Natural History and Epidemiology of Breast Cancer

2018 Dialogue I Prevent Cancer Foundation

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lombardi
RESEARCH EDUCATION TREATMENT

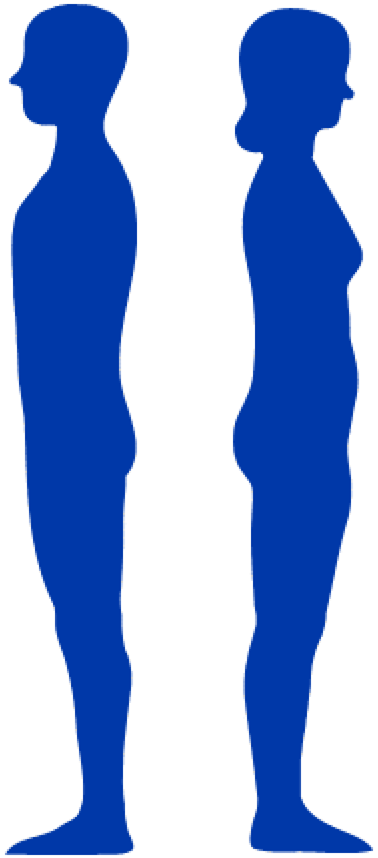
Objectives

- Ø Epidemiology of breast cancer
- Ø Risk factors for breast cancer
- Ø Controversies in screening

Estimated New Cancer Cases* in the US in 2017

Males **836,150**

Prostate	19%
Lung & bronchus	14%
Colon & rectum	9%
Urinary bladder	7%
Melanoma of skin	6%
Kidney & renal pelvis	5%
Non-Hodgkin lymphoma	5%
Leukemia	4%
Oral cavity & pharynx	4%
Liver & intrahepatic bile duct	3%
All other sites	23%



Females **852,630**

30%	Breast
12%	Lung & bronchus
8%	Colon & rectum
7%	Uterine corpus
5%	Thyroid
4%	Melanoma of skin
4%	Non-Hodgkin lymphoma
3%	Leukemia
3%	Pancreas
3%	Kidney & renal pelvis
22%	All other sites

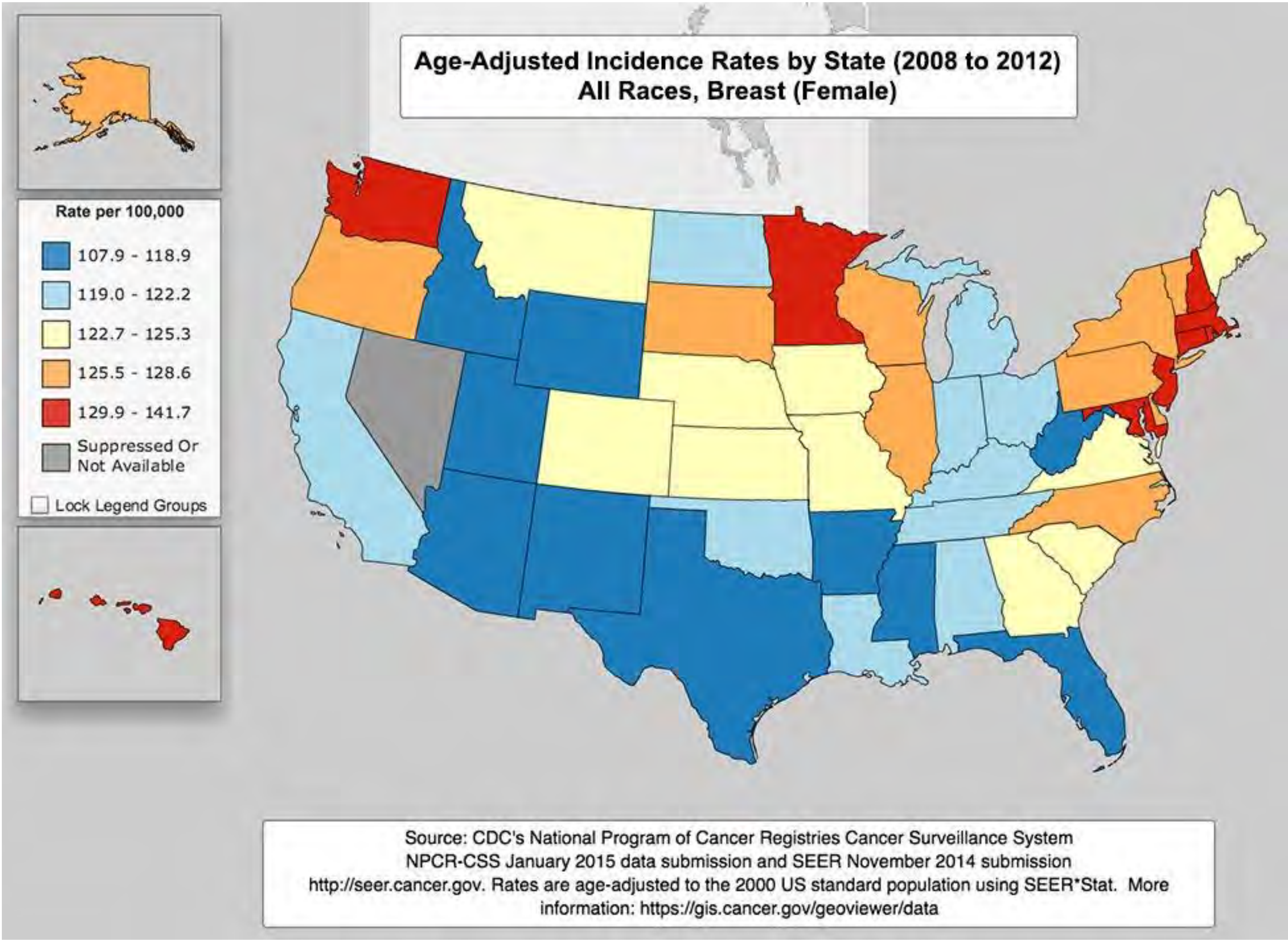
*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Breast specific data

- Breast cancer is the most commonly diagnosed cancer in U.S. women (1/8)
  - Every 3 minutes a female in U.S. diagnosed
- In 2018, an estimated 266,120 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S.
  - 63,960 new cases of non-invasive (in situ) breast cancer

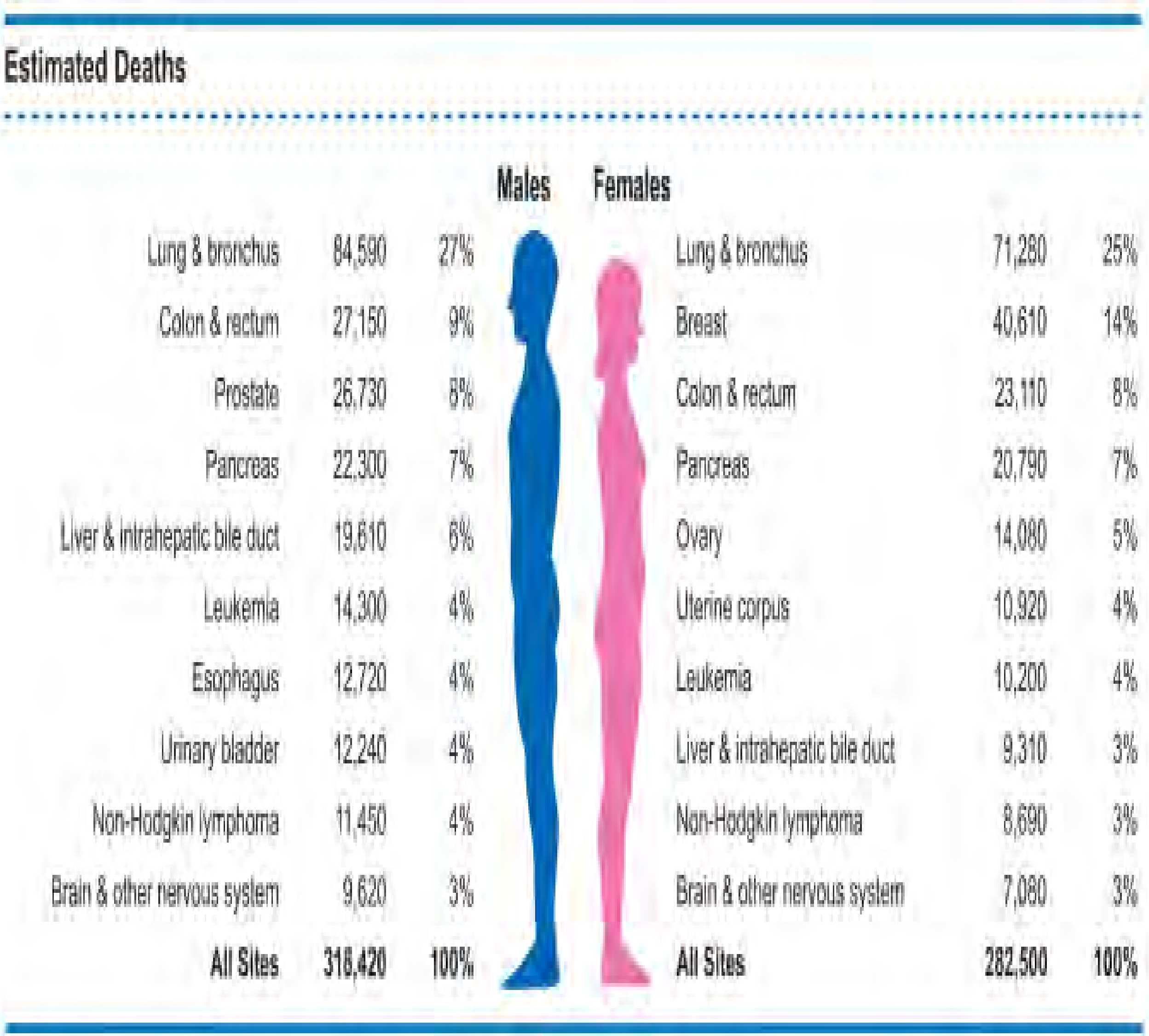
Male breast cancer

- 1% of breast cancers are in men
- About 2,550 new cases of invasive breast cancer are expected to be diagnosed in men in 2018
- A man's lifetime risk of breast cancer is about 1 in 1,000


Age-Adjusted Incidence Rates by State (2008 to 2012)
All Races, Breast (Female)
Rate per 100,000
107.9 - 118.9
119.0 - 122.2
122.7 - 125.3
125.5 - 128.6
129.9 - 141.7
Suppressed Or Not Available
Lock Legend Groups
Source: CDC's National Program of Cancer Registries Cancer Surveillance System
NPCR-CSS January 2015 data submission and SEER November 2014 submission
http://seer.cancer.gov. Rates are age-adjusted to the 2000 US standard population using SEER*Stat. More information: https://gis.cancer.gov/geoviewer/data

Mortality

- ACS- 2nd leading cause of cancer death
  - 40,920 breast cancer deaths est. 2018

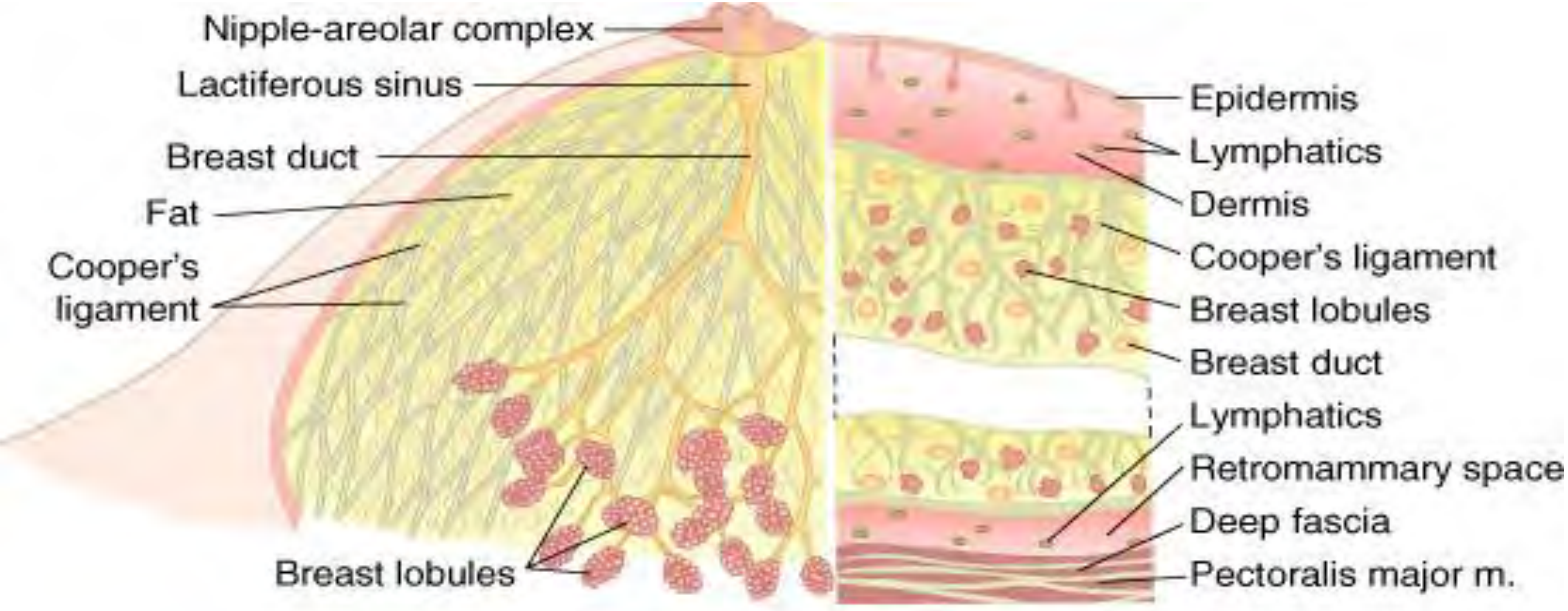


Estimated Deaths

Males			Females		
Lung & bronchus	84,590	27%	Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%	Breast	40,610	14%
Prostate	26,730	8%	Colon & rectum	23,110	8%
Pancreas	22,300	7%	Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%	Ovary	14,080	5%
Leukemia	14,300	4%	Uterine corpus	10,920	4%
Esophagus	12,720	4%	Leukemia	10,200	4%
Urinary bladder	12,240	4%	Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%	Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%	Brain & other nervous system	7,080	3%
All Sites	**318,420**	**100%**	**All Sites**	**282,500**	**100%**

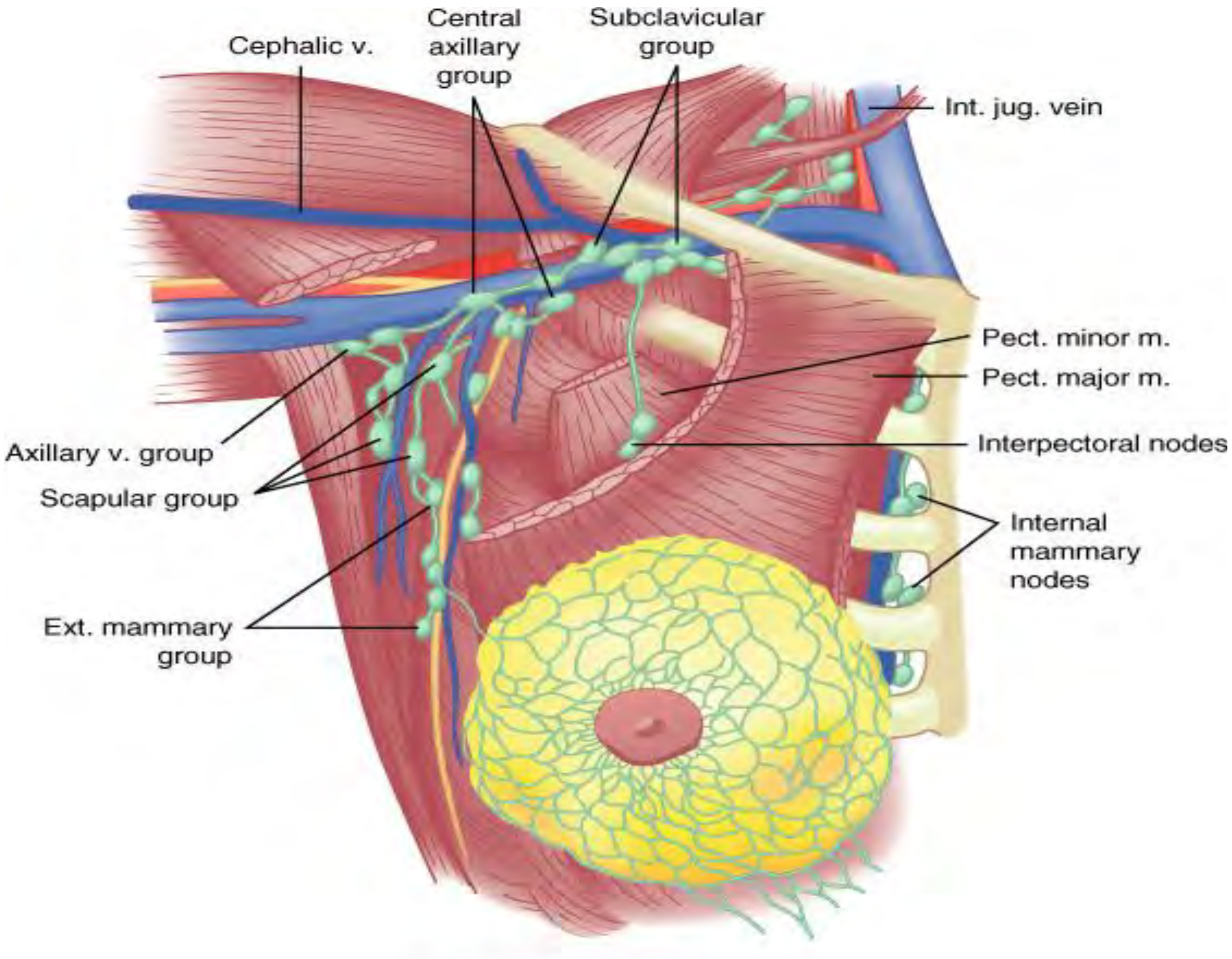
Breast cancer development

Anatomy of the Breast

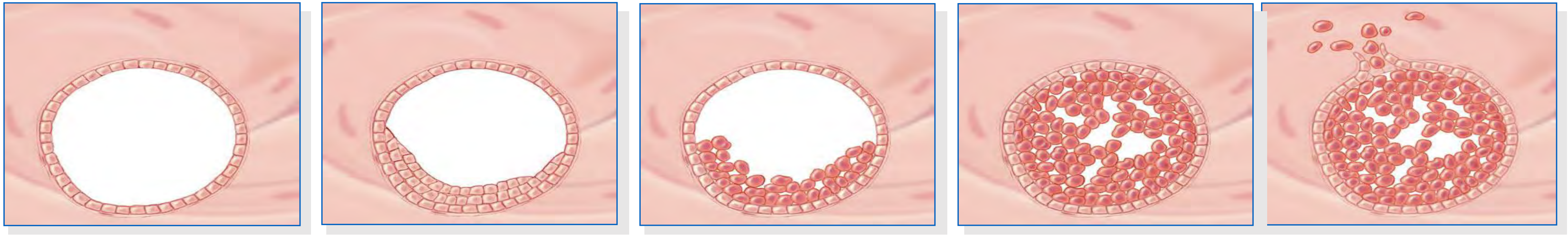


Lymphatics

- Sappey's plexus
  - >75% of lymphatic flow from breast into axillary lymph nodes



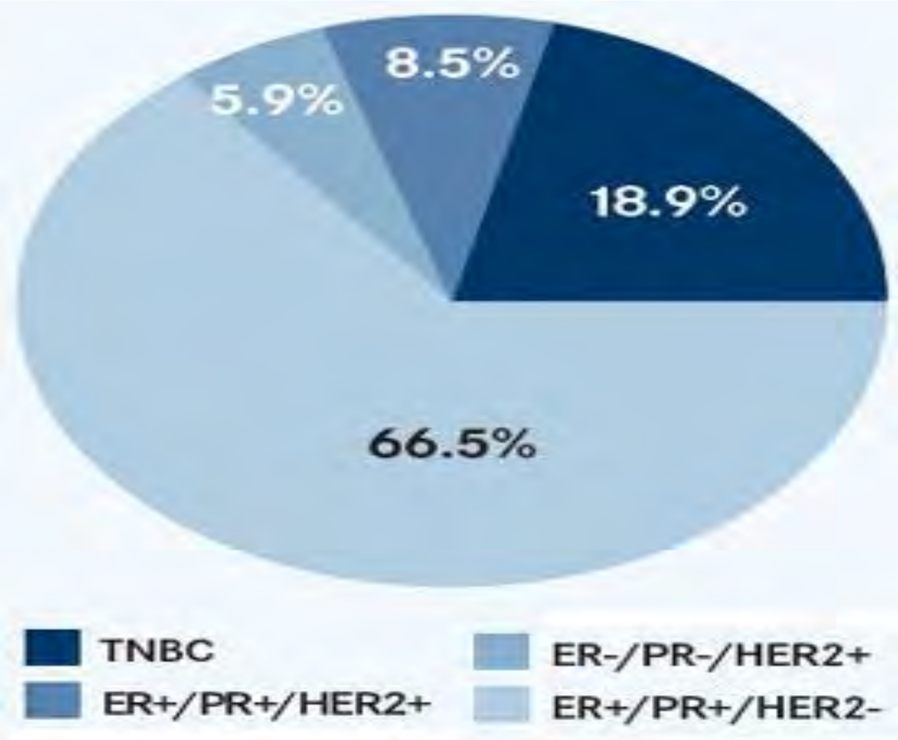
Breast cancer



Normal Duct | Intraductal Hyperplasia | Atypical Ductal Hyperplasia | Ductal Carcinoma *In Situ* | Invasive Ductal Carcinoma

95% of breast cancers originate in the epithelium of the ductal-lobular system.

Breast cancer subtypes



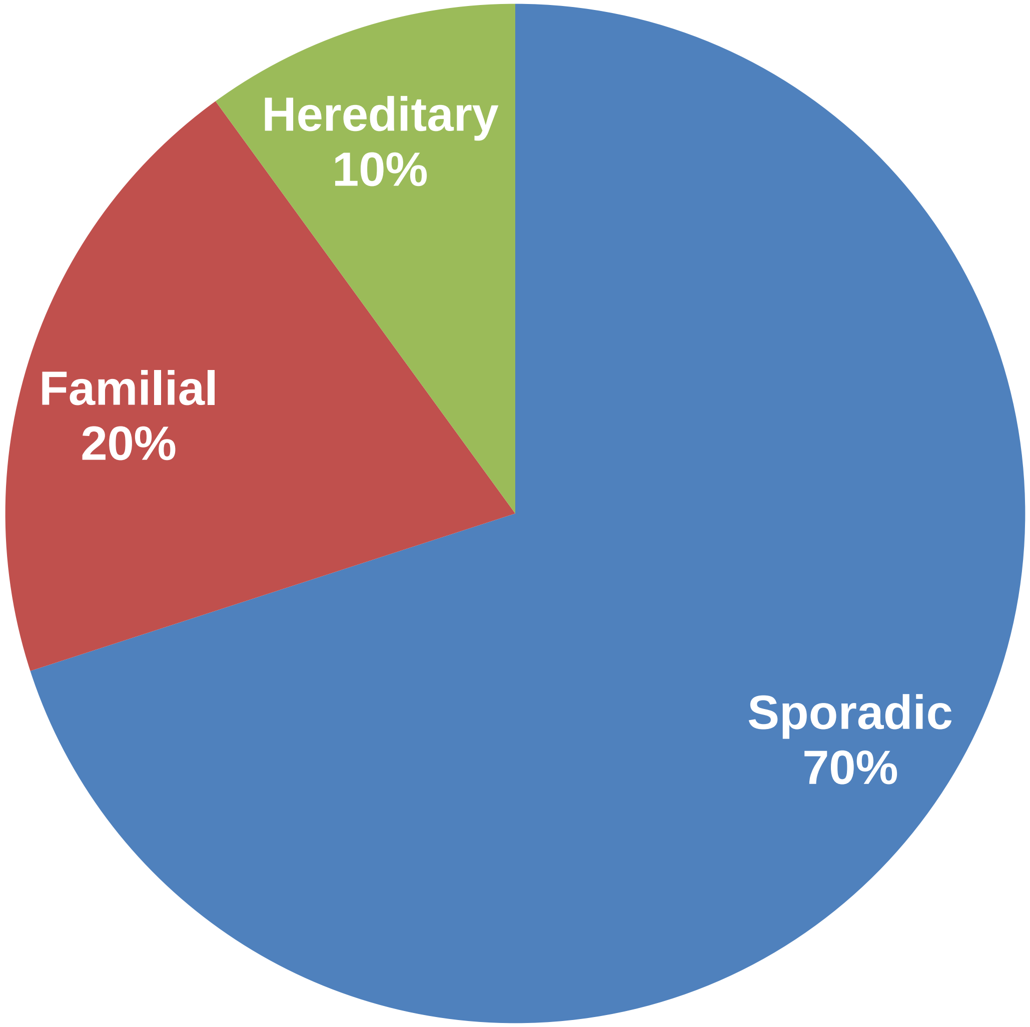
Incidence Among 1501 Women

A population-based study of the tumor status of women diagnosed with breast cancer in the Atlanta, Georgia, metropolitan area yielded these incidence rates by broad subtype. ER indicates estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; TNBC, triple-negative breast cancer.

Adapted from Lund MJ, Butler EN, Hair BY, et al. Age/race differences in HER2 testing and in incidence rates for breast cancer triple subtypes: a population-based study and first report. Cancer. 2010; 116(11):2549-2559.

Risk factors

BREAST CANCER RISK



General risk factors

- Being female
- Older age
- Having a mutation in the BRCA1 or BRCA2 breast cancer genes
- Having a previous biopsy showing hyperplasia
- Lobular carcinoma in situ (LCIS)
- A family history of breast cancer
- Having high breast density on a mammogram
- Radiation exposure (woman with hx. HD)
- A personal history of breast or ovarian cancer starting menopause after age 55
- Never having children
- Having your first child after age 35
- High bone density
- Early menarche (age less than 12)
- Alcohol intake
- Obesity

Hereditary breast cancer

- BRCA-1 and -2
- Tumor suppressor genes
- Estimated lifetime risk for breast cancer is up to 85%
- BRCA 1 55-85% risk
  - Ovarian cancer (15-45%), colon cancer, prostate cancer
- BRCA 2 37-85%
  - Ovarian cancer (20-30%), pancreatic and laryngeal cancer, prostate cancer
- Increased risk of local recurrence as well as contralateral breast cancer
- Genetic counseling and testing

Next generation sequencing

- The first evidence for the existence of a gene encoding for a DNA repair enzyme involved in breast cancer susceptibility was provided by Mary-Claire King's laboratory at UC Berkeley in 1990.

Table 1. DNA-repair genes that increase breast cancer risk and are included in the BROCA capture oligo set.

Gene	Syndrome	Biological pathway	Breast cancer risk	% of FBC**
ATM	Ataxia-telangectasia	Base excision repair	2-5x	<1%
BARD1		Tumor suppressor with *BRCA1*	2-5x	3%
BRCA1	*BrOv syndrome*	*ds break & nucl. excision repair*	*>5x*	*20%*
BRCA2	*BrOv & Fanconi anemia*	*ds break repair*	*>5x*	*10%*
BRIP1 (FANCJ)	Fanconi anemia	ds break repair	2-5x	<1%
CHEK2	Li-fraumeni	Nucleotide excision repair	2-5x	3%
MRE11	Nijmegen breakage synd.	MRN complex ds break repair	2-5x	2%
NBS1	Nijmegen breakage synd.	MRN complex ds break repair	2-5x	<1%
PALB2 (FANCN)	Fanconi anemia	DNA crosslink repair	2-5x	3%
PTEN	Cowden syndrome	Tumor suppressor of Rad51	>5x	1%
RAD50	Nijmegen breakage synd.	MRN complex ds break repair	2-5x	<1%
RAD51	Fanconi anemia	ds break repair	>5x	1%
STK11	Peutz-Jegher syndrome	Tumor suppressor	>5x	1%
TP53	Li-Fraumeni syndrome	Nucleotide excision repair	>5x	1%
			Total	50%

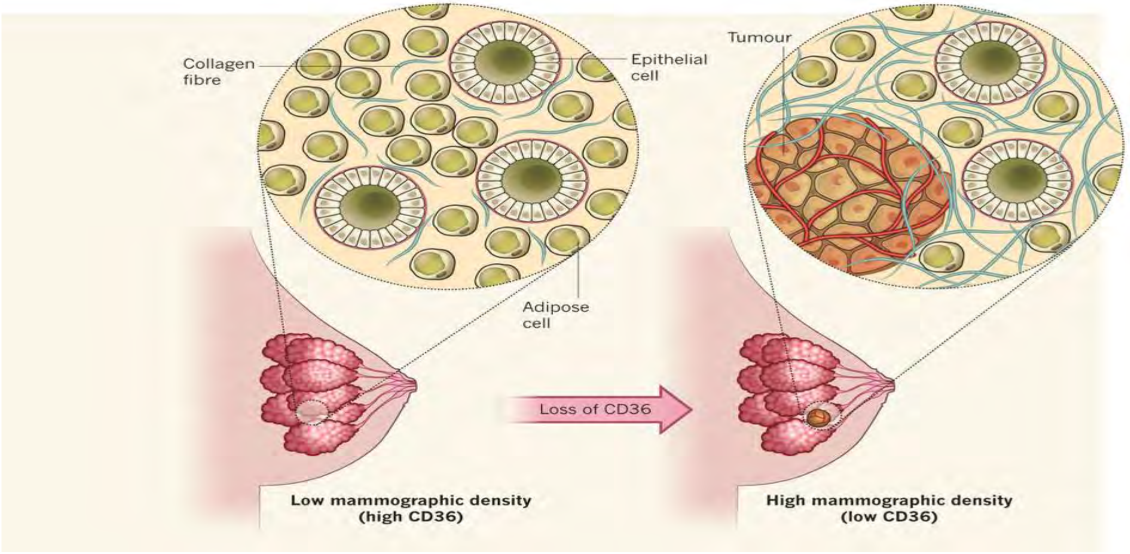
**FBC = familial breast cancer

Breast density

mammographic density

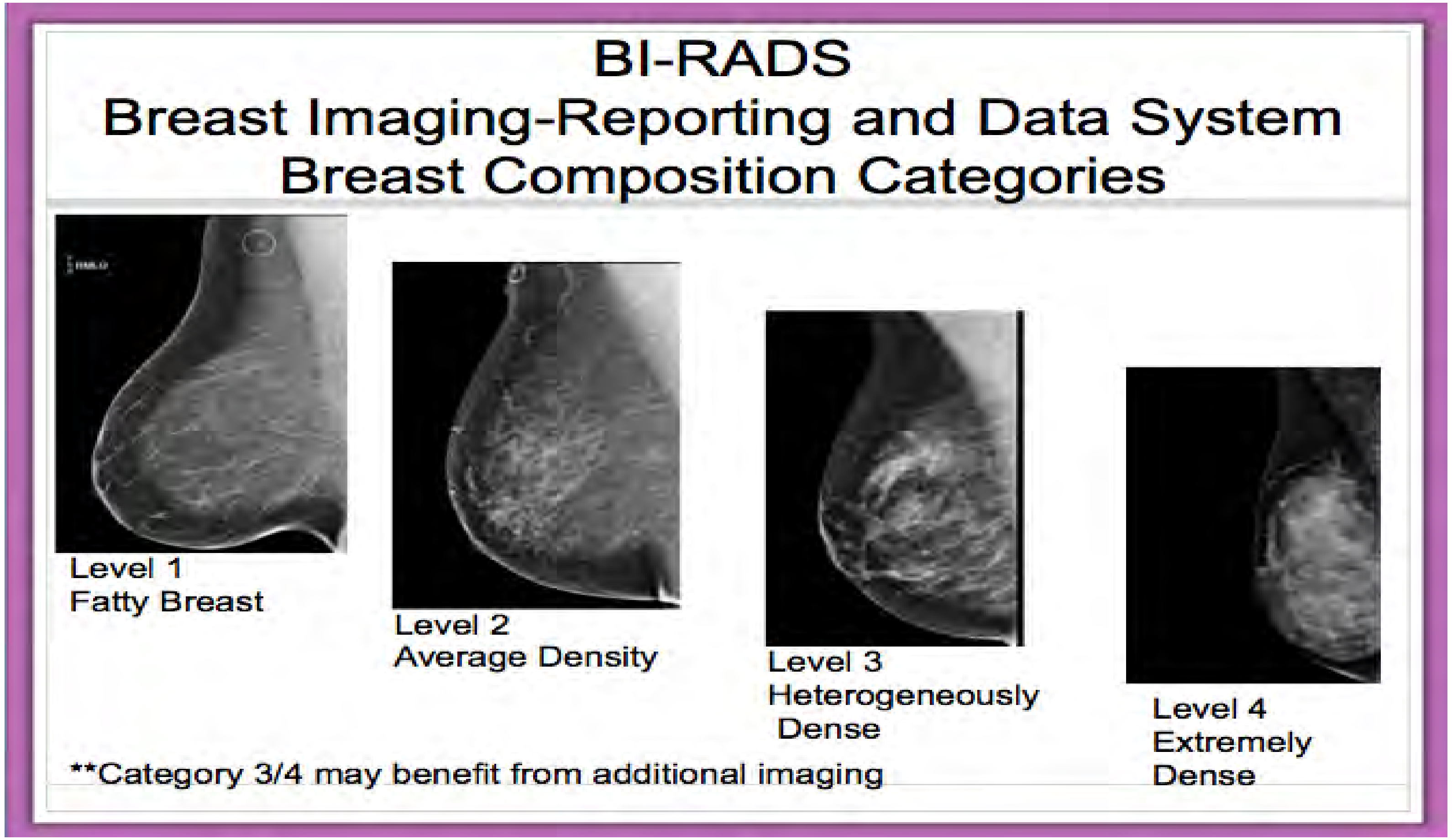
- The main tissue types in breasts are adipose tissue and stromal tissue, which contains collagen.

- The ratio of fat to collagen determines density of the breast.



Nature Volume: 490, Pages: 490–491 Date published: (25 October 2012)

Mammographic density



Categories of percentage mammographic density estimated by radiologists

A=0. B=10%. C=25%. D=50%. E=75%. F=75%.

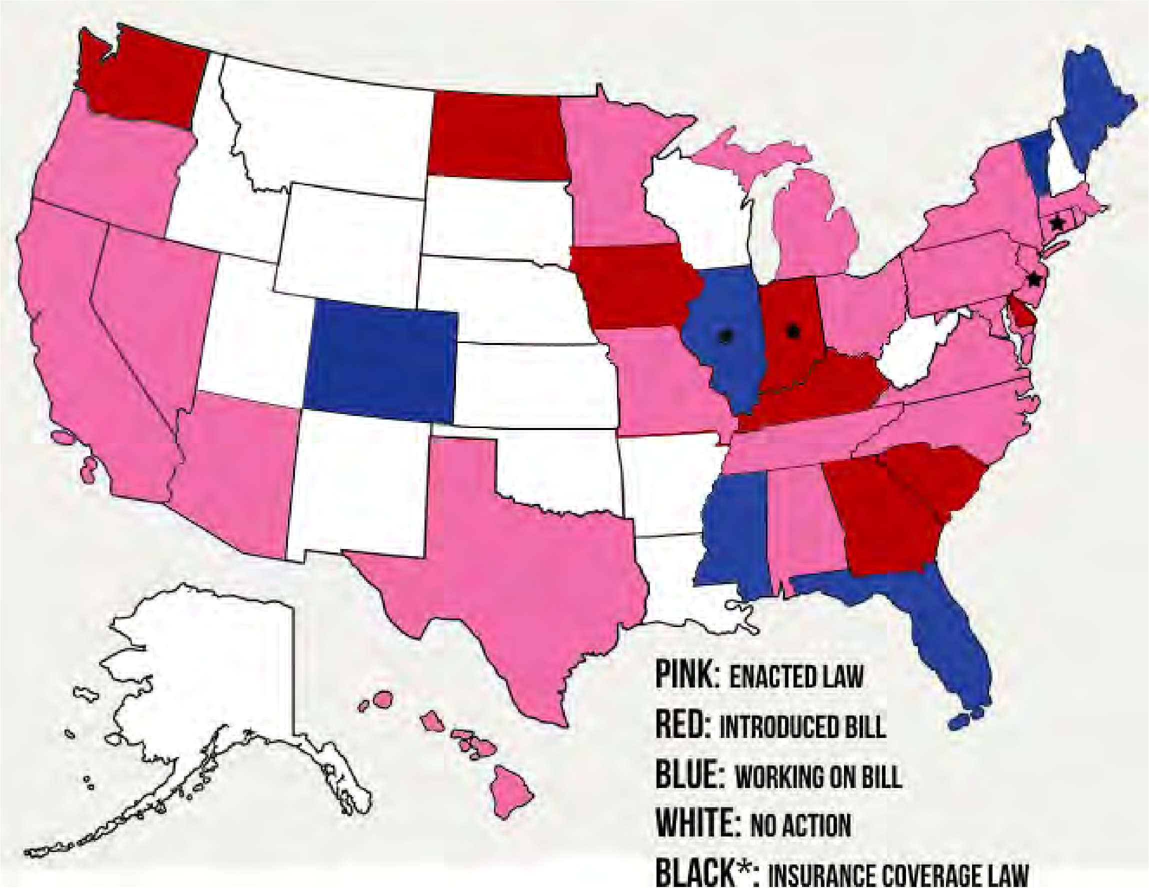
Boyd, et al. Lancet Oncol 2005; 6:10 798–808.

Breast density as a link?

- Women with greater than or equal to 75% breast density are at a four to six-fold greater risk of breast cancer compared to those with fatty breasts

Tamimi RM, Byrne C, Colditz GA, Hankinson SE. Endogenous hormone levels, mammographic density, and subsequent risk of breast cancer in postmenopausal women. J Natl Cancer Inst 2007; 99(15):1178–1187.
Boyd NF, Byng JW, Jong RA, et al. Quantitative classification of mammographic densities and breast cancer risk: results from the Canadian National Breast Screening Study. J Natl Cancer Inst 1995; 87(9):670–675.
Byrne C, Schairer C, Wolfe J, et al. Mammographic features and breast cancer risk: effects with time, age, and menopause status. J Natl Cancer Inst 1995; 87(21):1622–1629.
Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med 2007; 356(3):227–236

Legislation on breast density reporting



http://areyoudenseadvocacy.org/

Lifestyle factors

Alcohol consumption

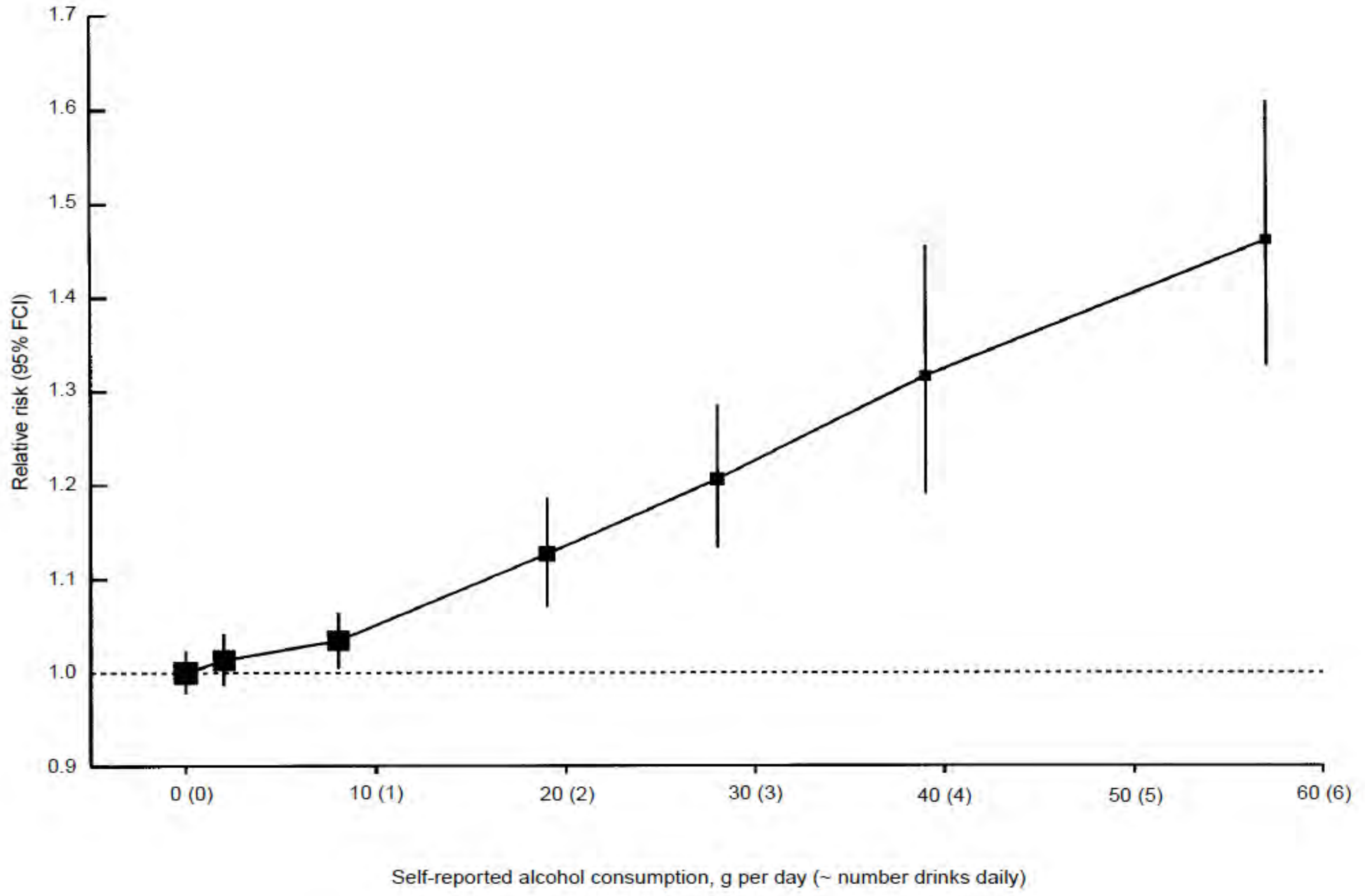


Figure 1 Relative risk of breast cancer in relation to reported intake of alcohol. Relative risks are calculated as floating absolute risk (FAR) and stratified by study, age, parity, age at first birth and smoking.

Alcohol, tobacco and breast cancer – collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the Disease
British Journal of Cancer (2002) 87, 1234 – 1245

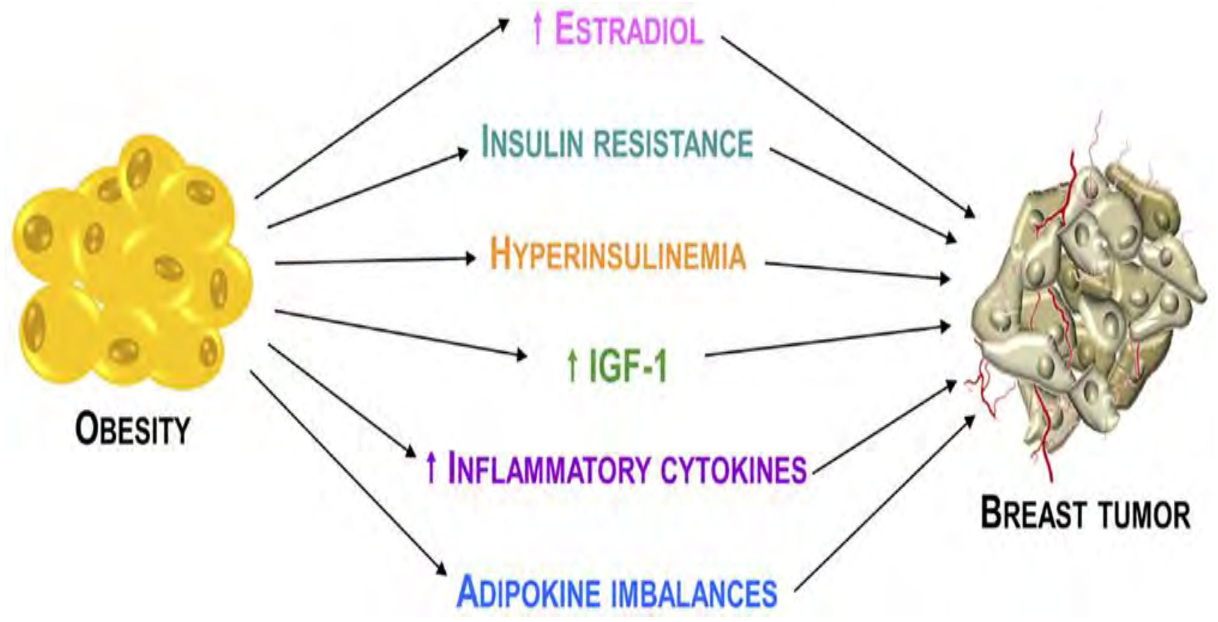
Limit Alcohol

1 alcoholic beverage per day

Shufelt C, et al "Red versus white wine as a nutritional Aromatase inhibitor in premenopausal women"
J Womens Health 2011; DOI:10.1089/jwh.2011.3001

Obesity and breast cancer

- Increased body fat increases risk in that fat produces more estrogen.

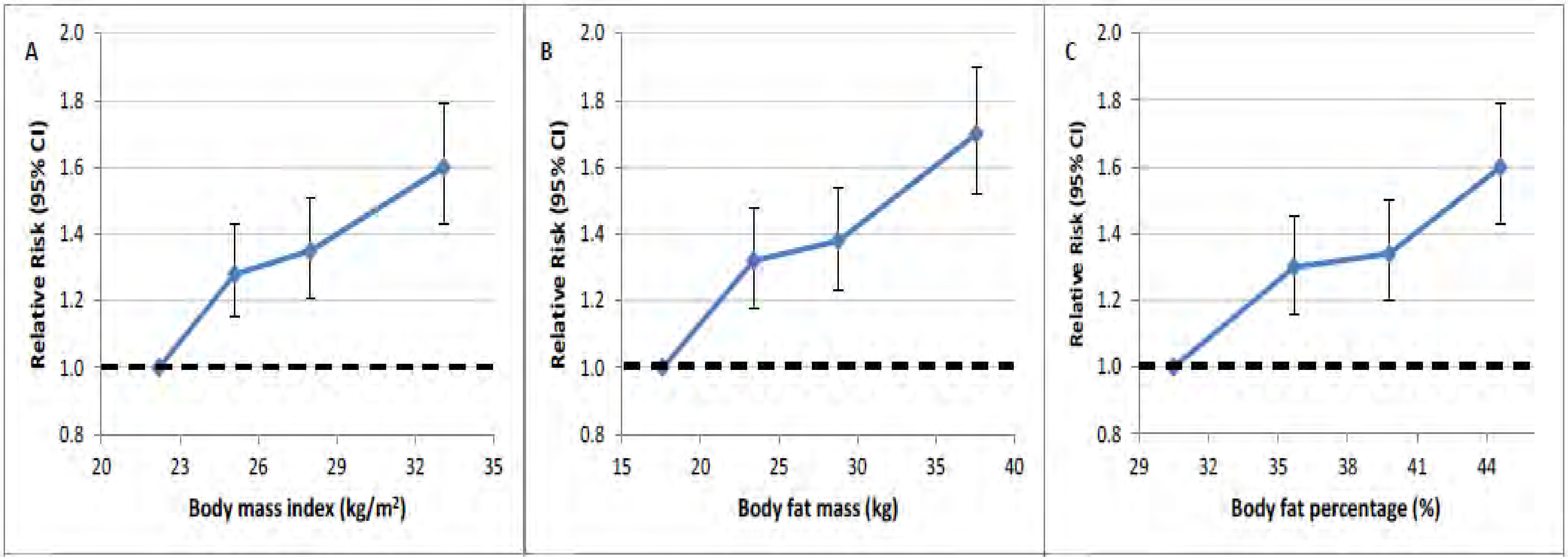


Relationship between obesity and breast cancer. Principal mechanisms through which the obesity condition may promote breast cancer development and progression.

Front. Oncol., 15 July 2015 | https://doi.org/10.3389/fonc.2015.00157

Adiposity and breast cancer risk in postmenopausal women: Results from the UK Biobank prospective cohort

Guo, et al. [Int J Cancer.](#) 2018



-162,691 postmenopausal women in UK Biobank followed from 2006-2014

-The magnitude of risk greater in women who had been postmenopausal for 12 or more years

Prevention with screening

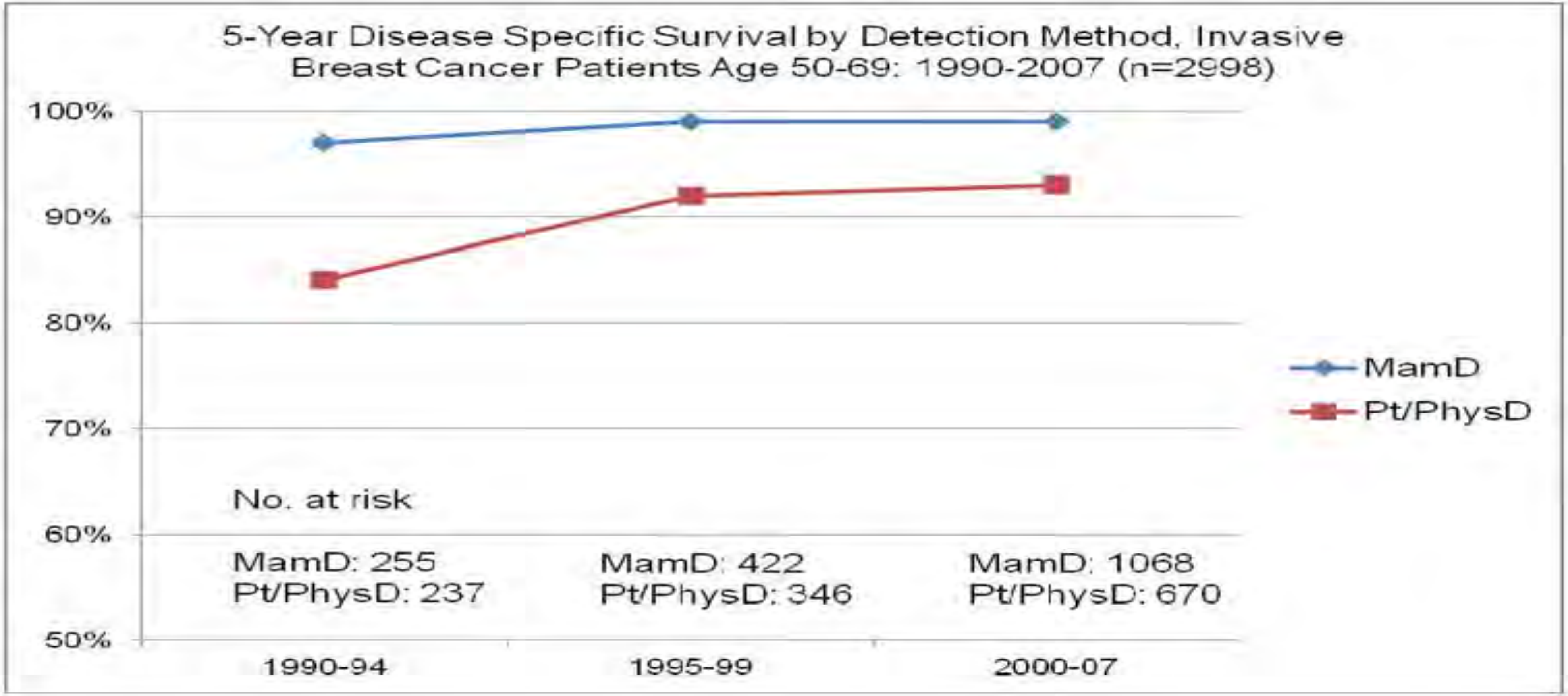
- Secondary prevention in the form of mammographic screening is recognized as an important strategy for reducing mortality from breast cancer.

- Mammography has been shown to reduce breast cancer mortality in women aged 50-69 years by as much as 30% .

- Younger women, ages 40-49, have also been shown to benefit from mammography with reduced breast cancer mortality.

- Loberg et al. **Benefits and harms of mammography screening** Breast Cancer Res. 2015; 17(1): 63

Survival rates from early detection

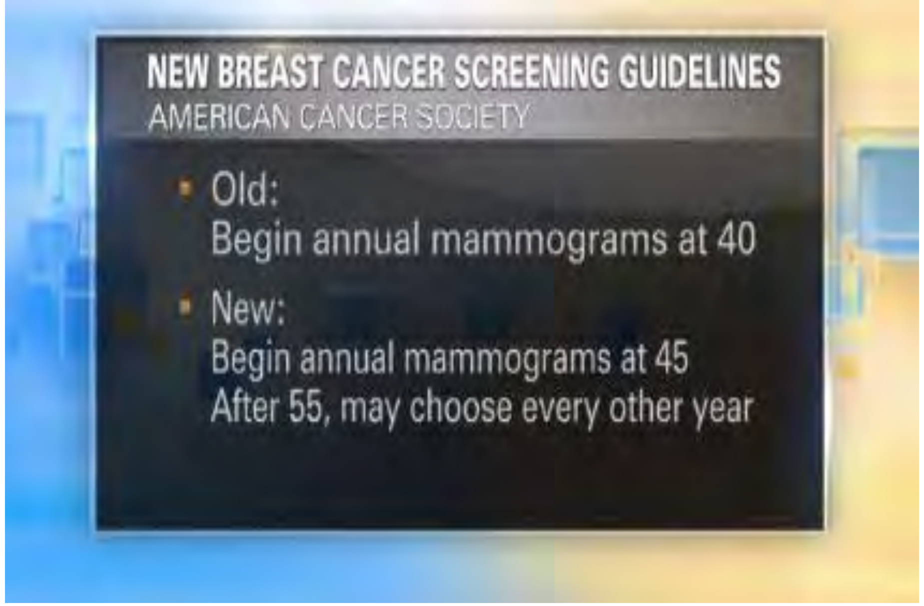


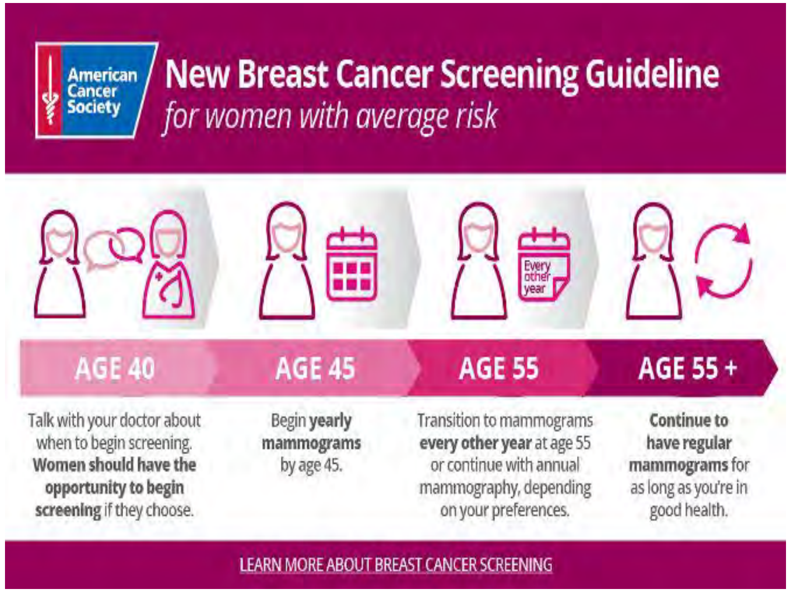
Kaplan et al. Cancer. 2015 Aug 1; 121(15): 2553–2561.

Breast cancer screening

- Tests can find breast cancer early, when it's most treatable
  - Clinical breast exam
  - Mammography screening

Recent Changes





Seeking Consensus on Mammograms

Some doctors are trying to reconcile various groups' recommendations for what age women should start getting mammograms and how often.

	USPSTF*	ACOG**	American Cancer Society
40s	No specific recommendation	Every year	45+ every year
50-74	Every two years	Every year	Every other year starting at 55
75+	No specific recommendation	No upper age limit for screening	Every other year while life expectancy is 10 years or more

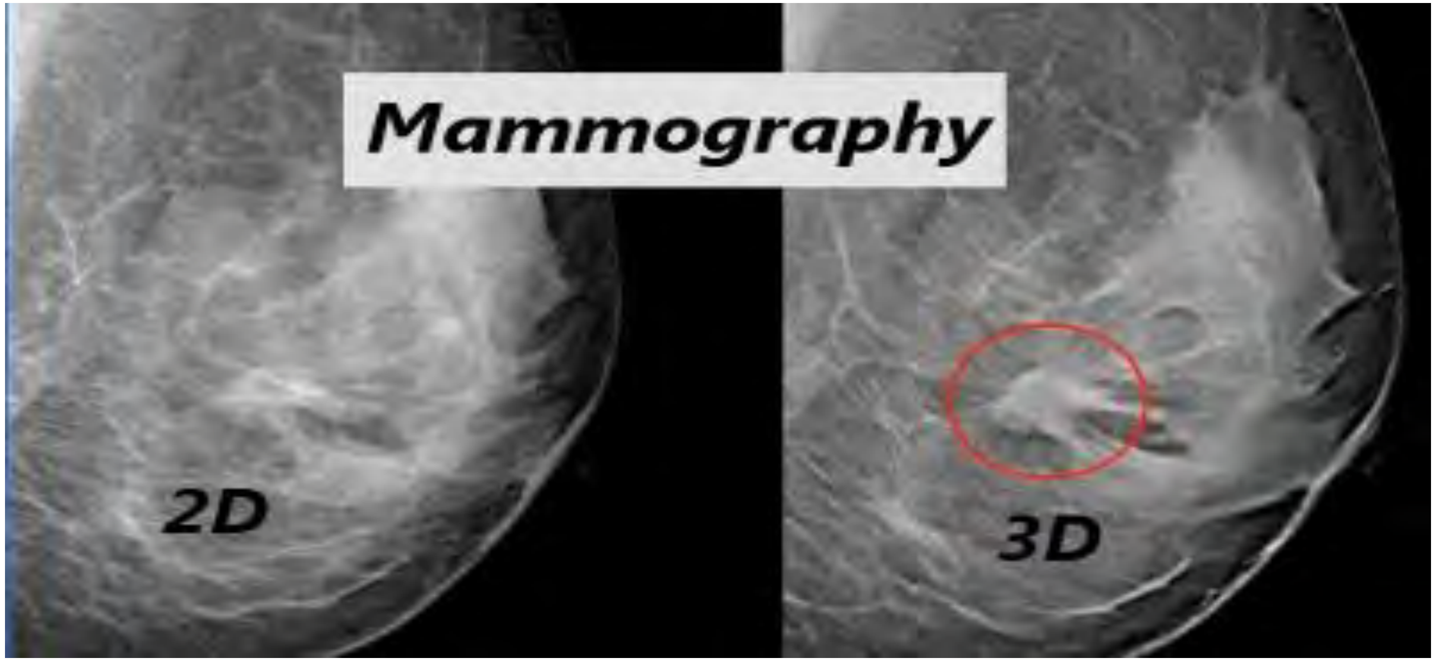
*U.S. Preventive Services Task Force
**American College of Obstetricians and Gynecologists

Controversities on screening

- Frequency
- Adopting advanced technology (i.e. 3D)
- Supplemental imaging

New technology

- Tomosynthesis (3D mammography)
- 4.1 cancers for every 1,000 patients vs. 2.9 cancers for every 1,000 patients with digital mammography alone. That's a more than 35 percent improvement in detection!



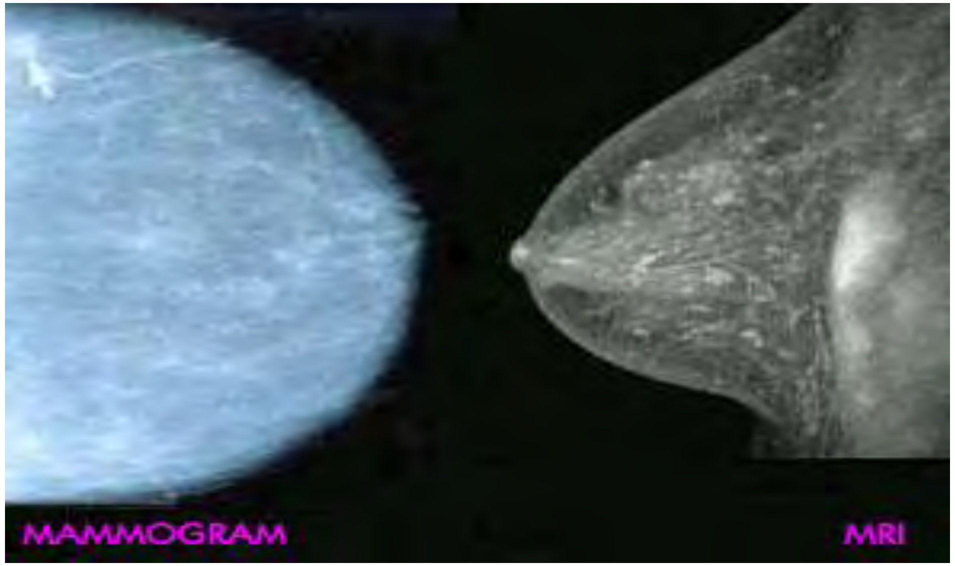
Friedewald, et al. **Breast Cancer Screening Using Tomosynthesis in Combination With Digital Mammography**
JAMA. 2014;311(24):2499-2507

Supplemental imaging?

- Ultrasound

Supplemental imaging?

- MRI



Current screening statistics

HP 2020 Target C-17: 81.1%
Source: Centers for Disease Control and Prevention, National Center for Health Statistics. National Health Interview Survey.
Data are age-adjusted to the 2000 US standard population using age groups: 50-64, 65-74.
Weighted regression lines are calculated using the Joinpoint Regression Program, Version 4.3.1.0 April 2016, National Cancer Institute.
The AAPC is the Average Annual Percent Change and is based on the APCs calculated by Joinpoint.
* The Annual Percent Change (APC)/Average Annual Percent Change (AAPC) is statistically significant.

- A recent systematic review and meta-analysis of racial disparities in screening mammography shows that disparities in utilization of screening mammography are still evident in black and Hispanic populations in the U.S.

- Ahmed, et al. Racial disparities in screening mammography in the United States: A Systemic Review and Meta-analysis. J Am Coll Radiol 2016.

Barriers to mammography

- Poverty, lower education, worse health status, no insurance or absence of private insurance, not having a regular source of care, and fewer physician visits

- In addition, lack of knowledge of breast cancer and breast cancer screening, cultural beliefs/fatalism, bad experience from prior mammograms, and lack of social support

Komenka IK, JNCI 2010
Stanley S, J Public Health 2012

Conclusion

- To improve breast cancer outcomes in women we need to:
  - Stress prevention:
    - Follow screening guidelines
    - Healthy lifestyle
    - Increase awareness and education, with focus on black and Hispanic women who continue to have lower screening rates

Acknowledgements

- My mentor Dr. Lucile Adams Campbell- Director of Minority Health and Health Disparities
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