Breast Cancer Screening:
Consensus and Controversies

Michael Morris, MD

Case #1

- 41 y/o women comes for her annual exam
  - No PMH; No FH cancer
  - Social EtOH; non-smoker
  - BMI 29
- You perform routine exam, including clinical breast exam

"should I have a mammogram?"

Family/friend with hx breast cancer:
1. Yes 2. No

No family/friend with hx breast cancer:
3. Yes 4. No

Case #2

- 51 y/o women comes for her annual exam
  - No PMH; No FH cancer
  - Social EtOH; non-smoker
  - BMI 29
- You perform routine exam, including clinical breast exam

"should I have a mammogram?"

Family/friend with hx breast cancer:
1. Yes 2. No

No family/friend with hx breast cancer:
3. Yes 4. No

Case #2

- 52 y/o women comes for her annual exam
  - No PMH; No FH cancer
  - Social EtOH; non-smoker
  - BMI 29

"should I have a yearly mammogram?"

Family/friend with hx breast cancer:
1. Yes 2. No

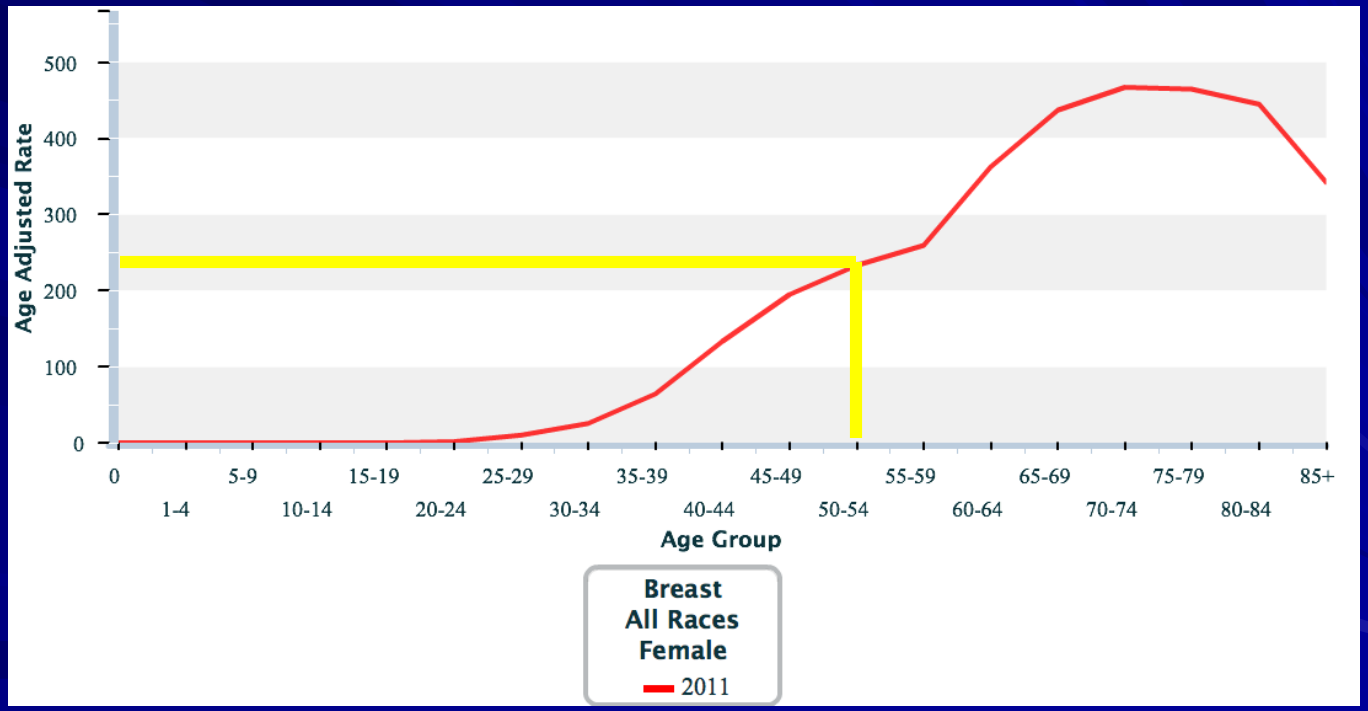
No family/friend with hx breast cancer:
3. Yes 4. No

What is the probability of a 50 year old women having breast cancer in the next 10 years?

1. 2%
2. 12%
3. 20%

What is the probability of a 50 year old women having breast cancer in the next 10 years?

1. 2%
2. 12%
3. 20%



http://seer.cancer.gov/canstat/animator

What is the probability of a 50 year old women having breast cancer in the next 10 years?

1. 2%
2. 12%
3. 20%

Table 2. Perceived and calculated risks and risk reductions

	Median (interquartile range)		
	All subjects	Numerate	Innumerate
Probability of developing breast cancer within the next 10 years			
Perceived, %	20.0 (10.0-30.0)		
Calculated, %	2.3 (2.0-2.8)		
Ratio	5.9 (3.1-13.6)	4.6†	9.7

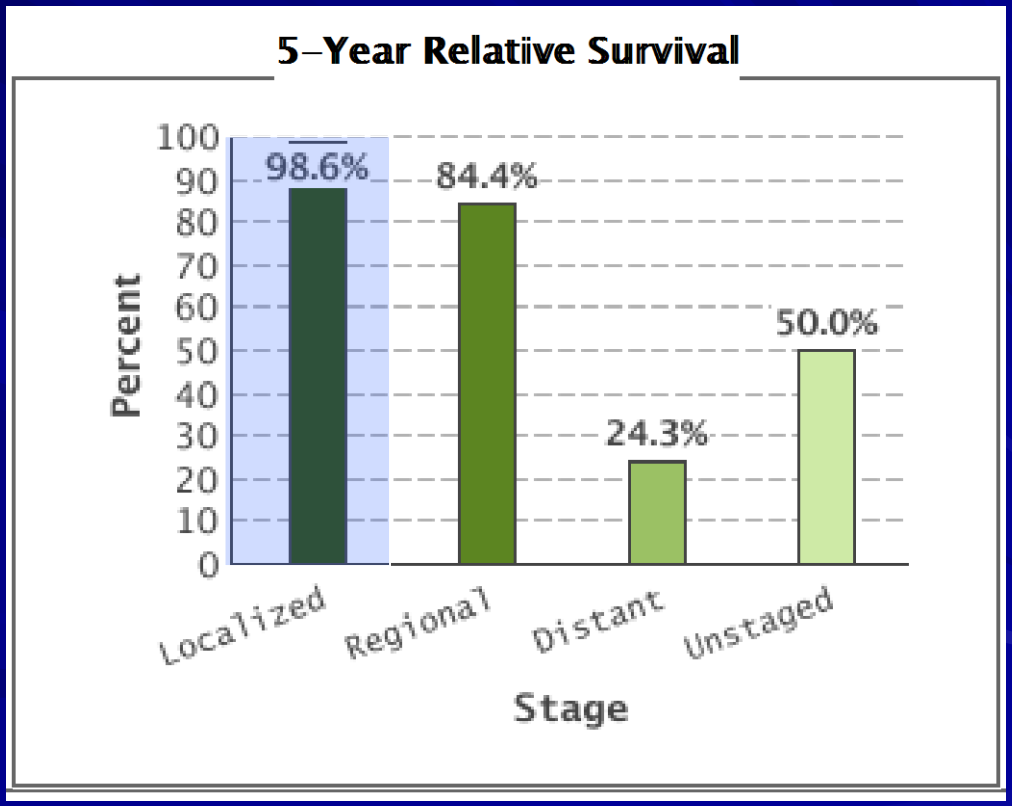
J Natl Cancer Inst. 1995;87(10):720-31

What is the risk of dying from early stage breast cancer?

1. 1%
2. 10%
3. 20%
4. 30%

What is the risk of dying from early stage breast cancer?

1. 1%
2. 10%
3. 20%
4. 30%



http://seer.cancer.gov/statfacts/html/breast.html

What is the risk of dying from early stage breast cancer?

1. 1%
2. 10%
3. 20%
4. 30%

Table 2. Perceptions of risk reported by women with breast cancer[a]

	DCIS ($N = 64$)	EIBC ($N = 164$)
How likely is it that you will die of breast cancer?		
Mean score	1.8	2.0
Unlikely (score ≤ 2)	43/59 (73%)	110/151 (73%)
Likely (score ≥ 3)	16/59 (27%)	41/151 (27%)
Likely/very likely (score $4 + 5$)	2/59 (3%)	20/151 (13%)
How likely is it that you will die of something other than breast cancer?		
Mean score	3.6	3.5
Unlikely (score ≤ 2)	11/58 (19%)	36/150 (24%)
Likely/very likely (score $4 + 5$)	32/58 (55%)	78/150 (52%)

[a] DCIS: ductal carcinoma *in situ*; EIBC: early stage invasive breast cancer.

Breast Cancer Res Treat. 2003;77(3):285-93

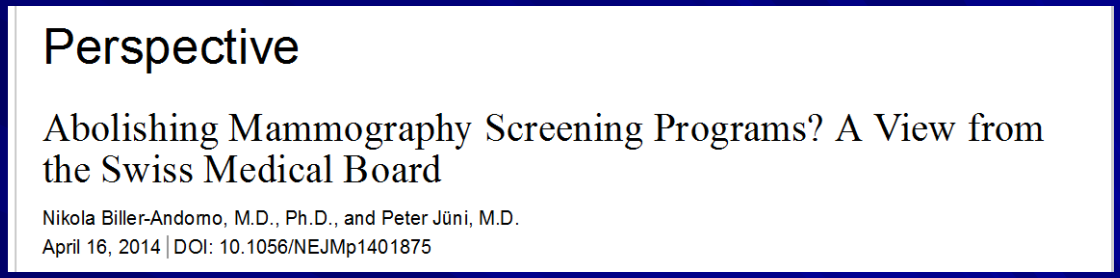
	Common Types of Cancer	Estimated New Cases 2014	Estimated Deaths 2014
1.	Prostate Cancer	233,000	29,480
2.	**Breast Cancer (Female)**	**232,670**	**40,000**
3.	Lung and Bronchus Cancer	224,210	159,260
4.	Colon and Rectum Cancer	136,830	50,310
5.	Melanoma of the Skin	76,100	9,710
6.	Bladder Cancer	74,690	15,580
7.	Non-Hodgkin Lymphoma	70,800	18,990
8.	Kidney and Renal Pelvis Cancer	63,920	13,860
9.	Thyroid Cancer	62,980	1,890
10.	Endometrial Cancer	52,630	8,590

Breast cancer represents 14.0% of all new cancer cases in the U.S.

14.0%

http://seer.cancer.gov/statfacts/html/breast.html

Breast Cancer Screening


Perspective

Abolishing Mammography Screening Programs? A View from the Swiss Medical Board

Nikola Biller-Andorno, M.D., Ph.D., and Peter Jüni, M.D.

April 16, 2014 | DOI: 10.1056/NEJMp1401875

- Where there is consensus I say so
- Where there is controversy I say so

- Make your own informed decision

Methods of Breast Cancer Screening

- Physical Exam
  - Breast self exam
  - Clinical breast exam
- Imaging
  - Mammography
  - MRI
  - *Ultrasound*
  - *Tomosynthesis, molecular breast imaging, contrast mammography*
- *Blood biomarkers*

Methods of Breast Cancer Screening

- Physical Exam
  - Breast self exam
  - Clinical breast exam
- Imaging
  - Mammography
  - MRI
  - *Ultrasound*
  - *Tomosynthesis, molecular breast imaging, contrast mammography*
- *Blood biomarkers*

Definitions

- Screening Exam:
  - Look for breast cancer in asymptomatic women
- Diagnostic Exam:
  - Referred for specific concern
  - Palpable lump, focal pain, nipple discharge (*clear, bloody*)

Definitions

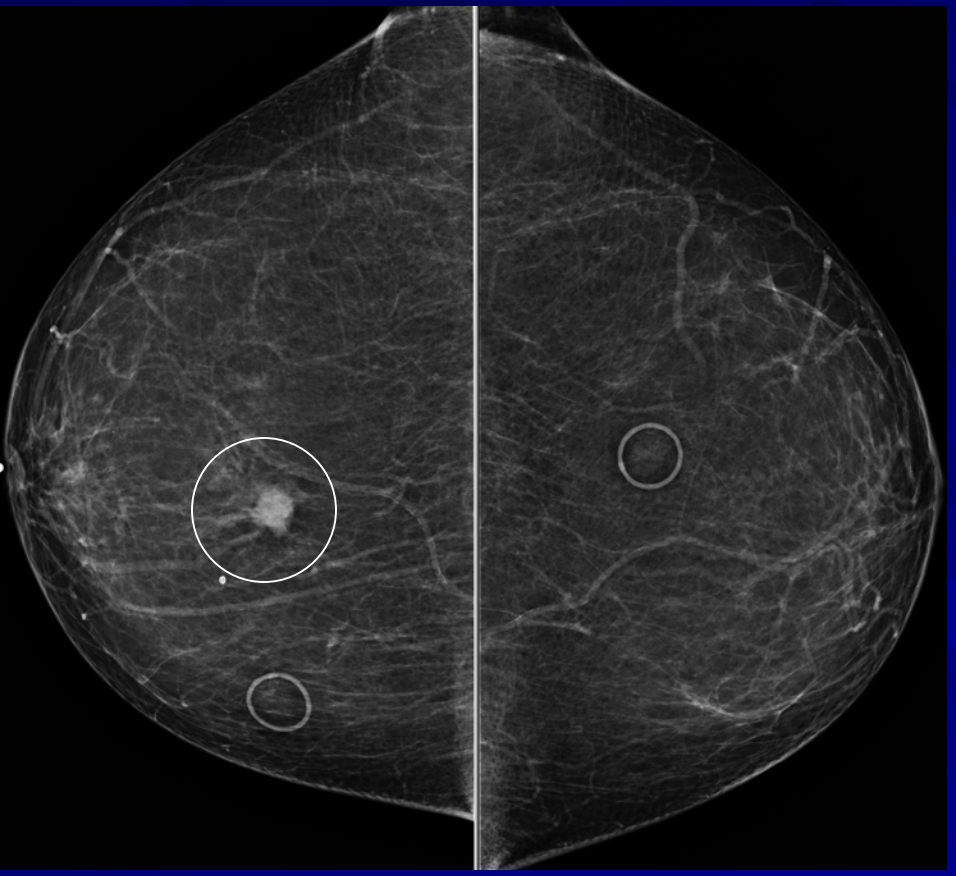
- Screening Exam:
  - Look for breast cancer in asymptomatic women

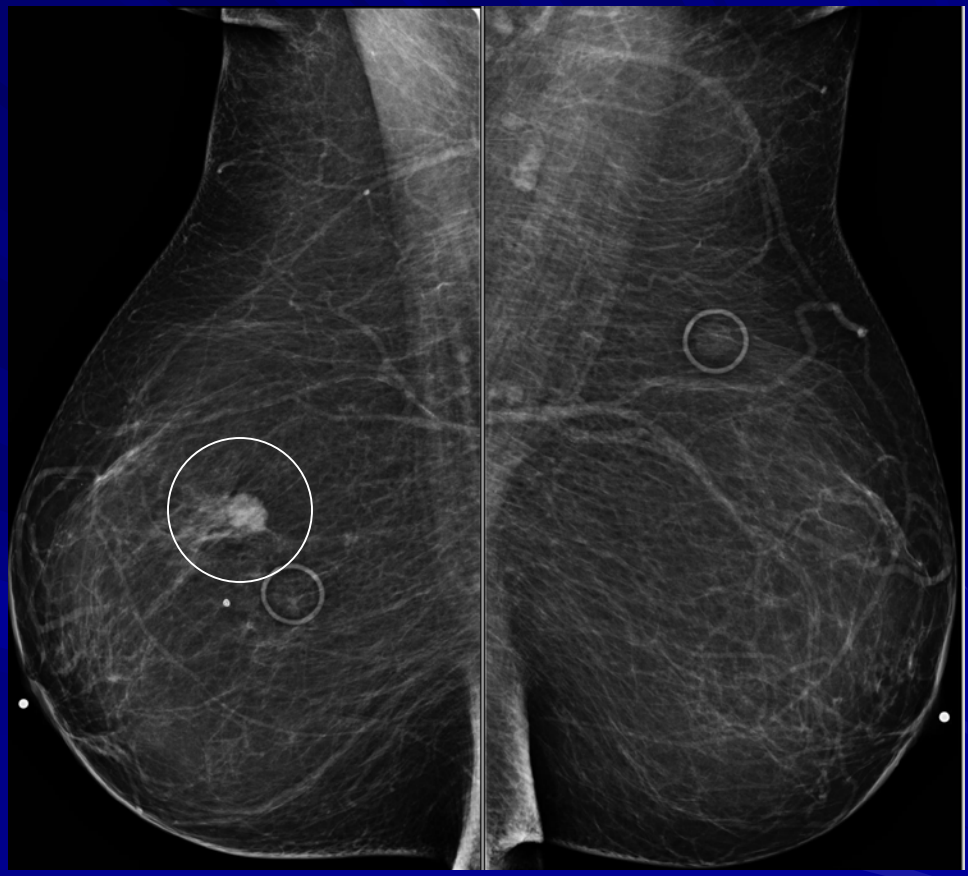
- Diagnostic Exam:
  - Referred for specific concern
  - Palpable lump, focal pain, nipple discharge (*clear, bloody*)

Case #1

- 51 y/o women comes for her annual exam
  - No PMH; No FH cancer
  - Social EtOH; non-smoker
  - BMI 29
- You perform routine exam, including clinical breast exam

"should I have a mammogram?"





Consensus

- Only screening method to reduce breast ca mortality in RCT
  - Ages 40-74
- Overall ~20% mortality reduction
  - Sensitivity 84.9%
  - Specificity 90.3%

- Yes: *ACS, NCI, USPSTF, AAFP, ACOG, ACR, ACP*
- No: 0

Lancet. 2012; 380:1778-86
http://breastscreening.cancer.gov/data

Benefits of Screening vs **“Harms” of Screening**

Benefits of Screening

- 20% mortality reduction*
  - If 1000 women screened
  - Absolute decrease 5 → 4

"Harms" of Screening

- Very big benefits, few people

Among 1000 women, # avoid dying of breast cancer per 10 years of screening:

- 40 y/o: 0.1-1.6
- 50 y/o: 0.3-3.2
- 60 y/o: 0.5-4.9

JAMA Int Med 2014;174:448
JAMA 2015;314(15):1599-1614
Ann Intern Med. 2016;164(4):279-96

Benefits of Screening

- 20% mortality reduction* → Very big benefits, few people
  - If 1000 women screened
  - Absolute decrease 5 → 4

"Harms" of Screening

- False Positives → Small harms, many people
  - ~10% recalled; ~1% biopsy
  - Anxiety, morbidity, cost
- High NNS when younger → Small harms, many people
  - 40-50: 1/1770-3300
  - 60-70: 1/377-500

JAMA 2015;314(15):1599-1614
Ann Intern Med. 2016;164(4):279-96

Benefits of Screening

- 20% mortality reduction* → Very big benefits, few people

"Harms" of Screening

- False Positives
- High NNS when younger → Small harms, many people

- Overdiagnosis
  - ~5-50% women with cancer Rx unnecessarily → Big harms, very few people

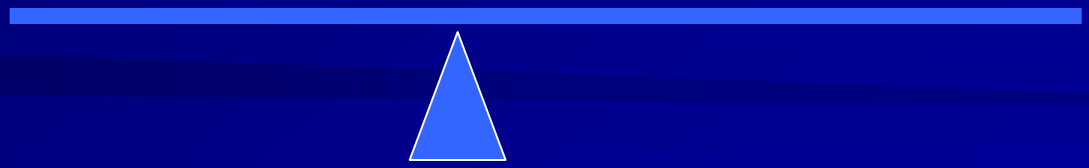
JAMA 2015;314(15):1599-1614
Ann Intern Med. 2016;164(4):279-96

- When to start screening?
  - Age 40 or 50
- Screening frequency?
  - Yearly or biennial
- When to stop?
  - Age 75, 80, 85

Small harms,
many people

Very big benefits,
few people

Big harms,
very few people

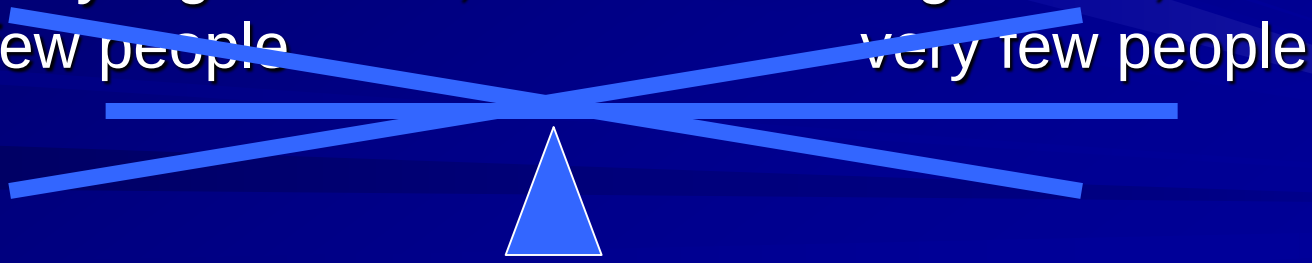


- When to start screening?
  - Age 40 or 50
- Screening frequency?
  - Yearly or biennial
- When to stop?
  - Age 75, 80, 85

Small harms, many people

Big harms, very few people

Very big benefits, few people



When to Start Screening?
(average risk women)

Age 40

- RCT trials start age 40
- 15% mortality reduction* in women 40-49
  - *relative decrease
- Yes: *NCI, ACR, ACOG*, ACS**

Wait until age 50

- High NNS <40
  - 40-50: 1/1770-3300
- Harms outweigh benefits
  - Increased stress from false positive mammogram
  - Increased biopsies
- Yes: *USPSTF, AAFP*

Ann Intern Med. 2007;146(7):511-5
Ann Intern Med. 2016;164(4):279-96

Society and expert recommendations for routine mammographic screening in women at average risk

Group (date)	Frequency of screening (years)	Initiation of screening		
		40 to 49 years of age	50 to 69 years of age	≥70 years of age
Government-sponsored groups				
US Preventive Services Task Force (2016)[1]	2	Individualize*	Yes	Yes, to age 74
Canadian Task Force on Preventive Health Care (2011)[2]	2 to 3	Recommend against*	Yes	Yes, to age 74
National Health Service, United Kingdom (2013)[3]	3	Yes, start age 47	Yes	Yes, to age 73
Royal Australian College of General Practitioners (2012)[4]	2	No (eligible but not targeted)	Yes	No (eligible but not targeted)
Medical societies				
American College of Obstetricians and Gynecologists (2011)[5]	1	Yes	Yes	Yes¶
American College of Physicians (2015)[6]	1 to 2	Individualize*	Yes	Yes, to age 74
American Academy of Family Physicians (2009)[7]	2	Individualize*	Yes	Yes, to age 74
American Cancer Society (2015)[8]	1 year age 45 to 54	Yes, start age 45	Yes	YesΔ
	2 years age ≥55			
American College of Radiology (2013)[9]	1	Yes	Yes	Yes◇
Coalitions				
National Comprehensive Cancer Network (2014)[10]	1	Yes	Yes	Yes

Very big benefits, few people

Small harms, many people

Big harms, very few people

Uptodate.com

When to Stop Screening?

- RCT data stop @ age 74
- Mortality benefit mammography 7-10 yrs

- Consider stop screening if:
  - Life expectancy <7-10yrs
  - Not willing to undergo f/u if abnrml mammo

  - *ACS, ACR, ACOG, AAFP, USPSTF, etc.*

JACR 2010;7:18-27
JAMA 2015;314(15):1599-1614

Case #2

- 36 y/o women, new patient visit
  - Healthy
  - Mom breast ca age 44
    - No other FH ca
  - G2P2, first birth age 32

Case #2

- 36 y/o women, new patient visit
  - Healthy
  - Mom breast ca age 44
    - No other FH ca
  - G2P2, first birth age 32

"should I have a mammogram?"

1. Yes
2. No

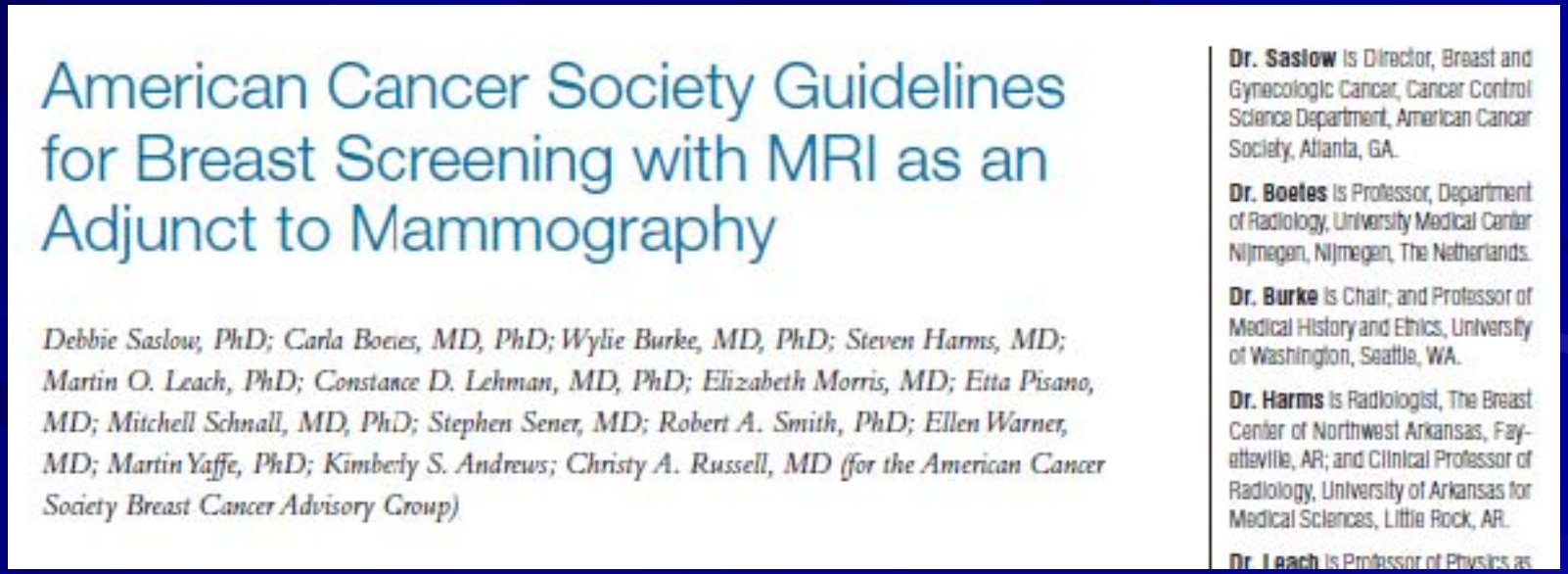
Should you refer this patient for a breast MRI?

- 36 y/o women, new patient visit
  - Healthy
  - Mom breast ca age 45
    - No other FH ca
  - G2P2, first birth age 32

Is she at ‘high risk’ for breast cancer?

Who is High Risk?

- ACS expert panel review of evidence
- High risk = 20-25% lifetime risk breast ca
  - Supplement mammography screening with MRI



American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography

Debbie Saslow, PhD; Carla Boetes, MD, PhD; Wylie Burke, MD, PhD; Steven Harms, MD; Martin O. Leach, PhD; Constance D. Lehman, MD, PhD; Elizabeth Morris, MD; Etta Pisano, MD; Mitchell Schnall, MD, PhD; Stephen Sener, MD; Robert A. Smith, PhD; Ellen Warner, MD; Martin Yaffe, PhD; Kimberly S. Andrews; Christy A. Russell, MD (for the American Cancer Society Breast Cancer Advisory Group)

Dr. Saslow is Director, Breast and Gynecologic Cancer, Cancer Control Science Department, American Cancer Society, Atlanta, GA.

Dr. Boetes is Professor, Department of Radiology, University Medical Center Nijmegen, Nijmegen, The Netherlands.

Dr. Burke is Chair; and Professor of Medical History and Ethics, University of Washington, Seattle, WA.

Dr. Harms is Radiologist, The Breast Center of Northwest Arkansas, Fayetteville, AR; and Clinical Professor of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR.

Dr. Leach is Professor of Physics as

CA Cancer J Clin 2007;57:75-89

When to Start High Risk Screening?

- Chest wall radiation
  - 10 years after chest wall radiation
- Family history or BRCA
  - 10 years before onset of cancer in relative
- MRI does not replace mammography

JACR 2010;7:18-27
J Clin Oncol. 2010; 28(9):1450-7

Who is High Risk?

20-25% Lifetime Risk:

- BRCA
  - Untested 1st degree relative
- Chest wall radiation 10-30 year old
- Li Fraumeni, Cowden
- Calculated lifetime risk by models (PMH, FH)
  - Gail
  - Tyrer-Cuzick
  - BRCAPRO

www.cancer.gov/bcrisktool/
CA Cancer J Clin 2007;57:75-89

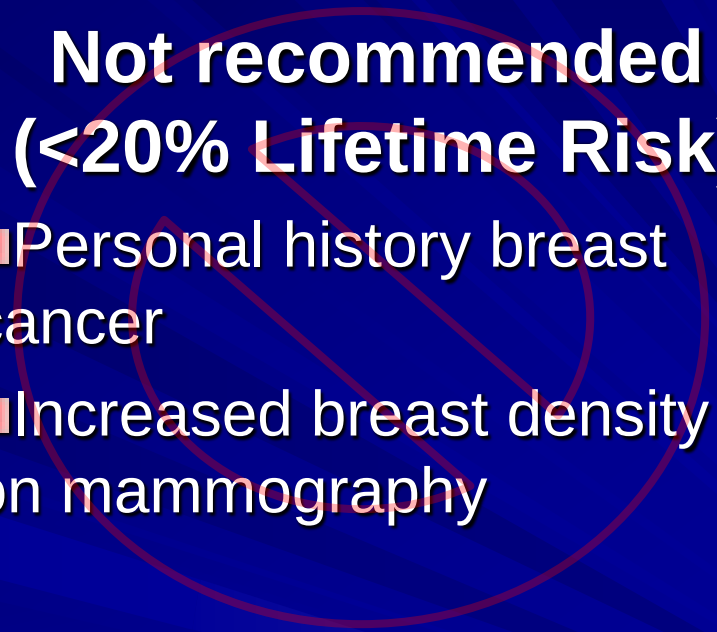
Who is (Not) High Risk?

20-25% Lifetime Risk:

- BRCA
  - Untested 1st degree relative
- Chest wall radiation 10-30 year old
- Li Fraumeni, Cowden
- Calculated lifetime risk by models (PMH, FH)
  - Gail
  - Tyrer-Cuzick
  - BRCAPRO

Not recommended (<20% Lifetime Risk)

- Personal history breast cancer
- Increased breast density on mammography

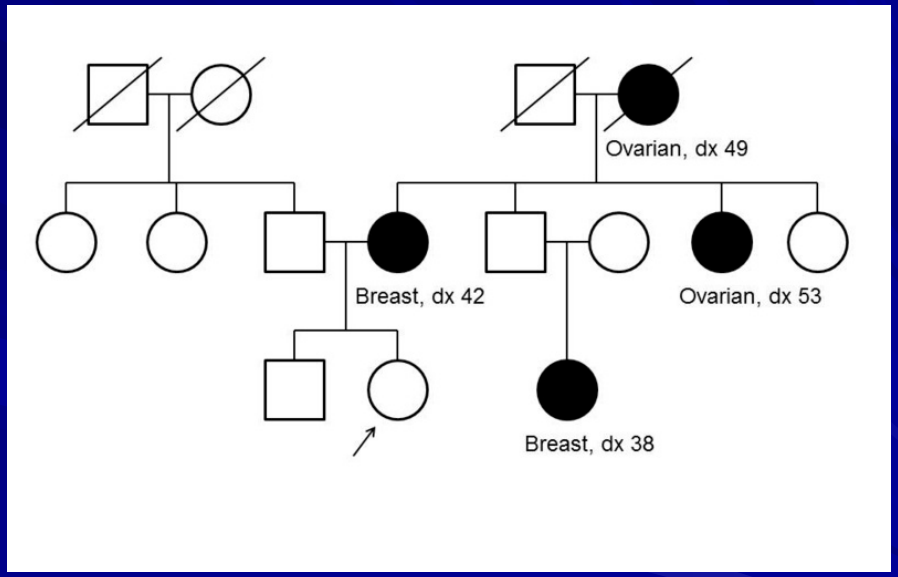


www.cancer.gov/bcrisktool/
CA Cancer J Clin 2007;57:75-89

Who should be referred to genetic counseling?

NCCN Guidelines:

- 2 or more breast ca on same side of family
- Breast ca in 1st or 2nd degree relative <45 y/o
- Male breast ca
- Ovarian ca
- Gene mutation in susceptibly gene



J Natl Compr Canc Netw. 2009;7(10):1060-96

Case #3

- 53 y/o women calls your office
  - Mammogram report states: “dense breasts, which can lower the sensitivity of mammography”
- “What does this mean?”
- “Do I need additional testing?”

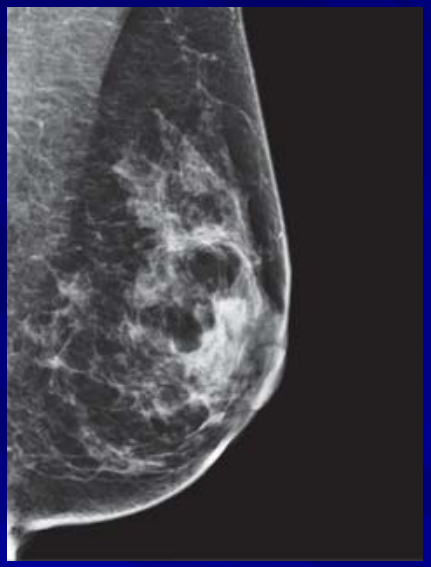
Breast Density

Entirely fat (~10%)

Sens: 88.2
Spec: 96.5

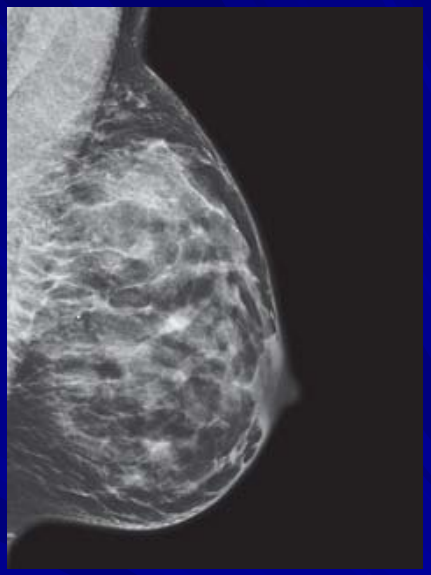
Scattered fibroglandular (~40%)

Sens: 82.1
Spec: 93



Heterogeneously dense (~40%)

Sens: 68.9
Spec: 90.8



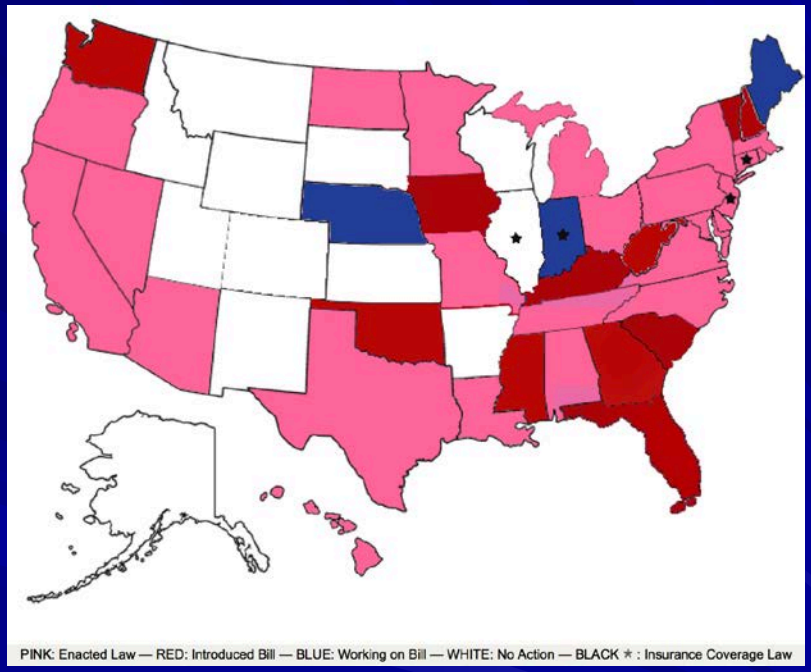
Extremely dense (~10%)

Sens: 62.2
Spec: 89.9

Ann Intern Med 2003;138:168-175

Breast Density – Emerging Controversy

- Higher breast density
  - lower sensitivity
  - Independent risk factor? (~2-4x)
- Mandated reporting



Are You DENSE?
exposing the best-kept secret®

- Your mammogram indicates that you have dense breast tissue. Dense breast tissue is common and is found in 50% of women. However, dense breast tissue can make it difficult to detect cancers in the breast by mammography and may also be associated with an increased risk of breast cancer. This information is being provided to raise your awareness and to encourage you to discuss with your health care providers your dense breast tissue and other breast cancer risk factors. Together, you and your physician can decide if additional screening options are right for you.

Summary

Consensus

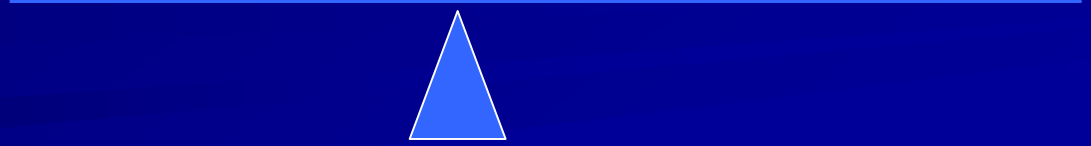
- Screening mammography in average risk women
- Screening mammography & MRI in high risk women

Controversy

- When to start?
- How often?
- When to stop?
- Breast density?

Very big benefits, few people

Small harms, many people
Big harms, very few people



My Advice:

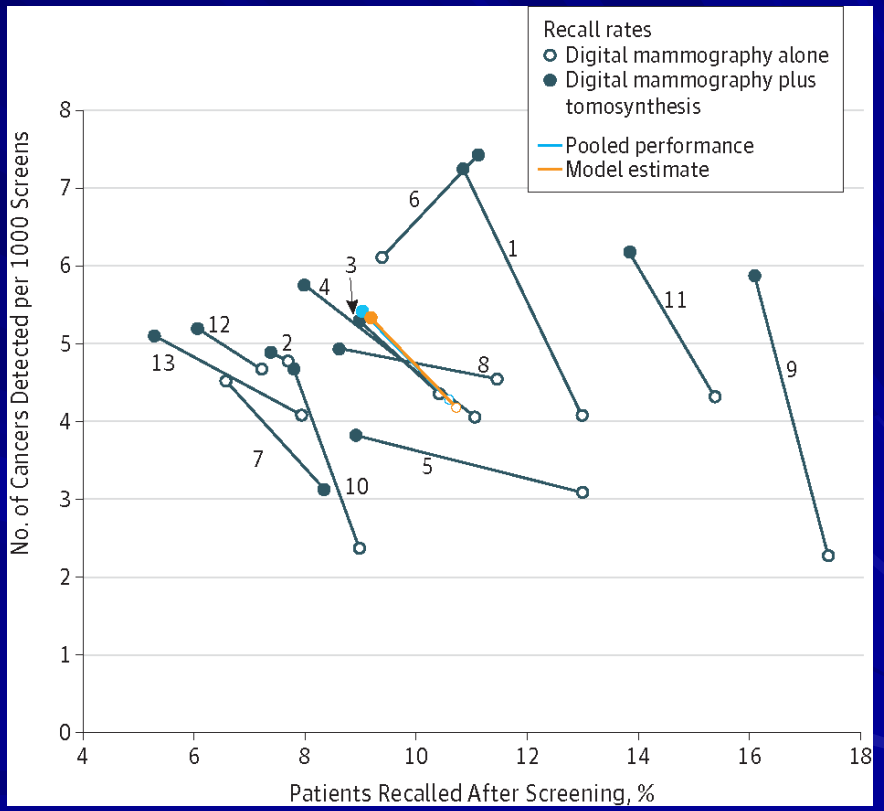
- Stick with recommendations of major medical societies
  - *ACS* (American Cancer Society)
  - *NCI* (National Cancer Institute)
  - *USPSTF* (US Preventative Services Task Force)
  - ACP (American College of Physicians)
  - AAFP (American Academy of Family Physicians)
  - *ACR* (American College of Radiology)
  - *ACOG* (American College of Obstetrics & Gynecology

Future

- Standardization → Individualization
  - Screening based on density
    - Fatty breasts screened less often?
  - New technologies
    - Tomosynthesis (3D mammography)
    - Automated breast ultrasound
    - Molecular imaging & genomics

Tomosynthesis

- 15-20% reduced recall rate
  - improved specificity



JAMA 2014;311:2499-2507

Thank You

Summary

Co... ...ersy

- Clinical b... ...to start?
- & MRI in ... ...t density?

Ve... ...s,
few ... ...ople

Annals of Internal Medicine ORIGINAL RESEARCH

Collaborative Modeling of the Benefits and Harms Associated With Different U.S. Breast Cancer Screening Strategies

Jeanne S. Mandelblatt, MD, MPH; Natasha K. Stout, PhD; Clyde B. Schechter, MA, MD; Jeroen J. van den Broek, MS; Diana L. Miglioretti, PhD; Martin Krapcho, BS; Amy Trentham-Dietz, PhD, MS; Diego Munoz, PhD, MS; Sandra J. Lee, ScD; Donald A. Berry, PhD; Nicolien T. van Ravesteyn, PhD; Oguzhan Alagoz, PhD; Karla Kerlikowske, MD; Anna N.A. Tosteson, ScD; Aimee M. Near, MPH; Amanda Hoeffken, MPH; Yaojen Chang, DrPH, MS, MPH; Eveline A. Heijnsdijk, PhD; Gary Chisholm, MS; Xuelin Huang, PhD; Hui Huang, MS; Mehmet Ali Ergun, MSc; Ronald Gangnon, PhD; Brian L. Sprague, PhD; Sylvia Plevritis, PhD; Eric Feuer, PhD; Harry J. de Koning, MD, PhD; and Kathleen A. Cronin, PhD, MPH

Background: Controversy persists about optimal mammography screening strategies.

Objective: To evaluate screening outcomes, taking into ac-

Results: Biennial strategies were consistently the most efficient for average-risk women. Biennial screening from age 50 to 74 years avoided a median of 7 breast cancer deaths versus no screening; annual screening from age 40 to 74 years avoided an

Conclusion: Biennial screening for breast cancer is efficient for average-risk populations. Decisions about starting ages and intervals will depend on population characteristics and the decision makers' weight given to the harms and benefits of screening.

screens.

This article was published at www.annals.org on 12 January 2016.

Despite decades of mammography screening for early detection of breast cancer, there is no consensus on optimal strategies, target populations, or the magnitude of harms and benefits (1–11). The 2009 US Preventive Services Task Force (USPSTF) recommended biennial film mammography from age 50 to 74 years and suggested shared decision making about screening for women in their 40s (12). Since that recommendation was formulated, new data on the benefits of screening have emerged (2, 6, 8, 9, 11, 13, 14), digital mammography has essentially replaced plain film (15), and increasingly effective systemic treatment regimens for breast cancer have become standard (16). There has also been growing interest in consumer preferences and personalized screening approaches (17–20). These factors could each affect the outcomes of breast cancer screening programs or alter policy decisions about population screening strategies (17).

Modeling can inform screening policy decisions because it uses the best available evidence to evaluate a wide range of strategies while holding selected conditions (such as treatment effects) constant, facilitating strategy comparisons (21, 22). Modeling also provides a quantitative summary of outcomes in different groups and assesses how preferences affect results. Collaboration of several models provides a range of plausible effects and illustrates the effects of differences in model assumptions on results (1, 7, 23).

We used 6 well-established simulation models to synthesize current data and examine the outcomes of digital mammography screening at various starting ages and intervals among average-risk women. We also examined how breast density, risk, or comorbidity levels affect results and whether preferences for health

See also:

Related articles . . . 205, 226, 236, 244, 256, 268, 279
Editorial comment 303

Web-Only
CME quiz

Benefits of Screening

- Overall 20% reduction in mortality
  - Relative decreases

Harms of Screening

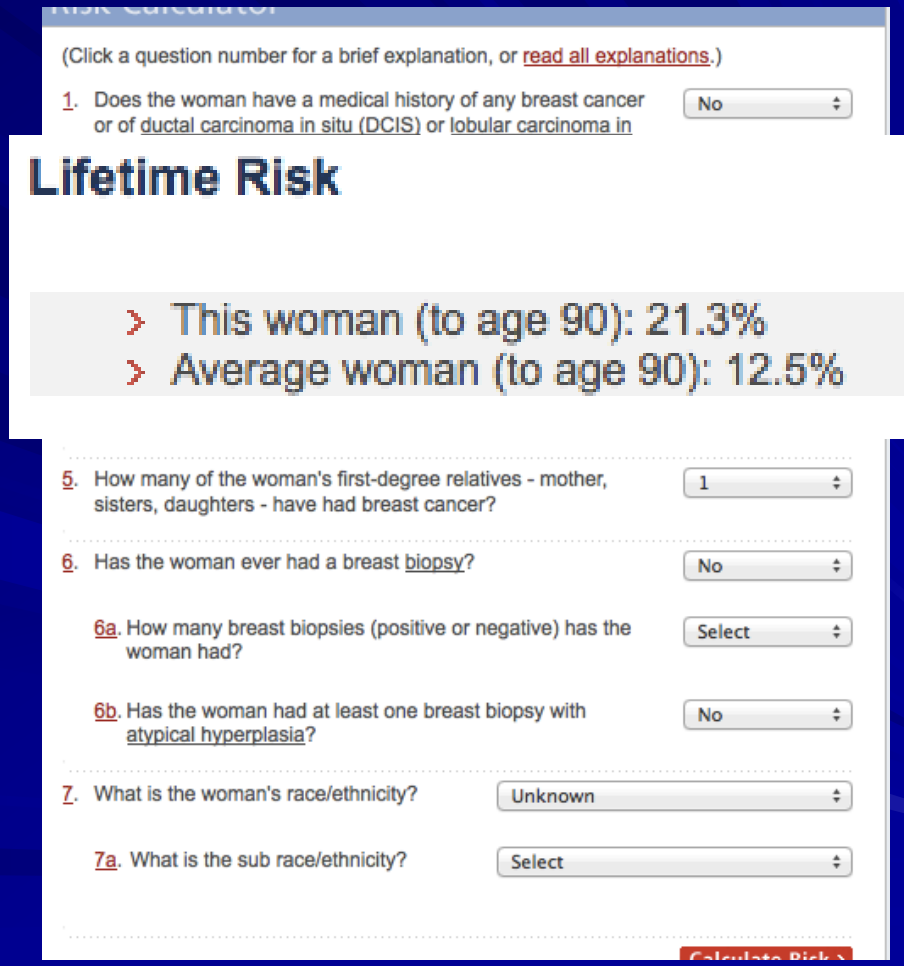
- For every 1000 women screened:
- Absolute decrease in mortality is small
  - 4 → 3
- Overdiagnosis
  - 5-15 women will be treated for an asx cancer
- False Positives
  - ~150 undergo beast bx

Methods of Breast Cancer Screening

- Physical Exam
  - Breast self exam
  - Clinical breast exam
- Imaging
  - Mammography
  - MRI
  - *Ultrasound*
  - *Tomosynthesis, molecular breast imaging, contrast mammography*
- *Blood biomarkers*

Who is High Risk?

- 32 y/o women, new patient visit
  - Healthy
  - Mom breast ca age 45
    - No other FH ca
  - Onset menses age 11
  - G2P2, first birth age 32



www.cancer.gov/bcrisktool/
CA Cancer J Clin 2007;57:75-89

Screening Mammography - Controversies

Benefits of Screening

- Overall 20% relative reduction in mortality → Very big benefits, few people

"Harms" of Screening

- False Positives
- High NNT when younger → Small harms, many people

- Overdiagnosis → Big harms, very few people

Screening Mammography - Controversies

Benefits of Screening

- Overall 20% relative reduction in mortality

→ Very big benefits, few people

When to start mammography

Age 40 or 50?

"Harms" of Screening

Screening frequency

- False Positives
- High NNT when younger

Yearly or biennial?

→ Small harms, many people

When to stop?

- Overdiagnosis

Age 75? 80? 85?

→ Big harms, very few people

Benefits of Screening

- 20% mortality reduction* → Very big benefits, few people

"Harms" of Screening

- False Positives
- High NNT when younger → Small harms, many people

- Overdiagnosis
  - ~1-10% women with cancer Rx unnecessarily → Big harms, very few people

Controversies

Benefits of Screening

- 20% mortality reduction*
  - If 1000 women screened
  - Absolute decrease 5 → 4

→ Very big benefits, few people

"Harms" of Screening

- False Positives
  - ~10% recalled, ~1% biopsy
  - Anxiety, morbidity, cost
- High NNT when younger
  - 40-50: 1/1900
  - 60-70: 1/377

→ Small harms, many people

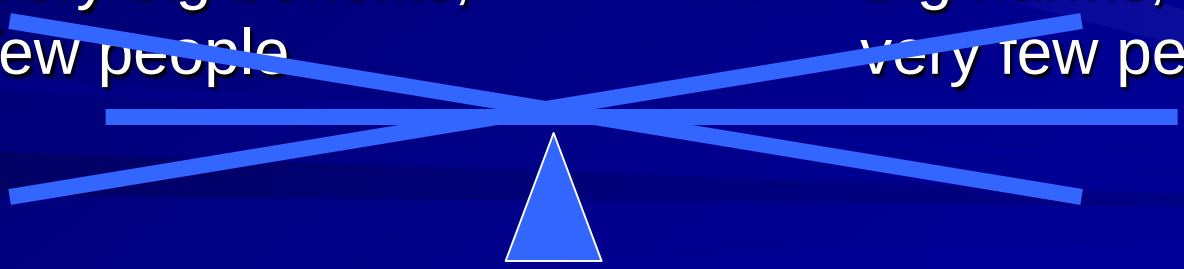
Ann Intern Med. 2009;151:727-37
J Med Screen 2012:19 s1:42-56

- When to start screening?
  - Age 40 or 50
- Screening frequency?
  - Yearly or biennial
- When to stop?
  - Age 75, 80, 85

Small harms, many people

Big harms, very few people

Very big benefits, few people

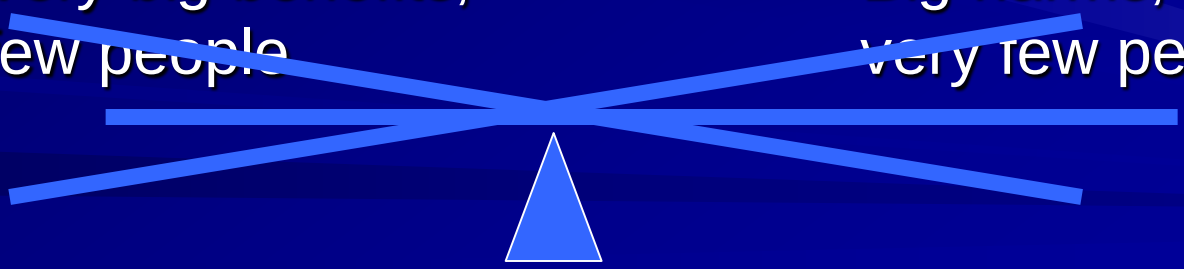


- When to start screening?
  - Age 40 or 50
- Screening frequency?
  - Yearly or biennial
- When to stop?
  - Age 75, 80, 85

Small harms, many people

Big harms, very few people

Very big benefits, few people



Organization and Year of Guidelines		Recommendations Regarding Mammography Screening	
American Cancer Society (United States),	2015	Yearly mammograms	45-55y, then biennial
National Health Service Breast Screening Program (United Kingdom), 2010[3,a]		Screening mammography every 3 y for women aged 47-73 y	

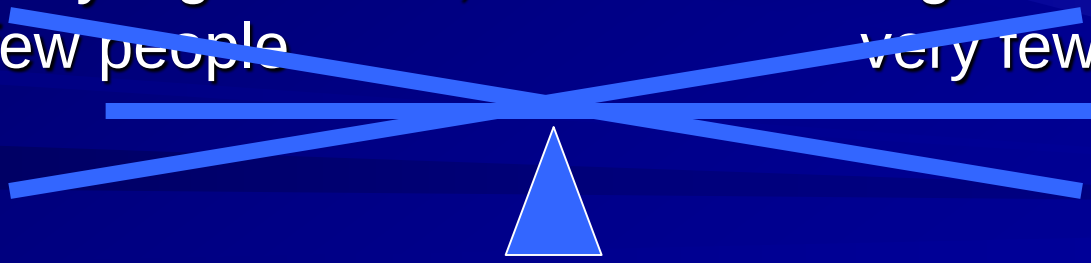
US Breast Cancer Mortality: 22/100,000

UK Breast Cancer Mortality: 24/100,000

Small harms, many people

Very big benefits, few people

Big harms, very few people



JAMA 2014;311(13):1327-35

Organization and Year of Guidelines	Recommendations Regarding Mammography Screening
Norwegian Breast Cancer Screening Program, 1996[4]	Screening mammography every 2 y for women between ages 50 y and 69 y
US Preventive Services Task Force, 2016	Biennial screening mammography for women between ages 50 y and 74 y The decision to start regular, biennial screening mammography before age 50 y should be an individual one and take into account patient context, including the patient's values regarding specific benefits and harms
National Health Service Breast Screening Program (United Kingdom), 2010[3,a]	Screening mammography every 3 y for women aged 47-73 y
Canadian Task Force on Preventive Health Care, 2011[81]	Routine screening mammography for women aged 50-74 y
National Cancer Institute (United States), 2012[6]	Screening mammograms every 1 to 2 y in women ≥40 y
American Cancer Society (United States), 2015	Yearly mammograms 45-55y, then biennial

Very big benefits,
few people

Small harms,
many people

Big harms,
very few people

JAMA 2014;311(13):1327-35
JAMA 2015;314(15):1599-1614

Organization and Year of Guidelines	Recommendations Regarding Mammography Screening
American Cancer Society (United States), 2013[5]	Yearly mammograms starting at age 40 y
National Health Service Breast Screening Program (United Kingdom), 2010[3,a]	Screening mammography every 3 y for women aged 47-73 y

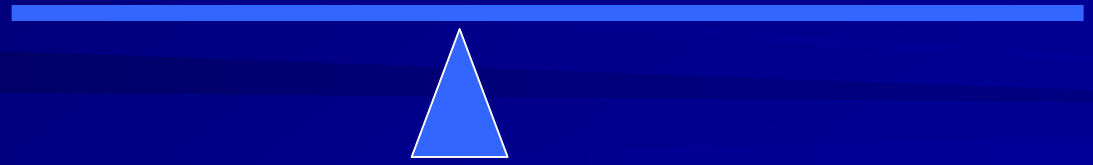
US Breast Cancer Mortality: 22/100,000

UK Breast Cancer Mortality: 24/100,000

Small harms,
many people

Very big benefits,
few people

Big harms,
very few people



JAMA 2014;311(13):1327-35

Physical Exam Screening

CLINICAL BREAST EXAM

- Yes:
  - *NCI, ACOG*
- Insufficient data/No:
  - *ACS, USPSTF, AAFP*

BREAST SELF EXAM

- Yes:
  - *ACOG*
- No:
  - *USPSTF, AAFP, ACS, NCI*