UCSF Helen Diller Family Comprehensive Cancer Center

# WHO IS AT Risk for Breast Cancer?
## "*What to do with that risk*"

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# Take Home Points

- **Who is at risk for breast cancer?**

- **Genetic Testing.**

- **Tools for Screening and Prevention.**

# Breast Cancer Statistics

- About 1 in 8 U.S. women (about 12%) will develop invasive breast cancer.

- In 2022, an estimated 281,550 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S.

- 49,290 new cases of non-invasive (in situ) breast cancer.

- About 2,650 new cases of invasive breast cancer are expected to be diagnosed in men in 2021. A man's lifetime risk of breast cancer is about 1 in 833.

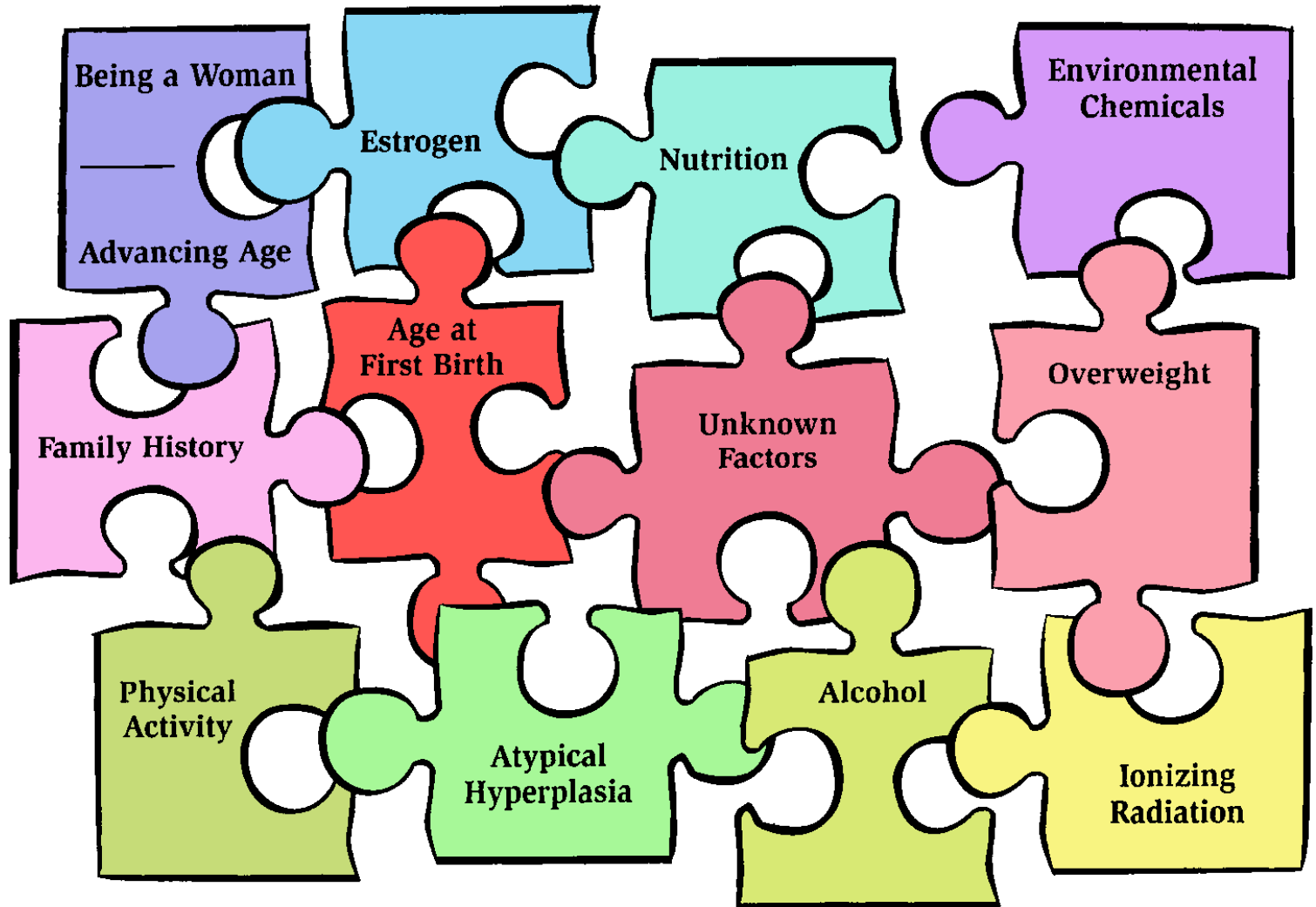- About 43,600 women in the U.S. are expected to die in 2021 from breast cancer.

Breastcancer.org

# Breast Cancer Risk

Who is at Risk?

# OUR FRIENDS

# OUR FAMILY

# The Puzzle of Breast Cancer

Being a Woman ___ Advancing Age

Estrogen

Nutrition

Environmental Chemicals

Family History

Age at First Birth

Unknown Factors

Overweight

Physical Activity

Atypical Hyperplasia

Alcohol

Ionizing Radiation

Cornell University Program on Breast Cancer and Environmental Risk Factors • www.cfe.cornell.edu/bcerf/

What to watch out for:

- Breast lump
- Nipple discharge
- Nipple inversion
- Skin dimpling
- Change in size of breast

# Breast Cancer Risk

- **Genetic Risk**

- **Non Genetic Risk, combination Genes and environment.**

# **Breast Cancer Risk**

How Much Risk?

Risk Assessment Models to help determine your risk.

Your primary doctor or NP can help you with this assessment. Self-Assessment online.

**Table 1.** Known risk factors and their incorporation into existing risk models*

| Variable | Relative risk at extremes† | Gail | Claus | BRCAPRO | IBIS | BOADICEA | Jonker |
|---|---|---|---|---|---|---|---|
| **Personal information** | | | | | | | |
| Age | 30 | Yes | Yes | Yes | Yes | Yes | Yes |
| Body mass index | 2 | No | No | No | Yes | No | No |
| Alcohol intake | 1.24 | No | No | No | No | No | No |
| **Hormonal and reproductive factors** | | | | | | | |
| Age at menarche | 2 | Yes | No | No | Yes | No | No |
| Age at first live birth | 3 | Yes | No | No | Yes | No | No |
| Age at menopause | 4 | No | No | No | Yes | No | No |
| Hormone replacement therapy use | 2 | No | No | No | Yes | No | No |
| Oral contraceptive pill use | 1.24 | No | No | No | No | No | No |
| Breast feeding | 0.8 | No | No | No | No | No | No |
| Plasma estrogen level | 5 | No | No | No | No | No | No |
| **Personal history of breast disease** | | | | | | | |
| Breast biopsies | 2 | Yes | No | No | Yes | No | No |
| Atypical ductal hyperplasia | 3 | Yes | No | No | Yes | No | No |
| Lobular carcinoma in situ | 4 | No | No | No | Yes | No | No |
| Breast density | 6 | No | No | No | No | No | No |
| **Family history of breast and/or ovarian cancer** | | | | | | | |
| First-degree relatives with breast cancer | 3 | Yes | Yes | Yes | Yes | Yes | Yes |
| Second-degree relatives with breast cancer | 1.5 | No | Yes | Yes | Yes | Yes | Yes |
| Third-degree relatives with breast cancer | 1.3 | No | No | No | No | Yes | No |
| Age of onset of breast cancer in a relative | 3 | No | Yes | Yes | Yes | Yes | Yes |
| Bilateral breast cancer in a relative | 3 | No | No | Yes | Yes | Yes | Yes |
| Ovarian cancer in a relative | 1.5 | No | No | Yes | Yes | Yes | Yes |
| Male breast cancer | 3–5 | No | No | Yes | No | Yes | Yes |

# Risk Factors for Breast Cancer

- **Family History**

- **Age of Menarche**

- **Age of Menopause**

- **Age of first parity/parity status**

- **Previous diagnosis of breast cancer**

- **ADH/LCIS**

# Risk Factors for Breast Cancer

- **Early radiation exposure**

- **Exogenous Estrogen**

- **Previous Biopsy  (atypia/LCIS)**
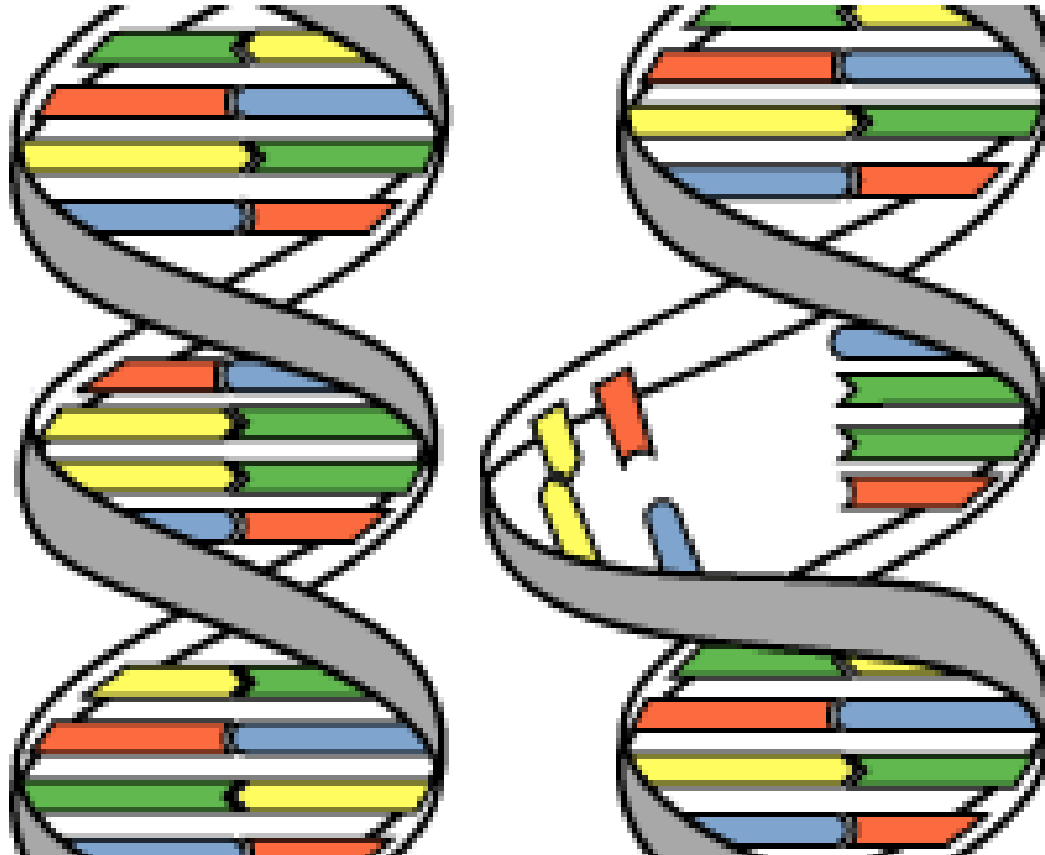
- **Alcohol factor**

# Who Should get tested for BRCA 1 and BRCA 2 Mutations and other mutations?
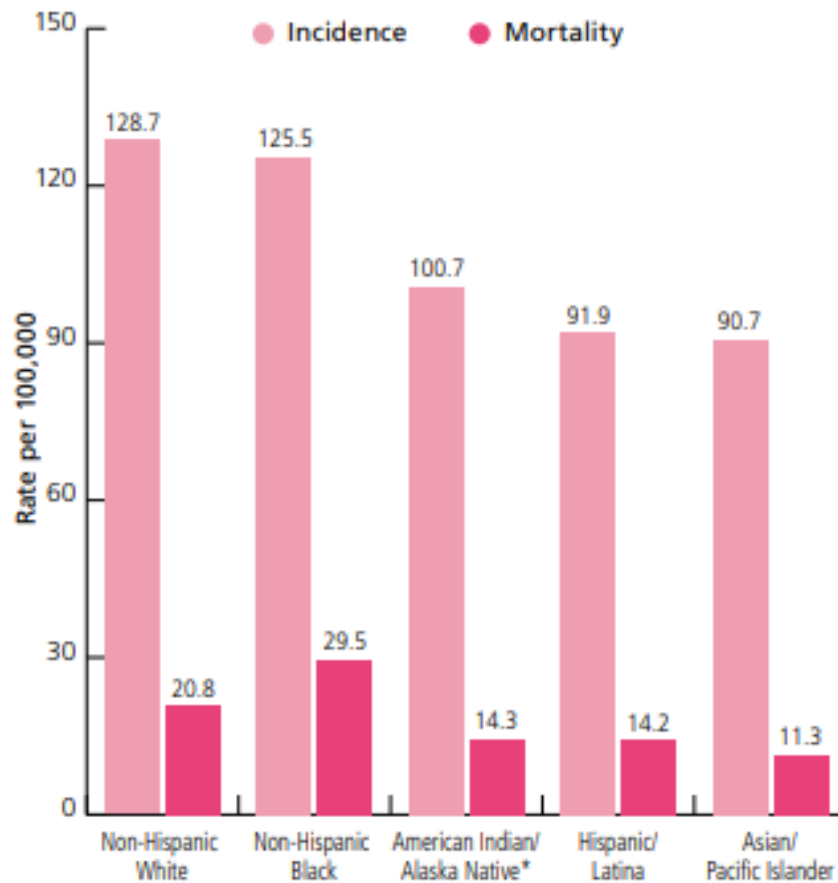
# Breast Cancer Risk-Genetics

**Mutations in the DNA that lead to the development of breast cancer.**

# Breast Cancer Risk-Genetic



BRCA 1 and 2

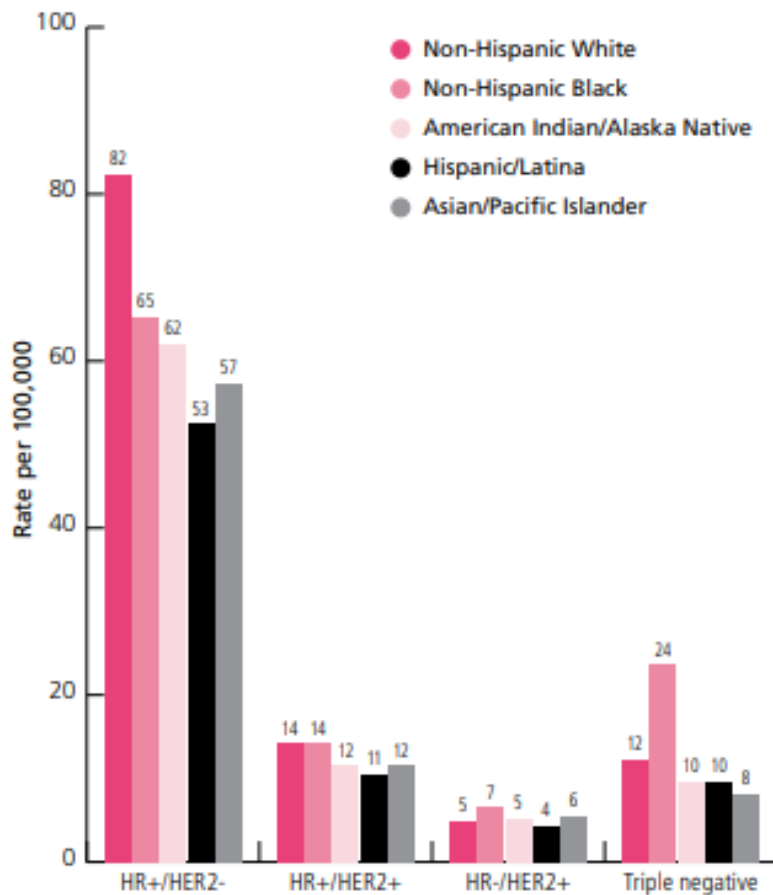Figure 2. Female Breast Cancer Incidence (2010-2014) and Mortality (2011-2015) Rates by Race/Ethnicity, US

➤ Black women have the highest breast cancer mortality rate.

➤ Among women younger than 40, black women have higher rates of breast cancer compared to white women.

Figure 3. Female Breast Cancer Incidence Rates by Subtype and Race/Ethnicity, 2010-2014, US

HR = hormone receptor, HER2 = human epidermal growth factor receptor 2.
Note: Rates are age adjusted to the 2000 US standard population.
Source: NAACCR, 2017.

©2017, American Cancer Society, Inc., Surveillance Research

**New subtypes inform:**

- The amount of risk.
- The timing of risk for recurrence- early vs late.
- The type of therapy that will provide the most benefit.

# Genetic Risk

## BRCA1 mutation rates vary by race and ethnicity, age

Researchers have found that a gene mutation linked to breast cancer is more common in some ethnic or racial groups of breast cancer patients than others. In all groups, a larger percentage of younger breast cancer patients had the mutation than older patients.

| ETHNICITY/RACE | BRCA1 PREVALENCE, ALL AGES | UNDER 35 YEARS IN AGE |
|---|---|---|
| Asian-American | 0.5 % | 2.4 % |
| African-American | 1.3 % | 16.7 % |
| White, non-Hispanic | 2.2 % | 7.2 % |
| Hispanic | 3.5 % | 8.9 % |
| Ashkenazi Jewish | 8.3 % | 66.7 % (*) |

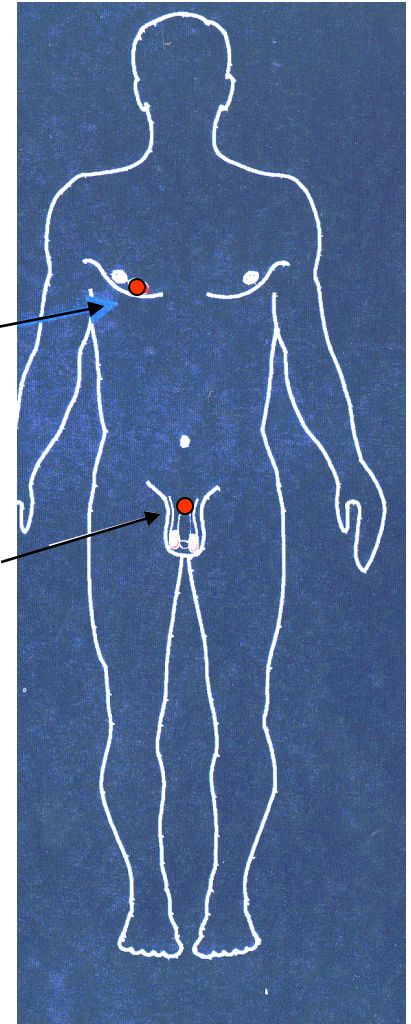*(*) based on three patients tested*

# *BRCA1*-Associated Cancers: Lifetime Risk
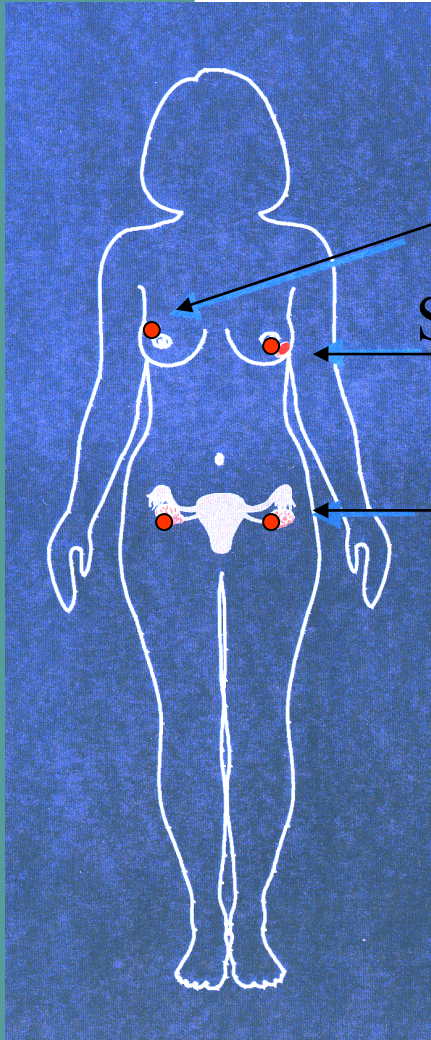
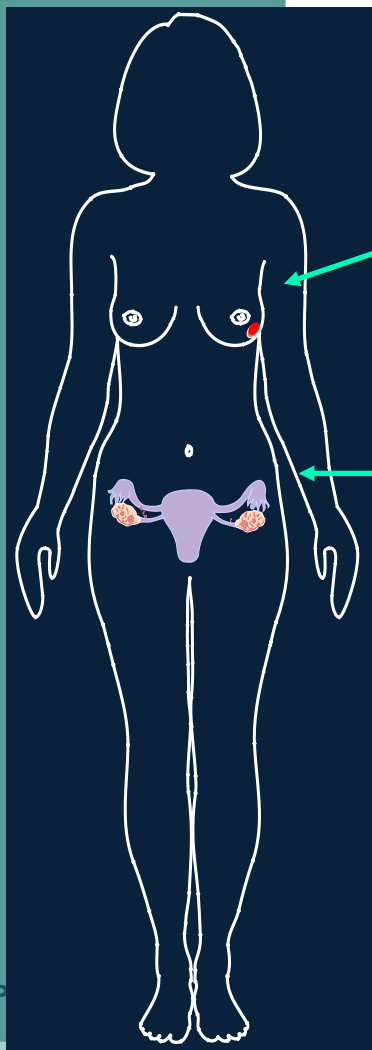Breast Cancer
85%

Second Primary
Breast Cancer
3% per year

Ovarian Cancer
30-54%

Male
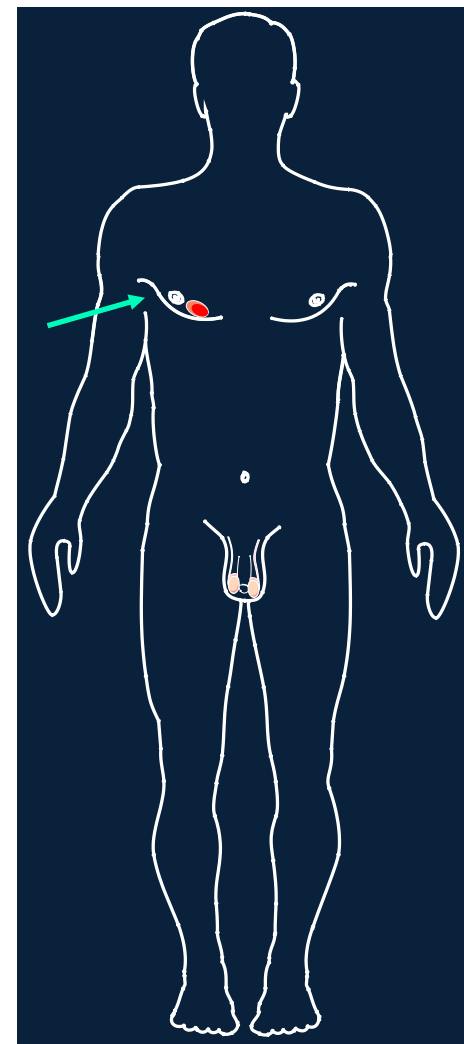Breast
Cancer
?%

Prostate
Cancer
30 to
50%

# *BRCA2*-Associated Cancers: Lifetime Risk

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breast cancer
(56%–85%)

ovarian cancer
(20%–30%)

male breast cancer
(6-8%)

# Breast Cancer Risk

Special Risk for being a mutation carrier for the BRCA 1 and 2 gene and other mutations.

1. Any women diagnosed with breast cancer under the age of 40 years or multifocal, bilateral breast cancer under the age of 60 years.

2. Any women under the age of 60 and triple Negative ER(-), PR(-), HER-2 (-).

3. Any women of Jewish Ancestry (Ashkenazi), Hispanic, Mediterranean, Norwegian diagnosed with breast cancer under the age of 60 years.

4. Breast cancer diagnosis and family history of breast and ovarian cancer including 2nd degree relatives. Maternal and Paternal.

5. Family history with two 1st degree relatives with breast cancer and any one 2nd degree relative with ovarian cancer.

# Breast Cancer Risk

All men with a breast cancer diagnosis should be tested for the BRCA 1 and 2 gene.

Special attention for TP53 mutation in melanoma families and colon carcinoma.

Others to screen are Cowden's and Li Fraumeni families. Li-Fraumeni strong family history of Leukemia, brain cancer, sarcoma, skin cancers.

Cowden's Disease (multiple hamatomas) multiple hamatomas on nose by age 20 and in nasal and oral mucosa. Lifetime risk for breast cancer is 81%. Other associated cancers are thyroid, renal, pancreatic cancer. Benign disorders multi-nodular goiters and fibroadenomatosis.

# Breast Cancer Risk

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**Oncology Genetic Test Report**
BRCA1/2 Sequencing and Del/Dup Analysis

*Sample Report*
Gene Dx
DNA DIAGNOSTIC EXPERTS

| PHYSICIAN | PATIENT | SAMPLE |
|---|---|---|
| | **LAST, FIRST** <br> DOB:        Age:    Sex: <br> Ethnicity: <br> Patient ID:  Ramos, Maria | Specimen ID: <br> Date of Report: <br> Date Collected: <br> Date Received: <br> Source:  EDTA Whole Blood |

### OncoGeneDx: BRCA1/2 Sequencing and Del/Dup Analysis

**Genes Evaluated:** BRCA1, BRCA2

**Test Indication**
Personal history of breast cancer. Family history of breast cancer.

### Results Summary: POSITIVE

| Gene | Results | Classification |
|---|---|---|
| BRCA1 | c.68_69delAG(p.Glu23ValfsX17) | PATHOGENIC |

This individual is heterozygous for a mutation in the BRCA1 gene, consistent with Hereditary Breast and Ovarian Cancer syndrome.

No additional reportable variants were detected by sequencing or deletion/duplication analysis in the BRCA1 or BRCA2 genes.

**Lifetime Cancer Risks**

- Lifetime cancer risks due to a BRCA1 mutation include:  approximately 57-84% risk for breast cancer in women and 24- 54% risk for ovarian cancer.  See interpretation. **

** Only the most commonly associated cancer risks are listed

| Mutation | Absolute breast cancer risk - lifetime |
|----------|----------------------------------------|
| BRCA1 | Up to 65% |
| BRCA2 | Up to 50% |
| TP53 | Up to 80% (Li-Fraumeni syndrome) |
| CDH1 | 40-50% |
| STK11 | 30-55% |
| PTEN | Up to 85% (Cowden syndrome) |
| CHEK2 | 37% |
| PALB2 | 30-35% |
| ATM | 33% |

High penetrance

Moderate penetrance

Antoniou Am J Hum Genet 2003
Valencia JAMA Surgery 2017
http://www.ncbi.nlm.nih.gov/books/NBK1236

# Seek Genetic Counseling and risk prevention program
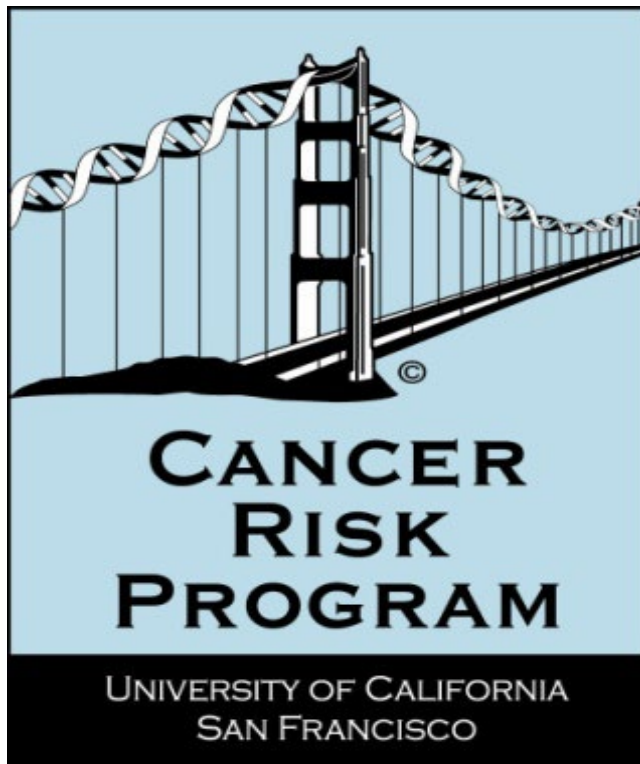
# What to do if you are Mutation Positive?

- Consult with a breast surgeon.

- Consult with a genetic counselor.

- Consult with a Gynecologist.

# Breast Cancer Risk

Surveillance Tools

◆ Recommend clinical breast examination every 6 months.

◆ Annual Mammogram and Bilateral Breast MRI.

◆ If indicated consultation with a genetic counselor.

◆ Chemoprevention with Tamoxifen or Raloxifene.

◆ Discuss risk reducing prophylactic surgery, mastectomy or BSO.

# TOOLS FOR PREVENTION

- **Know you maybe at increase risk for breast cancer due to your family history or history of atypia/LCIS on a breast biopsy.**

- **Screening mammogram or if appropriate breast MRI.**

- **Annual breast examination by an experience provider.**

- **Early Genetic Testing.**

# TOOLS FOR PREVENTION

- **Maintain healthy weight.**

- **Exercise regularly.**

- **Mini dose Aspirin, 81 mg daily.**

- **Reduce stress.**

# TOOLS FOR PREVENTION

**Eat fresh fruit and vegetables, Kale, spinach, blueberries, apple, pears, tomatoes.**

**October is Breast Cancer awareness month!**

## Thank you.

**Remember to get your mammogram and take a friend**