Harms and Costs of Not Screening

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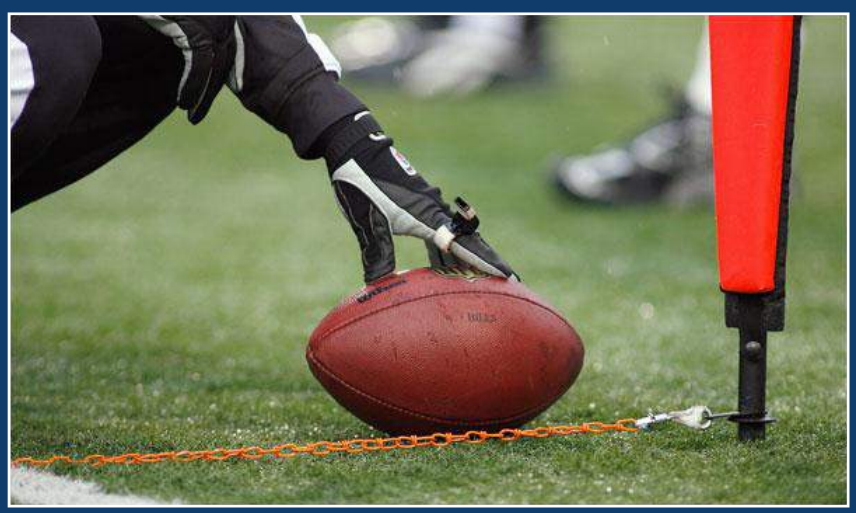
Overview

- Absence of screening does not mean absence of breast related problems
- There are harms of omission – that is of ***not*** screening
- Harms of omission should be considered along with harms of commission



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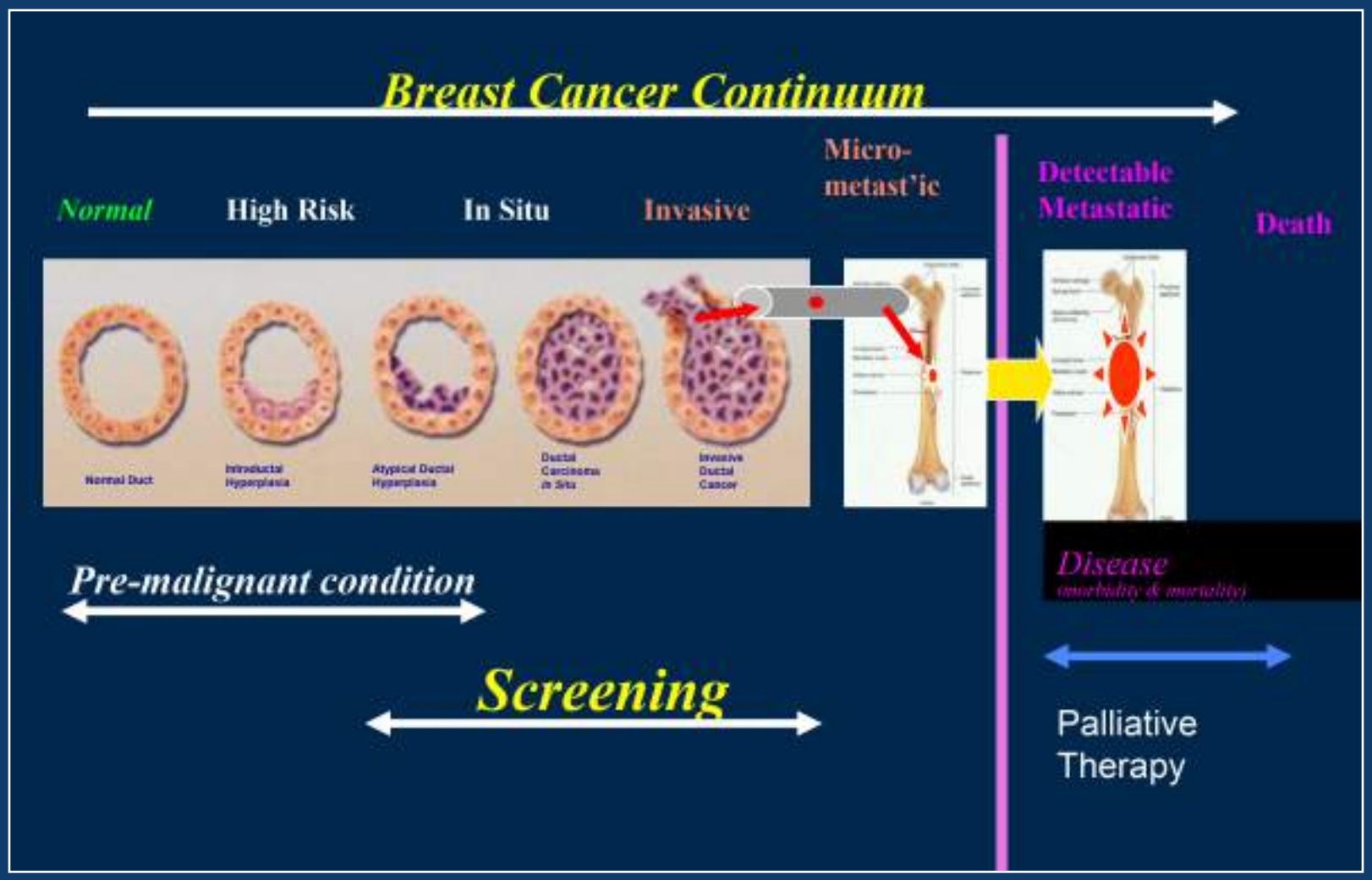
Breast Cancer Continuum

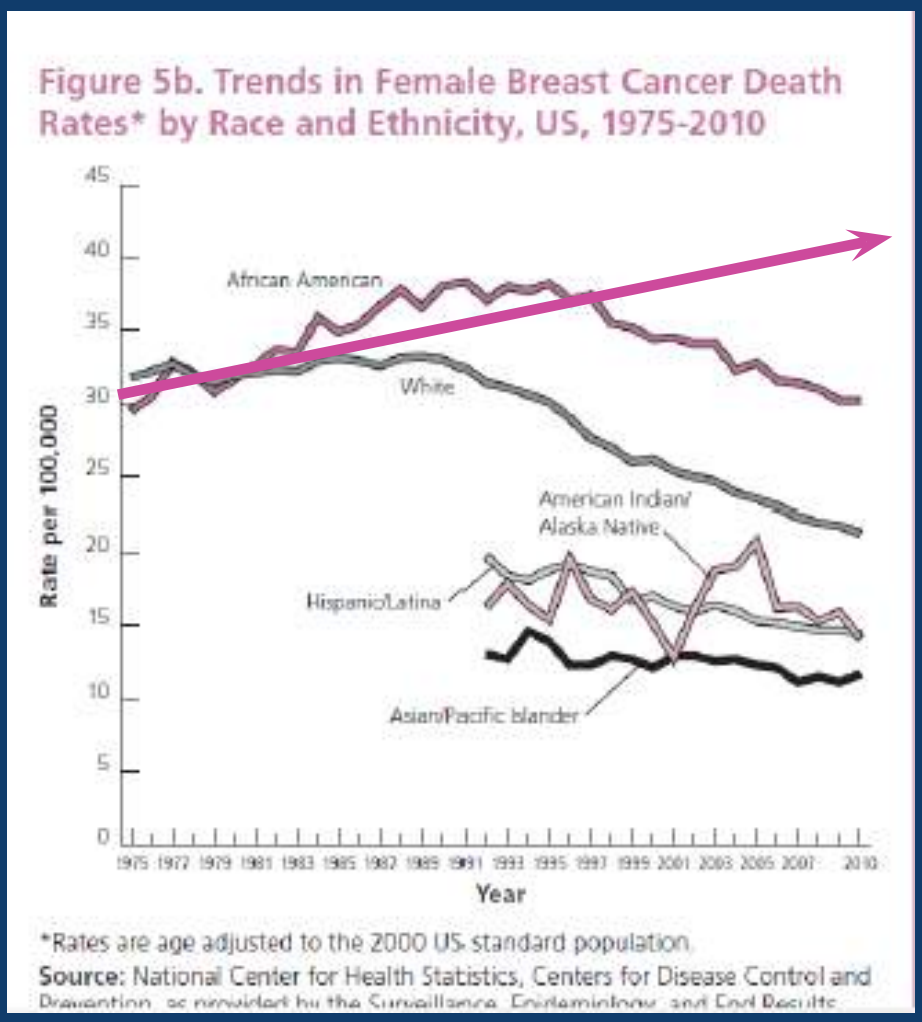


From D Hayes MD

Mammographic Screening

- Screening mammography saves lives for women age 39-69 based upon meta analysis of 8 RCT
- Screening recommended for normal risk by all major groups but different opinions when to start/ frequency
- Imperfect test, “harms” exist
- Qualitative rating of benefit and harms - a value judgment regarding a human life

USA Female Breast Ca Mortality Rate is now declining



-2 % / yr

1990-2009 = 33.2%

Screening and Treatment

Greater decline if Mortality trend used

ACS 2014

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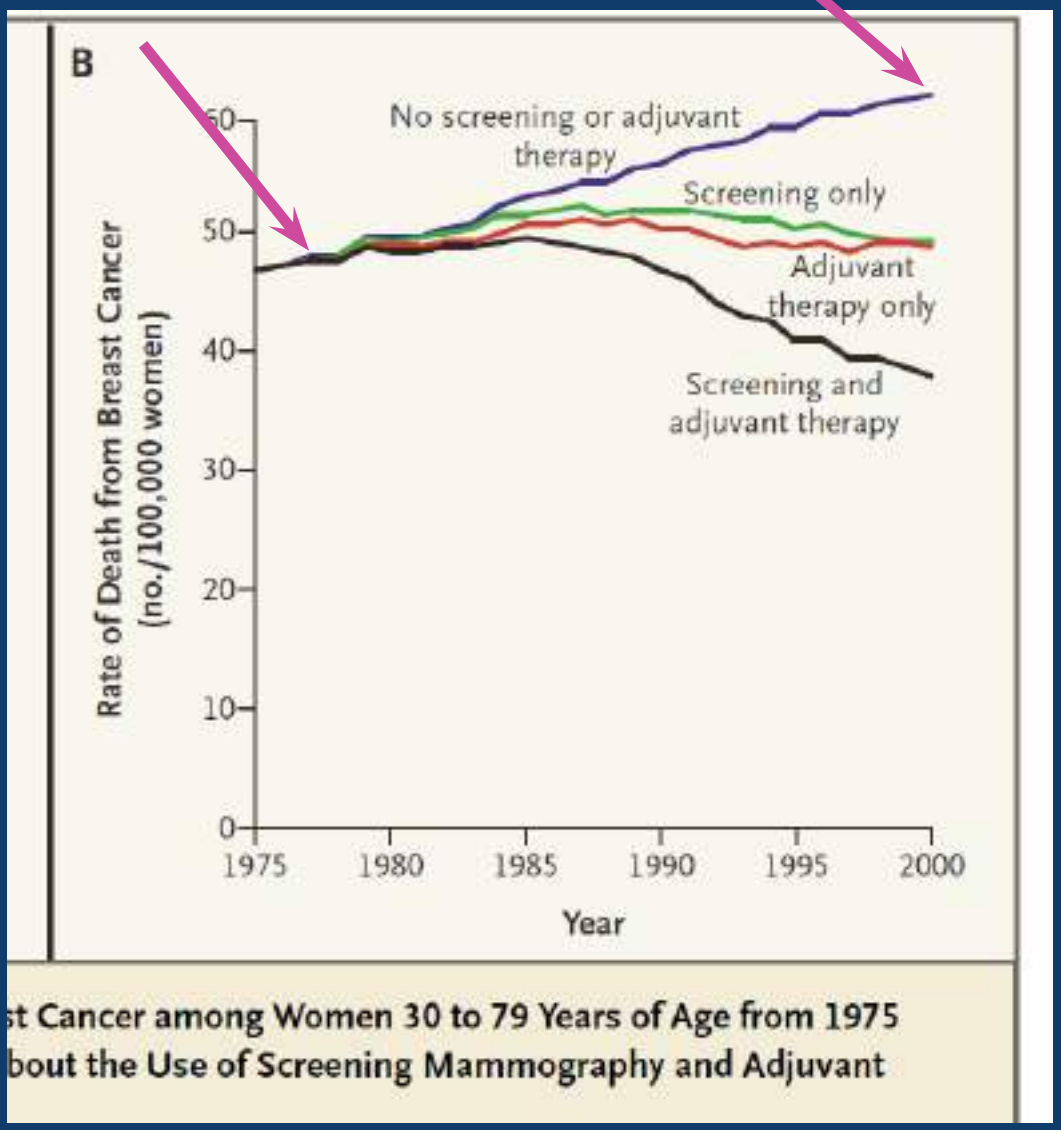
USA Female Breast Ca Mortality Rate is now declining



st Cancer among Women 30 to 79 Years of Age from 1975
bout the Use of Screening Mammography and Adjuvant

-2 % / yr

1990-2009 = 33.2%

Screening and Treatment

Greater decline if Mortality trend used

Berry et al N Engl J Med 2005;353:1784-92.

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International Agency for Research on Cancer

World Health Organization

PRESS RELEASE
N° 223

12 December 2013

Latest world cancer statistics
Global cancer burden rises to 14.1 million new cases in 2012:
Marked increase in breast cancers must be addressed

From 2008 to 2012, Breast Cancer Worldwide:

1. Incidence increased 20% (4% per year)
2. Mortality increased 14% (3% per year)
3. Most Common female cancer death: 522,000

US data is divergent from world trends

Harms of not Screening Harms of Omission

1. Under diagnosis/Death
2. Increased morbidity
3. FP – physical exam/bx
4. Costs: financial and human
5. Lack of identification and treatment of pre invasive breast cancer

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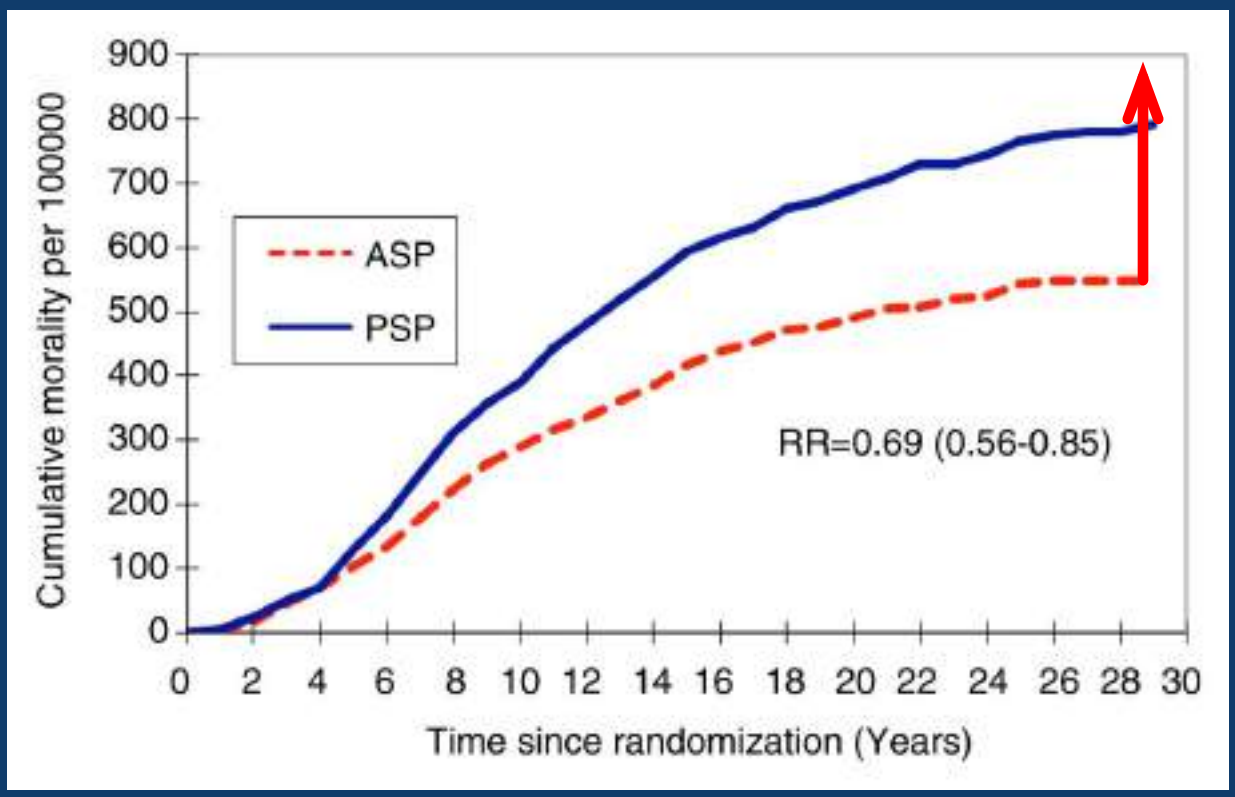
Harms of not Screening Evidence: Lack of mortality reduction

- RCT (invitation NOT as treated)
- Service screening of populations
- Computer models (CISNET)

Breast specific mortality reduction

Life Years Gained or lives saved/1000

Harms of not Screening Evidence: Lack of mortality reduction



Significant 20% reduction by meta-analysis 8 trials

Excess deaths in non screened groups

Tabár L et al. Radiology 2011;260:658-663 Radiology

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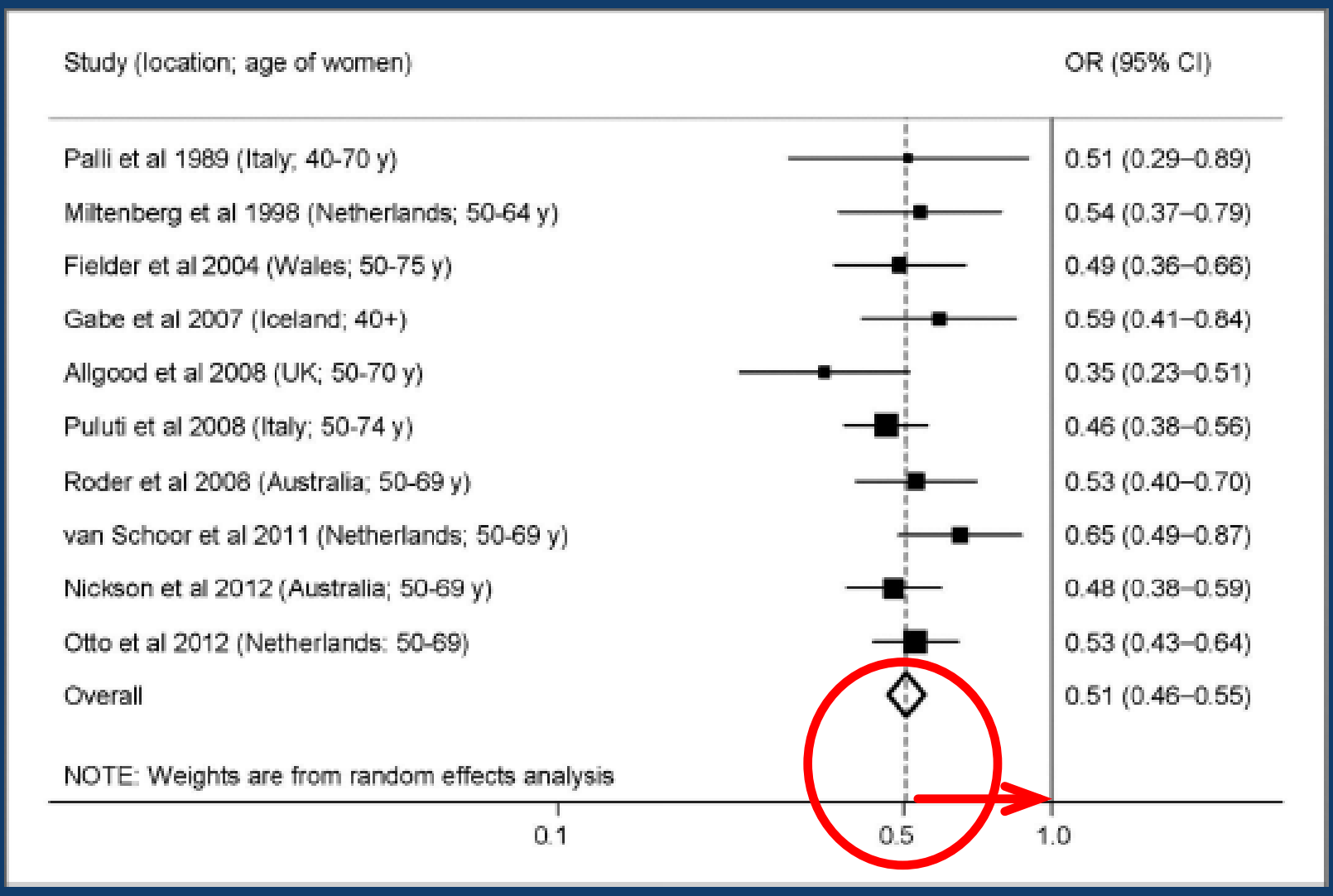
10 observational studies: Meta-analysis 49% Mortality Reduction



Nickson C et al. Cancer Epidemiol Biomarkers Prev 2012;21:1479-1488

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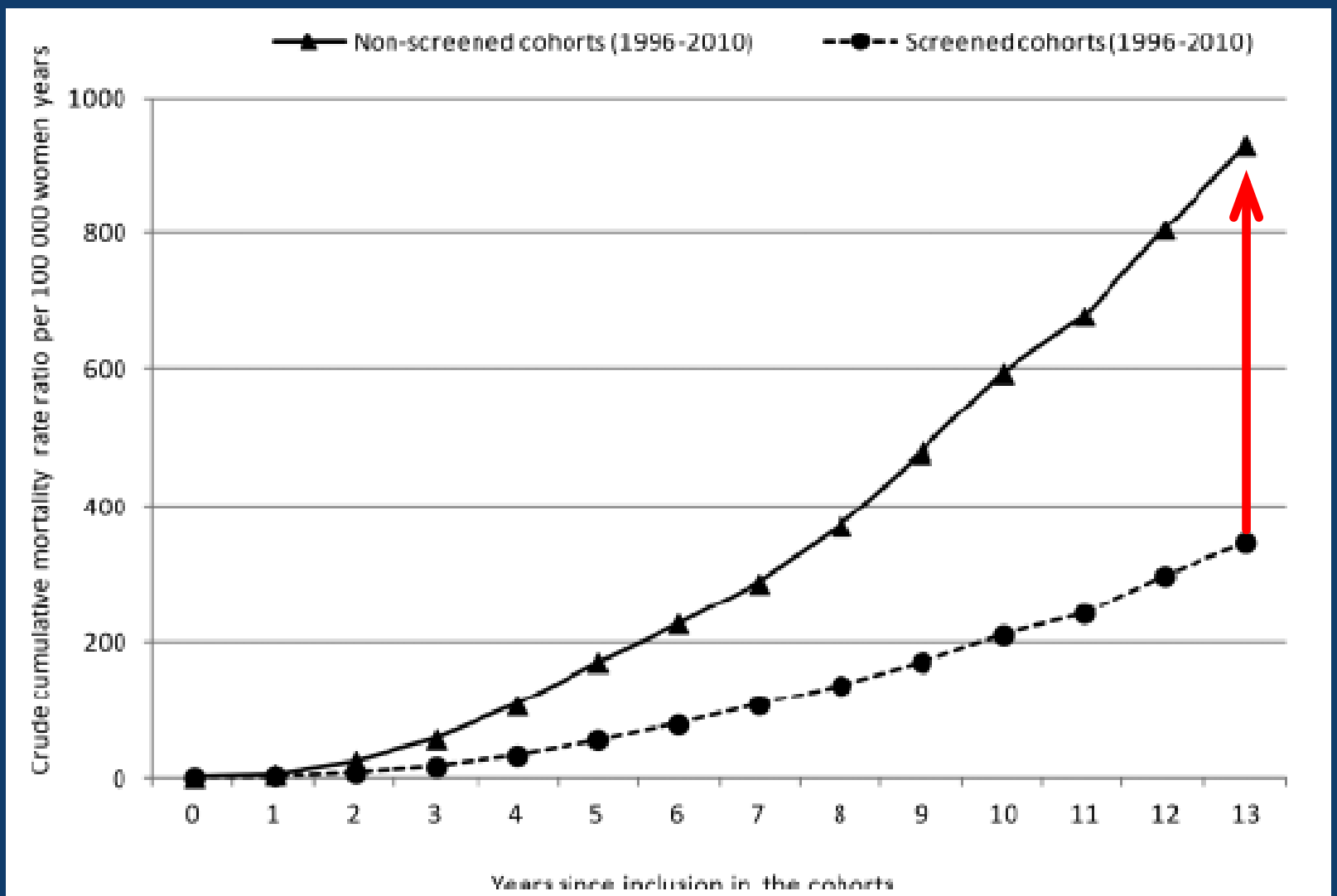
Breast cancer mortality in participants of the Norwegian Breast Cancer Screening Program (Cancer Registry of Norway)



48% crude reduction

43% adjusted reduction

62% crude reduction at 13 yrs

Hofvind et al Cancer 29 MAY 2013 DOI: 10.1002/cncr.28174

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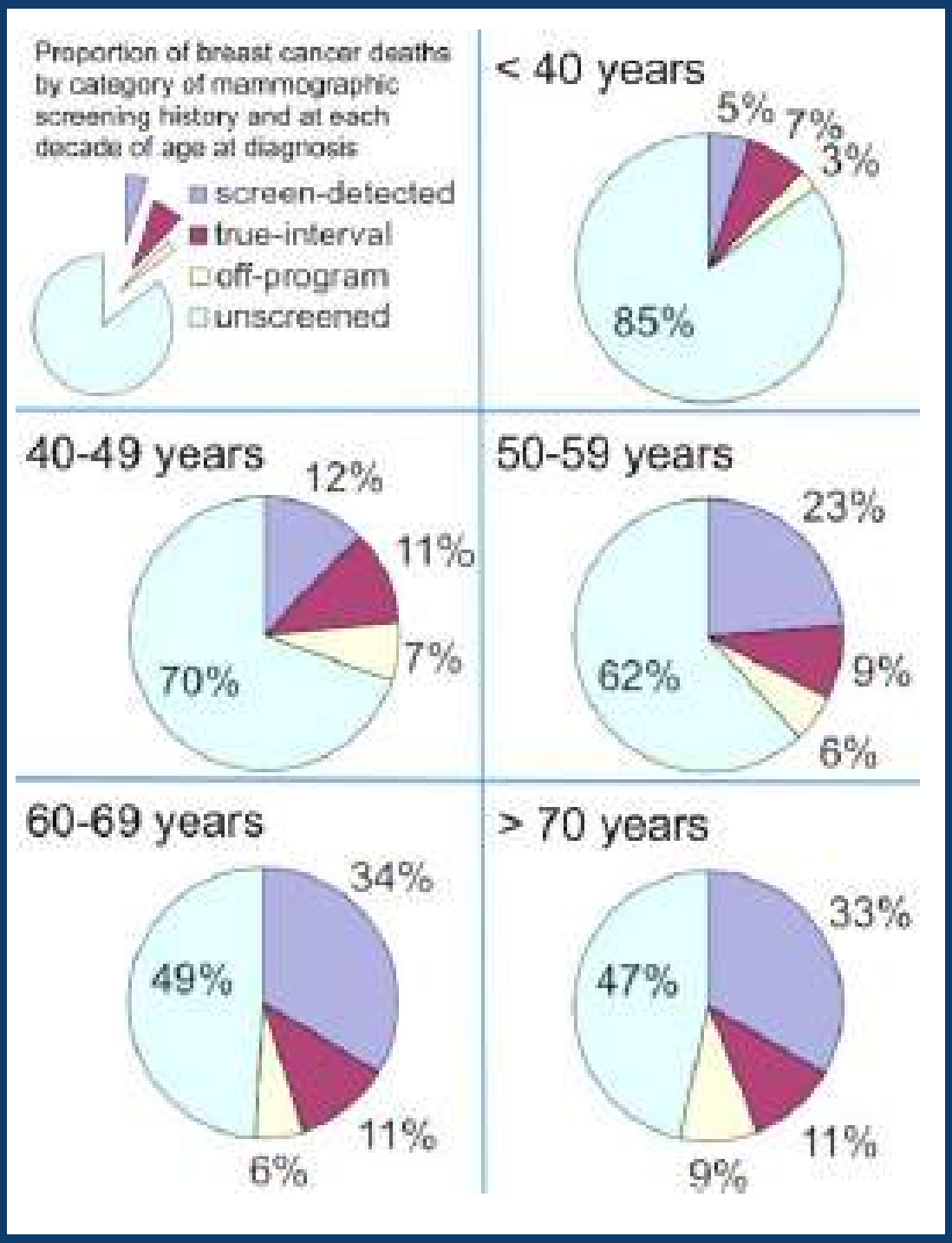
A failure analysis of invasive breast cancer



1990 -2007

Partners HealthCare Boston

71% of deaths occurred in 20% of women NOT screened (q 2 yr)

Webb et al Cancer

9 SEP 2013 DOI: 10.1002/cncr.28199

http://onlinelibrary.wiley.com/doi/10.1002/cncr.28199/full#cncr28199-fig-0002

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Less frequent Screening means higher mortality
Biennial 50-74 vs Annual 40-84 (mean 6 CISNET models)

	LYG/1000	Mortality Reduction (%)
B 50-74	110	23
A 40-84	189	40
Difference(%)	*79 (72%)*	*16.3 (71%)*

Hendrick and Helvie, AJR 2011 Derived from: Mandelblatt J S et al. Ann Intern Med 2009;151:738-747

Mortality reduction by screen frequency (UK) Less frequent screening means higher mortality

Screen Method	Mortality Reduction	Difference to A 40-73
50-70 triennial	16%	131%
40-73 triennial	20%	85%
40-73 annual	37%	-

Source: Gunsoy, British Journal of Cancer (2014) 110, 2412–2419

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Treatment Morbidity

- In general, more advanced stage requires more treatment
- Chemotherapy, hormonal therapy and full axillary dissection carries associated harms of treatment

Increase in late stage Cancer "Biennial" vs. Annual Screening

	Biennial	Annual	Difference
Recall (10 yr)	42%	61%	47%
Biopsy (10 yr)	5%	7%	42%
Stage III/IV (age 40-49)	14.9	10.1	-32%*

*Significant

Hubbard et al, *Ann Intern Med* 2011; 155

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Increased Morbidity Screen vs Palpable Detection Age 40-49

	Screened	Symptoms
Mastectomy	25%	47%
BCT	67%	48%
Chemotherapy	45%	81%

Malmgren J A et al. Radiology 2012;262:797-806

Advanced Cancer more common in non screened
RCT Blue = not invited (PSP)

Long-Term Incidence of Breast Cancer/Yen et al

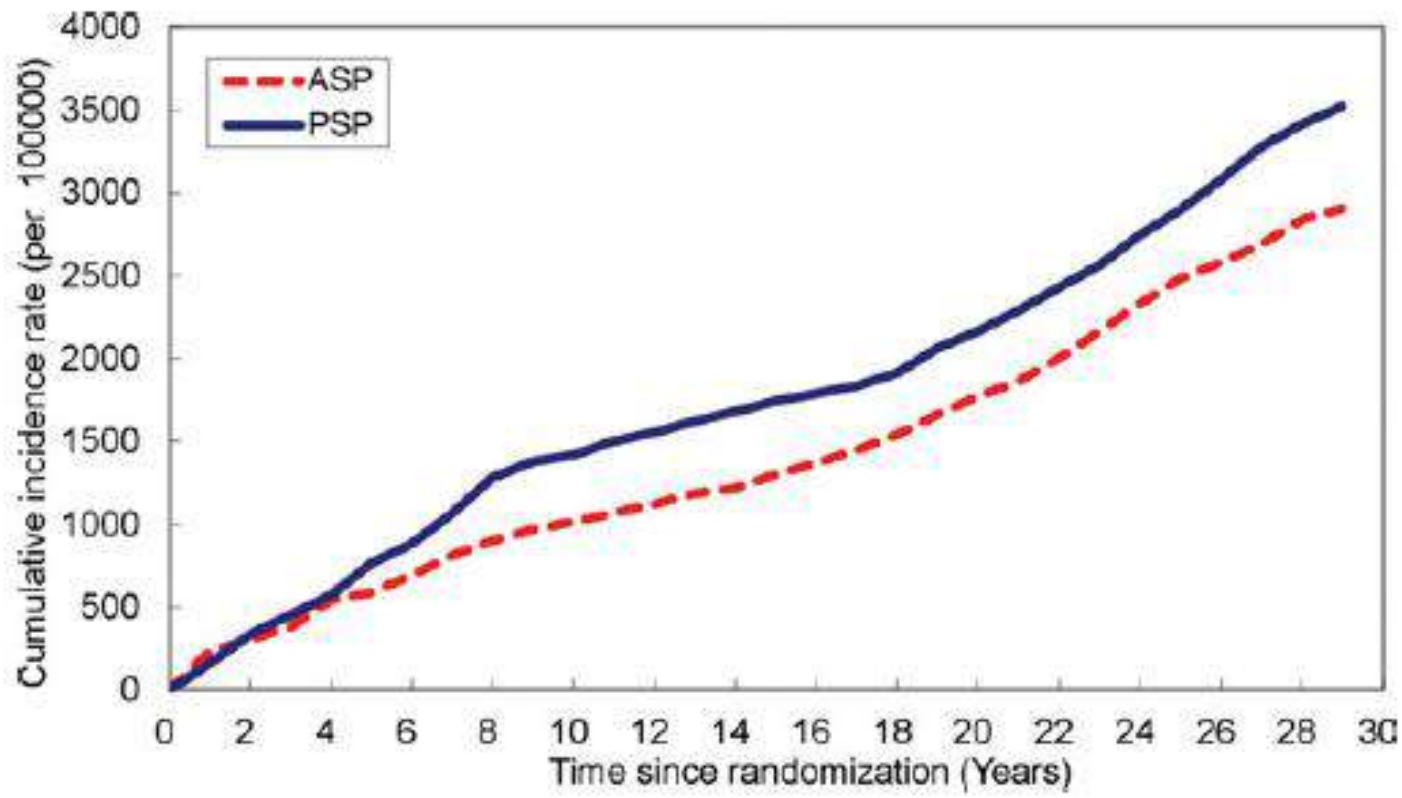

Figure 5. Cumulative 29-year incidence of advanced invasive cancers (node positive or ≥20 mm or both) in the ASP and PSP, Dalarna County, Sweden.

Yen et al Cancer. 2012 Dec 1;118(23):5728-32

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Morbidity: Age 40-79, British Columbia

Int. J. Cancer: **120,** 2185–2190 (2007)

A retrospective study of the effect of participation in screening mammography on the use of chemotherapy and breast conserving surgery

Andrew J. Coldman[1]*, Norm Phillips[2] and Caroline Speers[3]

46% less Chemotherapy among screened

47% higher use of BCT among screened

TABLE V – REGULAR SMPBC PARTICIPANTS VERSUS NONSMPBC PARTICIPANTS OBSERVED AND MODEL-PREDICTED ODDS RATIOS OF USE OF BREAST CONSERVING SURGERY AND CHEMOTHERAPY WITH CONFIDENCE INTERVALS

	Observed odds ratio (95% CI)	Age-adjusted odds ratio (95% CI)	Predicted odds ratio
Chemotherapy			
Nonparticipants	1.0	1.0	1.0
Participants	0.54 (0.42, 0.68)	0.53 (0.41, 0.69)	0.54
BCS			
Nonparticipants	1.0	1.0	1.0
Participants	2.2 (1.76, 2.78)	2.3 (1.79, 2.86)	1.47

Breast Symptoms Evaluation: 10 yrs

- 1983-93, 2400 women Harvard HMO
- 23% symptoms

  32% for age 40s
- 6.5 % had invasive procedures
- 4% PPV per episode (96% False positive)
- Fewer (.59) symptom evaluation if mammo screened

Elmore et al Ann Intern Med. 1999;130:651-657.

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False Positive biopsies per 10 year period Annual Screening (age 40-79)

FP Biopsy 4.3-6.7%

or 149 – 233 years of screening per biopsy

Hendrick and Helvie, AJR 2011

Derived from: Nelson, et al. Annals of Internal Med. 2009:151

Symptomatic Evaluations 10 year period

	Symptoms	Screen
Age 40-49	23%	
Age 50-69	32%	
FP Biopsy	5.5 %	5.5%
PPV Biopsy	15%	15-40%

Derived from: Elmore et al Ann Intern Med. 1999;130:651-657,

*Hendrick and Helvie, AJR 2011

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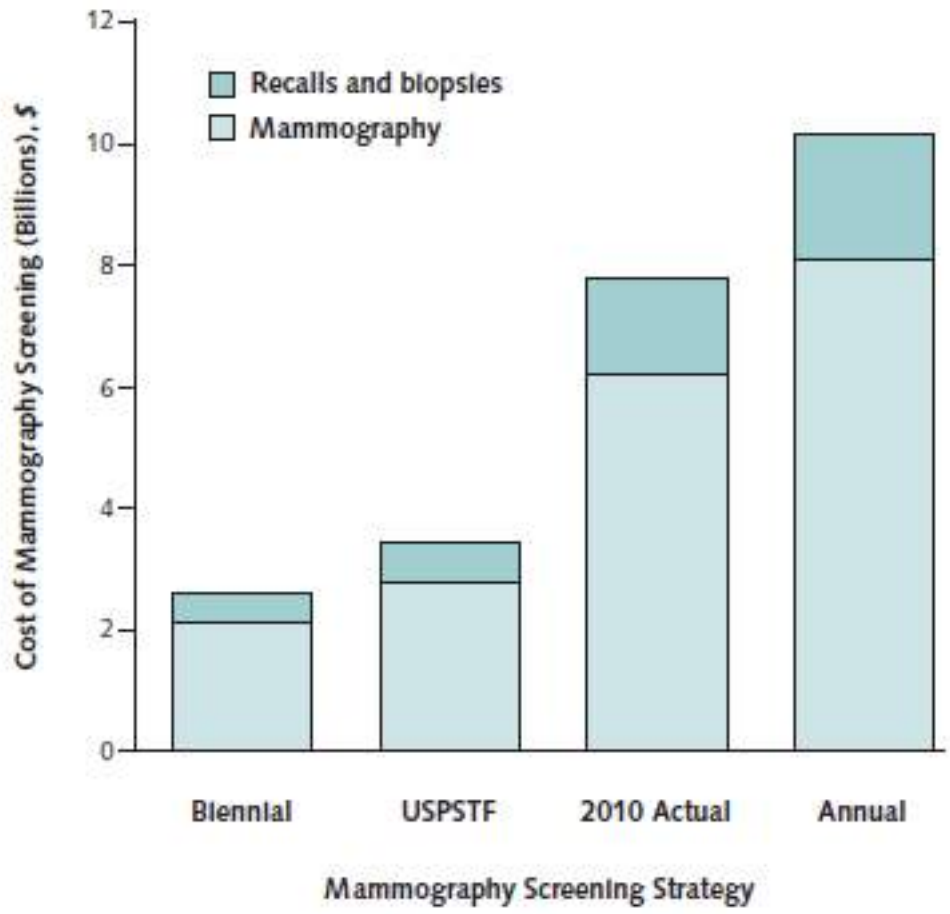
Aggregate Cost of Mammography Screening in the United States: Comparison of Current Practice and Advocated Guidelines

Cristina O'Donoghue, MD, MPH; Martin Eklund, PhD; Elissa M. Ozanne, PhD; and Laura J. Esserman, MD, MBA

Figure 1. Comparison of the costs of screening strategies per year.



Each bar represents the total cost of mammography screening per year, demarcating the costs from screening mammography and the subsequent recalls and biopsies. USPSTF = U.S. Preventive Services Task Force.

Ann Intern Med. 2014.;160:145-153.

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Cost of Not Screening

- Very complex financial analysis
- Cost of screening should not be isolated from down stream cost of not screening
- Cost of treating more advanced and metastatic disease
- Loss of economic productivity cost due to disability and death
- Human cost

Helvie MA. Ann Intern Med. 2014 Aug 19;161(4):304-5

Breast Cancer Res Treat (2012) 134:815–822
DOI 10.1007/s10549-012-2097-2

EPIDEMIOLOGY

The economic burden of metastatic breast cancer: a U.S. managed care perspective

Alberto J. Montero · Sara Eapen · Brian Gorin · Paulette Adler

non-Medicare patient population. Assuming average PPPM costs of $9,788 and an average life expectancy of 2.2 years, the total average expenditure to treat mBC would be ~$250,000 per patient.

Cost to treat metastatic Breast Cancer:

$250,000 per patient

($ 4 billion if 16,000 deaths averted)

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Productivity Costs of Cancer Mortality in the United States: 2000–2020

Cathy J. Bradley, K. Robin Yabroff, Bassam Dahman, Eric J. Feuer, Angela Mariotto, Martin L. Brown

Table 2. Site-specific present value of lifetime earnings (PVLE) among adults 20 and older in 2010

Cancer site	PVLE, $US	Percentage of total cost
Total (all cancers)	142 373 887 175	100.00
Lung and bronchus	38 953 476 028	27.36
Colon and rectum	12 802 283 437	8.99
Female breast	10 878 840 020	7.64

Breast Cancer Mortality Productivity cost:

$10.9 billion

Employment and caregiver cost by Age at Death

Age 40-44 $1.6 million

Age 50-54 $1.1 Million

Age 60-64 $0.6 million

Age 70-74 $0.2 million

Table 1. Model inputs and average PVLE for the year 2000*

Sex and age, y	No. of deaths	Mean person-years of life lost	Person-years of life lost	Percent employed	Percent employed full time	Percent employed part time	Annual mean full-time earnings, $US	Annual mean part-time earnings, $US	Mean PVLE, $US	Proportion of persons living in households	Adjusted caregiving and household wages, $US	Mean PVLE including caregiving and household wages in $US
Females												
20–24	394	61.39	24 190	73.3	69.0	31.0	27 050	12 188	1 338 188	91.5	9806	2 230 023
25–29	657	56.12	36 870	77.1	82.0	18.0	39 271	17 694	1 284 081	99.2	13 233	2 142 912
30–34	1378	51.07	70 370	75.6	82.0	18.0	41 308	18 612	1 167 549	99.2	13 233	1 972 799
35–39	3148	45.94	144 600	75.8	80.0	20.0	43 917	19 788	1 019 631	99.5	15 000	1 767 713
40–44	5956	40.93	243 760	78.7	80.0	20.0	43 917	19 788	873 166	99.5	15 000	1 551 323
45–49	9442	35.98	339 710	77.0	82.0	18.0	45 954	20 706	704 211	99.3	14 958	1 309 721
50–54	14 010	31.18	436 830	74.1	82.0	18.0	48 182	21 709	519 640	99.3	14 958	1 050 032
55–59	17 675	26.57	469 680	59.7	75.0	25.0	45 572	20 533	335 524	99.3	16 334	791 482
60–64	22 199	22.27	494 290	39.1	75.0	25.0	43 217	19 472	179 874	99.3	16 334	555 047
65–69	28 540	18.29	522 110	18.8	41.0	59.0	34 115	15 371	72 285	98.1	15 871	363 558
70–74	37 440	14.67	549 330	9.7	41.0	59.0	32 651	14 712	33 291	98.1	15 871	240 800
75–79	42 004	11.37	477 460	3.5	41.0	59.0	32 651	14 712	16 821	87.3	13 606	174 422
80–84	36 395	8.48	308 500	3.5	41.0	59.0	32 651	14 712	11 531	87.3	13 606	114 175
≥85	42 777	5.30	226 850	3.5	41.0	59.0	32 651	14 712	6144	87.3	13 606	81 229

J Natl Cancer Inst 2008;100:1763–1770

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Sweden age 40-49 Overdiagnosis

1% in situ plus invasive

negative 5% invasive

Overdiagnosis in the population-based service screening programme with mammography for women aged 40 to 49 years in Sweden

Barbro Numan Hellquist, Stephen W Duffy, Lennarth Nyström and Håkan Jonsson

J Med Screen 2012;**19**:14–19
DOI: 10.1258/jms.2012.011104

Results The prescreening incidence rate ratio was estimated at 0.92 (95% confidence interval [CI]: 0.88–0.97). The number of breast cancer cases and person-years were 6047 and 3.8 million, and 7790 and 5.2 million, in the study group and control group respectively during the study period. The RR estimate for all cancers was 1.01 (95% CI: 0.94–1.08) when adjusted for prescreening difference and a lead time of 1.2 years. The corresponding estimate for invasive breast cancers was 0.95 (95% CI: 0.88–1.02).

Conclusions We found no significant overdiagnosis for women aged 40–49 in the Swedish service screening programme with mammography.

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Reduction in Late-Stage Breast Cancer Incidence in the Mammography Era

Observed vs projected (adjusted) incidence 1977-1979 to 2007-2009

	2007 to 2009			
	Observed	APC of 1.3%		
		Projected	Change	% Change
Early stage				
DCIS	58.4	9.2	49.2	537
Localized disease	181.2	152.6	28.6	19
Total	239.6	161.8	77.9	48
Late stage				
Regional	77.2	126.8	−49.6	−39
Distant	17.7	24.0	−6.3	−26
Total	94.9	150.8	−55.8	−37
Total invasive cancer	276.2	303.4	−27.2	−9
Total breast cancer	334.6	312.6	22.0	7

Abbreviations: APC, annual percent change;
[a] Incidence indicates the number of cases p

Early 48%

Late -37%

Invasive -9%

All CA 7%

Helvie et al Cancer. 2014 Sep1;120(17):2649-56.

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Harms of Not Screening

- RCT, observational, and computer models show mortality reduction among screened women age 40 and older
- The harms of omission should be considered with harms of commission
- The harms of omission include death, excess morbidity, costs, and possibly excess incidence of invasive cancer

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