

# **“Words shape reality: the need for a new definition of success in ART”**

**L. Gianaroli, MD, FRCOG**

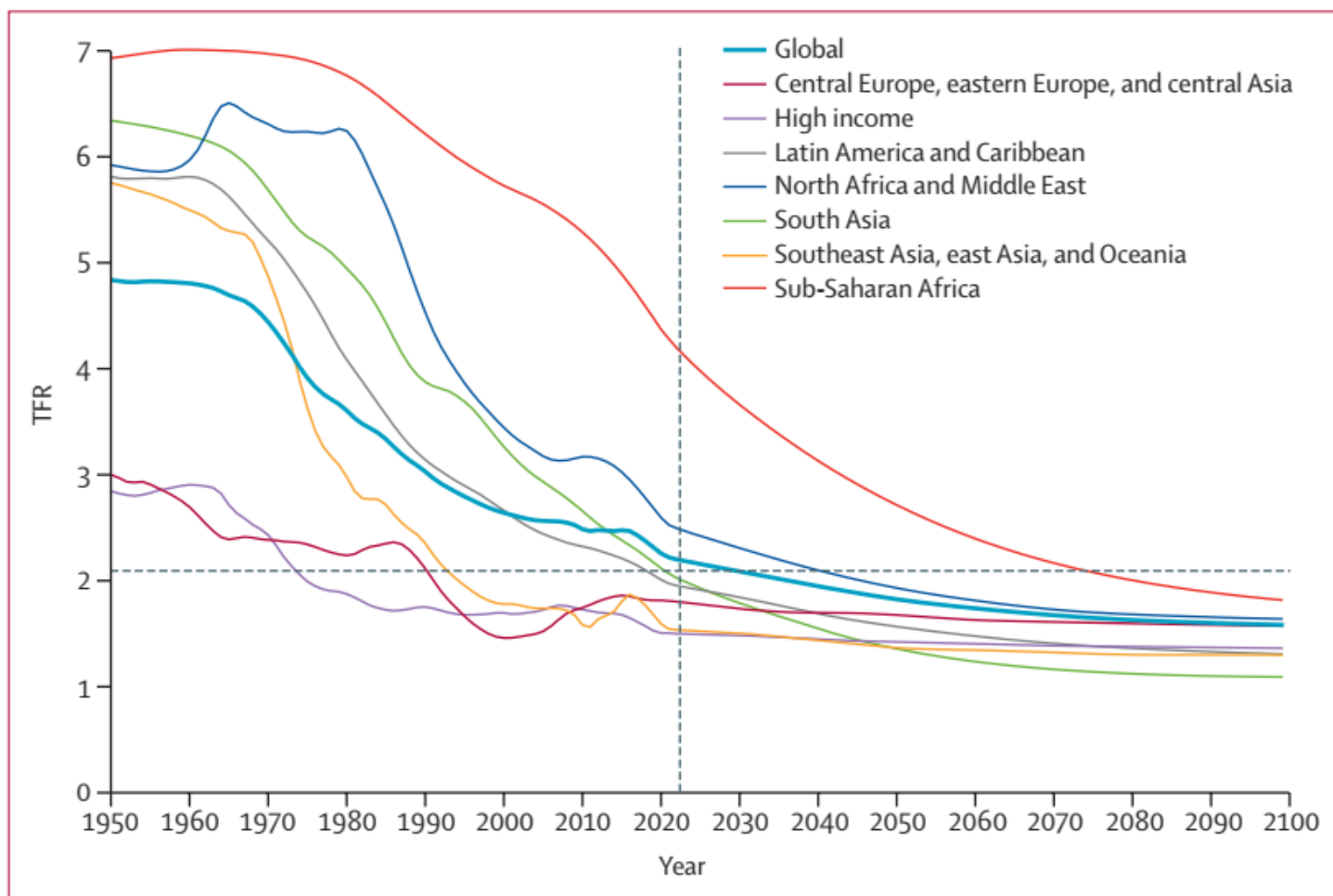
**H-Index (Google Scholar): 84**

**IIRM – Interdisciplinary Institute of Reproductive Medicine, Bologna, Italy**

**Leuven, 9<sup>th</sup> April 2025**



[illegible]

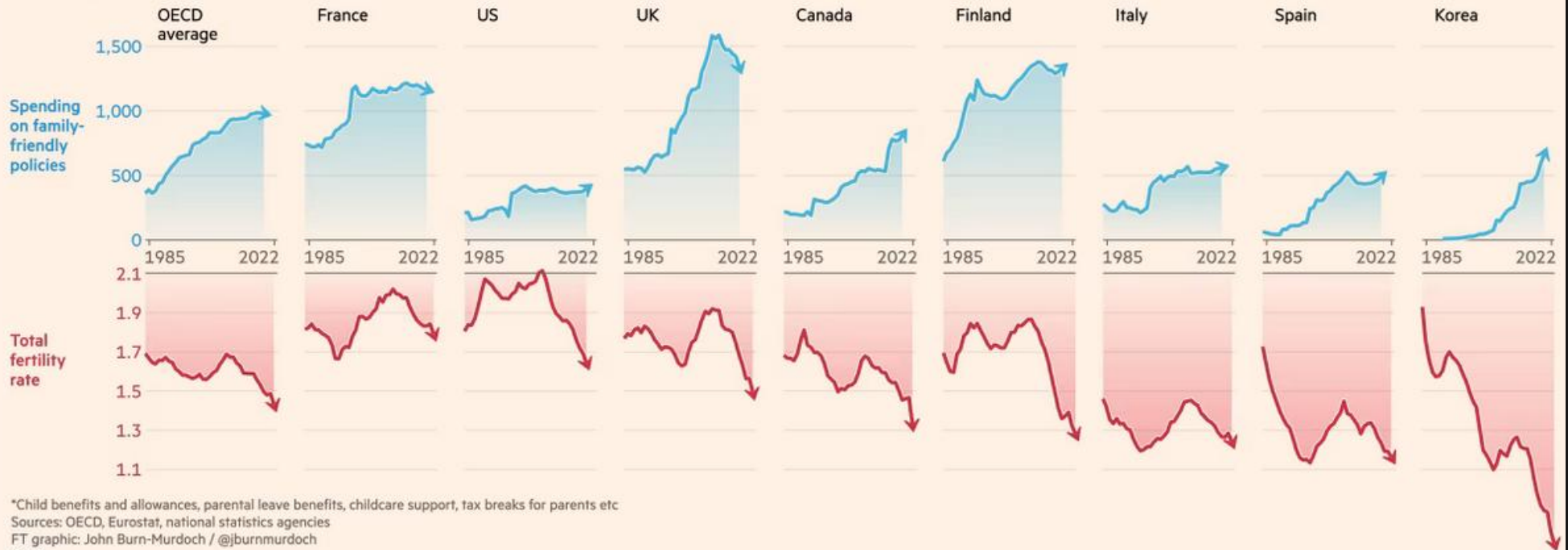


**Figure 1: TFR, globally and by GBD super-region, 1950-2100**

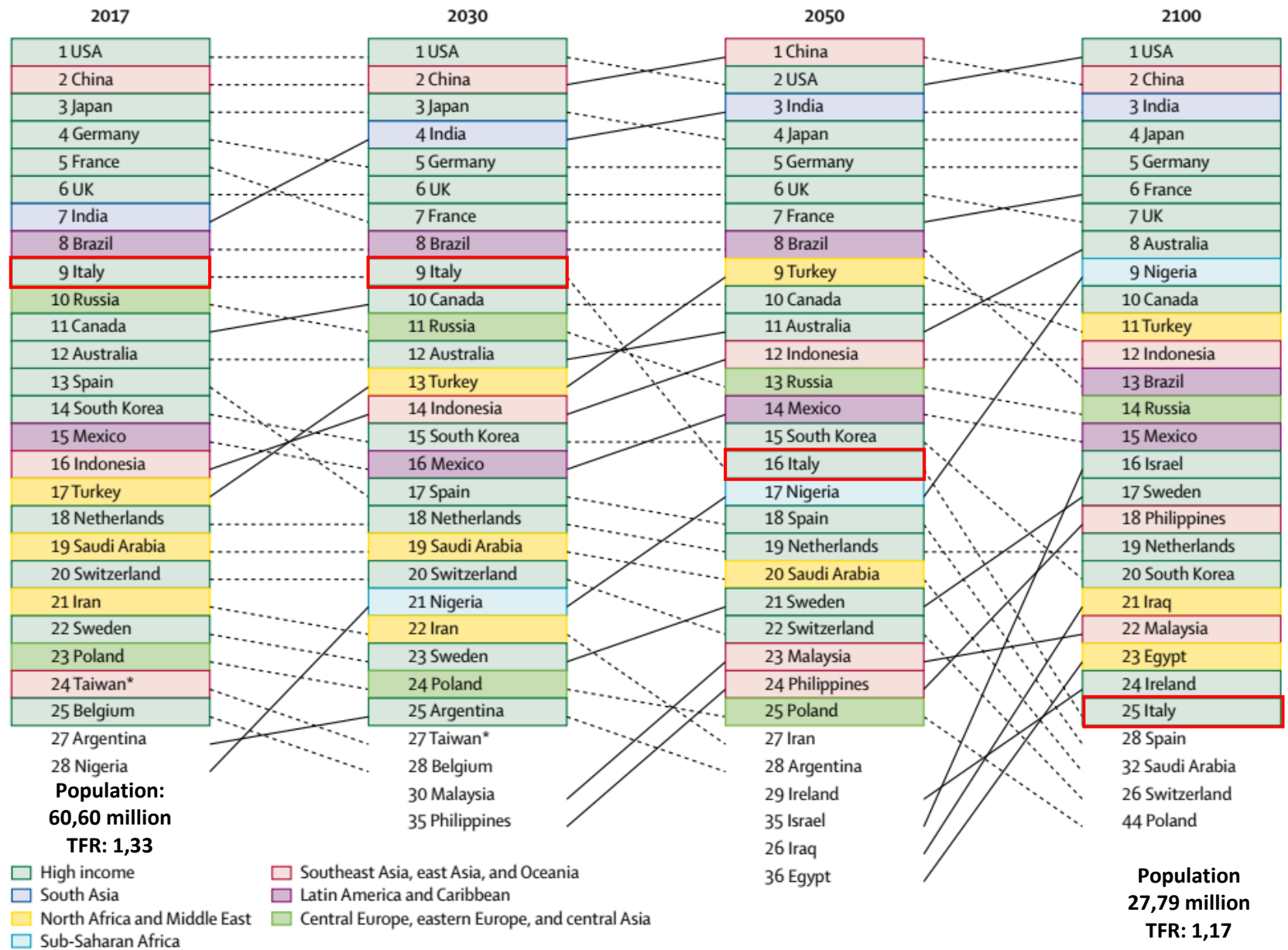
The dashed horizontal line indicates replacement TFR (2.1), and the dashed vertical line indicates the year 2022 (the first forecast year). GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. TFR=total fertility rate.

## Countries have greatly expanded spending on family-friendly policies, but birth rates continue to fall far below the replacement level

Public spending on pro-child policies\* (constant USD per capita) vs total fertility rate



# Ranking of the first 25 world economies according to GDP: projections



Brief Communication | Published: 13 January 2025

# Lifetime risk and projected burden of dementia

[Michael Fang](#), [Jiaqi Hu](#), [Jordan Weiss](#), [David S. Knopman](#), [Marilyn Albert](#), [B. Gwen Windham](#), [Keenan A. Walker](#), [A. Richey Sharrett](#), [Rebecca F. Gottesman](#), [Pamela L. Lutsey](#), [Thomas Mosley](#), [Elizabeth Selvin](#) & [Josef Coresh](#) 

[Nature Medicine](#) (2025) | [Cite this article](#)

**4374** Accesses | **2518** Altmetric | [Metrics](#)

**Overall lifetime risk for dementia among middle-aged Americans of 42 percent  
35 percent risk in men and 48 percent risk in women.**

**“Our study results forecast a dramatic rise in the burden from dementia in the  
United States over the coming decades, with one in two Americans expected to  
experience cognitive difficulties after age 55”**





nytimes 12/11/2024

...

A growing number of Americans are choosing not to have children. Some of their parents are grappling with what that means for them and may experience a deep sense of longing and loss when their children opt out of parenthood. [nyti.ms/4hHDf...](https://www.nytimes.com/2024/12/11/us/never-having-children-grief.html) Traduci



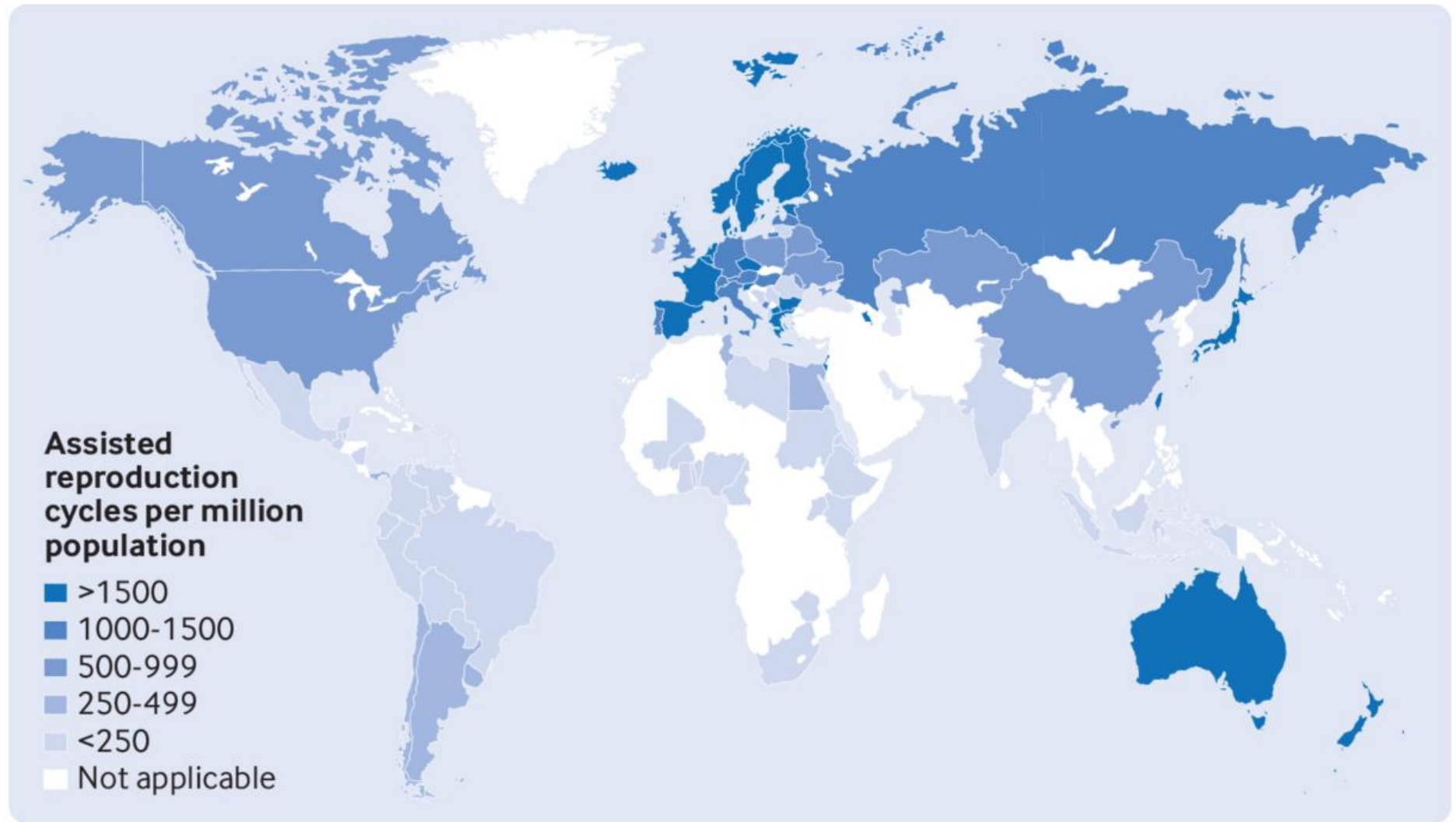
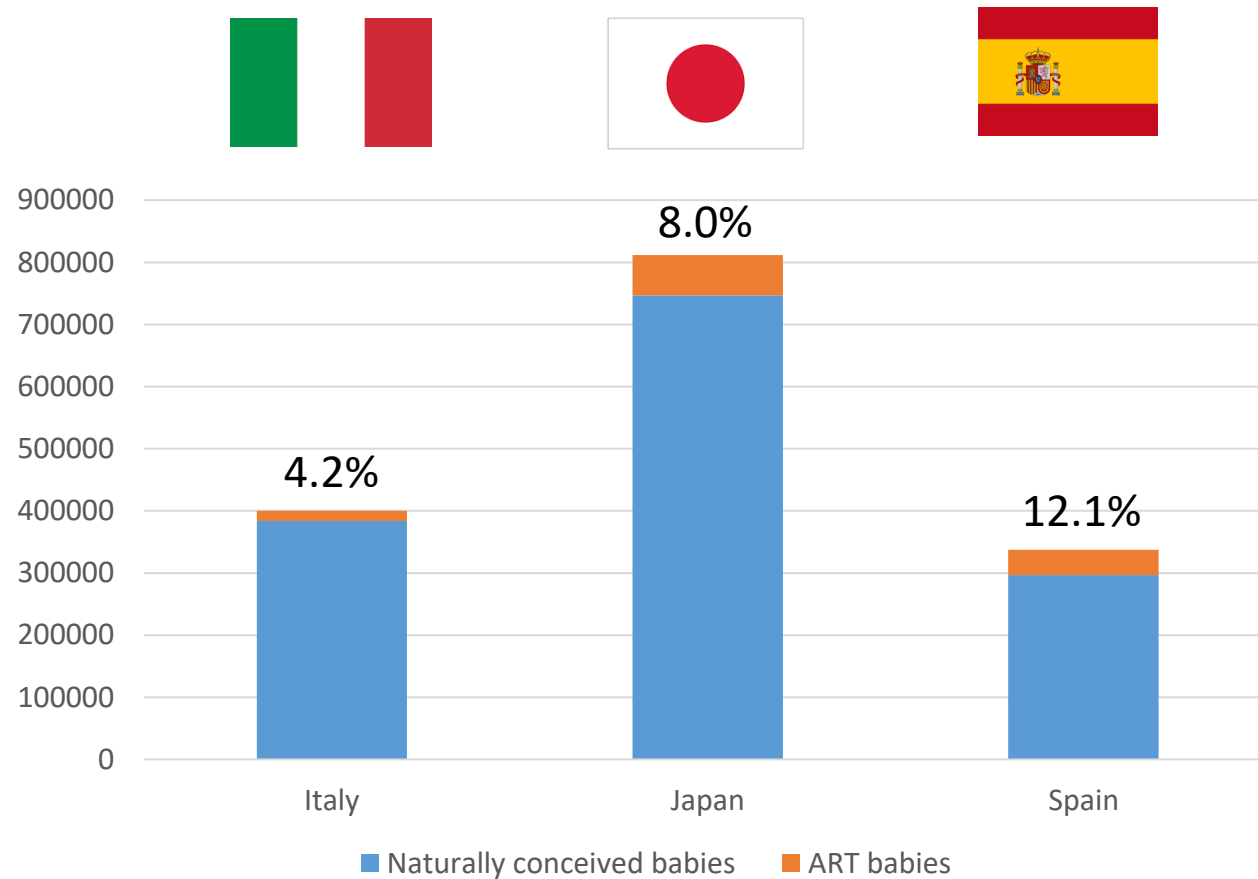
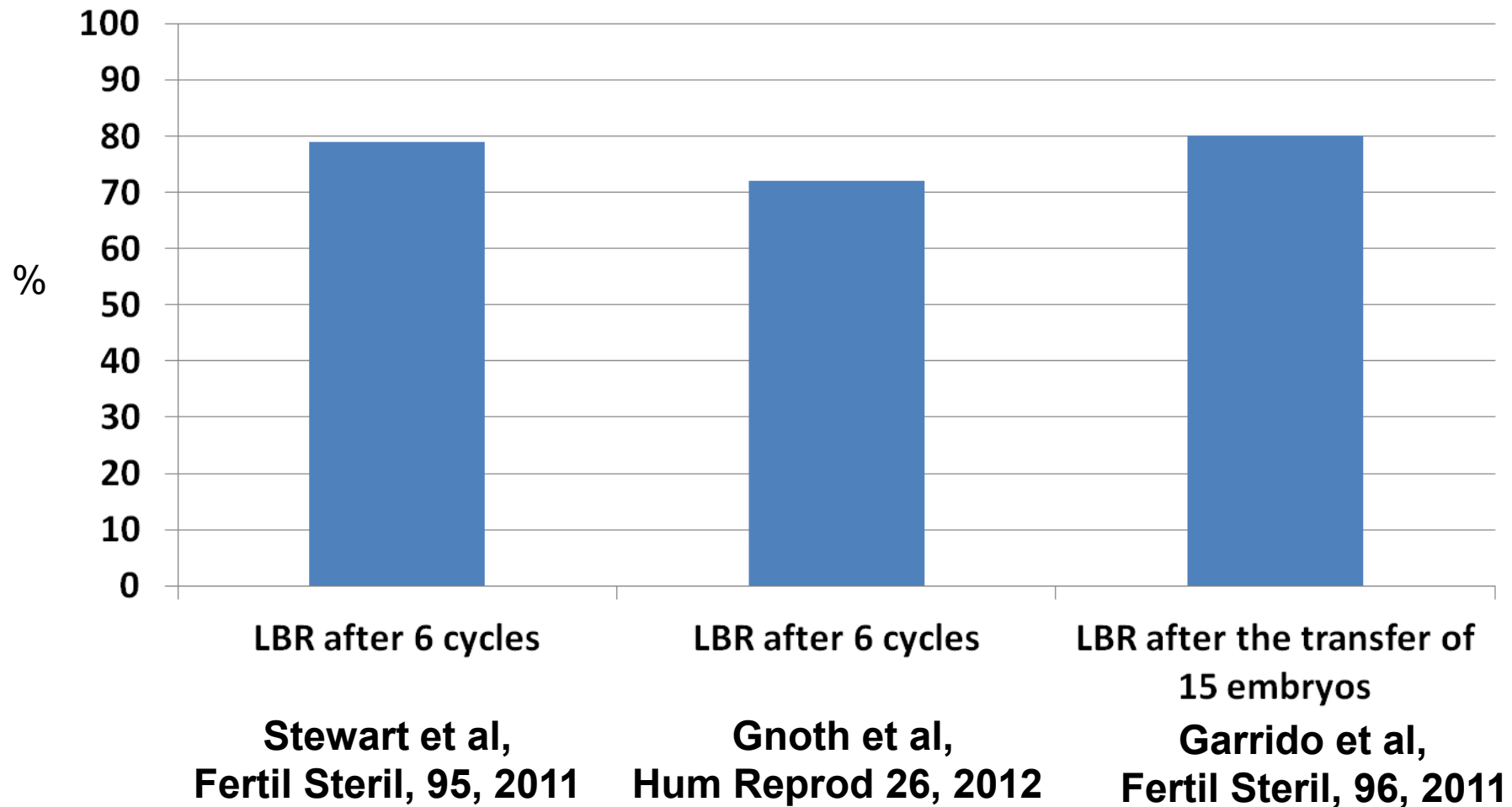


Fig 1 | Global use of assisted reproduction (cycles per million population) by country, 2018<sup>2</sup>

# Incidence of ART babies (2021)



# Cumulative live delivery after the exposure to multiple cycles of IVF (more than the usual 2 or 3 !)



# Treatment drop-out

## Causes of drop-out

**Financial  
reasons**

**Psychological  
factors**

**Unrealistic  
expectations**

**RIF**

- Couple distress
- Depression
- Anxiety
- Loss of trust in clinicians



# Treatment drop-out

## Causes of drop-out

**Financial reasons**

**Psychological factors**

- Couple distress
- Depression
- Anxiety
- Loss of trust in clinicians

**Unrealistic expectations**

- Life table
- Oncology

**RIF**

**Accurate diagnosis patients/ gametes/ embryos**

**Personalized Medicine**

**Precision Medicine**



# Personalized Medicine VS Precision Medicine

**Personalized Medicine:** tailoring investigations and therapies to each patient based on evidence, consideration of circumstances and clinical skills.



**Precision Medicine:** tailoring of diagnostics or therapeutics to individual patients based on their unique genetic and physiologic characteristics (emphasis on genomics, proteomics and other biologic omics).

In current evidence-based medicine, even efficacious therapies benefit only a minority of patients to whom they are administered, but all treated patients are exposed to the costs and potential harms.

Although there have been impressive advances in precision medicine in the past decade, better health outcomes require advances not only in omics-based medicine but also in traditional elements of personalized care.

## Personalized Medicine + Precision Medicine



**PERSONALIZED**

**PRECISION**

OK



Originators of Knowledge



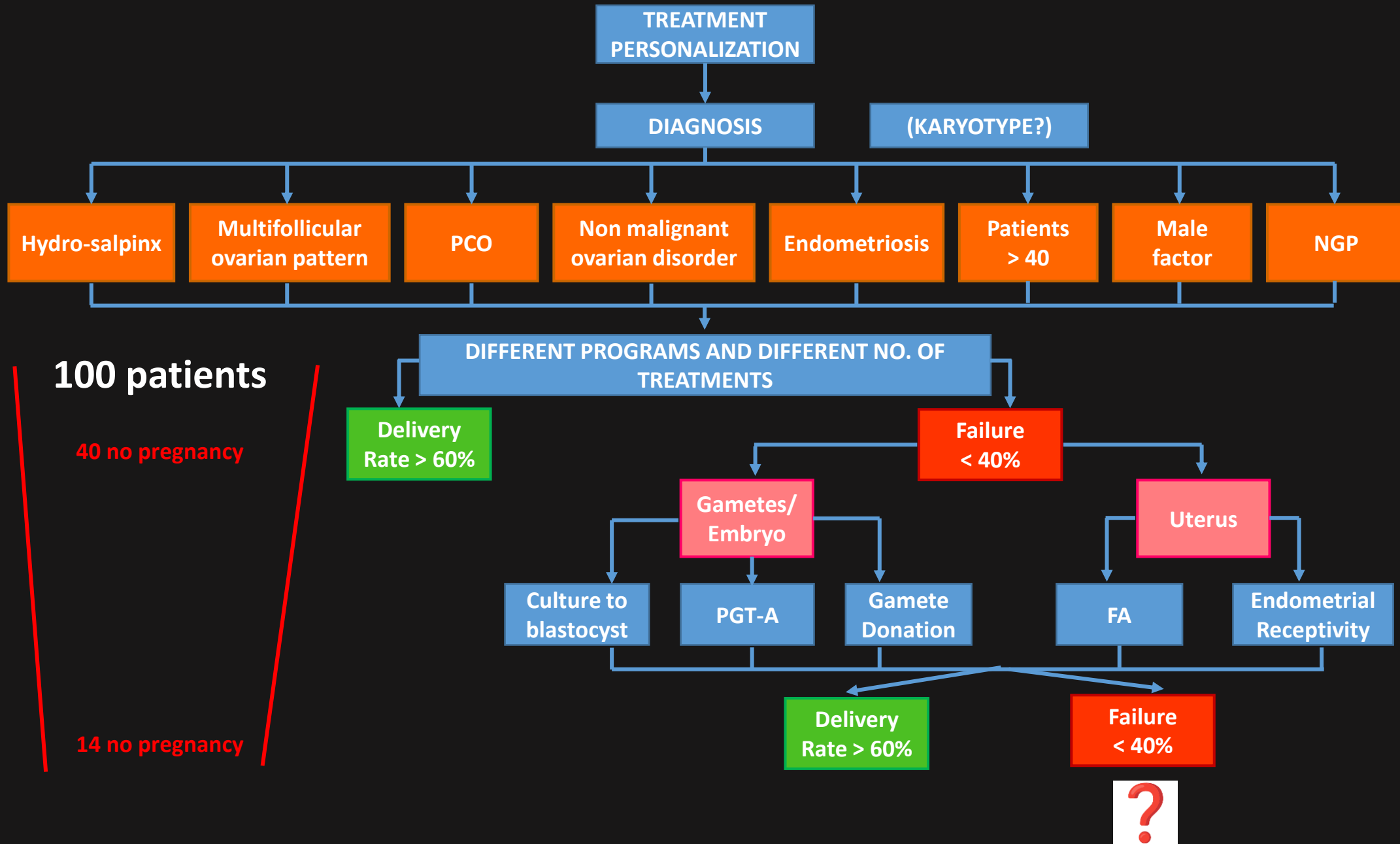
**MEDICINE**

**PERSONALIZED**

**PRECISION**

**EMBRYOLOGY  
BIOLOGY**





## Gestation vs pregnancy



Giuseppe Benagiano, MD, PhD; Salvatore Mancuso, MD, PhD;  
Luca Gianaroli, MD, PhD; Gian Carlo Di Renzo, MD, PhD

**Gestation:** the period from fertilization (whether in vitro or in utero) to birth

**Pregnancy:** the period after implantation has been completed.



# EARLY PREGNANCY FAILURE

221  
HEALTHY WOMEN  
ATTEMPTING TO  
CONCEIVE (707 cycles)

The New England  
**Journal of Medicine**  
©Copyright, 1988, by the Massachusetts Medical Society  
Volume 319 JULY 28, 1988 Number 4

**INCIDENCE OF EARLY LOSS OF PREGNANCY**  
ALLEN J. WILCOX, M.D., PH.D., CLARICE R. WEINBERG, PH.D., JOHN F. O'CONNOR, PH.D.,  
DONNA D. BAIRD, PH.D., JOHN P. SCHLATTERER, M.S., ROBERT E. CANFIELD, M.D.,  
E. GLENN ARMSTRONG, PH.D., AND BRUCE C. NISULA, M.D.

 DAILY URINARY  
LEVEL OF hCG

198  
INCREASED  
LEVELS OF hCG

19 (10%)  
MISCARRIAGES

136 (68%)  
CLINICAL  
PREGNANCIES

23 WOMAN:  
NO hCG  
INCREASE

43 (22%)  
NO  
GESTATIONAL  
SAC

PRECLINICAL  
LOSSES

**EARLY**  
PREGNANCY  
FAILURE  
(30%)

A NOTABLE PROPORTION OF EMBRYOS NEVER IMPLANT AND MANY THAT DO, ARE LOST WITHOUT CLINICAL RECOGNITION OF PREGNANCY



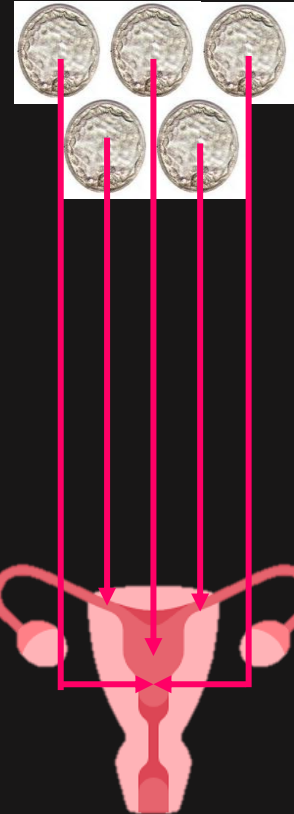
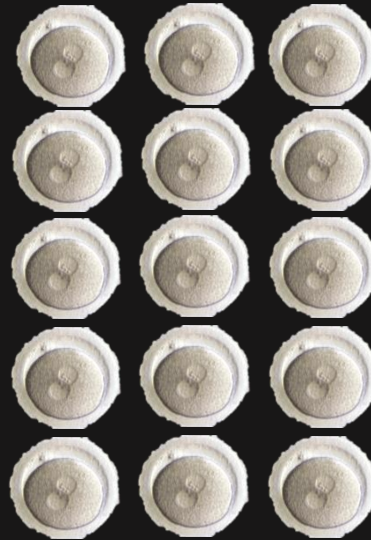
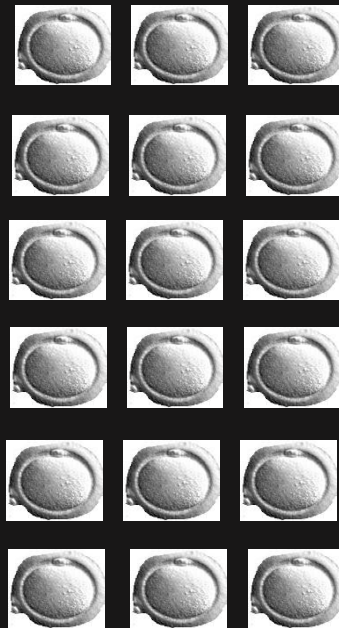
# Definitions

**Treatment cycle**

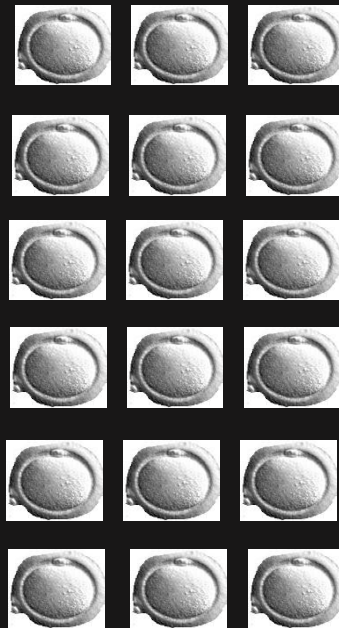
**A period of treatment followed by a period of rest.**

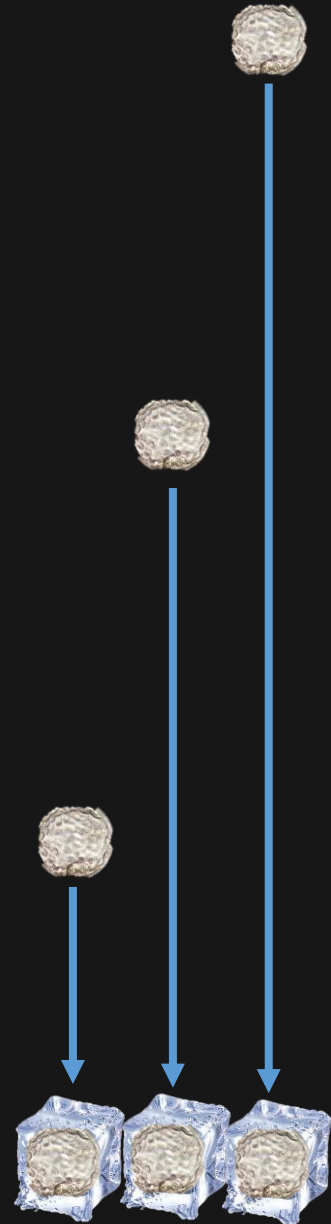
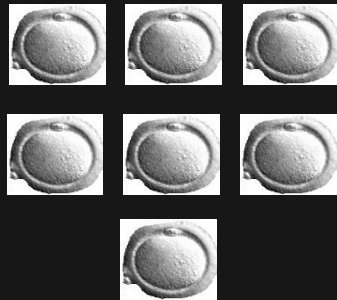
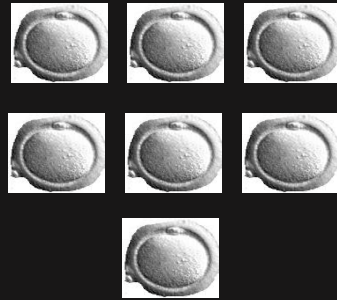
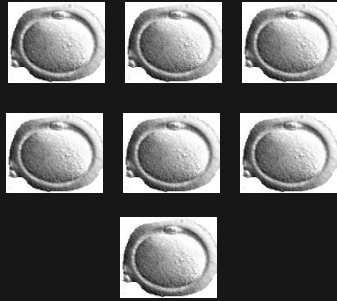
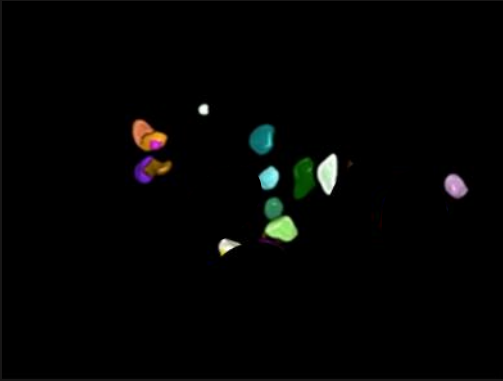
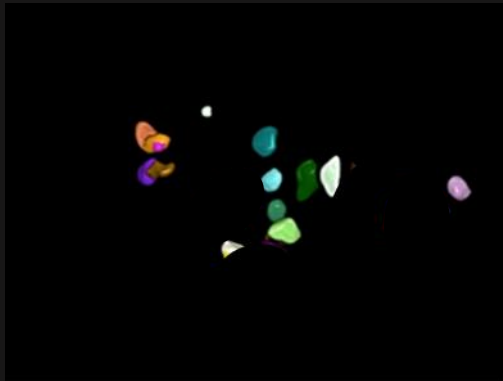
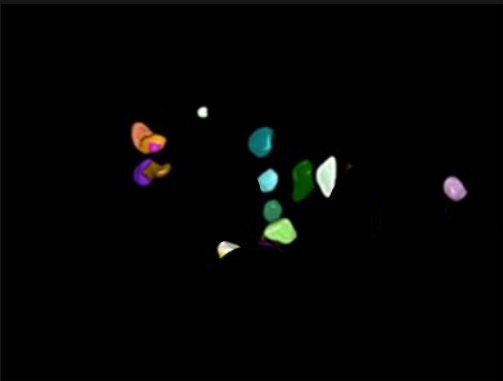


# What we get



# What we get



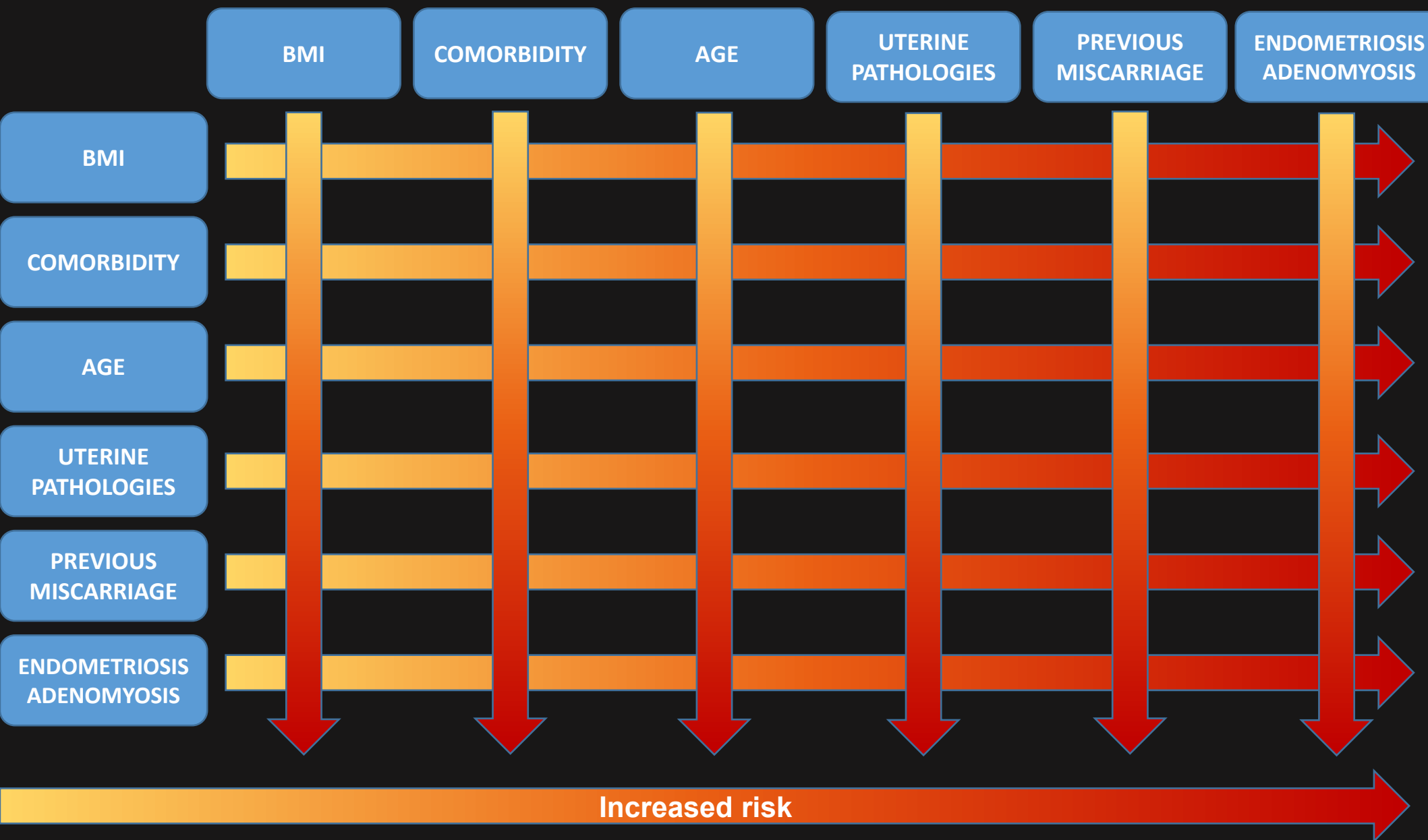


OK



Originators of Knowledge





OK



Originators of Knowledge



# IVF LITE Program

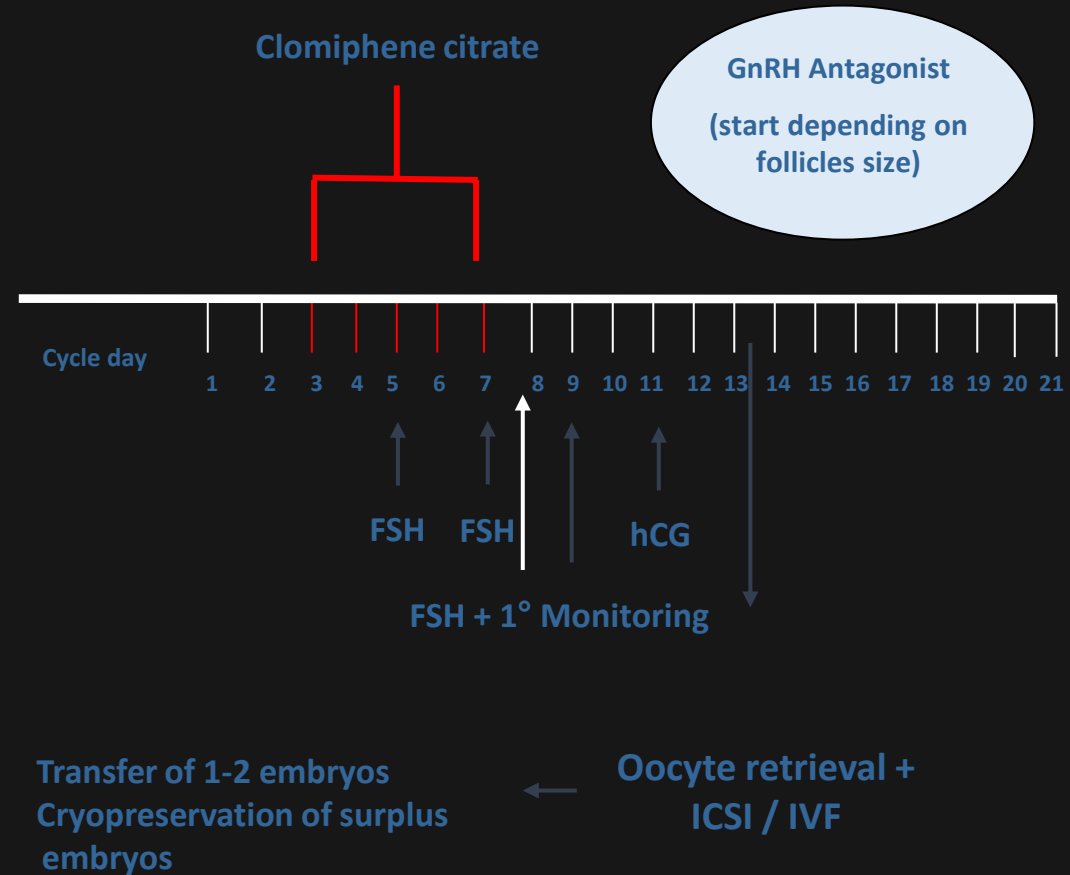
It is a protocol that implies a maximum of 3 embryo transfers (fresh or frozen, regardless of the number of oocyte retrievals), to be completed within 12 months.

## IVF LITE - INDICATIONS

- ✓ Age female partner  $\leq 38$  years
- ✓ No previous IVF/ICSI cycles
- ✓ No severe male factor of infertility
- ✓ No endometriosis
- ✓ AMH  $\geq 1.5$  ng/ml and/or FSH  $\leq 10$  mIU/ml
- ✓ Regular menstrual cycles (28-30 days)
- ✓ Normal karyotype

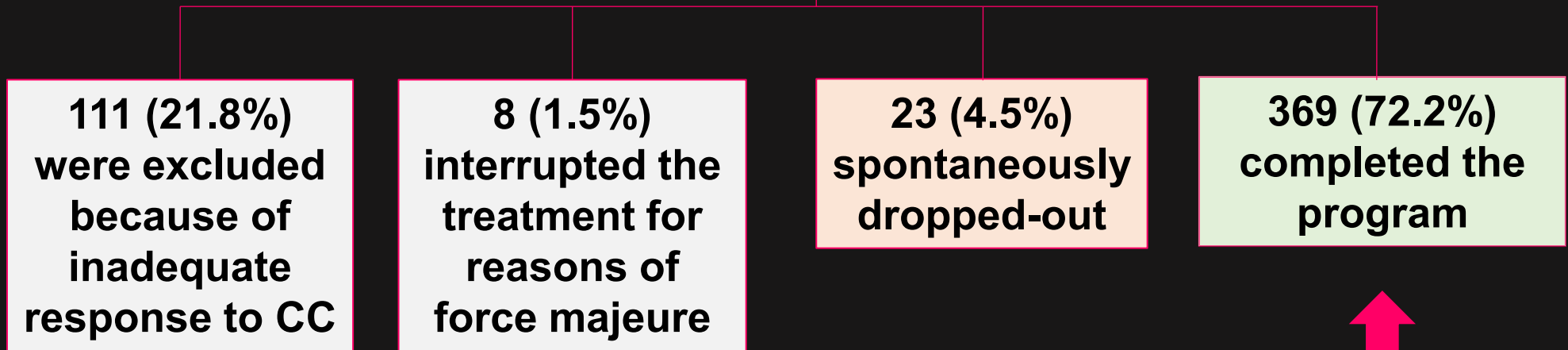
## CONCLUSION OF THE PROGRAM

- ✓ Pregnancy to term, regardless of the number of embryo transfers
- ✓ Three embryo transfers



# IVF LITE Program

**511 eligible consecutive infertile couples**



# Clinical outcome at the first, second and third ET

773 embryo transfers

	1 <sup>st</sup> ET	2 <sup>nd</sup> ET	3 <sup>rd</sup> ET
Transferred cycles	369	237	167
Age	33.4±3.1	33.6±3.2	34.0±3.3
Transferred embryos (mean±SD)	572 (1.6±0.6) <sup>a</sup>	384 (1.6±0.6) <sup>b</sup>	295 (1.8±0.6) <sup>a,b</sup>
Clinical pregnancies (% per ET )	148 (40.1) <sup>c</sup>	78 (32.9)	46 (27.5) <sup>c</sup>
Implantation rate	29.0 <sup>d</sup>	25.5 <sup>e</sup>	17.3 <sup>d,e</sup>
Live births (% per ET)	132 (35.8) <sup>f</sup>	70 (29.5)	37 (22.2) <sup>f</sup>

<sup>a</sup>  $p=0.0002$

<sup>b</sup>  $p=0.0174$

<sup>c</sup>  $p=0.0068$

<sup>d</sup>  $p=0.001$

<sup>e</sup>  $p=0.0133$

<sup>f</sup>  $p=0.0024$



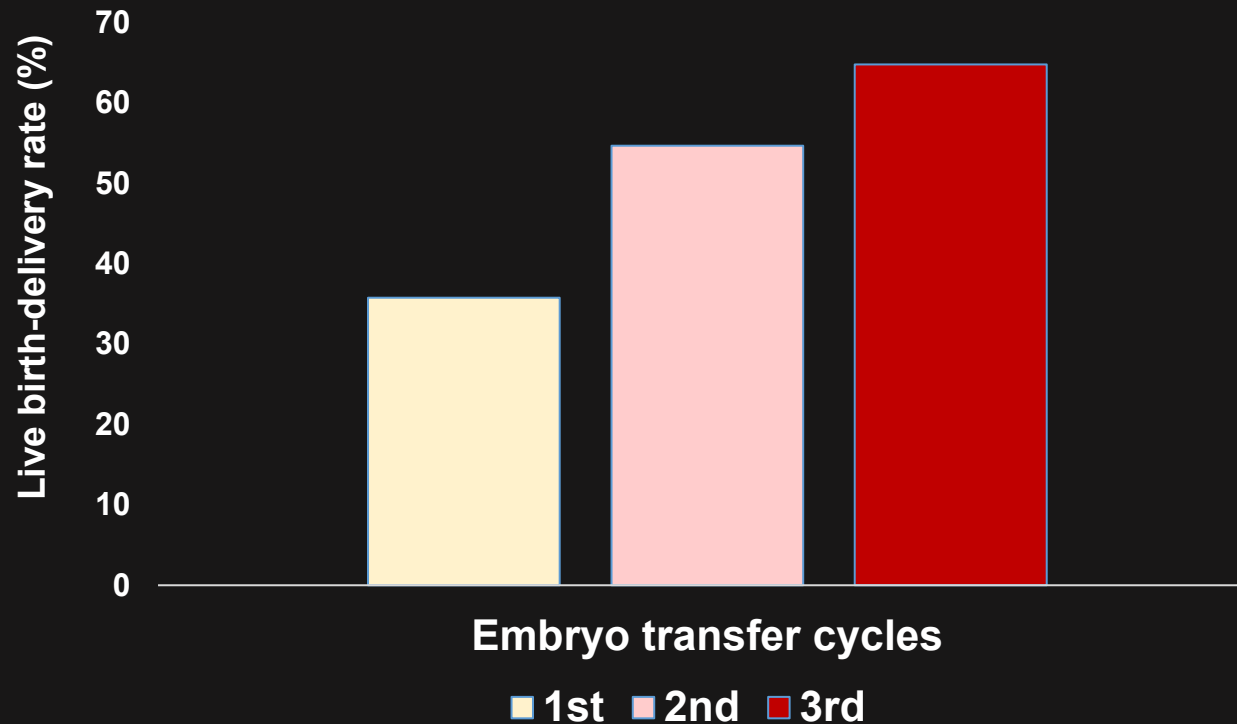
# Clinical outcome in relation to maternal age

	23-30 yrs	31-32 yrs	33-34 yrs	35-38 yrs
No. of patients	61	67	90	151
Age	28.5±1.6	31.5±0.5	33.5±0.5	36.2±1.4
Transferred cycles	131	133	182	327
Cumulative live births	39	49	59	92
% per patient	63.9	73.1	65.6	60.9
% per ET	29.8	36.8	32.4	28.1

**no significant difference in terms of cumulative LBR per patient**



# Cumulative live birth-delivery rate per patient after up to three consecutive embryo transfers



Exposure to one embryo transfer resulted in 35.8% LBR per patient, exposure to up to two embryo transfers yielded a cumulative LBR of 54.7%, and the completion of the IVF Lite program gave a **cumulative LBR per patient of 64.8%**



# Reproductive follow-up after completion of the IVF-Lite program

At completion of the IVF-Lite program,  
141 couples had 304 supernumerary cryopreserved embryos.



**50 couples returned to perform a thawing cycle**



**24 searching for a second pregnancy**



**9 term pregnancies  
37.5% live birth rate**



**26 searching for their first pregnancy**



**9 term pregnancies  
34.6% live birth rate**



# Reproductive follow-up after completion of the IVF-Lite program

A PGT-A cycle was performed in 15 of the patients who had failed the program and did not have supernumerary cryopreserved embryos



92 blastocysts were analyzed resulting in  
49 with an abnormal chromosome complement (53.2%)



22 single aneuploidies (44.9%)  
27 multiple aneuploidies (55.1%)

Embryo transfer was performed in all 15 patients

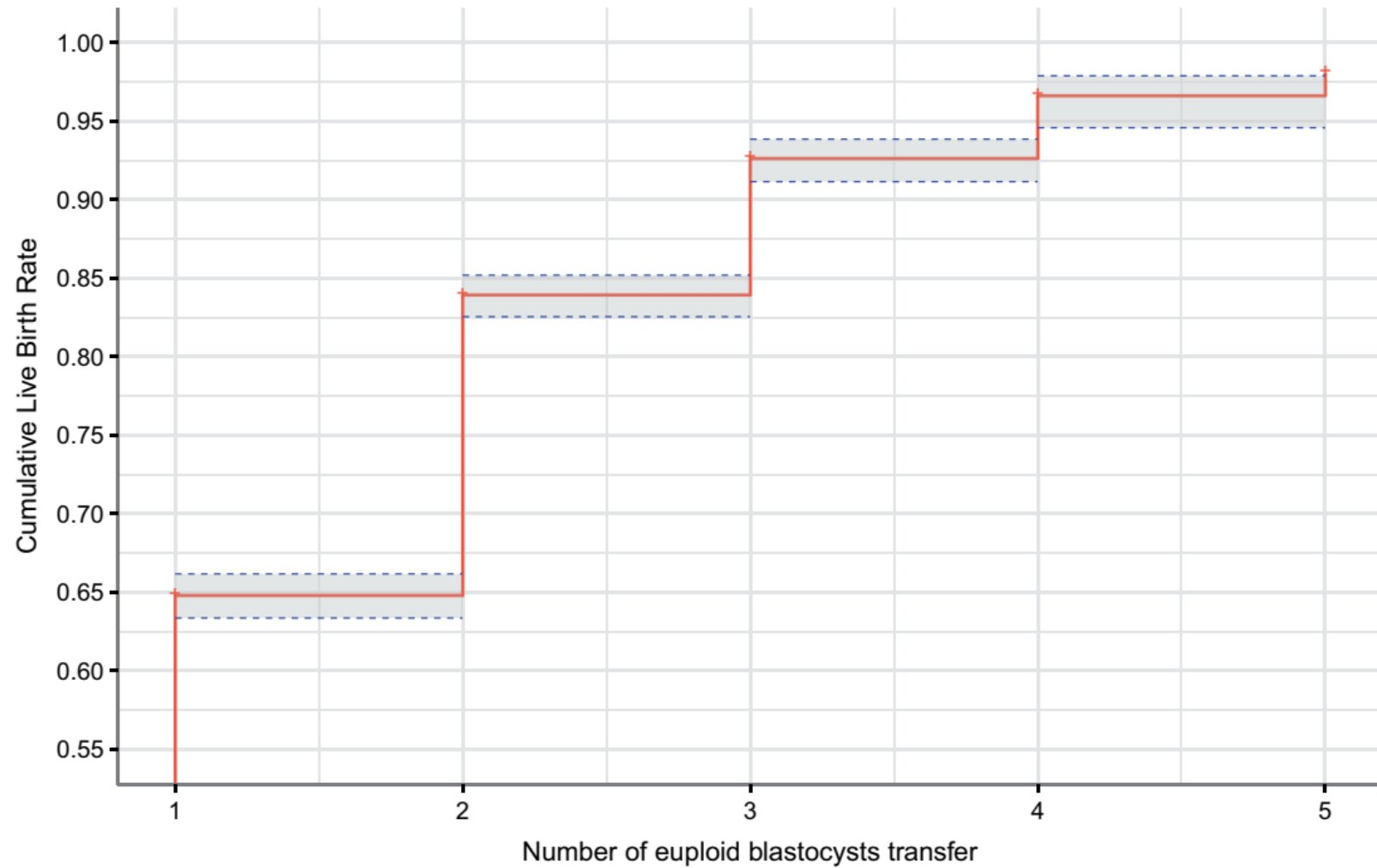


9 term pregnancies (60.0% per patient)

## **EXCLUSION CRITERIA:**

- history of any embryo transfer in another clinic
- history of any unscreened embryo transfer in participating clinics
- parental karyotype abnormalities
- use of donor oocytes or gestational carrier
- intracavity uterine pathology
- congenital uterine anomalies
- intramural fibroids distorting uterine cavity
- adenomyosis
- communicating hydrosalpinx
- endometrial thickness <6 mm prior to initiating of progesterone
- use of testicular sperm due to non-obstructive azoospermia
- transfer of an embryo with a reported intermediate chromosome copy number (i.e. mosaic)
- PGT cycles for monogenic disorders, or structural chromosome rearrangements
- Patients who received a double-euploid blastocyst transfer (DET) were excluded if only one of the embryos implanted

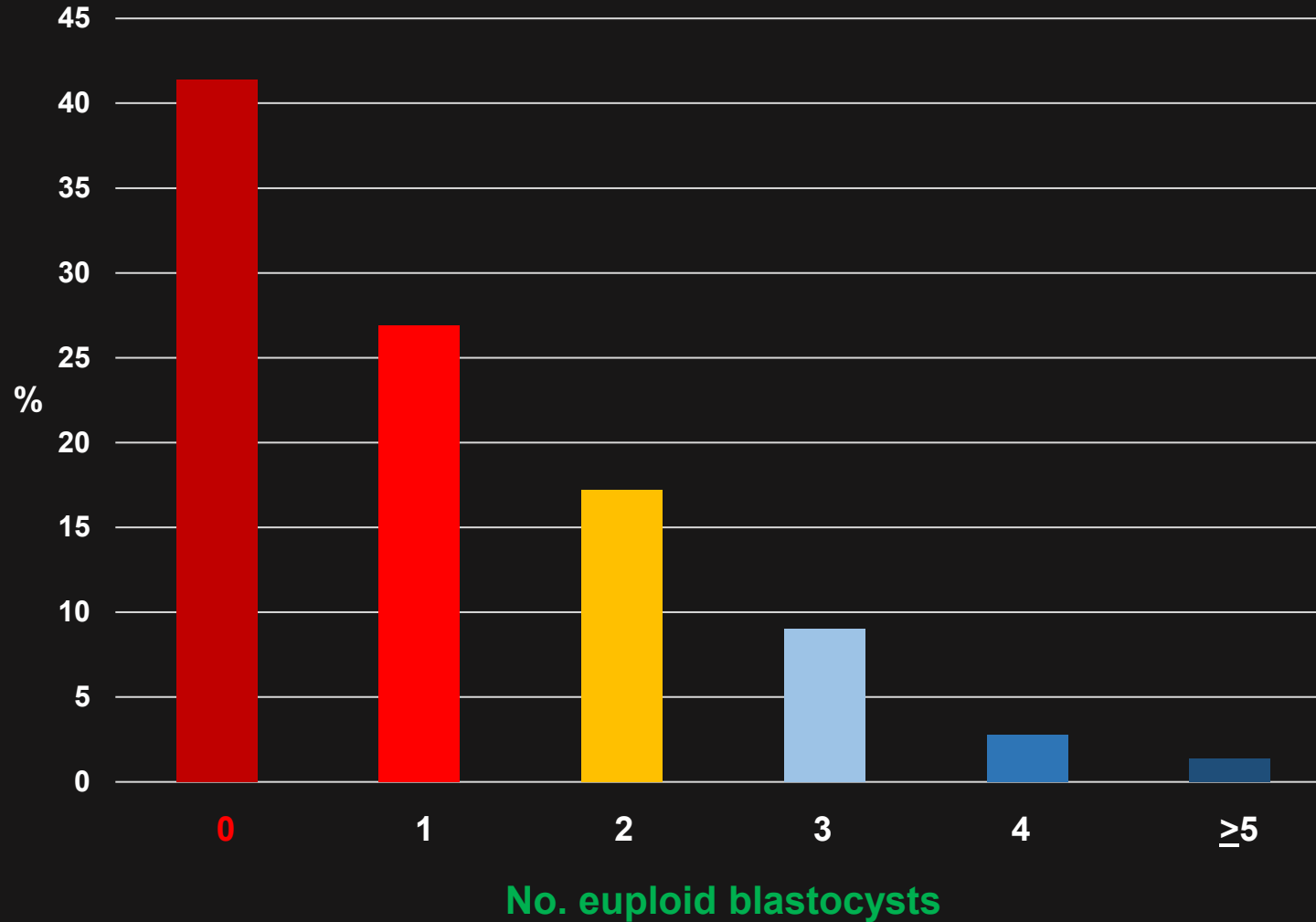




**Figure 1.** Cumulative live birth rate after subsequent euploid blastocyst transfer. Red line shows the cumulative live birth. Blue dotted lines show upper and lower bounds of the CI.



# Proportion of cycles with TE-euploid blastocysts



SISMER data up to February 2023

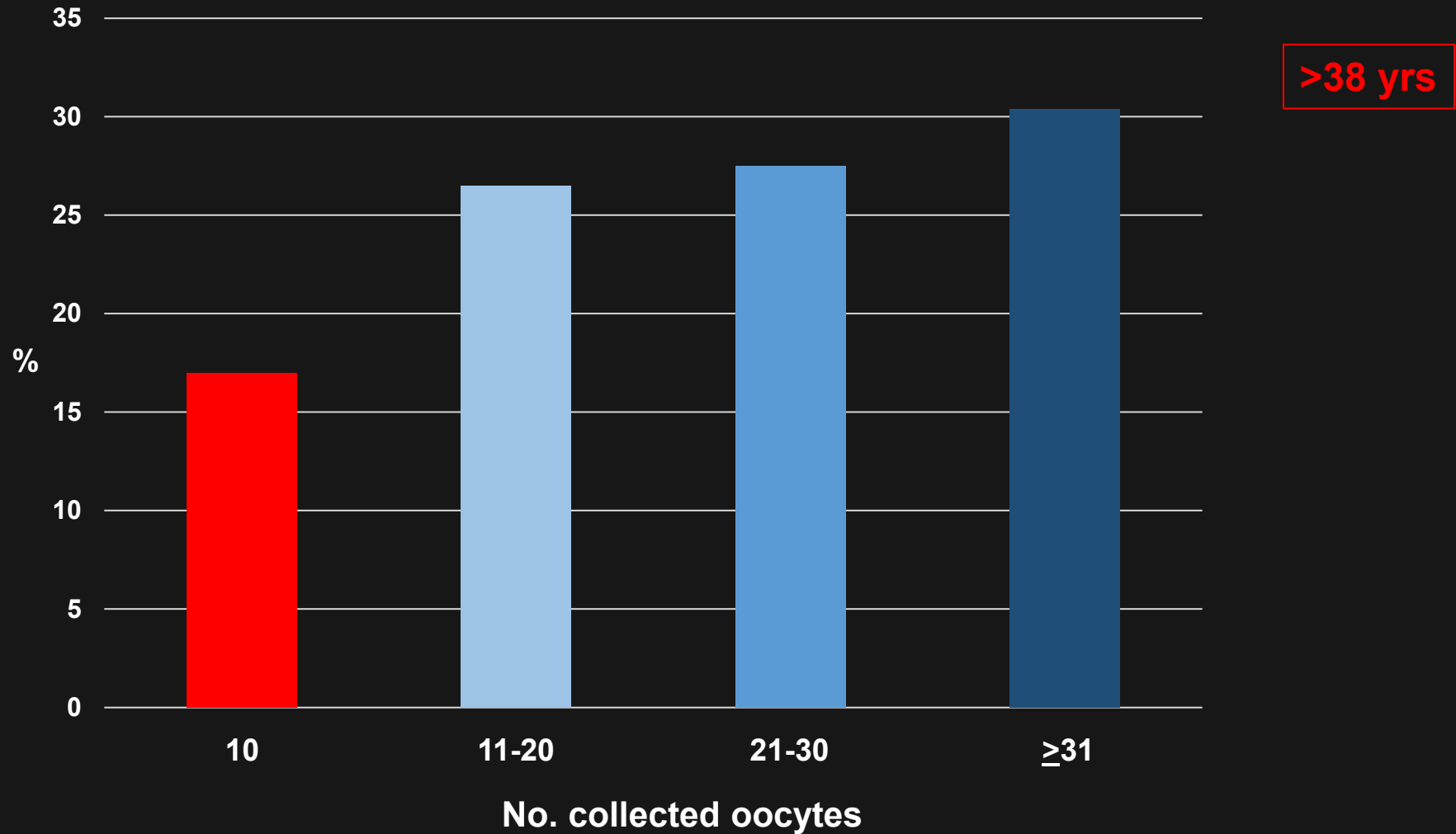
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Originators of Knowledge



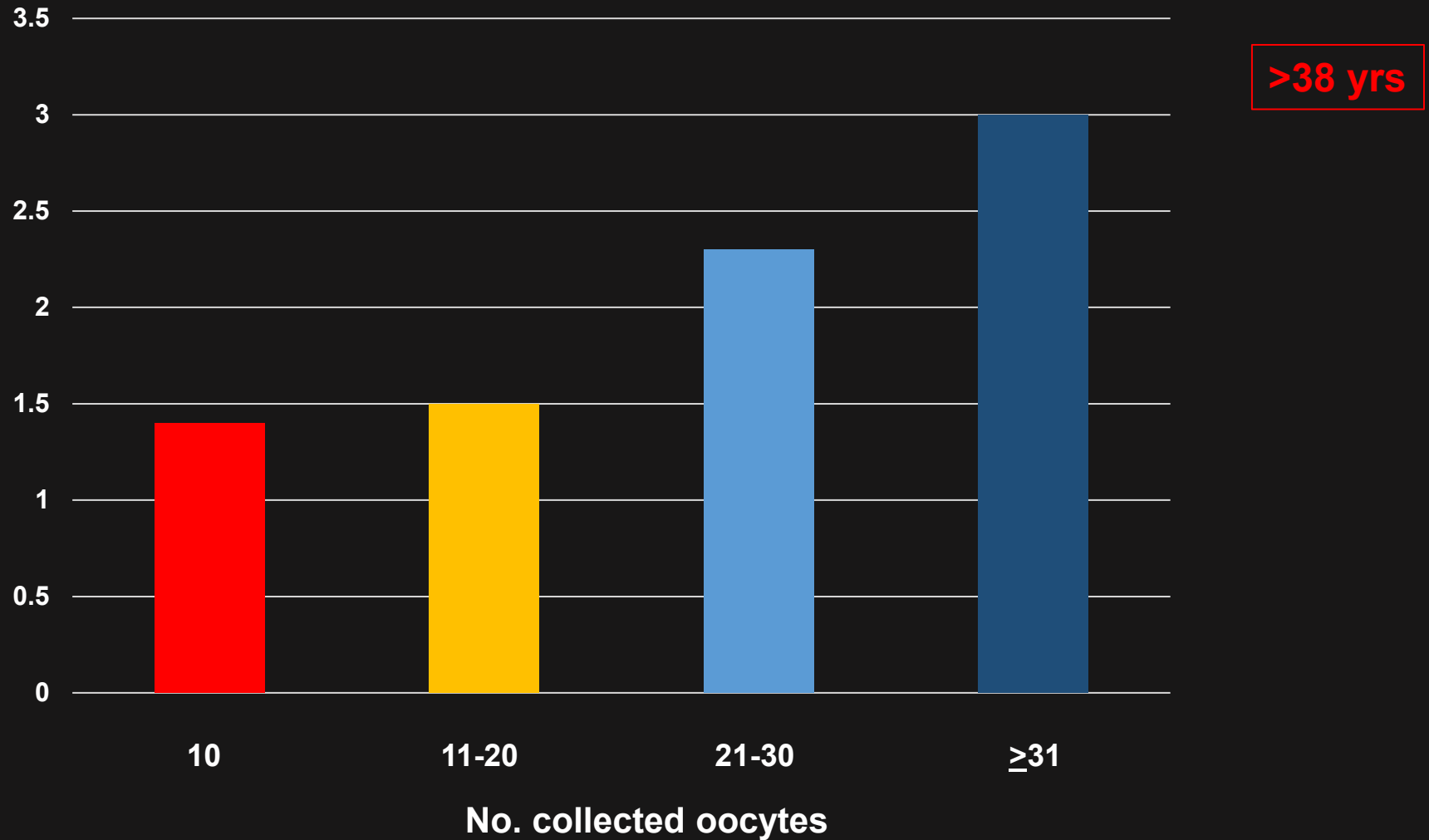
# Proportion of TE-euploid blastocysts in relation to the number of collected oocytes



SISMER data up to February 2023



# Number of pick-ups in relation to the number of collected oocytes



SISMER data up to February 2023



# Definitions

**Treatment cycle**

**A period of treatment followed by a period of rest.**

**Course of treatments**

**A treatment plan made up of several cycles of treatment. When a treatment cycle is repeated multiple times on a regular schedule, it makes up a course of treatment. A course of treatment can last for several months.**



# Life tables

A life table (or a cohort life table) in epidemiology is defined as “a table depicting the survival data of a cohort of individuals in a clinical study or trial. Although it is generally used for studying mortality, the life table format can be used to summarize any duration variable.

## The importance of life tables in ART

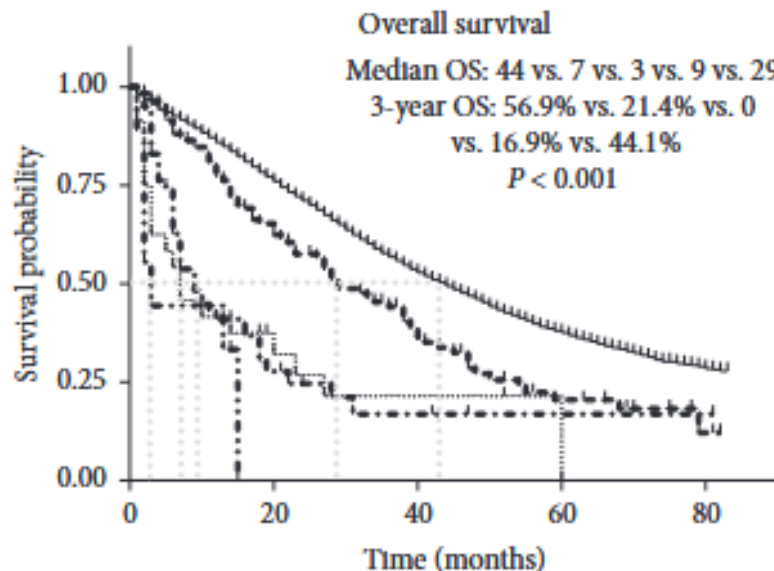
Life tables in ART can help develop a **NEW PARADIGM** based on courses of treatments instead of single treatment cycles.

This might be useful to reconsider several aspects, including:

- Cost-effectiveness
- Rules for access to treatment
- Outcomes



# Ovarian cancer



## Patients at risk

	11657	7599	3571	1339	155
Non-RT	11657	7599	3571	1339	155
R	29	7	3	1	1
R + S	9	2	2	2	2
R + C	59	12	5	2	2
R + S + C	118	68	30	11	3

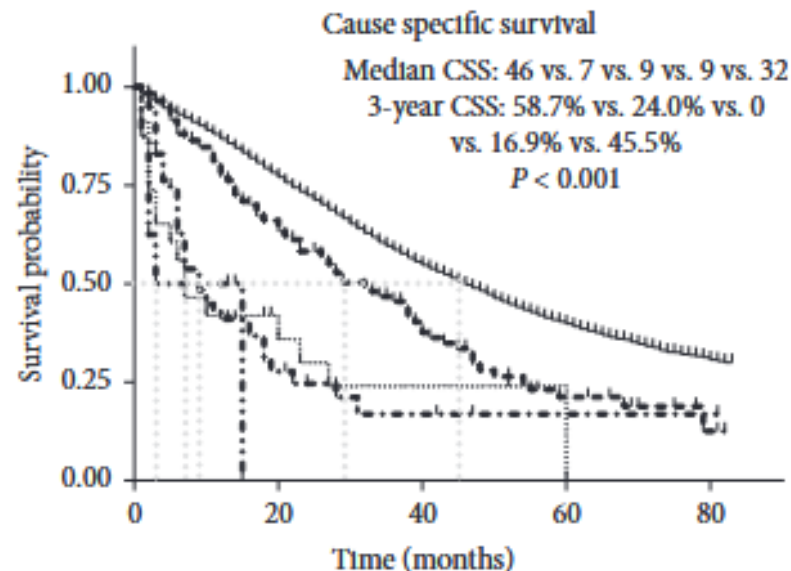
— Non-RT

... R

- - - R + S

- . - R + C

- - - R + S + C



## Patients at risk

	11593	7562	3559	1337	155
Non-RT	11593	7562	3559	1337	155
R	27	7	3	1	1
R + S	8	2	2	2	2
R + C	59	12	5	2	2
R + S + C	118	68	30	12	3

— Non-RT

... R

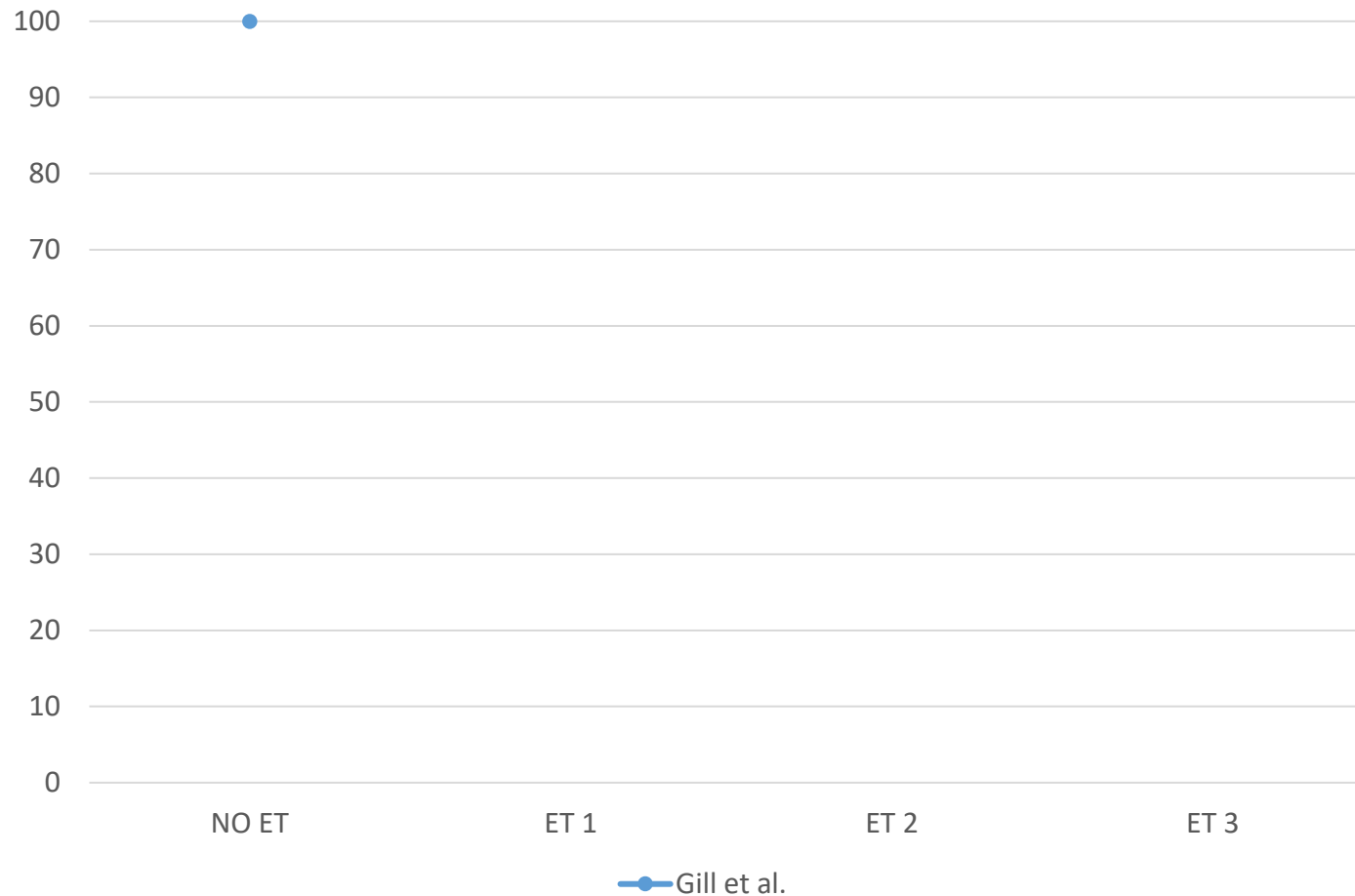
- - - R + S

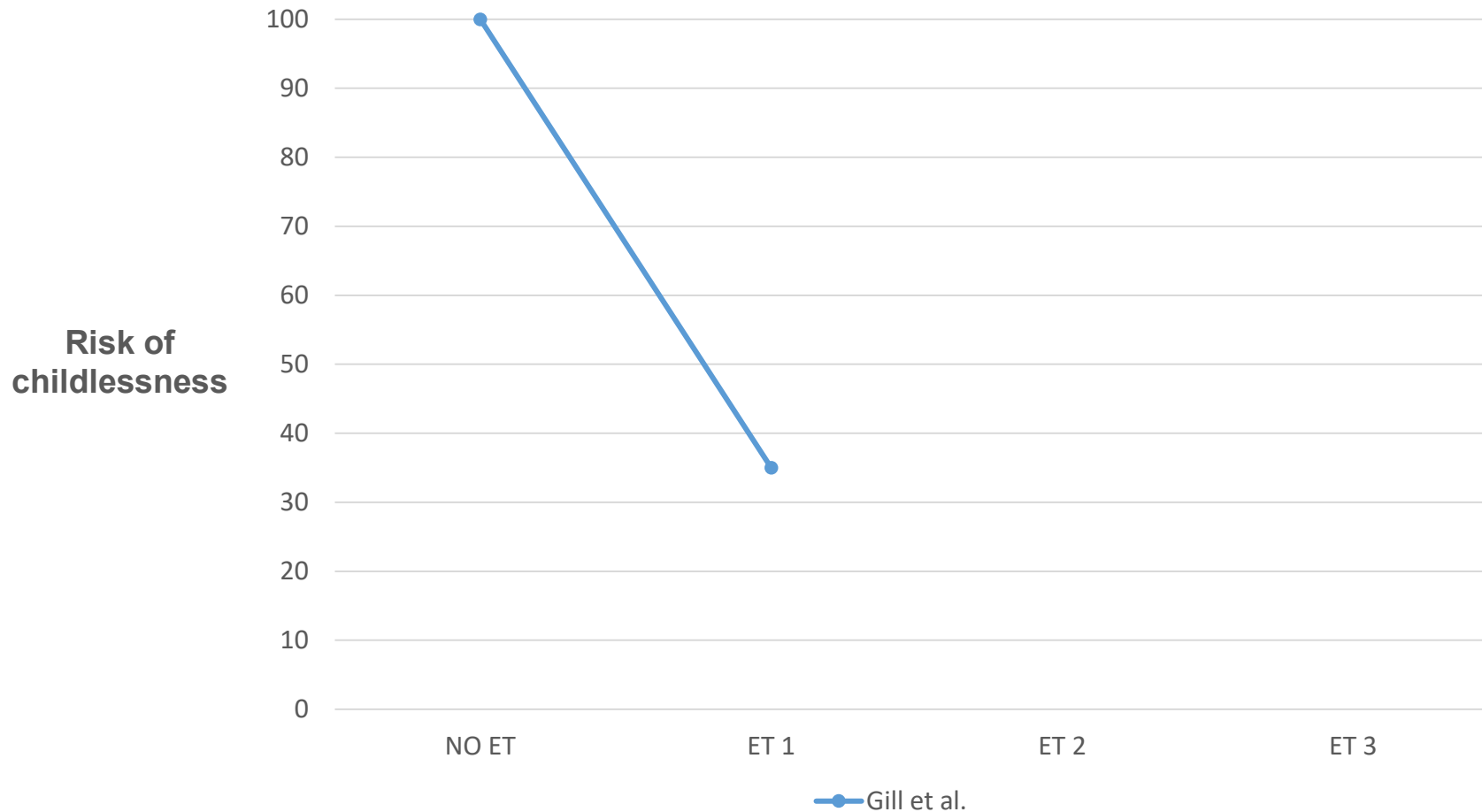
- . - R + C

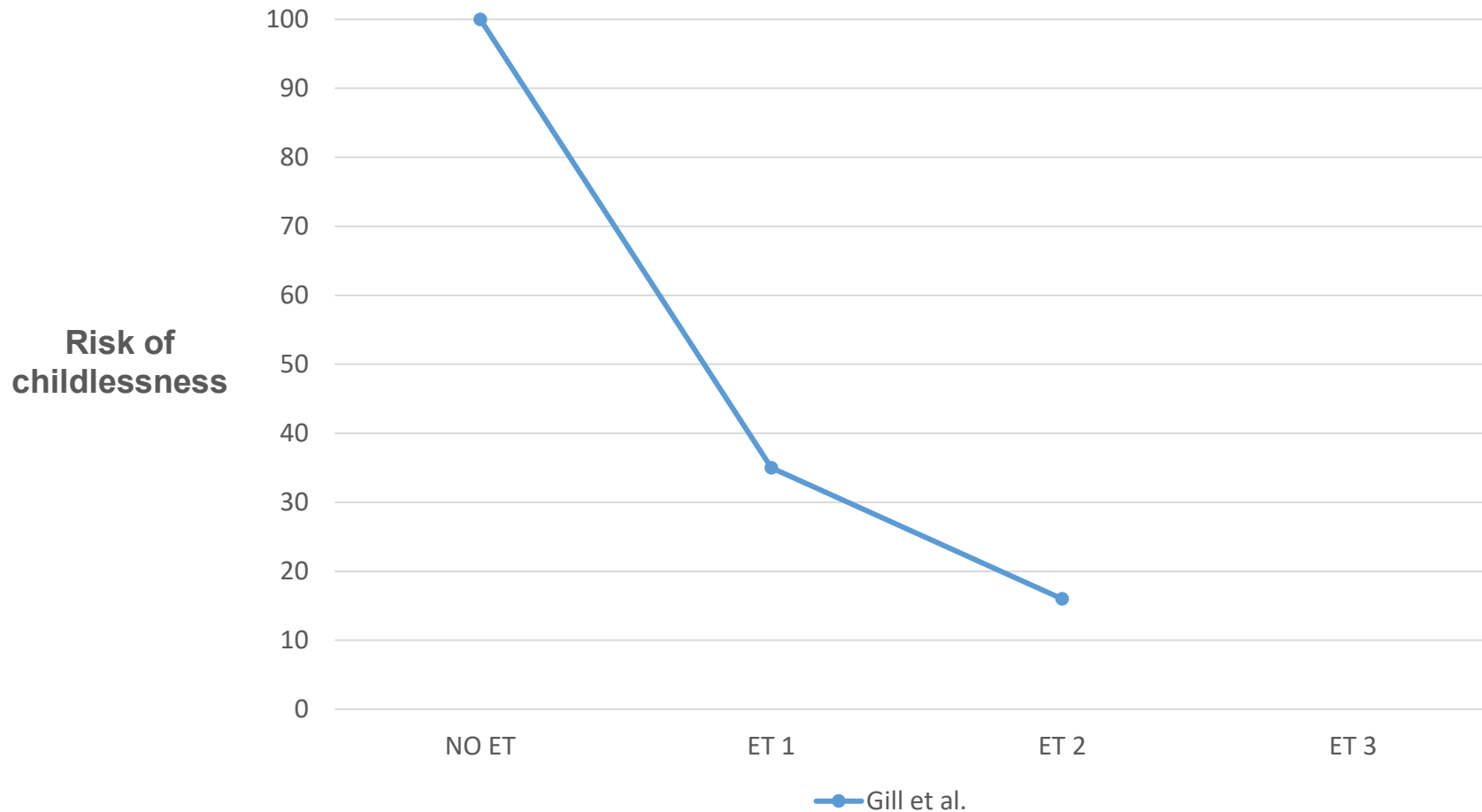
- - - R + S + C

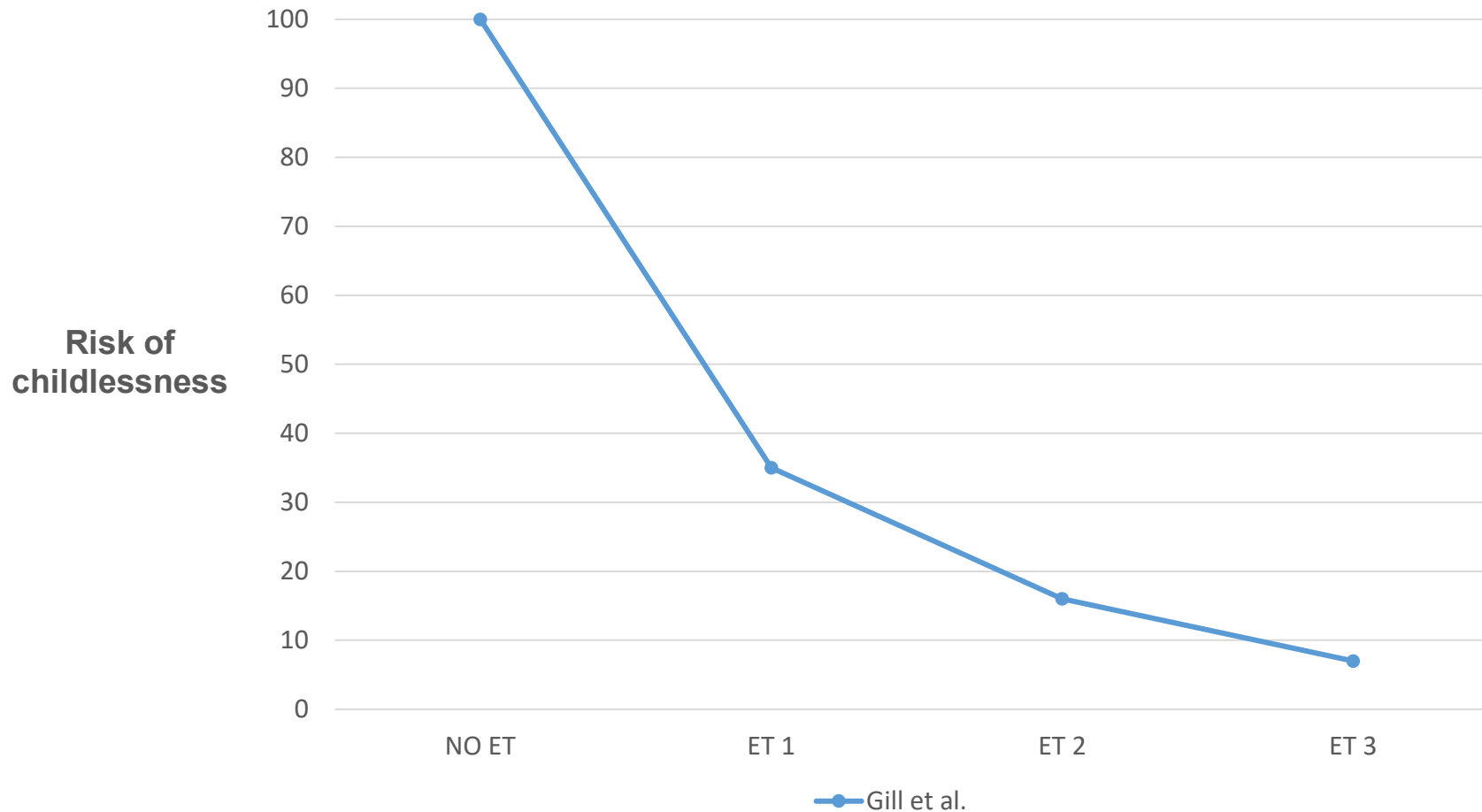


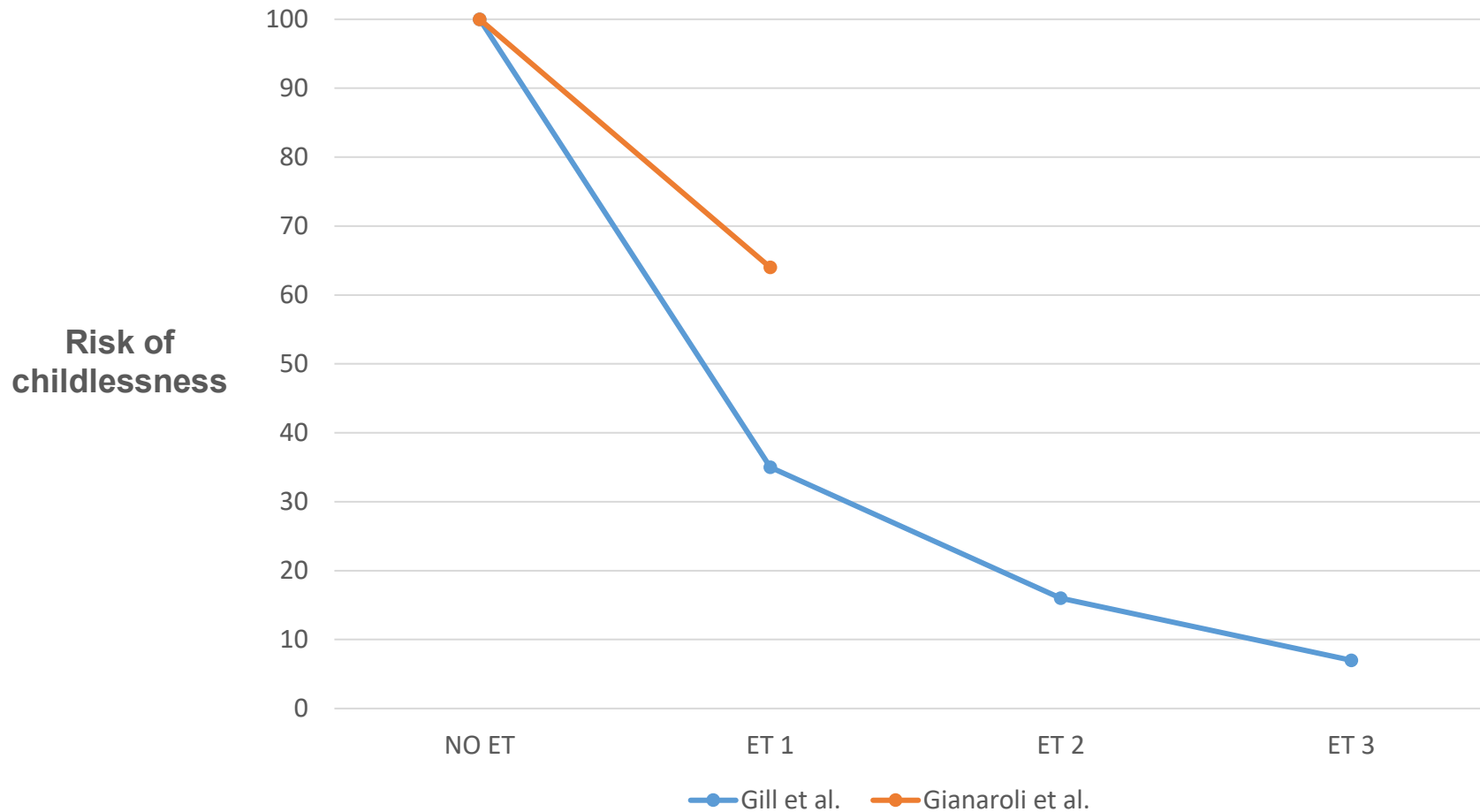
**Risk of  
childlessness**

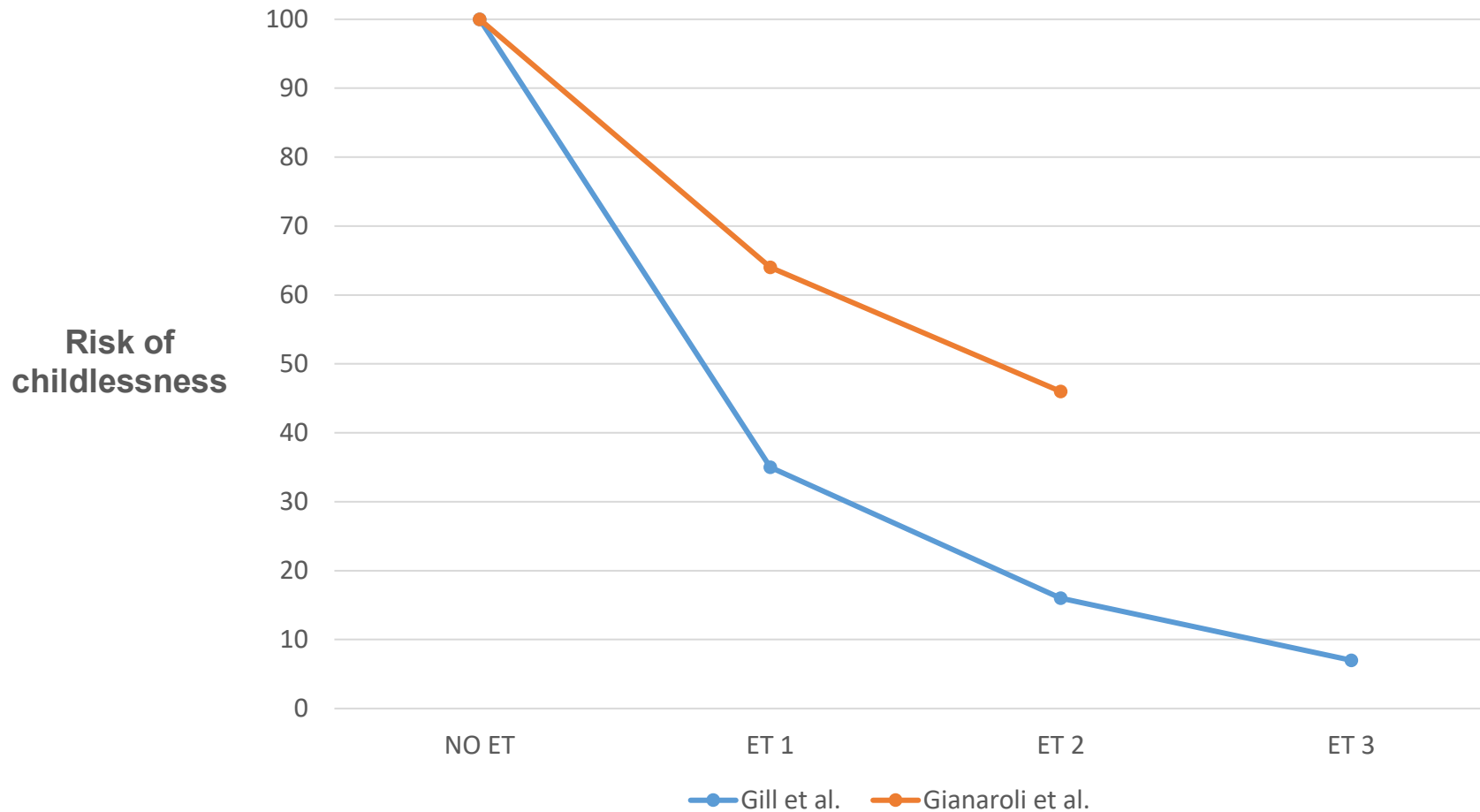


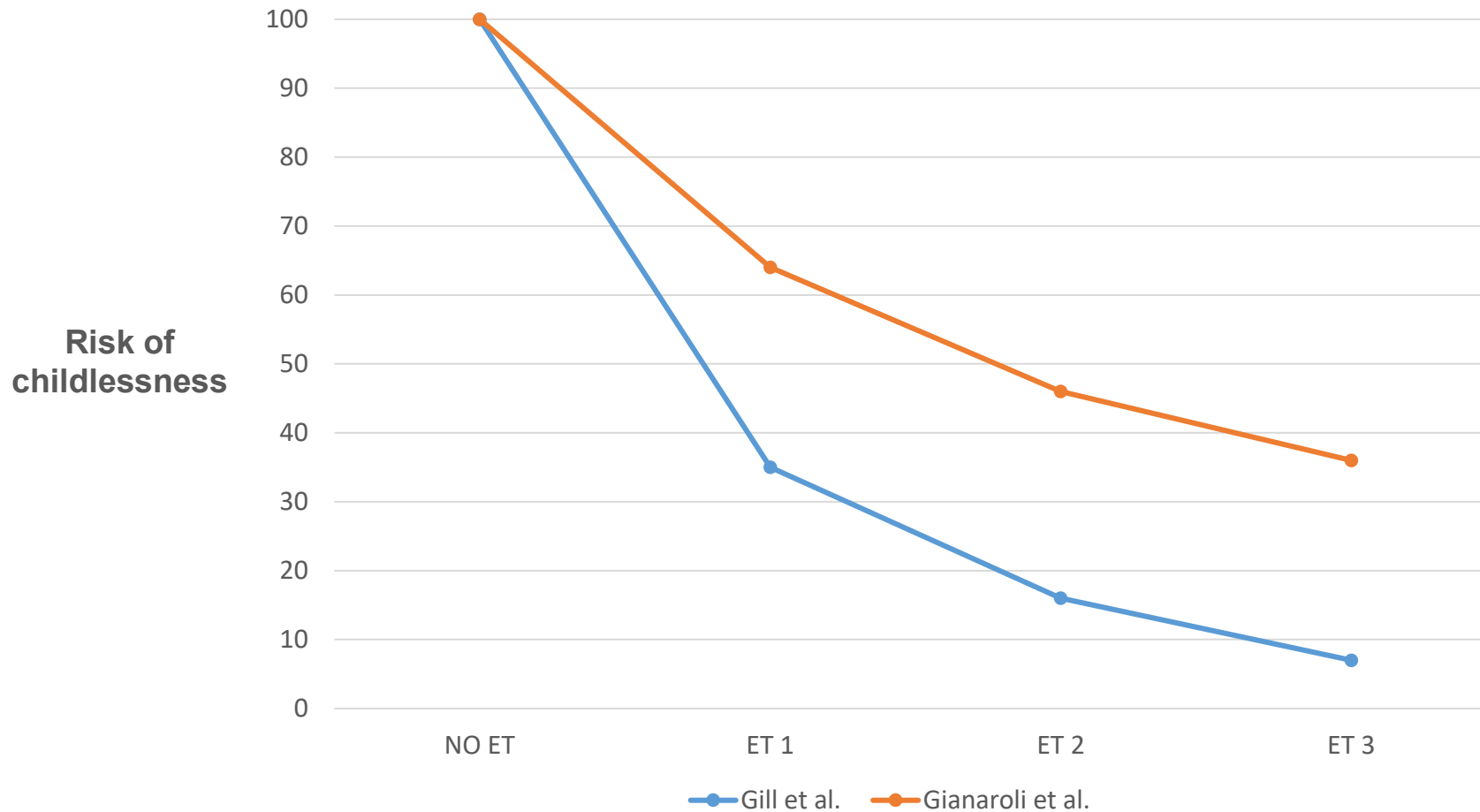












# PGT-A

65

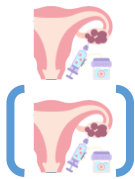
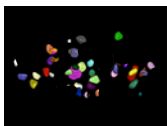
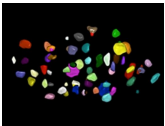


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# PGT-A










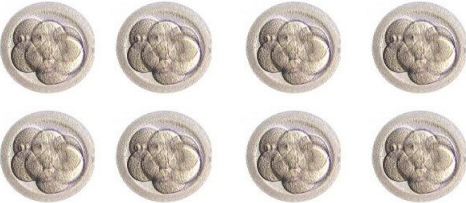


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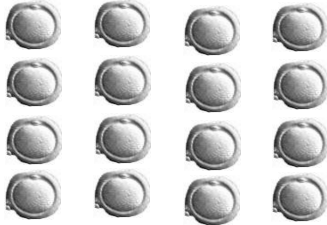
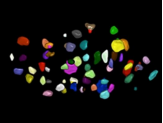
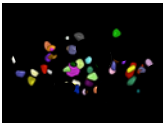

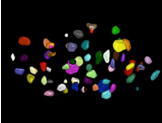
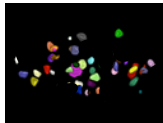


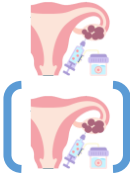







# PGT-A

65	84
	
 	   
	
	

















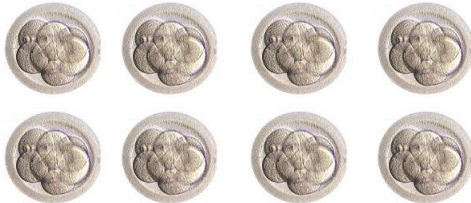
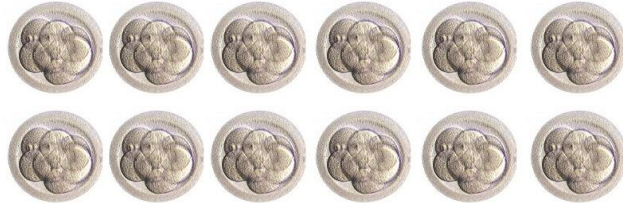





# PGT-A

65	84
	
  	  
  	   


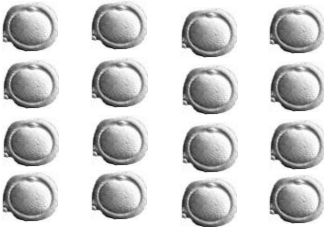
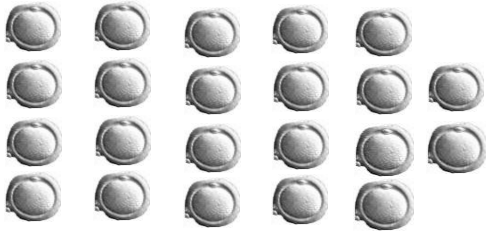
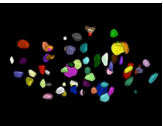
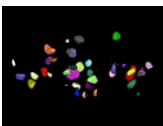
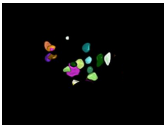
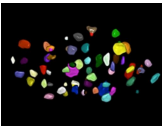
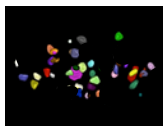
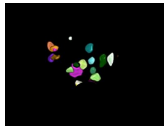
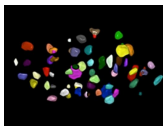
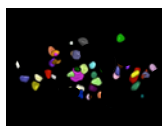


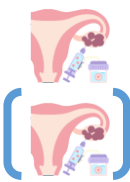





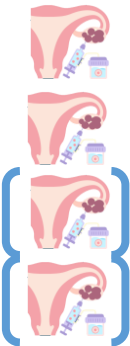
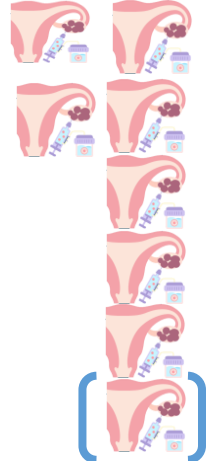


# PGT-A

65	84	93
		
 	   	     
		
		



# PGT-A

65	84	93
		
  	  	  
  	  	  



# IVF Lite

64



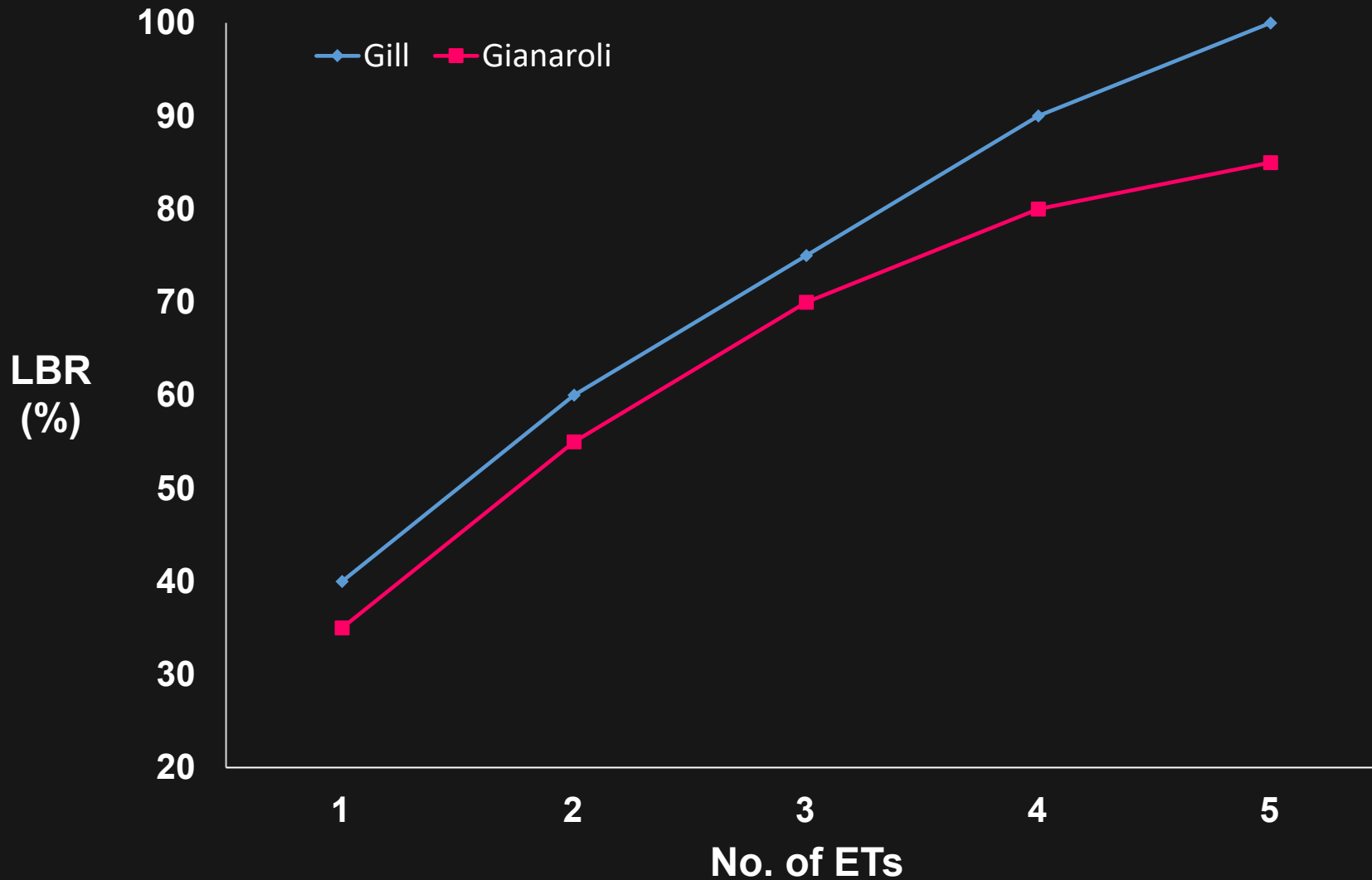
# CONCLUSIONS

**(Don't take these messages home....take them to your clinic!)**

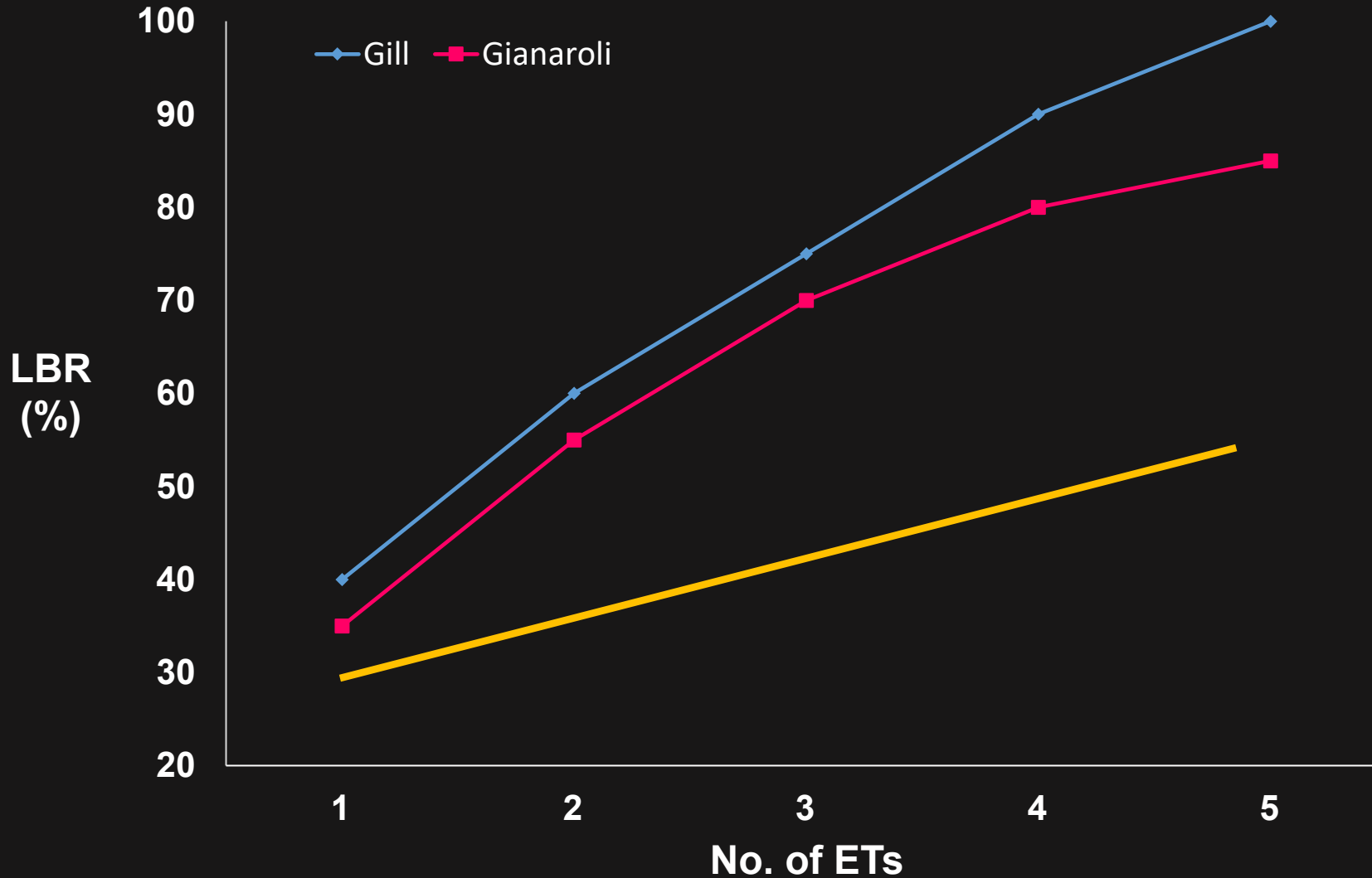
- **In nature RIF exists and it is normal**
- **Why should it be considered differently in ART?**
- **Strategies to reduce RIF cannot be «one fits all»**
- **The only proven strategy to decrease the incidence of RIF is the drastic reduction of drop out**
- **RIF criteria should be defined in each ART clinic for different sub-groups of patients and they should be used as KPI**
- **ART clinic effort is useless without patients' commitment.**



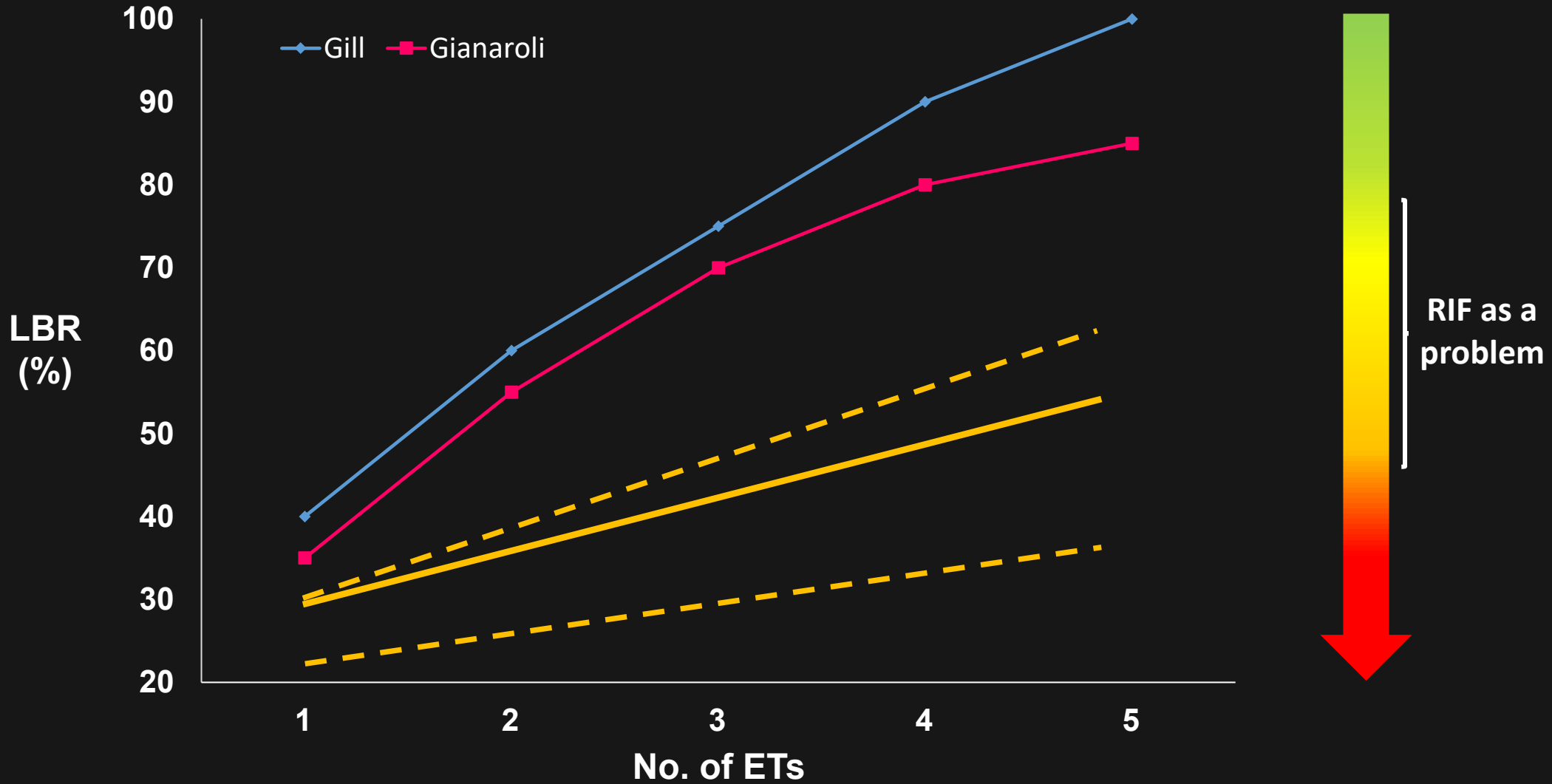
# How to calculate your RIF rate?



# How to calculate your RIF rate?



# How to calculate your RIF rate?



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# 3 euploid blastocysts

	<35	35-37	38-40	>40
No. of blastocysts needed	5-6	7-8	10	15
No. of 2 PN needed	12	16	20	30
No. of oocytes needed	18	20	24	36
No. of oocyte retrievals required				
Hyper response	1	1	2	3
Normal response	1-2	2	3-4	4
POR	4-5	6-7	7-8	10

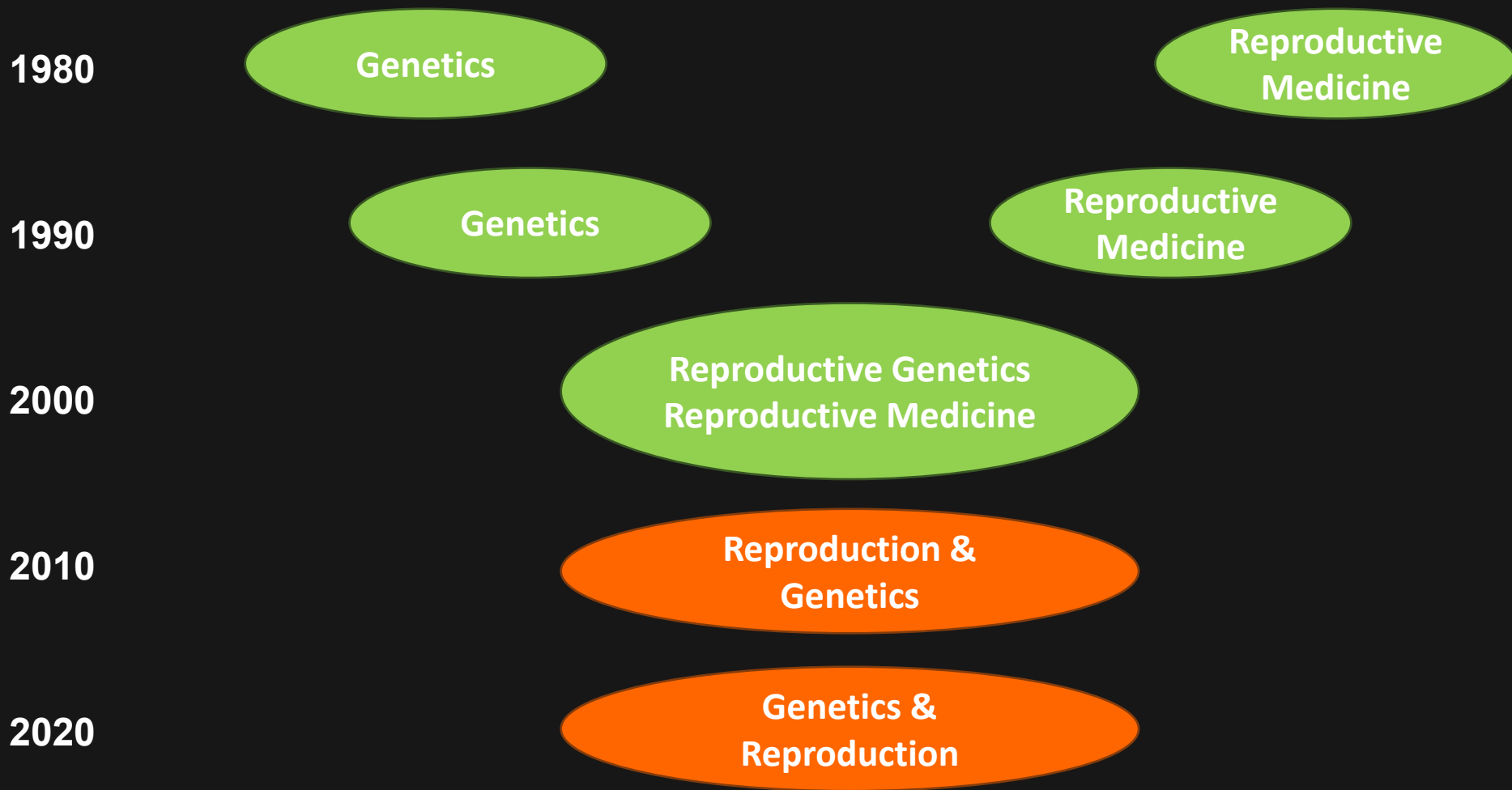


# 3 euploid blastocysts

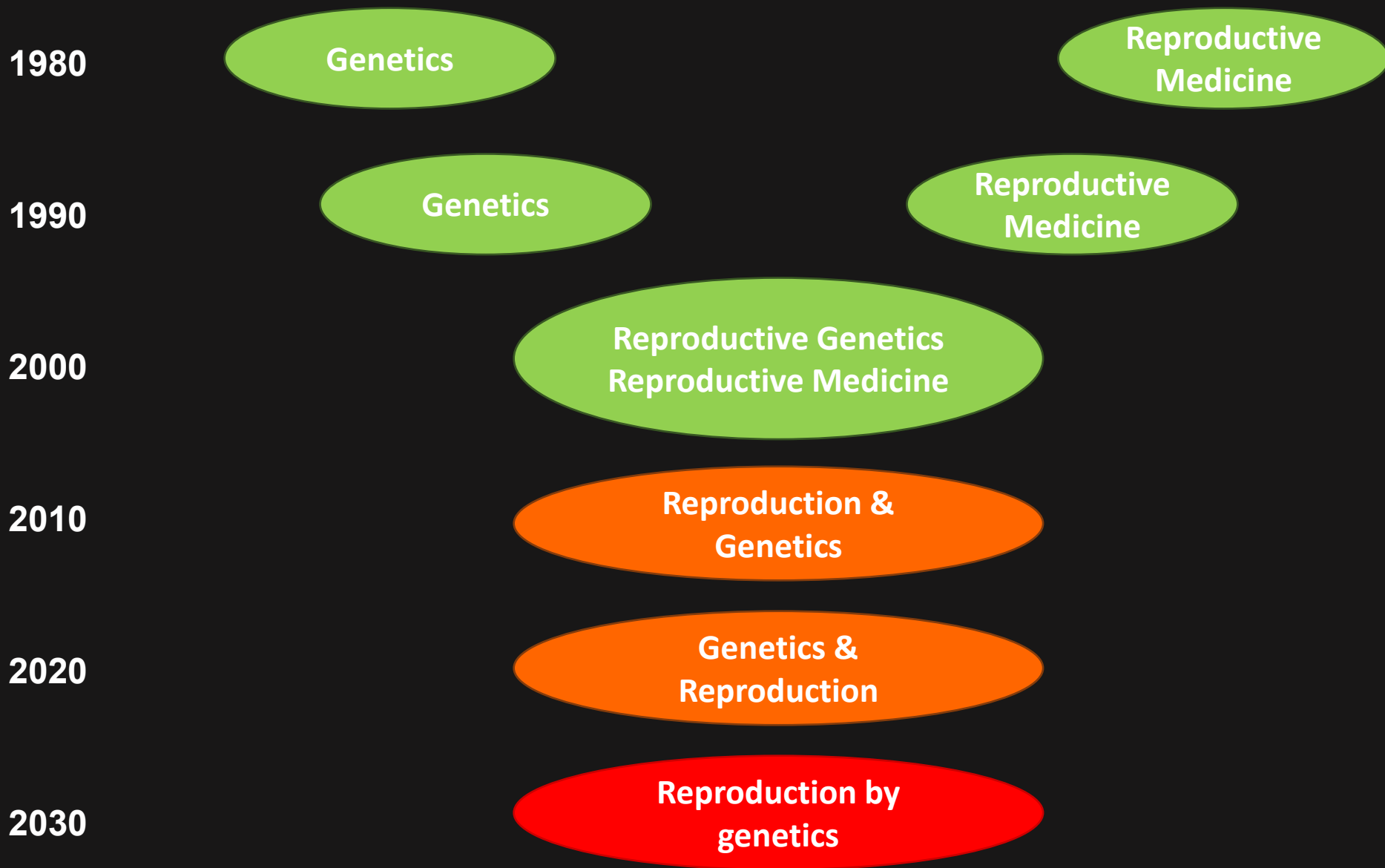
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# Reproductive Genetics in the ART Era



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Diversity, Sustainability and Resilience  
in Reproductive Medicine



International Federation of Fertility Societies

# IFFS WORLD CONGRESS 2025

Dates

**April 26-29, 2025**

(Sat) (Tue)

Venue

**Tokyo International Forum**

