Breast Cancer Screening and Prevention

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Learning Objectives

At the conclusion of this presentation, the participant will be able to:

- Explain to patients the harm that unnecessary radiographic imaging can cause and the benefits that mammography offer.
- Routinely calculate the risk for breast cancer for each woman at appropriate ages.
- Routinely offer chemoprevention for breast cancer to appropriate candidates

GYN Care	cinoma	Incidence	in
U.S.	Wome	n, 2020	

Carcinoma	New Cases	Deaths
Ovarian	21,750	13,940
Uterine corpus	65,620	12,590
Uterine cervix	13,800	4,290
Vulvar	6,120	1,350
Vaginal & other	6,230	1,450
Breast	276,480	42,170

https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2020.html.

Table 2. Age-specific Ten-year Probability of Breast Cancer Diagnosis or Death for US Women

Current age	Diagnosed with invasive breast cancer	Dying from breast cancer
20	0.1% (1 in 1,479)	<0.1% (1 in 18,503)
30	0.5% (1 in 209)	<0.1% (1 in 2,016)
40	1.5% (1 in 65)	0.2% (1 in 645)
50	2.4% (1 in 42)	0.3% (1 in 310)
60	3.5% (1 in 28)	0.5% (1 in 193)
70	4.1% (1 in 25)	0.8% (1 in 132)
80	3.0% (1 in 33)	1.0% (1 in 101)
Lifetime risk	12.8% (1 in 8)	2.6% (1 in 39)

Note: Probability is among those who have not been previously diagnosed with cancer. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.

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Dependencies Dependencies Dependencis

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Takkouche B, et al. *J Natl Cancer Inst.* 2008;100(29):1439-47. Col NF, et al. *Breast Cancer Rest Treat.* 2012:135(3):639-46.

Factors Shown To Have No Effect on Risk of Breast Cancer Breast augmentation Smoking Abortion Breast feeding <1 year

- Fat intake
- Selenium in diet
- Caffeine
- Short term postmenopausal hormone therapy (HT)

ACOG Comm. Opinion # 434. Obstet Gynecol. 2009;113(6):1417-8.

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Breast Cancer Incidence by Risk Status

- 1 in 8 average risk women will develop breast cancer by age 80-90
- 1 in 3 high risk women will develop breast cancer by age 50
- Testing to identify to identify high risk women expanding
 - Tests used to screen high risk women now start earlier, conducted more frequently and involve more modality
 - Prevention often involves surgery

Average Risk for Breast Cancer

- No personal history of breast cancer
- No confirmed or suspected genetic mutation known to increase risk of breast cancer
- No history of radiotherapy to the chest at a young age
- No significant family history of breast cancer
- No prior diagnosis of benign proliferative breast disease or worse
- No significant mammographic breast density

Yates J. OBG Mgmt. 2015;27(12):19-24.

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Breast Cancer Screening Recommendations: Average Risk

Mam		ammog	raphy	C	BE	SBE
ACOG	Offer	40	Q1-2	May be	e offered	*Not
	Initiate	40-49	Q1-2	25-39	Q1-3	recommended
	Recommend	50	Q1-2	40+	Q1	
	Offer	40-45		N1 . 4		N1 - 4
ACS ²	Recommend	45	Q1	Not		NOI
		>55y	Q1-2	recom	nenaca	recommended
USPSTF ³	Recommend Q2	50-7	4	Insuffic eviden	cient ce	Recommended against

*Replaced by "breast self-awareness"

ACOG Practice Bulletin No. 122. *Obstet Gynecol.* 2017;130:e1-e16.
 Oeffinger KC, et al. *JAMA*. 2015;314(15):1599-1614.
 Siu AL, et al. *Ann Intern Med.* 2016;164(4):279-96.

Shanghai SBE Trial

- Initial instruction, 1 year & 3 year reinforcement lessons
- SBE practice under medical supervision every 6 months for 5 years
- Ongoing reminders to practice monthly
- 1989-91 instructions followed for morbidity to 2000

	BSE	Control	SRR (95% CI)
Ν	132,979	133,085	
Cancer deaths			1.04 (0.82-
	135	131	1.33)
Benign lesions	2,387	1,296	

Cummings SR, et al. JAMA. 1999;281(23):2189-97.

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Clinical Breast Examination Limitations

- Physicians tested on artificial models detected:
 - ♦ 44% of lumps
 - ♦ 87% of 1 cm masses
 - ◆ 33% of 0.5 cm masses
 - 14% of 0.3 cm masses
 - 50% of hard masses
 - 36-40% of soft masses
 - 44% of deep or medium depth masses

Mammographic Screening Impacts

- Lead time is longest in cancers that don't prove fatal
 - Very short in fatal cancer
- 95% of breast cancer deaths occur in 20 years
- Study compared risk of death at 10 and 20 years following diagnosis of breast cancer among women who participate in mammographic screening in a Swedish county 1977-2015 vs. not
- Risk of breast cancer death among participants
 - 60% reduced within 10 years of diagnosis
 - 47% reduced within 20 years of diagnosis
- Screening reduced advanced cancers

Tabár L, et al. Cancer. 2019;125(4):515-523.

Breast Cancer Screening Recommendations: Average Risk

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ACOG	Offer	40	Q1-2	May be	e offered	*Not	
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	Offer	40-45					
ACS ²	Recommend	45	Q1	Not		Not	
		>55y	Q1-2	recom	nenueu	recommended	
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Controversies Surrounding Mammography

- Overdiagnosis leading to unnecessary procedures and treatments
- Lack of impact reducing late state disease
- Demand for mammography inflated by fears and personal testimonials
- New follow-up requirements for dense breasts

Benefits and Harms of Mammograms 10,000 Women Screened Annually for 10 Years

	Estimated No. by Decade/Age/Year			
	40	50	60	
Diagnosed with invasive breast cancer	147	231	345	
Breast cancer deaths	32	62	88	
Deaths averted because of mammogram	3	10	43	
≥1 False positive	6130	6130	4970	
≥1 Unnecessary biopsy	700	940	980	
Over diagnosed	28	44	66	

Keating NL. JAMA. 2018;319(17):1814-15.

Incidence Over Time of Cancer Metastatic at First Presentation















What Should We Be Doing?

- Stop screening women with no benefit¹
 - 48% of primary care physicians said they would recommend breast cancer screening for women diagnosed with terminal lung cancer
- Calculate patient's individual breast cancer risk²
 - Use estimate to determine screening frequency and modality
 - Low accuracy in predicting probability of breast cancer in individuals³
- Provide chemoprevention or other interventions when appropriate

Leach CR, et al. *Cancer*. 2012;118(1):27-37.
 Sameer D, et al. *JAMA*. 2014;312(21):2211-12.
 Nelson HD, et al. *JAMA* 2019;322(9):868-86.



Breast Cancer Risk Calculator Questions

Calculate risk for next 5 years and lifetime

- Q1: History of DCIS or LCIS?
- ◆ Q2: Current age?
- Q3: Age at time of first menstrual period?
- Q4: Age at time of first birth?
- Q5: No. of 1st degree relatives with breast cancer?
- ◆ Q6: Number of breast biopsies?
 - Any atypical hyperplasia?
- Q7: Race/ethnicity?

Available at: <u>http://www.cancer.gov/bcrisktool/</u>

Breast Cancer Risk Calculator Questions

 Does the woman have a history of breast cancer or of ductal carcinoma in situ (DCIS), breast augmentation, or mastectomy? 	a) Yes b) No
2. What is the woman's age	<35 - < 74
3. What is the woman's race/ethnicity?	
4. Have any of the woman's first-degree relatives (mother, sister or daughter) been diagnosed with breast cancer?	a) Yes b) No c) Unknown
5. Has the woman had prior breast biopsies (positive or negative)?	 a) None (no prior biopsy) b) Prior biopsy, unknown diagnosis c) Non-proliferative lesion d) Proliferative changes without atypia e) Proliferative changes with atypia f) Lobular carcinoma in situ
6. What is the woman's BI-RADS breast density (radiologic assessment of the density of breast tissue by radiologists who interpret mammograms?	 a) Almost entirely fatty b) Scattered fibroglandular densities c) Heterogeneously dense d) Extremely dense



Prevention Strategies: Healthy Lifestyle

- 23% of breast cancer cases in UK thought to be preventable
- Cancer research UK factors to reduce¹
 - Healthy weight reduced risk 13.9%
 - Obesity accounts for 8%
 - Regular exercise reduced risk 12.2%
 - ◆ ≤3 alcohol/week reduced risk 10.7%
 - ETOH account for 8%
 - Avoiding HT reduced risk 22.9%
- Unhealthy lifestyle increases more than genetic risk²

^{1.} Cancer Research UK. Breast Cancer statistics. https://www.cancerresearchuk.org/ health-professional/cancer-statistics/statistics-bycancer-type/breast-cancer#heading-Four. Accessed 8/26/20 2. Al Ajmi K, et al. JAMA Network Open. 2020;3(4):e203760.

USPSTF Draft Recommendation 2019

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P	opulation	Recommendation	Grade (What's This?)
W	Vomen at increased risk for reast cancer	The USPSTF recommends that 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.	В
W	Vomen not at increased risk for reast cancer	The USPSTF 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

https://w

USPSTF Recommendations for Medication Use to Reduce Risk of Breast Cancer 2019

- 5 year risk >3% (benefits > risks)
 - National Cancer Institute Brest Cancer Risk Assessment Tool
 - Breast cancer surveillance consortium risk calculator
- Treat those with any combination:
 - ◆ Age ≥65 with 1° relative with breast cancer
 - Age ≥45 with > 1° relative with breast cancer OR
 - 1° relative with breast cancer <50 yrs
 - Age ≥40 with 1° relative with bilateral breast cancer OR
 - Atypical ductal or lobular hyperplasia OR
 - Lobular carcinoma in situ
- Balance benefits and risks of treatment

US Preventative Task Force, et al. JAMA. 2019;322(9):857-67.



Absolute Risk Reduction with Chemoprevention

- Based on 5 year risk of 1.66% (60 yo woman)
 - 50% reduction = absolute risk reduction 0.85%
 - Number needed to treat = 120 to prevent one cancer
- 1,000 women treated 5 years
 - 7 breast cancers prevented
 - ◆ NNT = 143
- Chemoprevention does not reduce breast cancer mortality
 - Tends to reduce risk of more treatable cancers
- Consider higher thresholds to treat

Pace LE, et al. *JAMA*. 2019;322(9):821-23.

Future Developments

- Lower dose tamoxifen (5mg x 3 years) given^{1,2}
 - Intraepithelial neoplasia (atypical ductal hyperplasia)
 - Reduced hormone receptor positive DCIS and invasive for 5.1 years follow-up
 - Limited toxicity
- Denosumab to reduce premenopausal breast density
 - Reduces fibrous mammary gland structures²
- Online decision aids³
 - Ongoing RCT with younger, higher risk women
- DeCensi A, et al. J Clin Oncol. 2019;37(19):1629-37.
 Strait JE. https://medicine.wustl.edu/news/breast-cancer-prevention-trial-underway/
 Pace LE, et al. JAMA. 2019;322(9):821-23.

Preventing Breast Cancer: What We Know Works Now

Health Messages	Risk Group	Approximate % of US Female Population Aged <50 Years Affected, %	Possible Reduction in Risk, %	Time Until Benefit, y
Premenopausal women				
Alcohol intake: None	Youth (ages 12-17y), drinking at least one drink in past 30/d	13	20-30	10-20
Alcohol intake: ≤1 serving/d	Young adults (ages 18- 24y) drinking ≥4 drinks/wk	15	20-30	10-20
Healthy weight: Avoid weight gain	All women	13	25	10-20
Physical activity: ≥30 min/d	Women not meeting physical activity guidelines	54	20	10-30

Colditz GA et al. CA Cancer J Clin. 2014;64(3):186-94.

Preventing Breast Cancer: What We Know Works Now

Health Messages	Risk Group	Approximate % of US Female Population Aged <50 Years Affected, %	Possible Reduction in Risk, %	Time Until Benefit, y
Premenopausal wome	n			
Healthy diet: Fruits, vegetables, & whole grains	Youth eating very few fruits & vegetables	5-11	20-50	5-20
Breastfeed: One y total across all children	Women who have given birth	81	18	5
Prophylactic bilateral oophorectomy	BRCA 1 and 2 carriers	<1	50	≥2
Tamoxifen	High-risk women aged ≥35 y (greater than or equal to the risk for average woman aged 60 y)	3	50	2

Colditz GA et al. CA Cancer J Clin. 2014;64(3):186-94.

Preventing Breast Cancer: What We Know Works Now

Health Messages	Risk Group	Approximate % of US Female Population Aged <50 Years Affected, %	Possible Reduction in Risk, %	Time Until Benefit, y
Postmenopausal women				
Alcohol intake: Serving/d	Adults drinking ≥4 drinks/wk	13	35	5-10
Healthy weight: Weight loss	Overweight and obese (eg 5'4" and >145 lbs)	64	50	2-5
Physical activity: ≥30 min/d	Women not meeting physical activity guidelines	54	20	10-20
Estrogen-plus-progestin postmenopausal hormones: Avoid	Current users	1.7	10	1
Tamoxifen and raloxifene	High-risk women (greater than or equal to the risk for an average woman aged 60y	30	50	2

Colditz GA et al. CA Cancer J Clin. 2014;64(3):186-94.