

"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, 9th April 2025



DISCLOSURES

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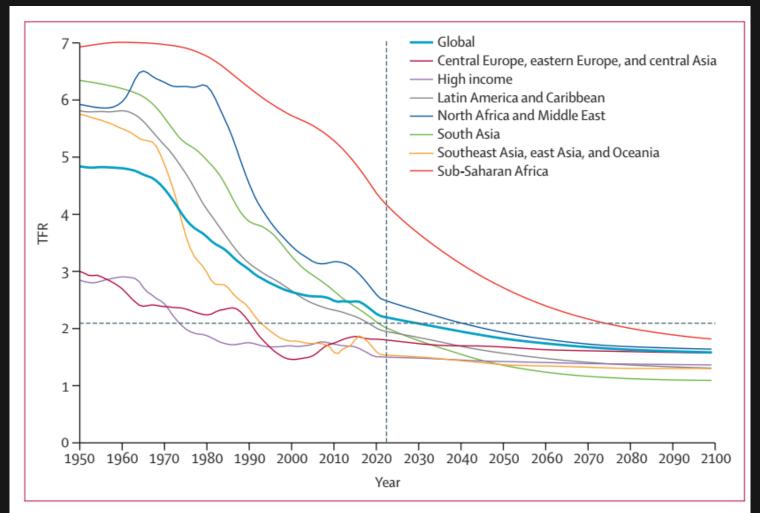


Figure 1: TFR, globally and by GBD super-region, 1950-2100

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

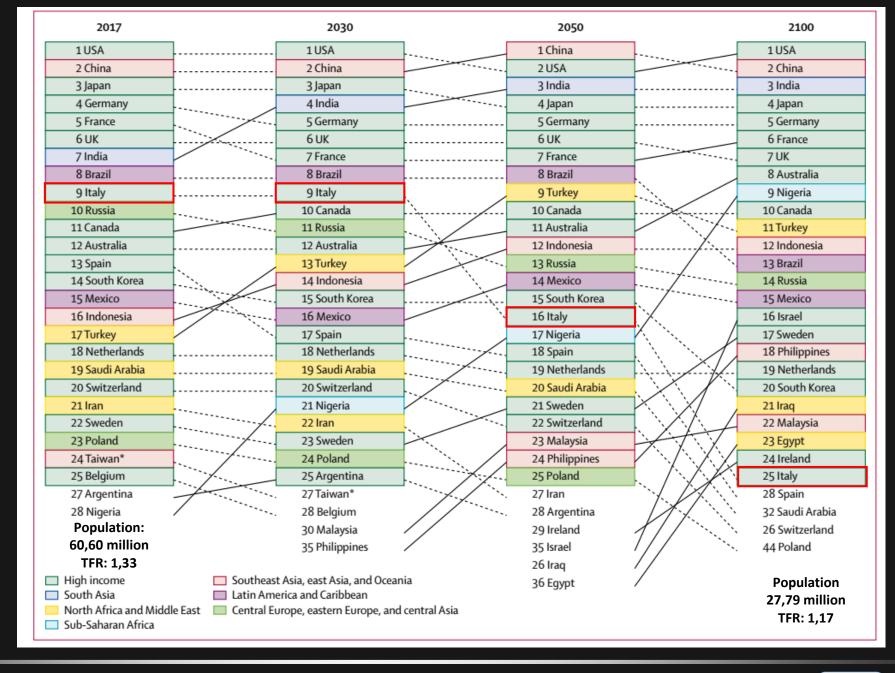
Public spending on pro-child policies* (constant USD per capita) vs total fertility rate







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

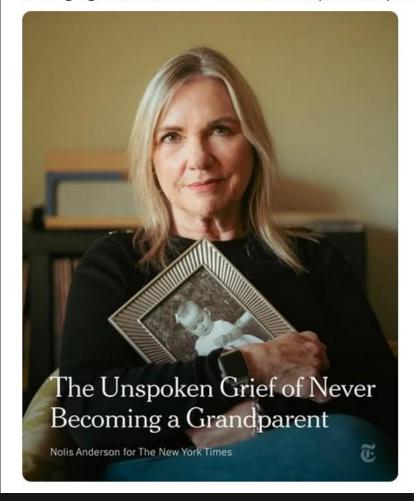
Overall lifetime risk for dementia among middle-aged Americans of 42 percent 35 percent risk in men and 48 percent risk in women.

"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"





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... Traduci





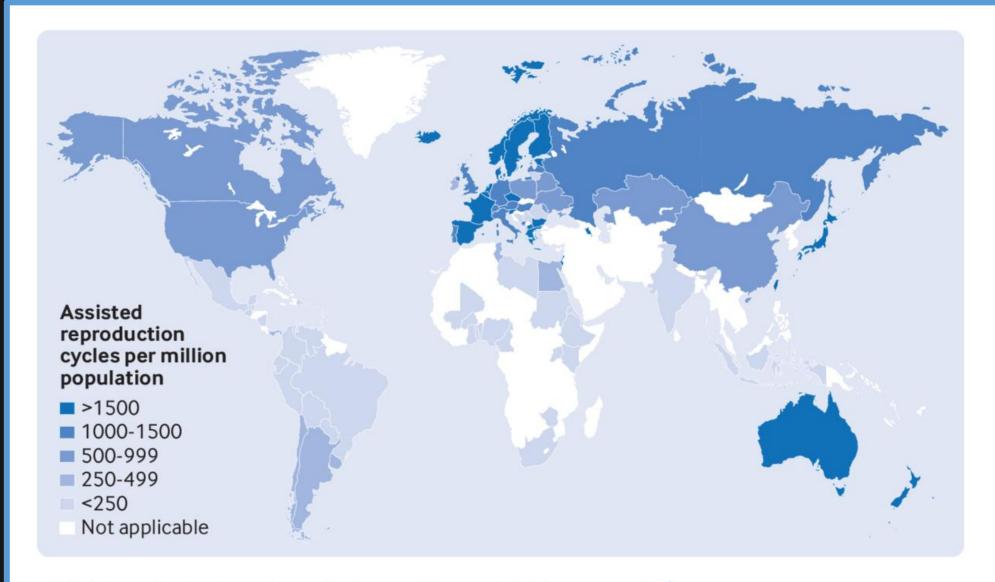
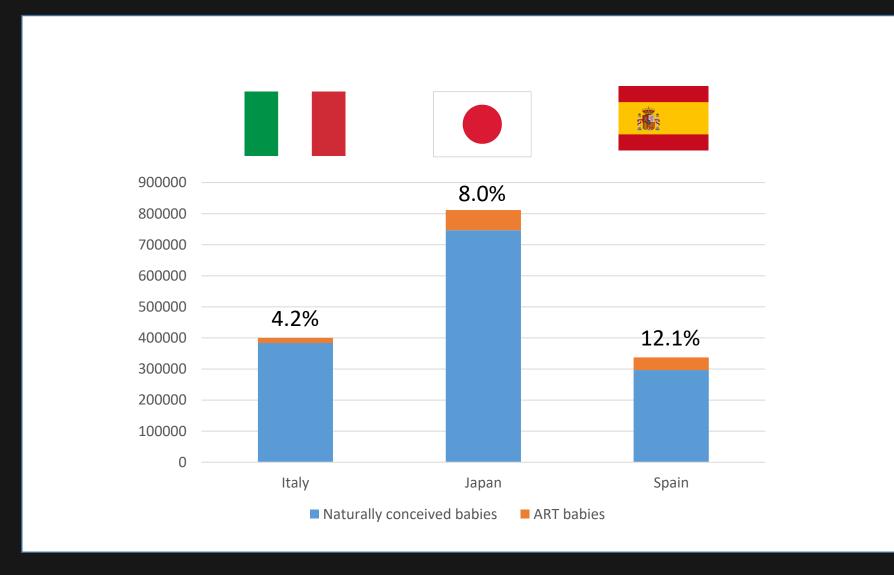


Fig 1 | Global use of assisted reproduction (cycles per million population) by country, 2018²





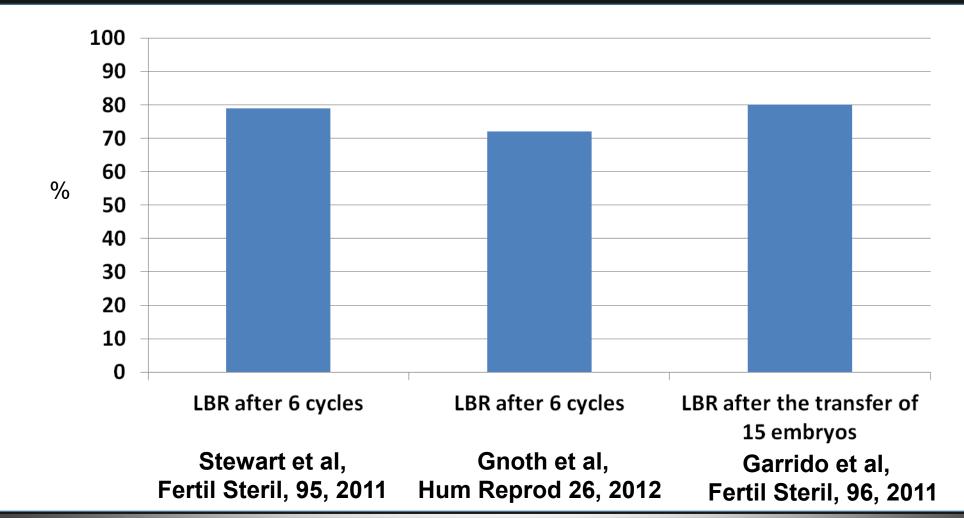
Incidence of ART babies (2021)







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







Treatment drop-outCauses of drop-out

Financial reasons

Psychological factors

Unrealistic expectations

RIF

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



Treatment drop-outCauses of drop-out

Financial reasons

Psychological factors

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

Unrealistic expectations

- Life table
- Oncology

Accurate diagnosis patients/ gametes/ embryos

RIF

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





MEDICINE

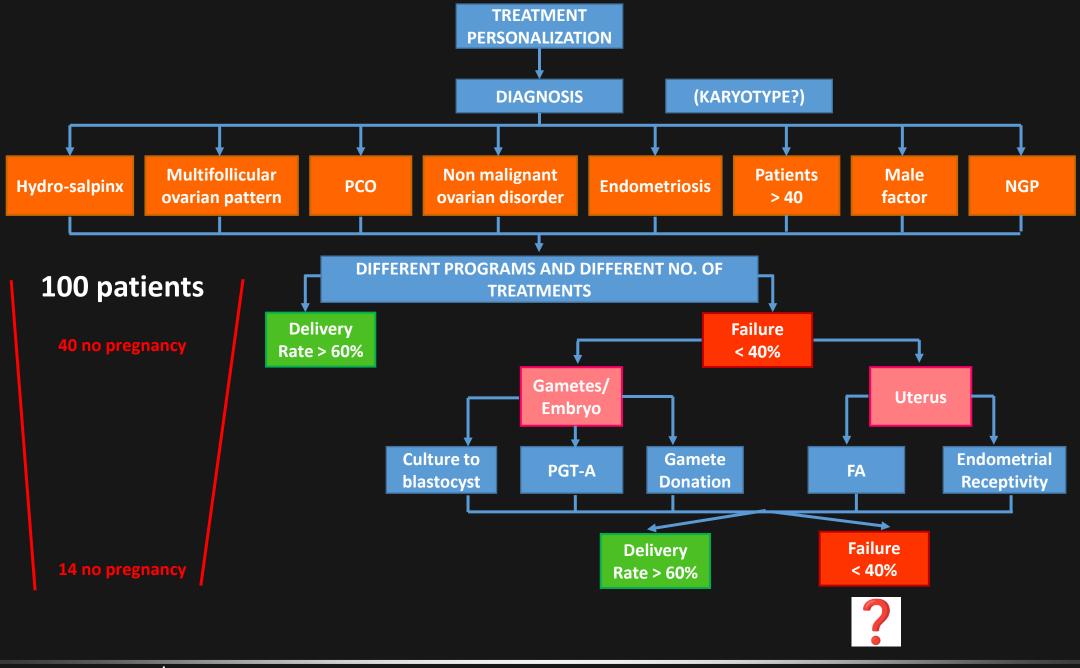
PERSONALIZED

PRECISION

EMBRYOLOGY BIOLOGY











Perspective

ajog.org

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)

DAILY URINARY LEVEL OF hCG

The New England Journal of Medicine

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Volume 319 JULY 28, 1988

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 ARMSTROMO, PH.D., AND BRUCE C. NISULA, M.D.

EARLY
PREGNANCY
FAILURE
(30%)

43 (22%) NO GESTATIONAL

SAC

PRECLINICAL LOSSES

198
INCREASED
LEVELS OF hCG

19 (10%)
MISCARRIAGES

136(68%)
CLINICAL
PREGNANCIES

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





Number 4

Definitions

Treatment cycle

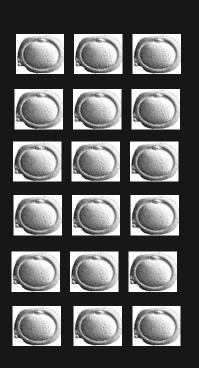
A period of treatment followed by a period of rest.





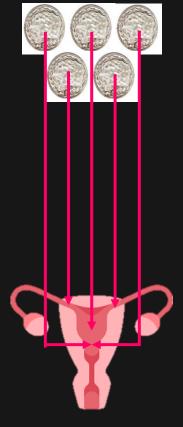
What we get





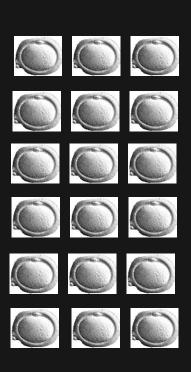




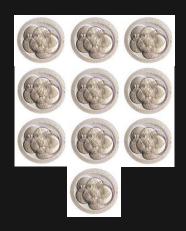


What we get





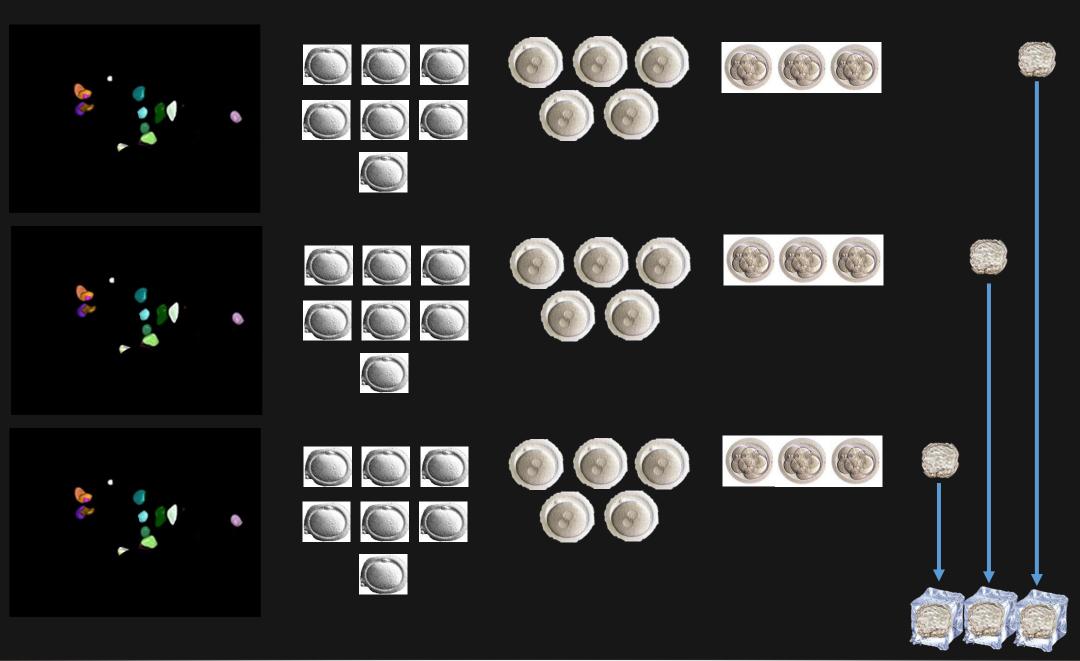








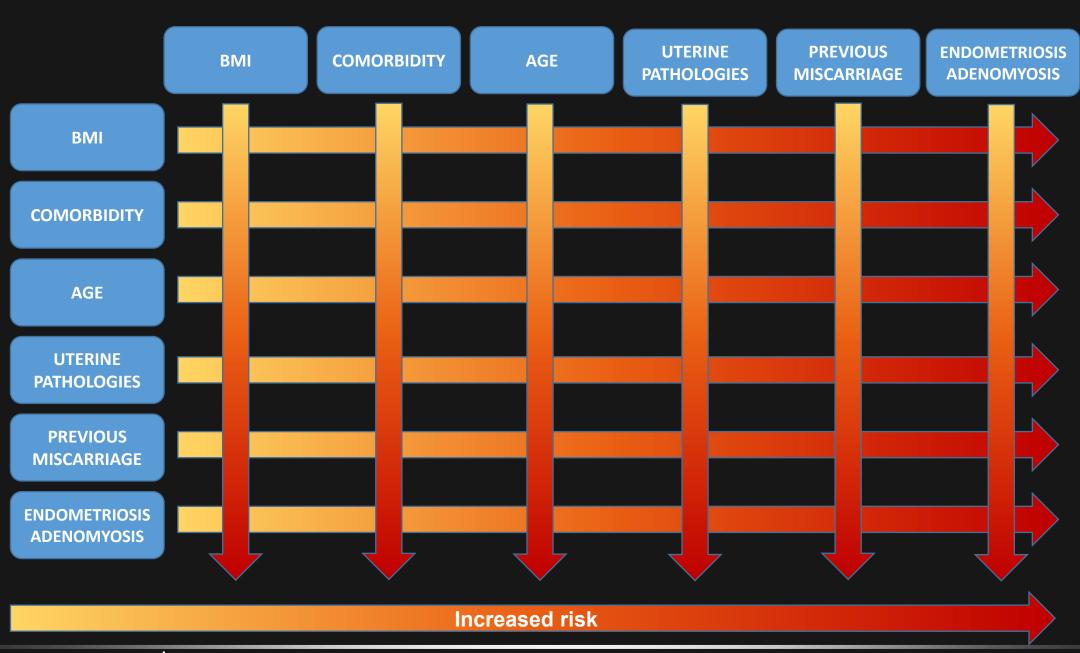






OK







OK



IVF LITE Program

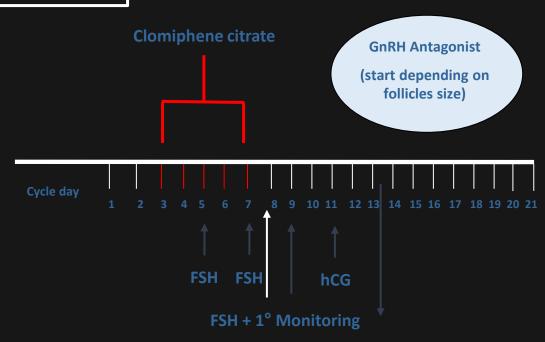
It is a protocol that implies a maximum of 3 embryo transfers (fresh or frozen, regardless of the number of oocyte retrievals), to be completed within 12 months.

IVF LITE - INDICATIONS

- ✓ Age female partner ≤ 38 years
- √ No previous IVF/ICSI cycles
- ✓ No severe male factor of infertility
- ✓ No endometriosis
- ✓ AMH ≥1.5 ng/ml and/or FSH ≤10 mlU/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



- Transfer of 1-2 embryos
- Cryopreservation of surplus embryos

Oocyte retrieval +







IVF LITE Program

511 eligible consecutive infertile couples

111 (21.8%)
were excluded
because of
inadequate
response to CC

8 (1.5%)
interrupted the
treatment for
reasons of
force majeure

23 (4.5%) spontaneously dropped-out 369 (72.2%) completed the program







Clinical outcome at the first, second and third ET

773 embryo transfers

	<u> </u>			
	1 st ET	2 nd ET	3 rd 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) ^a	384 (1.6±0.6) ^b	295 (1.8±0.6) ^{a,b}	
Clinical pregnancies (% per ET)	148 (40.1) ^c	78 (32.9)	46 (27.5) ^c	
Implantation rate	29.0 ^d	25.5 ^e	17.3 ^{d,e}	
Live births (% per ET)	132 (35.8) ^f	70 (29.5)	37 (22.2) ^f	

a p=0.0002 bp=0.0174 cp=0.0068 dp=0.001 ep=0.0133 fp=0.0024





Clinical outcome in relation to maternal age

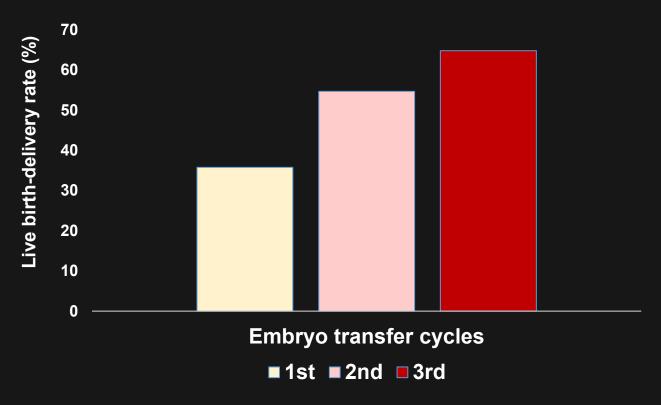
	23-30 yrs	31-32 yrs	33-34 yrs	35-38 yrs
No. of patients	61	67	90	151
Age	28.5±1.6	31.5±0.5	33.5±0.5	36.2±1.4
Transferred cycles	131	133	182	327
Cumulative live births	39	49	59	92
% per patient	63.9	73.1	65.6	60.9
% per ET	29.8	36.8	32.4	28.1

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





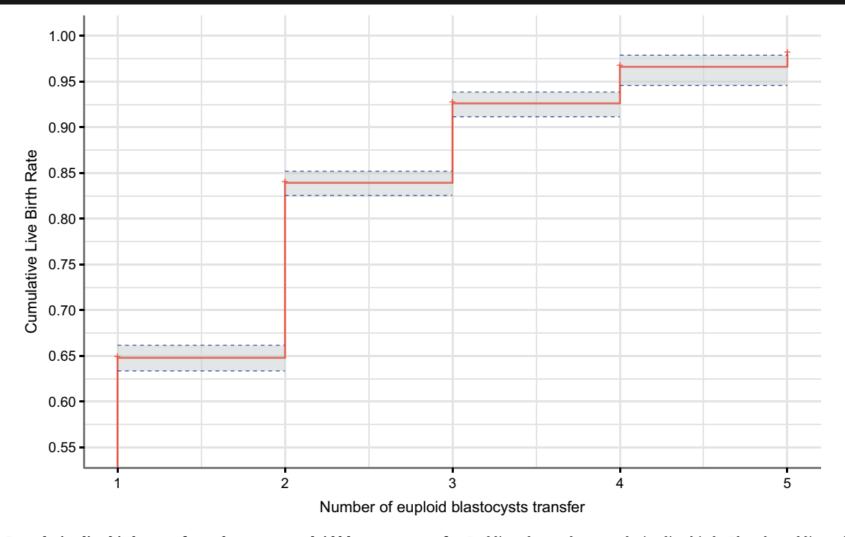
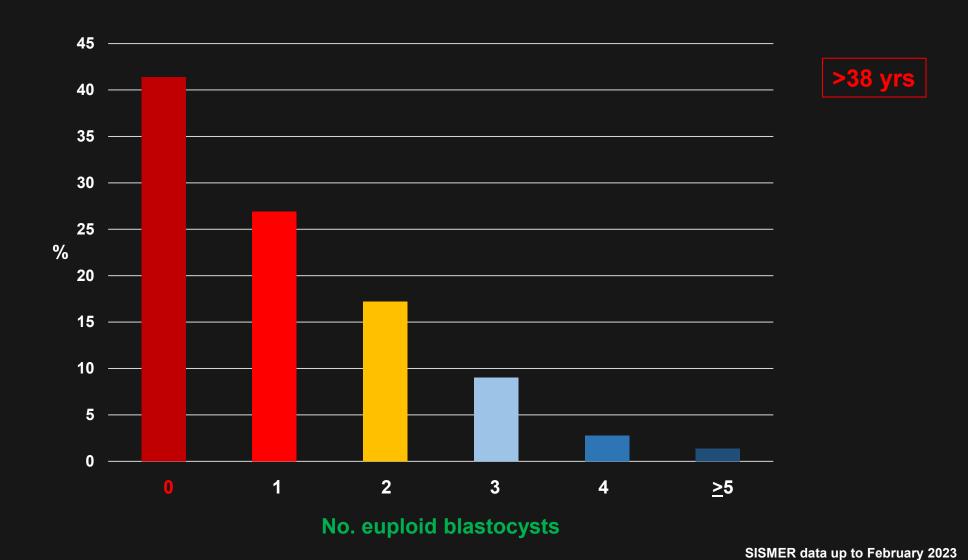


Figure 1. Cumulative live birth rate after subsequent euploid blastocyst transfer. Red line shows the cumulative live birth. Blue dotted lines show upper and lower bounds of the CI.





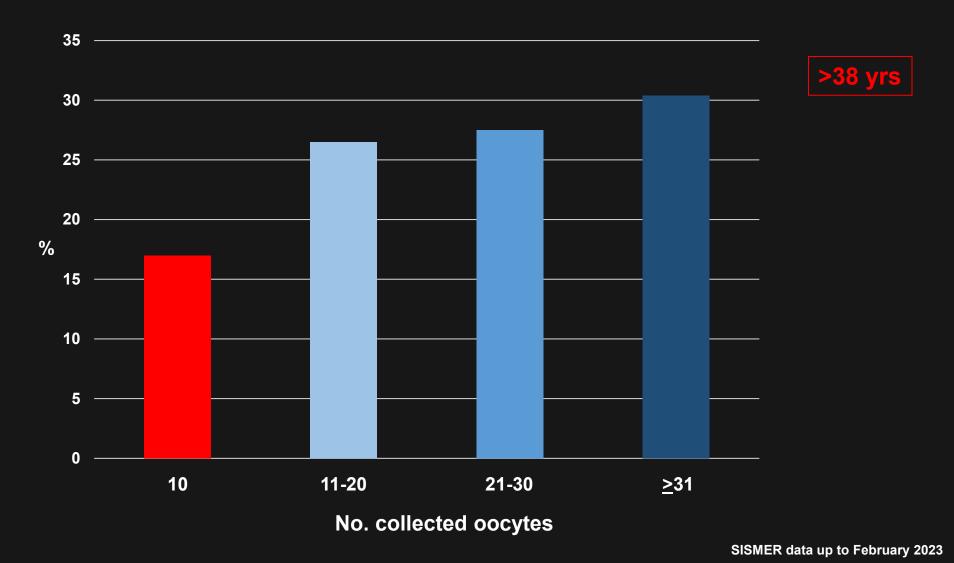
Proportion of cycles with TE-euploid blastocysts







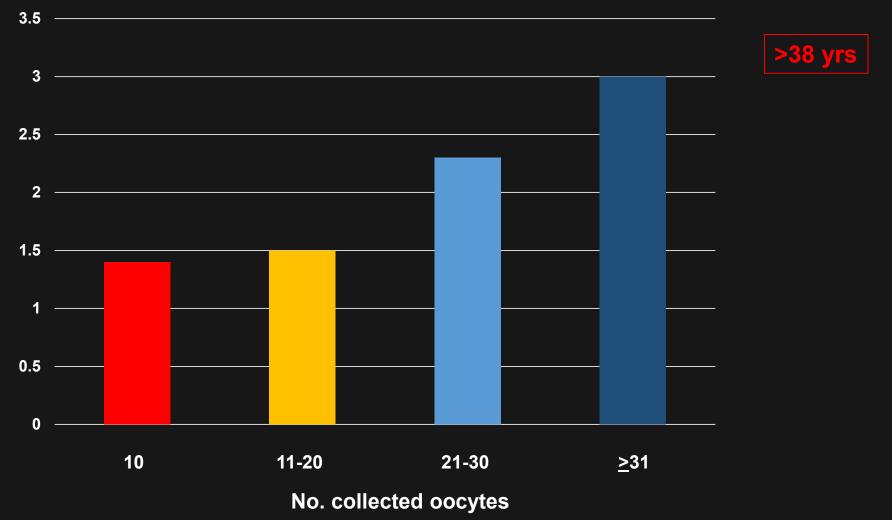
Proportion of TE-euploid blastocysts in relation to the number of collected oocytes







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









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.

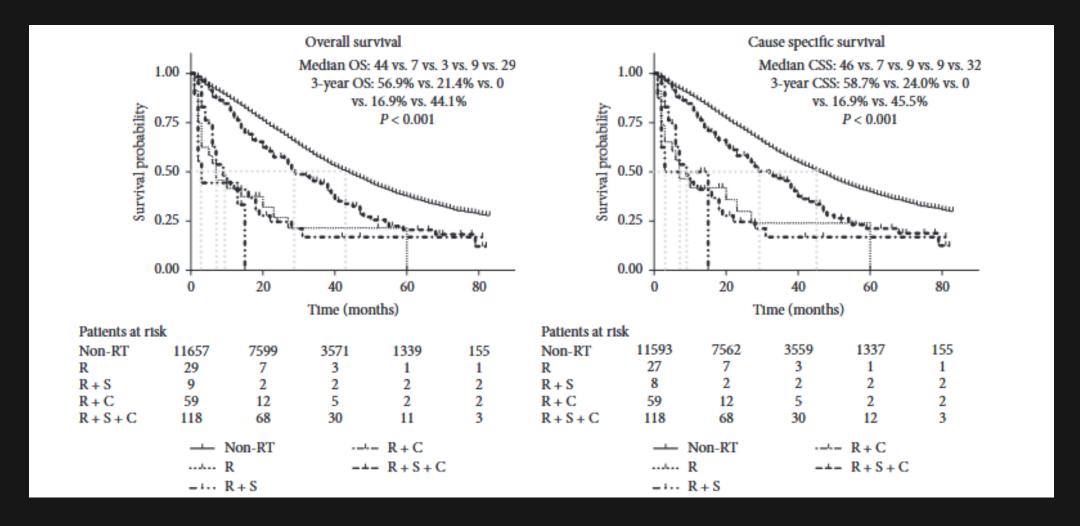
This might be useful to reconsider several aspects, including:

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



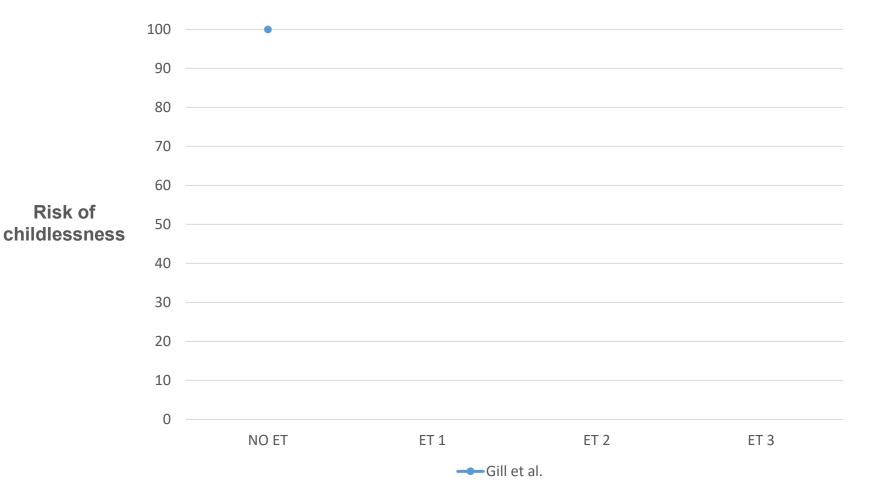


Ovarian cancer



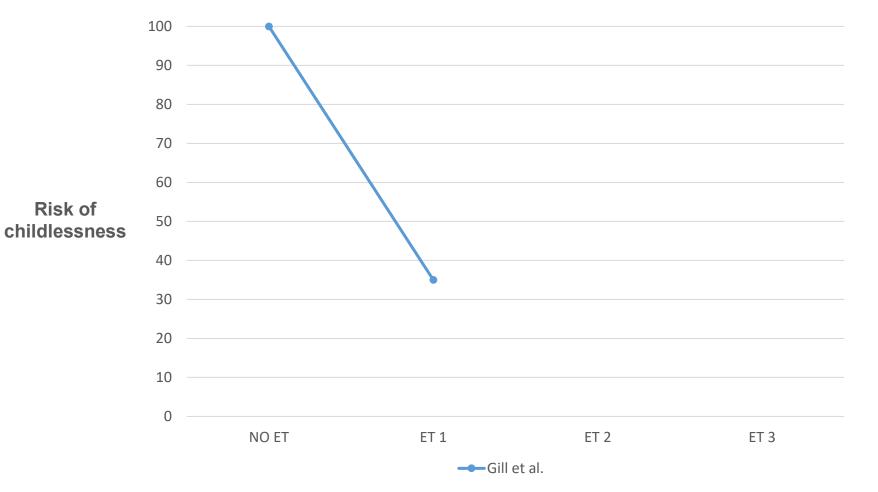






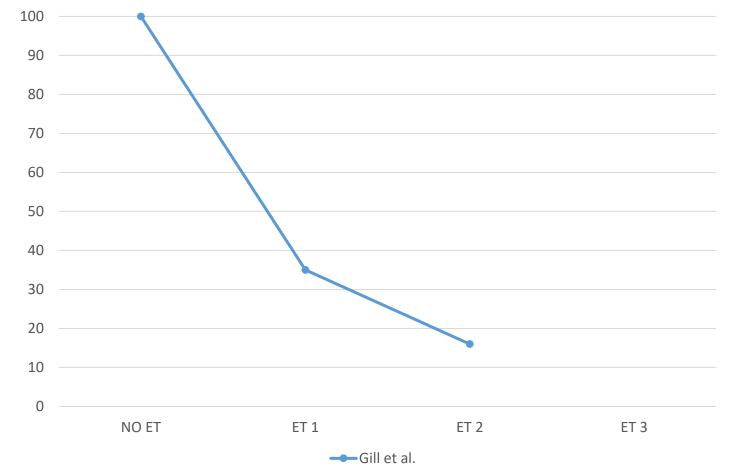






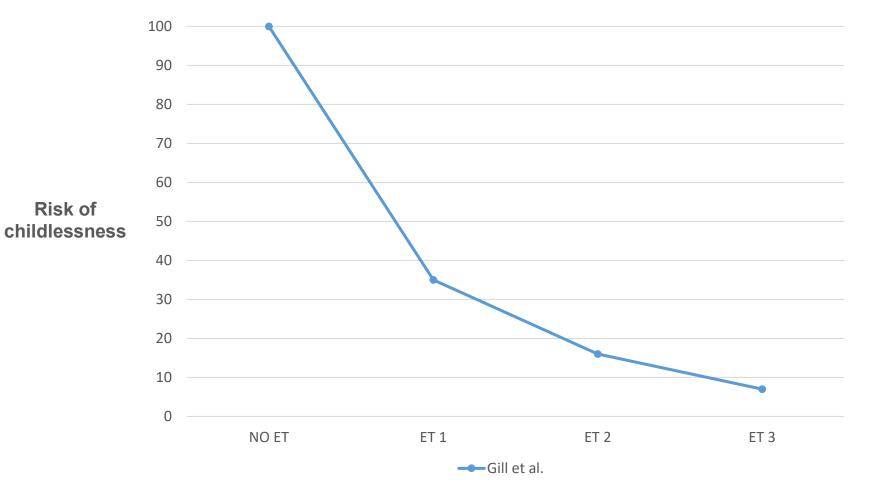






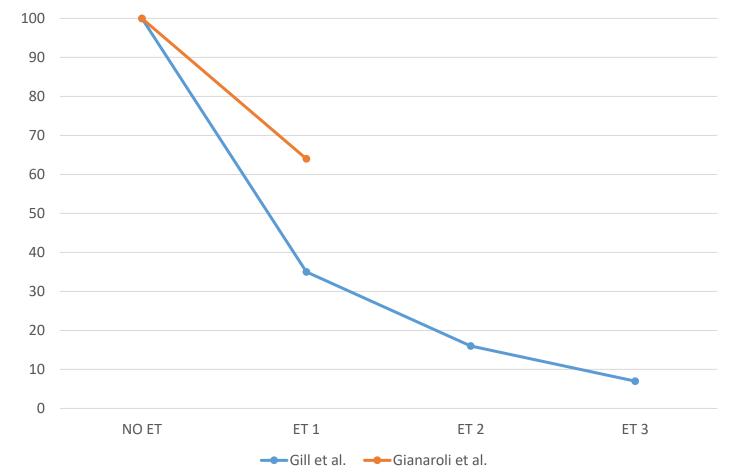






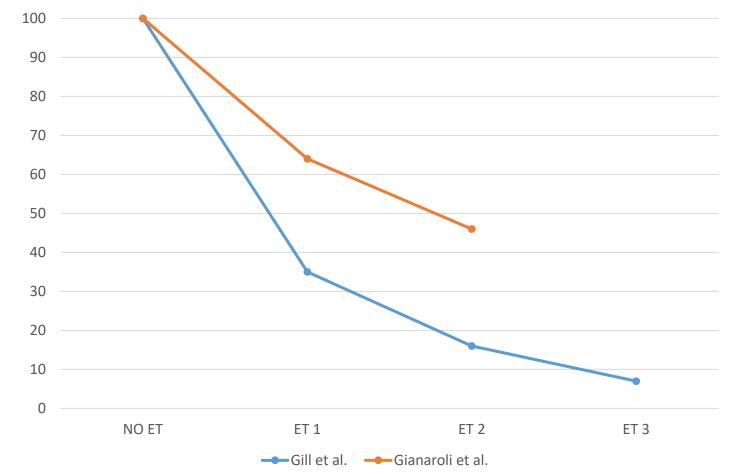






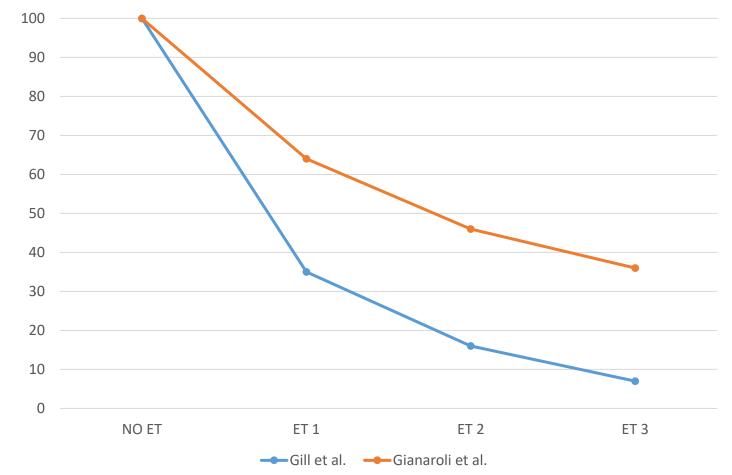
Risk of childlessness





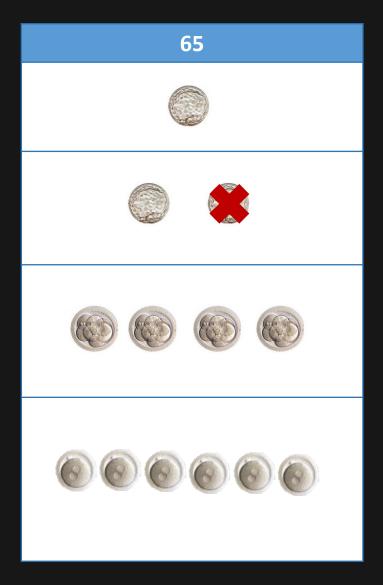
Risk of childlessness





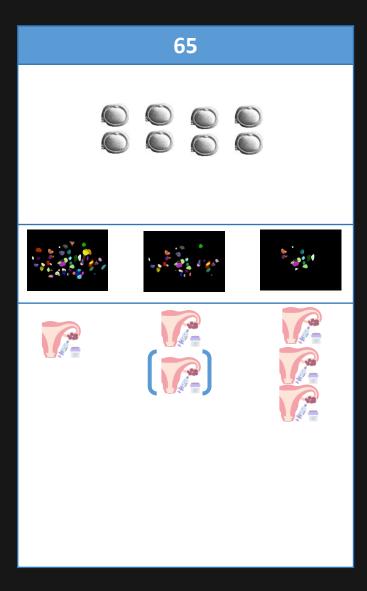
Risk of childlessness













IIRM 🗑

PGT-A

65	84





PGT-A

	65			84	
		****			****





65	84	93





IIRM 🗑

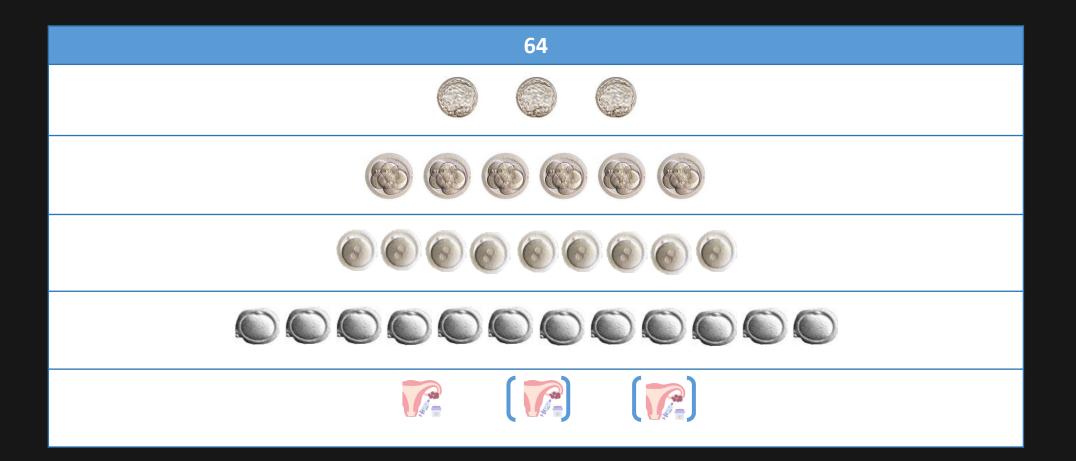
PGT-A

65		84			93	
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IVF Lite







CONCLUSIONS

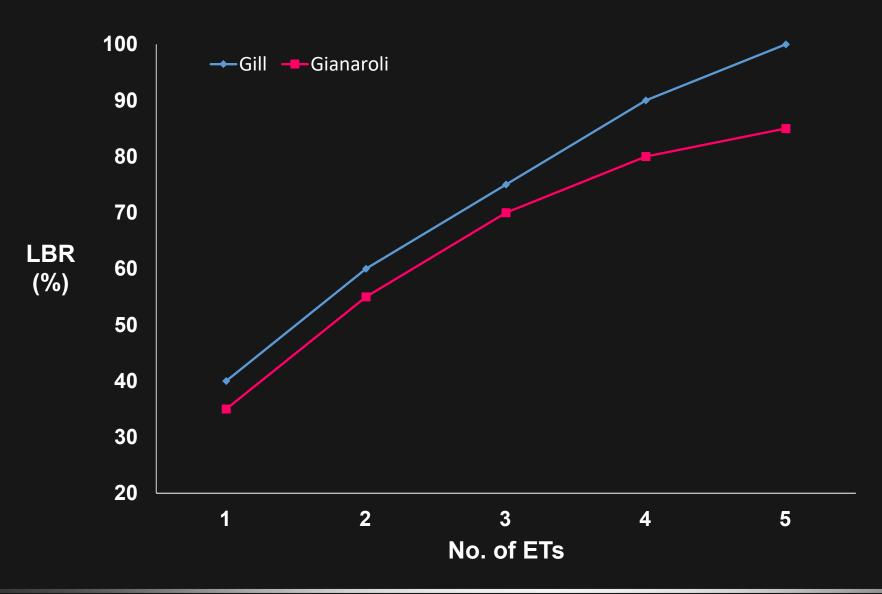
(Don't take these messages home....take them to your clinic!)

- 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' committment.





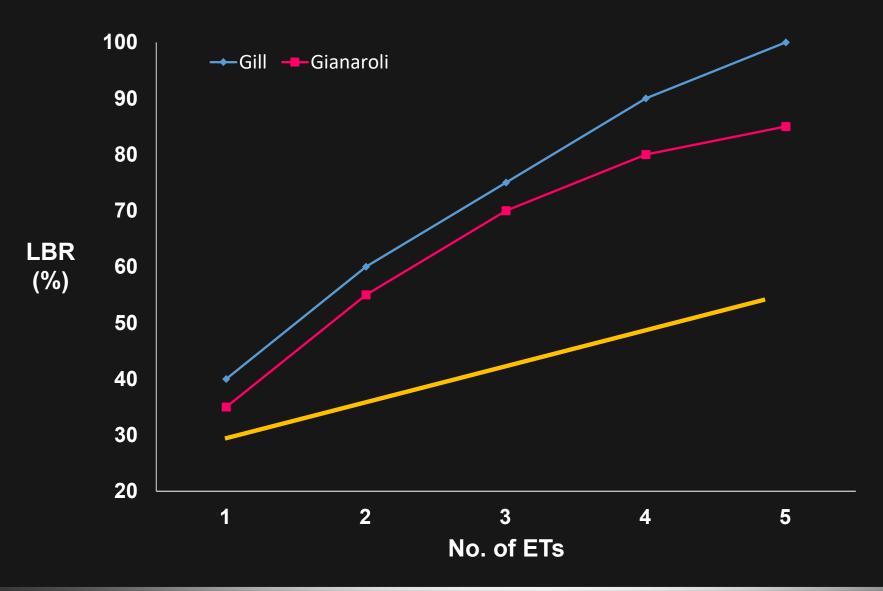
How to calculate your RIF rate?







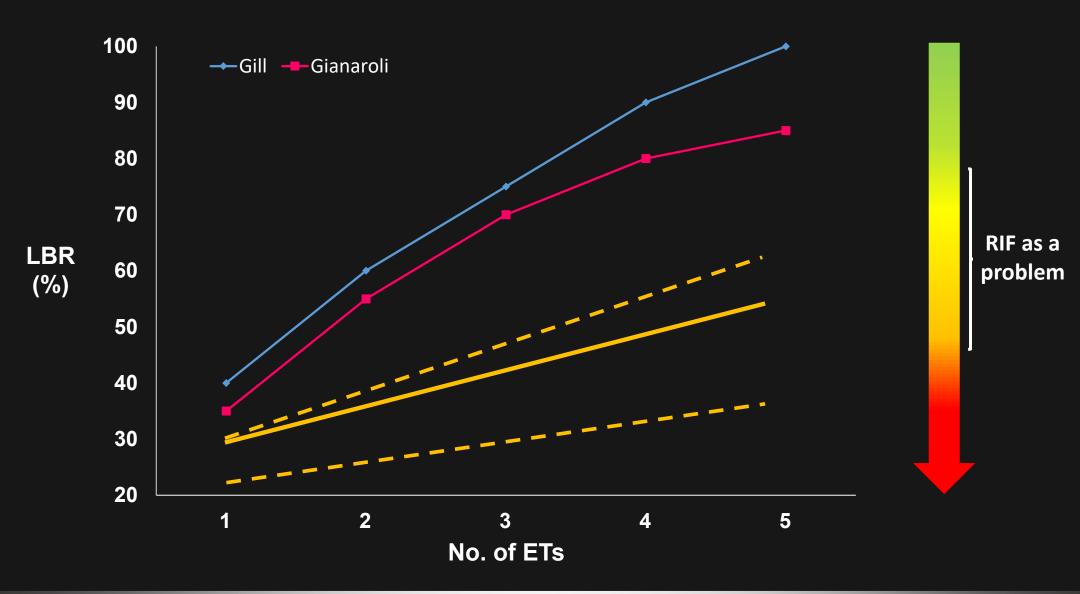
How to calculate your RIF rate?







How to calculate your RIF rate?







3 euploid blastocysts

	<35	35-37	38-40	>40
No. of blastocysts needed	5-6	5-6 7-8 10		15
No. of 2 PN needed	12	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





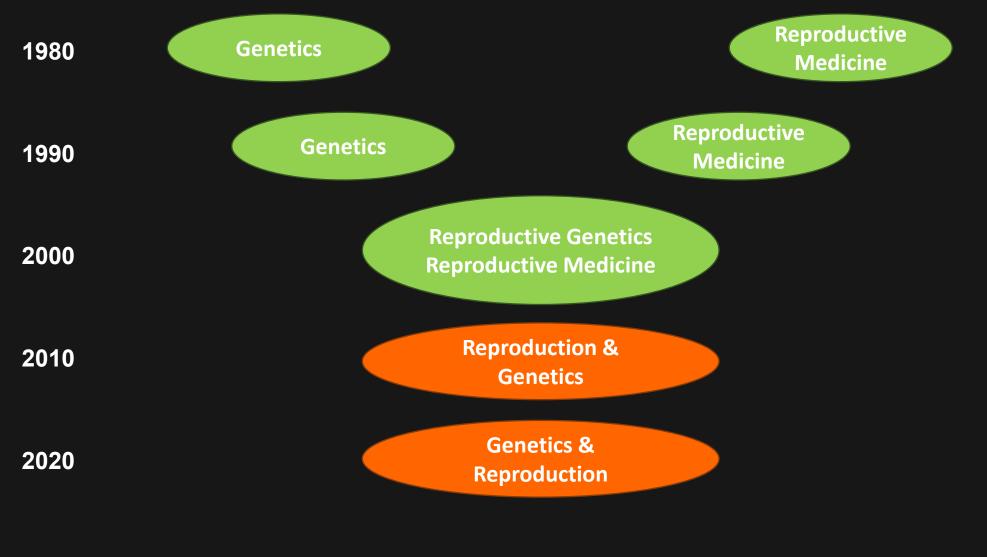
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No. of oocyte retrievals required					
Н	lyper response	1	1	2	3
N	lormal response	1-2	2	3-4	4
P	POR	4-5	6-7	7-8	10





Reproductive Genetics in the ART Era

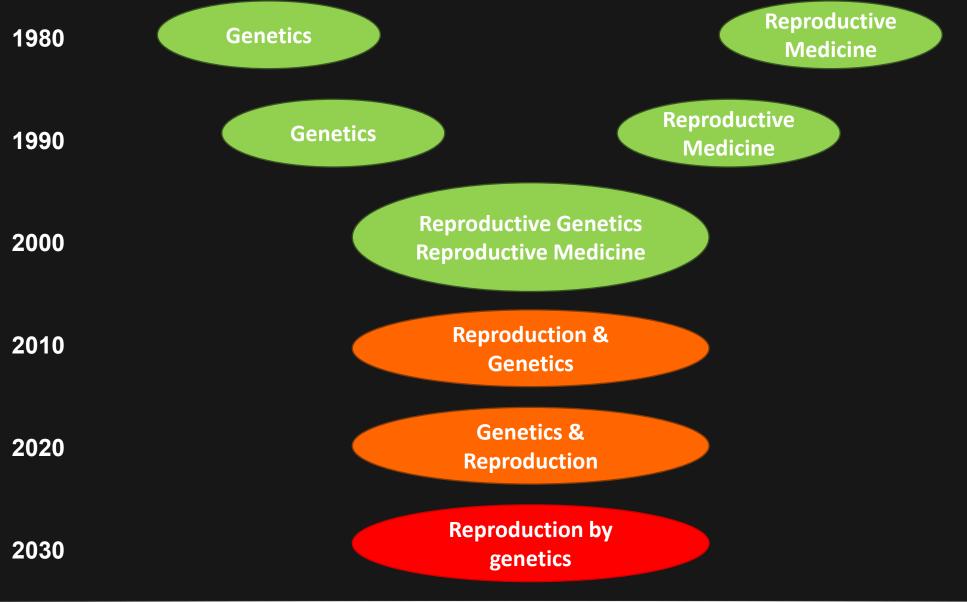








Reproductive Genetics in the ART Era











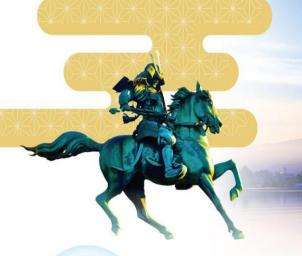












Diversity, Sustainability and Resilience in Reproductive Medicine



International Federation of Fertility Societies

FS WORLD CONGRESS



April 26-29,2025

Tokyo International Forum

