Dr Michelle Bailey

Fertility Associates

St Georges Hospital

Christchurch

Saturday, August 10, 2019 (Room 2)

8:30 - 9:25 WS #65: How to Achieve Better Fertility - An Interactive Session

9:35 - 10:30 WS #75: How to Achieve Better Fertility - An Interactive Session (Repeated)

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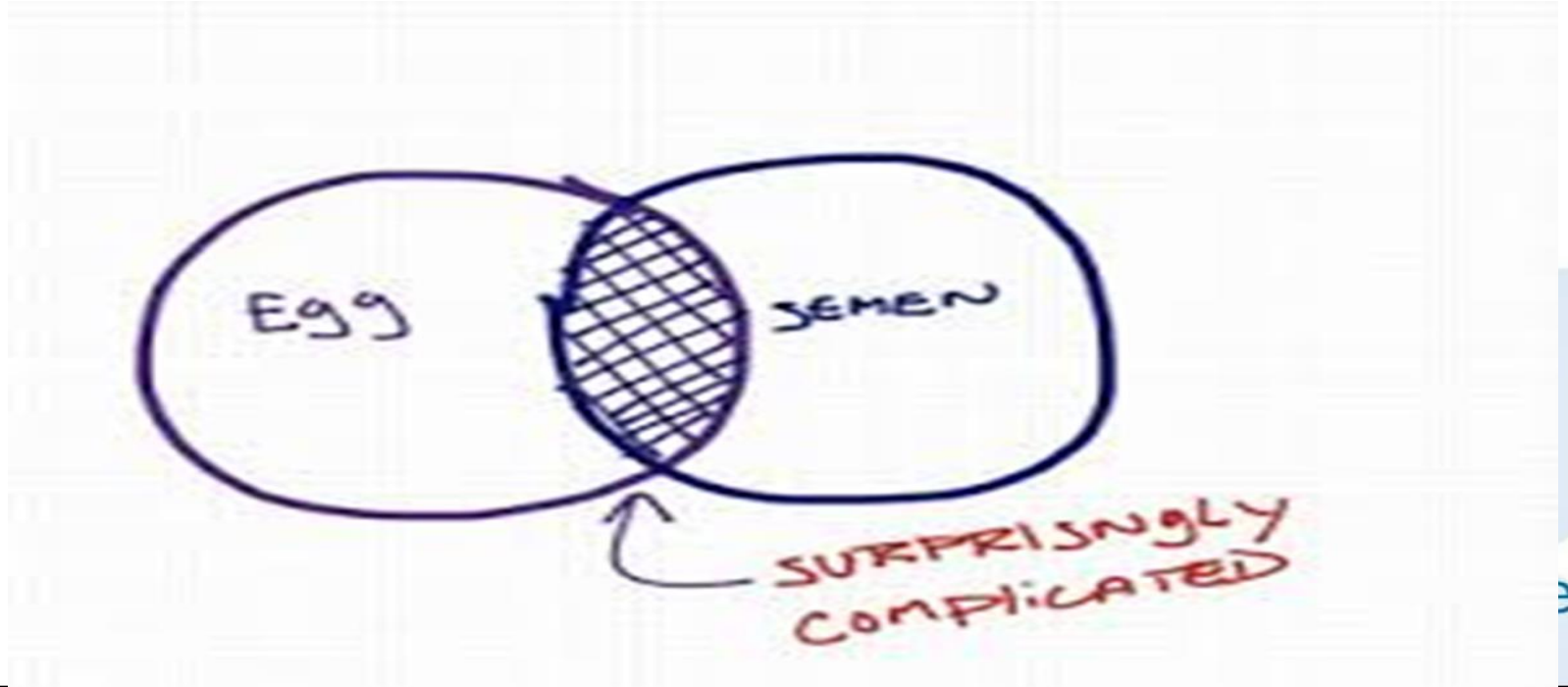
How to Achieve Better Fertility

Dr Michelle Bailey
Fertility Associates Christchurch
MBChB, FRANZCOG, CREI

Leaders in Fertility

THE MAGIC PILL TO SUCCESS



What Will We Cover Today ?

- What can your patients do to achieve better fertility
- What you can do to help your patients achieve better fertility
- What we can we do to help your patients

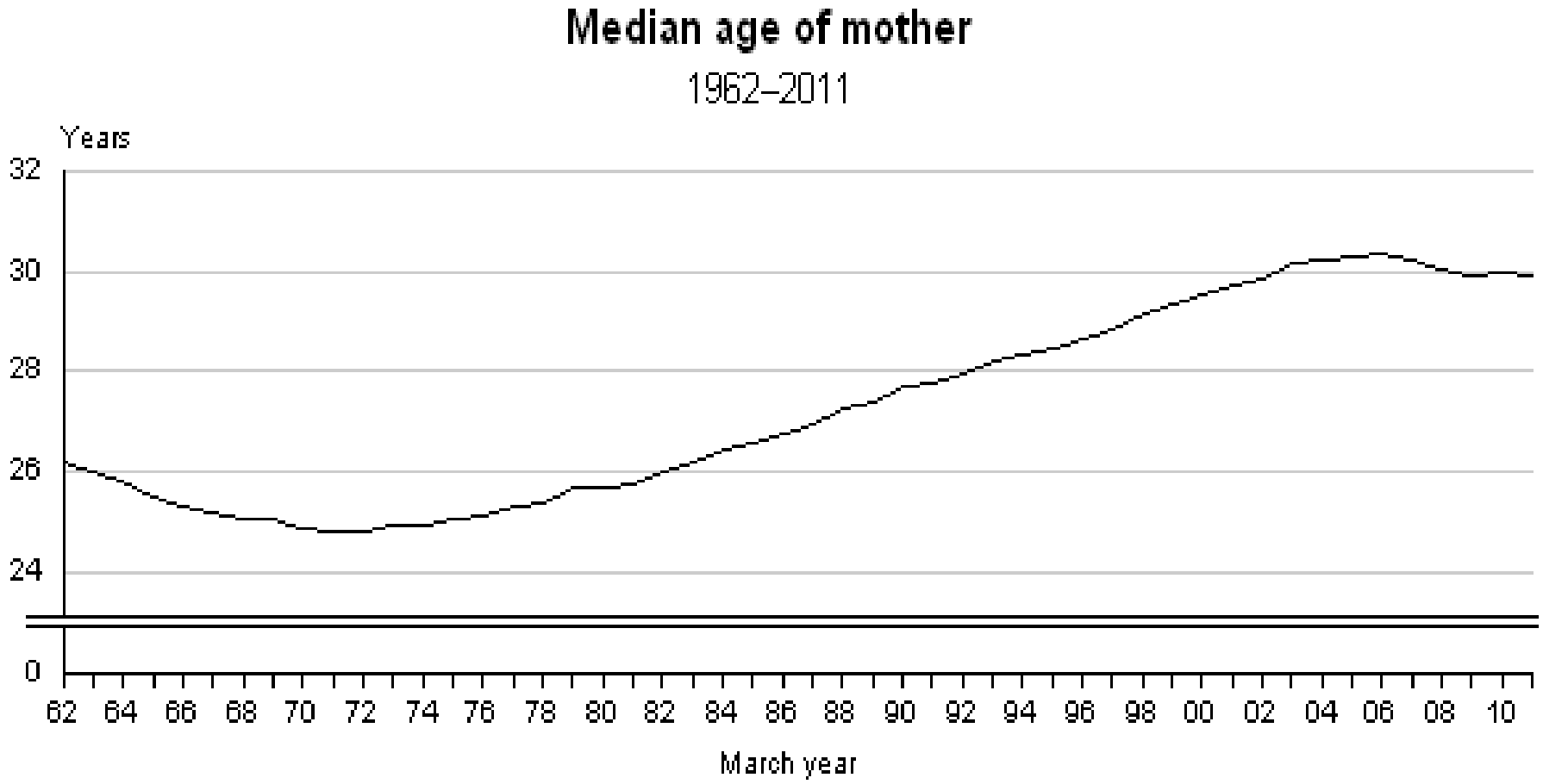
NZ research has found infertility is more common than previously thought.

By the age of 38 years infertility was experienced by

- *Infertility was defined as having tried for 12 months or more or having sought medical help to conceive.*

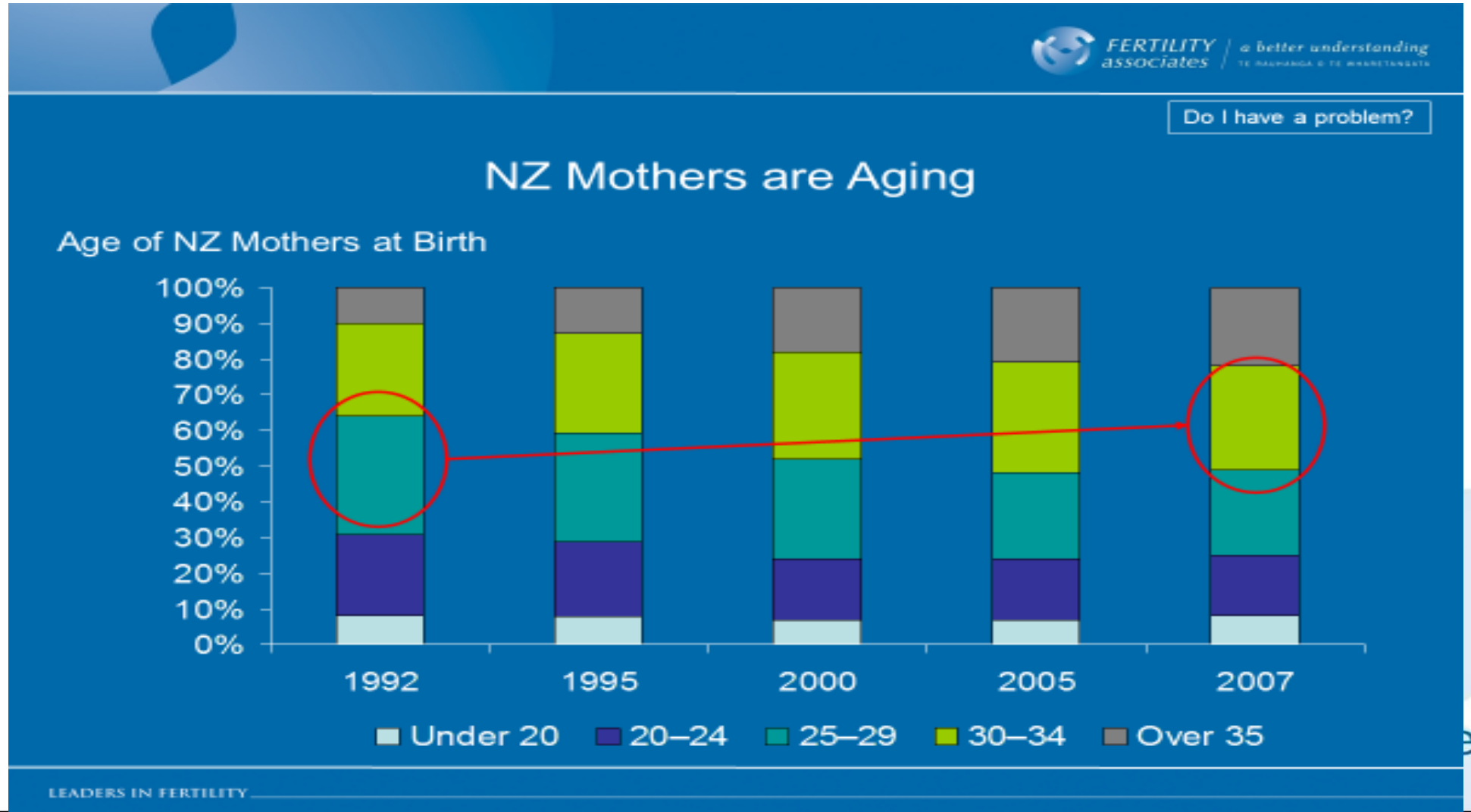
What Patients Can Do To Achieve Better Fertility ?

Female Age



Source: Statistics New Zealand

Female Age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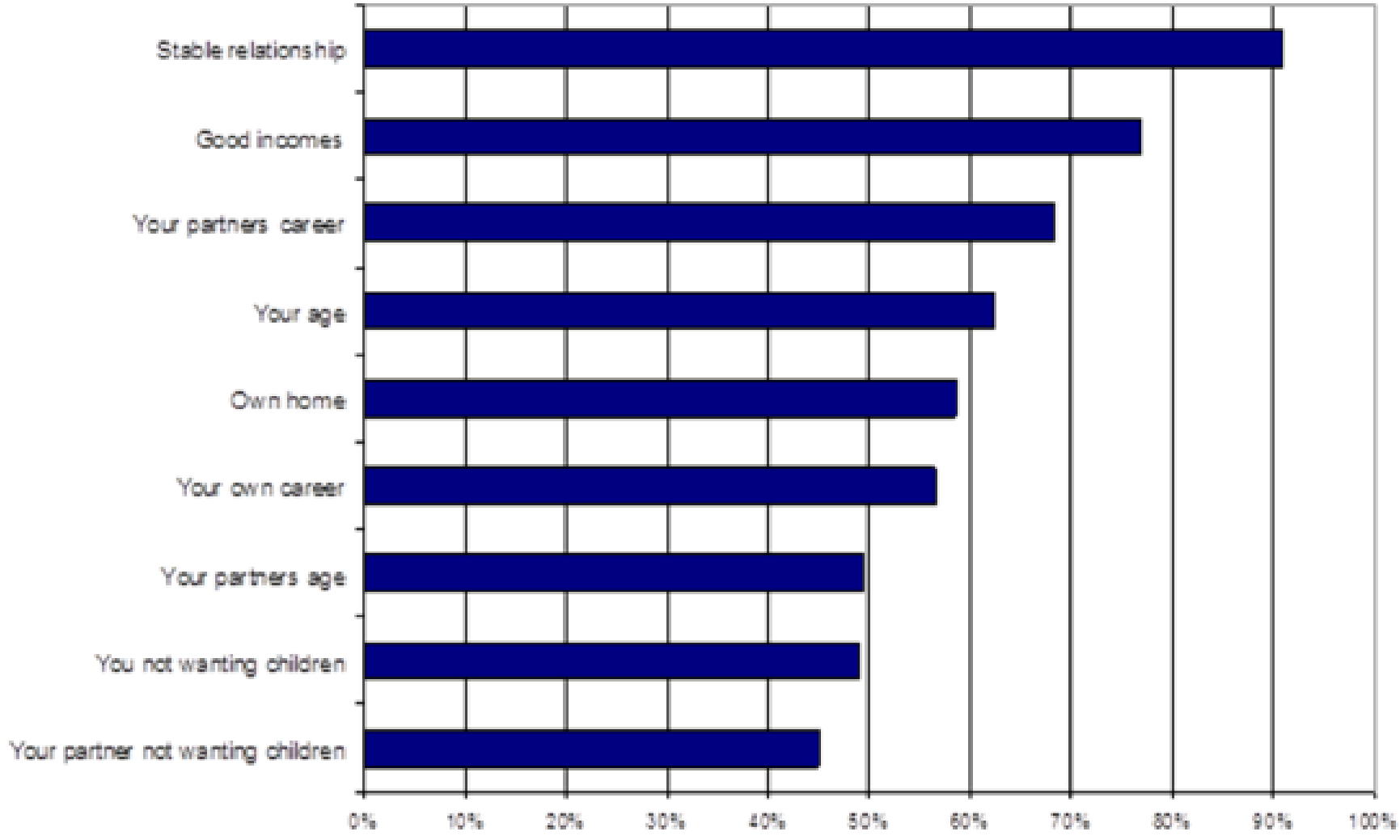
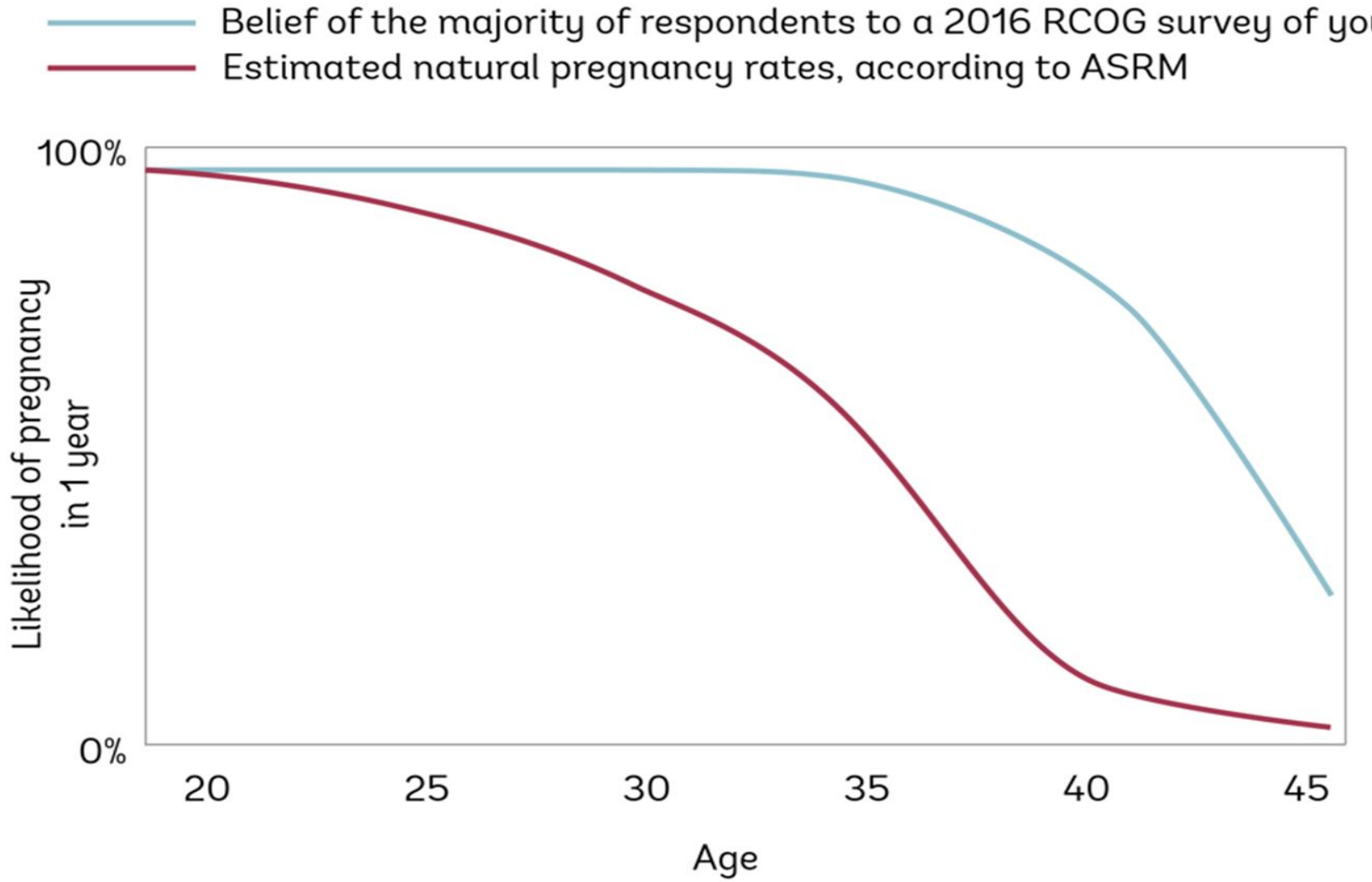
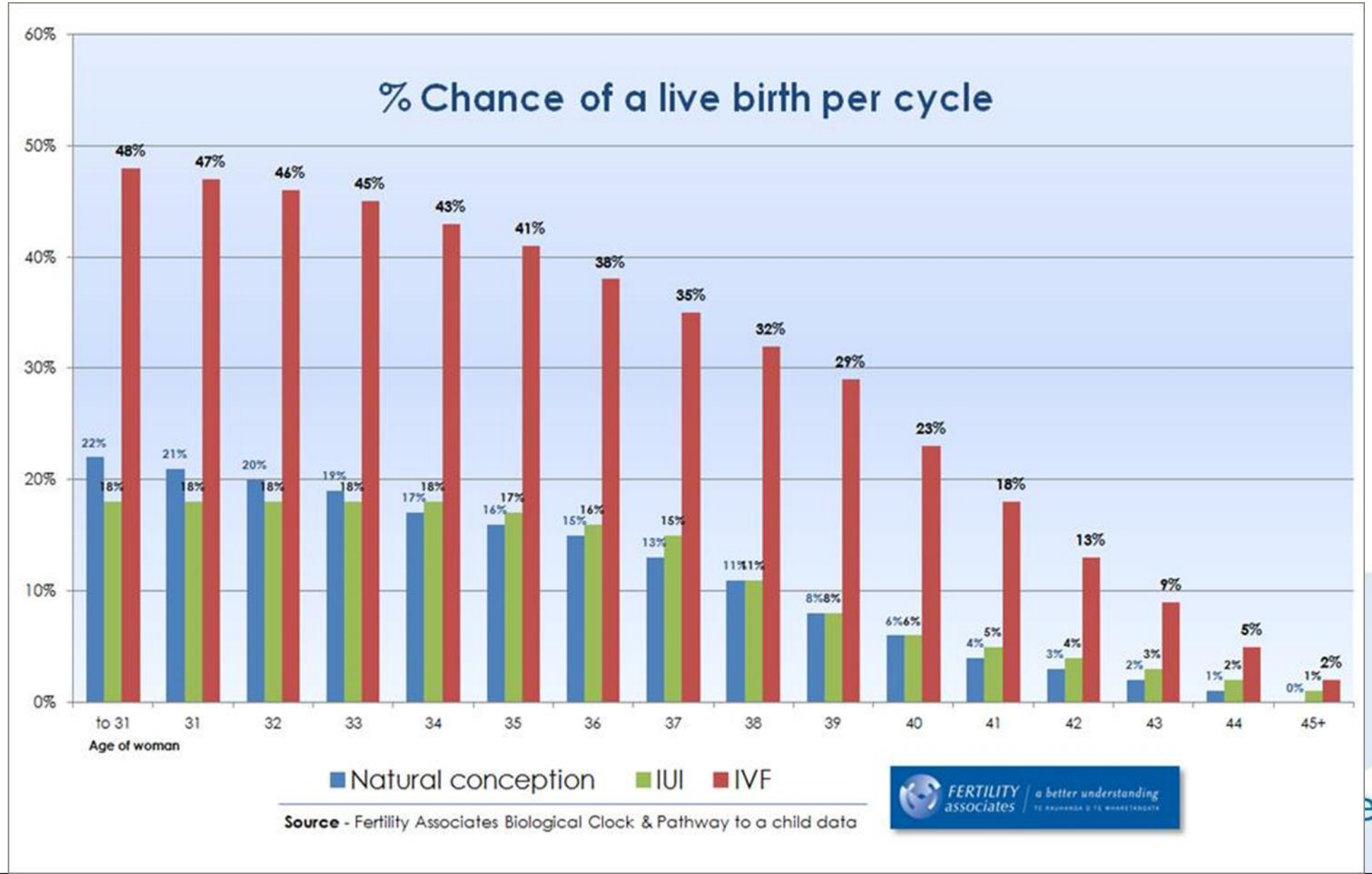
Do I have a problem?
NZ Mothers are Aging
Age of NZ Mothers at Birth
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1992
1995
2000
2005
2007
Under 20
20–24
25–29
30–34
Over 35
LEADERS IN FERTILITY

Reasons for Delaying Childbearing




Belief of the majority of respondents to a 2016 RCOG survey of youth
Estimated natural pregnancy rates, according to ASRM
100%
0%
Likelihood of pregnancy in 1 year
20
25
30
35
40
45
Age


% Chance of a live birth per cycle
60%
50%
40%
30%
20%
10%
0%
48%
47%
46%
45%
43%
41%
38%
35%
32%
29%
23%
18%
13%
9%
5%
2%
22%
21%
20%
19%
17%
16%
15%
13%
11%
8%
6%
4%
3%
2%
1%
0%
18%
18%
18%
18%
18%
17%
16%
15%
11%
8%
6%
5%
4%
3%
2%
1%
to 31
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45+
Age of woman
Natural conception
IUI
IVF
Source - Fertility Associates Biological Clock & Pathway to a child data
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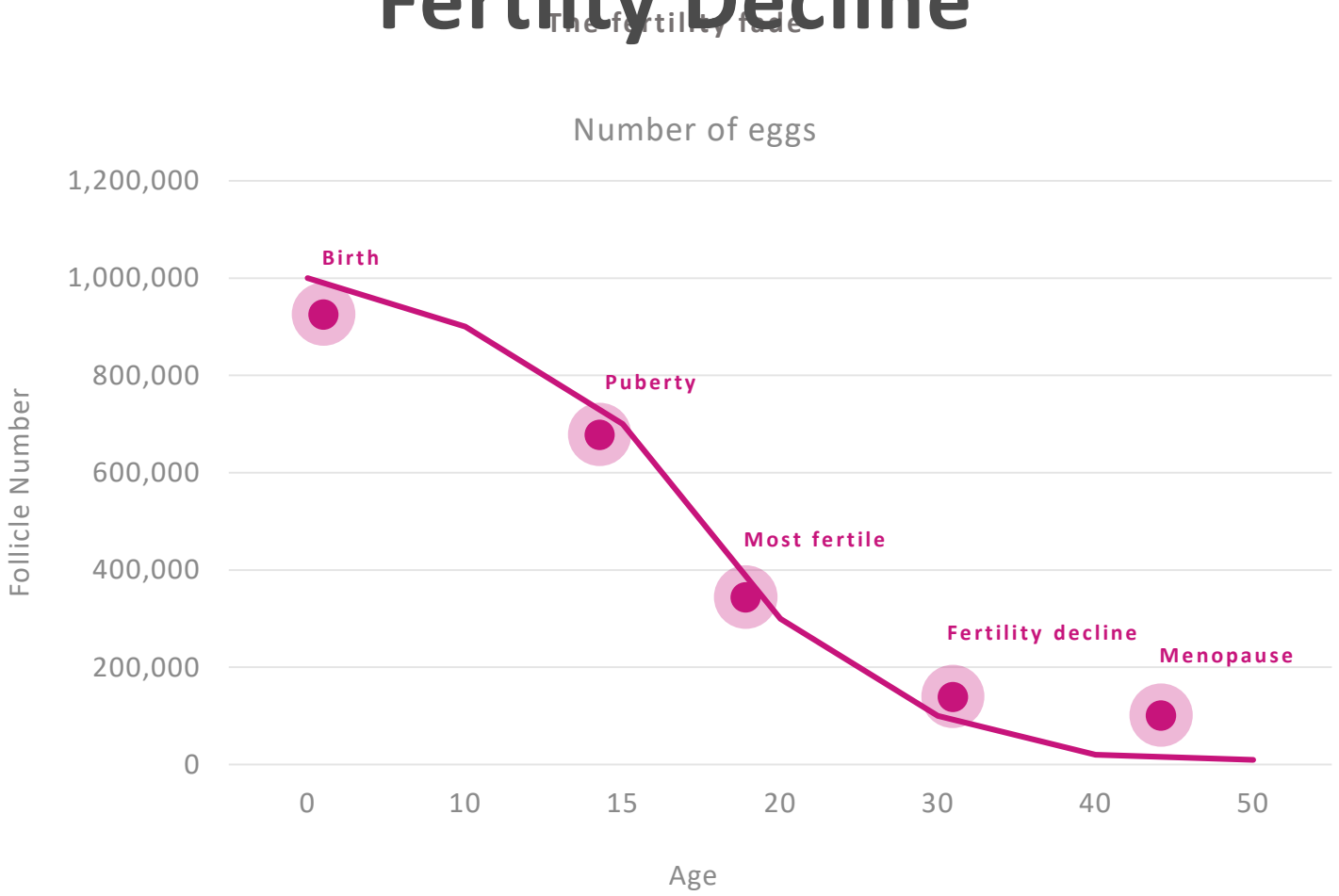
Egg Quantity Fertilty Decline



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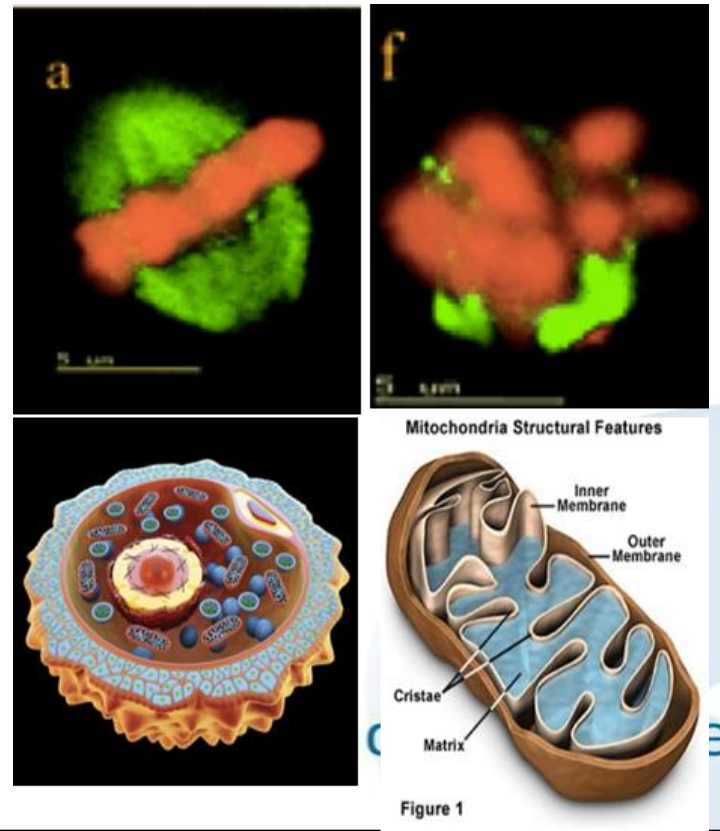
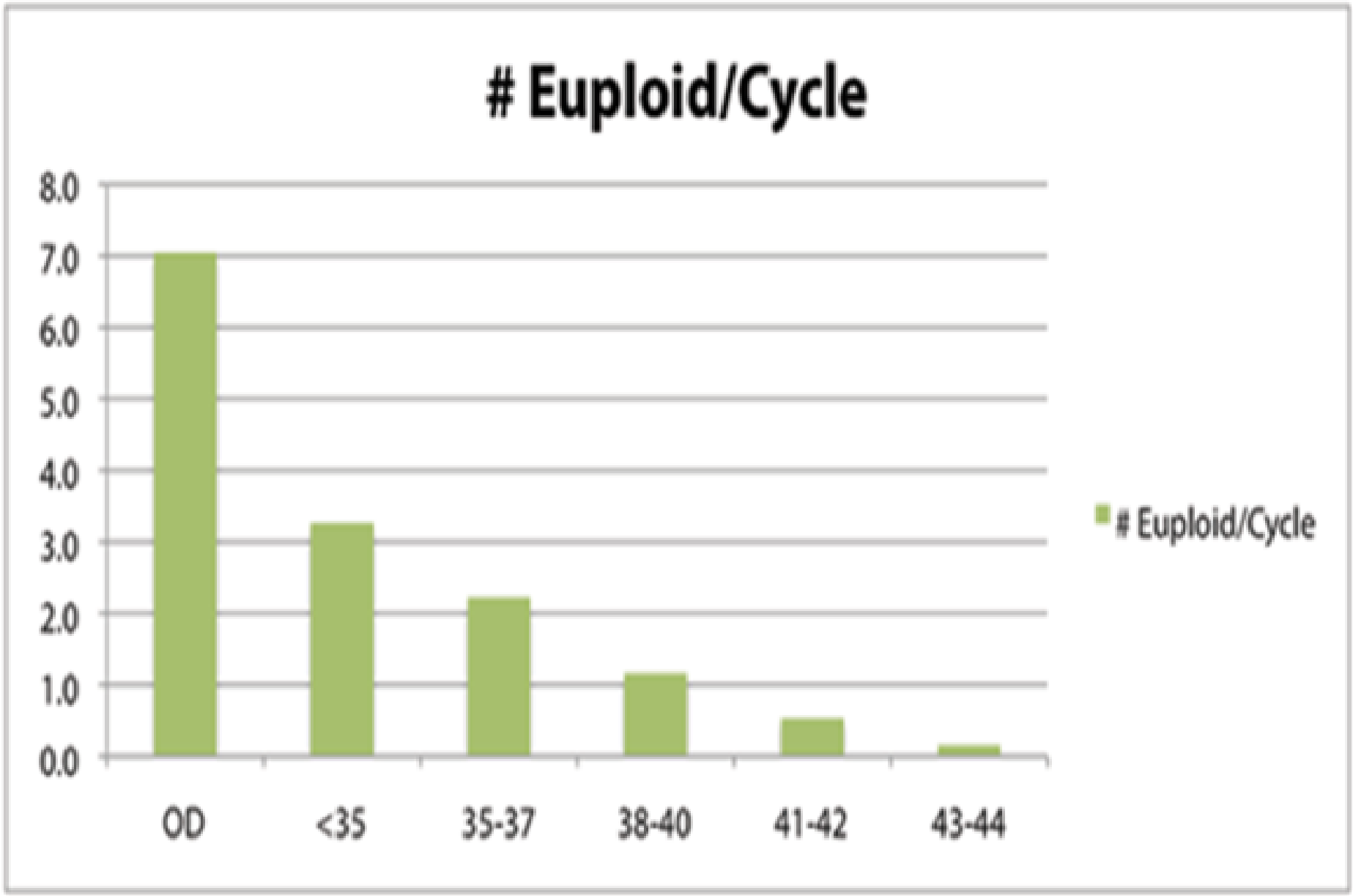
Egg Quality

- Increased Chromosomal Errors
- Mitochondrial aging

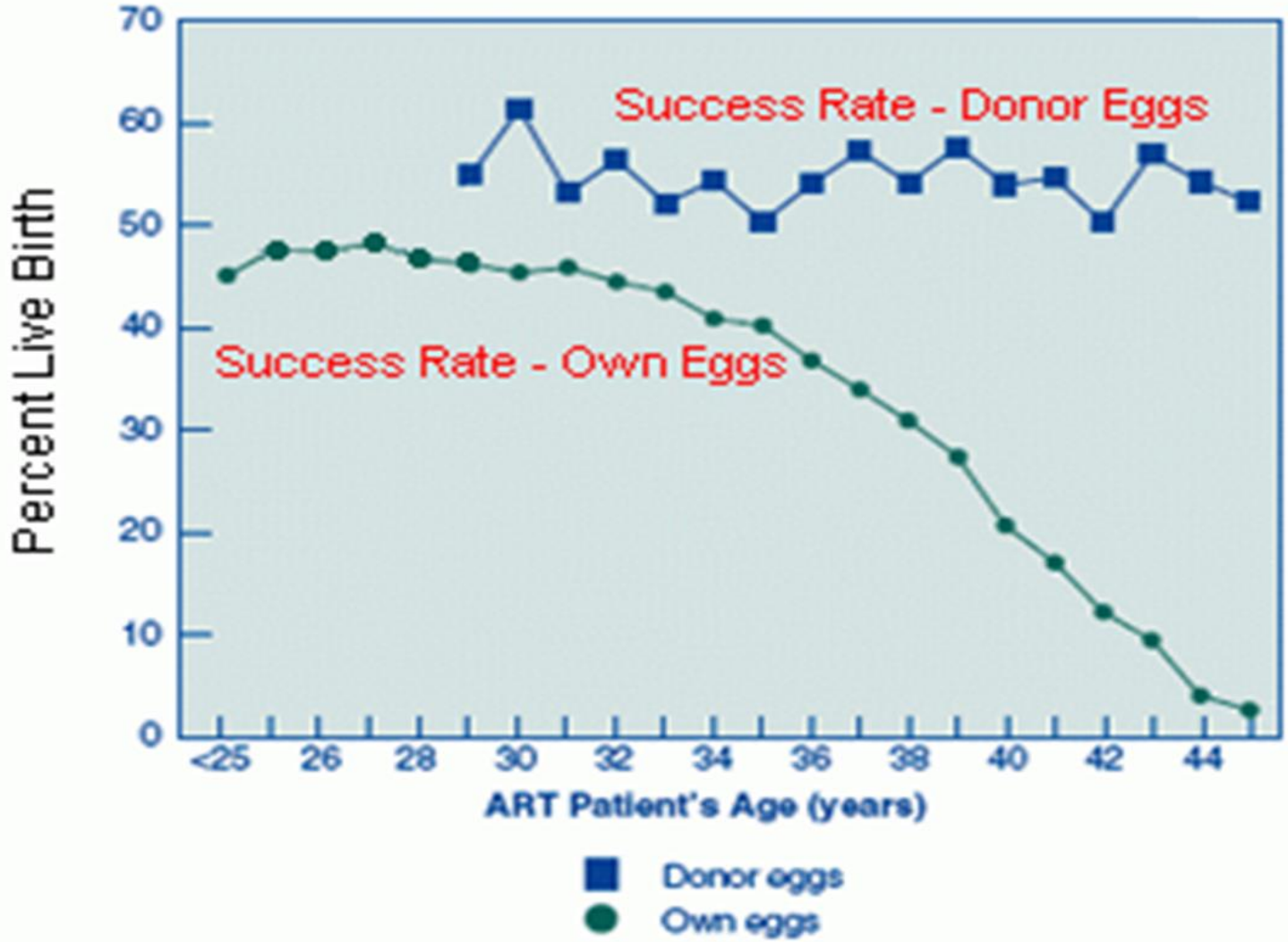



Euploid/Cycle
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
OD
<35
35-37
38-40
41-42
43-44
Euploid/Cycle

- A 46yo woman is having treatment with an egg donor. She is healthy. The donor is aged 25 years. What are the chances of success

- A 25% of the chance of the egg donor
- B 50% of the chance of the egg donor
- C 75% of the chance of the egg donor
- D Same chance as the egg donor
- E No chance

Percentages of Transfers That Resulted in Live Births for ART Cycles Using Fresh Embryos from Own and Donor Eggs, by ART Patient's Age, 2006



What You Can Do To Address The Effect Of Age On Fertility ?

- Talk to your female patients early in their lives about their **Family Planning Goals**
  - Plan for their last child, not first
- Ask them if they would consider fertility treatment if needed
- Consider assessing ovarian reserve

Chance of realization	1-child family	2-child family	3-child family
Without IVF			
50%	41	38	35
75%	37	34	31
90%	32	27	23
With IVF			
50%	42	39	36
75%	39	35	33
90%	35	31	28

Older men

- Age of paternity rising in Western countries including NZ
- In studies older men are >45 or >50 years
- Semen volume, sperm count, motility and morphology all decrease with age
- DNA damage to sperm increases with age
- Females longer time to pregnancy with older male partners
  - IVF – some evidence of lower success rates
  - Donor egg treatment -variable

Older men – what about their children?

- Increased risk late pregnancy loss and stillbirth with older fathers
- Increased risk schizophrenia and autism
- Increased risk of some rare syndromes
  - Achondroplasia, osteogenesis imperfecta, neurofibromatosis, Marfan syndrome
- Increased risk childhood ALL and possibly retinoblastoma
- Probable increased risk aneuploidies

Will a Poor Lifestyle Make you Infertile?

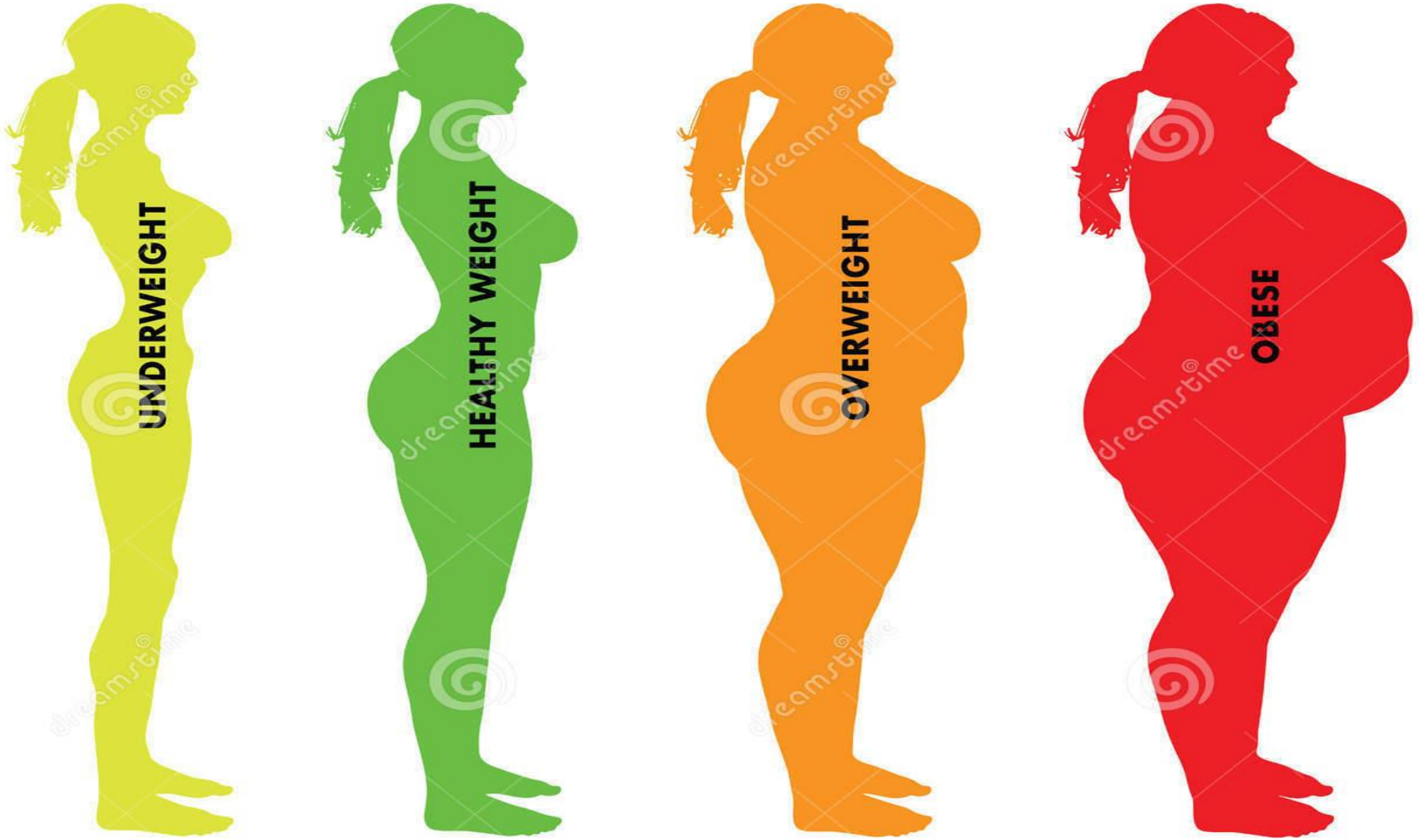
A It is vital to improve lifestyle factors to help fertility

B Probably it does to some extent

C Probably it doesn't

D We have not evidence to suggest this

Female Weight



Female Weight

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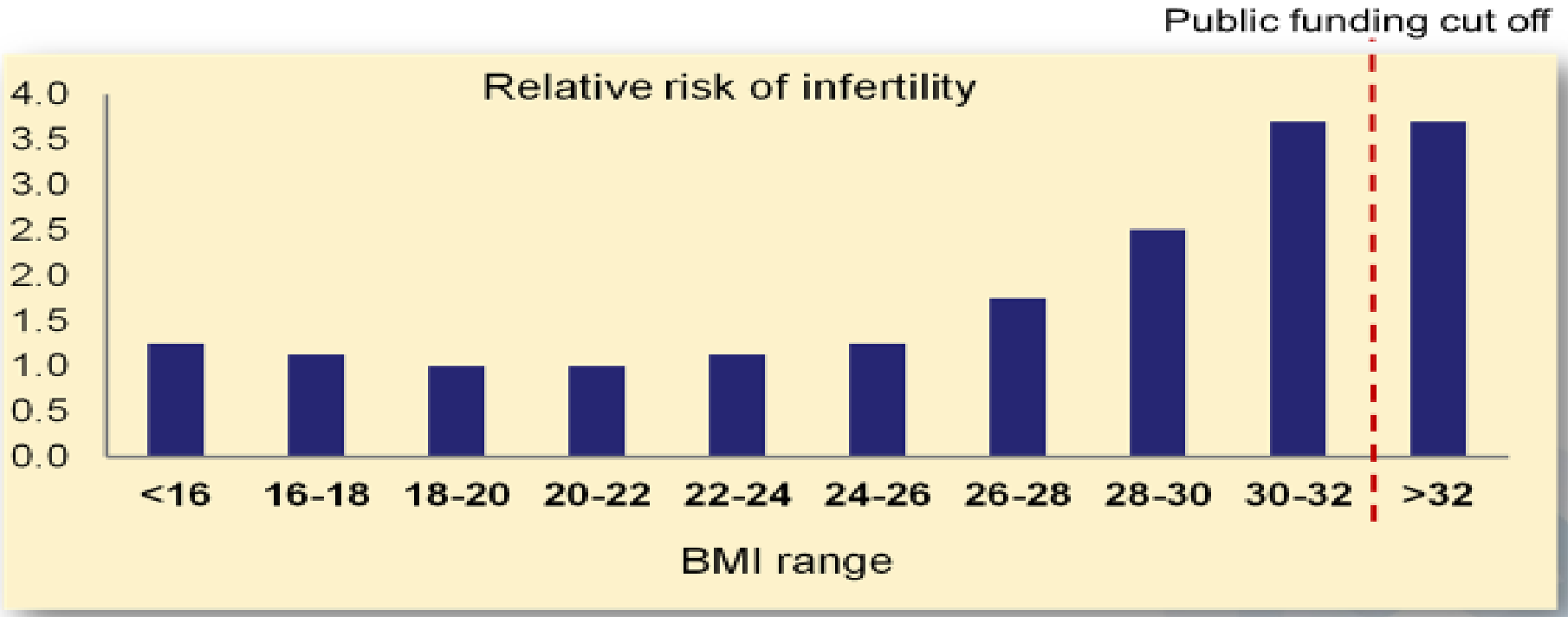
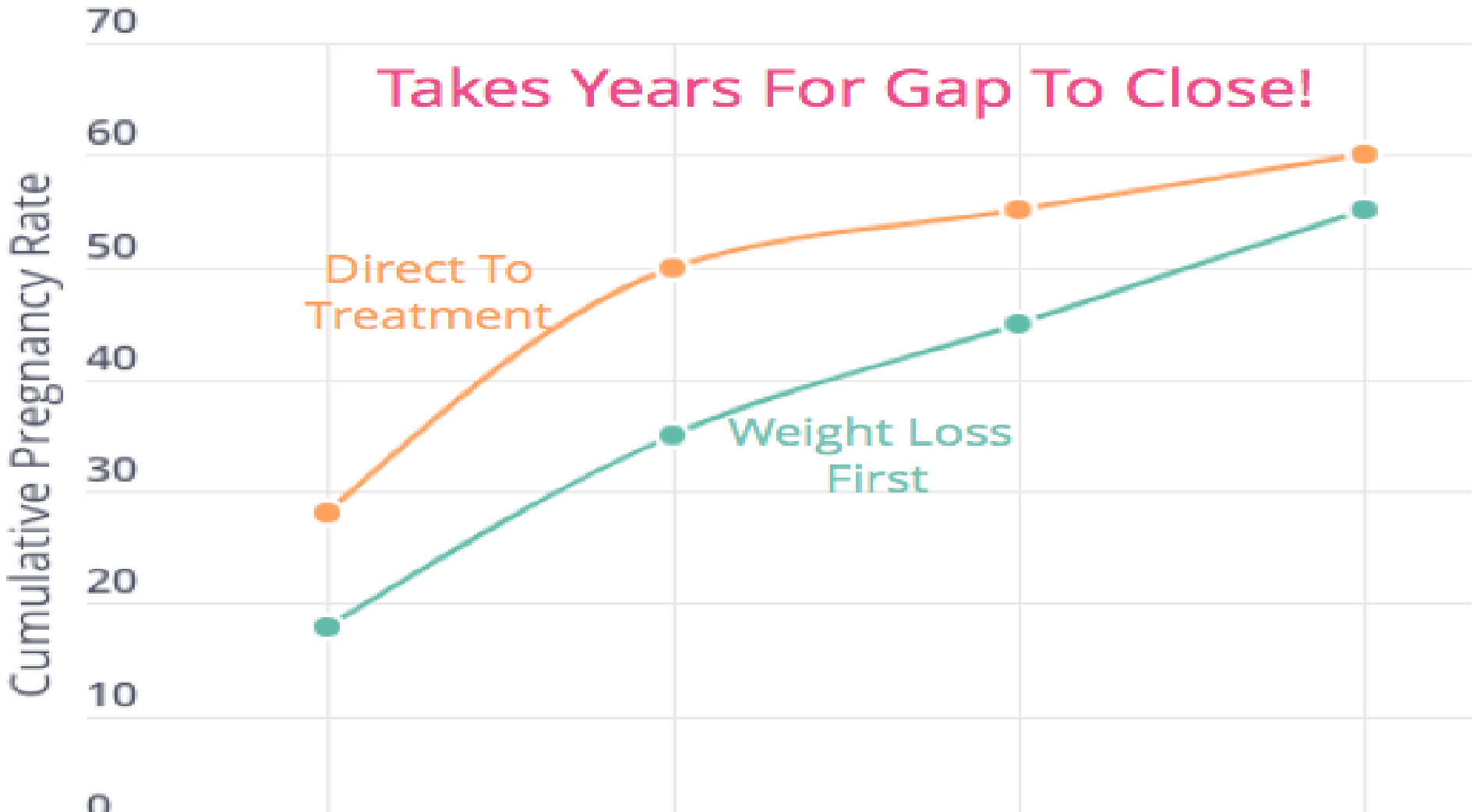
Impact of BMI on female fertility



Human Reproduction Update

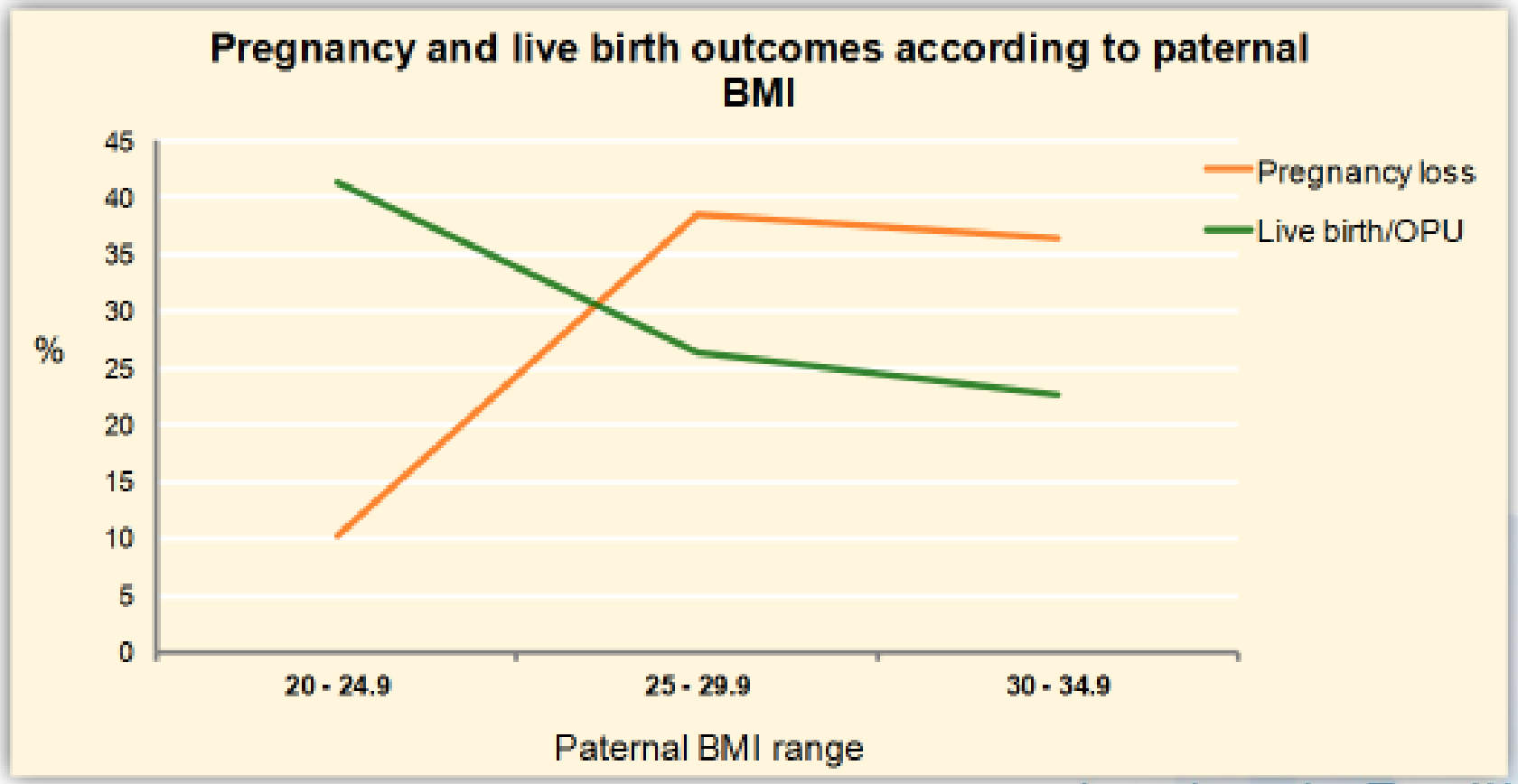
Homan, G.F. et al. Hum Reprod Update 2007 13:209-223; doi:10.1093/humupd/dml056

Value of Proceeding To Treatment



Impact of BMI on male fertility

- Overweight men (BMI over 28) have sperm counts 22% lower



Bakos et al., 2011, *Paternal Obesity and ART Pregnancy*

Diet

Exercise

- Moderate exercise is advised
- Get started on it before pregnancy as generally not advised to start exercising in pregnancy if not used to it
- Make sure not overexercising
  - Eating enough to cover exercise
  - Not got an eating disorder
  - Some women may be genetically predisposed to hypothalamic suppression
  - Can effect quality of ovulation

What You Can Do To Address The Effect Of Weight and Diet On Fertility

- Try to encourage patients to optomise their health and weight as much as realistically possible
- Ideally do this long before trying to conceive as may delay fertility treatments otherwise
- Encourage them to look at diet composition
- Try to assist very young patients from becoming morbidly obese
- ??Consider bariatric surgery if they have the means and other comorbidity

Female Smoking

- Toxins found in ovarian follicular fluid
- Menopause up to 4 years earlier
- Increased time to conceive - dose response
- Increased miscarriage/ectopic
- Damages gonads of foetuses
- Reversible in 1 year

Male Smoking

- Increase in childhood cancers if dad smokes
- Increase in Sperm DNA damage
- Dose dependant decrease in semen quality in men who smoke:
  - 23% red sperm concentration
  - 13% red sperm motility
- But no clear link to infertility

Alcohol

- Is a recognised teratogen – unknown safe level in pregnancy
- Moderate/heavy female drinkers take longer to conceive and are more likely to undergo an infertility evaluation
- Women:who drink more than 4 drinks/week had a 16% lower chance of a live birth
- Males drinking > 20/wk have a reduced number of pregnancies

Having the odd glass of wine is OK

Caffiene

- Most popular pharmacologically active substance consumed- Often perceived as an unhealthy habit
- Typical' caffeine consumption does not appear to be associated with:
  - inability to conceive
  - adverse reproductive outcomes such as congenital abnormalities, miscarriage, growth restriction, preterm birth
- Fertility outcomes unchanged by up to 200 mg caffeine/day

How much is 200 mg of Caffiene ?

Coffee, brewed
100 – 200 mg

Tea 50 mg

Espresso 40 mg

Coke 35 – 50 mg

Red bull 80 mg

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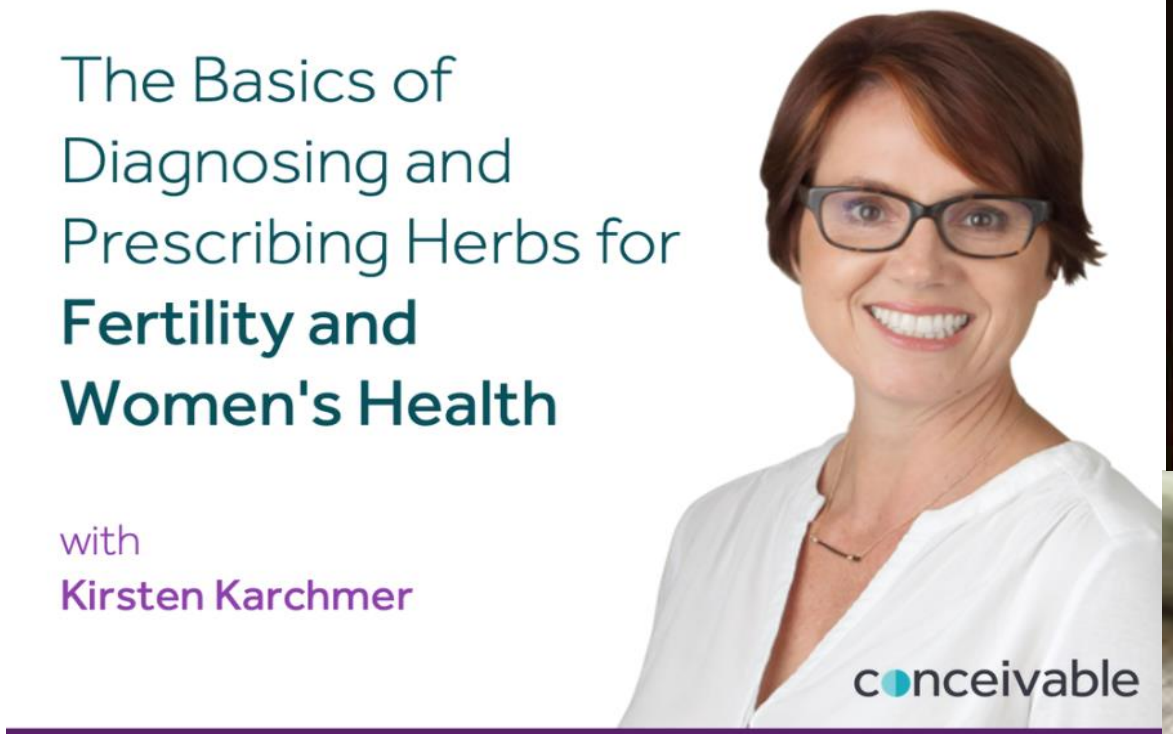
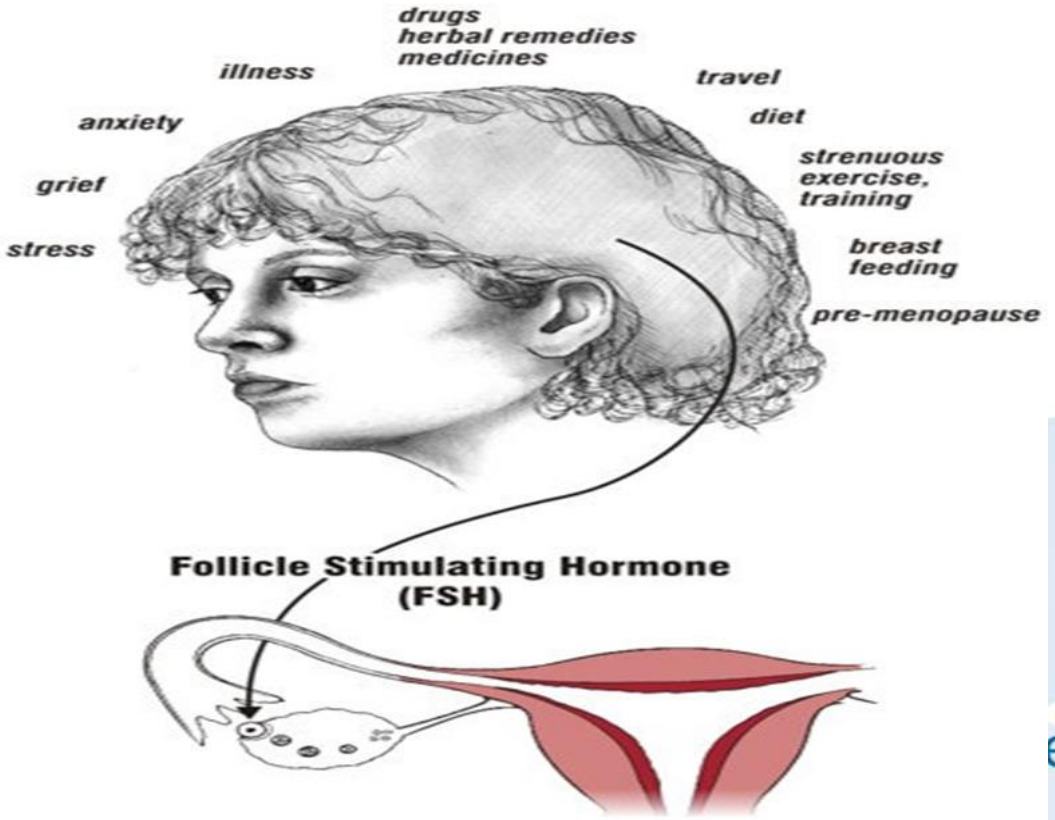
Herbs and Complementary Care



ertility

Stress

- No clinical trial has demonstrated definitively that reducing stress prior to infertility treatment improves pregnancy rates



Pollution/Toxins

- Still a new field of research in fertility medicine
- Heat
- Wifi
- Heavy metals
- Air pollution
- Endocrine disruptors
  - Pthalates
  - Bisphenols
  - Exogenous hormones

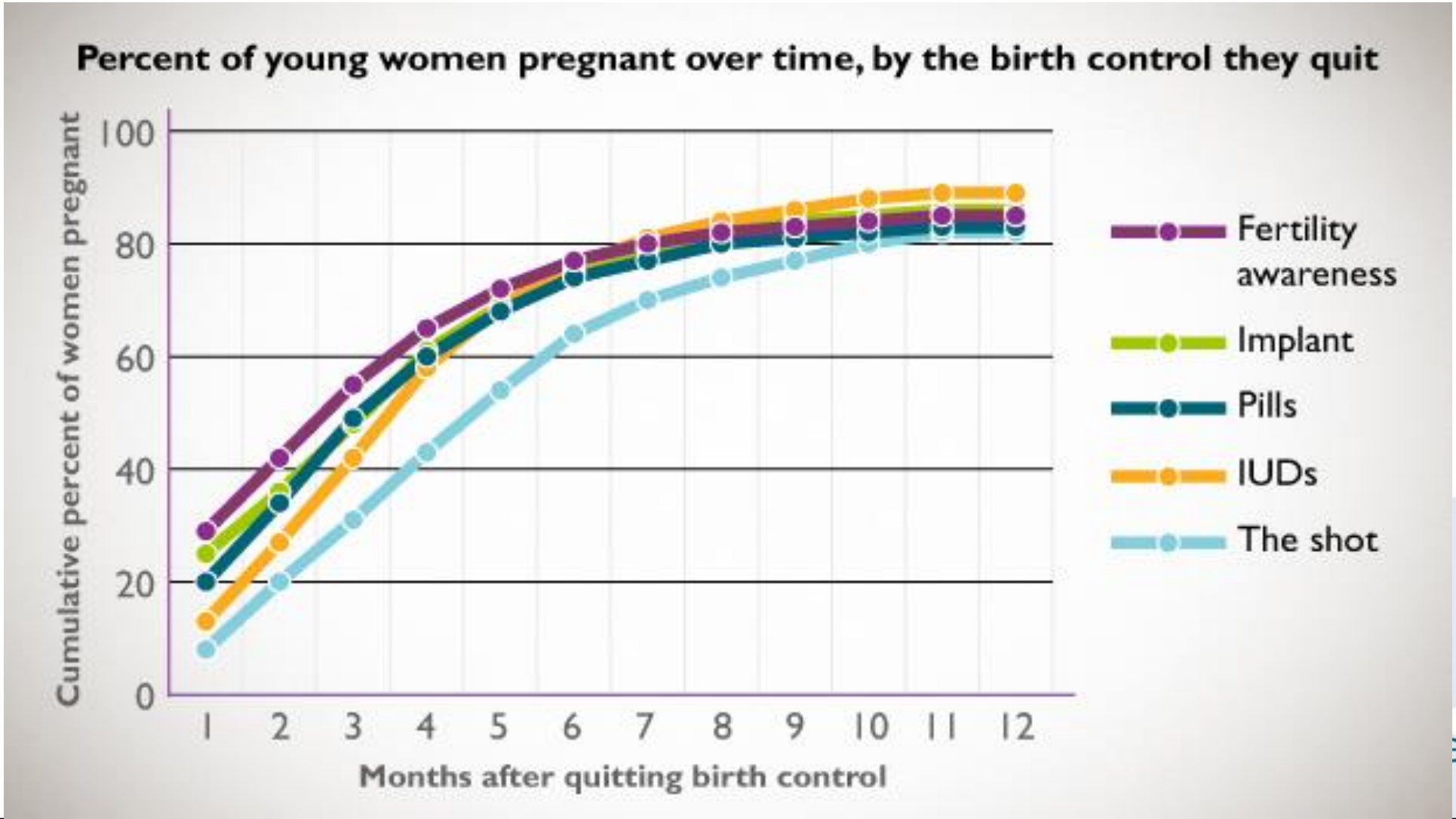
What Can You do to Help Your Patients ?

- Correctly establish onset of infertility
- Give them the correct information about normal fertility, and also when they may have sub-fertility
- Give them the correct pre-conceptual advice
- Consider assessing Ovarian Reserve for women in late 20's or early 30's or refer for this
- Look for Red Flags for early referral

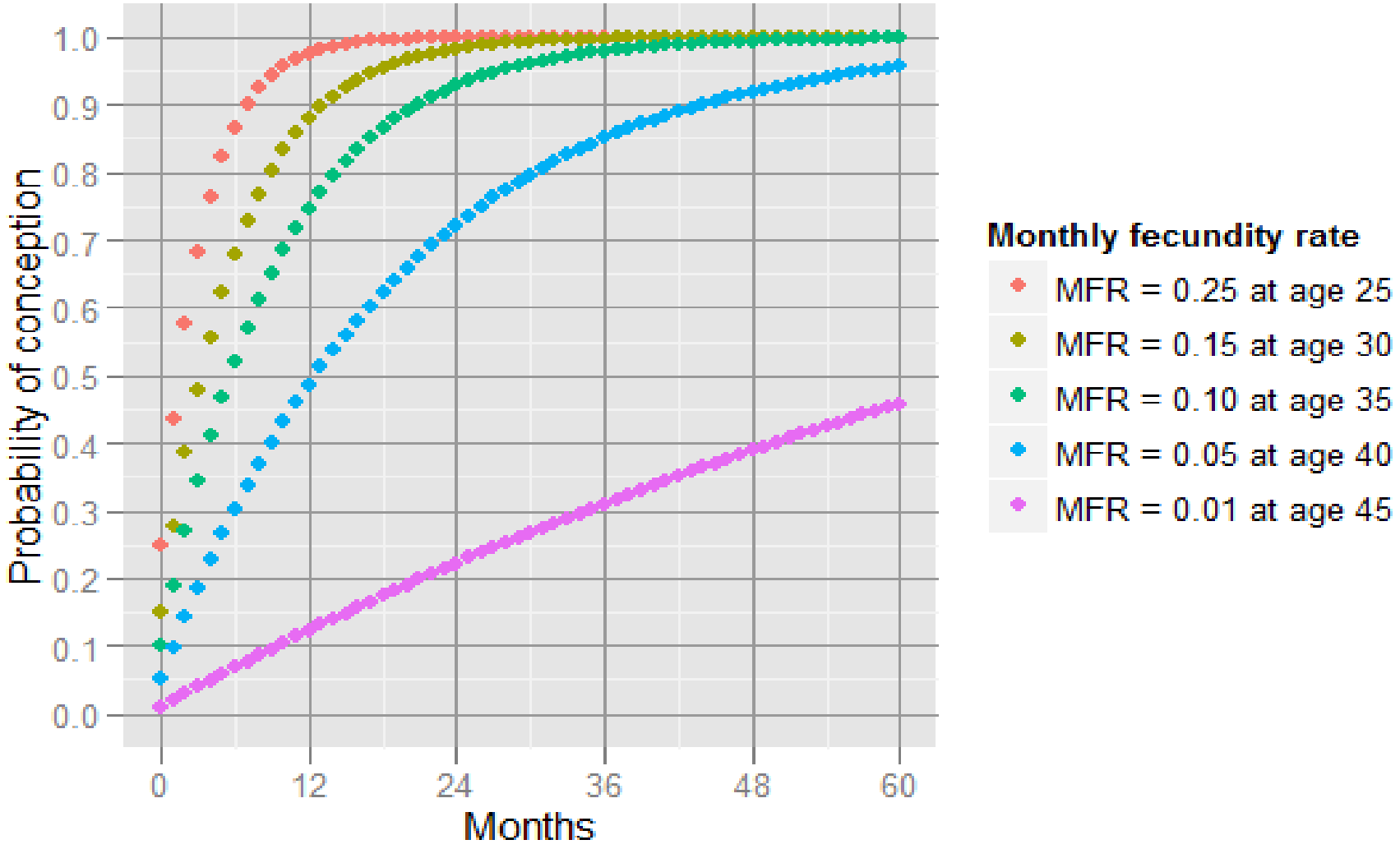
- What is the average time it takes for fertility to return after stopping the COCP?

- A 1 month
- B 3 months
- C 6 months
- D up to 1 year
- E 24 - 48 hours

Onset of Infertility



Time to Conceive

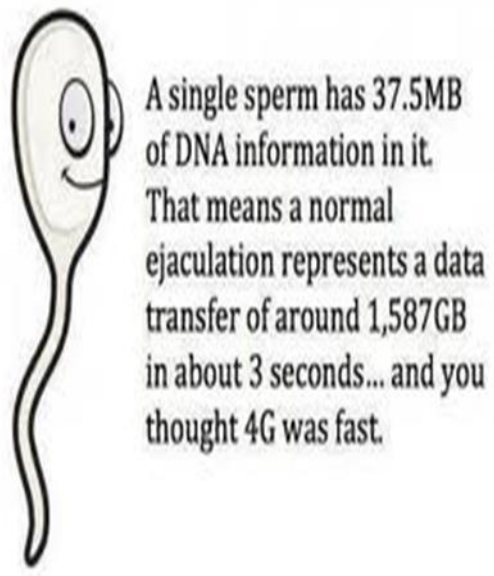


Basic Housekeeping – Women

- Take folic acid (minimum 800mcg), and use higher does if overweight or past or family risk of neural tube defects
  - Higher dose if on anti-seizure meds and ? Antidepressants
- Make sure Smear and STI screen is up to date
- Check basic antenatal bloods
- Make sure vaccinations are up to date

Basic Housekeeping – Men

- Loose underwear
- Reduce testis heating
- Avoid prolonged use of lap top computers
- Avoid close use of WiFi
- Regular ejaculation
- If want to take a supplement- use antioxidant
- Avoid testosterone

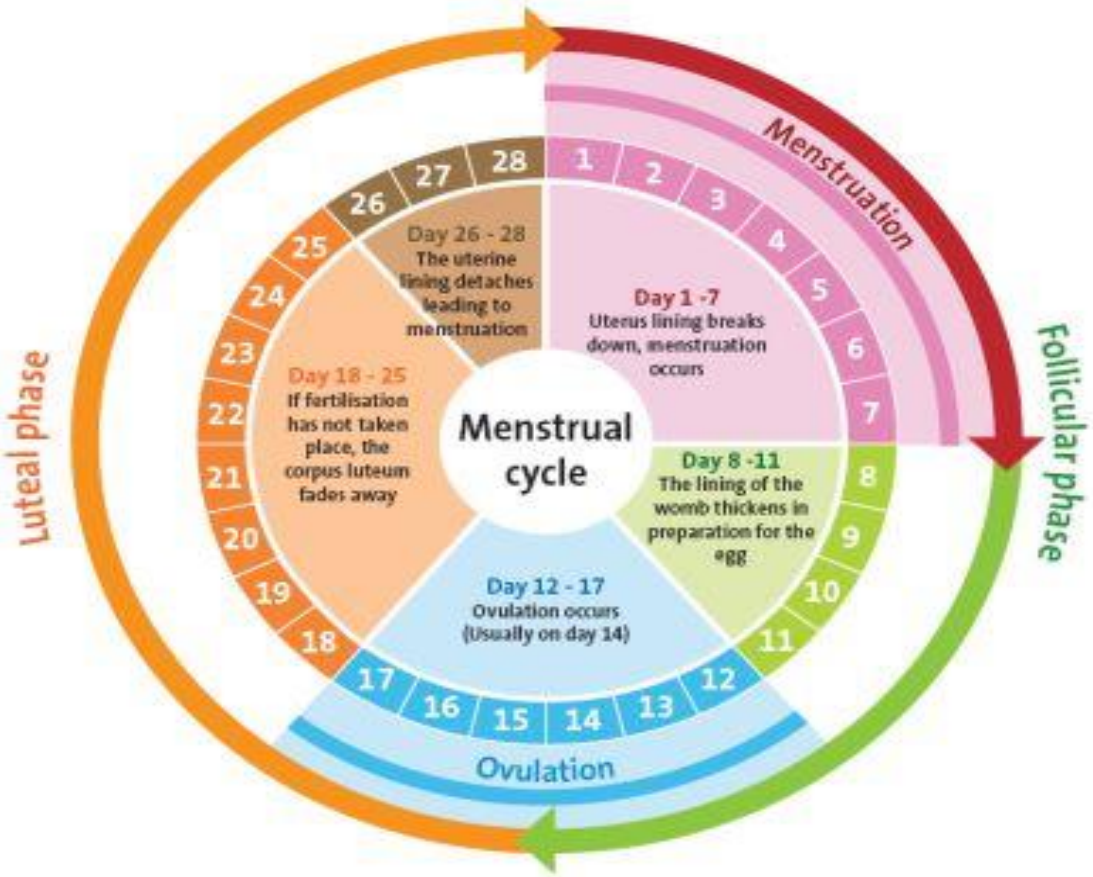


Have Regular Intercourse

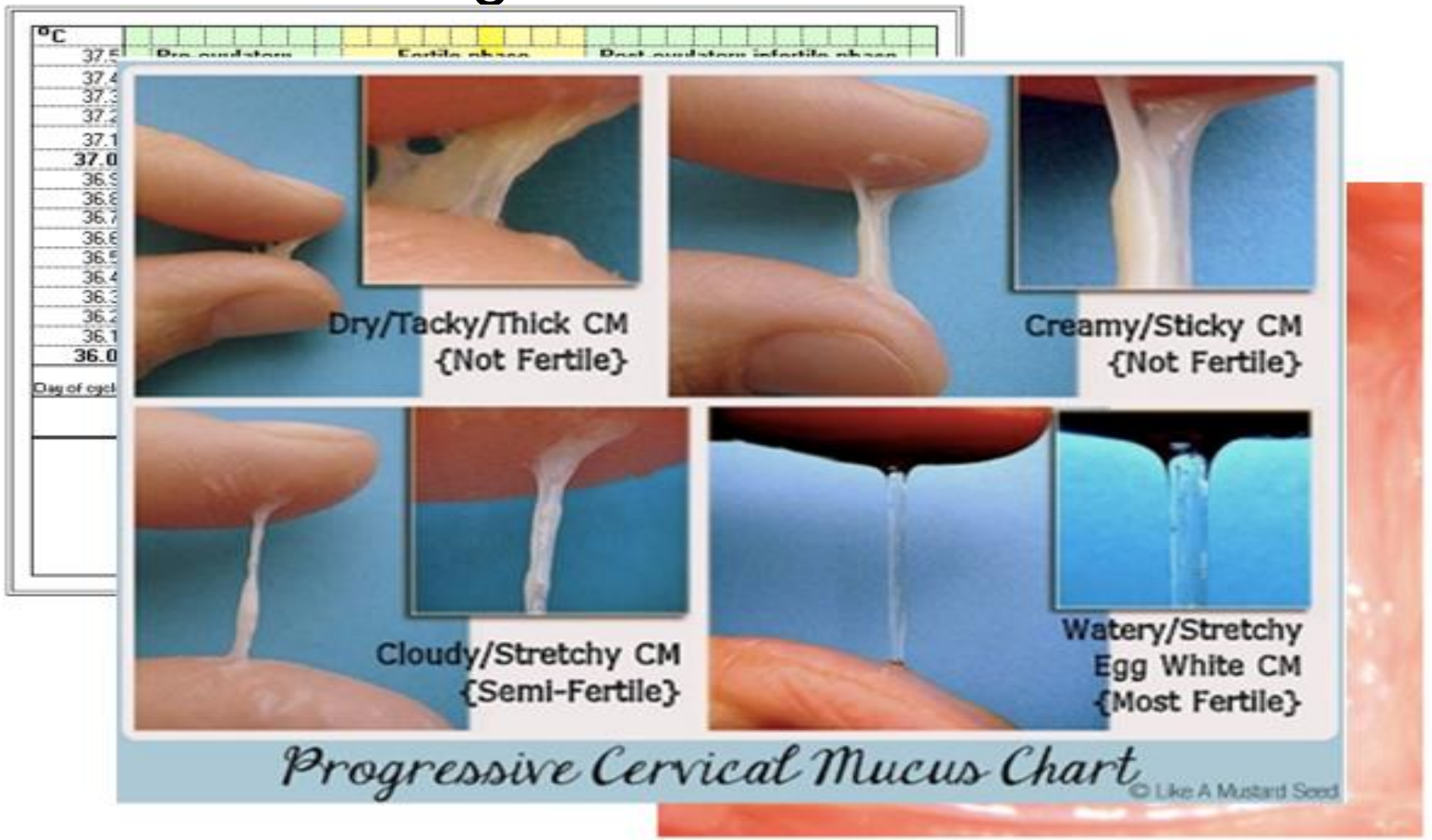
Correctly Timed Intercourse

"My husband and I had to try 70 times before I got pregnant —that was one weekend I'll never forget!"

Fertile Time of Cycle ?



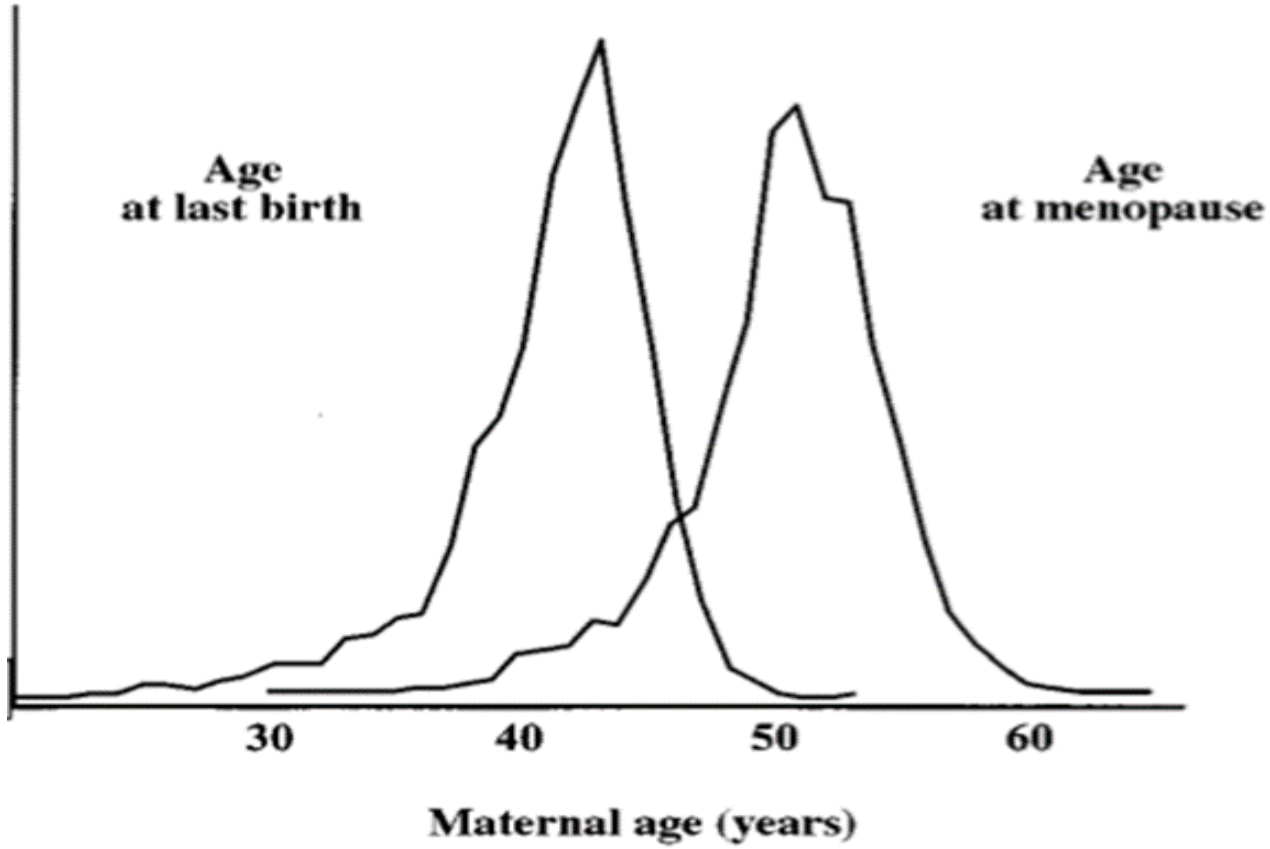
Changes in cervical mucus



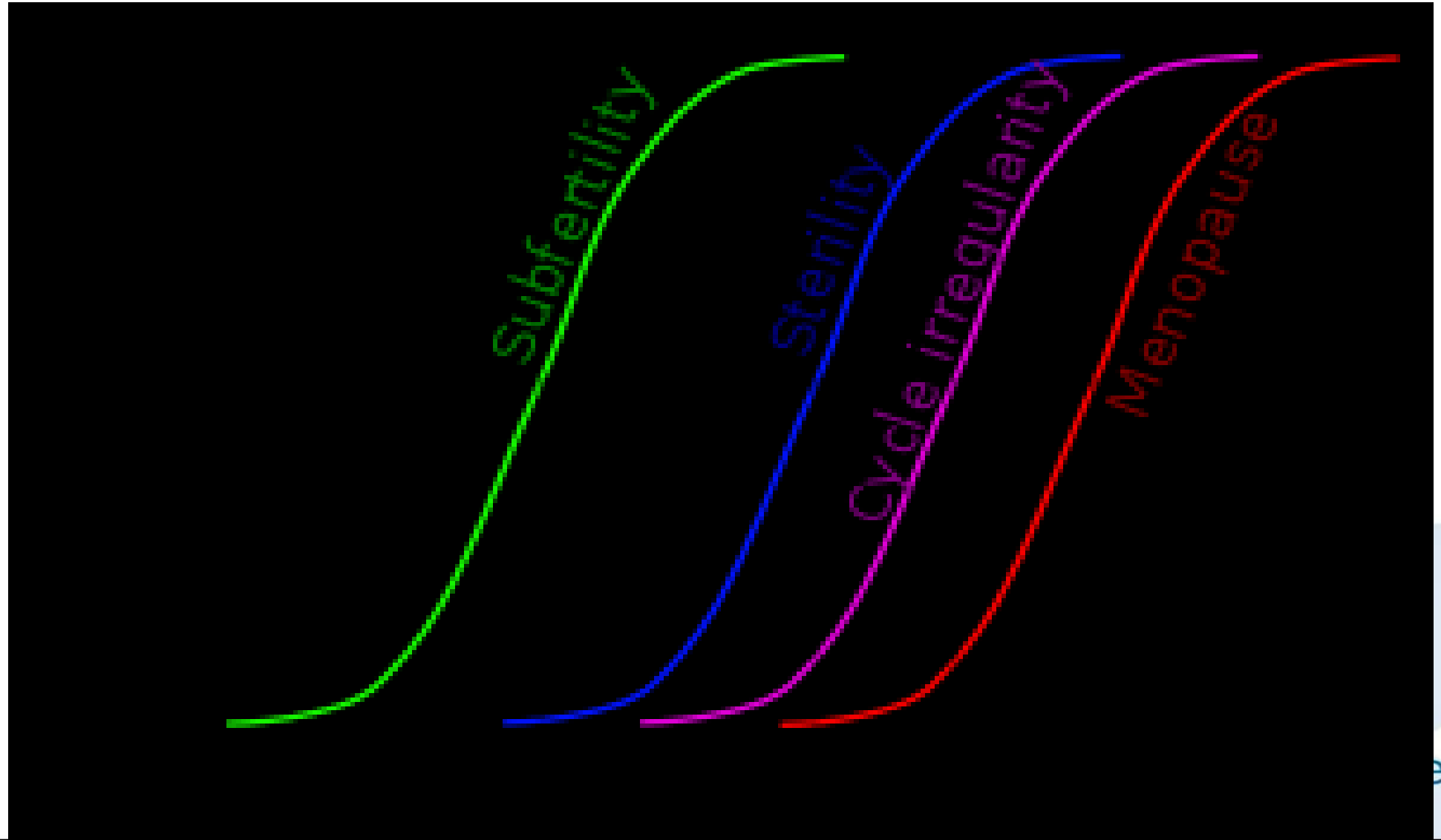
Ask About Gynaecology Symptoms

- Endometriosis
- PID
- PCOS
- Fibroids
- Cervical surgery
- Uterine surgery including TOP
- Recurrent Miscarriage
- Pelvic surgery

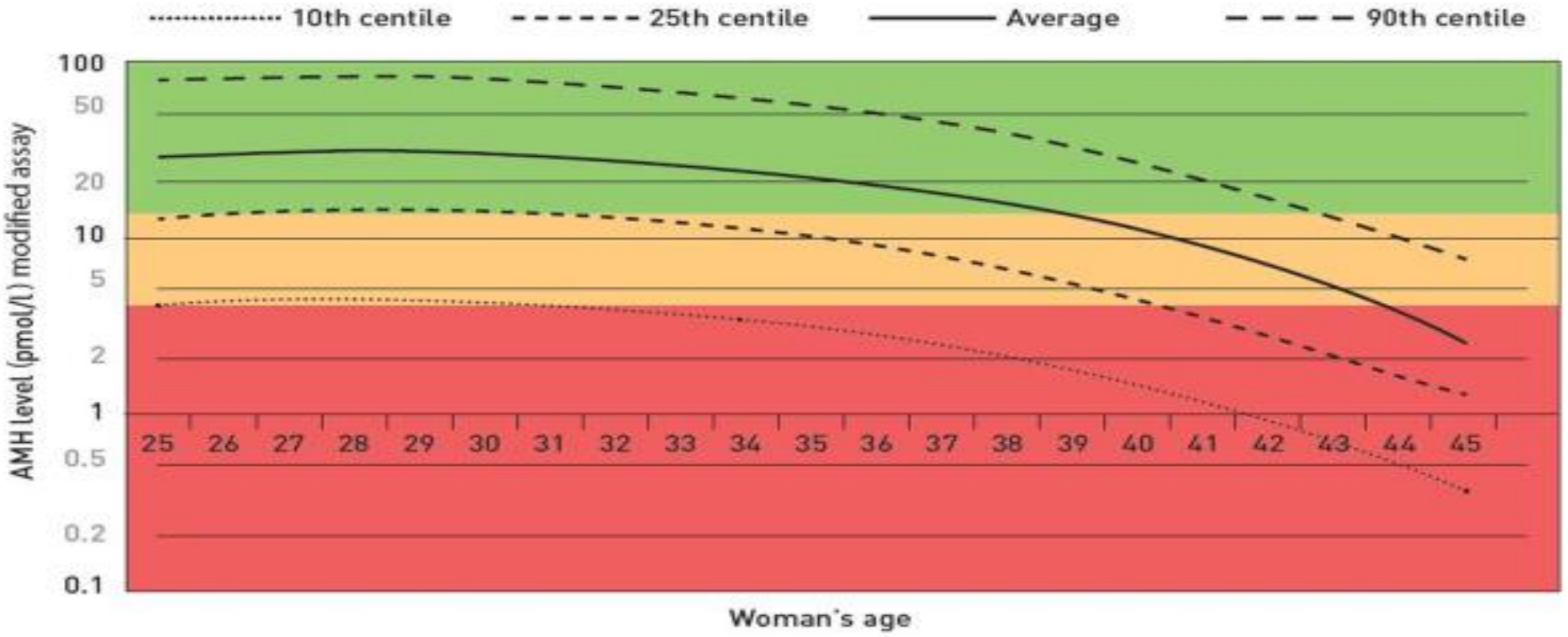
Ask about Premature Menopause



Change in cycle before menopause



Consider Assessing Ovarian Reserve



Green zone	Above the 25th centile for younger, fertile women	Very likely normal ovarian reserve – age is the best predictor of your future fertility	80% chance of 6 or more eggs in IVF
Orange zone	Between the 25th and 10th centiles for younger, fertile women	Some women in this range will have reduced ovarian reserve	50% chance of 6 or more eggs in IVF
Red zone	Below the 10th centile for younger, fertile women	Very likely reduced ovarian reserve	20% chance of 6 or more eggs in IVF

The Red Flags – refer early

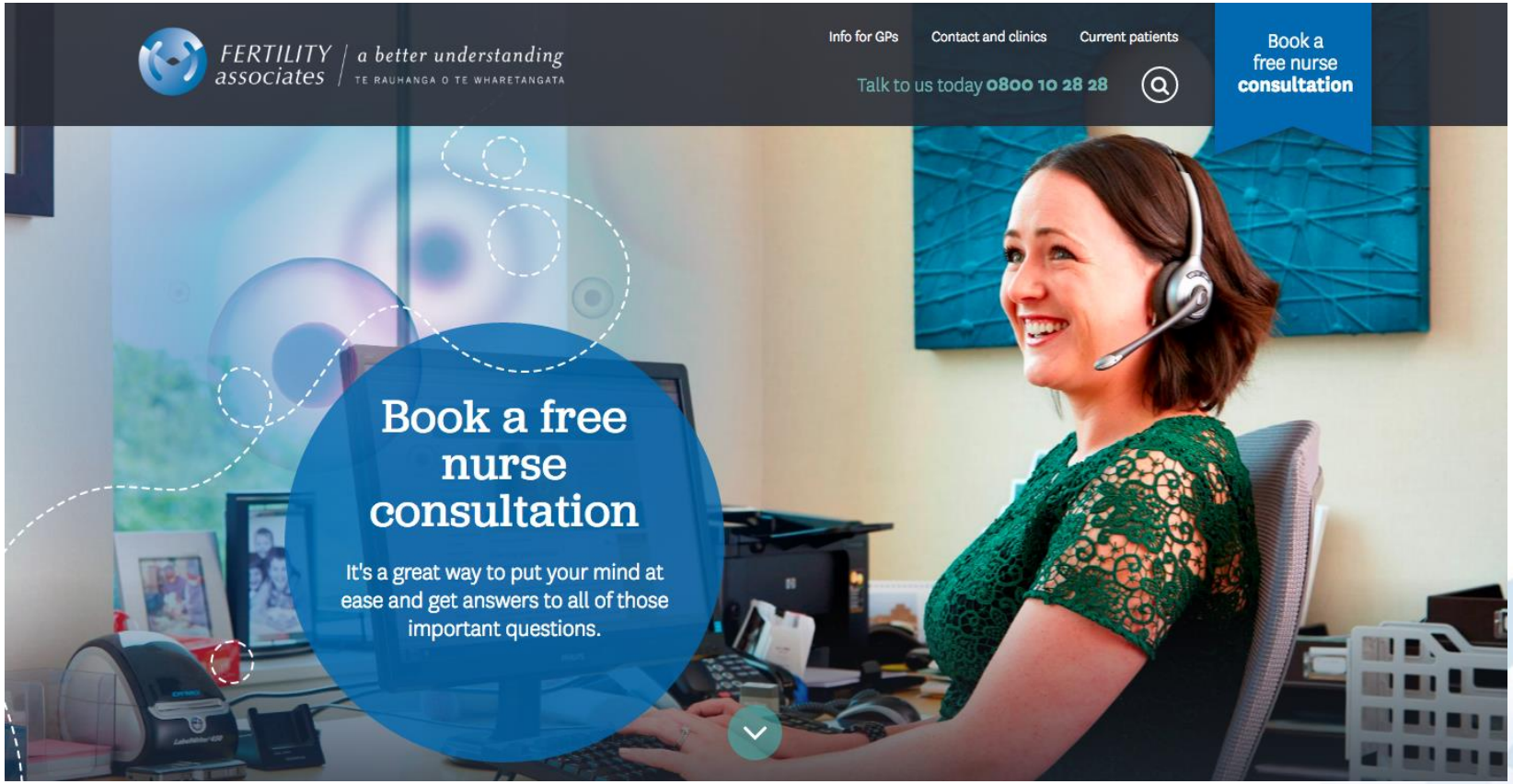
- Female age
- Previous cancer treatment
- Infrequent periods
- Significant Gynae/Urology history
- Risk factors for tubal/pelvic adhesions
- Family history of early menopause
- Genetic conditions
- Recurrent miscarriage
- Problems having sex

When to Refer ?

Couples who have not conceived after 12 months of unprotected intercourse should be offered referral for specialist assessment

BUT In the presence of negative prognostic factors couples or if woman is >35 yrs old, should be offered referral for specialist assessment after 6 months of unprotected intercourse

Referral - If Patients Are Not Quite Ready To See a Dr



Referral

- Refer themselves to FAC – will pay for consult, may be eligible for funded treatment
- Private referral – patients will pay for consult, may be eligible for funded treatment
- Public referral
  - Referral to FAC, funded from MOH for First Specialist Assessment (wait 4 months)
  - Referral to Christchurch Womens Hospital fertility clinic (wait approx. 4 months, can vary a bit)
  - May be eligible for funded treatment

We will always assess eligibility for funded treatment

Funded FSA – eligibility criteria

- > 1 year fertility delay (CWH sl diff)
- Both NZ residency or suitable visa
- Female non smoker
- Female under 40 years old
- < 2 children - 12 years or under
- BMI criteria – currently 35 at FAC

What Services are offered at CWH and FAC

Services	CWH	FAC
	FSA	FSA
	SIS	SIS (public if FSA appt)
	SA (SCL)	SA (SCL or FAC)
	Surgery	Surgery (private or refer CWH)
	Cycle monitoring	Cycle monitoring
		IUI
		IVF/ICSI
		PGD/PGS
		Donor sperm/egg/embryo
		Surrogacy

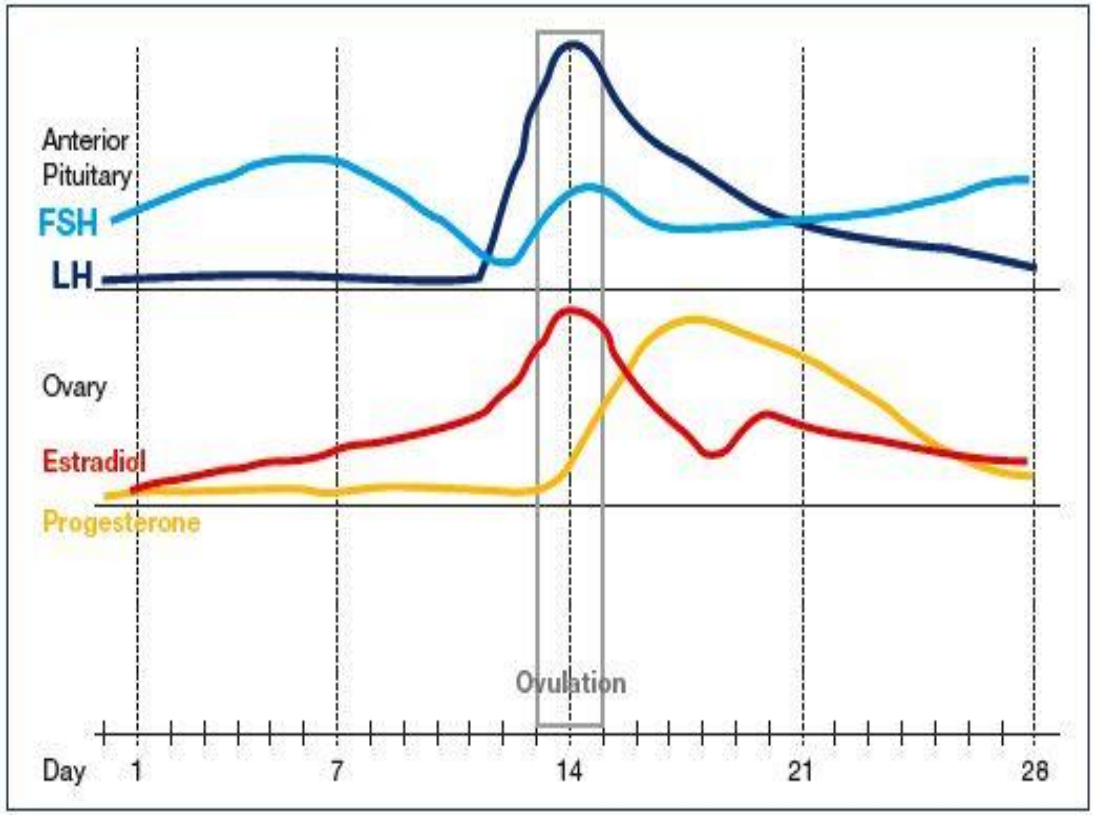
Funded Fertility Treatment - CPAC

- FSA eligibility doesn't mean funded treatment treatment
- Threshold is 65 points
- **Criteria**
- Duration of delay – up to 5 yrs max points
- BMI 32 or less, < 40, Non smoker
- Causes of infertility are assessed – endo, ovulation, sperm, tubal, other
- If sterility is iatrogenic
- If have a child < 12 yrs

So which tests do you need to perform and why?

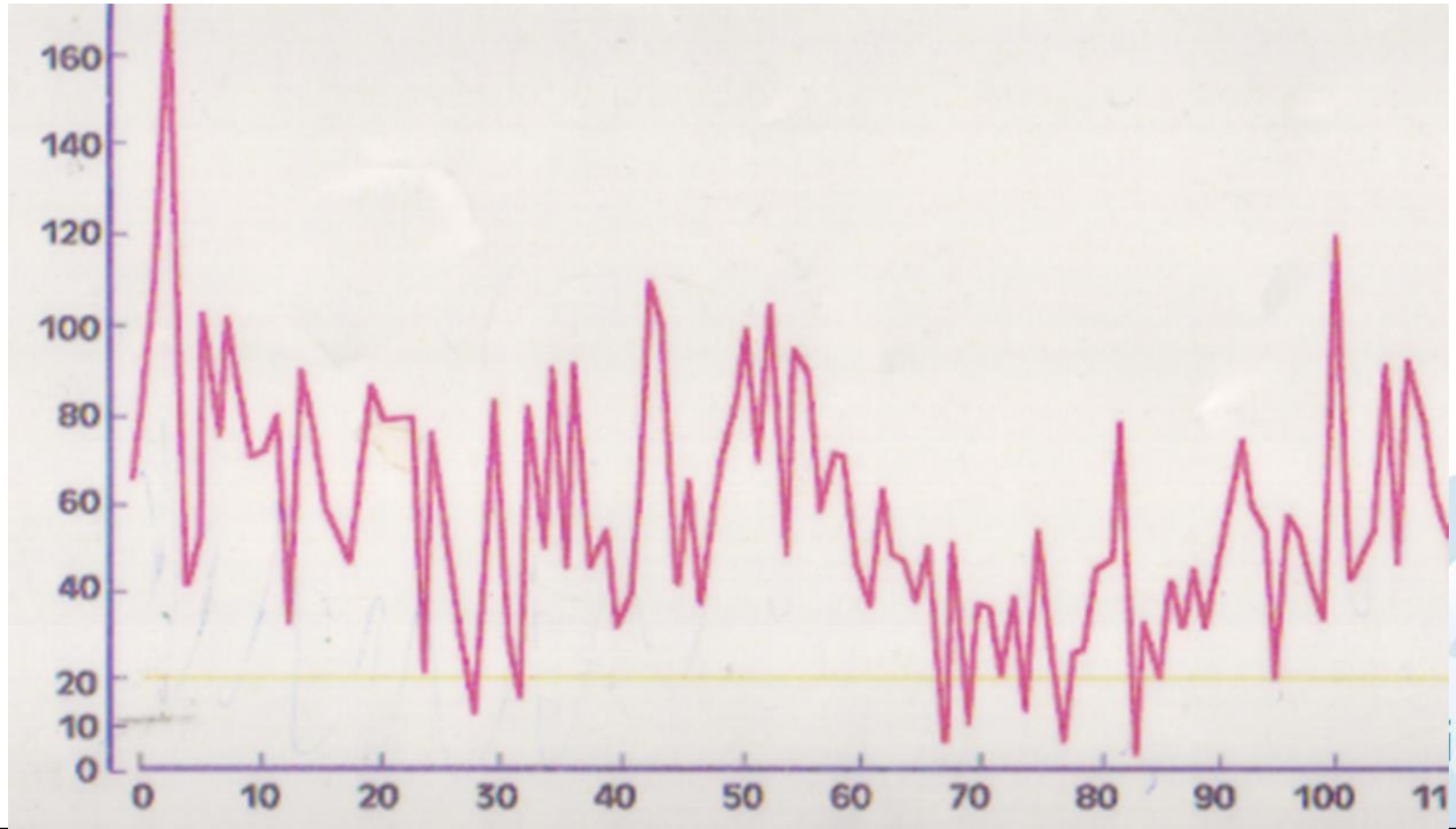
GP Investigations - Female

- Antenatal bloods
- If irregular cycles – Testo, SHBG, 17-OH prog
- Baseline FSH, E2
- Luteal prog
- Smear,swabs
- ? AMH
- USS – SIS or we can do



GP Investigations – Male

- Hep B,C,HIV
- Semen analysis – if abnormal, repeat

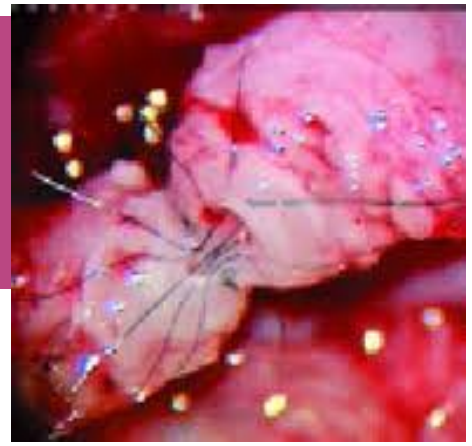


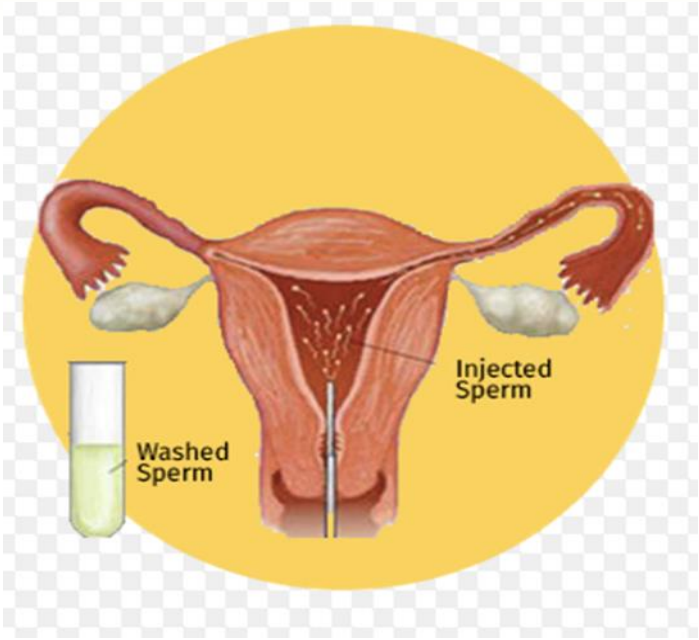
So … What happens Next?

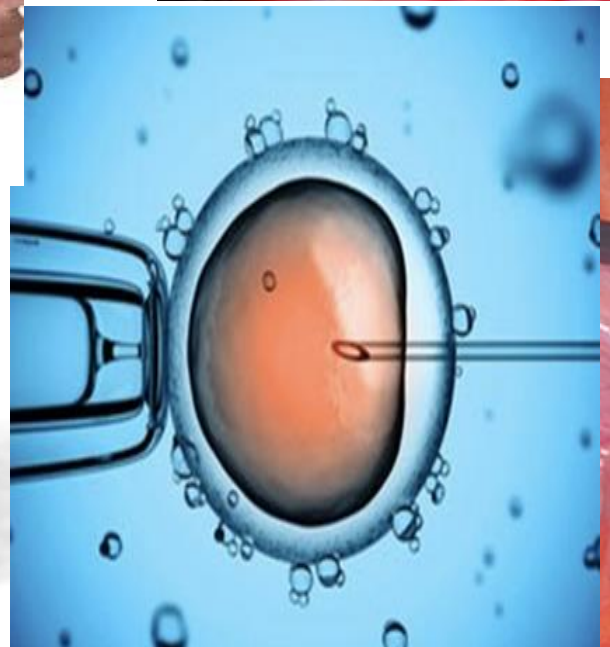
"And here we have the basis of our revolutionary new technique."

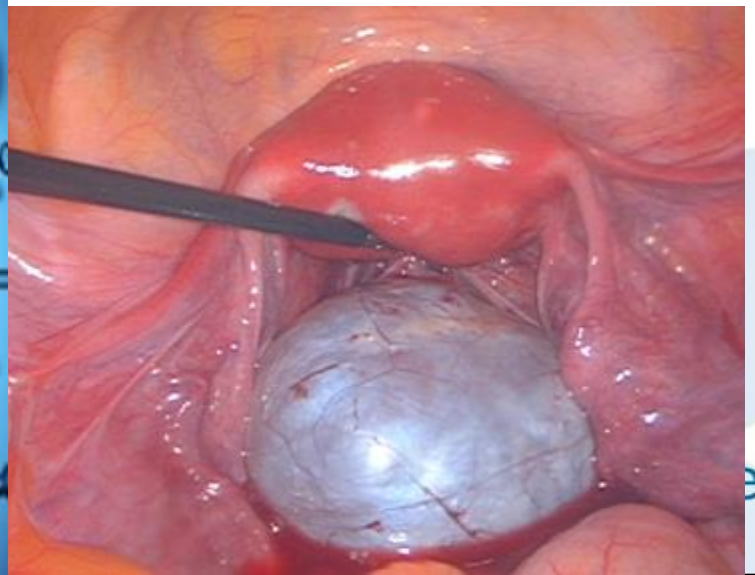
One of a few roads to take ...

IVF with Donor Eggs



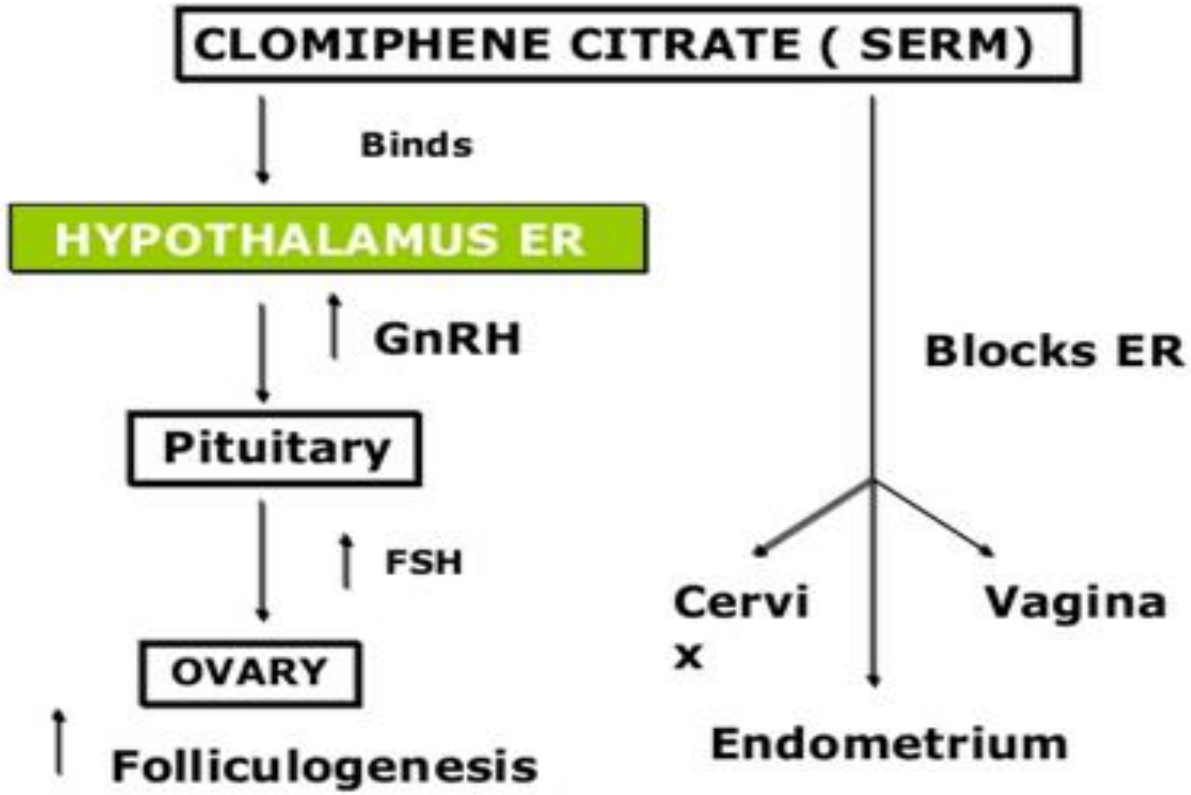




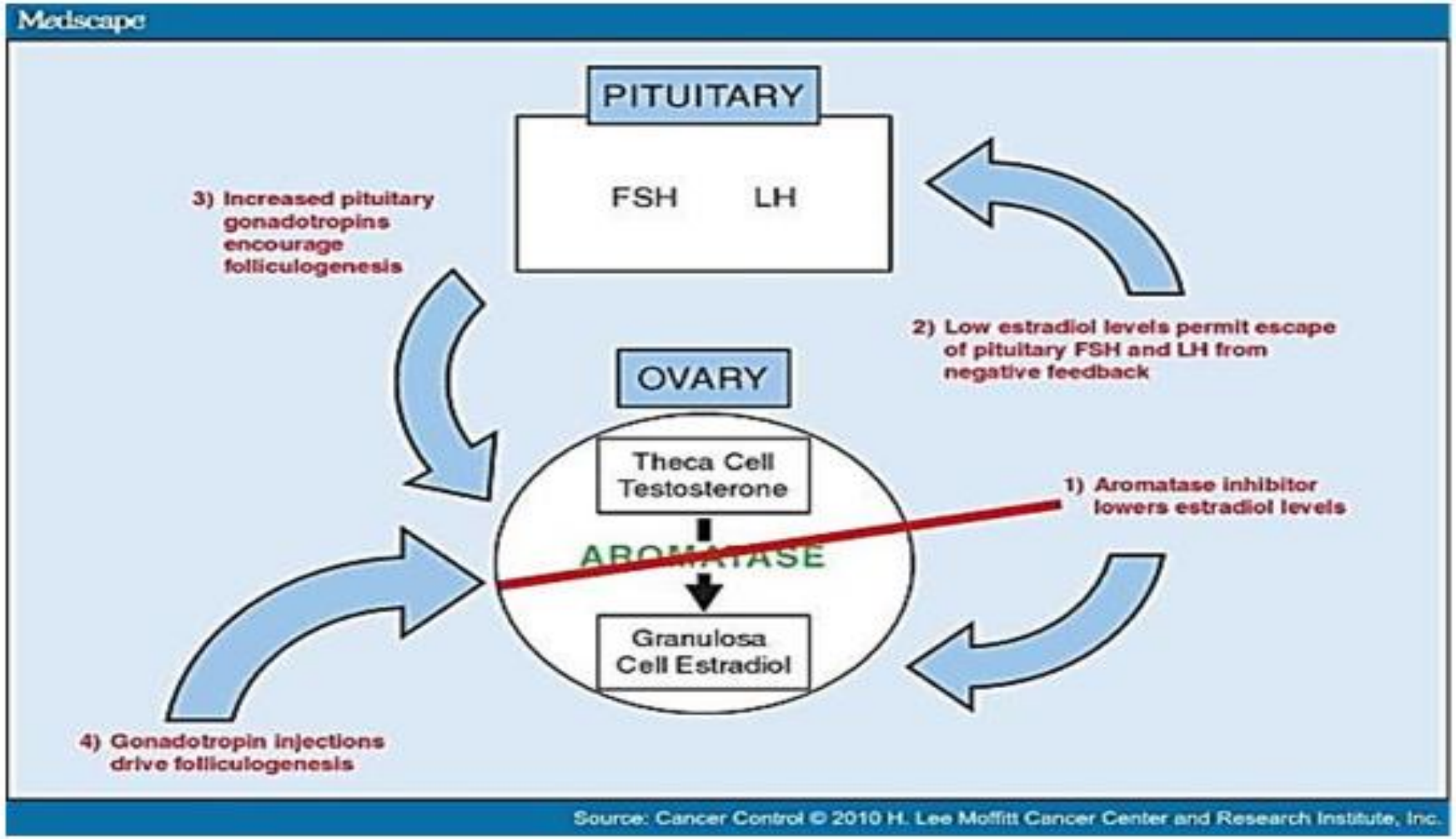


ertility

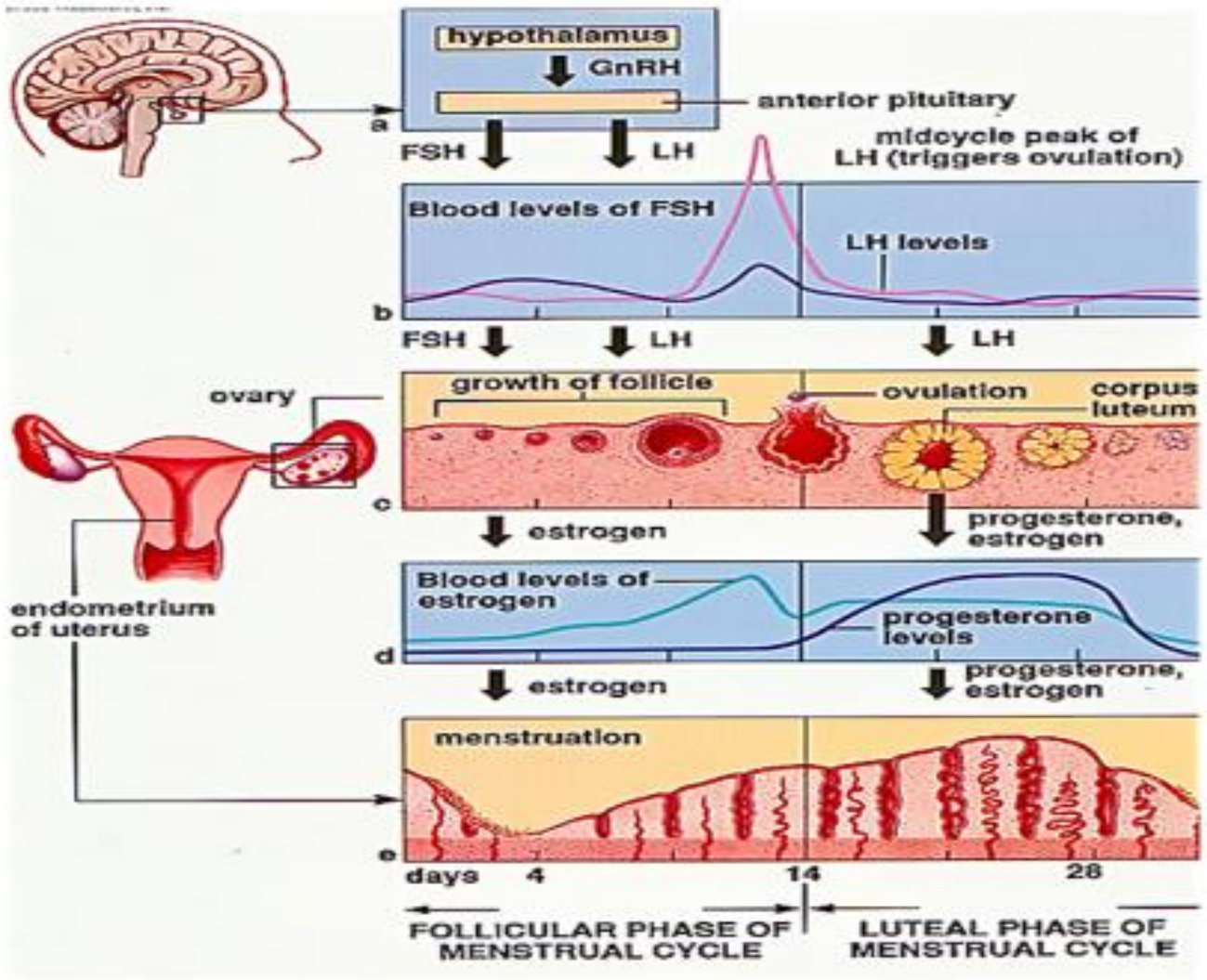
Ovulation Induction- Clomiphene



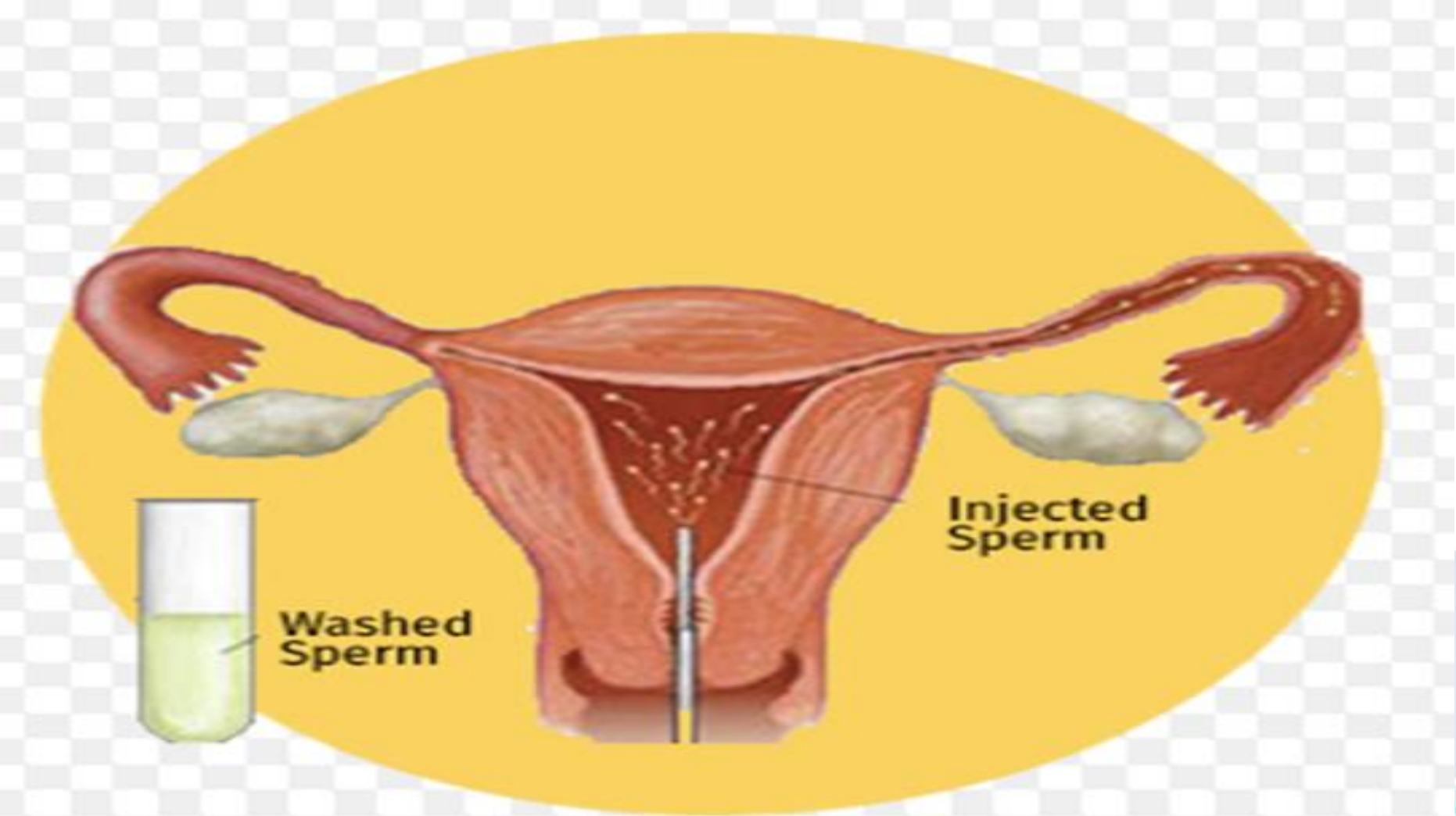
Ovulation Induction- Letrozole



Cycle Monitoring

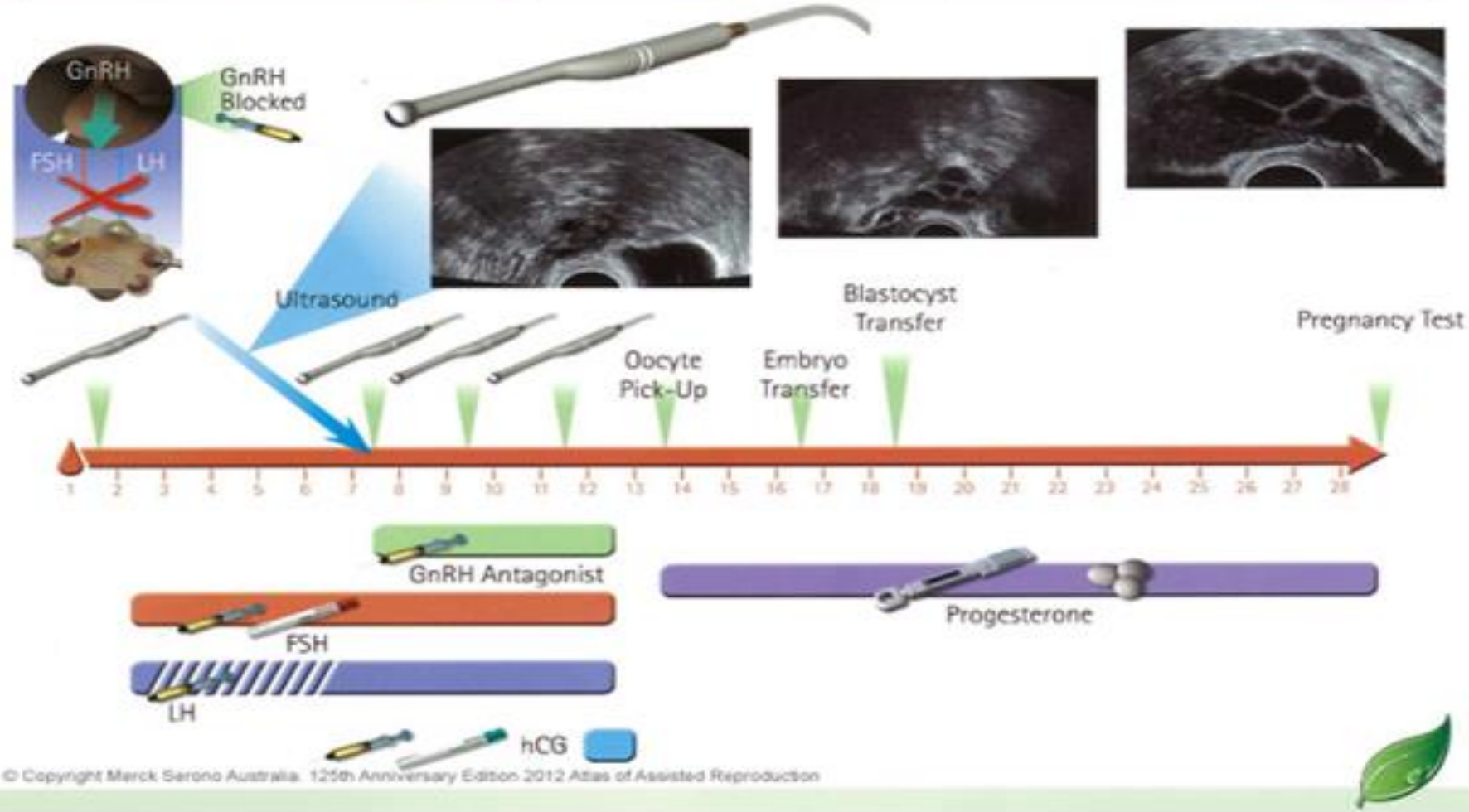


Intrauterine insemination

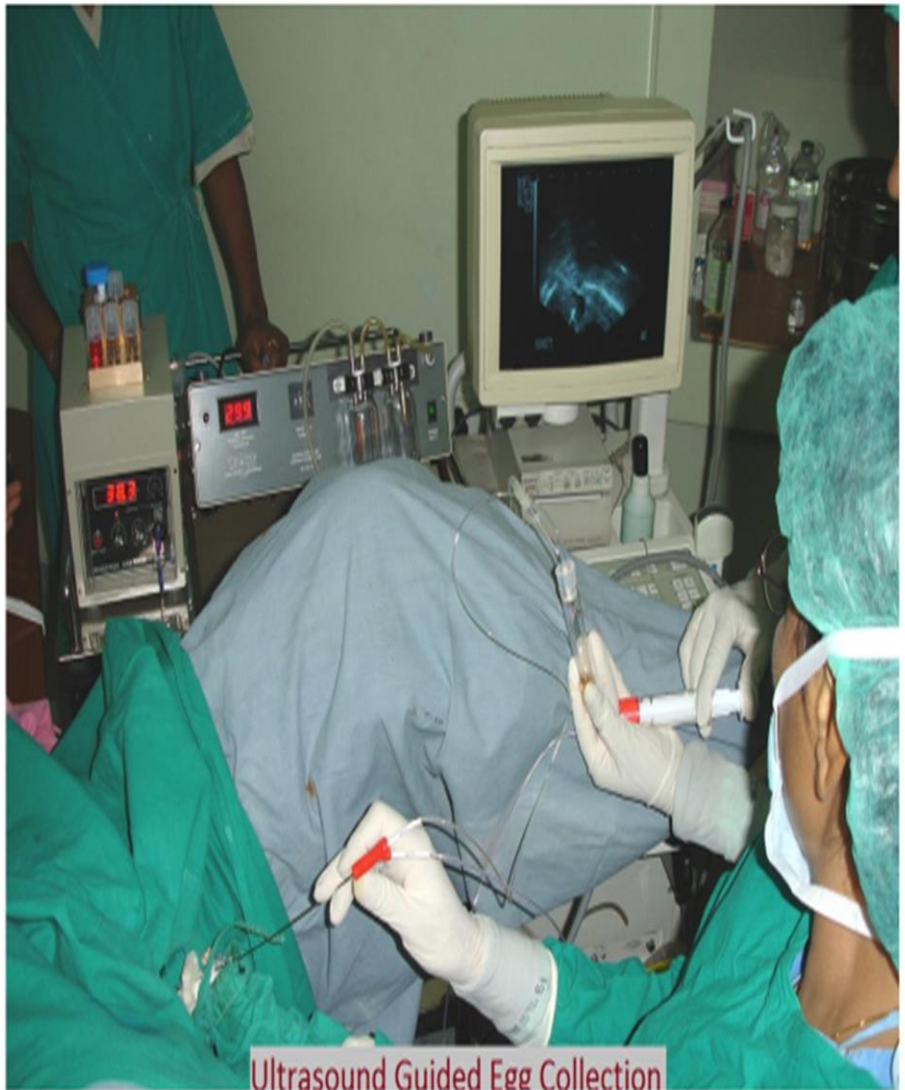


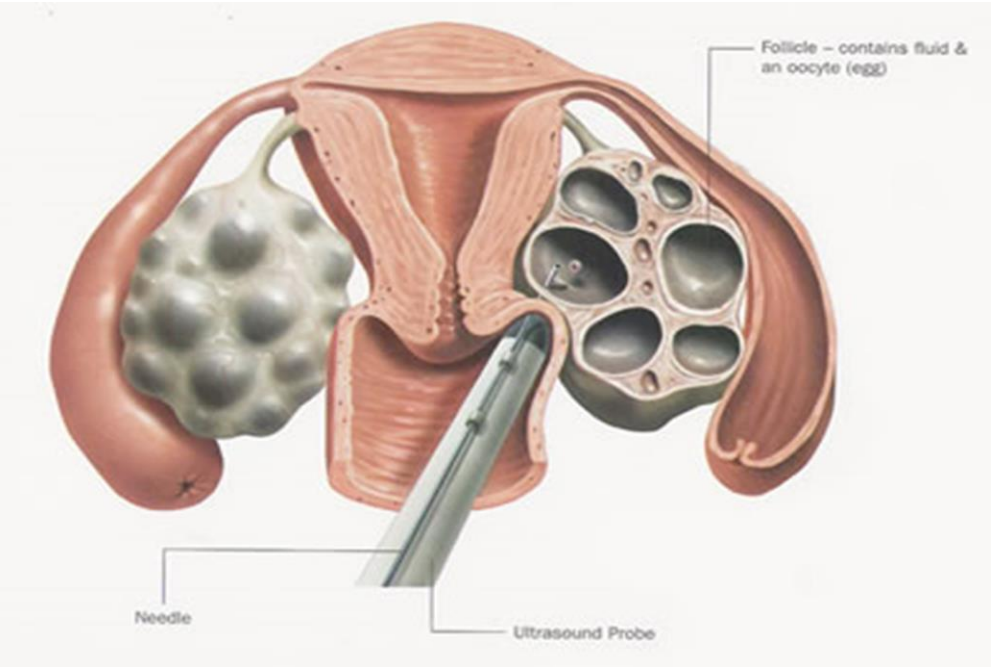
IVF Protocols – antagonist

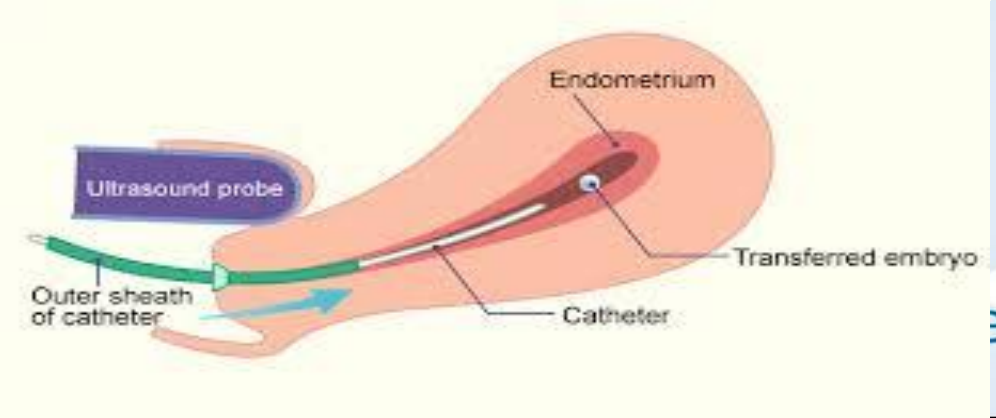
GnRH Antagonist Protocol



Egg Collection

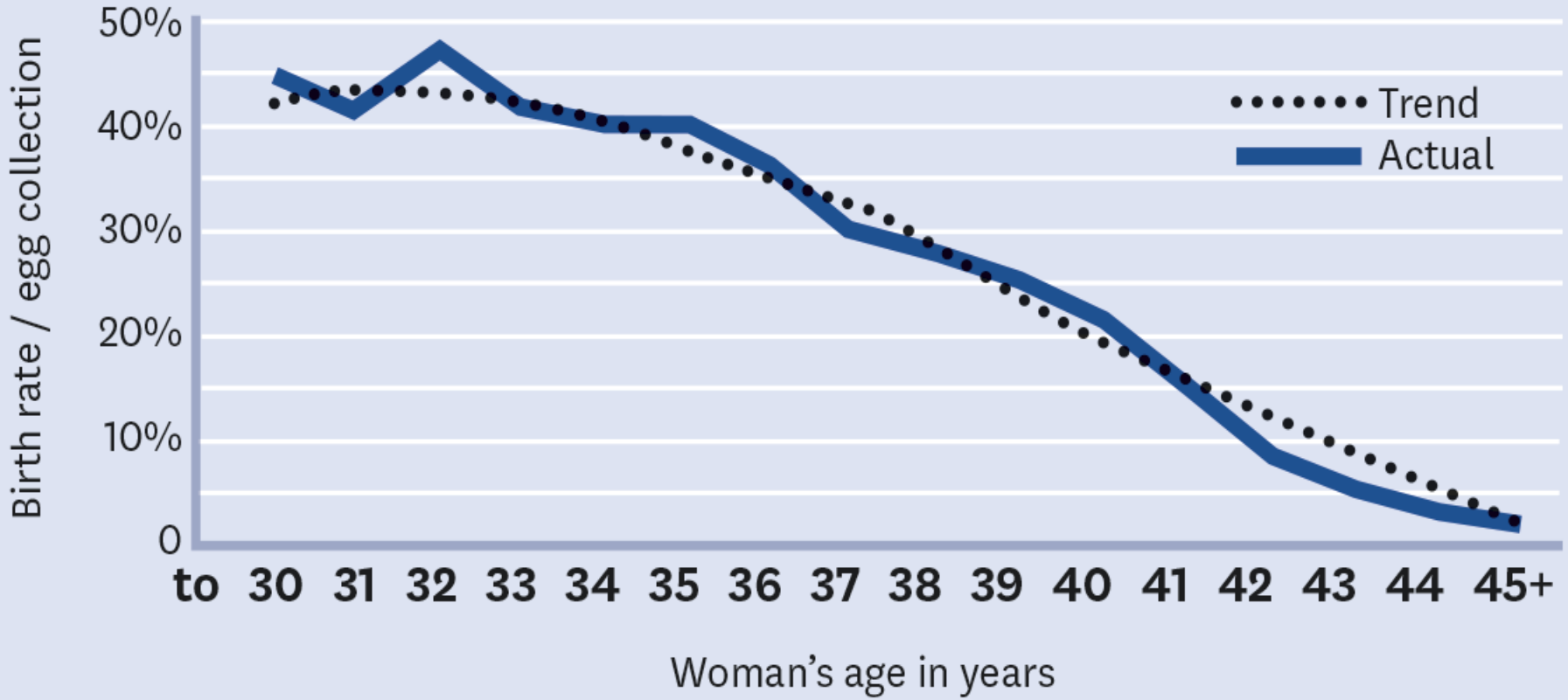






Birth rate from a single IVF egg collection

including use of any frozen embryos within 6 months



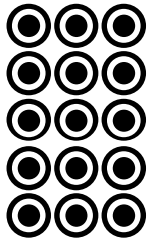
Egg Freezing – social or medical

How many eggs do I need?

- Studies demonstrate how many eggs are required per baby (50% chance)

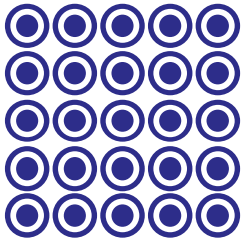
25-37 YEARS

10 eggs



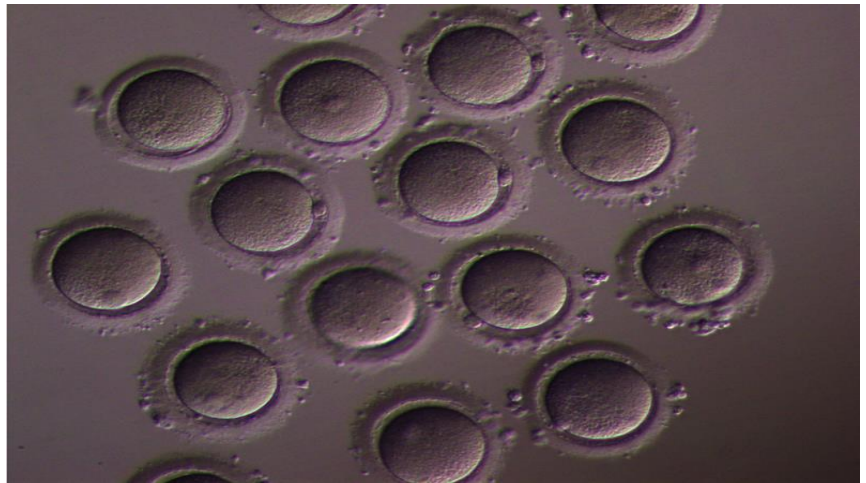
38-40 YEARS

15 eggs



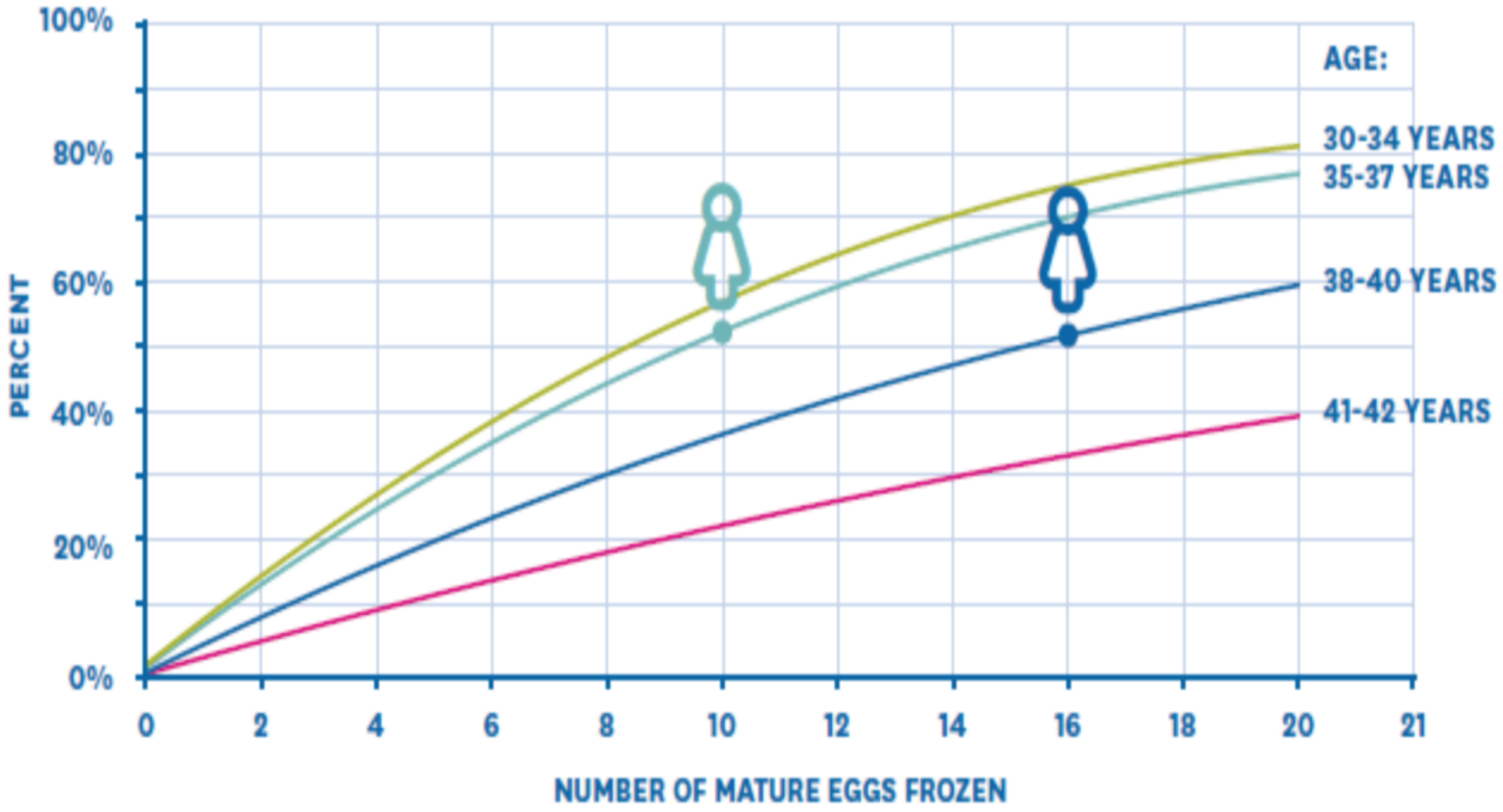
41-42 YEARS

25 eggs



FERTILITY associates

Predicted Chance of a Child by Number of Eggs Frozen (from Doyle et al 2016)



ertility

Take home messages

- Avoid depot provera
- Family Planning-Plan for your last child
- Have regular unprotected sex
- Make sensible lifestyle choices
- Assess risk factors & timely referral
- Consider Egg freezing

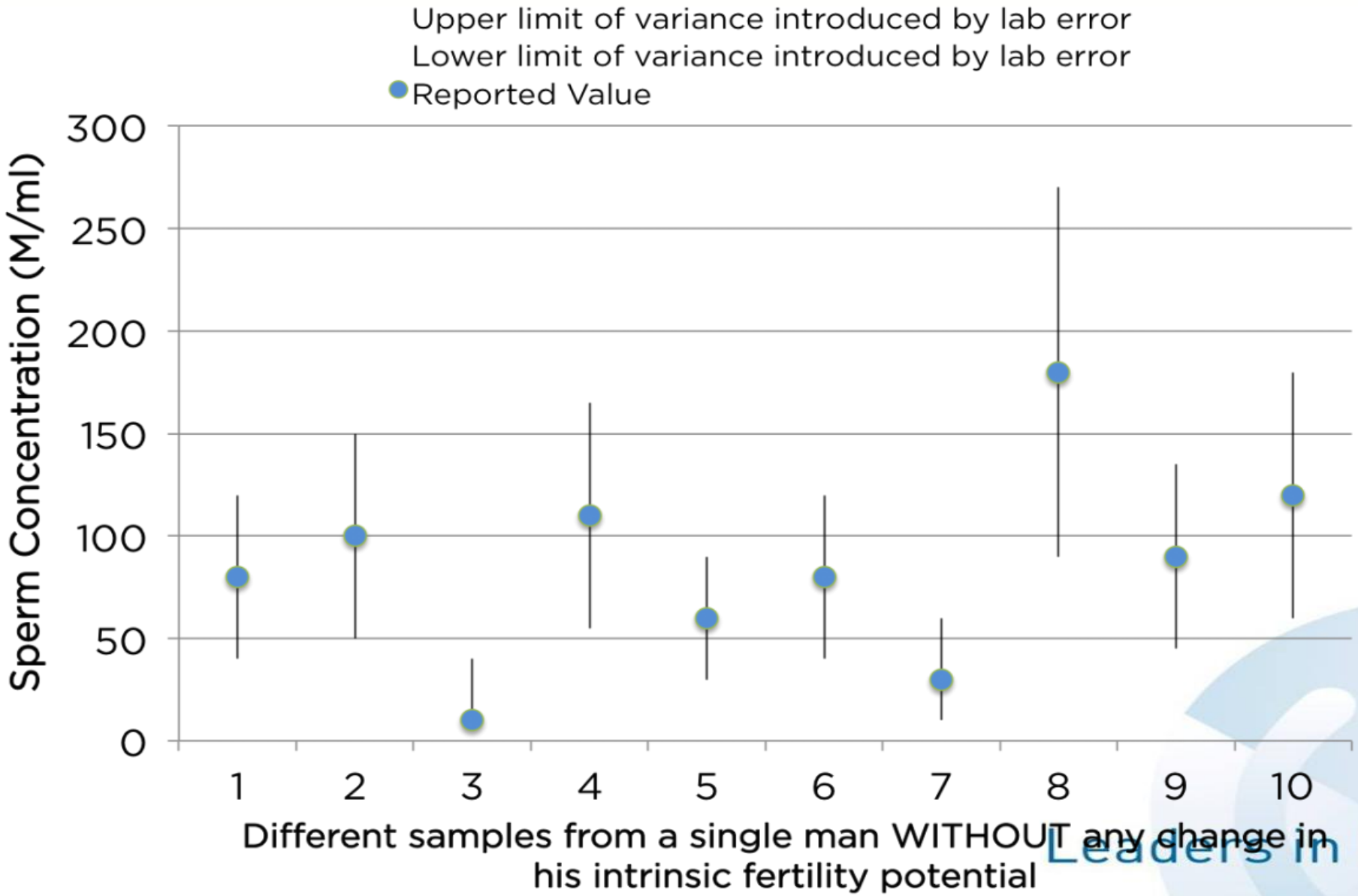
www.fertilityassociates.co.nz
www.yourfertility.org.au

Leaders in Fertility

Leaders in Fertility

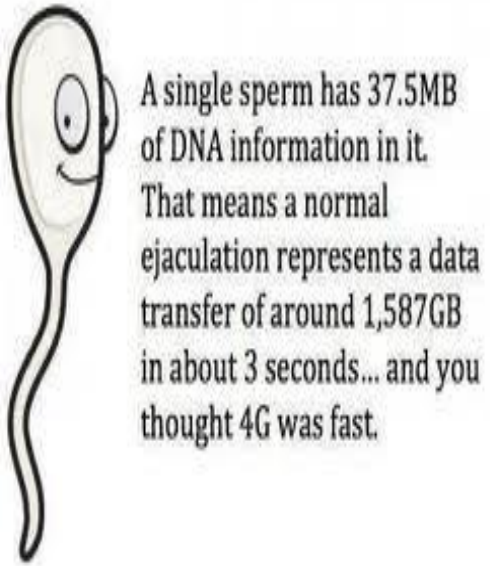
Leaders in Fertility

Leaders in Fertility

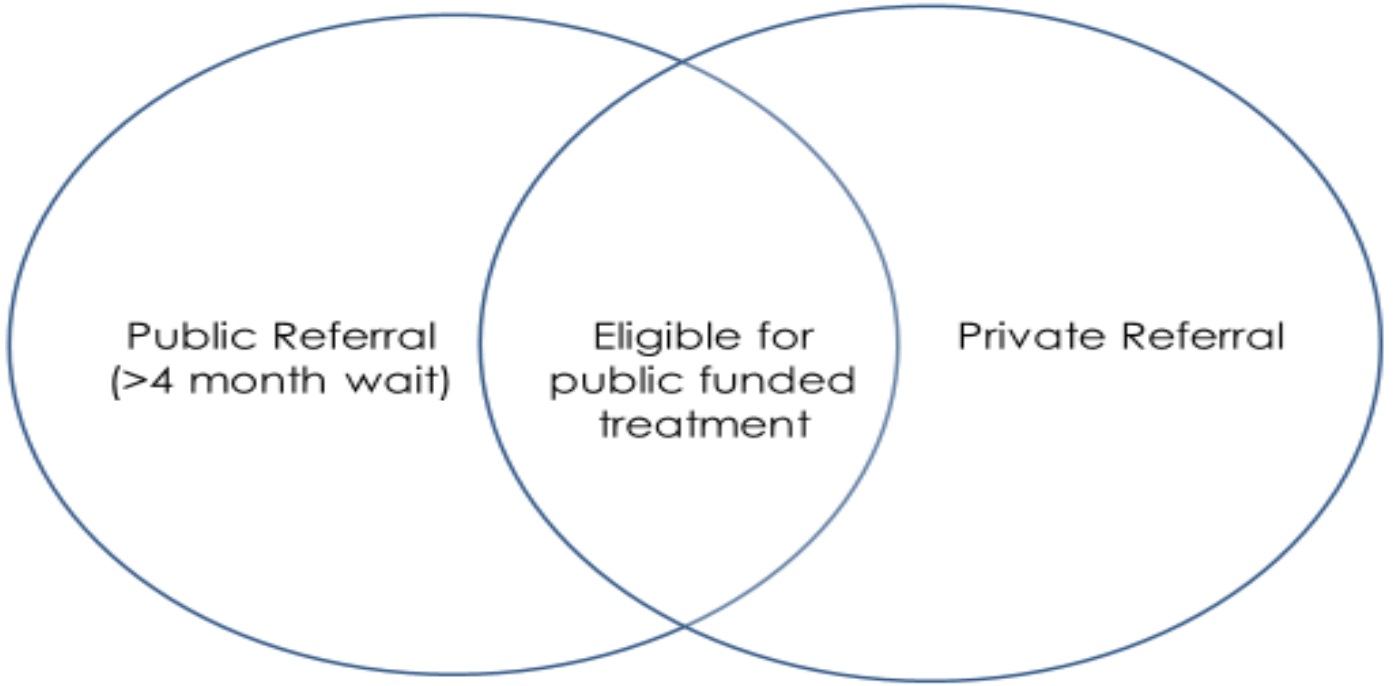

Upper limit of variance introduced by lab error
Lower limit of variance introduced by lab error
Reported Value
Sperm Concentration (M/ml)
300
250
200
150
100
50
0
1
2
3
4
5
6
7
8
9
10
Different samples from a single man WITHOUT any change in his intrinsic fertility potential

Semen Analysis

- 2-3 days abstinence
- Sample to lab within 60min
- WHO Criteria (2010)
  - Concentration > 15 Million/m
  - Motility > 40%
  - Morphology > 4% normal
- IF ABNORMAL REPEAT



Referral Pathway



We will always assess eligibility for funded treatment

CPAC SCORING SHEET – FAC, FAD

Ovulation	8	Anovulation due to hypogonadism/ Ovulatory but not pregnant after 9 months Rx/ Resistant to CC +/- Metformin +/- LOD
	3	< 9 ovulatory cycles/year
	0	Other
Male	8	Any of: Strict morphology < 4% Sperm concentration < 1 million/ml Sperm Mar > 40% positive >= 2 years since vasectomy reversal and not preg < 1 million motile after sperm wash IUI and < 2 million motile 3 x IUI for male infertility and not pregnant
	3	< 40% total motile or < 15 million/ml in 2 samples
	0	Other
Endo	6	Stage IV
	3	Stage III
	2	Stage II
	1	Stage I
	0	None
Tubal	8	Occlusion/ severe adhesions/ 12 months surgery
	3	Mod adhesions/ 6 months surgery
	2	Polyps/ mild adhesions/ normal tube one side
	1	Minimal adhesions best side
	0	No tubo-peritoneal pathology
Other	8	Severe
	3	Moderate
	2	Mild
	1	Minimal
	0	None

Name: Ref number:

Date scored: **Doctor scoring:**

Signature:

Height: **Weight:** **BMI:**

Date taken:
Day 3 FSH:
E2:

Smoker: Y / N
Onset of infertility (month/year):

IVF/ICSI IUI DI OI DO
(circle treatment, scoring can not be completed without treatment type)

Comments:

If for 1st FSA appointment 20 or 40 min required
Please circle appropriate duration

		Now	At:	At:
Duration of infertility = sum of all durations > 12 months without live birth	> 5 years	6	6	6
	≥ 4 and < 5 years	3	3	3
	≥ 3 and < 4 years	2	2	2
	< 3 years	1	1	1
Total diagnostic score				

	OBJECTIVE CRITERIA		Points	Now	At:	At:
Diagnostic (O1)	Total diagnostic score	≥ 6	10			
		3 – 5	7			
		2	4			
		0 – 1	2			
Woman's age (O2)		≤ 39 y	10			
		= 40, 41	5			
		≥ 42 y	1			
Objective score	*OS = O1 x O2 ÷ 100*					
	SOCIAL CRITERIA					
Duration of infertility over time (S1)	Less than 1 year		5			
	1 or 2 years		20			
	3 or 4 years		40			
	5 years or more		50			
Children at home (50% of time or more and under the age of 12. (S2)	None		50			
	1 by relationship		10			
	1 by previous relationship		8			
	+ 2 or more children at home excludes eligibility					
Sterilisation (S3)	Neither partner		20			
	One or both partners		10			
Social score	*SS = S1 + S2 + S3*					
FINAL SCORE	*=OS x SS*					

FERTILITY associates | a better understanding
TE RAUHANGA O TE WHARETANGATA

We have 18 fertility clinics across the country

Clinics


Auckland


Hamilton


Wellington


Christchurch


Dunedin

Other locations

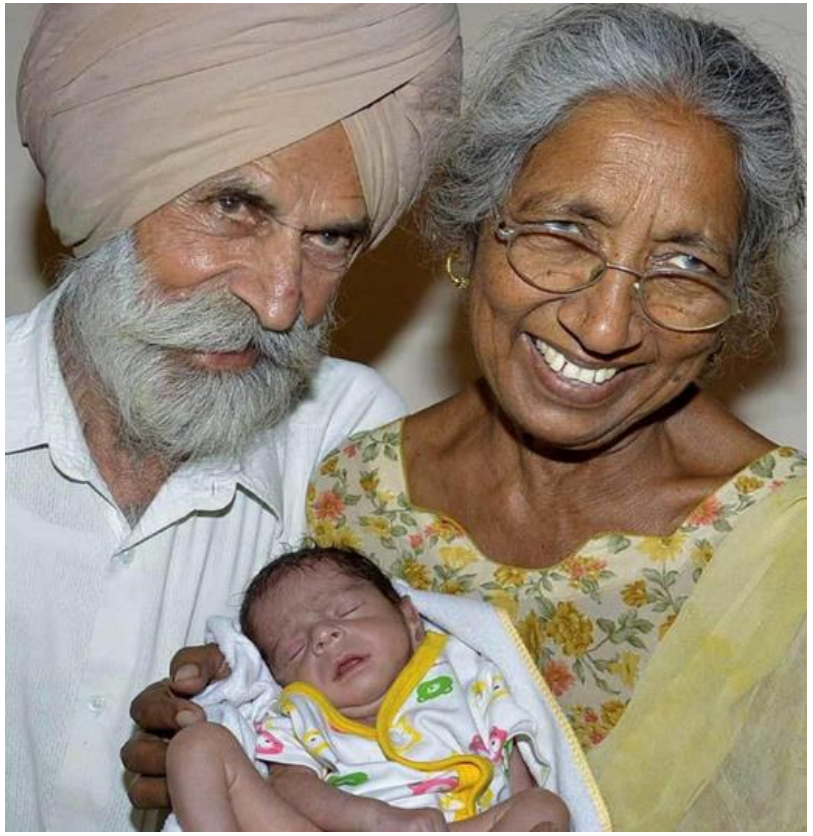
Auckland – Remuera
Auckland – Albany
Auckland East
Wellington
Hawke's Bay
Whanganui
Dunedin
Invercargill
National Management Group

Auckland - Karaka
Auckland West
Whangarei
Palmerston North
Gisborne
Lower Hutt

Hamilton
Tauranga
New Plymouth
Christchurch
Nelson
Cromwell / Queenstown
Fertility Associates Board

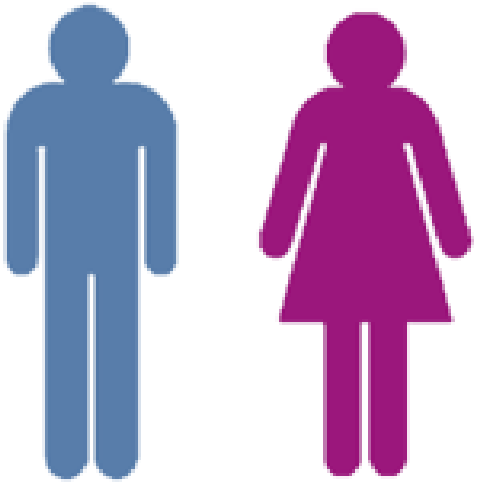
ertility

Female Age



Causes of Infertility

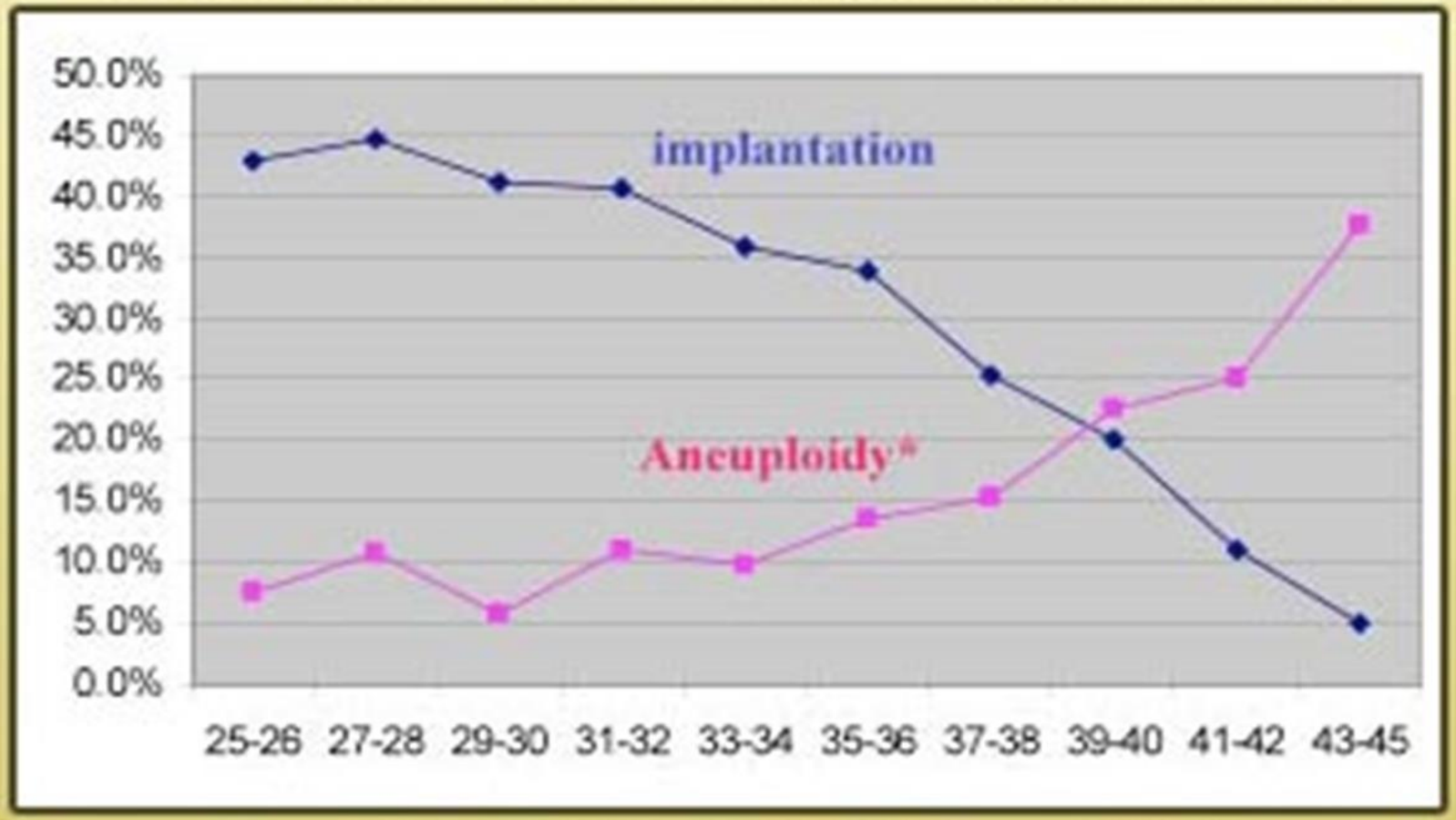
Male	40%
Female	40%
Combined/unknown	20%



Childlessness- Census Data

Woman's Age	1981	1996	2006
40-44	9 %	12 %	16 %
45-49	9 %	10 %	13 %

CHROMOSOME ABNORMALITIES CONTRIBUTE TO LOW IMPLANTATION

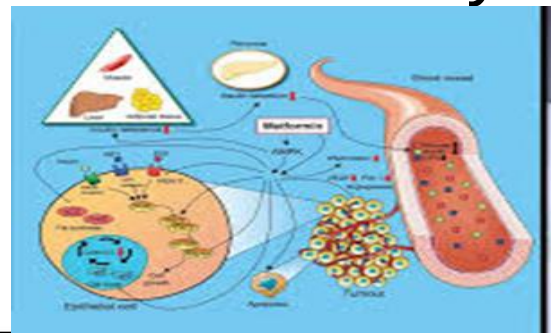


*Aneuploidy for XY,13,15,16,18,21,22 (Munne et al 2004)


2014
2015
2016

Metformin

- Use if T2DM or IGT
- Consider if want weight loss and fertility
- Can use for PCOS, but can take a number of months to work
  - If not having menses – unlikely to be working, also no endometrial protection
- May increase sensitivity to OI meds
- Side - effects can limit use - start slowly



So … What happens next?

Specialist tests for male infertility

- Semen analysis at FAC – antibodies, morph
- Swabs/urine for STIs
- If azoospermic/severe oligospermia
  - FSH, LH, testosterone (prolactin, TSH)
  - Genetic tests (specialist level)
- Scrotal USS
  - Masses
  - Varicocoeles
  - Testis volume, vas present