Controversies in breast cancer screening

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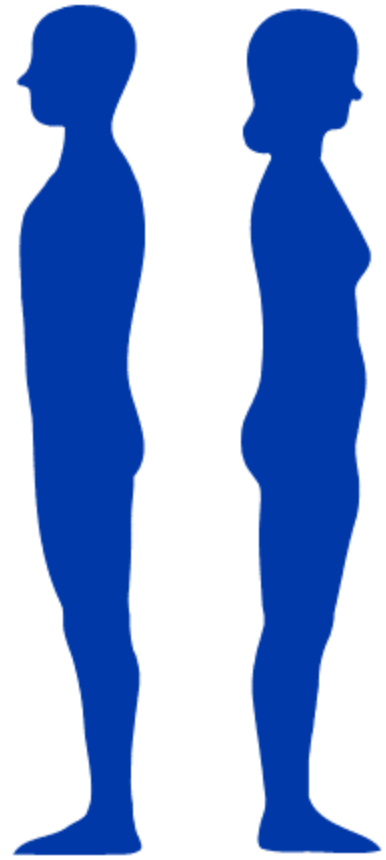
Objectives

- Ø Epidemiology of breast cancer
- Ø Genetics and breast cancer
- Ø Risk factors for breast cancer
- Ø Breast cancer screening as part of breast health
- Ø Screening options and the issue of dense breasts

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.

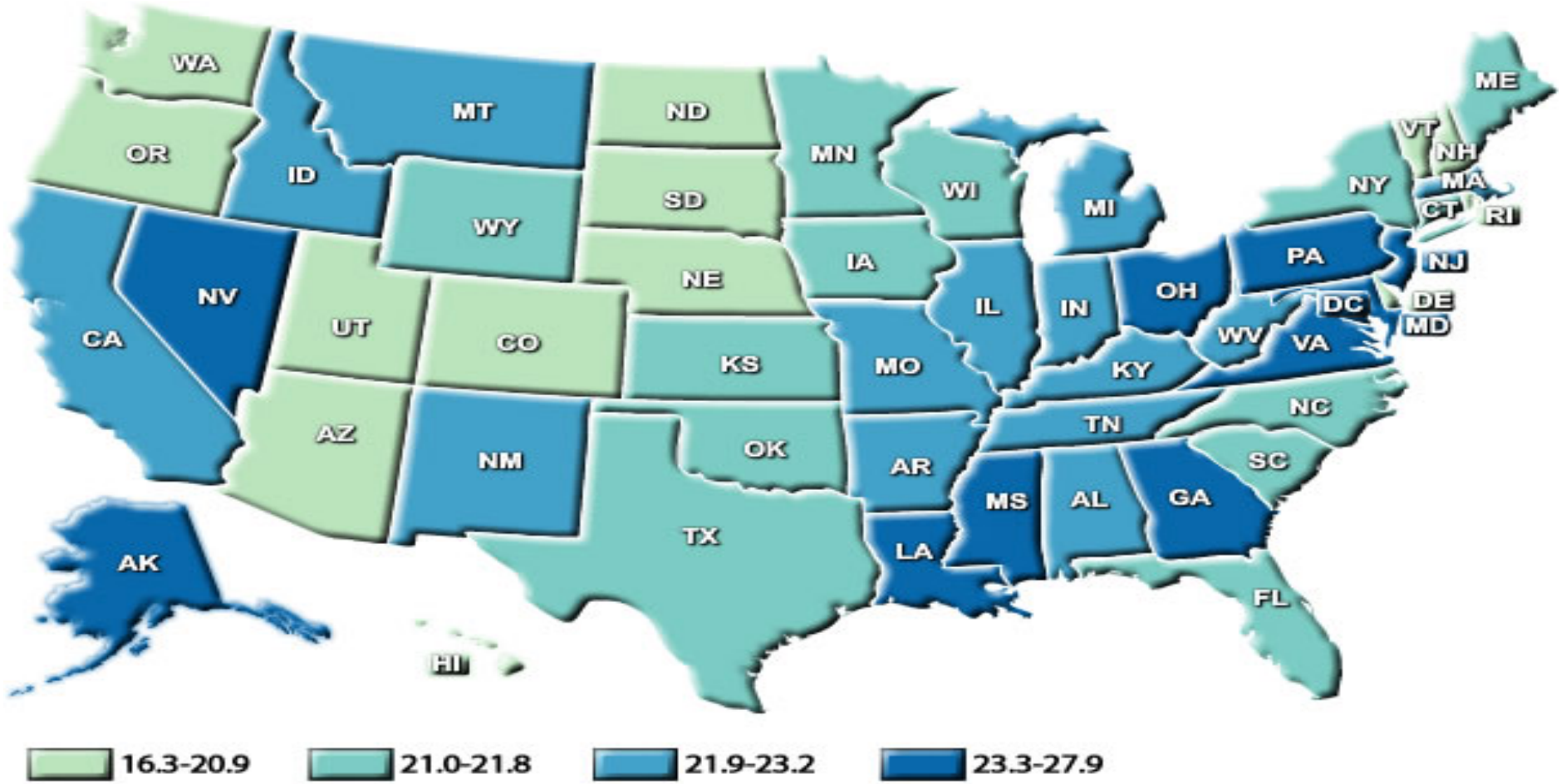
Statistics

- Breast cancer most common form of cancer for females
- Estimated that 178,480 females diagnosed
- 40,460 women will die in 2007
- 1 in 8 women diagnosed in their lifetime
- Every three minutes a female in U.S. diagnosed

Breast specific data

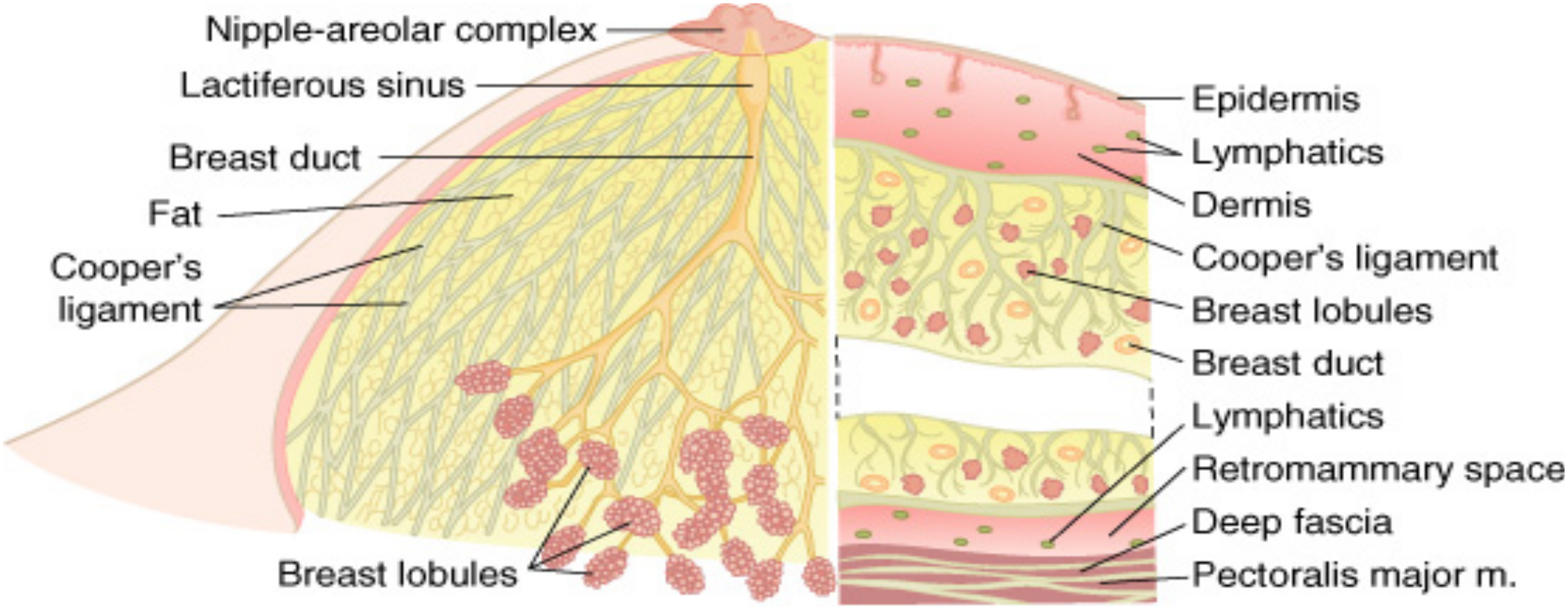
- Breast cancer is the most commonly diagnosed cancer in U.S. women (1/8)
- 2nd leading cause of cancer death
- In 2016, est. 246,660 new cases of invasive breast cancer are expected
  - 61,000 new cases of non-invasive (in situ)
  - 40,450 breast cancer deaths
- 1% of breast cancers are in men

Female Breast Cancer Incidence Rates* by State, 2009†



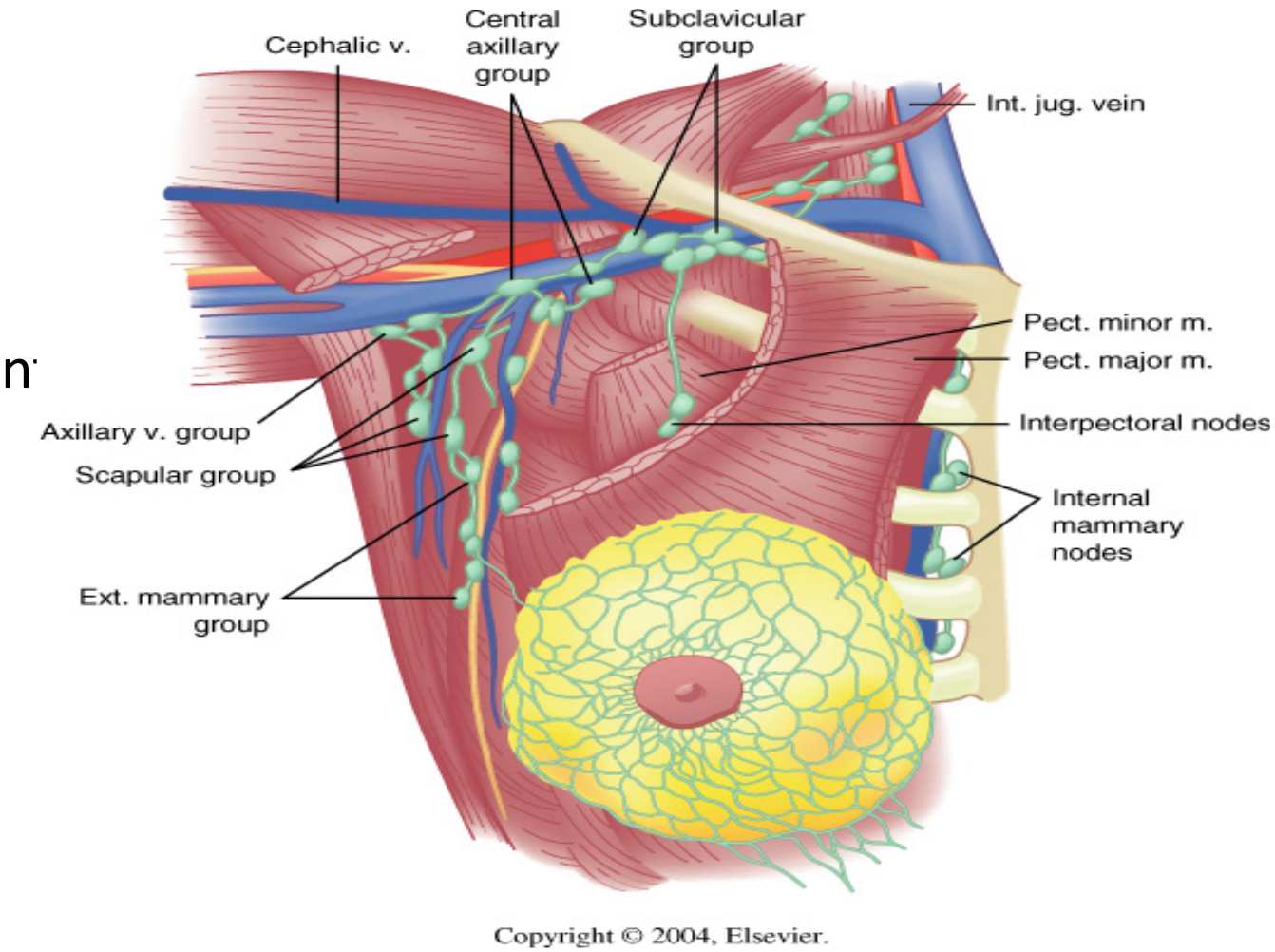
Breast cancer development

Anatomy of the Breast

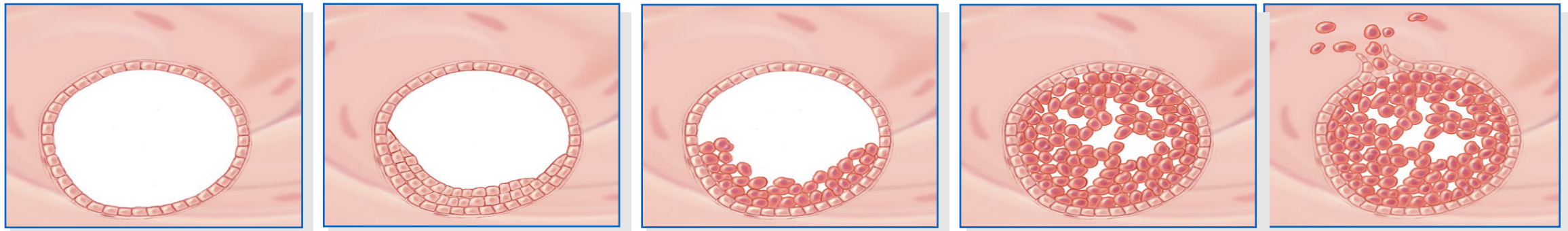


Lymphatics

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



Breast cancer



Normal Duct

Intraductal Hyperplasia

Atypical Ductal Hyperplasia

Ductal Carcinoma *In Situ*

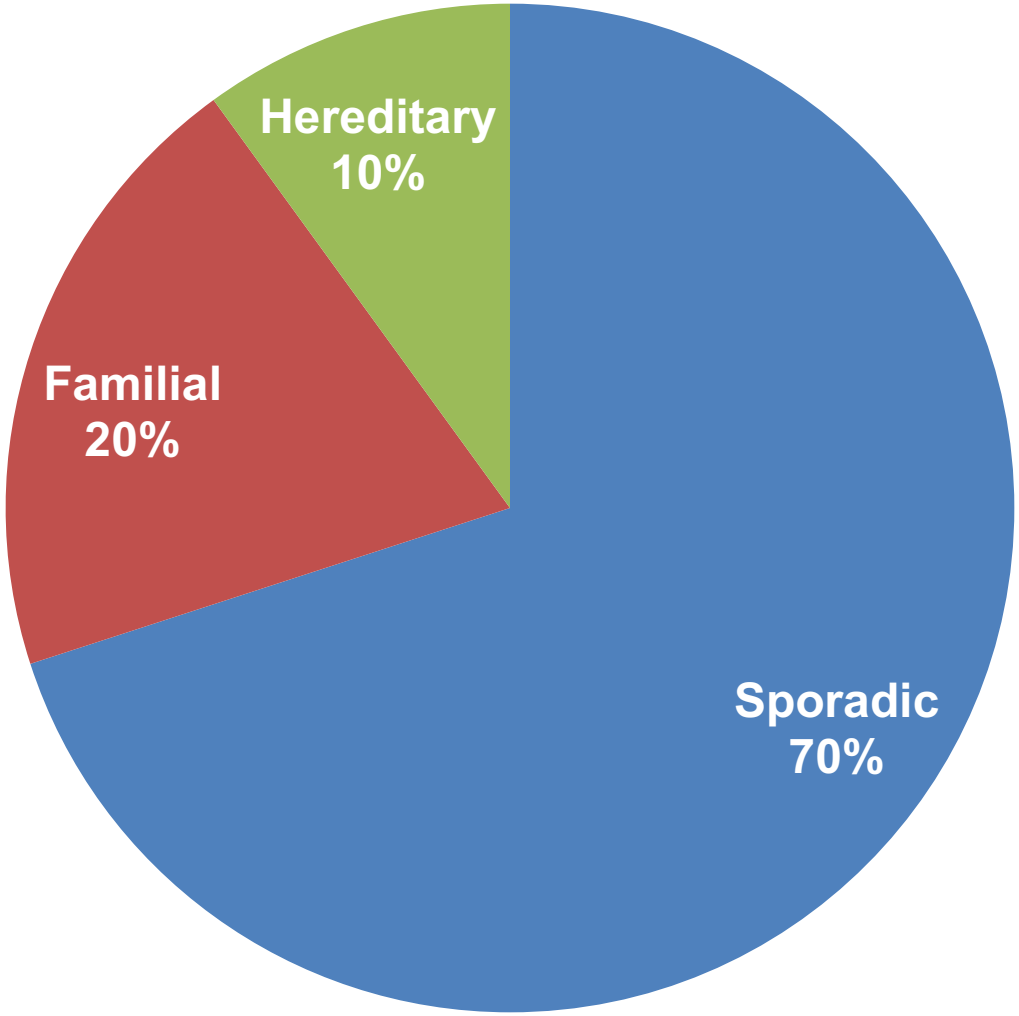
Invasive Ductal Carcinoma

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

Risk factors

Georgetown University Hospital
MedStar Health

BREAST CANCER RISK



BRCA Genes

- 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%
**FBC = familial breast cancer			Total	50%

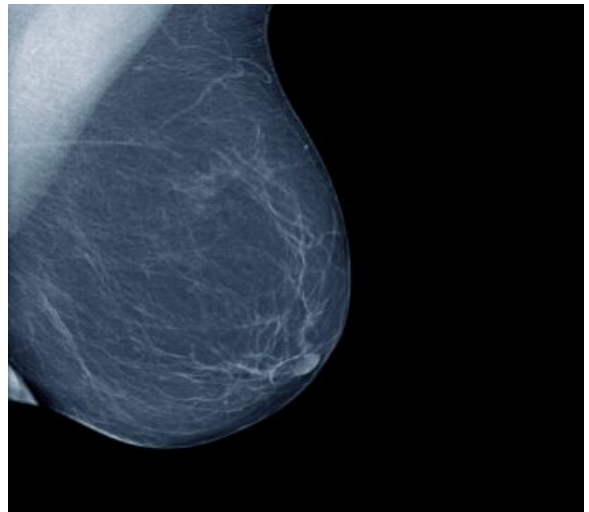
General risk factors

- 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)
- Obesity

Prevention with screening

Breast cancer screening

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



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

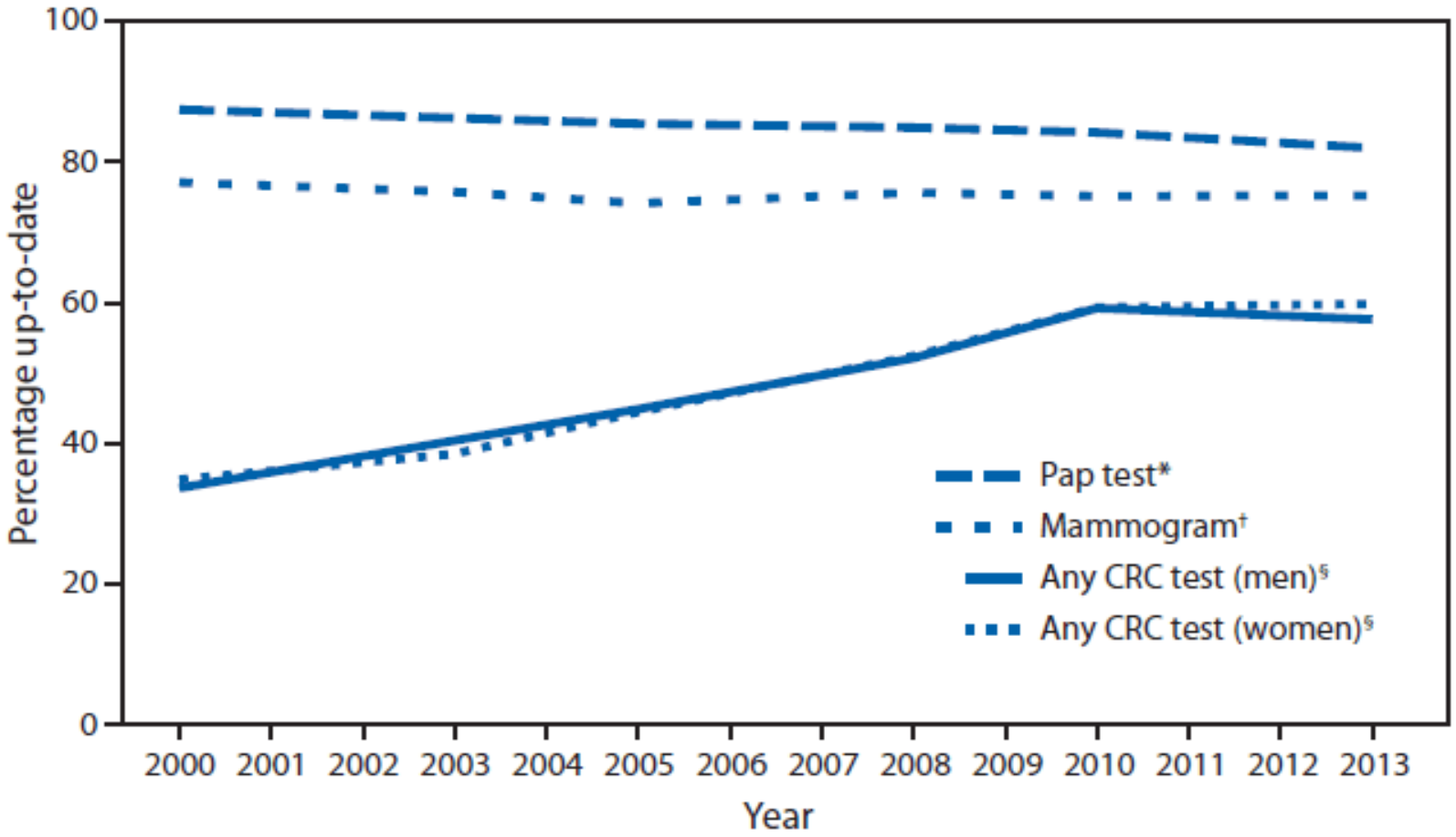
- Mammography has been shown to reduce breast cancer mortality in women aged 50-69 years by as much as 30% .

- 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

- A Healthy People 2010 goal set by the U.S. Departments of Health and Human Services was at least 70% of women 40 and over to have received a mammogram within the last two years.

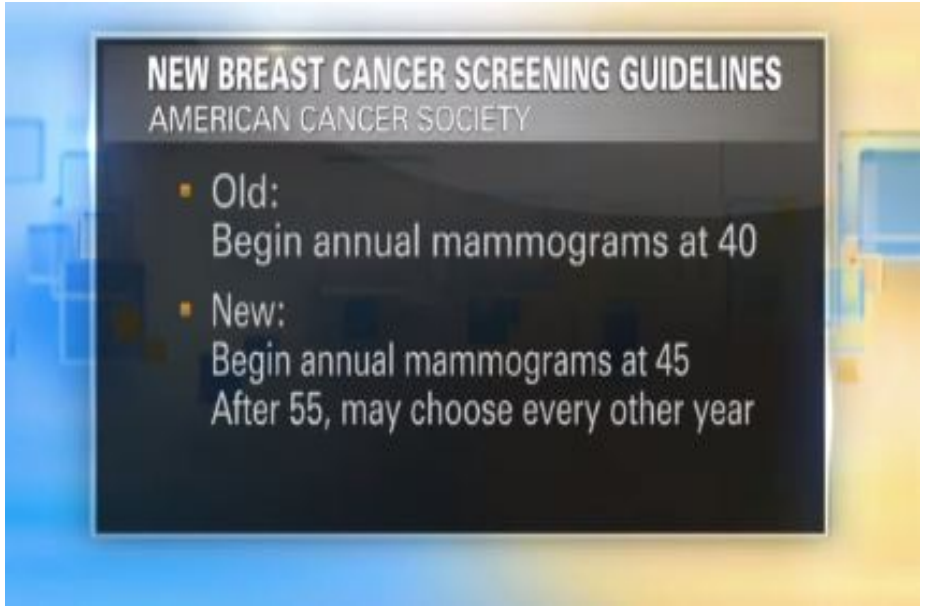
- Healthypeople.gov

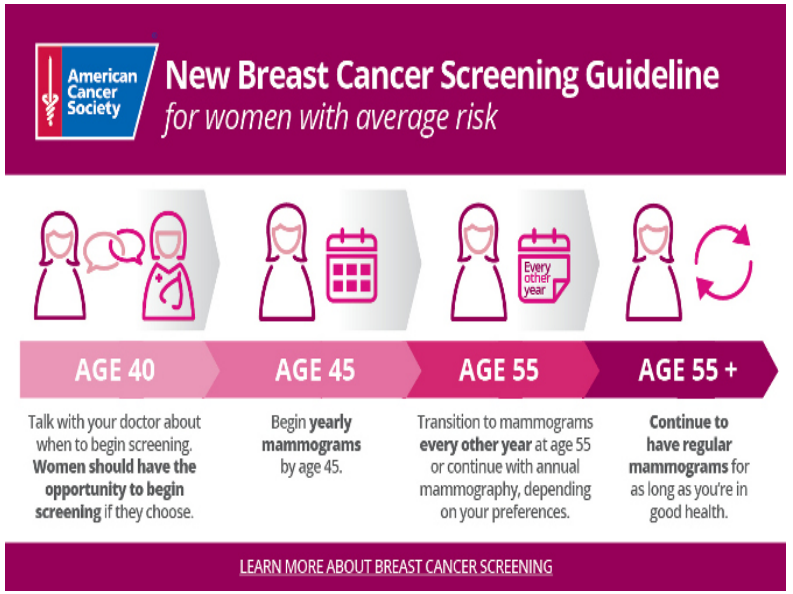


The figure above is a line chart showing the percentage of adults up-to-date with screening for breast, cervical, and colorectal cancers by test, sex, and year, in the United States during 2000-2013.

Sabatino et al. MMWR / May8,2015 / Vol.64 / No.17

Recent Changes





Oeffinger KC et al, *JAMA* 2015

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

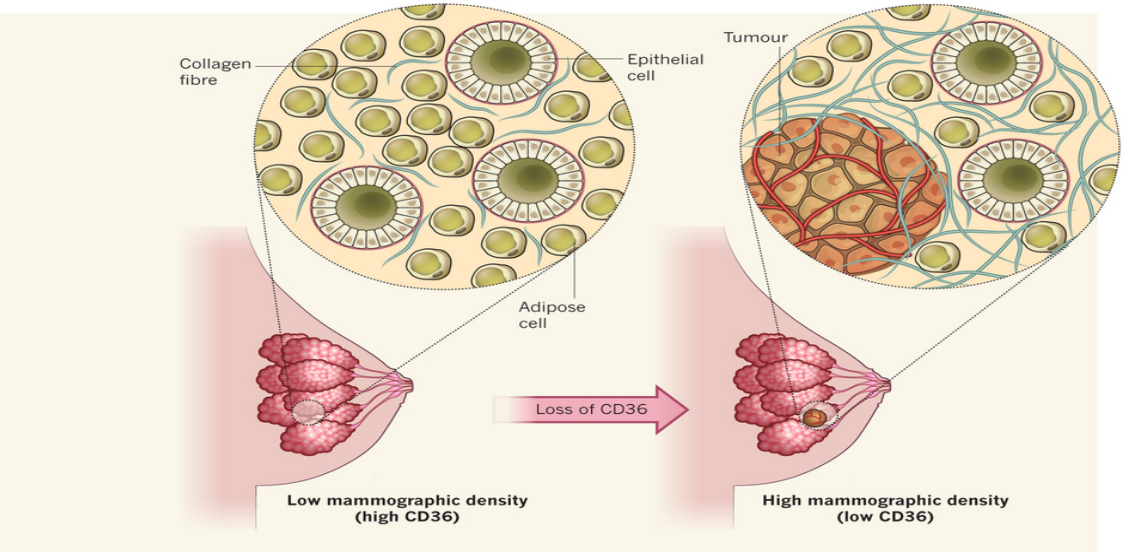
*U.S. Preventive Services Task Force
**American College of Obstetricians and Gynecologists

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.



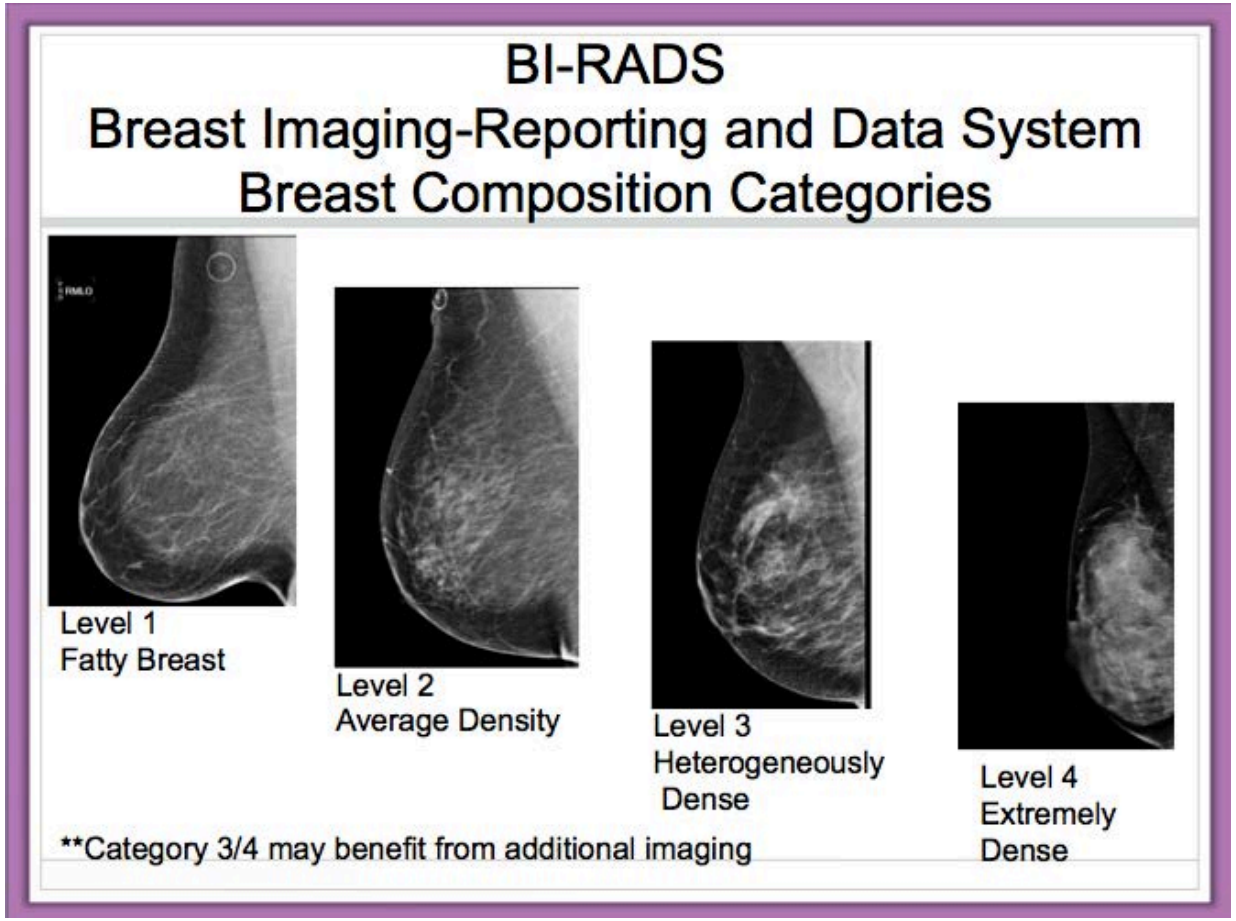
Nature Volume: 490, Pages: 490–491 Date published: (25 October 2012)

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

Mammographic density

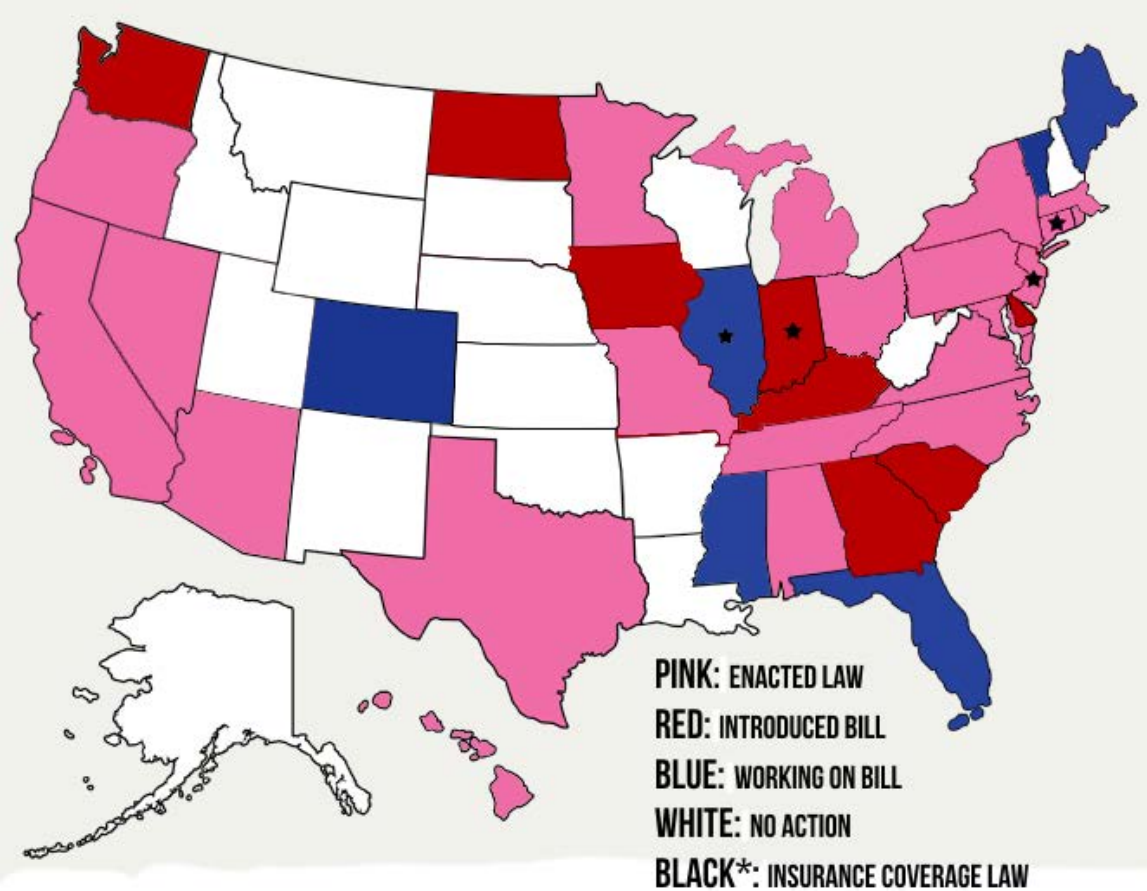


Categories of percentage mammographic density estimated by radiologists

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

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

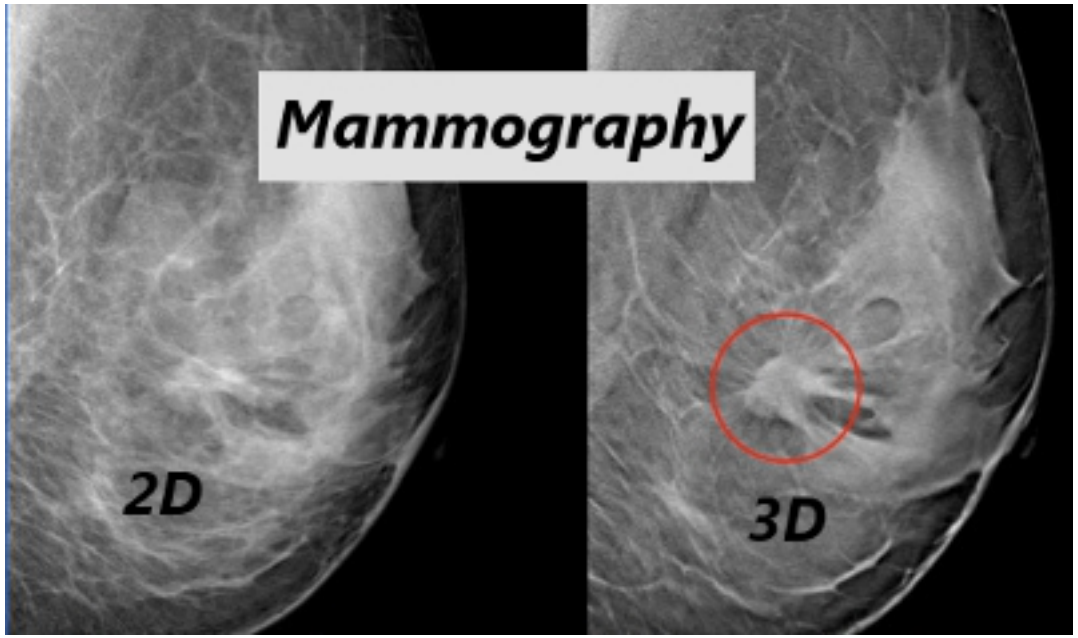
Legislation on breast density reporting



http://areyoudenseadvocacy.org/

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!



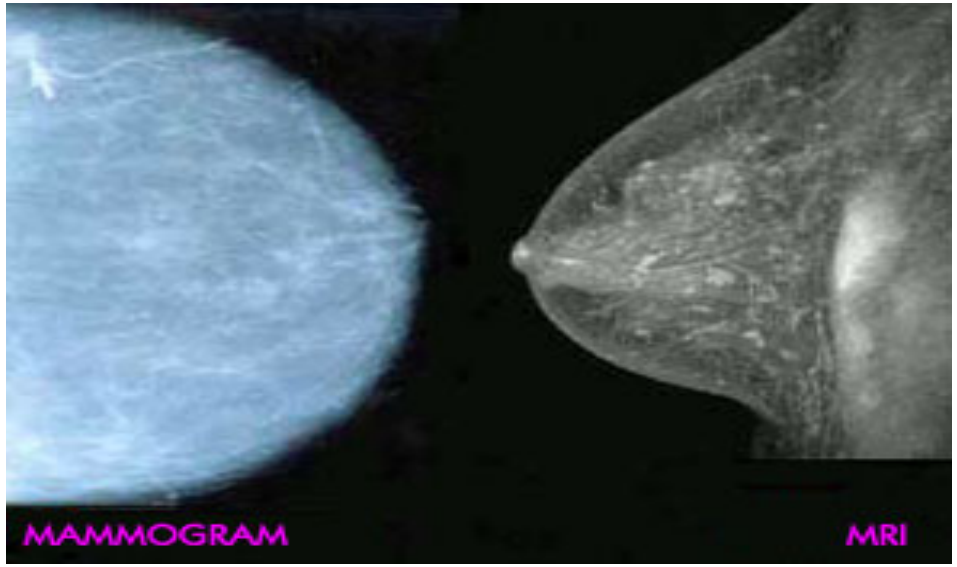
Friedewald, et al. **Breast Cancer Screening Using Tomosynthesis in Combination With Digital Mammography**
JAMA. 2014;311(24):2499-2507

Supplemental imaging?

- Ultrasound

Supplemental imaging?

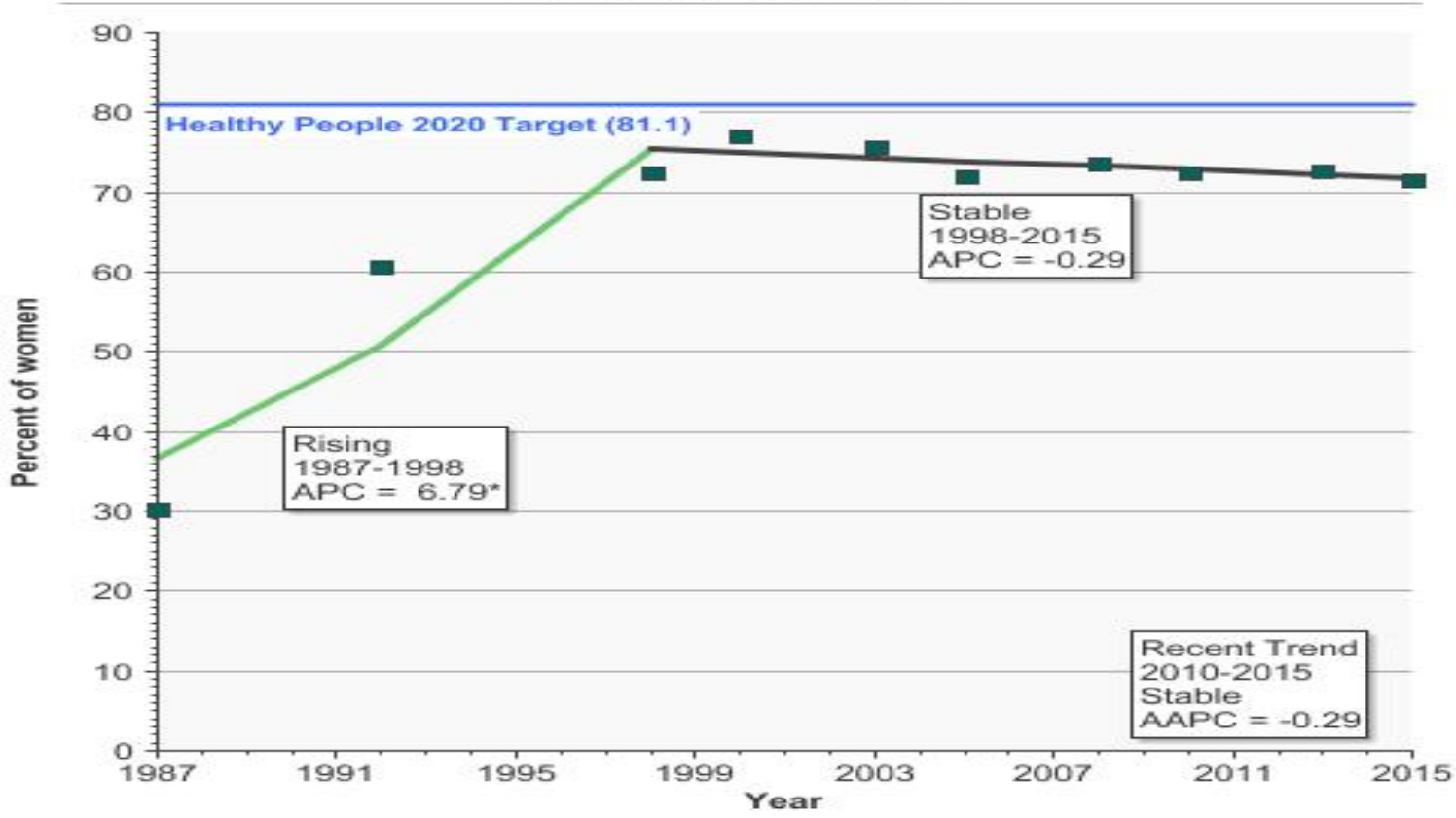
- MRI



Current screening statistics

Healthy People 2020

Percent of women aged 50-74 years who had mammography within the past 2 years, All Races, 1987-2015



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

- 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
- Emphasis should now be on addressing unacceptably low mammography utilization in certain subgroups within the black community

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
- Capital Breast Care Center

Capital Breast Care Center

OF GEORGETOWN LOMBARDI COMPREHENSIVE CANCER CENTER