



Memorial Sloan-Kettering Cancer Center
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Prophylactic Mastectomy

State of the Art

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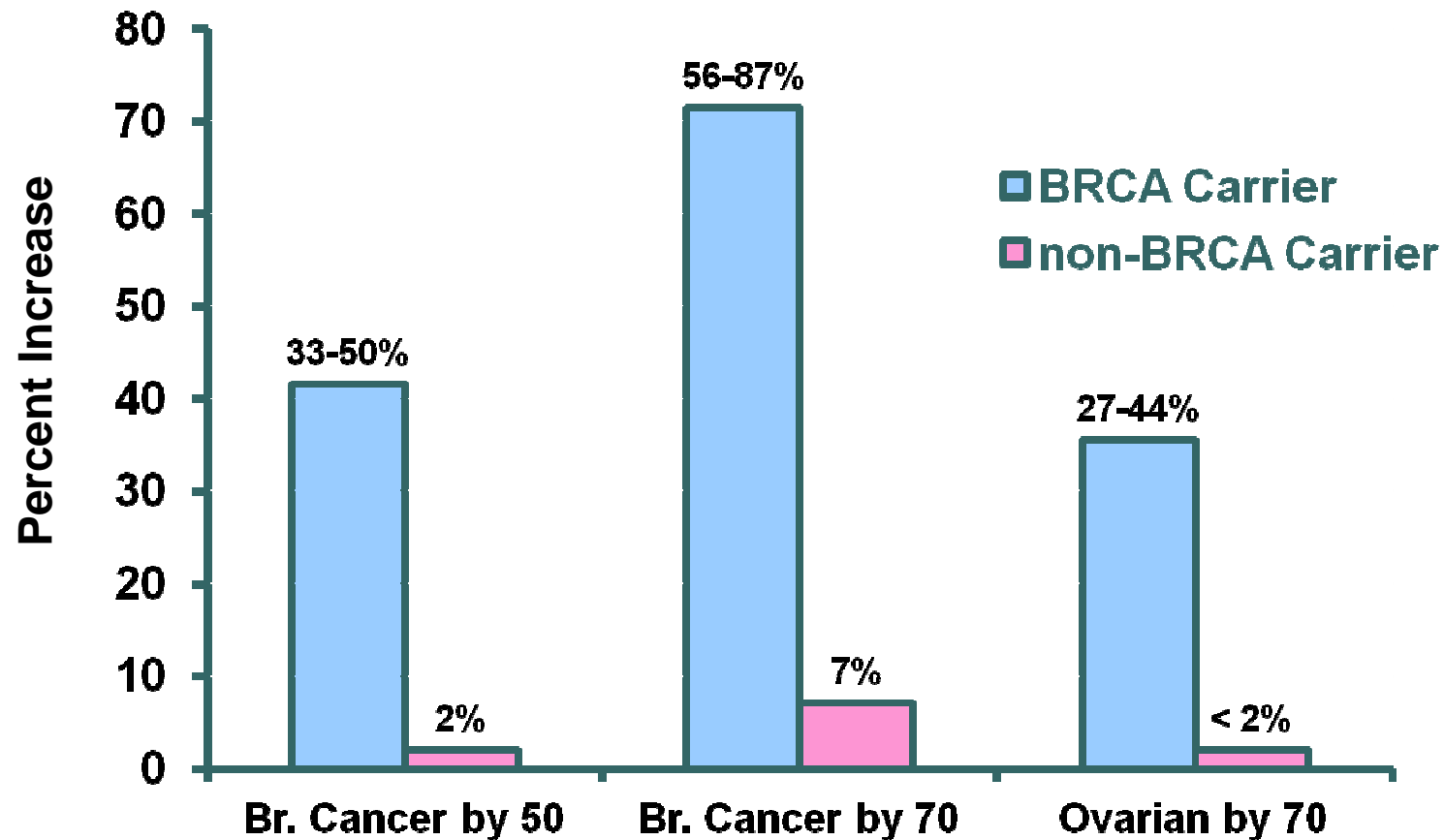
Prophylactic Mastectomy: Who and How

- Bilateral PM
Selection
Efficacy
- CPM
Selection
- Surgical Technique
SN biopsy

When Should PM Be Considered? Magnitude of Known Risk Factors

Relative Risk		
< 2	2-4	> 4
Early menarche	Family hx 1 ^o relative	BRCA mutation
Late menopause	> 35 first birth	Radiation exposure
Nulliparity	Dense breasts	LCIS
Obesity		Atypical hyperplasia
Alcohol		
HRT		

BRCA Mutations: Risk of Breast/Ovarian Cancer by Age



Risk of Breast Cancer After RT for Hodgkin's Lymphoma

Age at Diagnosis

<u>Age at Diagnosis</u>	<u>Relative Risk</u>
0-14	34-136
15-19	12-32
20-24	5-19
25-29	4-8
30-39	0.6-3.7
≥ 40	No increase

Absolute Risk of Cancer After LCIS Diagnosis

Study	F/u	Ipsilateral CA	Contralateral CA
7 studies (74-93) n = 610	14 yrs (5-24)	12% (74/602)	9% 37/610
Fisher 2004 n = 180	12 yrs	9% 16/180	8% 14/180

How Effective Is PM?

	Moderate Risk			High Risk		
	O	E	% Reduction	O	E	% Reduction
Incidence	4	37.4	89.5	3	30	90
Death	0	10.4	100	2	19.4	89.7

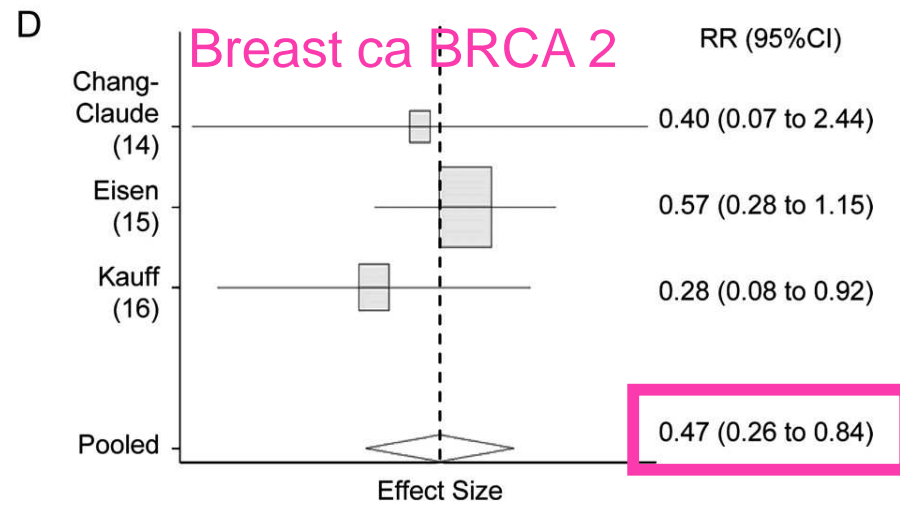
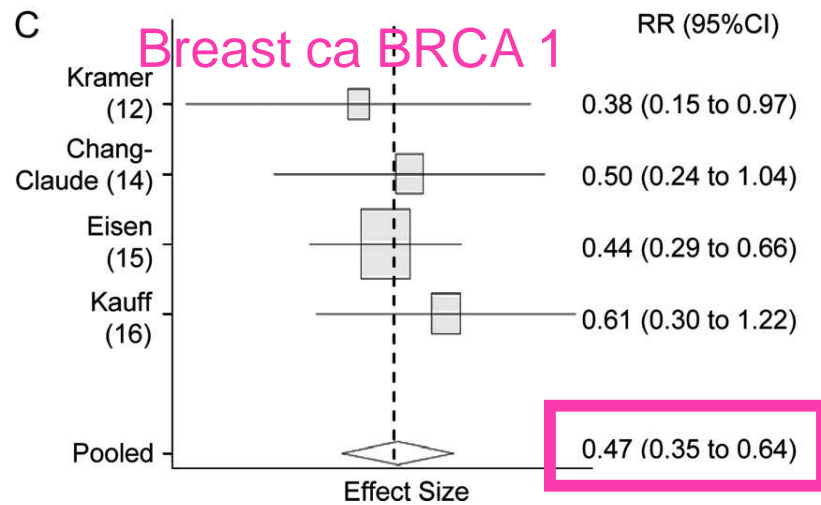
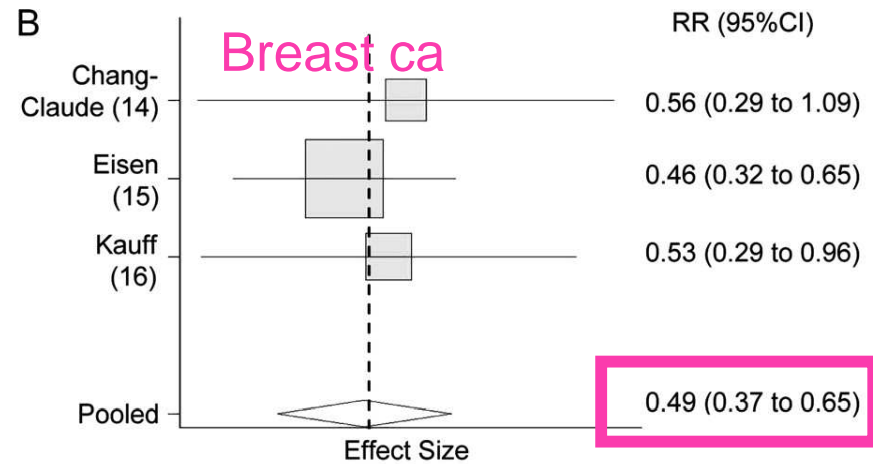
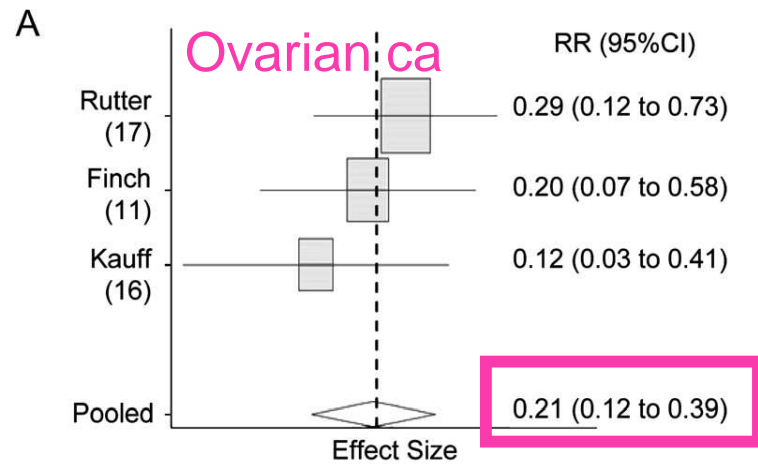
How Effective Is PM in BRCA Mutation Carriers?

Study	<u>PROSE</u>	<u>Meijers-Heijboer</u>
Follow-up	6.4 yrs	3.0 yrs
PM	1.9% (2/105)	0 (76)
No PM	48.7% (184/378)	12.7% (8/63)
	HR 0.05; 95% CI, 0.01-0.22	p = 0.003

Rebbeck T, J Clin Oncol 2004;22:1055

Meijers-Heijboer H, NEJM 2001;345:159

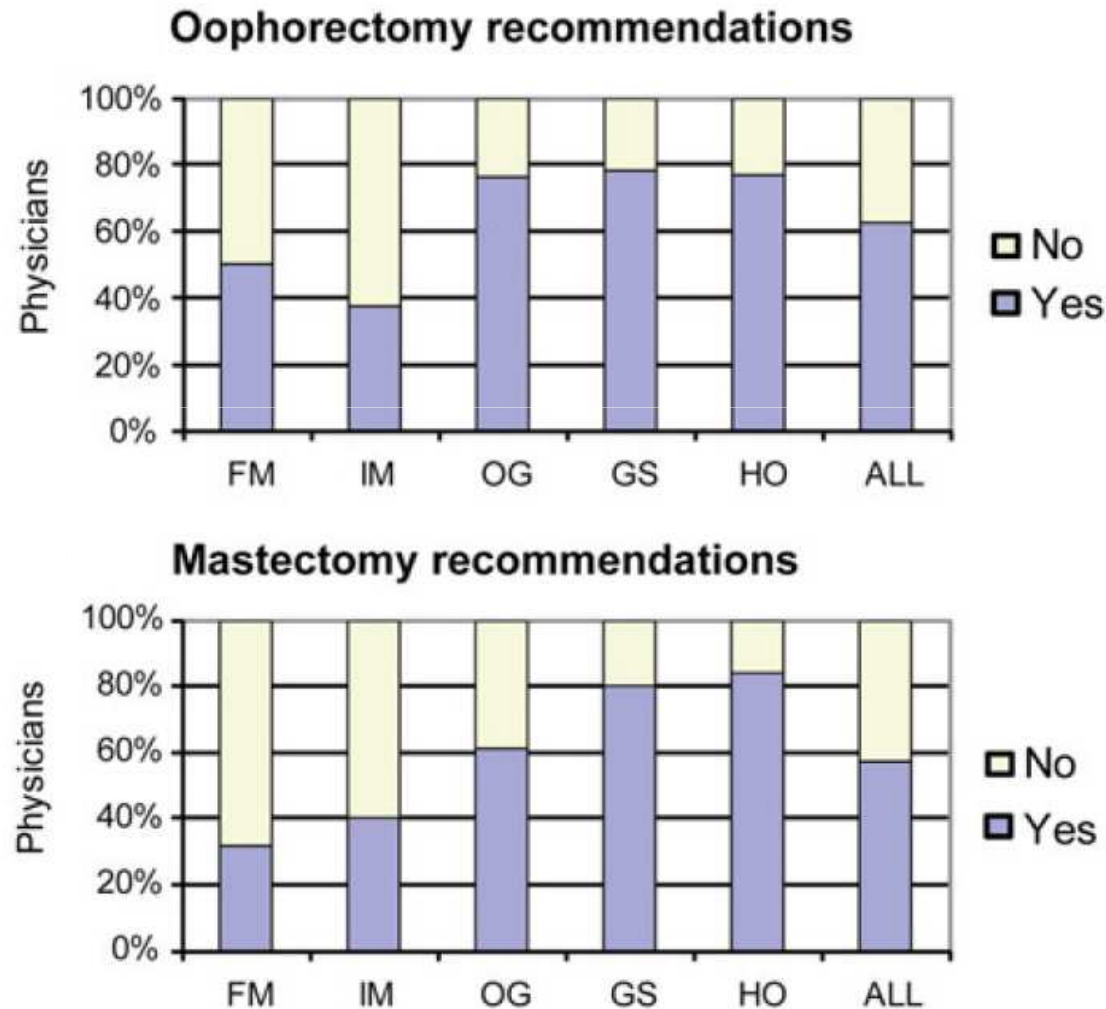
Metaanalysis of Risk-Reducing Estimates Associated with RRSO



Acceptability of Prophylactic Surgery

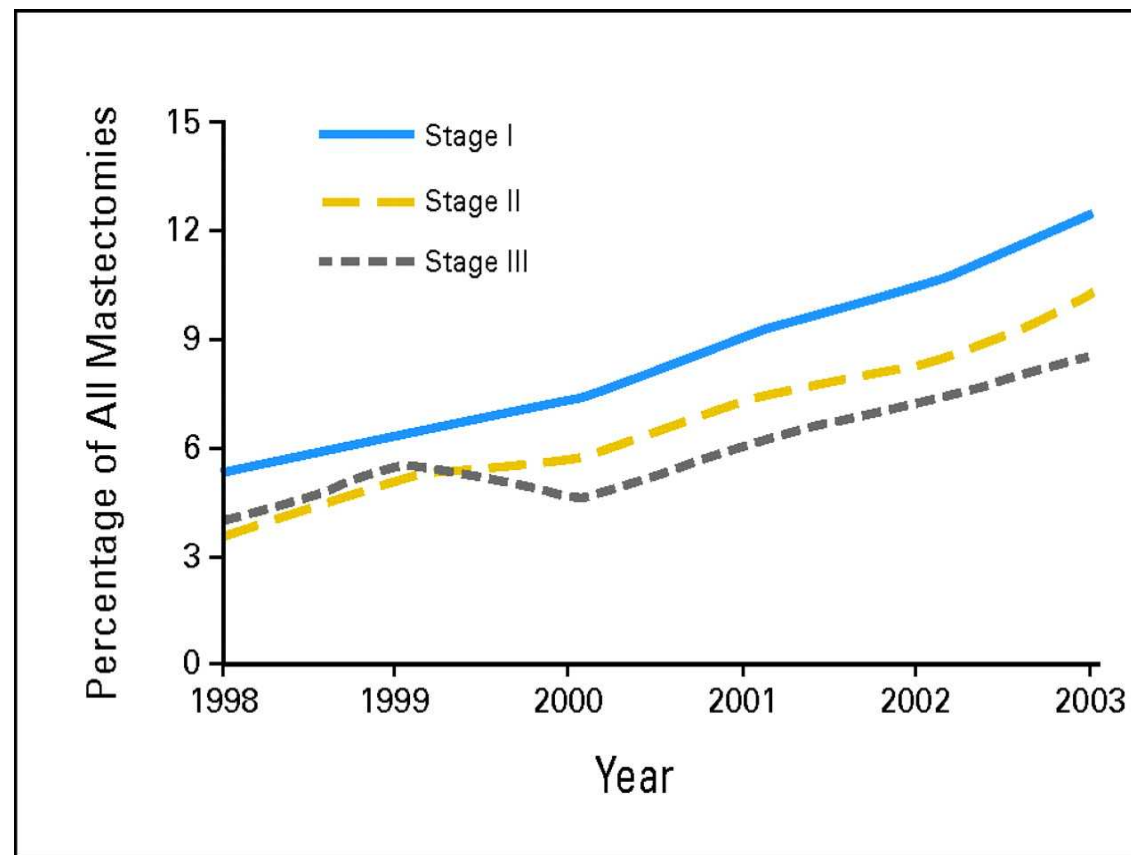
<u>Author</u>	<u>Group</u>	<u>% Accepting</u>	
		<u>PM</u>	<u>PO</u>
Wagner	Austrian BRCA 1/2 carriers	21	50
Lehrman	Unaffected U.S. carries	17	53
Meijers-Heijboer	Unaffected Dutch carriers	51	64
Eisinger	French women attending cancer genetics clinics	4	16

BRCA1 Management by Specialty



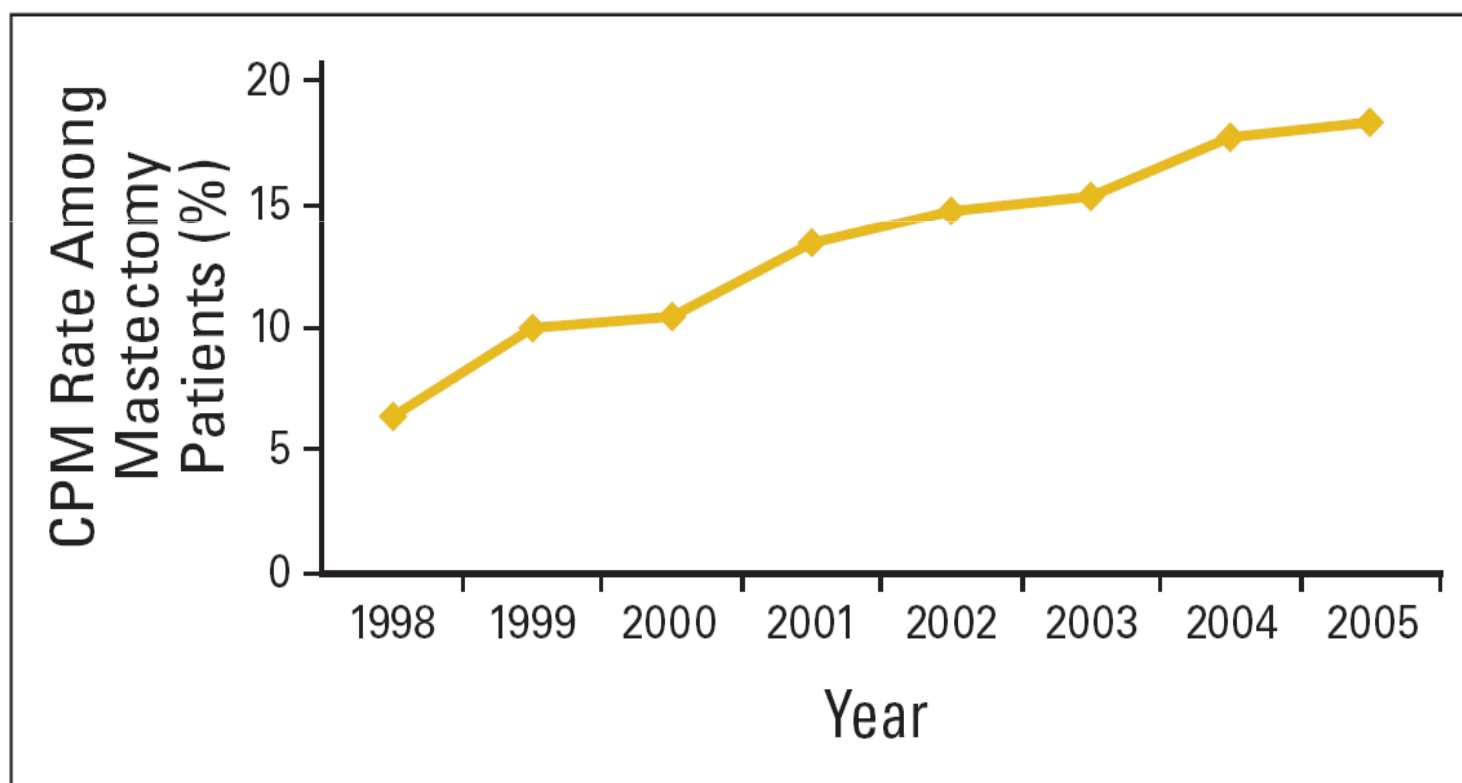
Contralateral Prophylactic Mastectomy Rates Among All Patients Undergoing Mastectomy

Invasive Cancer



Contralateral Prophylactic Mastectomy Rates Among All Patients Undergoing Mastectomy

DCIS



Who Gets CPM?

Patient

Younger

White

Insured

Family Hx

BRCA testing
(regardless of result)

Tumor

Lobular cancer

DCIS

Treatment

Reconstruction

MRI

Yi M, Cancer Prev Res 2010;3:1026

Stucky CC, Ann Surg Oncol 2010;17(Suppl 3):330

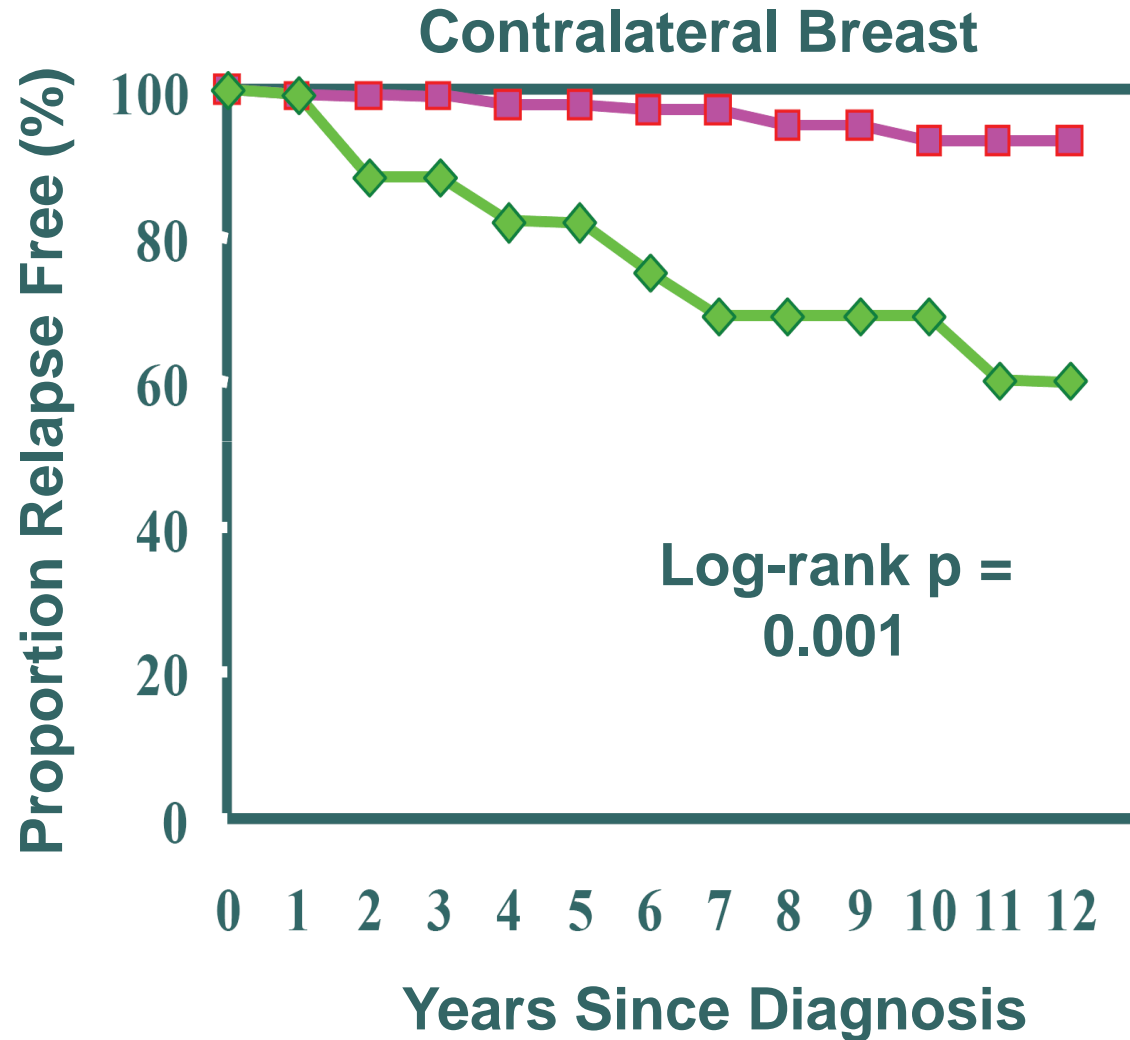
Yao K, Ann Surg Oncol 2010;17:2554

King TA, JCO 2011;29(16):2158

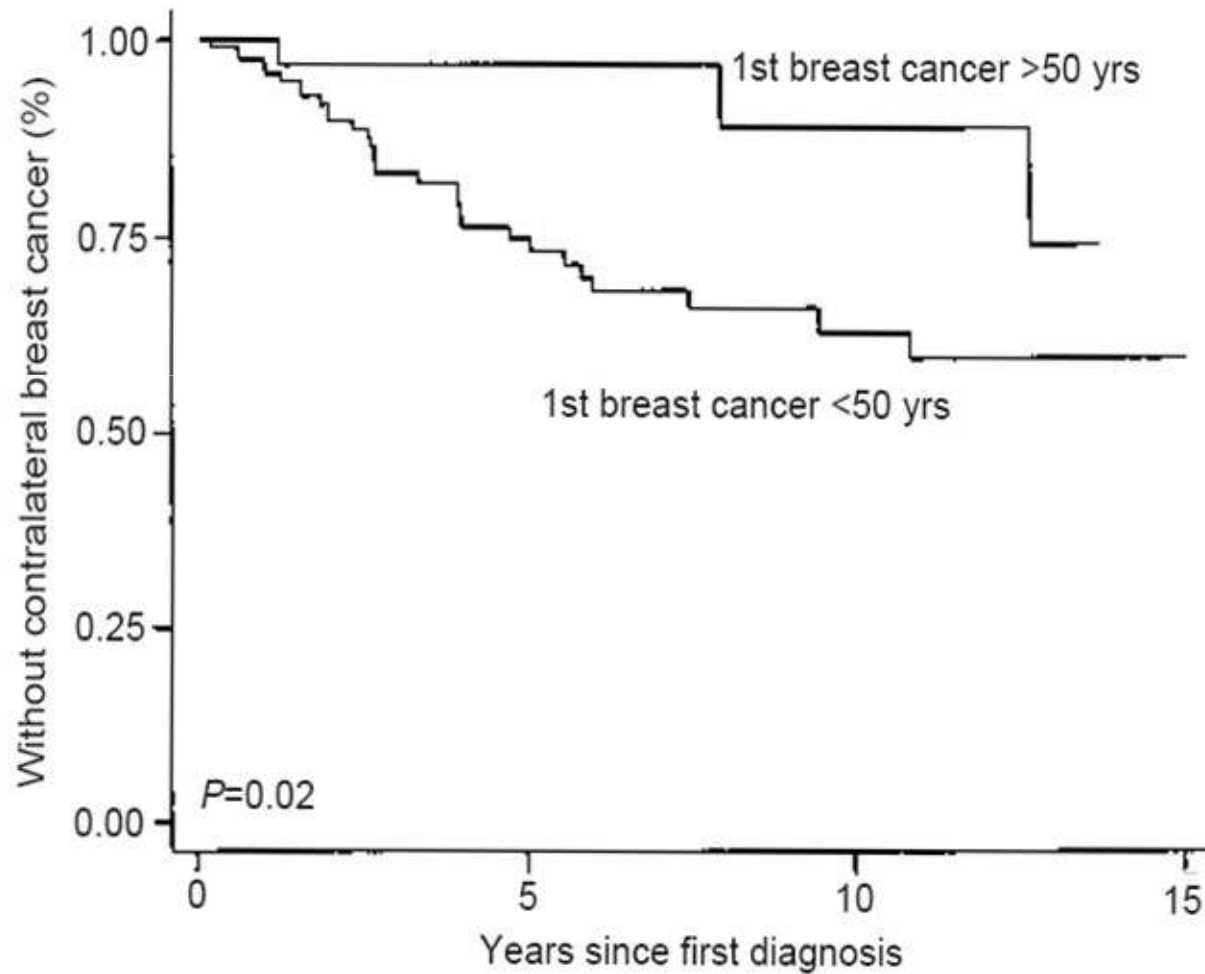
Why Is CPM Performed?

- High Risk of Contralateral Cancer
- Improve Survival
- Optimize Cosmetic Outcome of Reconstruction

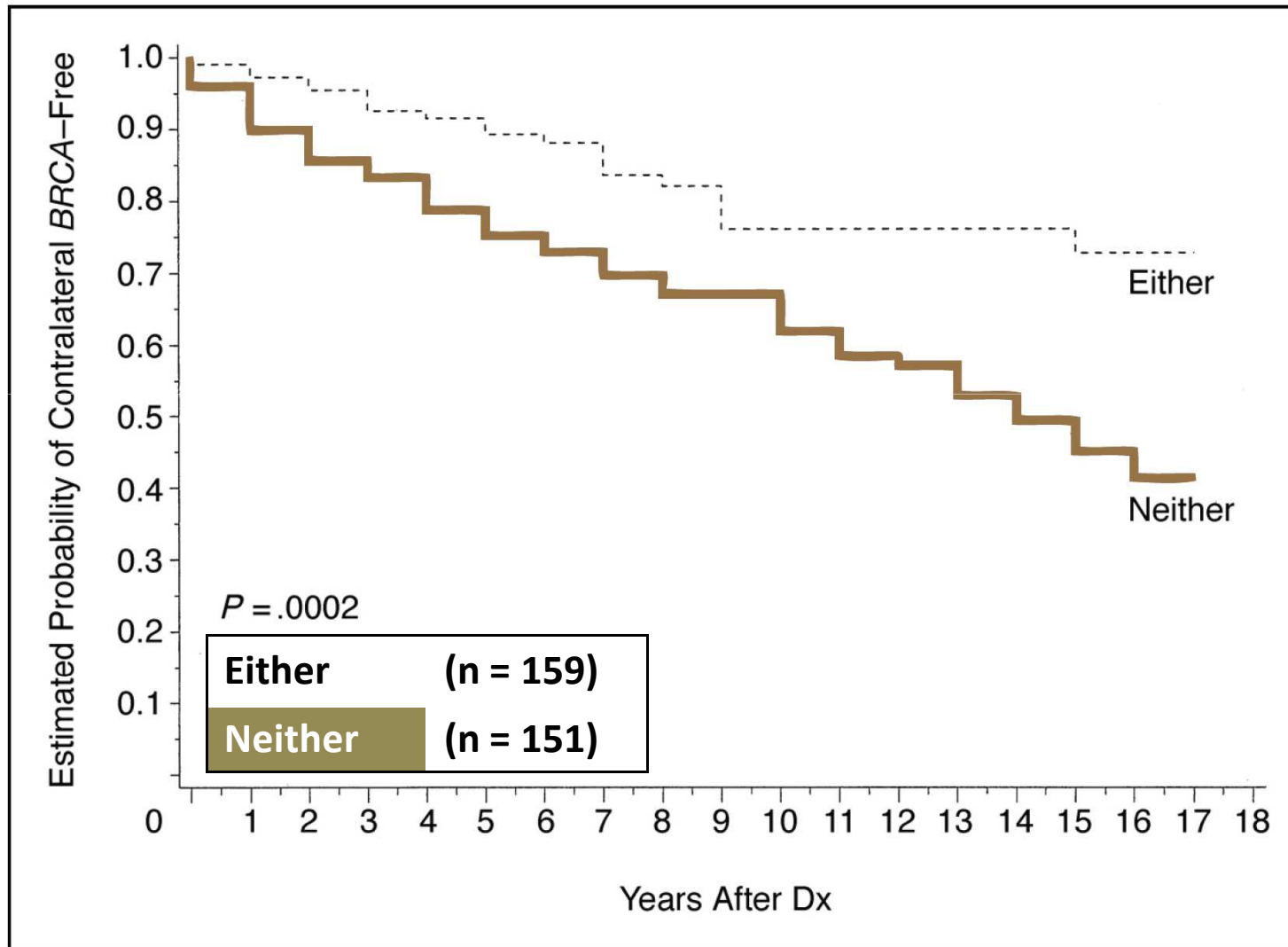
Risk of Contralateral Cancer in BRCA Mutation Carriers



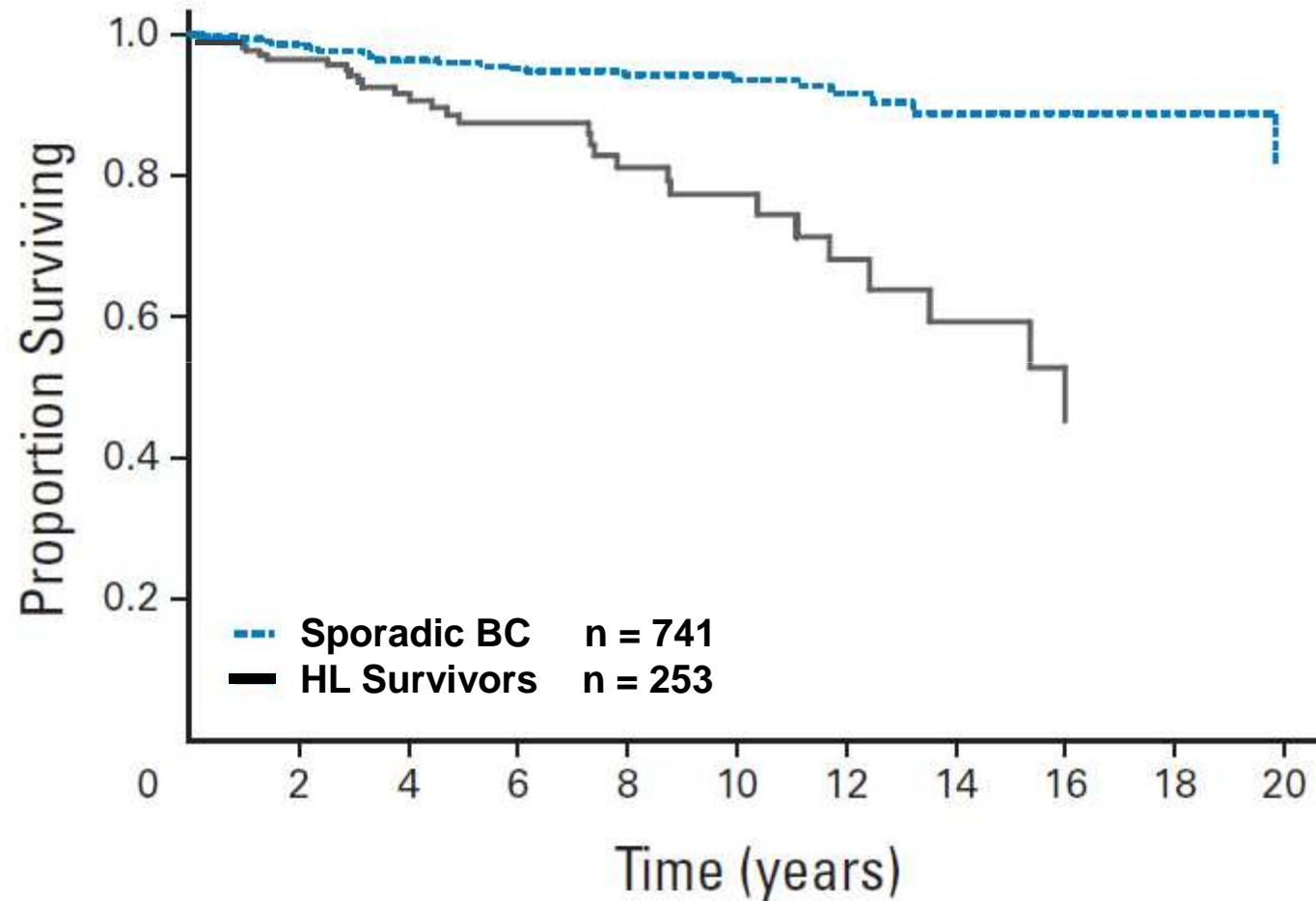
Effect of Age on Contralateral Cancer in BRCA 1 Carriers



Impact of Tamoxifen or Oophorectomy on CBC Risk in BRCA Carriers



Contralateral Cancer After RT for Hodgkins Lymphoma



What Is the Risk of Contralateral Cancer?

SEER 1973 - 1996

134,501 unilateral DCIS, Stage I+II cancer
4.2% incidence contralateral ca

10-year actuarial risk: 6.1%

20-year actuarial risk: 12.0%

What Is the Risk of Contralateral Cancer?

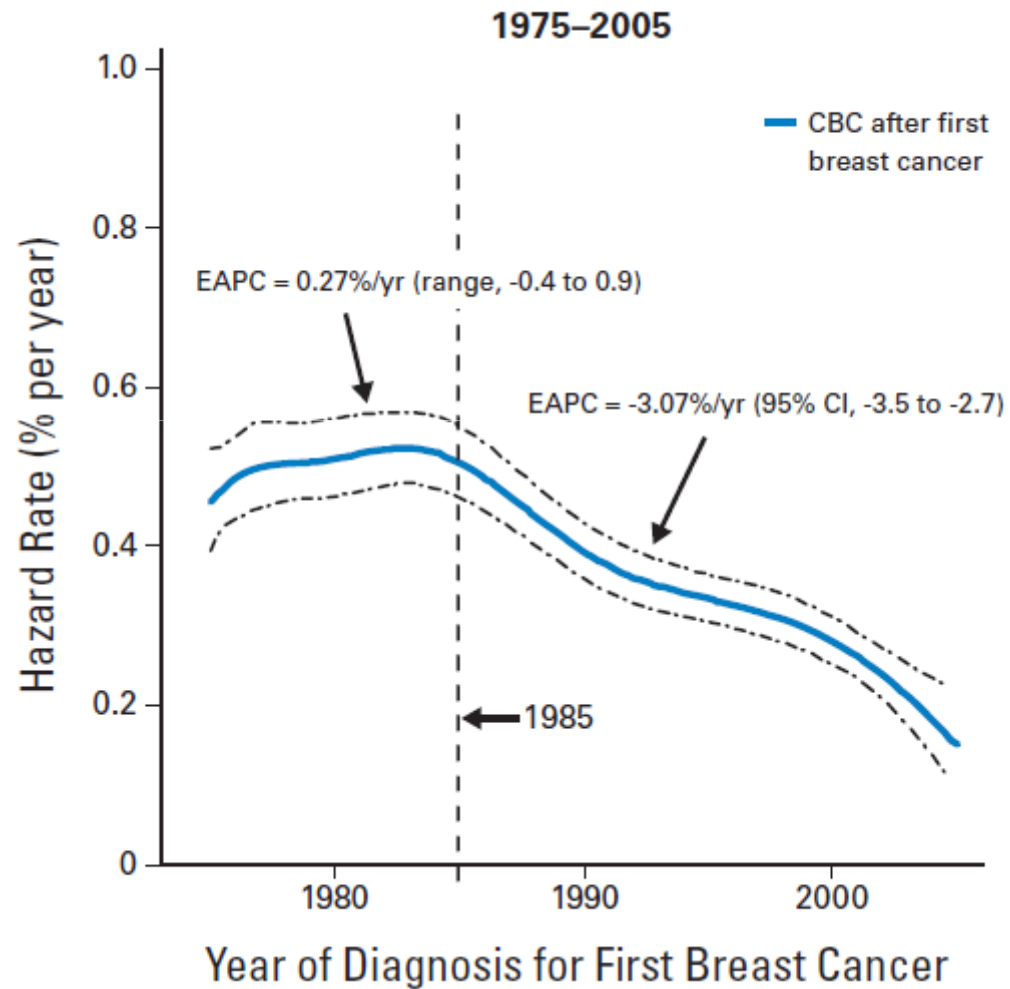
	Time (years)				p-value
	5	10	15	20	
<u>Histology</u>					
DCIS	3.3	6.0	8.7	10.6	
Ductal	2.9	6.0	9.1	12.1	.02
Lobular	3.2	6.4	9.0	11.7	
Medullary	3.2	7.5	10.8	17.0	

How Does Treatment Modify Risk?

- ↓ 50% - 60% by endocrine rx
- ↓ 20% by chemotherapy
- ↓ By trastuzumab

- Older studies prior to widespread use of adjuvant therapy overestimate risk

Incidence of Contralateral Cancer



Annual Incidence of Contralateral Breast Cancer 2001-2005

<u>Age First Diagnosis</u>	<u>Per 100/yr</u>	
	ER Positive	ER Negative
25-29	0.45	1.26
30-34	0.31	0.85
35-39	0.25	0.64
40-45	0.24	0.47
50-54	0.26	0.45
60-64	0.36	0.51
70-74	0.37	0.55
80-84	0.26	0.63

Do Increasing Rates of CPM Reflect Greater Awareness of Breast Cancer Risk?

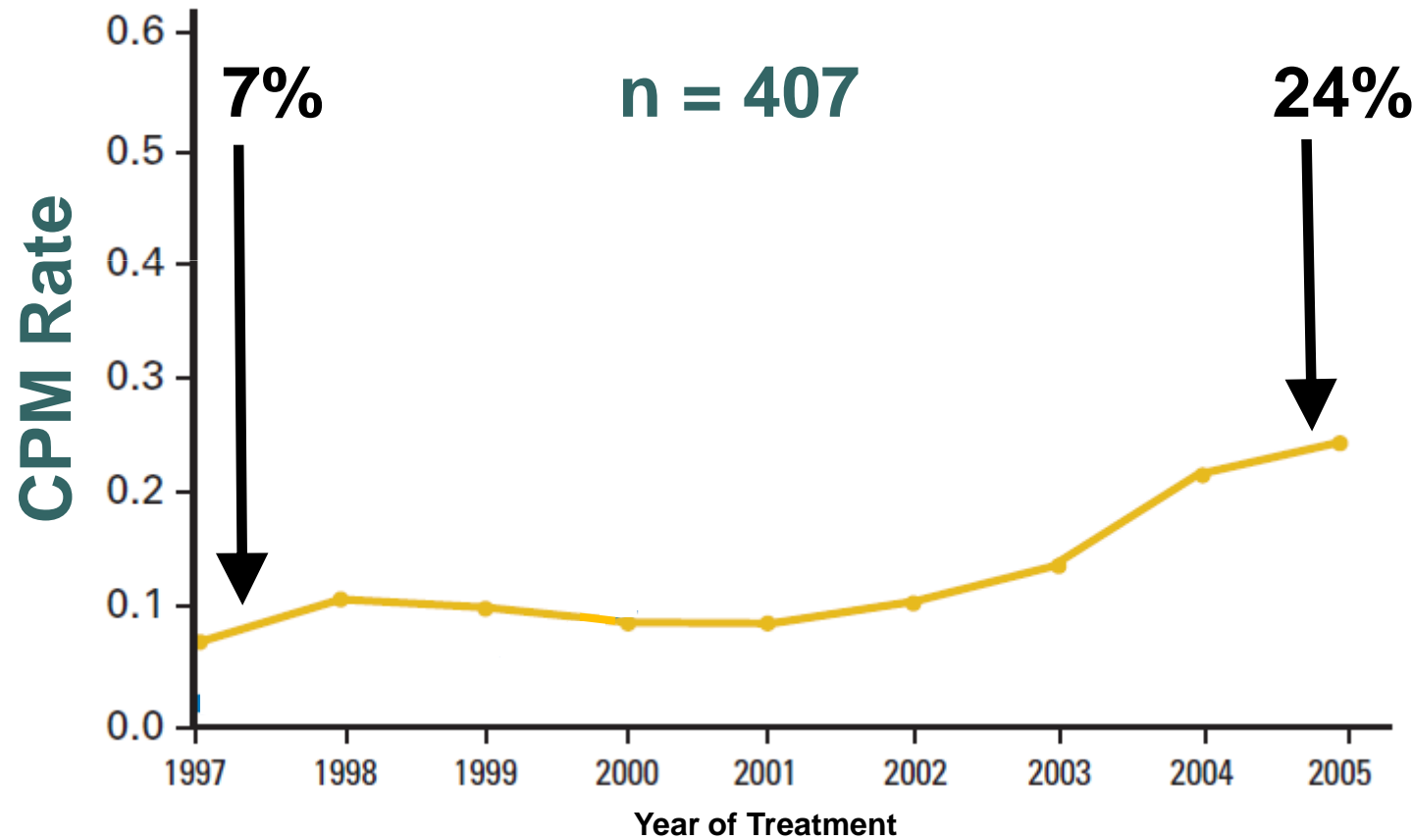
MSKCC Experience

n = 2965

- Unilateral breast cancer
- Stage 0-III
- Jan 1997 – Dec 2005
- CPM \leq 12 months of dx

Results

CPM Rate by Year of Surgery



Contralateral Prophylactic Mastectomy “High Risk” Population (n = 407)

BRCA mutation carriers = 37
Prior mantle radiation = 15

- 52 (13%) patients having CPM

Contralateral Prophylactic Mastectomy Patient Characteristics

	No-CPM (n=2558)	CPM (n=407)	p-value
Age at surgery			
Mean	54.7 yrs	45.6 yrs	<.0001
Race			
Non White	628 (25%)	29 (7%)	<.0001
White	1912 (75%)	378 (93%)	
Family History			
No	1525 (60%)	127 (32%)	<.0001
Yes	1010 (40%)	276 (68%)	

Contralateral Prophylactic Mastectomy

Familial Risk Factors

	No-CPM (n=2558)	CPM (n=407)	p-value
Number of FDR w/ BC			
0	558 (55%)	118 (43%)	.02
1	397 (39%)	135 (49%)	
2 or more	59 (6%)	23 (8%)	
Genetic testing			
Yes	243 (10%)	118 (29%)	<.0001
Mutation Carrier			
Yes	30 (12%)	37 (31%)	<.0001

Contralateral Prophylactic Mastectomy Clinical Management Factors

	No-CPM (n=2558)	CPM (n=407)	p-value
MRI at cancer diagnosis			
Yes	413(16%)	174(43%)	<.0001
Additional biopsy due to MRI			
Yes	252 (61%)	108 (62%)	NS
Ipsilateral	235 (57%)	58 (33%)	
Contralateral/Bilateral	17 (4%)	50 (29%)	<.0001

Contralateral Prophylactic Mastectomy Clinical Management Factors

	No-CPM (n=2558)	CPM (n=407)	p-value
Attempted BCS			
Yes	421 (16%)	112 (28%)	<.0001
Breast Reconstruction			
Yes	1306 (51%)	354 (87%)	<.0001

Predictors of CPM

Multivariate Random-Effects Logistic Regression

	OR	p-value
Age \geq 50 vs age < 50	0.321	<.0001
Race (Other vs White)	0.271	<.0001
Family hx of Breast Cancer	2.918	<.0001
DCIS only vs IFDC	1.912	0.0003
IFLC vs IFDC	0.902	0.6465
MRI at DX	3.177	<.0001
BCT Attempted	1.736	0.0014

Adjusted for surgeon

Does CPM Improve Survival?

Cochrane Review 2010

15yr Overall Survival

4 studies, 246 patients

CPM

n = 64

64%

No CPM

n = 182

48%

P = .26

Disease-Specific Survival

- 6 studies
- Heterogenous results
- Lack of adjustment for differences in prognostic factors

**Conclusions: Methodologic limitations.
Little good data to indicate CPM will improve survival**

Is CPM Likely to Increase Survival?

SEER 1998-2003
107,106 unilateral ductal cancers

CPM in 8.3% n = 8902

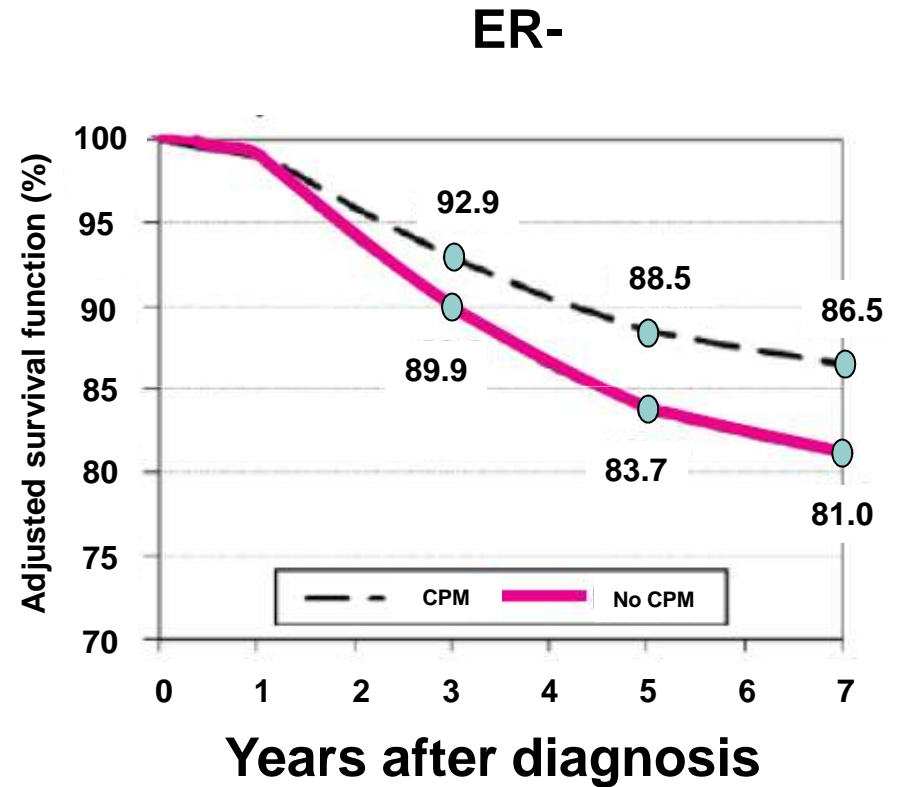
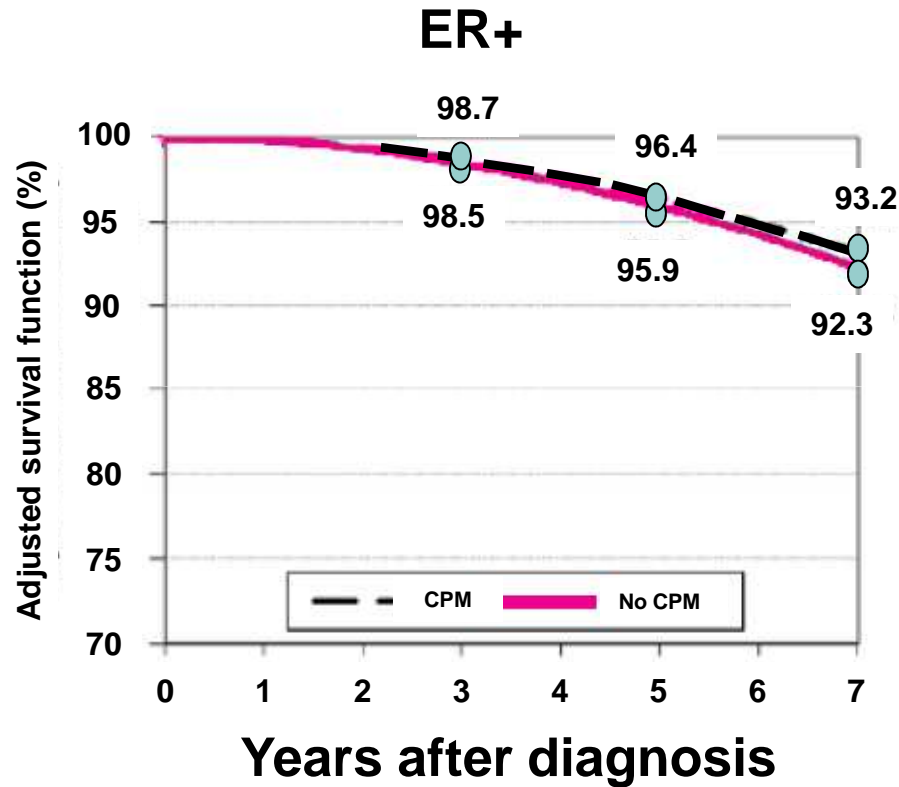
Rates of CBC

Age < 50, Stage I, II

	ER+	ER-	p-value
No CPM	0.46%	0.90%	<.001
CPM	0.13%	0.16%	.90
p	.07	.05	

Median follow-up 47 months

CPM and Survival



* Adjusted analysis

CPM and Survival

- No benefit in ER+ patients
- No benefit in ER- \geq 60 years
- Survival difference in ER- < 50 much greater than expected for < 1% difference in incidence.

Patient Satisfaction

Unilateral vs Bilateral Mastectomy

- Single institution survey of all reconstruction patients
- Jan 1999-Dec 2006
- Response rate 75%
- Minimum 13 months follow-up, mean 49 months

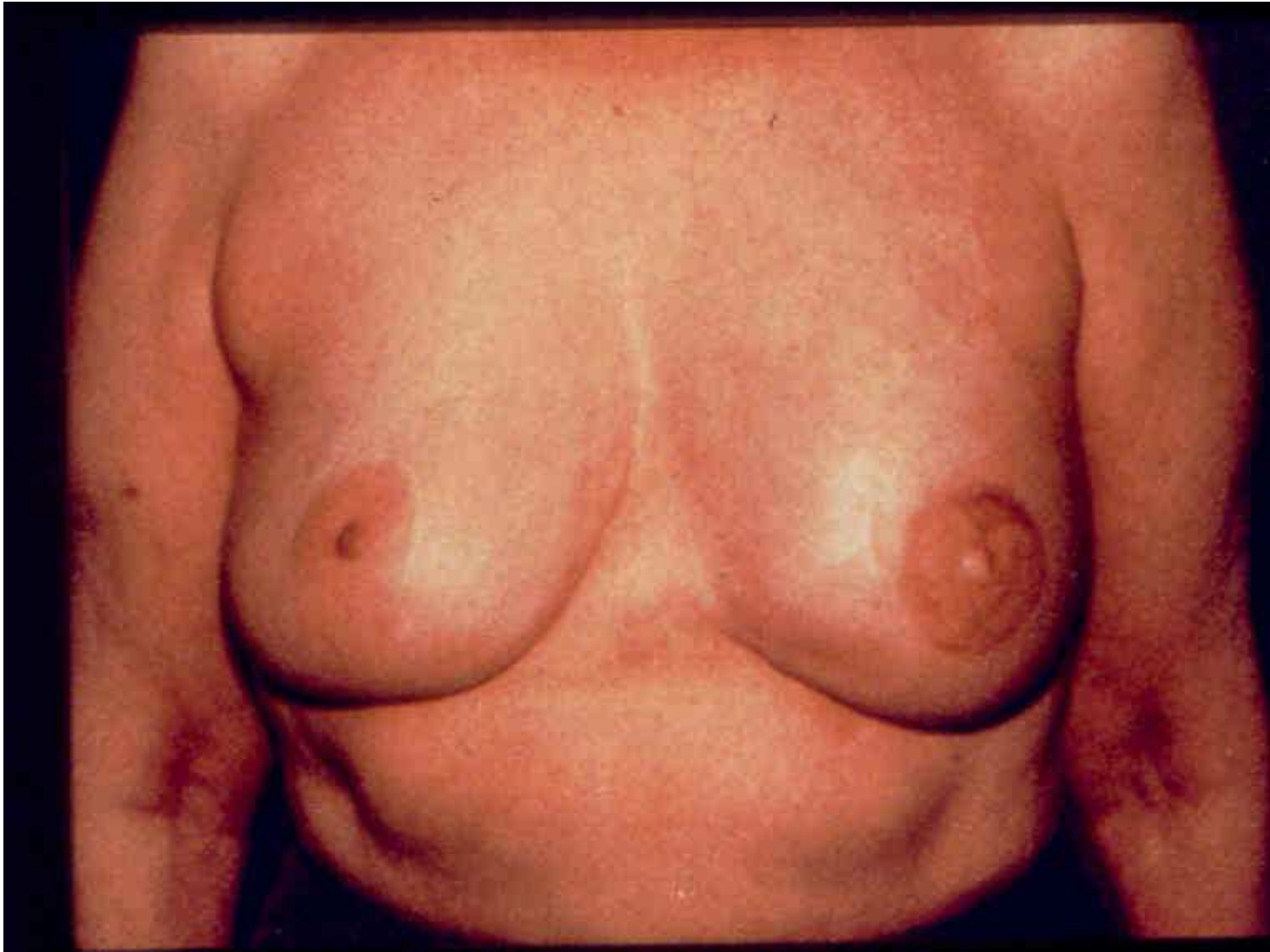
Outcome

Unilateral vs Bilateral Mastectomy + Recon

	<u>Unilateral</u>	<u>Bilateral</u>	<u>P-value</u>
# Patients	451	176	
General satisfaction	66.8%	66.9%	0.99
Aesthetic satisfaction	64.8%	62.6%	0.65
Mean # addl. surgeries	2.2	2.1	
Total complications	34.6%	34.1%	0.93

Technique of PM

- Same anatomic limits, flap thickness as therapeutic mastectomy
- Skin sparing routine



Sentinel Node Bx in PM

Metaanalysis: 6 studies, 1343 PM

Invasive ca: 1.7% 95% CI 1.1-2.5

Positive SN: 1.9% 95% CI 1.2-2.6

MSKCC Experience: 625 CPM 1997-2005

Invasive ca: 5 (0.8%)

Positive SN: 1 (0.2%)

Zhou WB, Can J Surg 2011;54:300

King TA, Ann Surg 2011; 254:2-7

Sentinel Node Bx in PM

- Not routine — incidence of side effects exceeds benefit.
- Older studies overestimate incidence of nodal metastases due to inclusion of isolated tumor cells, micrometastases.
- Reserve for patients with unsampled imaging abnormalities or core bx of atypia where risk of cancer is increased.

When Is CPM Indicated?

Unilateral cancer and

- BRCA 1/2 mutation carrier
- Hx mantle irradiation Hodgkins lymphoma

Physician-initiated discussion

When Is CPM Indicated?

Unlikely to benefit

- Poor prognosis from current cancer
 - Node positive, large primary, triple negative
- Effective risk-reducing therapy for current cancer
 - ER, PR positive, will get endocrine rx
 - ? HER2 positive, will get trastuzumab

When Is CPM Indicated?

- MD-initiated discussion rarely appropriate outside setting of known/suspected mutation carrier.
- May be appropriate if patient-initiated AND:
 - Young age
 - DCIS/favorable prognosis invasive ca
 - Significant family Hx
 - Breasts difficult to monitor: dense, multiple bx