

# Hereditary Cancer

## Breast and Ovarian Cancer

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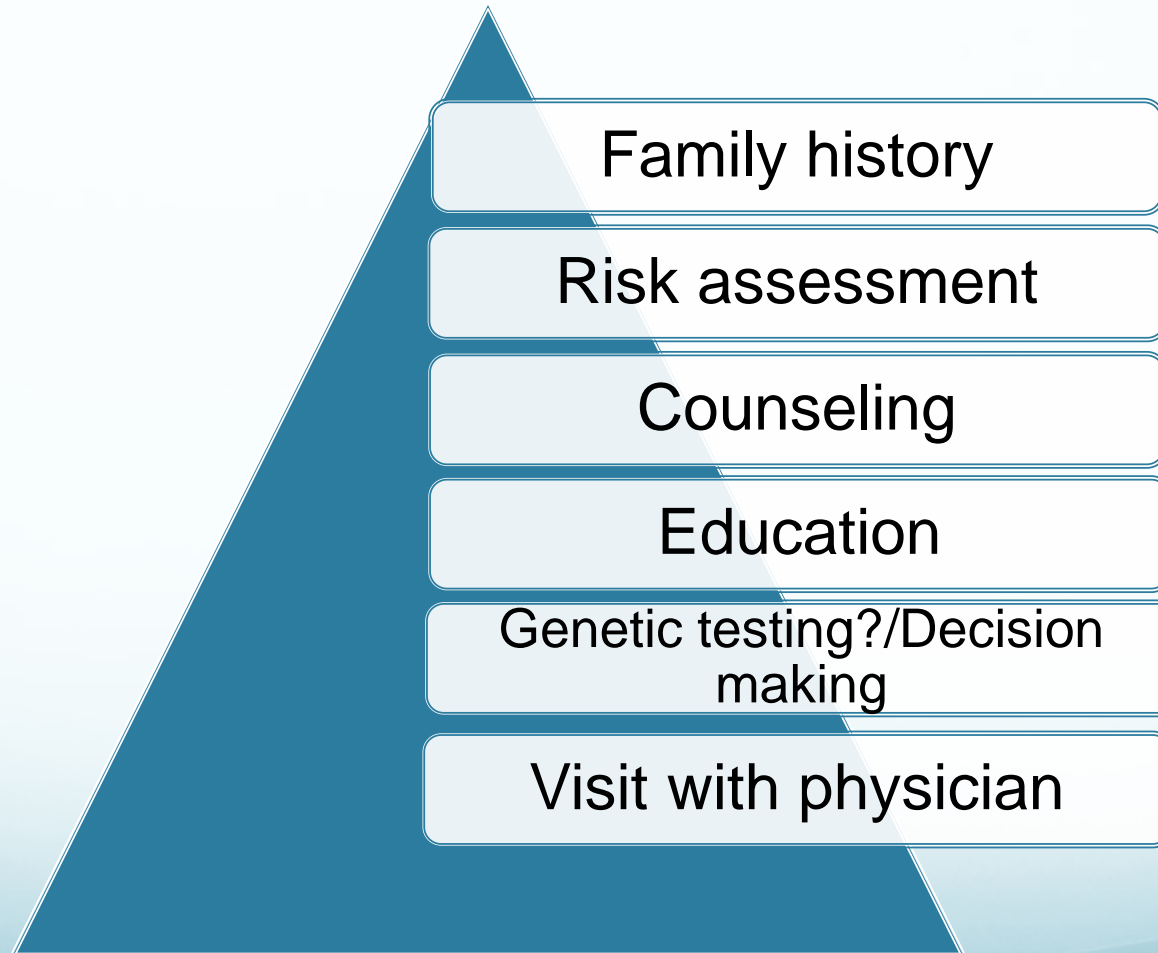
April 20, 2013

# What is the Educational Background of a Genetic Counselor?

- Master's degree in human genetics or a related major
- Certified by the American Board of Genetic Counseling
- Qualified to work in a variety of settings:
  - clinics-(majority)
  - commercial labs
  - research labs
  - state health departments
  - pharmaceutical companies etc.



# Clinic appointment

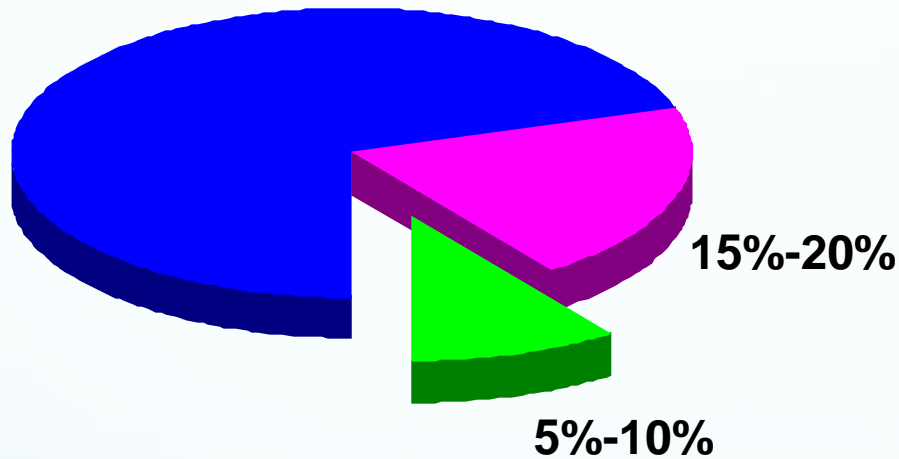


# Who Is at High Risk for Hereditary Cancer?



Hereditary cancers account for only a **small** proportion of all cancer

# How Much Cancer is Hereditary?



Cancer

- Sporadic= *environment*
- Family clusters= *genes & environment*
- Hereditary= *genes*

# Patient Concerns

- Personal risk/relatives risk vs. population risk?
- Reduce risk of cancer?
- Management of cancer?
- Cancer screening-personal/relatives?
- Encouragement by relatives
- Gene mutation in the family



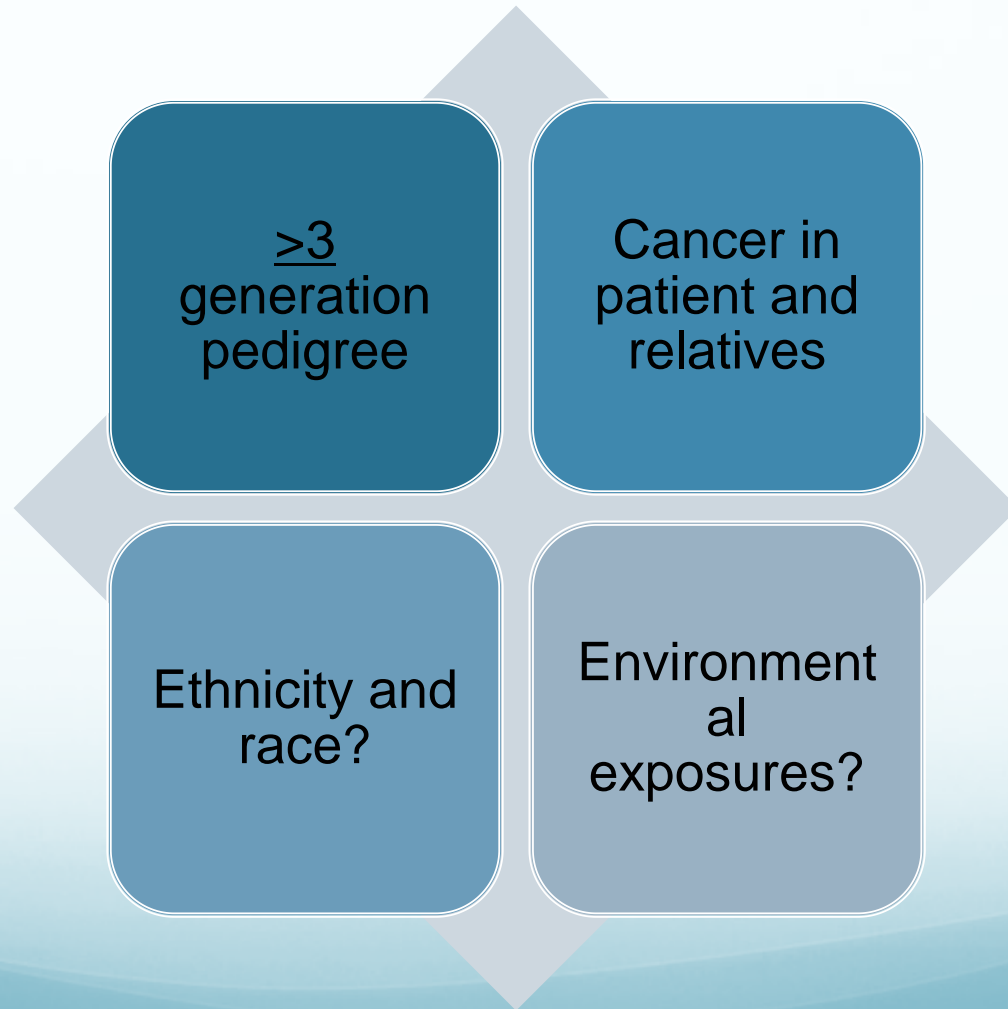
# The Cancer Family History Is the Key to:



- ❑ Accurate risk assessment
- ❑ Effective genetic counseling
- ❑ Appropriate medical follow-up

# Taking a Cancer Family History

## “Key” information





# Family History Questions

Who has had cancer? Their relationship to the patient?

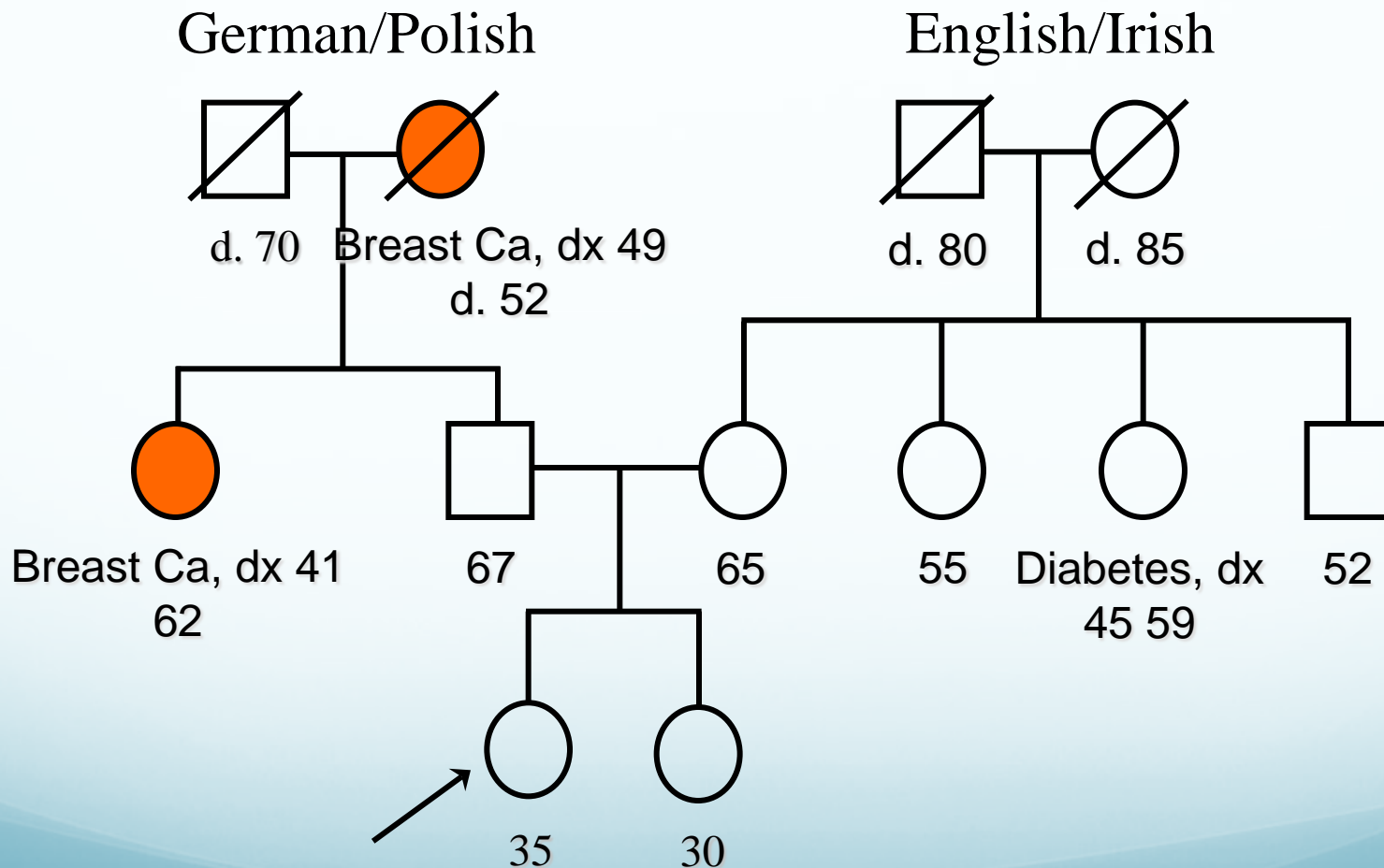
Primary cancer diagnosed in the patient/relative?

Age of the original cancer diagnosis?

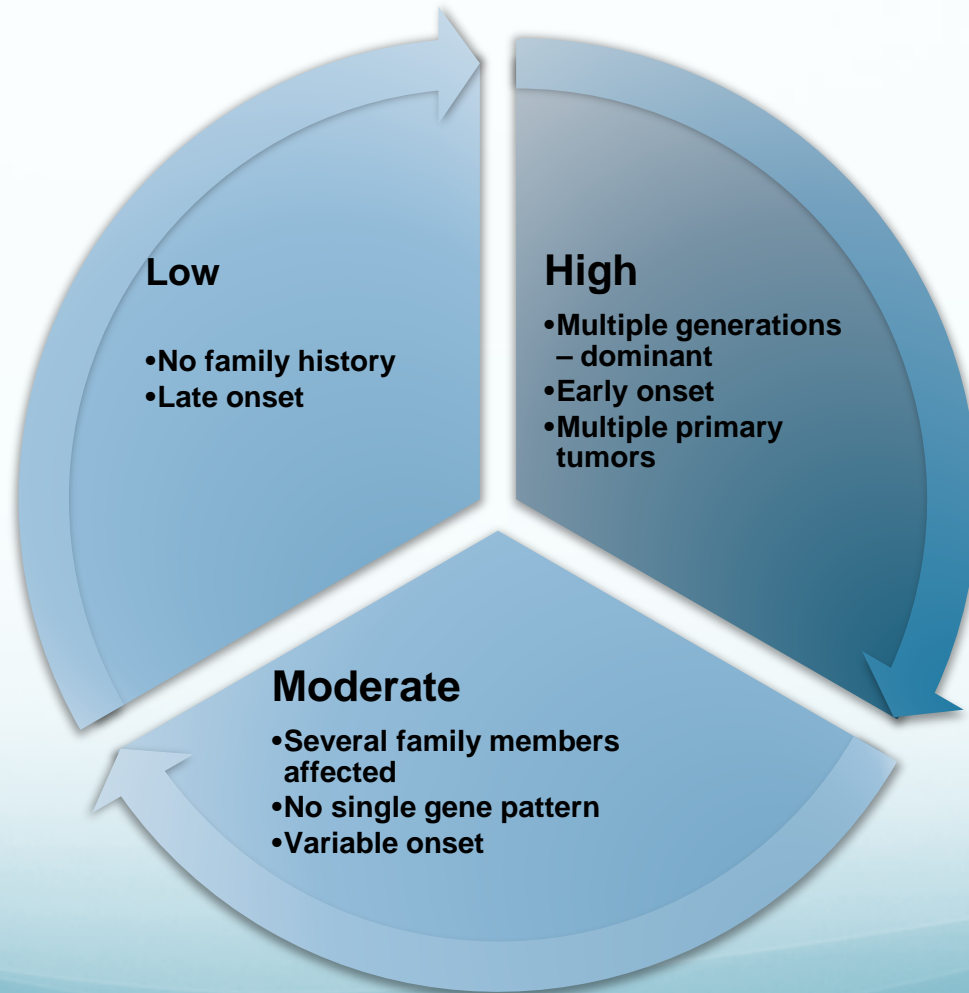
Environmental/personal health risks may have contributed to the risk of cancer?

Surgery (patient/relative) that may reduce their risk of cancer?

# Three-Generation Pedigree

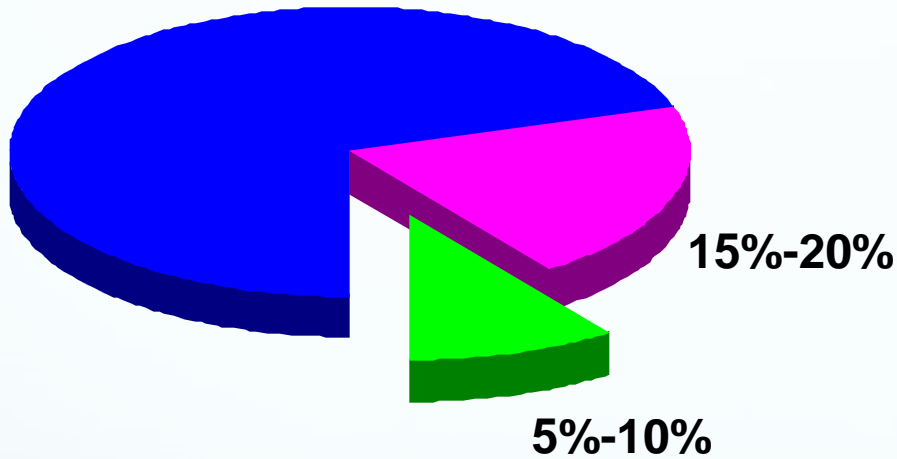


# CANCER RISK

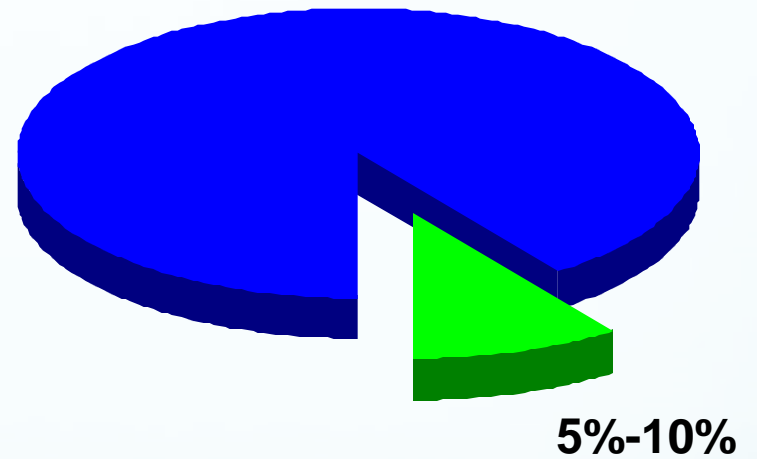


# How Much Breast and Ovarian Cancer is Hereditary?




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**Breast Cancer**



**Ovarian Cancer**

-  Sporadic
-  Family clusters
-  Hereditary



## **When to Suspect Hereditary Cancer Syndrome (5-10% of cancer in families)**

- **Cancer in 2 or more close relatives (on same side of family)**
- **Early age at diagnosis**
- **Multiple primary tumors**
- **Bilateral or multiple rare cancers (e.g. male breast cancer)**
- **Family history associated with syndrome**
- **Autosomal dominant transmission**



# Hereditary Ovarian Cancer

## Two Examples

Hereditary  
Breast and  
Ovarian  
Cancer

A Venn diagram consisting of two overlapping light blue circles. The left circle is labeled 'Hereditary Breast and Ovarian Cancer' and lists 'BRCA1 and BRCA2'. The right circle is labeled 'Lynch syndrome' and lists 'MLH1, MSH2, MSH6, PMS2'. The overlapping area in the center is a darker shade of blue.

- BRCA1 and BRCA2

Lynch  
syndrome


- MLH1,  
MSH2,  
MSH6,  
PMS2

# BRCA1 and BRCA2

BRCA1 and BRCA2 most common cause of hereditary ovarian (fallopian, peritoneal) cancer



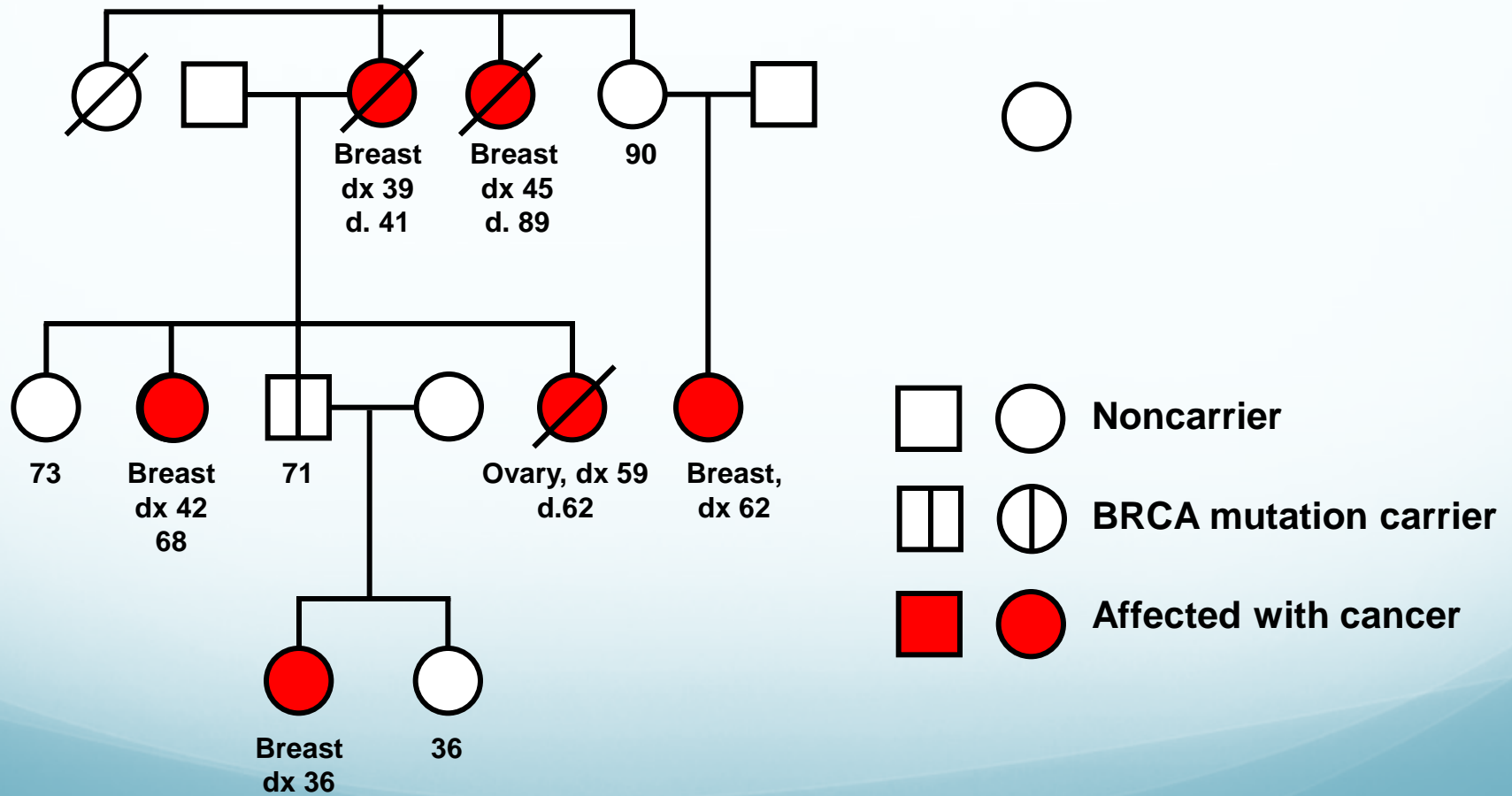
15% of women with ovarian cancer have a mutation in BRCA1 or BRCA2 genes



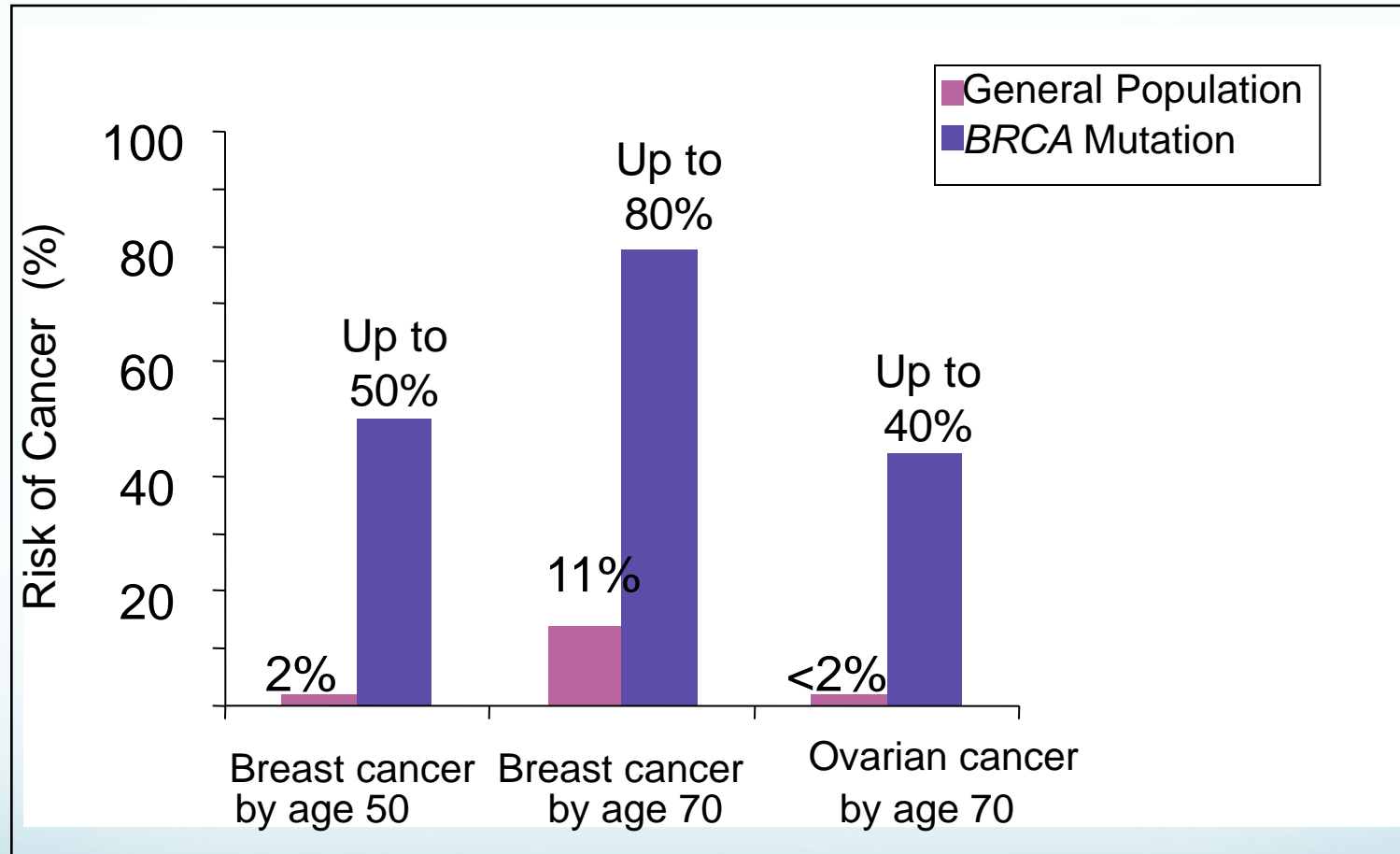
Risk of ovarian cancer is lower in BRCA2. Risk of breast cancer is the same in both genes.



# BRCA Linked Hereditary Breast and Ovarian Cancer



# A *BRCA* Mutation Increases Breast and Ovarian Cancer Risks



*Lancet* 1994;343:692-699

*NEJM* 1997;336:1401-1406

*AJHG* 2003;72:1117-1123

*AJHG* 1995;56:265-271

*Science* 2003; 299:643-646

# Screening for women +BRCA

## Breast

- ❖ Monthly breast self-exams (begin by age 18) *and*
- ❖ Early clinical surveillance (begin at age 25)
  - ❖ annual or semi-annual clinical breast exams
  - ❖ annual mammography
  - ❖ annual MRI (alternating every 6 mos with mammogram)

Modified from: Cancer Genetics Studies Consortium Consensus Statement  
Burke W et al. *JAMA* 277:997, 1997

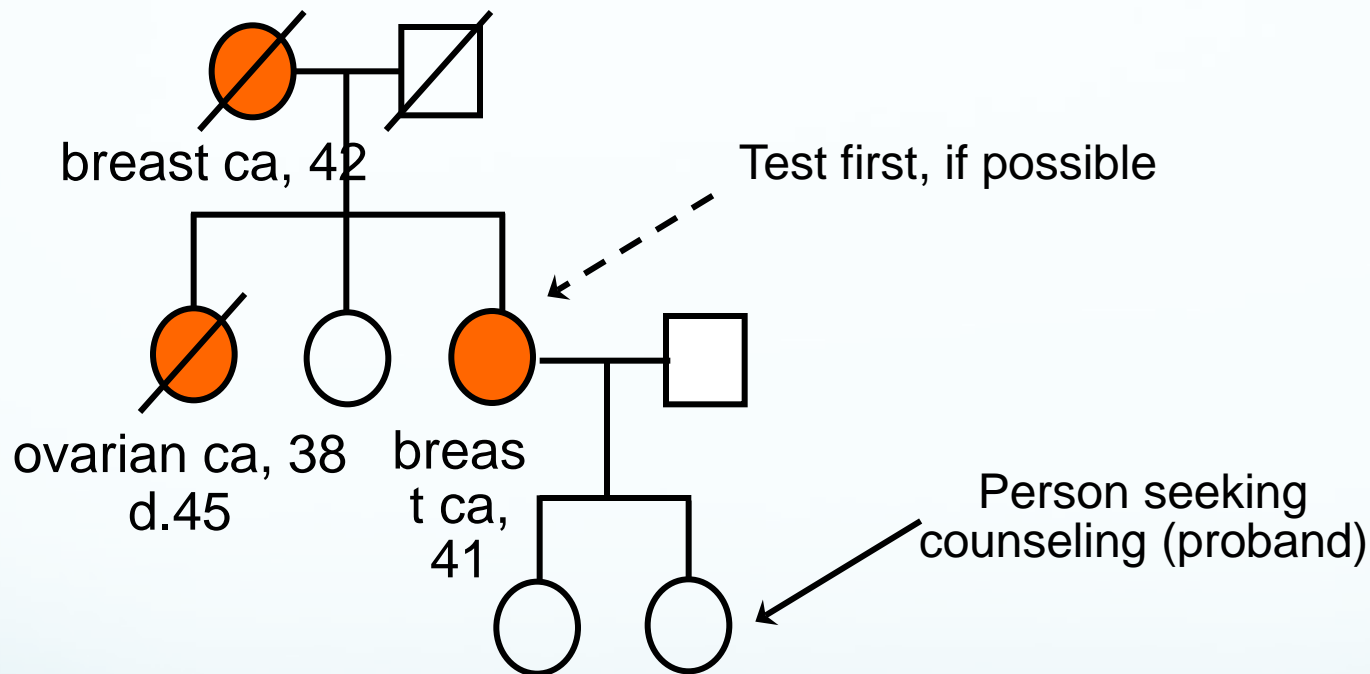
## Ovarian

- ❖ No proven methodology
- ❖ Annually or semiannually, starting at 25–35
  - ❖ transvaginal ultrasound w/color Doppler imaging
  - ❖ CA-125
  - ❖ Pelvic exam

“There are no data demonstrating that screening these high-risk women reduces their mortality from ovarian cancer. Nonetheless, [these measures] are recommended.”\*

\*NIH Consensus Conference, *JAMA* 273:491, 1995

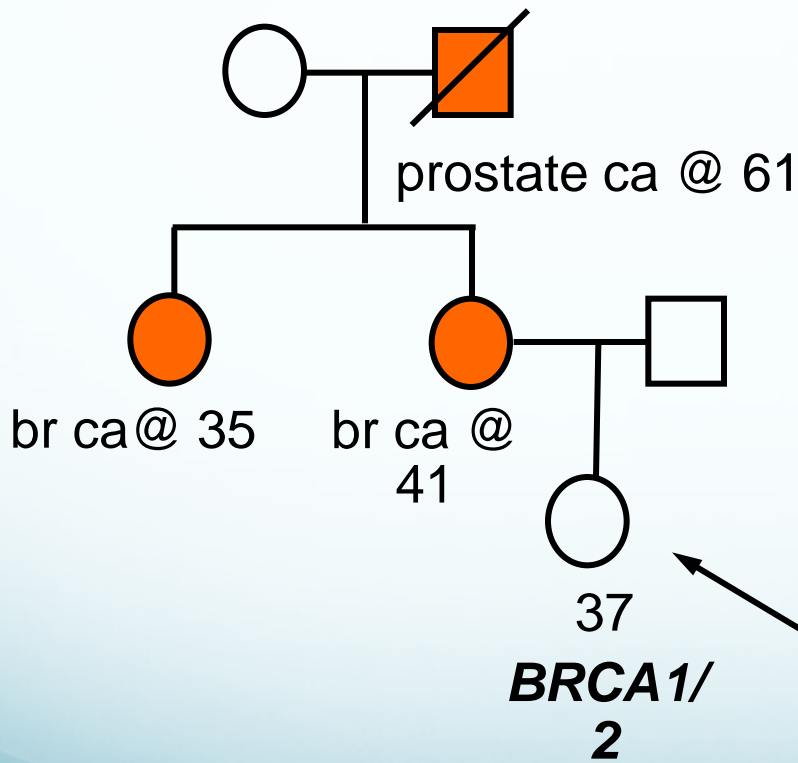
# Ideally, Begin Testing With an Affected Person



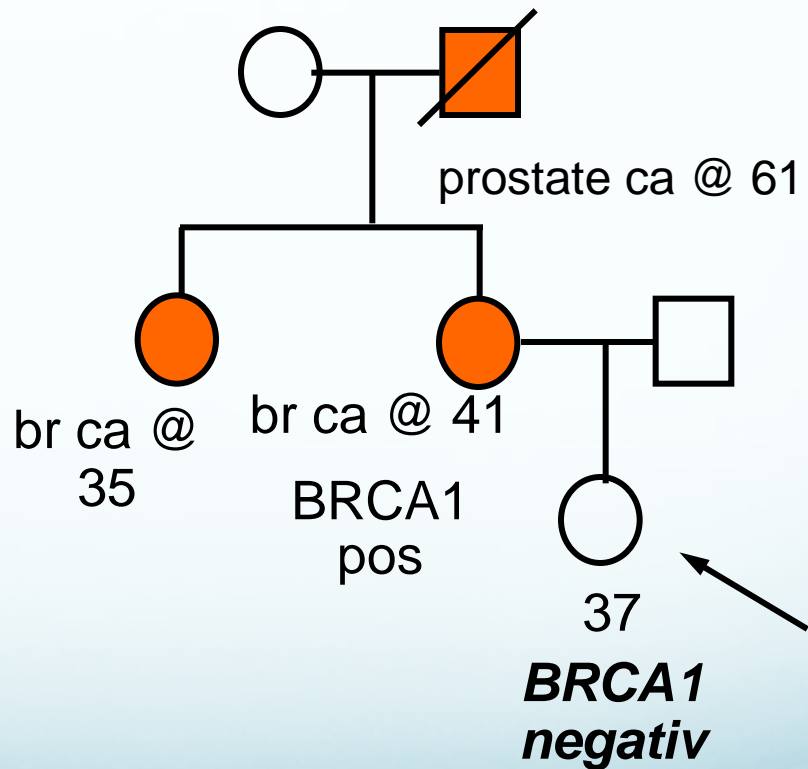
If a mutation is found in an affected person, testing will be more informative for other family members

# Interpreting a Negative Result

No identified mutation in family Family with known BRCA1 mutation



Inconclusive-risk due to family history



True negative-pop risk

# Lynch syndrome

2-4% of ovarian cancer is associated with Lynch syndrome.

Associated with colon cancer, uterine cancer, ovarian cancer and others

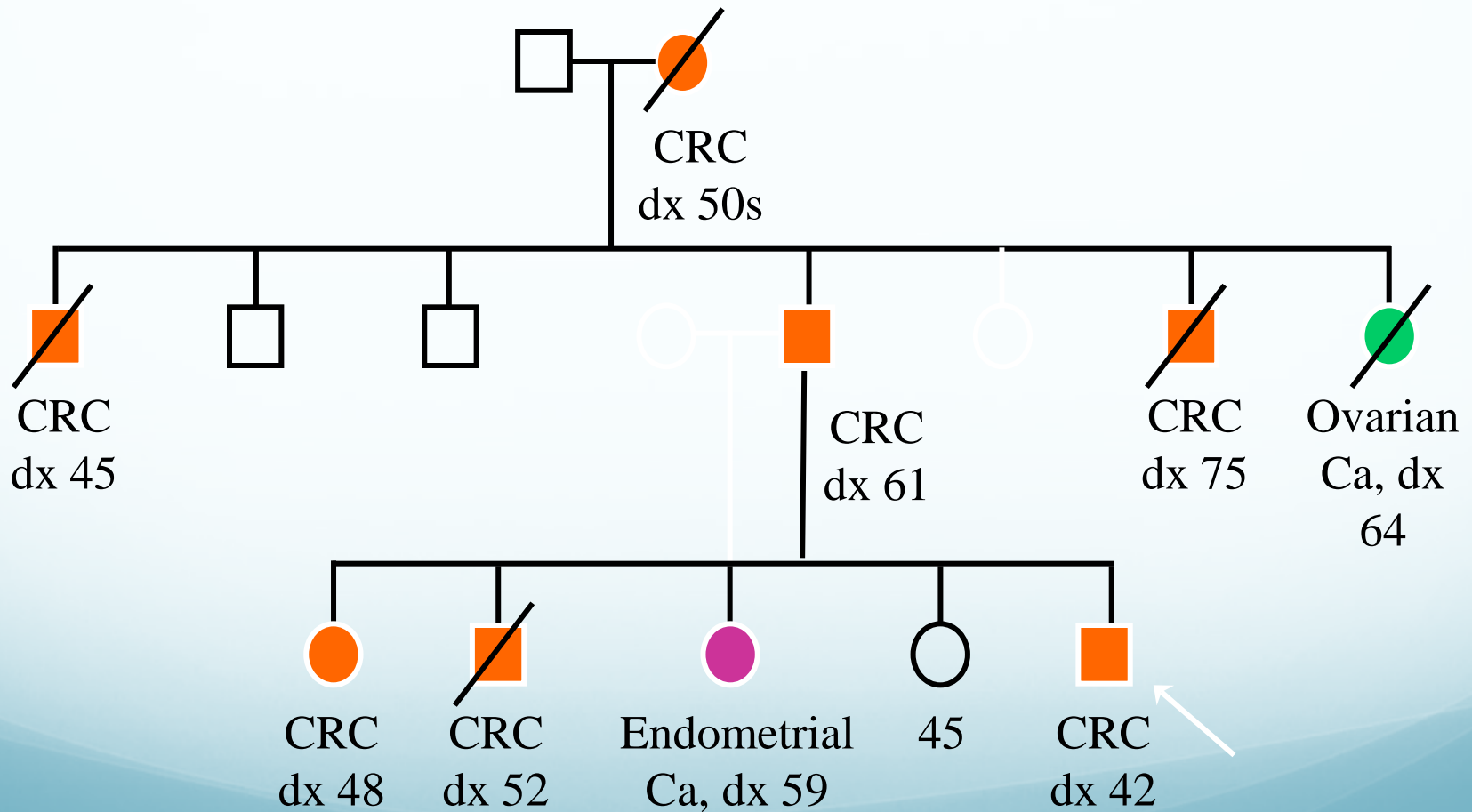
Ovarian cancer lifetime risk is up to 12%

Preventative surgery uterus & ovaries after childbearing is complete

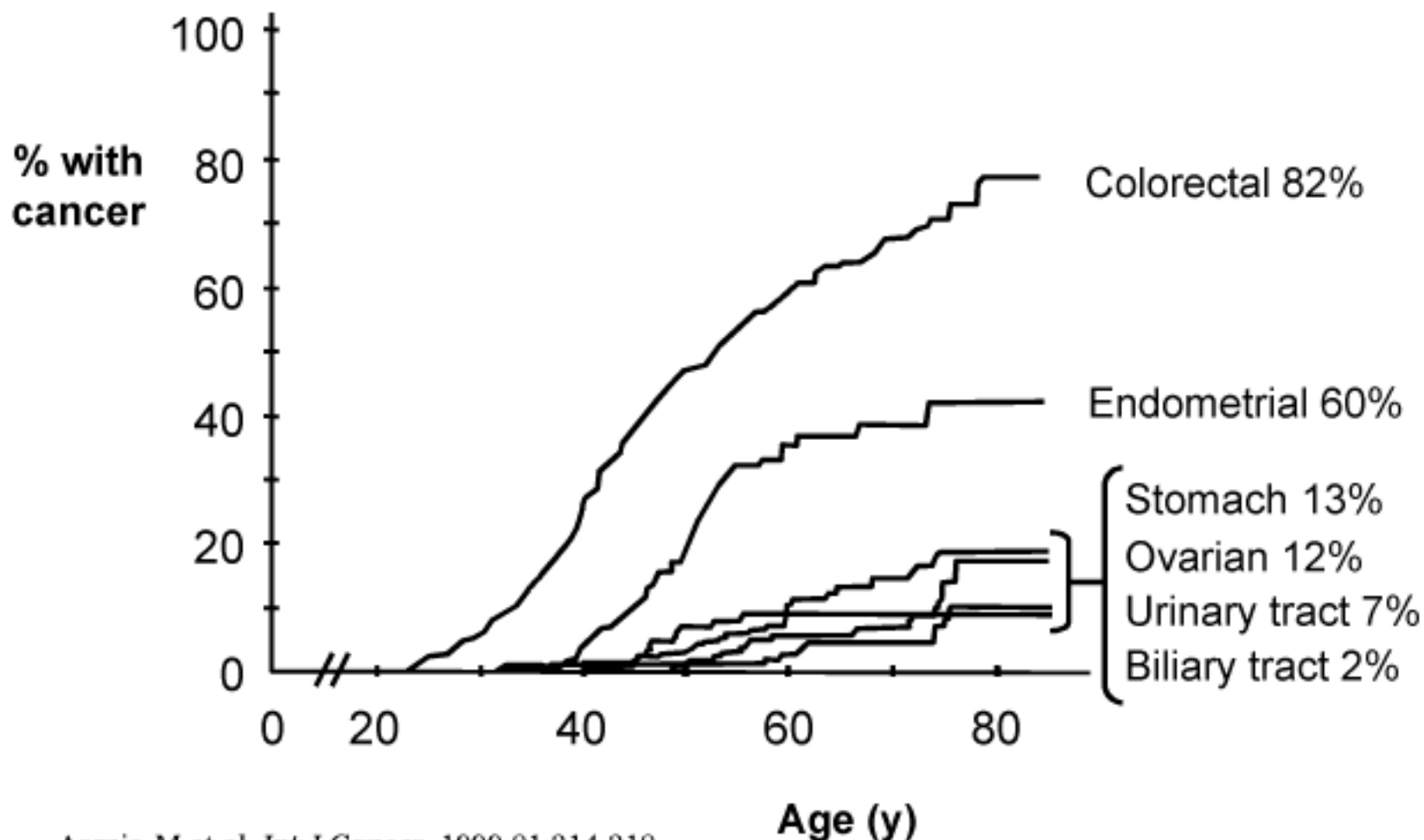
In most ovarian cancer patients, DNA testing is best

- MLH1, MSH2, MSH6, PMS2

# The Family History Is Key to Diagnosing Lynch syndrome



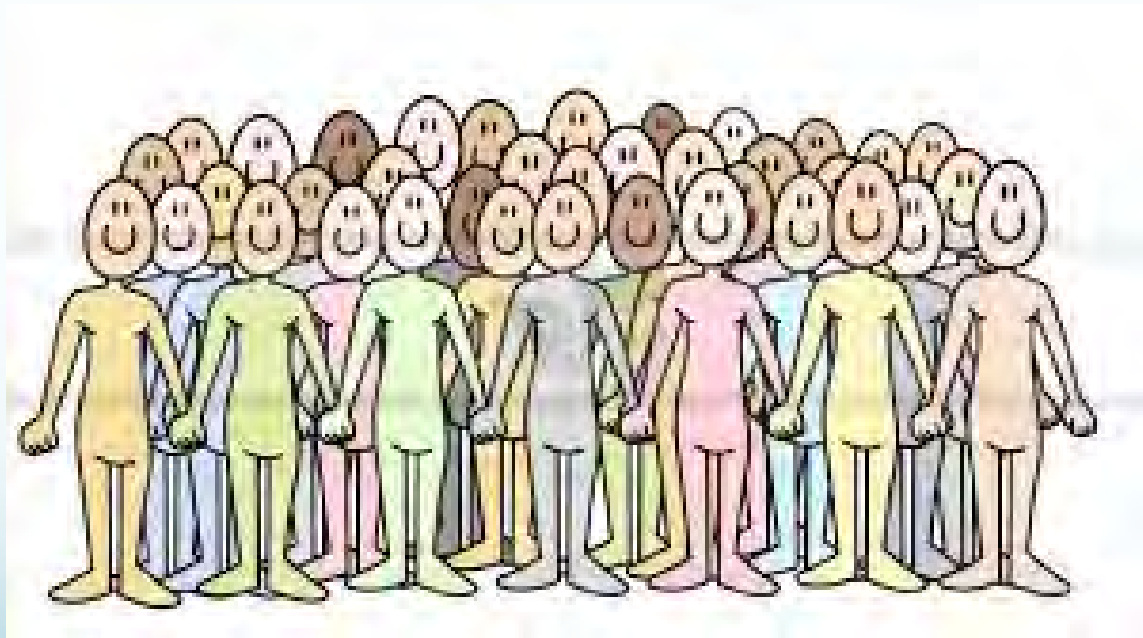
# Cancer Risks in HNPCC



Aarnio M et al. *Int J Cancer*. 1999;81:214-218.



# Who should be screened for HNPC/Lynch syndrome?



# Modified Amsterdam Criteria

- 3 or more relatives with Lynch related cancers in family
- One case a first-degree relative of the other two
- Two or more generations
- One or more Lynch related cancers by age 50
- FAP excluded
- Verification of tumors when possible

Failure to meet these criteria  
does *not* exclude Lynch syndrome

## Revised Bethesda Guidelines (Umar A et al, 2004)

MSI/IHC testing (screening for Lynch syndrome) on a colon cancer tumor should be offered to individuals meeting one or more of the following criteria:

Colorectal cancer diagnosed in a patient who is less than 50 yr. of age

Presence of synchronous, metachronous colorectal cancer or other Lynch syndrome associated tumors (colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, small bowel, brain and sebaceous gland adenomas and keatoacanthomas), regardless of age

Colorectal cancer with the MSI-high histology (presence of tumor infiltrating lymphocytes, Crohn's-like lymphocytic reaction mucinous/signet ring differentiation, or medullary growth pattern) diagnosed in a patient who is less than 60 yrs of age

Colorectal cancer diagnosed in one or more first degree relatives with an Lynch syndrome-related tumor, with one of the cancers being diagnosed under age 50 yr.

Colorectal cancer diagnosed in 2 or more first or second degree relatives with Lynch syndrome related tumors, regardless of age.



# Risk of ovarian cancer with a family history

**Table 2. Lifetime Probability of Getting Ovarian Carcinoma Based on Different Familial Risk Factors**<sup>3,7,13,19,24</sup>

	<b>Relative risk</b>	<b>Lifetime probability (%)*</b>
No family history	1.0	1.6%
Family history	2.9–7.2	4.6%–11.5%
One affected second-degree relative	2.9	4.6%
One affected first-degree relative	3.1–3.6	5.0%–5.7%
Two or three affected relatives	4.6	7.2%
Familial ovarian cancer syndrome	25–30	40%–50%

\* Lifetime chance of developing ovarian cancer in a 35-year-old woman.

Nguyen, H.N et al. Ovarian Carcinoma, 1994, *Cancer*, 74(2): 545-555.

# Genetic Testing



## Potential Benefits of Genetic Testing

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**Improved  
cancer risk  
management**

**Relief from  
uncertainty  
and anxiety  
about  
cancer risk**

**Information  
for  
individual  
and family  
members**

**Lifestyle  
decision  
making**

# Potential Risks of Genetic Testing

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# Genetic Information Nondiscrimination Law (GINA)

## What **Will** GINA Do?

- Effective 2009
- GINA generally will prohibit discrimination in **health coverage** and **employment** on the basis of genetic information.
- Not part of the new healthcare plan-President Obama



*President George W. Bush signs H.R. 493, the Genetic Information Nondiscrimination Act of 2008, Wednesday, May 21, 2008, in the Oval Office. White House photo by Eric Draper.*

# Summary

Only a small amount of cancer is hereditary (5-10%).

Genetic counseling is an assessment of family history and may or may not include genetic testing

The two most common cancer genetic syndromes associated with hereditary ovarian cancer are hereditary breast and ovarian cancer syndrome and Lynch syndrome



# Screening for women +BRCA

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