# Adolescents and Young Adults (AYA) with Cancer

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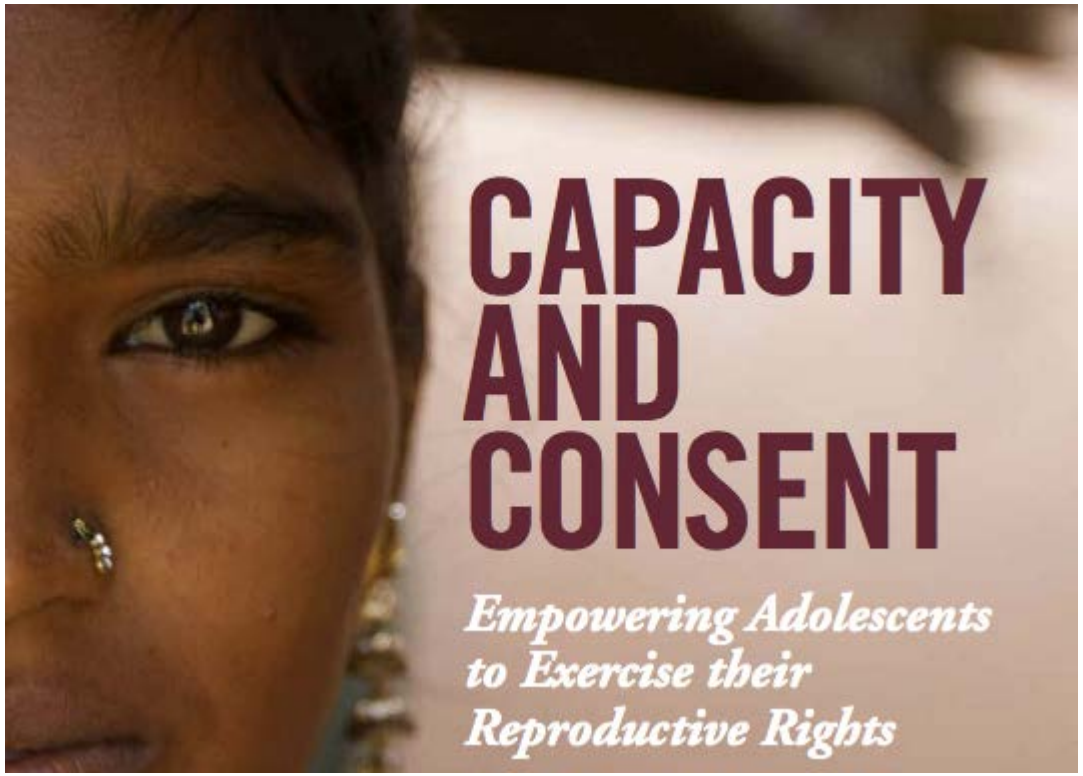
# Who are AYA?

- Aged 15-39
- Why this age group?
- What are the issues that differ from older adults?

* Adults survivors of pediatric cancer

# Issues

- Reproductive health
  - Fertility, body image, sexual health, sexual dysfunction, contraception, sexual orientation, gender identity, fluidity, genetics
- Insurance
- Social support
- Relationships
- Late diagnosis
- Health literacy
- Clinician knowledge/comfort



# Patient Population

- Annually >140,000 cancer patients diagnosed in reproductive years (up to 45) [1]
- > 11,000 breast cancer patients diagnosed under 40 each year [2]
  - 21% of gyn cancer <45 [3]
  - 12,000 children (0-19) diagnosed each year [4]
- Cancer Survivorship Rates are high
  - 77% patients under 45 survive five years[5]
- US Trend: Delayed Childbearing
  - Average age for first child is 25.2 – all time high[6]
  - More patients not had children

[1] *American Cancer Society & U.S. Census Bureau*
[2] *Young Survival Coalition*
[3] Liou WS, Yap S, et al., *Fertility and Sterility,* 2005.
[4] Goodwin T, Ooosterhuis BE, et al., *Pediatric Blood Cancer,* 2007.
[5] SEER *Cancer Statistics Review,* 1997-2004.
[6] CDC, 2004.

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# Risk Factors

- Disease
- Age
- Gender
- Treatment
  - Type, Cumulative Dosage & Location
    - Radiation
    - Chemotherapy
    - Bone Marrow or Stem Cell Transplant
    - Surgery
- Pre-treatment fertility status of patient
  - Often not known or considered


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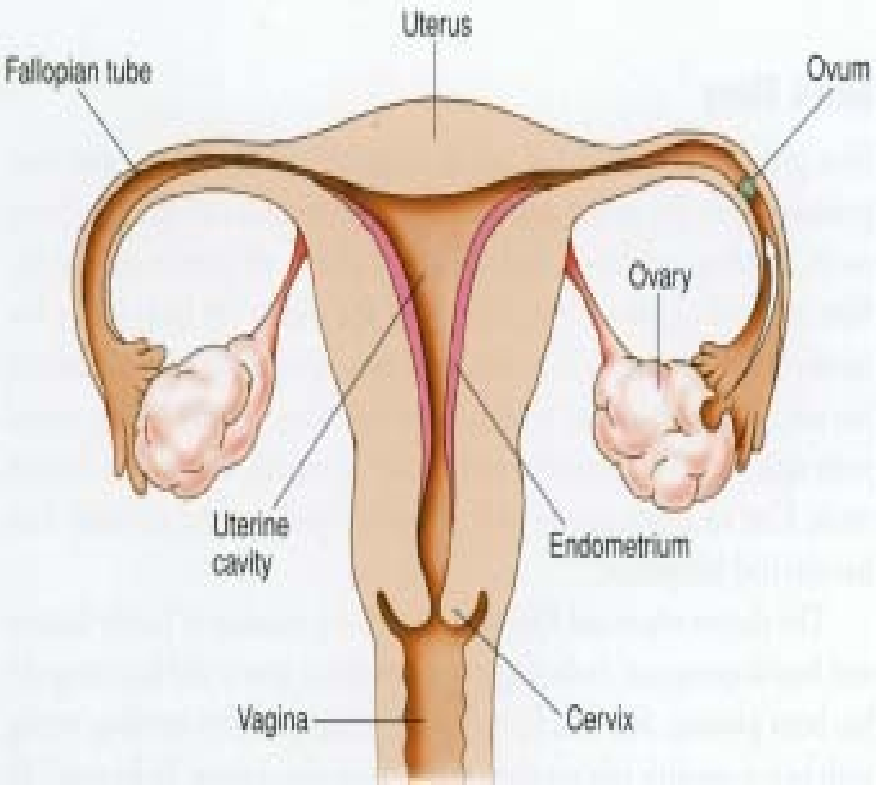
Lee SJ, Schover LR, et al., *Journal of Clinical Oncology,* 2006.

# Potential Impact After Cancer




WOMEN

- Depletion in number of oocytes = early menopause
- Germ Cell failure = premature ovarian failure (POF)
- Reduced production of ovarian hormones = early menopause
- Uterine/tube fibrosis = interference with fertilization and implantation
- Uterine vascular insufficiency = inability to maintain pregnancy

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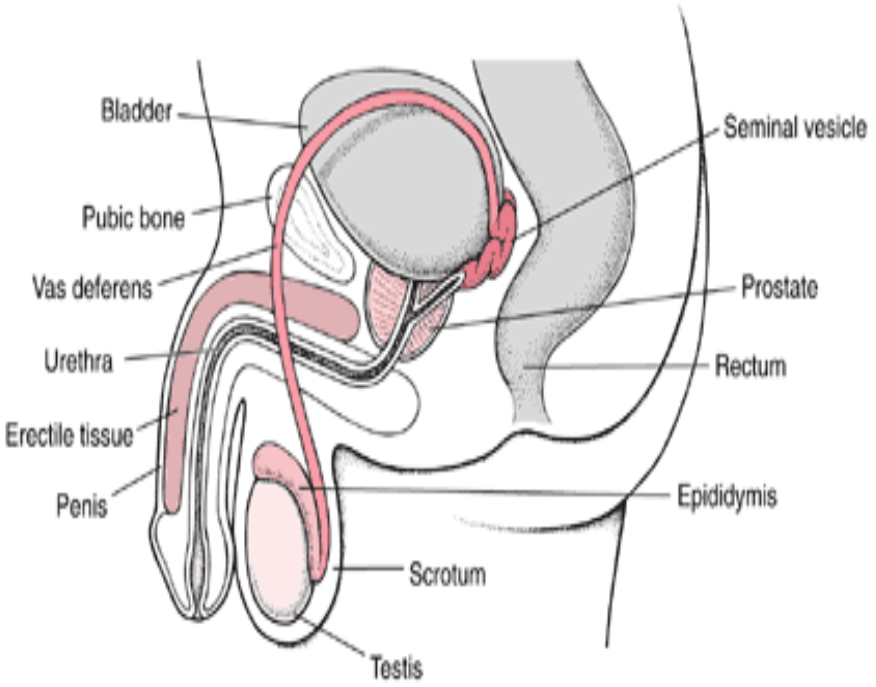
# Potential Impact After Cancer

MEN

- Reduced testosterone
  - Leydig cell dysfunction
- Germ cell failure
  - Decreased, damaged, or absent sperm
- Damage to duct system to transport sperm
  - Ejaculatory dysfunction
- Damage to pelvic nerves
  - Sexual and ejaculatory dysfunction

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# Survivorship & Quality of Life

- AYA patients and survivors cite infertility as significant survival concern
  - Diagnosis of infertility can be as devastating for patients as cancer diagnosis
  - Many young adult survivors remain unsure of their reproductive status
  - Many report significant anxiety about their ability to have children
  - Patients who received information regarding their sexual and reproductive health have lower levels of psychological distress than patients who did not receive this information

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

# Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update

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K.O. and A.W.L. were Expert Panel co-chairs and contributed equally to this work.

Clinical Practice Guideline Committee approved: January 25, 2018

Editor's note: This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including an abbreviated Data Supplement with new studies, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/survivorship-guidelines.

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0732-183X/18/3699-1/$20.00

## ABSTRACT

**Purpose**
To provide current recommendations about fertility preservation for adults and children with cancer.

**Methods**
A systematic review of the literature published from January 2013 to March 2017 was completed using PubMed and the Cochrane Library. An Update Panel reviewed the identified publications.

**Results**
There were 61 publications identified and reviewed. None of these publications prompted a significant change in the 2013 recommendations.

**Recommendations**
Health care providers should initiate the discussion on the possibility of infertility with patients with cancer treated during their reproductive years or with parents/guardians of children as early as possible. Providers should be prepared to discuss fertility preservation options and/or to refer all potential patients to appropriate reproductive specialists. Although patients may be focused initially on their cancer diagnosis, providers should advise patients regarding potential threats to fertility as early as possible in the treatment process so as to allow for the widest array of options for fertility preservation. The discussion should be documented. Sperm, oocyte, and embryo cryopreservation are considered standard practice and are widely available. There is conflicting evidence to recommend gonadotrophin-releasing hormone agonists (GnRHa) and other means of ovarian suppression for fertility preservation. The Panel recognizes that, when proven fertility preservation methods are not feasible, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency. GnRHa should not be used in place of proven fertility preservation methods. The panel notes that the field of ovarian tissue cryopreservation is advancing quickly and may evolve to become standard therapy in the future. Additional information is available at www.asco.org/survivorship-guidelines.

*J Clin Oncol 36. © 2018 by American Society of Clinical Oncology*

## INTRODUCTION

The goal of this update is to provide oncologists, other health care providers, and caregivers with recommendations regarding fertility preservation for adults, adolescents, and children with cancer.

The American Society of Clinical Oncology (ASCO) first published evidence-based clinical practice guidelines on fertility preservation in 2006, and an updated guideline was published in 2013.[1] The goal of this 2018 guideline update is to provide current guidance regarding fertility preservation options for people with cancer anticipating treatment. The current 2018 update assesses whether the 2013 recommendations remain valid. A complete list of 2013 and 2018 recommendations is available at www.asco.org/survivorship-guidelines and in Data Supplement 1.

## METHODS

### *Guideline Update Process*

ASCO uses a signals[2] approach to facilitate guideline updating. This approach is intended to identify new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on routine literature searching and the expertise of ASCO guideline panel members to identify signals. The Methodology Supplement

ASSOCIATED CONTENT

Appendix
DOI: https://doi.org/10.1200/JCO.2018.78.1914

Data Supplement
DOI: https://doi.org/10.1200/JCO.2018.78.1914

DOI: https://doi.org/10.1200/JCO.2018.78.1914





The discussion should be documented.

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# Fertility Preservation Options for Women

| | Before | During | After | Status |
|---|---|---|---|---|
| Embryo Freezing | X | | X | Std |
| Egg Freezing | X | | X | Std |
| Ovarian Tissue Freezing | X | | X | Std |
| In Vitro Maturation | X | | X | Exp |
| Ovarian Transposition | X | | | Std |
| Radical Trachelectomy | | X | | Std |
| GnRHa | | X | | Exp |
| Natural Conception | | | X | Std |
| In Vitro Fertilization | | | X | Std |
| Donor eggs or embryos | | | X | Std |
| Adoption | | | X | Std |
| Gestational Surrogacy | | | X | Std |

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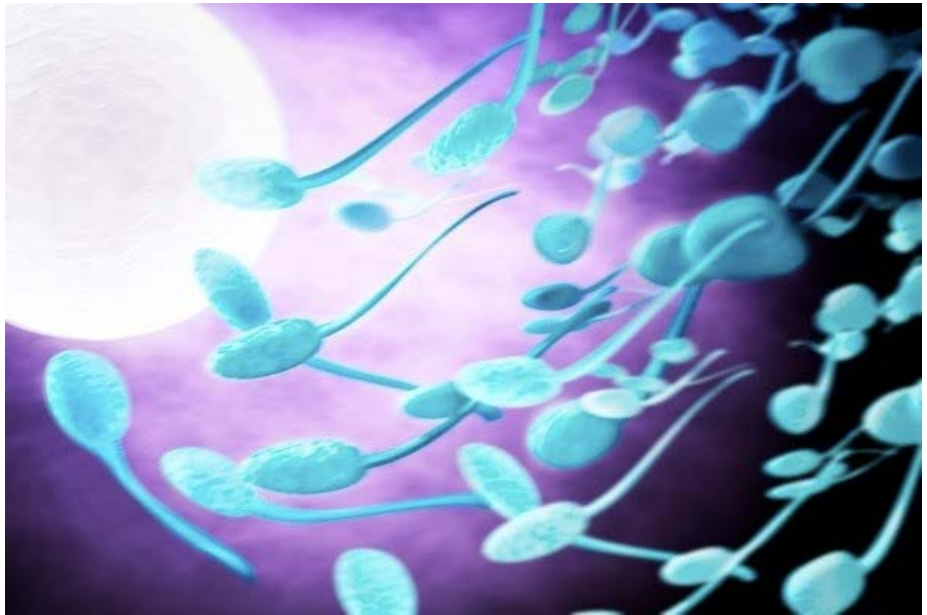
# Parenthood Options: Men

| | Before | During | After | Status |
|---|---|---|---|---|
| Sperm Banking | X | | | Std |
| Testicular Tissue Freezing | X | | | Exp |
| Natural Conception | | | X | Std |
| Assisted Reproduction | | | X | Std |
| Testicular Sperm Extraction | | | X | Std |
| Sperm Donation | | | X | Std |
| Adoption | | | X | Std |



# “You have a 20% chance of survival – have you ever thought about having kids?”

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# “My patients usually start treatment within 24 hours”

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# “I’ve had to find shoes for my patients to go home in”


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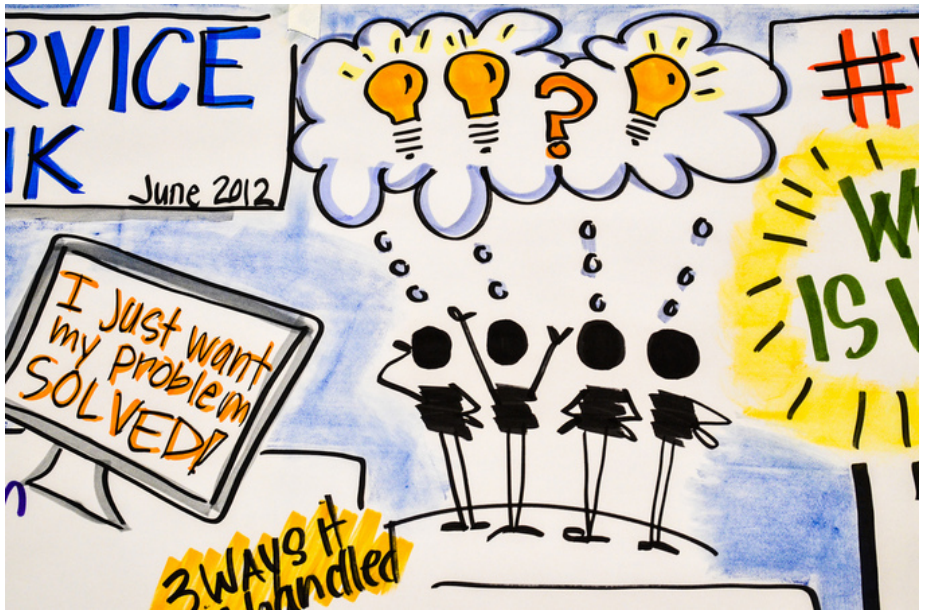
# Decision Making




- I don’t have a partner
- I’m gay
- I just want to live
- I going to be bald who will want me
- I don’t want to delay treatment
- I don’t want to pass this cancer on to a child
- I may not be around to see a child
- I’m transgender and I don’t associate with sperm/eggs/pregnancy

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# The mixed message

- Contraception
- I’m sterile right?
- I can’t get pregnant or impregnate someone on treatment?
- I’m in a same-sex relationship
- You will not be feeling well enough to have sex
- I trained in oncology, not REI or sexual health stuff
- Parents won’t leave the room


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# Oncofertility Interventions for Health Care Professionals

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# ECHO Content

**Module 1:** Orientation

**Module 2:** Reproductive Health in AYA Male Patients

**Module 3:** Reproductive Health in AYA Female Patients

**Module 4:** Reproductive Health in Pre-Pubertal Children with Cancer

**Module 5:** AYA Psychosocial Issues

**Module 6:** AYA Sexual Health

**Module 7:** Communication

**Module 8:** Overcoming System Barriers to Reproductive Health

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# Web-Based Lectures

Each Module has a web-based lecture, which participants view in chronological order


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# AYA and Parents/Families Issues

- Barriers
- Developmental understanding of reproductive health
- Lack of ability for future thinking
- Mental health co-morbidities
- Total focus on transition
- Finances
- Dysphoria/dissonance
- Adoption option


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# LOVE ECHO

0% COMPLETE 0/10 Steps

Welcome to the newest ECHO module. LOVE ECHO focuses on providing affirming care to LGBTQIA cancer survivors, including collecting sexual orientation and gender identity (SOGI) data, tailoring care, referrals and environment, and applying this to psychosocial care.

This pilot module includes a lecture and interactive cases, a glossary and resource list, and starts and ends with a pre and post test. You will also have the opportunity to provide some feedback on this new module upon completion.


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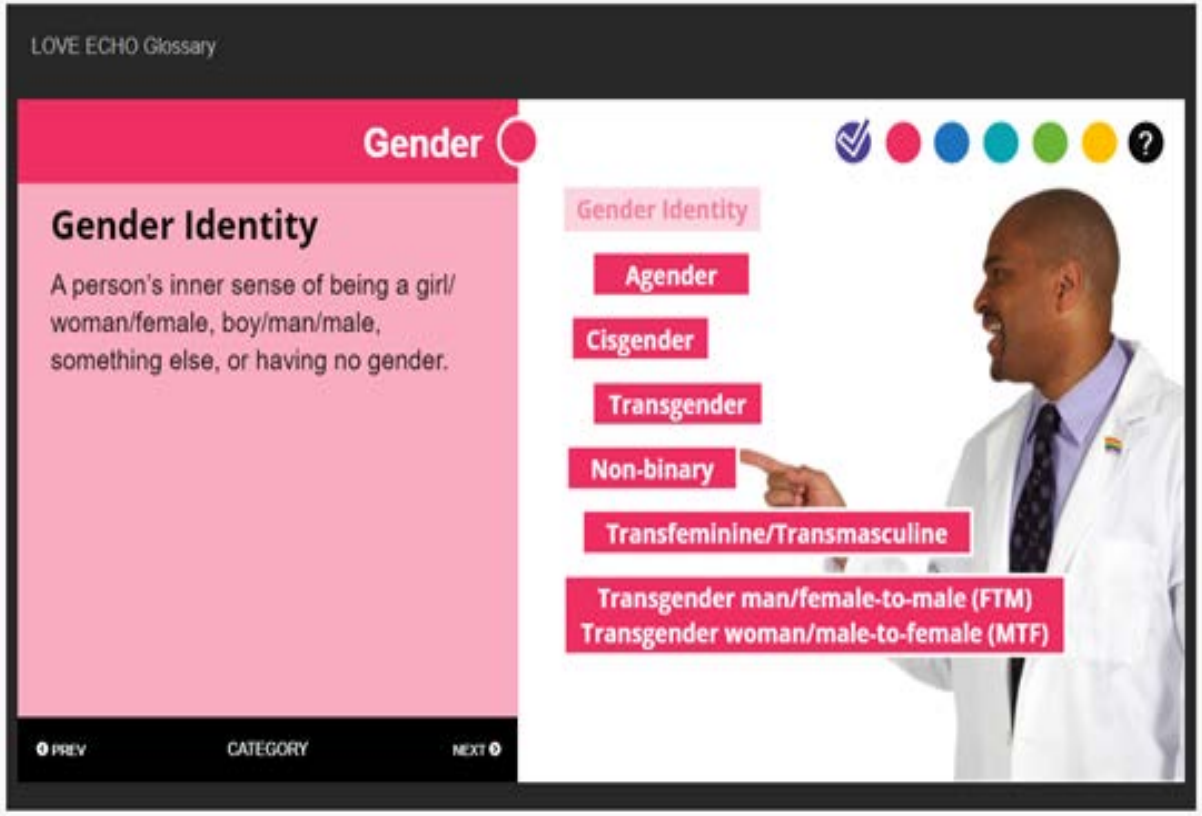
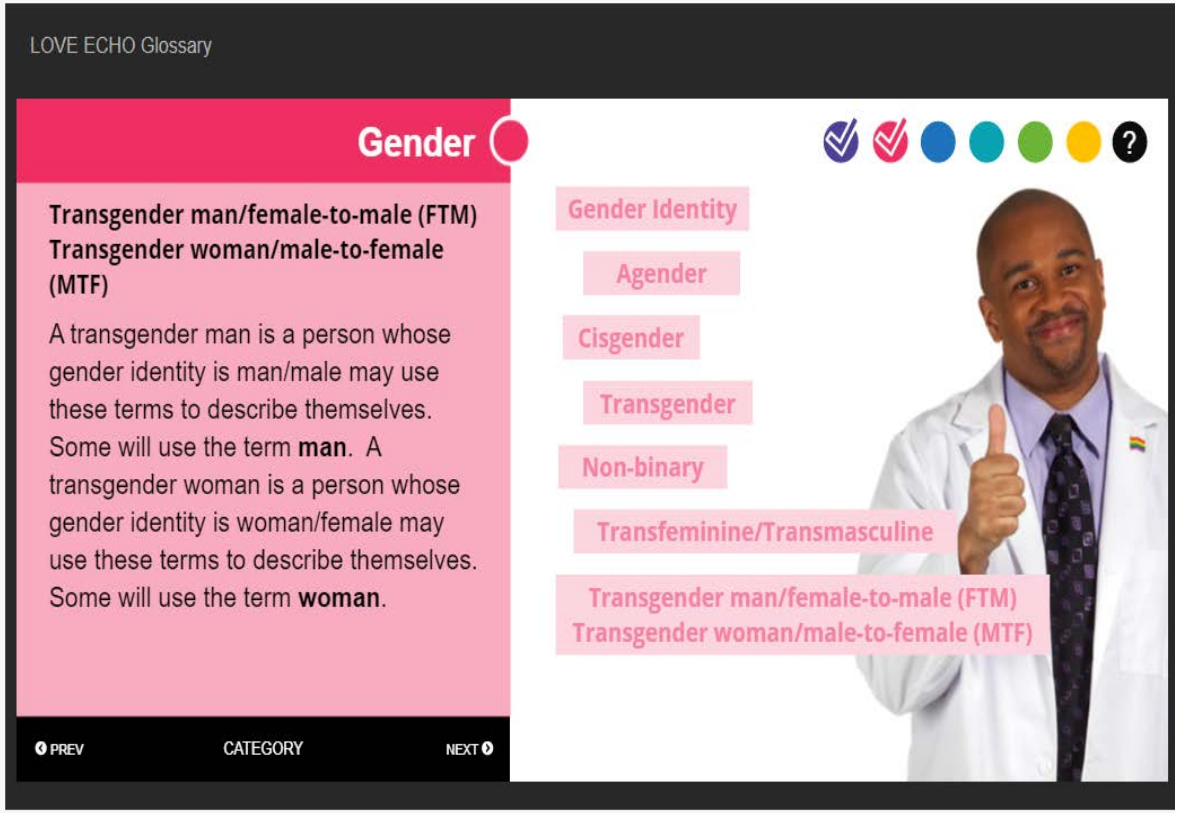
# ACTIVITY: INTERACTIVE GLOSSARY




# ACTIVITY: INTERACTIVE GLOSSARY

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Case Study 3: Horace

THE CASE

# MEET HORACE

Horace is 31-year-old Black cis man who identifies as bisexual (SOGI data was collected on intake forms). Horace was recently diagnosed with colorectal cancer and is here after discussing the treatment plan (starting with surgery) with the oncologist.

BEGIN ▶

PREV NEXT

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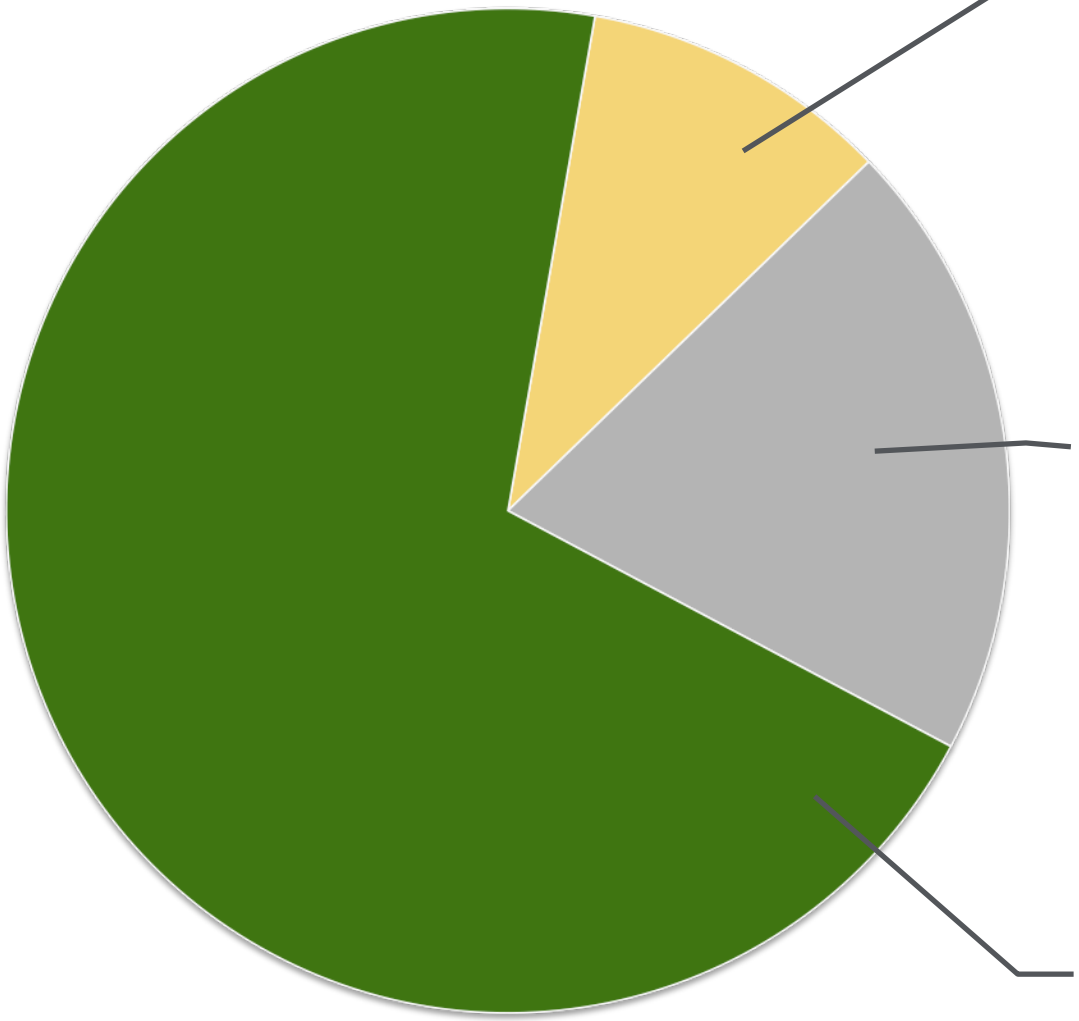
# Distribution of Cancer



## Hereditary (5 – 10%)

- Gene Mutation is inherited in family
- Significantly increased cancer risk

## Familial (20%)

- Multiple genes and environmental factors may be involved
- Some increase in cancer risk

## Sporadic (70%)

- Cancer occurs by chance or related to environmental factors
- General population cancer risk

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# Concerns

| Concern | Patients on TX | Patients off TX | Providers |
|---|---|---|---|
| Depression | X | | X |
| Body image | X | X | |
| Lack of independence | X | X | X |
| Transportation | X | | |
| Financial issues | X | X | X |
| Mental health services | X | | X |
| Fertility | X | X | X |
| Poor communication | X | X | X |
| Care coordination | X | | X |
| Uncertainty | X | X | X |

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# Provider Feedback: Unprepared for the Unexpected

**Providers noted AYAs are unprepared for the unexpected**

*“I think that, first and foremost you're not supposed to get cancer when you're a young adult so I think the patients come here unprepared.  Unprepared because they haven't had experiences in their life that require a hospital setting.  Unprepared because, you know, on their to do list of things to do fighting cancer was not anywhere near it.”*

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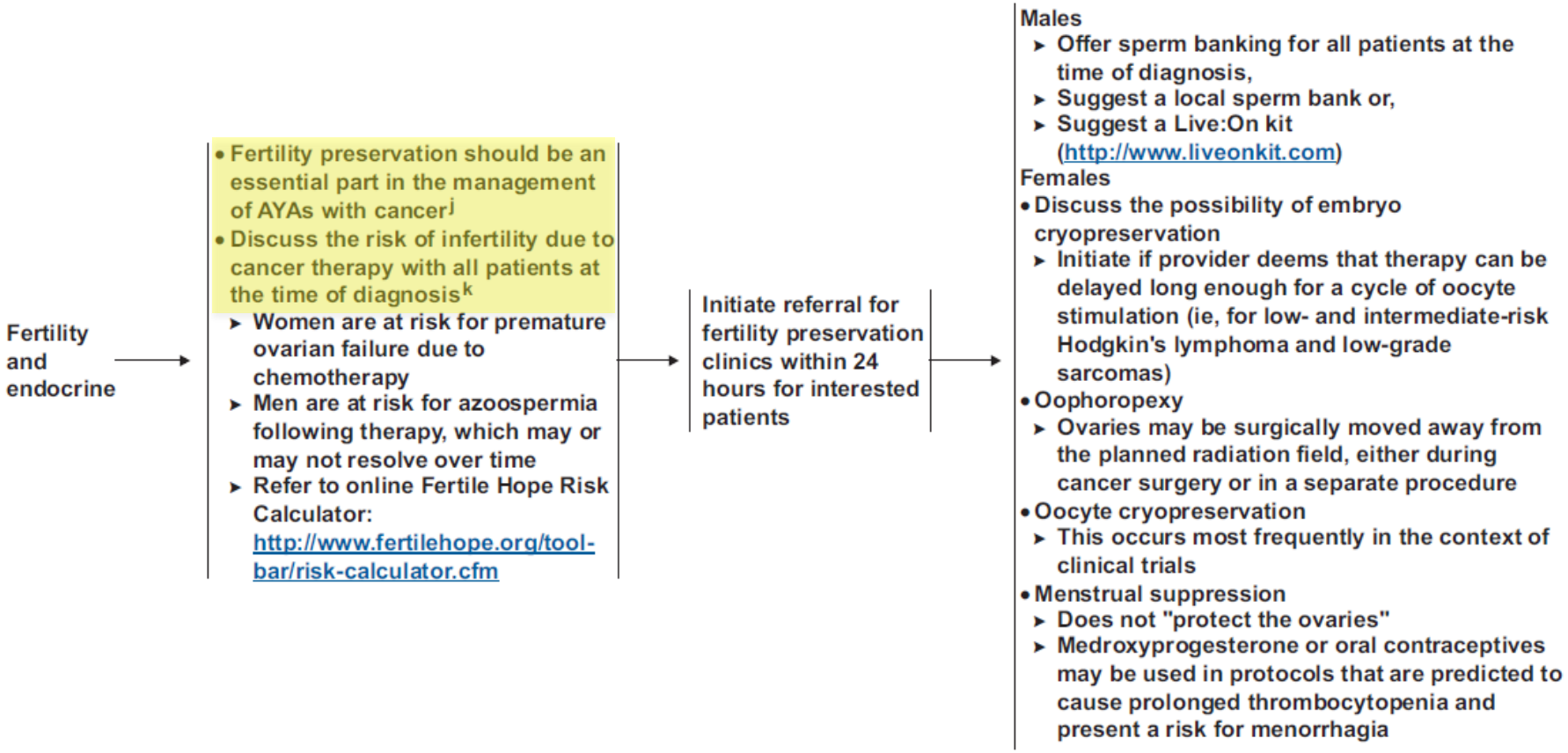
# Backgr
# NCCN

National Comprehensive Cancer Network®

## NCCN Guidelines Version 1.2012
## Adolescent and Young Adult Oncology

NCCN Guidelines Index
AYA Oncology Table of Contents
Discussion

### FERTILITY/ENDOCRINE CONSIDERATIONS




[j] Levine J, Canada A, Stern CJ. Fertility preservation in adolescents and young adults with cancer. *J Clin Oncol.* 2010;28:4831-4841. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20458029.

[k] The impact of cancer therapy on fertility is related to the age of the patient at the time of treatment and is dependent on the duration, dose intensity, and type of treatment. See NCCN Guidelines for Breast Cancer for the management of women with breast cancer during pregnancy.

**Note: All recommendations are category 2A unless otherwise indicated.**
**Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.**





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# Background

- For AYA patients at increased risk of hereditary cancer, National Comprehensive Cancer Network (NCCN) recommends that patients of reproductive age should be counseled about options of:
  - pre-implantation genetic testing (for several hereditary cancer syndromes)


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# General Hereditary Cancer Red Flags

- Multiple family members with cancer
- Cancers occur on the same side of the family
- Cancer diagnoses occur at a younger than expected age
- Clustering of certain types of cancer is present
- Multiple primary cancers are diagnosed in the same individual
- Bilateral cancers

# Red Flags: Pediatric/Adolescent Cancer PLUS

- ≥1 congenital anomaly
- Developmental delay, intellectual disability
- Facial dysmorphology
- Aberrant Growth (length, macrocephaly, asymmetry)
- Skin (café-au-lait macules, vascular changes, benign tumors, hypersensitivity)
- Known or suspected genetic predisposition (i.e. somatic test results)
- Mutation positive family member (syndrome with younger onset manifestations
- Hematologic disorders: pancytopenia, anemia, neutropenia, thrombocytopeni

*Modified slide from Shelly Weiss, MS, CGC

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# Red Flags in children and AYA population for more common hereditary cancer syndromes

| Syndrome | Gene | Red Flags |
|---|---|---|
| Wilms Tumor | *WT1* | Bilateral Wilms tumors |
| Familial Adenomatous Polyposis | *APC* | Colorectal polyps, hepatoblastoma, GI and/or thyroid carcinoma, desmoid tumors, osteomas, etc. |
| Multiple Endocrine Neoplasia type II | *RET* | Medullary thyroid carcinoma |
| Li-Fraumeni syndrome | *TP53* | Young diagnoses in multiple family members of Breast, adrenocortical, choroid plexus carcinoma, leukemia, osteosarcoma <10, embryonal rhabdomyosarcoma. More than one primary tumor. Bilateral or multifocal tumors. |
| Rhabdoid Predisposition | *SMARB1/INI* | Rhabdoid tumors (e.g. heart, kidney) and absence of TSC related findings |
| Von-Hippel Lindau | *VHL* | hemangioblastoma (retinal, CNS), pheochromocytoma, paraganglioma |
| Gorlin syndrome | *PTCH1* | Macrocephaly, bifid uvula, dental pits, palmar pits, basal cell cancer, medulloblastoma |
| Peutz-Jeghers syndrome | *STK11* | GI hamartomas, breast ca, ovarian ca, h/o intussusception, mucosal freckling (lips, around and inside of mouth, near the eyes, nostrils, anus, hands and feet |

*Modified slide from Shelly Weiss, MS, CGC



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# Red Flags in children and AYA population for more common hereditary cancer syndromes

| Syndrome | Gene | Red Flags |
|---|---|---|
| Familial Pleuropulmonaryblastoma | *DICER1* | Goiter, papillary thyroid carcinoma, serrtoli-leydig cell ovarian tumor, pleuropulmonary blastoma, lung cysts, rhabdomyosarcoma, medulloblastoma |
| Ataxia-Telangiectasia | *ATM* | Breast cancer in carriers; higher incidence after radiotherapy |
| Constitutional Mismatch Repair Deficiency | *MLH1, MSH2, MSH6, PMS2, EPCAM* | Bilineal family history of Lynch-associated cancers (e.g. colon, uterine, ovarian cancer); multiple café-au-lait macules, pilomatricomas) |
| Retinoblastoma | *RB1* | Bilateral or trilateral retinoblastoma; sarcoma, melanoma; often no family history |
| Familial Neuroblastoma | *ALK, PHOXB2* | family history of “neuroblastic” tumors; consider when 2 FDRs have a neuroblastic tumor, individual with bilateral or multifocal neuroblastomas |
| Juvenile Polyposis | *BMPR1A, SMAD4* | Juvenile polyp pathology, colon cancer |
| Cowden syndrome | *PTEN* | Macrocephaly, multiple café-au-lait spots, facial papules, skin tags, intellectual disability, breast cancer, colon cancer, uterine fibroids and/or cancer, ovarian cancer, meningioma, |

*Modified slide from Shelly Weiss, MS, CGC

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*Worry, despite reassurance*
Female; 17 years old;
Hodgkin lymphoma

"Sometimes I think about … could it be passed down to my child if I had a child? She [oncologist] says no because it's not a hereditary thing, but …"

# What do we know?

- The majority of studies have been done in the context of *BRCA1/2* positive women.
  - Overall low levels of awareness (Quinn et al., 2009; Vadaparampil et al., 2009; Rich et al., 2014)
  - Mixed perspectives on personal acceptability (Staton et al., 2008; Quinn et al., 2009; Vadaparampil et al., 2009; Rich et al., 2014)
  - Patients should receive information about PGT (Vadaparampil et al., 2009; Hurley et al., 2012)Rich et al., 2014)
  - Feel that printed material is best (Hurley et al., 2012)
  - Mixed thoughts about timing and provider (Hurley et al., 2012)

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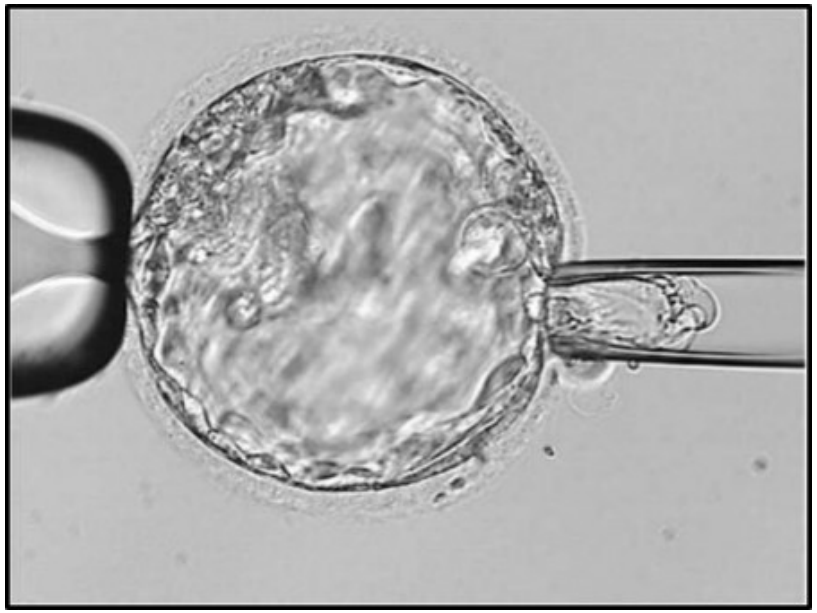
# Preimplantation Genetic Testing (PGT)

- PGT is the genetic testing of embryos for inherited genetic abnormalities
- PGT allows families to achieve a pregnancy free from the known genetic mutation in the family
- The first child was born as the result of *in vitro* fertilization and PGD in 1990 (Handyside, 1990)



**Trophectoderm Biopsy.** *Washington University.*

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