

# Reproduction, Menopause and Survivorship

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# Oncofertility = Cancer & Reproductive Health

Increasing Cancer Survival Rates



Increased Emphasis on Quality of Life

+

Several Successful Fertility Preservation & Post-treatment Parenthood Options

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Improved treatments for menopausal symptoms

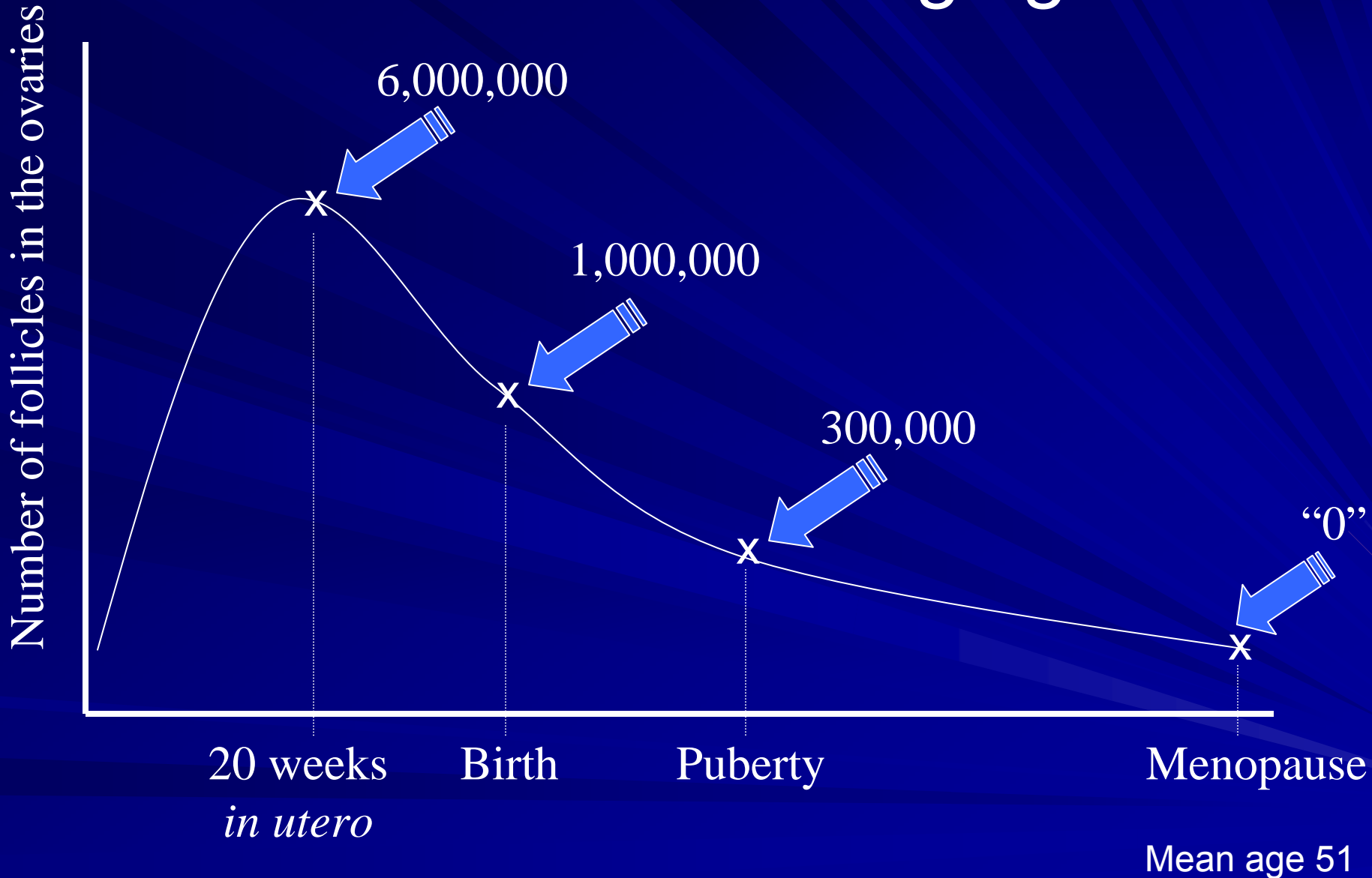
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**Patients Need Information About Reproductive Risks & Options**

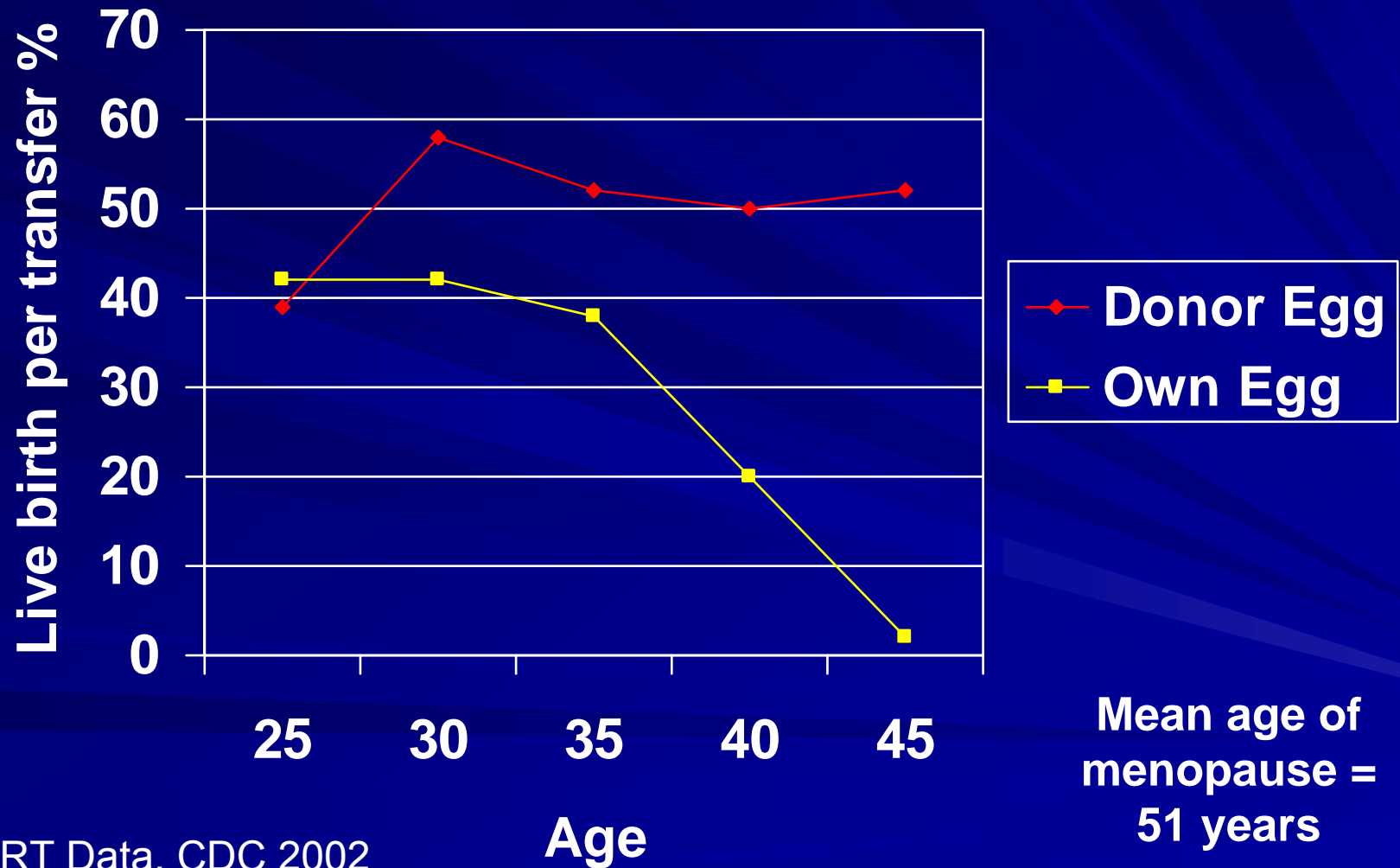
# Patient Population Facts

- Annually more than 130,000 cancer patients are diagnosed in their reproductive years
  - 11,000 breast cancer patients are diagnosed under the age of 40 each year
- Cancer Survivorship Rates are High
  - 77% percent of patients under 45 survive at least 5 yrs
- US Trend: Delayed Childbearing
  - Average age for first child is 25.2
  - More patients have not had children when diagnosed

# Natural Ovarian Aging



# Fertility depends on the age of a woman's eggs



# Effect of Cancer Therapy on Reproductive Function

- Cancer treatments accelerate ovarian aging
  - May lead to infertility
  - Early menopause
  - Menopausal symptoms: sexual dysfunction, hot flashes, sleep problems, mood changes
  - Long term health risks
- Reproductive Effects depend on :
  - Type chemotherapy – alkylating agents
  - Cumulative Dose
  - Radiotherapy – pelvic, cranial
  - Bone Marrow Transplant
  - Age of patient and how long pregnancy is delayed

# ASCO Guideline Summary

JOURNAL OF CLINICAL ONCOLOGY

A S C O S P E C I A L A R T I C L E

## American Society of Clinical Oncology Recommendations on Fertility Preservation in Cancer Patients

*Stephanie J. Lee, Leslie R. Schover, Ann H. Partridge, Pasquale Patrizio, W. Hamish Wallace, Karen Hagerty,  
Lindsay N. Beck, Lawrence V. Brennan, and Kutluk Oktay*

As part of informed consent prior to therapy, oncologists should address the possibility of infertility with patients as early in treatment planning as possible <sup>1</sup>

<sup>1</sup> Lee SJ, Schover LR, et al., *Journal of Clinical Oncology*, 2006.

# Oncofertility Program at Penn

## ■ Clinical Program

- Dedicated outpatient office sessions
- Dedicated physicians and nurses
- Psychosocial counseling
- Financial Counselling/Support
  - Fertile Hope/Donations
- Inpatient consult service at HUP and CHOP

## ■ Research Program

- Experimental fertility preservation procedures
- Observational studies
- Core member of Oncofertility Consortium – NIH funded multi-center grant to study fertility preservation

# Oncofertility Program at Penn

- Comprehensive fertility preservation program
  - Standard treatments
    - Embryo banking (Alternative protocols may reduce risk of ovarian stimulation in hormone sensitive cancers)
    - Ovarian Transposition
  - Experimental treatments:
    - Egg banking
    - Ovarian tissue banking – as part of Oncofertility Consortium
    - GnRH agonists
- Managing Late Effects of Treatment
  - Fertility treatments including donor egg, adoption counselling
  - Contraception
  - Non-hormonal menopause symptom management
  - Therapies to improve sexual function and bone health

# Pregnancy after Cancer

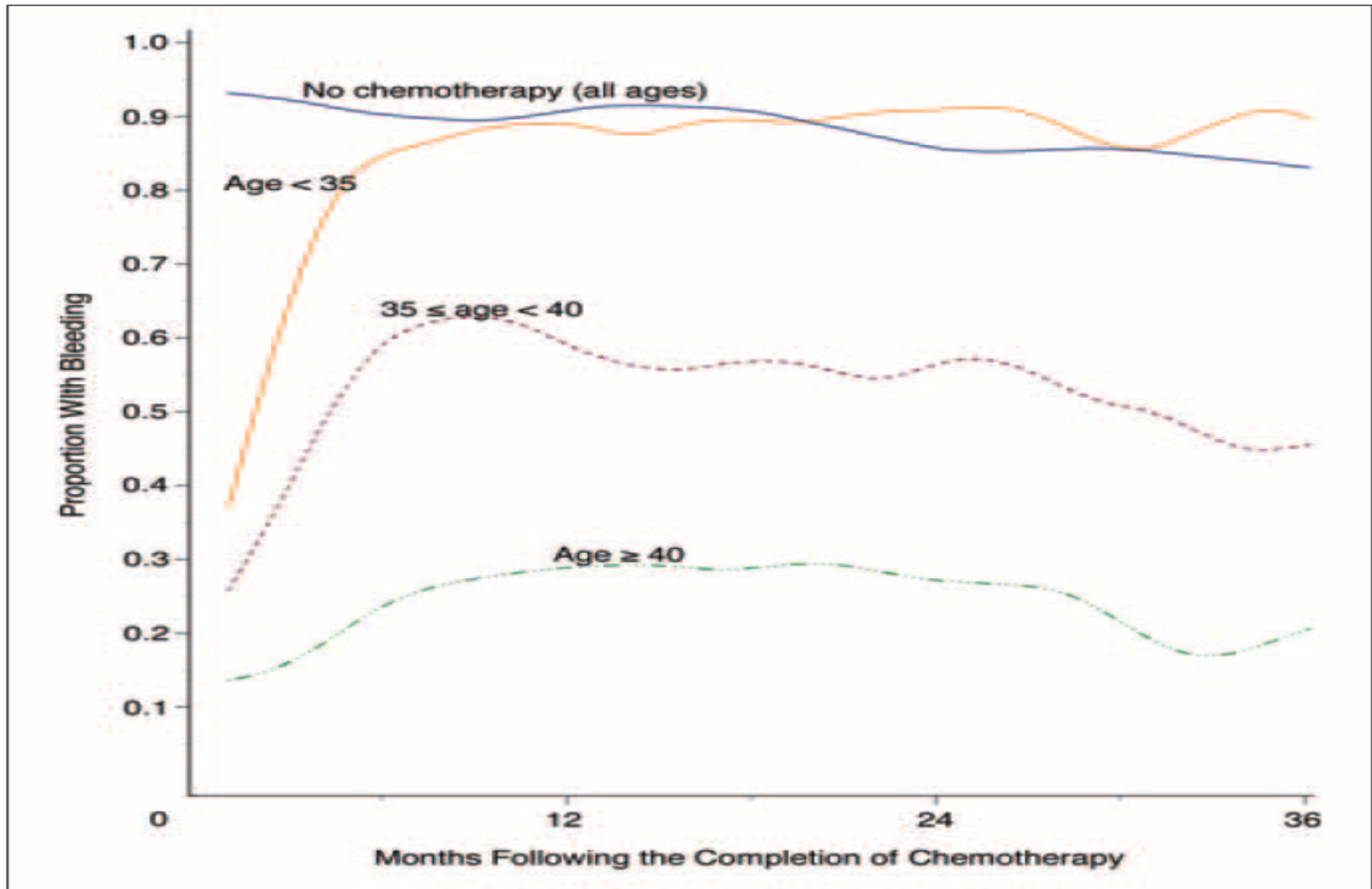
- Pregnancy does not trigger cancer recurrence, even after breast cancer
  - Relative Risk of Death = 0.44 - 0.8
  - Ideal timing of pregnancy unclear
- No increased risk of genetic or birth defects
- Pregnancy may be higher risk
  - Toxicities of cancer therapies
  - Increased surveillance
- Gestational Surrogacy is an option
  - Allows biological offspring even if unable to carry a pregnancy

Blakely et al. Cancer 2004;100:4659.  
Gelbert et al. 2001;19:1671.  
Ives et al. BMJ 2007;334:194.

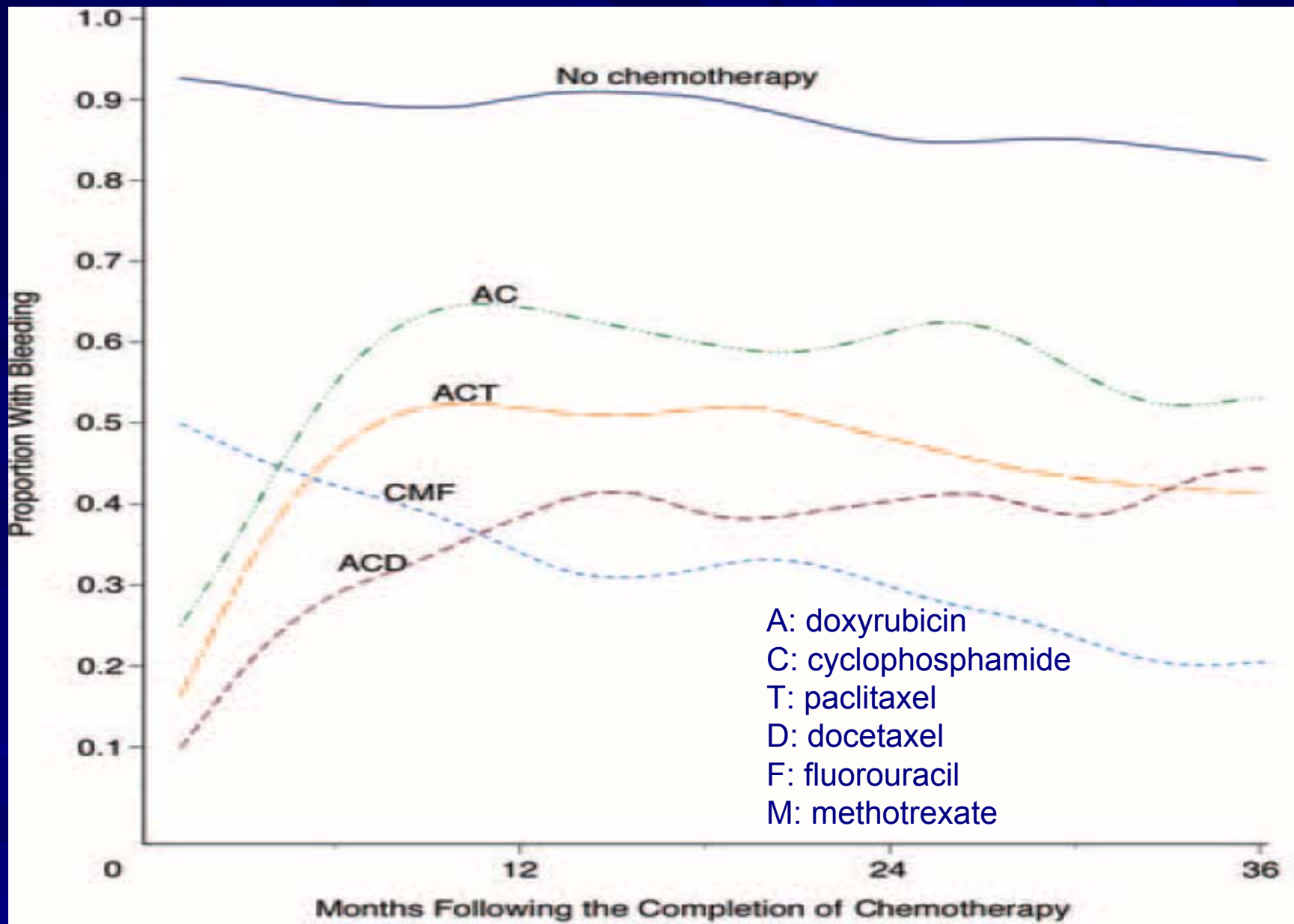
# Oncofertility Research Program at Penn

How can we help to predict the  
effect of cancer therapy on  
reproductive function?

# Breast Cancer



**Fig 2.** Bleeding after chemotherapy by patient age.



# Fertility after Cancer

- Menstrual function  $\neq$  Fertility
- Decreases in fertility occur well before menopause
- Limited studies
- Fertility depends on multiple factors:
  - age, availability of partner, fertility of partner, coital frequency, use of birth control, willingness to conceive
- To answer this question we need large prospective time to pregnancy studies
  - Expensive and challenging to conduct

# Measures of Ovarian Reserve: surrogate markers for fertility?

- Follicle Stimulating Hormone, Estradiol, Inhibin B, Anti-Mullerian Hormone
- Ovarian ultrasonography
  - Antral follicle counts
  - Ovarian volume
- Do measures of ovarian reserve predict fertility, premature ovarian failure, age at menopause?

# Preliminary Data: Childhood Cancer Survivors (Mean Age 26 years)

	Survivors ( <i>n</i> =60)	Controls ( <i>n</i> =59)	P-value
<b>FSH (Miu/ml)</b>	<b>13.33</b>	<b>8.88</b>	<b>0.002</b>
Estradiol (pg/ml)	8.52	10.31	0.14
Inhibin B (pg/ml)	11.9	14.5	0.25
<b>AMH (ng/L)</b>	<b>545.9</b>	<b>2069.3</b>	<b>&lt;0.001</b>
Ovarian volume (mm <sup>3</sup> )	961.2	1,609.6	0.57
<b>AFC</b>	<b>31.43</b>	<b>44.8</b>	<b>&lt;0.001</b>

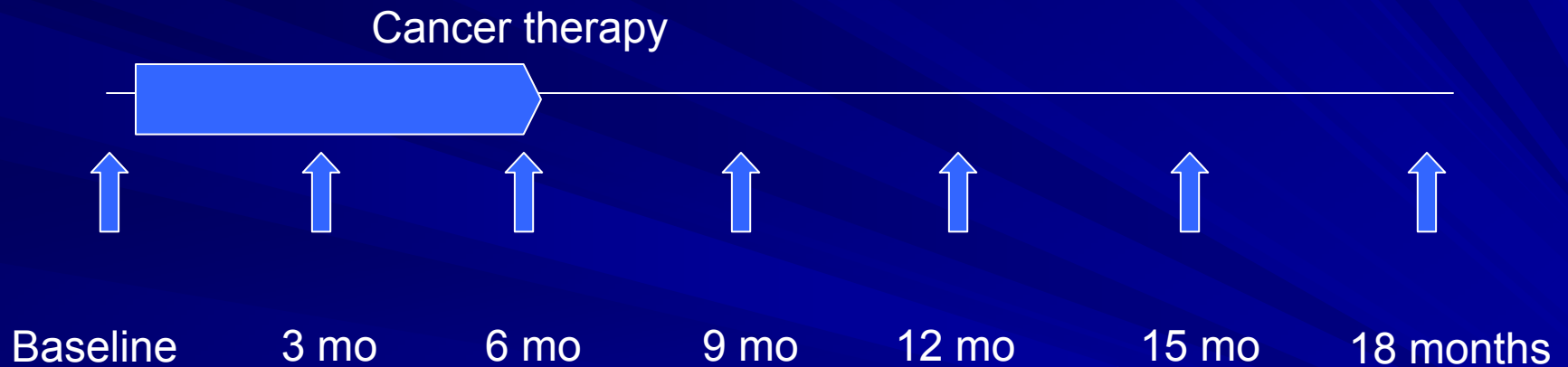
Linear regression model adjusted for BMI, Race, Age  
Geometric hormone means presented

Even in regularly menstruating women, measures are different

# ORACLE Study – Part 1

## New Diagnosis

Eligibility: reproductive aged women exposed to alkylators compared to controls



Study visit: questionnaire, menstrual diary, brief physical exam, pelvic  
Ultrasound and blood draw for hormones

# ORACLE – Part 2

## Yearly Visits in Survivors

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1-2 years after  
treatment



1 year



2 years



3 years



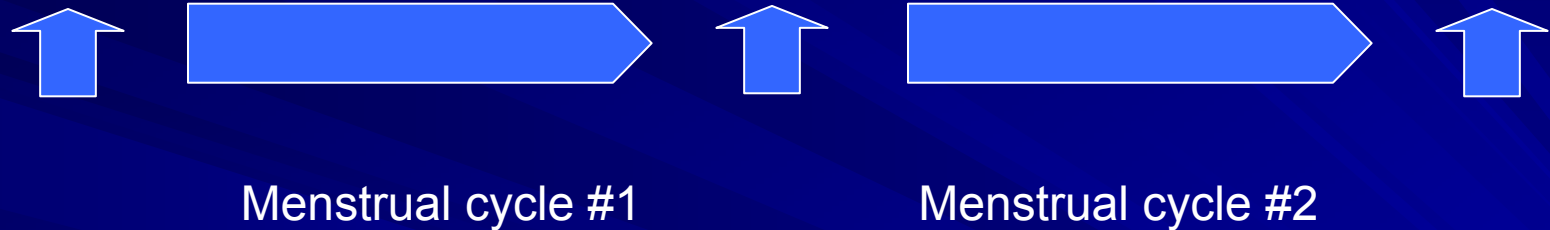
4 years

Eligibility: Cancer survivors, and 2 groups of women never treated for cancer.

Study visit: questionnaire, menstrual diary, brief physical exam, pelvic Ultrasound and blood draw for hormones

# ORACLE – Part 3

## Daily Urine Collection



Eligibility: Cancer survivors, and 2 groups of women never treated for cancer

Study visit: questionnaire, menstrual diary, brief physical exam, pelvic Ultrasound and blood draw for hormones

**We hope that our clinical and research efforts will help to expand the long term reproductive options for cancer survivors**

**Thank You!!**

To participate in a study email  
[Maureen.Prewitt@uphs.upenn.edu](mailto:Maureen.Prewitt@uphs.upenn.edu)

[www.myOncofertility.org](http://www.myOncofertility.org)

[www.fertilehope.org](http://www.fertilehope.org)