Breast Cancer Screening in the Elderly

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Objectives

- Develop a systematic way to think about benefits and harms of cancer screening in older adults

- Consider life expectancy when making screening recommendations

- Understand the importance of factoring patient preferences into screening decisions

The Problem

- Breast cancer in the elderly will be an increasing health care issue over the next two decades due to demographics and increased use of screening mammography.
- 30-40% of breast cancer occur in women ≥ 70 years.
- US Census Bureau projects that between the years 2000 and 2030, those ≥ 65 years will approximately double form 35 to 71 million, with older women substantially outnumbering men.

Breast Caner Risk for American Women by age

By age	
50	One in 50
60	One in 24
70	One in 14
80	One in 10
85	One in 9

Cases

- ## <u>Mrs. A</u>

  70 y/o woman with Alzheimer's dementia (MMSE=10/30) and functionally dependent in many ADLs. She lives with her daughter who brings her in for a routine check-up. She has no history of any cancer screening tests.

- ## <u>Mrs. B</u>

  80 y/o woman with a history of osteoarthritis. She walks 2 miles a day and cares for her older sister. She has not seen a doctor in several years but decides to come in for a routine check-up. She has no history of any cancer screening tests.

Uncertainty

Uncertainty about when to screen asymptomatic elderly patients for breast cancer

- Most trials of breast cancer screening tests have excluded patients over age 74
  - Extrapolate data to older patients

- Data from randomized trials not always applicable to an individual patient
  - Trials do not address individual characteristics that may change the likelihood of benefit vs. harm

What to Do?

- Guidelines used to be based on age cutoffs and were conflicting

  Mammography Guidelines (until 2002)
  - USPSTF: Stop mammography at age 70
  - American College of Physicians: Stop at age 75
  - American Geriatrics Society: Stop at age 85
  - American Cancer Society: Never stop

- Now the SIOG: International Society of Geriatric Oncology (2012) guidelines agree that screening:
  - Beyond 70 years of age should be made by the individual and the clinician based on risks and benefits of screening, patient preferences, and life expectancy.

Framework for Individualized Decisions

- The natural history of breast cancer in the elderly. Is breast cancer "less aggressive in the elderly?"
- Estimate life expectancy
- Weigh potential benefits and harms according to according to an individual's values/preferences
- Determine potential harms of screening

Is breast cancer less aggressive in the elderly?

University of Chicago Study on the Natural History of Breast Cancer

- ◉ 2136 patients treated with mastectomy from 1927-1987
- ◉ This era is prior to screening
- ◉ 75% did not receive systemic therapy
- ◉ Looked at 3 age groups:
  - ≤ 40
  - 41-70
  - > 70

University of Chicago Study on the Natural History of Breast Cancer

Heimann and Hellman **J Clin Oncol. 2000;18:591-599**

		< 40	41-70	> 70
T size cm	< 2	32	32	36
	2-5	49	49	46
	> 5	19	19	18
+ nodes	0	40	42	44
	1-3	32	28	28
	≥ 4	28	27	17
	X	<1	3	17

University of Chicago Study on the Natural History of Breast Cancer

Heimann and Hellman **J Clin Oncol. 2000;18:591-599**

- Multivariate analysis showed that age was not a significant factor for distant disease free survival

Natural History of Breast Cancer

- Italian study, 2999 post menopausal women who underwent surgery between 1997-2002

- Looked at 3 age groups: 50-64, 65-74, ≥75

- No difference seen in the 3 age groups for: proportion of patients with
  - Grade 1,2,3
  - High Ki 67
  - ER neg
  - 1-3, 4-9 + nodes

Natural History of Breast Cancer

◉ But women aged ≥ 75 had:
- Fewer p T 1 (tumor < 2 cm)

  p N O
- More 10+ positive nodes

**Probably reflects
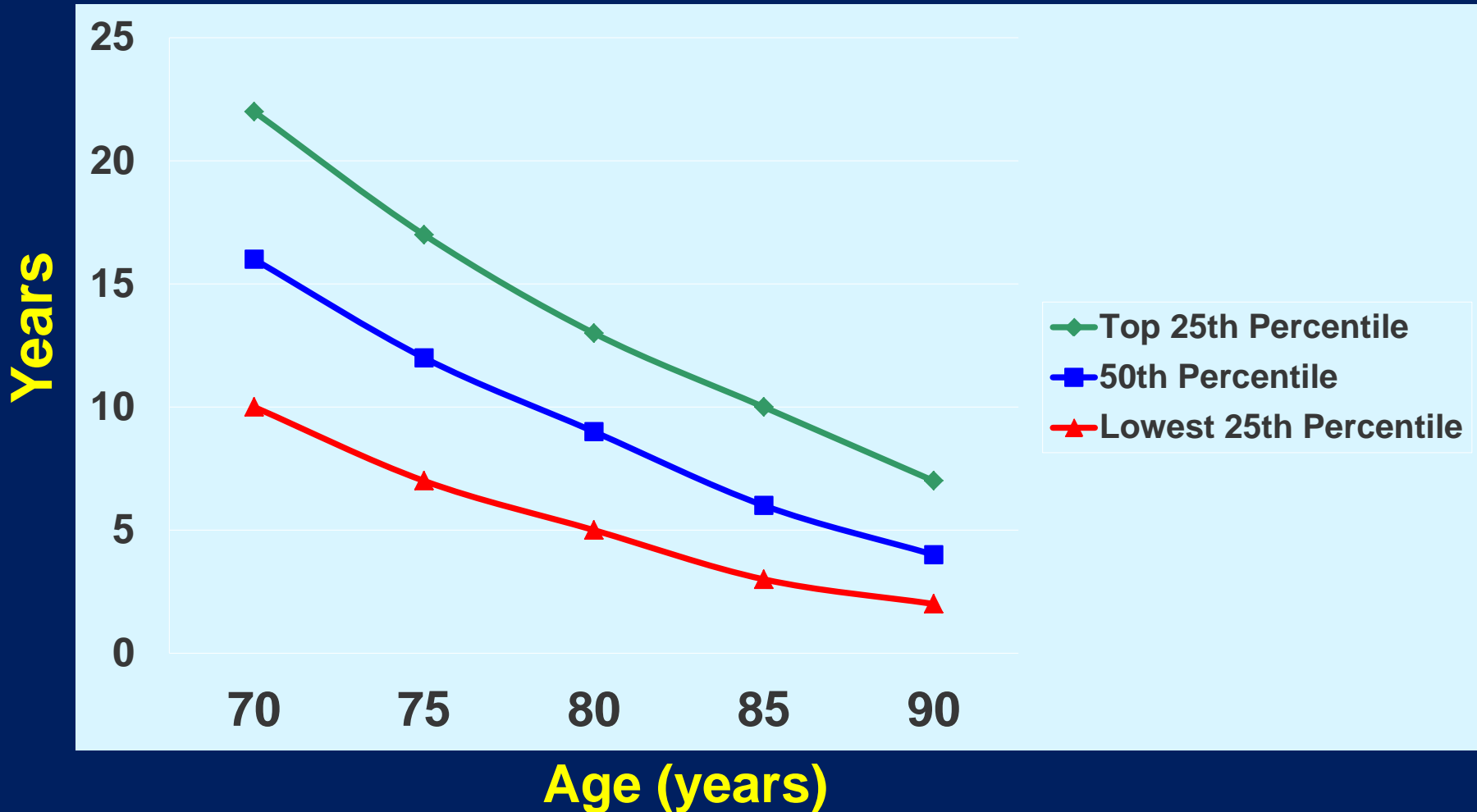Less screening**

- Fewer Her 2+

  LVI (lymphovascular invasion)
- More ER/PR+ cancers

Life Expectancy for Women

Walter LC. *JAMA* 2001;285:2750-2756

Life expectancy for women at different ages

Age (years)	Life expectancy	
	Median (years)	Quartiles* (years)
50	33	(40-24.5)
70	15.7	(21.3-9.5)
75	11.9	(17.0-6.8)
80	8.6	(9.6-2.9)

Data are from the Life Tables of the US. Modified from Walter and Covinsky J Am Med Assoc 2001;285:2750-6.

*Correspond to upper and lower quartiles

Independent Risk Factors for 4-Year Mortality (Lee et al. JAMA 2006;295:805)

Age (y)	Adjusted OR (95% CI)*	Points
60-64	1.9 (1.4-2.5)	1
65-69	2.8 (2.1-3.7)	2
70-74	3.7 (2.8-4.9)	3
75-79	5.4 (4.1-7.1)	4
80-84	8.3 (6.3-11.0)	5
≥ 85	16.2 (12.2-21.6)	7
* Each OR was adjusted for the risk factors in the table		

Independent Risk Factors for 4-Year Mortality
(Lee et al. JAMA 2006;295:805)

Demographics	Adjusted OR (95% CI)*	Points
Male gender	2.0 (1.8-2.3)	2
Comorbidities and Behaviors		
Diabetes mellitus	1.8 (1.5-2.1)	1
Cancer	2.1 (1.7-2.4)	2
Lung Disease	2.3 (1.8-2.9)	2
Heart Failure	2.3 (1.8-3.1)	2
BMI < 25 kg/m^2	1.7 (1.4-1.9)	1
Current smoker	2.1 (1.7-2.5)	2
* Each OR was adjusted for the risk factors in the table		

Independent Risk Factors for 4-Year Mortality
(Lee et al. JAMA 2006;295:805)

Functional Measures	Adjusted OR (95% CI)*	Points
Bathing	2.0 (1.6-2.4)	2
Managing finances	1.9 (1.6-2.3)	2
Walking several blocks	2.1 (1.8-2.4)	2
Pushing/pulling	1.5 (1.3-1.8)	1
* Each OR was adjusted for the risk factors in the table		

4-year Mortality Risk

Score	4-year Mortality Risk
0 - 5	≤ 4%
6 – 9	15%
10 – 13	42%
≥ 14	64%

Life Expectancy

Social Security
Official Social Security Website

http://www.ssa.gov/oact/STATS/table4c6.html

Exact Age	Death Probability[a]	Number of lives[b]	Life expectancy[c]
70	0.01644	82,424	16.33
75	0.026706	74,443	12.79
80	0.043899	62,957	9.65
85	0.075729	47,412	6.95
90	0.131146	28,649	4.85
95	0.213849	11,795	3.39
100	0.299455	2,813	2.49

a = Probability of dying within one year
b = Number of survivors out of 100,000 born alive
c = Average number of remaining years

Benefits of Screening (randomized Controlled Trials
Pooled RRs for Breast Cancer Mortality From Mammography
Screening Trials for All Ages

| Age	Trials included, n	RR for Breast Cancer Mortality (95% CrI)	NNI to Prevent 1 breast Cancer Death (95% CrI)
39-49	8	0.85 (0.75-0.96)	1904 (929-6378)
50-59	6	0.86 (0.75-0.99)	1339 (322-7455)
60-69	2	0.68 (0.54-0.87)	377 (230-1050)
70-74	1	1.12 (0.73-1.72)	Not available

Lag-Time to Benefit

- Benefit of screening does NOT occur immediately

- Screening results in benefit by finding cancers at an early stage, which would have caused symptoms or killed a person years later

- A life expectancy of > 5 yrs is required to have some chance of survival benefit from screening
  - RCTs of mammography show survival curves of screened vs. unscreened do not separate significantly until > 5 years after start of screening

Screening Mammography RCTs

◉ RCTs in women aged 50-69 years

**Cumulative Breast Cancer Mortality
by Study Group**

**Mortality/
100,000**

Legend:
- ◆ Screening
- ■ Control

Time (years)

Nystrom L. *Lancet.* 2002:909-919
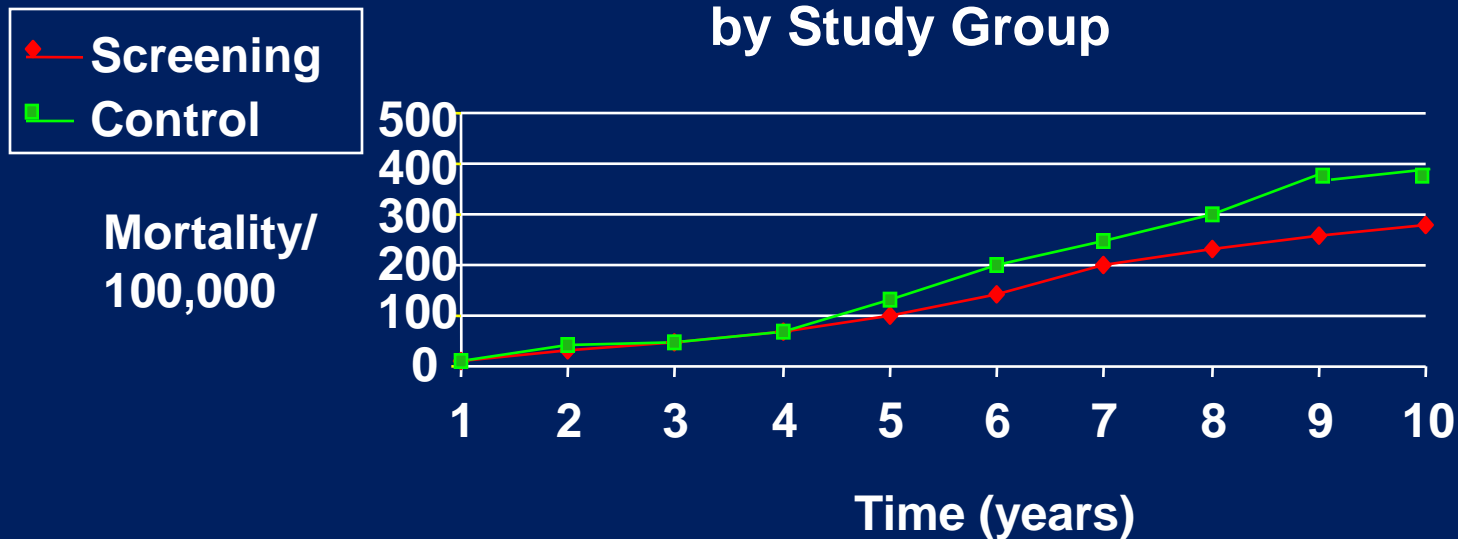
Are there studies indicating a benefit of screening the elderly for breast cancer?

⦿ Study by Fracheboud et al. (EUR J Cancer 2008;6:48)

- In 1998-2006, 737 million screening examinations performed; 862,655 involved women 70-75 years. The participation rate was 81% for ages 50-69 and 72% for ages 70-75. As of 2003, breast cancer mortality among women aged 75-79 started to decline and was 29.5% lower in 2006 than the mean rate during 1986-1997

Are there studies indicating a benefit of screening the elderly for breast cancer?

- Lash et al (J Clin Oncol 2007:25;3001-6)
  - 1,846 stage I and II breast cancer patients ≥ 65 years old were enrolled in a mammographic study. They matched 4 controls to each breast cancer decendent to estimate the association between receipt of surveillance mammogram and breast cancer mortality.
  - 178 women died of breast cancer during 5-year followup. The authors reported that each additional surveillance mammogram was associated with a 0.69-fold decrease in the odds of breast cancer mortality (95% CI:0.52-0.92). The protective association was strongest among women with stage I disease, with those who received mastectomy, and those in the oldest group

Benefits of Screening

- Unlikely to benefit if life expectancy < 5 years

- If life expectancy > 5 years benefit should be considered in terms of absolute risk reduction (ARR) rather than relative risk reduction (RRR)
  - RRR usually reported in studies or advertisements:

  "TEST REDUCES RISK OF CANCER BY 25%!"

  - A 25% RRR describes a reduction from 40% to 30% or 4% to 3%

Absolute Benefit

- More benefit from test that reduces risk from 40% to 30% → ARR = 10% rather than 4% to 3% → ARR = 1%

- Absolute benefit presented as Number Needed to Screen (NNS) = 1/ARR
  40% to 30% → NNS = 1/0.1 = 10
  4% to 3% → NNS = 1/0.01 = 100

- Absolute benefit is fair way to present benefit because accounts for baseline risk of disease

Number Needed to Screen

NNS over remaining lifetime to prevent one cancer death for women at selected ages and life expectancies

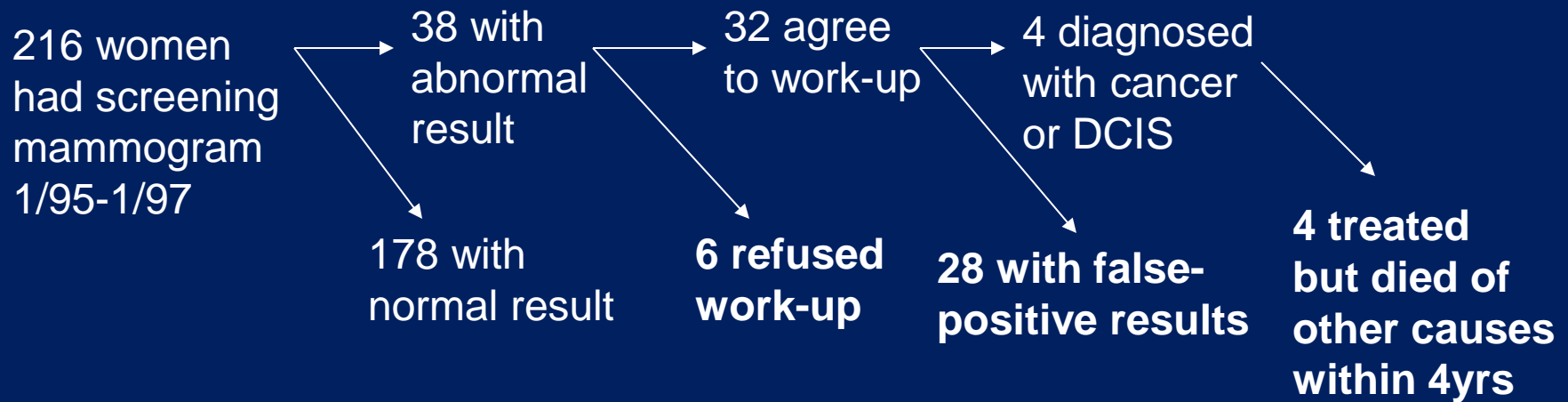| Screening Test	RRR	AGE 70 Life Expectancy			AGE 80 Life Expectancy			AGE 90 Life Expectancy		
		U	M	L	U	M	L	U	M	L
Mammography	**26%**	**142**	**242**	**642**	**240**	**533**	**-**	**1,066**	**-**	**-**
FOBT	18%	178	340	1,046	262	581	-	1,163	-	-
Pap Smear	60%	934	1,521	4,070	1,694	3,764	-	7,528	-	-

- indicates life expectancy < 5 years

Harms of Screening

- Complications from additional diagnostic procedures due to inaccurate test results

- Identification and treatment of clinically unimportant disease that would not have progressed to symptoms in patient's lifetime

- Psychological distress

Harms of Screening Mammography

- Conducted study at On Lok (PACE): Health program for frail elderly

- State auditors insisted mammograms be performed in all women despite poor health and advanced age (per American Cancer Society)
  - 50% of patients have dementia
  - Median life expectancy is 4 years

- The harms of this universal screening mammography policy in frail older women was assessed

Screening mammography in frail elderly women frequently led to harm

216 women had screening mammogram 1/95-1/97

→ 38 with abnormal result

178 with normal result

→ 32 agree to work-up

6 refused work-up

→ 4 diagnosed with cancer or DCIS

28 with false-positive results

4 treated but died of other causes within 4yrs

Walter LC. *J Gen Intern Med* 2001:779-784

Harm of Finding Clinically Unimportant Cancers

80 y/o woman with severe dementia from multiple strokes who underwent screening mammography on enrollment

- Abnormal mammogram
- 2 biopsy attempts—inconclusive results
- Underwent surgery—ductal carcinoma in situ
- Developed wound infection—daily trips to wound clinic for 3 months
- Second surgery to close wound
- Died of large stroke 9 months later

Walter LC. *J Gen Intern Med* 2001:779-784

Preferences

- Assess how patients view potential harms/benefits and integrate values/preferences into decisions

- Different from public health strategy in which experts weigh benefits/risks and decide what is best for a population

- Since many decisions in older patients are "close calls," need to consider values/preferences
  - Harms look larger to some people
  - Non-mortality benefits considered more substantial to some people (e.g., "peace of mind")

Other Considerations

- Perhaps older adults would have less need for reassurance from continued screening if:
    - Used less alarming language about cancer risk
        - Ex: Breast cancer responsible for ~1% of deaths in women $\geq$ 80 yrs
    - Talk about screening as a choice (not an obligation)
        - 41% of Americans labeled an 80 y/o woman "irresponsible" if she did not have mammography

- Need to encourage informed discussions: Screening is a "double-edged sword"

Welch HG. *Ann Intern Med*. 2004;140:754-5

Discuss Preferences for Work-up

- Prior to screening, discuss possible procedures or treatments required to work-up abnormal result

- Patients who would not want work-up/treatment for an abnormal result should NOT be screened

Cases

Mrs. A – 70 y/o woman with severe dementia

Mrs. B – 80 y/o woman with osteoarthritis

- ◉ Estimate life expectancy
  - Mrs. A is younger but has severe dementia and functional dependency, so life expectancy < 5 years
  - Mrs. B is probably in upper quartile of life expectancy for her age, so likely to live > 13 years

- ◉ Probability of benefit
  - Mrs. A unlikely to benefit since life expectancy < 5 yrs
  - Mrs. B has reasonable likelihood of benefit (NNS)
    - ○ 240 for mammography; 262 for FOBT; (1,694 for Paps)

Cases

- Probability of harm
  - Mrs. A has severe dementia so tests may cause distress and if cancer identified likely is unimportant
  - Mrs. B understands and accepts risks of tests

- Values and preferences
  - Mrs. A has avoided doctors and becomes agitated if anything interrupts her daily routine
  - Mrs. B worries about her health and wants a mammogram, FOBT, and Pap smear

- Screening recommendations
  - Recommend AGAINST screening Mrs. A
  - Recommend screening Mrs. B

Summary

Do Screen

Don't Screen

Likelihood of Benefit

Likelihood of Harm

Patient Preferences (moveable fulcrum)

Questions