Breast Cancer Screening: U.S. Preventive Services Task Force Recommendations

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U.S. Preventive Services TASK FORCE

Disclosures

Includes, per IOM standards: "Any current and planned commercial (including services from which a clinician derives a substantial proportion of income), noncommercial, intellectual, institutional, and patient/public activities pertinent to the potential scope of the clinical practice guideline."

Task Force Member	Potential Conflicts of Interest
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Disclosures (continued)

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Our Goals

- We are here to present our recommendations and the evidence that supports them
- We believe there are **many common areas of agreement** about breast cancer screening held by the organizations present here
- There may be areas where disagreement remains:
  - This conference presents an opportunity to better understand those residual areas of discordance
- We have noted several critical misunderstandings of our processes and our breast cancer screening recommendations:
  - We want to use this time to correct those areas of confusion

Misinterpretations of the USPSTF Processes and Our Breast Cancer Screening Recommendations

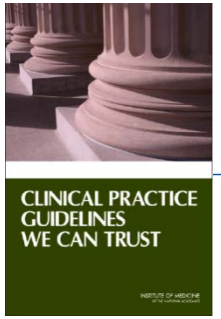
- **Myth**: "The USPSTF does not have the requisite expertise to make recommendations about breast cancer screening"
- **Myth**: "The USPSTF recommendation development process does not meet IOM standards for trustworthy guidelines"
- **Myth**: "The USPSTF "C" recommendation for women ages 40 to 49 years and its "I" statement for women ages 75 and older are recommendations *against* mammography screening"
- **Myth**: "The USPSTF is recommending against insurance coverage for screening mammograms for women in their 40s"

The U.S. Preventive Services Task Force (USPSTF)

- Independent panel of volunteer, non-federal experts (N=16)
- Makes recommendations on clinical preventive services offered in the primary care setting (screening tests, preventive medications, counseling)
- Members with expertise in primary care and in evidence-based medicine/research
    - Family Medicine, Obstetrics and Gynecology, Internal Medicine, Geriatrics, Nursing, Pediatrics, Behavioral Health, Health Systems
- Explicit process of evidence review with input from sub-specialists with content expertise and public throughout the recommendation development process

USPSTF Recommendation Process and IOM Standards

- 2011 IOM Report ("Clinical Practice Guidelines We Can Trust") calls out the USPSTF as a leader and a reference standard for guideline development processes:
  - "The USPSTF…is noted for its early use of transparent standards and inclusion of multidisciplinary experts in the [CPG] development process." (p.36)
  - "Increasing transparency of the guideline process has long been recommended by the authors of CPG development appraisal tools…and the following leading guidelines development organizations: the U.S. Preventive Services Task Force (USPSTF)…." (p.76)



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USPSTF Recommendation Process and IOM Standards

- 2015, Dr. Sheldon Greenfield, Chair of the 2011 IOM Report, reaffirmed the leadership role of the USPSTF in developing clinical practice guidelines in accordance with that report, specifically in regards to the breast cancer screening recommendations:
  - "Both the ACS and the Task Force used similar processes as outlined in the IOM report; they relied on experts who have been vetted for lack of conflicts of interest and utilized evidence from independent researchers who also did not have conflicts of interest. This may explain why these two organizations are more aligned than ever — and it is a step forward in the harmonization of their independent assessments of the evidence."

Rebuilding Trust In Medicine: How the Public Can Interpret Differing Guidelines. Health Affairs Blog. November 17, 2015.

Steps the USPSTF Takes to Solicit Input & make a Recommendation

At each stage –

1) Solicit feedback from content experts, sub-specialists
2) Draft posted for public comment
3) Peer-review of evidence report prior to public posting

Basic USPSTF Methods for Developing Recommendations

- The USPSTF assesses the evidence across the analytic framework:
  - Judges the ***certainty*** of the estimates of the potential benefits and harms
  - Judges the ***magnitude*** of the potential benefits and harms
  - The ultimate goal is to judge the ***balance*** of the benefits and harms, or the ***magnitude of the net benefit*** of the preventive service

Basic USPSTF Methods for Developing Recommendations: The Letter Grades

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	I			

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USPSTF Grades

- **A**
- **B**
- **C**

All three grades are recommendations in favor of screening

They differ by the level of certainty of the evidence and the magnitude of potential net benefit

- **I**

Not enough evidence to make a recommendation

NOT a recommendation against screening – rather it's a call for more research

USPSTF Breast Cancer Screening Recommendations for Women 50-74 years

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	I			

- The USPSTF recommends biennial screening mammography for women aged 50 to 74 years. **B recommendation.**
  - The USPSTF concludes with ***moderate certainty*** that the ***net benefit*** of screening mammography in women aged 50 to 74 years is ***moderate***.

USPSTF Breast Cancer Screening Recommendations for Women 40-49 years

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	**A**	**B**	**C**	**D**
Moderate	**B**	**B**	**C**	**D**
Low	**I**			

- The 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 and 49 years. **C recommendation.**
  - The USPSTF concludes with ***moderate certainty*** that the ***net benefit*** of screening mammography in the general population of women aged 40 to 49 years, **while positive**, is ***small***.
  - This is a **positive** recommendation—*not* a recommendation against screening

USPSTF Breast Cancer Screening Recommendations for Women 75 years and older

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	I			

- The current evidence is *insufficient* to assess the *balance of benefits and harms* of screening mammography in women age 75 years and older. **I statement.**
  - Not a recommendation for or against screening – a call for more research
  - In the absence of evidence, clinicians and patients must use clinical judgment to determine age to stop screening

USPSTF Grades and the Affordable Care Act

- **Private insurers** "…shall provide coverage for and shall not impose any cost sharing requirements for evidence-based items or services that have in effect a rating of 'A' or 'B' in the current recommendations of the USPSTF"

- **The law also states** "…nothing in this subsection shall be construed to prohibit a plan or issuer from providing coverage for services in addition to those recommended by USPSTF or to deny coverage for services that are not recommended by the Task Force"

USPSTF Grades and the Affordable Care Act

- The ACA expands access to evidence-based preventive services, but is the "floor" and not the "ceiling" for coverage
- USPSTF evaluates science, but does not determine coverage - that role is left to insurers, regulators, and lawmakers
- As physicians, we value access for our patients, but as a Task Force, we cannot reinterpret the science to arrive at an A or B recommendation
- In the case of mammography for women in their 40's, lawmakers acted in 2009 and 2015 to ensure private insurance coverage

Systematic Evidence Review

POTENTIAL BENEFITS OF SCREENING

Nelson HD, et al. Screening for Breast Cancer. Ann Intern Med. 2016; 164: doi:10.7326/M15-0969

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Screening Target Population

Women age 40 and older

Screening Pool
Average-risk women with no previous or current breast abnormalities

Not in Screening Pool
- Current physical finding
- Previous breast cancer or other breast abnormality (DCIS, LCIS, ADH, ALH)
- BRCA mutation
- Strong family history (>15% risk)
- Chest radiation, familial cancer syndromes

Effectiveness: Outcomes of Interest

Final Health Outcomes

- All-cause mortality
- Breast cancer-specific mortality

Intermediate Outcomes

- Treatment-related morbidity
- Incidence of advanced breast cancer

All outcomes were evaluated by how they differed by age, risk factor, and screening interval, although data were often lacking

Effectiveness of Screening: Study Designs Included in Review

- Randomized controlled trials (**8**)
- Observational studies (**200+** in review; **81** directly about effectiveness)
- Meta-analyses of both experimental and observational evidence

All-Cause Mortality: RCT Findings

- All trials reported all-cause mortality outcomes
- No trial found a reduction in all-cause mortality with mammography screening either for the entire intervention group or by age:
  - Combined RR (>600,000 women), all ages/trials: **0.99 (95% CI, 0.97-1.002)**
    - 39-49 y: RR 0.99 (0.94-1.05)
    - 50-59 y: RR 1.02 (0.94-1.10)
    - 60-69 y: RR 0.97 (0.90-1.04)
    - 70-74 y: RR 0.98 (0.86-1.14)

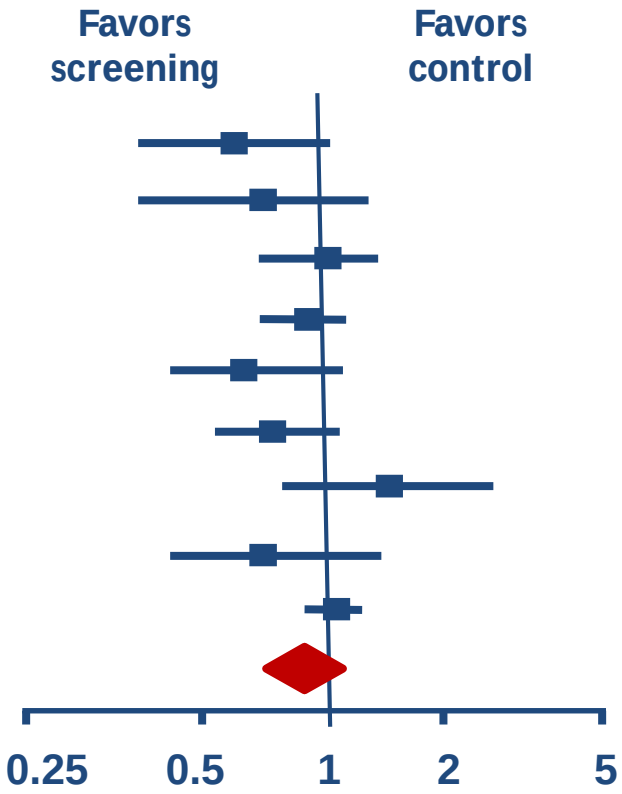
Breast Cancer-Specific Mortality: RCT Findings

Age-Specific Rates of Breast Cancer Mortality Reduction With Screening: Meta-analysis (Long Case Accrual)		
Age, y	Breast Cancer Mortality Reduction: RR (95% CI)	Deaths Averted With Screening 10,000 Women Over 10 Years (95% CI)
39-49	0.92 (0.75-1.02)	**3** (0-9)
50-59	0.86 (0.68-0.97)	**8** (2-17)
60-69	0.67 (0.54-0.83)	**21** (11-32)
70-74	0.80 (0.51-1.28)	**13** (0-32)
75+	Not Reported	**Unknown**
50-69	0.78 (0.68-0.90)	13 (6-20)

No trials included women 75 years of age and older

Meta-analysis of Screening Trials
Breast Cancer Deaths, Ages 39 to 49 Years

Study (mean FU)	RR breast cancer death (95% CI)
Malmö II (11.2)	0.64 (0.39 to 1.06)
Kopparberg (12.5)	0.73 (0.37 to 1.41)
Östergötland (12.5)	1.02 (0.52 to 1.99)
*Age (17.5)	0.93 (0.80 to 1.09)
Gothenburg (13.8)	0.69 (0.45 to 1.05)
HIP (14.0)	0.75 (0.53 to 1.05)
Stockholm (14.3)	1.52 (0.80 to 2.88)
Malmö I (18.2)	0.74 (0.42 to 1.29)
*CNBSS-1 (21.9)	1.04 (0.87 to 1.24)
Total	**0.92 (0.75 to 1.02)**
2009 meta-analysis	0.85 (0.75 to 0.96)



Meta-analysis uses the longest follow-up times available.
**Updated results available since previous recommendation.*

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Breast Cancer-Specific Mortality: Observational Evidence, Women, Ages 50 to 69 Years

- **EUROSCREEN** systematic reviews of mammography screening:
  - Time-trend studies with adequate follow-up—mortality reductions range **28%-35%**
  - Incidence-based mortality studies--pooled **RR 0.75** (95% CI 0.69-81) for women invited to screening
  - Case-control studies--pooled **OR 0.69** (95% CI 0.57-0.83) for women invited to screening
- **Harris et al** systematic review of mammography screening:
  - 17 observational studies, all noted to have quality concerns
  - Found **wide variation** in their estimates of effect size:
    - 4 found a ***large effect*** (>33% RRR),
    - **8** found a ***moderate effect*** (13-33% RRR),
    - **5** found ***small or no effect*** (0-12% RRR)

Breast Cancer-Specific Mortality: Observational Evidence
Women 40-49 Years

- Hellquist et al (Swedish Screening of Young Women Cohort):
  - **RR 0.74** (95% CI 0.66-0.83) for women invited to screening
- Coldman et al (Pan-Canadian cohort study):
  - **Standardized Mortality Ratio (SMR) 0.56** (95% CI 0.45-0.67) in women who chose to be screened versus those who did not

Potential Benefits of Mammography Screening: Breast Cancer Deaths

- Does mammography screening reduce deaths from breast cancer?
  - **Yes**, and the totality of evidence provides high confidence about the magnitude of benefit for women 50 to 74 years
    - The effect sizes between the RCTs and the observational evidence are generally congruent for this age group (**22%** versus **25%-31%**)
  - The totality of evidence provides less agreement between RCTs and observational studies for women in their 40s

Breast Cancer Screening Trials

Strengths

- Trials enrolled >557,000 women
- Study populations and interventions relevant to practice
- Long term follow-up
- Adherence high for some trials

Limitations

- Trials began 20-50 years ago (except the AGE trial that is more recent) and do not reflect more recent changes in:
  - Technology (digital)
  - Treatment (tamoxifen)
  - Breast cancer risk factors
- Variation in:
  - Usual care
  - Follow-up
  - Methods

Observational Evidence of Breast Cancer Screening

Strengths

- Studies can incorporate recent changes in:
  - Technology (digital)
  - Treatments (tamoxifen)
  - Breast cancer risk factors
- Can look at large numbers of participants
- Can assess changes over time

Limitations

- Comparison groups are likely to be dissimilar.
- Impossible to ensure complete elimination of biases and confounders:
  - **Healthy volunteer bias**
  - Lead-time bias
  - Length-biased sampling, etc.
- Wide variability in study quality

Healthy Volunteer Bias—Why It Matters

Example: Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Trial

Pinsky et al. Evidence of a healthy volunteer effect in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Am J Epidemiol*. 2007.

Standardized Mortality Ratios (SMRs) for Selected Causes (1993-2003)

	Men		Women	
Cause	**SMR**	95% CI	**SMR**	95% CI
All-cause*	**46**	44-47	**38**	36-39
Cardiovascular	**39**	37-41	**32**	30-35
Diabetes	**33**	27-39	**21**	16-26
Injuries & Poisonings	**66**	59-74	**59**	48-70

SMR: The ratio of observed deaths in the trial (both screening and control arms) to expected deaths in the general (non-participating) population. ***An SMR < 100 means there were less deaths observed in the trial than expected in the general population.***

**Except deaths from prostate, lung, colorectal, or ovarian cancers (the screened cancers).*

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Randomized Trials vs. Observational Evidence Case Study: Hormone "Replacement" Therapy and CVD Prevention

- Late 1980s-mid 1990s:
  - Multiple observational studies of hormone "replacement" therapy (HRT) and coronary heart disease (CHD) consistently show associations between HRT use and lower rates of re-infarction, CHD-related death, and coronary artery restenosis among women with CHD
  - Fewer observational studies of HRT for primary prevention of CHD, but consistent in direction and magnitude of effect with the studies in women with established disease
- 1990's
  - The seemingly overwhelming nature of the observational data cause many clinicians to question the ethics of a randomized trial testing the hypothesis in primary prevention (calling it "unethical to randomize women to no treatment")
- **2000's**
  - Randomized controlled trial of HRT - **Women's Health Initiative** (RCT) finds a trend towards **increased** risk of CHD in users of combined hormone therapy, which persisted through nearly 9 years of follow-up (**HR1.22 , 95% CI, 0.99 to 1.50**)

Interval and the Effectiveness of Mammography Screening

- No trials compared different intervals
- Two observational studies found no differences in breast cancer mortality with annual versus biennial or triennial screening
- Modeling represents current best approach to estimating the trade-offs to be gained with different intervals (more later)

Potential Benefits of Mammography Screening: Treatment-Related Morbidity

- Does mammography screening decrease morbidity caused by breast cancer treatments?
  - **The body of evidence is mixed.**
  - Pooled analysis of the trials, and some of the observational evidence, suggest a paradoxical increase in treatment intensity related to screening, whereas other observational evidence suggests a decrease in treatment intensity with the use of screening.

Treatment-Related Morbidity: RCT Findings

- Compared to the control group, women assigned to screening were more likely to:
  - Receive mastectomy: **RR 1.20** (95% CI 1.11-1.30)
  - Receive any surgical therapy (mastectomy + lumpectomy): **RR 1.35** (95% CI 1.26-1.44)
  - Receive radiation therapy: **RR 1.32** (95% CI 1.16-1.50)
- Women assigned to screening were *less* likely to receive hormone therapy: **RR 0.73** (95% CI 0.55-0.95)
- Receipt of chemotherapy was similar between the two groups: **RR 0.96 (95% CI 0.78-1.19)**

Treatment-Related Morbidity: Observational Evidence (Case Series)

Author	Setting	Age	Results
Buseman, 2003	U.S.	42-49	Lumpectomy and radiation: RR 1.00 (95% CI, 0.75-1.33) Chemo: RR 1.06 (95% CI, 0.85-1.33)
Garcia Fernandez, 2014	Spain	50-69	Overall differences, P<0.001 "Conservative surgery": 83% v. 57% Chemo: 0.4% v. 0.8% Radiation: 87% v. 75%
Jensen, 2003	Denmark and Sweden	50-69	Overall differences, P< 0.001 Mastectomy: 61% v. 85% Lumpectomy: 32% v. 6.8%
Olivotto, 1999	Canada	40-89	Overall differences, P<0.001 Total mastectomy: 35% v. 46% Breast conservation 65% v. 54% Chemo: 23% v. 27%

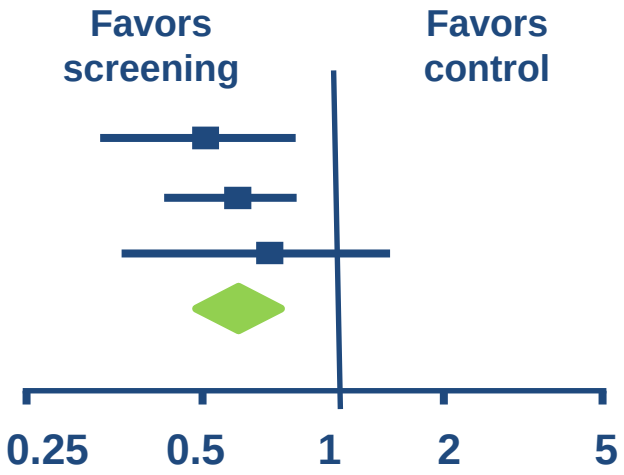
Potential Benefits of Mammography Screening: Incidence of Advanced Breast Cancer

- Does mammography screening reduce the incidence of advanced breast cancer?
  - **The body of evidence is mixed.**

Meta-analysis of Screening Trials

Advanced Breast Cancer Age ≥50

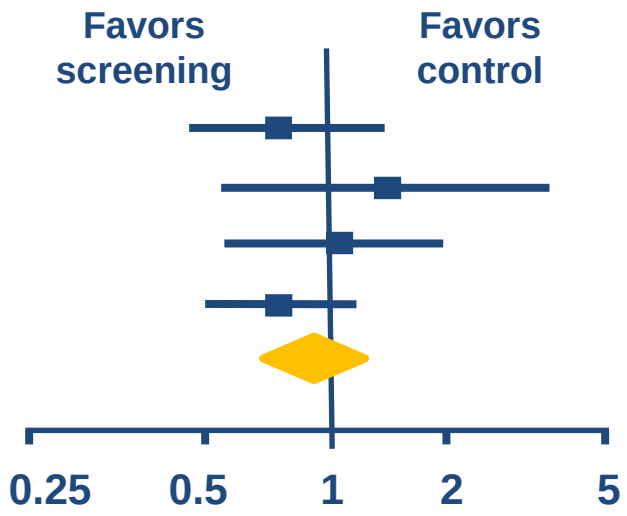
Study (mean FU)	RR advanced cancer (95% CI)
HIP (Stage III+)	0.52 (0.31 to 0.88)
Swedish (≥50 mm)	0.63 (0.45 to 0.89)
CNBSS-2 (≥40 mm)	0.75 (0.38 to 1.46)
Total	0.62 (0.46 to 0.83)



Meta-analysis of Screening Trials

Advanced Breast Cancer Age 39 to 49

Study (mean FU)	RR advanced cancer (95% CI)
HIP (Stage III+)	0.87 (0.48 to 1.58)
Swedish (≥50 mm)	1.57 (0.63 to 3.90)
CNBSS-1 (≥40 mm)	1.18 (0.67 to 2.08)
Age (≥50 mm)	0.85 (0.57 to 1.28)
Total	0.98 (0.74 to 1.37)

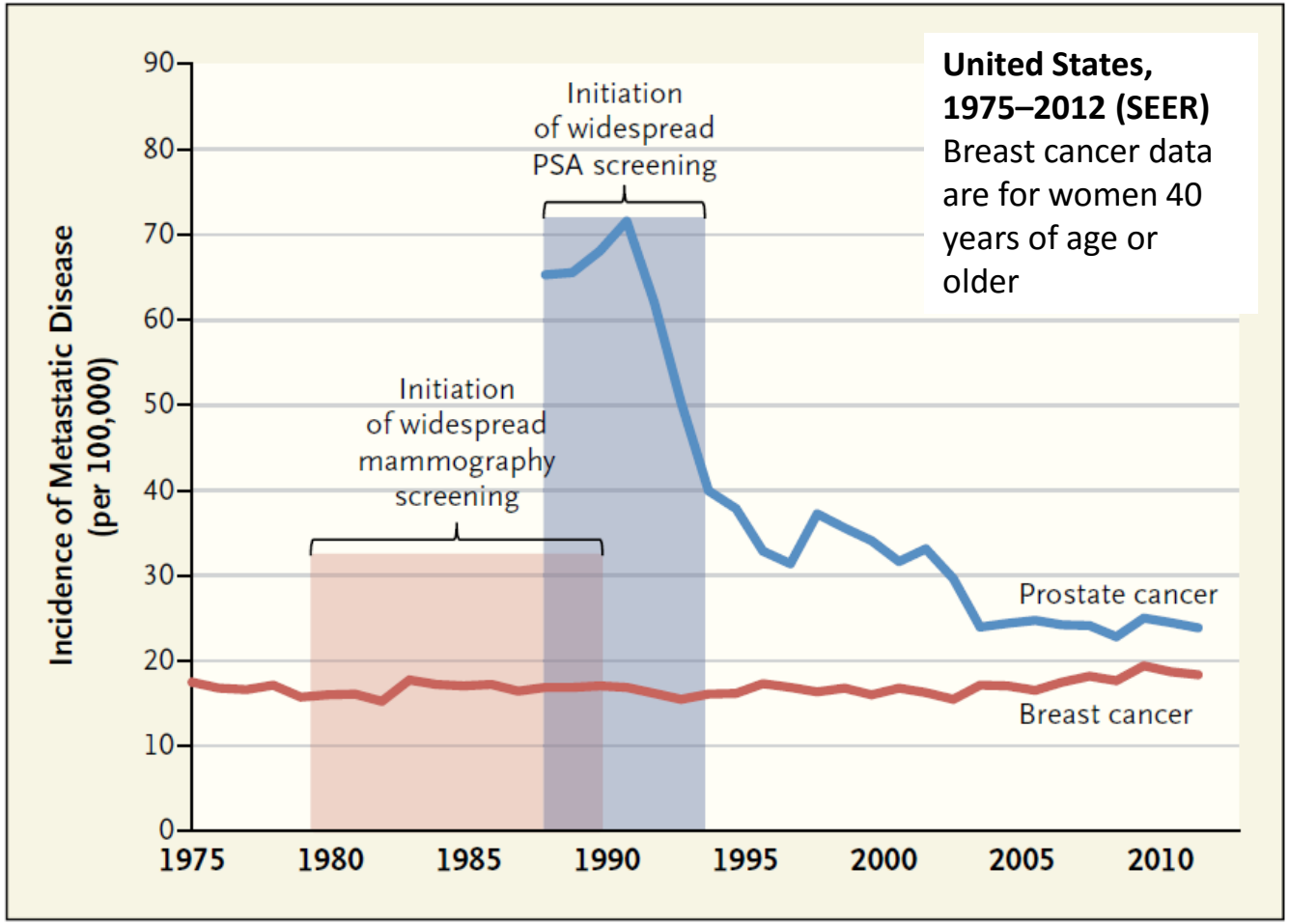


To combine results, the meta-analyses used the most severe disease categories available from the trials (stage III and IV disease, size 50 mm or greater tumors, or 4 or more positive lymph nodes)

Incidence of Advanced Breast Cancer: Observational Evidence

- 5 case series compared breast cancer diagnoses in populations of women with previous screening versus not
- Most used thresholds indicating early stages of disease or proportions instead of incidence rates, so this data was inadequate to determine whether there was an effect of screening

Incidence of Advanced Breast Cancer: Observational Evidence



Welch HG, et al. Trends in Metastatic Breast and Prostate Cancer—Lessons in Cancer Dynamics. *NEJM*. 2015; 373: 1685-7.

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Potential Benefits of Mammography Screening: Incidence of Advanced Breast Cancer

- Does mammography screening reduce the incidence of advanced breast cancer?
  - The body of evidence is mixed. RCT evidence suggests:
    - **Women 50 years and older** had a **reduced risk** of advanced disease with breast cancer screening
    - **Women ages 39 to 49 years** had **no difference** in the incidence of advanced breast cancer in the screening versus the control arms

Potential Benefits of Mammography Screening: Summary

- Reduces breast cancer deaths in women ages 40 to 74, with the likelihood of benefit increasing with age
  - Women 50 to 74 years most likely to benefit from screening
  - There is insufficient evidence about the benefits of screening mammography in women ages 75 years and older
- Has not been shown to decrease all-cause mortality
- Evidence is mixed as to whether it decreases treatment-related morbidity or the incidence of advanced cancers
  - Stronger evidence for reduction in advanced cancers in women ages 50+
- Empiric evidence cannot definitely answer the questions of whether screening at more frequent intervals generally (i.e., annual v. biennial), improve health outcomes

Impact of Race on Effectiveness of Mammography Screening

- African American women are more likely to die of breast cancer than white women (31 v. 22 deaths per 100,000 women per year)
  - Reason for the disparity not entirely clear:
    - **Biology**: African American women more likely to develop triple-negative phenotypes and other aggressive tumors
    - **Socioeconomic**: Associations between being African American and experiencing delays in receipt of health care services for cancer (even lack of treatment altogether)
  - African American women severely underrepresented in the RCTs of screening (largely performed in Europe in white women)
  - Direct evidence is lacking for this population and this represents a critical research need

Reminder: Basic USPSTF Methods for Developing Recommendations

- The USPSTF assesses the evidence across the analytic framework:
  - Judges the ***certainty*** of the estimates of the potential benefits and harms
  - Judges the ***magnitude*** of the potential benefits and harms
  - The ultimate goal is to judge the ***balance*** of the benefits and harms, or the ***magnitude of the net benefit*** of the preventive service

Systematic Evidence Review

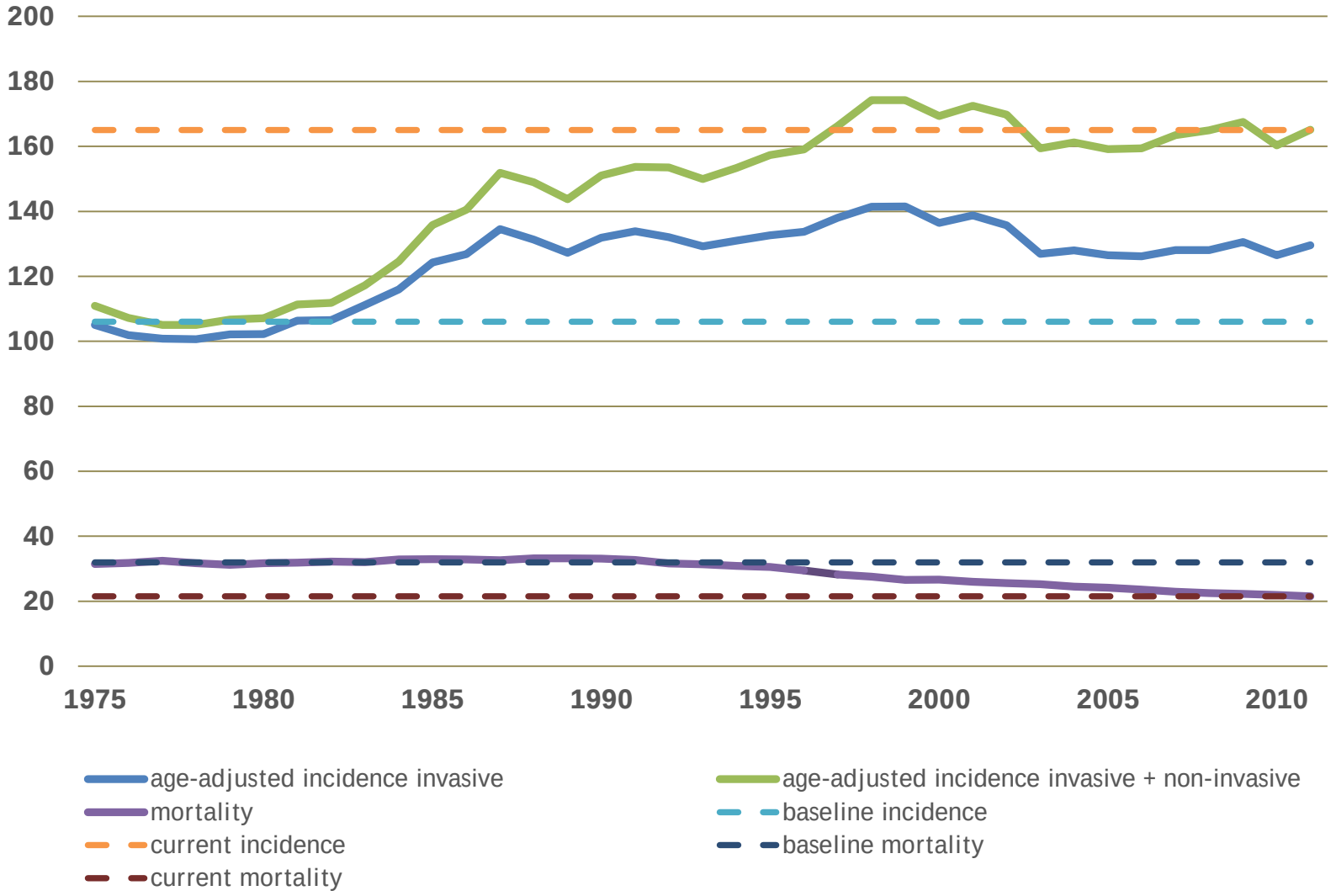
POTENTIAL HARMS OF MAMMOGRAPHY SCREENING

Nelson HD, et al. Harms of Screening for Breast Cancer. Ann Intern Med. 2016; 164: doi:10.7326/M15-0970.

Overdiagnosis

- Diagnosis of cancer that would never have progressed to become clinically detectable or threaten health in the absence of screening
- Most important harm of screening
- Impossible to directly measure, must be indirectly quantified from studies
- Multiple methods are available for estimating the magnitude
  - Currently, there is no scientific consensus as to the optimal approach
  - Accordingly, estimates vary widely in the literature:
    - Full range is 0%-50% across all study designs

Breast Cancer Incidence and Mortality Per 100,000 Women (SEER Data)



Howlander N, et al. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, April 2015.

Breast Cancer Incidence and Mortality Per 100,000 Women (SEER Data)

- The previous slide illustrates changes in breast cancer incidence and mortality in the United States between 1975 and 2011:
  - Prior to mass mammography screening, the breast cancer incidence rate (invasive disease and DCIS together) was 111 cases per 100,000 women
  - With widespread screening, breast cancer **incidence** increased to 165 cases per 100,000 women, an **excess of 54 cases**, or about a **50% increase**
    - No one can say with certainty what proportion would have occurred without screening, but it is likely that part is the result of screening (i.e., overdiagnosis)
  - Breast cancer **mortality** declined at a slower rate, from 31 to 22 **(or 9 fewer) deaths** per 100,000 women over the same time period
    - No one can say with certainty what proportion can be attributed to screening versus better treatment, but both are responsible

Overdiagnosis

- Estimates from the RCTs with no screening in the control arms: 19% from the individual woman's perspective; 11% from the population perspective
- Estimates from the CISNET models: median 12-18%, depending on screening strategy
- At an 11-12% overdiagnosis rate, this means for each woman who avoids a breast cancer death, 2 to 3 are diagnosed and treated for a breast cancer that was not destined to harm them
- Ultimately, given the wide variability of estimates, it is critical for researchers to work together to critically evaluate and agree on uniform definitions and standards to optimally measure and monitor overdiagnosis

Harms of Screening: False Positives, False Negatives, Additional Imaging, and Breast Biopsies

Harms of One-Time Mammography Screening per 10,000 Women Screened: Breast Cancer Surveillance Consortium Registry Data				
Outcome	Ages 40-49 y	Ages 50-59 y	Ages 60-69 y	Ages 70-74 y
False-positive mammograms, *n*	1,212	932	808	696
Breast biopsies recommended, *n*	164	159	165	175
False-negative mammograms, *n*	10	11	12	15

10-Year Cumulative Probabilities (BCSC Data)

- False-positive result: **41%-61%,** depending on screening frequency and age (more at younger ages).
- Biopsy with no cancer found: **5%-9%**

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Cancer Intervention and Surveillance Modeling Network (CISNET)

MODELING

Mandelblatt J, et al. Collaborative Modeling of the Benefits and Harms Associated With Different U.S. Breast Cancer Screening Strategies. Ann Intern Med. 2016; 164: 215-225.

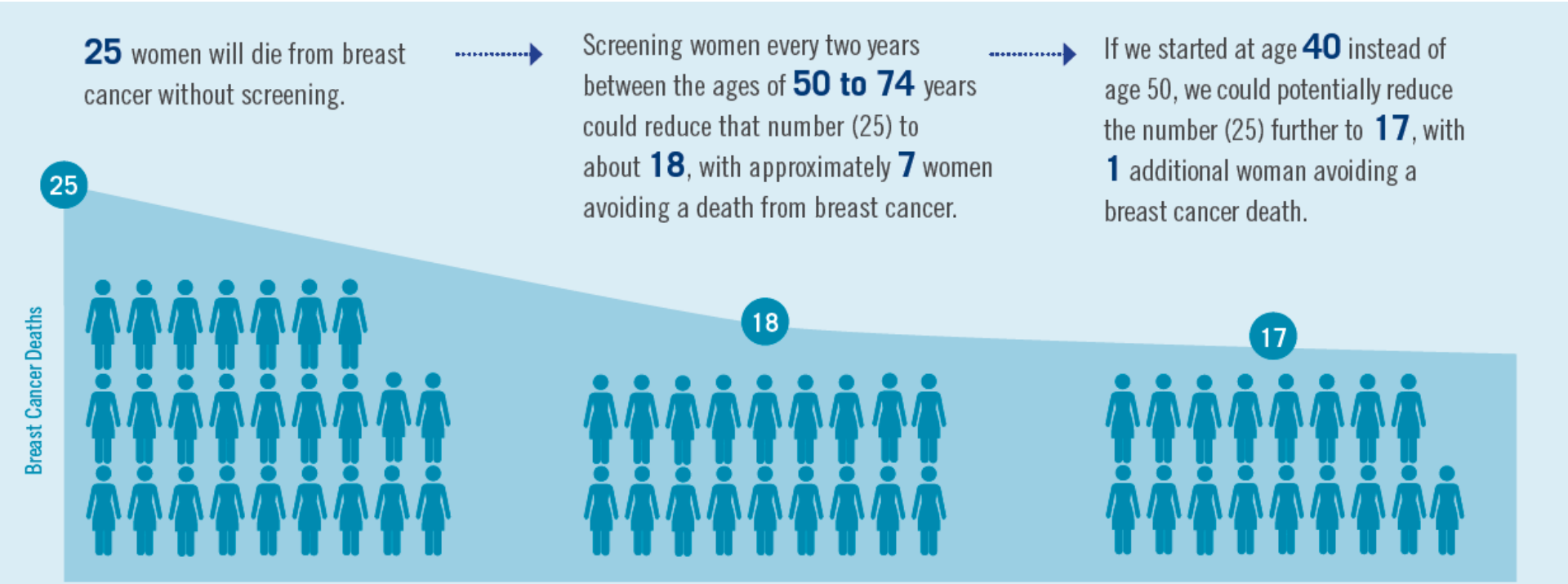
CISNET Modeling

- Complemented the systematic evidence review
- Used data from multiple sources to project what would happen under different screening scenarios
- Designed to address important questions unanswered by the empiric evidence:
  - What's the optimal age to start screening?
  - How do different screening intervals affect potential benefits and risks?

Findings

- What's the optimal age to start screening? (Beginning at age 40 versus 50 years)

Out of 1,000 women followed today until their deaths:



Benefit and Harms: 40 vs 50

- Potential benefits:
  - Beginning screening at 40 years old instead of 50 years old is expected to help one more woman out of 1,000 women prevent death from breast cancer.
- Potential harms
  - 2-3 additional overdiagnosed breast cancers
  - 67 additional breast biopsies
  - 576 additional false positive mammograms

Frequency

What are the benefits and harms of annual versus biennial screening?

For 1,000 women who begin screening at age 40:

Potential benefits of screening more often:

- 1-2 additional women avert death from breast cancer (increasing from 8 to 9-10 women)

Potential harms of screening more often:

- 9 additional overdiagnosed breast cancers
- 125 additional unnecessary breast biopsies
- 1,421 additional false positives (10-year probability is 40% with biennial vs. 60% with annual screening)

Task Force Conclusions from Models

- At what age do the potential benefits of screening outweigh the potential harms by at least a moderate amount?
  - **Age 50**. Screening beginning at age 40 produces a small gain in breast cancer deaths averted but a moderate increase in harms
- What screening interval provides the best balance of benefits to harms?
  - **Every other year**. The six models produced a consistent ranking of strategies and concluded biennial screening achieved the best balance of benefits and harms
    - For every one additional death from breast cancer averted, approximately four women would be overdiagnosed and overtreated

USPSTF Mammography Screening Recommendations: Women 40-49 Years

- The 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 and 49 years. **C recommendation**.
  - For women who are at average risk for breast cancer, most of the benefit of mammography results from biennial screening during ages 50 to 74 years. Of all of the age groups, women aged 60 to 69 years are most likely to avoid breast cancer death through mammography screening. While screening mammography in women aged 40 to 49 years may reduce the risk for breast cancer death, the number of deaths averted is smaller than that in older women and the number of false-positive results and unnecessary biopsies is larger. The balance of benefits and harms is likely to improve as women move from their early to late 40s.

USPSTF Mammography Screening Recommendations: Women 40-49 Years

- In addition to false-positive results and unnecessary biopsies, all women undergoing regular screening mammography are at risk for the diagnosis and treatment of noninvasive and invasive breast cancer that would otherwise not have become a threat to their health, or even apparent, during their lifetime (known as "overdiagnosis"). Beginning mammography screening at a younger age and screening more frequently may increase the risk for overdiagnosis and subsequent overtreatment.
- Women with a parent, sibling, or child with breast cancer are at higher risk for breast cancer and thus may benefit more than average-risk women from beginning screening in their 40s.

More Conservative Screening Practices for Women 40-49 Years Are Common Internationally

- **Canadian Task Force on Preventive Health Care**:
  - Recommends not routinely screening women ages 40 to 49 years with mammography
  - Recommends routine screening mammography every 2 to 3 years in women ages 50 to 74 years
- **International Agency for Research on Cancer (IARC) Breast Cancer Screening Working Group**:
  - Limited Strength of Evidence that it reduces breast cancer mortality in women 40-49 years of age
  - Sufficient Strength of Evidence that mammography has a net benefit for women 50 to 69 years of age who are invited to attend organized mammographic screening programs

There is Increasing Convergence About Individualized Decision-Making for Women in their 40s

- **American College of Physicians:**
  - Recommends that screening mammography decisions in women ages 40 to 49 years should be based on individualized assessment of risk for breast cancer

- **American Academy of Family Physicians:**
  - The 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 and 49 years

- **American Cancer Society:**
  - Women should have the opportunity to begin annual screening between the ages of 40 and 44 years

There is Increasing Convergence About Individualized Decision-Making for Women in their 40s

- **USPSTF**: For women in their 40s, the benefit still outweighs the harms, but to a smaller degree; *this balance may therefore be more subject to individual values and preferences than it is in older women.* Women in their 40s must weigh a very important but infrequent benefit (reduction in breast cancer deaths) against a group of meaningful and more common harms….*Women who value the possible benefit of screening mammography more than they value avoiding its harms can make an informed decision to begin screening.*

- **ACS**: The GDG concluded that the lesser, but not insignificant, burden of disease for women ages 40-44 and the higher cumulative risk of adverse outcomes no longer warranted a direct recommendation to begin screening at age 40. However, the GDG also concluded that women in this age group *should have the choice to begin screening at age 40 or before age 45, based on their preferences and their consideration of the tradeoffs. Some women will value the potential early detection benefit and will be willing to accept the risk of additional testing, and will thus choose to begin screening earlier. Others will choose to defer beginning screening, based on the relatively lower risk of breast cancer.*

Strong Points of Agreement Between Many Current Breast Cancer Screening Recommendations

- Mammography screening is an important tool in reducing the risk of dying from breast cancer
- The benefit of regular mammography screening increases with age, with the greatest benefit for women occurring between the ages of 50 and 74 years
- Women, starting at age 40, should consider the potential benefits and harms of mammography screening and make an informed decision for themselves, in consultation with a trusted clinician, based on their own values, preferences, and family and personal health history about when to begin screening
- There is not a one-size fits all correct age at which to stop mammography screening. The evidence is very limited regarding the screening of women over 75. Most experts agree that mammography screening is not beneficial for women who are approaching the end of life (likely to die within 10 years)

Thank You