NCCN Guidelines Prognostic/Predictive Tools for Adjuvant Decision Making

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Clinical Practice Guidelines in Oncology – v2.2008

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Biological Application of Adjuvant Therapy

- **Chemotherapy:** benefit in all endocrine and HER2 subtypes.
- **Trastuzumab:** active only in HER2 amplified or over-expressed disease
- **Endocrine therapies:** only effective in estrogen and/or progesterone receptor positive disease

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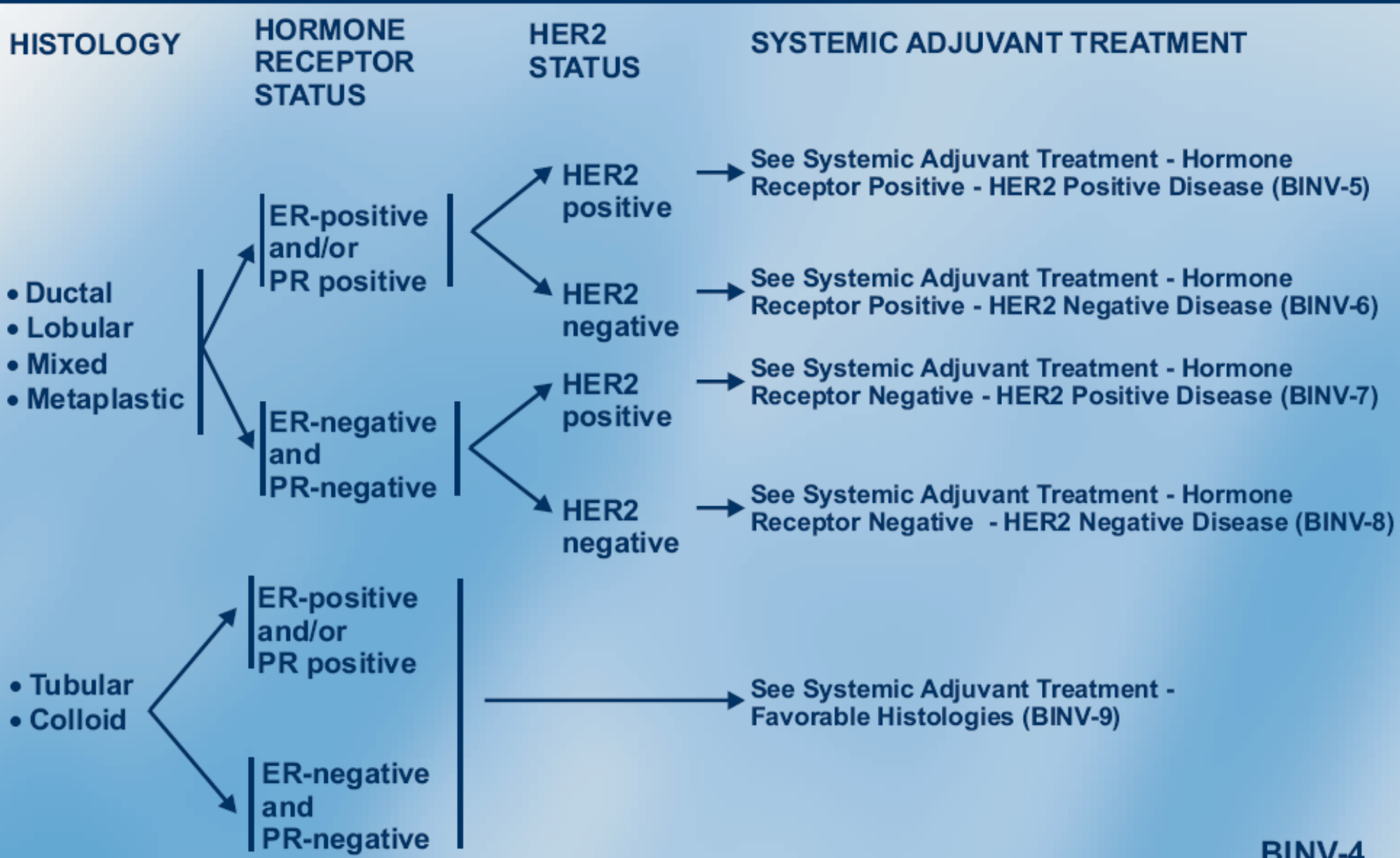

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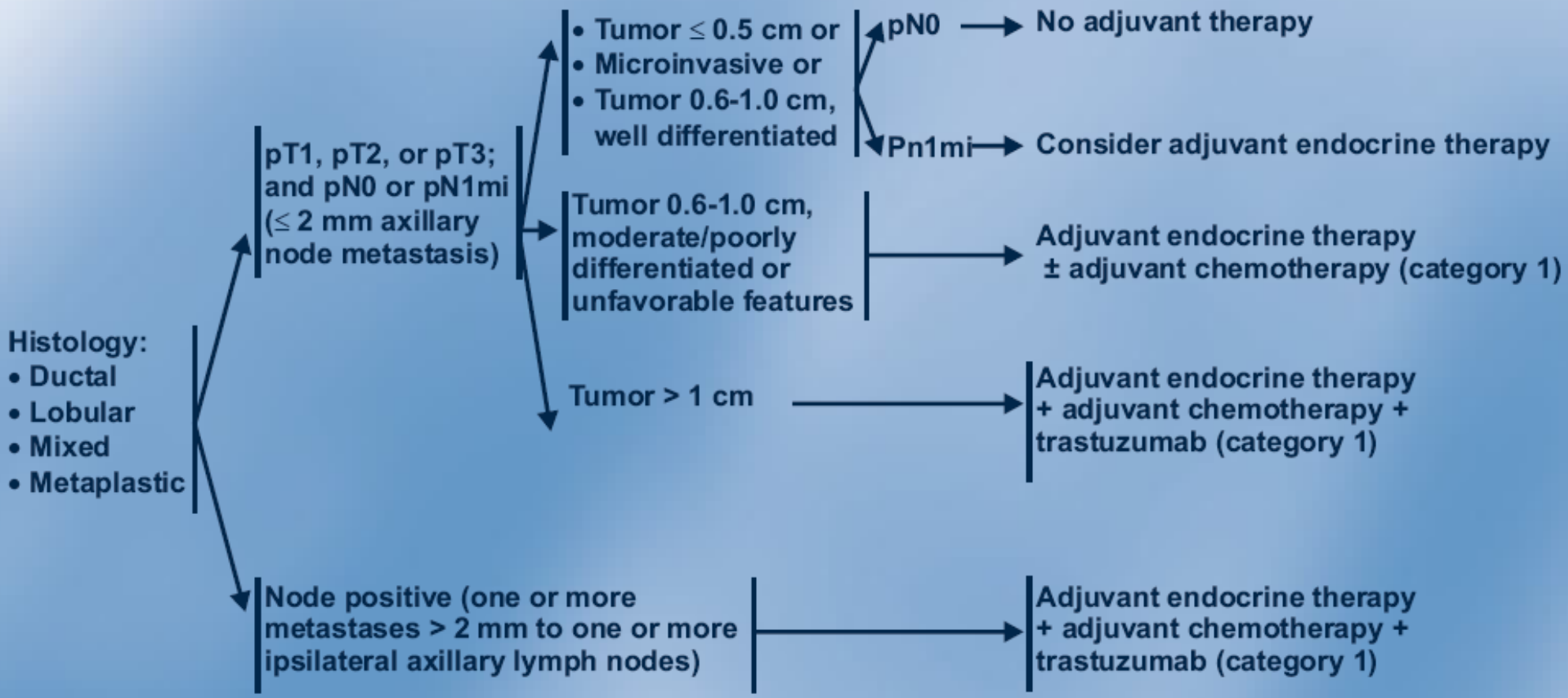
SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR POSITIVE - HER2 POSITIVE DISEASE



Prognostic/Predictive Factors

	Prognostic	Predictive
Lymph nodes	Yes	
Tumor size	Yes	
Tumor type	Yes	
Tumor grade	Yes	
LVI	Yes	
Proliferation	Yes	
ER/PR status	Yes	Yes
HER2 stat\us	Yes	Yes
Genomics	Yes	Yes

Adjuvant! Online

Decision making tools for health care professionals

Adjuvant! for Breast Cancer (Version 8.0)

Patient Information

Age: 54

Comorbidity: Perfect Health

ER Status: Positive

Tumor Grade: Grade 3

Tumor Size: 1.1 - 2.0 cm

Positive Nodes: 1 - 3

Calculate For: Relapse

10 Year Risk: 52 Prognostic

Adjuvant Therapy Effectiveness

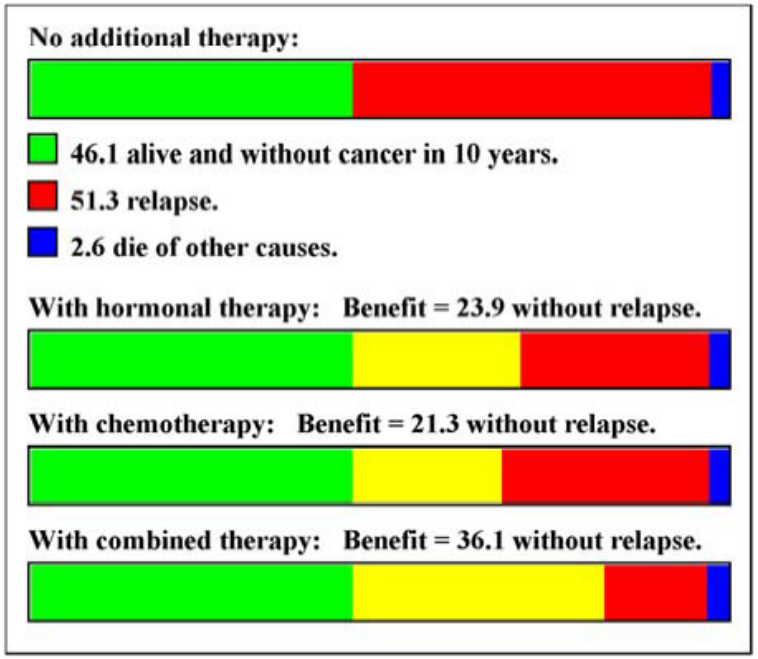
Horm: Aromatase Inhibitor for 5 yrs

Chemo: 3rd Generation Regimens

Hormonal Therapy: 56

Chemotherapy: 51

Combined Therapy: 78



Print Results PDF | Access Help and Clinical Evidence

Images for Consultations

AdjuvantOnline Validation 10-Year DFS

Characteristic	Adjuvant Prediction (%)	Observed (%)
Age (years)		
20-35	67.9	54.3
36-50	69.8	67.6
51-65	70.5	71.2
66-75	71.7	72.3
>75	74.8	72.0
Tumor Grade		
1	82.8	82.7
2	74.5	73.4
3	63.9	62.1
Unknown	70.7	73.3

Olivotto et al. J Clin Oncol 23:2716,2005

AdjuvantOnline Validation 10-Year DFS

Characteristic	Adjuvant Prediction (%)	Observed (%)
Tumor size, mm		
1-10	80.8	79.7
11-20	74.5	73.3
21-50	60.0	59.5
ER status		
Negative	65.5	66.1
Positive	72.0	69.6
Unknown	74.5	76.2

Olivotto et al. J Clin Oncol 23:2716,2005

AdjuvantOnline

- Pros
  - Widely available
  - Free of cost
  - Easy to use
  - Validated
  - Objective, unbiased
- Cons
  - Lack of HER2 and trastuzumab consideration
  - Mix of qualitative/quantitative factors
  - Lack of quality control over biomarkers input

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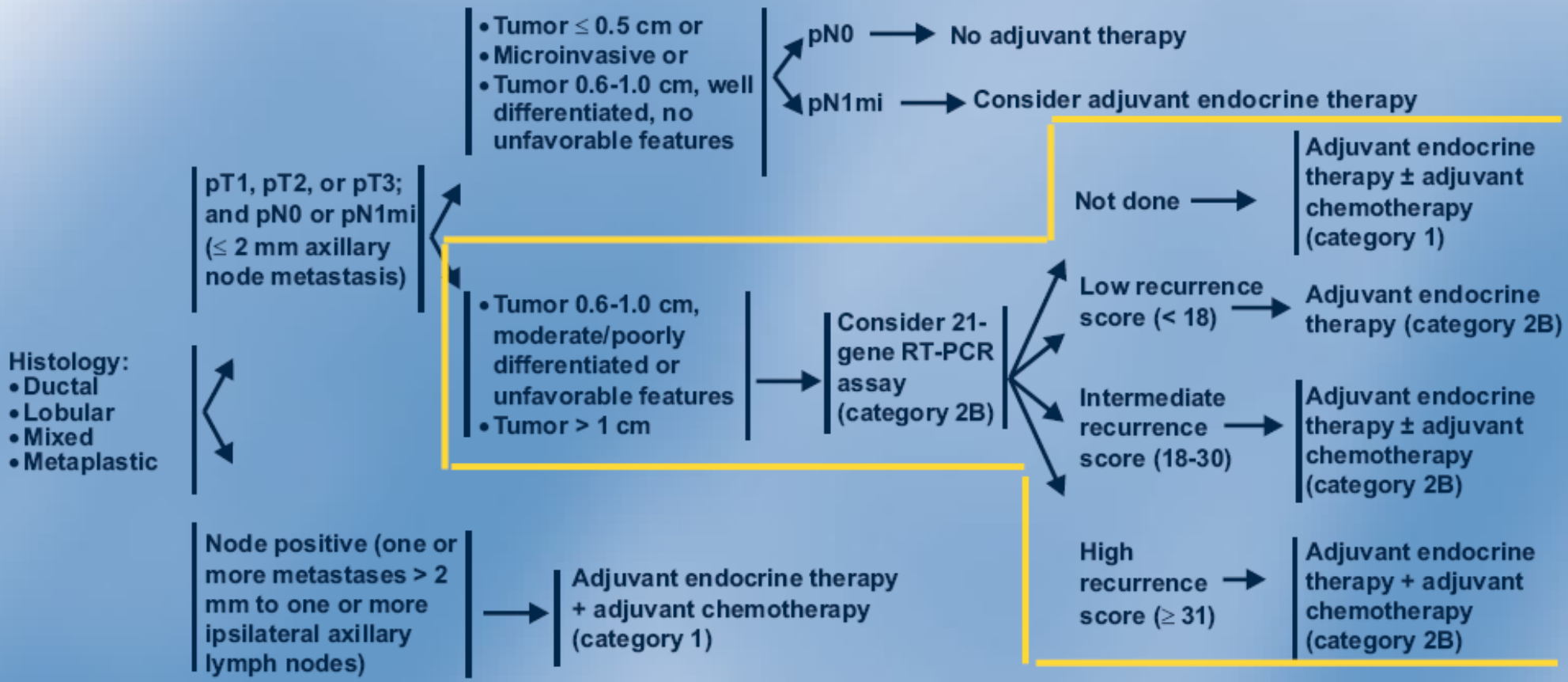
SYSTEMIC ADJUVANT TREATMENT - HORMONE RECEPTOR POSITIVE - HER2 NEGATIVE DISEASE



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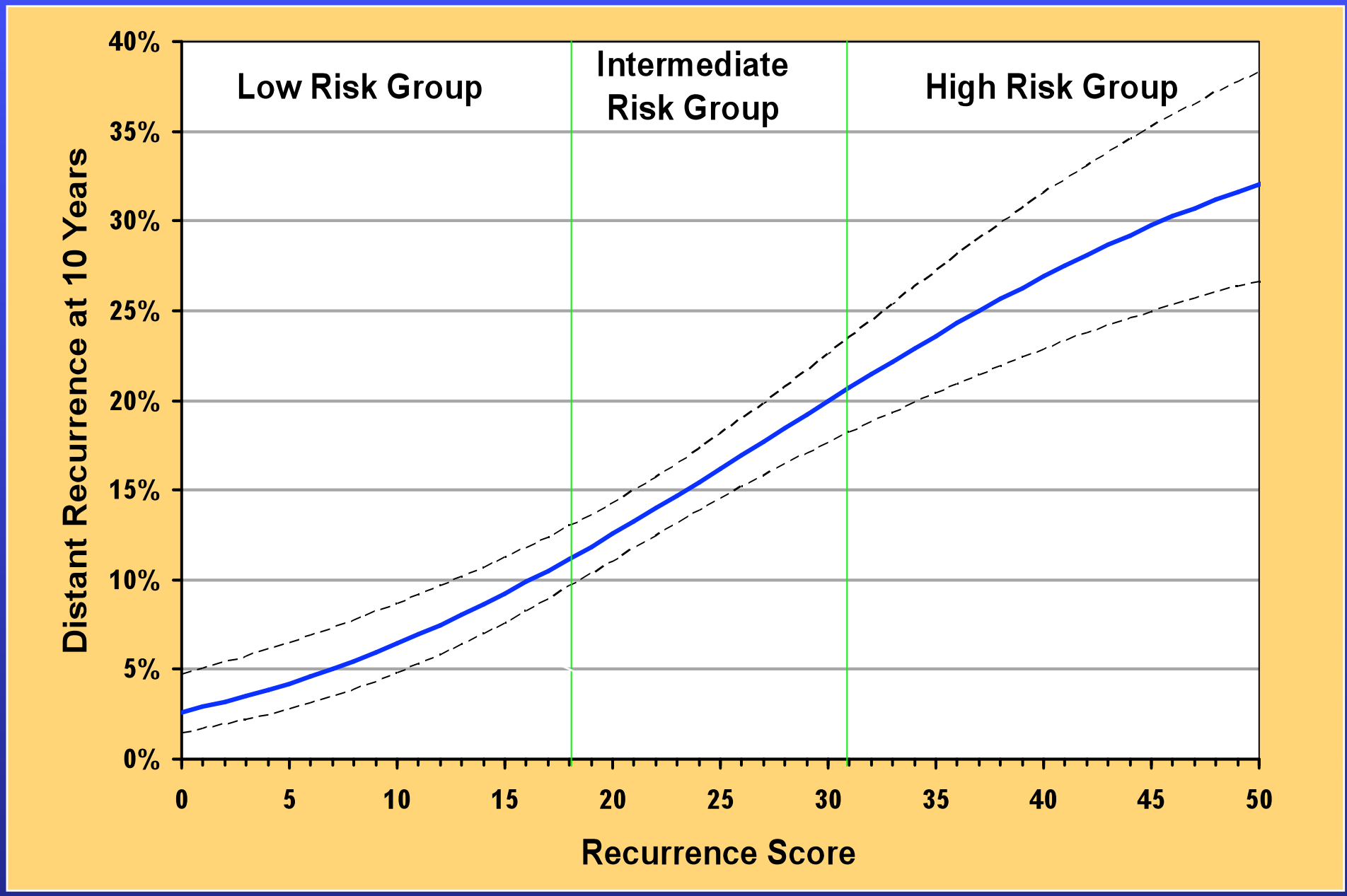
Gene Profiling Technology:

Oncotype DX™ Technology: Algorithm and Recurrence Score (RS)

RS = +0.47 x HER2 Group Score
-0.34 x ER Group Score
+1.04 x Proliferation Score
+0.10 x Invasion Group Score
+0.05 x CD68
-0.08 x GSTM1
-0.07 x BAG1

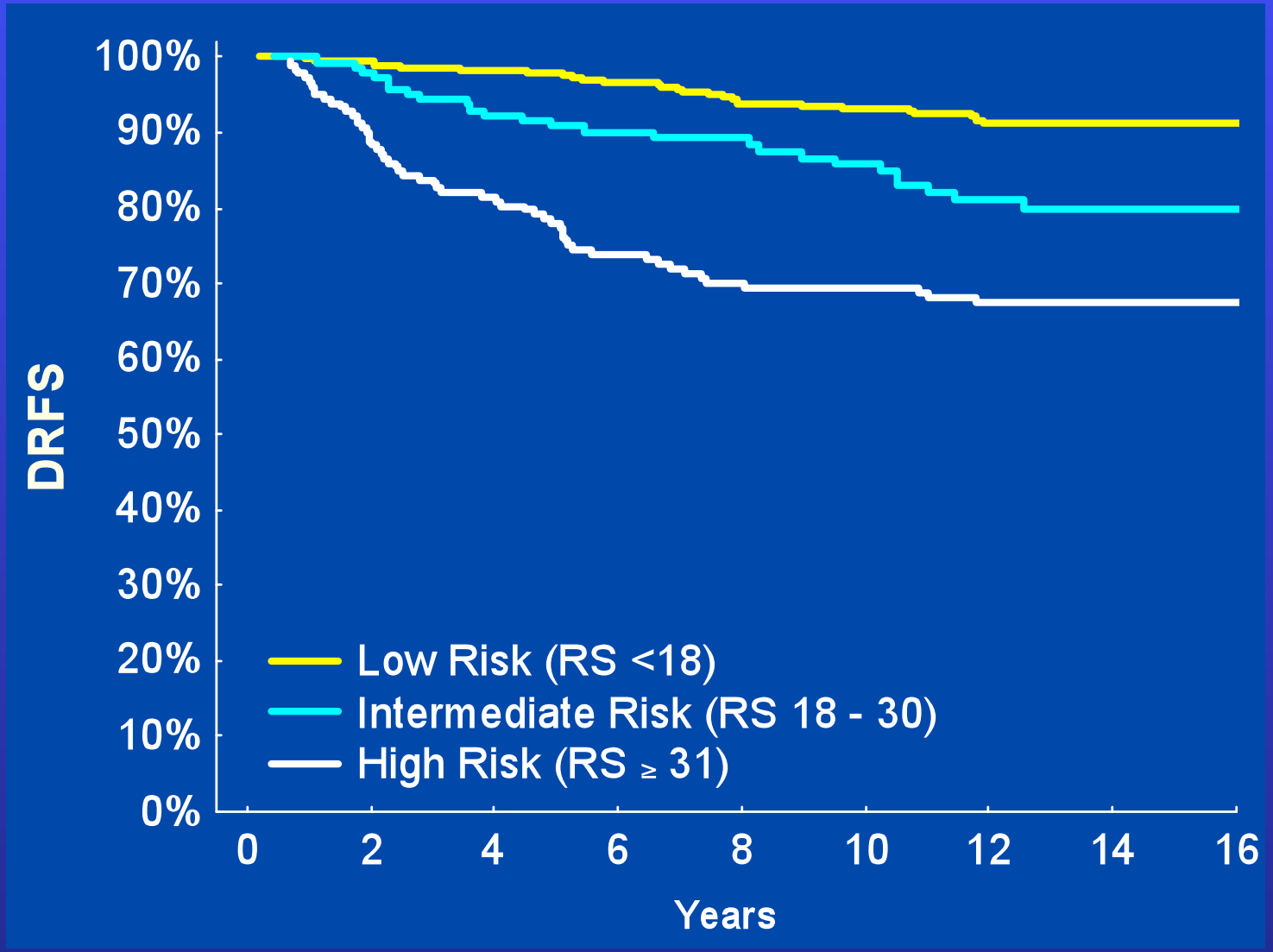
Recurrence Category	RS (0-100)
Low risk	<18
Intermediate risk	18-30
High risk	≥31

Recurrence Score as a Continuous Predictor



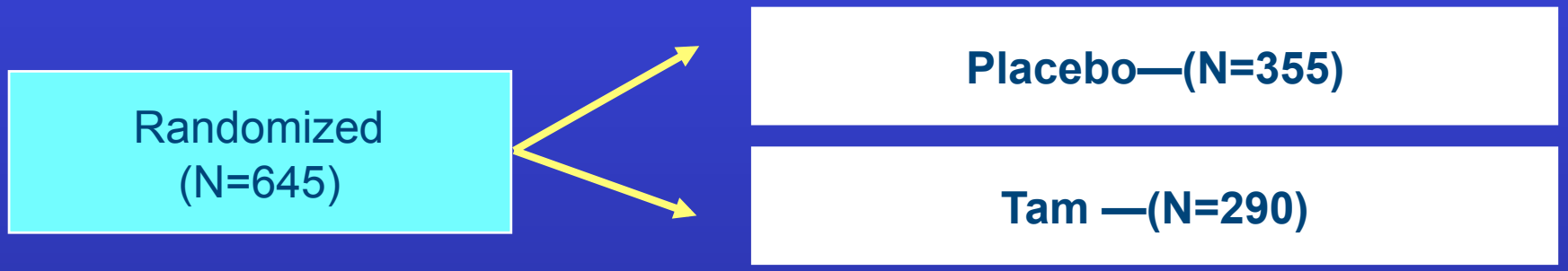
B14-Results

DRFS—Low, Intermediate, High RS Groups

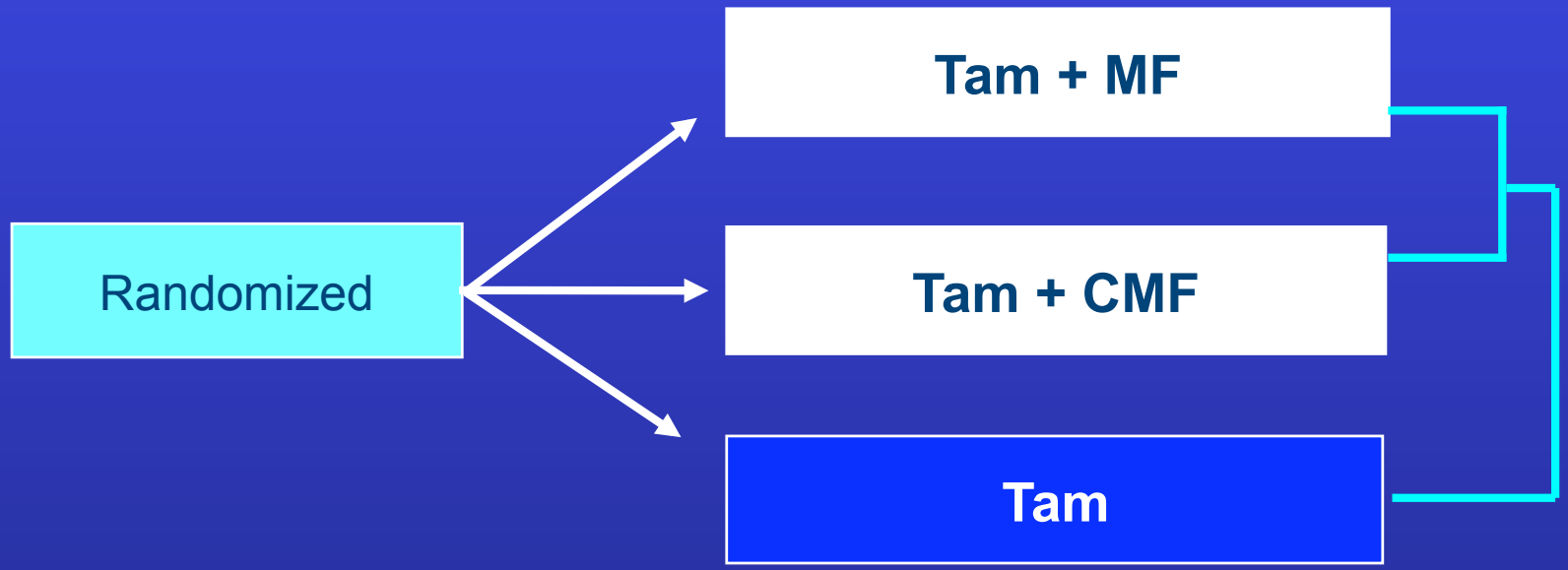


Paik et al, SABCS 2003

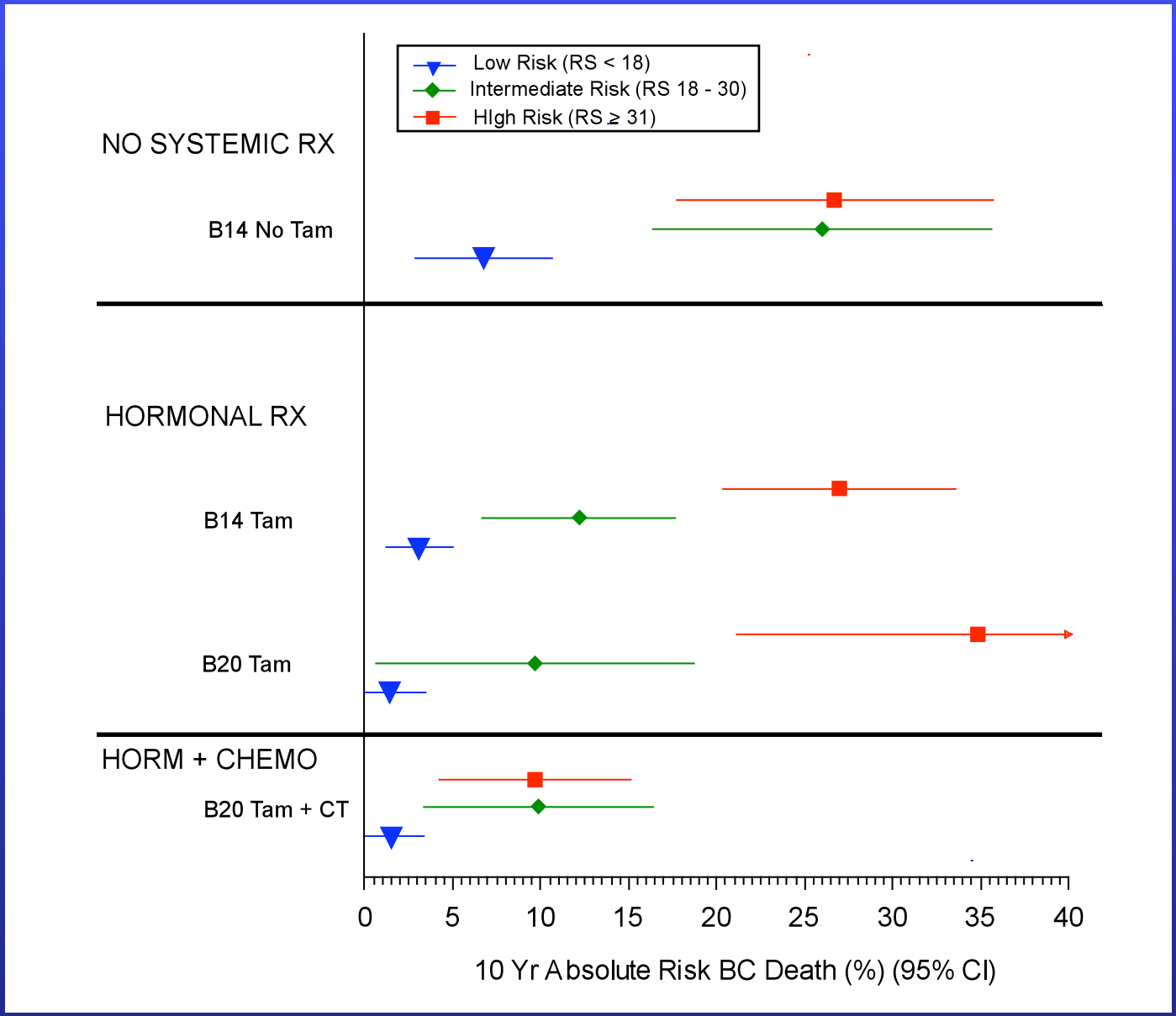
RS as a predictive factor for benefit from tamoxifen: NSABP B-14



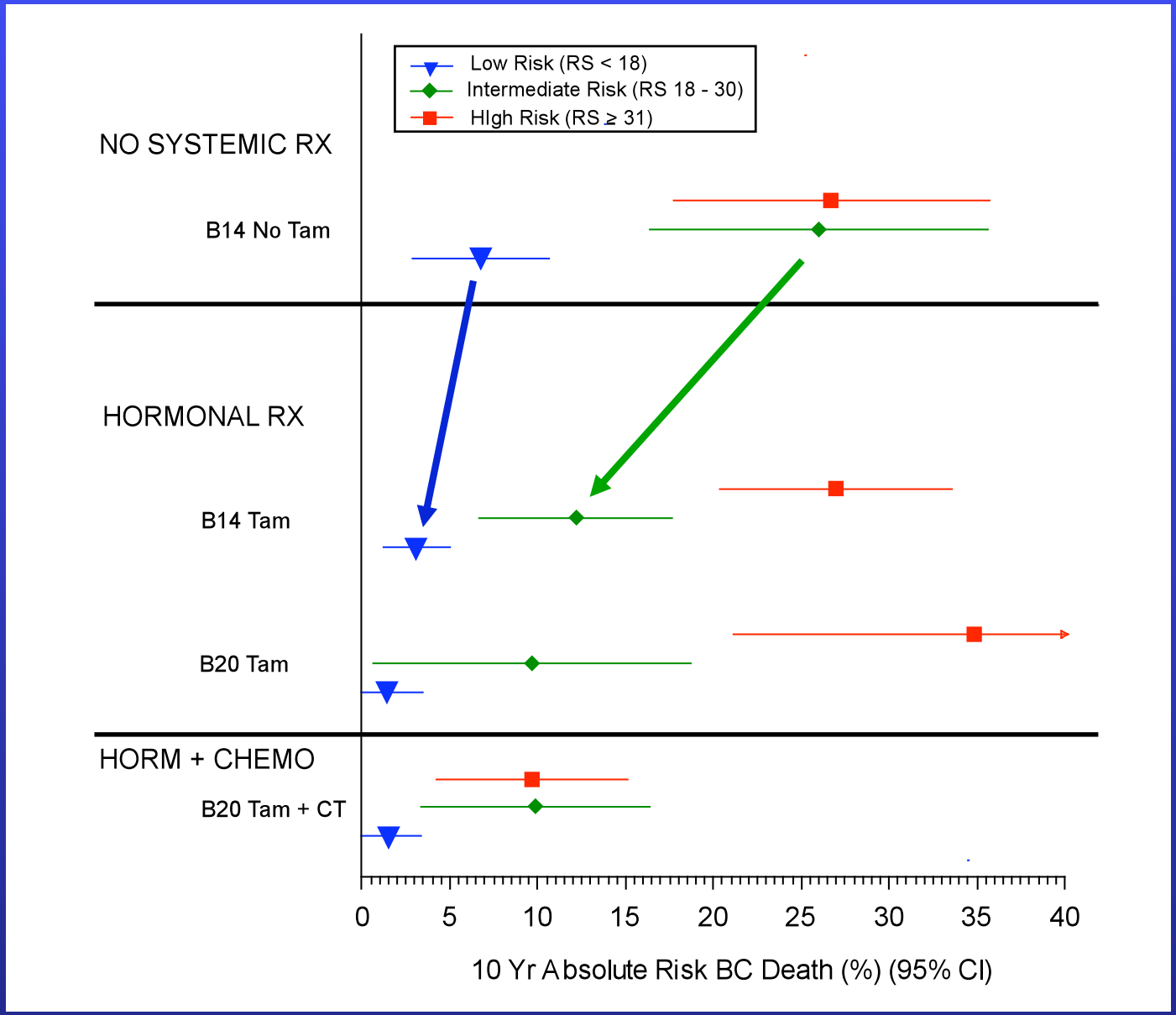
RS as a predictive factor for benefit from adjuvant chemotherapy: NSABP B-20



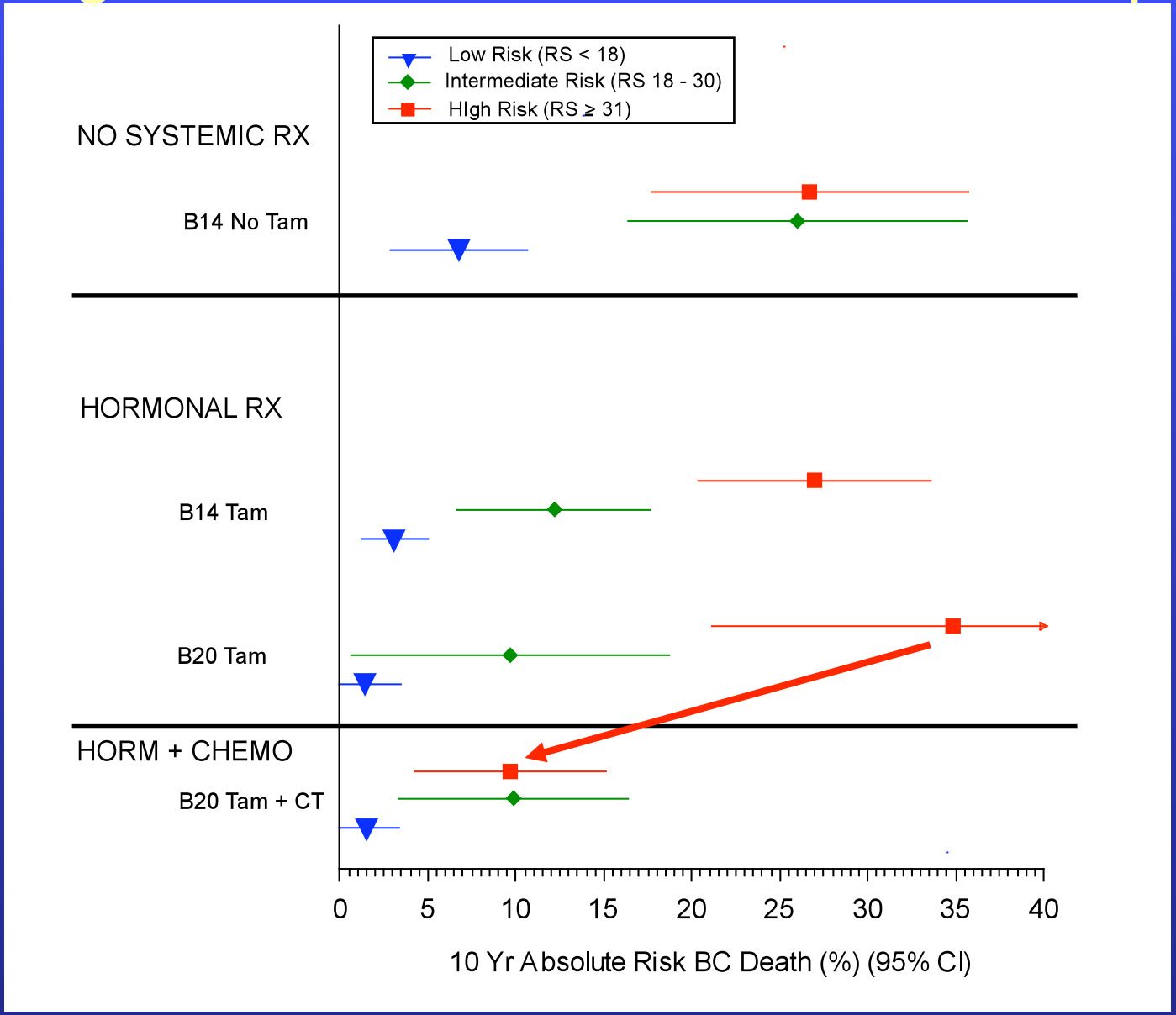
RS and Breast Cancer Death in NSABP B-14 and B-20



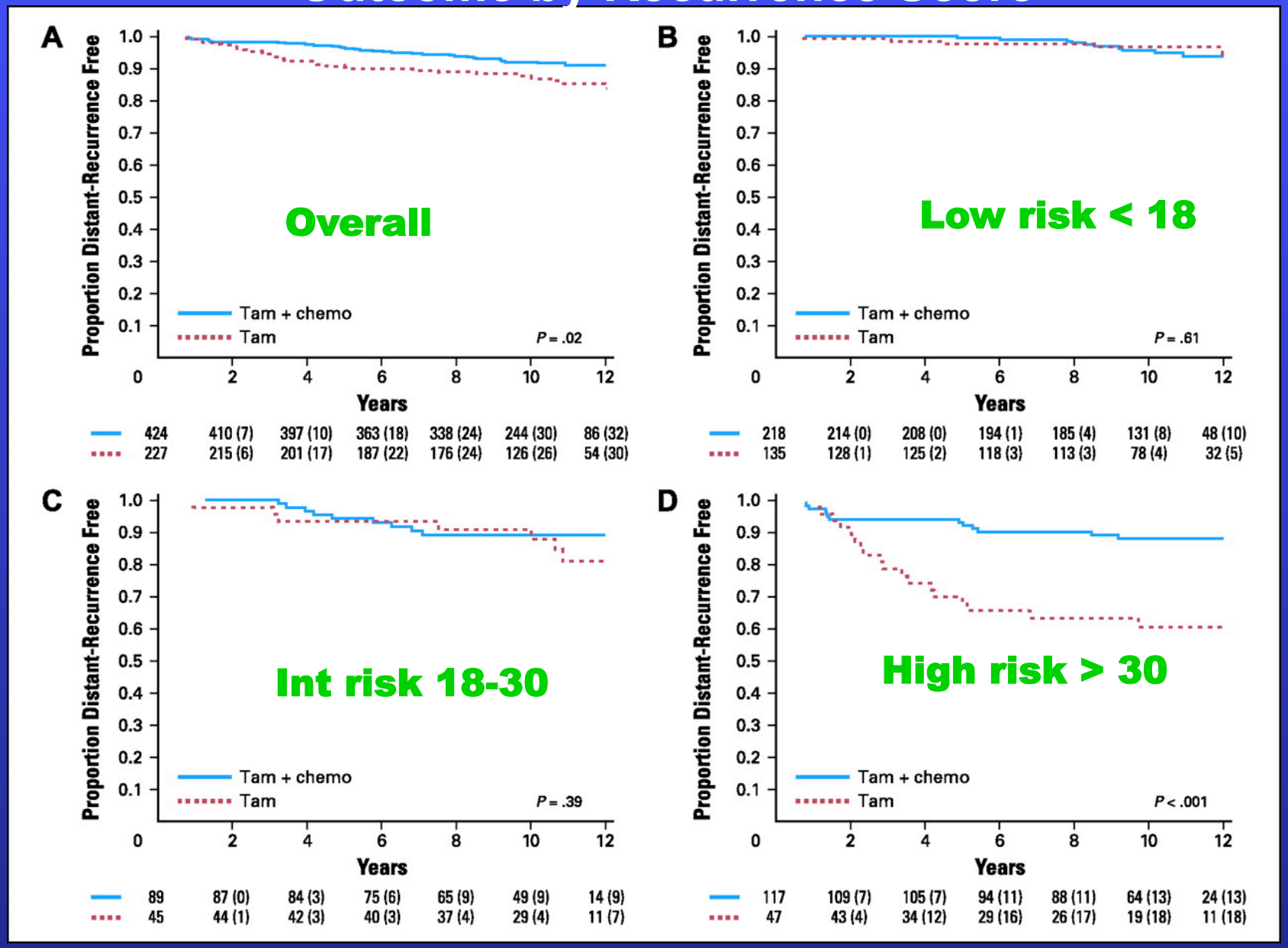
Largest Tamoxifen Benefit Observed in Low and Intermediate Recurrence Score Groups



Largest Chemotherapy Benefit Observed in High Risk Recurrence Score Group



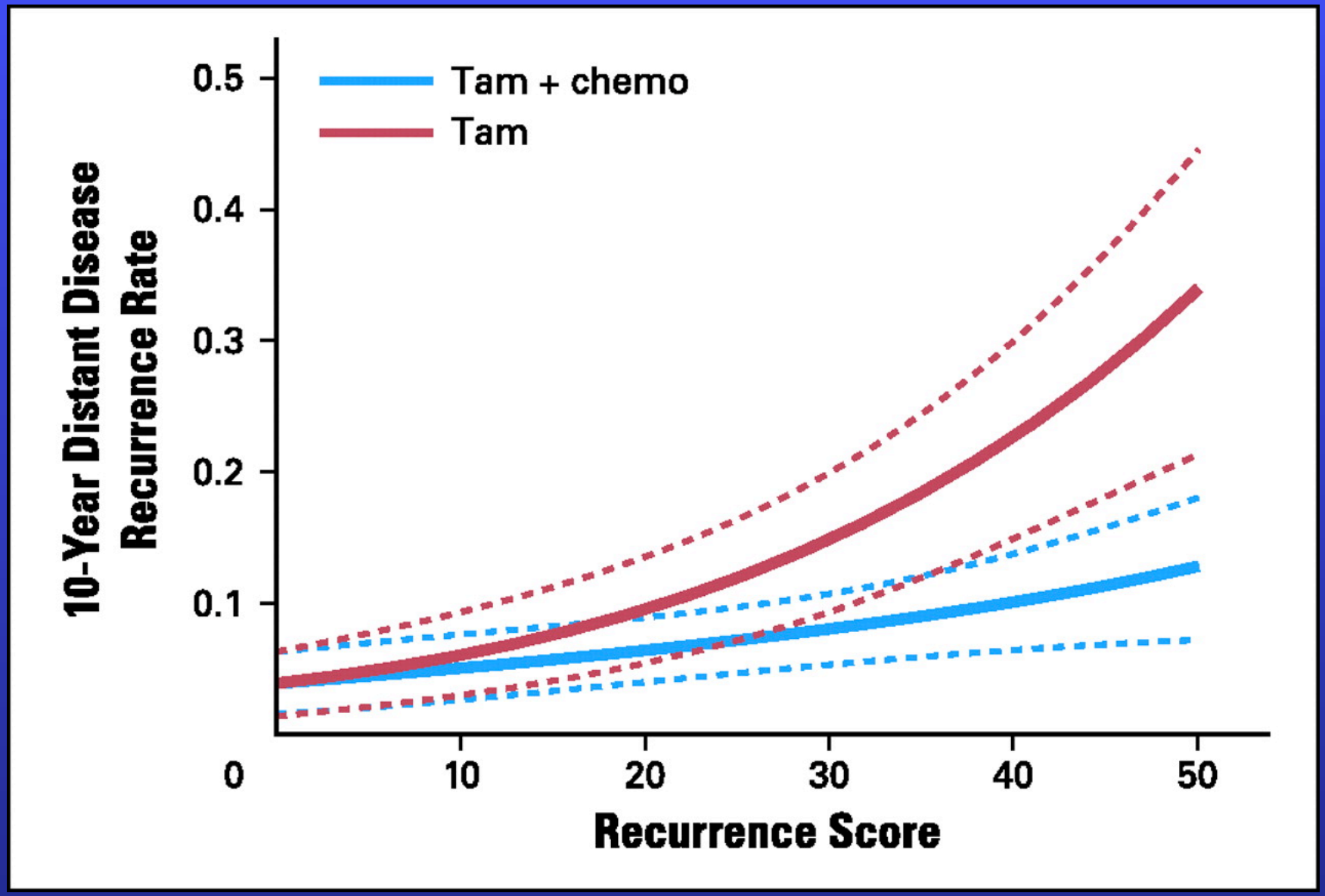
NSABP B-20
Outcome by Recurrence Score



JOURNAL OF CLINICAL ONCOLOGY

Paik, S. et al. J Clin Oncol; 24:3726-3734 2006

Fig 4. Linear fit of the likelihood of distant recurrence as a continuous function of recurrence score for the tamoxifen alone (TAM) and tamoxifen plus chemotherapy (TAM + chemo) treatment groups



Paik, S. et al. J Clin Oncol; 24:3726-3734 2006

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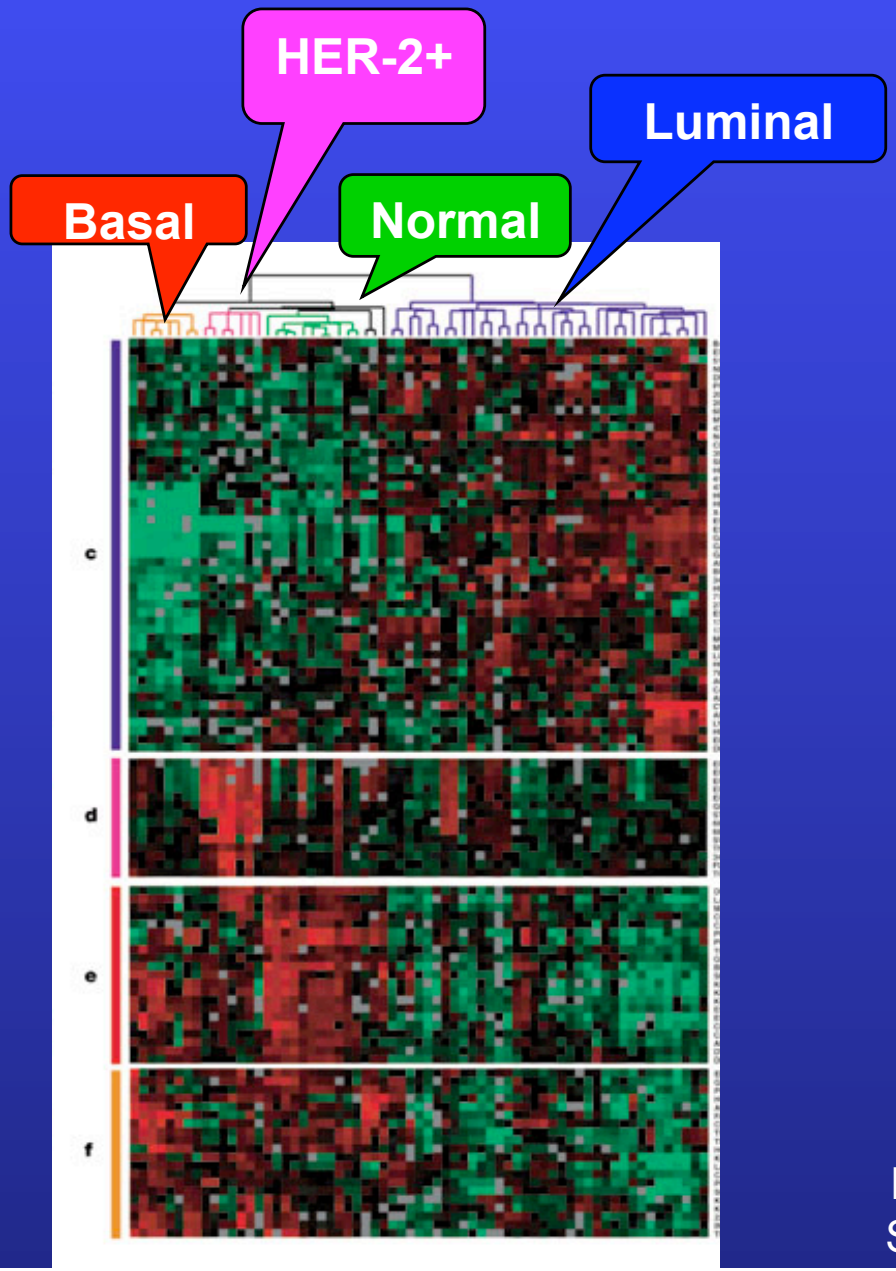
Use of 21-Gene RT-PCR Test

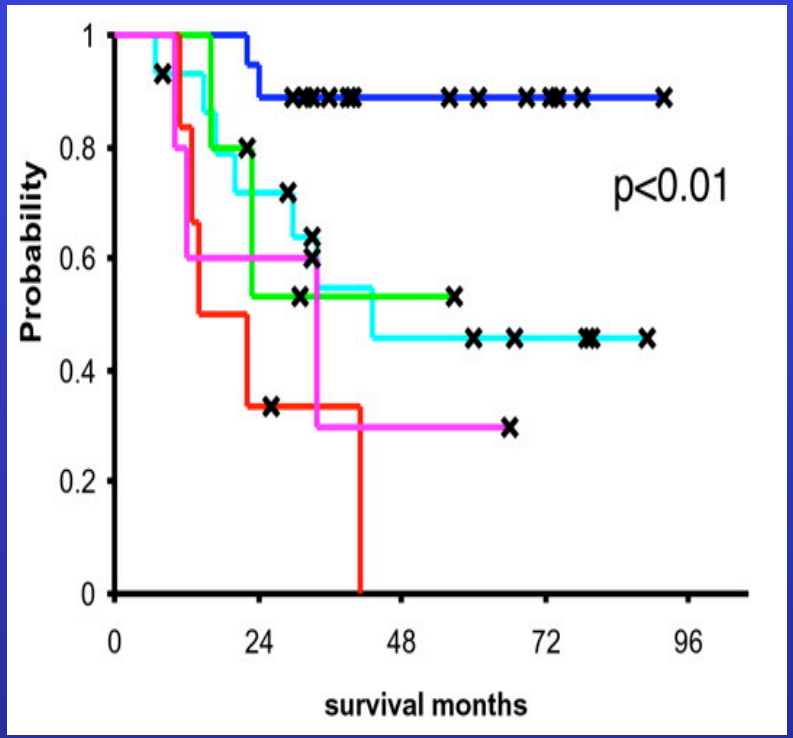
- Limited to ER+ node negative disease
- Validated only in tamoxifen treated patients with first generation chemotherapy
- Most HER2-positive disease has high RS
- Major use therefore is in ER+, HER2-negative, node negative disease.

21-Gene RT-PCR (OncotypeDX™)

- Pros
  - Highly reproducible
  - Quantitative
  - Based primarily upon known prognostic/ predictive factors
  - Utilizes paraffin embedded tissue
- Cons
  - Expensive
  - Not clearly superior to assessment of ER/PR/ HER2/Grade/Size/etc
  - Not US FDA approved

Molecular portraits of human breast tumors



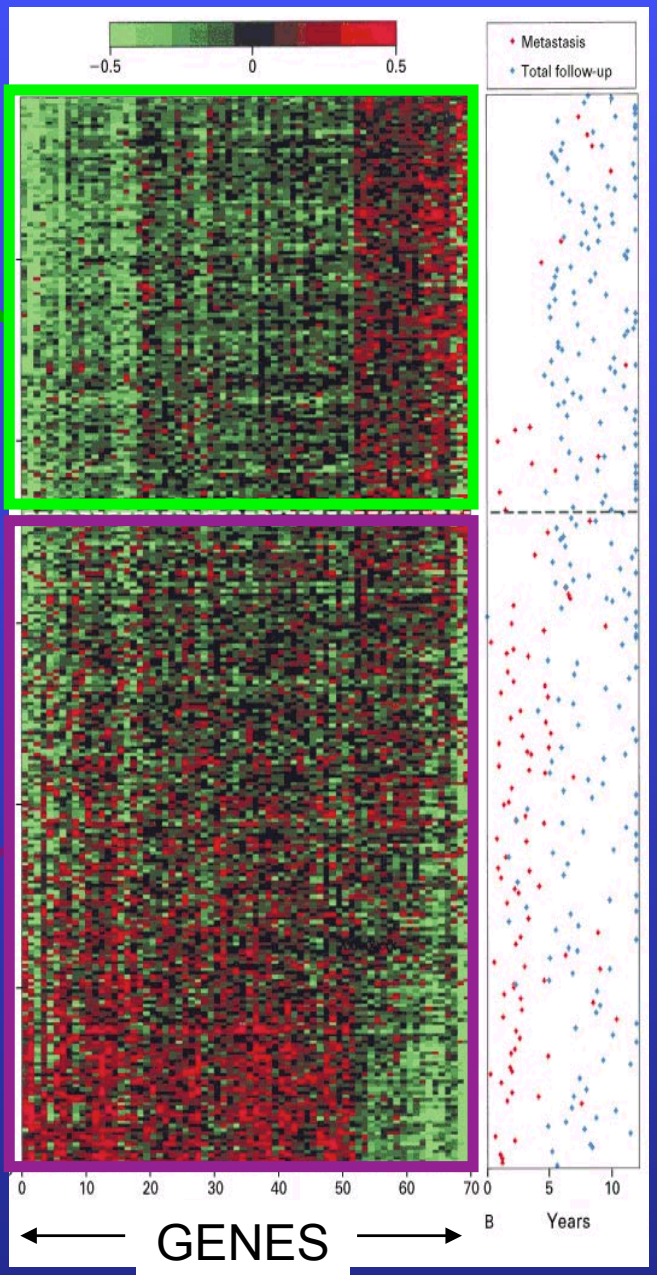


Perou, Sorlie, et al *Nature* **406:**747 2000
Sorlie, Perou et al, *PNAS* 98:10869 2001

Mammoprint

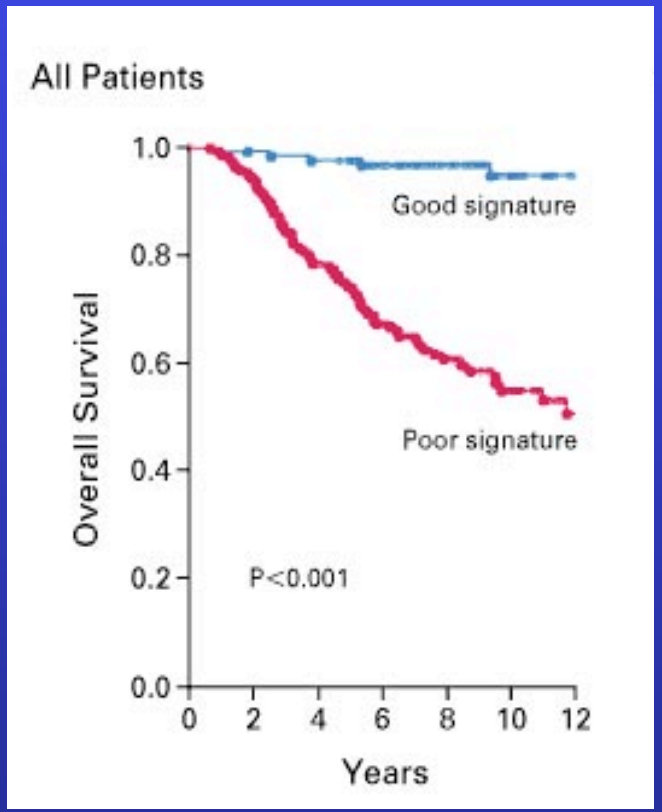
Good prognosis signature

Poor prognosis signature

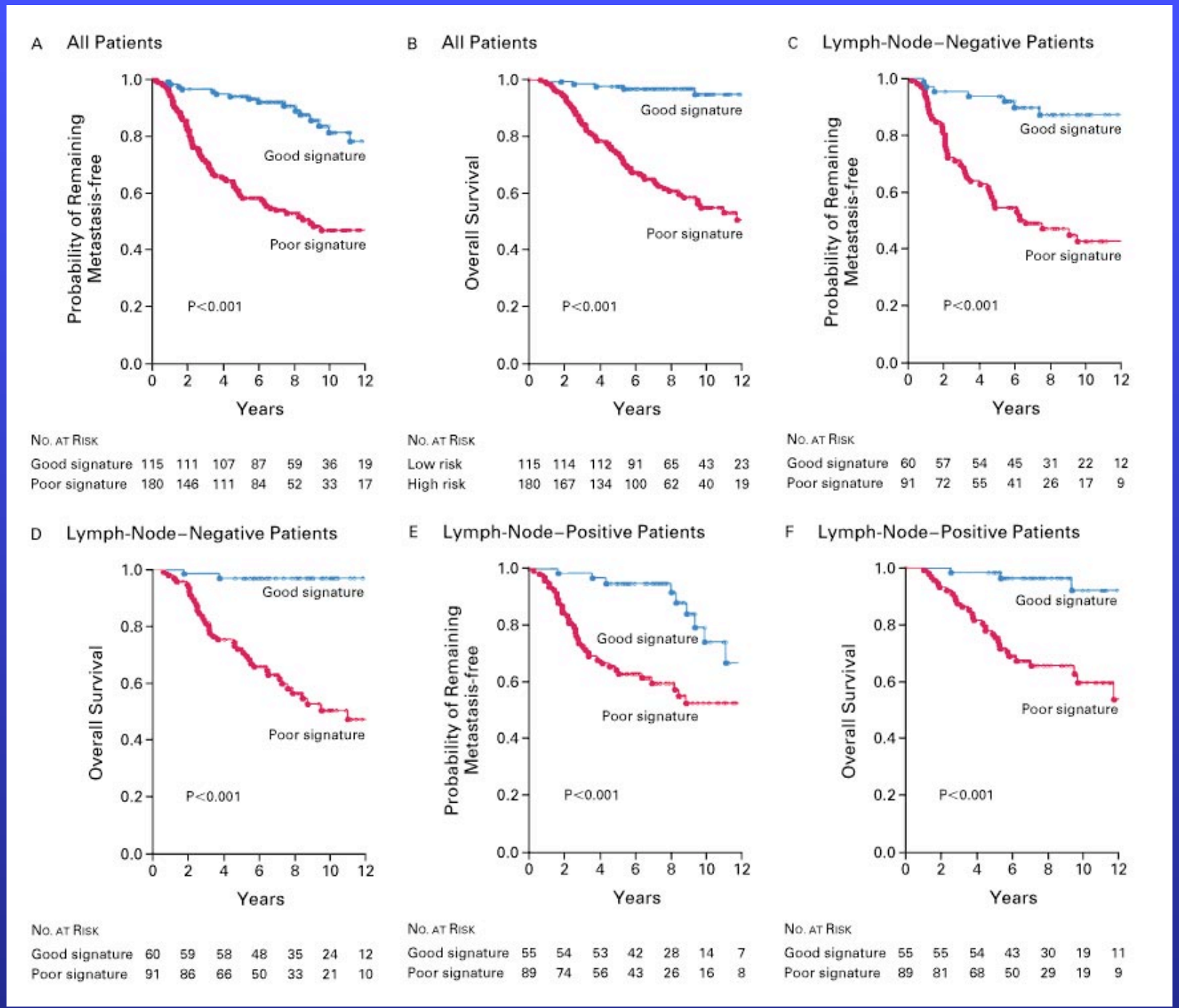


Which genes are associated with…?

Apply to dataset with known outcome



Van de Vijver, NEJM 2002



van de Vijver, M. et al. N Engl J Med 2002;347:1999-2009

Mammoprint

- Pros
  - Appears prognostic
  - Widely separate groups
  - US FDA approved
- Cons
  - Currently requires fresh frozen tissue
  - Unknown regarding prediction
  - Expensive

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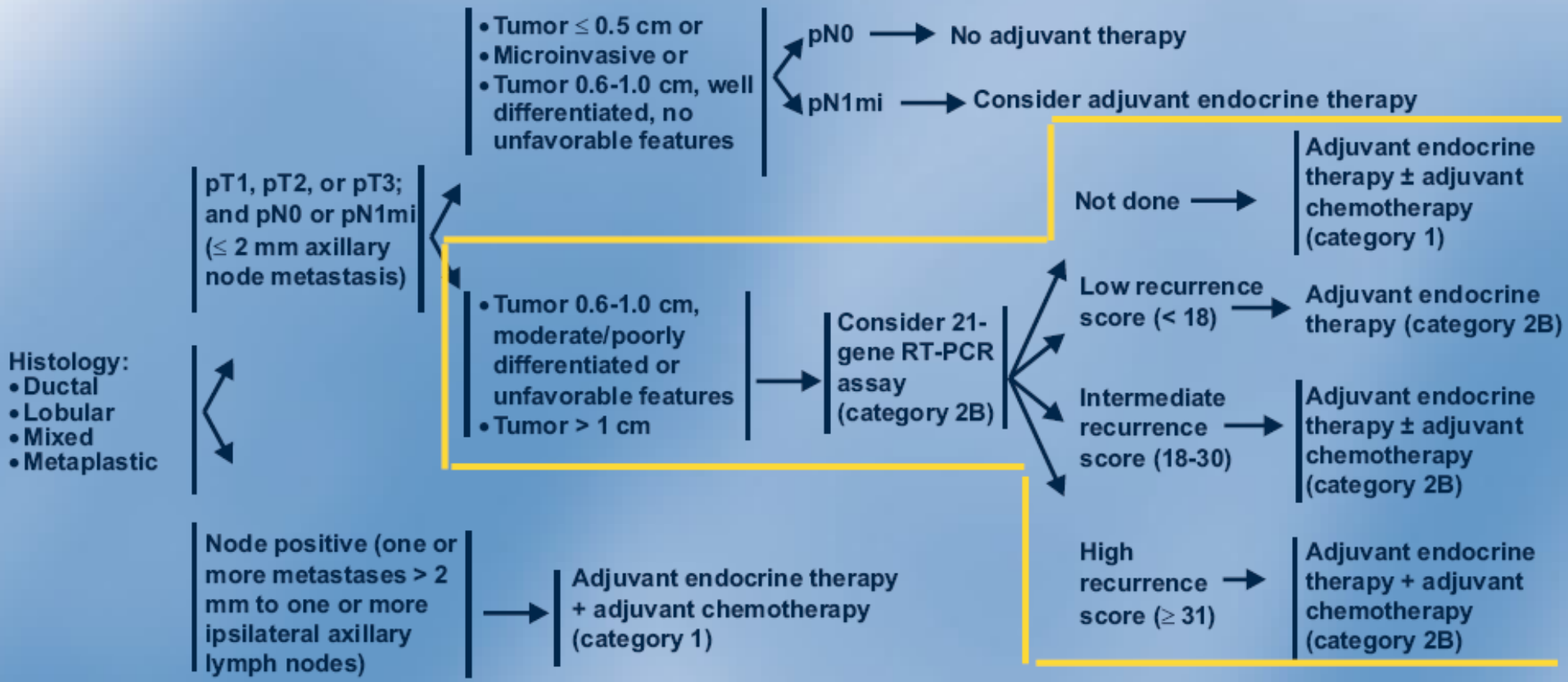

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