Fertility Preservation and Reproductive Late Effects in Adolescent and Young Adult Cancer

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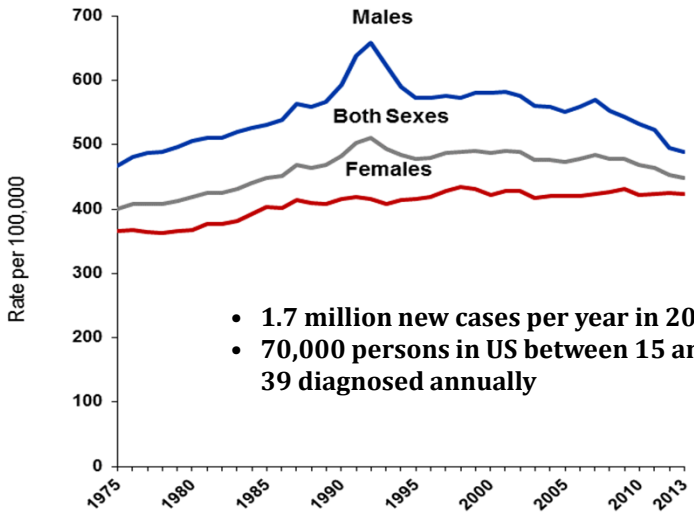
Learning Objectives

- Explain the effects of cancer treatments on fertility and limits of risk stratification.
- Discuss standard and novel fertility preservation therapies for patients with cancer.
- Describe reproductive late effects and management options in survivorship.
- Utilize the referral process to the Fertility Preservation and Reproductive Health program at The Ohio State University Wexner Medical Center James Cancer Hospital.

Trends in Cancer Incidence Rates*, US, 1975-2013

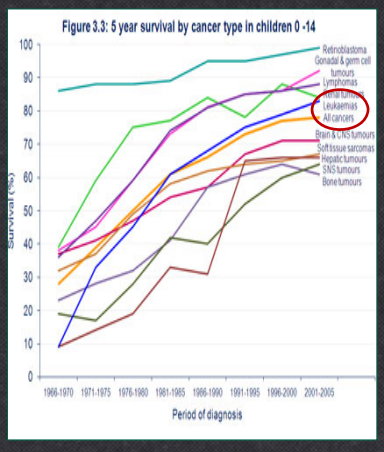


- **1.7 million new cases per year in 2018**
- **70,000 persons in US between 15 and 39 diagnosed annually**

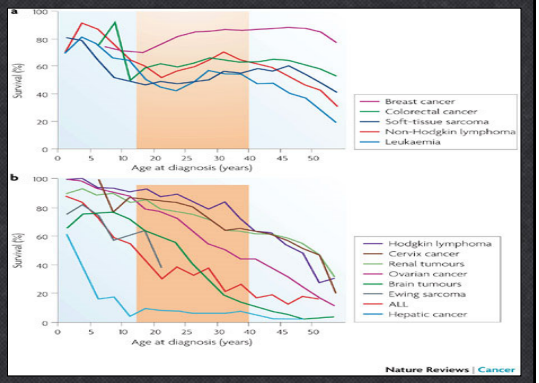
*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2016.

Survival

Pediatric



Adolescent and Young Adult



Cancer statistics, 2013. Siegel et al. CA Cancer J Clin. 2013 Jan;63 (1):11-30.

Clinical Ascertainment of Health Outcomes Among Adults Treated for Childhood Cancer

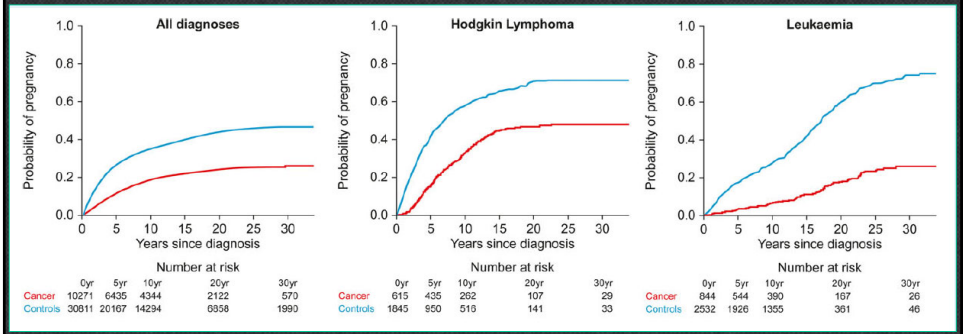
Melissa M Hudson et.al., JAMA. 2013;309(22):2371-2381

Prevalence of Cardiovascular, Pulmonary, and Endocrine or Reproductive Late Effects in At-Risk Populations Following Exposure-Based Screening

				No. (%) [95% CI]				
				SJLIFE Diagnosis				
Potential Late Effect	**Screening Test**	**Exposure Status**	**No. at Risk[a]**	**Before**	**Related**	**After**	**Overall Prevalence**	**CTCAE Version 4 Grade 3-4, %[b]**
Primary ovarian failure	Menstrual history, FSH, estradiol	Alkylating agents, radiation to female reproductive system	553	44 (8.0) [5.8-10.5]	20 (3.6) [2.2-5.5]	1 (0.2) [0.0-1.0]	65 (11.8) [9.2-14.7]	0
Male germ cell dysfunction	Semen sample analysis	Alkylating agents, radiation to male reproductive system	328	9 (2.7) [1.3-5.1]	209 (63.7) [58.3-68.9]	0	218 (66.4) [61.1-71.6]	97.7
Leydig cell failure	Morning testosteron, LH	Alkylating agents, radiation to male reproductive system	574	25 (4.4) [2.8-6.4]	37 (6.4) [4.6-8.8]	4 (0.7) [0.2-1.8]	66 (11.5) [9.0-14.4]	0

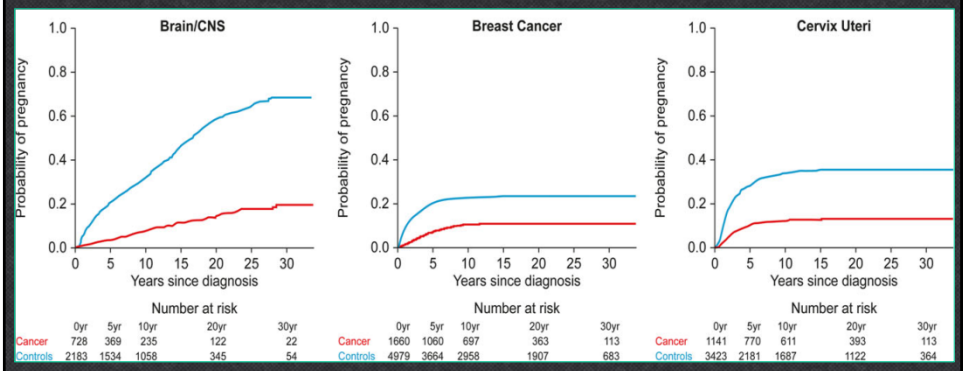
- Health outcomes in 1,713 survivors median age 32 yrs (18-60 yrs)
- Prevalence of primary ovarian failure 12% in at risk females
- Prevalence of male germ cell dysfunction 66%
- Prevalence of Leydig cell failure 12%

The impact of cancer on subsequent chance of pregnancy: a population based analysis



Hum Reprod. 2018 Jul 1;33(7):1281-1290.

The impact of cancer on subsequent chance of pregnancy: a population based analysis



Hum Reprod. 2018 Jul 1;33(7):1281-1290.

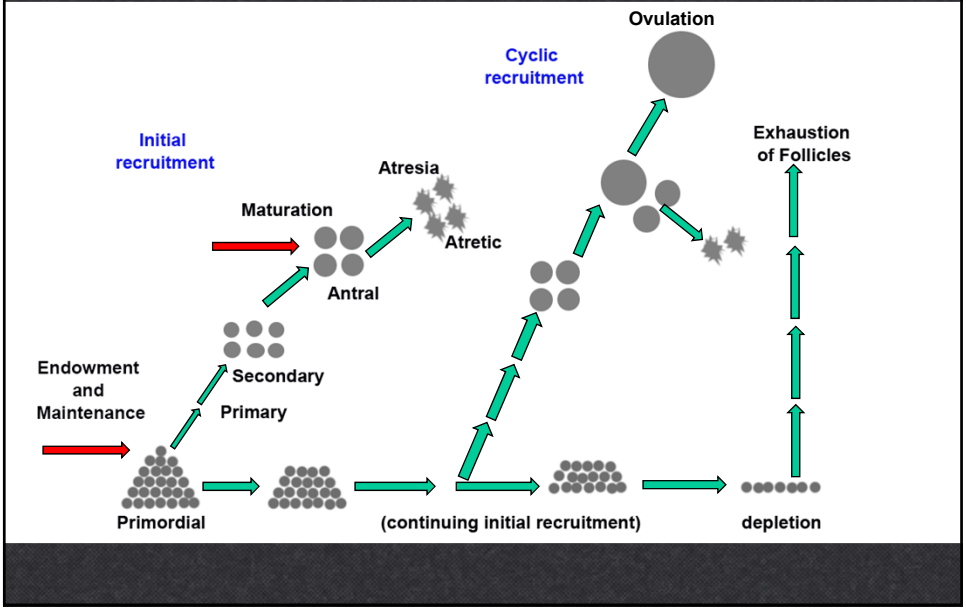
Cancer and Fertility

Implications of systemic malignancies on human fertility. Reproductive Biomedicine Online. Agarwal. 2004;9(6):67-9.

- Cytokines
  - Non-specific damage to gonadal tissue
- Metabolic disturbance
  - Fever
  - Anorexia
- Hormonal
  - Regional hormonal alterations
  - Down-regulation of HPO axis

Pal. Human Reprod.1998;13:1837-40

Chemoradiation and Follicular Development



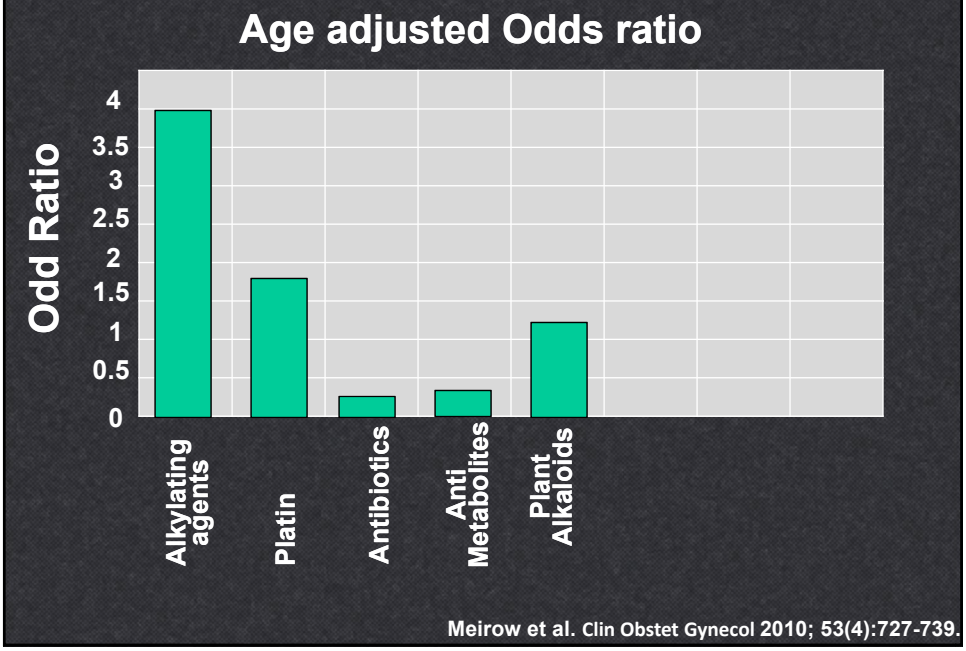
How is risk estimated?

Chemotherapy and Fertility

Gonadotoxicity of commonly used chemotherapy agents.		
Chemotherapeutic agent	Risk of gonadotoxicity	Mechanism of action
Alkylating agents Cyclophosphamide Ifosfamide	High	Induces single-stranded DNA breaks, targets primordial follicles and resting oocytes
Platinums Cisplatin Carboplatin	Intermediate	Induces chromosomal damage and DNA cross-links
Taxanes Paclitaxel	Intermediate	Inhibits microtubule formation and spindle function
Anthracyclines Doxorubicin	Intermediate	Inhibits DNA replication and transcription
Antimetabolites Gemcitabine 5-Fluorouracil	Low	Acts primarily on cells synthesizing DNA

Chan et al. Gynecol Oncol 2017; 144:631-636

Chemotherapy and Fertility



Meirow et al. Clin Obstet Gynecol 2010; 53(4):727-739.

Cyclophosphamide Equivalent Dose Calculation. The CED is calculated using the following equation: CED (mg/m^2) = 1.0 (cumulative cyclophosphamide dose (mg/m^2)) + 0.244 (cumulative ifosfamide dose (mg/m^2)) + 0.857 (cumulative procarbazine dose (mg/m^2)) + 14.286 (cumulative chlorambucil dose (mg/m^2)) + 15.0 (cumulative BCNU dose (mg/m^2)) + 16.0 (cumulative CCNU dose (mg/m^2)) + 40 (cumulative melphalan dose (mg/m^2)) + 50 (cumulative Thio-TEPA dose (mg/m^2)) + 100 (cumulative nitrogen mustard dose (mg/m^2)) + 8.823 (cumulative busulfan dose (mg/m^2)).

	A	B	C	D
1				
2	**Alkylating agent**	**Cumulative dose (mg/m2)**		
3	Cyclophosphamide			
4	Ifosfamide	101000		
5	Procarbazine			
6	Chlorambucil			
7	BCNU			
8	CCNU			
9	Melphalan			
10	Thiotepa			
11	Nitrogen Mustard			
12	Busulfan			
13				
14	Cyclophosphamide Equivalent Dose Score =		24644	mg/m2

http://oncofertility.northwestern.edu/sites/oncofertility.northwestern.edu/files/ced_calculator.xlsx

Estimating Risk - CED

TABLE IV. Rate Ratios for Non-Surgical Premature Menopause: Multiple Poisson Regression Model

	CED			AAD		
Variable	RR	95% CI	*P*-value	RR	95% CI	*P*-value
Age	**1.14**	**1.09–1.20**	**<0.001**	**1.13**	**1.07–1.19**	**<0.001**
Minimum ovarian dose						
Other cancers						
None	1.00			1.00		
1–99 cGy	2.96	0.92–9.50	0.069	**4.25**	**1.18–15.26**	**0.027**
≥100 cGy	**11.68**	**3.59–38.04**	**<0.001**	**16.77**	**4.55–61.88**	**<0.001**
Hodgkin lymphoma						
None	**13.86**	**4.04–47.57**	**<0.001**	**9.88**	**1.65–59.24**	**0.012**
1–99 cGy	**10.04**	**3.40–29.65**	**<0.001**	**12.73**	**3.55–45.57**	**<0.001**
≥100 cGy	**10.76**	**3.32–34.91**	**<0.001**	**10.73**	**2.70–42.64**	**<0.001**
CED (mg/m^2)						
0	1.00					
>0–<4,000	0.56	0.07–4.27	0.578			
≥4,000–<8,000	**2.74**	**1.13–6.61**	**0.025**			
≥8,000	**4.19**	**2.18–8.08**	**<0.001**			
AAD tertile						
0				1.00		
1–2				2.09	0.97–4.51	0.060
3				**4.99**	**2.53–9.84**	**<0.001**

CED, Cyclophosphamide Equivalent Dose; AAD, Alkylating Agent Dose score; RR, rate ratio; CI, confidence interval; values shown in bold are statistically significant.

Green et al. Pediatr Blood Cancer. 2014;61:53-67

Gonadotoxic Risk: >80% risk of loss of reproductive potential

- Alkylating-intensive chemotherapy
  - cyclophosphamide equivalent dose (CED) ≥ 7,500 mg/m2
  - any treatment regimen containing procarbazine
  - busulfan cumulative dose >600 mg/m2
  - alkylating chemotherapy conditioning prior to SCT
- Whole abdomen/pelvic irradiation to ovaries
  - ≥15 Gy pre-pubertal, >10 Gy post-pubertal, >6 Gy adult
- Whole abdomen/pelvic irradiation to uterus ≥30 Gy
- Total body irradiation and cranial radiation ≥30 Gy

Metzger ML. J Clin Oncol; 31(9), 2013

Subfertility/Infertility Risk

High risk > 80%	Medium Risk >20 and <80%	Low Risk < 20%
Conditioning for BMT	AML	ALL
Hodgkin's: w/ alkylating agents	Hepatoblastoma	Wilms' tumor
Soft-tissue sarcoma: metastatic	Osteosarcoma	Soft-tissue sarcoma: stage I
Ewing's sarcoma: metastatic	Ewing's sarcoma: non-metastatic	Retinoblastoma
	Soft-tissue sarcoma: stage II/III	Germ-cell tumors (fertility sparing)
	Neuroblastoma	
	Non-Hodgkin lymphoma	
	Hodgkin's: alternating alkylator tx	

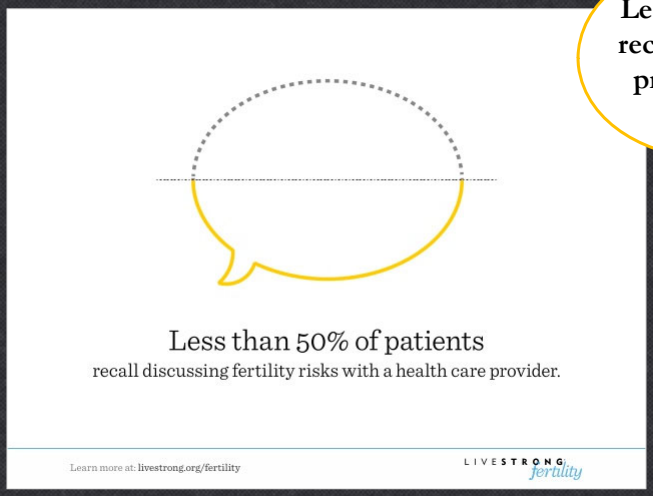
Can risk be minimized?

Expert Consensus Position Statements

- American Society of Clinical Oncology (ASCO)
- American Society for Reproductive Medicine (ASRM)
- Association of Pediatric Hematology/Oncology Nurses (APHON)
  - "Physicians should inform cancer patients about options for fertility preservation and future reproduction prior to treatment…"
  - "…regardless of the patient's age, gender, culture, socioeconomic status, or healthcare team bias…"
  - "…and continue throughout treatment and survivorship in a manner appropriate to the patient's developmental stage at that time."

Statements supported by American College of Obstetricians and Gynecologists (ACOG) and American Academy of Pediatrics (AAP).

Gap



Less than 30% receive fertility preservation therapies

Gwede CK et al. Pract Radiat Oncol. 2012;2:242-247.
Quinn GP et al. J Clin Oncol. 2009; 27:5952–5957

Fertility Preservation Methods

Standard Methods	Considerations
Mature oocyte cryopreservation (35 - 50% success rate)	No partner needed; 10 – 14 days stimulation; surgical procedure; costs; no ovarian function preserved Stimulation may occur at any phase of the cycle
Embryo cryopreservation (40% success rate)	Partner or sperm donor needed; 10 – 14 days stimulation; surgical procedure; costs; no preservation of ovarian function; embryo ownership concerns
Ovarian transposition (88-90% success rate)	Underutilized
Ovarian shielding (75-80% success rate)	Scatter effect; consider concomitant chemotherapy

Fertility Preservation Methods

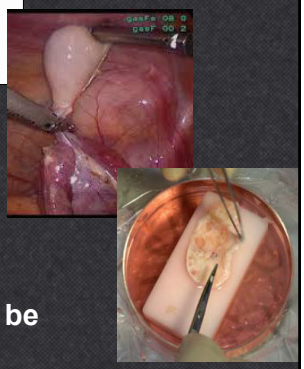
Investigational Methods	Considerations
Immature oocyte cryopreservation	No partner needed; no stimulation; surgical procedure; costs; no ovarian function preserved
Ovarian tissue freezing	Surgical procedure; costs; transplantation not suitable with high gonadal involvement; preservation of gonadal function
GnRHa ovarian suppression	Conflicting historical data; recent data supports use in breast cancer patients and when no other therapies available

Indications for Ovarian Tissue Cryopreservation

- Edinburgh criteria for malignant disorders (modified):
  - High risk of gonadal failure after cancer treatment
  - Absence of previous high gonadotoxic chemotherapy
  - Absence of surgical contraindication
  - Negative serologies
- Nonmalignant disorders treated with immunosuppression or SCT
- Individuals with gender and sex diversity
- Genetic predisposition to accelerated follicular loss

Wallace et al. The Lancet 2005;6(4):209-218

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



- 130 total children worldwide as of 2018
- Age range from adolescence to mid 30's
- Spontaneous and assisted conception
- 32% delivery rate - suggest OTC no longer be experimental
- Transplanted tissue shown to be viable for up to 10 years

Jensen et al. J Assist Reprod Genet (2017) 34: 325

Obstet Gynecol Int. 2010; 2010: 160386.

Rowell E. (2017) Optimal Technique for Laparoscopic Oophorectomy for Ovarian Tissue Cryopreservation in Pediatric Girls. In: Woodruff T., Gosiengfiao Y. (eds) Pediatric and Adolescent Oncofertility. Springer, Cham

In Vitro Maturation

First pregnancy and live birth resulting from cryopreserved embryos obtained from in vitro matured oocytes after oophorectomy in an ovarian cancer patient.

Prasath EB[1], Chan ML, Wong WH, Lim CJ, Tharmalingam MD, Hendricks M, Loh SF, Chia YN.

- 21 yo s/p interval bilateral oophorectomy for bilateral serous carcinoma of the ovary
- OTC performed at second surgery
- All visible follicles aspirated
- ICSI followed by 2 embryo transfer
- Delivery of healthy infant
- Several reports of live birth after IVM of growing follicles
- No reports of live birth after IVM of primordial follicles

Fertility Preservation Methods

Investigational Methods	Considerations
Immature oocyte cryopreservation	No partner needed; no stimulation; surgical procedure; costs; no ovarian function preserved
Ovarian tissue freezing	Surgical procedure; costs; transplantation not suitable with high gonadal involvement; preservation of gonadal function
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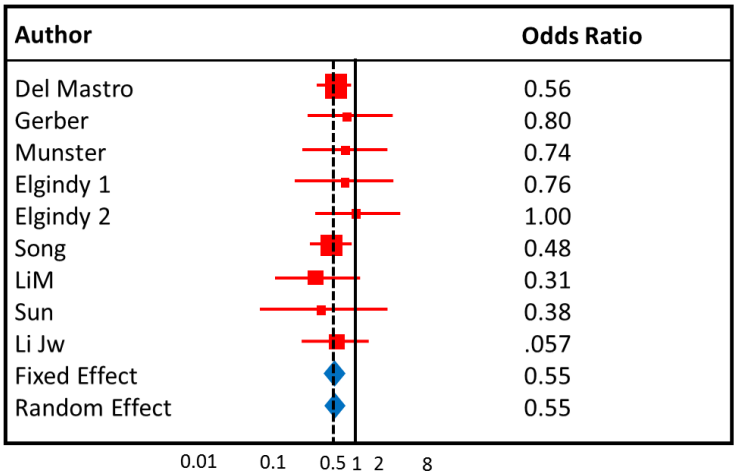
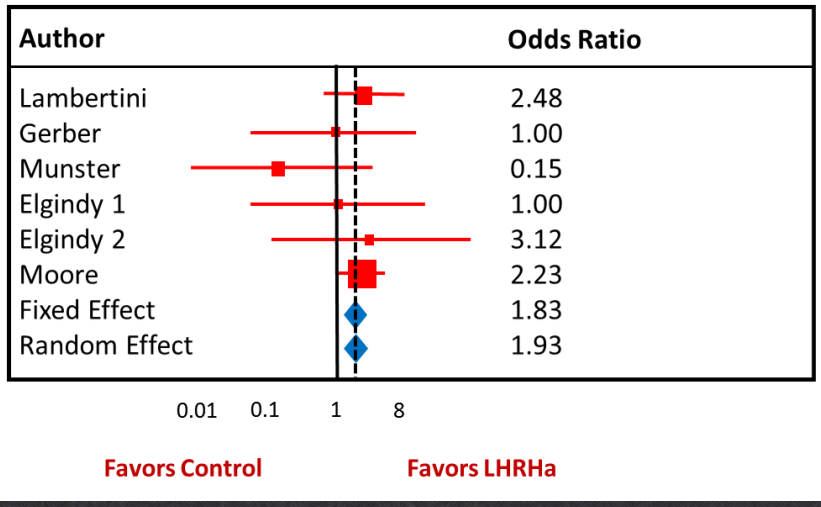
GnRHa therapy and ovarian protection: Premature ovarian failure



OR for premature ovarian failure: LHRHa versus chemotherapy alone

Lambertini et al. Annals of Oncology; 2015

GnRHa therapy and ovarian protection: Pregnancy



OR for pregnancy: LHRHa versus chemotherapy alone

Menstrual suppression

- Leuprolide acetate 11.25 mg IM or 22.5 mg SC every 12 weeks during chemotherapy for menstrual suppression for patients are risk of profound anemia Bates et al 2011.
  - administered prior to chemotherapy
  - final dose to be administered at final chemotherapy infusion.
- ASCO: when proven fertility preservation methods…are not feasible…GnRHa may be offered to individuals in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency Oktay 2018.
- Norethindrone acetate add-back to minimize hot flashes and protect bone DiVasta 2013.
  - start with or before leuprolide and discontinue 12 weeks after final dose

Bates et al.Pharmacotherapy 2011;31(11):1092–1110.
DiVasta et al. Curr Opin Obstet Gynecol 2013, 25:287–292
Oktay, K., et al., J Clin Oncol, 2018. 36(19): p. 1994-2001.

Minimizing Risk

Protective Agent	Mechanism of action	Treatment interactions
GnRH analog	Suppresses HPO axis; unclear	No interference
Imatinib	Inhibit c-Abl kinase apoptosis pathway	May interfere w/ apoptosis
Sphingosine-1-Phosphate	Inhibit sphingomyelin apoptosis pathway	May interfere w/ apoptosis
Tamoxifen	Anti-apoptotic activity; Antioxidant activity via IGF-1 axis; Possible HPO axis suppression	Concern for antagonism
AS101	Inhibits P13K/PTEN Akt follicle activation pathway; anti-apoptosis	No interference; may have additive/synergistic interaction
Bone marrow mesenchymal stem cells	Tissue differentiation, angiogenesis, anti-apoptosis	May cause drug resistance with Cisplatin
Growth-Colony Stimulating Factor (G-CSF)	Unclear: possibly angiogenesis; anti-apoptosis	No interference

Fertility Preservation Costs

Methods	Costs
Sperm cryopreservation	$400 + $175 for semen analysis
Oocyte cryopreservation	$8000 plus meds $4000 - $6000 (reduced costs through Livestrong) plus meds
Embryo cryopreservation	$6500 - $13000 $7800 - $12000 reduced costs plus meds
Long term storage	$275 $75 reduced costs
Ovarian tissue cryopreservation	$10000 - $30000 for oophorectomy (funding) $500 for tissue processing (funding)

Donor Embryos	Donor Oocytes	Gestational Surrogate	Adoption
• Embryos donated • Success rate > frozen embryo/ IVF transfers • $5,000-7,000 + IVF costs	• Oocytes donated • 40-50% success rate •$5,000-15,000 + IVF costs	• Pregnancy carried for patient • Success rate similar to fresh cycle IVF • $10,000-100,000	• Legal parent-child relationship created •$2500-35000

Levine J et al. J Clin Oncol 2010; 28: 1-11.

Is fertility preservation safe in breast cancer ?

Safety of Fertility Preservation by Ovarian Stimulation With Letrozole and Gonadotropins in Patients With Breast Cancer: A Prospective Controlled Study

Amr A. Azim, Maria Costantini-Ferrando, and Kutluk Oktay

- **Patients ages 18-45**
- **Histologically confirmed invasive breast carcinoma**
- **Stage III or less disease**
- **Normal baseline hormonal function**
- **79 elected to undergo COS with Letrozole and gonadotropins**
- **136 declined**
- **Type of chemotherapy similar and adjusted for tamoxifen use**

Controlled Ovarian Stimulation: Aromatase Inhibitors

	Study (n=79)	Controls (n=136)	P value
Time between surgery and chemotherapy (d)	45.08 +/- 31.64	33.46 +/- 27.3	< 0.01
Length of stimulation	9.87 +/- 2.28	n/a	
Mean Peak E2 levels pg/ml	405.94 +/- 256.64	n/a	
Oocytes retrieved	10.3 +/- 7.75	n/a	
Oocytes/embryos cryopreserved	5.97 +/- 4.97	n/a	
Median length follow-up after surgery (mos.)	23.4	33.05	<0.001
Recurrences	3 (3.8%)	11 (8.1%)	

Azim et al. J Clin Onc;2008(26);16:2630-2635

Time from definitive surgery to chemotherapy: survival rates

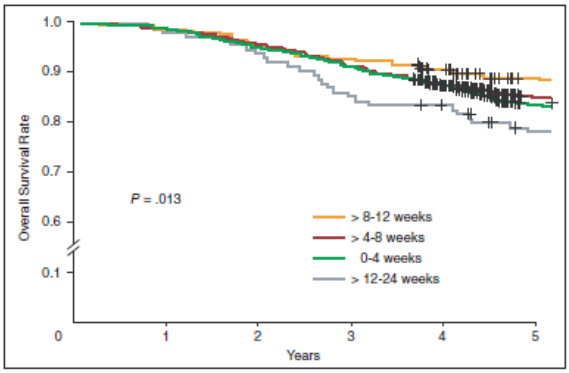
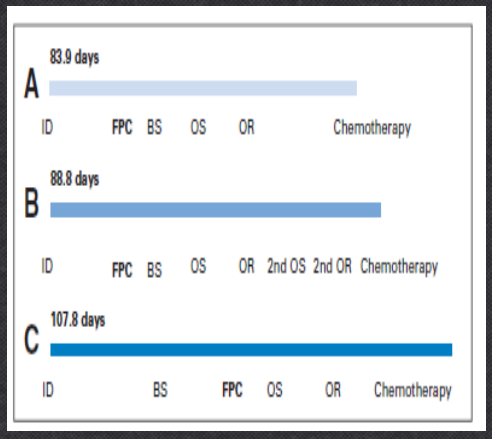


Fig 3. Kaplan-Meier plot for overall survival according to interval between surgery and chemotherapy initiation. Overall survival for the four groups: 0 to 4 weeks, longer than 4 to 8 weeks, longer than 8 to 12 weeks, and longer than 12 to 24 weeks from definitive surgery to start of adjuvant chemotherapy.

Lohrisch . J Clin Oncol. 2006; 24:4888–4894
Cold. Br J Cancer. 2005; 93:627–632.

Timing of Fertility Preservation Counseling

- 93 patients
- 35 referred prior to breast surgery (BS)
  - 42.6 days ID to OS
- 58 referred post BS
  - 71.9 days ID to OS



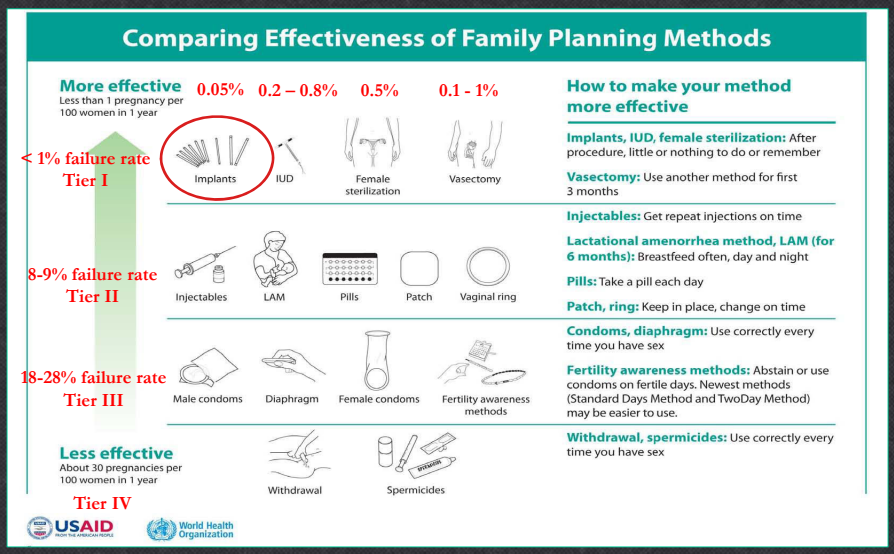
Lee et al. J Clin Oncol 2010;28(31):4683-4686

When is the optimal timing of conception?

Contraception

- Discuss risk of birth defects and early pregnancy loss with pregnancy during chemotherapy and need for abstinence or contraception.
- Recommend abstinence with low absolute neutrophil count (ANC) during chemotherapy due to risk of possible disruption of the vaginal mucosa during intercourse with risk for infection.
- Discuss contraception with non-estrogen containing long-acting reversible contraceptives (LARCs) due to theoretical risk of thrombosis with combined hormonal contraceptives.
  - LARCS have highest efficacy

Contraceptive Efficacy

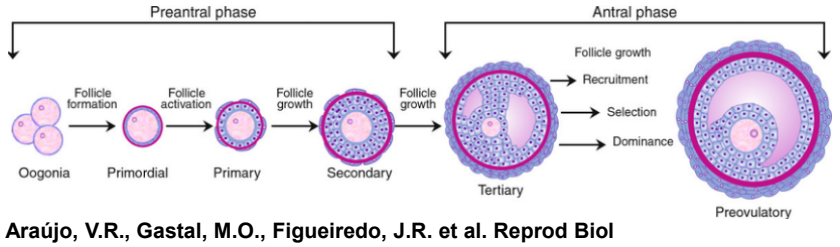


Intrauterine device during gonadotoxic therapy

- Limited data on Copper and Levonorgestrel IUD use in women immunosuppressed from cancer treatment
- Category 1 and 2
  - HIV immunosuppression
  - Systemic lupus erythematosus
  - Uncomplicated solid organ transplant
- Emergency Contraception (EC)
  - No studies to address the use of EC in cancer
  - Considered safe due to short duration of use

Regulation of ovarian follicular development in primates: facts and hypotheses.

Gougeon A[1].



Araújo, V.R., Gastal, M.O., Figueiredo, J.R. et al. Reprod Biol Endocrinol (2014) 12: 78. https://doi.org/10.1186/1477-7827-12-78

- Growth span from primordial to pre-ovulatory follicle: 6 months
- Risk of mutagenesis maximal during this maturation phase
- Recommendation: delay conception for 6 months after completion of treatment

Gougeon et al., Endocr Rev. 1996 Apr;17(2):121-55
Meirow et al., J Natl Cancer Inst Monogr. 2005;34:21–5
Chung et al., Fertil Steril 2013;99:1534-42
Mahajan. J Human Reprod Sci. 2015 Jan-Mar; 8(1): 3–13

Offspring of patients treated for cancer in childhood.

Li FP, Fine W, Jaffe N, Holmes GE, Holmes FF.

CONGENITAL ANOMALIES IN CHILDREN OF PATIENTS WHO RECEIVED CHEMOTHERAPY FOR CANCER IN CHILDHOOD AND ADOLESCENCE

DANIEL M. GREEN, M.D., MICHAEL A. ZEVON, PH.D., GEOFFREY LOWRIE, M.A., NINA SEIGELSTEIN, B.S., AND BRENDA HALL, R.N., C.N.P.

- 243 study progeny Li et al. 1979 May;62(5):1193-7
  - Incidence of fetal chromosomal or congenital abnormalities after chemotherapy remains the same as for the general population
- 202 pregnancies in 302 subjects Green et al. 1991 July;325:141-146
  - No relation between number or cumulative dose of mutagens received and the frequency of congenital anomalies in offspring

Childbearing after breast cancer

TABLE II. Influence of Interval Between Breast Cancer Diagnosis and Pregnancy on Survival

Refs.	Level of evidence[a]	Survival according to interval between diagnosis and pregnancy
Harvey et al. [32]	4	No differences
Mignot et al. [33]	3b	No differences
Clark and Chua [34]	4	<6 months: 54% 5-year survival 6–24 months: 78% 5-year survival >5 years: 100% 5-year survival
Sankila et al. [18]	3b	No differences
Mueller et al. [23]	2b	<3 months[b]: RR 1.7 (95% CI, 1.2–2.6)[c] 4–12 months: no difference 2–3 years: RR 0.49 (95% CI, 0.27–0.86) 3–4 years: RR 0.30 (95% CI, 0.12–0.71) 4–5 years: RR 0.19 (95% CI, 0.05–0.81)
Ives et al. [25]	2b	<6 months: RR 2.20 (95% CI, 0.14–35.42; $P = 0.58$)[d] 6–24 months: RR 0.45 (95% CI, 0.16–1.28; $P = 0.14$) >24 months: RR 0.48 (95% CI, 0.27–0.83; $P = 0.009$)

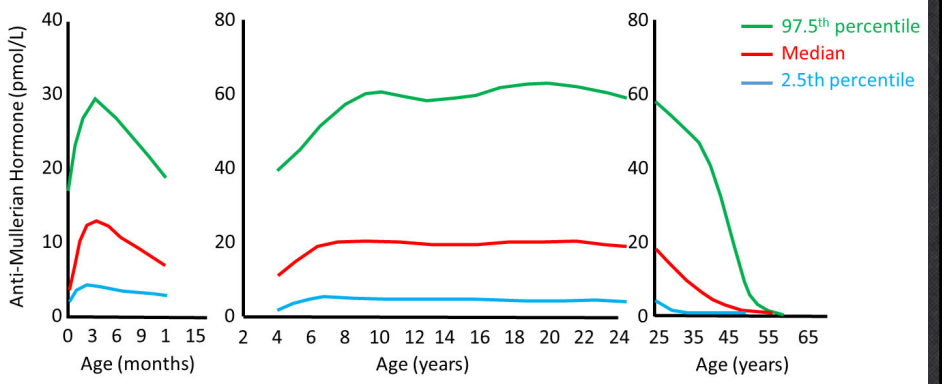
RR, relative risk; CI, confidence interval.
[a]Level of evidence according to the Oxford Centre for Evidence-Based Medicine (www.cebm.net/index.aspx?0=1025).
[b]Interval between diagnosis and live birth instead of pregnancy.
[c]Mortality compared with breast cancer patients without subsequent births.
[d]Mortality compared with breast cancer patients without subsequent pregnancy.

De Bree et al. J Surg Onc 2010

Childbearing after breast cancer

- **Conception 6 months after diagnosis is unlikely to compromise survival in localized breast cancer and good prognosis.**
- **Most clinicians advise women treated for early breast cancer to wait at least 2 years from diagnosis before attempting conception, to allow early recurrences to manifest.**
- **Patients with regional spread advised to wait 3 years from diagnosis.**

Anti-Mullerian Hormone



Serum AMH (picomoles per liter) in 926 healthy infants, girls, adolescents, and adult women.

Hagen et al. J Clin Endocrinol Metab, November 2010, 95(11):5003–5010

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Ovarian Reserve Testing

AMH ng/ml	Clinical Situation	Implications
Very Low (<0.5)	Impending onset of premature menopause	Predicts low ovarian response to stimulation
Low (0.5 - 1.0)	Limited egg supply Diminished reserve	Shortened reproductive window
Mid-range (> 1-3.5)	Normal testing	Consider preservation if high risk treatment
Elevated (>3.5)	Polycystic ovaries	Risk of ovarian hyperstimulation syndrome (OHSS)

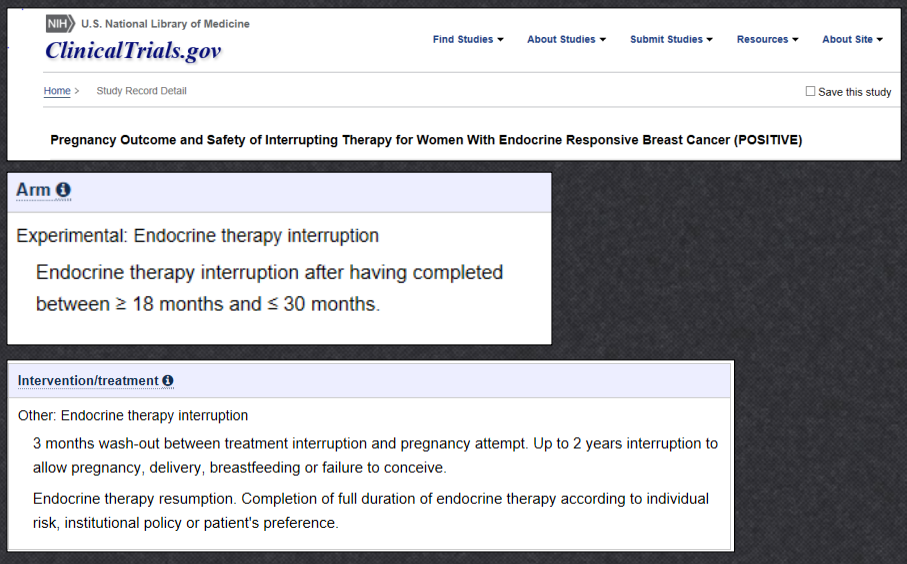
[1]Modified, Toner. Fertil Steril 2013
[2]Broer. Hum Reprod Update. 2013;19(1):26-36

Assessing the Reproductive Window

- Baseline AMH to assess ovarian reserve prior to cancer treatment
- Serial AMH yearly to follow rate of decline
- Serial FSH yearly to follow rate of rise
- Refer to REI for fertility treatment when AMH levels fall below norms for age, FSH rises > 10 mIU/ml, or if patient desires preservation.

Guzy and Demeestere. Minerva Gineocologica 2017 Feb;69(1):57-67
Van Dorp et al., 2016

Treatment "holiday" for conception



Treatment "holiday" for conception

- Tamoxifen should be discontinued 3 months prior to conception.
- Aromatase inhibitors should be discontinued 2 months prior to conception.
- HER2/nue antagonists should be discontinued 4 months prior to conception.
- May pursue spontaneous conception or IVF with aromatase inhibitor.
- Resume Tamoxifen after pregnancy or breastfeeding to complete 10 years.

Reproductive Health Concerns in Survivorship

- Primary ovarian insufficiency:
  - Infertility, diminished bone density and early-onset dementia, genitourinary symptoms, sexual dysfunction, and GVHD.
- Radiation therapy:
  - Risk of miscarriage, preterm labor and low birth weight.
  - Vaginal fibrosis, stenosis and fistula formation at ≥ 90-100 Gy.

Faubion 2016; Jackson 2016

Recommendations: Reproductive Health

- Early evaluation for GVHD and vaginal stenosis with early Gyn referral.
- Vasomotor and genitourinary symptoms may be managed with hormonal and non-hormonal therapies.
  - hormonal therapy should be used with caution in breast cancer
- Sexual dysfunction screening throughout survivorship with referral to a therapist upon positive screening.
- Pregnancy is safe in survivorship after optimization of maternal health and assessment of recurrence risk.

Edgar et al., 2013
Henderson et al., 2010

How do we improve outcomes at OSU Wexner Medical Center?

Fertility Preservation and Reproductive Health Consult

- Eligibility:
  - Ages: 18 through 45 at diagnosis
  - Planned removal of a gonad and/or
  - Chemotherapy, radiation or surgical procedures that affect fertility
- Fertility Preservation
  - Oocyte cryopreservation - patients 18-42 years
  - Embryo cryopreservation - patients 18-42 years
  - Ovarian tissue cryopreservation - patients 18-42 years under IRB
- Reproductive health: all ages
  - Endocrine function post-treatment
  - Contraceptive and STI counseling
  - HPV screening and immunization counseling
  - Sexual dysfunction screening and referral as indicated

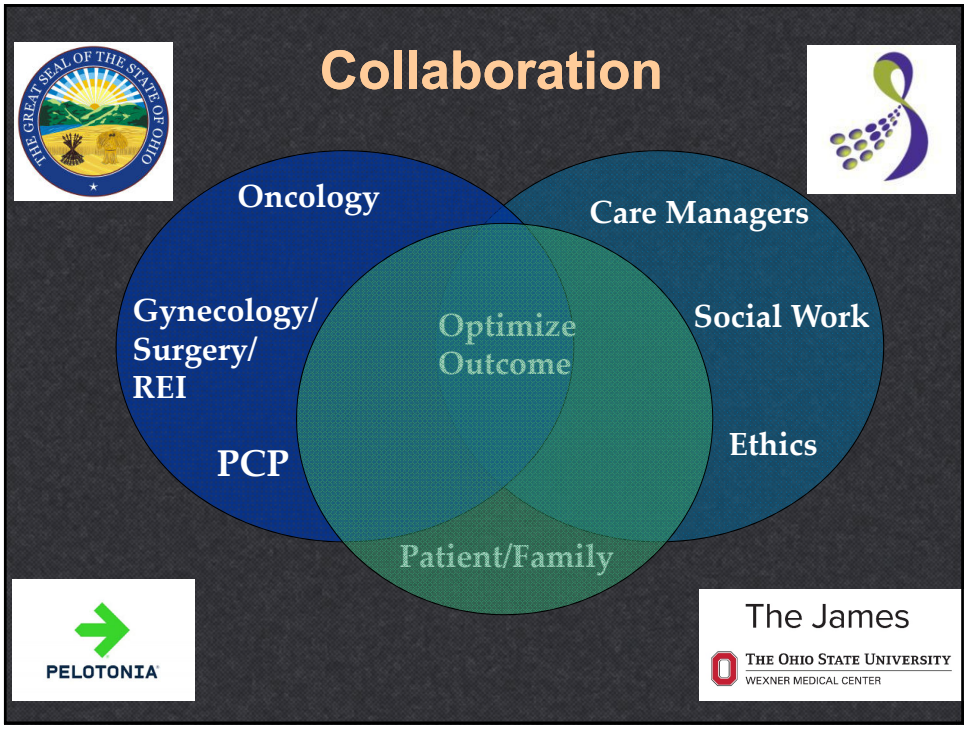
Patient Experiences

"75% of cancer survivors without children stated they wanted to have children in the future. "

"Women counseled about their risk of infertility by an oncologist and a fertility specialist had significantly less regret about their decision to preserve fertility that those counseled only by an oncology team."

"Patients experience less regret and have improved quality of life when counseled about fertility preservation options even if no option is pursued."

Moffat et al. Arch Gynecol Obstet. 2012;286(6):1521-1527.
Letourneau. Cancer. 2012;118(6):1710-1717.
Partridge et al. Clin Breast Cancer. 2008;8(1):65-69
Chandra et al. Fertil Steril.2010;93(3):725-736


Collaboration
Oncology
Gynecology/
Surgery/
REI
PCP
Care Managers
Social Work
Ethics
Optimize
Outcome
Patient/Family
PELOTONIA
The James
The Ohio State University
Wexner Medical Center