. et al. (2025). Preimplantation genetic testing and disorders of placental implantation: a systematic review and meta-analysis. *Journal of assisted reproduction and genetics*, *42*(5), 1539–1546.

Hum Reprod. 2023 Apr 3;38(4):739-750. doi: 10.1093/humrep/dead021.

Preimplantation genetic testing and child health: a national register-based study

Erica Ginström Ernstad [1], Charles Hanson [2], Kjell Wånggren [3], Ann Thurin-Kjellberg [2], Cecilia Hulthe Söderberg [4], Elisabeth Syk Lundberg [5 6], Max Petzold [7], Ulla-Britt Wennerholm [1], Christina Bergh [2]

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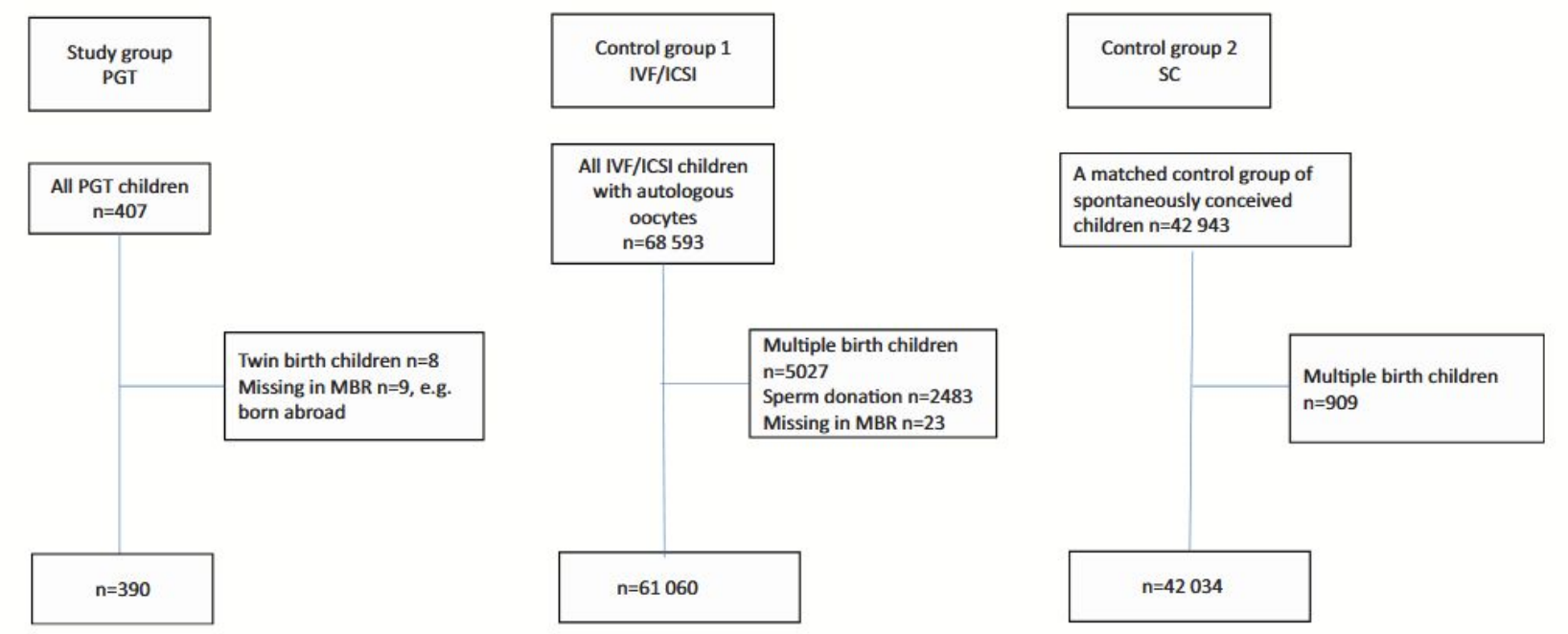

Ginström Ernstad, E. et al. (2023). Preimplantation genetic testing and child health: a national register-based study. *Human reproduction (Oxford, England)*, *38*(4), 739–750.

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Table II Indications and procedures for singleton pregnancies after preimplantation genetic testing, (PGT) in Sweden 1996–2019.

Deliveries, n	390
Indication for treatment, n (%)	
Monogenic disorders	259 (66.4)
X-linked disorders	18 (4.6)
Chromosomal aberrations	113 (29.0)
Biopsy stage n, (%)	
Cleavage stage	193 (49.5)
Blastocyst stage	195 (50.0)
Missing	2 (0.5)
Zona opening, n (%)	
Laser	334 (85.6)
Acid	47 (12.1)
Missing	9 (2.3)
Genetic analyses, n (%)	
PCR	269 (69.0)
FISH	76 (19.5)
Array-CGH	43 (11.0)
NGS	2 (0.5)

FISH, fluorescence *in situ* hybridization; CGH, comparative genome hybridization; NGS, next generation sequencing.

Ginström Ernstad, E. et al. (2023). Preimplantation genetic testing and child health: a national register-based study. *Human reproduction (Oxford, England)*, *38*(4), 739–750.

Hum Reprod. 2023 Apr 3;38(4):739-750. doi: 10.1093/humrep/dead021.

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Table III Perinatal outcome in singleton pregnancies after preimplantation genetic testing (PGT), IVF/ICSI, and spontaneous conception (SC) in Sweden 1996–2019.

	PGT	IVF/ICSI	Spontaneous conception	Crude odds ratio (95% CI) PGT versus IVF/ICSI	Adjusted odds ratio[a] (95% CI) PGT versus IVF/ICSI	Crude odds ratio (95% CI) PGT versus SC	Adjusted odds ratio[a] (95% CI) PGT versus SC
Deliveries, n	390	61 060	42 034				
Male gender, n (%)	182 (46.7)	31 391 (51.4)	21 492 (51.1)	0.83 (0.68–1.01)	0.83 (0.68–1.01)	0.84 (0.69–1.02)	0.83 (0.68–1.02)
Gestational age, mean (days ±SD)	277 ± 15.0	277 ± 15.1	279 ± 13.1	–	–	–	–
Post-term birth ≥42 weeks, n (%)	24 (6.2)	3978 (6.5)	2834 (6.7)	0.94 (0.62–1.42)	1.20 (0.79–1.83)	0.91 (0.60–1.37)	0.88 (0.58–1.33)
Pre-term birth <37 weeks, n (%)	30 (7.7)	4434 (7.3)	1926 (4.6)	1.06 (0.73–1.55)	1.22 (0.82–1.81)	**1.74 (1.19–2.53)**	**1.73 (1.17–2.58)**
Very pre-term birth <32 weeks, n (%)	3 (0.8)	834 (1.4)	361 (0.9)	0.56 (0.18–1.75)	NA[c]	0.90 (0.29–2.80)	NA[c]
Birth weight, mean (grams ±SD)	3472 ± 601	3466 ± 613	3538 ± 564	–	–	–	–
<2500 g, n (%)	19 (4.9)	3145 (5.2)	1327 (3.2)	0.94 (0.59–1.49)	1.17 (0.71–1.91)	1.57 (0.99–2.50)	1.52 (0.93–2.49)
<1500 g, n (%)	4 (1.0)	719 (1.2)	326 (0.8)	0.87 (0.32–2.33)	NA[c]	1.33 (0.49–3.57)	NA[c]
≥4500 g, n (%)	13 (3.3)	1996 (3.3)	1450 (3.4)	1.02 (0.59–1.77)	0.96 (0.55–1.68)	0.96 (0.55–1.68)	0.97 (0.56–1.69)
SGA<−2 SD, n (%)	16 (4.1)	2685 (4.4)	1309 (3.1)	0.93 (0.56–1.54)	1.20 (0.72–1.98)	1.33 (0.81–2.20)	1.29 (0.78–2.14)
LGA>+2 SD, n (%)	18 (4.6)	2694 (4.4)	1835 (4.4)	1.05 (0.65–1.68)	0.87 (0.54–1.40)	1.06 (0.66–1.71)	1.07 (0.67–1.73)
Apgar score <4 at 5 min, n (%)	<3 (<0.8)[b]	337 (0.6)	251 (0.6)	NA[c]	NA[c]	NA[c]	NA[c]
Perinatal mortality, n (%)	<3 (<0.8)[b]	354 (0.6)	235 (0.6)	NA[c]	NA[c]	NA[c]	NA[c]
Neonatal mortality, n (%)	0 (0.0)	114 (0.2)	55 (0.1)	NA[c]	NA[c]	NA[c]	NA[c]
Infant mortality, n (%)	0 (0.0)	169 (0.3)	80 (0.2)	NA[c]	NA[c]	NA[c]	NA[c]
Any birth defects registered at birth, n (%)	18 (4.6)	2556 (4.2)	1538 (3.7)	1.11 (0.69–1.78)	1.20 (0.75–1.93)	1.27 (0.79–2.05)	1.26 (0.78–2.03)
Major birth defects registered at birth, n (%)	7 (1.8)	1594 (2.6)	854 (2.0)	0.68 (0.32–1.44)	NA[c]	0.88 (0.42–1.87)	NA[c]
Major birth defects registered up to 1 year of age, n (%)	21 (5.4)	3149 (5.2)	2028 (4.8)	1.05 (0.67–1.63)	0.96 (0.60–1.53)	1.12 (0.72–1.75)	1.05 (0.66–1.68)

Ginström Ernstad, E. et al. (2023). Preimplantation genetic testing and child health: a national register-based study. *Human reproduction (Oxford, England)*, *38*(4), 739–750.

Table IV Early childhood outcome in singleton pregnancies after preimplantation genetic testing (PGT), IVF/ICSI, and spontaneous conception (SC) for in Sweden 1996–2019.

	PGT	IVF/ICSI	SC	Crude hazard ratio (95% CI) PGT versus IVF/ICSI	Adjusted hazard ratio[a] (95% CI) PGT versus IVF/ICSI	Crude hazard ratio (95% CI) PGT versus SC	Adjusted hazard ratio (95% CI) PGT versus SC
Deliveries, n	390	61 060	42 034	–	–	–	–
Follow-up time in years, mean (SD)	4.62 ± 4.1	9.05 ± 6.2	5.12 ± 3.9	–	–	–	–
Asthma	38 (9.7)	6980 (11.4)	4016 (9.6)	1.25 (0.91–1.72)	1.03 (0.73–1.44)	1.14 (0.83–1.57)	1.11 (0.79–1.55)
Allergic disorders	34 (8.7)	7505 (12.3)	4451 (10.6)	1.08 (0.77–1.51)	0.97 (0.69–1.38)	0.89 (0.64–1.25)	0.88 (0.62–1.24)
Sepsis	<3 (<0.8)[b]	134 (0.2)	64 (0.2)	NA[c]	NA[c]	NA[c]	NA[c]
Hypothyroidism	<3 (<0.8)[b]	165 (0.3)	56 (0.1)	NA[c]	NA[c]	NA[c]	NA[c]
ADHD	3 (0.8)	1649 (2.7)	363 (0.9)	1.08 (0.35–3.34)	NA[c]	0.95 (0.31–2.97)	NA[c]
ASD	<3 (<0.8)[b]	1012 (1.7)	301 (0.7)	NA[c]	NA[c]	NA[c]	NA[c]
Affective disorders	0 (0.0)	641 (1.0)	77 (0.2)	NA[c]	NA[c]	NA[c]	NA[c]
Schizophrenia	0 (0.0)	20 (0.0)	4 (0.0)	NA[c]	NA[c]	NA[c]	NA[c]
Mental retardation	<3 (<0.8)[b]	343 (0.6)	112 (0.3)	NA[c]	NA[c]	NA[c]	NA[c]
Cerebral palsy	<3 (<0.8)[b]	128 (0.2)	56 (0.1)	NA[c]	NA[c]	NA[c]	NA[c]
Epilepsy	<3 (<0.8)[b]	486 (0.8)	171 (0.4)	NA[c]	NA[c]	NA[c]	NA[c]
Mortality[d]	0 (0.0)	220 (0.4)	89 (0.2)	NA[c]	NA[c]	NA[c]	NA[c]

NA, not applicable; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorders.

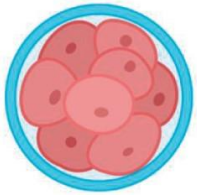
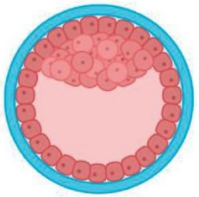
Sin diferencias en resultados finales evaluados en infancia temprana

Ginström Ernstad, E. et al. (2023). Preimplantation genetic testing and child health: a national register-based study. *Human reproduction (Oxford, England)*, *38*(4), 739–750.

Obstetric, neonatal, and child health outcomes following embryo biopsy for preimplantation genetic testing

Alessandra Alteri, Greta Chiara Cermisoni, Mirko Pozzoni, Gerarda Gaeta, Paolo Ivo Cavoretto, Paola Viganò

Escasa evidencia en general para resultados a largo plazo

PTD	PTD	PTD
HDP	HDP	HDP
Abnormal placentation	Abnormal placentation	Abnormal placentation
GDM	GDM	GDM

BW, LBW and VLBW	BW, LBW and VLBW	BW, LBW and VLBW
SGA and LGA	SGA and LGA	SGA and LGA
Apgar scores	Apgar scores	Apgar scores
NICU admission	NICU admission	NICU admission
Birth defects	Birth defects	Birth defects

Neurological outcomes	Neurological outcomes	Neurological outcomes
Blood pressure and anthropometric outcomes	Blood pressure and anthropometric outcomes	Blood pressure and anthropometric outcomes
Mental, psychomotor and cognitive development outcomes	Mental, psychomotor and cognitive development outcomes	Mental, psychomotor and cognitive development outcomes

Alteri, A. et al. (2023). Obstetric, neonatal, and child health outcomes following embryo biopsy for preimplantation genetic testing. *Human reproduction update*, *29*(3), 291–306.

The use of preimplantation genetic testing for aneuploidy: a committee opinion

Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology

American Society for Reproductive Medicine, Washington, DC

CERPO

- PGT-A: evidencia no apoya uso general para todos los pacientes IVF
- Resultados clínicos: RCTs muestran valores similares de nacido vivo y aborto entre IVF con o sin PGT-A
- Mejor evidencia a edades mayores (> 35 años)
- Sin evidencia en donante de ovocitos ni infertilidad de causa masculina

Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Electronic address: asrm@asrm.org (2024). The use of preimplantation genetic testing for aneuploidy: a committee opinion. *Fertility and sterility*, *122*(3), 421–434.

The use of preimplantation genetic testing for aneuploidy: a committee opinion

Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology

American Society for Reproductive Medicine, Washington, DC

CERPO

- NGS como estándar, aunque mosaicismo es complejo de interpretar
- Relevancia de consejería en mosaicismo
- Transferencia fresco versus congelado sin diferencias aparentes en resultados
- Biopsia trofoectodérmica preferida (menos dañina que en fase de clivado)
- Evidencia mixta en costoefectividad

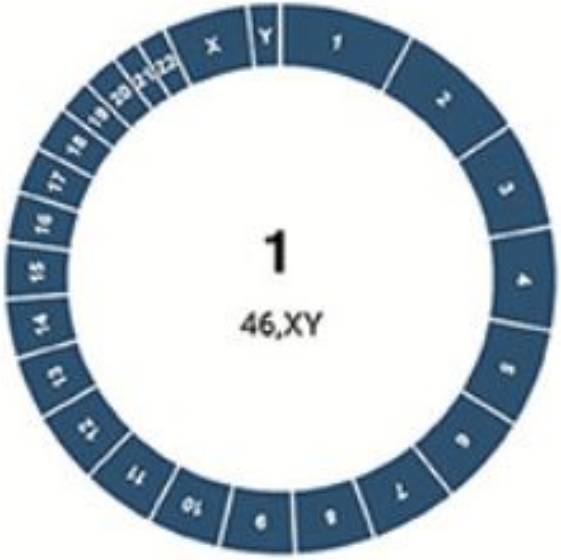
Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Electronic address: asrm@asrm.org (2024). The use of preimplantation genetic testing for aneuploidy: a committee opinion. *Fertility and sterility*, *122*(3), 421–434.

Utility and First Clinical Application of Screening Embryos for Polygenic Disease Risk Reduction

Nathan R. Treff[1,2*] Jennifer Eccles[1,2] Lou Lello[1,3] Elan Bechor[1]
Jeffrey Hsu[1] Kathryn Plunkett[1,2] Raymond Zimmerman[1,2] Bhavini Rana[1,2]
Artem Samoilenko[1] Steven Hsu[1] Laurent C. A. M. Tellier[1,2,3]

Otros: PGT-P

CERPO



	Risk		Avg Risk	Ratio	Risk Percentile
Type 1 Diabetes	0.20%	Normal	0.33%	0.6x	7%
Type 2 Diabetes	20%	Normal	35%	0.6x	6%
Testicular Cancer	0.33%	Normal	0.40%	0.8x	42%
Prostate Cancer	8.7%	Normal	11%	0.8x	46%
Basal Cell Carcinoma	32%	Normal	30%	1.1x	61%
Malignant Melanoma	2.0%	Normal	2.0%	1.0x	67%
Heart Attack	39%	Normal	35%	1.1x	76%
Atrial Fibrillation	43%	Normal	38%	1.1x	74%
Coronary Artery Disease	35%	Normal	30%	1.2x	78%
Hypertension	39%	Normal	40%	1.0x	46%
High Cholesterol	0.13%	Normal	0.30%	0.4x	8%

Conclusiones

CERPO

- Técnicas PGT en rápido desarrollo, con limitaciones por n° de células y mosaicismo
- Existen recomendaciones claras de uso para técnicas de PGT
- PGT-A con evidencia contradictoria de outcomes finales
- Aún evidencia escasa de resultados a largo plazo
- Es necesaria consejería detallada previo a proceso