



# What About My Kids?

Understanding the Genetics  
of Cancer through your  
Family History

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# Her Story



- Jennifer is a 40 year old woman who was previously diagnosed with breast cancer
- She has completed her cancer treatment and has just returned to work
- She feels she can finally move forward with her life

# Family Story

Jennifer always knew it wasn't **if** she was going to get cancer...but **when** it would happen

- Her mother had already had breast cancer
- One of her mother's sisters died young from ovarian cancer
- She had always assumed cancer would happen to her

It doesn't matter what you  
do because it's going to  
happen anyway

Leonard Cohen

PICTUREQUOTES.COM

As she settles into her desk at work knowing that she has conquered her cancer, she suddenly wonders...



WHAT DOES  
THIS MEAN  
FOR MY KIDS?



# Cancer & Genetics



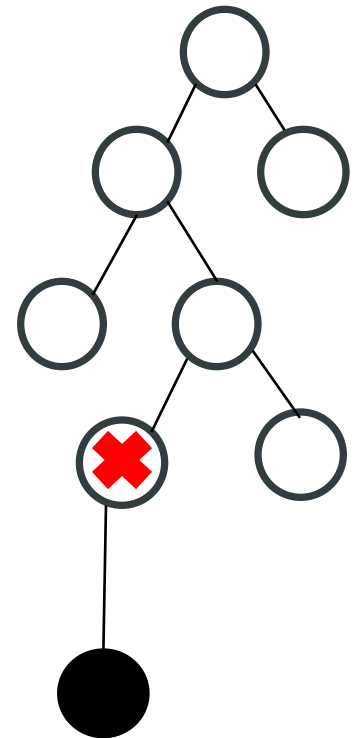
# Cancer is Common

- 1 in 2 men get cancer in their lifetime
- 1 in 3 women get cancer in their lifetime
- 1 in 8 women get breast cancer in their lifetime
- 1 in 20 individuals get colon cancer in their lifetime



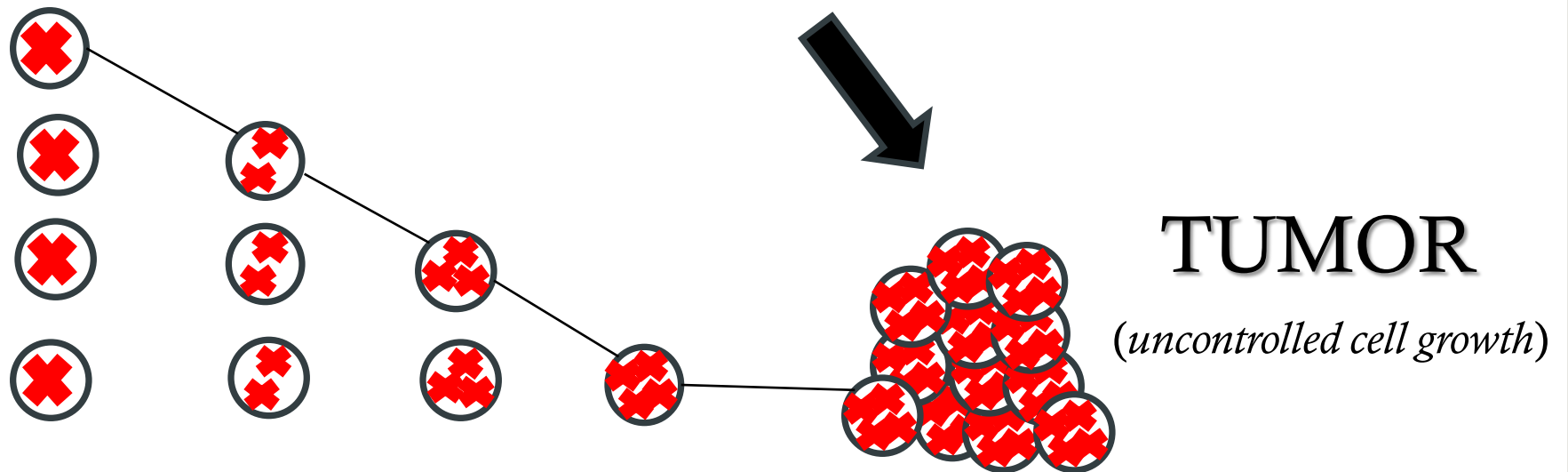
# What is Cancer?

- All cancer begins in cells within our body
- Cells contain our genetic information (DNA)
- Cells grow and divide to keep you healthy
  - Replace old and damaged cells
- When cells divide they copy DNA
- Sometimes cells make a mistake (mutation):
  - DNA can be repaired OR
  - Cell dies and is replaced

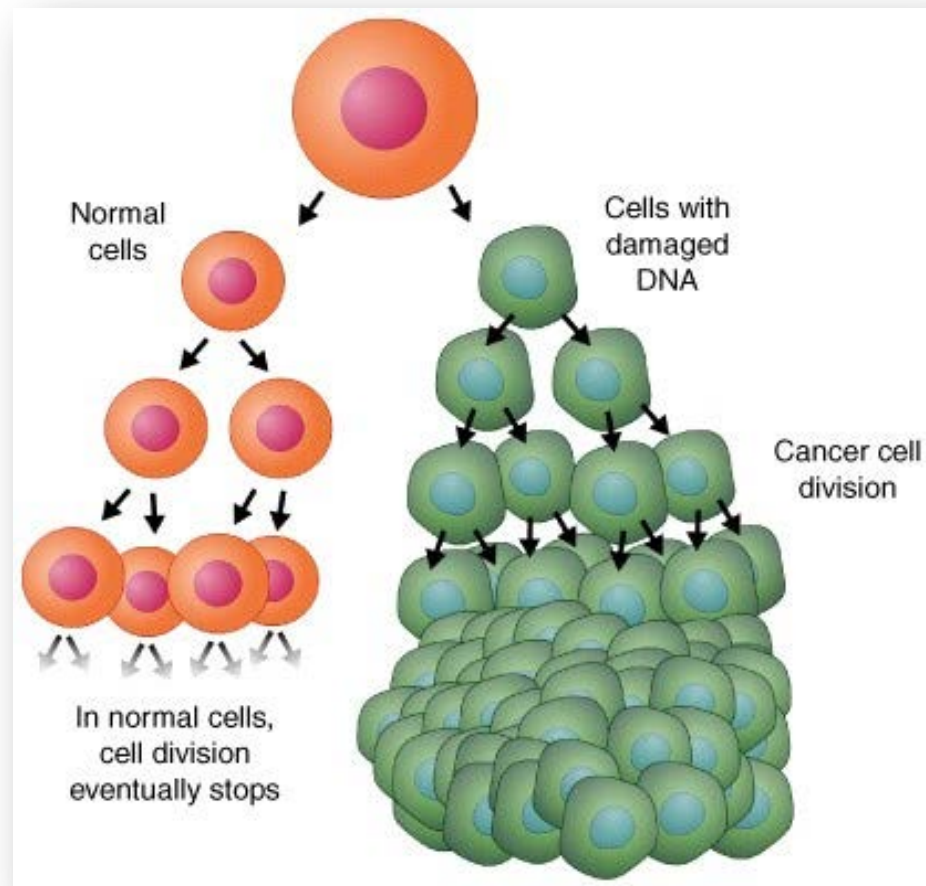


# What is Cancer?

- Sometimes mistakes or mutations are not recognized:
  - Cells do not die when they should
  - Cells grow without control making more cells
  - Cells create many copies of the mutation



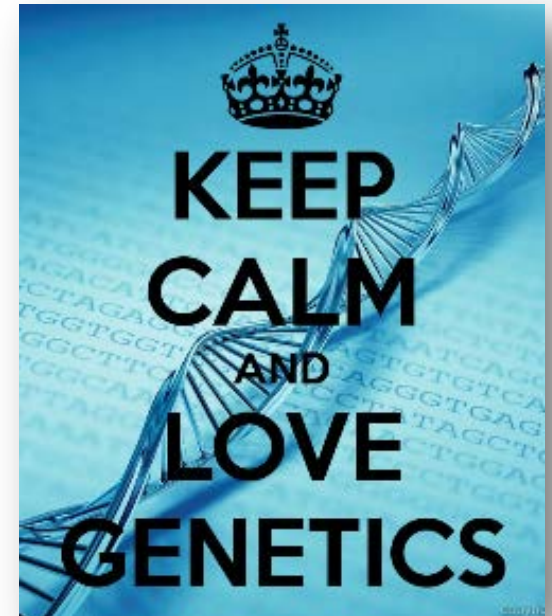




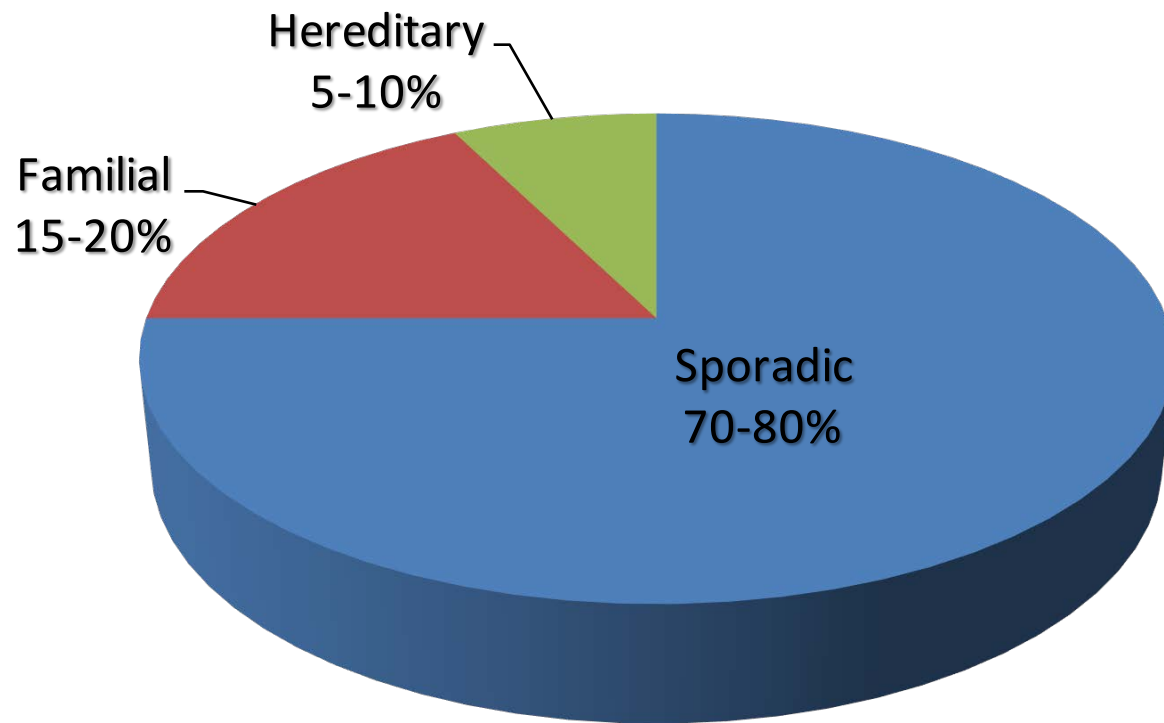
A single mutation in DNA does not cause cancer – it is the accumulation of multiple mutations over many years that allows a normal cell to become abnormal and grow without control (cancerous cell)

# All Cancer is Genetic

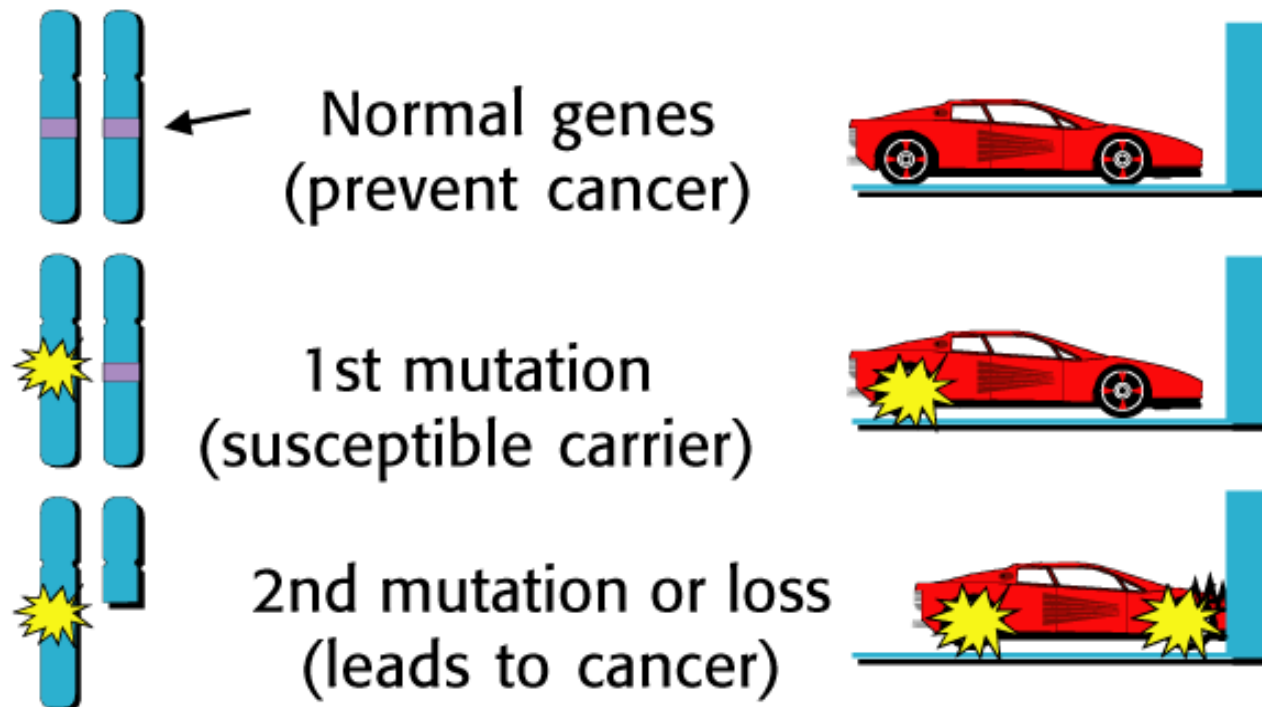
- Cancer starts from a mutation in our DNA
  - In normal cells, mutations are detected and repaired
  - In cancer cells, mutations are not detected or repaired and the cell continues to divide



# Most Cancer is Not Inherited



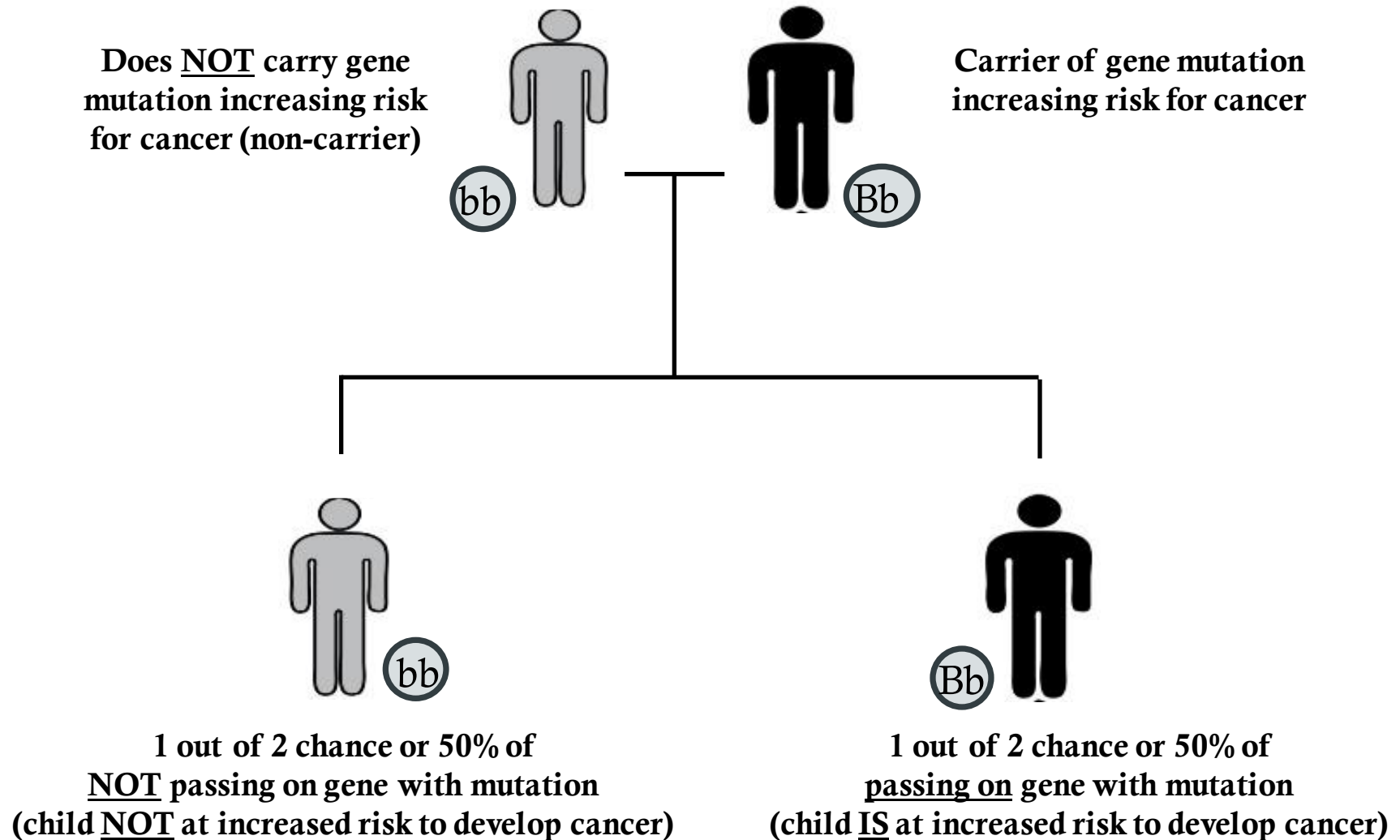
# Two Hits to Cancer



Weinberg RA. Oncogenes and tumor suppressor genes. *CA Cancer J Clin.* 1994;44:160-170.

Weinberg RA. Tumor suppressor genes. *Science.* 1991;254:1138-1146.

# Autosomal Dominant Inheritance





# Using Family History to Understand Cancer Risk



<http://www.temple-square.com/wp-content/uploads/2015/06/ThinkstockPhotos-153079734.jpg>

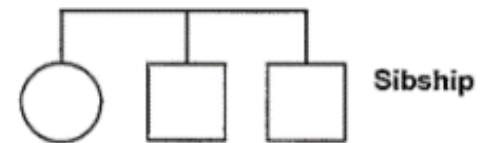
# Pedigree Symbols Chart



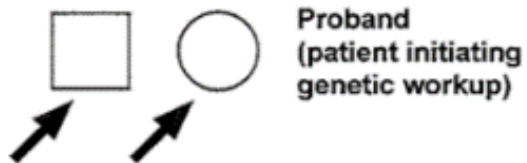
Male, Female



Mating



Sibship



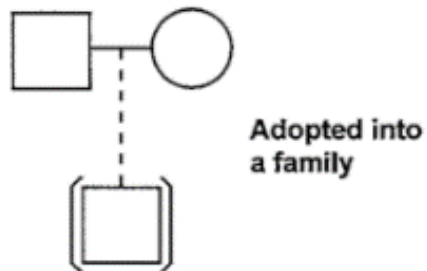
Proband  
(patient initiating  
genetic workup)



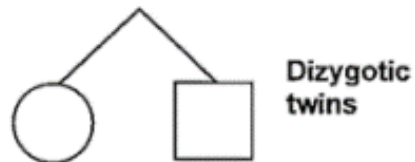
Affected  
with trait



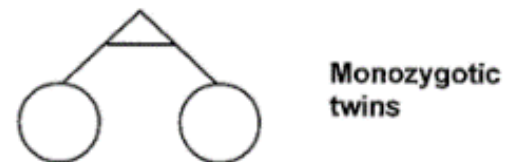
Deceased



Adopted into  
a family

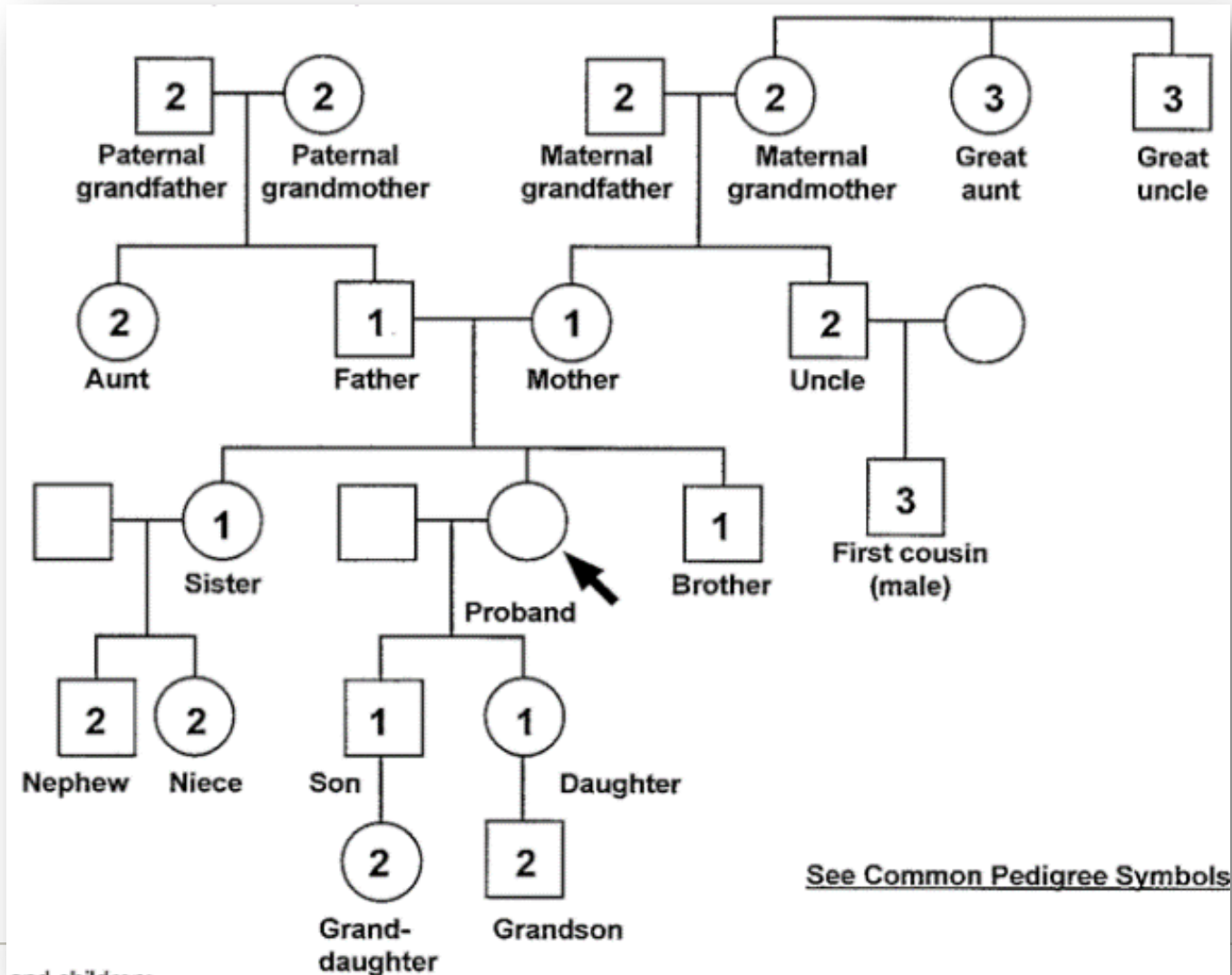


Dizygotic  
twins



Monozygotic  
twins

# Pedigree Relationship Chart



# Assessing Your Family History

- 3 generations
  - You/siblings, parents, grandparents
- General health history for all relatives
- Causes and age at time of death
- Exposures
  - Alcohol/drugs, occupational
- Ethnicity
- Specific cancer history





# Specific Cancer History

- Location of primary cancer
  - Breast, colon, kidney
- Age at time of diagnosis
- Current age or age at time of death
- Cancer on one side (unilateral) or both sides (bilateral)
- Relationship
- Environmental exposures
  - Smoking, occupational, sun
- Treatment provided
  - Chemotherapy, radiation, surgery
- Pathology reports
- Imaging/procedure results
  - Mammograms, colonoscopy
- Genetic test results
- Results from tumor testing
- Autopsy reports/death certificates



# Should I be Concerned about a Hereditary Cancer Syndrome?



<http://thumbs.dreamstime.com/x/adult-children-hands-holding-underwater-18174048.jpg>

# Give it the **CANCER** Test

**C** = Close blood relatives with cancer (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>)

**A** = Age of onset (<50 years)

**N** = Number of cancers (bilateral, multiple primaries)

**C** = Cancer types (same or related cancers)

**E** = Ethnicity (Ashkenazi Jewish)

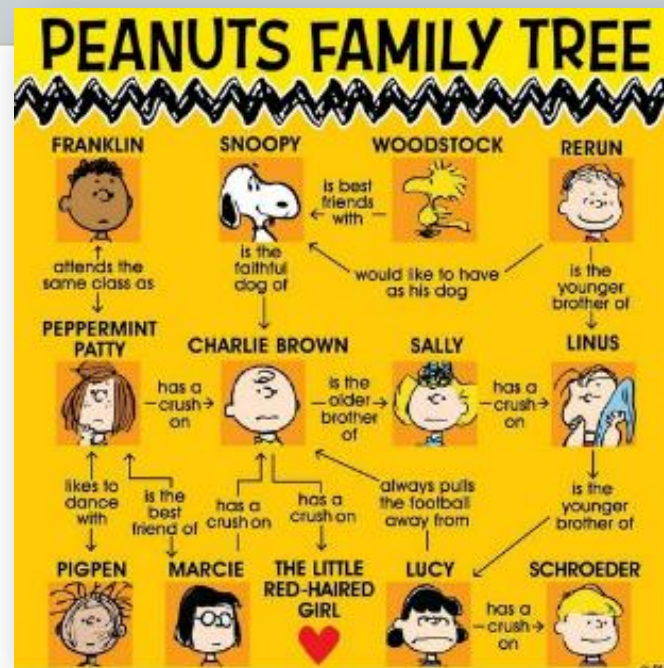
**R** = Rare cancers (sarcoma, male breast cancer)

# When Inherited Cancers are Hidden

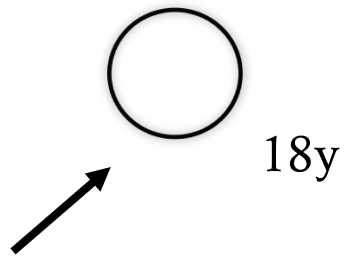
- Adopted
- Limited family members
- Early deaths
- Prophylactic surgeries (for other reasons)
- Limited gender representation (few females)



# Family History Example

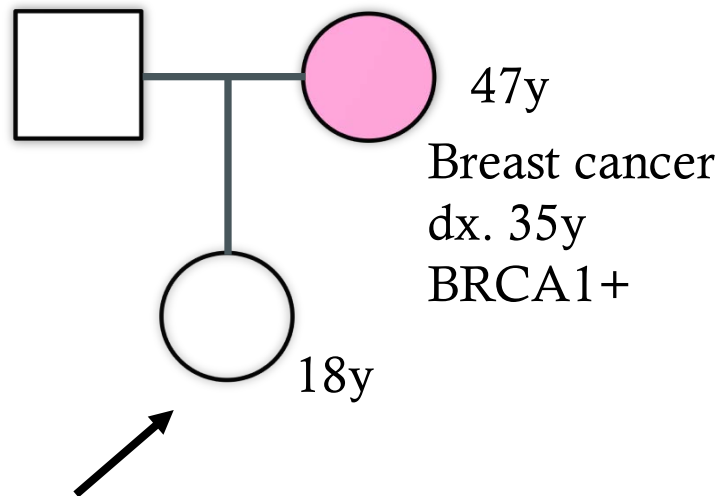


# Case Presentation

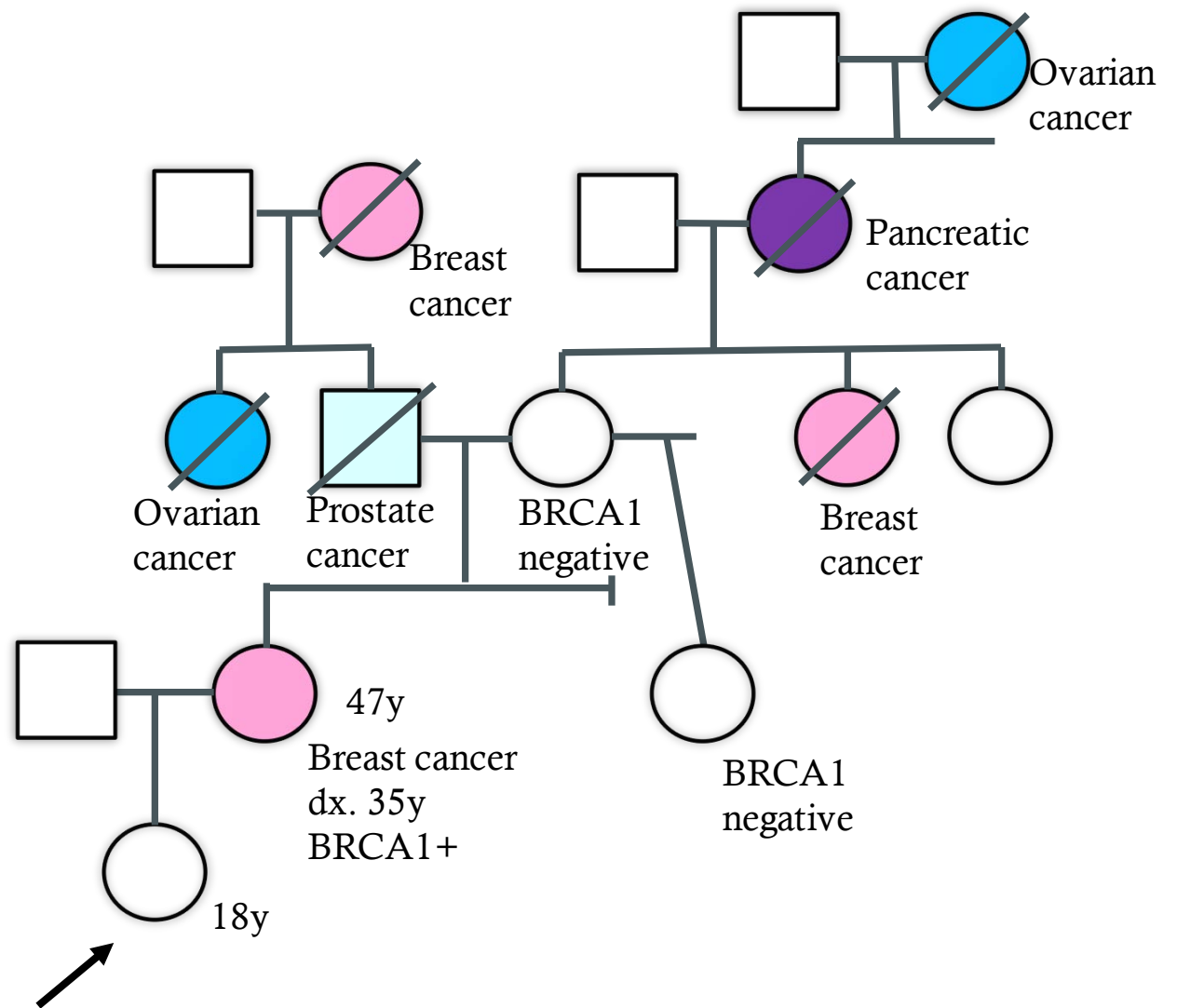




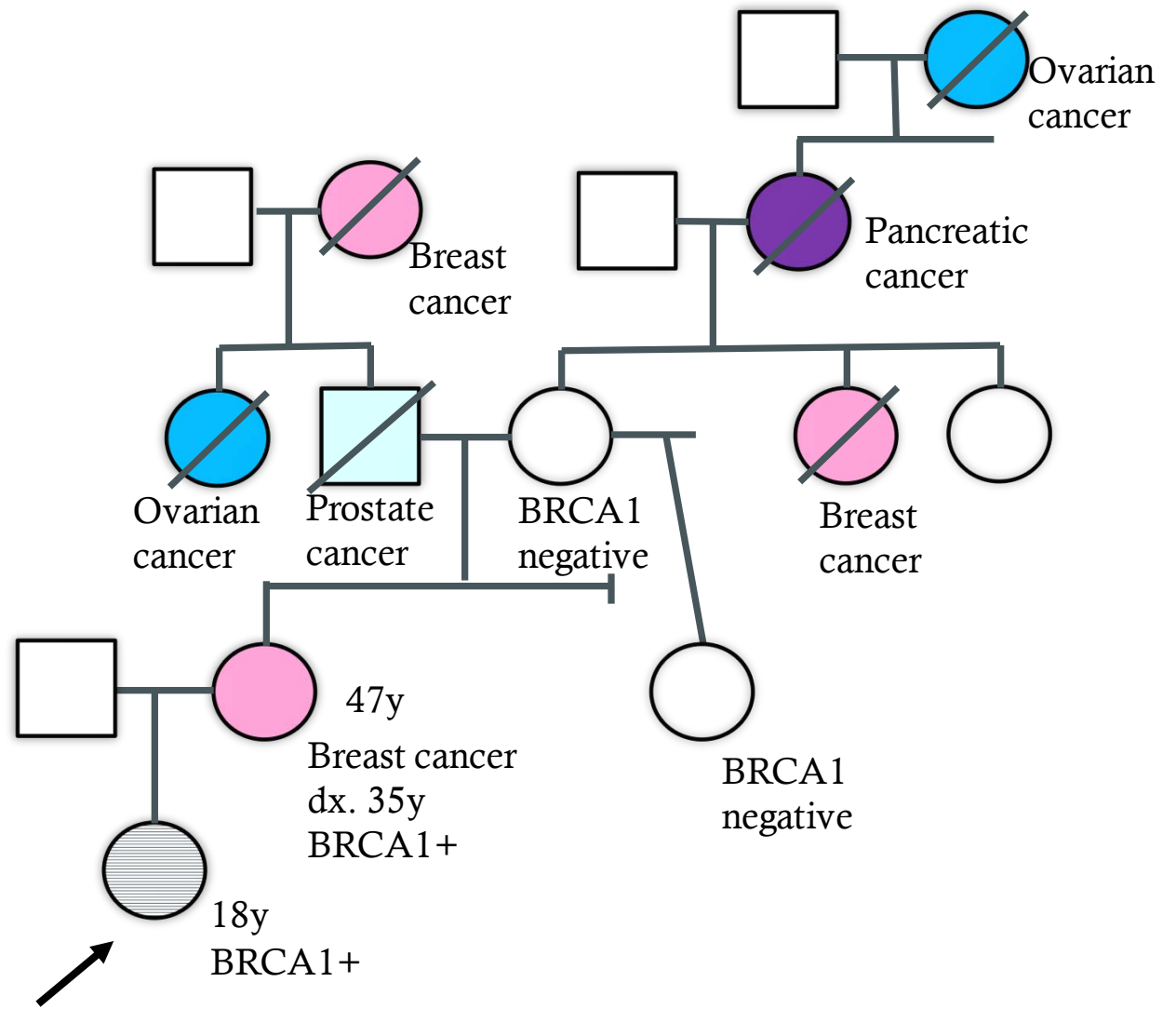
# Case Presentation



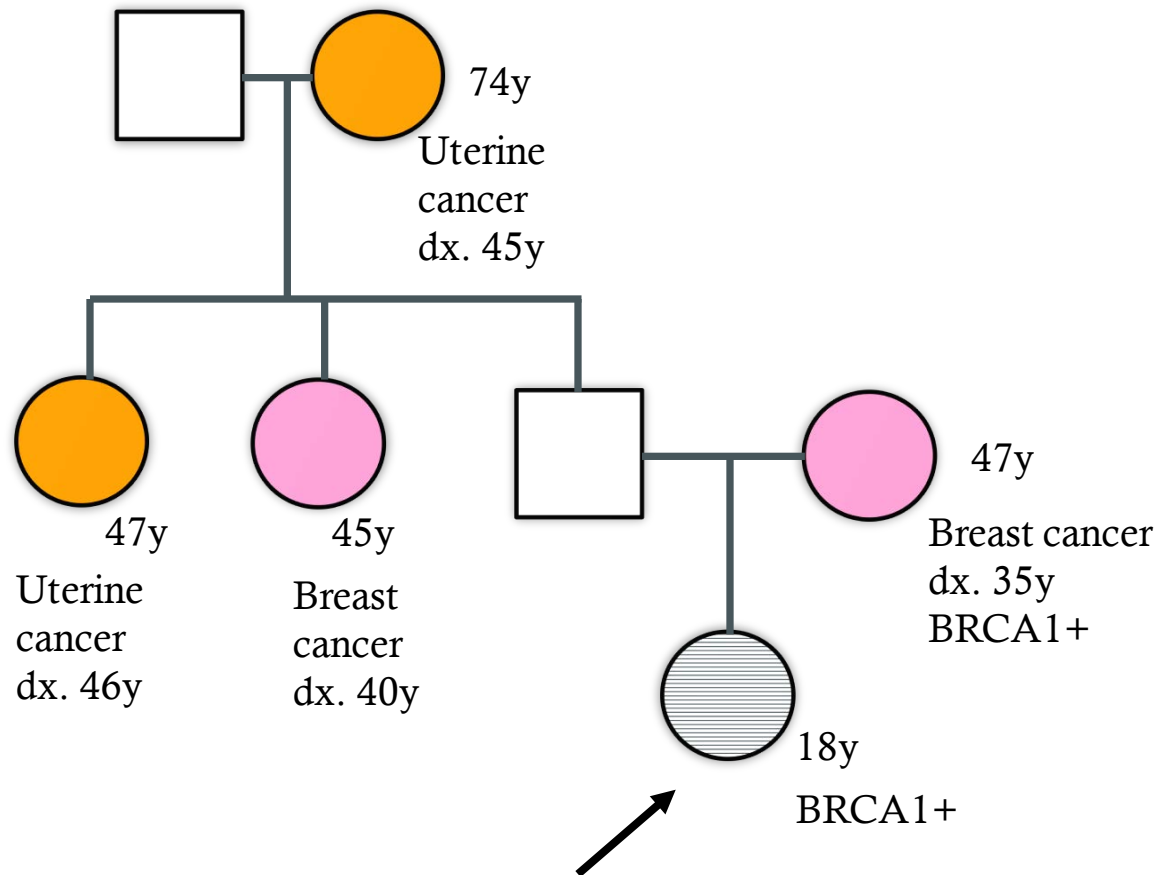
# Case Presentation



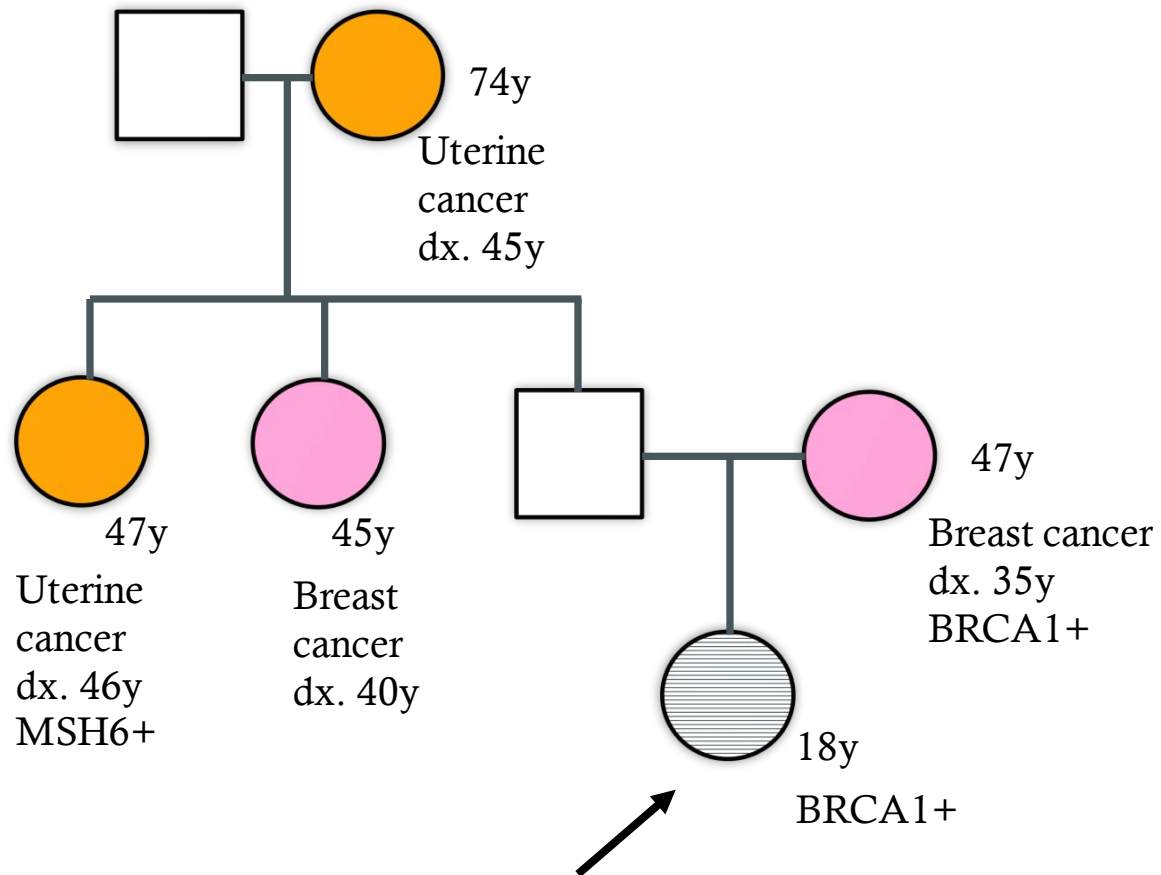
# Case Presentation



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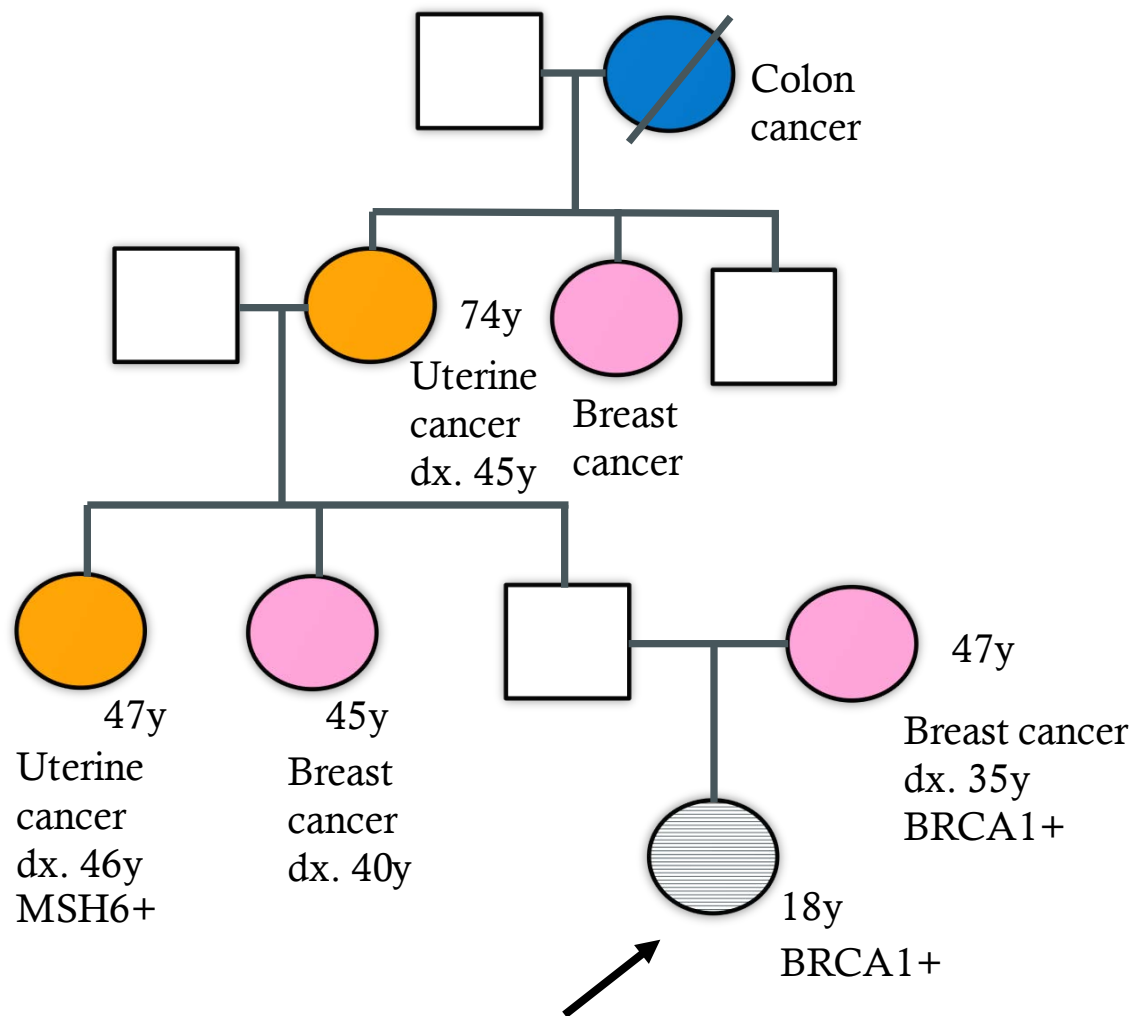


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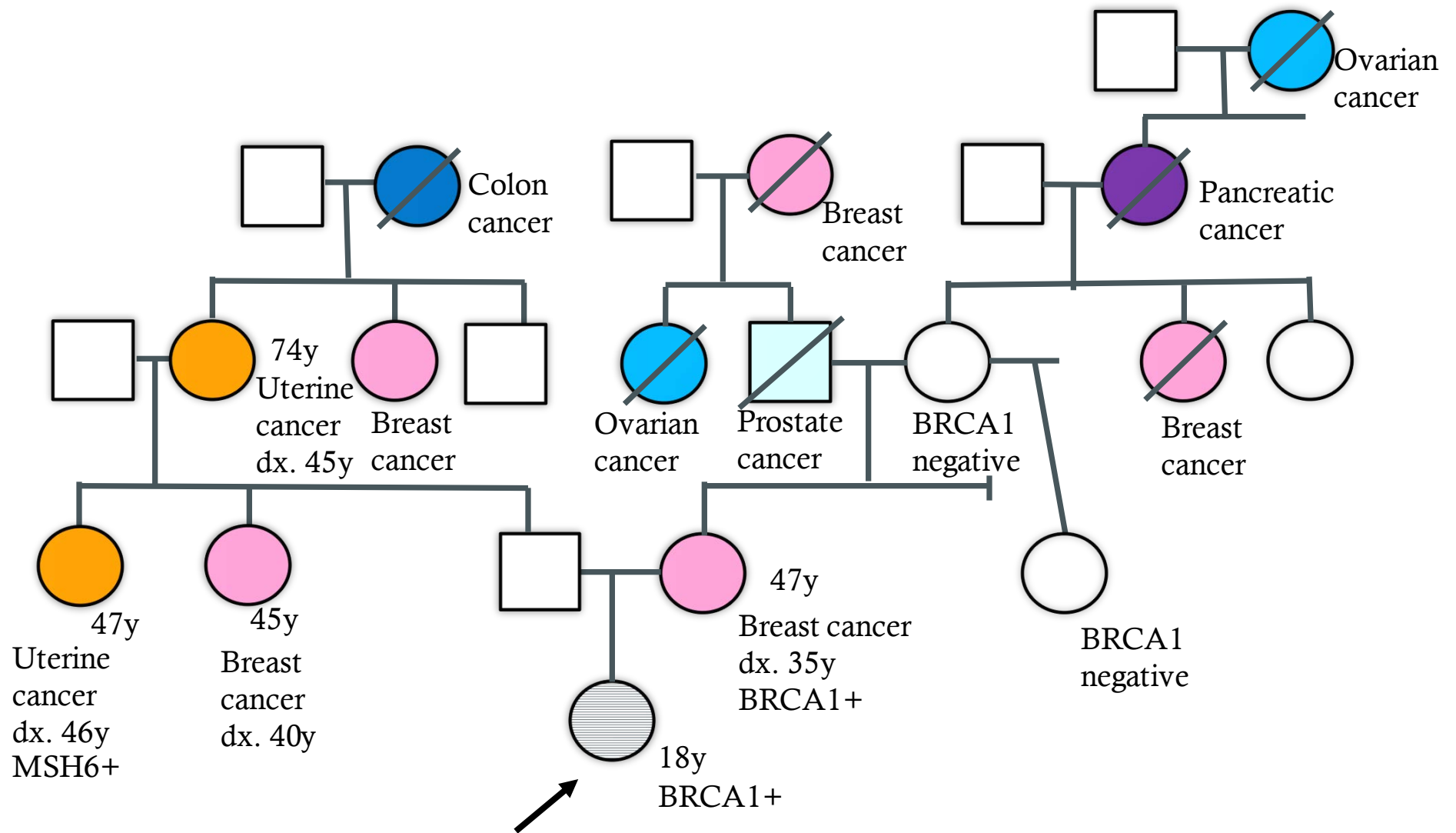




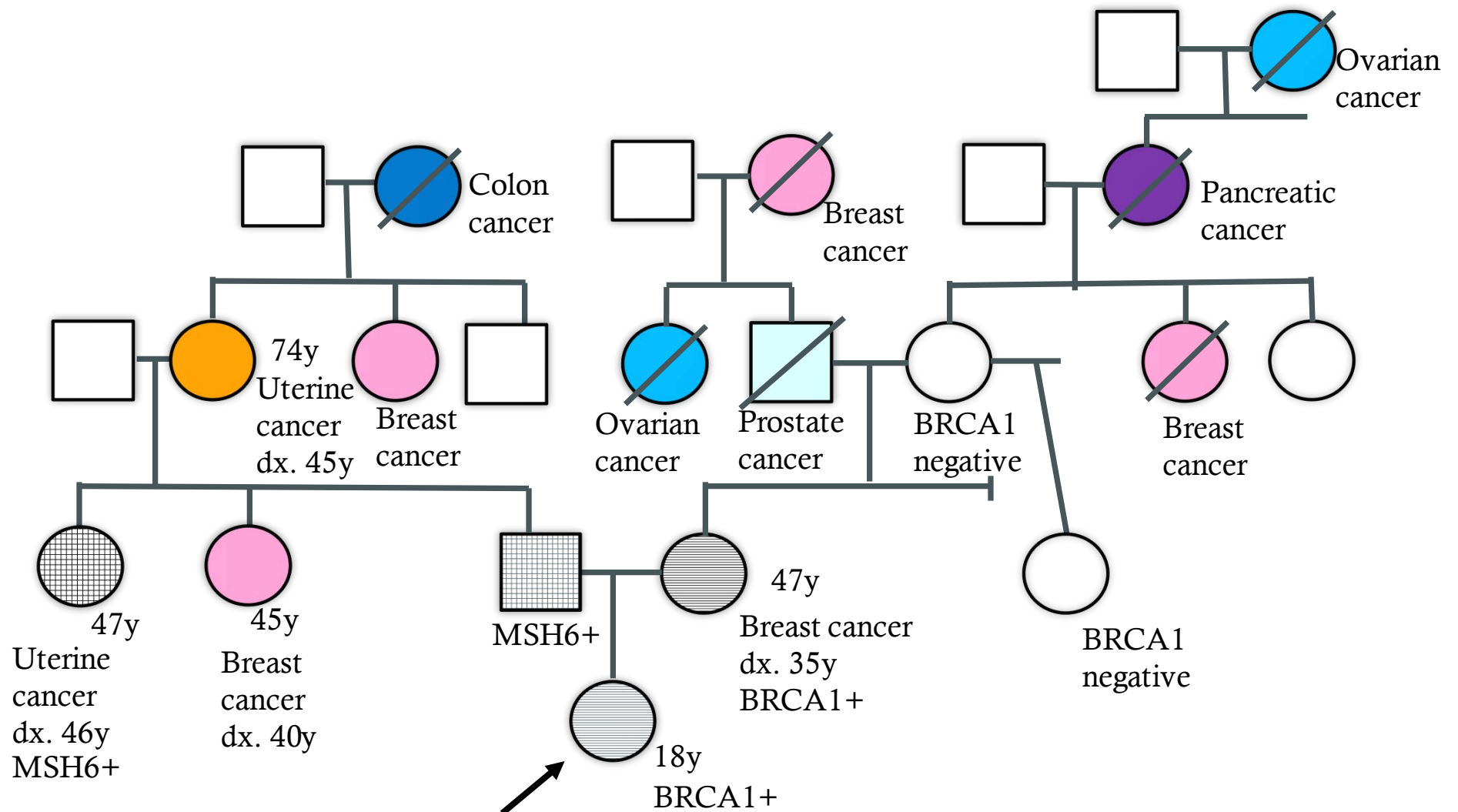
# Case Presentation



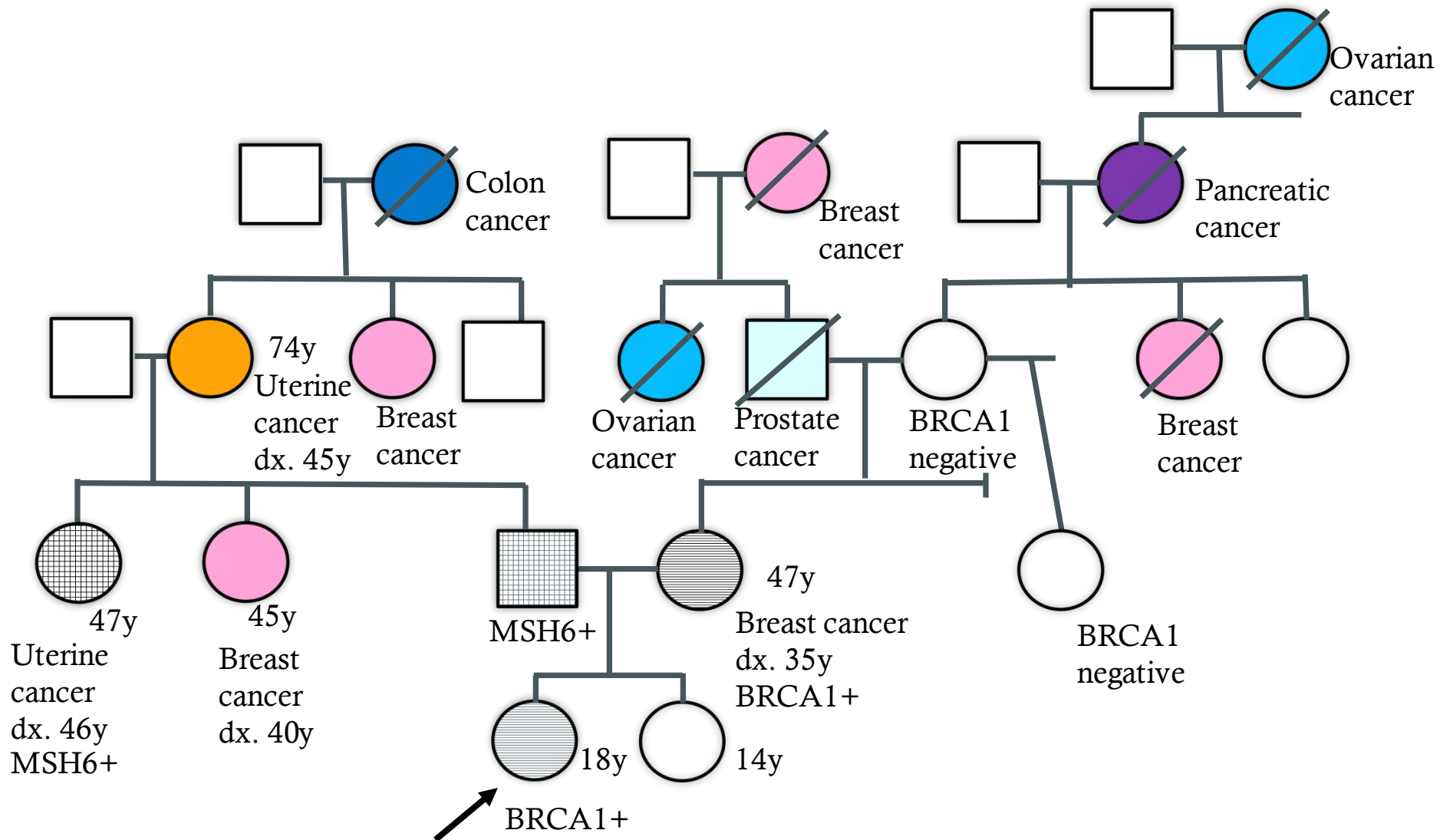
# Case Presentation



# Case Presentation



# Case Presentation



# Hereditary Cancer Syndromes



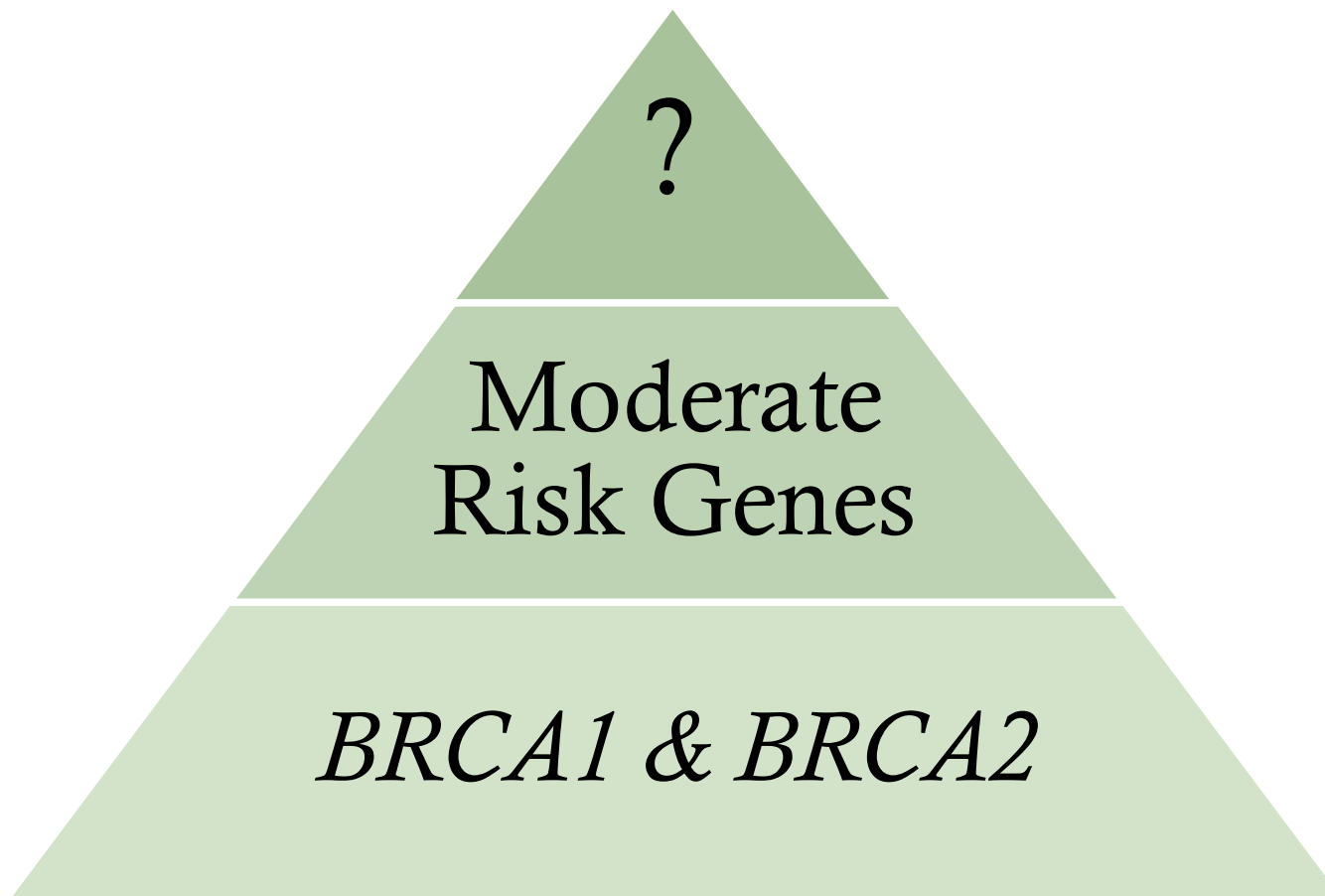
[http://i1.cpcache.com/product\\_zoom/619345252/purple\\_ribbon\\_awareness\\_tree\\_](http://i1.cpcache.com/product_zoom/619345252/purple_ribbon_awareness_tree_)

# Genes Identified in HCS

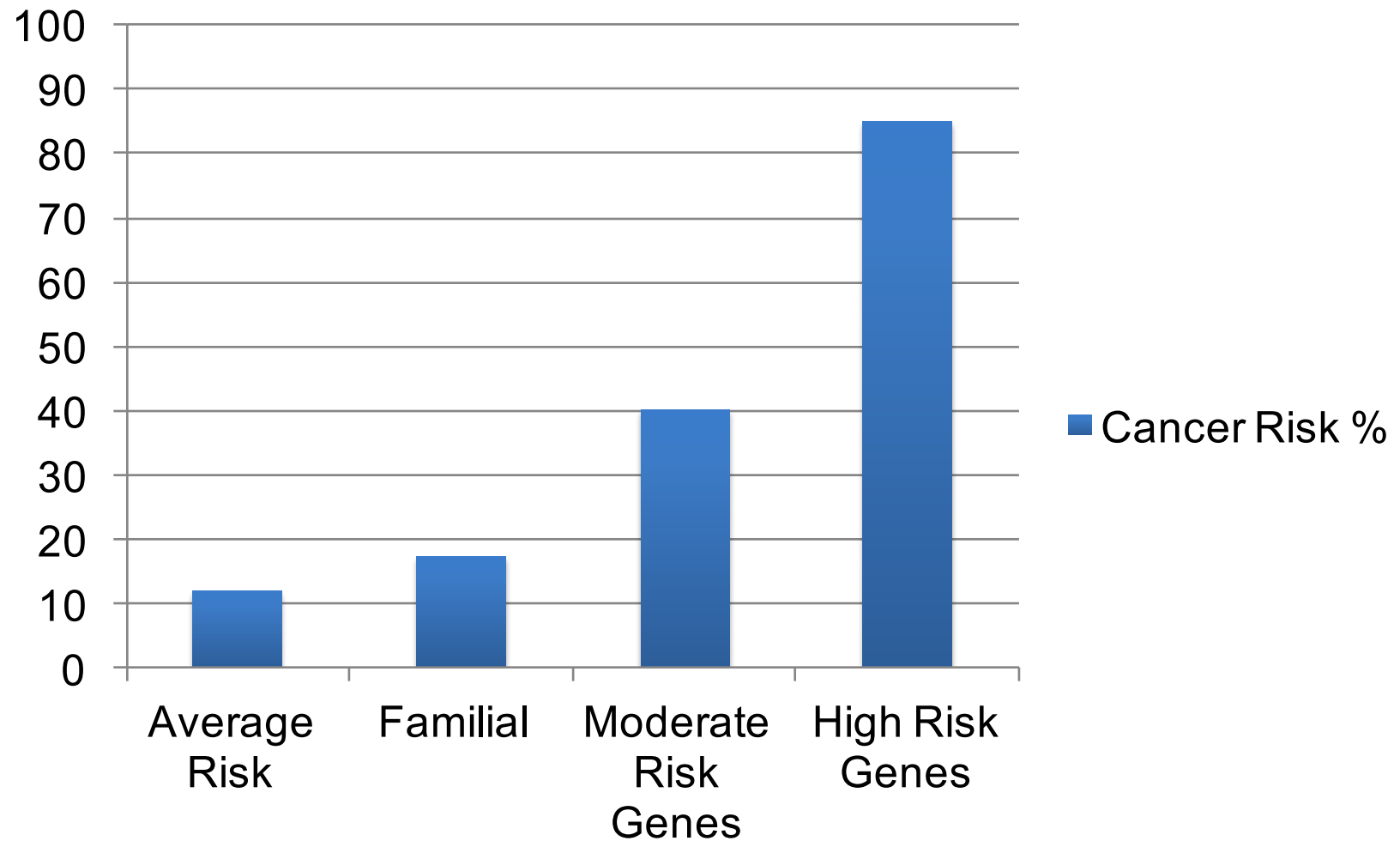
BREAST	COLON	OVARIAN	PANCREATIC	RENAL
<i>BRCA1</i>	<i>MLH1</i>	<i>BRCA1</i>	<i>APC</i>	<i>SDHA-SDHD</i>
<i>BRCA2</i>	<i>MSH2</i>	<i>BRCA2</i>	<i>BRCA1</i>	<i>TSC1</i>
<i>ATM</i>	<i>MSH6</i>	<i>CHEK2</i>	<i>BRCA2</i>	<i>TSC2</i>
<i>CHEK2</i>	<i>PMS2</i>	<i>CDH1</i>	<i>CDKN2A</i>	<i>VHL</i>
<i>PALB2</i>	<i>EPCAM</i>	<i>BRIP1</i>	<i>PALB2</i>	<i>BAP1</i>
<i>CDH1</i>	<i>MUTYH</i>	<i>MLH1</i>	<i>TP53</i>	<i>FLCN</i>
<i>TP53</i>	<i>APC</i>	<i>MSH2</i>	<i>MLH1</i>	<i>MLH1</i>
<i>BRIP1</i>	<i>POLE</i>	<i>MSH6</i>	<i>MSH2</i>	<i>MSH2</i>
<i>BARD1</i>	<i>POLD1</i>	<i>PMS2</i>	<i>MSH6</i>	<i>MSH6</i>
<i>STK11</i>	<i>PTEN</i>	<i>PALB2</i>	<i>PMS2</i>	<i>PMS2</i>
<i>PTEN</i>	<i>SMAD4</i>	<i>PTEN</i>	<i>STK11</i>	<i>TP53</i>



# Causes of Hereditary Breast Cancer



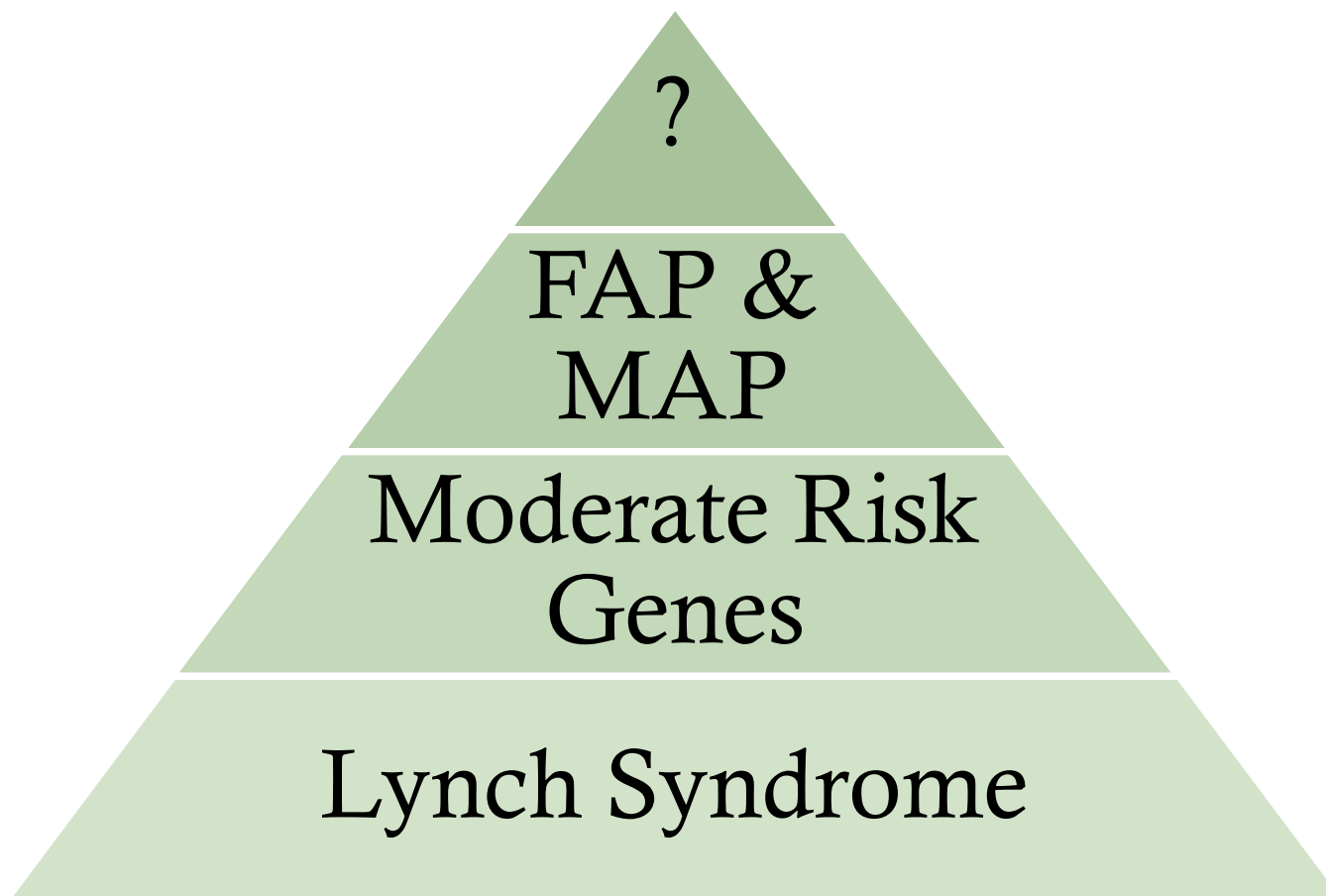
# Lifetime Risk for Breast Cancer



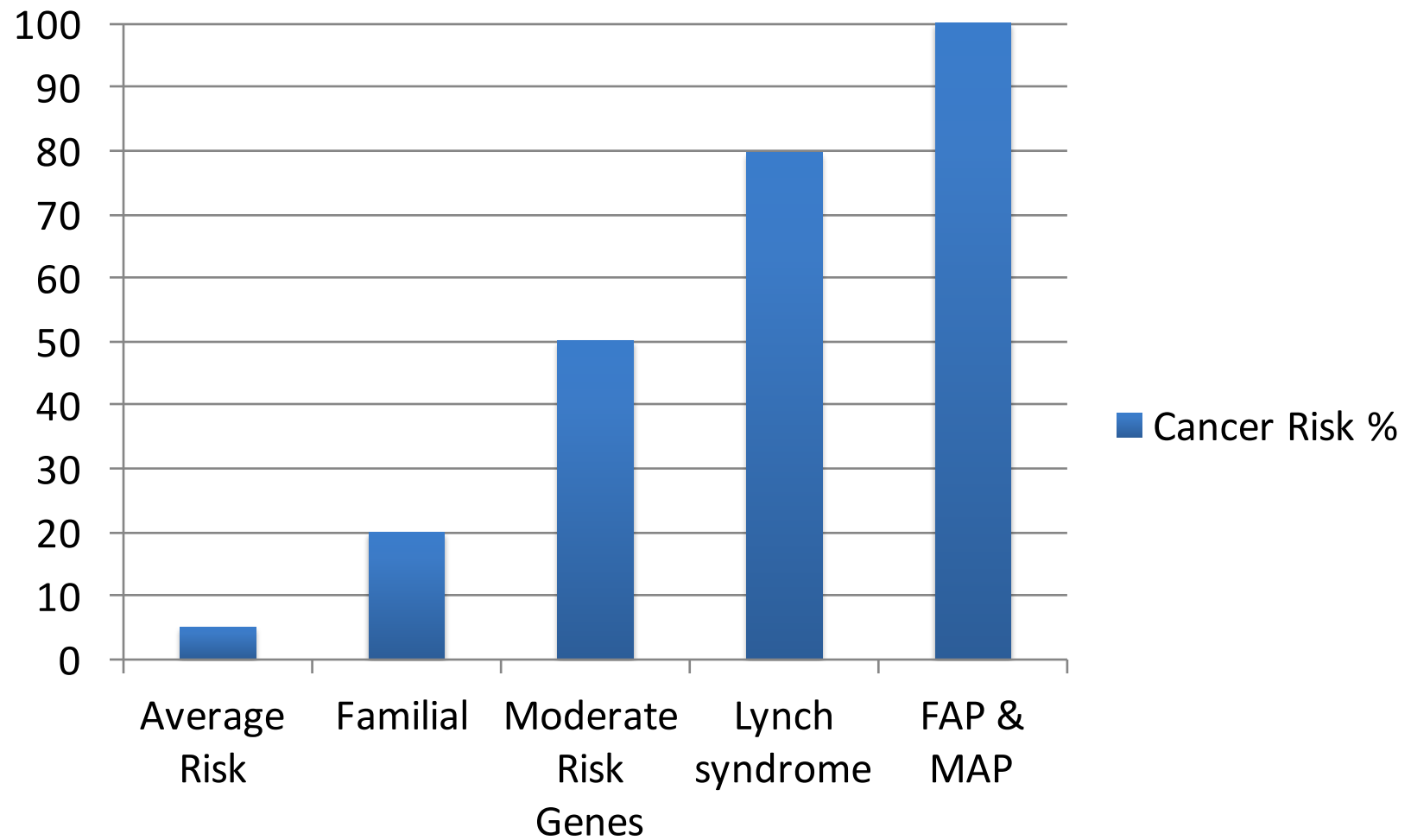
# Associated Cancers of Hereditary Breast and/or Ovarian Cancer Syndrome (HBOC)

<b>Cancer Type</b>	<b>General Population Risk</b>	<b><i>BRCA1</i> or <i>BRCA2</i> Lifetime Risk</b>
Breast	12%	40-80%
Second Breast	3.5-11% per year	27% within 5 years
Ovarian	1-2%	11-40%
Male Breast	0.1%	1-10%
Prostate	16%	Up to 39%
Pancreatic	0.9%	1-7%

# Causes of Hereditary Colon Cancer



# Lifetime Risk for Colon Cancer

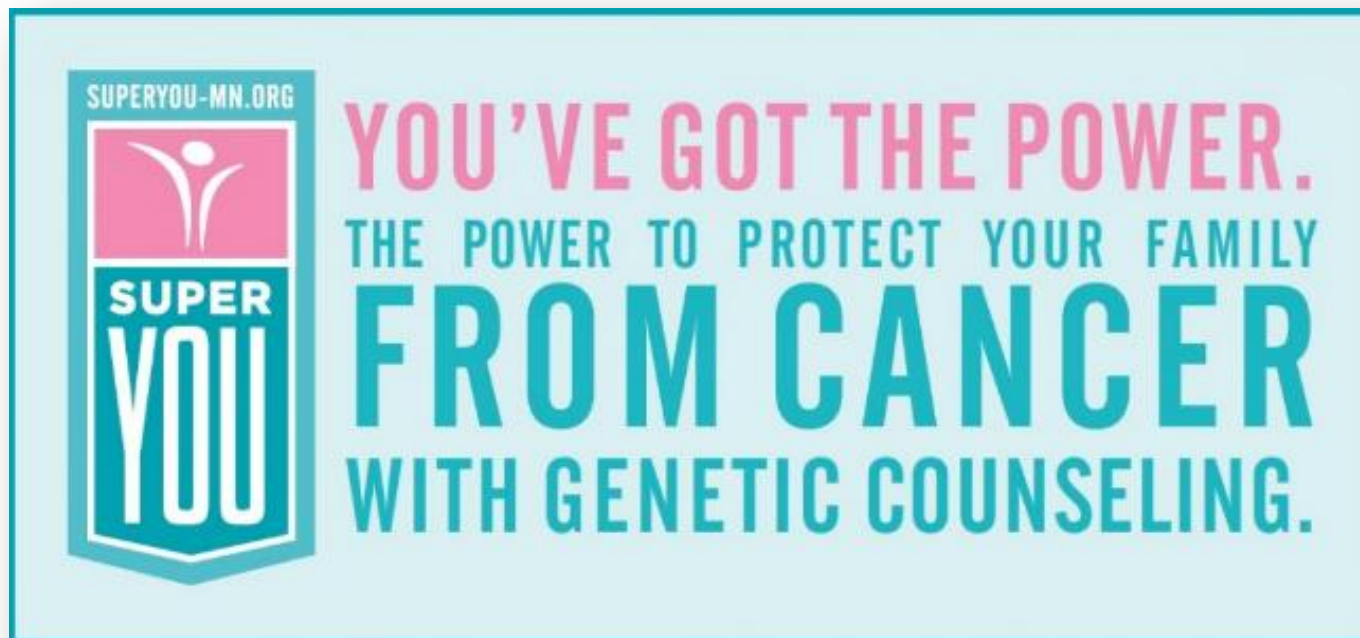


# Associated Cancers of Lynch Syndrome

Cancer Type	General Population Risk	LS-Associated Risk
Colon	4.8-5.5%	52-82%
Endometrial (uterine)	2.7% for women	25-60%
Gastric	<1%	6-13%
Ovarian	1-2% for women	4-12%
Urinary Tract	<1%	1-4%
Small bowel	<1%	3-6%
Brain/CNS	<1%	1-3%
Skin	<1%	1-9%



# Genetic Counseling & Testing



*Genetic counseling is the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease.*



# Oncology Genetic Counseling

- Collect detailed, cancer-focused personal & family history
- Assess risk for certain types of cancer based on history



# Oncology Genetic Counseling



- Determine likelihood of inherited cancer syndrome
- Coordinate genetic testing
- Discuss history and risks with providers to assist in care



# So What About My Kids?



<http://www.icebike.org/the-definitive-guide-to-kids-bike-sizes-dont-buy-the-wrong-bike/>

# What if My Cancer is Inherited?

- Follow management guidelines
  - Increase screening
  - Risk reducing surgeries



*By screening more frequently, the hope is to catch any cancer that forms as soon as possible to provide the best outcome.*



# What About My Kids?

- Each child has a 50% risk of inheriting the mutation
- Kids 18 years & older can be tested for the mutation
  - **Positive Result**
    - Increased risk, follow guidelines
  - **Negative Result**
    - Not at increased risk
    - General population screening
- No testing for kids under 18 yrs



# What About the Rest of My Family?



- Inherited cancer syndromes are typically passed generation to generation
  - Likely one of your parents carries the mutation
  - Your brothers/sisters are at 50% risk
  - Your aunts/uncles are at risk
  - Your cousins are at risk

# How Can My Relatives be Tested?



- Ideally, refer to Cancer Genetic Counselor
  - [www.nsgc.org](http://www.nsgc.org) “Find a Genetic Counselor”
- Testing is only for known mutation in family
  - No need to test for multiple genes!
- Result will be:
  - True **positive**:
    - They have the mutation
    - Increased cancer risk
  - True **negative**:
    - They do not have the mutation
    - Likely general population risk

# What if My Testing is Negative?

- Does not mean that the cancer in family is not inherited!
  - Could be other genes not yet identified
  - Could be other genes not tested
  - Could be in the family but you didn't inherit it
- Risk is based on personal and family history
- You may still qualify for increased screening



# Risk of Cancer Based on Family History

Type of Cancer	General Population Guidelines
Breast Cancer	Annual mammogram beginning at 40-45 years
Colon Cancer	Screening colonoscopy beginning at age 50 years (repeat 10 years)

# Risk of Cancer Based on Family History

Type of Cancer	General Population Guidelines	Increased Risk
Breast Cancer	Annual mammogram beginning at 40-45 years	Risk >20% = Annual mammogram <u>AND</u> annual breast MRI beginning 10 years before earliest diagnosis but not less than 30 years.
Colon Cancer	Screening colonoscopy beginning at age 50 years (repeat 10 years)	One FDR* with colon cancer diagnosed less than 60 years or two FDRs with colon cancer at any age: Colonoscopy beginning at age 40 years (or 10 years before earliest diagnosis) and repeat every 5 years

\*FDR: First Degree Relative



# What if Testing is Inconclusive?

- We do not act on result
  - If we don't know what it means we can't act on it
- Wait for time
  - More individuals need to be identified with same mutation
- Result may/will be updated
  - Most inclusive results turn into results with no clinical significance (aka: negative result)



# What Now?



<https://www.hiscox.co.uk/business-blog/wp-content/uploads/2014/05/Help-and-support-signpost.jpg>

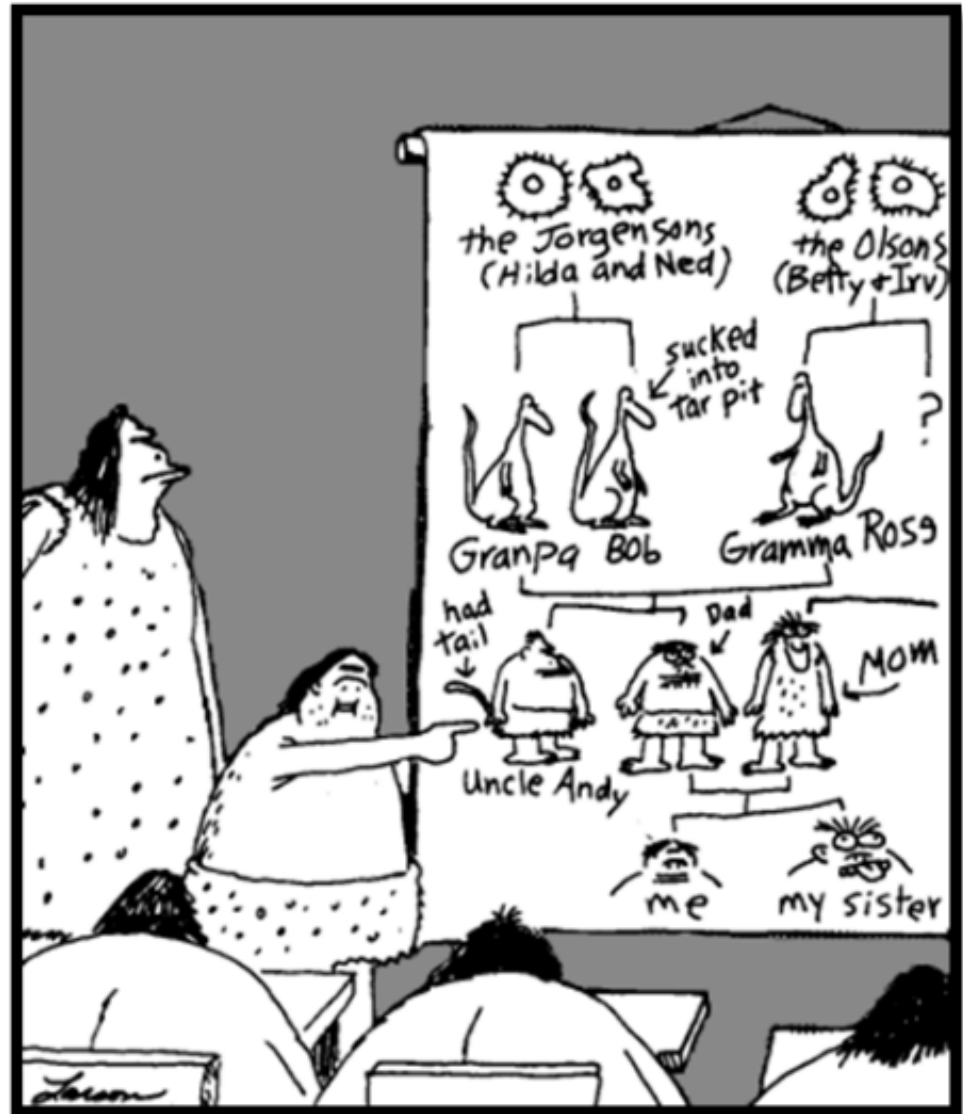
# From Questions to Hope



- **H**ereditary cancer syndrome diagnosis can provide the reason why cancer is in a family
- **O**utlining screening measures and improved understanding of risk can empower you and your relatives to take steps to reduce your risks
- **P**reventing cancers through better understanding of risk-reducing options
- **E**ducating about hereditary cancer syndromes and cancer risk can help you and your family “defy the hand you’re dealt”

# Thank You!

Dana Knutzen, MS, LCGC  
Licensed & Certified Genetic  
Counselor



“Dirk Brings His Family Tree to Class” (Gary Larson)