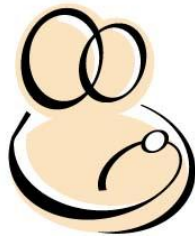


# Hopelessly Infertile: Are There Any Miracles?

*Raymond W. Ke, MD*

*University of Tennessee Health Science Center*

*Fertility Associates of Memphis*



FERTILITY  
ASSOCIATES  
of MEMPHIS

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*William H. Kutteh, MD, Ph.D Raymond W. Ke, MD*



# Objectives

- **Understand the scope and principles of assisted reproductive technologies (ART)**
- **Understand the benefits and limitations of current ART**
- **To be aware of state of the art and future directions for ART**

*When you absolutely cannot have children,  
it's called sterility.*

*When it seems to be taking an awfully long  
time, but you still hope, that's called  
infertility.*

*Infertility is worse.*

**Katherine Bouton**  
**Ms. Magazine**  
**April/97**

# LIFE

## 'CATS' LEAPS ONTO BROADWAY

The hottest theater  
ticket in the country

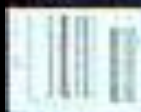
## SAVING AFRICA'S BIG ANIMALS

A radical plan to  
butcher some of them  
and sell their meat

November 1982 \$2.00

## TEST- TUBE BABY BOOM

Elizabeth Curo,  
America's first  
in vitro baby,  
at the lab  
where she  
was conceived



# **Assisted Reproductive Technology (ART)**

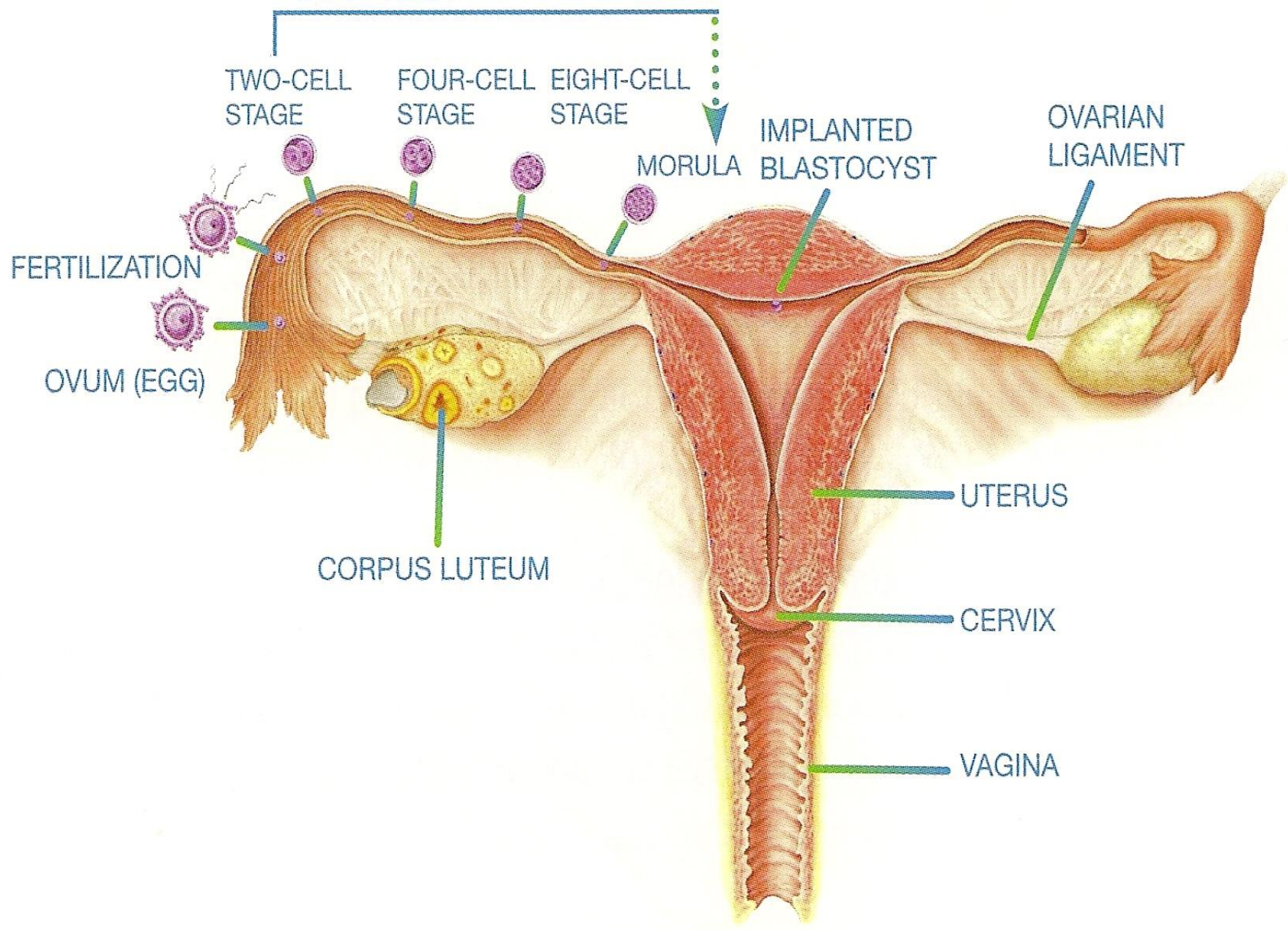
**“ Techniques that combine egg and sperm  
outside the female reproductive tract to  
enhance the probability of pregnancy.”**

# **In Vitro Fertilization (IVF)**

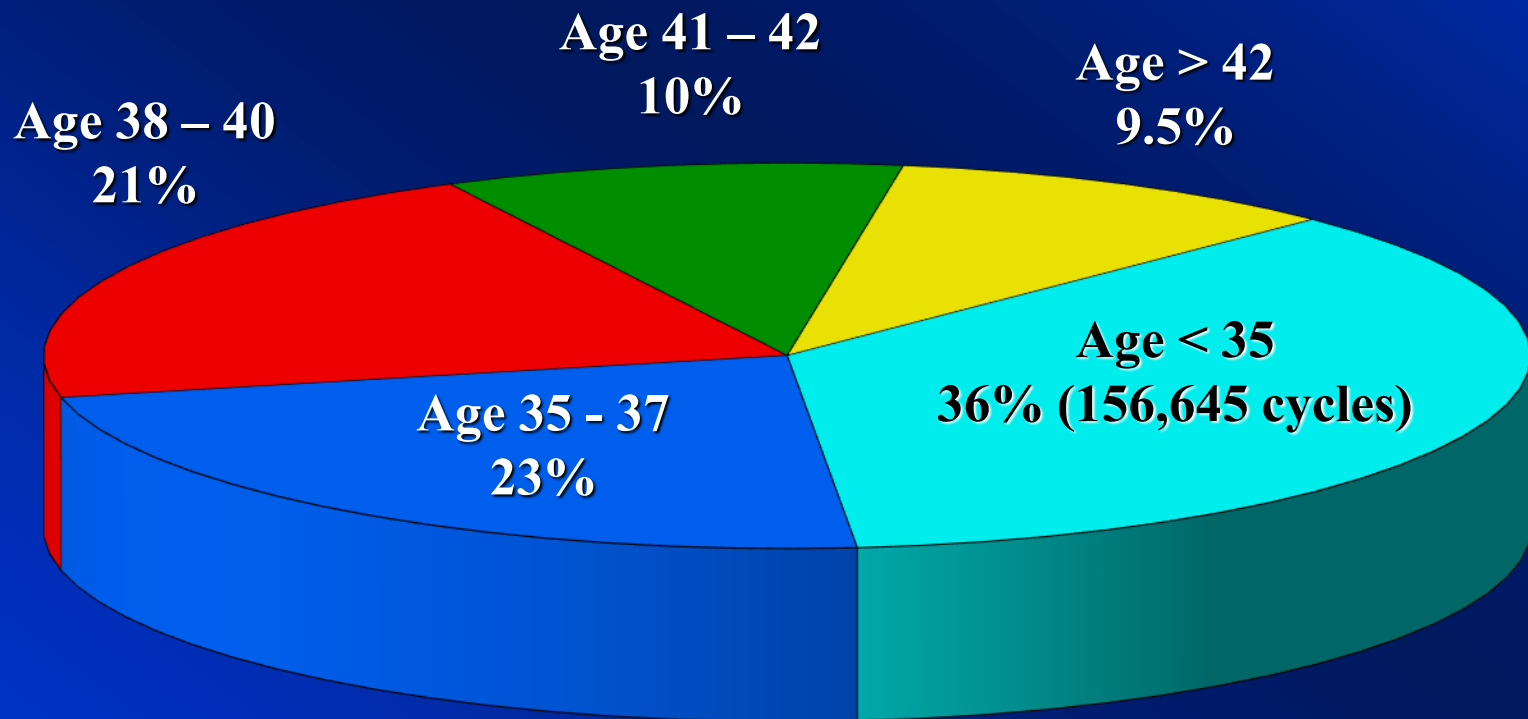
## **Technique**

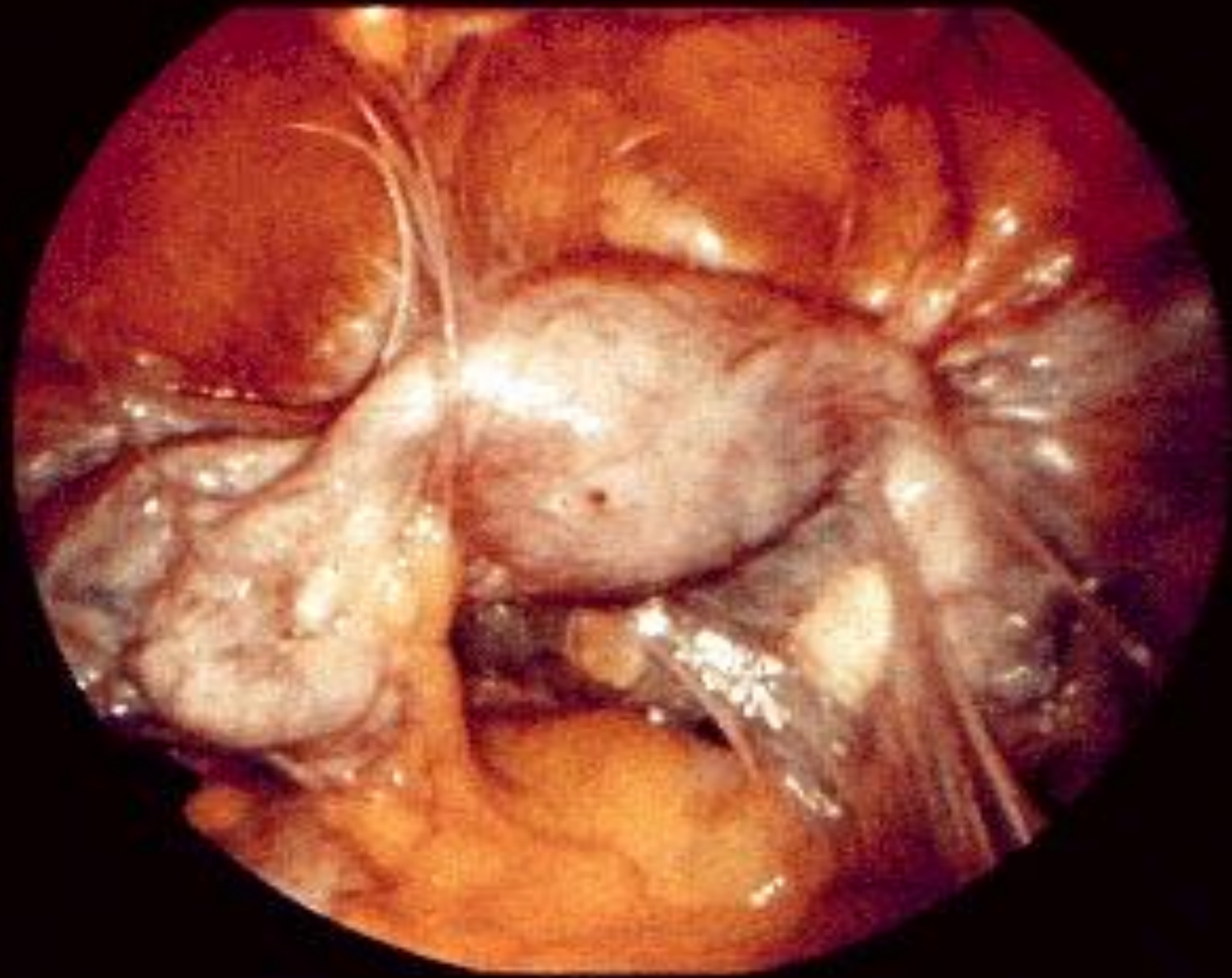
- **Controlled ovarian hyperstimulation (superovulation)**
- **Oocyte retrieval**
- **In vitro fertilization**
- **Embryo culture**
- **Transcervical embryo transfer**

EARLY CELL DIVISION OF ZYGOTE

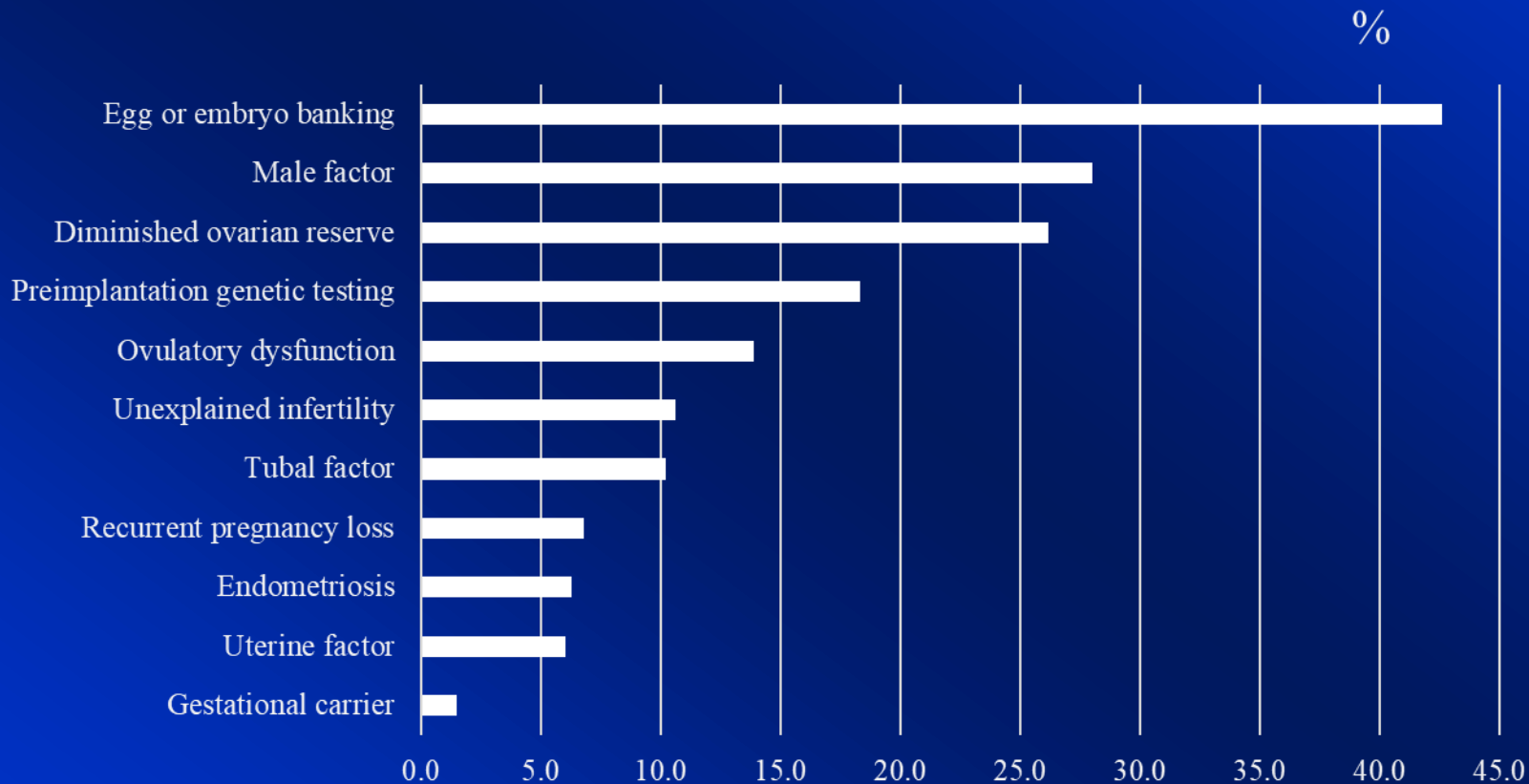


# ART Use By Age Group - United States, 2022



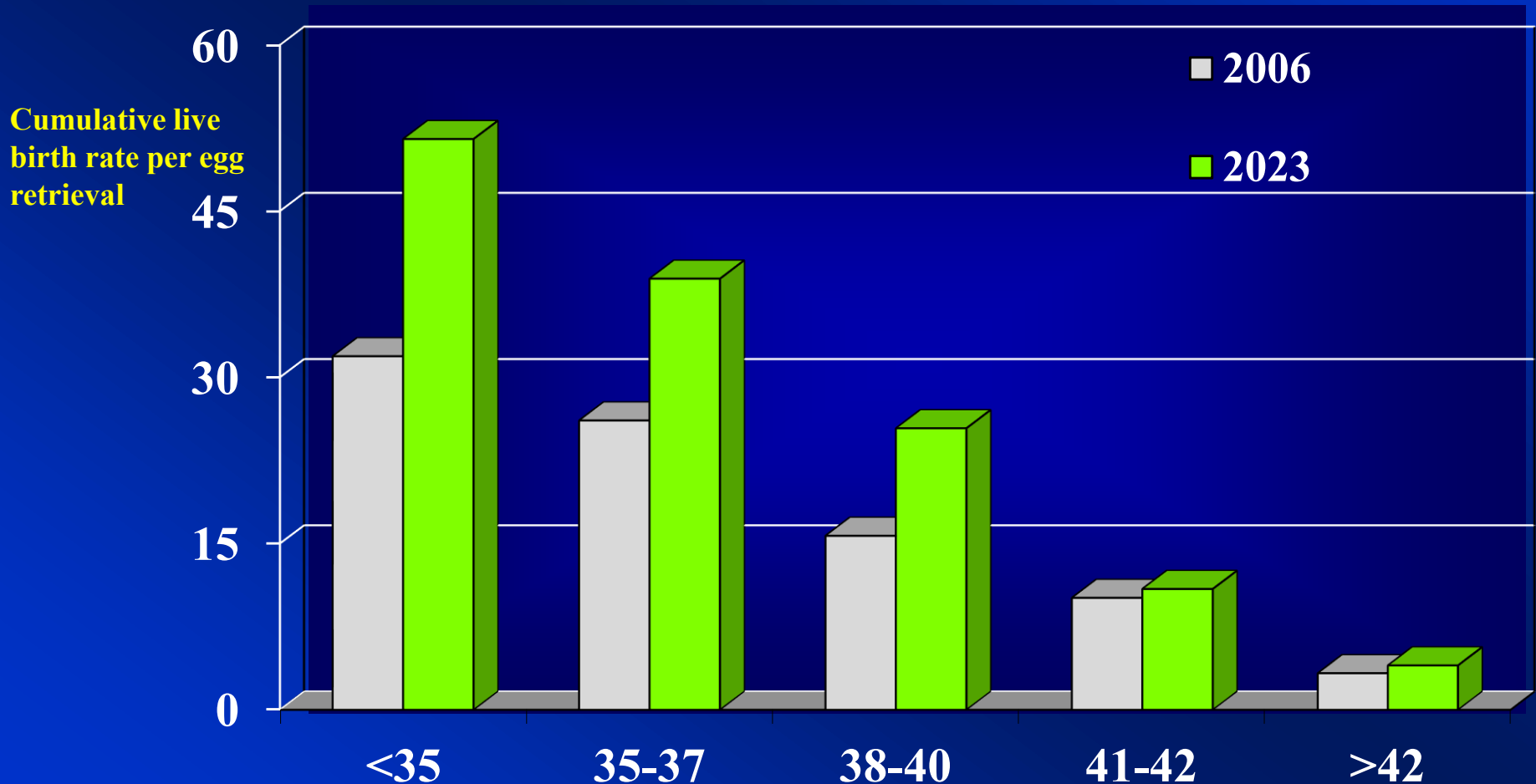


# Reasons for using ART – United States, 2022



# IVF Live Birth Rates by Age Groups

## SART 2023



Non-donor cycles only

<https://www.sartcorsonline.com/EmbryoOutcome/PublicSARTOutcomeTables>

# Monthly Fecundity Rate with Live Birth



NHS, 2003  
CDC/SART 2022

%

# ART

## Concerns in 2006

- **Exposure to superovulation**
  - discomfort
  - ovarian hyperstimulation syndrome
  - ?? risk of neoplasm
- **Risk of multiple pregnancy**
- **Risk to fetus**
  - ? increased incidence of low birthweight and preterm delivery
- **Cost**

LONG

A

B

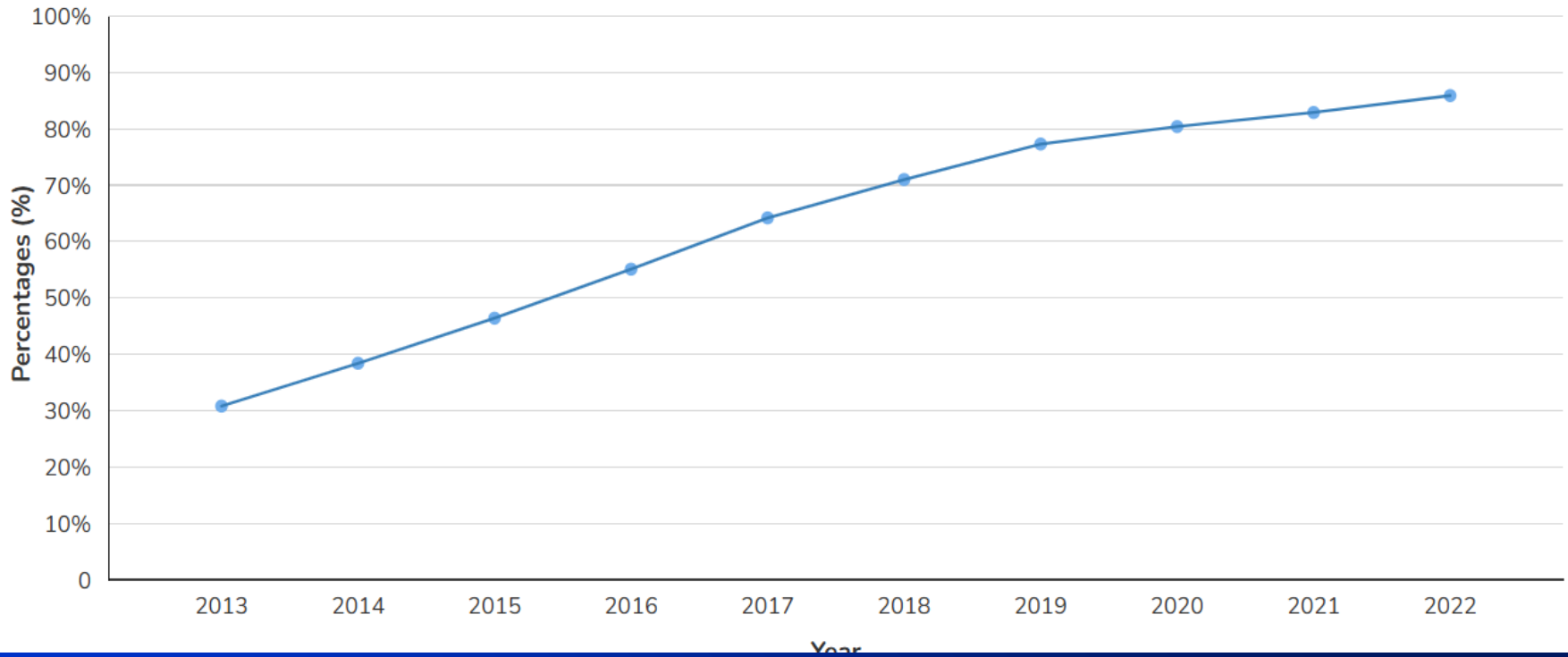
C

D

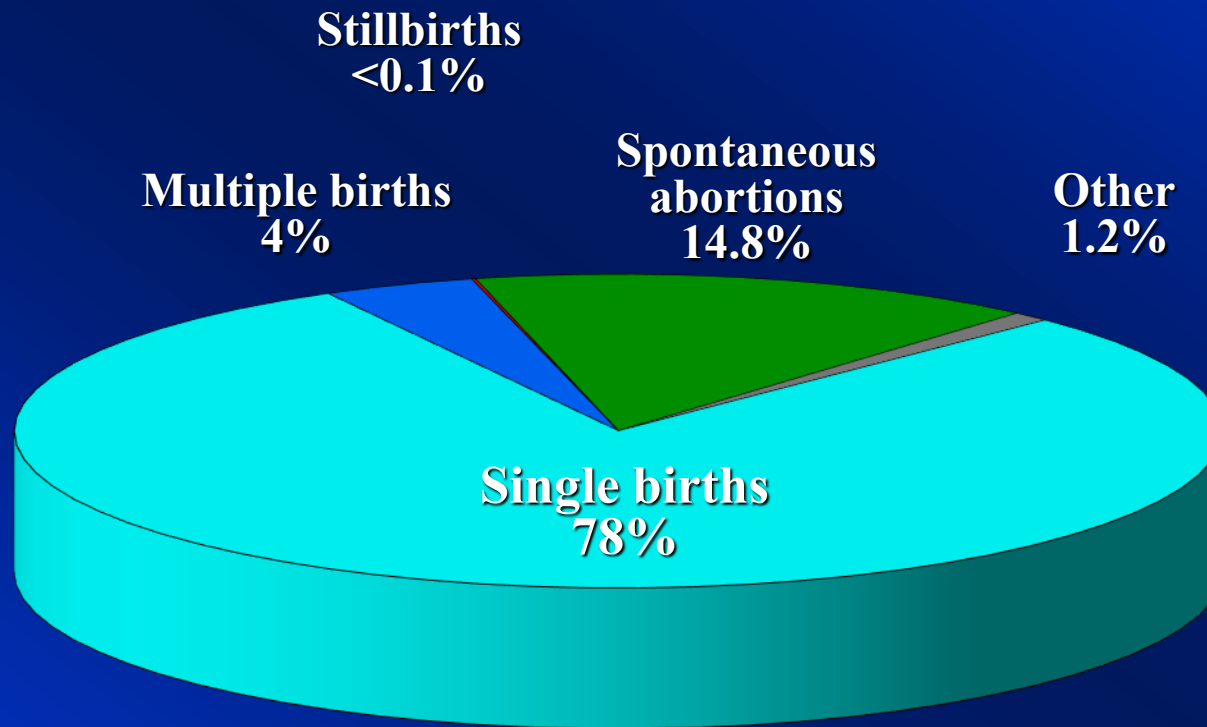


# Single Embryo Transfer

Percentage of Embryo Transfer Cycles in Which a Single Embryo Was Transferred, 2013–2022



# Outcomes of Pregnancies From ART 2022 CDC



# Cryopreservation: Vitrification

7.5% ethylene glycol  
7.5% DMSO  
20% SSS  
in M199-H

Equilibration  
Solution

15% ethylene glycol  
15% DMSO  
0.5 M sucrose  
20% SSS  
in M199-H

Vitrification  
Solution

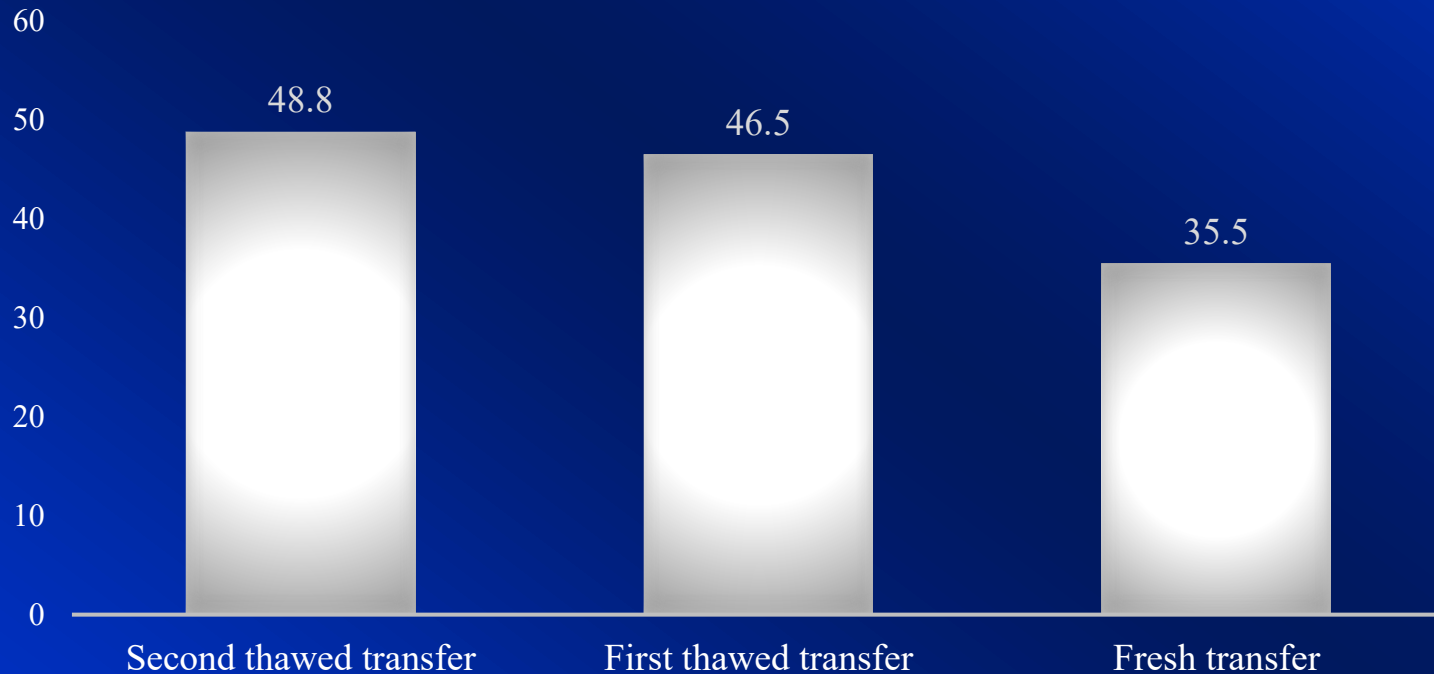
Liquid Nitrogen Plunge

Expose Time 50  
to 60 Sec.



# Fresh vs Thawed Embryo Transfer

LIVE BIRTH RATE PER RETRIEVAL/THAW (%)



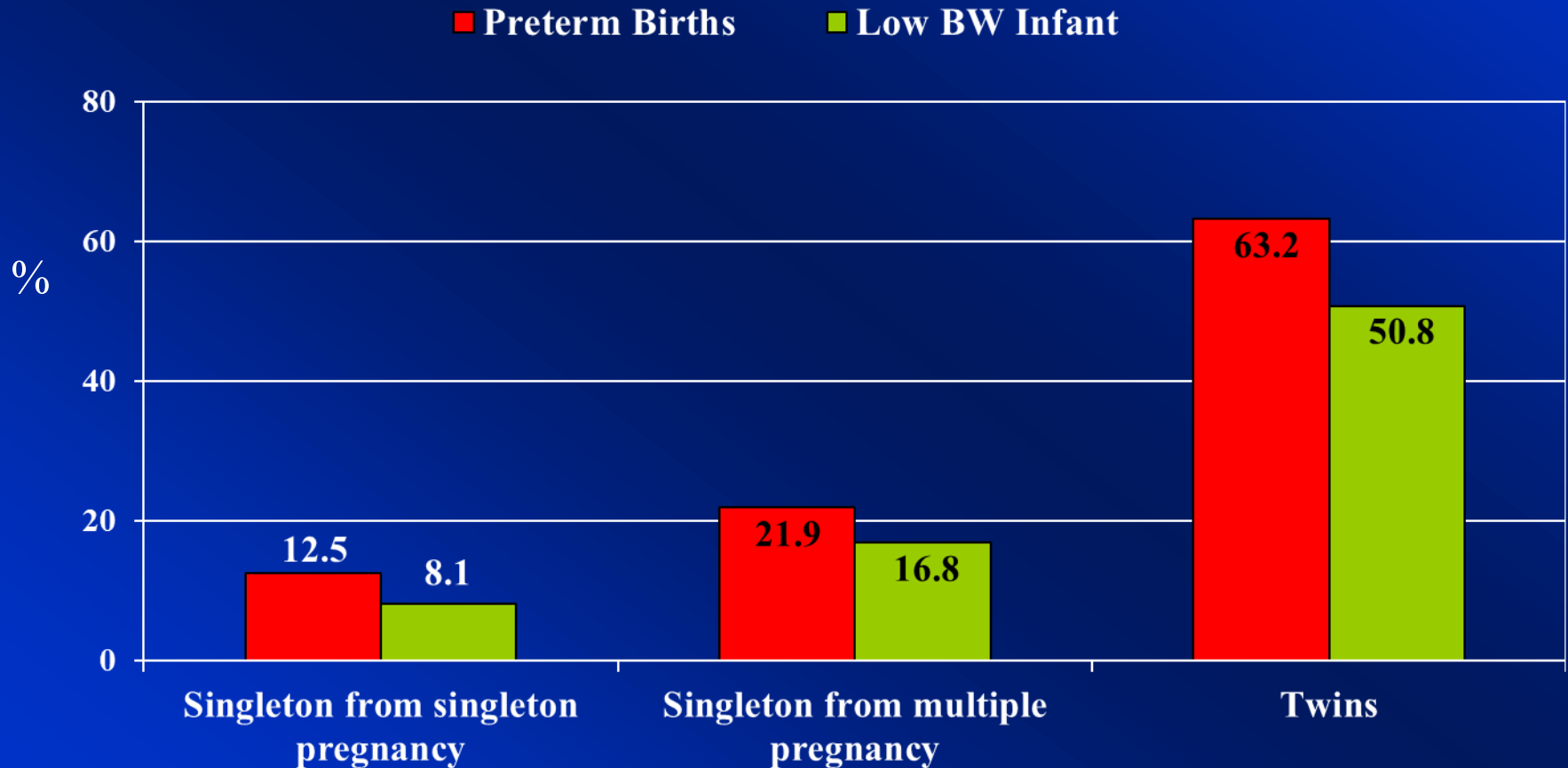
Based on 53,088 egg retrievals: under 35, non-donor oocytes

<https://www.sartcorsonline.com/EmbryoOutcome/PublicSARTOutcomeTables>

# Thawed Embryo Transfer

- **Vitrification of embryos preserves embryonic competence**
- **Controlled ovarian hyperstimulation may adversely affect uterine receptivity**
- **Allows for pre-implantation genetic testing**
- **Further reduces risk of ovarian hyperstimulation syndrome**
- **In 2023, only 12% of egg retrievals result in fresh embryo transfer**

# Risk of Pre-term Birth and Low Birthweight in Infants Conceived with ART – CDC 2022



# Risk of Congenital Anomalies

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	Absolute risk per 1000 ART Births	Odds Ratio
<b>Major birth defects</b>	<b>43</b>	<b>1.5</b>
<i>Hypospadias</i>	<i>7.6</i>	<i>3.1</i>
<b>Epigenetic or Imprinting Disorder</b>	<b>0.3</b>	<b>17.8</b>
Beckwith Wiedemann Angelman		
<b>ICSI-Sex chromosome aneuploidy</b>	<b>6</b>	<b>3.0</b>

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# ART

## Trends in 2026

- **Pre-implantation genetic testing**
- **Fertility preservation**
- **Cost**

# Preimplantation Genetic Testing

- **Identifies embryonic genotype**
  - **Aneuploidy - PGT-A**
  - **Single gene mutation - PGT-M**
  - **Chromosomal rearrangements - PGT-SR**
  - **Sex selection**
  - **Polygenic conditions?**
- **Avoids pregnancy termination**
- **Opportunity for gene therapy**

# PGT-A

- **Implantation rate improved with PGT-A in all age groups**
- **Miscarriage rate was lower with PGT-A in all age groups**
- **Livebirth rate improved in age > 37yo**

**Chang J et al. Fertil Steril 2016;105:394**

- **Number needed to treat for one additional livebirth :**
  - **21 cycles or 35 embryo transfers**

**Kushnir et al. Fertil Steril 2016;106:75**

ORIGINAL ARTICLE

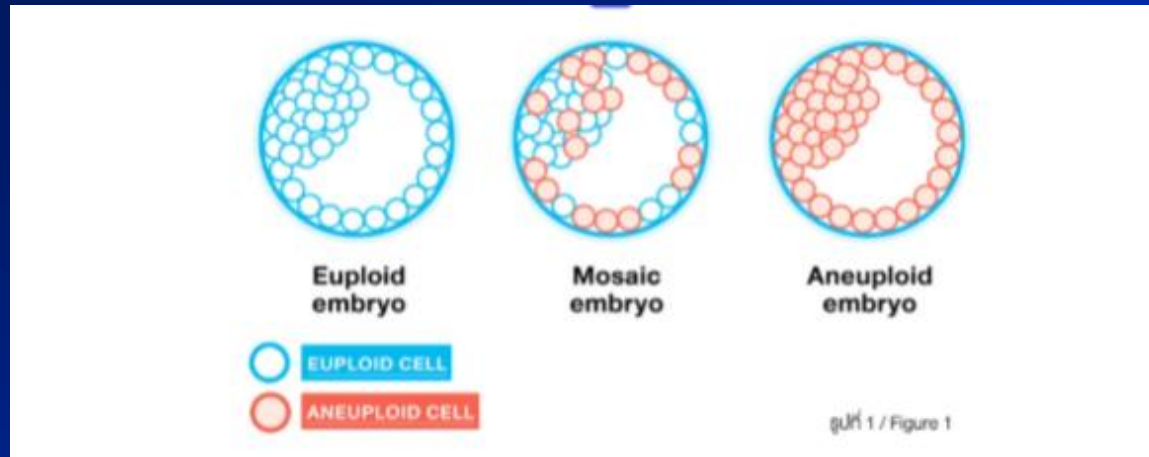
## Live Birth with or without Preimplantation Genetic Testing for Aneuploidy

J. Yan, Y. Qin, H. Zhao, Y. Sun, F. Gong, R. Li, X. Sun, X. Ling, H. Li, C. Hao, J. Tan, J. Yang, Y. Zhu, F. Liu, D. Chen, D. Wei, J. Lu, T. Ni, W. Zhou, K. Wu, Y. Gao, Y. Shi, Y. Lu, T. Zhang, W. Wu, X. Ma, H. Ma, J. Fu, J. Zhang, Q. Meng, H. Zhang, R.S. Legro, and Z.-J. Chen

ABSTRACT

- **1212 good-prognosis patients randomly assigned to PGT-A or no PGT-A**
- **69.8% of all biopsied embryos were euploid**
- **No difference in cumulative live birth rate (77.2% vs 81.8%)**
- **Pregnancy loss was decreased with PGT-A (8.7% vs 12.6%)**

# Embryonic Mosaicism



- 18 transfers of mosaic embryo in women with no available euploid embryos
- Results in six euploid healthy livebirths and two miscarriages

Greco E et al. NEJM 2015, 373: 2089

- False positive rate of 0-30% with next gen sequencing (NGS)

Goodrich D et al. J Assist Reprod Genet. 2016; 33:1473-1480

# Screen your embryos for thousands of diseases

Developmental Delay Celiac Disease Breast Cancer Prostate Cancer Heart Defects Ovarian Cancer

Stomach Cancer's Tumor Intellectual Disability Colorectal Cancer Hearing Loss Melanoma Thyroid Cancer

Heart Defects Type I Diabetes Bladder Cancer Kidney Cancer Pancreatic Cancer Hemophilia

Osteoarthritis Epilepsy Osteoarthritis Autism Spectrum Disorder

Atrial Fibrillation Inflammatory Bowel Disease Parkinson's Disease Glaucoma Atrial Fibrillation

Alzheimer's Disease Birth Defects Cystic Fibrosis Rheumatoid Arthritis Cystic Fibrosis

Deafness and Hearing Loss Obesity Cystic Fibrosis Lung Cancer Cell Vision and Hearing Loss

Neuroblastoma Autistic Spectrum Disorder Huntington's Disease Class I

Alzheimer's Disorder Schizophrenia Prostate Cancer



Intellectual Disability

Autism Spectrum Disorder

Birth Defects

SEE ALL WE SCREEN FOR

# **Fertility Preservation**

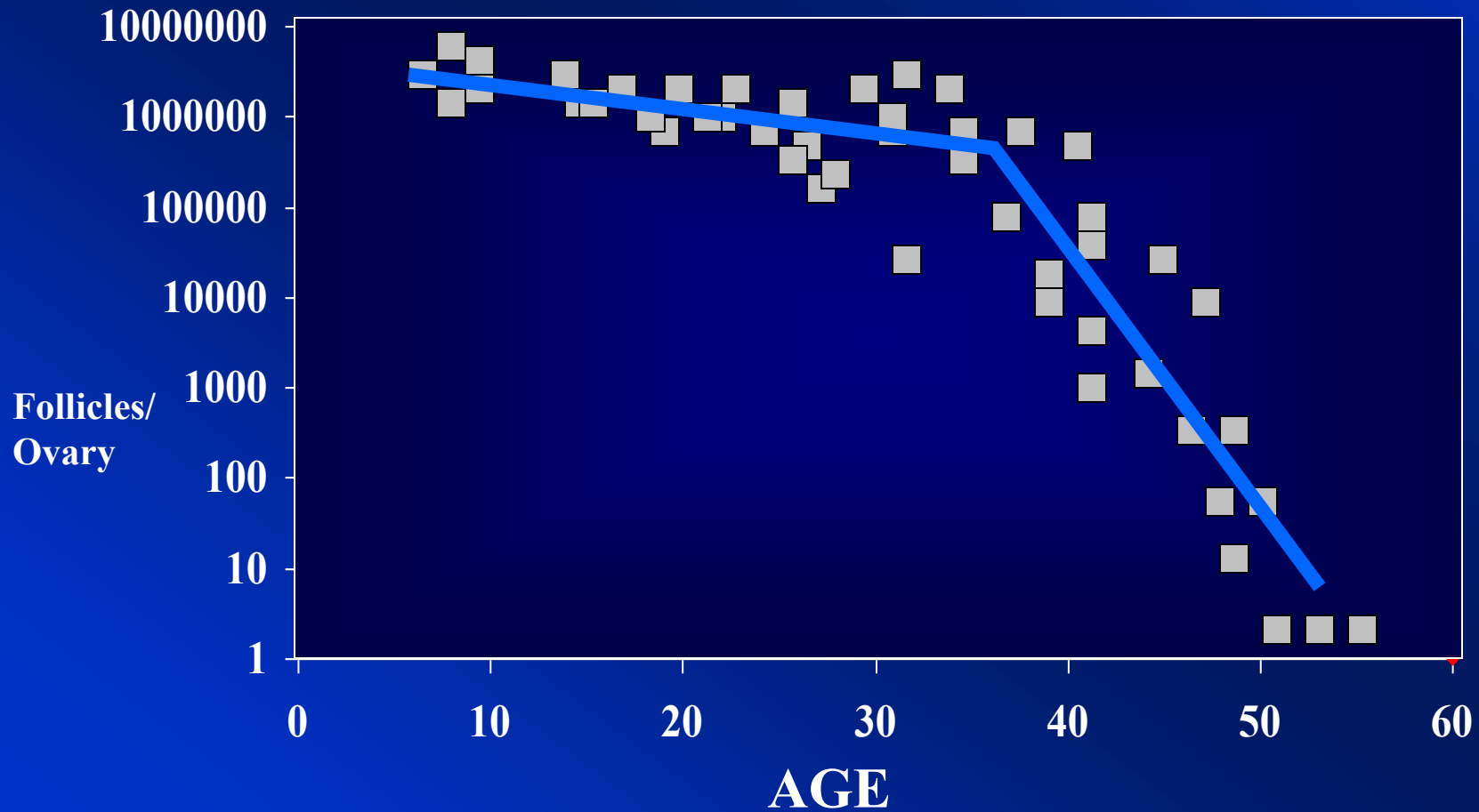
## **Mature Oocyte Cryopreservation**

- **Prior to gonadotoxic treatment or gonadectomy in reproductive age females**
- **Excessive available oocytes during IVF**
- **Unavailable male partner**
- **Elective fertility preservation (EFP)**

# **American Society of Clinical Oncology (ASCO) Guidelines**

- **As part of informed consent prior to therapy, oncologists should address the possibility of infertility with patients**
- **Referrals for interested patients to reproductive specialists**
- **Discussion at the earliest possible opportunity**
- **Sperm, oocyte and embryo cryopreservation for centers with expertise are standard practice**

# Age-Related Changes in Ovarian Reserve



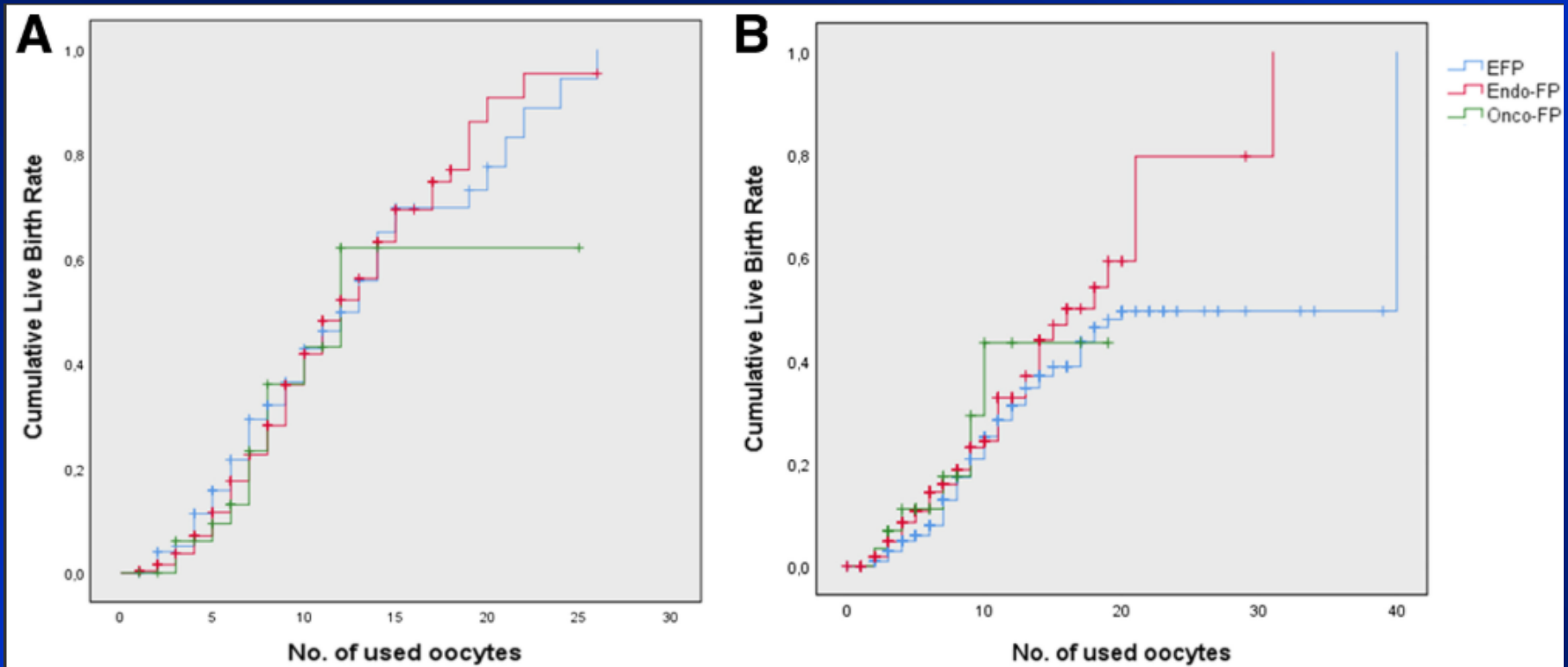
# Elective Fertility Preservation (EFP)

- **1468 patients**
  - mean age: 37.2
  - mean no. vitrified oocytes per retrieval: 9.8
- **137 patients returned for IVF**
  - Mean age at return: 39.2
  - 85.2% survival rate
  - 27% ongoing preg rate per patient

# Fertility Preservation

Age  $\leq 35$

Age  $> 35$



EFP: elective fertility preservation

Endo-FP: endometriosis

Onco-FP: oncologic

Cobo A, et al. Fertil Steril 2021;1091

A woman is shown in profile, kissing a baby who is lying down. The scene is bathed in a warm, reddish-orange light, creating a soft and intimate atmosphere. The woman's hand is visible, gently supporting the baby's head. At the top of the image, the word "TIME" is written in a large, bold, red, serif font.

**TIME**

**How a dazzling  
array of medical  
breakthroughs  
has made**

**CURING  
INFERTILITY**

**more than just  
a dream**