The US Preventive Services Task Force: Breast Cancer Screening.

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U.S. Preventive Services TASK FORCE

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
- 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 by Evidence-based Practice Centers (EPCs), with input from sub-specialists with content expertise and public throughout the recommendation development process

The U.S. Preventive Services Task Force

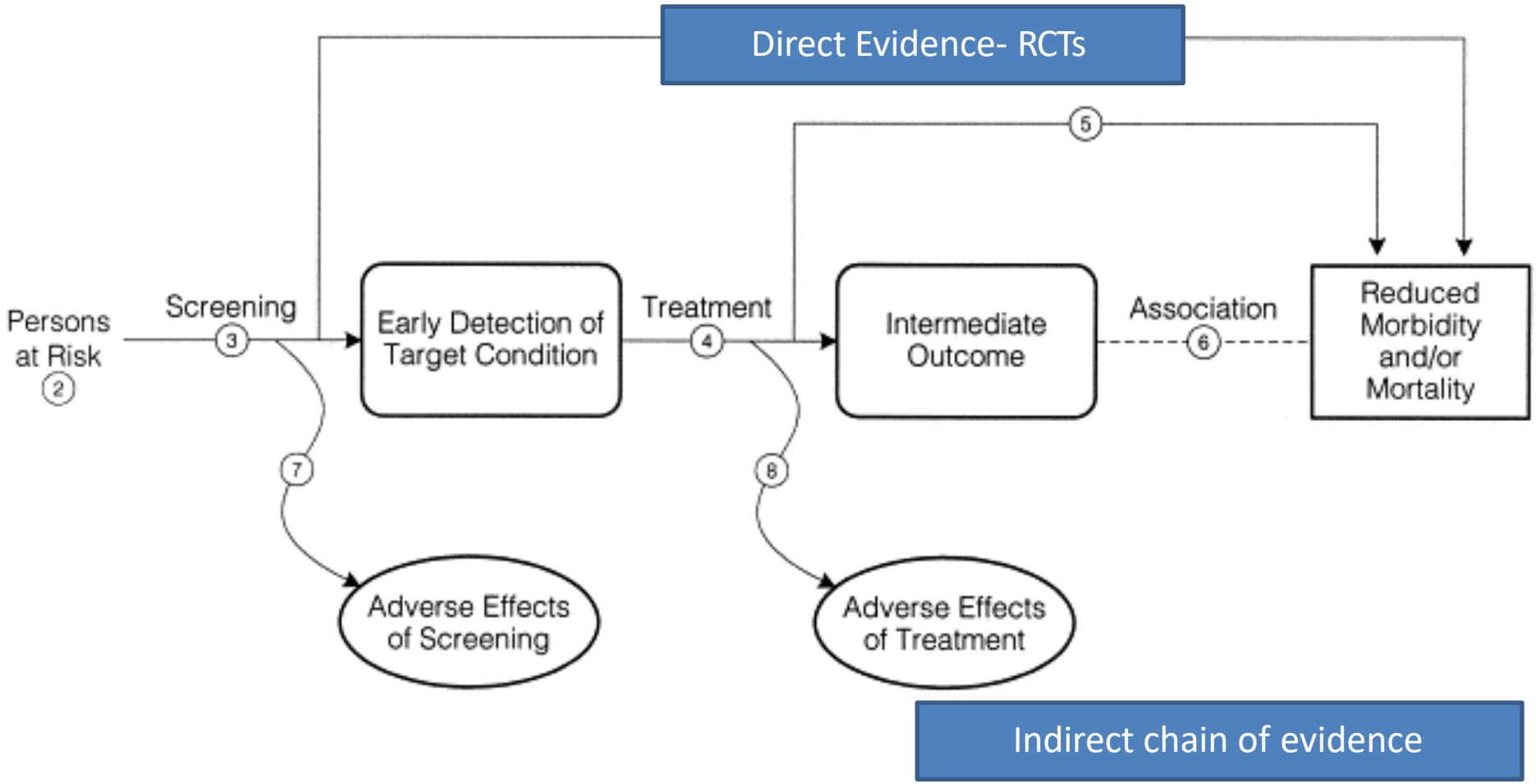
- The USPSTF scope for clinical preventive services includes:
  - screening tests
  - counseling
  - preventive medications
- Services are offered in a primary care setting
- Recommendations apply to adults and children with no signs or symptoms
- The Task Force evaluates benefits and harms of each service
- Costs are not considered in the balance of benefits and harms.

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

The USPSTF analytic framework for approaching the evidence (generic)



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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			

Grade	Definition
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.
I	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Grade	Definition
A	**DO**
B	
C	
D	**Don't Do**
I	**Don't Know**

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BREAST CANCER: SCREENING

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

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

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

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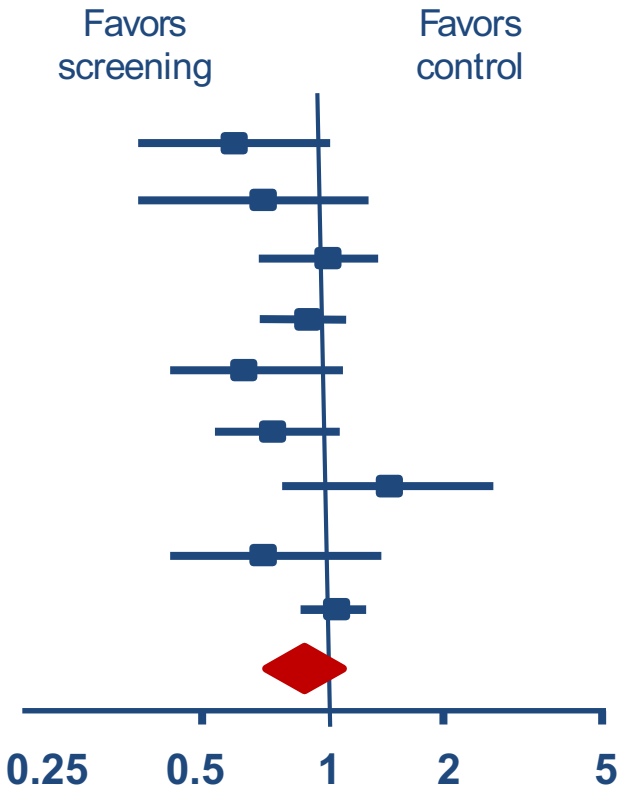
Meta-analysis of Screening Trials
Breast Cancer Deaths, Ages 39 to 49 Years

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 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

Breast Cancer-Specific Mortality: Observational Evidence Women

- 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)

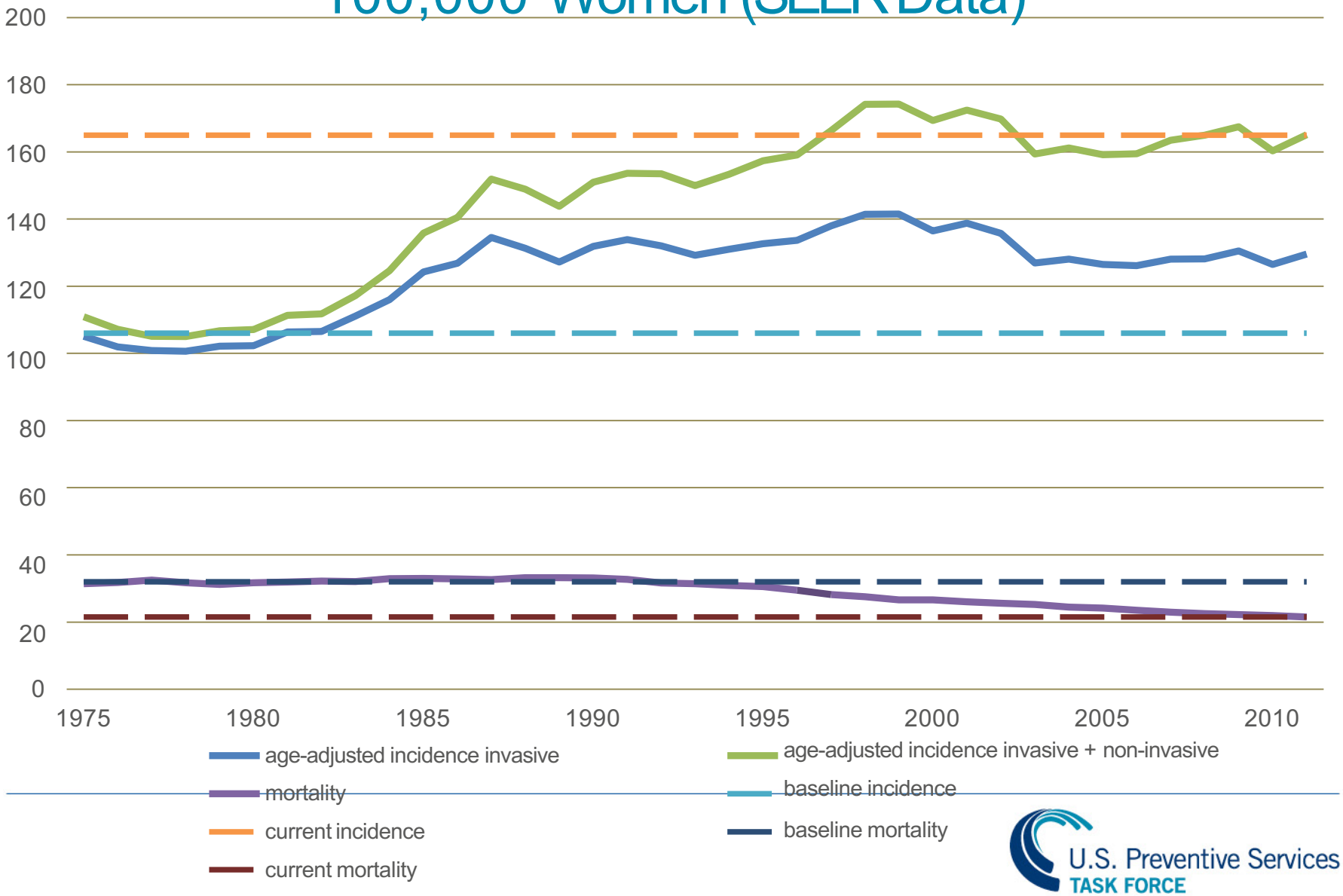
Potential Benefits of Mammography Screening: Summary

- Reduces breast cancer deaths in women ages 40 to 74, with the likelihood of benefit increasing with age
  - There is less agreement between RCTs and observational studies for women in their 40s
  - There is insufficient evidence about the benefits of screening mammography in women ages 75 years and older
- Empiric evidence cannot definitely answer the questions of whether screening at more frequent intervals generally (i.e., annual v. biennial) improve health outcomes

Potential harms: 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
- Currently, there is no scientific consensus as to the optimal approach for estimating the magnitude

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



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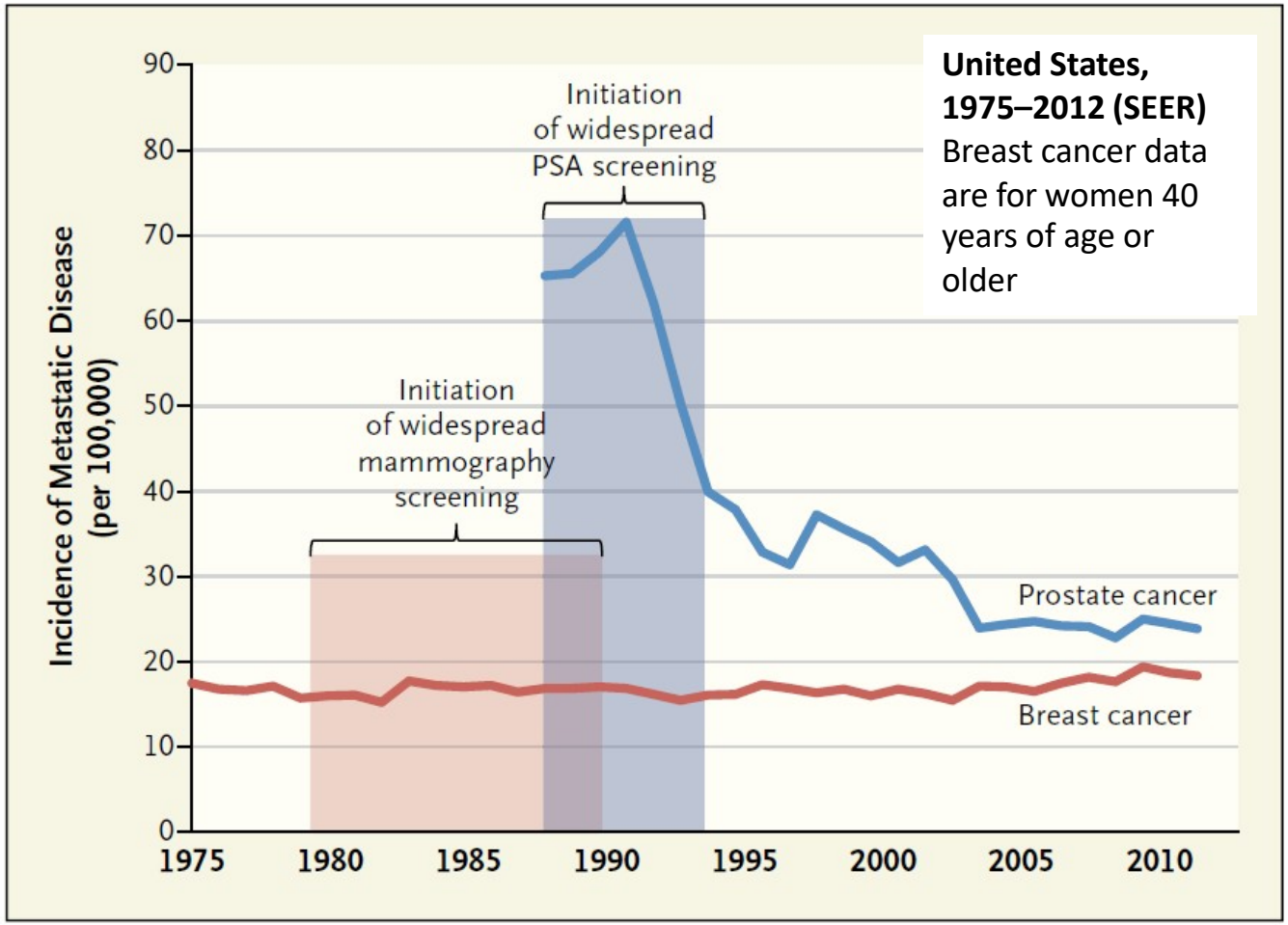
Incidence of Advanced Breast Cancer: Observational Evidence



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

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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%

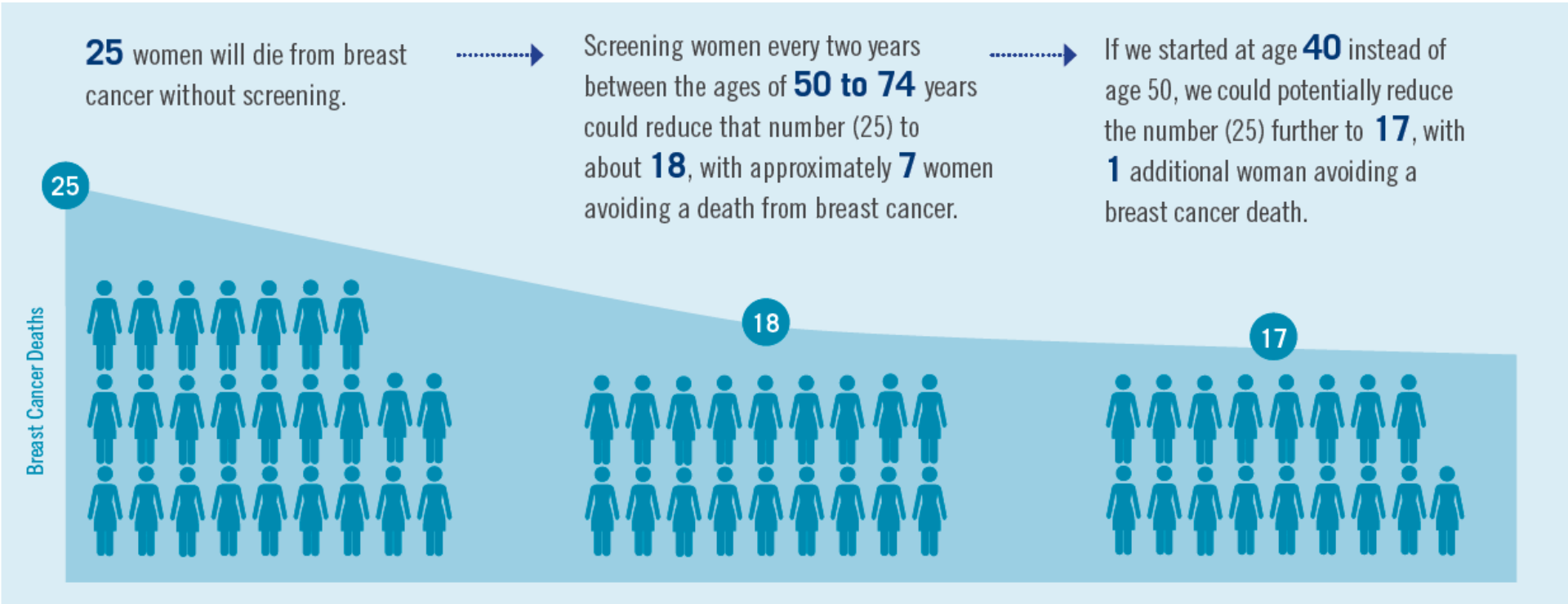
Putting it all together: CISNET Modeling

- 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 harms?

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

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				

- 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. Crecommendation.
  - 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

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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

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Women's Health Deserves Better than a "C"

Regular mammography for women aged 40-49 should be a "B" grade recommendation

Insurance companies and government agencies historically have limited coverage to USPSTF-recommended services given "A" or "B" rankings. **By rating mammography for women aged 40-49 as a "C" recommendation, millions of women could lose coverage for care that has been proven to detect a large**

I am asking the United States Preventive Services Task Force to revise its proposed recommendations for mammography because...

BASTARDS!!!

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
  - For mammography covered by federal legislation
- As clinicians, we value access for our patients, but as a Task Force, we cannot reinterpret the science to arrive at an A or B recommendation

The interests in clinical prevention are many, significant, and complex.


WHICH OF OUR
DAUGHTERS &
SISTERS
LOSE?
EARLY DETECTION SAVES LIVES...
STOP THE USPSTF DRAFT
RECOMMENDATIONS

Full page ads in major newspapers, @$500,000

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Financial interests in prevention

- Those who make and market
  - Screening tests
  - Preventive medications
  - Therapeutics
- Medical community -> primary care, specialists, radiologists
- Challenge to balance rigorous evaluation of science with goal of transparency

Conclusions

- The USPSTF is an independent entity that uses a structured systematic review of the scientific evidence, combined with expert judgment, to make recommendations about preventive services offered in primary care.
- The USPSTF offers a structure and process for arriving at evidence-based recommendations and strives for openness and transparency and seeks to expand discussion of healthcare preventive practices.
- Please read our reports! Our rationale and other clinical considerations are outlined there. Use them as a starting point to engage in the ongoing discussion of how to achieve effective evidence-based healthcare.
- Please stay engaged in the ongoing healthcare and policy discussions regarding access to evidence-based preventive services for all of our patients.