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fertilitySA

Maximising IVF Outcomes with Science and Innovation

Nicole McPherson

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“We acknowledge the **Kaurna** as the Traditional Custodians of the Country we live and work on. We recognise their continuing connection to the land and waters and thank them for protecting this coastline and its ecosystems since time immemorial. We pay our respects to Elders past and present and extend that respect to all First Nations people”

Artist: Jenna Oldaker, Wadawurrung artist
Artwork Description: This artwork represents the connection between our ancestors, land, sky and spirits. The spirits of those that have passed, live on in the night sky watching over us as we continue to care and learn from our beautiful Country home.

Director of Research

Nicole McPherson, PhD

Over a decade of experience in IVF research leadership.

Senior Lecture and Research Leader at University of Adelaide.

Research informed international/national pol icies, including the WHO.

2 Provisional Patents - in sperm selection.

Clinical trials development and management in human IVF.

Awarded two nationally competitive fellowships – NHMRC and Australian Research Council.

Strong advocate for promoting reproductive and sexual health - 20+ media coverage.
Developed pre-conception e-tools.

Associated editor - BMC Reproductive Health.

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What is ART and IVF

- Assisted reproductive technologies (ART) can be defined as a set of techniques and medical treatments that allow individuals and couples to start a family.
- Nowadays between 1 in 5 and 1 in 6 couples will suffer from infertility.
- Treatments include; timed intercourse, intrauterine insemination, ovulation induction and *in vitro* fertilization (IVF).
- Two methods of IVF (i) standard insemination and (iii) intracytoplasmic sperm injection (ICSI)

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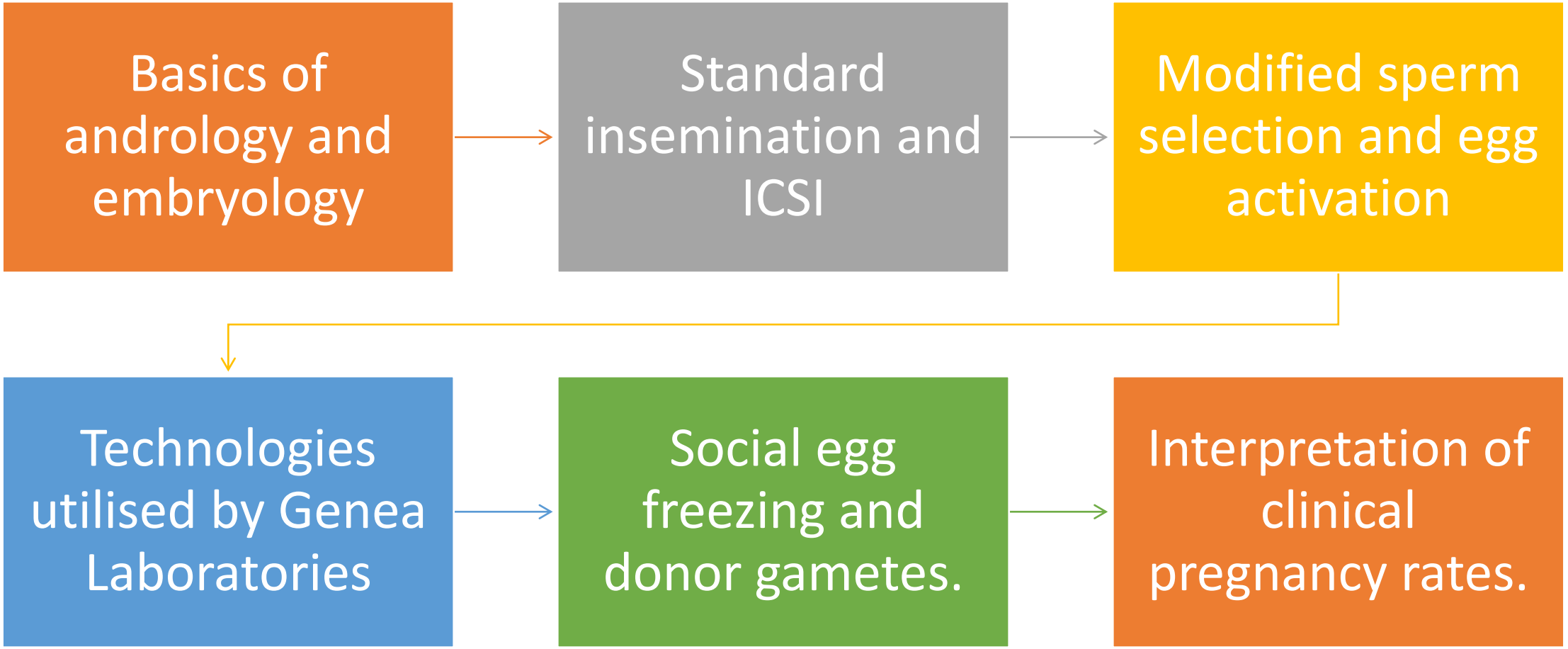
Items that will be covered in this talk



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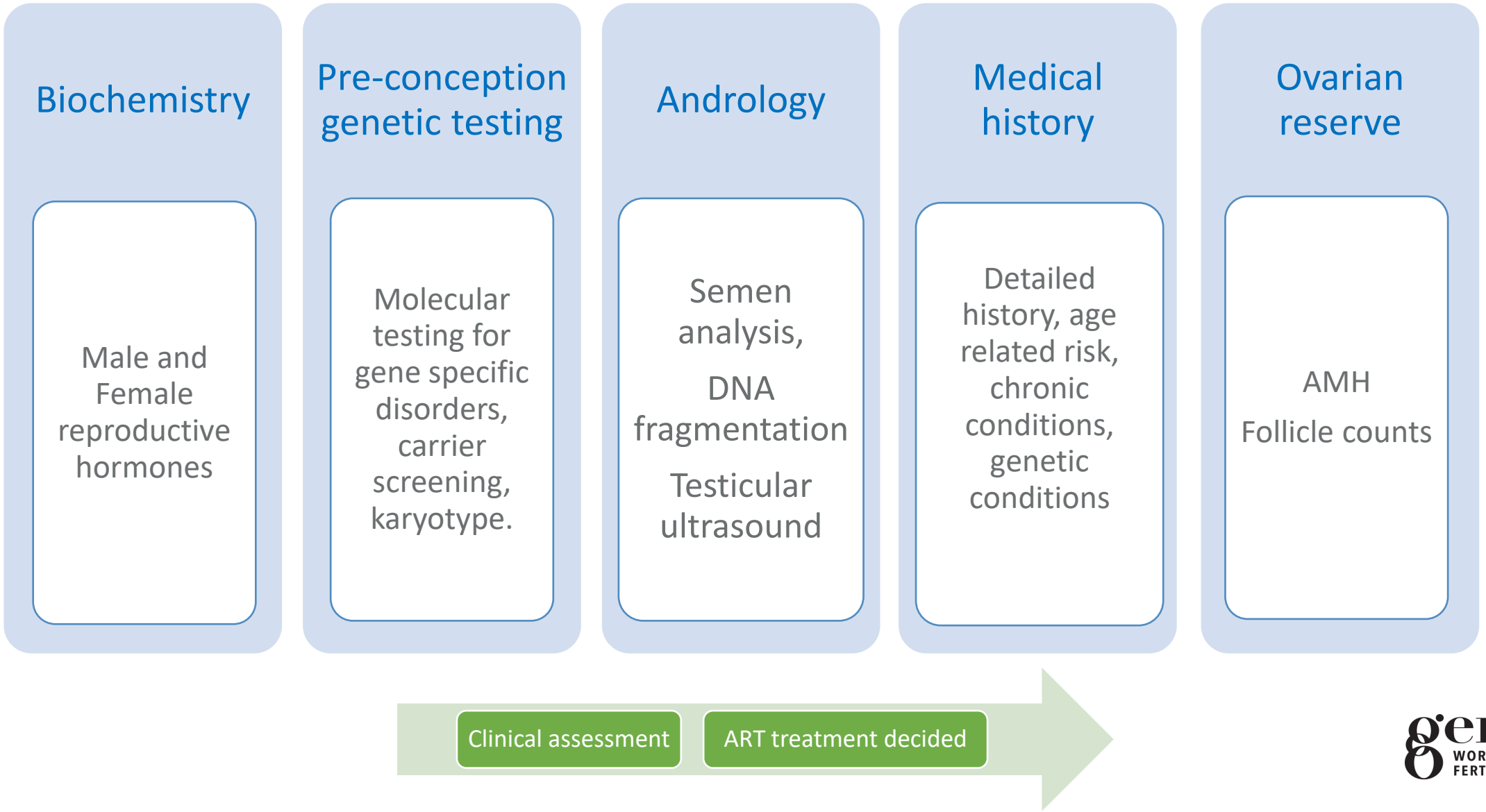
Fertility Assessment



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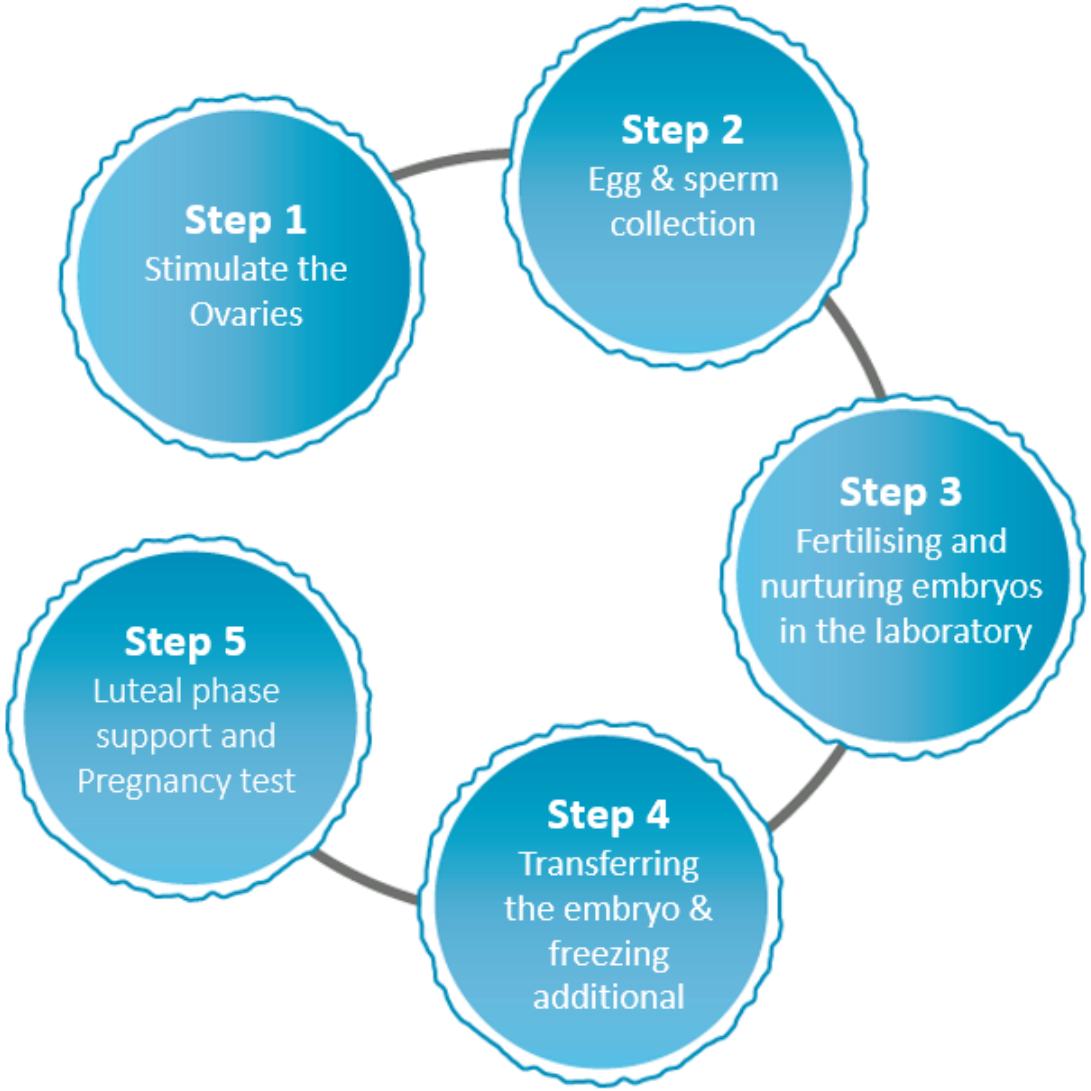
Process for standard IVF or ICSI



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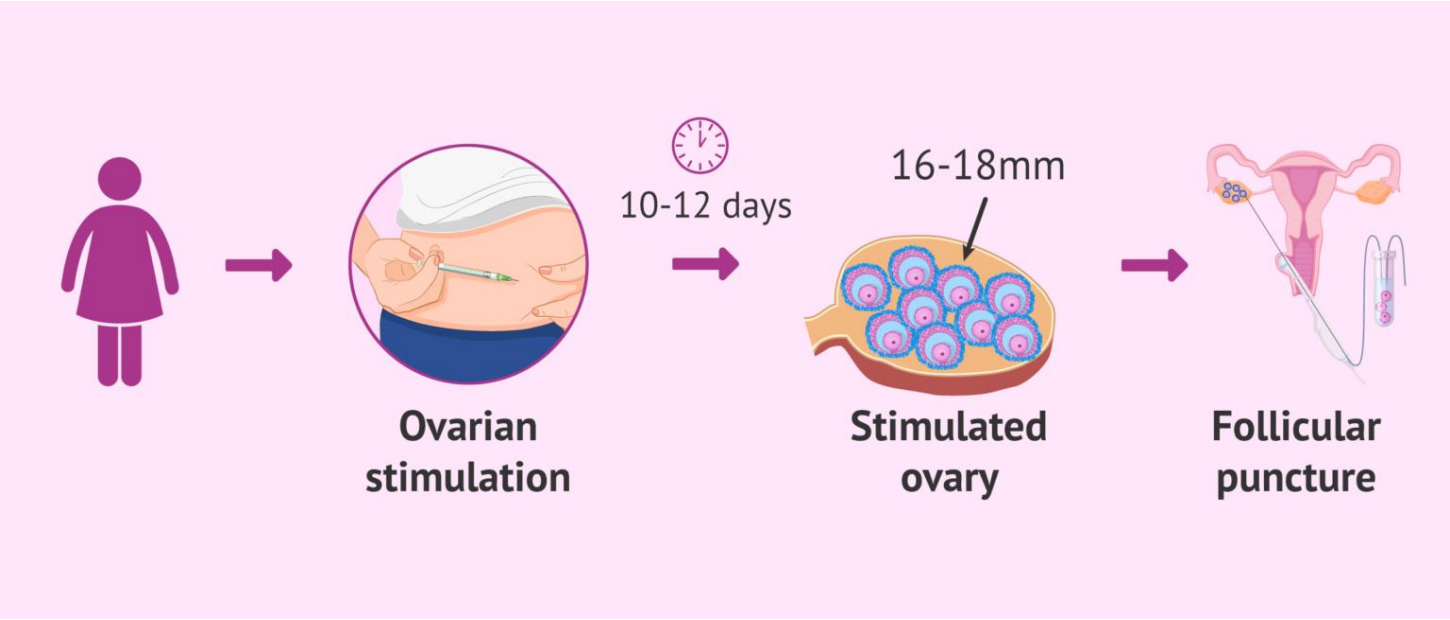
Ovarian stimulation

- Purpose – increase the number of eggs developing in the ovaries during a cycle.
- Different stimulation drugs can be prescribed to stimulate the ovaries with many aiming to produce between 5-20 mature eggs in a cycle.



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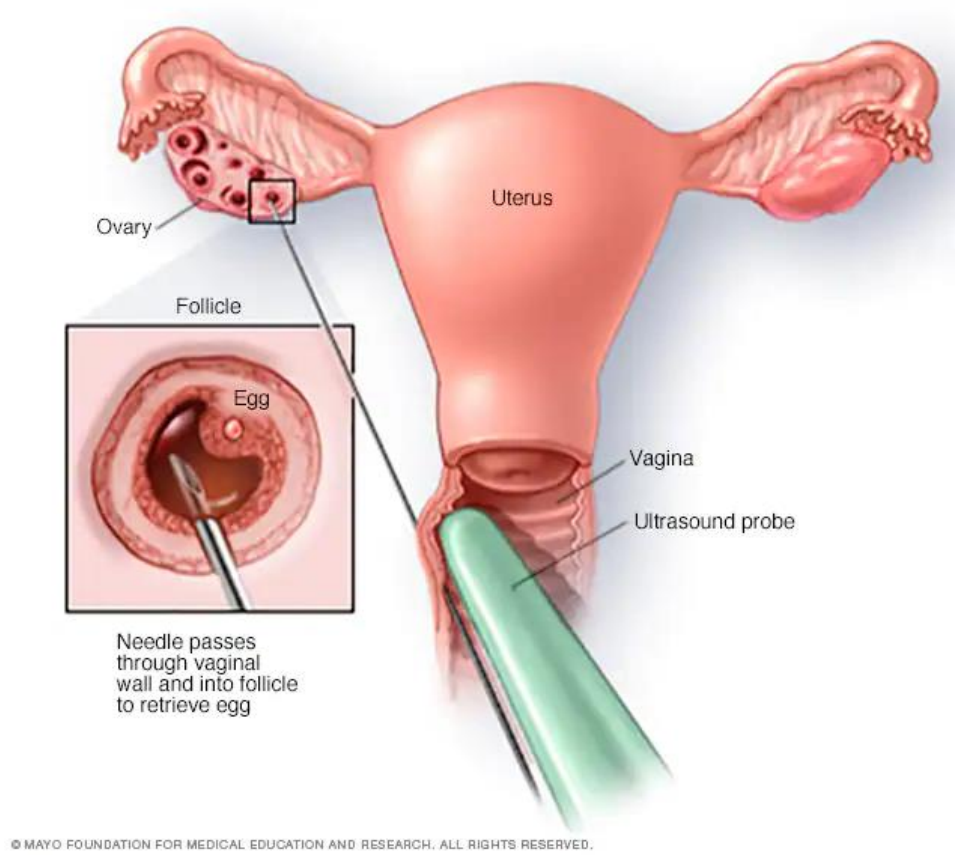
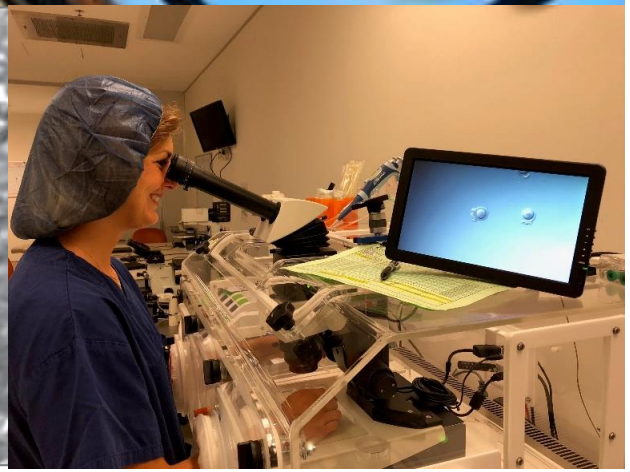
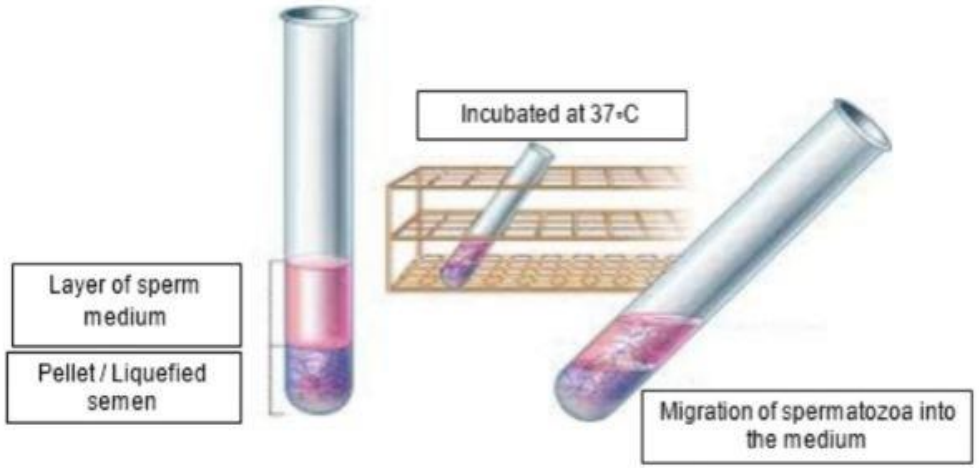
Egg collection



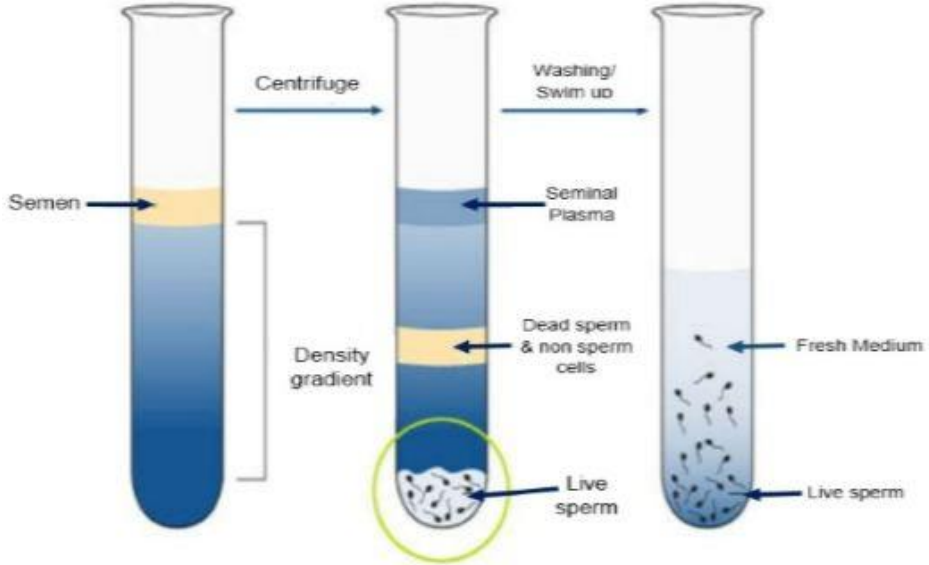


Sperm collection and preparation

Process within 1h



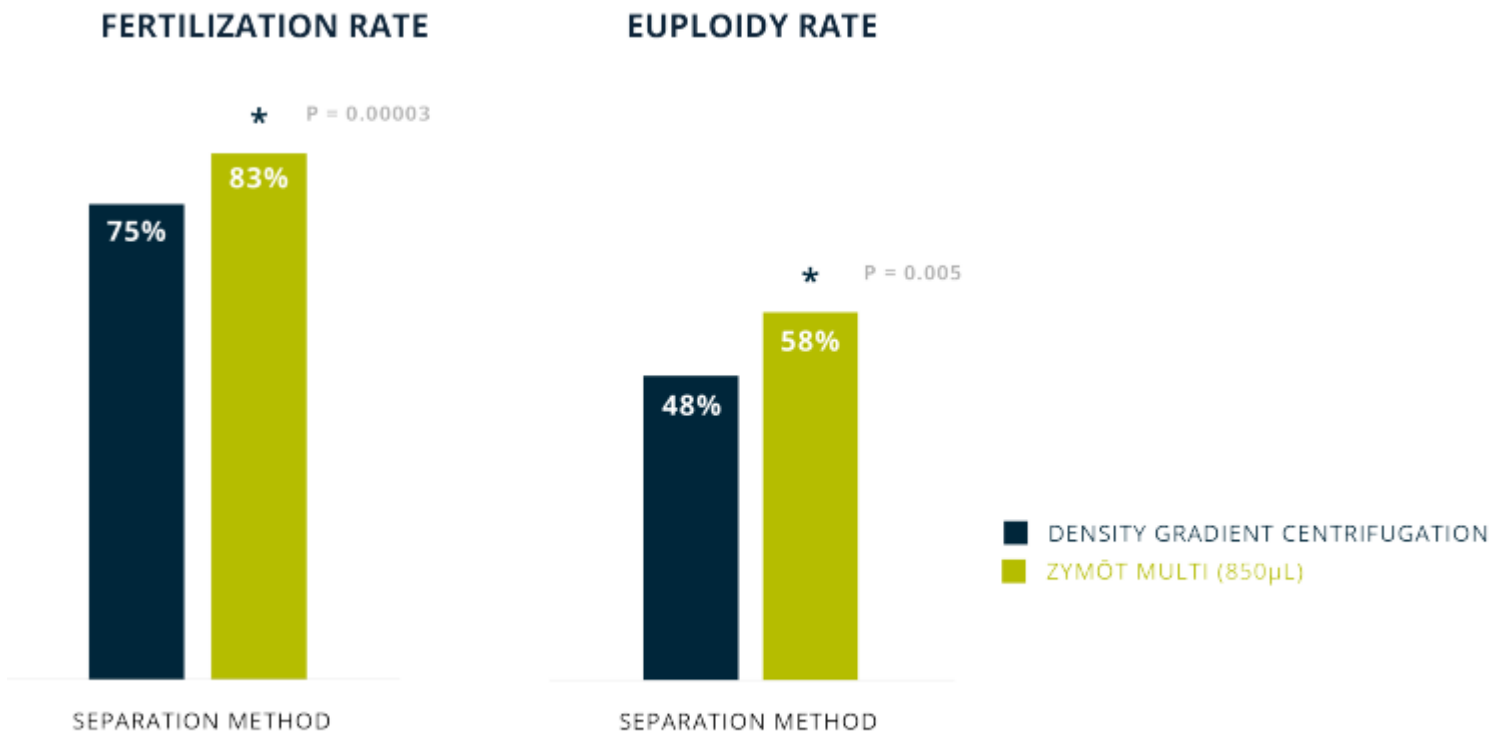
Swim-up



Density Gradient

What about those men with high DNA damage?

ZyMōt® FERTILITY, INC.



At The Fertility & IVF Center of Miami, using the ZyMōt Multi (850µL) Sperm Separation Device resulted in an 11% increase over the baseline fertilization rate (left) and a 21% increase over the baseline euploidy rate (right).

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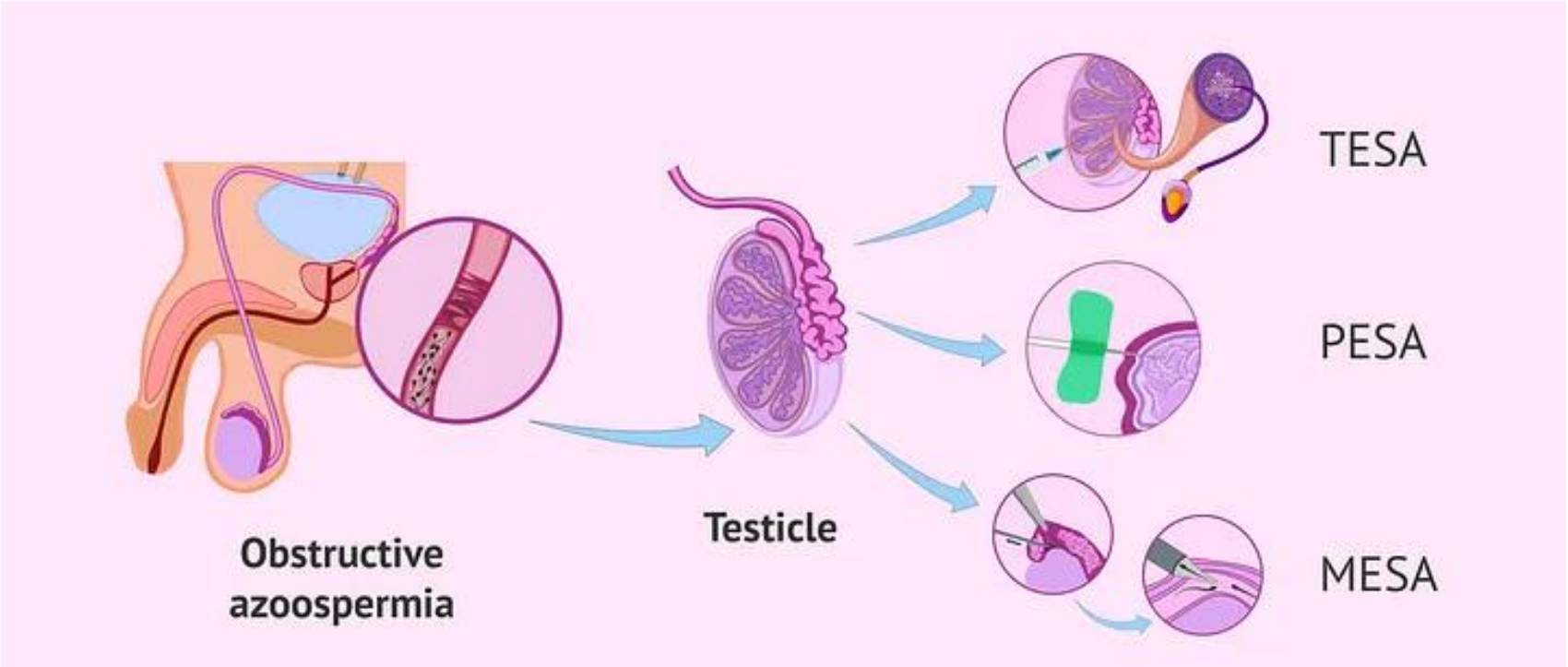
What about those men with no sperm in their ejaculate?



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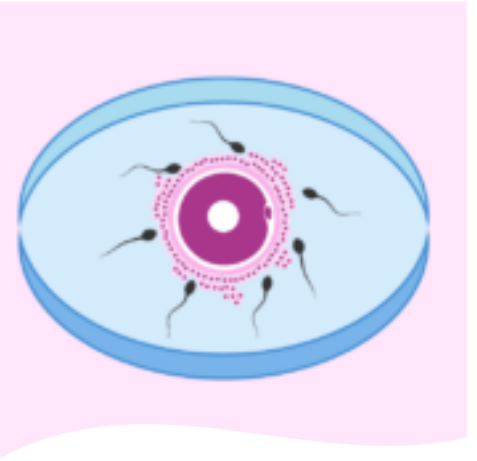
Standard insemination



- 10,000 motile sperm are co-incubated with eggs overnight in conditions that match the female reproductive tract.
- Performed in couples with female factor infertility.

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Intracytoplasmic sperm injection

- Direct injection of one sperm into the egg.
- Technique pioneered from a mistake back in the early 90's.
- Performed in couples with serve male-factor infertility and previously failed standard insemination.

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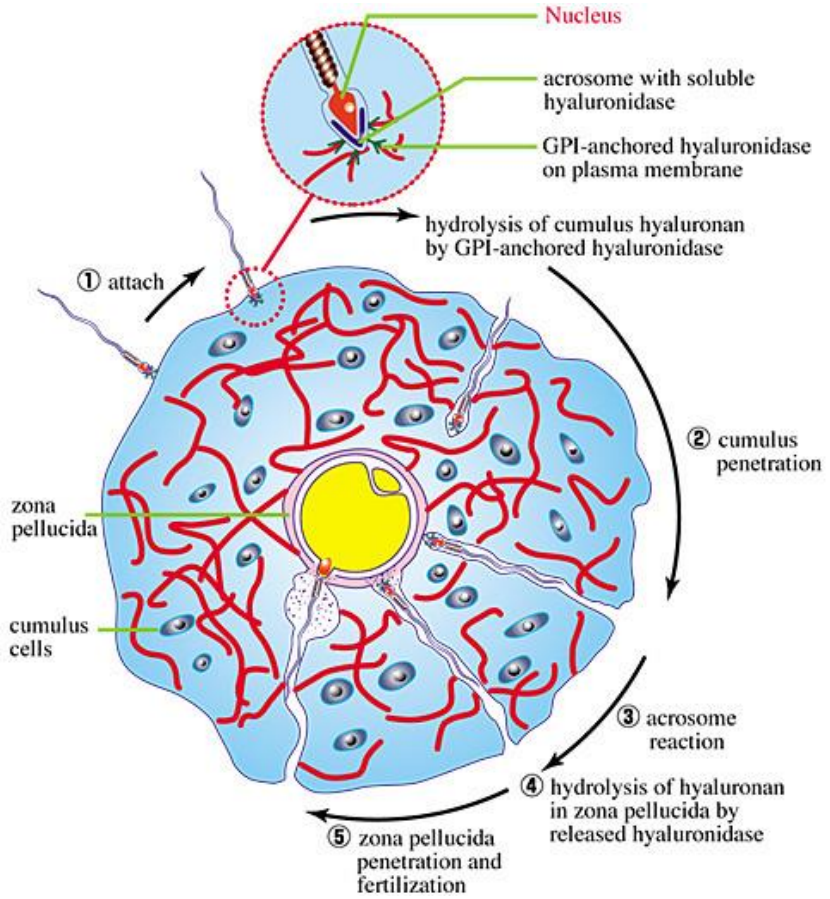

Modified sperm selection for ICSI – PICSI

- PICSI also known as sperm slow is the use of hyaluronan to help select better quality sperm.
- Improves live birth outcomes in men of an advanced age and selects for sperm with better DNA integrity *(West et al, 2022, Human Reproduction).*

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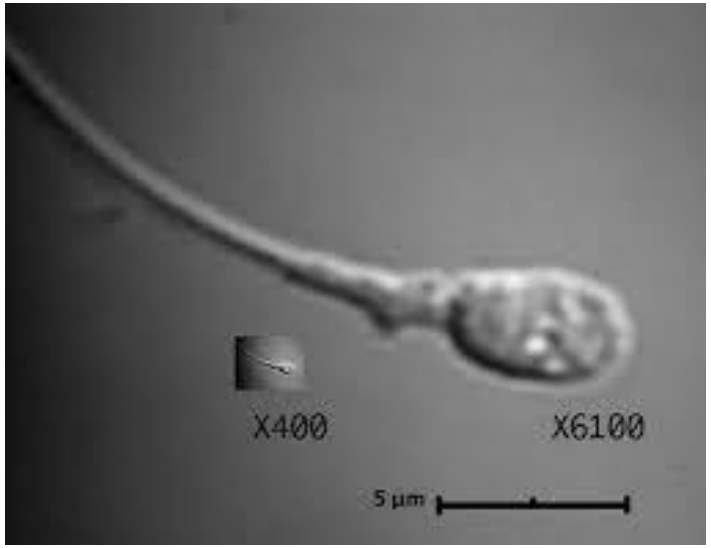

ANDROLOGY

Original Article | Free Access

Sperm morphological normality under high magnification is correlated to male infertility and predicts embryo development

B. F. Zanetti, D. P. A. F. Braga, R. R. Provenza, R. C. S. Figueira, A. Iaconelli Jr., E. Borges Jr.

First published: 18 February 2018 | https://doi.org/10.1111/andr.12473 | Citations: 2

Table 6 Linear and binary logistic regression analyses of MSOME grades correlation with ICSI outcomes, adjusted for male and female ages, ejaculatory abstinence, and retrieved oocytes

	MSOME I+II		MSOME III		MSOME IV	
	β	*p*	β	*p*	β	*p*
Fertilization rate	0.197	0.044	0.150	0.134	−0.192	0.052
High-quality embryos rate	0.306	0.013	0.379	0.002	−0.378	0.002
Blastocyst rate	0.248	0.047	0.008	0.954	−0.195	0.130
Implantation rate	−0.098	0.405	−0.137	0.252	0.138	0.244
	95% CI	*p*	95% CI	*p*	95% CI	*p*
Cancelation rate	0.95; 1.07	0.817	0.94; 1.12	0.557	0.95; 1.03	0.716
Pregnancy rate	0.90; 1.05	0.493	0.84;1.09	0.528	0.96; 1.09	0.396

ICSI, intracytoplasmic sperm injection; MSOME, motile sperm organelle morphology examination; β, standardized regression coefficient; 95% CI, 95% confidential interval for Exp(B).

Modified sperm selection for ICSI – IMSI

- Intracytoplasmic morphologically selected sperm injection (IMSI).
- Used in patients with very poor sperm morphology and in couples with poor embryo development.
- Selection of sperm based on normal morphological characteristics of head and neck at x6000 magnification.
- Latest Cochrane review (2020) – shows some low-quality evidence for increased pregnancy rates (PMID: 32083321).

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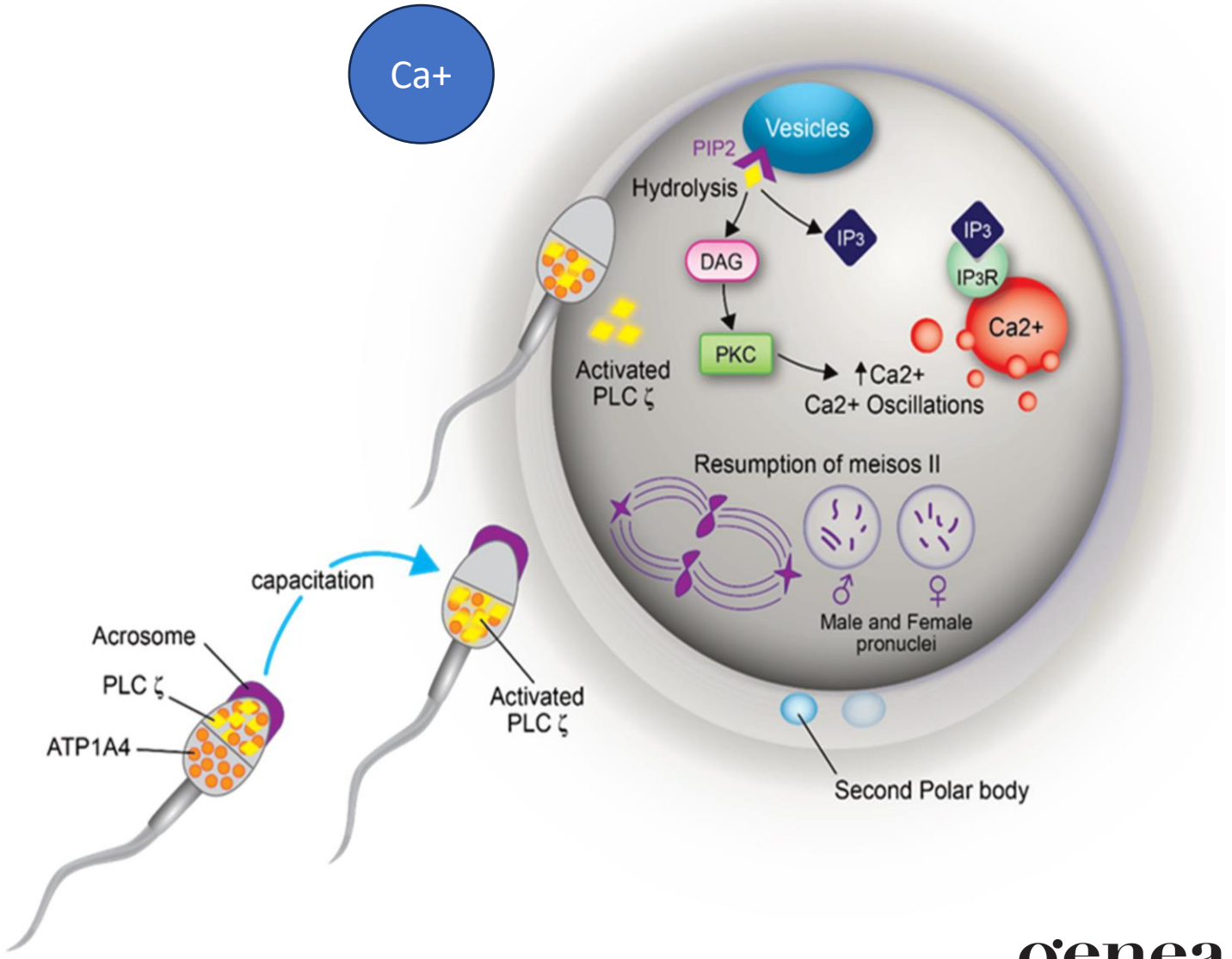
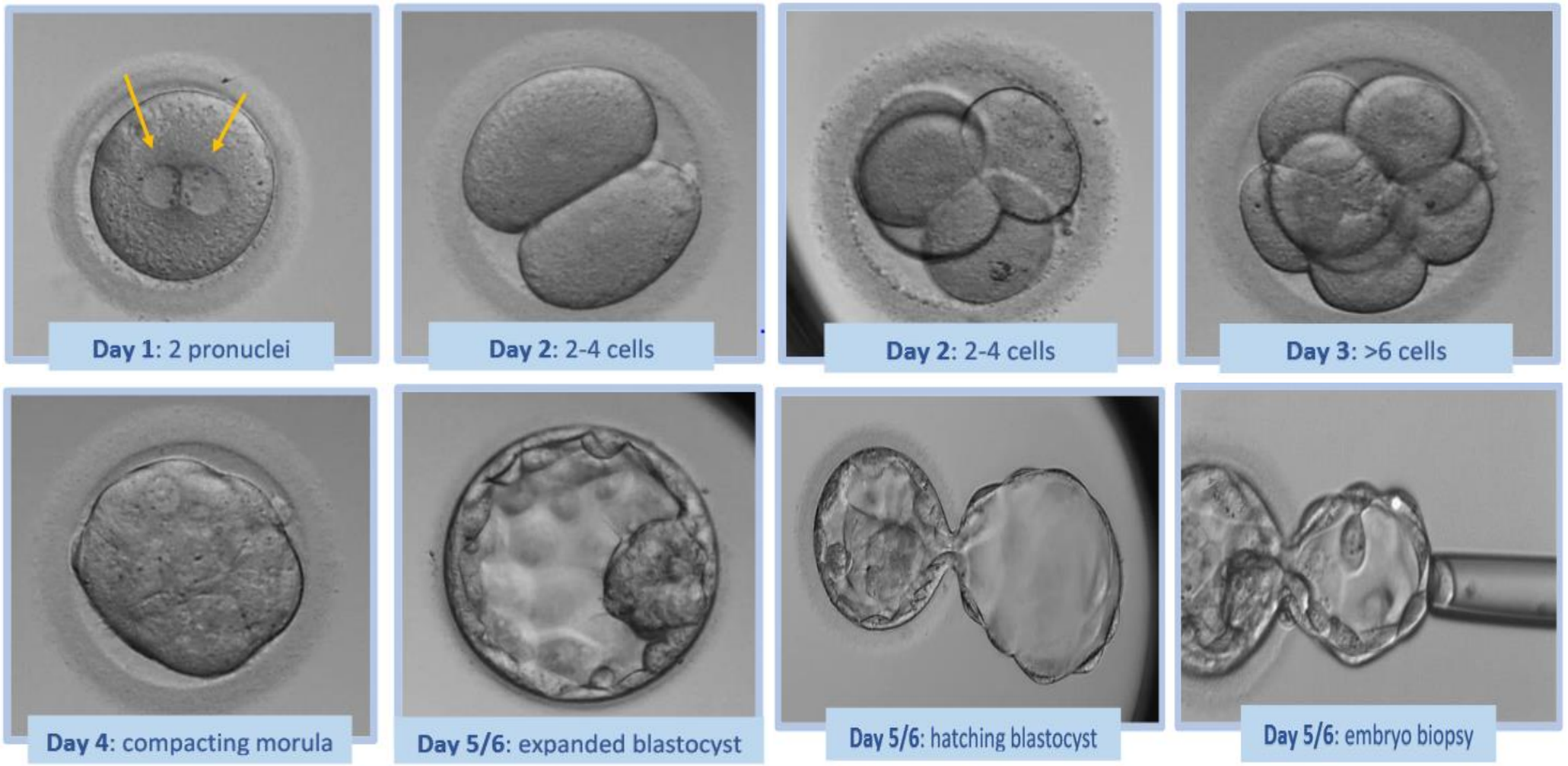
Modified ICSI – Oocyte activation

- Oocyte artificial activation following ICSI can occur with the help of calcium ionophore.
- Mimics the natural calcium oscillations that occur following fertilization, which are triggered by a protein (PLCζ) from the fertilising sperm *(Shafgat et al, 2022 Front Cell Dev Biol)*.
- Used in patients with failed fertilization or low (<25%) following ICSI.
- Systematic review (2021) shows that oocyte activation can increase fertlisation, embryo development and pregnancy rates in couples who respond poorly to standard ICSI *(Shan et al, 2021, Font Physiol)*.



In vitro embryo development



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Gems culture media – Invented by Genea

- Contains all the components (mimic the oviductal environment) including carbohydrates, amino acids, antioxidants and buffers to supports gametes during collection and embryos during development.
- Used exclusively by Genea clinics since 2013.

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Geri Timelapse Incubator

- Uninterrupted culture for 5-6 days.
- Individual chambers per patient.
- Mimics the uterine environment.
  - Temperature (37^{o}C)
  - Humidity
  - Hypoxic conditions (5% Oxygen, 6% Carbon dioxide)

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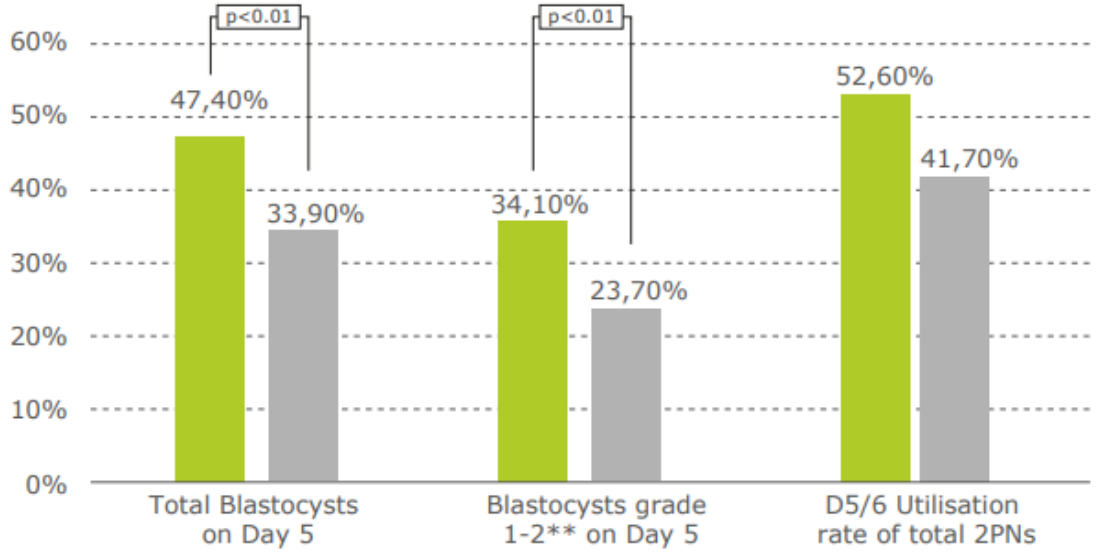
Gems + Geri increases the number of good quality blastocyst

Why Gems®?

THE PROOF IS IN THE RESULTS

After the implementation of a fully undisturbed culture system in all Genea labs, the use of the Geri® incubator alongside the Geri® Medium provided more supportive environmental conditions for embryos* compared to MINC incubator using Gems Sequential media[1]:

- **More blastocysts** developed to D5*
- **Better quality** blastocysts*
- **Higher** utilization rate



Genea Clinical Results

Quantity and quality of blastocysts produced from fertilized oocytes

(All clinics, all cycles, combined ages)[1]

Geri & Geri Medium
(Apr 2016-Dec 2017; Total # embryos 20173)

MINC & Gems sequential media
(Jan 2015-Apr 2016; Total # embryos 20554)

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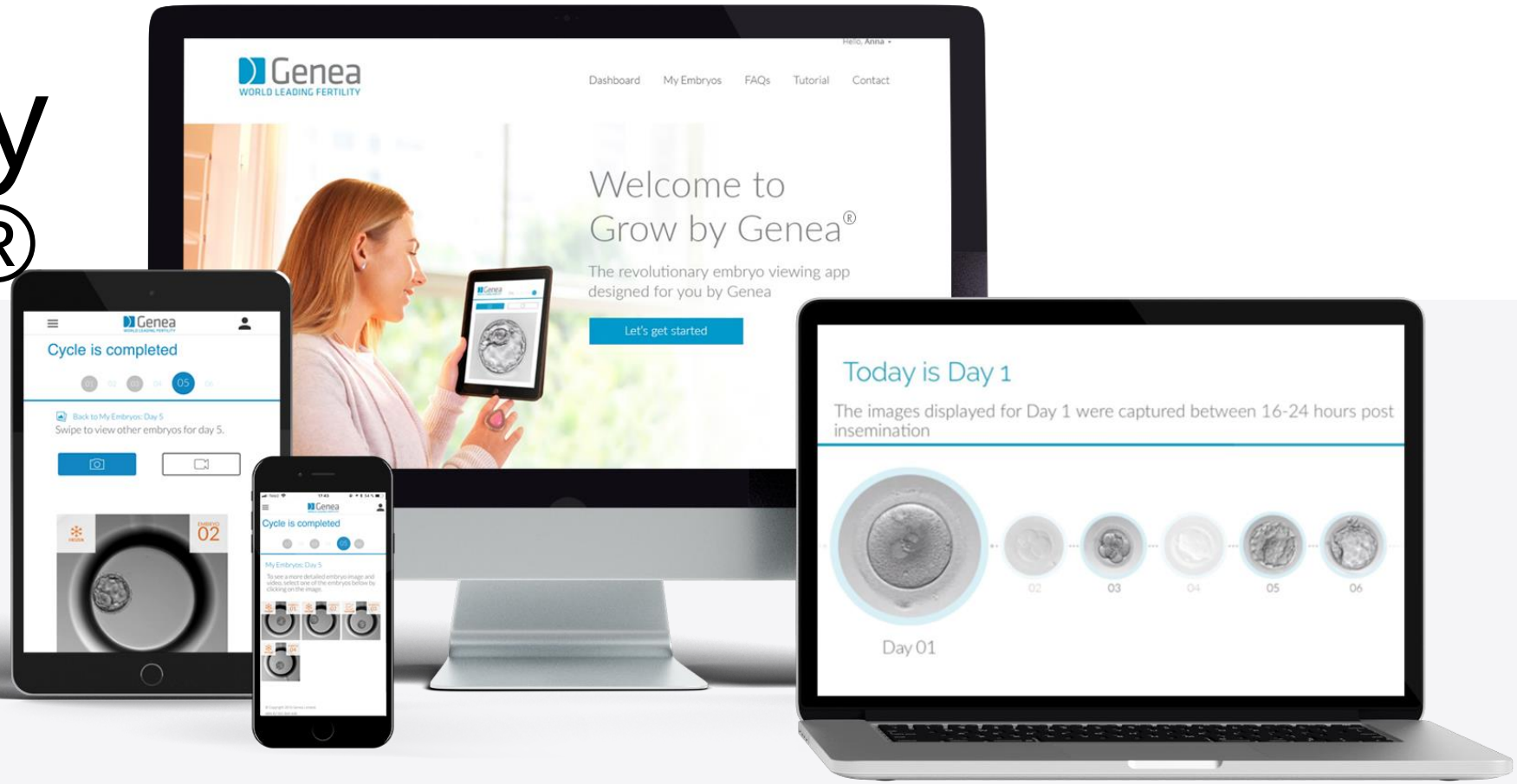
Grow by Genea®



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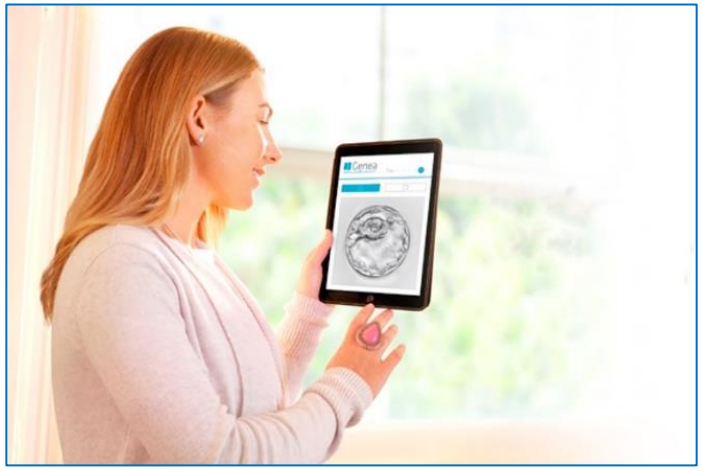
Overview

- Enhances the patient experience by allowing access to images and footage of their embryo development
- Still image and time-lapse video snippets are uploaded at specific time points
  - Evening of: Day 1, Day 3, Day 5 and Day 6
- Patients still receive ongoing communications from an embryologist regarding their embryo development.
- Management of Database by Embryology team in SA via specific email
  - adelaide.grow@genea.com.au

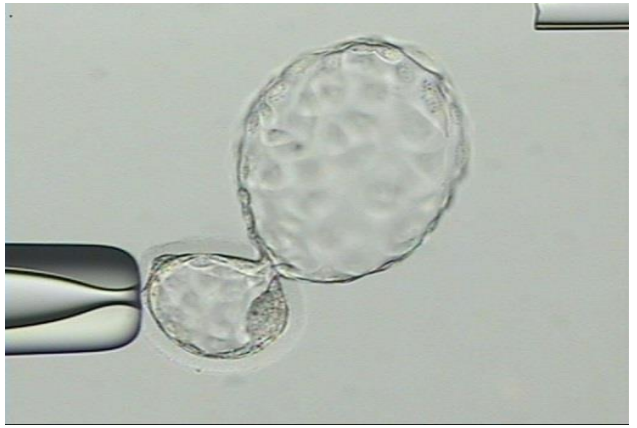


Biopsy for pre-implantation genetic screening

- To test an embryo for chromosomal or genetic disorders we need to take a small portion of the embryo.
- Two main different types of screening that we do:

  PGS: for whole chromosomes (age related)

  PGD: for chromosome regions and genes (known disorder or carrier)
- The biopsy consists of cells from the trophectoderm (6-8 cells).
- Need to know that whilst these cells are representative of the whole embryo, prenatal screening is still important.
- Embryos may be mosaic; made up of cells with differing chromosomes *(Chavli et al, 2024 JCI).*
- Different prenatal screening consists of NIPS, amnio and CVS.



PCR- for chromosome regions (and genes)

- NGS complete set of chromosomes (most common)

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Embryo Biopsy procedure

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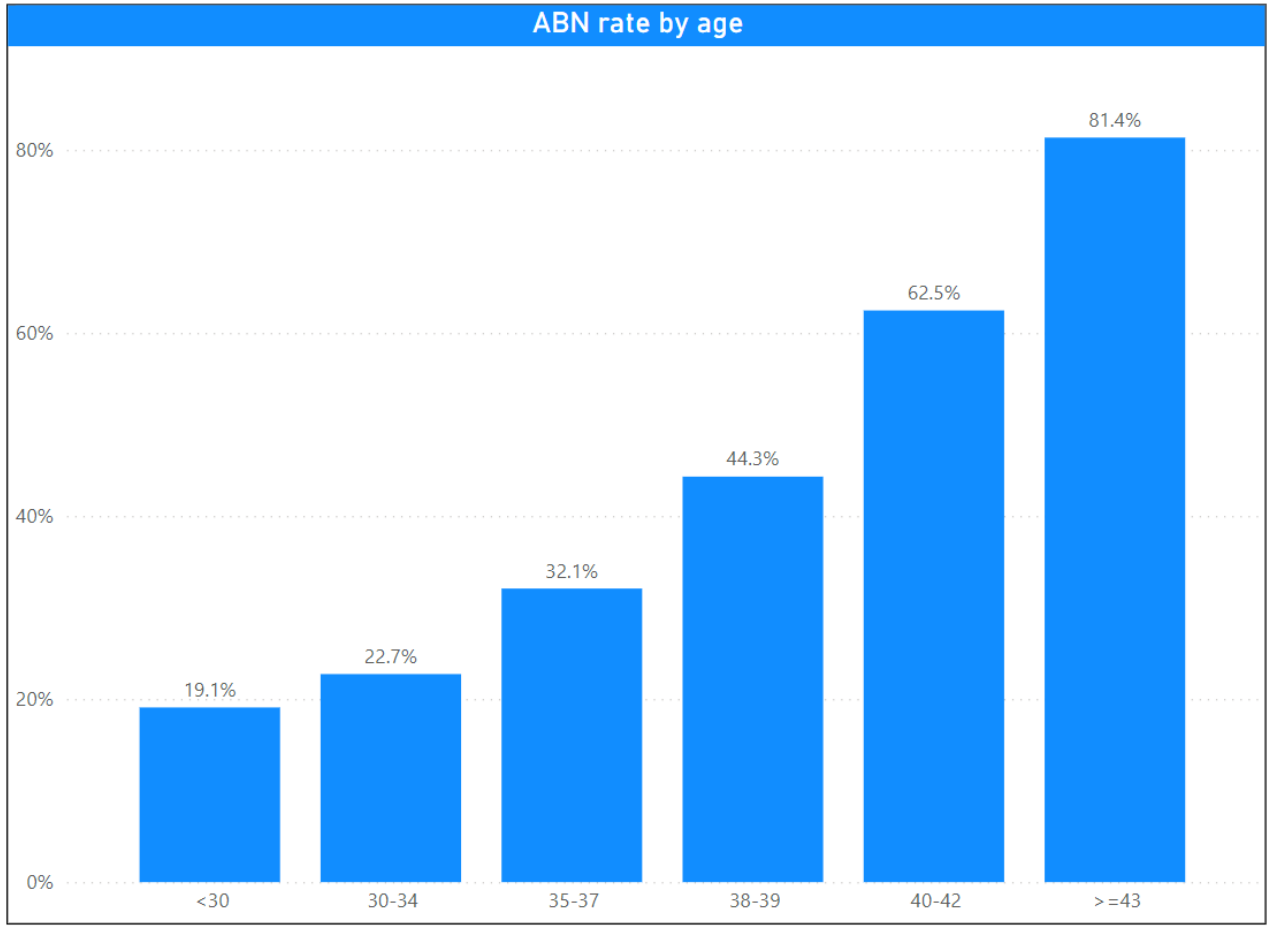
Why do pre-implantation genetic screening?



- To improve live birth rates by transferring a morphologically good & euploid embryo compared to just morphologic assessment.
- Indication: women older than 36 years and/or those that have had a repeated miscarriage.
- But be aware that the older a woman gets, the less eggs, poorer quality and unlikely to have a chromosomally normal embryo.

- Increases live births and ongoing pregnancies per embryo transfer and reduces miscarriage.
  (Kasaven et al 2023, JARG – Systematic review and meta-analysis)

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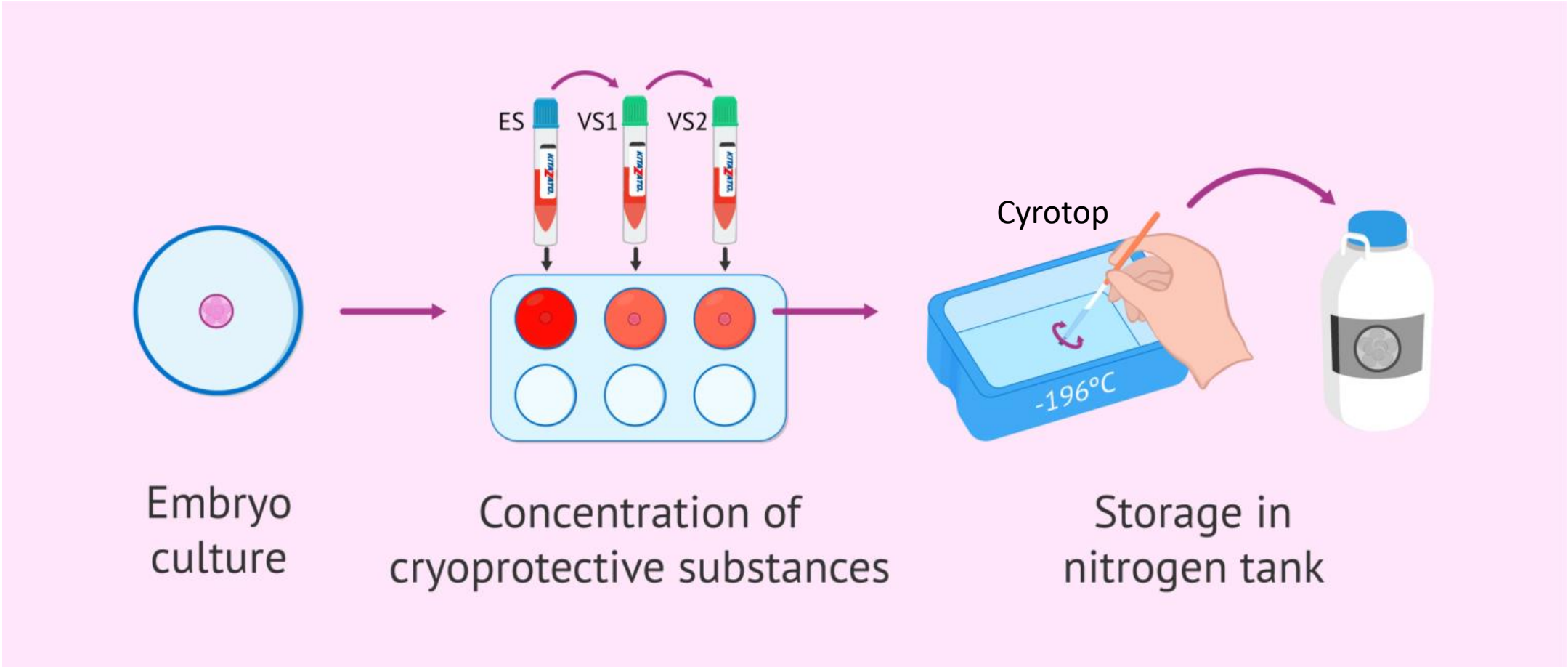
Vitrification to store eggs and embryos



- Utilises ultra-rapid freezing process that avoids ice crystal formation inside the embryo by removing water and replacing with a high concertation of cryoprotectants.
- Embryos can be stored in state of suspended animation forever.

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Embryo Transfer

- Most done on Day 5 of embryo development.
- A fine plastic catheter loaded with the embryo is passed through the cervix into the uterus under ultrasound
- A pregnancy test is taken 16 days following egg collection (~11 days after embryo transfer).

Safety: Traceability of samples

- Every movement between vessels or addition of material to a vessel requires an identification check in the laboratory.
- This is a two-step process where the scientist will ID the patients' paperwork against their dishes and then use our electronic system to perform a second ID.
- Regular audits are performed to ensure compliance in use.

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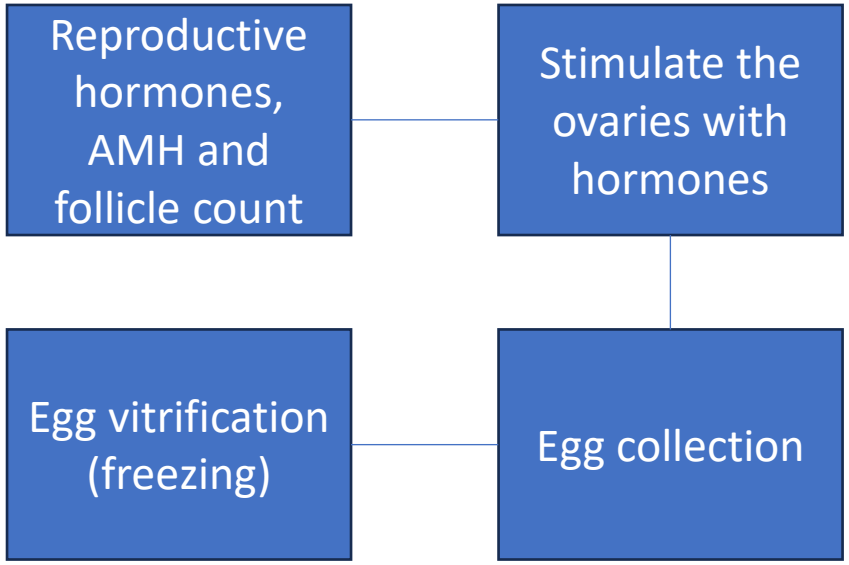
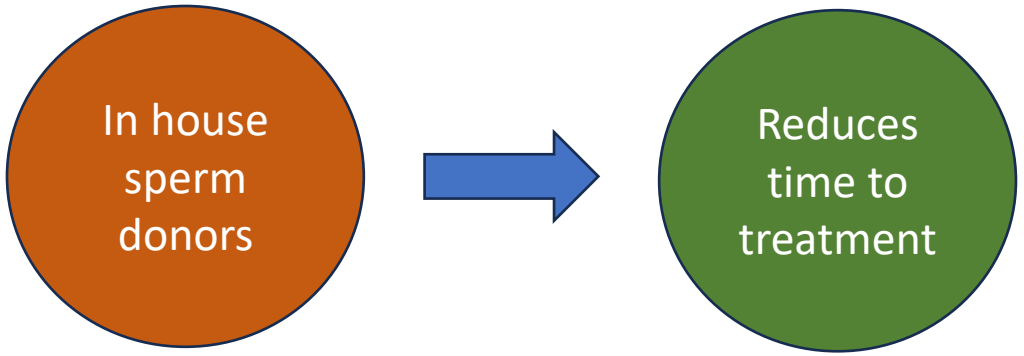
Social Egg Freezing and Donor Gametes



Age at time of freezing is the biggest indicators of later success.

> I froze my eggs because I had just broken up with my long term boyfriend, knew my fertility was declining and wanted to do something to feel as though I was investing in my future, giving myself an option for down the track.
> Dianne, 34

[Egg freezing - Genea Fertility]



Seattle Sperm Bank

THE WORLD EGG BANK

rainbow families
connecting • supporting • empowering

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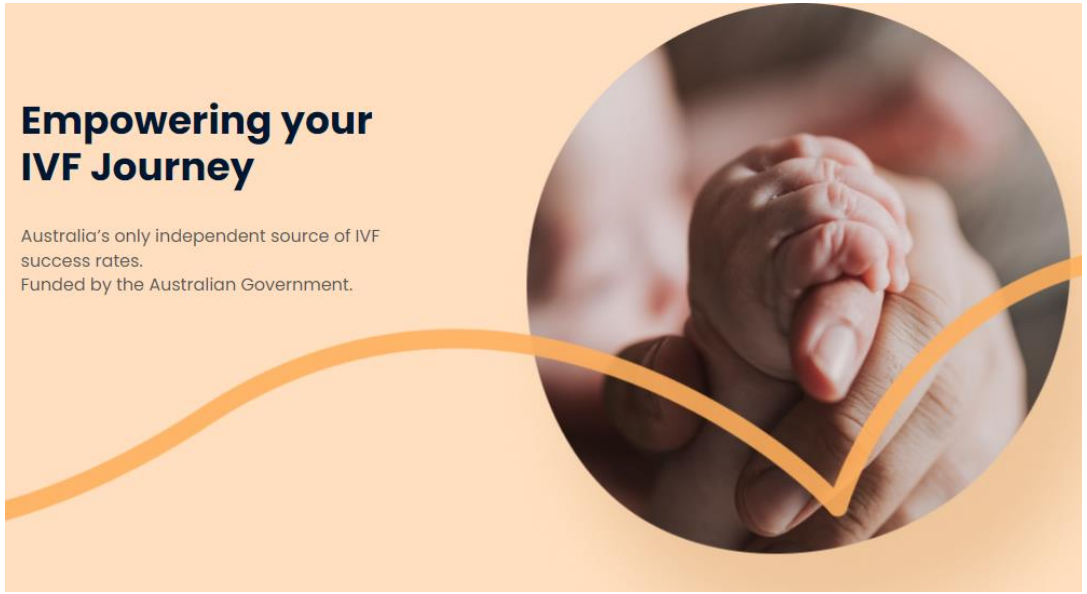
Understanding clinic results

- All results reported yearly to NPESU at UNSW.
- Includes all cycles and pregnancy outcomes from the previous year.
- This data set makes up the Australian and New Zealand Reproductive Database (ANZARD).
- After being reviewed by independent statisticians, individual reports are issued back to each clinic and the data is combined to create national averages.
- Each clinic is aware of their results and were they sit Nationally however up until 2021 this was never advertised.
- This has made comparing clinics hard as there are many different measures of success and many ways to manipulate data to inflate this success such as restricting age or treatment type.

YourIVFSuccess

YourIVFSuccess



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YourIVFSuccess

[YourIVFSuccess]

Genea Fertility SA

RTAC Accredited | Established 2009

Level 9 431 King William Street Adelaide SA 5000

www.fertilitysa.com.au

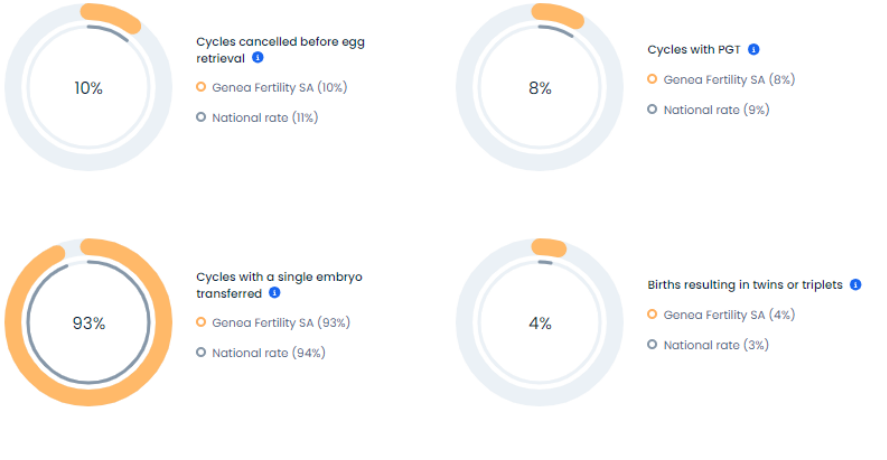
Success Rates | Clinic Profile | **Clinic Services**

Provided Services

- ✓ IVF
- ✓ ICSI
- ✓ Cryopreservation
  - ✓ Eggs
  - ✓ Sperm
  - ✓ Embryos
- ✗ Surrogacy
- ✓ Counselling
- ✓ Intrauterine insemination
- ✓ Surgical sperm collection
- ✓ Egg donation
- ✓ Donated sperm
- ✓ In vitro maturation
- ✓ Preimplantation genetic testing - chromosomal
- ✓ Preimplantation genetic testing - single gene
- ✓ Non IVF fertility care

About this clinic

This clinic performed 500-1000 individual treatment cycles in 2022.



Patients at this clinic

These statistics are based on cycles performed in 2022 at this clinic.

Pregnancy rates measured on Your IVF Success

- Measure #1: Births per complete egg retrieval cycle (including the later transfer of resulting embryos)
- Description - This measure shows the chance of a live birth from fresh and frozen embryo transfer procedures resulting from each complete egg retrieval cycle.

- Measure #2: Births per complete egg retrieval cycle (including the later transfer of resulting embryos) for women having their first ever egg retrieval
- Description - This measure shows the chance of a live birth from fresh and frozen embryo transfer procedures resulting from each complete egg retrieval cycle for women having their first ever egg retrieval.

- Measure #5: Clinical Pregnancies per individual treatment attempt
- Description - This measure shows the chance of a clinical pregnancy from each individual treatment attempt involving an intended embryo transfer.

- NB: The above measures are for women using own eggs only (no surrogates, donor eggs or gestational carrier cycles). Current report is 2020 OPUs with FETs followed to end of 2021 for measures 1 and 2. Measures 1 and 2 are excluded for freeze all cycles where the patient does not return for an egg warm or FET cycle in the designated time-frame. Measure 5 is for Procedures in 2022.

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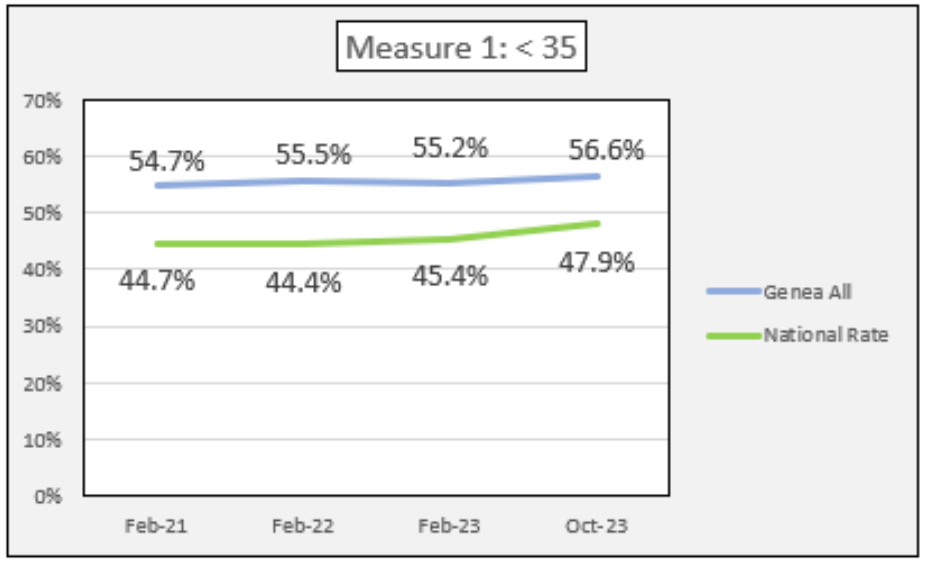
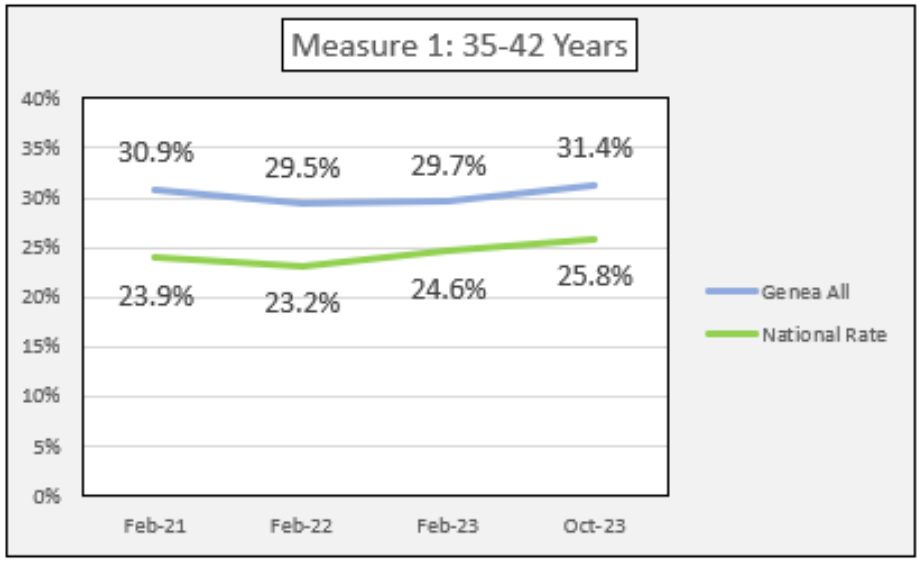
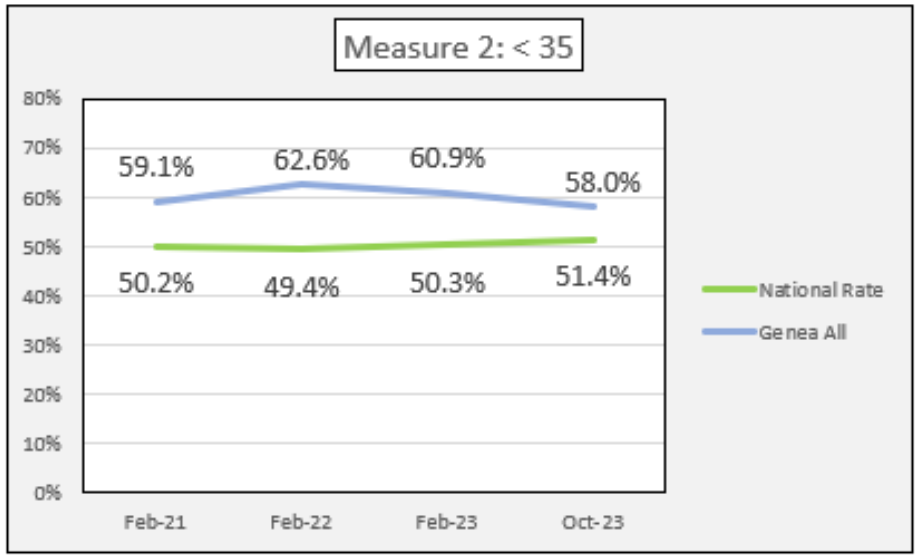
Measure 1/2: Genea vs National Average Trends

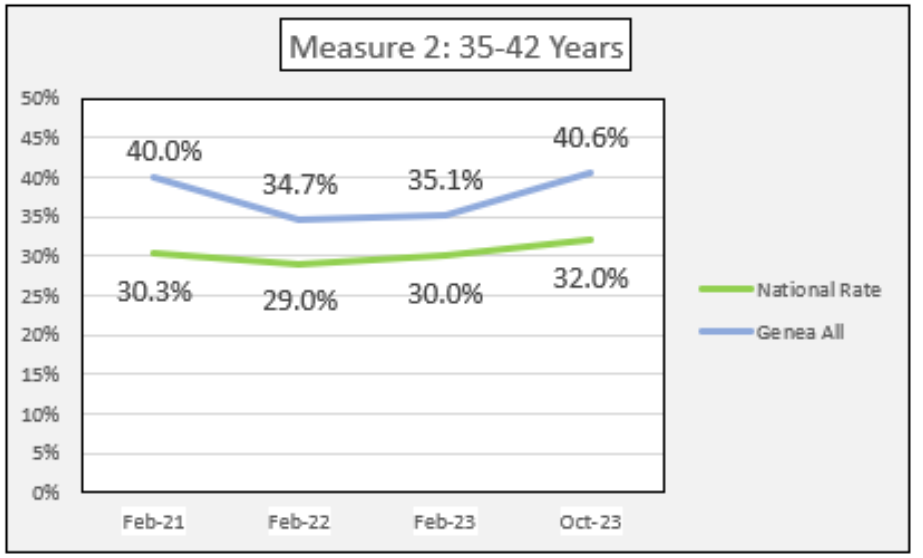
Births per completed egg retrieval (all)





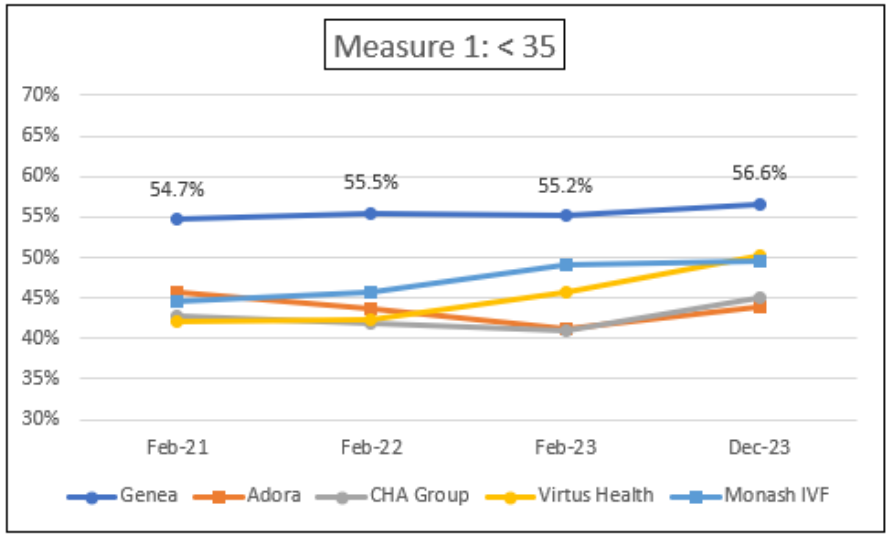
Births per completed egg retrieval (First cycle)

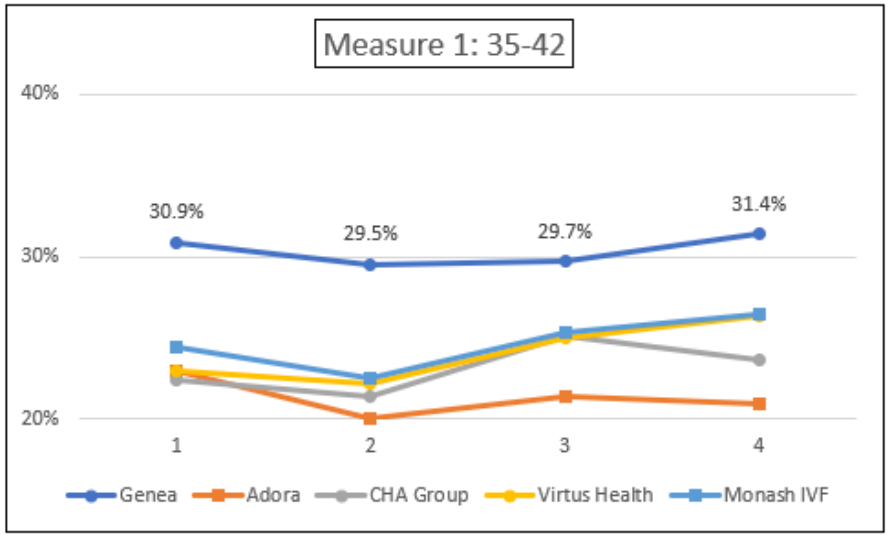




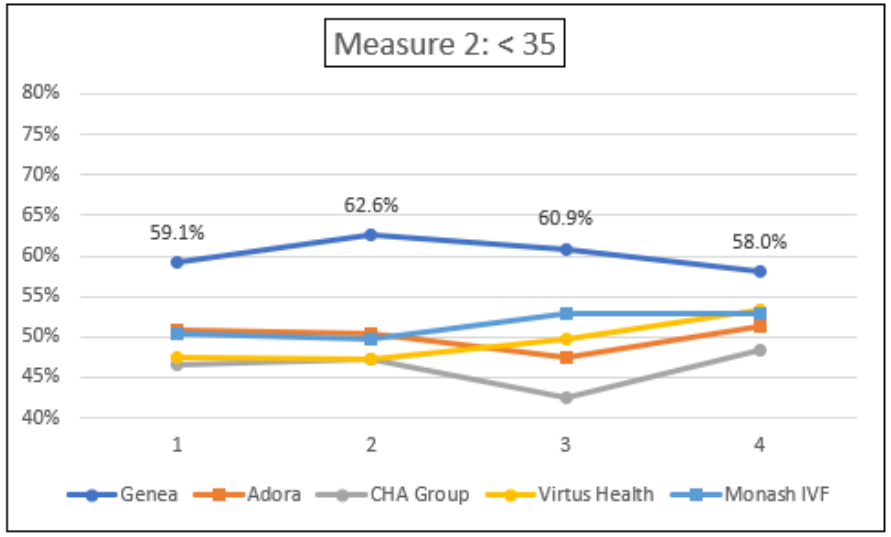
Measure 1/2: Genea IVF vs other main IVF Clinics

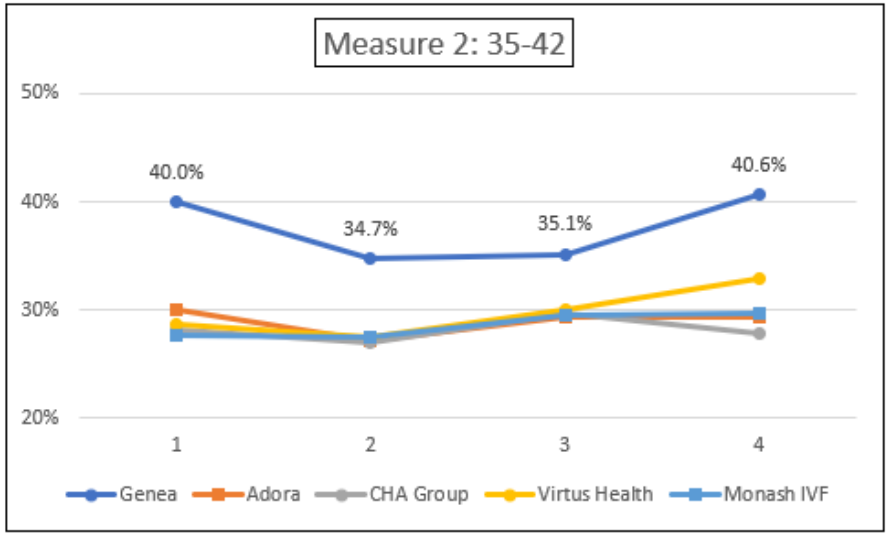
Births per completed egg retrieval (all)



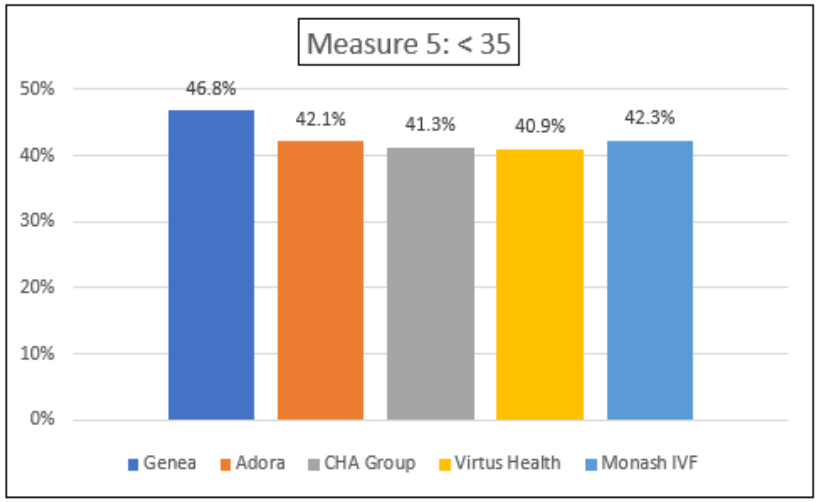


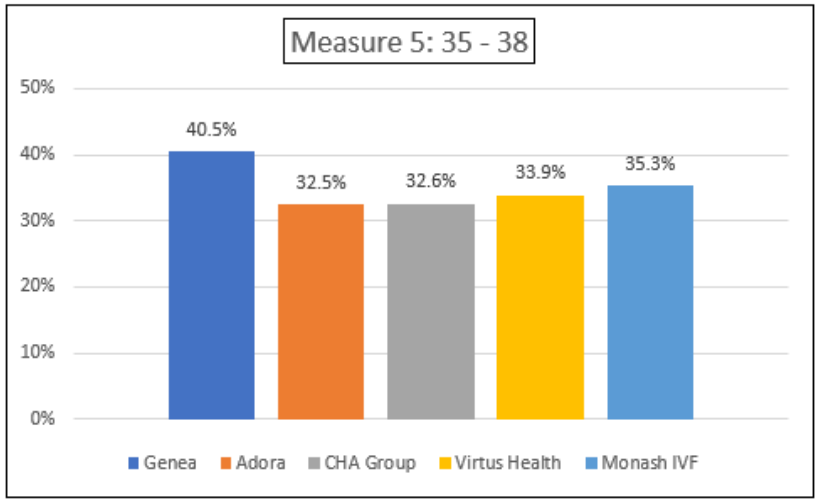
Births per completed egg retrieval (First cycle)

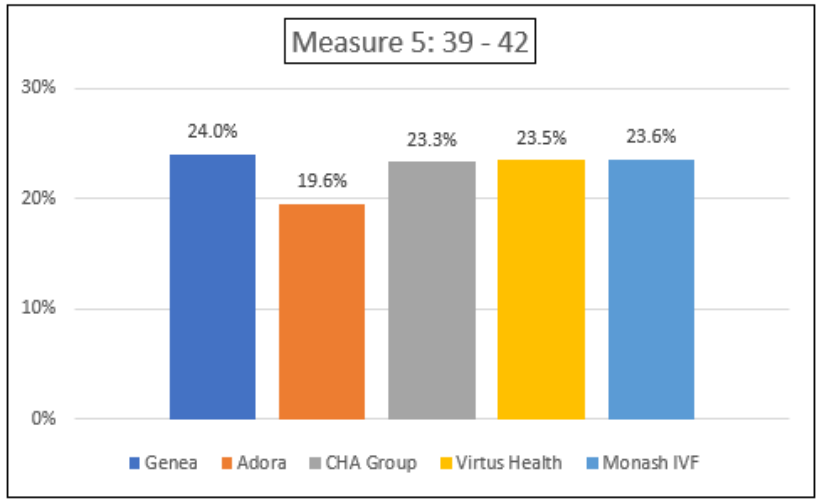




Measure 5: Genea IVF vs other clinics







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Thoughts?

Case: Female 36 years old and Male 40 years old have been trying for a child unsuccessfully for 8 months.

- What sort of medical history would you take?
- What types of testing would you perform?
- What type of information would you give?
- Would you tell them to keep trying or would you refer them on?

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Thank you