

# Staying abreast: Learn the facts about Breast Cancer Risk

Kala Visvanathan MD MHS

Professor of Oncology and Epidemiology

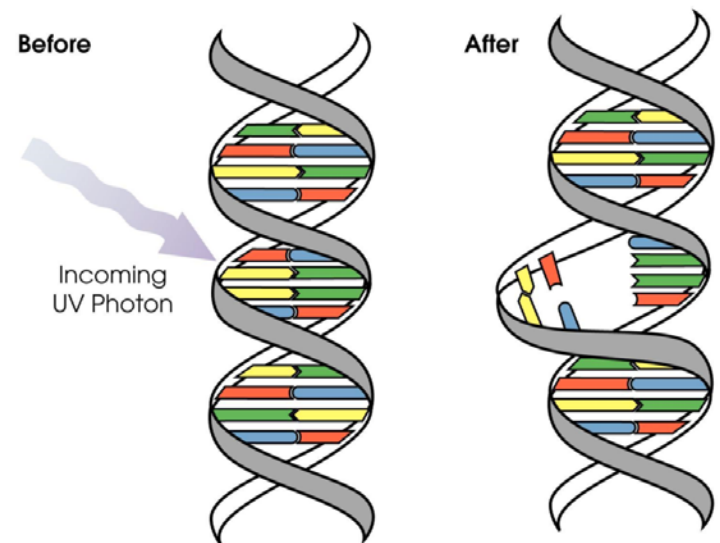
Johns Hopkins School of Medicine and Bloomberg School of Public Health



JOHNS HOPKINS  
M E D I C I N E

# DNA damage leads to Cancer

- Is fundamentally a disease caused by **damage to the DNA**
- These mutations can be inherited from
  1. Your parents
  2. Increasing age



Source: NASA.gov

# Normal Cells vs. Cancer Cells

Normal cell



Example of one type of abnormal or cancerous cell



[curecancernaturally.net](http://curecancernaturally.net)

Normally, cells grow and divide to form new cells as needed. When cells grow old, they die and new cells replace them.

Sometimes, this process goes **wrong**.

# CARCINOGENESIS

INITIATION

PROMOTION

TRANSFORMATION

PROGRESSION

Carcinogen

Genetic Change

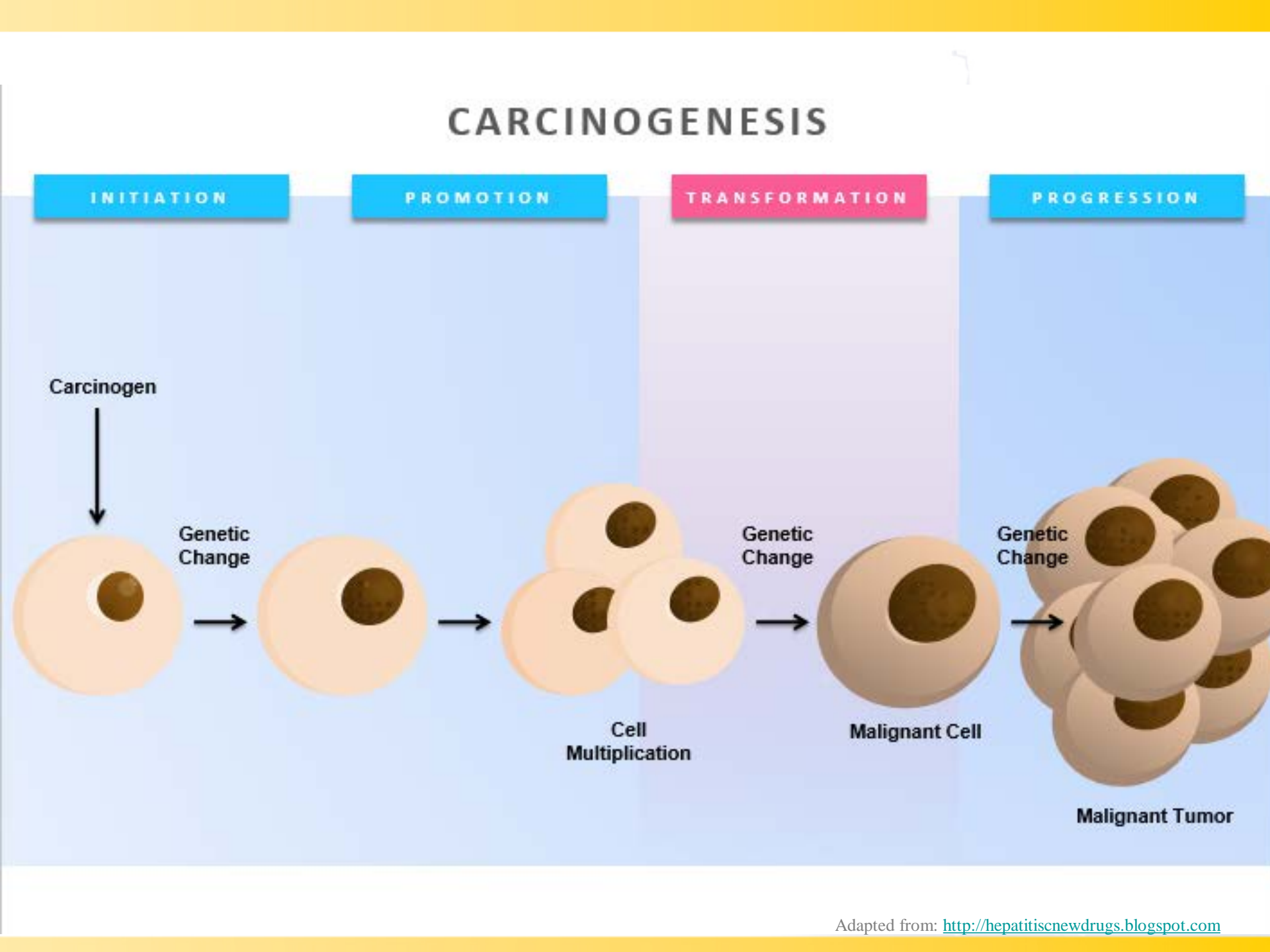
Genetic Change

Genetic Change

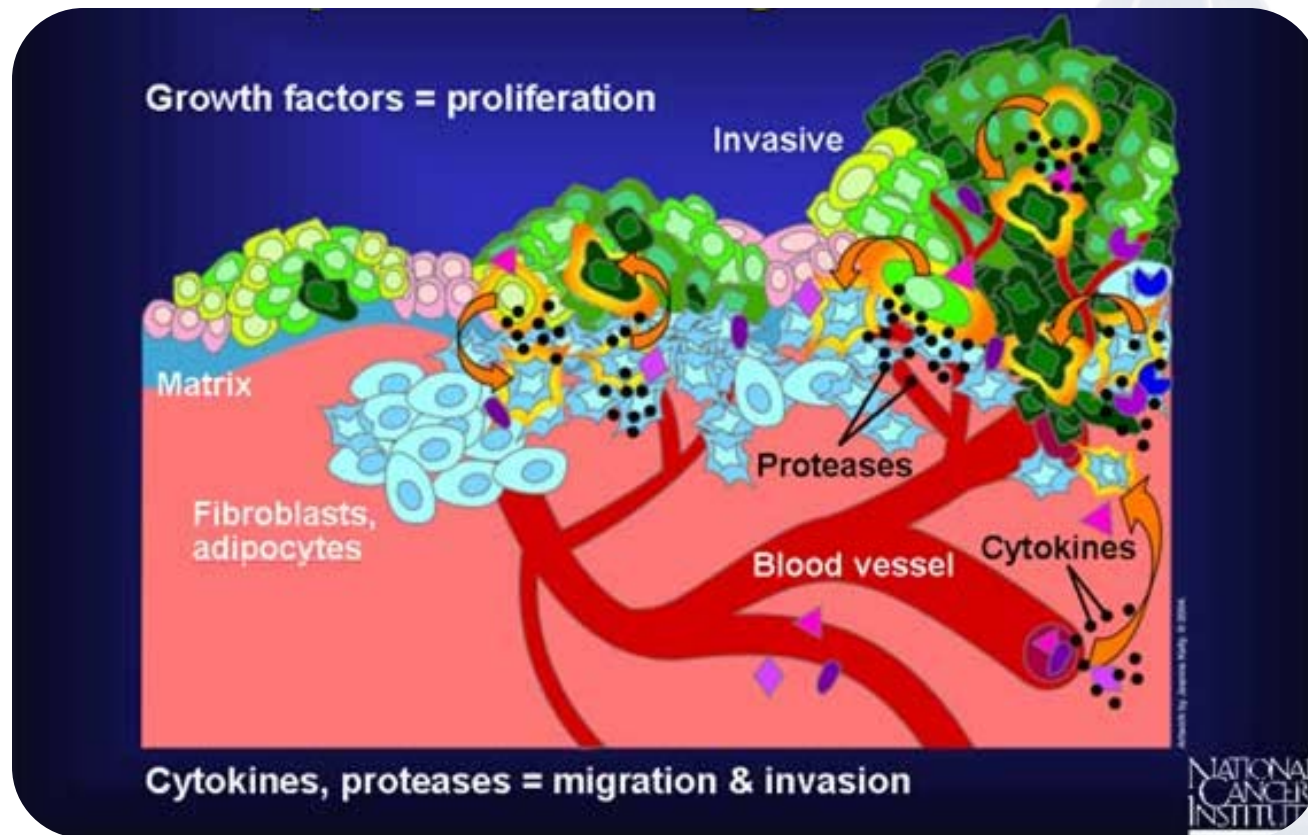
Cell Multiplication

Malignant Cell

Malignant Tumor



# Cancer Tends to Corrupt Surrounding Environment



Source: National Cancer Institute

# Breast Cancer

- **In situ breast cancer**
  - “Stage 0”
- **Invasive breast cancer**
  - Stage I-IV
- **Local:** still confined to the primary site
- **Regional:** spread to regional lymph nodes or directly beyond the primary site
- **Distant:** metastasized

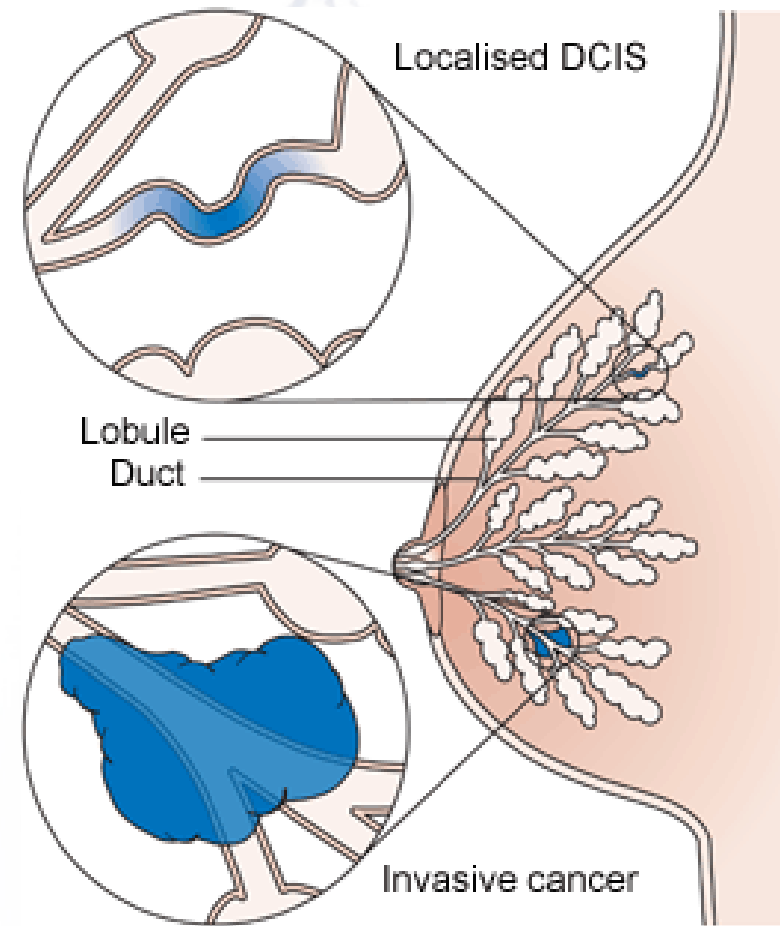
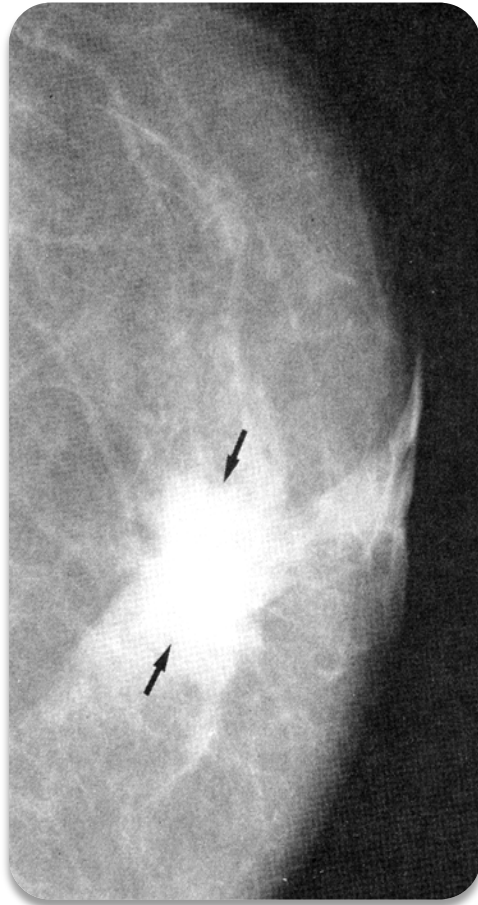
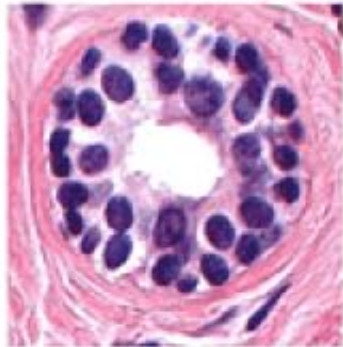


Diagram showing ductal cancer in situ (DCIS)  
Copyright © CancerHelp UK

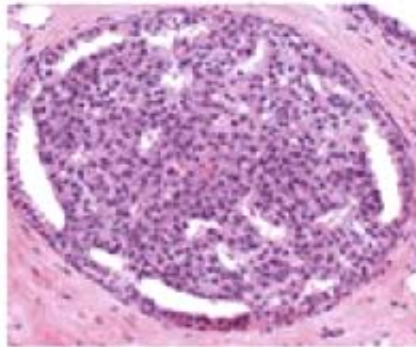
# Mammogram and corresponding gross specimen demonstrating a dense discrete mass within the breast



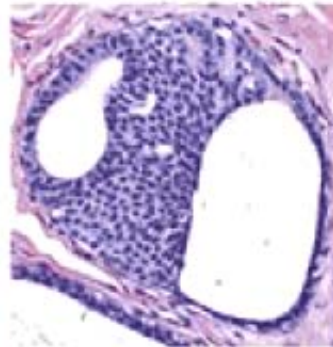
# Tumor Types



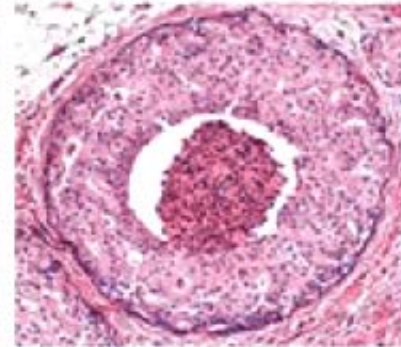
**Normal  
Ductal Lumen**



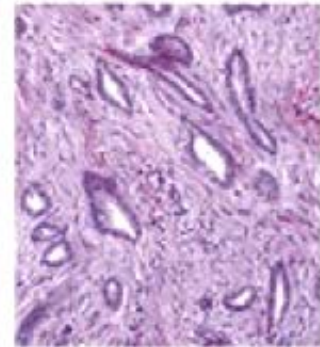
**Benign Proliferative  
Changes**



**Atypical Hyperplasia**



**Ductal Carcinoma  
In Situ**



**Invasive Carcinoma**

**Accumulation of genetic and epigenetic changes**



# What Causes Cancer?

**1. GENETICS**

**2. THINGS YOU'RE  
EXPOSED TO**

**3. THINGS YOU DO  
and DON'T DO**

# Risk Factors

## What are risk factors?

- A risk factor is anything that affects your chance of getting the disease

### Examples:

- Sun exposure increases likelihood of skin cancer
- Smoking increases likelihood of lung cancer



# Cancer Risk and Aging



# Probability of Developing Breast Cancer

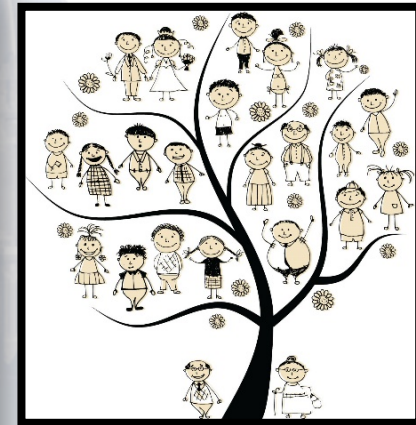
**Table 4. Age-Specific Probabilities of Developing Invasive Breast Cancer\***

<b>If current age is:</b>	<b>The probability of developing breast cancer in the next 10 years is:</b>
20	0.05%
30	0.43%
40	1.43%
50	2.51%
60	3.51%
70	3.88%
<b>Lifetime risk</b>	<b>12.28%</b>

# Risk Factors

**Table 3. Factors That Increase the Relative Risk for Breast Cancer in Women**

Relative Risk	Factor
>4.0	<ul style="list-style-type: none"> <li>• Female</li> <li>• Age (65+ versus &lt;65 years, although risk increases across all ages until age 80)</li> <li>• Certain inherited genetic mutations for breast cancer (BRCA1 and/or BRCA2)</li> <li>• Two or more first-degree relatives with breast cancer diagnosed at an early age</li> <li>• Personal history of breast cancer</li> <li>• High breast tissue density</li> <li>• Biopsy-confirmed atypical hyperplasia</li> </ul>
2.1-4.0	<ul style="list-style-type: none"> <li>• One first-degree relative with breast cancer</li> <li>• High-dose radiation to chest</li> <li>• High bone density (postmenopausal)</li> </ul>
1.1-2.0	
Factors that affect circulating hormones	<ul style="list-style-type: none"> <li>• Late age at first full-term pregnancy (&gt;30 years)</li> <li>• Early menarche (&lt;12 years)</li> <li>• Late menopause (&gt;55 years)</li> <li>• No full-term pregnancies</li> <li>• Never breastfed a child</li> <li>• Recent oral contraceptive use</li> <li>• Recent and long-term use of hormone replacement therapy</li> <li>• Obesity (postmenopausal)</li> </ul>
Other factors	<ul style="list-style-type: none"> <li>• Personal history of endometrium, ovary, or colon cancer</li> <li>• Alcohol consumption</li> <li>• Height (tall)</li> <li>• High socioeconomic status</li> <li>• Jewish heritage</li> </ul>



[www.johngraycentre.org](http://www.johngraycentre.org)



[www.scientificamerican.com](http://www.scientificamerican.com)

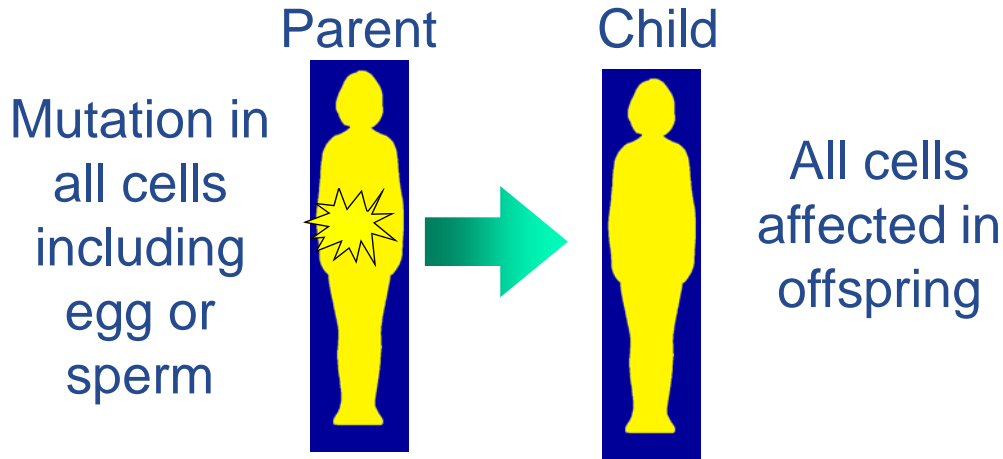
Adapted with permission from Hulka et al, 2001.

# Who is at high risk for breast cancer?



# All Cancers Arise from Gene Mutations

## Germline mutations



- Present in egg or sperm
- Are heritable
- Cause cancer family syndromes

## Somatic mutations

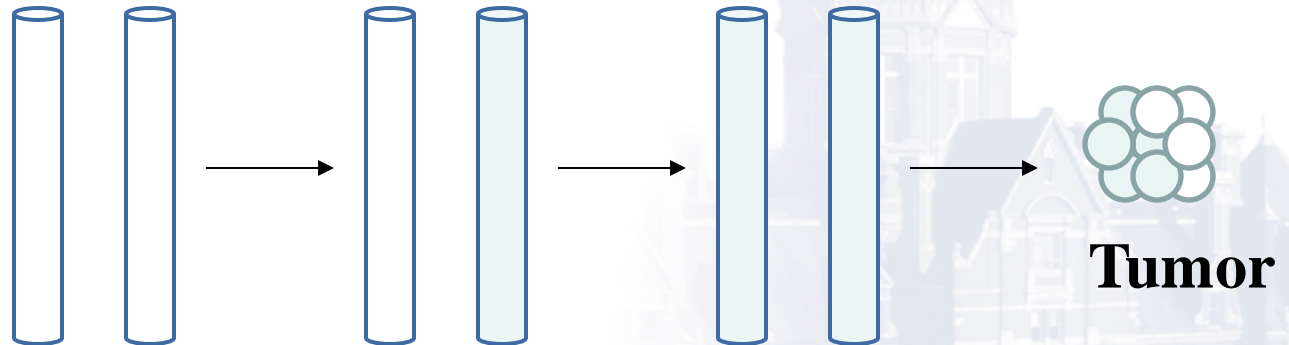


- Occur in tumor only
- Are not heritable
- Are more common

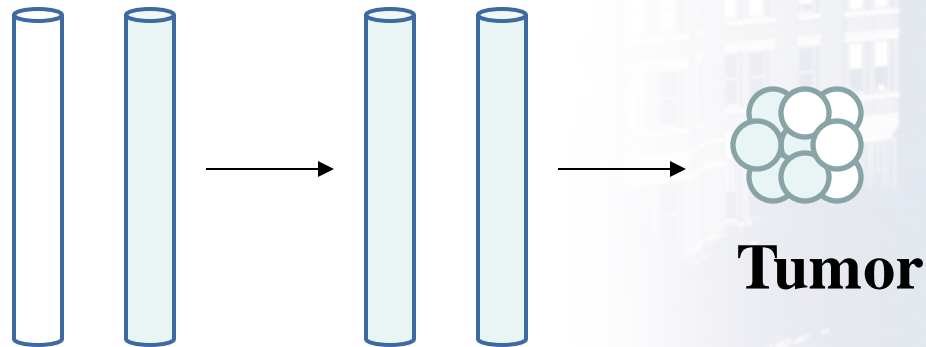
# Inherited Cancers

## Knudson's 2 Hit Hypothesis

**Sporadic Cancer:**  
2 acquired mutations

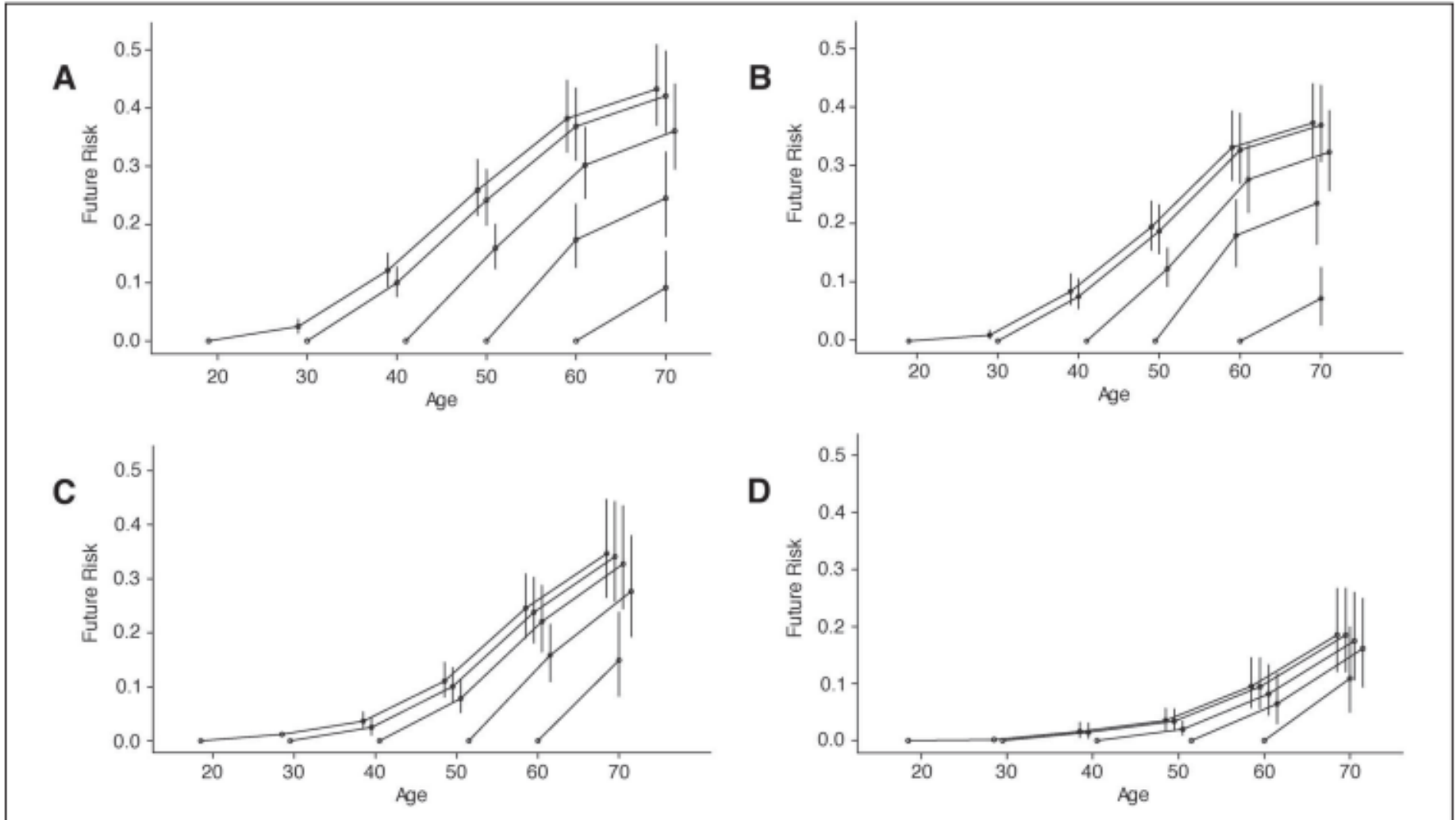


**Hereditary Cancer:**  
1 inherited and  
1 acquired mutation





# Natural History of Breast and Ovarian Cancer in BRCA1/BRCA2 Mutation Carriers



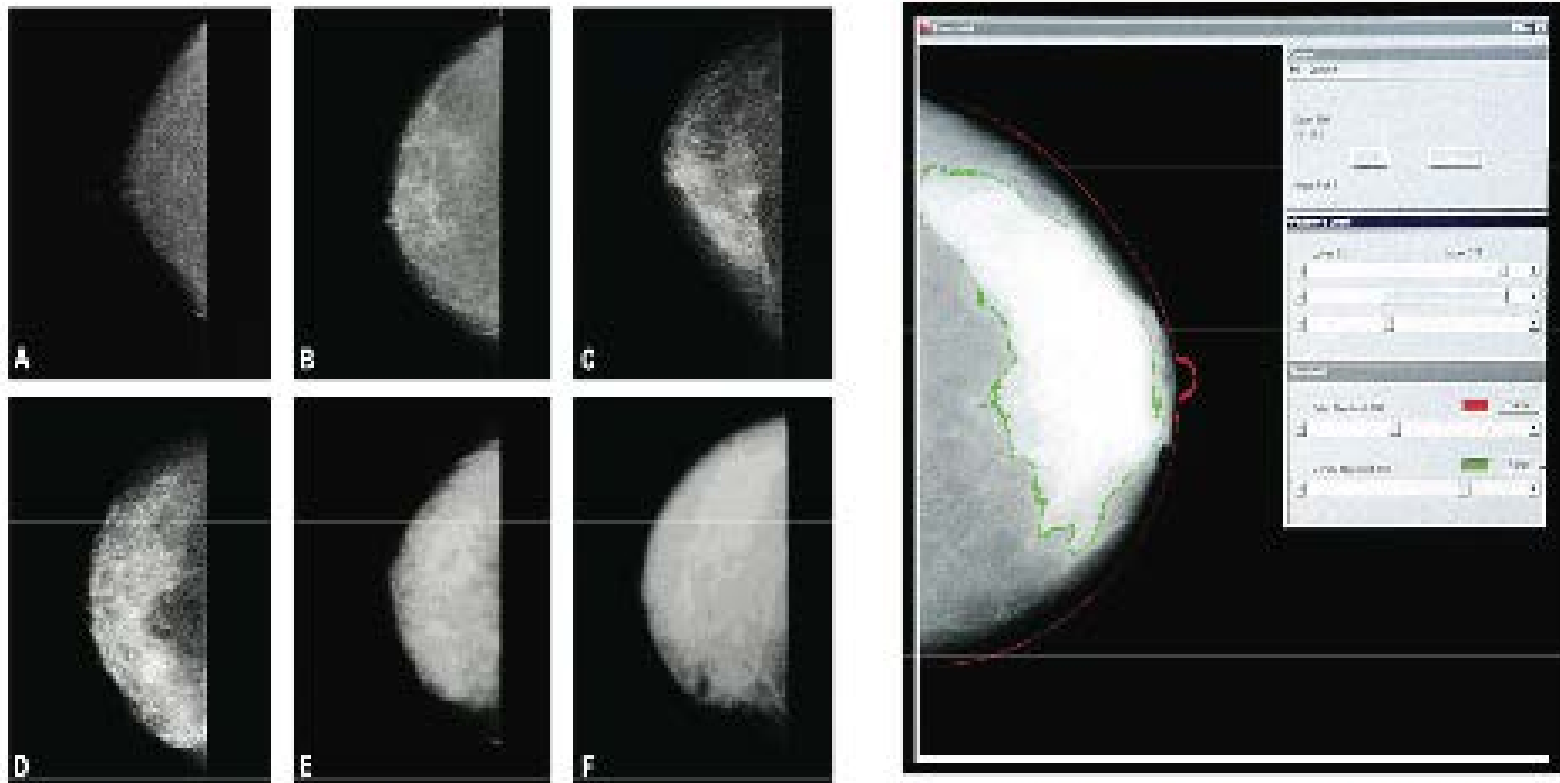
# General Indications for Referral to Genetic Counseling

- Unusually early age of onset for a specific cancer
- Multiple primary cancers in a single individual
- Bilateral cancer in paired organs or multifocal disease
- Clustering of the same type of cancer in close relatives
- Cancers occurring in multiple generations of a family
- Occurrence of rare tumors (e.g., retinoblastoma, adrenocortical carcinoma, ocular melanoma, paraganglioma, or duodenal cancer)
- Unusual presentation of cancer (e.g., male breast cancer)
- Uncommon tumor histology (e.g., medullary thyroid carcinoma, type 2 papillary kidney cancer)

# Breast Density

- The relative risk of women with 75% or more percent mammographic density (PMD) compared to 10% or less is between 4-6 fold
- PMD is associated inversely with greater age, parity and weight menopause, and tamoxifen
- PMD is positively associated with greater height, family history of breast cancer and HT
- 16% of all breast cancers have been attributed to a density of 50% or more
- Although can mask the diagnosis of breast cancer from longitudinal study, believed to be an independent risk factor

# Breast Density



**Figure 1. Examples of mammographic density. (a) 0% mammographic density, (b) less than 10%, (c) less than 25%, (d) less than 50%, (e) less than 75%, and (f) greater than 75%. On the right is an illustration of Cumulus in the measurement of mammographic density. The red line outlines the breast, and the green line outlines the area of density. Republished with permission from [2].**

# Tools to Assess Breast Cancer Risk

### Risk Calculator

(Click a question number for a brief explanation, or [read all explanations.](#))

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?
2. What is the woman's age?  
*This tool only calculates risk for women 35 years of age or older.*
3. What was the woman's age at the time of her first menstrual period?
4. What was the woman's age at the time of her first live birth of a child?
5. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?
6. Has the woman ever had a breast biopsy? 
  - 6a. How many breast biopsies (positive or negative) has the woman had?
  - 6b. Has the woman had at least one breast biopsy with atypical hyperplasia?
7. What is the woman's race/ethnicity? 
  - 7a. What is the sub race/ethnicity?

**Breast Cancer Risk Assessment Tool**  
(<http://www.ems-trials.org/riskevaluator/>)

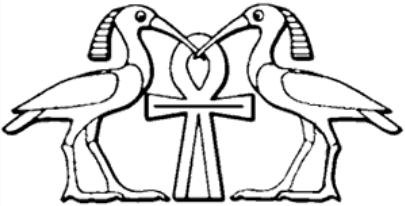
**IBIS Assessment Tool**  
(<http://www.ems-trials.org/riskevaluator/>)

### IBIS Breast Cancer Risk Evaluation Tool

Description	Software Downloads	Documentation	Screenshots & Examples	Software Change Log
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FAQs

**NEW! Version 7 released** [[Download ZIP](#)]



#### Description of breast cancer risk program

The program assumes that there is a gene predisposing to breast cancer in addition to the BRCA genes. The woman's family history is used to calculate the likelihood of her carrying an adverse gene, which in turn affects her likelihood of developing breast cancer. The risks of developing breast cancer for the general population were taken from data on the first breast cancer diagnosis (ICD-10 code C50) in Thames Cancer Registry area (UK) between 2005-2009.

The risk from family history (caused by the adverse genes) is modelled to fit the results in "Familial Breast and Ovarian Cancer: A Swedish Population-based Register Study, Anderson H et al., American Journal of Epidemiology 2000, 152: 1154-1163".

#### Contact Details

Prof. Jack Cuzick  
Centre for Cancer Prevention,  
Wolfson Institute of Preventive Medicine,  
Charterhouse Square,  
London  
EC1M 6BQ  
email: [riskevaluator@ems-trials.org](mailto:riskevaluator@ems-trials.org)

# Lifestyle Approaches to Reducing Breast Risk Cancer



# Causes of Overweight



Family  
History and  
Genetics

Metabolism



Overweight

Environment

Behavior  
and Habits



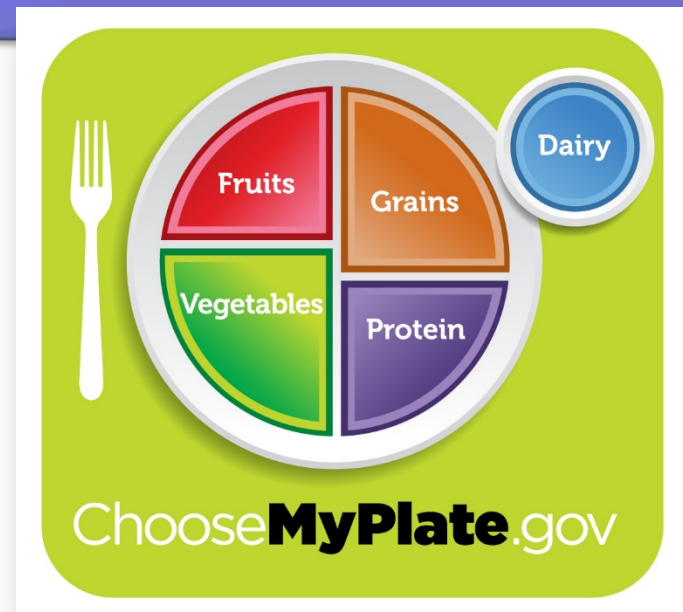
# Energy Balance

## Energy Balance

- Important to maintain a healthy weight
- Amount you take in needs to include what your body uses
- If overweight, reduce caloric intake to lose weight



[originalstrength.net](http://originalstrength.net)





# Healthy Weight

Español

STANDARD | METRIC

Your Height:    
(feet) (inches)

Your Weight:   
(pounds)

Compute BMI

Your BMI:

## BMI Categories:

- Underweight = <18.5
- Normal weight = 18.5–24.9
- Overweight = 25–29.9
- Obesity = BMI of 30 or greater

## The BMI Tables

### Aim for a Healthy Weight:

- Limitations of the BMI
- Assessing Your Risk
- Controlling Your Weight
- Recipes



Download the BMI Calculator iPhone App

## Body Mass Index

- Measurement of body fat based on height and weight
- To calculate:  
<http://www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm>

# Sustained weight loss and breast cancer risk in postmenopausal women who never used postmenopausal hormones



Wolin, K. Y. et al. *Oncologist* 2010;15:556-565

# Hormones

## Combination of Hormones



## Estrogen only

NDC 0046-1101-81 100 Tablets

**PREMARIN<sup>®</sup>**  
(conjugated estrogens tablets, USP)

**0.45 mg**

SEALED FOR YOUR PROTECTION

**R<sub>x</sub> only**  
**Wyeth<sup>®</sup>**

Visit us at [www.PREMARIN.com](http://www.PREMARIN.com)

Each tablet contains 0.45 mg of conjugated estrogens, USP, in their naturally occurring conjugated form. Usual Dosage: See accompanying descriptive literature. The appearance of these tablets is a trademark of Wyeth Pharmaceuticals, Inc. Wyeth Pharmaceuticals Inc. Philadelphia, PA 19101 PAA010991

(01)00300461101811

Dispenser: Include "Information for the Patient" leaflet with each prescription dispensed. Store at 20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F). [See USP Controlled Room Temperature] Dispense in a well-closed container as defined in the USP.

FPO

LOT  
EXP

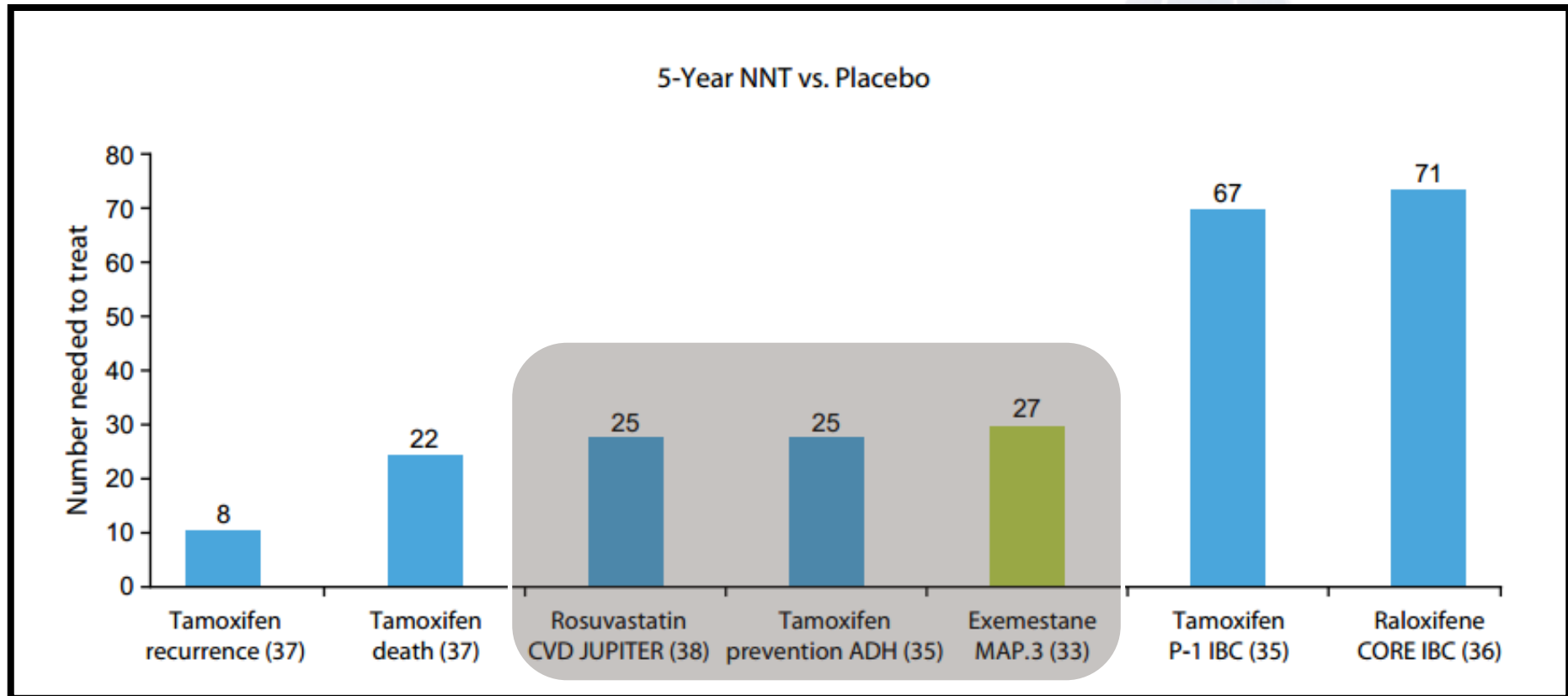
Source: drugs.com

# Making the case for breast cancer prevention

- Since 1998 8 phase III breast cancer prevention trials have been conducted and ALL of them have demonstrated a reduction in breast cancer incidence
- Four national guidelines ASCO, USPTF, NCCN and the UK Nice guidelines are all in support of the use of chemoprevention for women at higher risk
- Tamoxifen, Raloxifene, Aromatase Inhibitors

Visvanathan K ASCO risk reduction guidelines JCO 2013  
[http://www.nccn.org/professionals/physician\\_gls/f\\_guidelines.asp](http://www.nccn.org/professionals/physician_gls/f_guidelines.asp)  
[www.nice.org.uk/](http://www.nice.org.uk/)

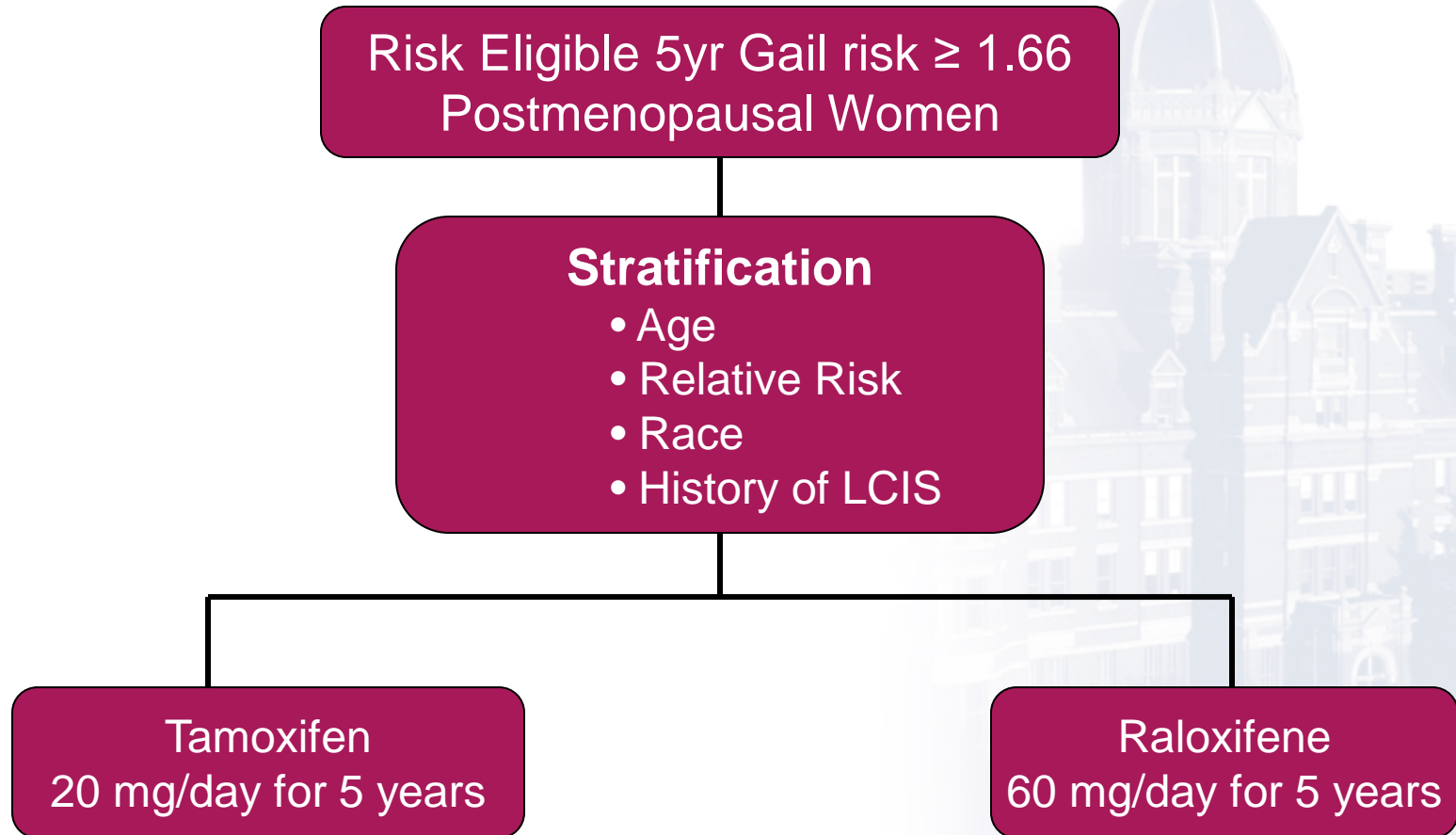
# Comparison of NNT in primary prevention trials in oncology and cardiology



Abbreviations: CVD, cardiovascular; IBC, invasive breast cancer; JUPITER, Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin.

# Study of Tamoxifen and Raloxifene

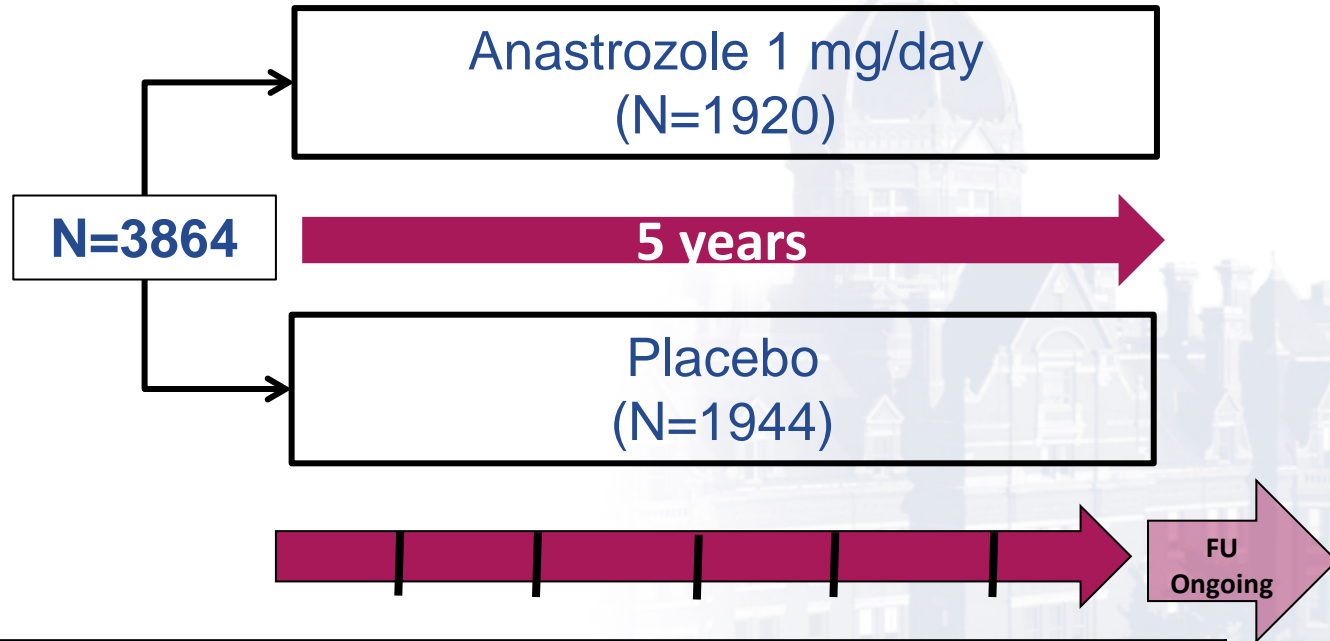
NSABP Protocol P-2 Schema



# Trial Schema

## Postmenopausal women:

- Ages 40-70
- Increased risk of breast cancer:
  - Family history
  - Atypia / LCIS
  - Breast density
- No HRT



- Exclusion
- On HRT
  - Severe osteoporosis T score < 4
  - 2 vertebral fracture
  - Life expectancy 10 yrs

	Baseline	6 M	12 M	24 M	36 M	48 M	60M
Clinic visit	X	X	X	X	X	X	X
Mammogram	X			X		X	
Blood	X		X				X
DXA	X						

# Summary of Recommendations

1. Chemoprevention should be discussed in women at increased risk for breast cancer. There are now many options. In conjunction with discussion of risks and benefits

2. Particularly women with ADH, LCIS, higher risk women

3. Need to factor in age, race and presence of uterus in decision with respect to SERMs

4. In terms of toxicity younger women have less toxicity but also often less risk.

5. AI (not FDA approved yet) but clearly have a role in chemoprevention.



# Overall Cancer Prevention



1. Stop using tobacco
  2. Maintain a reasonable weight
  3. Increase physical activity
  4. Eat 5-9 fruits and vegetables daily
  5. Increase fiber and reduce saturated fat
  6. Limit alcohol consumption
  7. Limit exposure to the sun
  8. Get immunized (younger)
  9. Avoid risky behaviors
  10. Treat precursor lesions
- \* Become aware of your cancer risk

# Take Home Messages

1. Be aware of your risk factors for breast cancer
2. Be aware of your breast cancer risk
3. Optimize lifestyle factors to minimize risk
4. If you have a strong family history consider a referral to a genetics clinic
5. If you are at moderately increased risk discuss chemoprevention with your doctors
6. Screen
7. Inform other women so they can also optimize their breast health

**Thank you!**