FERTILITY PRESERVATION –THE FUTURE IS BRIGHT

Stephanie Gunderson MD

OBJECTIVES

- Understand who should be offered fertility preservation
- Understand which treatments affect the ovaries
- Review options for females undergoing gonadotoxic treatment
- Discuss outcomes as it relates to fertility preservation treatment options
- Briefly review cost of fertility preservation options

I HAVE NOTHING TO DISCLOSE

INTRODUCTION

70,000 AYA (15-39 YO) cancer diagnoses a year in the US

Survival rates are increasing (some 5-year survivals are as high as 80%)

We need a plan for the future!

ASCO guidelines recommend that all patients of childbearing age be offered fertility preservation services

Del-pozo-Lerida,S et al. Preservation of fertility in patients with cancer (review). Oncology reports 41 no.5 (2019): 2607-2614
Loren AW et al. Fertility preservation for patients with cancer: American society of clinical oncology clinical practice guideline update. Journal of Clinical oncology 2013:19,2500-2510

WHO SHOULD BE OFFERED FERTILITY PRESERVATION SERVICES?

Cancer – before or after treatment

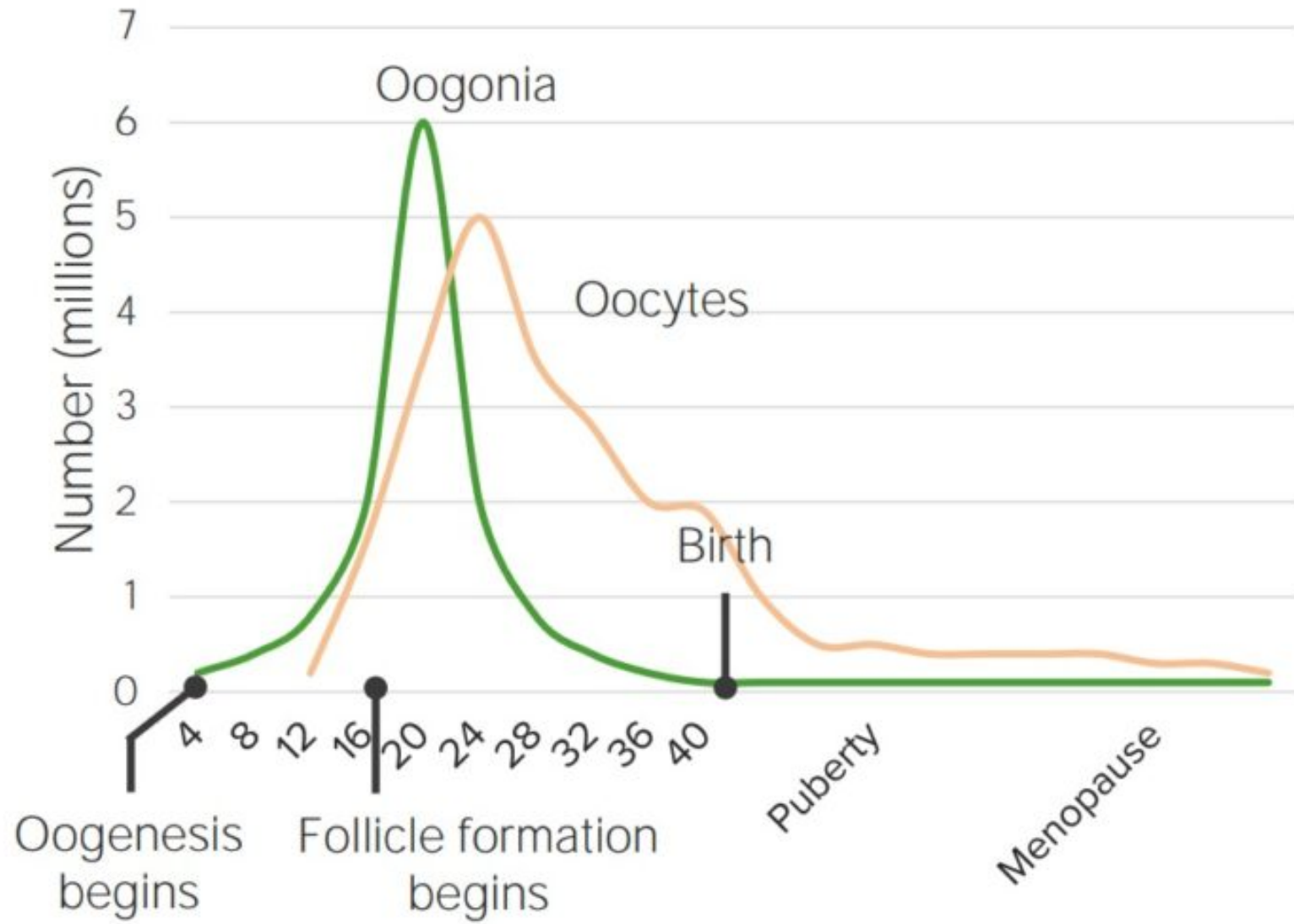
Nonmalignant conditions requiring treatment with gonadotoxic therapy– examples being rheumatoid arthritis, vasculitis, renal disease

Severe hemoglobinopathies requiring stem cell transplant

Congenital/genetic conditions- Fragile X premutation carriers, Turner's syndrome

Gender dysphoria

Anyone wanting to preserve their fertility!

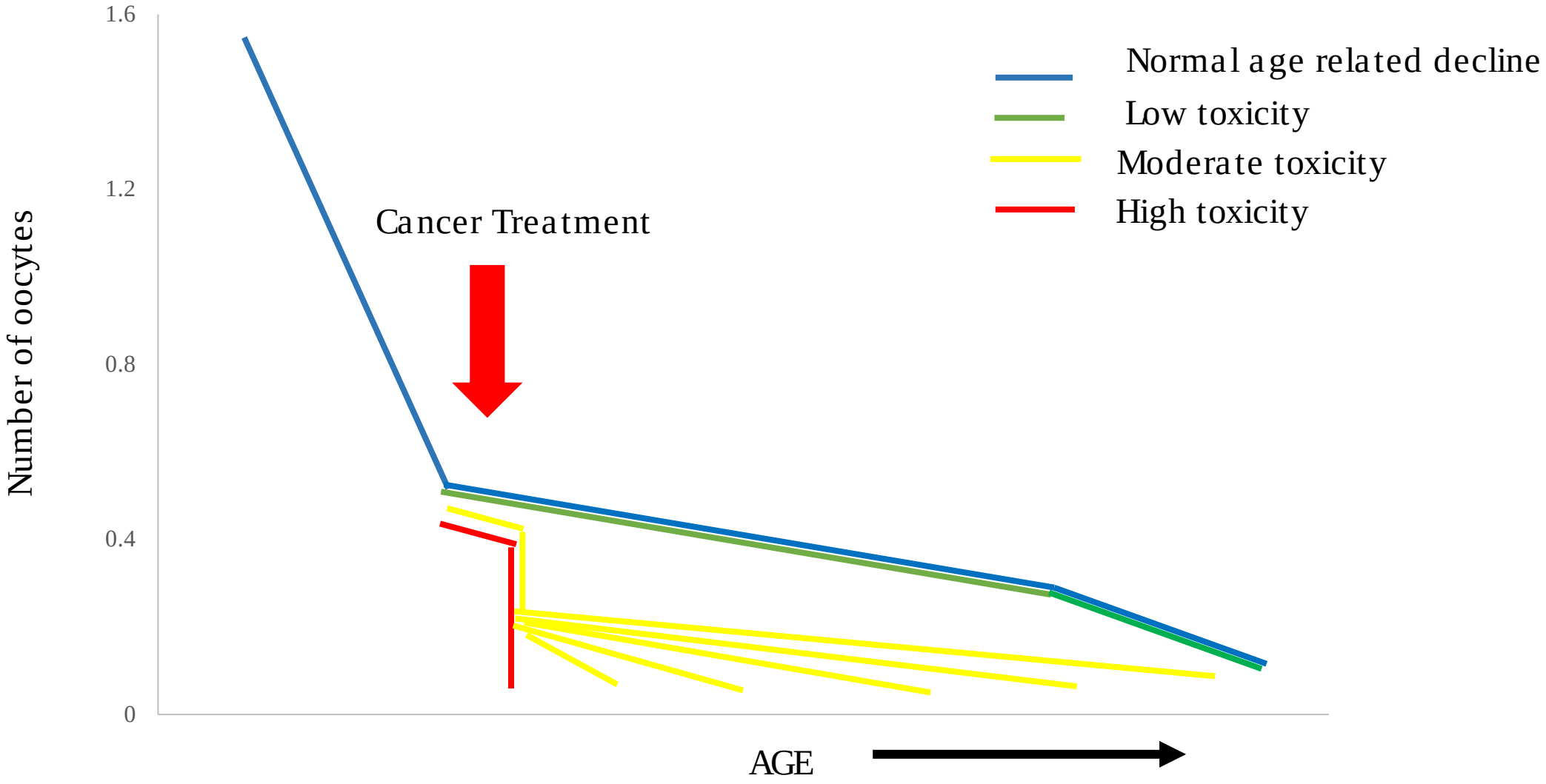

Number (millions)
7
6
5
4
3
2
1
0
Oogonia
Oocytes
Birth
4
8
12
16
20
24
28
32
36
40
Puberty
Menopause
Oogenesis begins
Follicle formation begins

WHO IS AT RISK?

			Minimally Increased Risk	Significantly Increased risk	High level of Increased risk
Alkylators CED* gm/m2		Prepubertal	CED < 8	8-12	> 12
		Pubertal	CED < 4	4-8	>8
Heavy Metal			Cisplatin Carboplatin		
Hematopoietic Stem Cell Transplant					Alkylator +/-Total body irradiation Myeloablative and Reduced intensity regimens
Radiation exposure	Ovary	Prepubertal		< 15 Gy	≥ 15 Gy
		Pubertal		< 10 Gy	≥ 10 Gy
	Hypothalamus		22-29.9	> 30-39.9 Gy	> 40 Gy

Meacham LR, Burns K, Orwig KE, Levine J. Standardizing Risk Assessment for Treatment-Related Gonadal Insufficiency and Infertility in Childhood Adolescent and Young Adult Cancer: The Pediatric Initiative Network Risk Stratification System. J Adolesc Young Adult Oncol. 2020 Dec;9(6):662-666. doi: 10.1089/jayao.2020.0012. Epub 2020 May 26. PMID: 32456570.

WHAT IS THE RISK?



RISK OF PREMATURE OVARIAN INSUFFICIENCY

- 921 participants
- Median age 31.7
- Median years after cancer diagnosis was 24.

Exposure	Dose	HR	95%CI
Ovarian RT	<1000 cGY	13.85	6.5-29.51
	>1000 cGY	132.34	62.88-278.53
CED	8,000-11,999 mg/m^2	2.77	1.18-6.51
	12,000-19,999 mg/m^2	3.9	1.8-8.43
	>20,000 mg/m^2	4.13	1.63-10.5

Chemaitilly W, Li Z, Krasin MJ, Brooke RJ, Wilson CL, Green DM, Klosky JL, Barnes N, Clark KL, Farr JB, Fernandez-Pineda I, Bishop MW, Metzger M, Pui CH, Kaste SC, Ness KK, Srivastava DK, Robison LL, Hudson MM, Yasui Y, Sklar CA. Premature Ovarian Insufficiency in Childhood Cancer Survivors: A Report From the St. Jude Lifetime Cohort. J Clin Endocrinol Metab. 2017 Jul 1;102(7):2242-2250. doi: 10.1210/jc.2016-3723. PMID: 28368472; PMCID: PMC5505200.

RISK OF PREMATURE OVARIAN INSUFFICIENCY

		POI (n = 100)				
Characteristic	**N**	**n[a]**	**%**	**HR**	**CI**	***P* Value**
Age at cancer diagnosis (years)[b]						
Mean (SD)		8.10 (5.57)		1.02	0.98–1.06	0.41
Oophoropexy						
No	863	80	9.27	1.00		
Yes	58	20	34.48	0.72	0.42–1.23	0.23
Body mass index						
≥18.5–24.99 kg/m^2	338	42	12.43	1.00		
<18.5 kg/m^2	43	12	27.91	1.87	0.97–3.59	0.06
25.0–29.9 kg/m^2	224	29	12.95	0.92	0.56–1.52	0.74
≥30 kg/m^2	316	17	5.38	0.36	0.20–0.65	0.001
Treatment exposure						
No alkylating agent nor ovarian radiotherapy	318[c]	2	0.63	1.00		
Alkylating agent only	400[c]	8	2.00	2.98	0.63–14.06	0.17
Ovarian radiotherapy only	59[c]	17	28.81	71.70	16.50–311.58	<0.001
Both	141[c]	73	51.77	95.56	23.30–391.93	<0.001

Chemaitilly W, Li Z, Krasin MJ, Brooke RJ, Wilson CL, Green DM, Klosky JL, Barnes N, Clark KL, Farr JB, Fernandez-Pineda I, Bishop MW, Metzger M, Pui CH, Kaste SC, Ness KK, Srivastava DK, Robison LL, Hudson MM, Yasui Y, Sklar CA. Premature Ovarian Insufficiency in Childhood Cancer Survivors: A Report From the St. Jude Lifetime Cohort. J Clin Endocrinol Metab. 2017 Jul 1;102(7):2242-2250. doi: 10.1210/jc.2016-3723. PMID: 28368472; PMCID: PMC5505200.

REDUCED INTENSITY CONDITIONING FOR SCT

- Traditional conditioning for SCT results in POI 95-100%of the time
- RIC resulted in POI 86.3%and amenorrhea was seen in 68.1%

Assouline E, Crocchiolo R, Prebet T, Broussais F, Coso D, Gamerre M *et al.* Impact of Reduced-Intensity Conditioning Allogeneic Stem Cell Transplantation on Women's Fertility. Clinical Lymphoma Myeloma and Leukemia 2013;13:704-10.

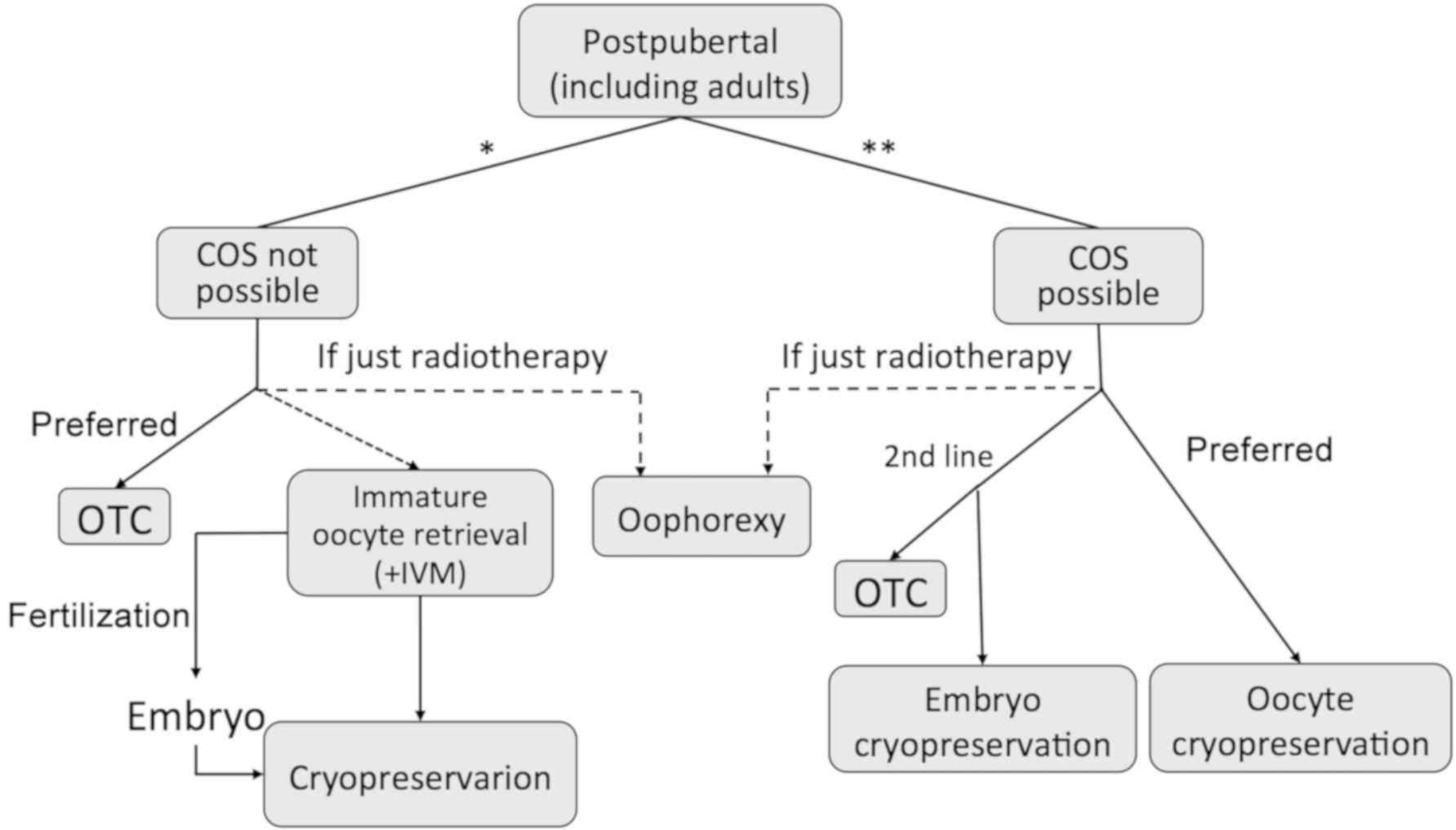
CED calculators

FERTILITY RISK CALCULATOR - FERTILITY PRESERVATION PROGRAM IN PITTSBURGH (.ORG) FERTILITYPRESERVATIONPITTSBURGH

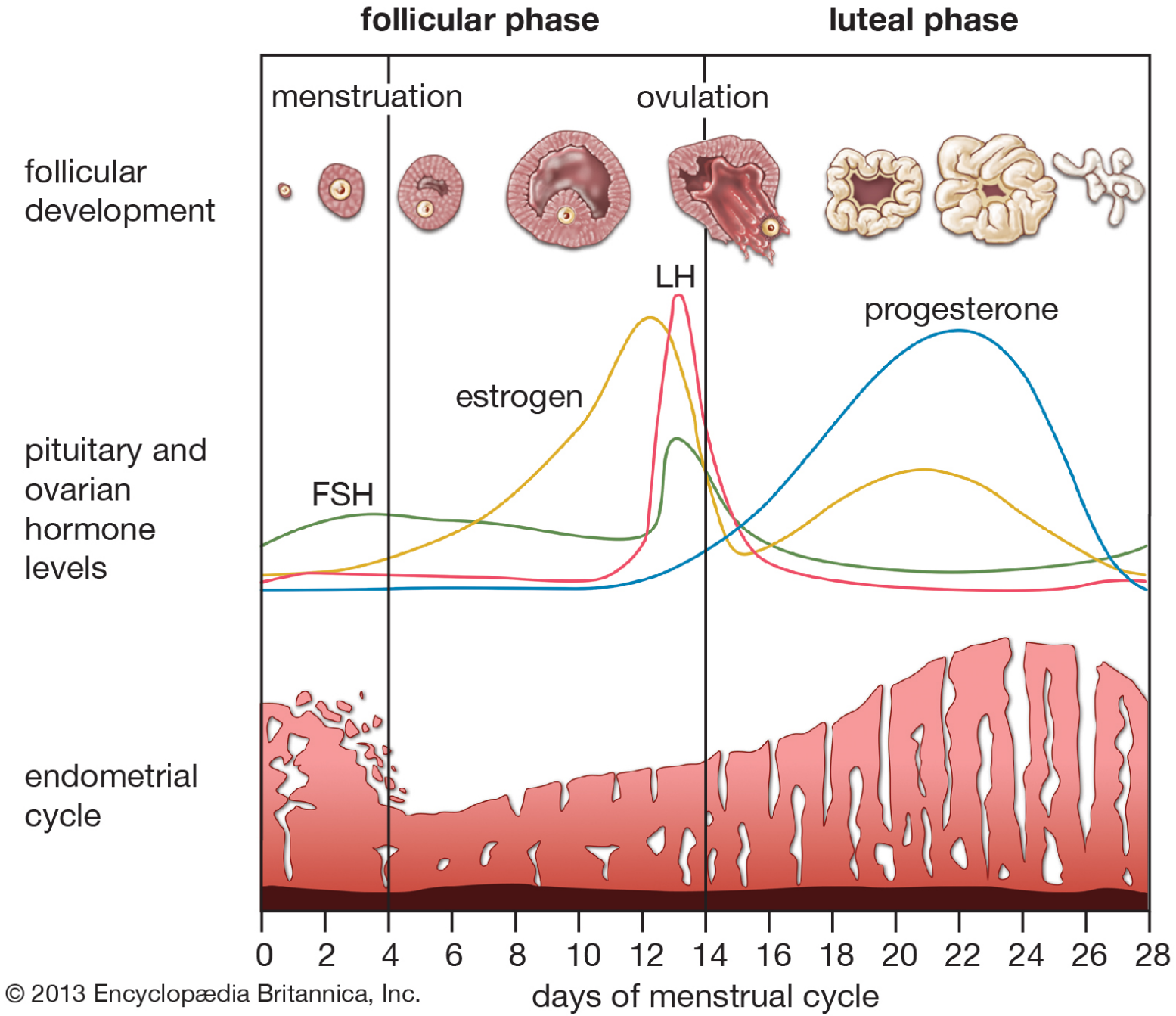
POSTPUBERTAL FEMALES

Oocyte cryopreservation

Embryo cryopreservation


Postpubertal
(including adults)
*
**
COS not
possible
COS
possible
If just radiotherapy
If just radiotherapy
Preferred
OTC
Immature
oocyte retrieval
(+IVM)
Oophorexy
2nd line
Preferred
OTC
Fertilization
Embryo
Cryopreservarion
Embryo
cryopreservation
Oocyte
cryopreservation

The menstrual cycle



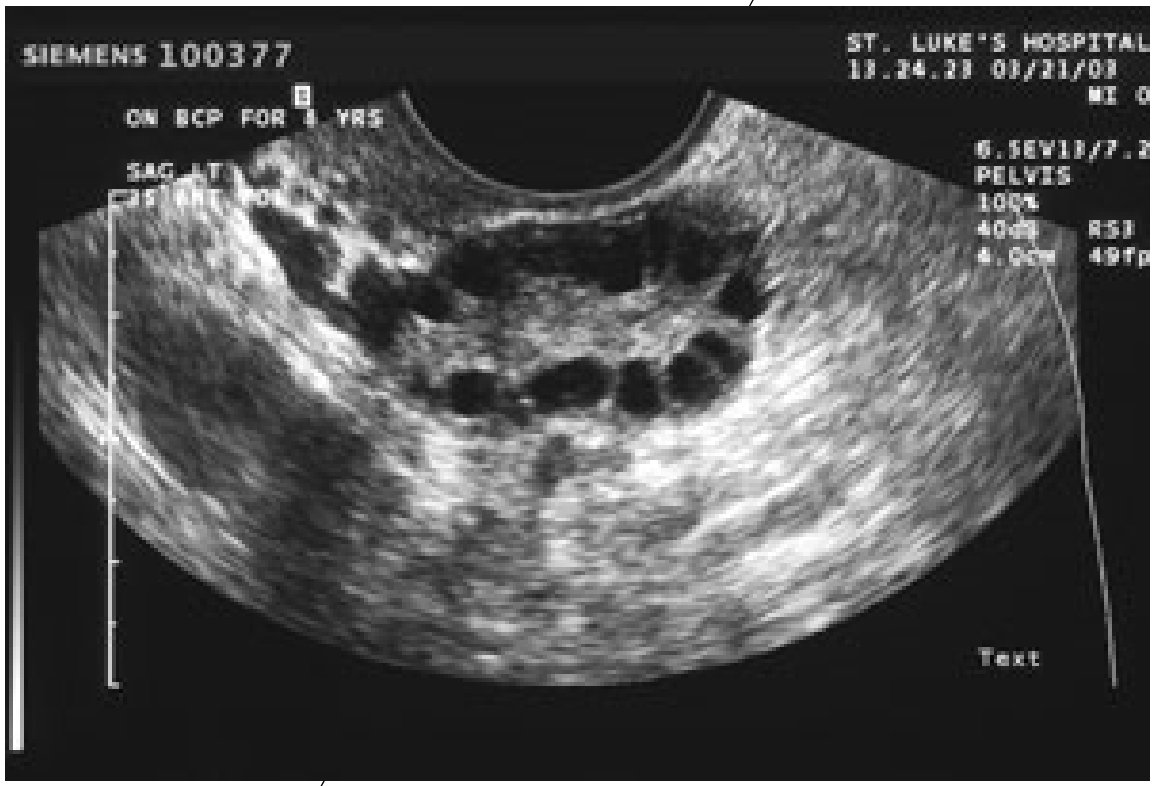
ASSESSING OVARIAN RESERVE

Day 2/3 FSH and estradiol in menstruating patients

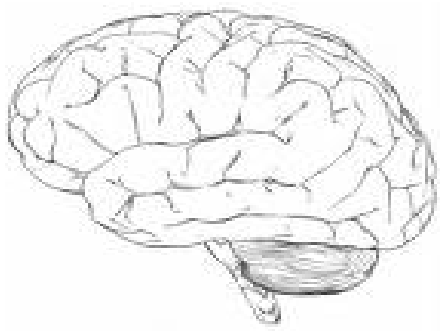
- FSH>10 miu/mL, E2>70 pg/mL = diminished ovarian reserve
- Random level in amenorrheic patient

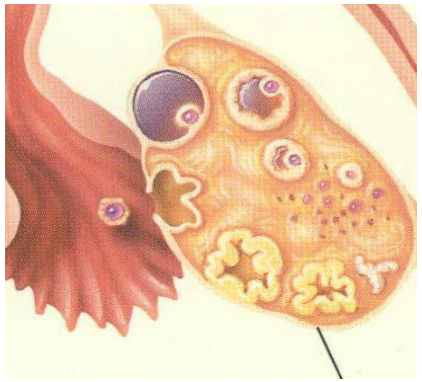
Anti-mullerian Hormone

Antral follicle Count



FSH
LH
+

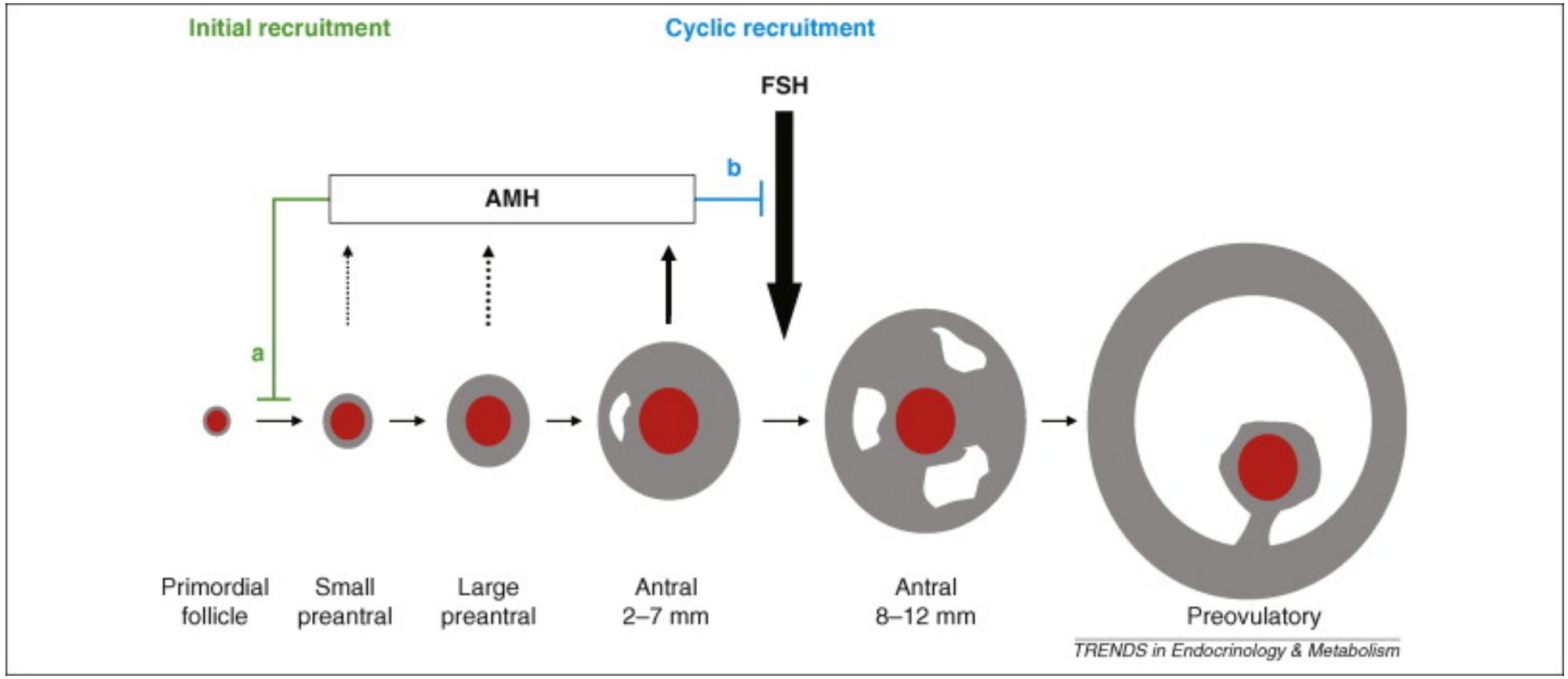




Estradiol
-

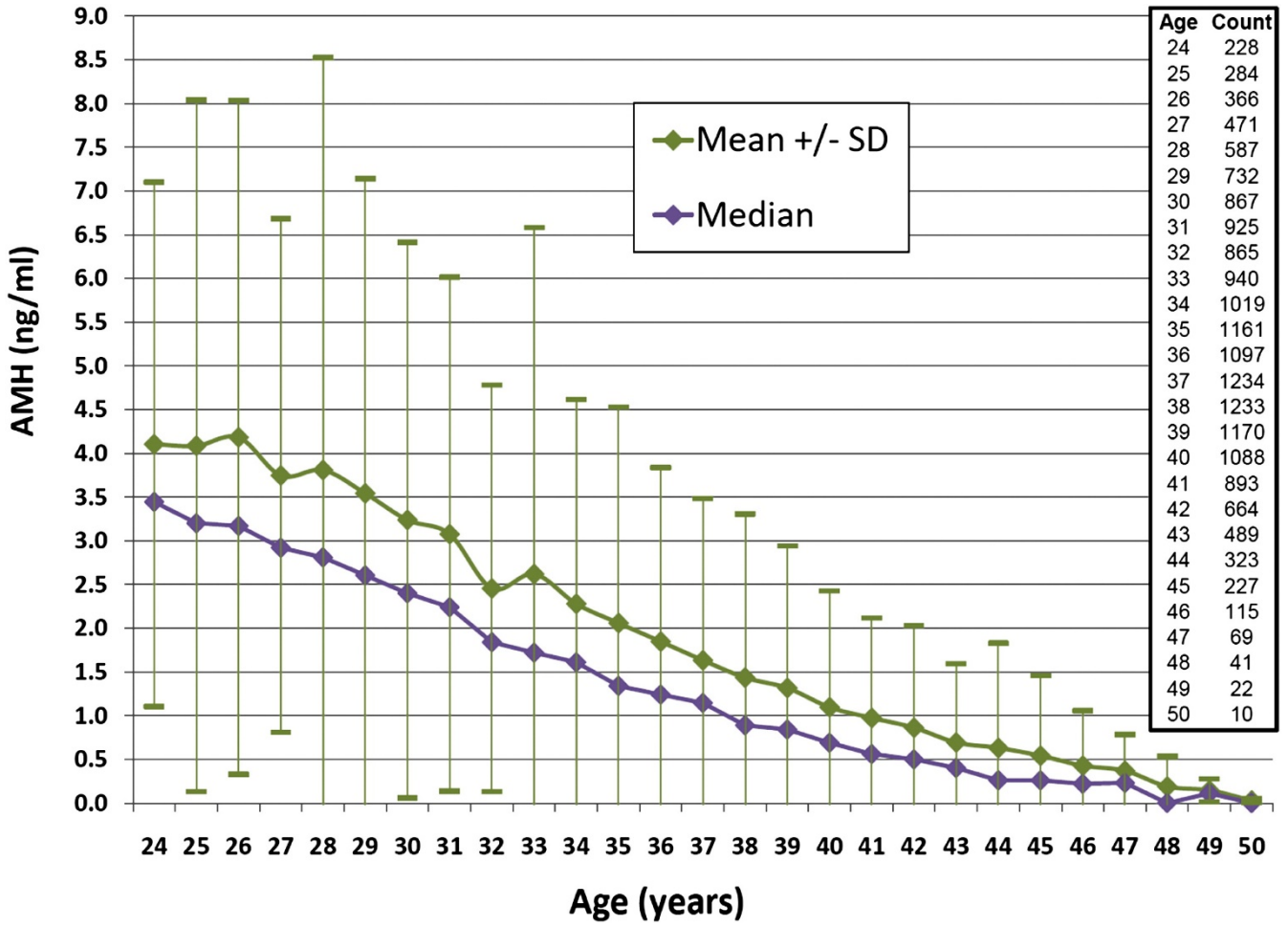
Normal:
FSH < 10 mIU/mL
Estradiol < 70 pg/ml

ANTI- MULLERIAN HORMONE



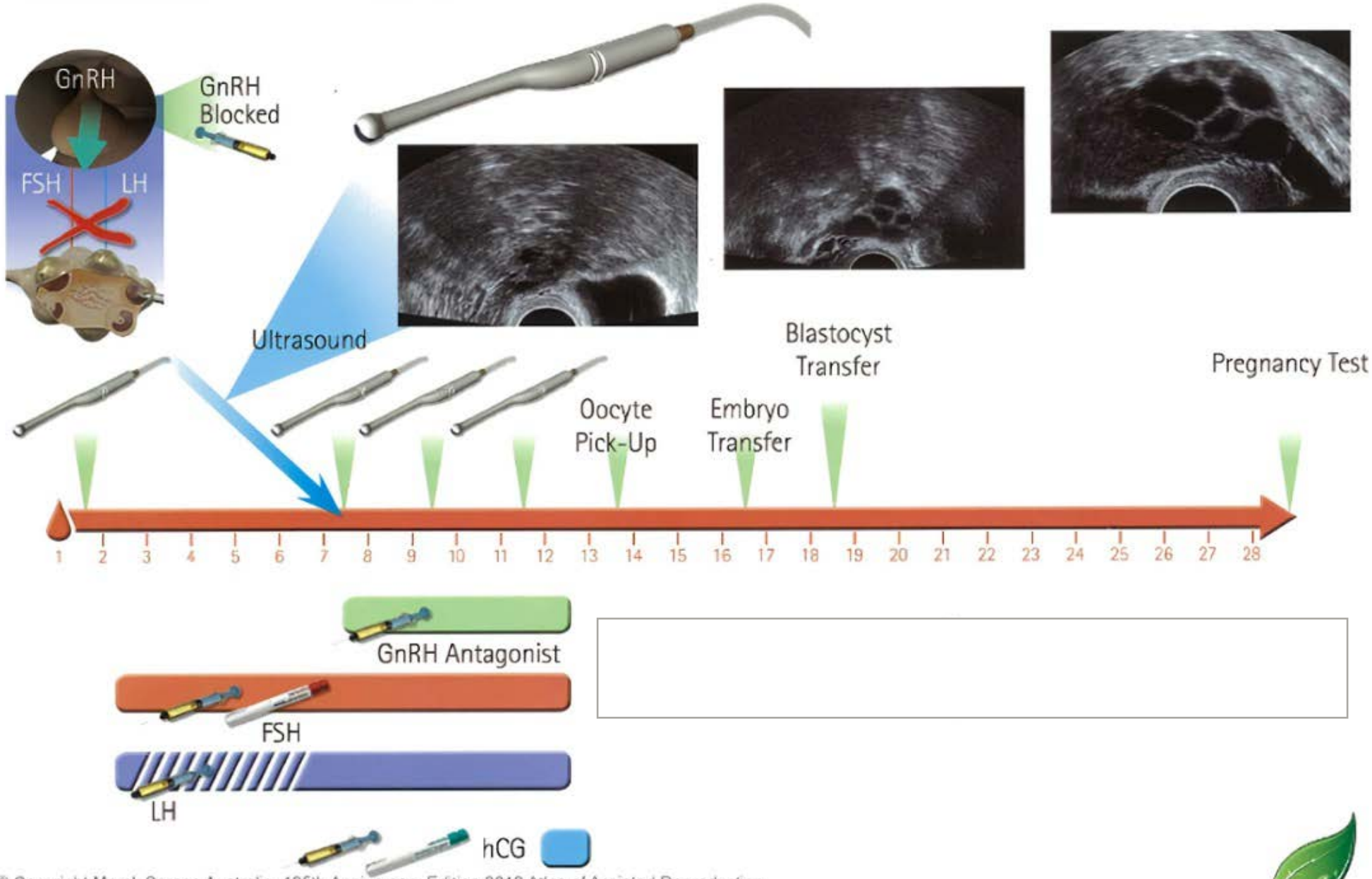
Sowers et al., J Clin Endoc Metab 2008

AGE SPECIFIC AMH LEVELS



Seifer DB et al., Fertility and Sterility 2011; 95)2): 747-750

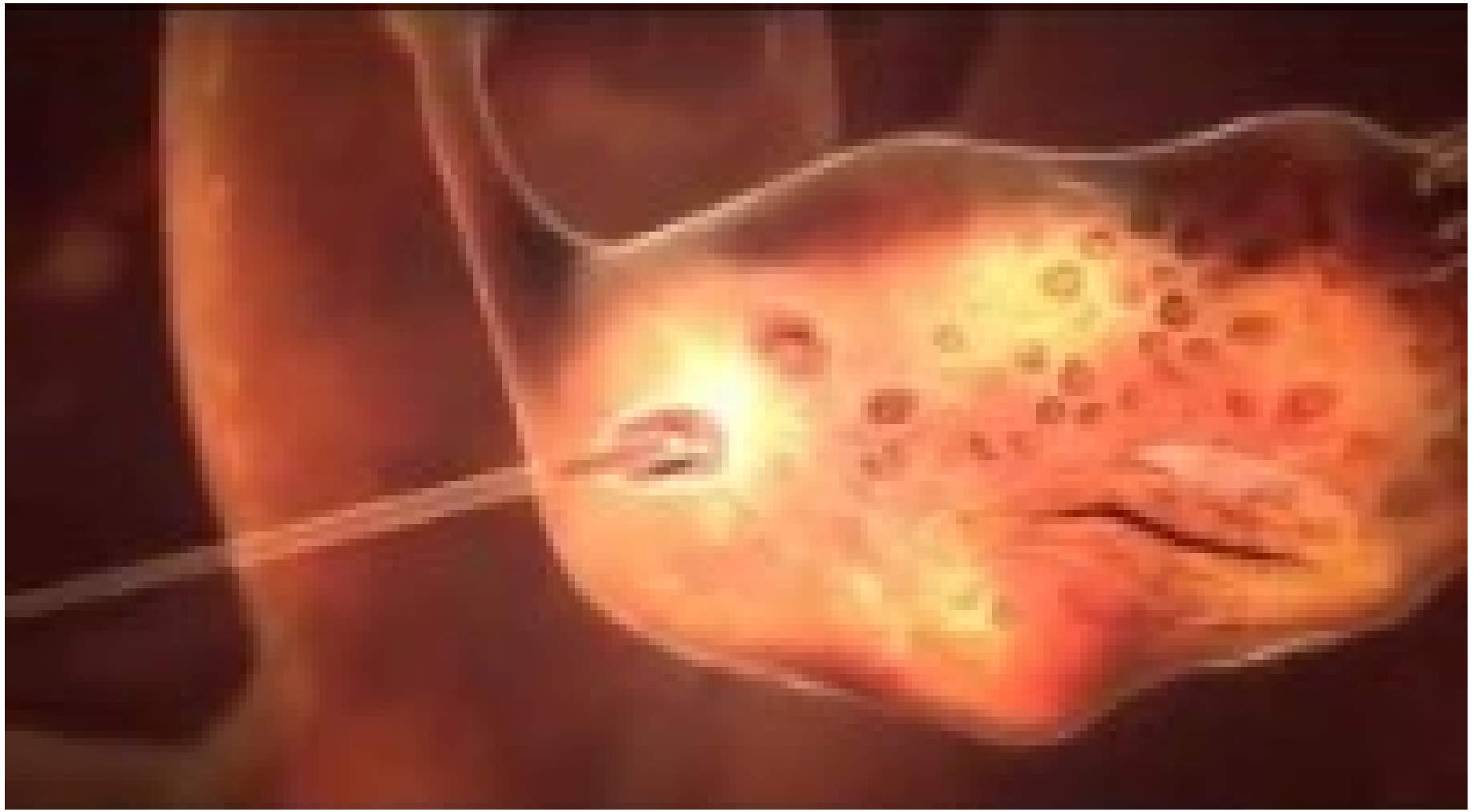
GnRH Antagonist Protocol



INVITRO FERTILIZATION

- 10-14 days of injections
- Injections are subcutaneous
- Frequent ultrasounds and blood work
- Side effects: abdominal bloating, pelvic discomfort, headache, nausea, emotional lability

OOCYTE CRYOPRESERVATION



RANDOM START

GnRH Antagonist Protocol

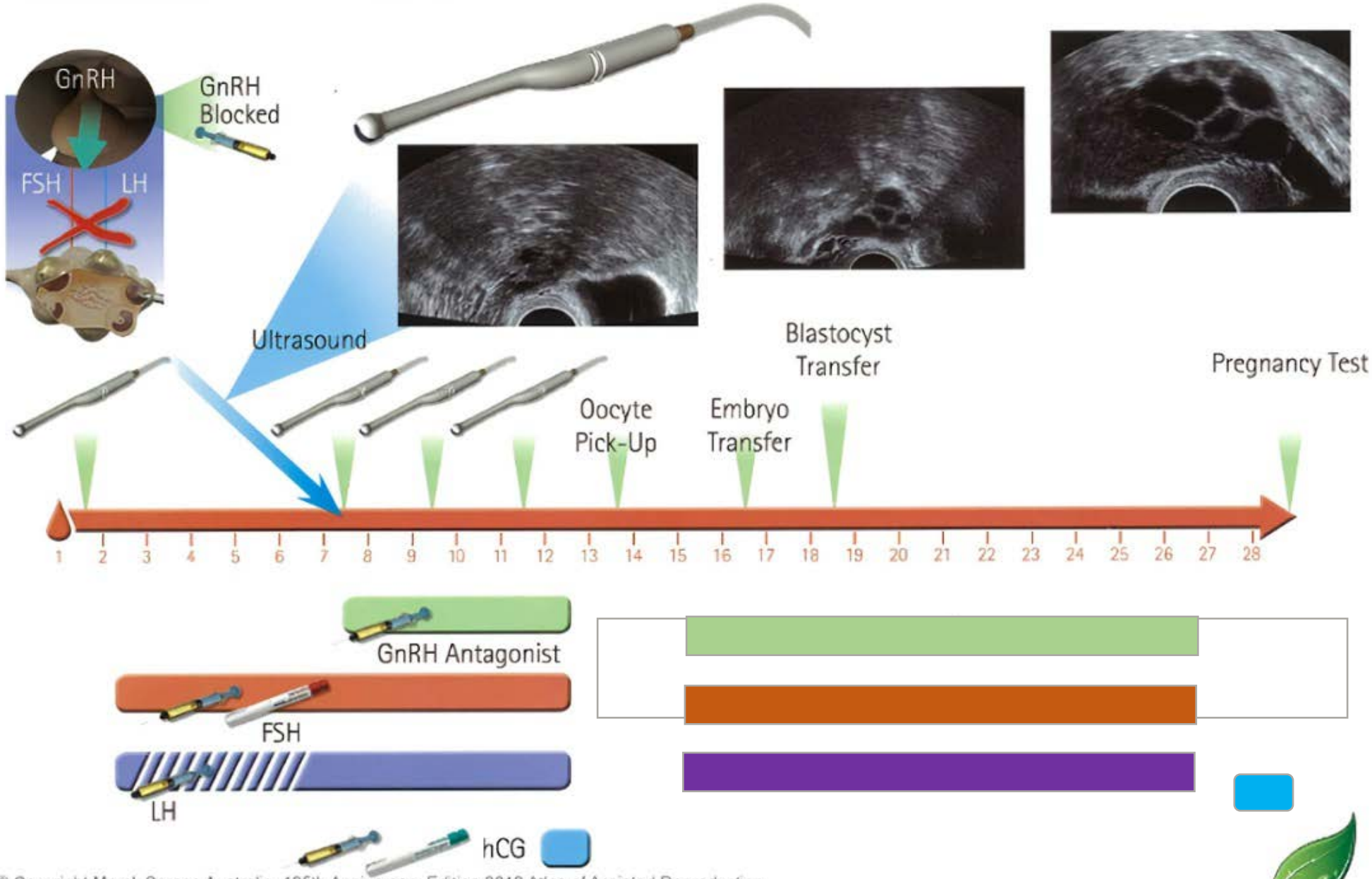


Table 2

Outcome of stimulations, Outcome of stimulations in all women and in those who initiated stimulation in the early (day 1–5), mid-late proliferative (day 6–14) and luteal (day ≥ 15) phases of the menstrual cycle. Statistical significance is marked as: difference between early and mid-late proliferation initiation (a), between early and luteal initiation (b) and between mid-late and luteal initiation of stimulation (c). ∅ = "mean".

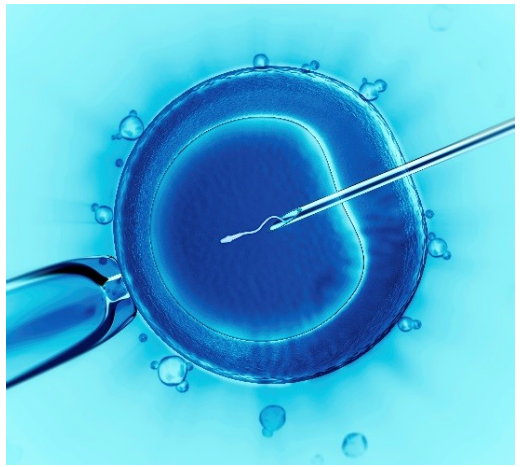
	All patients (n = 684)	Day 1–5 (n = 472)	Day 6–14 (n = 109)	Day ≥15 (n = 103)	p
Days of gonadotropin stimulation (∅ n ± SD)	10.8 ± 2.4	10.8 ± 2.4	10.6 ± 2.7	11.5 ± 2.2	0.022[b,c]
Total dose of gonadotropins (∅ IU ± SD)	2574 ± 1013	2496 ± 980	2529 ± 940	2970 ± 1145	<0.001[b,c]
Total dose of gonadotropins/day (∅ IU)	238	231	239	258	<0.002[b,c]
OHSS III° (n/total))	1/684	1/472	0/109	0/103	0.799
Obtained oocytes (∅ n/ ± SD/total)	12.3 ± 4.4/684	11.6 ± 7.7/472	13.9 ± 9.1/109	13.6 ± 7.9/103	0.006[a,b]
Only cryopreservation of oocytes (∅ n ± SD/total)	11.2 ± 8.1/265	12.1 ± 8.6/179	11.5 ± 9.0/53	13.6 ± 6.8/33	
Only cryopreservation of zygotes (∅ n ± SD/total)	6.5 ± 3.5/341	6.6 ± 4.2/241	6.6 ± 3.6/46	6.3 ± 3.2/54	
Cryopreservation of both, oocytes and zygotes					
oocytes (∅ n ± SD/total)	6.5 ± 3.5/56	6.4 ± 3.5/38	6.5 ± 2.8/8	6.7 ± 4.0/10	
zygotes (∅ n ± SD/total)	5.1 ± 2.9/56	4.9 ± 3.1/38	6.8 ± 2.7/8	4.4 ± 1.6/10	

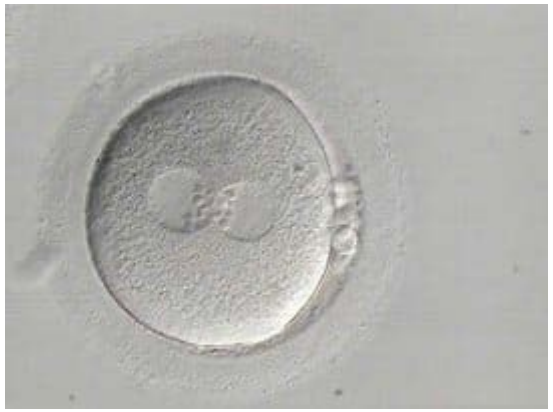
von Wolff M, Capp E, Jauckus J, Strowitzki T, Germeyer A, FertiPROTEKT study group. Timing of ovarian stimulation in patients prior to gonadotoxic therapy: an analysis of 684 stimulations. Eur J Obstet Gynecol Reprod Biol 2016;199:146–9

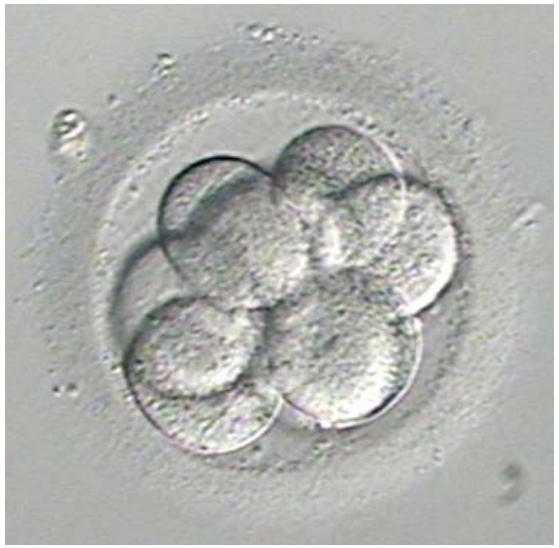
OOCYTE CRYOPRESERAVTION

- 

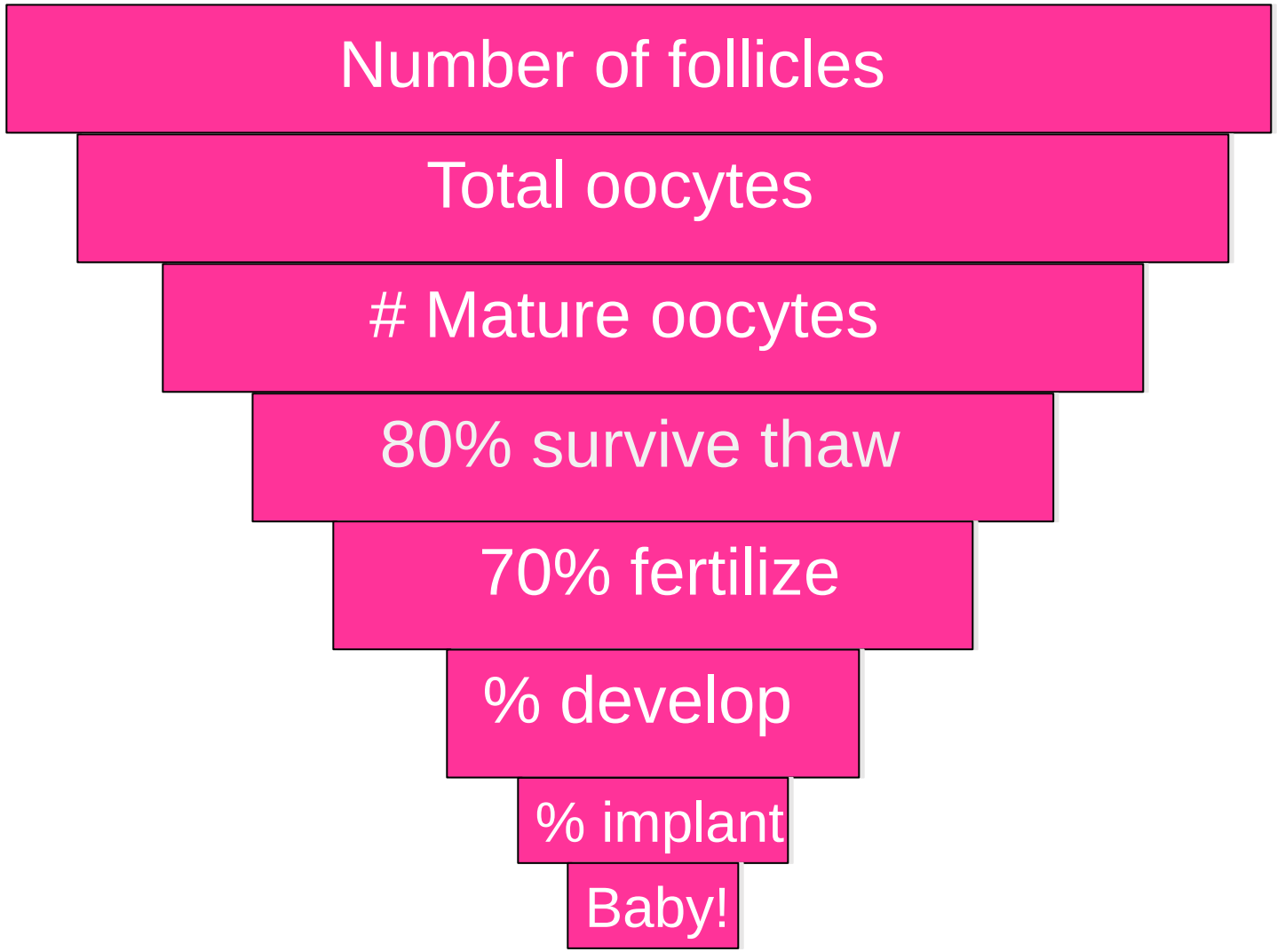
EMBRYO CRYOPRESERAVTION







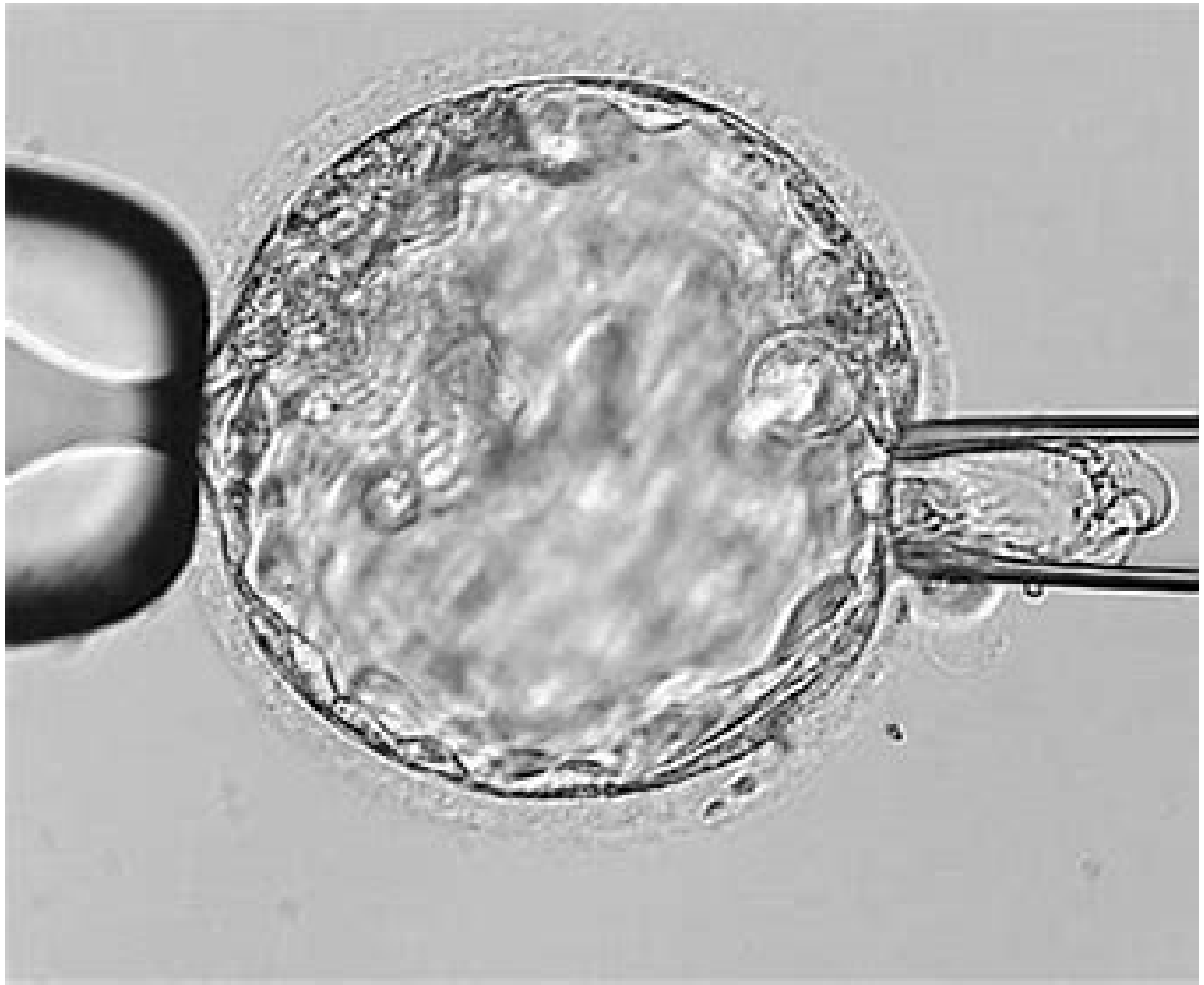
THERE IS ATTRITION ALONG THE WAY



Survival Rates

- 80%of oocytes frozen will survive the thaw
- 95%of good quality blastocysts frozen will survive the thaw

PREIMPLANTATION GENETIC TESTING



UTILIZATION OF OOCYTES AND EMBRYOS

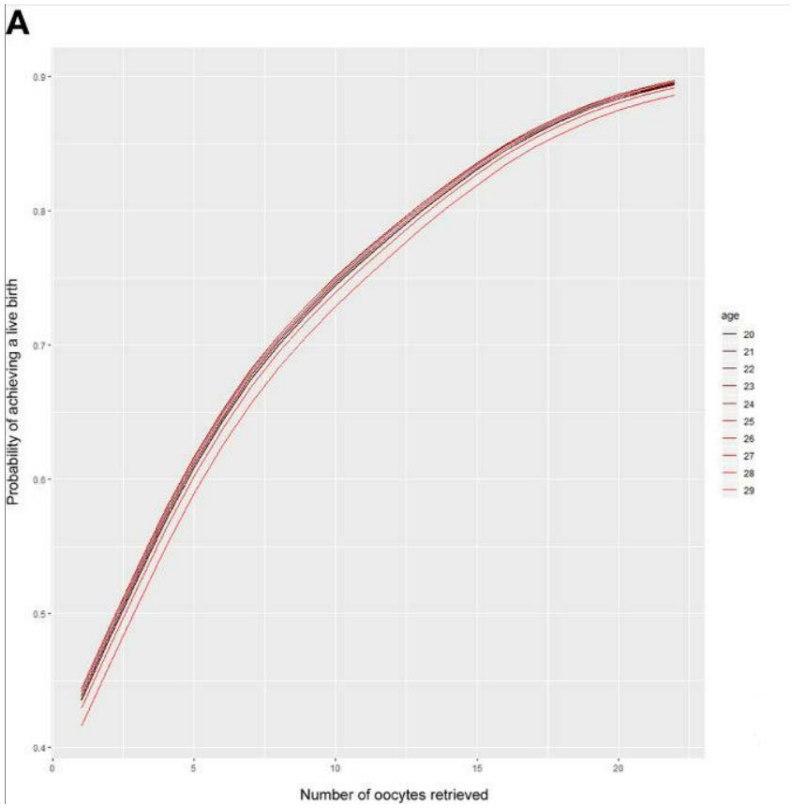
- In one cohort study that collected data from 2005-2009 on 231 patients with 280 cycles showed a utilization rate of 38%
- Another study collecting data from 2006-2020 showed that of the 921 patients who electively froze oocytes only 68 (7.4%) has utilized them
- A smaller study looked at 66 patients undergoing oocyte cryopreservation prior to gonadotoxic treatment, the utilization rate was 23%

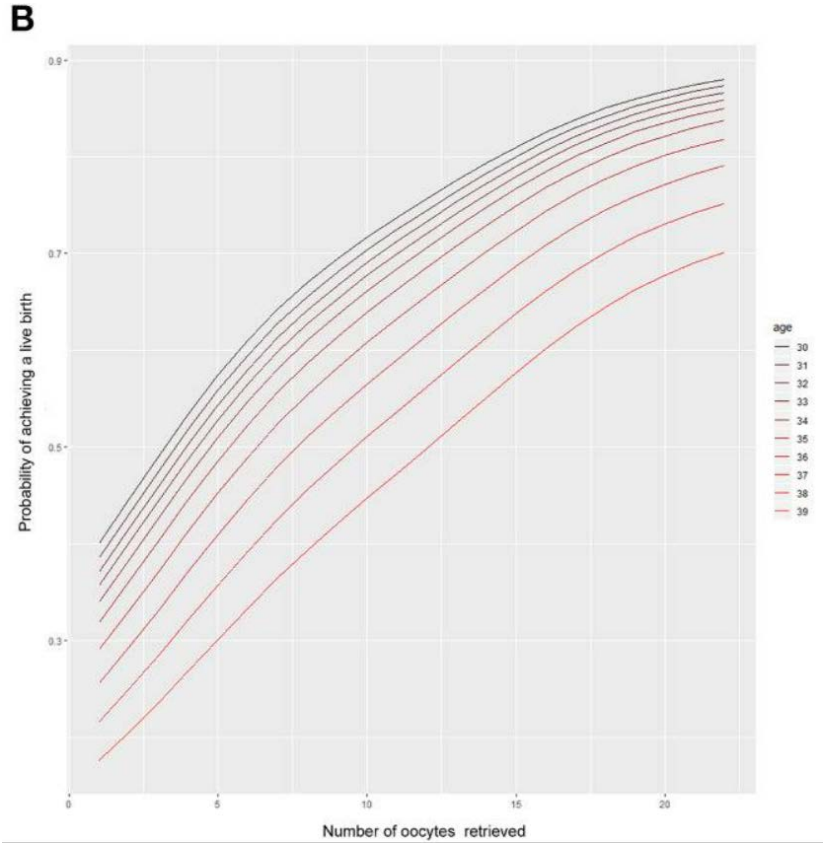
Blakemore JK, Grifo JA, DeVore SM, Hodes-Wertz B, Berkeley AS. Planned oocyte cryopreservation-10-15-year follow-up: return rates and cycle outcomes. Fertil Steril. 2021 Jun;115(6):1511-1520. doi: 10.1016/j.fertnstert.2021.01.011. Epub 2021 Mar 9. PMID: 33712289.

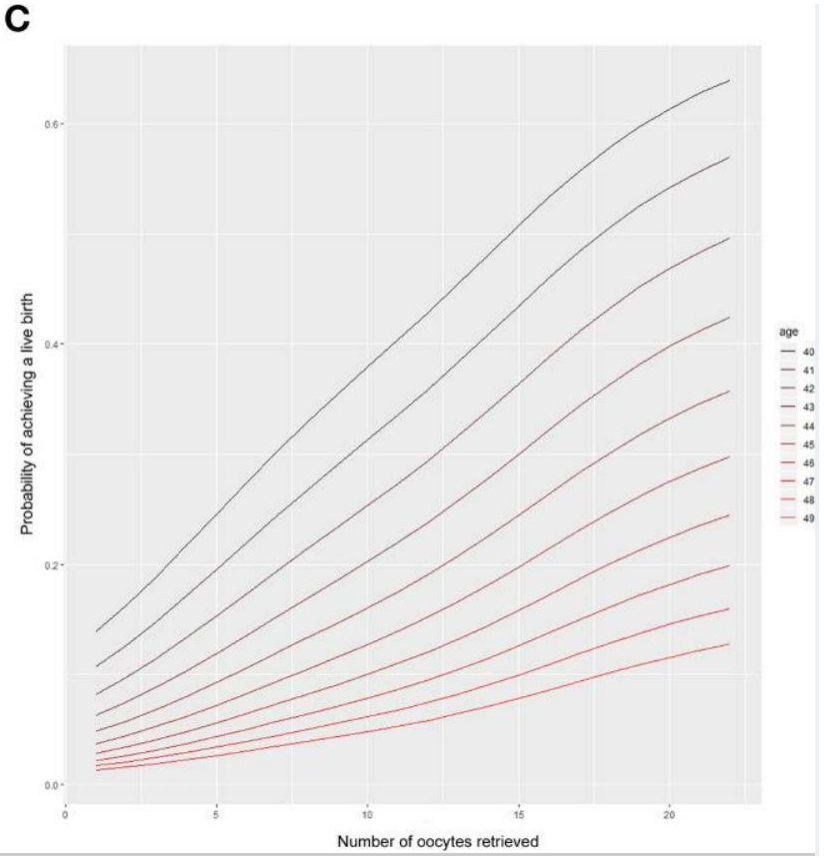
Leung AQ, Baker K, Vaughan D, Shah JS, Korkidakis A, Ryley DA, Sakkas D, Toth TL. Clinical outcomes and utilization from over a decade of planned oocyte cryopreservation. Reprod Biomed Online. 2021 Jul 1:S1472-6483(21)00308-4. doi: 10.1016/j.rbmo.2021.06.024. Epub ahead of print. PMID: 34474973.

Dolmans, M.M., Hollanders de Ouderaen, S., Demylle, D. *et al.* Utilization rates and results of long-term embryo cryopreservation before gonadotoxic treatment. *J Assist Reprod Genet* **32,** 1233–1237 (2015). https://doi.org/10.1007/s10815-015-0533-z

LIVE BIRTH WITH VITRIFIED OOCYTES







Zhu, Haiyan et al. “Predicting the Likelihood of Live Birth in Assisted Reproductive Technology According to the Number of Oocytes Retrieved and Female Age Using a Generalized Additive Model: A Retrospective Cohort Analysis of 17,948 Cycles.” *Frontiers in endocrinology* vol. 12 606231. 30 Apr. 2021, doi:10.3389/fendo.2021.606231

THE MAJORITY OF WOMEN DO NOT RETRIEVE THE OPTIMAL NUMBER OF OOCYTES

58%of women who undergo planned oocyte cryopreservation do not bank sufficient number of oocytes to yield an 80%chance of live birth

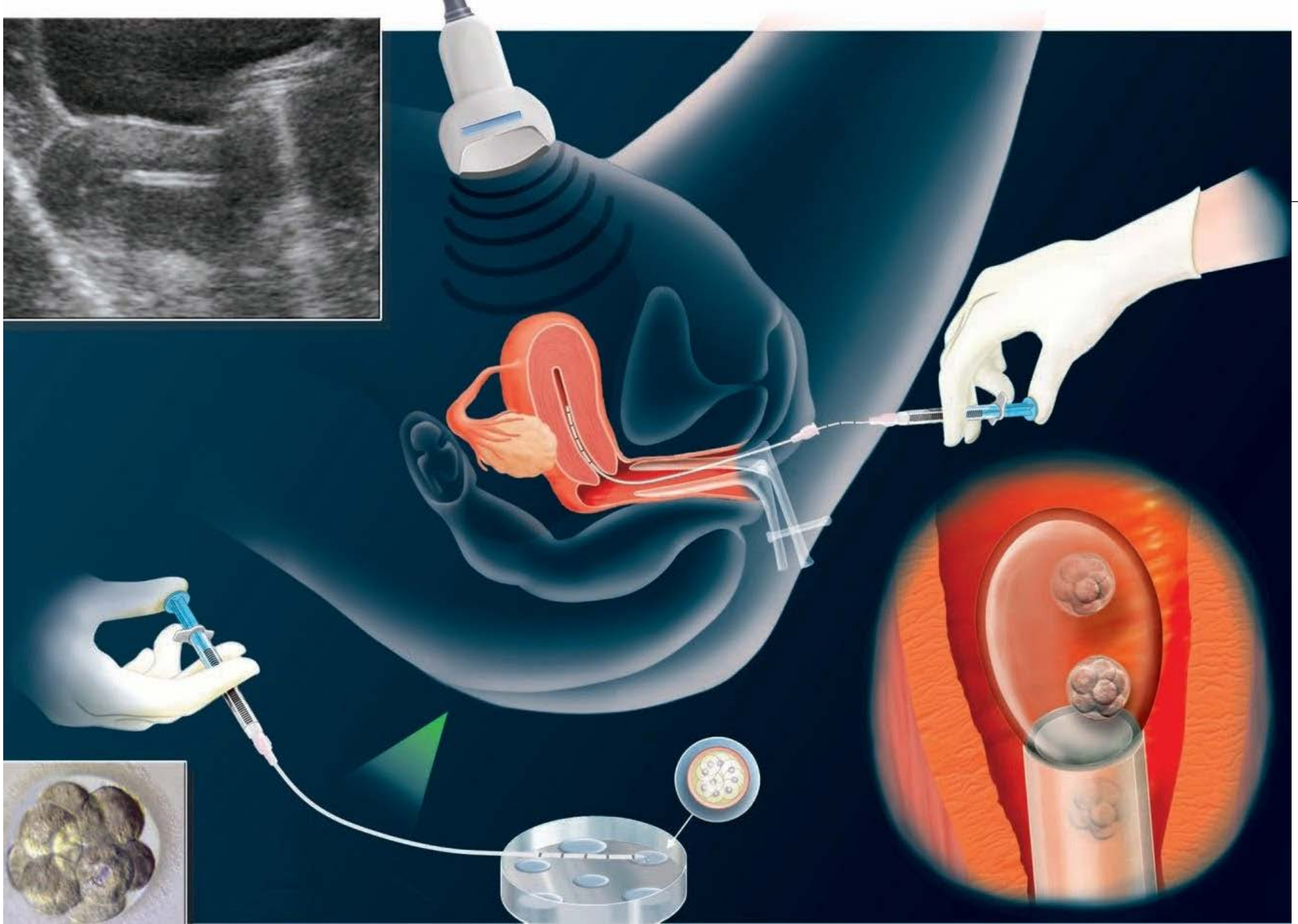
Median number of cycles needed to achieve adequate number of oocytes was 1.3-2.2 (depending on age)

ASRM 2020 Abstract Majority of women undergoing elective oocyte cryopreservation do not attain optimal number of oocytes cryopreserved for reasonable likelihood of future live birth. UCSF

WHEN TO DO AN EMBRYO TRANSFER?

Discussion with oncologist

Typically, 6 months post chemotherapy



EMBRYO CRYOPRESERVATION SUCCESS

TABLE 1

Data from 2017 live-birth rates per cycle start.

	Age range, y				
Variable	< 35	35–37	38–40	41–42	> 42
Live-birth rate/cycle start	46.8	34.4	21.0	10.1	3.1
Confidence range	46.3–47.3	33.8–35.0	20.5–21.5	9.5–10.6	2.8–3.5

ASRM. Fertility preservation before gonadotoxic therapy. Fertil Steril 2019.

Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. ASRM Fertility and Sterility 2019

EMBRYO TRANSFER SUCCESS (PER SINGLE EMBRYO TRANSFER WITH GOOD QUALITY EMBRYO)

<35 years old – 50%live birth

35-37 years old – 35-40%live birth

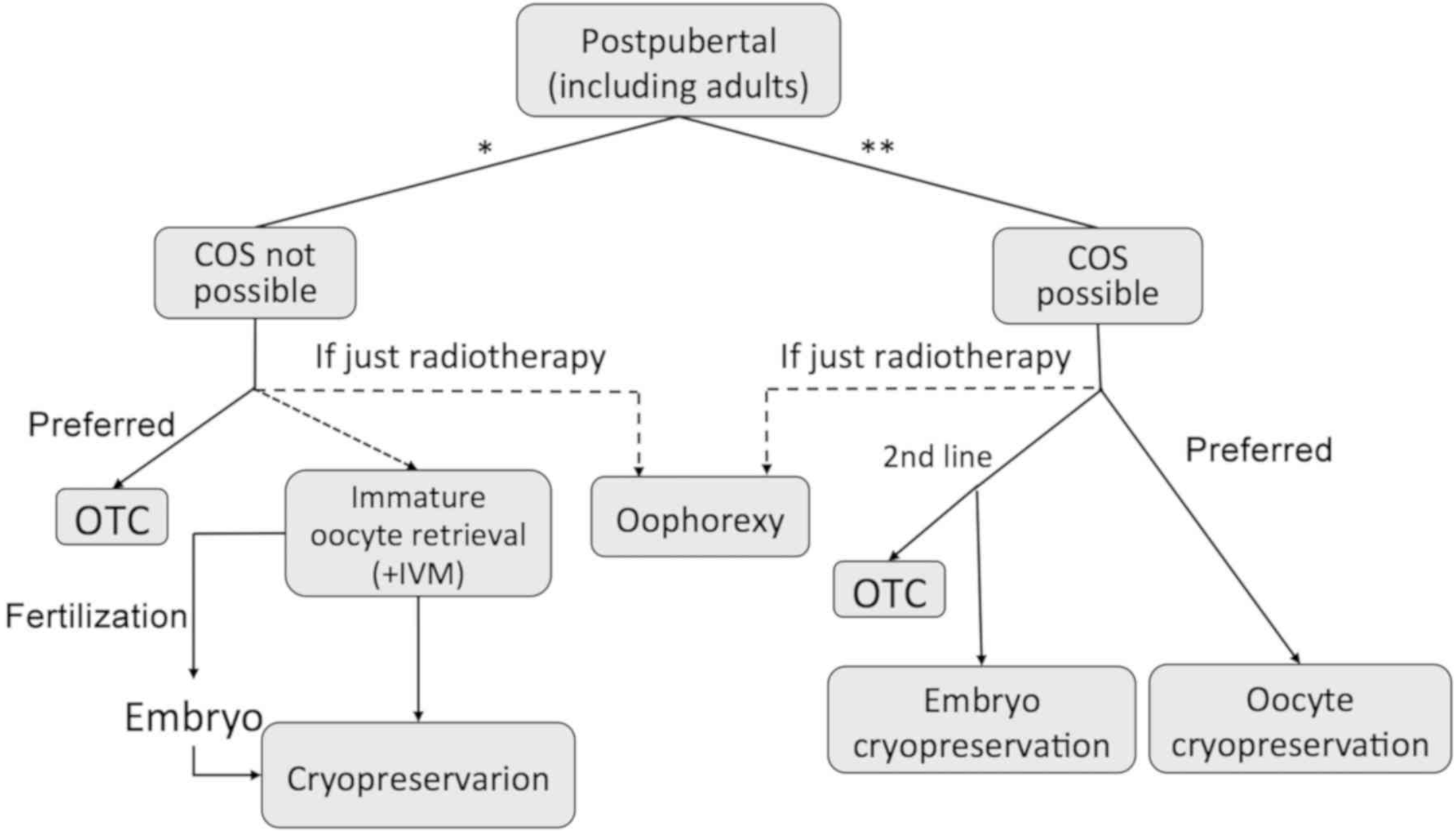
38-40 years old – 25%live birth

41-42 years old – 15%live birth

>42 years old – 5%live birth

PREPUBERTAL FEMALES

- Ovarian tissue cryopreservation
- In vitro maturation


Postpubertal
(including adults)
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COS not
possible
COS
possible
If just radiotherapy
If just radiotherapy
Preferred
OTC
Immature
oocyte retrieval
(+IVM)
Oophorexy
2nd line
Preferred
OTC
Fertilization
Embryo
Cryopreservarion
Embryo
cryopreservation
Oocyte
cryopreservation

OVARIAN TISSUE CRYOPRESERVATION

NOT EXPERIMENTAL (2019)

Prepubertal patients

Patients who cannot delay chemotherapy start

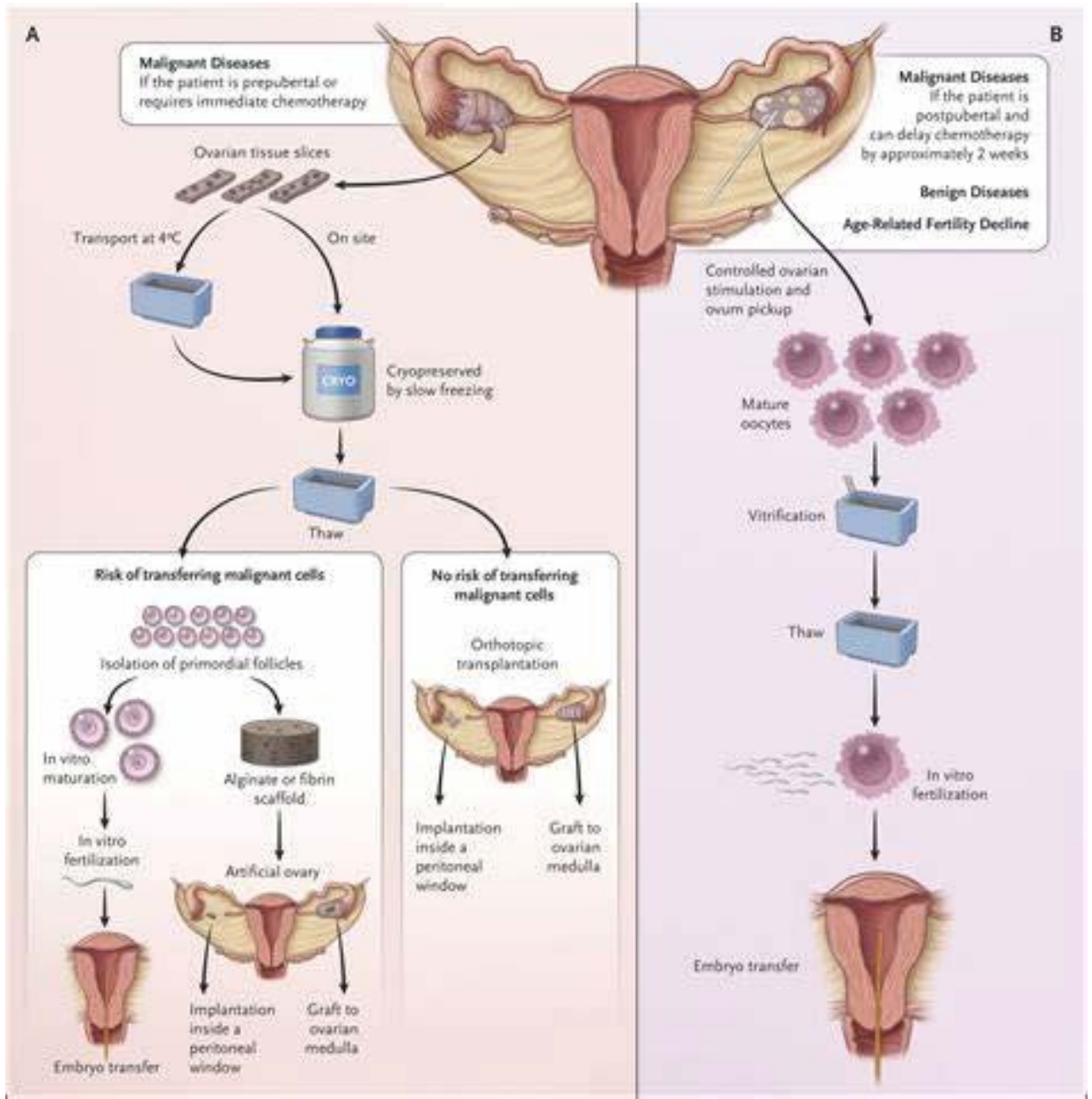
Patients having surgery for another reason

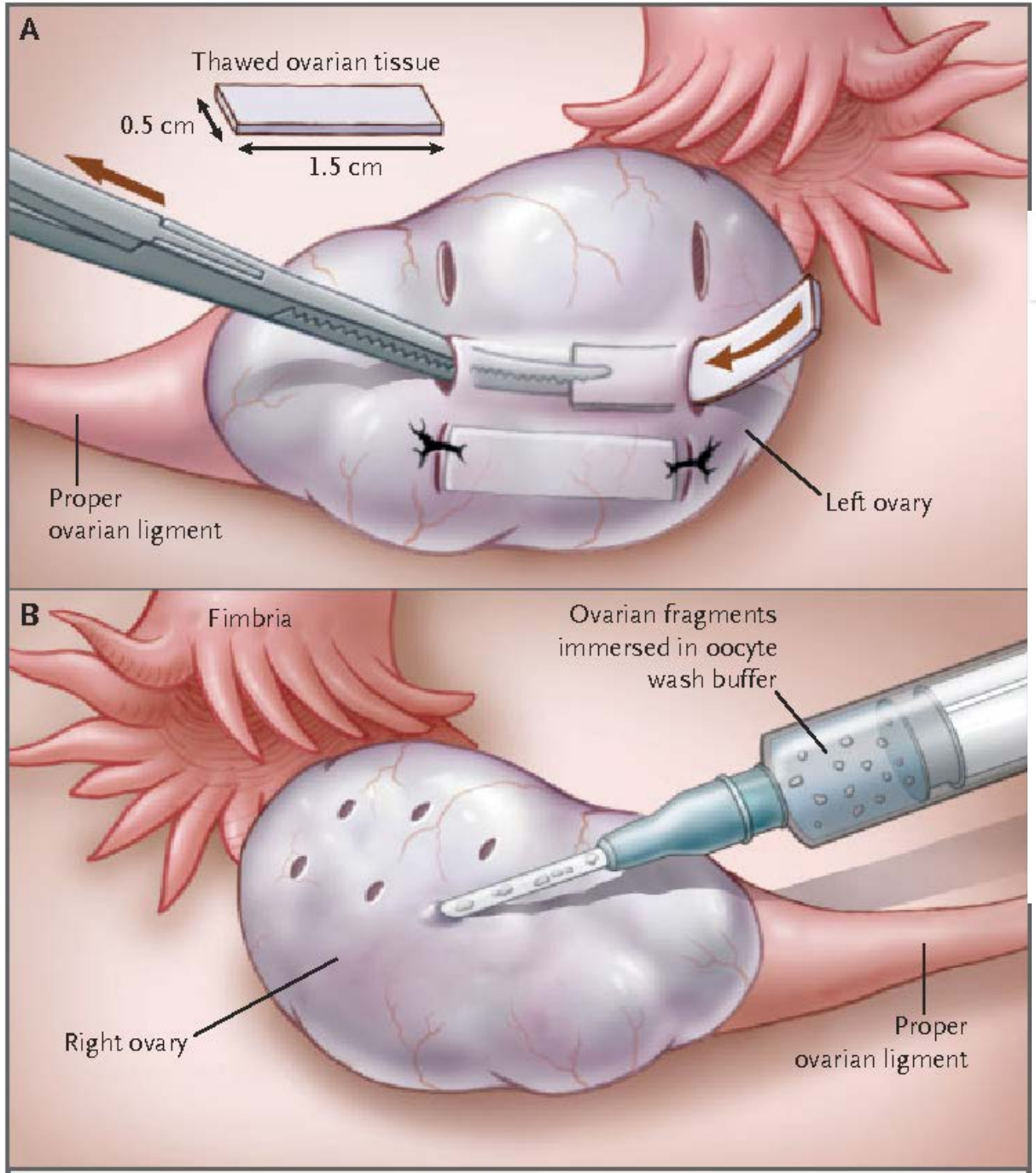
Not recommended for patients >40 YO, have large ovarian cyst, received prior chemotherapy

Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. ASRM Fertility and Sterility 2019

Ovarian Tissue Cryopreservation (OTC) | The Oncofertility Consortium (msu.edu)

PREPUBERTAL FEMALES





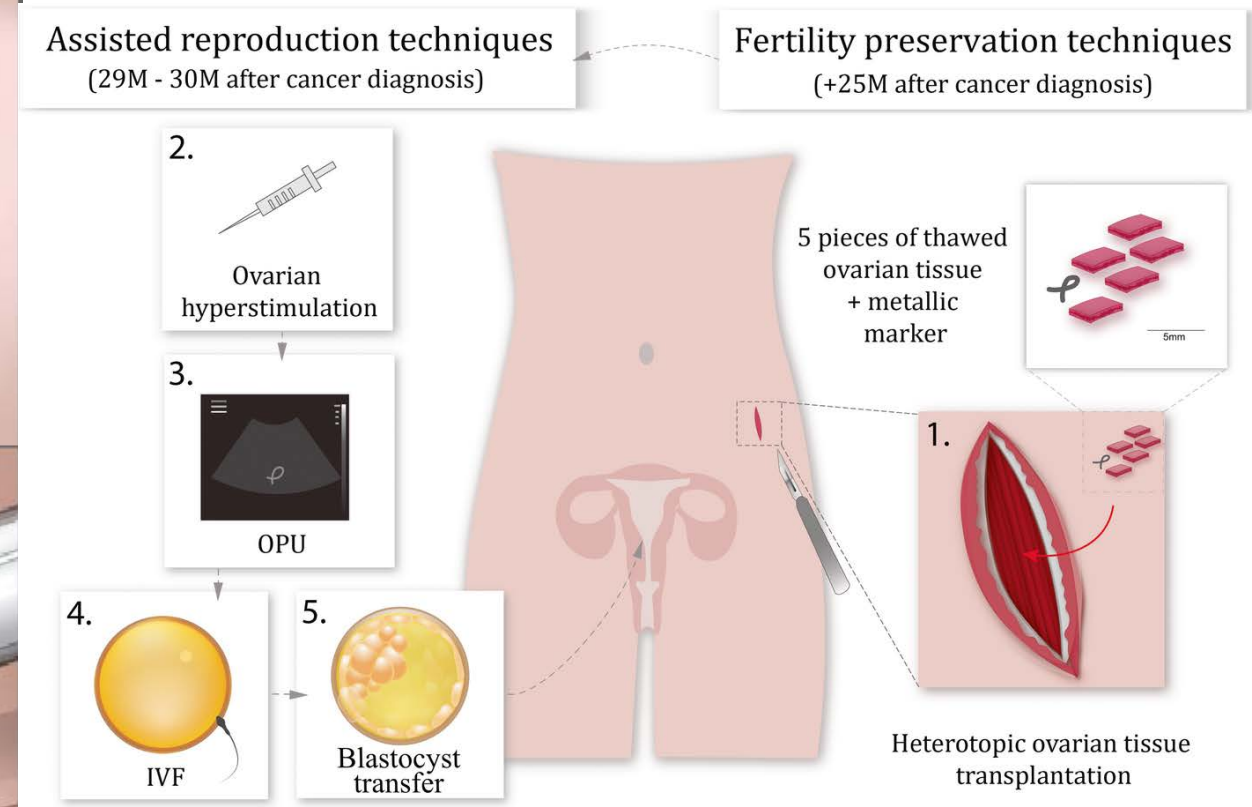
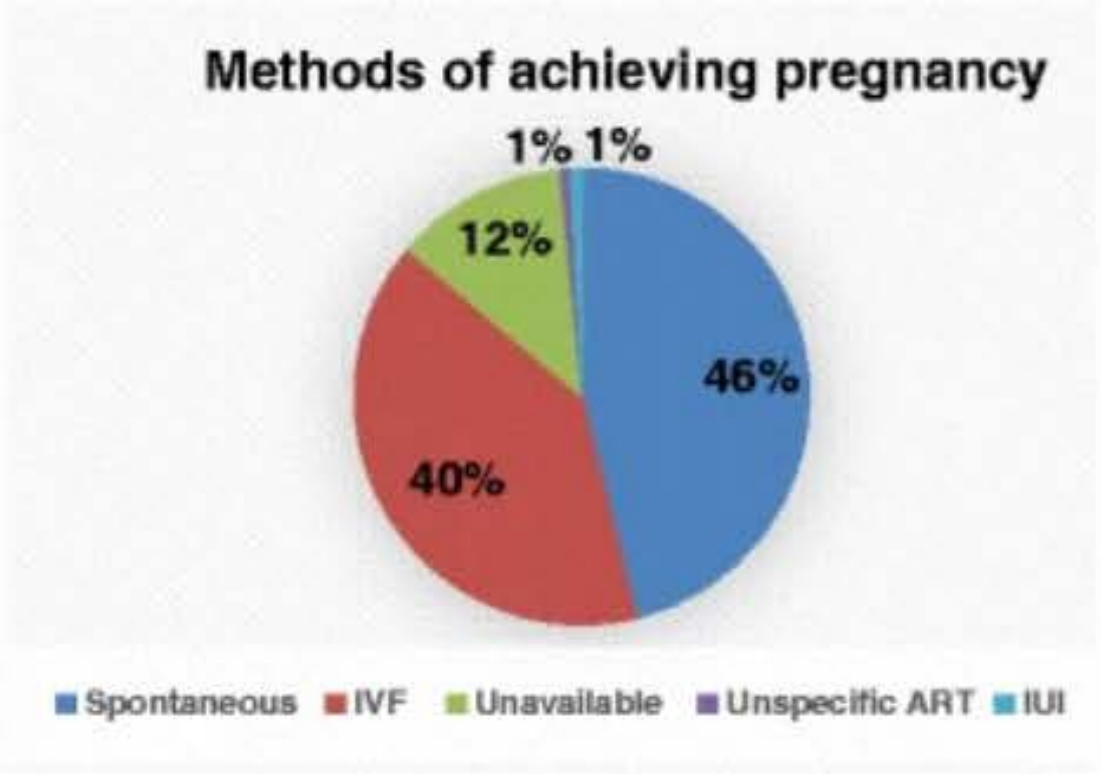
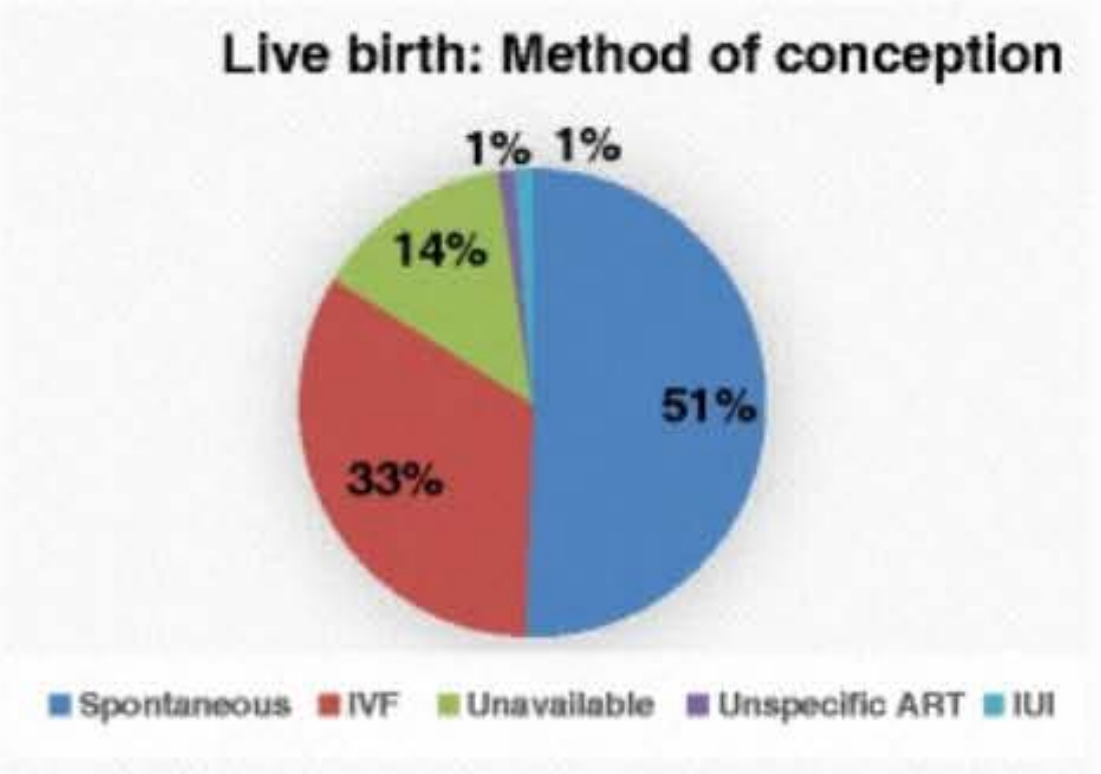


Figure 2. Surgical Technique.

en-thawed ovarian tissue: an update on worldwide activity published in peer-reviewed pa





obtain **a** pregnancy ($N = 131$) and **b** live birth ($N = 87$)

Gellert, S.E., Pors, S.E., Kristensen, S.G. *et al.* Transplantation of frozen-thawed ovarian tissue: an update on worldwide activity published in peer-reviewed papers and on the Danish cohort. *J Assist Reprod Genet* **35,** 561–570 (2018). https://doi.org/10.1007/s10815-018-1144-2

OVARIAN TISSUE CRYOPRESERVATION OUTCOMES

- Live birth between 25-37%
- Hormonal function resumes 60-240 days after transplant
  - Median duration of return is 7 years

Table 4 Gestational age (GA) and birth weight of 40 children, 34 singletons, and 3 sets of twins published in peer-reviewed journals and 9 new Danish cases presented in this paper

From: 86 successful births and 9 ongoing pregnancies worldwide in women transplanted with frozen-thawed ovarian tissue: focus on birth and perinatal outcome in 40 of these children

	NC/IVF/IUI	Delivery mode (CS/VD/NS)	GA (weeks) Median	GA (weeks) Mean ± SEM (range)	Birth weight (g) Median	Birth weight (g) Mean ± SEM (range)	Girls *N*	Boys *N*
Singletons[a]	17/16/1	15/12/7	38	39 ± 0.2 (36–41)	3168	3217 ± 82 (2370–4230)	17	17
Twins	3 sets IVF	2 sets/1 set	37	36 ± 1 (33–38)	2650	2560 ± 286 (1650–3320)	2	4

NC naturally conceived, *IVF* in vitro fertilization, *IUI* intrauterine insemination, *CS* caesarean section, *VD* vaginal delivery, *NS* not specified

[a]The GA on 3 singleton births is not available

Jensen, A.K., Macklon, K.T., Fedder, J. *et al.* 86 successful births and 9 ongoing pregnancies worldwide in women transplanted with frozen-thawed ovarian tissue: focus on birth and perinatal outcome in 40 of these children. *J Assist Reprod Genet* **34,** 325–336 (2017). https://doi.org/10.1007/s10815-016-0843-9

NO EVIDENCE TO SUPPORT THAT OTC INCREASES CHANCE OF DISEASE RECURRENCE

***This should not be offered to patients with known BRCA variants

Gellert, S.E., Pors, S.E., Kristensen, S.G. *et al.* Transplantation of frozen-thawed ovarian tissue: an update on worldwide activity published in peer-reviewed papers and on the Danish cohort. *J Assist Reprod Genet* **35,** 561–570 (2018). https://doi.org/10.1007/s10815-018-1144-2

LIMITED DATA IN PATIENTS <18 YEARS OLD

18 patients were under 21 (9-20.3 years) years old when they cryopreserved their tissue and auto-transplantation of thawed tissue in each of these patients resulted in 10 live births for 9 mothers

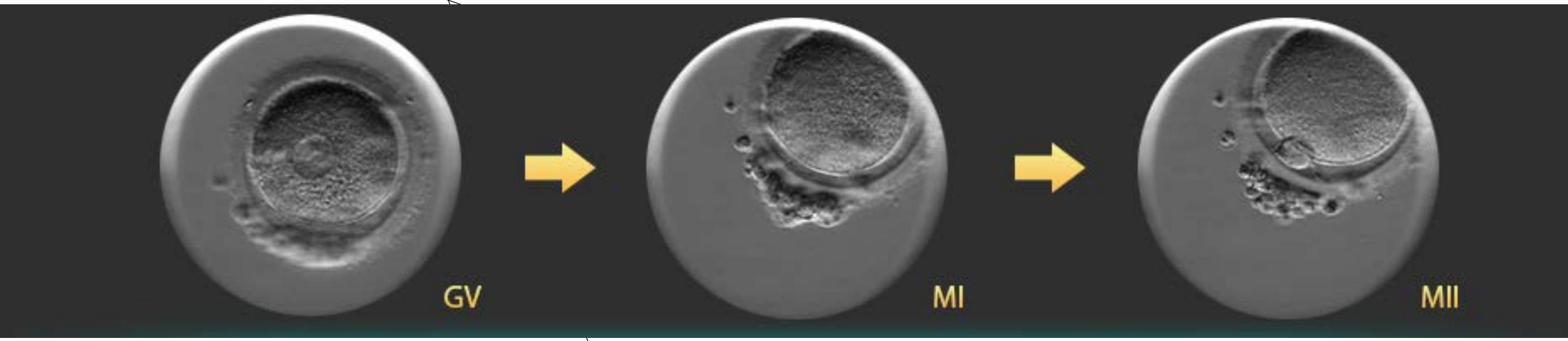
Pacheco F, Oktay K. Current Success and Efficiency of Autologous Ovarian Transplantation: A Meta-Analysis. Reprod Sci 2017;24(8):1111 1120.
Corkum KS, Rhee DS, Wafford EQ, Demeestere I, Dasgupta R, Baertschiger R, et al. Fertility and hormone preservation and restoration for female children and adolescents receiving gonadotoxic cancer treatments: A systematic review. J Pediatr Surg 2019;(Pediatr Blood Cancer 60 2012):ahead of print.

Ann & Robert H. Lurie
Children's Hospital of Chicago®

Children's
Hospital of Wisconsin
Kids deserve the best.

CURRENTLY CHW/ RMC IS WORKING WITH LURIE'S CHILDREN'S HOSPITAL TO PROVIDE THE OPTION OF OVARIAN TISSUE CRYOPRESERVATION TO OUR PATIENTS!

IVM



IN VITRO MATURATION

- Best in women with PCOS
- Has been utilized in patients undergoing gonadotoxic therapy
- Maturation rates from GV to MII are 50-55%
- Fertilization rates similar to in vivo matured oocytes – 70%
- Blast rate much lower 5-6%
- High rate of chromosomal abnormalities (DNA methylation and imprinting disorders)
- First live birth in 2009

Khalili MA, Shahedi A, Ashourzadeh S, Nottola SA, Macchiarelli G, Palmerini MG. Vitrification of human immature oocytes before and after in vitro maturation: a review. *J Assist Reprod Genet*. 2017;34(11):1413-1426. doi:10.1007/s10815-017-1005-4

Characteristic	Singleton pregnancy (n = 345)			Multiple pregnancy (n = 205)		
	IVM group (n =	IVF group (n = 230)	*P* value	IVM group (n = 69; 34	IVF group (n = 136; 68	*P* value
Gestational age (wk)	38.7 ± 1.8	38.8 ± 1.3	.68	35.3 ± 2.5	35.9 ± 1.8	.28
Preterm labor[b]	7 (6%)	9 (3.9%)	.34	16 (47.0%)	34 (50%)	.24
Birth weight (g)	3,306.2 ± 473.9	3,272.4 ± 390.4	.51	2,416.7 ± 580.8	2,380.1 ± 375.3	.74
Sex						.15
Male	60 (52.2%)	128 (55.7%)	.54	34 (49.2%)	63 (46.3%)	
Female	55 (47.8%)	102 (44.3%)		35 (50.7%)	73 (53.6%)	
Fetal malformation	3 (2.6%)[c]	7 (3.0%)[d]	.64	5 (7.2%)[e]	8 (5.9%)[f]	.22

Yu EJ, Yoon TK, Lee WS, Park EA, Heo JY, Ko YK *et al*. Obstetrical, neonatal, and long-term outcomes of children conceived from in vitro matured oocytes. Fertil Steril 2019;112:691-9.

LUPRON

ASRM statement “Given the evidence of efficacy, GnRH agonists may be offered to breast cancer patients to reduce the risk of premature ovarian insufficiency, but should not be used in place of other fertility preservation alternatives”

Blumenfeld Z, Katz G, Evron A. 'An ounce of prevention is worth a pound of cure': the case for and against GnRH-agonist for fertility preservation. Ann Oncol. 2014 Sep;25(9):1719-1728. doi: 10.1093/annonc/mdu036. Epub 2014 Mar 20. PMID: 24651411.

LUPRON AND DMPA FOR MENSTRUAL SUPPRESSION DURING CHEMOTHERAPY

Vaginal bleeding	No. of patients (%)			
	Untreated	DMPA	GnRH-a	Total
No bleeding	7 (35.0)	19 (45.2)	30 (76.9)	56 (55.4)
Mild bleeding*	5 (25.0)	14 (33.3)	9 (23.1)	28 (27.7)
Moderate bleeding†	5 (25.0)	4 (9.5)	0	9 (8.9)
Severe bleeding‡	3 (15.0)	5 (11.9)	0	8 (7.9)
Total number of patients	20	42	39	101
Moderate and severe bleeding§	8 (40.0)	9 (21.4)	0	17 (16.8)

Meriow D et al. Prevention of severe menorrhagia in oncology patients with treatment-induced thrombocytopenia by luteinizing hormone-releasing hormone agonist and depo-medroxyprogesterone acetate. Cancer 2006 107(7):1634-1641

ALWAYS AN OPTION TO DO NOTHING

Patients should have been given the opportunity to hear about and discuss their options so that they can make informed decision that is right for them!

SPECIAL CIRCUMSTANCES

Fertility preservation after chemotherapy

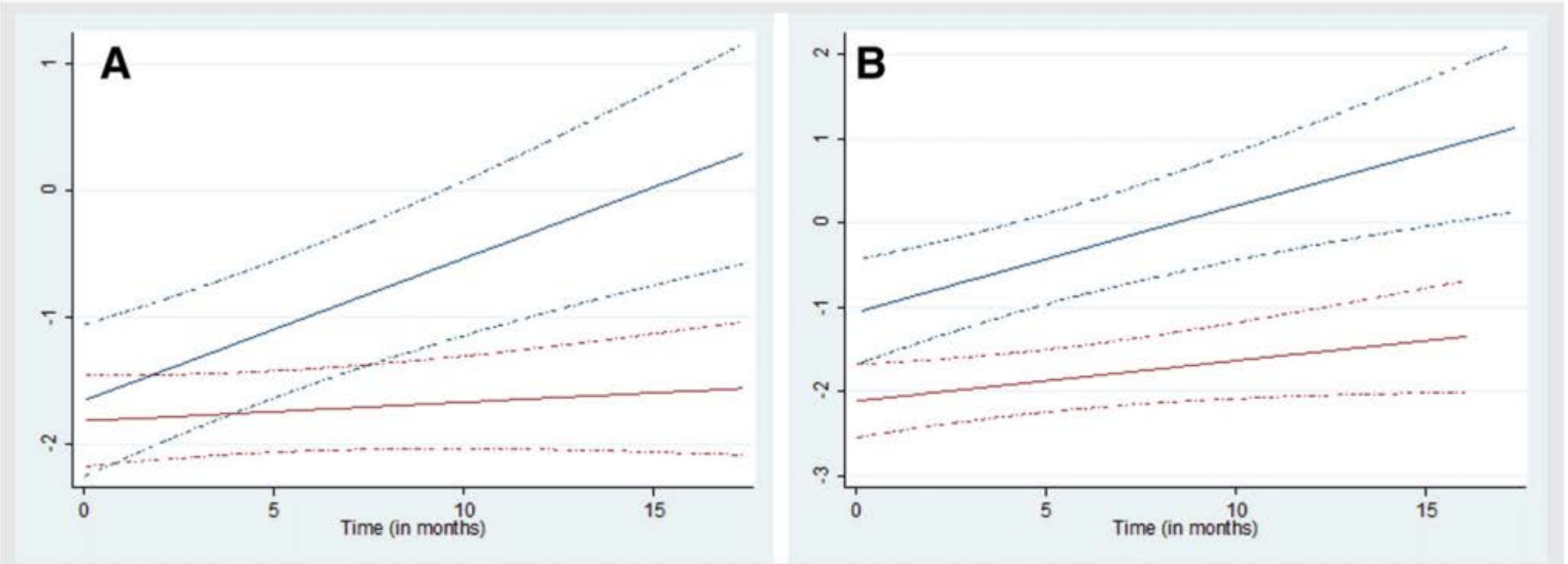
Breast cancer

FERTILITY PRESERVATION FOLLOWING CHEMOTHERAPY

- A safe interval between chemotherapy completion and oocyte/embryo cryopreservation has not been established
- Chemotherapeutic agents can cause DNA abnormalities and oxidative damage
- In mouse models, conception that occurred 3 months after cyclophosphamide exposure were at higher risk of fetal anomalies and pregnancy loss

Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. ASRM Fertility and Sterility 2019

AMH PRIOR TO CHEMOTHERAPY, CAN IT PREDICT OVARIAN RECOVERY?



Rate of recovery of antimüllerian hormone after cancer therapy. (A) *Blue*: Pretreatment antimüllerian hormone (AMH) >2. Slope is 11.9% per month. *Red*: Pretreatment AMH ≤2. Slope is 2.6% per month (interaction *P*=.003). Dashed lines = 95% CI. (B) *Blue*: No alkylator use. Slope is 13.4% per month. *Red*: Alkylator use. Slope is 4.9% per month (interaction *P*=.062). Dashed lines = 95% CI.

Dillon. Pretreatment AMH determines posttreatment recovery. Fertil Steril 2013.

AMH POST TREATMENT

Modeling of reproductive lifespan in female AYA cancer survivors based upon AMH

Breast (26.9%), Lymphoma (24.8%), Thyroid (18%)

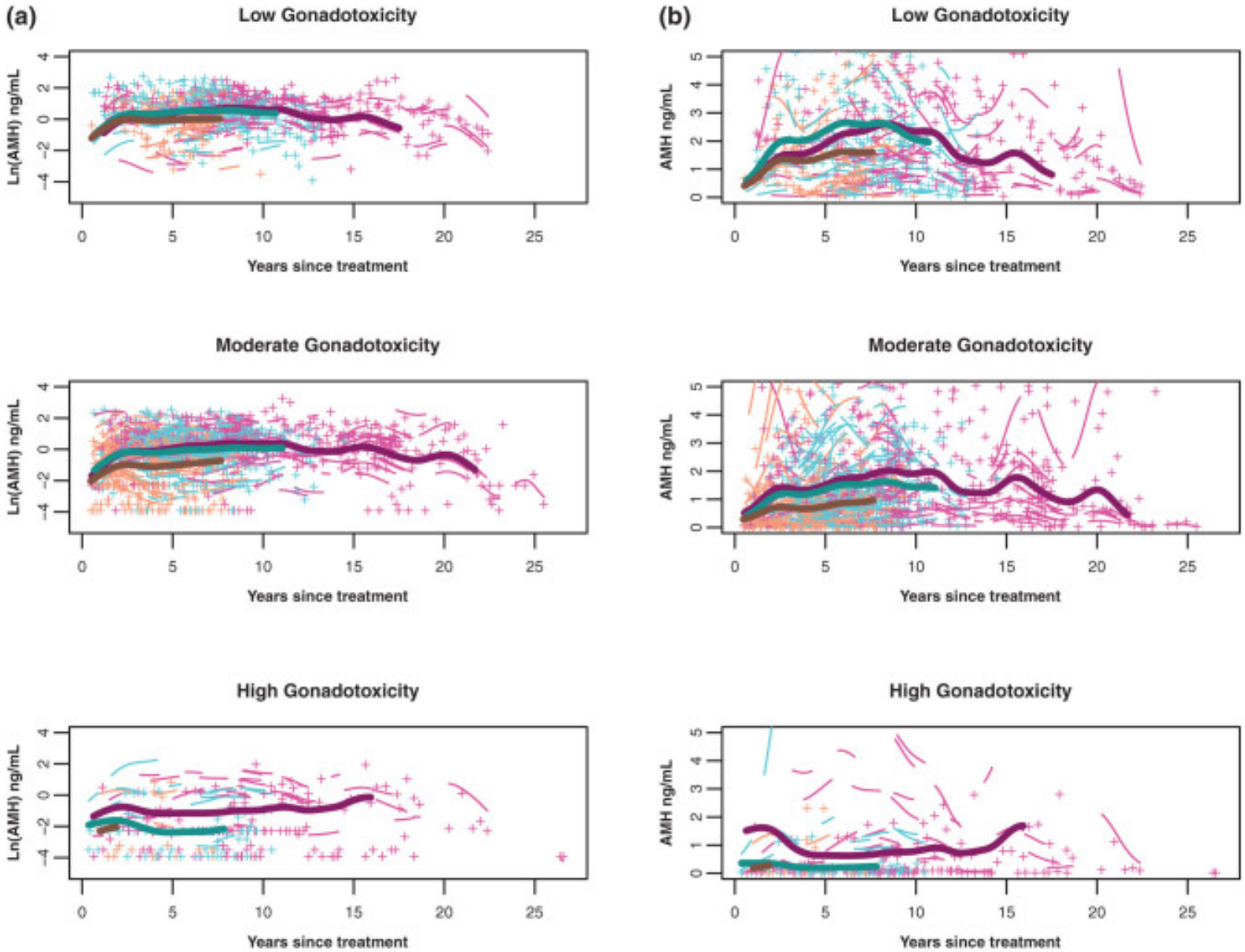
AMH trajectories differed by treatment gonadotoxicity

Moderate gonadotoxicity- AMH increased over 2-3 years post treatment then declined over 15 years

High gonadotoxicity- AMH lower overall and declined shortly after peak at 2-3 years

Protective effect of age not observed in high gonadotoxic group

Su IH et al. JCEM 2020;Aug 105 (8):2740-2751


(a)
Low Gonadotoxicity
Ln(AMH) ng/mL
Years since treatment
(b)
Low Gonadotoxicity
AMH ng/mL
Years since treatment
Moderate Gonadotoxicity
Ln(AMH) ng/mL
Years since treatment
Moderate Gonadotoxicity
AMH ng/mL
Years since treatment
High Gonadotoxicity
Ln(AMH) ng/mL
Years since treatment
High Gonadotoxicity
AMH ng/mL
Years since treatment
Age < 25
Age 25–30
Age > 30

OPTIMAL TIMING OF AMH MEASUREMENT POST CHEMO

- No current data
- Ok to measure 6-10 months post treatment
- Follow every 6 months
- No opportune time to intervene based on percent drop
- Likely best time to intervene is 2-3 years post treatment

BREAST CANCER

Need to keep estradiol levels low, especially in hormone responsive cancer

BREAST CANCER

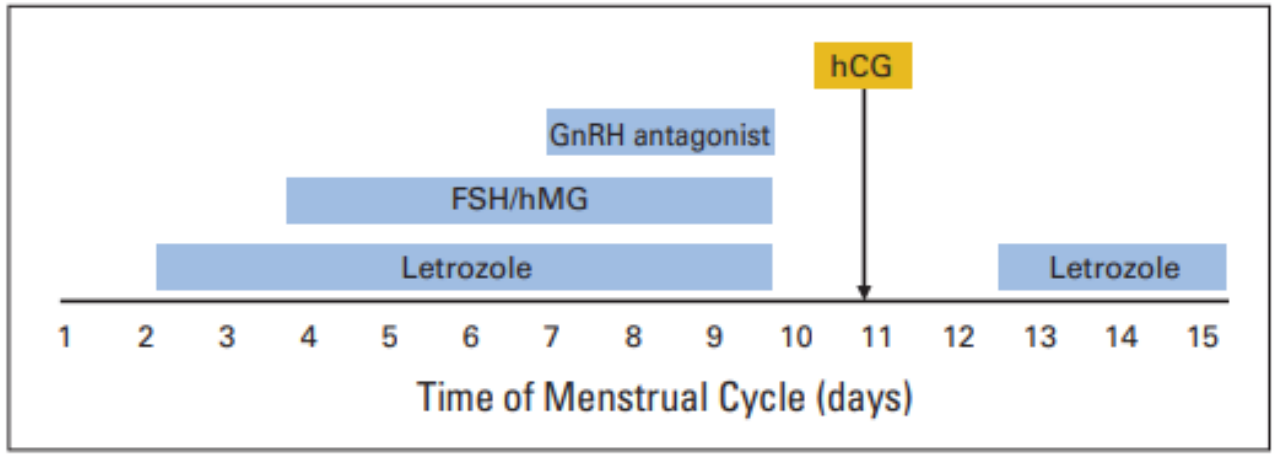


Fig 1. Protocol for ovarian stimulation with letrozole and gonadotropins in patients diagnosed with breast carcinoma. In this regimen, letrozole is initiated on the second day of menstrual cycle and gonadotropins are started 2 days later. A gonadotropin-releasing hormone (GnRH) antagonist is administered when estradiol levels reach ≥ 250 pg/mL or the lead follicle size reaches 14 mm. Human chorionic gonadotropin (hCG) is administered when the leading follicle reaches 19 to 20 mm in diameter. Letrozole treatment is restarted after oocyte retrieval until the estradiol levels are lower than 50 pg/mL. FSH, follicle-stimulating hormone; hMG, human menopausal gonadotropin.

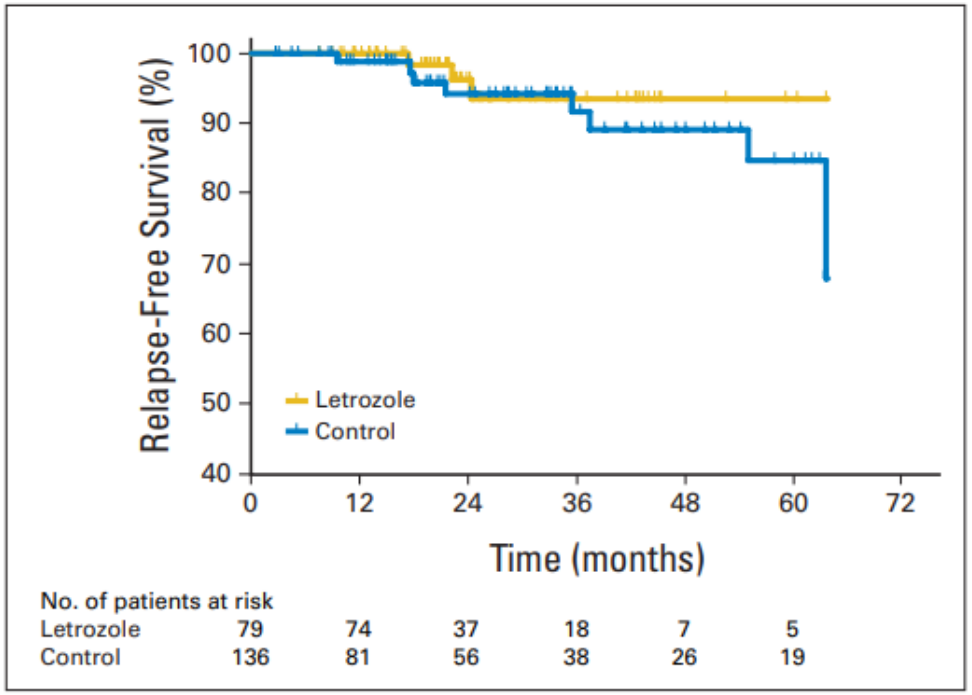


Fig 2. Relapse-free survival in ovarian stimulation and control groups. Kaplan-Meier plot for relapse-free survival in letrozole and control groups. $P = .36$ (log-rank test), hazard ratio = 0.56. The number of patients at risk at each year is shown below the graph.

Azim AA, Costantini-Ferrando M, Oktay K. Safety of fertility preservation by ovarian stimulation with letrozole and gonadotropins in patients with breast cancer: a prospective controlled study. J Clin Oncol. 2008 Jun 1;26(16):2630-5. doi: 10.1200/JCO.2007.14.8700. PMID: 18509175.

LETROZOLE UTILIZATION FOR ESTRADIOL SUPPRESSION

Patients at increased risk of clots

- Post operatively
- Sickle cell disease

ASRM – WHAT SHOULD BE AVAILABLE

Rapid access

Interdisciplinary team: oncology, endocrinology, reproductive medicine, urology, anesthesiology

Lab: ability to vitrify oocytes and embryos

Counseling: genetic, mental health, financial

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WRAP UP

Ideal to know dose and duration of chemotherapeutics at time of referral

Patients have the best outcome if they undergo fertility preservation options prior to chemotherapy/radiation

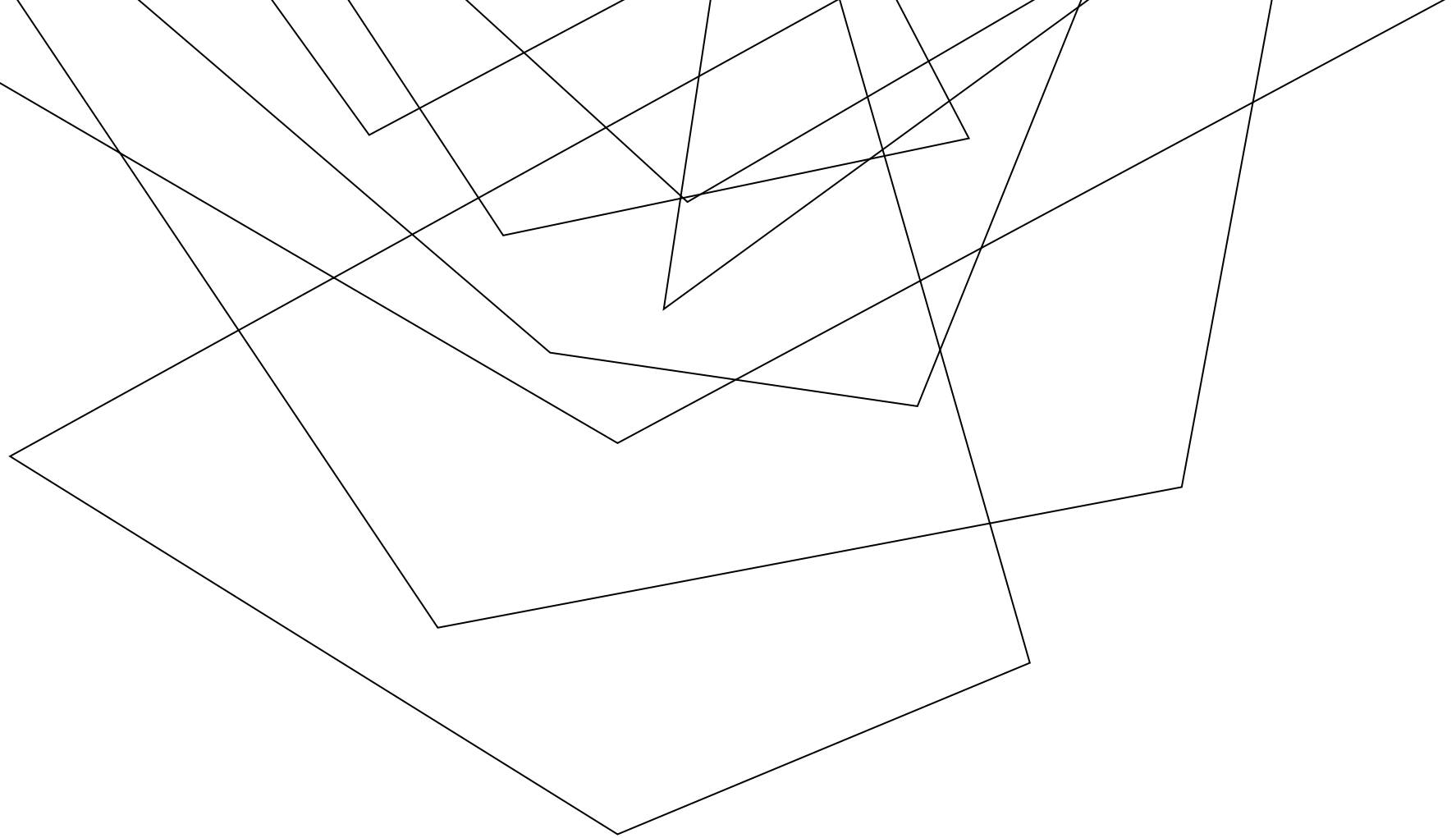
- If not, follow AMH 6-10 months post treatment every 6 months

If able obtain AMH prior to appointment

Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. ASRM Fertility and Sterility 2019

FINANCIAL ASPECT

- IVF without assistance (ARCě as an option)
  - Oocyte cryopreservation ~$10,000 + meds
  - Embryo cryopreservation ~$13,000 + meds
- Livestrong (Single <$100k and couple <$135k annual income)
  - Oocyte cryopreservation $7,433
  - Embryo cryopreservation $8,640
  - Post treatment $9,922
  - Meds usually covered
  - Reprotech for gamete/embryo storage
  - Pre-chemo and post-chemo



QUESTIONS?

#MCWFertility

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