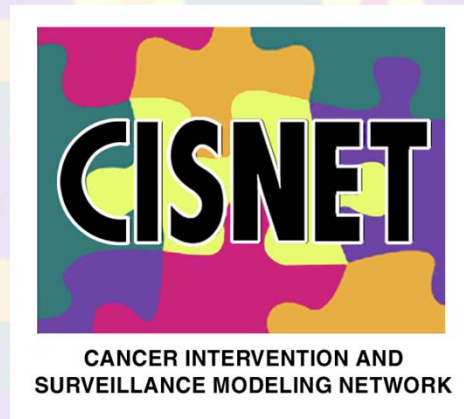


Cancer Intervention and Surveillance Modeling Network: Scientific Update

Breast Cancer Initiative

National Cancer Advisory Board
June 14, 2006



Donald Berry PhD.

M.D. Anderson Cancer Center

Houston, TX



Joint Analysis: Breast Cancer Base Case

**Assess Impact of Adjuvant Therapy &
Screening Mammography on US Breast
Cancer Mortality, 1975-2000**

Population Models

Common inputs

Background trends

Screening behavior

Diffusion of new treatments

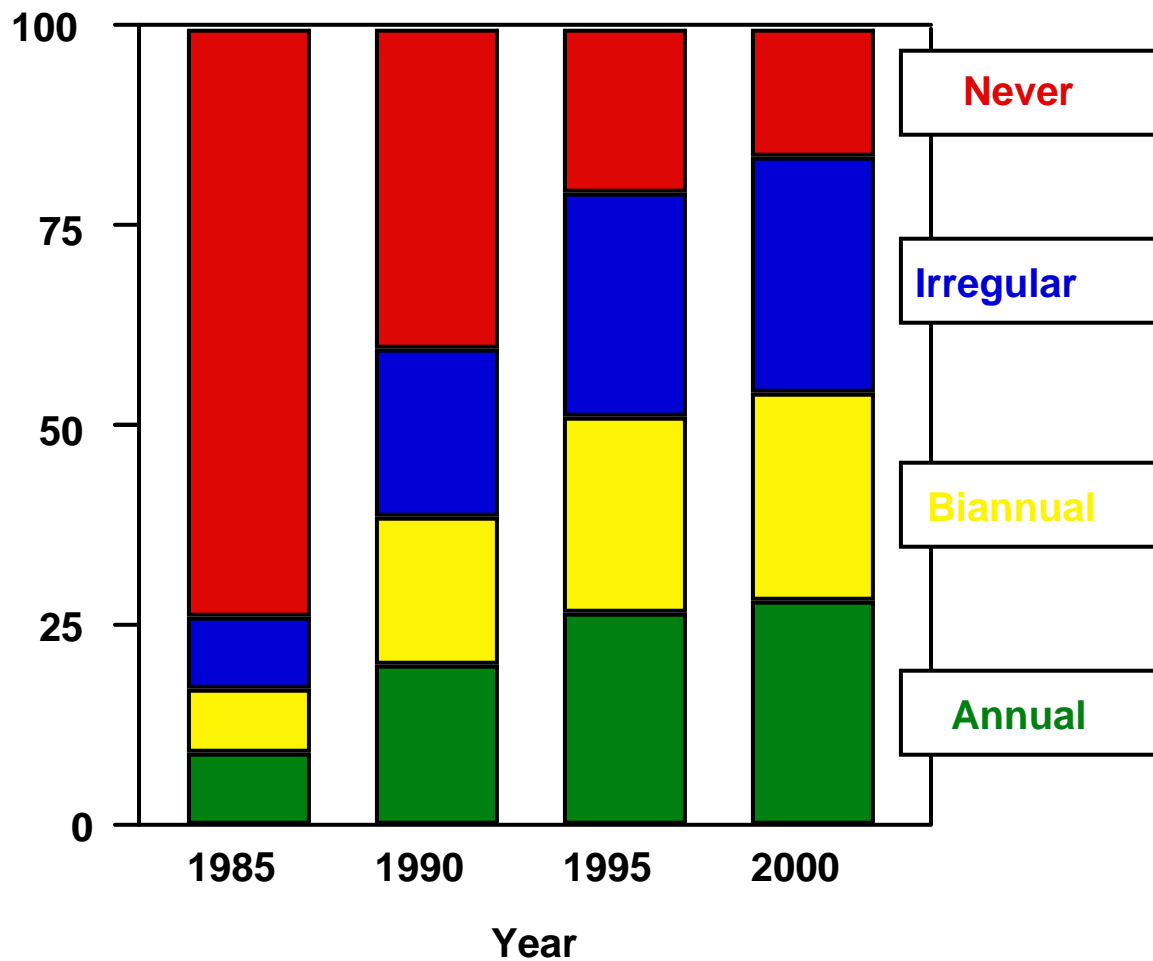
Other common inputs

Unique simulation or analytical model

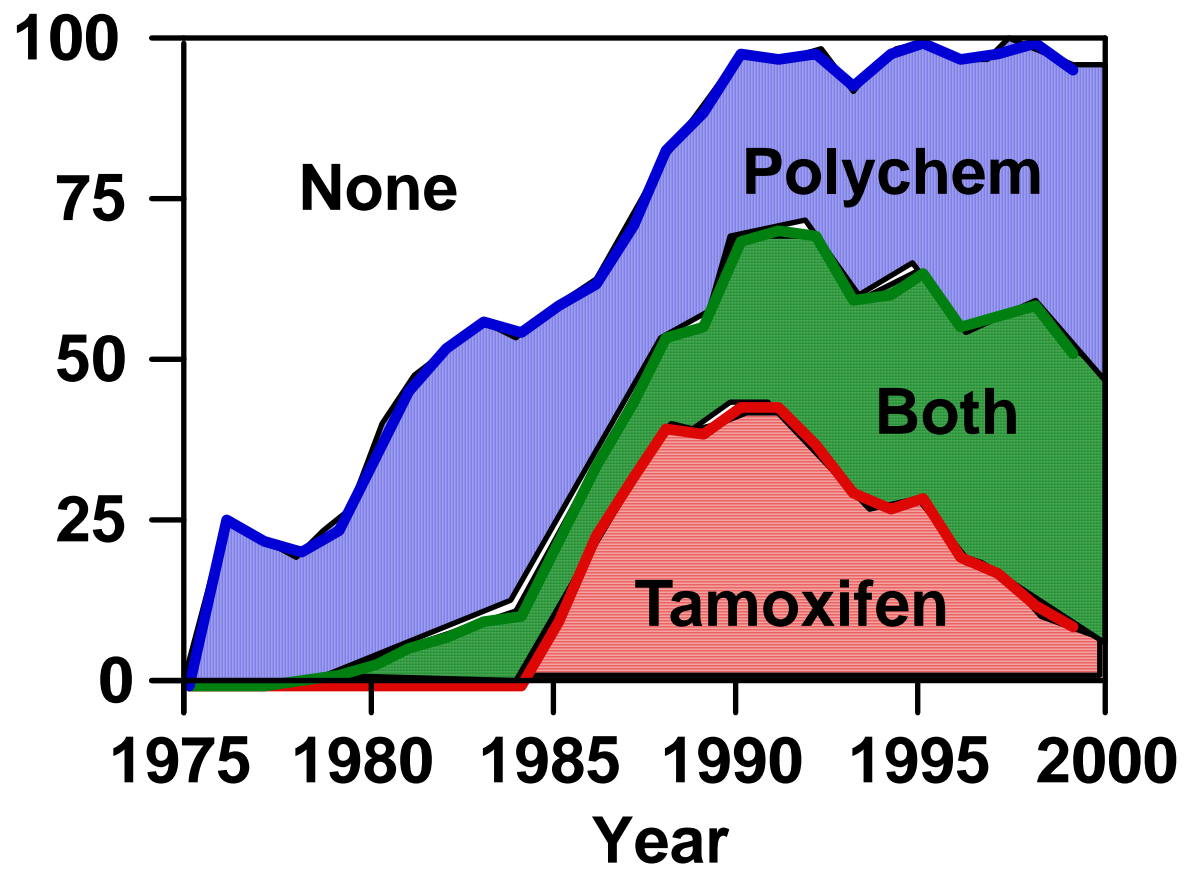
7 different breast cancer models

BC incidence & mortality

Mammography Screening Over Time, Women ages 40-79



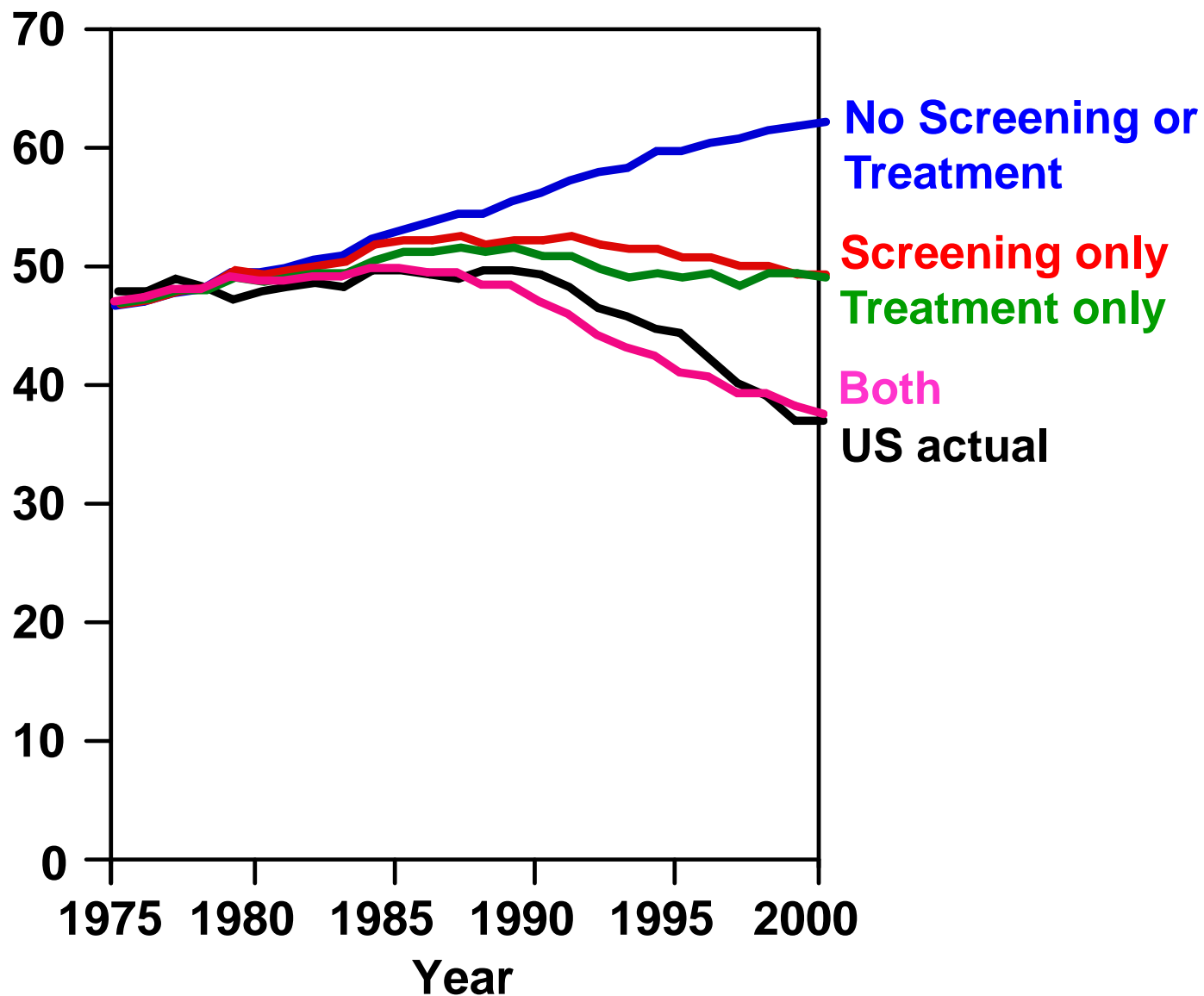
Dissemination of Adjuvant Therapy Ages 50-69, node-positive, stages II/IIIA





Modeling Results

One Group's Mortality Rate per 100,000 Women 40-79 under Various Scenarios

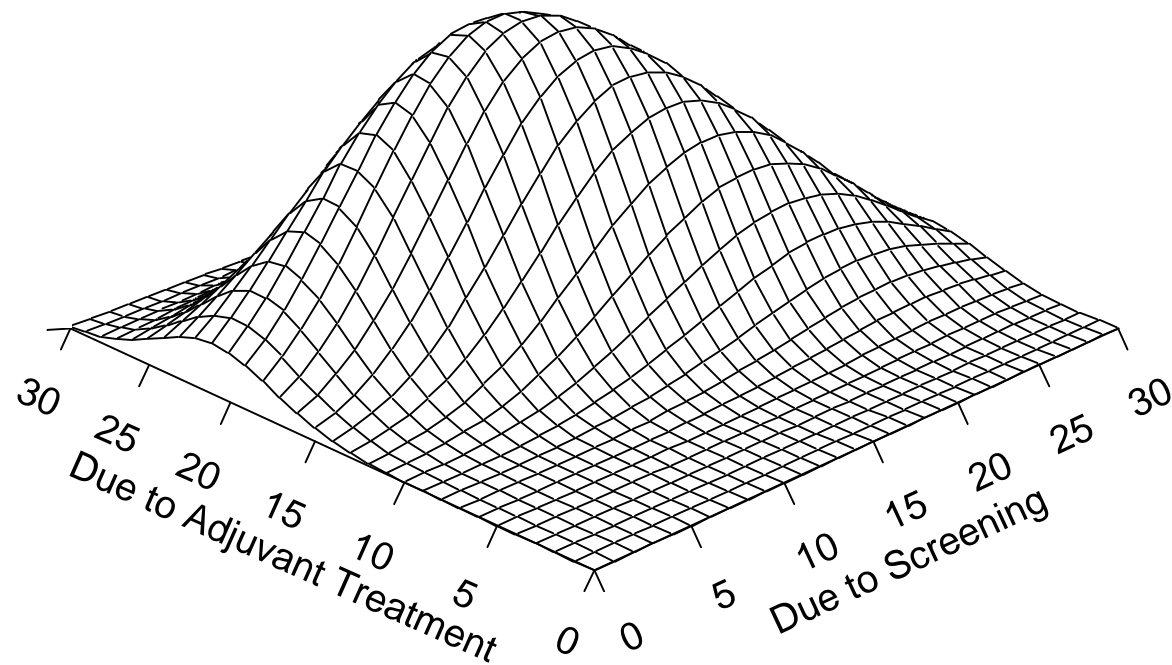


Percent reductions in BC mortality due to adjuvant Rx and screening



Model	Tamoxifen	Chemotherapy	Both therapies	Screening	Overall
D	6.1	6.1	12.0 (35%)	22.7 (65%)	32.9
E	12.0	9.6	20.9 (58%)	15.3 (42%)	30.9
G	7.7	7.0	14.6 (54%)	12.4 (46%)	24.9
M	10.7	9.5	19.5 (65%)	10.6 (35%)	27.5
R	NA	NA	19.0 (72%)	7.5 (28%)	25.6
S	8.9	6.9	14.9 (47%)	16.9 (53%)	29.9
W	12.5	8.9	20.8 (51%)	20.3 (49%)	38.3

Percent reductions in BC mortality due to adjuvant Rx and screening



- **Screening lowers BC mortality**
- **Population treatment benefit similar to clinical trials**
- **Little evidence for synergy**
- **Some model differences**
- **Overall robustness across models**

“What seems most important is that each team found at least some benefit from mammograms. The likelihood that they are beneficial seems a lot more solid today than it did four years ago, although the size of the benefit remains in dispute”

Berry et al. *NEJM* 2005;353:1784-1792

***JNCI* Monograph, summer 2006**

- Common inputs**
- Model descriptions**
- Comparisons of
 - ◆ Modeling assumptions**
 - ◆ Intermediate outcomes**
 - ◆ Mortality outcomes****



The Future

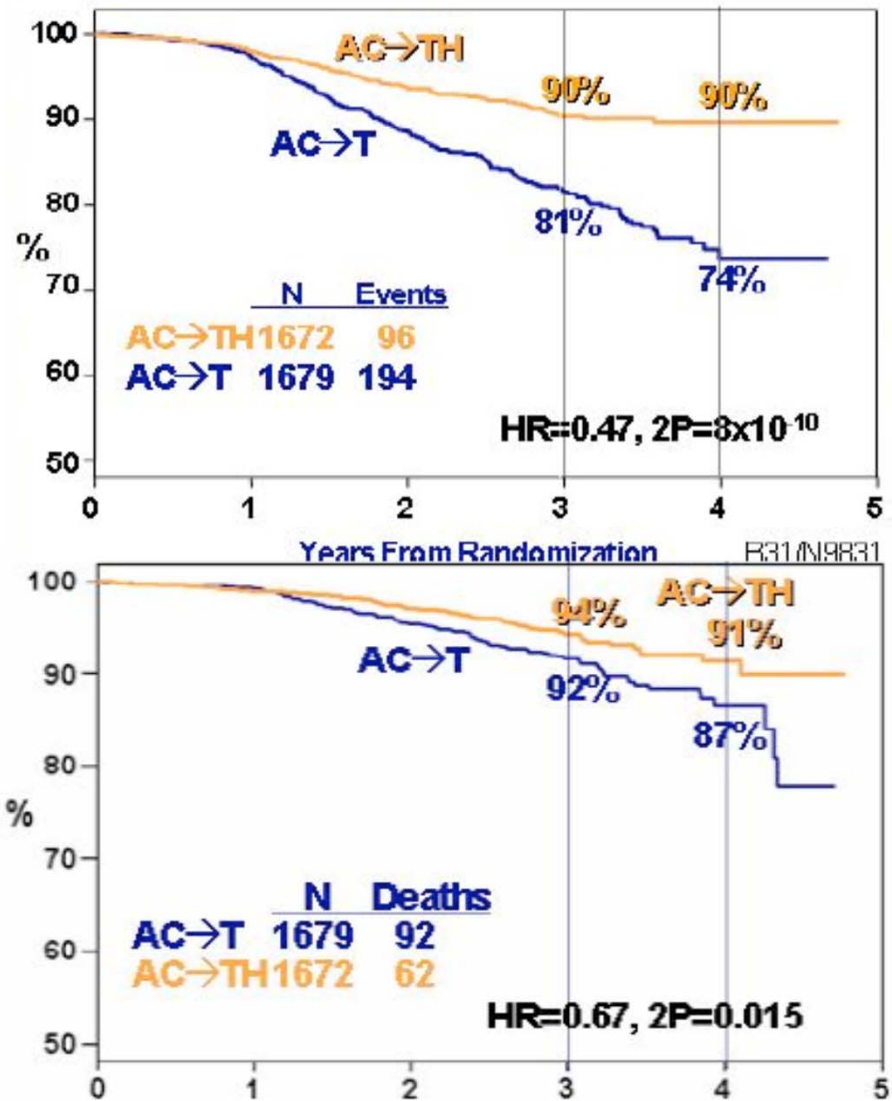
- **Individual groups modeling risk factors, optimal screening schedules, high-risk populations, disparities**
- **Some groups participating in HP2010**
- **Base case II: Modeling impact of new (mostly individualized) treatments on breast cancer mortality rates**

- **New targeted treatments:**
 - ◆ Trastuzumab (Herceptin)
 - ◆ Lapatinib (Tykerb)
 - ◆ Bevacizumab (Avastin)
 - ◆ Aromatase inhibitors

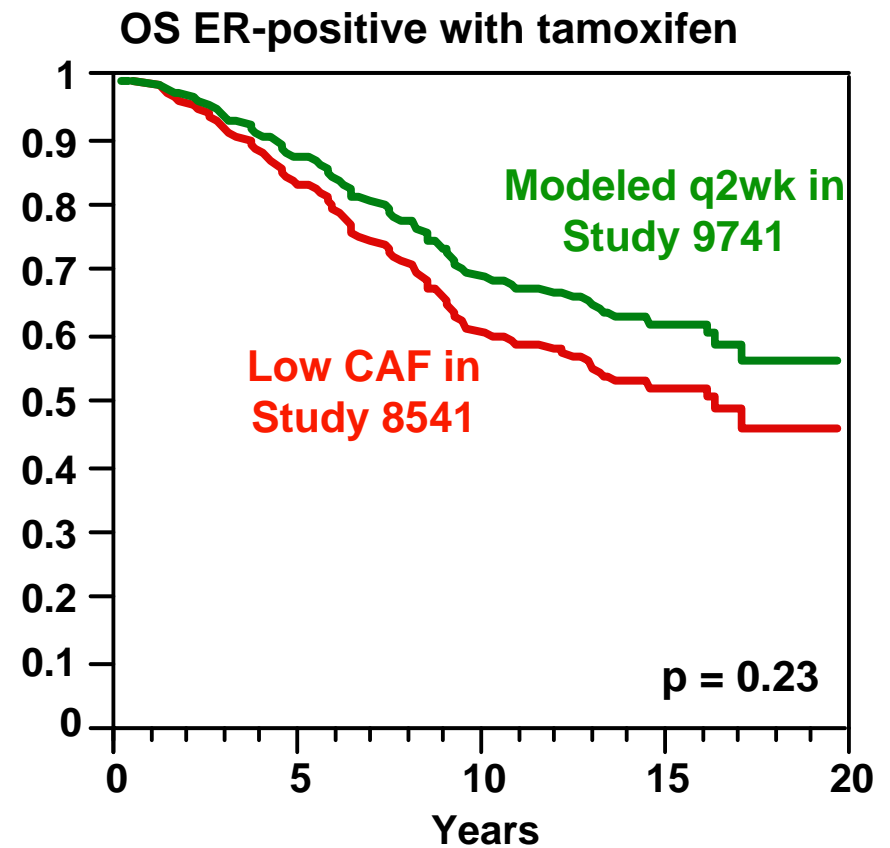
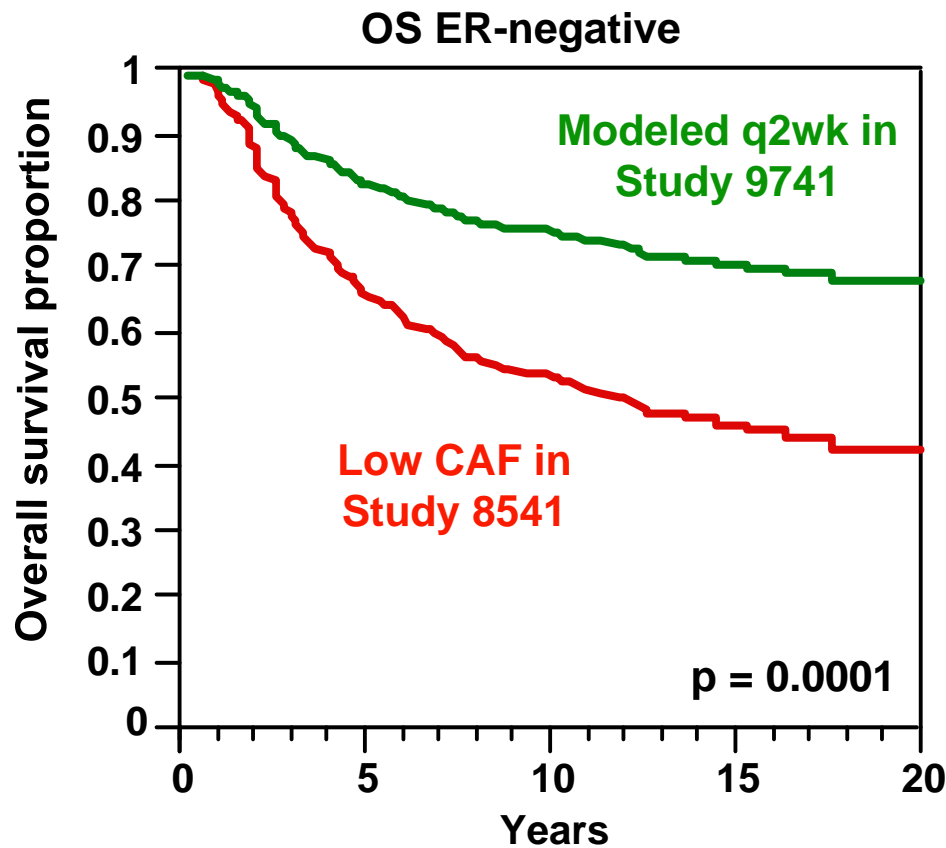
- **Individualized therapy:**
 - ◆ Adjuvant!Online
 - ◆ OncoType Dx
 - ◆ Chemotherapy benefit by ER/HER2

- **Chemoprevention:**
 - ◆ Tamoxifen
 - ◆ Raloxifene

**Relapse-free
and Overall
Survival
Benefit of
Trastuzumab
(Herceptin)
in HER2+
Adjuvant
Breast
Cancer:
B31/N9831**



Cumulative Effects: Higher Dose Doxorubicin + Paclitaxel + Dose-Dense by ER Status

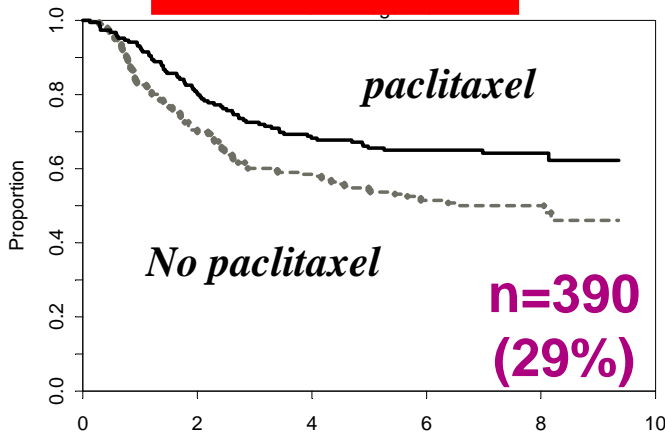


Benefits of Paclitaxel on Disease-Free Survival by HER2 and ER Status

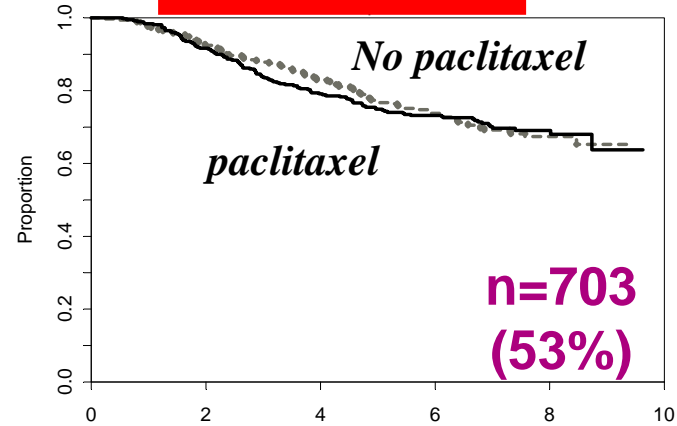


HER2 NEG

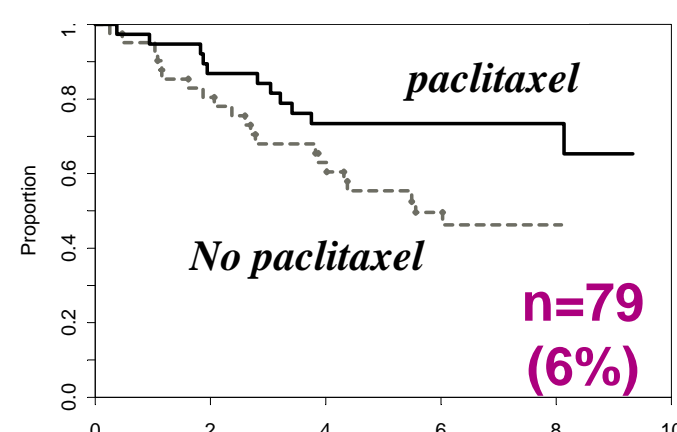
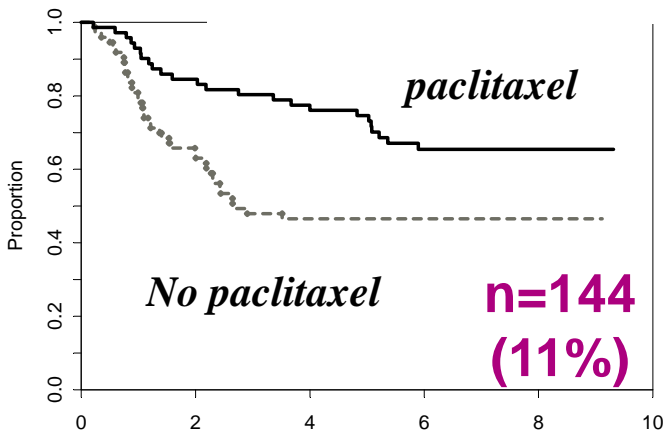
ER Neg



ER Pos



HER2 POS



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