Breast Cancer and Breast Disease

Are we overscreening?

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Learning Objectives

- Discuss the epidemiology of breast disease.
- Review factors in breast cancer prevention.
- Use an evidence-based approach to recommendations in evaluating breast disease.
- State the USPSTF recommendations on screening for breast cancer.

Breast Cancer

- Most common cause (with exception of skin) of cancer in women in the US and the 2nd leading cause of cancer death
  - 1/8 women will develop breast cancer (12%)
    - 5-year survival rate 90%
  - 1/36 will die (3%)
    - Death rates have been dropping since 1989 with larger decreases in women younger than 50
      - Thought to be the result of earlier screening, increased awareness and better treatments
- Breast cancer is the leading cause of death from cancer in women worldwide
- Risk assessment tools can identify the risk of breast cancer, and patients at high risk may be candidates for risk-reducing medications
  - choice of medication varies with menopausal status

48 yo female

HPI:
10 days – right breast lump
Denies pain, skin changes, or nipple discharge.

No family history of breast cancer

Mammogram – BiRADS 3

U/S 3.4cm spiculated mass

U/S guided Core BX:
Invasive ductal CA (Clip placed)

Histology:
ER(+), PR(+), her2neu (-)

Adjuvant chemo prior to surgery

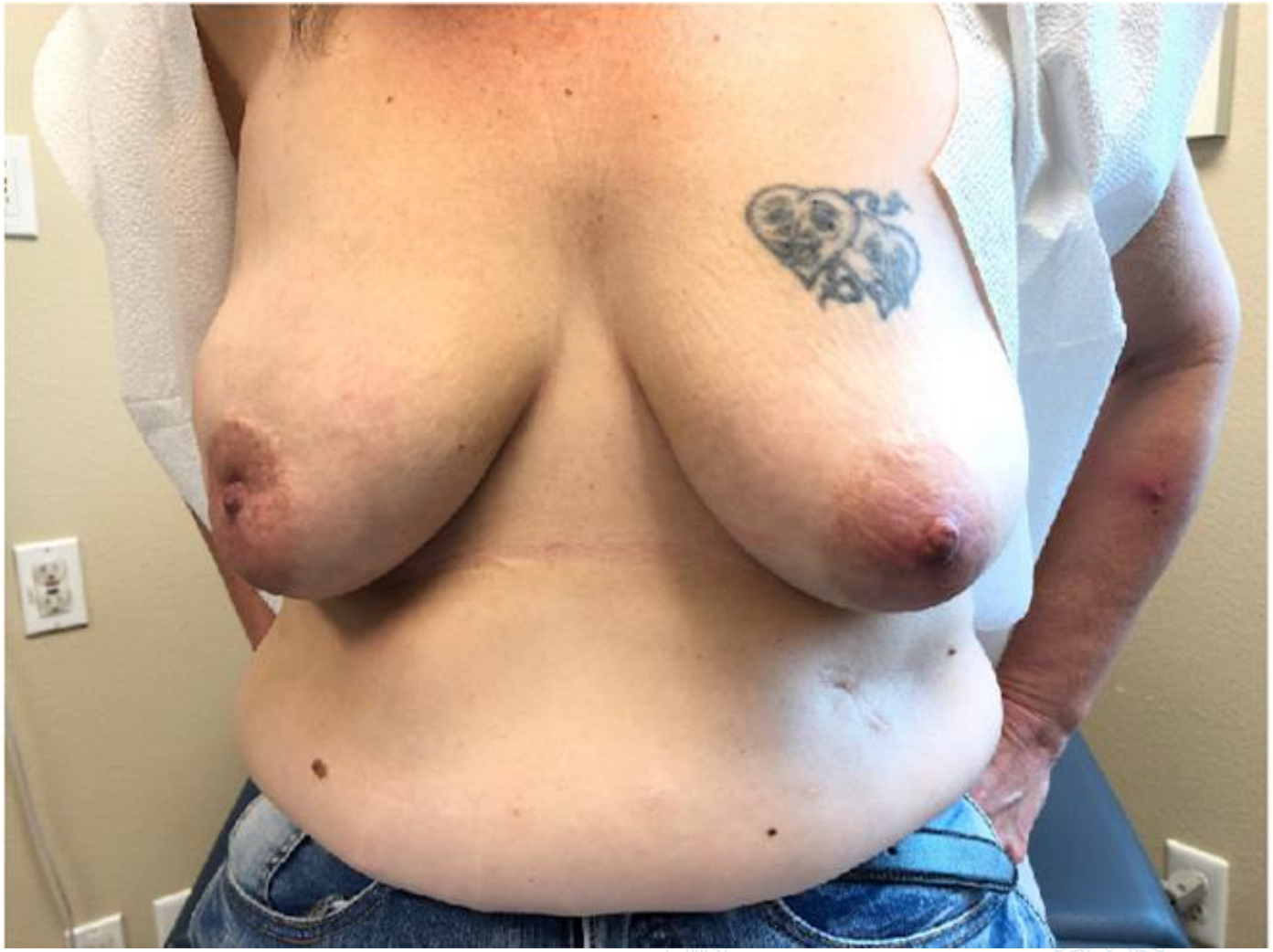
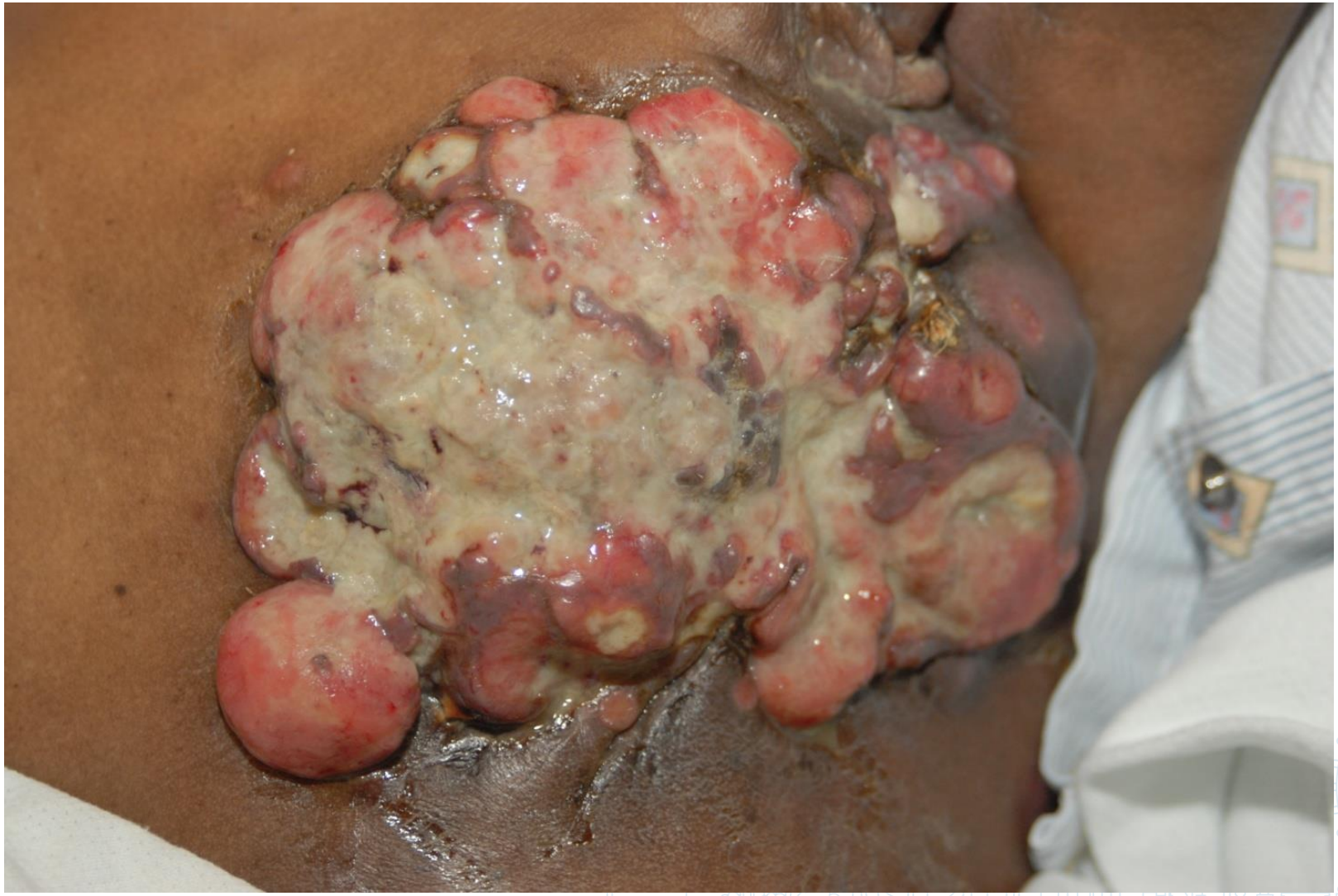
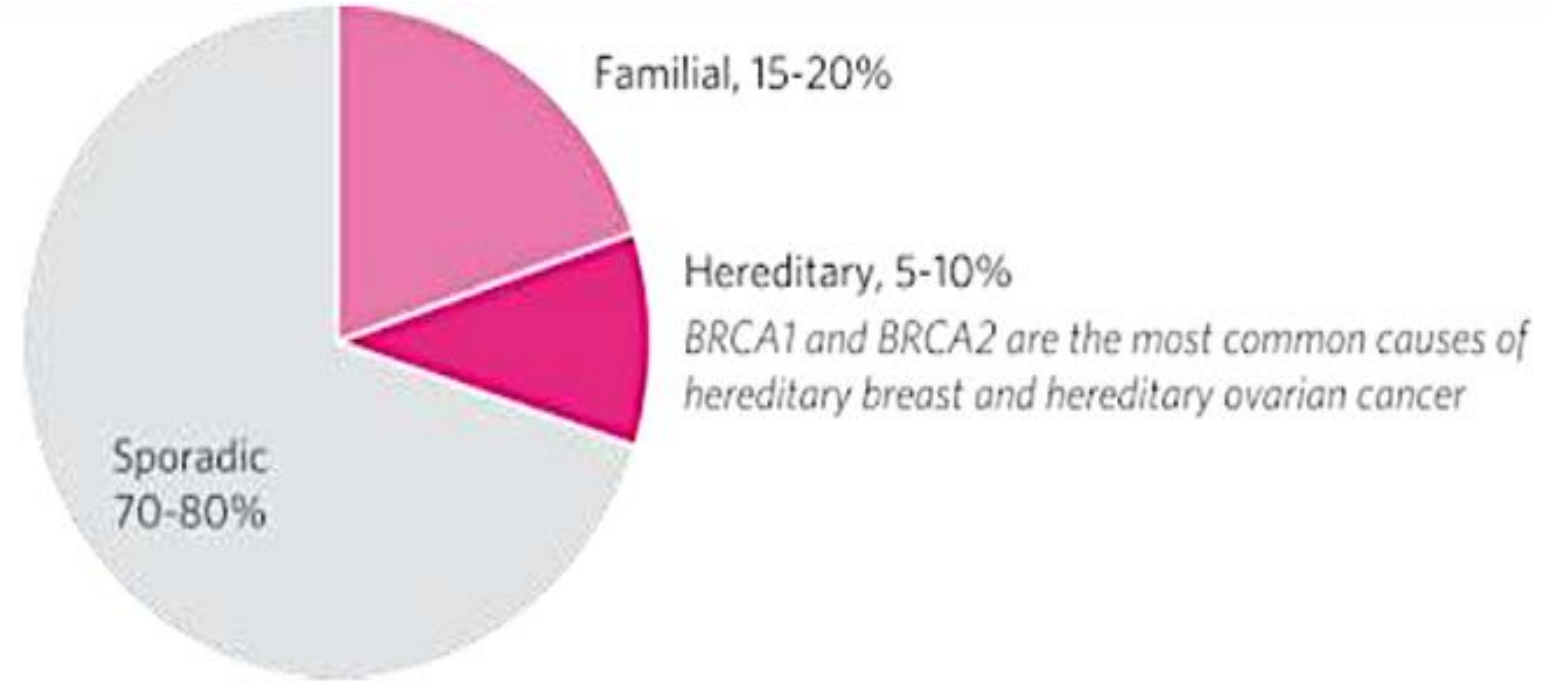


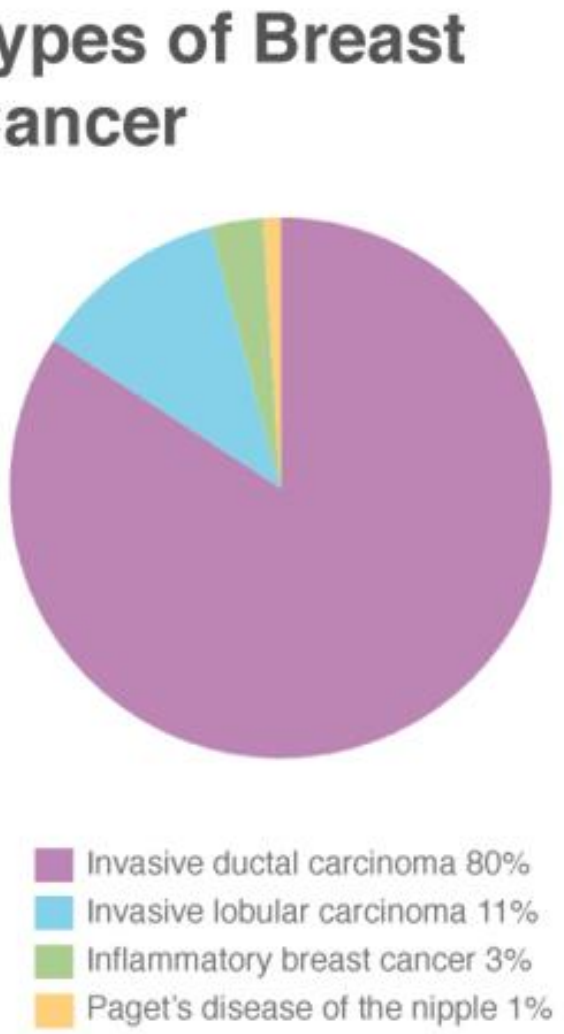
Photo Courtesy: David Glenn Weismiller, MD, ScM, FAAFP

Breast Cancer



Breast Cancer Type Breakdown





Communication

- Survivorship Care Plan (SCP)
  - Patient-Centered communication tool to improve the quality of follow-up care for survivors
  - IOM recommends that, after primary treatment, all patients receive an SCP
    - Treatment summary
    - Individualized follow-up plan that makes clear which physician will be responsible for carrying out the plan

Breast Cancer: Screening

(USPSTF – 2016; Topic Update in Progress)

Population	Recommendation	Grade
Women aged 50-74 years	Biennial screening mammography for women aged 50 to 74 y.	B
Women aged 40-49 years	Decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40-49y	C
Women aged 75 years or older	Current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older.	I
All women	Current evidence is insufficient to assess the benefits and harms of digital breast tomosynthesis (DBT) as a primary screening method for breast cancer.	I
Women with dense breasts	Current evidence is insufficient to assess the balance of benefits and harms of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging, DBT, or other methods in women identified to have dense breasts on an otherwise negative screening mammogram.	I

Question 1

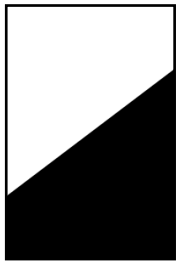
Sarah, a 45-year-old woman, presents to her family physician for a wellness visit. She has no significant past medical history and no family history of breast cancer. She leads a healthy lifestyle, exercises regularly, and has no complaints. During the conversation, Sarah mentions that she has never had a mammogram before and asks about the necessity of screening for breast cancer. Based on the best scientific evidence which one of the following statements is true when considering **1000 women** who start mammography at **40 years compared with 50 years**?

A. Five women diagnosed with breast cancer will not die.
B. More than 500 more women will have a false-positive test result.
C. Ten women will be diagnosed and treated for breast tumors that would not have caused symptoms or problems or needed treatment.
D. 27 more women will have breast biopsies with normal results.

USPSTF *Draft* Statement – May 2023

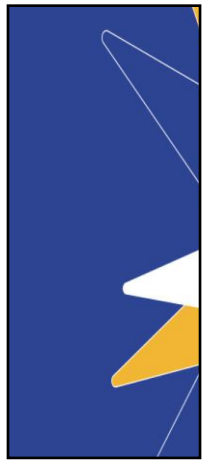
- Recommends all women should get screened for breast cancer every other year, starting at age 40.
  - This applies to women at average risk of breast cancer
  - Includes:
    - People with a family history of breast cancer
    - People with other risk factors, e.g., dense breasts
- Imaging –both are effective
  - Digital Mammography (DM) – images of the breast with X-rays from 2 angles
  - Digital breast tomosynthesis (DBT or 3-D mammography) – Images breast with X-rays from multiple angles

What did the USPSTF Systematic Review also say?



Most studies were performed in “White European” populations and called out the need for additional research to address the glaring disparities in diagnosis and outcomes for Black women in the US.

Did not explicitly support **changing** the 2016 USPTSF grade C recommendation for screening women between 40 to 49 years; **instead** cited its modeling study’s conclusions and increasing prevalence of breast cancer in younger women to justify this change.



Details the use of six sophisticated “microsimulation and analytic models ... in a hypothetical cohort of average-risk US 40-year-old female persons” and found that “strategies with biennial screening, start ages at 40 or 45, and cessation age 79 resulted in greater incremental gains in mortality reduction per mammogram compared with most strategies involving annual screening, start age 50, and/or cessation age 74.”

Unfortunately, breast cancers that occur in premenopausal persons (which is most of the most controversial 40 to 49 yoa group) tend to be more aggressive, diagnosed at a later stage, and result in early mortality.

(In fairness, the models in the modeling study did use age-adjusted data regarding cancer outcomes in their analyses, but not all of the models treated survival rates similarly.)

- If breast cancers in younger persons are, in fact, "etiologically distinct from breast cancers arising in older women," then the USPSTF's assumption that increasing screening in younger persons will result in improved outcomes just as it does for older women **may be** questionable.

Table 1. Lifetime Benefits and Harms of Biennial Screening Mammography per 1,000 Women Screened

Variable	*Median value for women age 40 to 74 years of age (range)*	*Median value for women age 50 to 74 years of age (range)*
Possible benefits		
Reduced breast cancer deaths	8 (5 to 10)	7 (4 to 9)
Life-years gained	152 (99 to 195)	122 (75 to 154)
Possible harms		
False-positive results	1,529 (1,100 to 1,976)	953 (830 to 1,325)
Breast biopsies that turn out to be normal	213 (153 to 276)	146 (121 to 205)
Overdiagnosed breast tumors	21 (12 to 38)	19 (11 to 34)

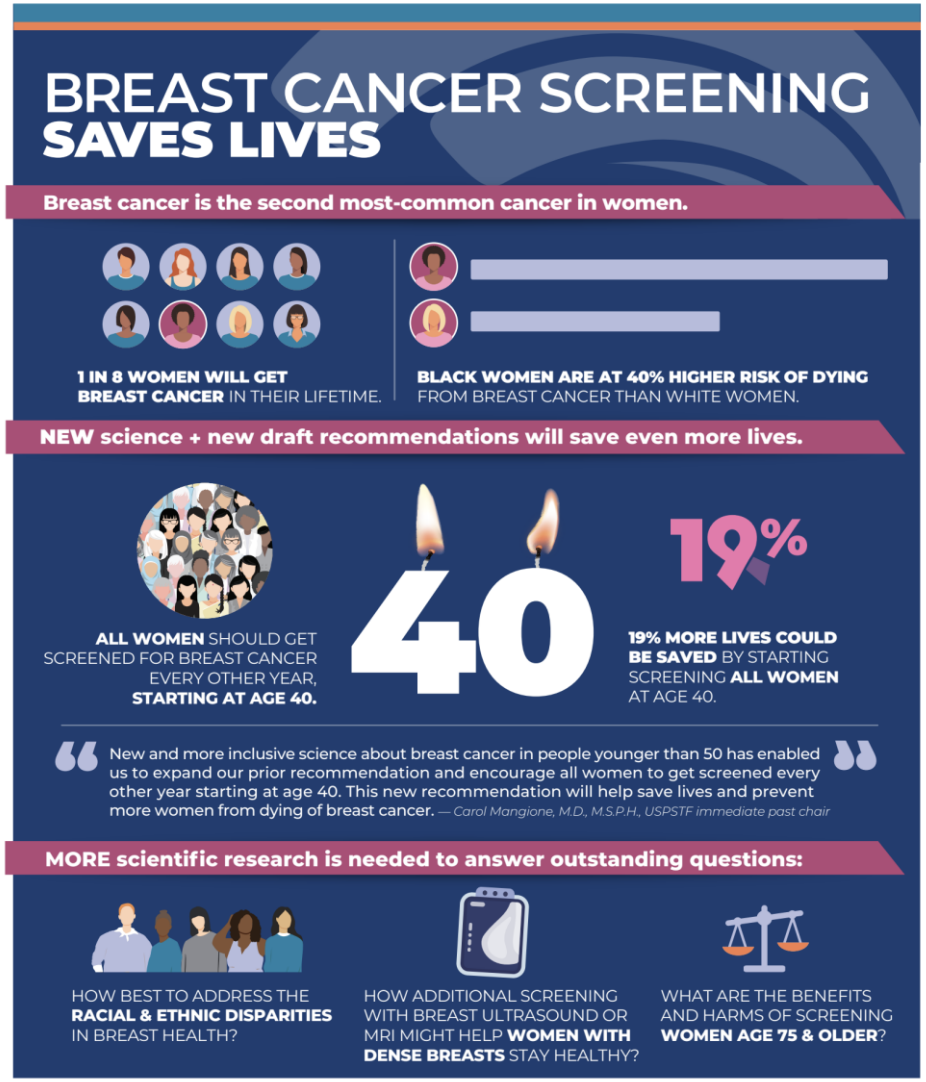
Adapted from U.S. Preventive Services Task Force. Final recommendation statement: breast cancer: screening. February 2016. http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/breast-cancer-screening1. Accessed March 3, 2016.

Ebell MH, Lin KW. Counseling Women About Breast Cancer Screening. Am Fam Physician. 2016 Apr 15;93(8):652-3. PMID: 27175837.

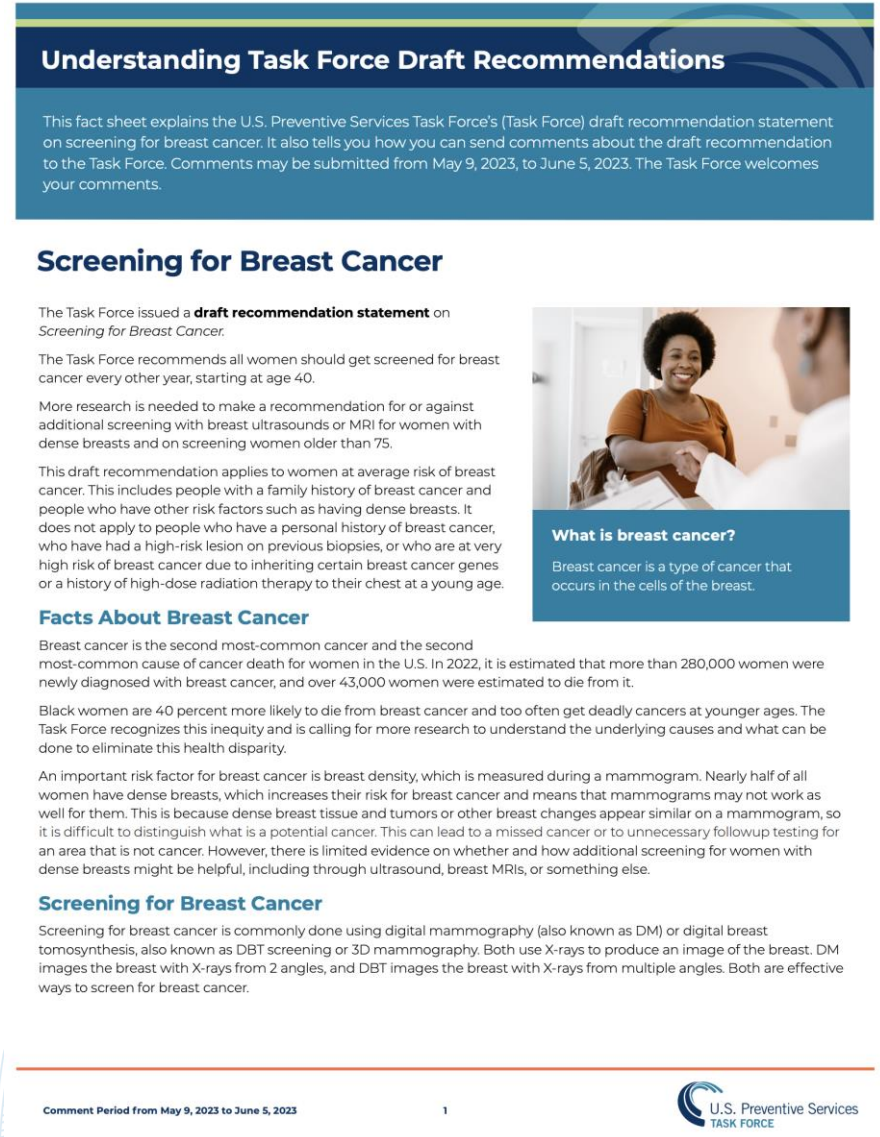
What to explain to women in their 40's…

- Based on the best scientific evidence, here are the potential benefits and harms for **1000 women** who start mammography at **40 years compared with 50 years:**

• **One woman diagnosed with breast cancer will NOT die**
• **576 more women will have a false-positive test result** Patients are called back for more imaging because something unusual was seen on the first mammogram, but it turns out not to be cancer.
• **67 more women will have breast biopsies with normal results**
• **Two women will be diagnosed and treated for breast tumors that would not have caused symptoms or problems or needed treatment** Over diagnosed breast tumor: Some cancers (about one out of five) grow very slowly, to the point where they would never have caused symptoms or problems, and the patient would have eventually died of something else. Finding and treating these tumors in women who get mammograms leads to unneeded worry and treatment.



https://www.uspreventiveservicestaskforce.org/files/breast-cancer/Breast_Cancer_DRS_infographic.pdf



https://www.uspreventiveservicestaskforce.org/files/breast-cancer/Breast_Cancer_DRS_Consumer_Guide.pdf

Breast Cancer

- Most common cause (with exception of skin) of cancer in women and the 2nd leading cause of cancer death
  - 1/8 women will develop breast cancer
  - 1/36 will die
- Presence of dominant inherited cancer susceptibility genes (BRCA 1 and BRCA 2) occur in about 1/300-500 of general population
  - Screening for inherited risk (USPSTF 2013)
    - Assessment of risk for significant BRCA mutations
    - Genetic testing of high-risk women (Level A)
  - The lifetime risk of breast cancer for a woman with a BRCA1 or BRCA 2 mutation is 65-74%

USPSTF

August 2019

- Recommends that primary care clinicians assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer **or** who have an ancestry associated with breast cancer susceptibility 1 and 2 (*BRCA1/2)* gene mutations with an **appropriate brief familial risk assessment tool**. Women with a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing. B Recommendation
- Recommends AGAINST routine risk assessment, genetic counseling, or genetic testing for women whose personal or family history or ancestry is not associated with potentially harmful *BRCA1/2* gene mutations. D Recommendation

Screening Tools Evaluated by the USPSTF

Tool
Ontario Family History Assessment Tool
Manchester Scoring System
Referral Screening Tool*
Pedigree Assessment Tool
FHS 7*

** Simplest and quickest to administer*

Since 2005, family history risk stratification tools have been developed and validated for use in primary care practice to guide referral for BRCA genetic counseling. In addition, the potential benefits and harms of medications for breast cancer risk reduction have been studied for longer follow-up periods, and more information is available about the potential psychological effects of genetic counseling and risk-reducing surgery.

http://www.uspreventiveservicestaskforce.org/uspstf12/brcatest/brcatestfinalrstab.htm#tab1

Translation

- Family history that raises concerns about hereditary breast and ovarian cancer includes:
  - Ashkenazi Jewish heritage with a family history of breast and/or ovarian cancer
  - Breast cancer diagnosed before age 50
  - Both breast and ovarian cancer in the same family member
    - In a woman with breast cancer, the 10-year risk of developing ovarian cancer is 12.7% for women with a BRCA1 mutation and a 6.8% for women with a BRCA2 mutation.
  - Bilateral breast cancer or multiple primary breast cancers
  - Male breast cancer
  - Breast cancer diagnosed before age 60 with triple-negative (estrogen-receptor negative, progesterone-receptor negative, HER2-negative) pathology
  - Known BRCA1 or BRCA2 mutation

Testing

- **Commercially available tests** for genetic sequencing are often **not approved for clinical use** and may **not** have adequate coverage of genes like *BRCA1/BRCA2* to rule out the presence of deleterious mutations
- A thorough personal and family history of breast and ovarian cancer should be obtained to help direct additional testing of the patient and possibly family members
  - It is important to refer patients like this to a medical genetics professional and affiliated genetic counselor for additional evaluation, given the complexity of such testing and the high stakes of false reassurance or unnecessary testing and treatment

BRCA1 or BRCA 2 Mutation

- **Can be considered for prophylactic oophorectomy and mastectomy**
  - Prophylactic therapy
    - Decreases incidence of breast and ovarian cancer
    - Inadequate evidence for mortality benefits
- ***Cancer Genetics Studies Consortium Recommendations for Screening***
  - Monthly BSE: Age 21
  - CBE q 6-12 m starting at age 25-35 years
  - Annual mammograms starting at age 25-35 years
  - Ovarian cancer screening (US, CA-125 levels) q 6-12 months starting at age 25-35 years

Risk Factors for Breast Cancer

(typically, a combination of factors)

- **Non-modifiable**
  - Gender
  - Age
  - Family history
    - Genetic ($BRCA_1$ or $BRCA_2$ or other
  - Personal History
  - Race
  - Radiation therapy to chest
  - Exposure to estrogen
    - Early menstruation
    - Late menopause (>55)
  - Pregnancy (>30 or never) and breastfeeding (1.5-2 years)
- **Modifiable**
  - Weight
  - Diet
    - Very low in fat?
  - Physical activity
  - Alcohol consumption
  - Smoking
  - Exposure to **progesterone**
  - OCP?

Hormone Therapy

*Women's Health Initiative Study**

- **Increased risk**
  - Breast cancer (26%)§
    - Not breast cancer deaths
  - CVA (41%)
  - MI (29%)§
  - Venous thromboembolic events*§
- **Proven benefits**
  - Reduced risk of osteoporosis and related fractures (34%)
  - Decreased colon cancer risk (37%)
  - Improvement of vasomotor symptoms

Previous thromboembolic disease is the only **ABSOLUTE contraindication to HT. Heart disease, breast cancer, and endometrial cancer are **RELATIVE** contraindications.*

*§ **Among women receiving estrogen ONLY, there was increased risk of thromboembolic events, but NOT an increased risk of CV events or breast cancer.***

** Writing Group for the Women's Health Initiative. JAMA. 2002;288:321-333.*

Timing of Screening

- Evidence indicates that biennial screening is optimal.
- Biennial schedule preserves most of the benefit of annual screening AND cuts the harms nearly in half.

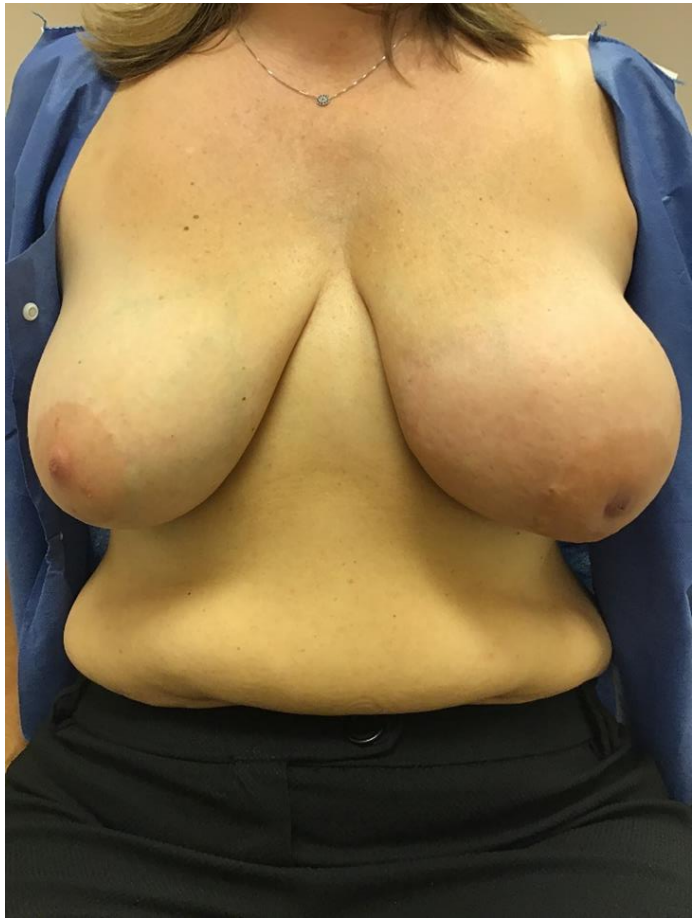
Breast Imaging Reporting and Data System Classification (BI-RADS) and Recommended Management

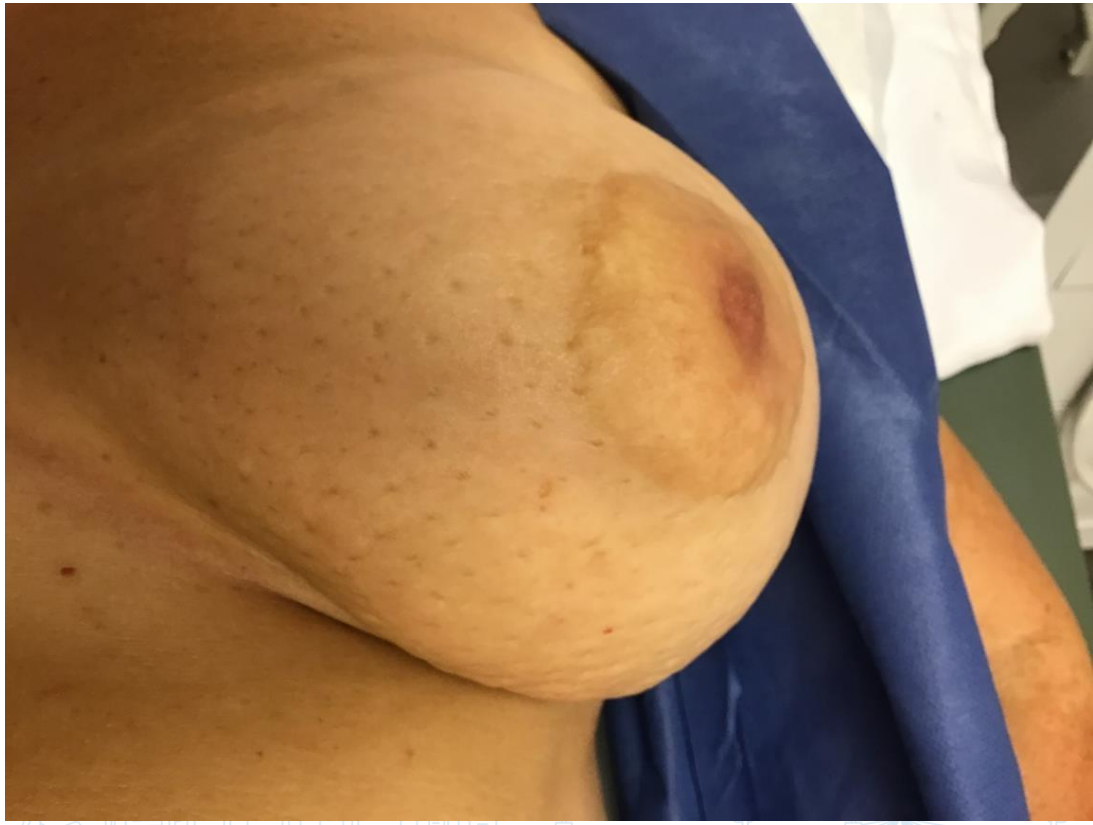
BI-RADS Assessment Category	Likelihood of Cancer	Management		
		Mammography	**Ultrasonography**	**MRI**
0: Incomplete – need additional imaging evaluation	N/A	Recall for additional imaging, comparison with prior examination(s) or both	Recall for additional imaging	Recommend additional imaging: mammography or targeted US
1: Negative	Essentially 0% likelihood of malignancy	Routine mammography screening	Routine screening	Routine breast MRI screening if cumulative lifetime risk ≥20%
2: Benign	Essentially 0% likelihood of malignancy	Routine mammography screening	Routine screening	Routine breast MRI screening if cumulative lifetime risk ≥20%
3: Probably benign	>0% but ≤2% likelihood of malignancy	Short-interval (6-month) follow-up or continued surveillance mammography	Short-interval (6-month) follow-up or continued surveillance	Short-interval (6-month) follow-up
4: Suspicious (4a-4c)	>2% but <95% likelihood of malignancy	Tissue Diagnosis		
5: Highly suggestive of malignancy	≥95% likelihood of malignancy	Tissue Diagnosis		
6: Known biopsy-proven malignancy	N/A	Surgical excision when clinically appropriate		

Breast Cancer
Screening Methods

- Breast self-examination (BSE)
  - Studies have not clearly demonstrated BSE as beneficial for cancer screening.
  - Any benefits must be balanced against potential harms – such as excessive invasive procedures performed as a result of the discovery of noncancerous lesions.
- Breast Self-Awareness?

BREAST SELF-AWARENESS

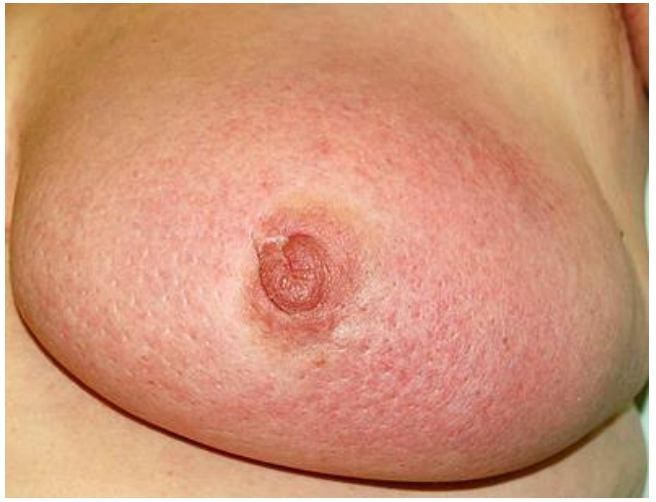




peau d'orange

Inflammatory Breast Cancer

(Non)lactational Mastitis



- Plugged ducts
- Galactoceles
- Inflammatory breast cancer
  - In inflammatory breast cancer, the skin examination will demonstrate thickening, erythema, peau d'orange, and there is often associated axillary lymphadenopathy
  - It is important to rule out inflammatory breast cancer if a suspected breast infection does not respond to antibiotics.

Breast Cancer
Screening Methods

- Clinical breast exam (CBE)
  - Insufficient evidence to recommend it as a singular screening modality.
  - RCTS demonstrate varying detection rates: 3%-57%.
  - Most advocates have supported CBE as a complementary technique to mammography.
  - About 5% of screening-detected cancers are found using CBE alone.

Recommendations of Others

Organization	Year	Recommendation
ACS	**2015**[§]	Women with average risk of breast cancer should undergo regular screening mammography starting at age 45. (45-54 years, annual; ≥55 biennial). **NO CBE for screening at ANY AGE**
AMA	2002	Similar to ACS, except for inclusion of a positive recommendation for BSE
AAFP	**2016**	Endorsed the USPSTF recommendation
ACOG	2011*	Mammography (Level B) and CBE (Level C) **annually starting at the age of 40**. No consensus on upper age limit of mammograms. **All women should be encouraged to practice breast "self-awareness."**
WHO	**2009**	Mammography q 1-2 years (Age 50-59). Does NOT recommend CBE or BSE

[§] *JAMA 2015;314(15)1599-1614.*
**Obstet Gynecol. 2011;118:372-382*

Screening Breast MRI

- The *American Cancer Society* recommends screening breast MRI (impact on breast cancer mortality is uncertain):
  - Women with BRCA1 or BRCA2 gene mutations
  - Women with a first-degree relative with BRCA1 or BRCA2 gene mutations who have not as yet had genetic testing
  - Women with a lifetime risk of more than 25% as defined by risk assessment tools largely dependent on family history
  - Women who underwent radiation to the chest between ages 10-30 for Hodgkin's disease
  - Women known to have a hereditary breast cancer syndrome, ie, Li Fraumeni, Cowden, and Bannayan-Riley-Ruvalcaba, and their first-degree relatives

Breast Cancer Screening

Conclusions

- Has resulted in an increase in diagnosis of localized disease without a commensurate decrease in the incidence of more widespread disease
- It cannot predict which of the discovered cancers are more aggressive, and cannot accurately detect premalignant lesions.
- <u>The decrease in the mortality rate of breast cancer is due BOTH to earlier detection and better follow-up medical care.</u>

2. A 53-year-old premenopausal female sees you to discuss chemoprevention after having a breast biopsy that showed atypical ductal hyperplasia. She is still having periods and her family history includes invasive breast cancer in a sister at age 48. After a conversation about risks and benefits of chemoprevention and possible side effects she decides to start medication to reduce her risk. *Which **ONE** of the following would you recommend for this patient?*

A. Combined oral contraceptives
B. Letrozole (Femara)
C. Medroxyprogesterone (Provera)
D. Raloxifene (Evista)
E. Tamoxifen (Soltamox)

USPSTF
2019

Population	Recommendation	Grade
Women at increased risk for breast cancer*	Clinicians offer to prescribe risk-reducing medications, such as tamoxifen, raloxifene, or aromatase inhibitors, to women who are at increased risk for breast cancer and at low risk for adverse medication effects	**B**
Women not at increased risk for breast cancer	Recommends against the routine use of risk-reducing medications, such as tamoxifen, raloxifene, or aromatase inhibitors, in women who are not at increased risk for breast cancer.	**D**

- National Cancer Institute (NCI) Breast Cancer Risk Assessment Tool, estimate a woman's risk of developing breast cancer over the next 5 years. There is no single cutoff for defining increased risk for all women.*
- **Women at greater risk, at least a 3% risk for breast cancer in the next 5 years, are likely to derive more benefit than harm from risk-reducing medications and should be offered these medications if their risk of harms is low**.
- Some women at lower risk for breast cancer have also been included in trials documenting reduced risk for breast cancer when taking tamoxifen, raloxifene, or aromatase inhibitors. However, when balancing the harms associated with these medications, the net benefit will be lower among women at lower risk.

https://bcrisktool.cancer.gov/

NIH NATIONAL CANCER INSTITUTE

Breast Cancer Risk Assessment Tool

RISK CALCULATOR ABOUT THE CALCULATOR

The Breast Cancer Risk Assessment Tool

The Breast Cancer Risk Assessment Tool allows health professionals to estimate a woman's risk of developing invasive breast cancer over the next 5 years and up to age 90 (lifetime risk).

The tool uses a woman's personal medical and reproductive history and the history of breast cancer among her first-degree relatives (mother, sisters, daughters) to estimate absolute breast cancer risk—her chance or probability of developing invasive breast cancer in a defined age interval.

Assess Patient Risk

The tool has been validated for white women, black/African American women, Hispanic women and for Asian and Pacific Islander women in the United States. The tool may underestimate risk in black women with previous biopsies and Hispanic women born outside the United States. Because data on American Indian/Alaska Native women are limited, their risk estimates are partly based on data for white women and may be inaccurate. Further studies are needed to refine and validate these models.

This tool cannot accurately estimate breast cancer risk for:

- Women carrying a breast-cancer-producing mutation in *BRCA1* or *BRCA2*
- Women with a previous history of invasive or in situ breast cancer
- Women in certain other subgroups

Chemoprevention

Agent	Type	Comment	SOR
Tamoxifen	SERM	FDA-approved; primary prevention of breast cancer in high-risk women. It can decrease the risk of developing breast cancer (specifically estrogen-receptor–positive breast cancer) by up to 48%; only FDA-approved medication for the chemoprevention of breast cancer in **premenopausal women**	**A**
Raloxifene	SERM	Approved for the chemoprevention of breast cancer in postmenopausal women, but **not** premenopausal women	**A**
Letrozole	Aromatase inhibitor	Approved for chemoprevention of breast cancer in **postmenopausal** women but are **not** approved for **premenopausal** women. *Aromatase inhibitors block the conversion of androgens to estrogen but cannot block ovarian production of estrogen, so they do not work in premenopausal women unless the woman is also taking a gonadotropin-releasing hormone inhibitor.*	**A**
Combined OCPs	-	Can be used for the **prevention of ovarian cancer and endometrial cancer** but does **NOT** prevent breast cancer	**C**
Progesterone	-	Does **NOT** reduce the risk for breast cancer	**A**

3. A 51 yo female presents to the office with the complaint of a left breast mass. She reports she was in an automobile accident 5 months ago and first noted the mass at that time. She thought it was due to the seat belt she was wearing. On examination you note a 1 cm hard mass in the upper outer quadrant of the left breast. It is mobile and nontender. There is no overlying change in the skin, nipple discharge, or nipple retraction. You review her chart and note she had a negative screening mammogram 6 months ago. ***Which of the following is the first diagnostic imaging study that should be performed in evaluating this new palpable breast mass?***

A. Ultrasound
B. MRI
C. Mammogram
D. CT

Breast Mass

- May be benign or malignant
  - ~90% of palpable breast masses in women 20s to early 50s are benign
- Benign mass may be solid or cystic
- Malignant mass is TYPICALLY solid
- Cystic mass with solid components (complex cyst) can also be malignant

Differential

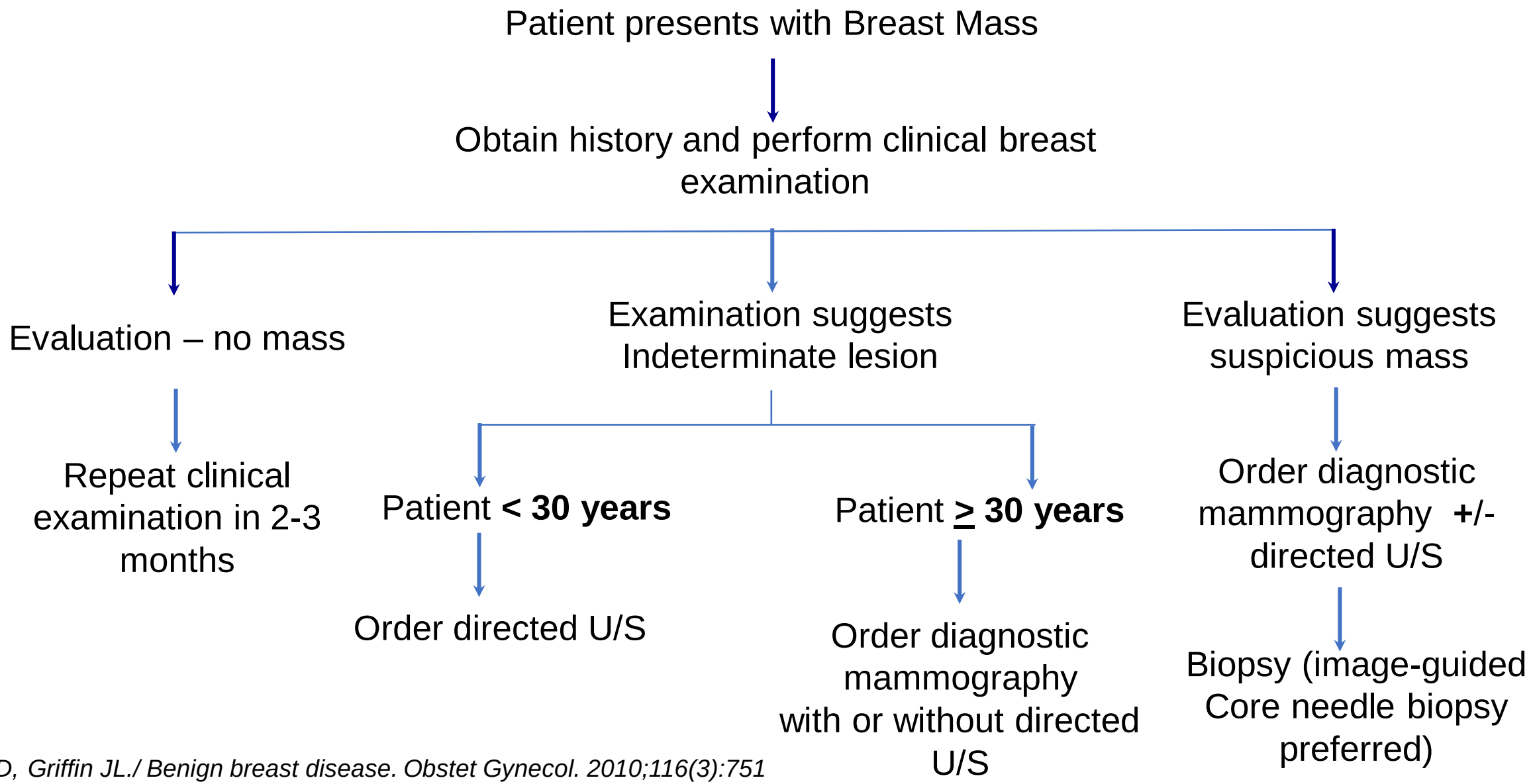
- Fibroadenoma
- Cyst
- Fibrocystic changes
- Galactocele
- Fat necrosis


BREAST CANCER
RISK FACTORS AND PREVENTION
RISK FACTORS
UNCONTROLLABLE RISK FACTORS
Incidence increases particularly after the age of 40.
AGE
Incidence is much higher in females than in males
GENDER
5 - 10% of cases are hereditary
GENETIC FACTORS
Before 12 years of age
EARLY MENARCHE
Of any type of cancer
FAMILY HISTORY
After 55 years of age
LATE MENOPAUSE
Radiation therapy in the chest area
EXPOSURE TO RADIATION
OBESITY
particularly after menopause
LACK OF EXERCISE
EATING LOTS OF PROCESSED AND FATTY FOOD
USING HORMONAL BIRTH CONTROL METHODS
risk decreases after stopping their use
USING HORMONE REPLACEMENT THERAPY
to treat menopausal symptoms
NOT BREASTFEEDING
after giving birth puts women at a higher risk
GIVING BIRTH AT AN OLDER AGE
After 35 years of age
HAVING NO CHILDREN
Incidence decreases when women give birth
CONTROLLABLE RISK FACTORS
PREVENTION
EXERCISING
MAINTAINING A HEALTHY WEIGHT
LIMITING ALCOHOL INTAKE
+962 6 5530800
+962 6 5530870
JBCPjordan
Jordan Breast Cancer Program
www.jbcp.jo

Evaluation of Breast Mass

- Detailed clinical history and physical examination to determine degree of suspicion for malignant disease (risk factors)
- Characterization of mass (CBE)
  - Duration, location, size, margin irregularity, relationship to the chest wall, density of the breast tissue; evaluation of the skin overlying the mass and nipple; relationship to menstrual cycle; presence of pain, redness, fever, or discharge.
- Supraclavicular, cervical, axillary nodes

Approach to the Patient with a Palpable Breast Mass



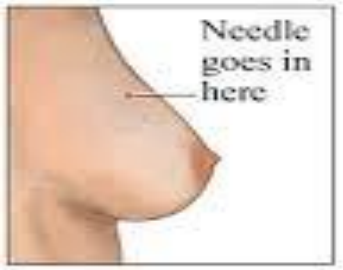
Pearlman MD, Griffin JL./ Benign breast disease. Obstet Gynecol. 2010;116(3):751

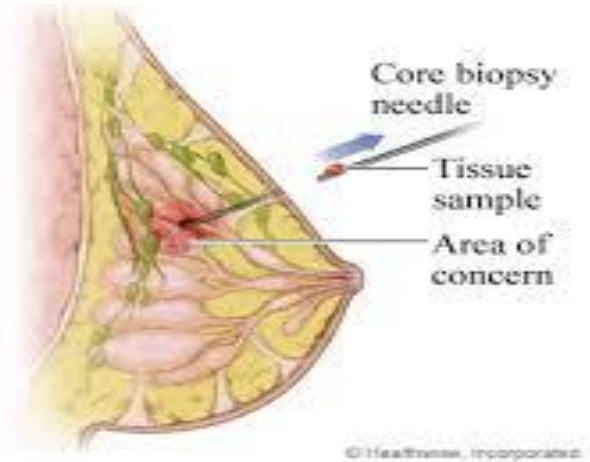
Imaging

- **Palpable mass**
  - Unilateral diagnostic mammogram
    - First imaging study for a woman with a new, palpable breast mass, and should be performed even if recent mammogram was negative
    - A normal mammogram DOES NOT eliminate the need for further evaluation of a suspicious mass [even though the false (-) rate of mammograms is <5% for clinically palpable breast cancers].
  - Ultrasound
    - Always perform in setting of new palpable abnormality – help differentiate benign cyst from a benign or malignant solid mass
    - For young women with a clinically benign mass e.g. fibroadenoma and no family history of premenopausal breast cancer, US is a useful initial diagnostic imaging study
  - MRI is NOT indicated for the work-up of an undiagnosed mass – reserved for diagnostic dilemmas

Biopsy

- Diagnosis of benign or malignant mass is confirmed by a breast biopsy
- Core needle biopsy using image guidance (or FNA with experienced cytopathologist) for ANY mass not identified as a simple cyst
- Image guidance ensures adequate localization of the mass and placement of localizing clip for future identification of the mass if required for surgical intervention (open biopsy)





SUMMARY

Practice Recommendations

Recommendation	SOR
Teaching breast self-examination does NOT reduce mortality and is NOT recommended	A
For average-risk women 40-49 years of age, the risks of mammography are closely balanced. The decision to perform screening mammography should take into consideration the individual patient risk, values, and comfort level of the patient and physician	B
Biennial screening should be offered to average risk women 50-74 years of age.	B
Screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with 1 of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2)	B

Thank You

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