Hypothesis #3: Hormone therapy influences cancer etiology

Breast Cancer Trends, Etiology

And Related Phenomena

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http://cancercontrolplanet.cancer.gov/breast_cancer.html

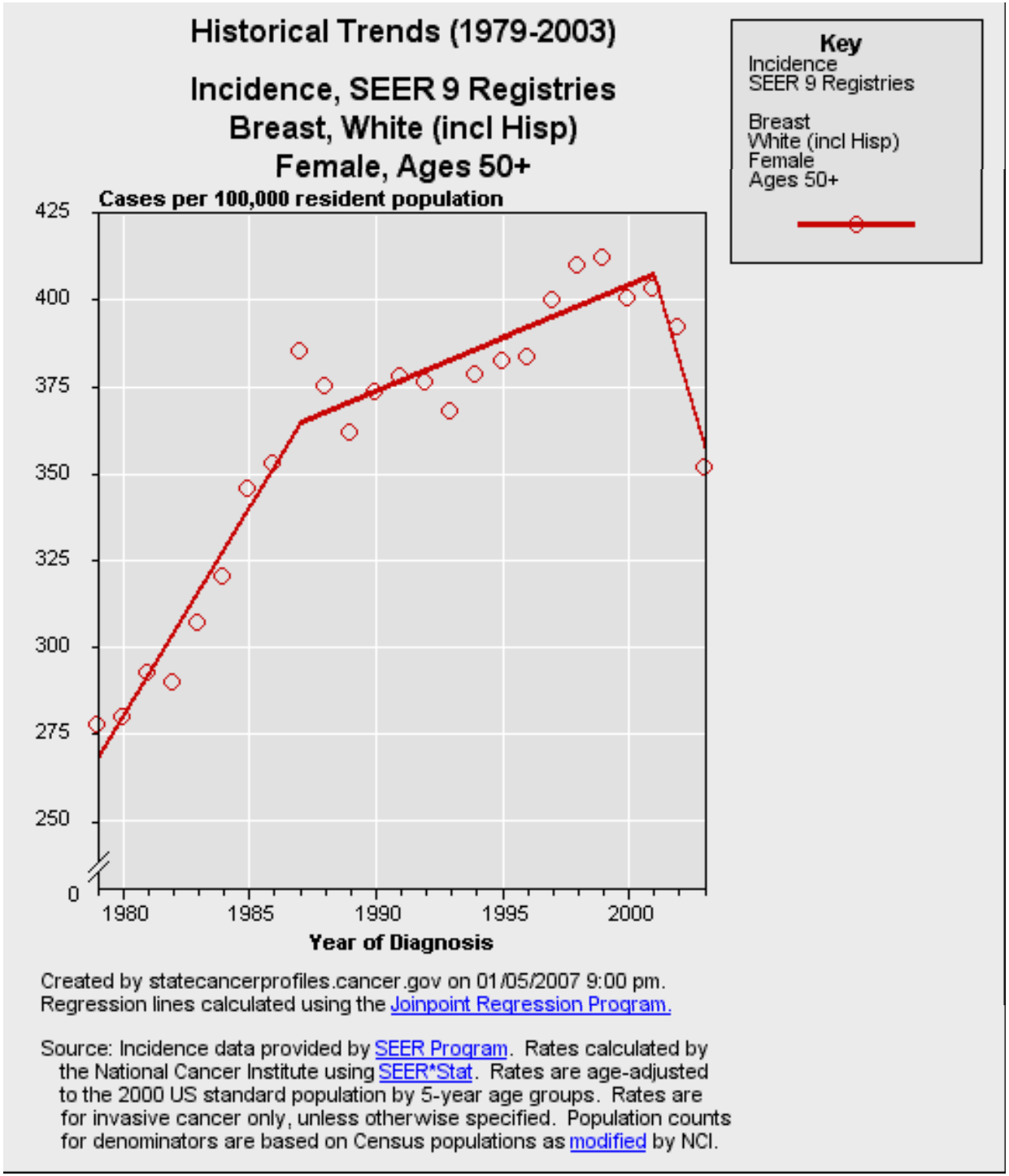
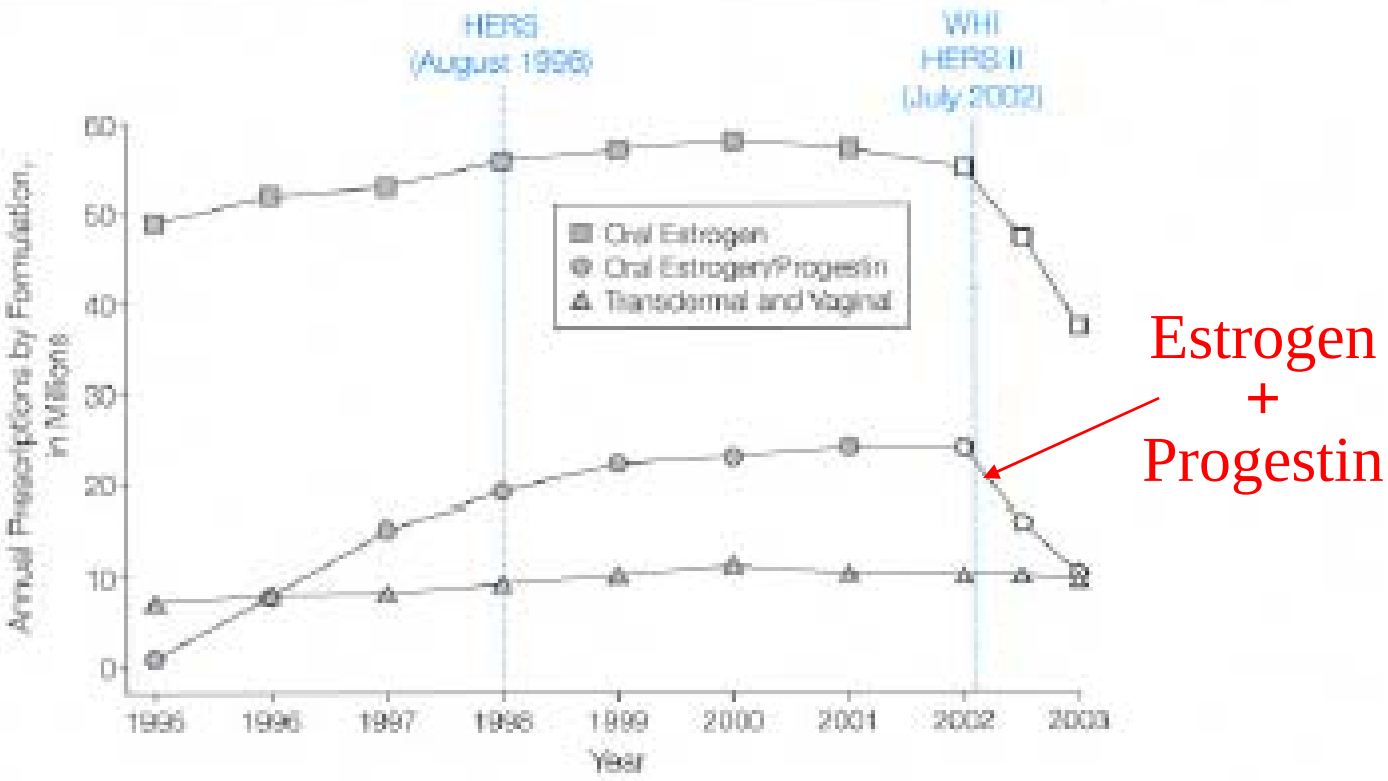


Figure 3. Annual Number of US Prescriptions for Hormone Therapy by Formulation, 1995-July 2003



Annualized data for January to June 2002, July to December 2002, and January to July 2003 are included (open symbols). Data are from the National Prescription Audit Plus, IMS HEALTH. HERS indicates Heart and Estrogen/Progestin Replacement Study; WHI, Women's Health Initiative.

Rate of Cancer and 95% CI Among Postmenopausal Women Who Underwent Screening Mammography From 1996 to 2000, by Duration of HT Use

		Duration of Use*	
		Estrogen and Progestin	
	No HT	< 5 Years	≥ 5 Years
No. of examinations	382,435	24,819	47,979
No. of cancers	1,803	81	298
Cancers per 1,000 exams	4.3	3.7	6.5
95% CI†	4.2 to 4.5	3.2 to 4.3	6.0 to 7.0
Relative risk	Referent	0.85	1.49
95% CI†		0.73 to 0.98	1.36 to 1.63

* Estrogen and progestin group: HT users with a uterus.

† Adjusted for age, family history of breast cancer, examination year, time between mammography examinations, and mammography registry using Poisson regression and standardized to the total population.

Excerpted from:
Kerlikowske et al,
J Clin Oncol 21:4314-21, 2003

Relative Risk of Breast Cancer for a Given Tumor Characteristic (type, stage, size, grade, and estrogen receptor status) Among Postmenopausal Women Using Hormone Therapy Relative

Tumor Characteristic	Estrogen and Progestin Users for ≥ 5 Years Versus Nonusers*	
	RR	95% CI
More favorable prognosis		
DCIS	1.41	1.24 to 1.60
Stage 0 or I	1.51	1.37 to 1.66
Tumor size ≤ 20 mm§	1.59	1.43 to 1.76
Grade 1 or 2§	1.60	1.44 to 1.77
Estrogen receptor-positive§	1.72	1.55 to 1.90
Less favorable prognosis		
Invasive	1.51	1.38 to 1.66
Stage II, III, or IV	1.46	1.30 to 1.63
Tumor size > 20 mm§	1.24	1.09 to 1.42
Grade 3 or 4§	1.54	1.37 to 1.73
Estrogen receptor-negative§	0.89	0.77 to 1.03

§Invasive cancer only.

Kerlikowske et al,
J Clin Oncol 21:4314-21, 200

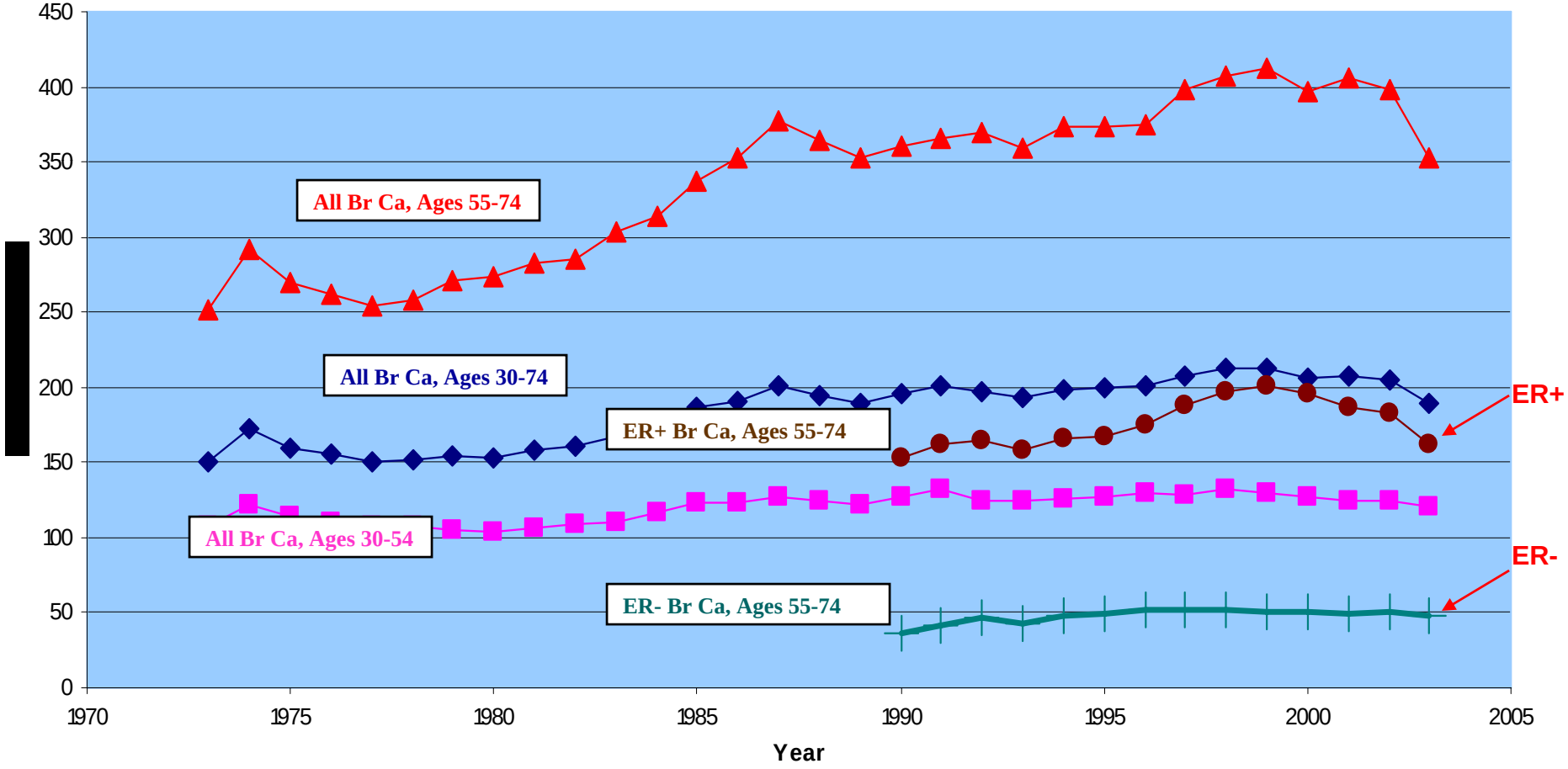
Examples of Studies That Have Examined for Certain Effects Of Combination Hormone Replacement Therapy on the Risk of All Breast Cancer, or Lobular Breast Cancer

Author (year)	Study Group	Duration Effect	Currency Effect	Cessation Effect	Lean Effect	ER+ over ER- Risk
Schairer (1994)	BCDDP F-U	**Yes**	na	na	na	na
Colditz (1995)	Nurses Health Stdy	**Yes**	**Yes**	na	na	na
Magnusson 1999)	Swedish case-contr.	**Yes**	na	na	**Yes**	na
Schairer (1999)	BCDDP F-U	**Yes**	**Yes**	**Yes**	**Yes**	na
Li (2000)	King Co. case-contr	**Yes**	**Yes**	na	na	na
Ursin (2002)	LA Co. case-contr.	**Yes**	**Yes**	na	**Yes**	**Yes**
Chen (2002)	GHC nested case-c	**Yes**	**Yes**	na	**Yes**	na
Newcomb (2002)	Multicenter case-co	na	**Yes**	na	**Yes**	na
WHI Grp. (2002)	Women's H. Initiat.	**Yes**	na	na	na	na
Daling (2002)	CARE (NICHHD)	**Yes**	na	**Yes**	na	na
Li (2003)	Wash. case-contr	**Yes**	**Yes**	**Yes**	na	**Yes**
Daling (2003)	CARE (NICHHD)	na	**Yes**	na	na	**Yes**
Kerlikowski ('03)	Mammo registry	**Yes**	na	na	na	**Yes**
Chen (2004)	Nurses Health Stdy	na	na	na	na	**Yes**
Rosenberg (2006)	Black WH Study	**Yes**	**Yes**	na	**Yes**	na
Li (2006)	WHI	**Yes**	na	**Yes**	na	**Yes**
Reeves (2006)	Million Women St.	**Yes**	na	na	**Yes**	na
Rosenberg (2006)	Swedish case-contr	**Yes**	na	na	na	**Yes**

na = not applicable because not examined

Incidence Rates of Breast Cancer by Histological Type and ER Status:

Women of all races, Original 9 SEER Registries (1973 to 2003)



How Does The Breast Cancer Incidence Decline Compare With Documented Changes in Mammography?

Women 55-74, Incidence in SEER (9 regions):

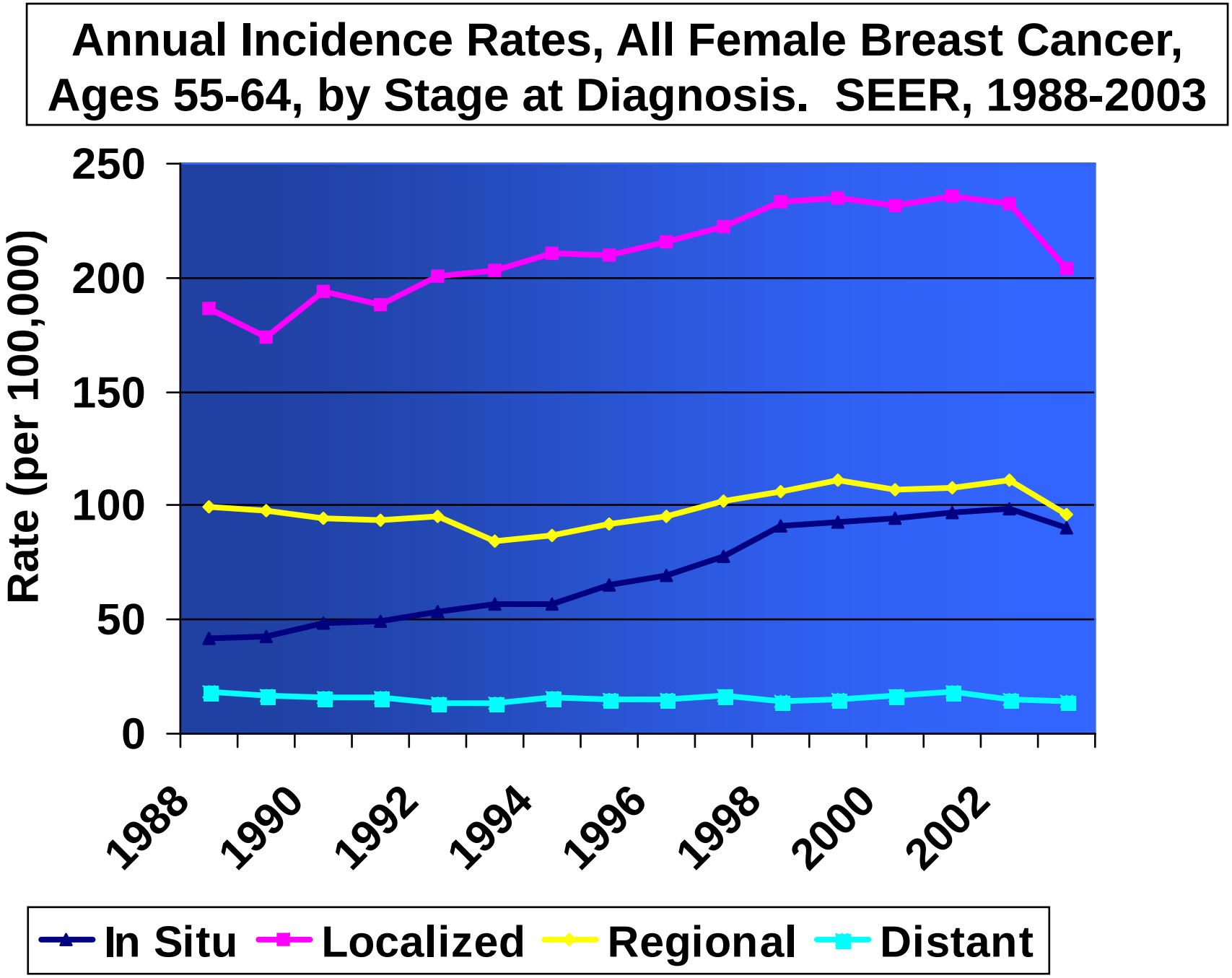
1999-2003 Reduction in ER+ Ductal Br Ca = 18%

2001-2003 Reduction in ER+ Ductal Br Ca = 13%

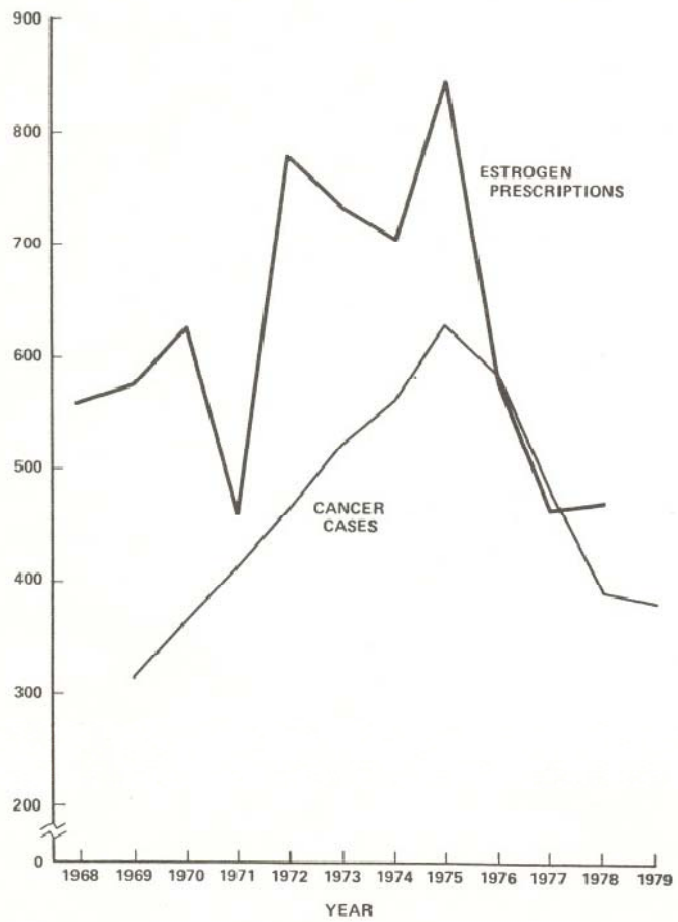
NCHS 2000-2003 Reduction in Mammography:

Ages 50-64 = 3.2%

Ages 65-74 = 0.8%


Annual Incidence Rates, All Female Breast Cancer, Ages 55-64, by Stage at Diagnosis. SEER, 1988-2003
Rate (per 100,000)
250
200
150
100
50
0
1988
1990
1992
1994
1996
1998
2000
2002
In Situ
Localized
Regional
Distant

Annual # of Estrogen Prescriptions, Western Region Sample, and # New Cases of Endometrial Ca

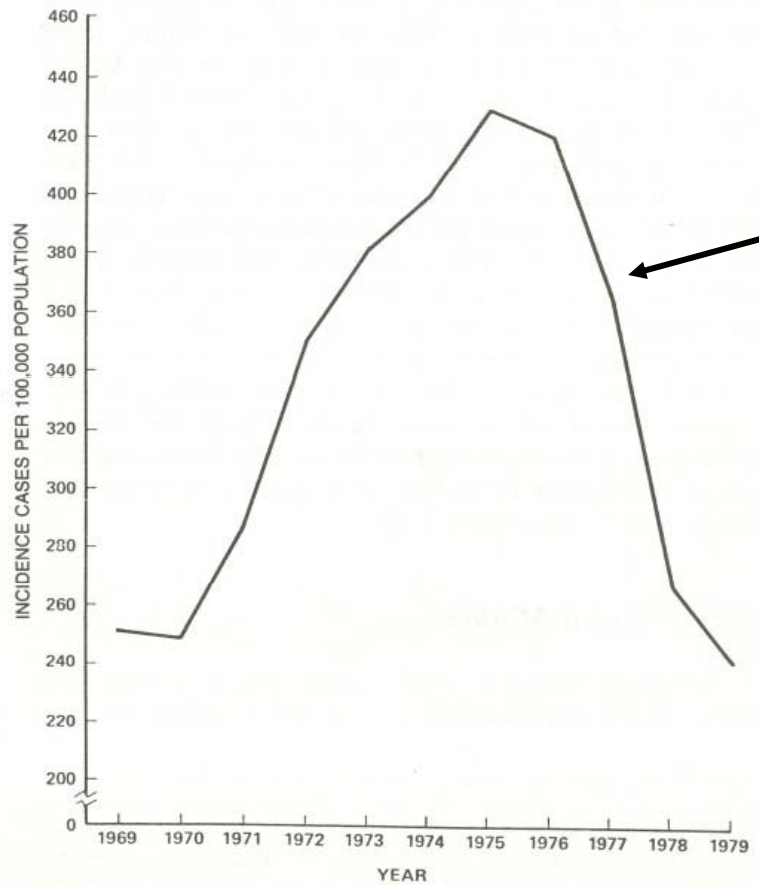


Source: RCE, California Department of Health Services; National Disease and Therapeutic Index, IMS America, Ltd.

FIGURE 2—Annual Number of Estrogen Prescriptions to Women, Ages 50–74 in Western Region Sample, 1968–1978, and Annual Number of New Cases of Endometrial Cancer Among White Women, Ages 50–74 in the San Francisco-Oakland SMSA, 1969–1979

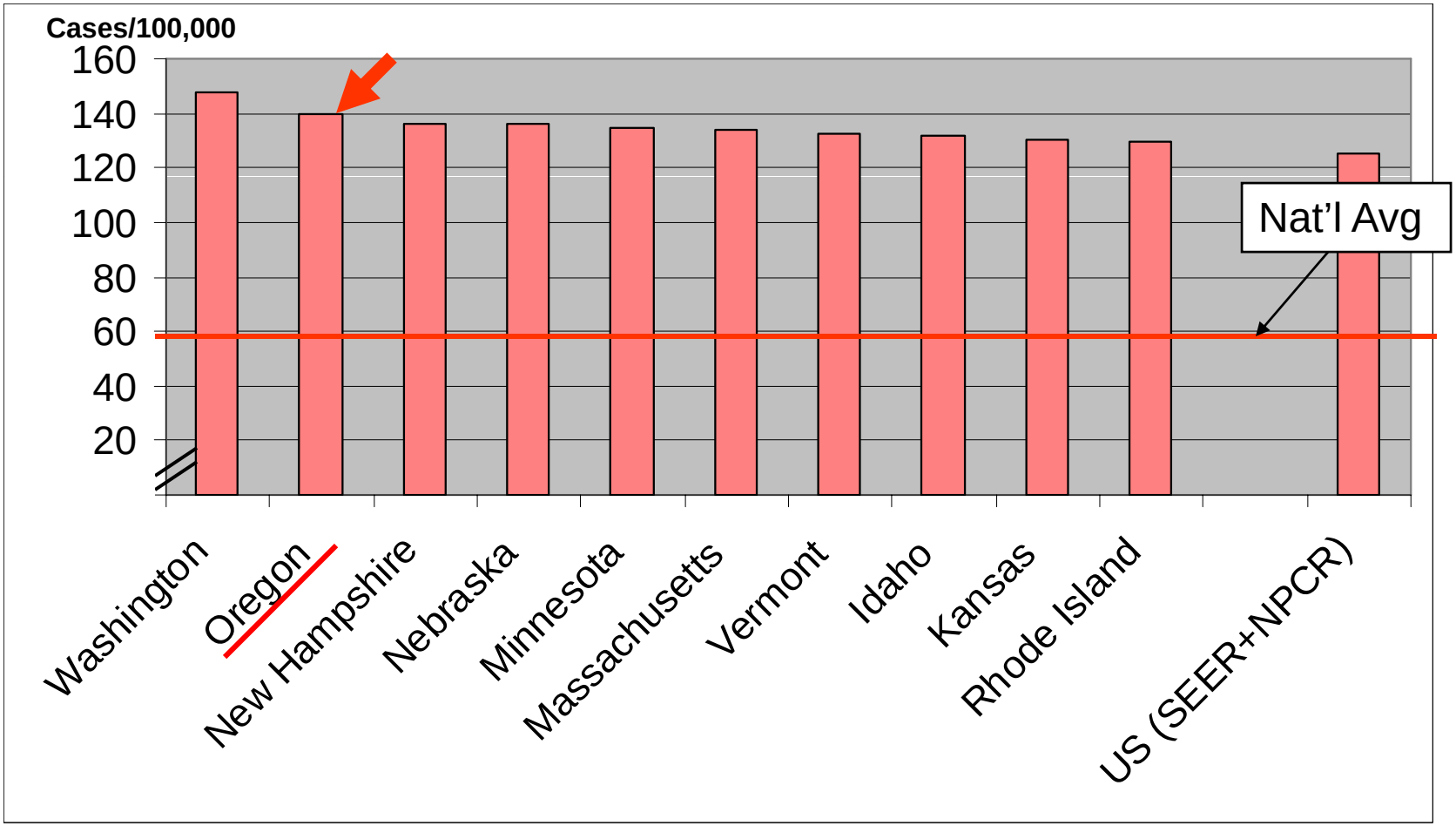
Endometrial Cancer Epidemic
Calif. SEER area, 1969-1979

Annual Incidence Rates (cases/100,000)



White Females Age 50-74

FIGURE 1—Endometrial Cancer Incidence Rates, White Females, Ages 50–74, Alameda and Contra Costa Counties, California, 1969–1979

Am J Public Health 1982; 72:65-68.

Female Breast Cancer
Top 10 States in the US
Age-Adjusted Incidence Rates, All Ages, All Races, 2002