Evaluation of Breast Pathology

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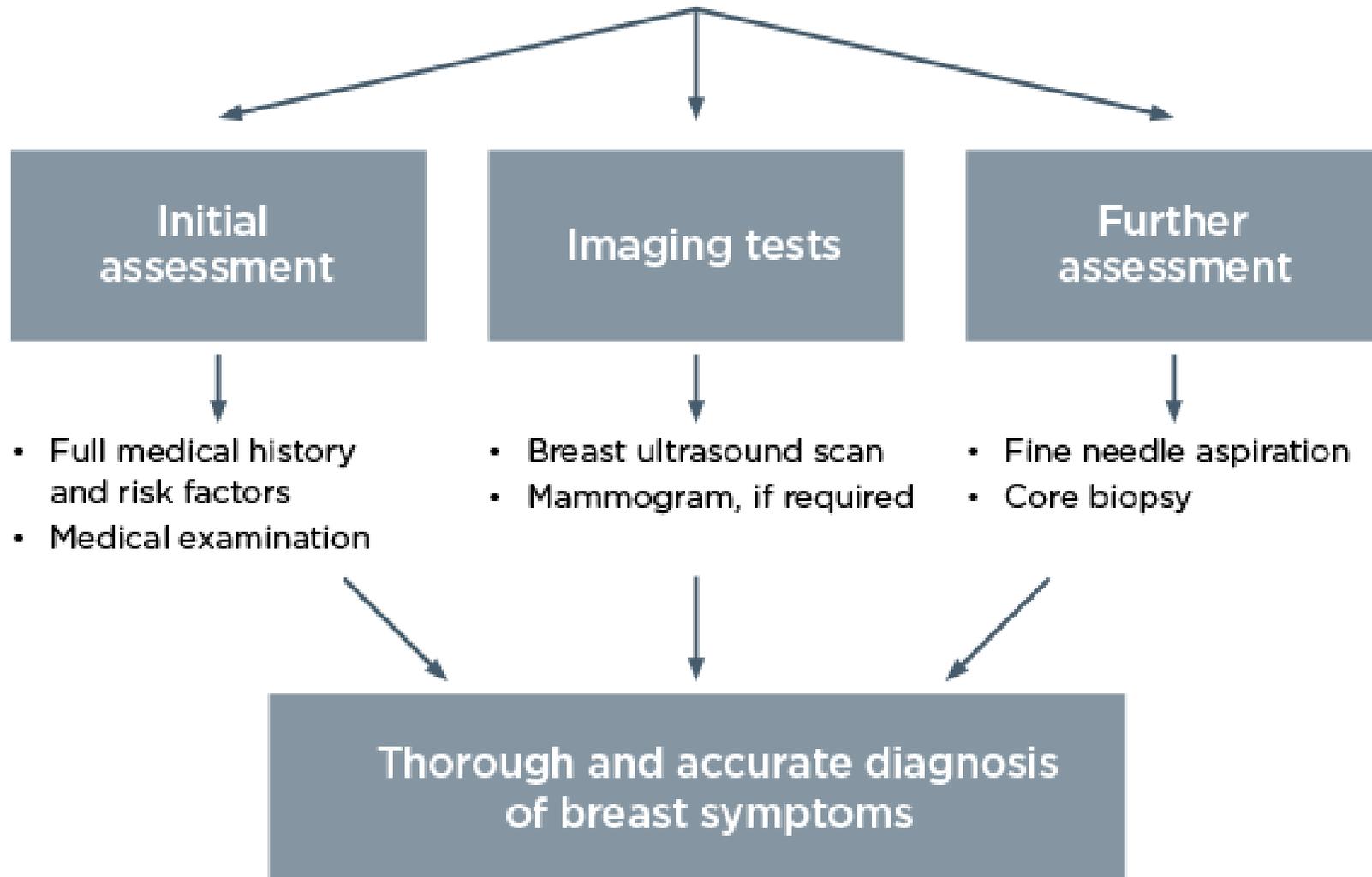ASSISTANT PROFESSOR OF SURGERY – HASHEMITE UNIVERSITY

Breast Pathology

❑A wide rage of disorders can affect breast at any age

❑Breast Pathology
  ❑Congenital Vs. Acquired
  ❑Inflammatory Vs. non-Inflammatory
  ❑Benign Vs. Malignant

Breast Pathology

(Medical History)

A) Patient Profile

- Name

- Age

- Occupation

- Living place

- Marital status

B) Chief complain and Duration

❑**Asymptomatic**

OR

❑**Symptomatic**
  ❑Pain (mastalgia): cyclic or non-cyclic; Acute vs. Chronic
  ❑Mass
  ❑Nipple discharge
  ❑Breast size changes
  ❑Breast skin changes
  ❑Nipple Changes
  ❑Axillary swelling

Duration?

C) Chief complain analysis:

Pain:

- Onset

- Duration

- Site and radiation or referral

- Character

- Relation to the cycle

- Severity

- Aggravating and relieving factors

- Predisposing factors

- Progression

Mass:

❑When was first discovered

❑How it was discovered

❑How did it change since being noticed

❑Did she experienced similar conditions before

❑Did she feel other masses or nodularity

❑History of trauma to the breast or chest wall

❑Skin changes at the site of the mass

Nipple discharge:

- Unilateral or bilateral
- Single duct or multiple ducts
- Painless or painful
- Color
- Spontaneous or induced
- Associated nipple changes

Nipple/areola changes:

❑Change in nipple position or protrusion

❑Change in nipple appearance (i.e thickening; ulceration; scaling)

❑Change in areola (pigmentation; ulceration; scaling; thickening)

Axillary Swelling:

❑Painful vs. Painless

❑Cyclic vs. non-cyclic changes

❑Skin changes

❑History of upper limb injury; vaccination; canulation; lactation

D) Obstetric and Gynecologic History

- Menarche
- Regularity of the cycle
- Menopause
- Marital status
- Parity and age of 1st full time pregnancy
- Last pregnancy
- History of lactation
- Hormonal treatment

E) Comprehensive medical and surgical history

F) Family history

❑Similar acute illness in one or more of the family members

❑Family history of malignant breast pathologies; degree of relativeness and age of diagnosis

❑Family history of ovarian cancer; degree of relativeness and age of diagnosis

❑Other malignancies

❑Known genetic disorders or mutations

G) Social history

❑Smoking

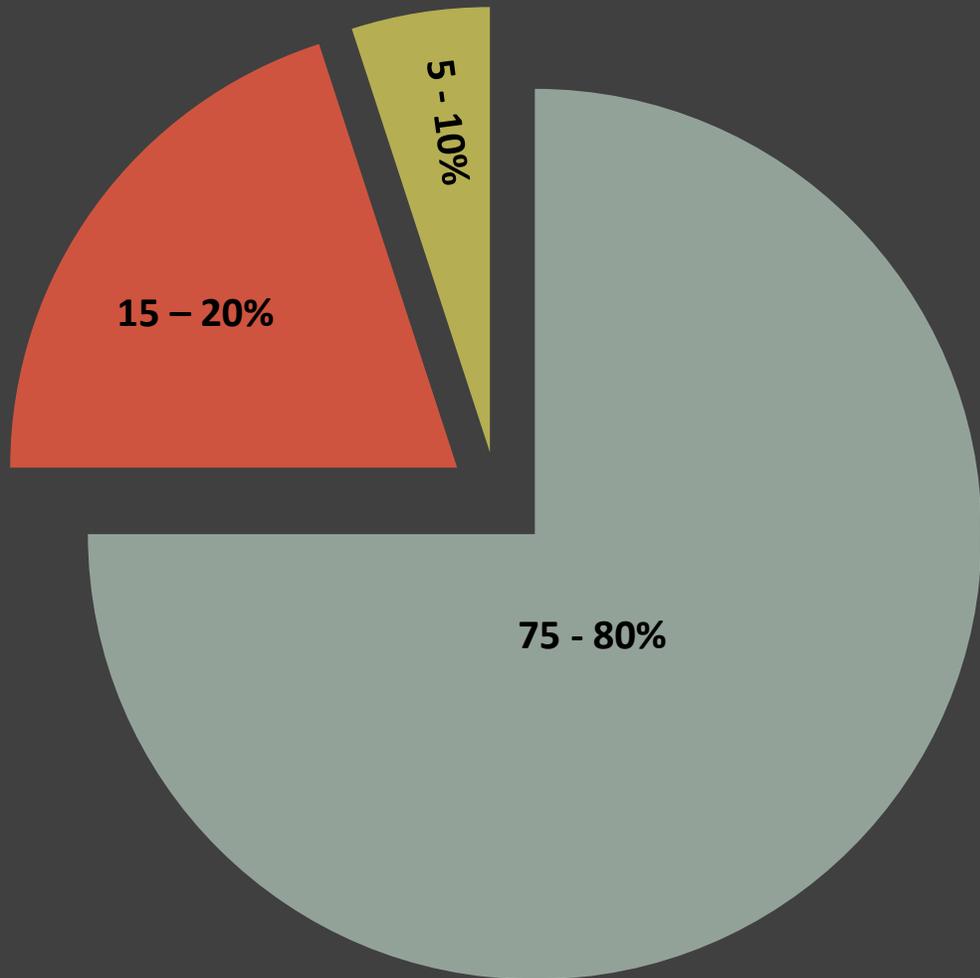❑Alcohol

❑Living circumstances and pets

Breast Cancer

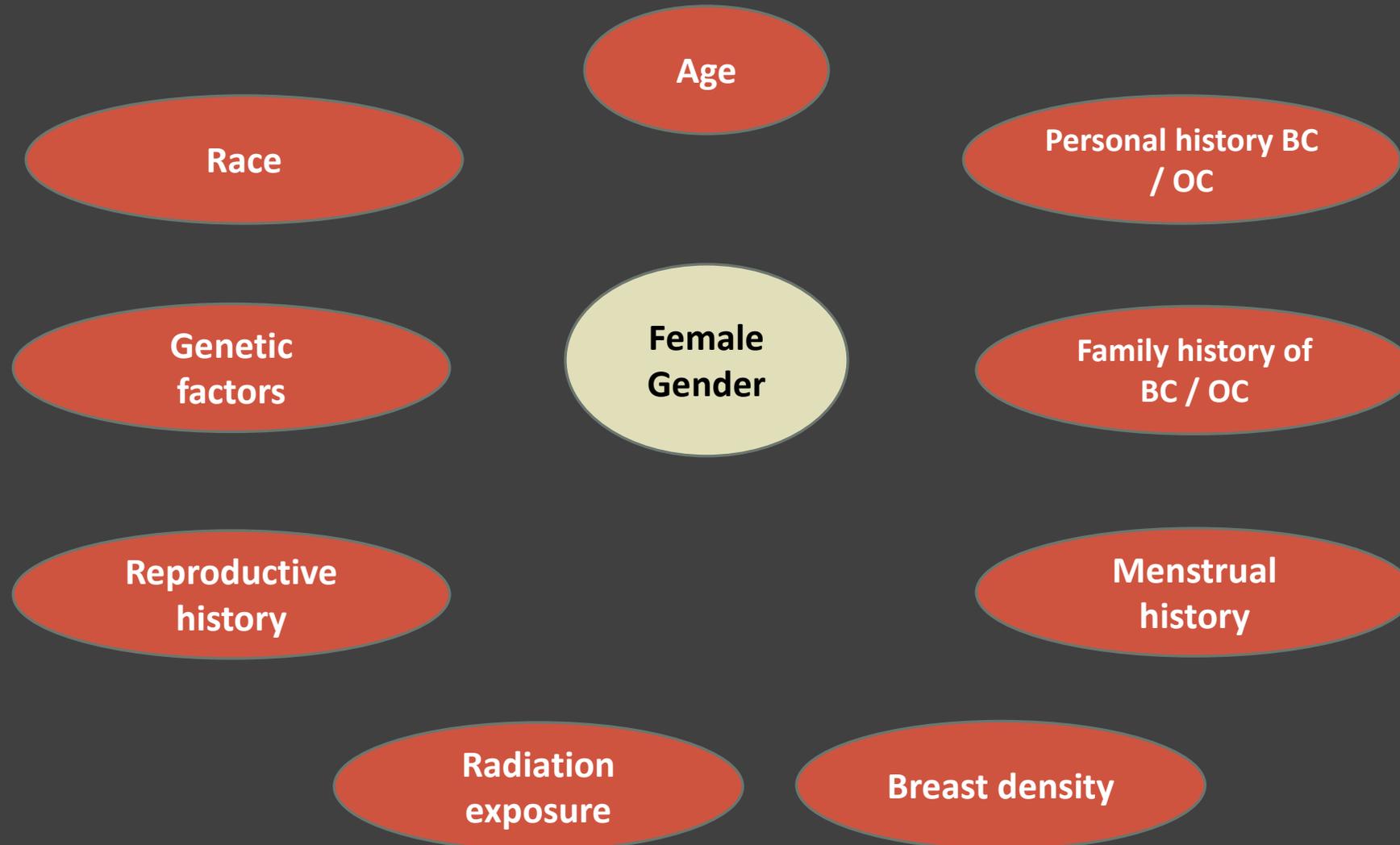# Risk Factors

Non modifiable risk factors

Age

Race

Personal history BC / OC

Genetic factors

Female Gender

Family history of BC / OC

Reproductive history

Menstrual history

Radiation exposure

Breast density

Modifiable risk factors

Obesity

Exercise

Nulliparity

HRT

Female Gender

Breast feeding

OCP ?

Alcohol consumption

Smoking ?

DR. MAHMOUD AL-BALAS; CONSULTANT BREAST AND GENERAL SURGERY
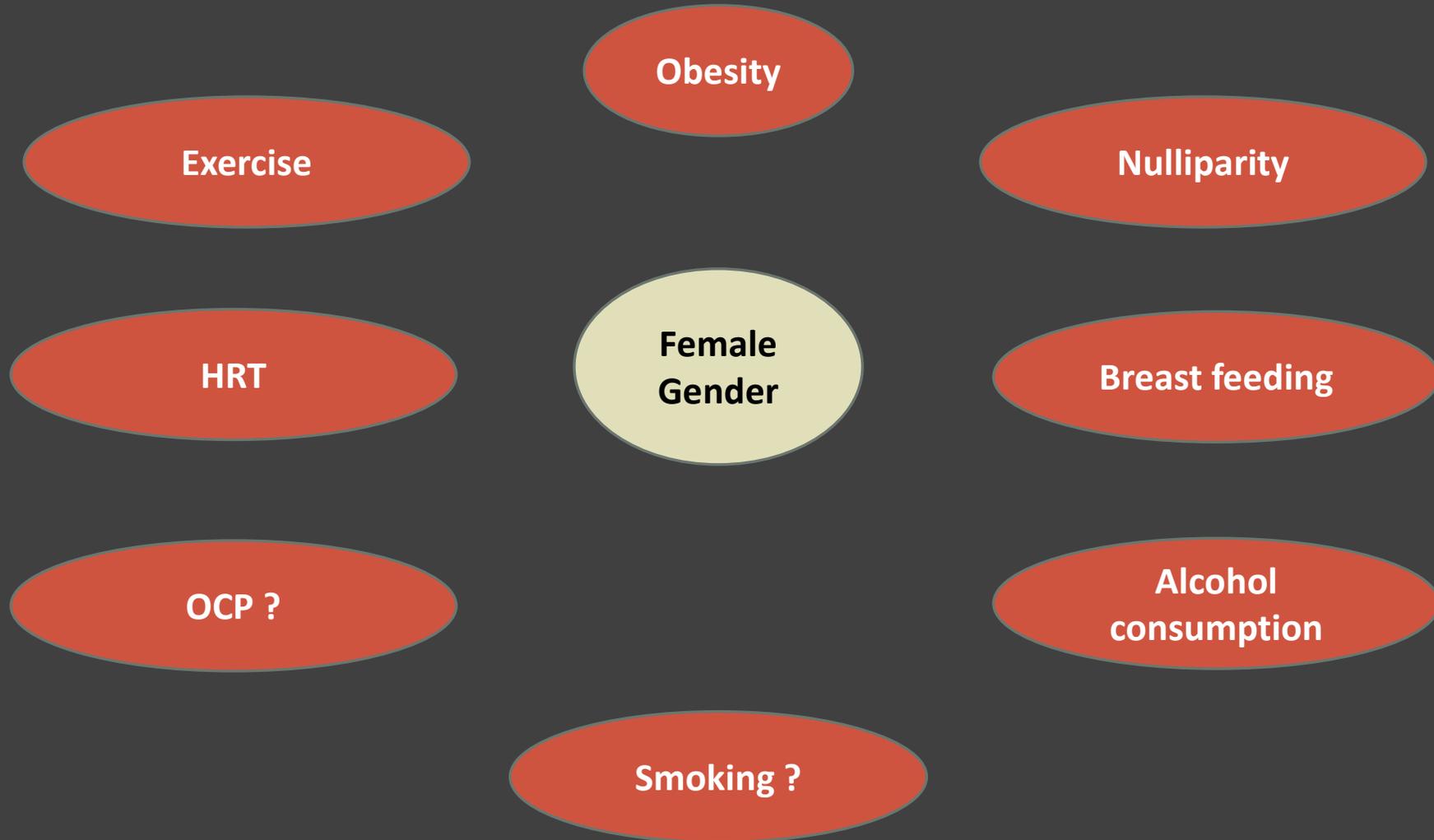
Gender

❑Breast cancer is the most common cancer among US women, accounting for 29% of newly diagnosed cancers.

❑Life time risk for BC is 1:8 (12.5%)

❑Men are generally at low risk for developing breast cancer

Age

❑Breast cancer incidence and death rates generally increase with age.

❑During 2008-2012, the median age at the time of breast cancer diagnosis was 61 years
   ❑50% of women who developed BC were 61 years of age or younger at the time of diagnosis
   ❑The median age of diagnosis is younger for black women than white women

Table 5. Age-specific Probabilities of Developing Invasive Female Breast Cancer*

| If current age is …	The probability of developing breast cancer in the next 10 years is:[†]	or 1 in:
20	0.1%	1,674
30	0.4%	225
40	1.4%	69
50	2.3%	44
60	3.5%	29
70	3.9%	26
Lifetime risk	12.3%	8

*Among those free of cancer at beginning of age interval. Based on cases diagnosed 2010-2012. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.

Source: 18 SEER Registries, National Cancer Institute. Probabilities derived using NCI DevCan Software, Version 6.7.3.

American Cancer Society, Inc., Surveillance Research, 2015

The decrease in incidence rates that occurs in women 80 years of age and older may reflect lower rates of screening, the detection of cancers by mammography before 80 years of age, and/or incomplete detection

Figure 1. Age-specific Female Breast Cancer Incidence and Mortality Rates, US, 2008-2012
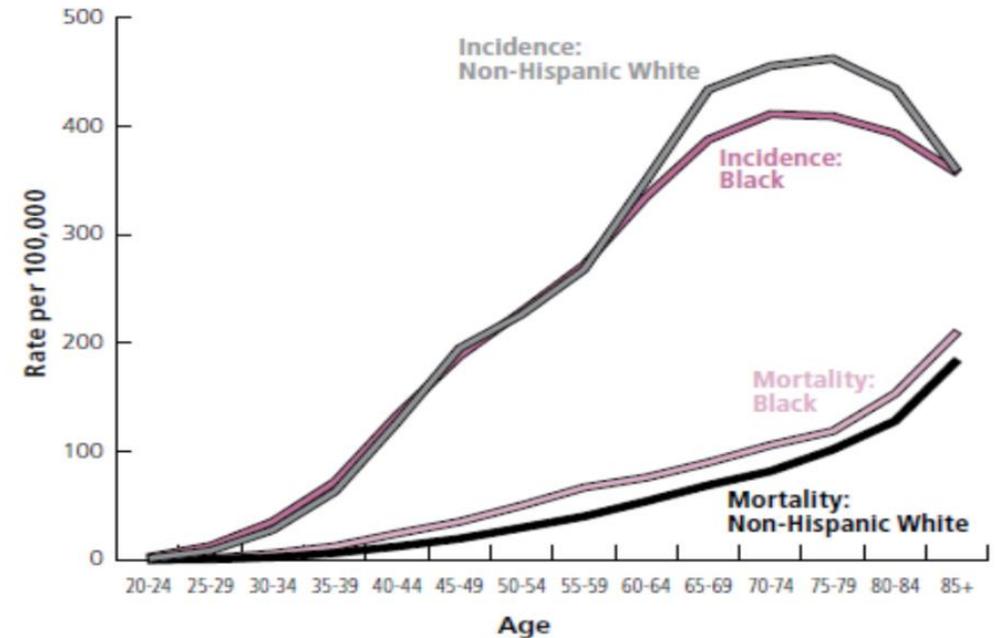
Sources: Incidence: North American Association of Central Cancer Registries (NAACCR), 2015. Mortality: US mortality data, National Center for Health Statistics, Centers for Disease Control and Prevention.

American Cancer Society, Inc., Surveillance Research, 2015

Race / Ethnicity

☐ Between the ages of 60 and 84, breast cancer incidence rates are markedly higher in white women than black women.

☐ Black women have a higher incidence rate before age 45.

☐ Black women with BC have higher mortality rates in all age groups.

Figure 5a. Trends in Female Breast Cancer Incidence Rates* by Race and Ethnicity, US, 1975-2012
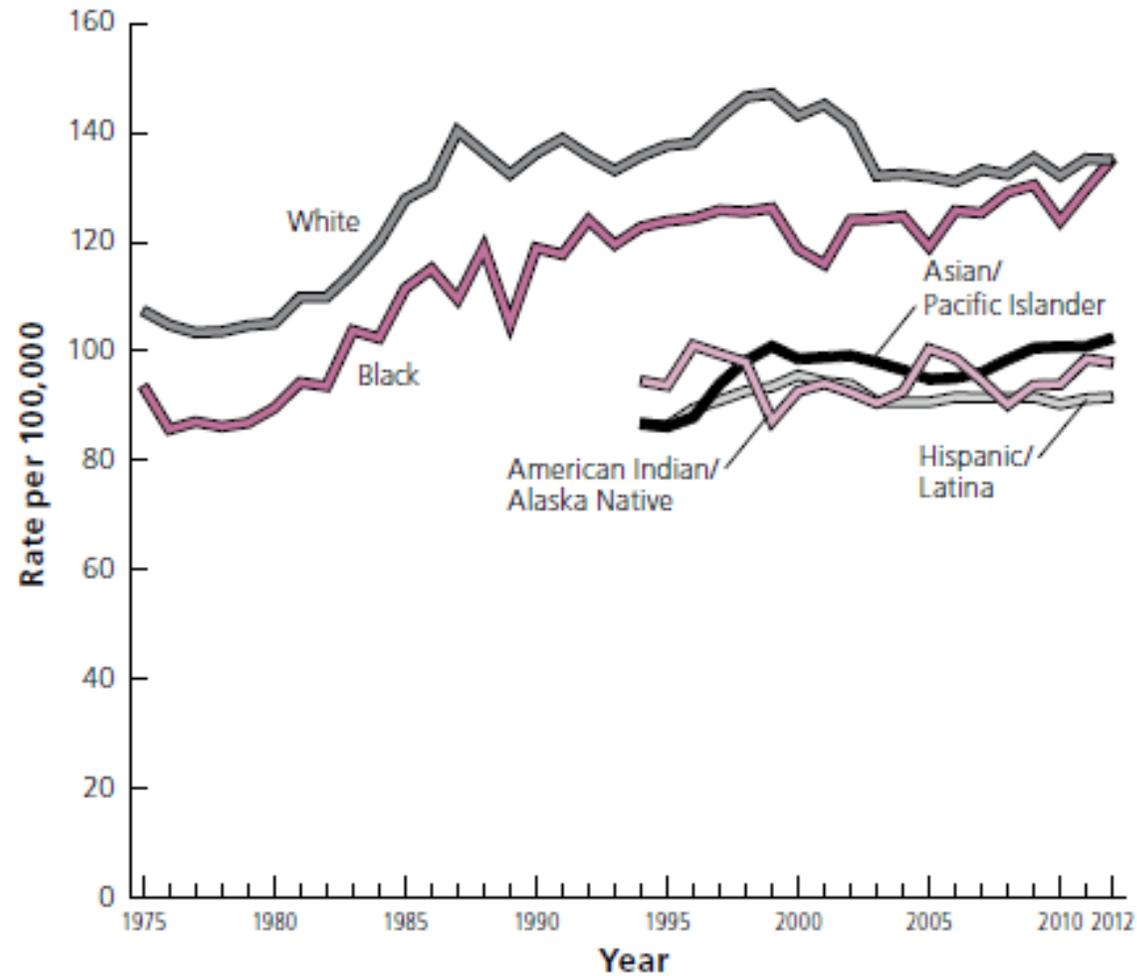
*Rates are age adjusted to the 2000 US standard population and adjusted for reporting delay.

Figure 5b. Trends in Female Breast Cancer Death Rates* by Race and Ethnicity, US, 1975-2012
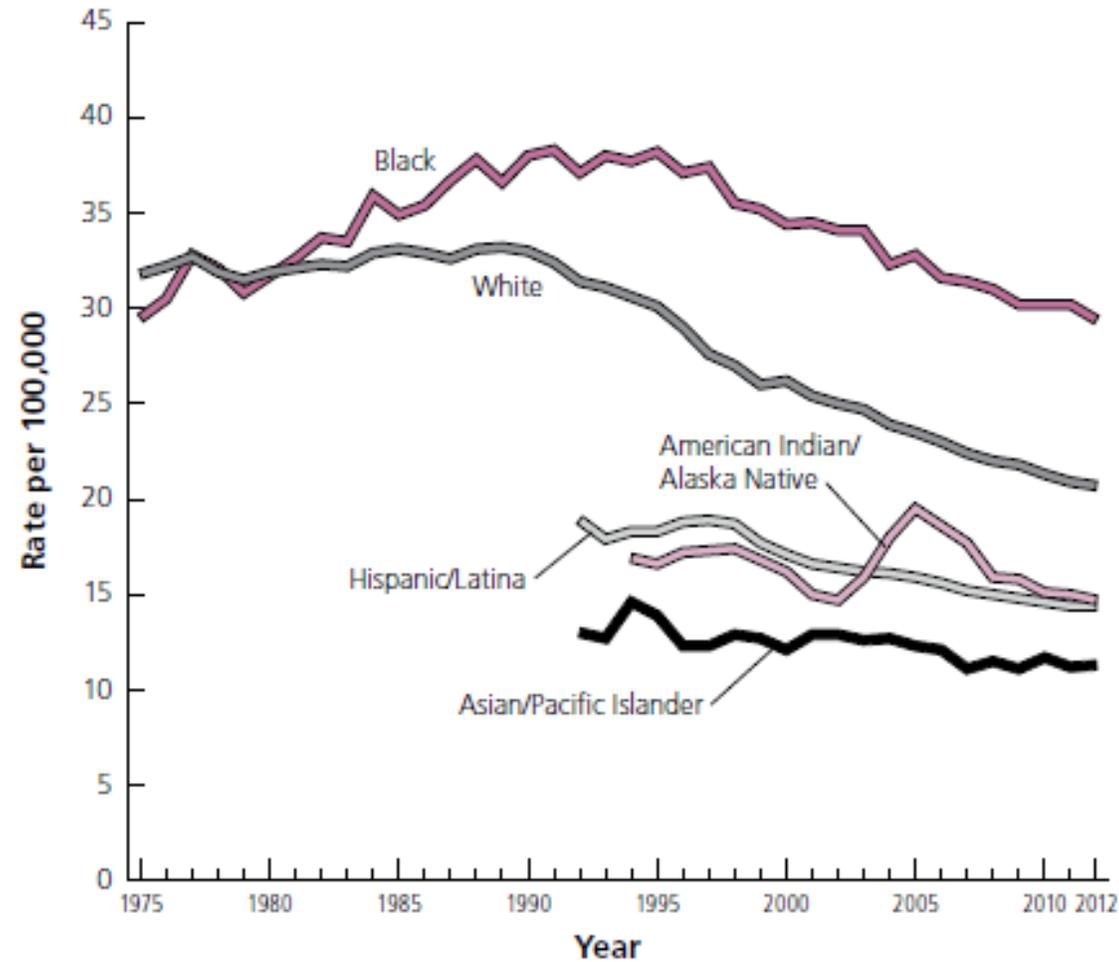
*Rates are age adjusted to the 2000 US standard population.

Family history

❑ Women / men with a family history of breast cancer, especially in a first-degree relative (mother, sister, daughter, father, brother, or son) are at increased risk of developing breast cancer

❑ Risk is higher with more than one affected first-degree relative.

❑ Risk is further increased when the affected relative was diagnosed at a young age.

❑ Compared to women without a family history, risk of breast cancer
  ❑ One 1st degree member → 2 times higher
  ❑ 2 1st degree relative → 3 times higher
  ❑ 3 or more 1st degree relatives → 4 times higher

The majority of women with one or more affected first-degree relatives will never develop breast cancer and that most women who develop breast cancer do not have a family history of the disease.

Genetic factors

BRCA 1 / 2 mutations

The most well-studied breast cancer susceptibility genes
  ◦ **5%-10% of all female breast cancers**
  ◦ **5%-20% of male breast cancer**
  ◦ **15%-20% of all familial breast cancers**

Very rare (much less than 1%) in the general population
  ◦ **Slightly more often in certain ethnic or geographically isolated groups, such as those of Ashkenazi (Eastern European) Jewish descent (about 2%).**

The average risk for *BRCA1* and *BRCA2* mutation carriers is estimated to be between 57%-65% and 45%-55%, respectively

Mutations in *PALB2,* a different gene that works with *BRCA2*, appear to confer risk similar to *BRCA2* mutations.

Risk by age of 70	Breast	Ovarian	Contralateral BC
BRCA 1	55-70%	40%	Up to 60%
BRCA 2	45-70%	15%	Up to 60%

BRCA 2 mutation are associated with increased risk of male breast cancer and prostate cancer

Other cancers → pancreatic cancer – fallopian tube cancers – primary peritoneal sarcoma

Other inherited conditions associated with a smaller increase in breast cancer risk include:

Li-Fraumeni syndrome

Cowden syndromes

Genetic tests

Molecular tests are commercially available to identify some of the *BRCA* mutations, as well as many of the family cancer syndromes

The interpretation of these tests and treatment decisions is complex.

It is not yet possible to predict if or when women who carry a particular genetic abnormality will develop breast cancer.

Tests are not available for all of the genetic variants that affect breast cancer risk

Personal history of BC

❑Women with a history of breast cancer are about 1.5 times more likely to develop a new breast cancer.

❑Women diagnosed with early onset breast cancer (age <40) have almost a 4.5-fold increased risk of subsequent breast cancer.

❑Genetic predisposition, such as mutations in *BRCA1* and *BRCA2* genes, contribute to some of the excess risk of subsequent breast cancers, particularly among women diagnosed at a young age

Proliferative ductal lesions

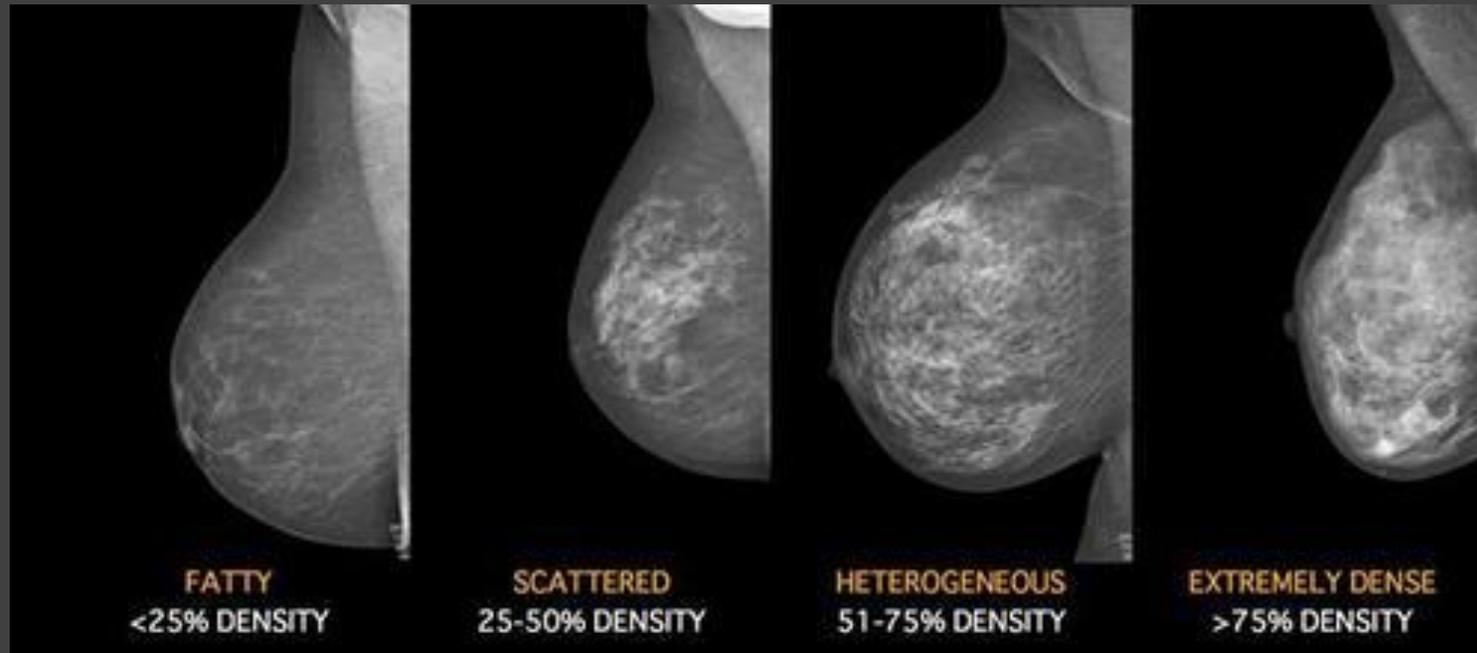| A correlation between ductal proliferative lesions and risk of breast cancer	
UDH	1.5-2 folds
ADH	4-5 folds
DCIS	9-10 folds

Lobular neoplasia

	Breast Cancer RR
ALH	4-5 folds
LCIS	8-9 folds

Note: LIN has been linked to increased risk for subsequent carcinoma in both breast

Breast Density

FATTY <25% DENSITY   SCATTERED 25-50% DENSITY   HETEROGENEOUS 51-75% DENSITY   EXTREMELY DENSE >75% DENSITY

(1.1 – 2) times higher risk for BC

(2.1 - 4) times higher risk for BC

Dense Breast

Factors affect breast density	
❑ Genetics	
❑ Increase Age ❑ Pregnancy ❑ Menopause ❑ Obesity ❑ Tamoxifen	Decrease in Breast Density
❑ Alcohol ❑ Combined HRT	Increase in Breast Density

Endogenous hormone levels

❑Postmenopausal women with naturally high levels of certain endogenous sex hormones have about **twice** the risk of developing breast cancer compared to women with the lowest levels.

❑It is harder to study the relationship of hormones in premenopausal women because levels vary across the menstrual cycle

  ❑a recent large review found that high levels of circulating estrogens and androgens are also associated with a small increased risk of breast cancer in premenopausal women.

Menstrual cycles

❏ Breast cancer risk increases slightly for each year earlier menstruation begins (by about 5%) and for each year later menopause begins (by about 3%).

❏ Breast cancer risk is about 20% higher among girls that begin menstruating before age 11 compared to those that begin at age 13.

❏ Women who experience menopause at age 55 or older have about a 12% higher risk compared to those who do so between ages 50-54.

❏ The increased risk may be due to longer lifetime exposure to reproductive hormones and has been more strongly linked to ER+ breast cancer than other subtypes.

Bone mineral density

❑High bone mineral density in postmenopausal women has been associated with increased risk for breast cancer in many, but not all, studies.

❑Risk appears to be most strongly related to ER+ disease

❑It is a marker for cumulative estrogen exposure.

❑It may be helpful for identifying women at increased risk for breast cancer

Pregnancy

❑Women with first child before 20 years of age have a 50% reduced lifetime risk of breast cancer compared to women who have not had children

❑A transient increase in breast cancer risk (lasting about 10 years) following a full-term pregnancy, particularly among women who are older at first birth

❑Women who have their first child after 35 years of age remain at higher risk of breast cancer compared to women have not had children

Fertility drugs

❑A review of 23 studies found that use of fertility drugs, including clomiphene, gonadotropins, and gonadotropin-releasing hormones, **was not** associated with breast cancer risk.

❑Recently published results of a long-term follow-up study of women seen at 5 US fertility clinics also found no association with ever use of clomiphene or gonadotropins

❑Risk of invasive breast cancer was increased among women who underwent **more than 12 clomiphene** treatment cycles compared to women who had never used fertility drugs.

❑More research is needed on the relationship between breast cancer risk and the long-term effects of ovulation-stimulating drugs.

Breastfeeding

❑Most studies suggest that breastfeeding for a year or more slightly reduces a woman's overall risk of breast cancer.

  ❑Breastfeeding for a longer duration is associated with greater risk reduction.

  ❑In a review of 47 studies; the risk of breast cancer was reduced by 4% for every 12 months of breastfeeding.

❑The protective effect may be stronger for or even limited to triple negative cancers.

Hormonal birth control

❑Studies suggest that recent use of OCP (combined E & P pill) is associated with a small increase in BC risk, particularly among women who begin use before 20 years of age or before first pregnancy.

❑Risk appears to diminish when women stop taking the pill, and after about 10 years, it is similar to those who have never taken OCPs.

❑Depo-Provera and Mirena have only been in use since the 1990s, thus more studies with additional years of follow-up data are needed to confirm if use of these drugs is associated with breast cancer risk

HRT

❑Combined estrogen and progestin increases the risk of developing breast cancer, with higher risk associated with longer use.

❑Risk is also greater for women who start hormone therapy soon after the onset of menopause compared to those who begin use later.

❑The increased risk appears to diminish within 5 years of discontinuation of hormone use.

Estrogen-only therapy

❑The effects of on breast cancer risk is less clear

❑The US Preventive Services Task Force has concluded that the use of estrogen alone is associated with reduced risk of breast cancer
   ❑(i.e. women who used estrogen-only therapy for an average of 6 years had a 23% lower risk of developing breast cancer)

❑Some observational studies have found a slight increase in risk among estrogen therapy users
   ❑Lean women
   ❑Women begin therapy soon after menopause.

Tobacco

❑Limited but accumulating research indicates that smoking may slightly **increase** breast cancer risk
  ❑Long-term, heavy smoking
  ❑Women who start smoking before their first pregnancy.

❑A recent review by American Cancer Society researchers found that women who initiated smoking before the birth of their first child had a 21% higher risk of breast cancer than did women who never smoked.

❑The 2014 US Surgeon General's report on smoking concluded that there is "suggestive but not sufficient" evidence that smoking increases the risk of breast cancer.

❑Some studies suggest secondhand smoke may increase risk, particularly for premenopausal breast cancer. The association is unclear

Obesity

premenopausal

Obesity decreases risk of BC

← **Obesity** →

postmenopausal

Obesity increases risk of BC

❑*Risk is about 1.5 times higher in overweight women and about 2 times higher in obese women than in lean postmenopausal women*

❑*A large meta-analysis recently concluded that each 5 kg (about 11 pounds) gained during adulthood increases the risk of postmenopausal breast cancer by 11%.*

❑*Breast cancer risk was 16% higher in women with type II diabetes independent of obesity*

Physical activity

❑Growing evidence suggests that women who get regular physical activity have a 10%-25% lower risk of breast cancer compared to women who are inactive

❑Stronger evidence for postmenopausal than premenopausal women.

❑An ACS study that included more than 73,000 postmenopausal women found that breast cancer risk was **14%** lower among women who reported walking 7 or more hours per week compared to women who walked 3 or less hours per week.

Diet

❑The effect of diet on breast cancer risk remains an active area of research.

❑Numerous studies have examined the relationship between food consumption (including fat, fiber, soy, dairy, meat, and fruits and vegetables) and breast cancer with mixed results

❑A recent meta-analysis showed no association between fat intake and BC
  ❑Nurses' Health Study showed that a high-fat diet during adolescence was associated with a moderate increase in premenopausal breast cancer risk

❑A meta-analysis showed that soy intake was inversely associated with breast cancer risk in Asian but not Western populations.

❑There is growing evidence that high levels of fruit and vegetable consumption may reduce the risk of hormone receptor-negative breast cancer

Alcohol

❑Numerous studies have confirmed that alcohol consumption increases the risk of breast cancer
   ❑7%-10% for each 10g (one drink) of alcohol consumed per day on average.
   ❑20% higher risk for 2-3 alcoholic drinks per day

❑Alcohol use has been more strongly related with increased risk for ER+ than ER- breast cancer

❑This effect is related to increasing estrogen and androgen levels.

Radiation

❑The link between radiation exposure and breast cancer has been demonstrated in studies of atomic bomb survivors and women who have received high-dose radiation therapy to the chest

❑Girls and women treated with high-dose radiation to the chest between 10 and 30 years of age, such as for Hodgkin lymphoma are at increased risk for breast cancer

❑Breast cancer risk among women with such exposure starts to rise about 8 years after radiation treatment and continues to be elevated for more than 25 years

Environmental pollutants

❑In general, epidemiological studies have not found clear relationships between environmental pollutants and breast cancer

❑Some have suggested that rising breast cancer incidence in the latter half of the 20th century may have been caused by environmental pollutants such as organochlorine pesticides

❑Risk increased in animal studies only

Occupational exposures

❏ A few occupations have been linked to breast cancer risk

❏ A recent meta-analysis concluded that evidence from high-quality studies suggests that night shift work increases breast cancer risk by 40%.

   ❏ Shift work at night is a common exposure, involving about 15% to 20% of workers in the US and Europe

   ❏ Exposure to light at night disrupts the production of melatonin

   ❏ Experimental evidence suggests that melatonin may inhibit the growth of small, established tumors and prevent new tumors from developing

❏ The International Agency for Research on Cancer concluded in 2007 that shift work, particularly at night, was probably carcinogenic to humans

Table 4. Factors That Increase the Relative Risk for Breast Cancer in Women

Relative Risk	Factor
>4.0	• Age (65+ vs. <65 years, although risk increases across all ages until age 80) • Biopsy-confirmed atypical hyperplasia • Certain inherited genetic mutations for breast cancer (*BRCA1* and/or *BRCA2*) • Ductal carcinoma in situ • Lobular carcinoma in situ • Personal history of early-onset (<40 years) breast cancer • Two or more first-degree relatives with breast cancer diagnosed at an early age
2.1-4.0	• High endogenous estrogen or testosterone levels (postmenopausal) • High-dose radiation to chest • Mammographically extremely dense (>50%) breasts compared to less dense (11%-25%) • One first-degree relative with breast cancer

Table 4. Factors That Increase the Relative Risk for Breast Cancer in Women

Relative Risk	Factor
1.1–2.0	• Alcohol consumption • Ashkenazi Jewish heritage • Diethylstilbestrol exposure • Early menarche (<12 years) • Height (>5 feet 3 inches) • High socioeconomic status • Late age at first full-term pregnancy (>30 years) • Late menopause (>55 years) • Mammographically dense (26%-50%) breasts compared to less dense (11%-25%) • Non-atypical ductal hyperplasia or fibroadenoma • Never breastfed a child • No full-term pregnancies • Obesity (postmenopausal)/adult weight gain • Personal history of breast cancer (40+ years) • Personal history of endometrium, ovary, or colon cancer • Recent and long-term use of menopausal hormone therapy containing estrogen and progestin • Recent oral contraceptive use

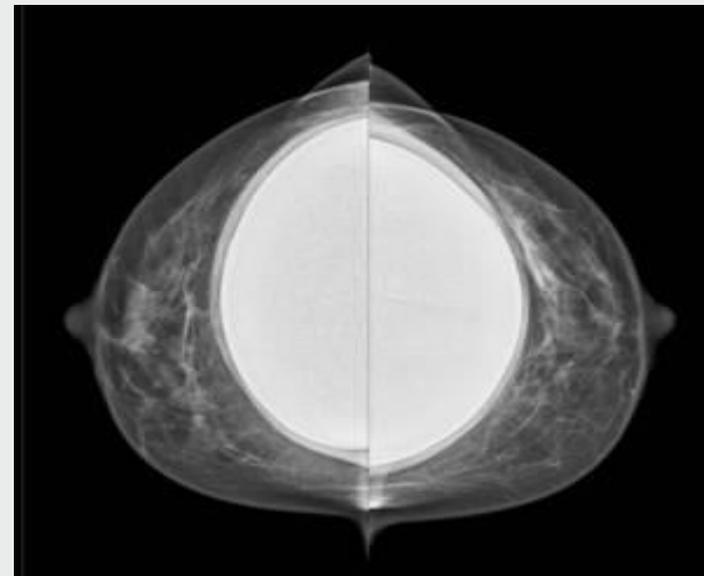# Factors that are not associated with breast cancer risk

Abortion

Hair dyes and antiperspirants

Breast implants

❑ **Can be associated with rare type of lymphoma**

❑ **Implant displacement view**

Questions?