Table 1. Mammography Screening Trials Included in Meta-analysis

Study; Author, Year	Baseline Study Year	Setting or Population (screening, *n*; control, *n*)	Enrollment Age, *y*	Randomization Method	Study Group	Screening Protocol				USPSTF Quality Rating
						Interval, *mo*	Round, *n*	View, *n*	Follow-up, *y*	
Health Insurance Plan (HIP) of Greater New York; Habbema et al,1986[70]	1963	New York health plan members (30,239; 30,256)	40-64	Pairs of women stratified by age and family size were individually randomly assigned by drawing from a list.	Mammography + CBE vs. usual care	12	4	2	18	Fair
Canadian National Breast Screening Study-1 (CNBSS-1); Miller et al, 2002[71]	1980	15 centers in Canada, self-selected participants (25,214; 25,216)	40-49	Blocks were stratified by center and 5-year age group after CBE.	Mammography + CBE vs. usual care (all women prescreened and instructed in BSE)	12	4-5	2	13	Fair
Gothenburg* Breast Screening trial; Bjurstam et al, 2003[67]	1982	All women born from 1923-1944, living in Gothenburg, Sweden (20,724; 28,809)	39-59	Cluster, based on day of birth (1923-1935 cohort [18%]), and individual (1936-1944 cohort [82%]).	Mammography vs. usual care; control participants offered screening after 5 years, completed screening at approximately 7 years.	18	5	1-2	12	Fair
Stockholm; Nystrom et al, 2002[68]	1981	Residents of southeast greater Stockholm, Sweden (40,318; 19,943)	40-64	Individual, by day of month; screening to control group ratio is 2:1.	Mammography vs. usual care	24-28	2	1	11.4	Fair
Malmo; Nystrom et al, 2002[68]	1976-1978	All women born from 1927-1945 living in Malmo, Sweden (21,088; 21,195)	45-70	Individual, within birth year.	Mammography vs. usual care; control participants offered screening after 14 years.	18-24	9	1-2	11-13 15.5	Fair
Swedish Two-County trial (2 trials); Nystrom et al, 2002[68]; Tabar et al, 1995[72]	1977	From Ostergotland and Kopparberg counties in Sweden (77,080; 55,985)	40-74	Clusters, based on geographic units; blocks designed to be demographically homogeneous.	Mammography vs. usual care; control participants offered screening after 7 years.	24-33	3	1	20 15.5	Fair
Age trial;* Moss et al, 2006[66]	1991	23 National Health Service breast screening units in England, Scotland, and Wales (53,884; 106,956)	39-41	Individual, stratified by general practitioner group with random number generation (1991-1992); randomization through Health Authority computer system (1992-onward).	Mammography vs. usual care; all women offered screening at age 50-52.	12	4-6, varied by center	2	10.7	Fair

*New data since the previous recommendation.

Abbreviations: BSE=breast self examination; CBE=clinical breast examination; USPSTF=U.S. Preventive Services Task Force.

Table 2. Summary of Statistical Model Features

Feature	Model[a]					
	D	E	G	M	S	W
Includes DCIS	No	Yes	Yes	Yes	No	Yes
Includes ER status	Yes	Yes	Yes	Yes	Yes	Yes
How treatment affects mortality	Hazard reduction	Cure fraction	Hazard reduction	Hazard reduction and cure fraction based on mode of diagnosis[b]	Hazard reduction	Cure fraction
Calibrated to mortality?	No	No	No	Yes	No	Yes[c]
Calibrated to incidence?	No	Yes	Yes	Yes	Yes	Yes
Factors affecting screening benefits[d]	Stage shift, age shift	Size (larger or smaller than fatal diameter)	Stage shift, age shift	Stage shift, age shift	Stage shift, size within stage, age shift	Effectiveness of treatment by stage and age shifts
Factors affecting treatment benefits (independent of screening)	ER status, age, calendar year	ER status, age	ER status, age	ER status, age, calendar year (and improvements in care)	ER status, age	ER status, age, calendar year (which affect cure probability)

DCIS = ductal carcinoma in situ; ER = estrogen receptor.

[a] Model group abbreviations: D = Dana-Farber Cancer Institute; E = Erasmus Medical Center; G = Georgetown University; M = M.D. Anderson Cancer Center; S = Stanford University; W = University of Wisconsin/Harvard.

[b] If cancer is clinically detected in model M, a hazard reduction is applied to the survival function. If cancer is detected by screening, then a cure fraction is applied for cases diagnosed in stages 1 and 2a. If cancer is detected by screening in stages 2b, 3, or 4, a similar hazard reduction is applied as for the clinically detected cases. This results in screening benefits due to stage shift and better prognosis for screening-detected versus clinically detected cases within early-stage disease. The use of a cure fraction for early-stage screening-detected cancer is a modification of the model published elsewhere (7, 11).

[c] Model W is calibrated only to mortality for a subset of the cure fraction variables after the natural history model was calibrated to incidence.

[d] Note that all models use age-specific inputs for sensitivity of mammography screening. Sensitivity, in turn, has a small effect on screening benefits.

Table 3 GRADING of recommendations: National Clearinghouse Guidelines (www.guideline.gov)

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
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.	Offer or provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is at least moderate certainty that the net benefit is small.	Offer or provide this service only if other considerations support the offering or providing the service in an individual patient.
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.	Discourage the use of this service.
I Statement	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.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

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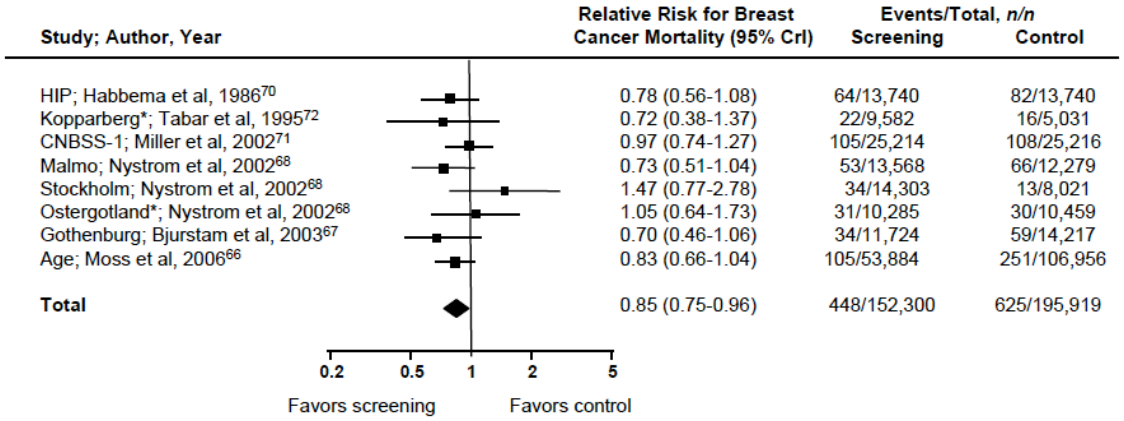
Table 4: Pooled relative risk for breast cancer mortality from mammography screening trials --Women age 39 to 49 years

The lines for each study represent the spread of the confidence or certainty in the findings of the study. If it crosses the midline or value of 1 then it means the study's conclusions are not statistically significant and the results could be secondary to chance. NOTE: the total falls in favor of screening.



*Swedish Two-County Trial.

Abbreviations: CrI=confidence interval for individual trial results and credible interval for meta-analysis results; CNBSS-1=Canadian National Breast Screening Study-1; HIP=Health Insurance Plan of Greater New York.

Table 5. Pooled Relative Risk for Breast Cancer Mortality from Mammography Screening Trials for All Ages

(The prevention of death from screening mammograms improves with aging due to the decline in the amount of glands vs. fat in the breast tissue)

Age, *y*	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)	1,904 (929-6,378)
50-59	6	0.86 (0.75-0.99)	1,339 (322-7,455)
60-69	2	0.68 (0.54-0.87)	377 (230-1,050)
70-74	1	1.12 (0.73-1.72)	Not available

*Trials and their acronyms are discussed in the text.

Abbreviations: CrI=confidence interval for individual trial results and credible interval for meta-analysis results; NNI=number needed to invite to screening; RR=relative risk.

Table 6. Benefits and Harms Comparison of Different Starting and Stopping Ages Using the Exemplar Model[a]

Strategy	Average Screenings per 1000 Women	Potential Benefits (vs. No Screening)			Potential Harms (vs. No Screening)[b]	
		Percentage of Mortality Reduction	Cancer Deaths Averted per 1000 Women	Life-Years Gained per 1000 Women	False-Positive Results per 1000 Women	Unnecessary Biopsies per 1000 Women
Comparison of different starting ages						
Biennial screening						
40–69 y	13,865	16[c]	6.1	120[c]	1,250	88
45–69 y	11,771	17[c]	6.2	116[c]	1,050	74
50–69 y	8,944	15	5.4	99	780	55
55–69 y	6,941	13	4.9	80	590	41
60–69 y	4,246	9	3.4	52	340	24
Annual screening						
40–69 y	27,583	22[c]	8.3	164[c]	2,250	158
45–69 y	22,623	22[c]	8.0	152[c]	1,800	126
50–69 y	17,759	20[c]	7.3	132[c]	1,350	95
55–69 y	13,003	16[c]	6.1	102[c]	950	67
60–69 y	8,406	12[c]	4.6	69[c]	600	42
Comparison of different stopping ages						
Biennial						
50–69 y	8,944	15	5.4	99	780	55
50-74 y	11,109	20	7.5	121	940	66
50–79 y	12,347	25	9.4	130	1,020	71
50-84 y	13,836	26	9.6	138	1,130	79
Annual						
50–69 y	17,759	20[c]	7.3	132[c]	1,350	95
50-74 y	21,357	26[c]	9.5	156[c]	1,570	1106
50–79 y	24,439	30	11.1	170	1,740	122
50-84 y	26,913	33	12.2	178	1,880	132

[a] Results are from model S (Stanford University). Model S was chosen as an exemplar model to summarize the balance of benefits and harms associated with screening 1000 women under a particular screening strategy.

[b] Overdiagnosis is another significant harm associated with screening. However, given the uncertainty in the knowledge base about ductal carcinoma in situ and small invasive tumors, we felt that the absolute estimates are not reliable. In general, overdiagnosis increases with age across all age groups but increases more sharply for women who are screened in their 70s and 80s.

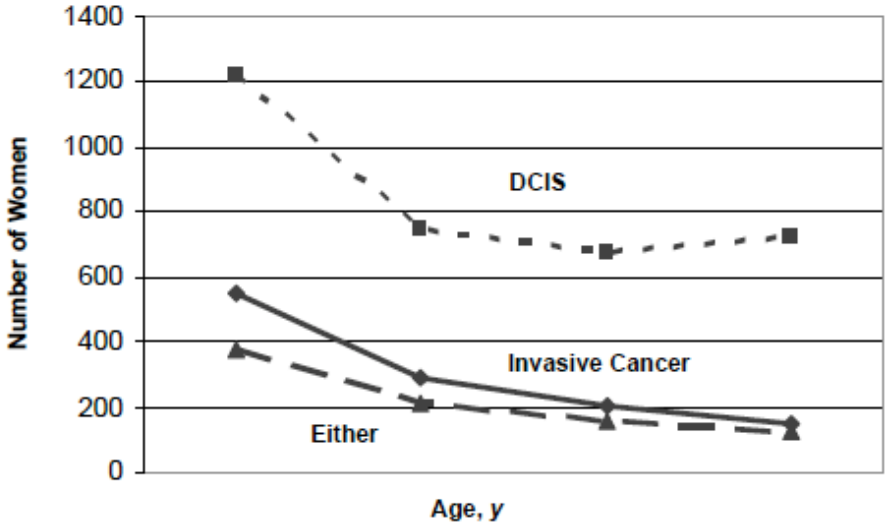
[c] Strategy is dominated by other strategies; the strategy that dominates may not be in this table.

Table 7. Percentage of Reduction in Breast Cancer Mortality Maintained When Moving From an Annual Screening Interval to a Biennial Interval, by Screening Strategy and Model

Model[a]	Maintained Reduction in Breast Cancer Mortality, by Screening Strategy, %[b]									
	Ages 50–69 y	Ages 40–69 y	Ages 45–69 y	Ages 40–79 y	Ages 40–84 y	Ages 55–69 y	Ages 60–69 y	Ages 50-74 y	Ages 50–79 y	Ages 50–84 y
D	76	75	78	79	82	83	79	81	78	83
E	75	73	74	75	75	75	73	76	75	76
G	85	86	91	87	88	91	86	89	88	89
M	90	96	97	97	99	92	84	95	93	95
S	74	73	78	76	77	80	74	79	85	79
W	68	67	70	70	71	71	70	72	70	73

[a]Model group abbreviations: D = Dana-Farber Cancer Institute; E = Erasmus Medical Center; G = Georgetown University; M = M.D. Anderson Cancer Center; S = Stanford University; W = University of Wisconsin/Harvard.
[b] Differences in the range of results reflect differences in modeling approaches. For example, the benefit of screening in model M is modeled through stage shift, as with most other models, but also includes a "beyond stage shift" factor based on a cure fraction for small tumors. However, because many of these "cures" occur among women with invasive cancer that is not fatal, finding such cancer 1 year earlier confers very little mortality advantage to annual (vs. biennial) screening.

Table 8. Number of Women Undergoing Routine Mammography to Diagnose 1 Case of Invasive Cancer, DCIS, or Either from the Breast Cancer Surveillance Consortium

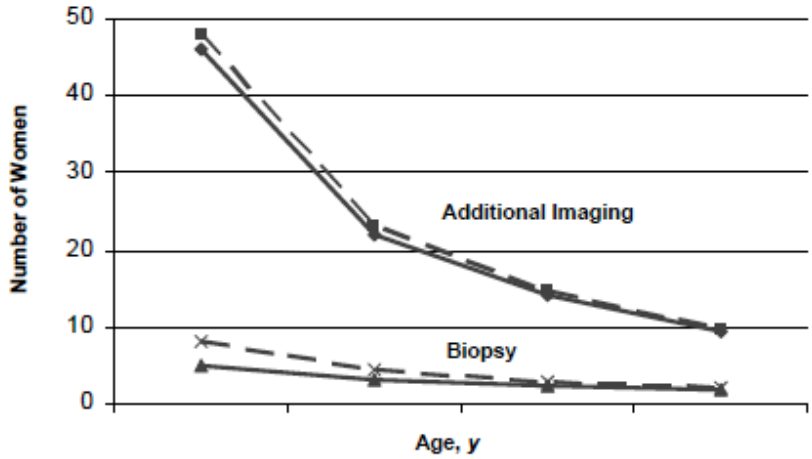


	40-49	50-59	60-69	70+
Invasive	556	294	200	148
DCIS	1,250	769	667	690
Either	385	213	154	122

Number undergoing mammography to diagnose 1 case of invasive cancer, DCIS or either = (# women screened/# cases detected among women by screening).

Abbreviation: DCIS=ductal carcinoma in situ.

Table 9. Number of Women Undergoing Additional Imaging and Number Undergoing Biopsy to Diagnose 1 Case of Invasive Cancer from the Breast Cancer Surveillance Consortium



		40-49	50-59	60-69	70+
Additional imaging	Assumes missing values do not undergo procedure	47	22	14	9
	Assumes missing values undergo procedure	48	23	15	10
Biopsy	Assumes missing values do not undergo procedure	5	3	2	2
	Assumes missing values undergo procedure	8	4	3	2

Number undergoing additional imaging to diagnose 1 case of invasive cancer = (# women undergoing additional imaging/# cases of invasive cancer detected among women by screening).

Number undergoing biopsy to diagnose 1 case of invasive cancer = (# women undergoing biopsy/# cases of invasive cancer detected among women by screening).

Table 10 Summary of USPSTF Meta-analysis Evidence

Number of Studies and Type	Design	Limitations	Consistency	Applicability	Overall Quality	Findings
KQ1a. Does screening with mammography (film and digital) and MRI decrease breast cancer mortality among women age 40-49 and over the age of 70?						
8 for women age 40-49 y; 1 for age 70-74 y; no screening trials of MRI or digital technologies	RCTs	Several trials were conducted before current mammography technology and treatment approaches; all trials met criteria for fair quality	Consistent	Fair: all but 1 trial were conducted outside of the U.S. but recruited large community-based populations	Fair	For women age 39-49 y, the combined relative risk for breast cancer mortality was 0.85 (95% CrI, 0.74-0.95; 8 trials) and the number needed to screen 1,894 (992-6,201). Evidence for women 70 y or older is insufficient
KQ1b. Does CBE screening decrease breast cancer mortality? Alone or with mammography?						
1 (2 in progress)	RCTs	The trial was discontinued after one round because of poor community acceptance	Not applicable	Poor	Poor	Inconclusive findings.
KQ1c. Does BSE practice decrease breast cancer mortality?						
2 trials + 3 systematic reviews	RCTs	Both trials were conducted in countries that do not have mass mammography screening	Consistent	Fair: Although trials were conducted in populations very different than the U.S., results could be useful for U.S. practice	Fair	Both trials indicated no reduction in mortality rates
KQ2a. What are the harms associated with screening with mammography (film and digital) and MRI?						
Several systematic reviews and primary studies; no studies of MRI for screening average-risk women	Several study designs and data sources including RCTs, observational studies, surveys, and data from the BCSC	Adverse effects have been studied in various ways, most studies are descriptive	Varies by type of harm	Poor to good: The applicability of some studies, such as those about radiation exposure, may be low because they provide indirect evidence for the association between radiation exposure from routine mammography and breast cancer; other studies, such as those of patient anxiety with false-positive mammography results, come from direct patient experiences	Poor to good	Evidence supports a relationship between radiation exposure and breast cancer with much higher doses of radiation than obtained through screening. Pain during procedures is common, brief, and not a barrier. Anxiety, distress, and other psychosocial effects of screening are usually transient and do not influence future screening practices. False-positive results are common. Younger women have more false-positive mammography results and more additional imaging than older women, but rates of biopsy are lower. Rates of overdiagnosis vary by study methodology and are 1-10%
KQ2b. What are the harms associated with CBE?						
3	1 RCT and 2 descriptive studies	Identified studies provide isolated descriptive data and are insufficient to address the question	Not applicable	Poor	Poor	Inconclusive findings
KQ2c. What are the harms associated with BSE?						
3	2 RCTs and 1 observational study	Both trials were conducted in countries that do not have mass mammography screening	Not applicable	Fair: Although trials were conducted in populations very different than the U.S., results could be useful for U.S. practice	Fair	2 trials indicated increased benign breast biopsies with breast self-examination; biopsies were not increased in the observational study

Abbreviations: BCSC=Breast Cancer Surveillance Consortium; BSE=breast self examination; CBE=clinical breast examination; CrI=credible interval; MRI=magnetic resonance imaging; RCTs=randomized controlled trials; U.S.=United States.

Table 11. Breast Cancer Screening Recommendations for Average-Risk Women

	American Academy of Family Physicians (AAFP)	American Cancer Society (ACS)	American College of Obstetricians and Gynecologists (ACOG)	American College of Physicians (ACP)*	American College of Preventive Medicine (ACPM)	American College of Radiology (ACR)	American Medical Association (AMA)	Canadian Task Force on Preventive Health Care (CTFPHC)	National Cancer Institute (NCI)	National Compre-hensive Cancer Network (NCCN)	US Preventive Services Task Force (USPSTF)	World Health Organization (WHO)
Mammography												
Age 40+, annual		x				x	x			x		
Age 40+, every 1-2 years	x							x	x		x	
Age 40-49, every 1-2 years			x									
Age 50+, annual			x									
Age 50-69, annual or biennial					x							x
Age 70+					x							
MRI												
Not recommended for average risk women		x								x		
CBE												
Age 40+, annual		x	x							x		
Periodic evaluation (1-3 years), ages vary		x					x	x ages 50-69	x	x		
Insufficient evidence											x	
Not recommended												x
BSE												
Recommended			x				x			x		
Insufficient evidence	x	x							x		x	
Not recommended								x				x

*Suggests periodic, individualized screening for women age 40-49 years.

Abbreviations: BSE=breast self examination; CBE=clinical breast examination; MRI=magnetic resonance imaging.