

GP Fertility Spring Series

To Freeze or Not to Freeze. A new medical dilemma

Speaker: Dr Michelle Wellman

Date: Thursday, May 9th, 2024.

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Dr Michelle Wellman

MBBS, DipRANZCOG, FRANZCOG

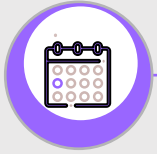


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AWARE
WOMEN'S
HEALTH

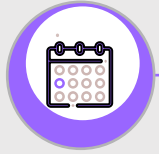
257 Melbourne Street
NORTH ADELAIDE



Egg Freezing

- Vitrification
- From 2012 no longer considered experimental





Egg Freezing

AUSTRALIA

133 percent increase in women freezing their oocytes in Australia and New Zealand between 2016 and 2020

EGG FREEZING CYCLES

ANZARD 2021

Table 12: Number of autologous fresh fertility preservation cycles for female patients by age and treatment type, Australia and New Zealand, 2021

Reason for fertility preservation	< 35	35–39	≥ 40	All
Medical reason – cancer diagnosis	412	163	42	617
Medical reason – other	1,198	1,527	395	3,120
Non-medical reason	770	1,172	202	2,144
Total	2,380	2,862	639	5,881



VARTA

ANNUAL REPORT 2022

Egg freezing

1,513 women froze their eggs during 2021-22, up 63% from the year before. There were 6,489 women with eggs in storage on June 30, 2022 – up 30% from the year before.



CELEBRITY MOMS
Celebrities Who've Opened Up About

Entertainment > TV

By **SO EGG-TRA** Kourtney Kardashian said family 'BULLIED' her into freezing her eggs before 'trying to have a baby' with Travis Barker

Caitlyn Hitt

Published: 23:58 ET, Mar 16 2022 | Updated: 0:58 ET, Mar 17 2022

ed To
ture

"I need to be aggressive about protecting my fertility, about protecting myself." - by Diandra Malivindi

Recent Adelaide Study

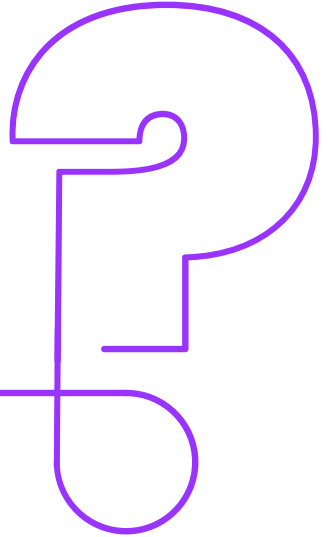
Br J Health Psychol. 2023;28:639–650

61.3% of Australian women in sample of 514 aged 18-44 years would consider non-medical egg freezing

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COMMON QUESTIONS



01

Should I freeze my eggs?

02

At what age should I freeze my eggs?

03

How many eggs will I get from a cycle?

04

How many cycles will I need to do?

05

How many eggs do I need to freeze?

06

What does the egg-freezing process involve?

I have been able to sign up to the poll

Yes

No

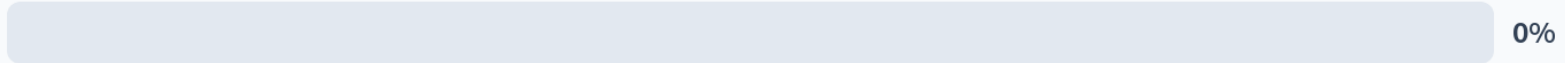
I have been able to sign up to the poll

Yes



100%

No



0%

I have been able to sign up to the poll

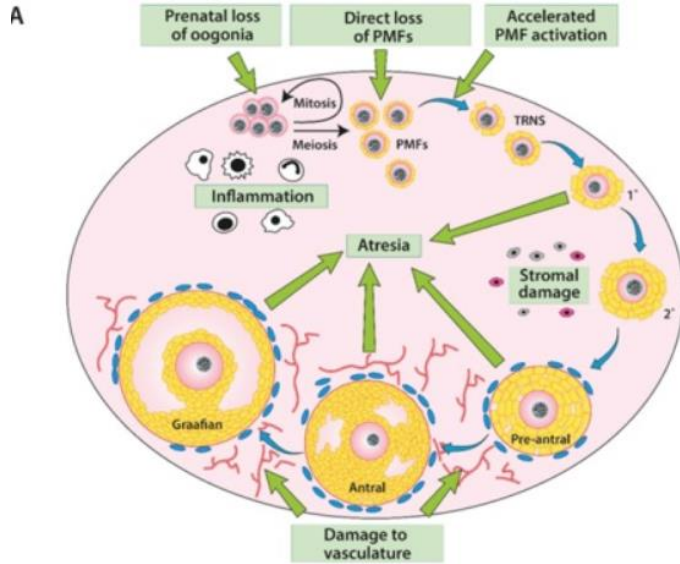
Yes

100%

No

0%

CANCER DIAGNOSIS



- Women with cancer diagnosis 38% less likely to have a pregnancy than general population
- Breast cancers, lymphomas
- Women prior to chemotherapy – cyclophosphamide, cisplatin, doxorubicin
- Radiotherapy

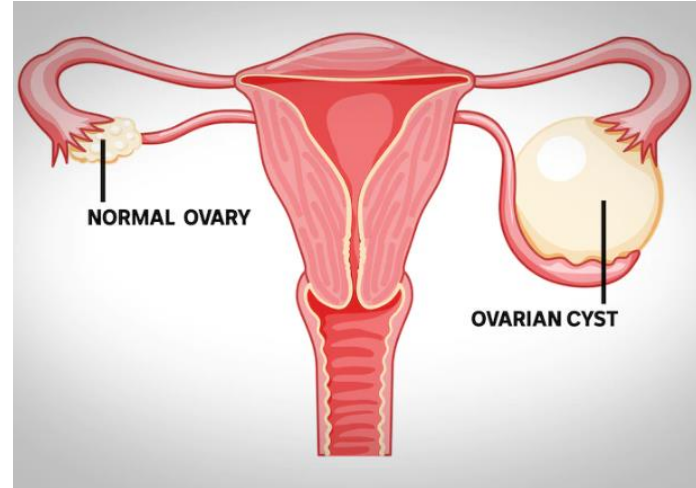
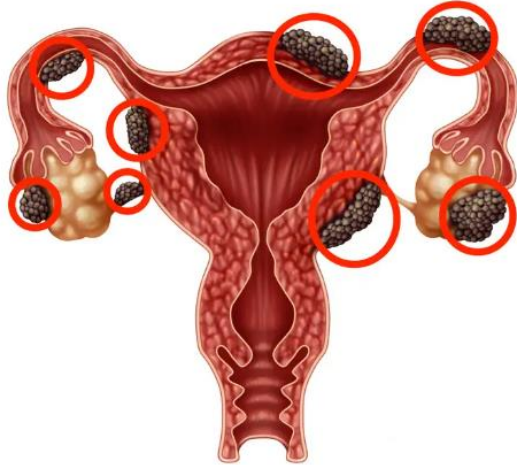
[Hum Reprod Update](#). 2019 Nov; 25(6): 673–693.

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MEDICAL 'OTHER'

Actual or potential risk to ovarian reserve



MEDICAL 'OTHER'

Diminished ovarian reserve e.g

- Genetic – fragile X
- Autoimmune – Addison's disease
- Family history
- Idiopathic

Prior to gender affirmation treatment



**SOCIAL
ELECTIVE
NON MEDICAL**

**AGE RELATED
FERTILITY DECLINE**

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MEET CAROLINE



35 years old

Just broke up
with BF of 7 years

Wants children some
time in the future

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What would you advise Caroline to do?

A Freeze eggs now

B Advise review in 12 months

C Request 'egg timer test'

D Advise donor sperm

E Refer to a fertility specialist

F None of the above

What would you advise Caroline to do?

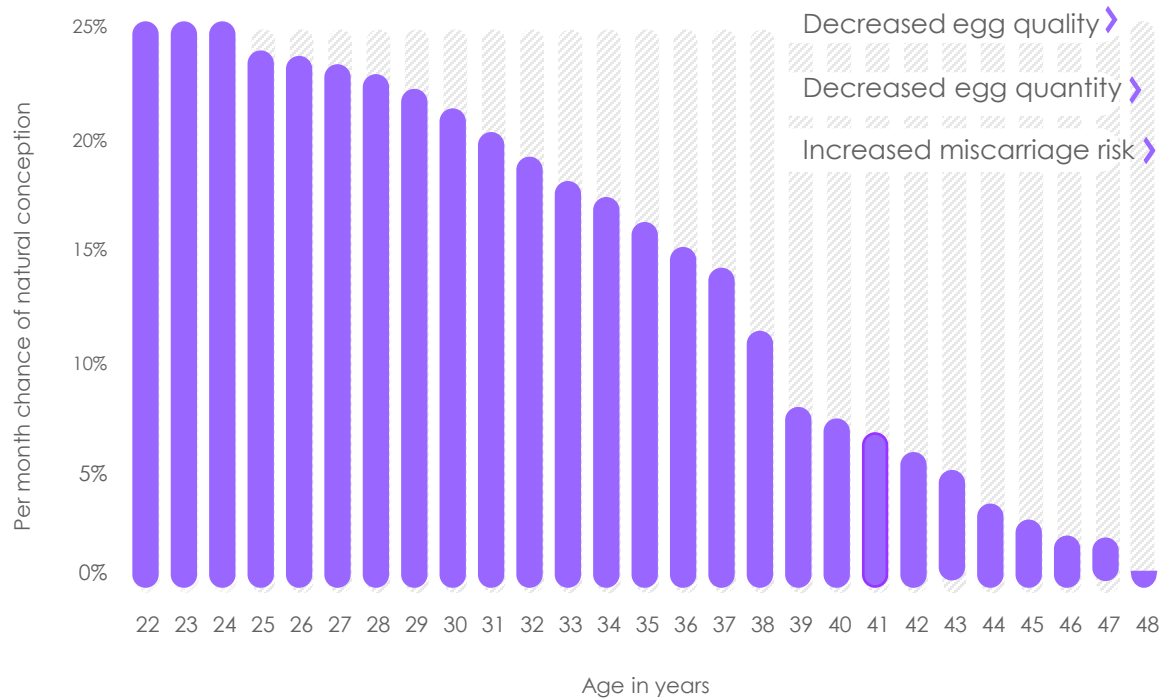
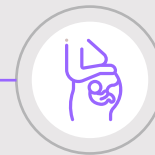


What would you advise Caroline to do?

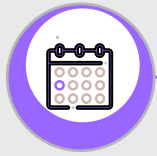


AGE IS **QUEEN**

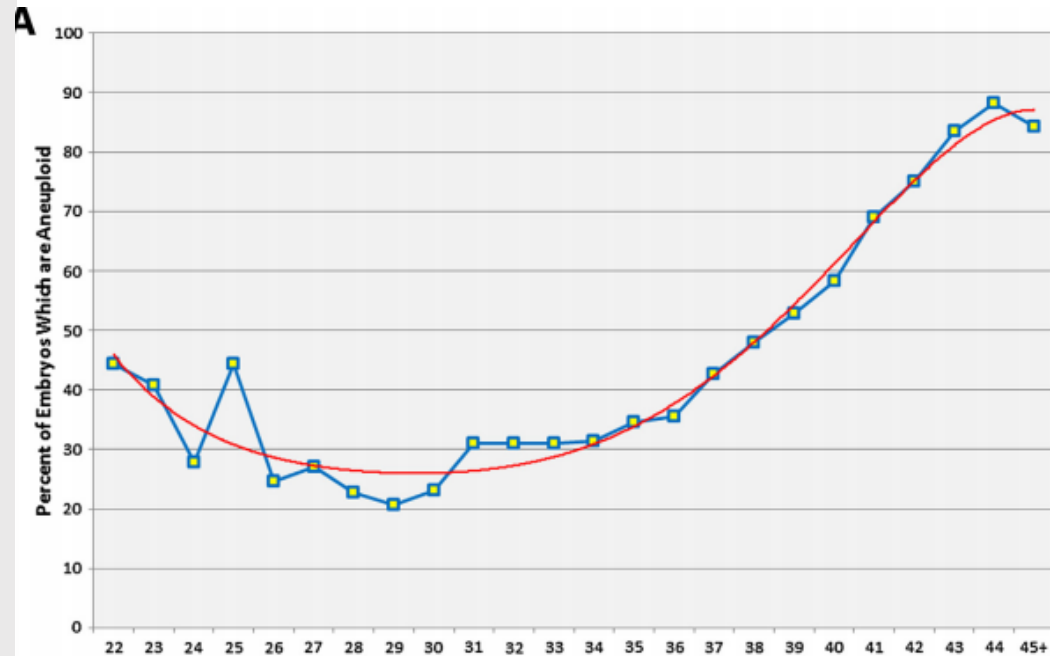


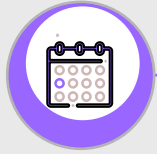


AGE AND FERTILITY

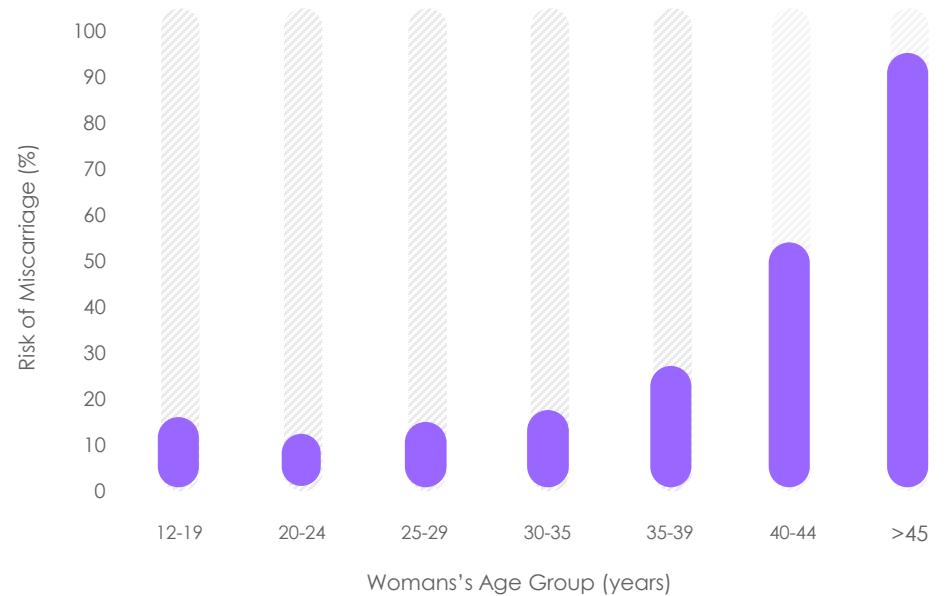


ANEUPLOIDY AND AGE





RISK OF MISCARRIAGE BY AGE



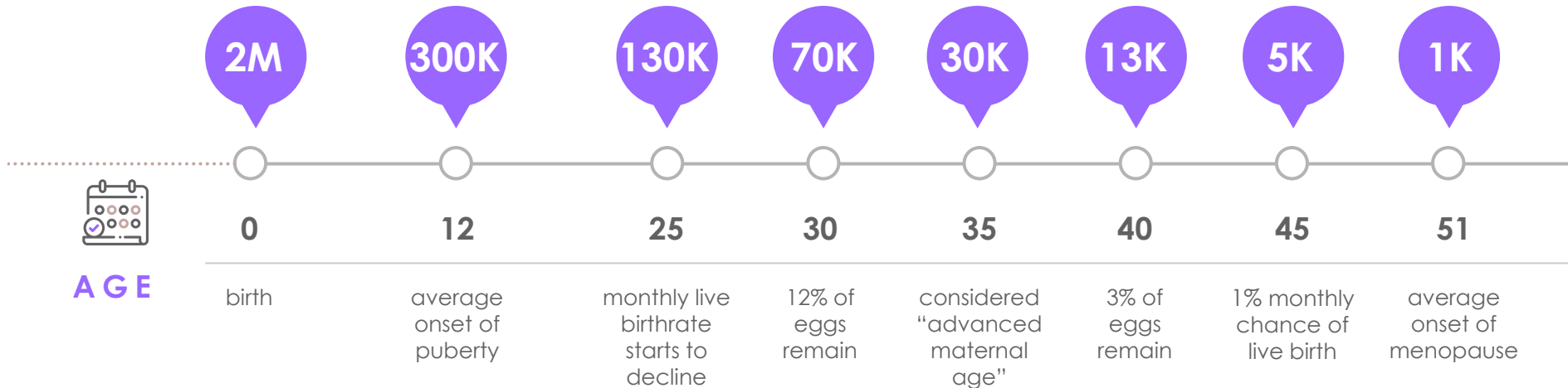


THE
'EGG TIMER'
TEST

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DECLINE IN EGG NUMBERS WITH AGE



ANTRAL
FOLLICLES



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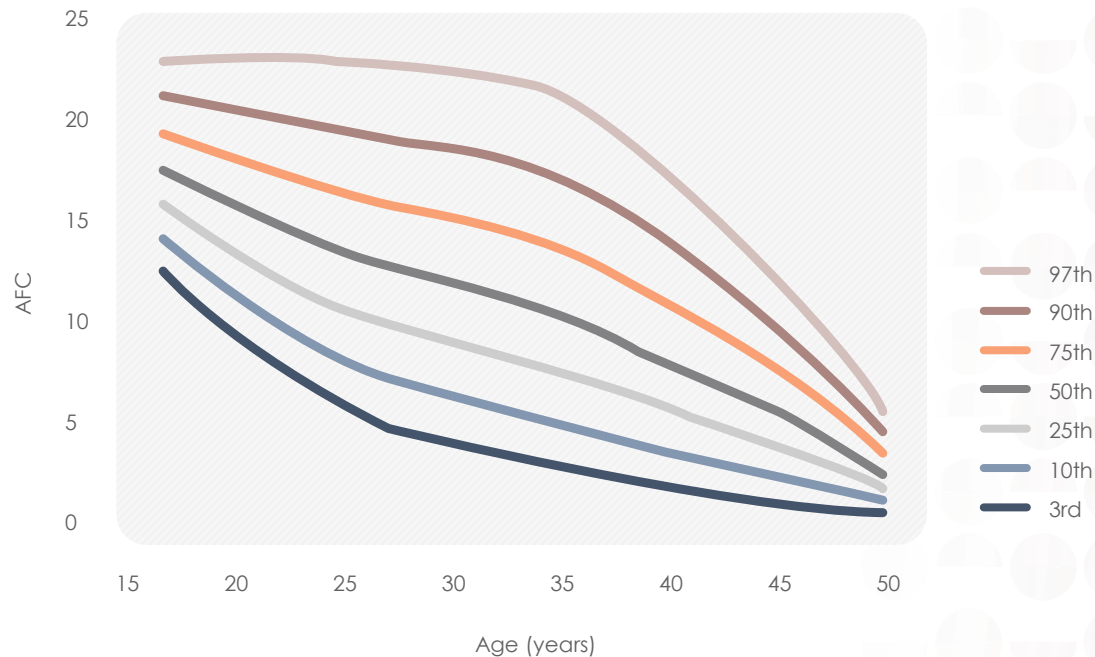


ANTRAL FOLLICLE COUNT



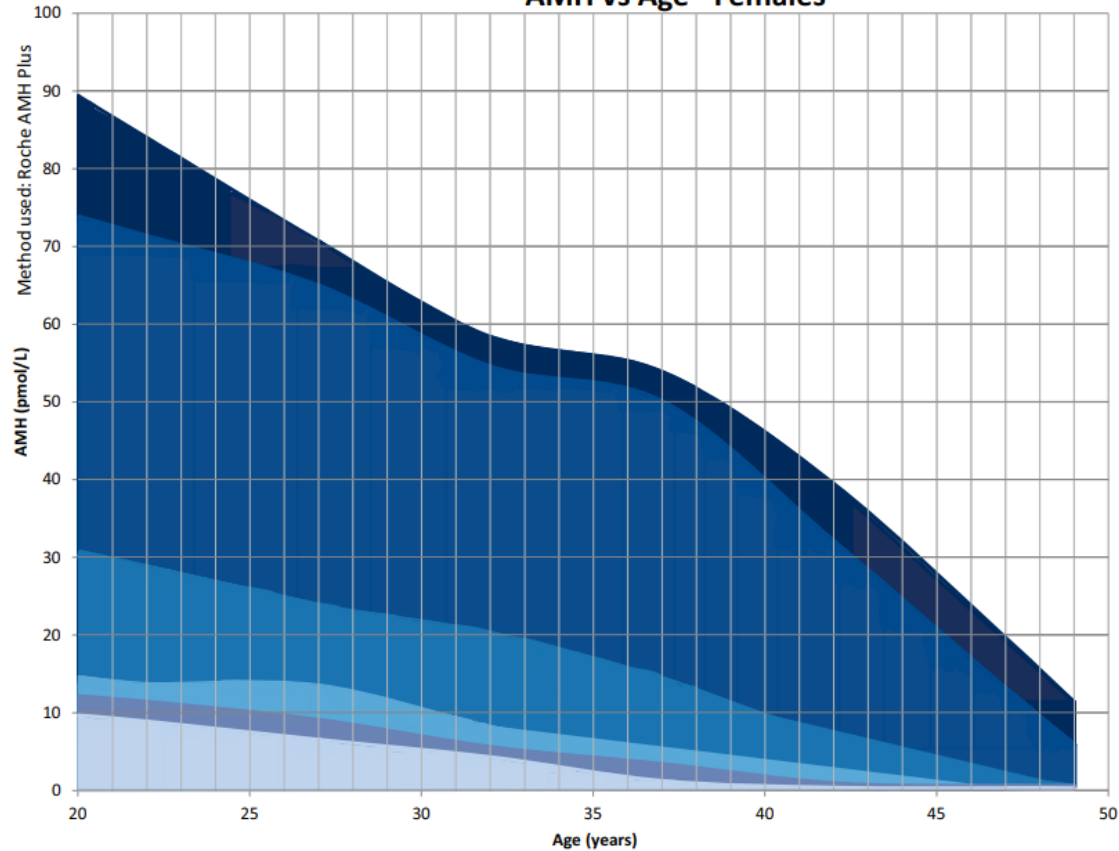
Ultrasound conducted
between cycle days 5-9

Follicles between 2 and 9mm



AMH RANGE

AMH vs Age - Females

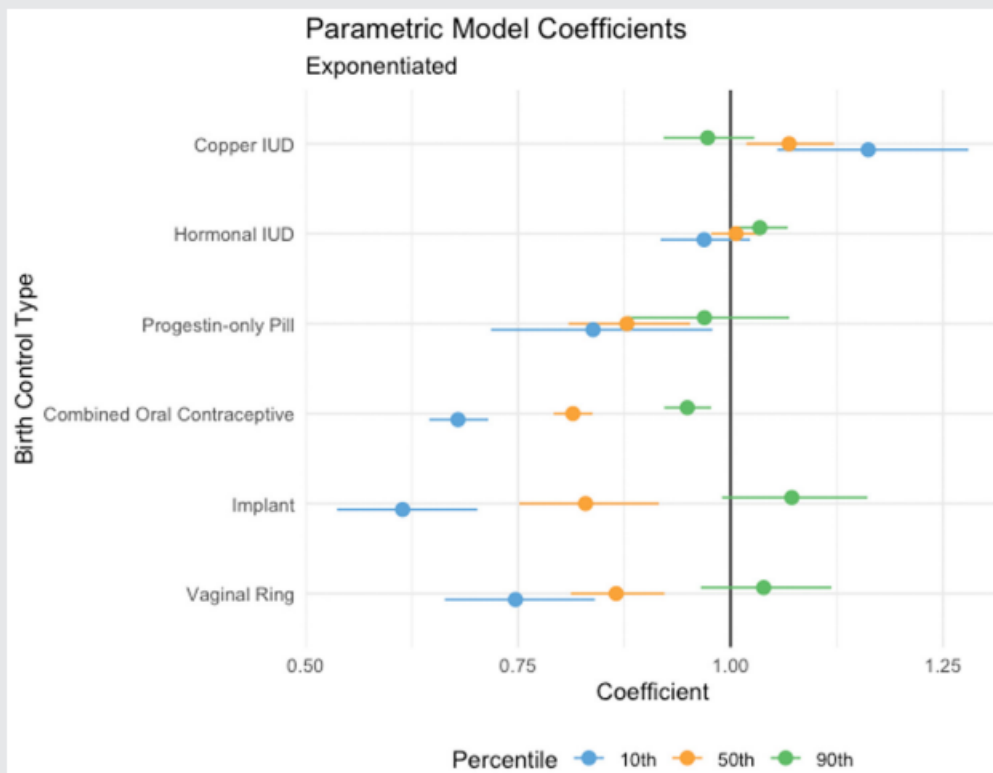


Conversion factor is as follows:
Roche AMH Plus Assay =
0.8 Beckman Access AMH Assay

Roche	Beckman
0.8	1
4	5
8	10
12	15
16	20
20	25
24	30
28	35
32	40
36	45
40	50
44	55
48	60
52	65
56	70
60	75
64	80
68	85
72	90

- 97.5 Percentile
- 95.0 Percentile
- 50.0 Percentile
- 10.0 Percentile
- 5.0 Percentile
- 2.5 percentile

FIGURE 2



Suppressive effects of contraceptives across antimüllerian hormone (AMH) percentiles. The exponentiated parametric model coefficients were shown for the 10th (blue), 50th (orange), and 90th (green) AMH percentiles. The results could be interpreted as the percentage change in the AMH values with no birth control as the reference group. For hormonal contraceptive methods, effects were largest at the 10th percentile. The circles indicate the point estimates; the horizontal lines indicate the 95% confidence intervals. IUD = intrauterine device.

Nelson. Contraceptive-specific AMH values. *Fertil Steril* 2023.

DOES AMH PREDICT CURRENT FERTILITY?

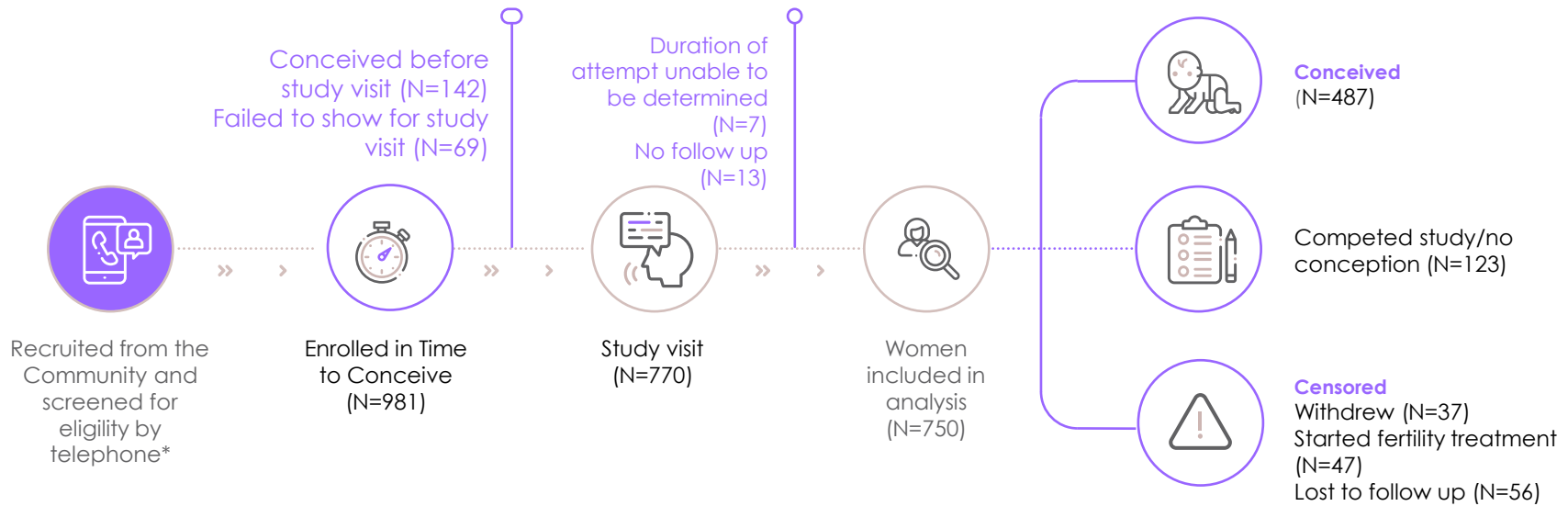
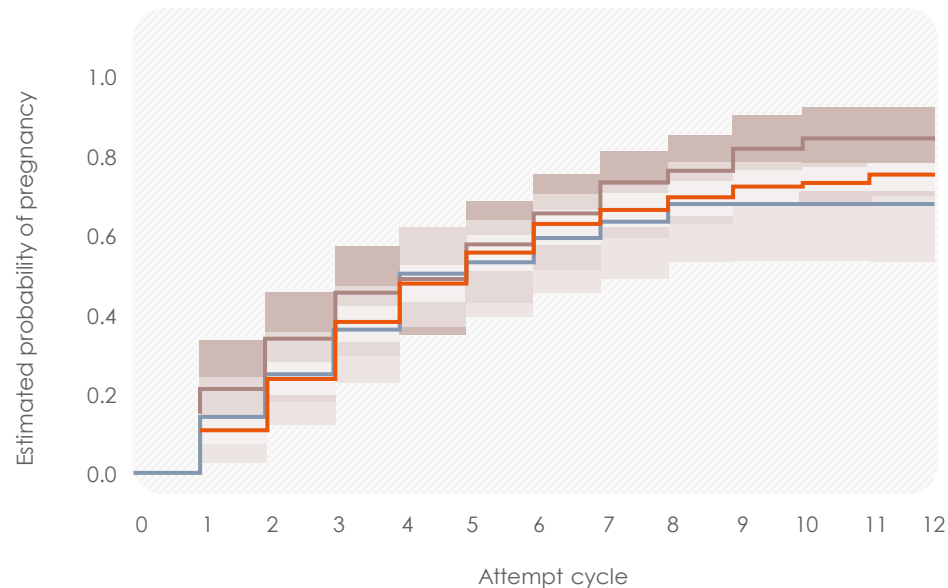


Figure 1 Study chart of participants in the cohort | *Number screened and reasons and numbers for exclusions are not available
JAMA 2017 Oct 10;318(14):1367-1376



CUMULATIVE PROBABILITY OF CONCEPTION STRATIFIED BY AMH LEVELS



AMH Categories — < 0.7 ng/ml — 0.7 - 8.4 ng/ml — >= 8.5 ng/ml

Figure 2
Adjusted Kaplan Meier Curves for time to pregnancy with 95% confidence intervals by AMH. Model adjusted for age, body mass index, race, current smoking status, history of prior pregnancy, and hormonal contraceptive use in the preceding year. The number of woman at risk during each cycle of attempt are provided in supplemental table 1. The median (interquartile range) number of cycles each woman contributed was 4 cycles (2-6).

DOES AMH PREDICT
TIME TO MENOPAUSE?

GRAPHICAL ABSTRACT



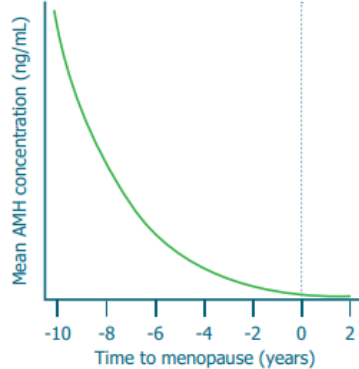
1. **Systematic review**
undertaken



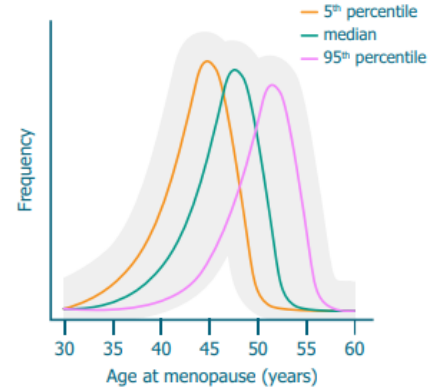
2. Publications screened
n=3207



3. Publications in the
analysis **n=41**



AMH becomes **undetectable** around
the time of menopause/POI



Lower age-specific AMH concentrations
(represented by different curves) are
associated with an **earlier age**
at **menopause** but high variation
limits clinical utility

Prediction of age at menopause remains imprecise when not imminent, but very low AMH in young women can indicate increased risk of developing POI. AMH, anti-Müllerian hormone; POI, premature ovarian insufficiency.

NUMBER OF MATURE EGGS per cycle **RELATIVE TO AMH**

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	AMH UNK	AMH 0-5	AMH 5-15	AMH 15-25	AMH 25-40	AMH 40+	TOTAL
Avg MII's	7.78	3.89	5.95	8.41	9.12	9.83	7.51
# Patients	76	9	22	22	8	6	143
Avg Age	36.86	38.16	38.35	37.38	34.32	36.66	36.99



ICSI

Avg MII's	6.6	4.14	5.97	7.06	9.21	9.75	6.59
# Patients	449	43	60	33	28	16	629
Avg Age	36.96	37.34	37.1	34.31	35.81	31.73	36.57

ANTI-MÜLLERIAN HORMONE (AMH)



Does NOT reflect quality of eggs.



May be used to assist in diagnosis of PCOS when diagnosis is unclear



Can still conceive successfully with very low levels.



Not predictive of fertility window or age of menopause in an individual

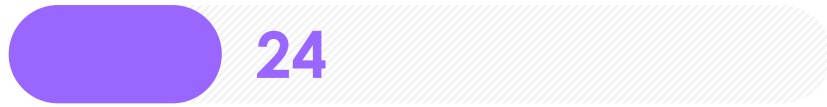


Gives an indication of expected yield in ovarian stimulation.

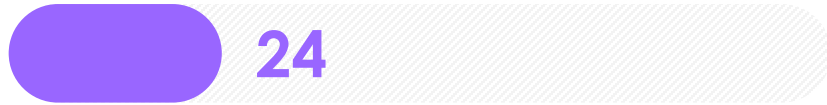


Test can be performed at any stage of the menstrual cycle.

DECISION MAKING HIGH RESERVE



Antral Follicle Count



Anti Müllerian Hormone



Necessary?

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HORIZON

What would you advise Caroline to do now? (high AMH)

A Advise freeze eggs now

B Advise to wait she has plenty of time

C Advise review in 12 months

D Advise donor sperm

E None of the above

What would you advise Caroline to do now? (high AMH)

A Advise freeze eggs now

0%

B Advise to wait she has plenty of time

100%

C Advise review in 12 months

0%

D Advise donor sperm

0%

E None of the above

0%

What would you advise Caroline to do now? (high AMH)

A Advise freeze eggs now

0%

B Advise to wait she has plenty of time

100%

C Advise review in 12 months

0%

D Advise donor sperm

0%

E None of the above

0%

DECISION MAKING

LOW RESERVE

04

Antral Follicle Count

02

Anti Müllerian Hormone



Necessary?

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HORIZON

What would you advise Caroline to do now? (low AMH)

A Advise to freeze eggs

B Advise to wait

C Advise review in 12 months

D Advise donor sperm

None of the above

What would you advise Caroline to do now? (low AMH)

A Advise to freeze eggs

0%

B Advise to wait

0%

C Advise review in 12 months

100%

D Advise donor sperm

0%

None of the above

0%

What would you advise Caroline to do now? (low AMH)

A Advise to freeze eggs

0%

B Advise to wait

0%

C Advise review in 12 months

100%

D Advise donor sperm

0%

None of the above

0%

DECISION MAKING

LOW RESERVE

04

Antral Follicle Count

02

Anti Müllerian Hormone



???
Freezing her
infertility?

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QUALITY



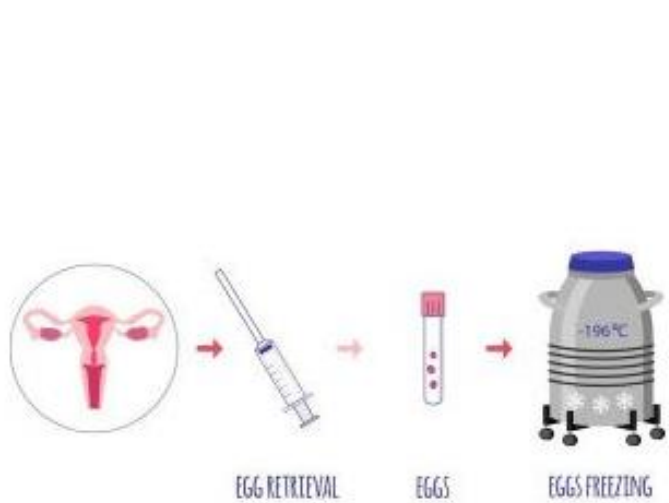
QUANTITY



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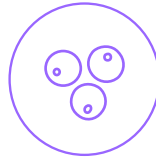
THE PROCESS



Pre-treatment investigations



Egg stimulation



Egg collection



Vitrification and storage

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TESTS THAT GPS CAN DO
BEFORE REFERRING TO A

FERTILITY SPECIALIST

Pathology tests

- Anti-Müllerian Hormone (AMH)
- Hepatitis B
- Hepatitis C
- HIV



Ultrasound

**Pelvic ultrasound to assess the
Antral Follicle Count (AFC):**

- Cycle days 5-9
- Ideally at specialised Ultrasound Centre



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STEPS

Egg
collection

02

03

Egg
vitrification
& storage

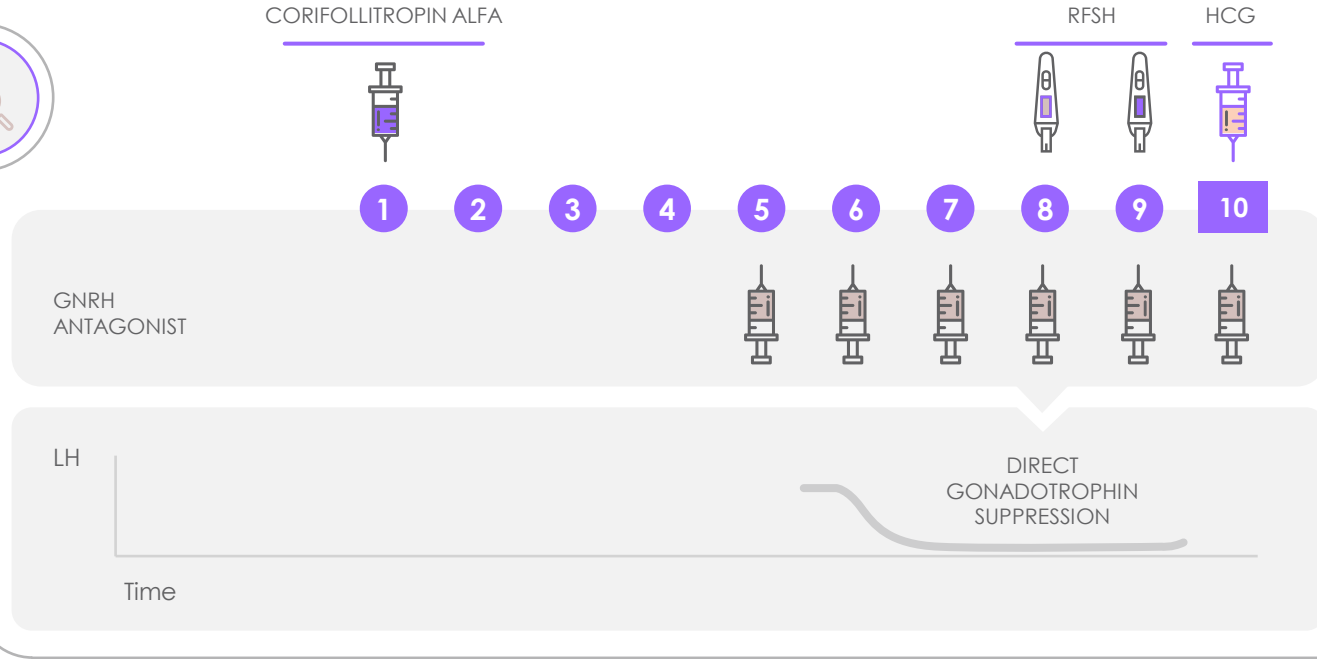
01

Stimulate
the ovaries

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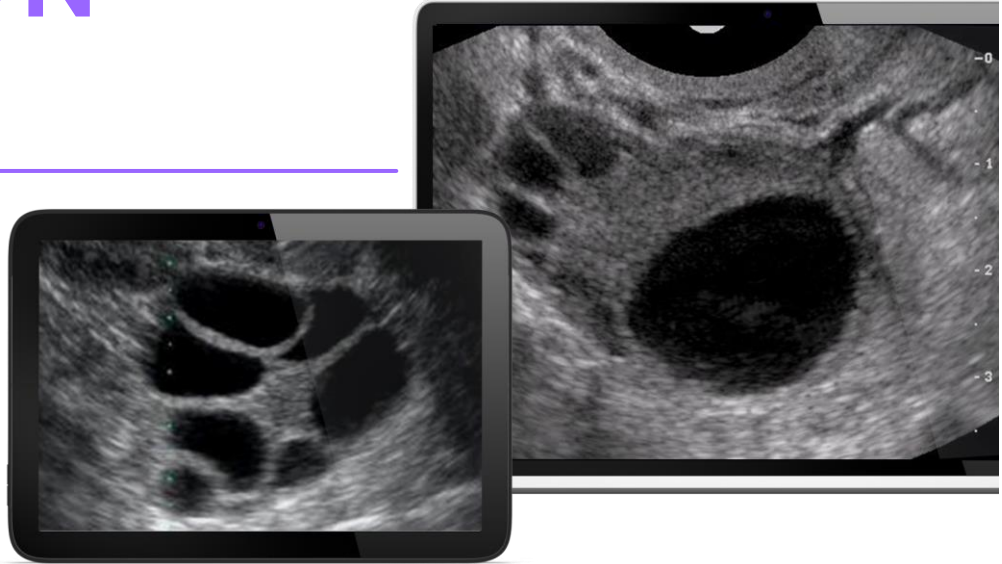
OVARIAN STIMULATION



OVARIAN STIMULATION

Ovary with natural
cycle or ovulation
induction treatment.

Stimulated
ovary with IVF.



STEPS



Egg
collection

02

03

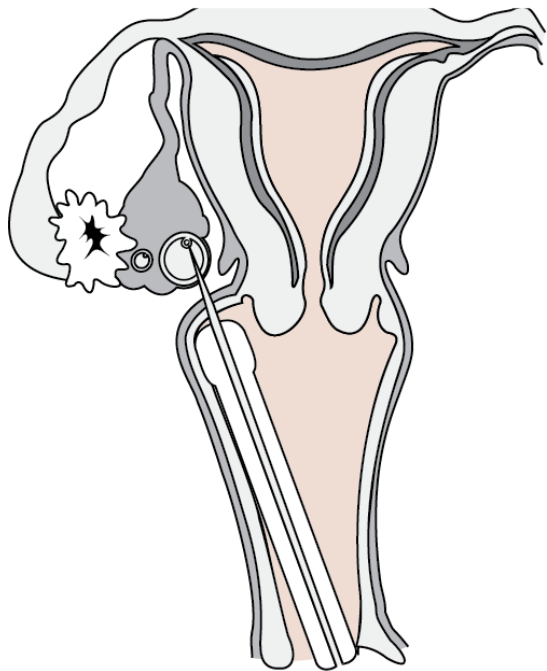
Egg
vitrification
& storage

01

Stimulate
the ovaries

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EGG COLLECTION



Takes place in Day Surgery.



Under ultrasound guidance,
follicles aspirated.



Takes around 20-30 minutes.

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STEPS

Egg
collection

02

03

Egg
vitrification
& storage

01

Stimulate
the ovaries

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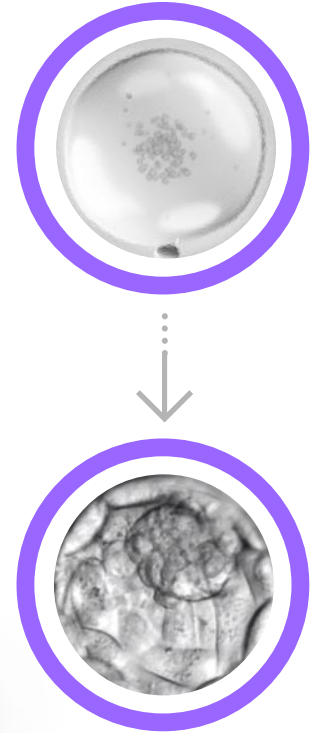
VITRIFICATION

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EGGS AND EMBRYOS



EMBRYO CULTURE AND DEVELOPMENT

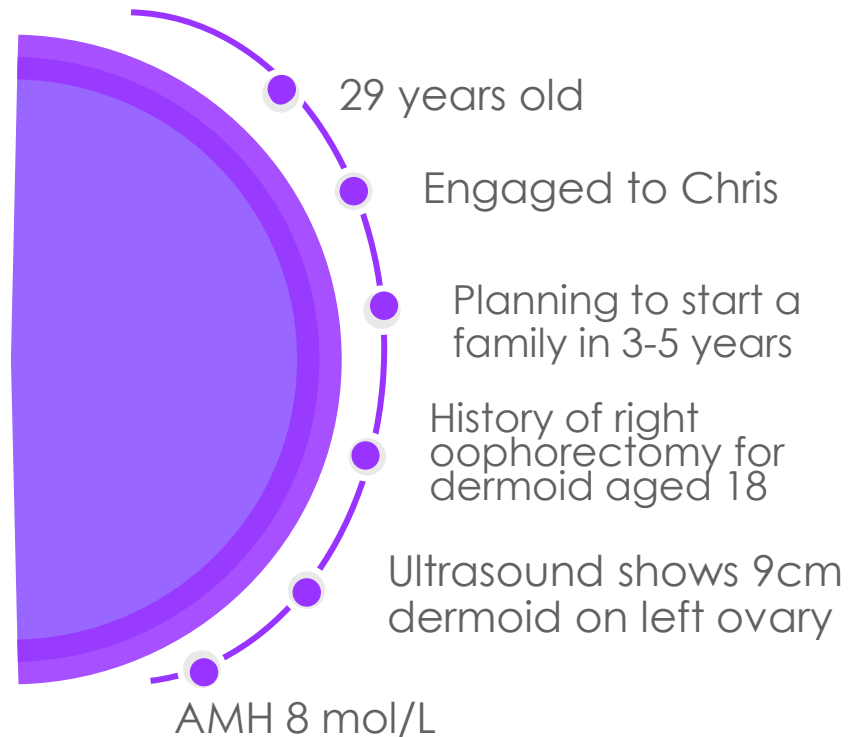


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MEET ALISON



What would you advise Alison?

A Start trying to conceive now

B Have dermoid cyst removed

C Freeze embryos and then have dermoid removed

D Freeze eggs and then have dermoid removed

E None of the above

What would you advise Alison?

A Start trying to conceive now

0%

B Have dermoid cyst removed

0%

C Freeze embryos and then have dermoid removed

0%

D Freeze eggs and then have dermoid removed

0%

E None of the above

0%

What would you advise Alison?

A Start trying to conceive now

0%

B Have dermoid cyst removed

0%

C Freeze embryos and then have dermoid removed

0%

D Freeze eggs and then have dermoid removed

0%

E None of the above

0%

SUCCESS OF **EMBRYOS**



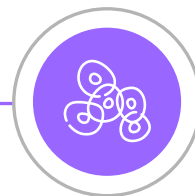
10

Eggs



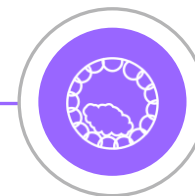
08

Fertilise



06

Cleavage-stage
(Day 3) embryos



2 – 3

Blastocyst
(Day 5 embryos)



SUCCESS OF

EGG FREEZING



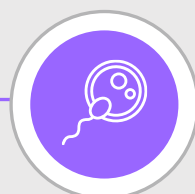
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Eggs



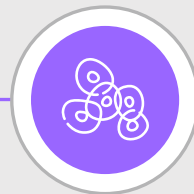
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Survive
thaw



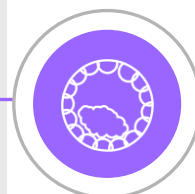
06

Fertilise



04

Cleavage-stage
embryos



1 - 2

Blastocyst

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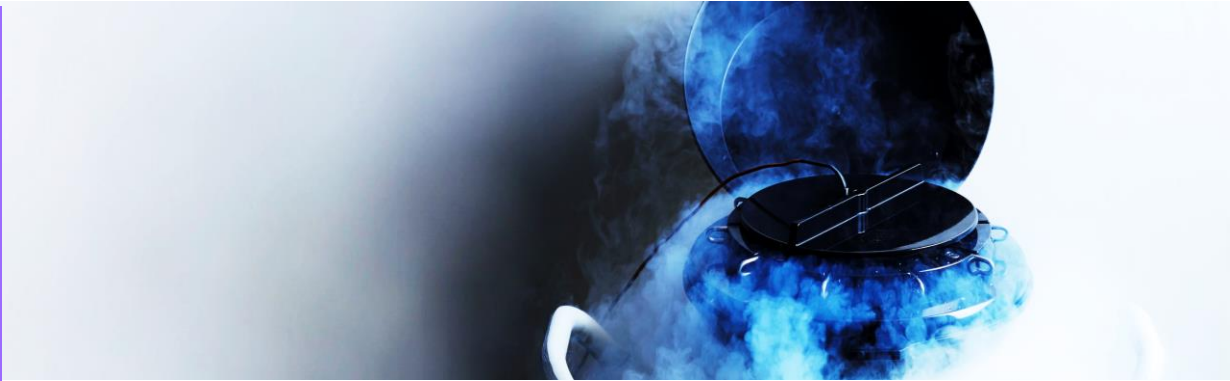
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SUCCESS RATES FOR EGG FREEZING



Probability of
achieving a live birth
– two key factors:

- Woman's age at egg collection
- Total number of eggs available



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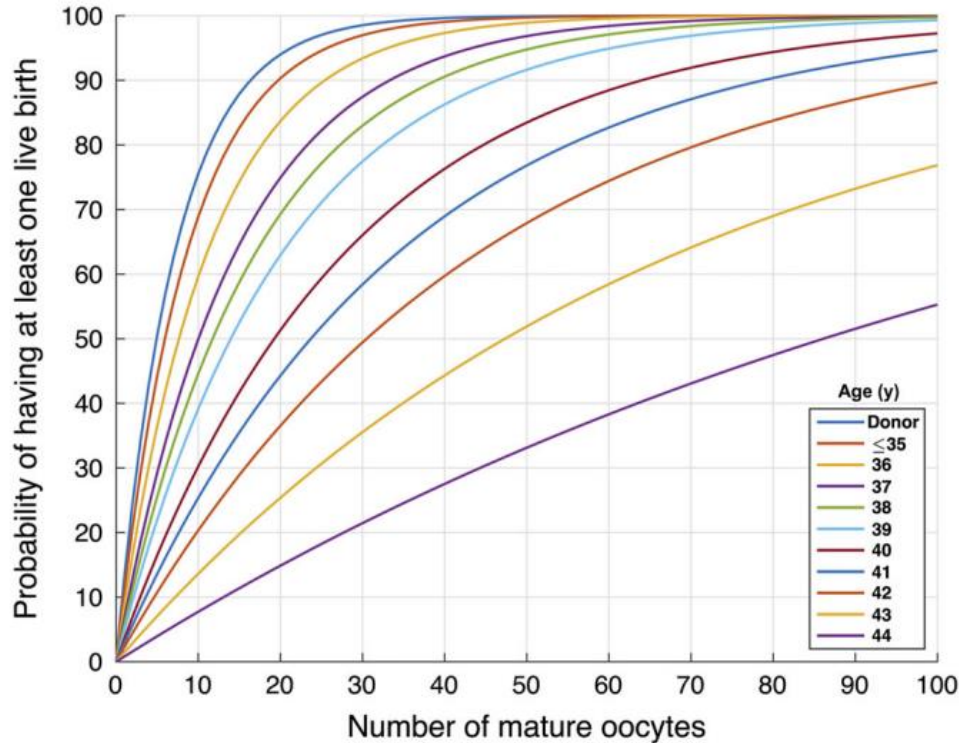
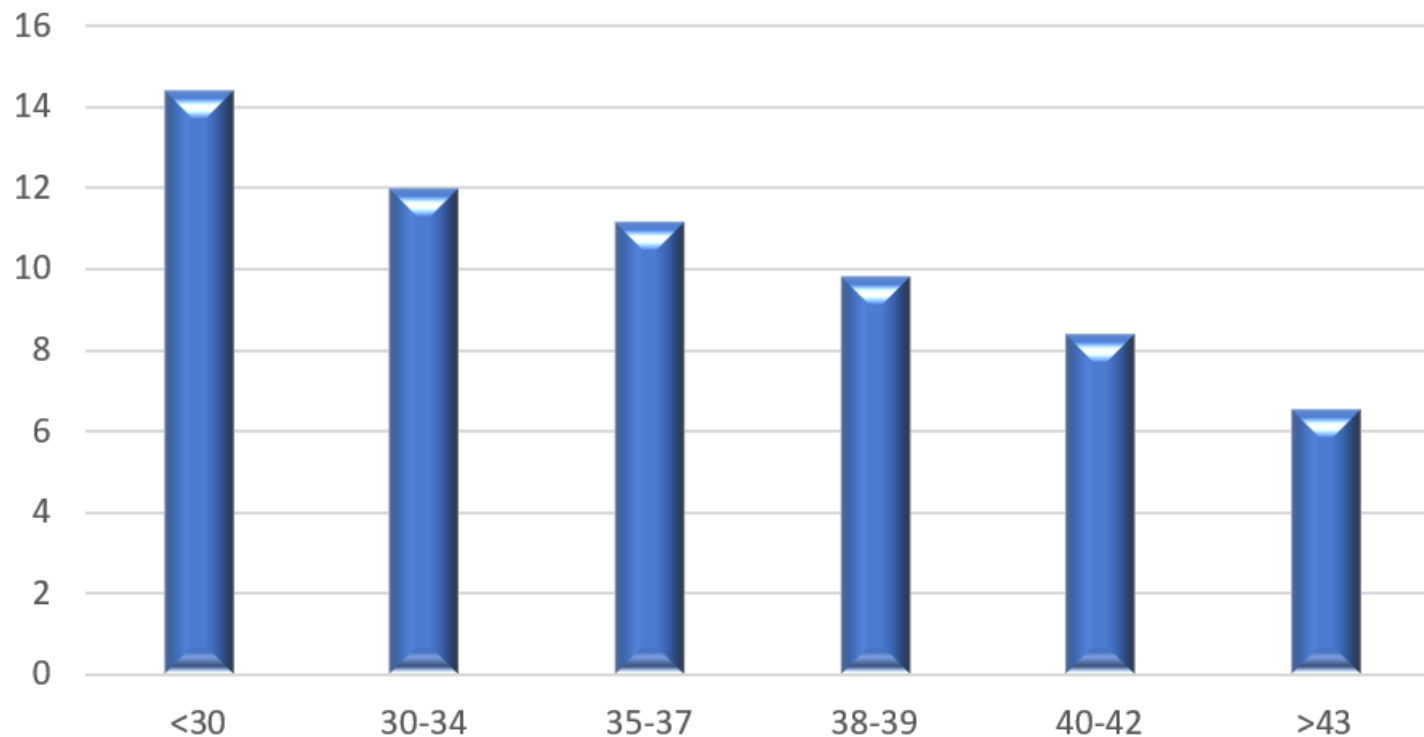


Figure 1 Live birth predictions by age and number of mature oocytes retrieved. Each curve shows the percent likelihood that a patient of a given age will have at least one live birth according to Equation 2, based on the number of mature oocytes retrieved and frozen.

Human Reproduction, Vol.32, No.4 pp. 853–859, 2017

This is based on ICSI cycles - Assumes 95% survival <36 years and 85% survival >36 years

Average Oocytes Collected by Age





DIMINISHING RETURNS BEYOND 3 CYCLES

HOW
LIKELY ARE
WOMEN
TO USE
THEIR
EGGS?

What do reproductive-age women who undergo oocyte cryopreservation think about the process as a means to preserve fertility? Hodes-Wertz B, et al. Fertil Steril 2013

INTENTION

Very likely

60%

Somewhat likely

34%

REALITY

10-20%

Unlikely

6%

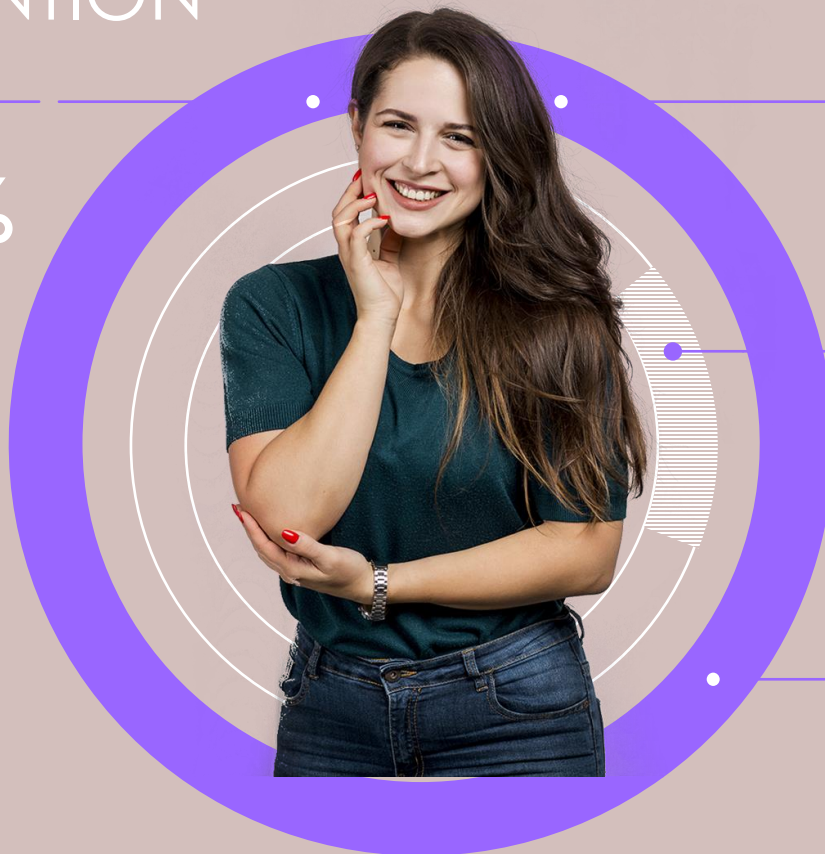


Table 3. Summary of the outcomes post oocyte thaw and comparison with the published literature.

Outcomes	Current Study	Worldwide Data	Collated Data
Mean age at freezing	37.1 years	37.3 years	37.2 years
Usage rate	16%	1006/8208 (12%)	1031/8375 (12%)
Thaw/survival rate per oocyte frozen	74%	6462/7904 (82%)	6508/8230 (79%)
Fertilisation rate per injected oocyte	67%	832/1239 (67%)	977/1439 (68%)
Live birth rate per ET	35%	196/558 (35%)	203/580 (35%)
Less than 38 years	38%	24/50 (48%)	29/65 (45%)
38 years of age and above	29%	20/94 (21%)	22/101 (22%)

J. Clin. Med. 2023, 12, 4182 (Guys Hospital)

Genea Horizon

- Since inception 1780 patients attended for oocyte freezing
- To date only 67 (3.8%) returned to use eggs
- Live birth data on 38 patients

Horizon ET snapshot 2020-2022	
Patients with an egg warm	38
Patients with an ET from egg warm	33
Bhcg	14 (36.8%)
FHP	10 (26.3%)
LB	10 (26.3%)

Often choosing to thaw only 8-10 eggs in cohort

Patients in older age group with eggs 15 >38, 6 patients aged 40-42

?

INSURANCE POLICY



“

Freezing my eggs was an empowering experience.



“

I'm someone who likes to consider all my options.



“

For me, freezing my eggs was an insurance against regret.



“

It's about investing in myself and giving me options down the track.



WHAT
WE HEAR
**FROM
PATIENTS**

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ANY POTENTIAL RISKS?

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No evidence of an increase in congenital anomaly rate.



Metanalysis including 4159 babies to maximum of 6 years appears safe but no longer term data.

Reprod Sci 2022 Nov;29(11):3222-3234

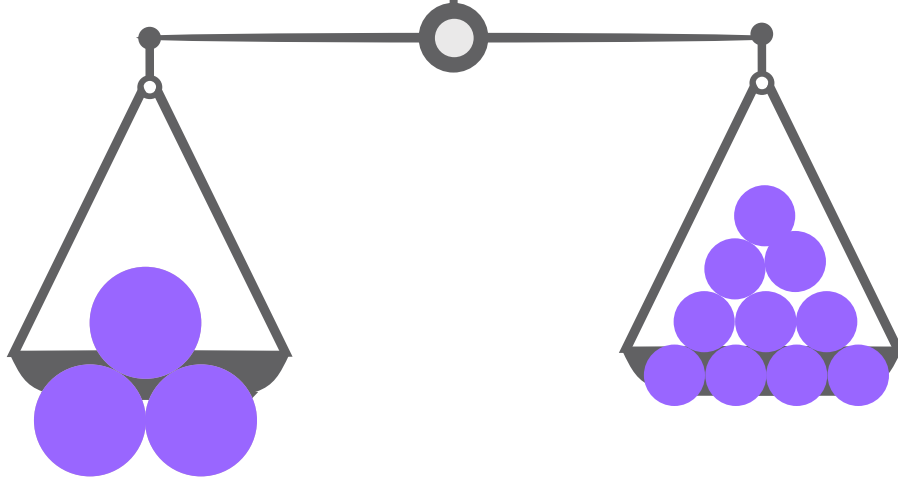


Small risk associated with stimulation (OHSS) and egg collection (bleeding, infection, torsion).

TIMING

TOO EARLY

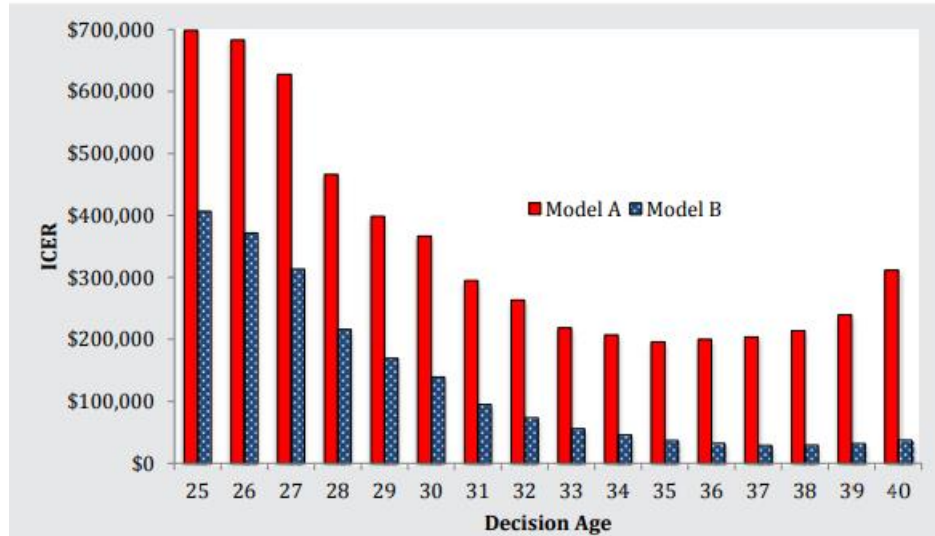
- ➔ Risk associated with stimulation and OPU
- ➔ Risk never using cryostored oocytes



TOO LATE

- ← Risk of lower success
- ← Risk higher aneuploidy rates
- ← Risk fewer number of oocytes

FIGURE 3



Cost per additional live birth at horizon age when electing to cryopreserve oocytes versus no action at decision age, which is presented on the x axis. Model A represents women requiring marriage before attempting pregnancy. Model B represents women who do not require marriage before attempting pregnancy (will attempt pregnancy with husband, donor sperm, or unmarried male partner).

Mesen. *Timing of elective egg freezing. Fertil Steril* 2015.

QUESTIONS?