Family planning after a diagnosis of cancer … What's the next step?

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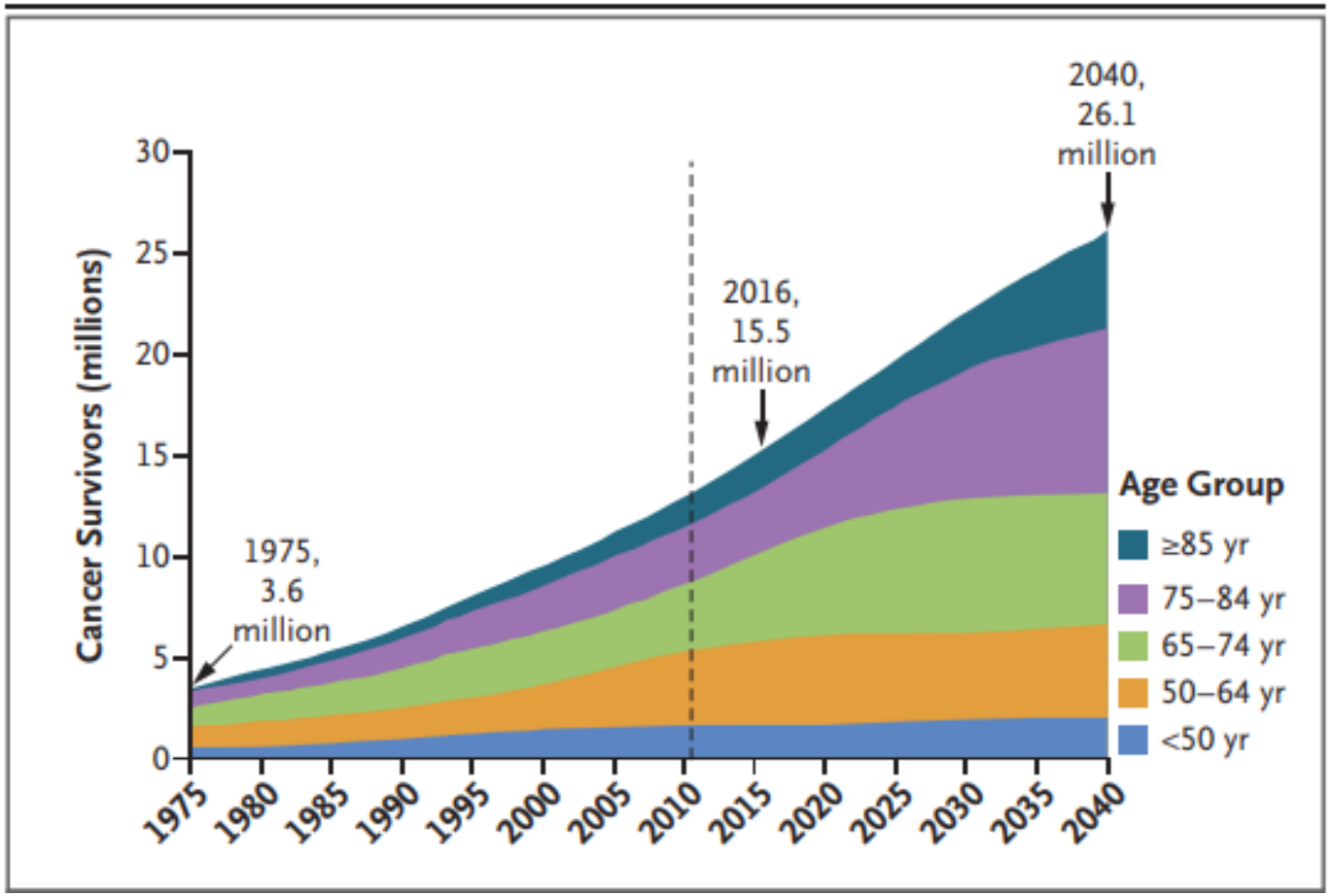
Better Treatment = Better Survival



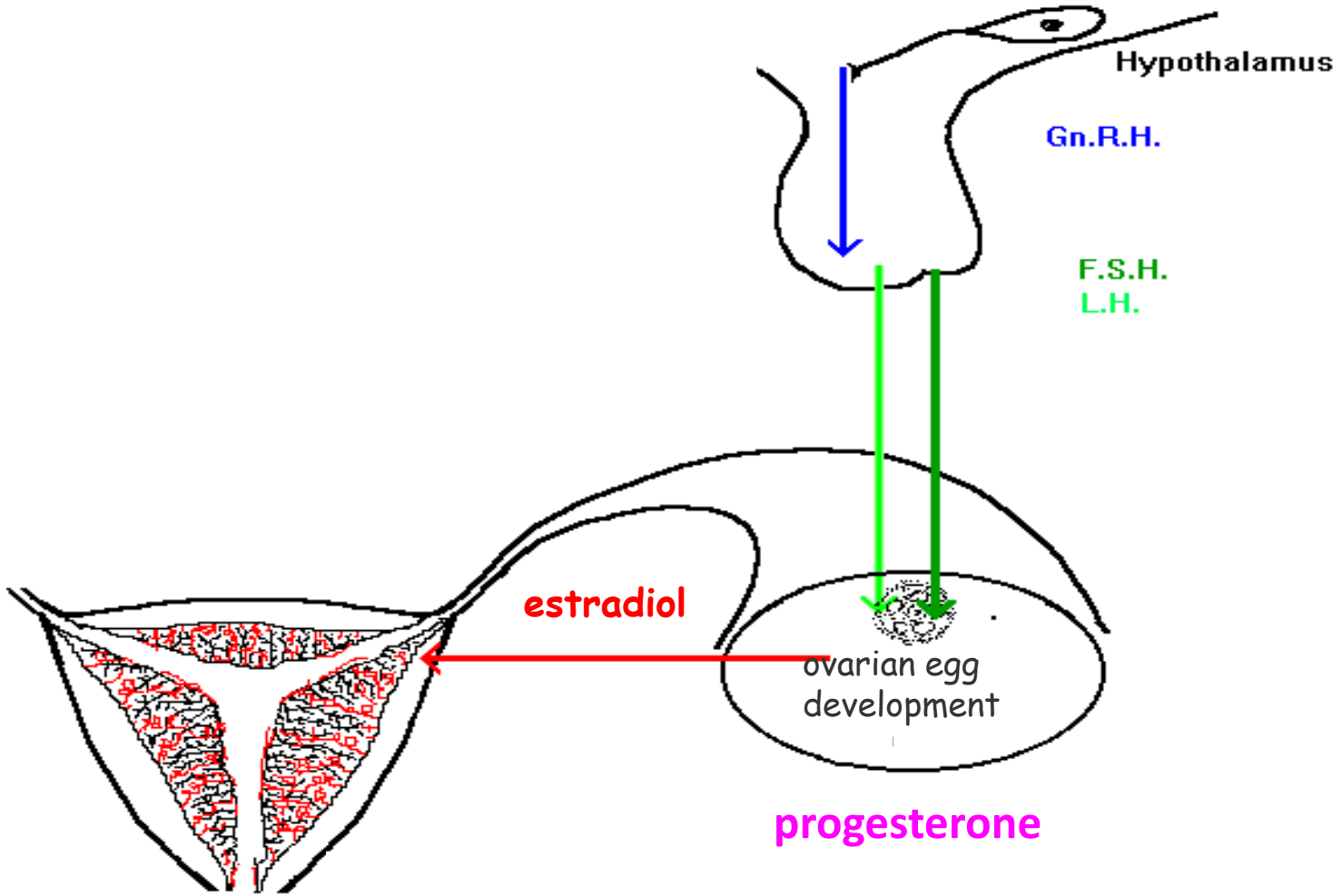
LIVING AFTER CANCER—NOT JUST SURVIVING

To be discussed..

- What determines the chance for a future pregnancy?
  - Basic fertility facts
  - Ovarian reserve
  - Cancer diagnosis
- Which treatments modify the chance for pregnancy?
- Which family planning options exist for women with a history of cancer?
  - Spontaneous pregnancy
  - Assisted Reproduction
  - Third Party Reproduction
  - Adoption
- What are the risks for pregnancy risks after a diagnosis of cancer?

FERTILITY AND FAMILY PLANNING BASICS: NEED TO KNOW FACTS

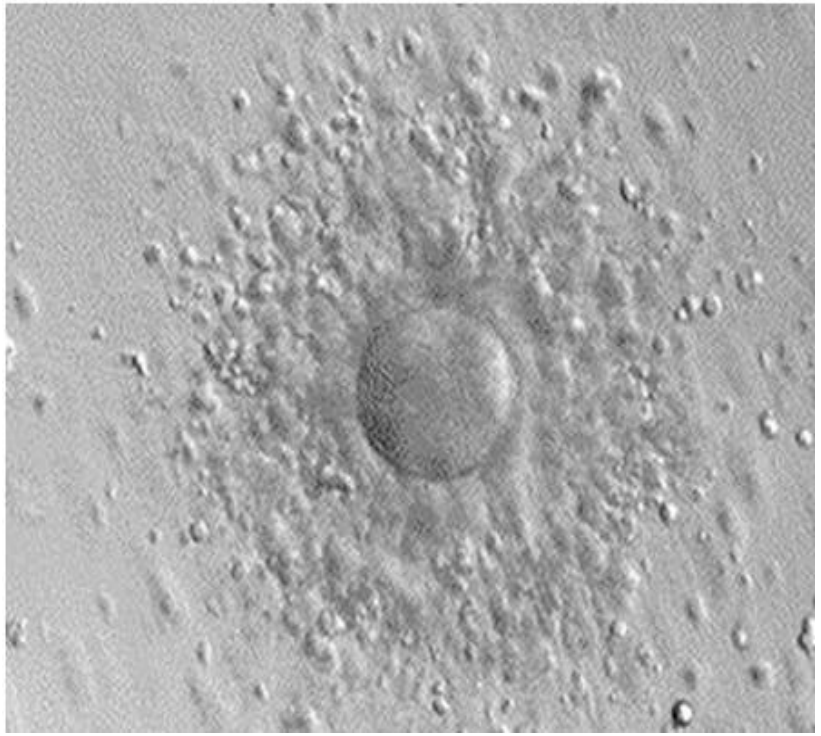
COMMUNICATION BETWEEN THE BRAIN-OVARY AND UTERUS IS CRITICAL FOR FERTILITY



DID YOU KNOW THAT……

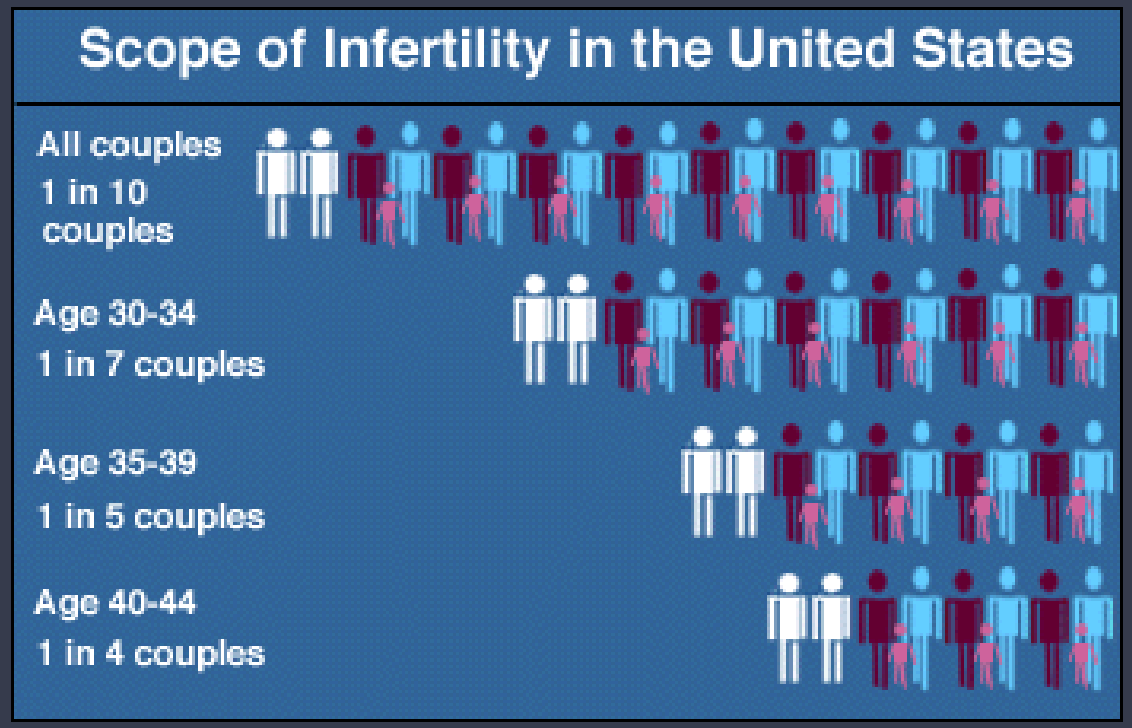
1. **The women amass their greatest number of eggs before birth (6-7 million)**
2. **At birth, the ovaries house about 1 million eggs**
3. **By the 1st menses about 300-400,000 eggs remain**

The average woman will release between 300-400 eggs over a lifetime



Broekmans et al., Endocrine Reviews 2009

Not all eggs are good=AGE matters

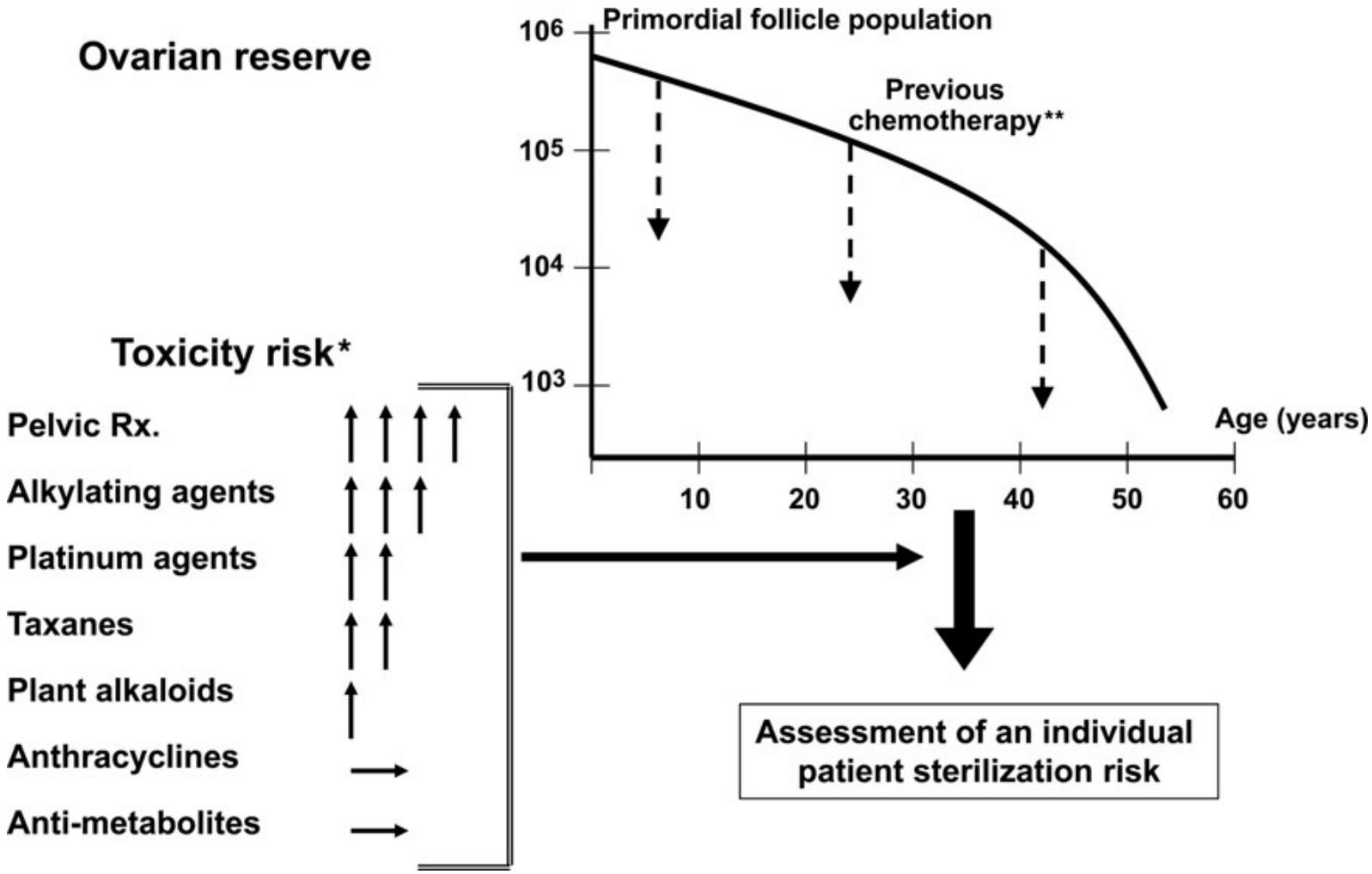


Maternal Age at Delivery	Risk of Miscarriage	Abnormal oocyte	Abnormal embryos
30	12	<40	<55
35	16	40	56.4
38	22	49	71.4
40	33-40	59	74.5
45	60	70	80.9

*Hook EB. Cross PK. Schreinemachers DM. (1983) Chromosomal abnormality rates at amniocentesis and in live-born infants. JAMA, 249(15):2034-8. *Hook EB. (1981) Rates of chromosomal abnormalities at different maternal ages, Obstetrics & Gynecology, 58(3):282-5.

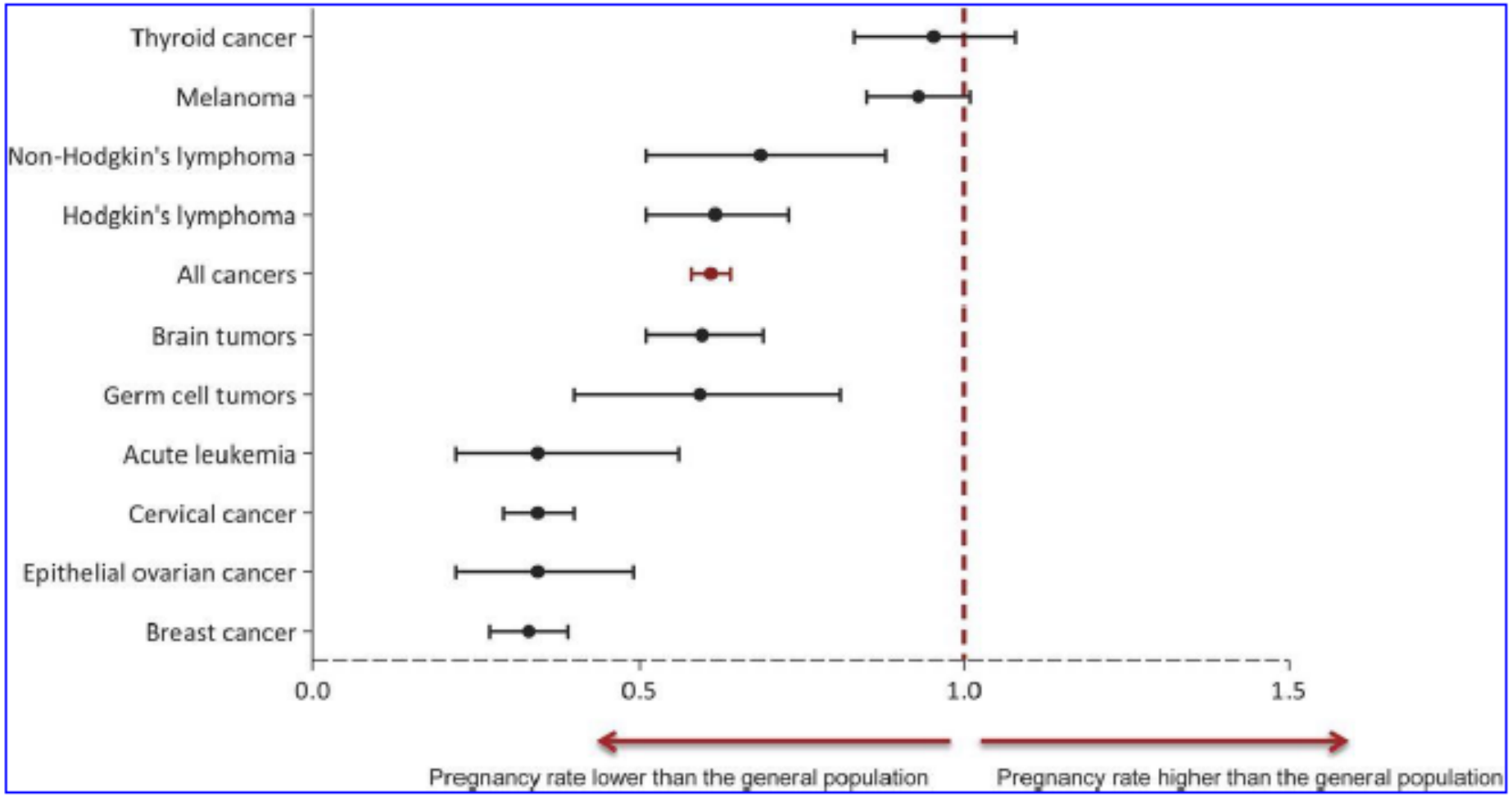
Modifiers of pregnancy success in women with a history of cancer therapy

RISK OF OVARIAN FAILURE POST-CHEMOTHERAPY




Does my history of cancer and cancer therapy affect my chance for pregnancy?

PREGNANCY RATES AND CANCER



- Stensheim H et al, Inter J of Cancer 2011.

CUMULATIVE PROBABILITY OF 1ST PREGNANCY AFTER CANCER DIAGNOSIS

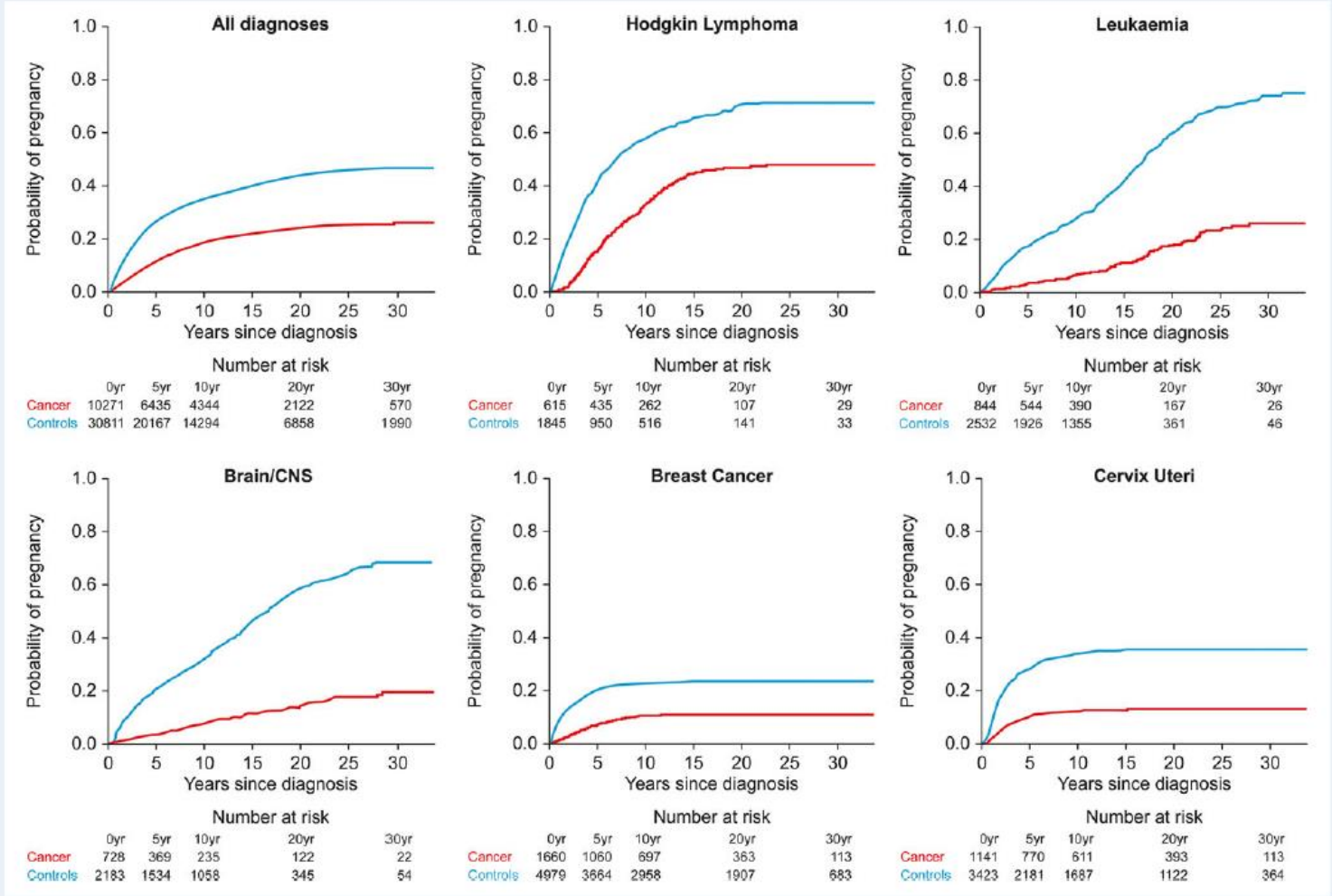


Figure 2 Cumulative probability of first pregnancy after cancer diagnosis (red) in all women with cancer compared to population controls (blue), and in women with breast, cervical, brain/CNS cancers, Hodgkin lymphoma and leukaemia. Tables under each panel indicate the number of women with cancer and controls at the time of diagnosis, and at subsequent time points up to 30 years.

Andersen et al., Human Reproduction 2018

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CUMULATIVE PROBABILITY OF 1ST PREGNANCY AFTER CANCER DIAGNOSIS

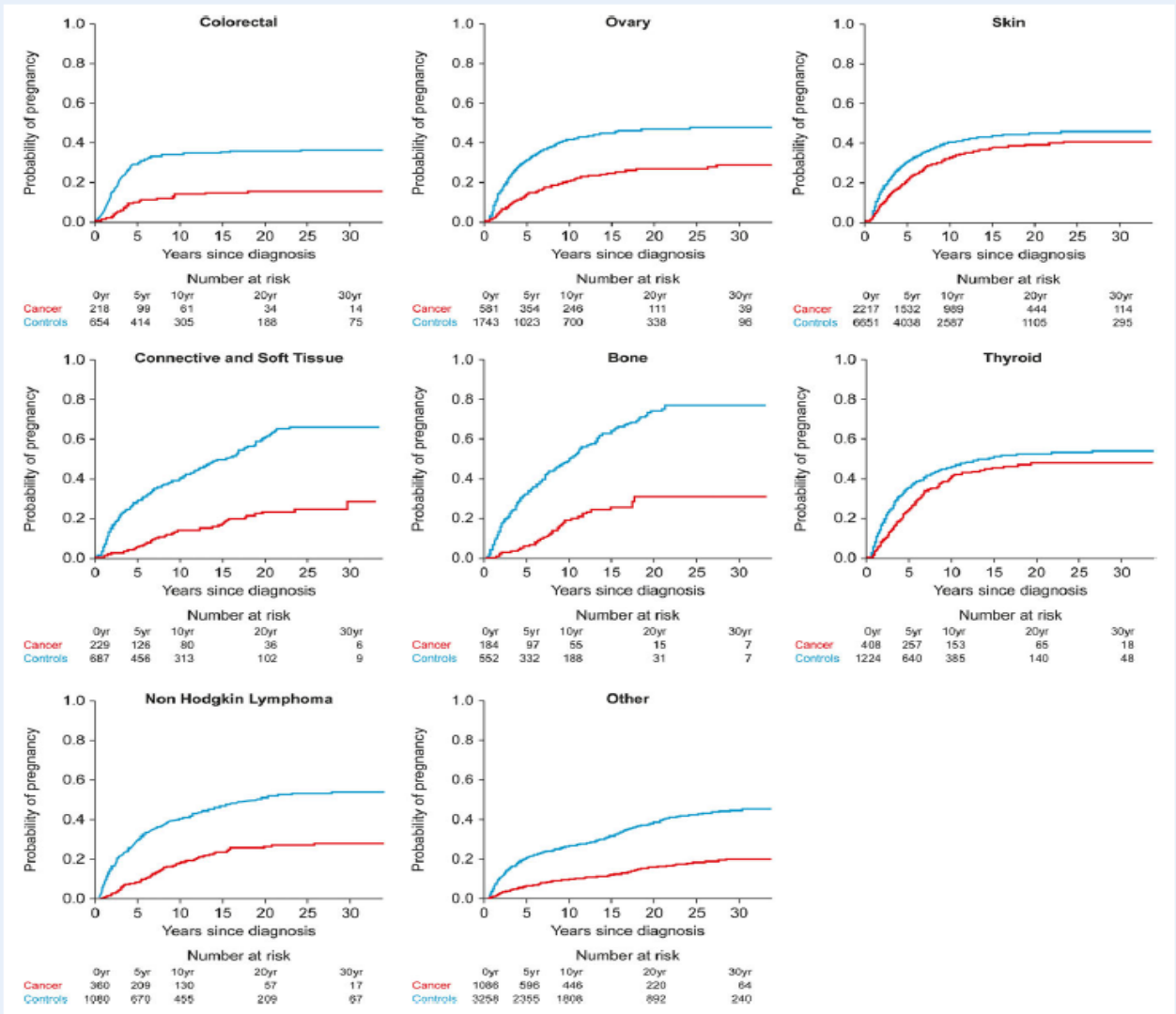


Figure 3 Cumulative probability of first pregnancy after cancer diagnosis (red) in women with diagnoses other than those shown in Fig. 2 compared to population controls (blue). Tables under each panel indicate the number of women with cancer and controls at the time of diagnosis, and at subsequent time points up to 30 years.

Andersen et al., Human Reproduction 2018

What is my best path forward when I want to start a family?

BIG questions???

- Is it OK to get pregnant after being treated for cancer?
- Can I get pregnant on my own and with my own eggs?
- Do I have enough eggs remaining in my ovary to get pregnant?
- Is my uterus OK to carry a pregnancy after pelvic radiation?
- Am I at increased risk for miscarriage?
- Can I breast feed after receiving whole body or chest radiation?
- What do I do if I do not have my own eggs?


Is it OK for me to be pregnant?

POTENTIAL RISKS TO PREGNANCY AFTER CANCER

Anatomical Region Affected	Cause/Therapeutic Exposure	Potential Risk	Screening/ Management
Cardiac Function	Chemotherapy • Anthracyclines Radiation • Mediastinal or chest • Scatter from abdominal	Restrictive or dilated cardiomyopathy and congestive heart failure • 1st and 3rd trimester of pregnancy and Postpartum	• Echocardiogram • ECG • Preconception consultation with MFM • Monitoring by MFM • Gestation carrier
Musculoskeletal	Radiation Pelvic and Abdominal	• Dysfunction labor	• Preconception consultation with MFM • Monitoring by MFM • Gestation carrier

POTENTIAL RISKS TO PREGNANCY AFTER CANCER THERAPY

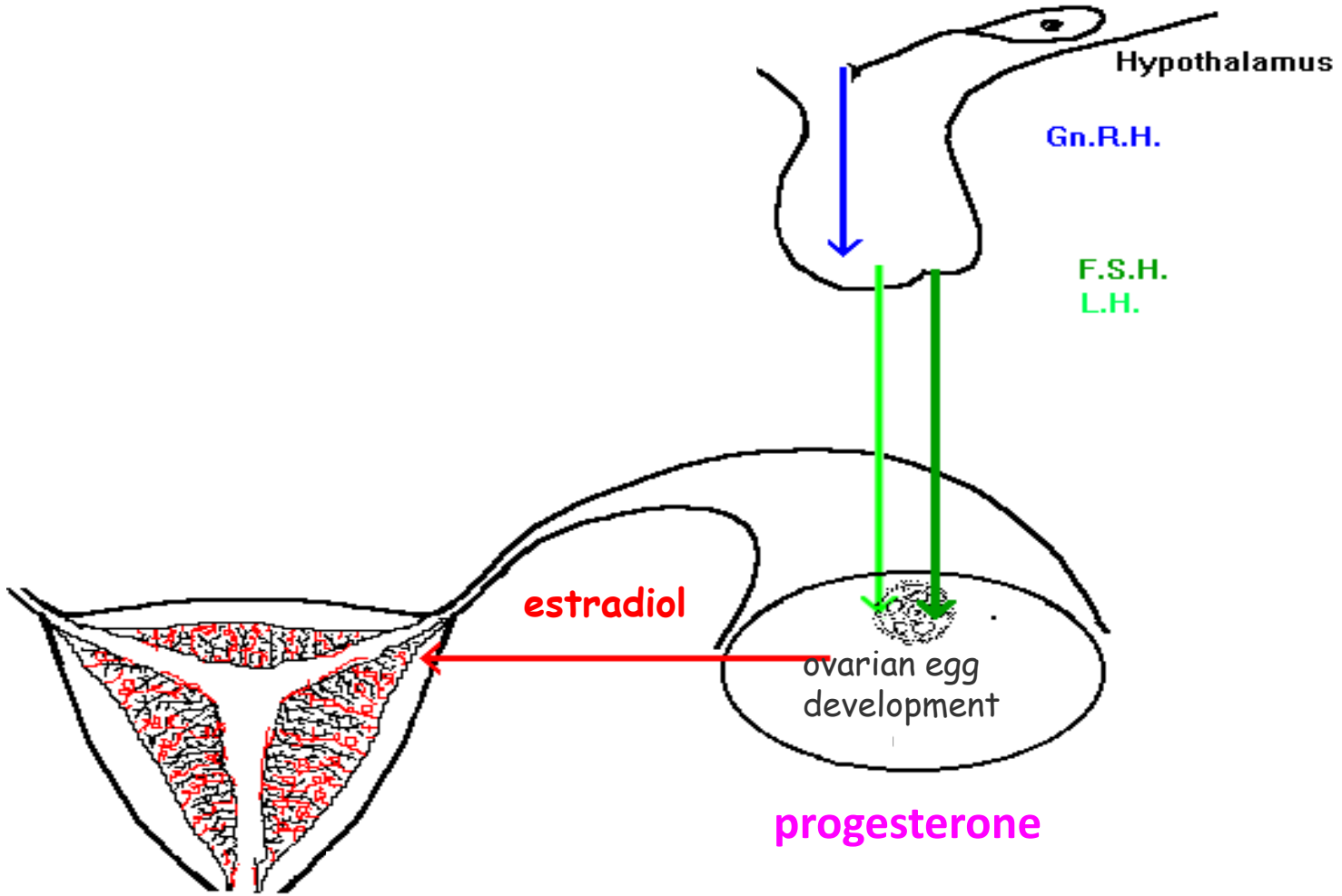
Anatomical Region Affected	ng/ ement
Pulmonary	ary Function onsult esia consult
Uterus	onception ultation itoring by MFM ation carrier

Toxicity Bear:

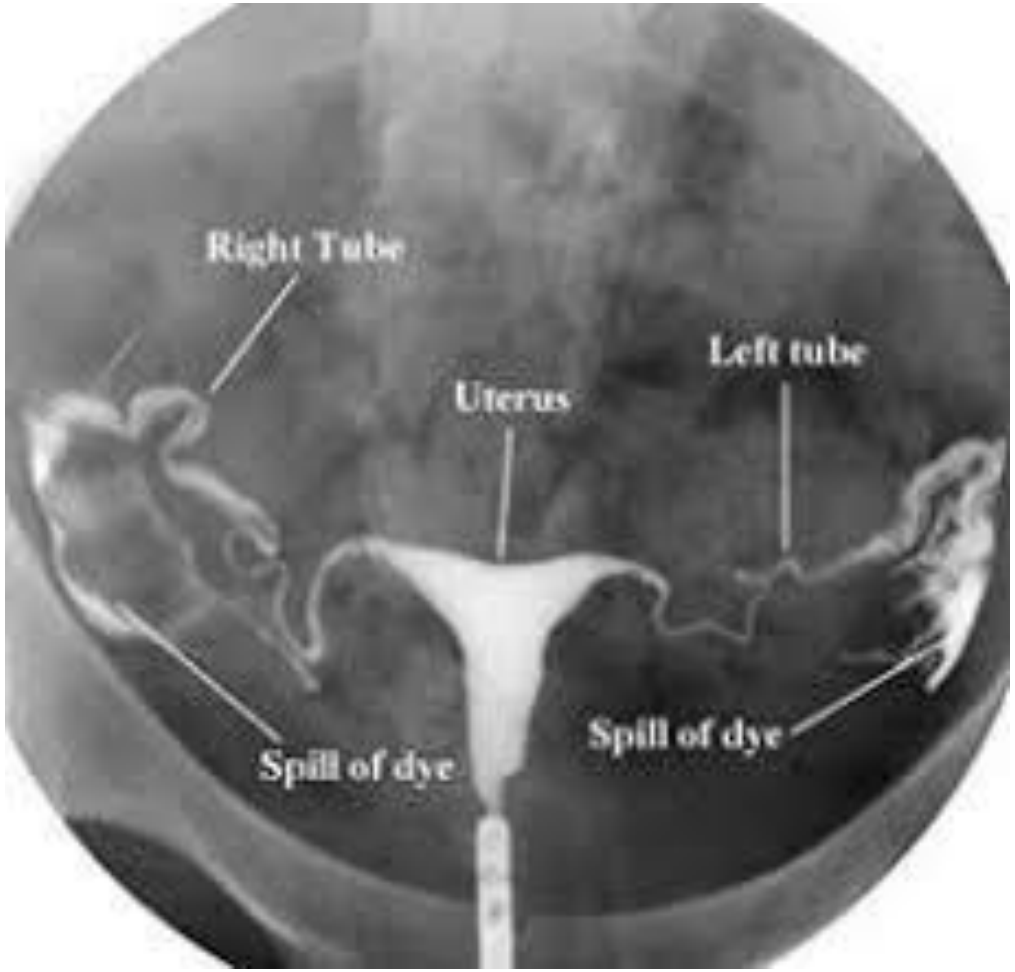
A = Asparagine
C = Cisplatin
V = Vincristine/Vinblastine
B = Bleomycin
D = Doxorubicin
Psi = Cyclophosphamide
M = Methotrexate


Can I get pregnant on my own and with my own eggs?
Do I have enough eggs in my ovaries to get pregnant?

COMMUNICATION BETWEEN THE HPG AXIS IS CRITICAL FOR FERTILITY.



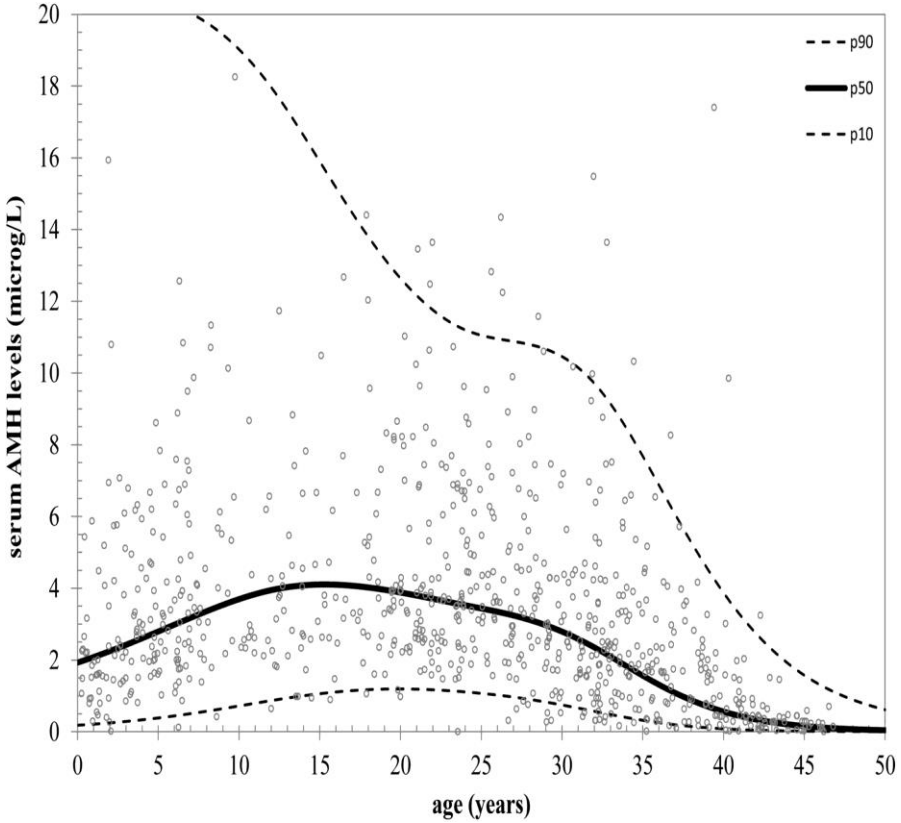
PATIENTS WITH A HISTORY OF PELVIC SURGERY SHOULD HAVE A HYSTEROSALPINGOGRAM



Ovarian Retirement Fund

ANTRAL FOLLICLES

AMH NOMOGRAM

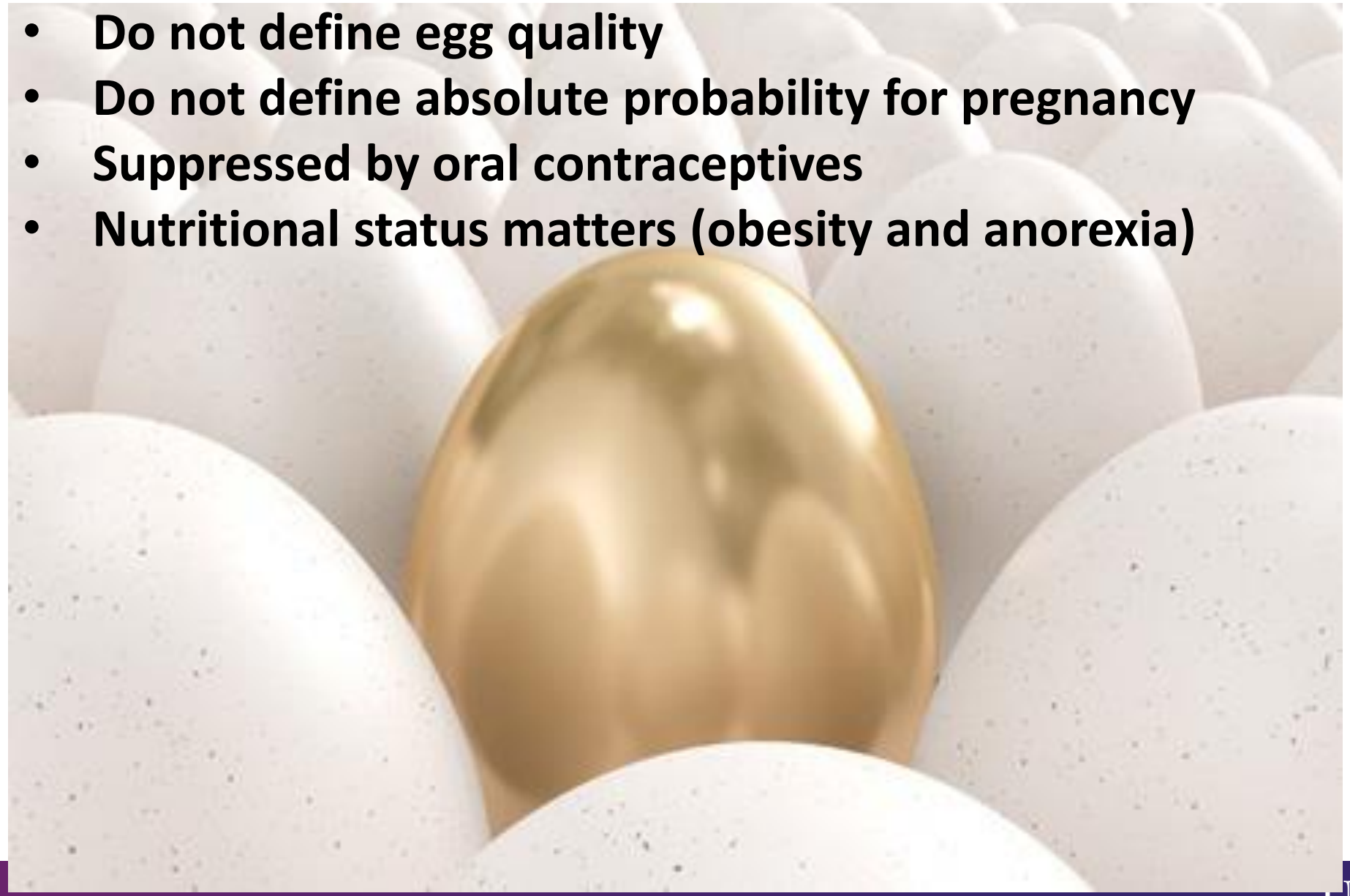


Interpretation	AMH Serum Level (ng/ml)
High (PCOS)	> 4.0
Normal	1.6-4.0
Low Normal	1.1-1.5
Low	0.5-1.0
Very low	<0.5

AMH nomogram from birth to menopause in 804 healthy females from Lie Fong et al.

LIMITATIONS OVARIAN RESERVE MARKERS……

- **Do not define egg quality**
- **Do not define absolute probability for pregnancy**
- **Suppressed by oral contraceptives**
- **Nutritional status matters (obesity and anorexia)**



FERTILITY PROFILE OF THE TYPICAL COUPLE

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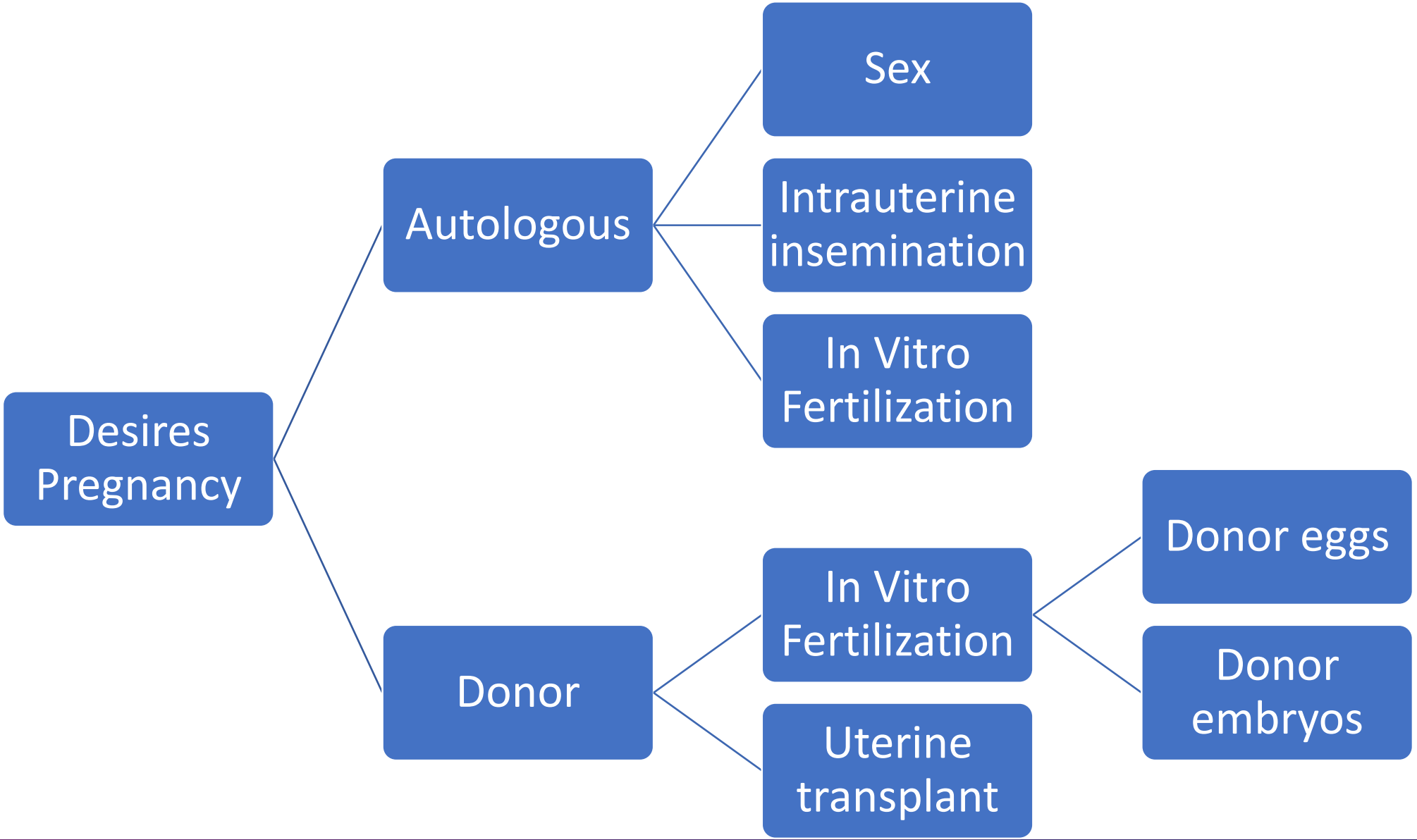
PATHWAYS TO PREGNANCY IN WOMEN DIAGNOSED WITH CANCER

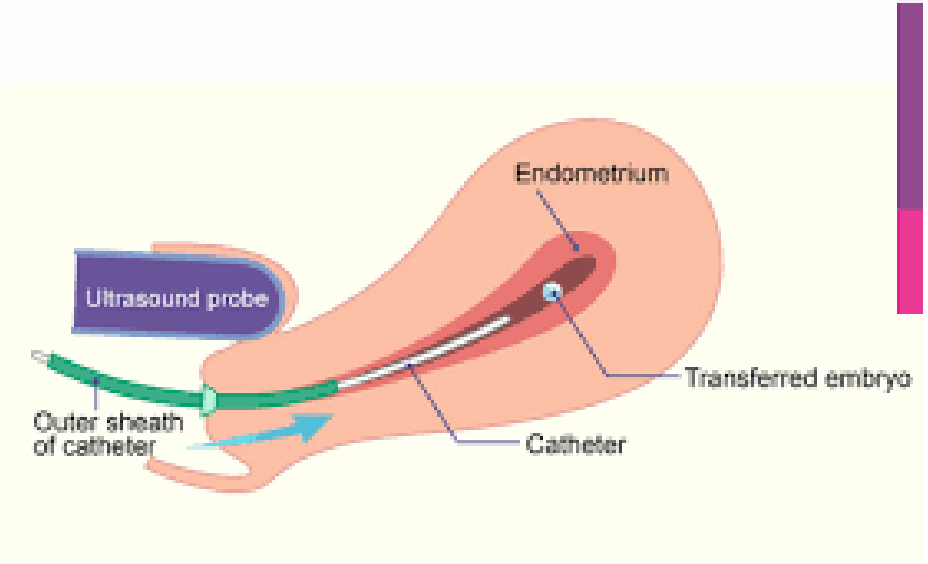


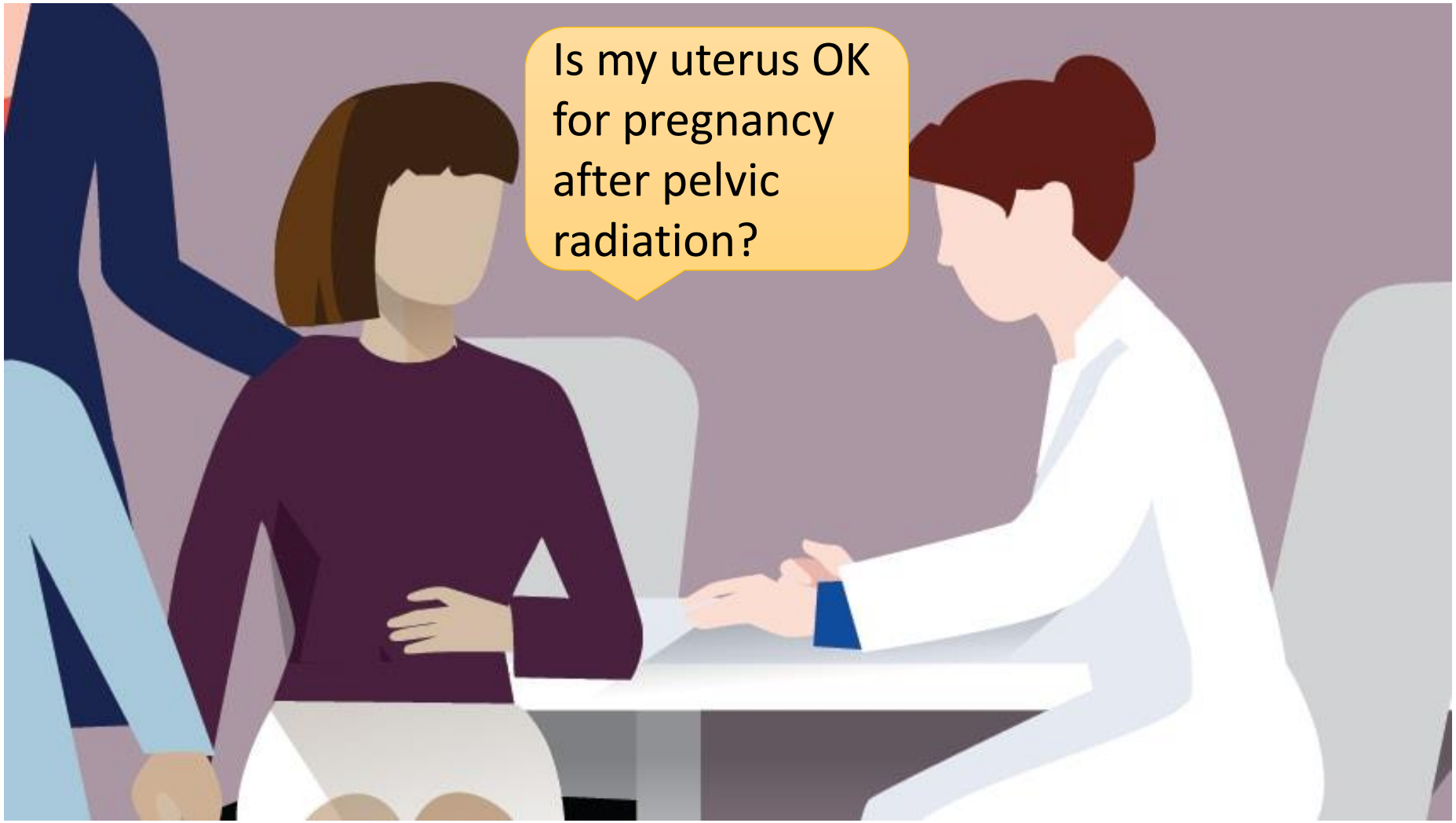

How do I use my frozen eggs or embryos to achieve pregnancy

Assisted Reproductive Technology

In Vitro Fertilization

Embryo Transfer




Is my uterus OK for pregnancy after pelvic radiation?

Fertility Risks and Pelvic and Total Body Radiation

Ovarian irradiation

- 20.3 Gy birth
- 18.4 Gy 10 yo
- 16.5 Gy 20 yo
- 14.3 Gy 30 yo
  - immediate gonadal failure
  - Premature menopause

Uterine irradiation

- 20-30 Gy
  - Miscarriage
  - Fetal growth restriction
  - High blood pressure during pregnancy
  - Preterm delivery
  - Dysfunctional labor
  - Placental dysfunction

Head irradiation

- 45 Gy adult
- 24-35 Gy children
  - increased risk for pituitary function
    - Diabetes
    - Hypogonadism
    - Lactation difficulty
    - Adrenal dysfunction

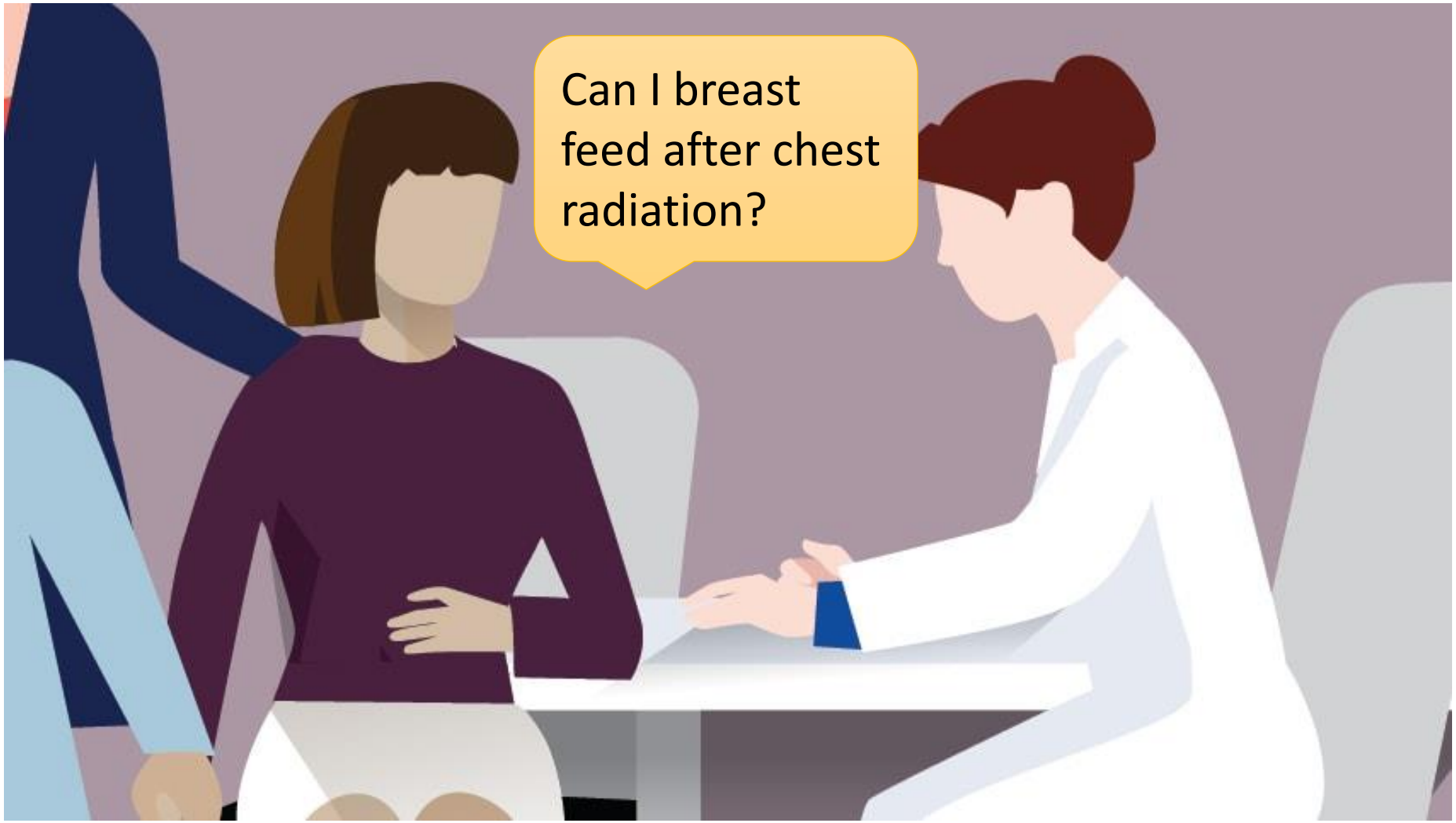

Am I at increased risk for miscarriage?

PREGNANCY OUTCOMES IN WOMEN WITH A HISTORY OF CANCER

Table III **Outcomes of singleton first pregnancies among nulliparous women with cancer onset at age ≤39 years, Scotland, 1981–2012 and matched controls.**

Singleton first pregnancies following cancer onset/matching date to 31 December 2014	Nulliparous women with cancer		Control women		Difference	95% CI	
	Number	%/rate*	Number	%/rate*		Lower	Upper
Total	2071	100	11772	100			
Miscarriage	203	9.8	1095	9.3	0.5	−0.9	1.9
Termination	231	11.2	1725	14.7	−3.5	−5.0	−2.0
Still birth	8	0.4	53	0.5	−0.1	−0.4	0.2
Live birth	1629	78.7	8899	75.6	3.1	1.1	5.0
Infant death	12	7.4	43	4.8	2.5	−1.9	6.9

*% of all first singleton pregnancies apart from for infant deaths which is per 1000 live births.


Can I breast feed after chest radiation?

- Most women can breast feed
- Breast irradiation many be associated with reduced milk production
- Women who receive chest irradiation may be less successful than their siblings with breast feeding
- Studies are needed to determine if breast milk quality is adversely affected after chest radiation

- Cancer 2010;116:4866–71.
- Int J Radiat Oncol Biol Phys. 1989;17:244.


What do I do if I did not freeze eggs or embryos before my cancer treatment?

DONOR CYCLES (POST-TREATMENT)

A. Eggs
- Directed
- Anonymous

B. Embryos
- Directed
- Anonymous

I. Advantage
- You do not need your own eggs
- You can use partner's sperm
- You can experience pregnancy and birth
- High success rates

II. Challenges
- Cost
- Personal beliefs
- Ethnic/racial egg availability
- Surrogate may be needed

WHEN PREGNANCY IS NOT POSSIBLE

Pathways to travel…..

1. Gestation carrier /surrogate
2. Adoption
3. Foster Parenting to Adoption

Challenges…..

1. $$$$$
2. Parental rights
3. A reproductive lawyer is needed

SUMMARY

1. Improved cancer treatment has resulted in more younger people living after a diagnosis of cancer.
2. Many cancer treatments are toxic to reproductive organs and have long term consequences.
3. Many young cancer patient survivors may have the opportunity for pregnancy with their own eggs.

PATIENTS EXPECT TO LIVE AFTER A CANCER DIAGNOSIS

QUESTIONS?

Thank You For Your Attention!

Angela Nicholson, Nurse Manager (206-598-7529)

Clinic Appointments (206-598-4225)