



DCIS: Strategies for Integrating Tumor Biology and Population Sciences

Overview of Treatment

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Standard Treatment in DCIS

- Mastectomy
 - Excision + RT
 - Excision
- } ± Tamoxifen

Which Rx for which patient?

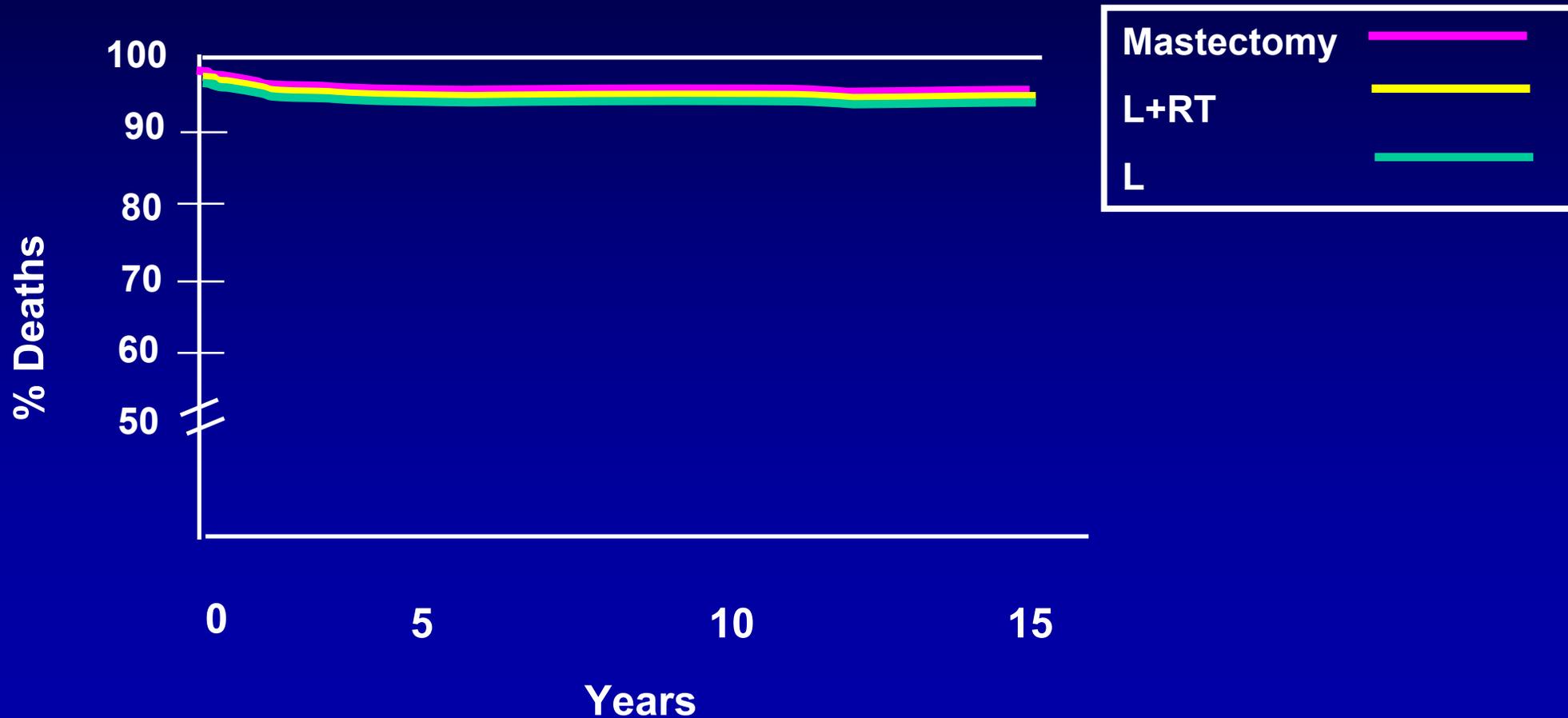
Key Management Concepts in DCIS

- The presence of invasive cancer cannot be reliably excluded without complete excision of the lesion

DCIS Diagnosed by Core Biopsy: How Common is Sampling Error?

Author	# Patients	% Invasive
Kestin 2000	130	7.7
Rosenfeld Darling 2000	289	14
Cox 2001	240	12.5
Cox 2003	499	9.4
Morrow	238	13.3

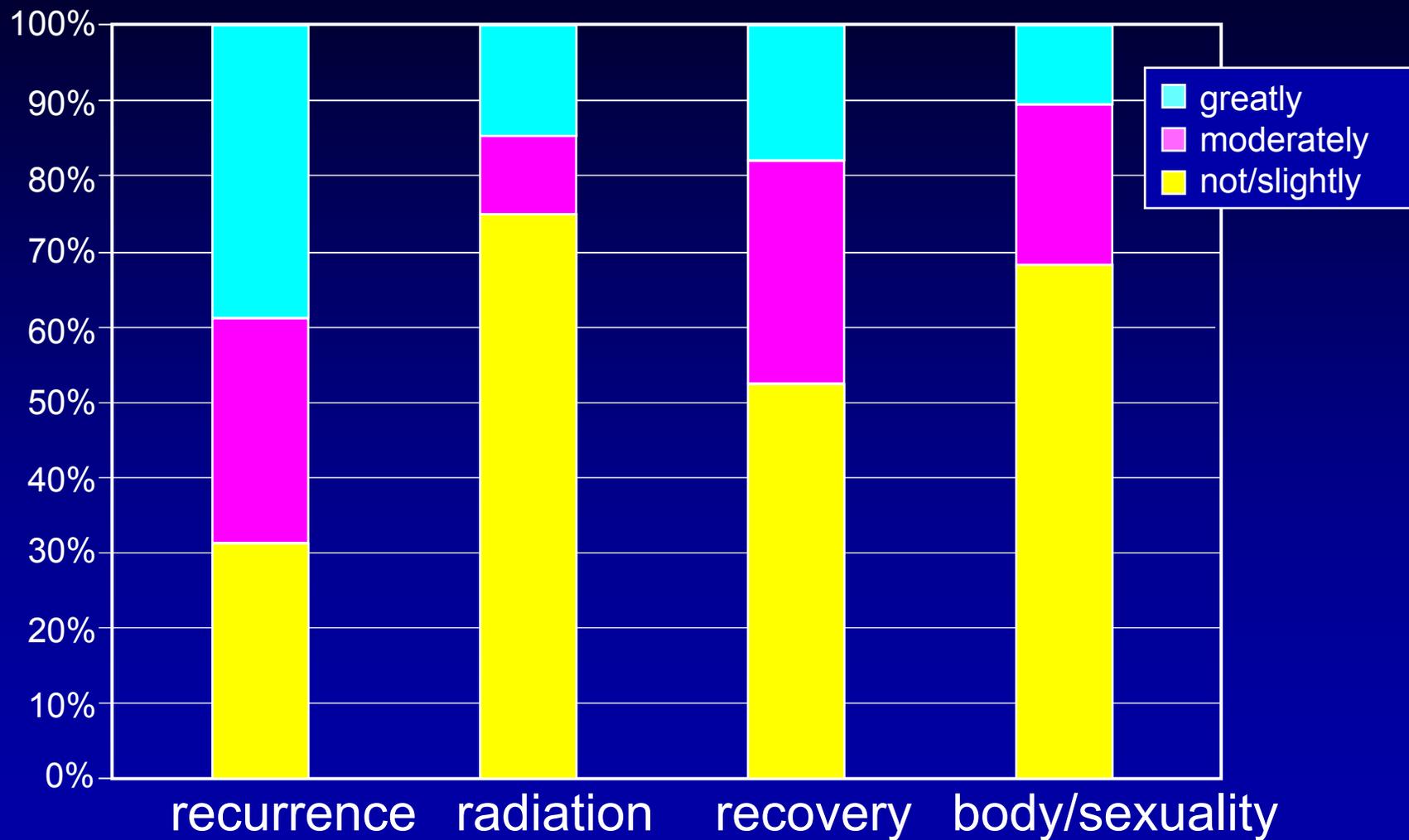
Cause Specific Survival in DCIS By Treatment



Key Management Concepts in DCIS

- Prevention of local recurrence (invasive and noninvasive) is a major goal of the treatment of DCIS

Factors Influencing Patient Decisions



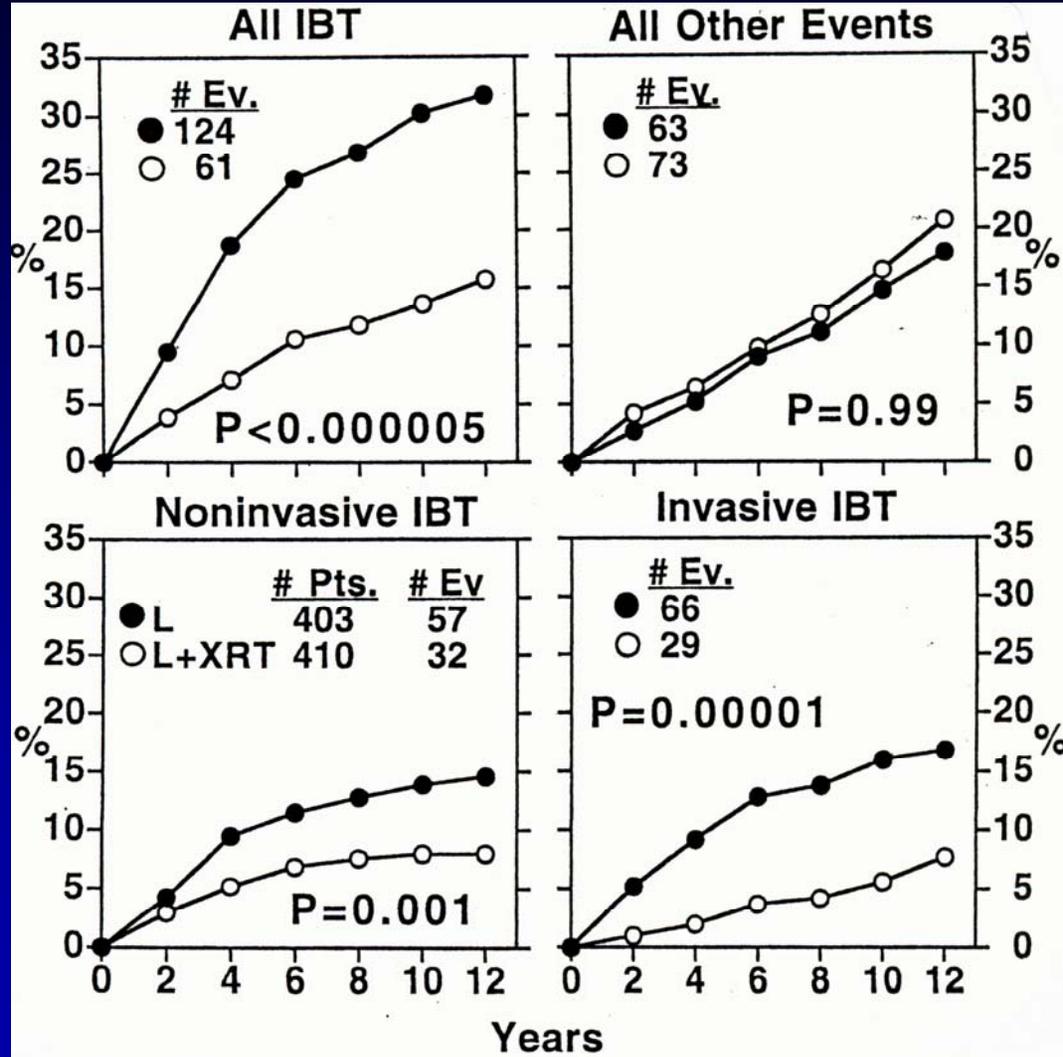
Katz, JCO 2005;23:5526

n=1079

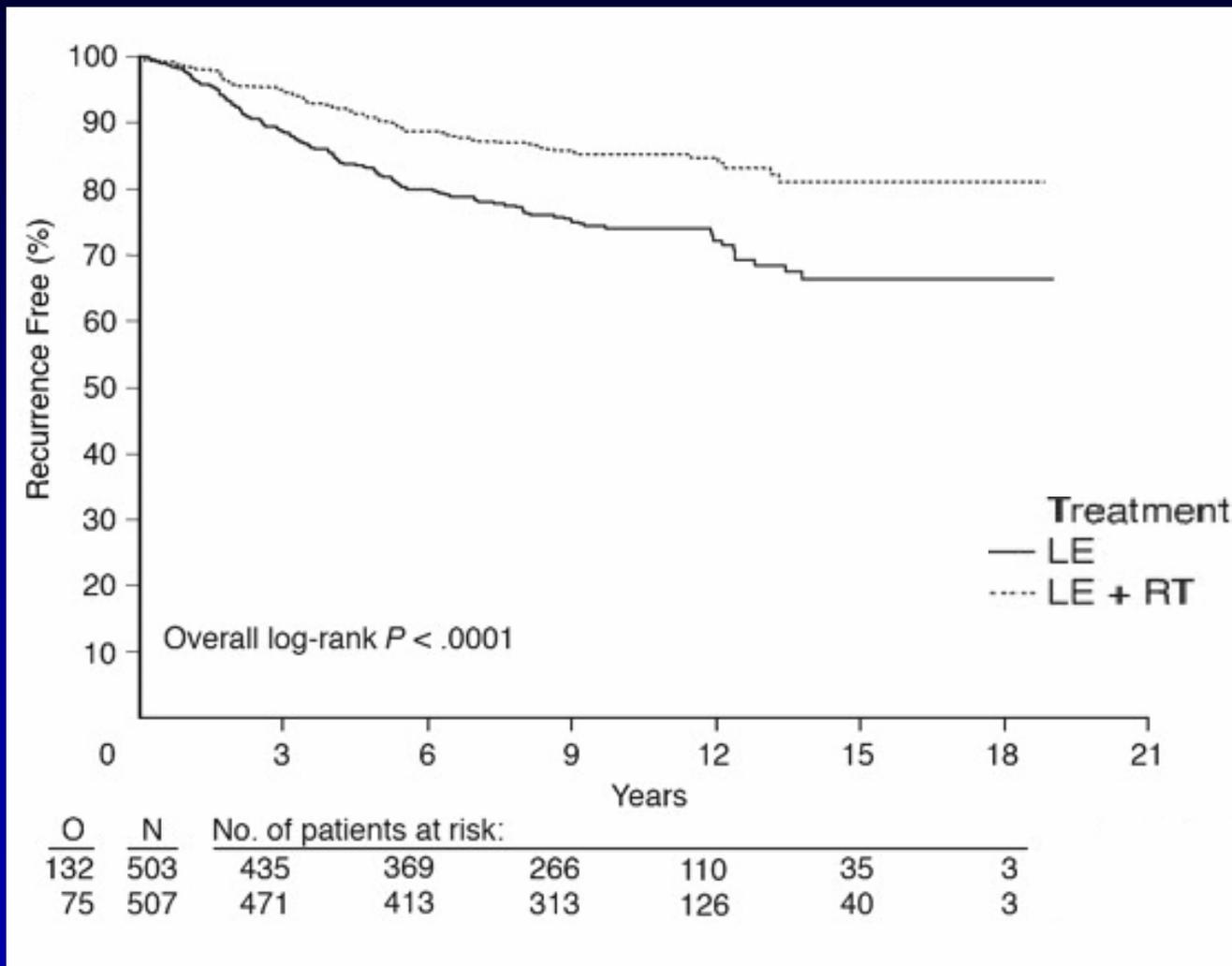
Randomized Trials of RT in DCIS

Trial	# Patients	% Mammo Detected	Boost	Tamoxifen
NSABP B17	813	80	No	No
EORTC 10853	1002	71	No	No
UK Trial	1030	100	No	Yes

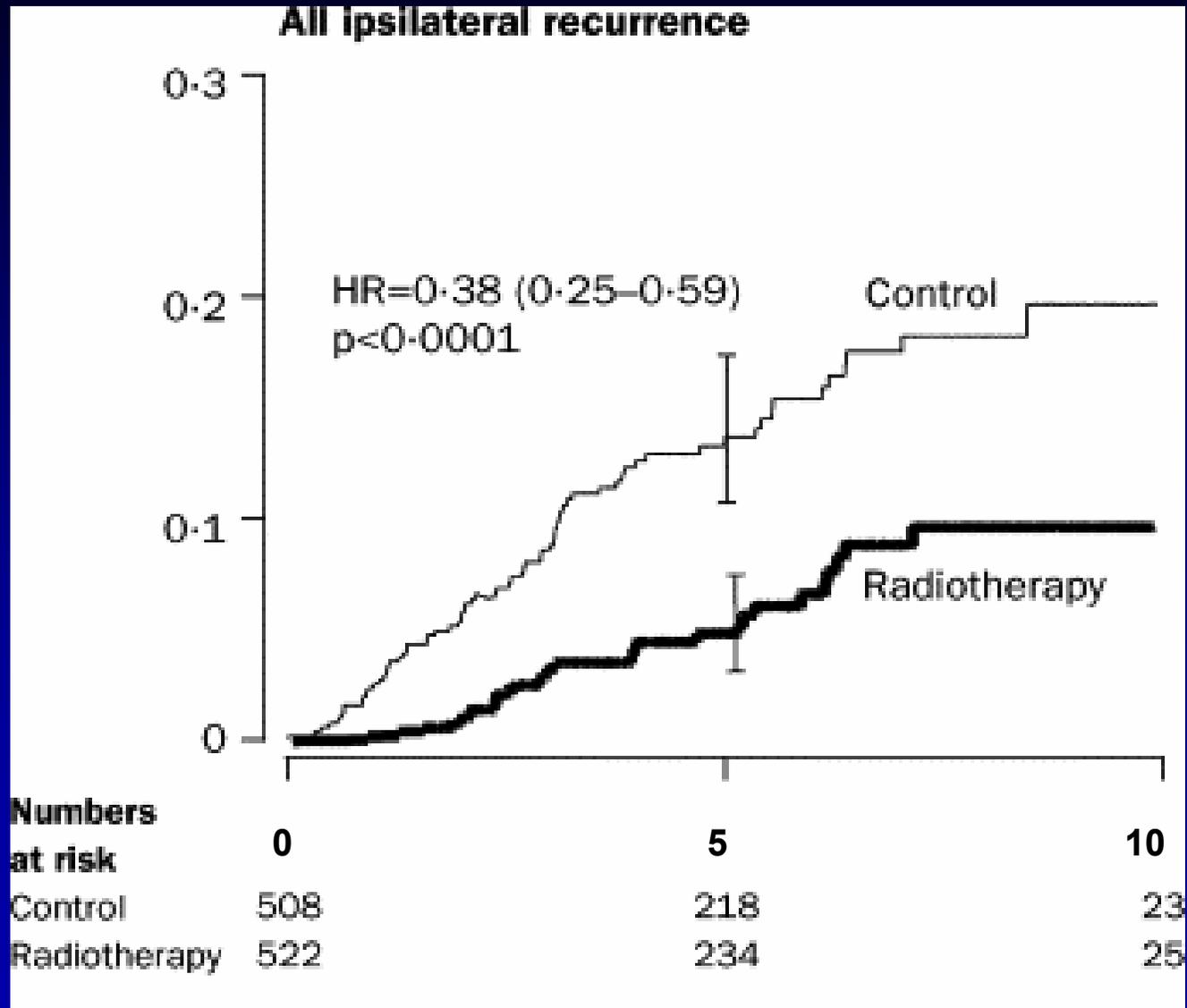
NSABP B17



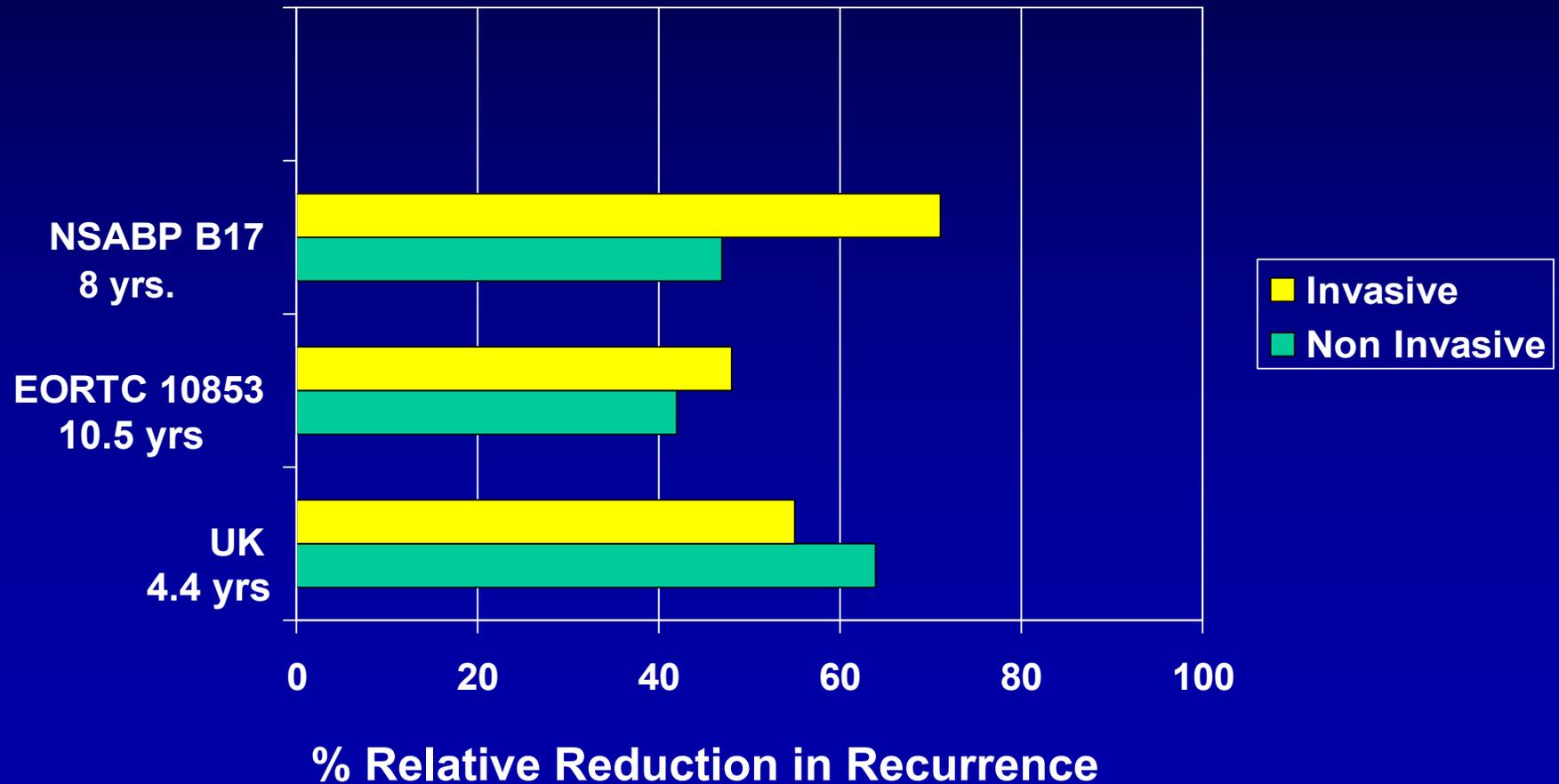
Local Recurrence in EORTC 10853



UK DCIS Trial



Effect of RT in DCIS



Key Management Concepts in DCIS

Prevention of local recurrence is a major goal of the treatment of DCIS

- The use of RT reduces LR

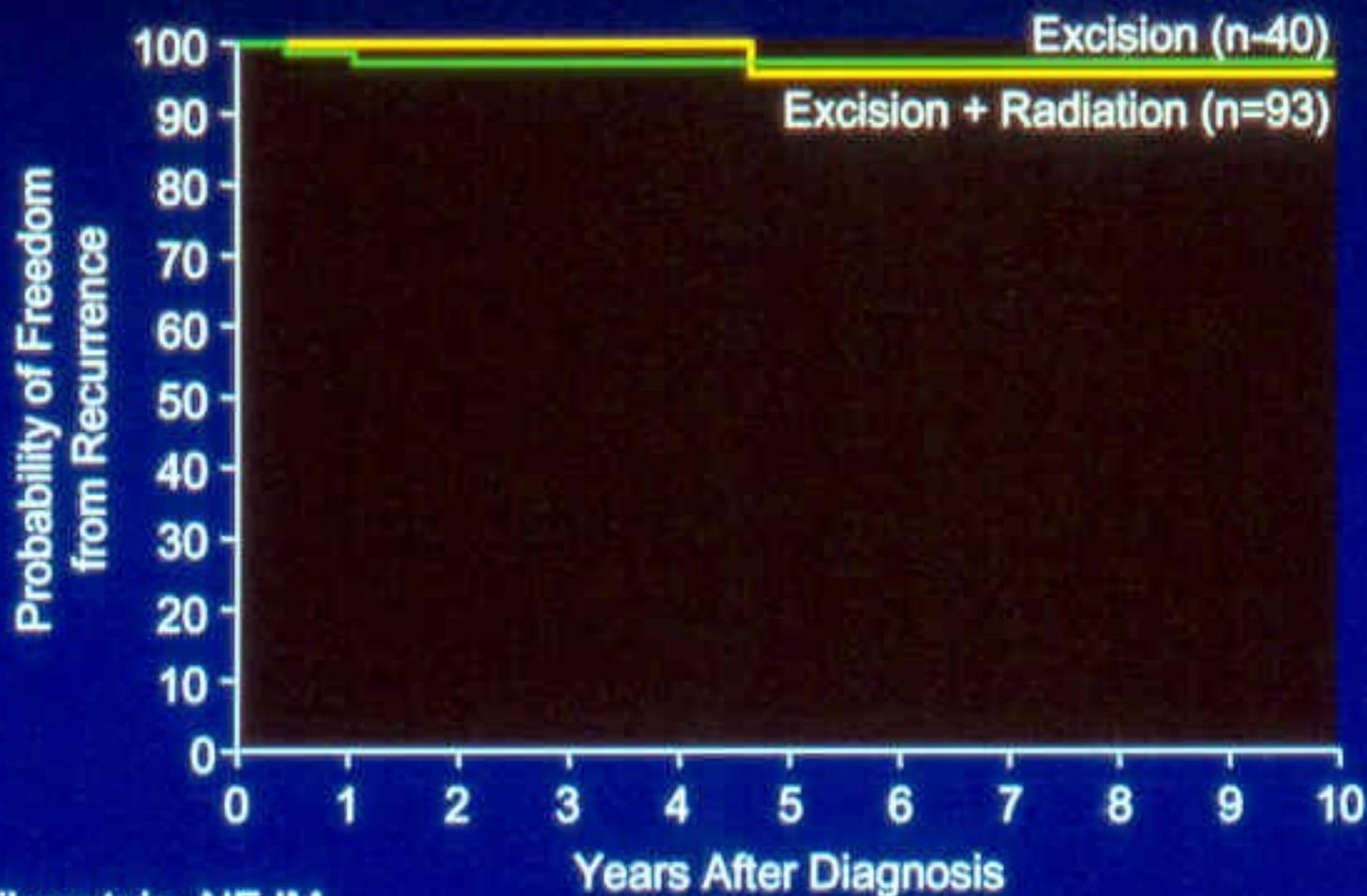
Subsets of patients NOT benefiting from RT have not been reproducibly identified.

Patient Population

	No RT	RT
# Patients	256	213
Mean F/U	72 mo	92 mo
# LR	38	37
% Invasive LR	42	51

Silverstein M, NEJM 1999;340:1455

Local Recurrence: Margins ≥ 10 mm



Wide Excision Alone for DCIS

Dana Farber Prospective Trial
11/94 – 7/02

Eligibility Criteria

DCIS \leq 2.5cm

Margin \geq 1cm

Predominant grade 1 or 2

No Tam

Wide Excision Alone for DCIS

Recruitment goal: 200; Closed after 158 patients

Mean age 51 years Median follow up 40 months

LR as first failure 2.4%/yr (95%CI 1.3 – 4.1%)

5 year LR 12%

Eligibility: E5194

- DCIS, locally excised, $\geq 3\text{mm}$ in size
- Low/intermediate grade $\leq 2.5\text{ cm}$
- High grade $\leq 1\text{ cm}$ (NG 3 + necrosis)
- Minimum margin width $\geq 3\text{mm}$
- Specimen sequentially sectioned and completely embedded to determine grade, size, and margins
- Post excision mag mammo negative for microcalcifications

SCHEMA: E5194

Stratification:

- Low/Int. Grade DCIS ≤ 2.5 cm
vs.
High Grade DCIS ≤ 1.0 cm
- Adj. TAM Planned
vs.
No Adjuvant TAM

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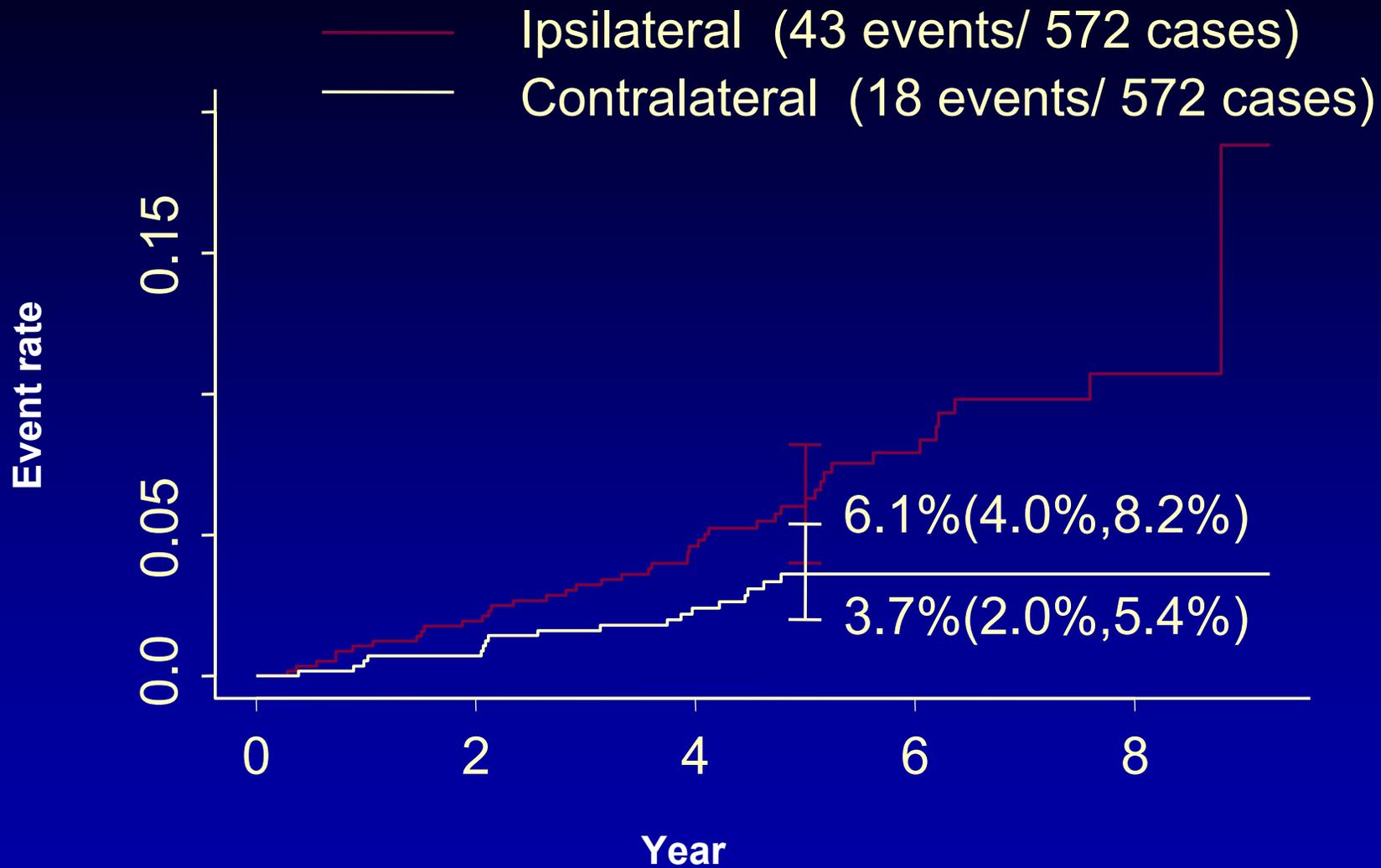
Central
Pathology
Review

Observation

Local recurrence/Disease
Progression Treated at
Investigator's Discretion
Central Path Review of
Recurrence

Low/Intermediate Grade Stratum

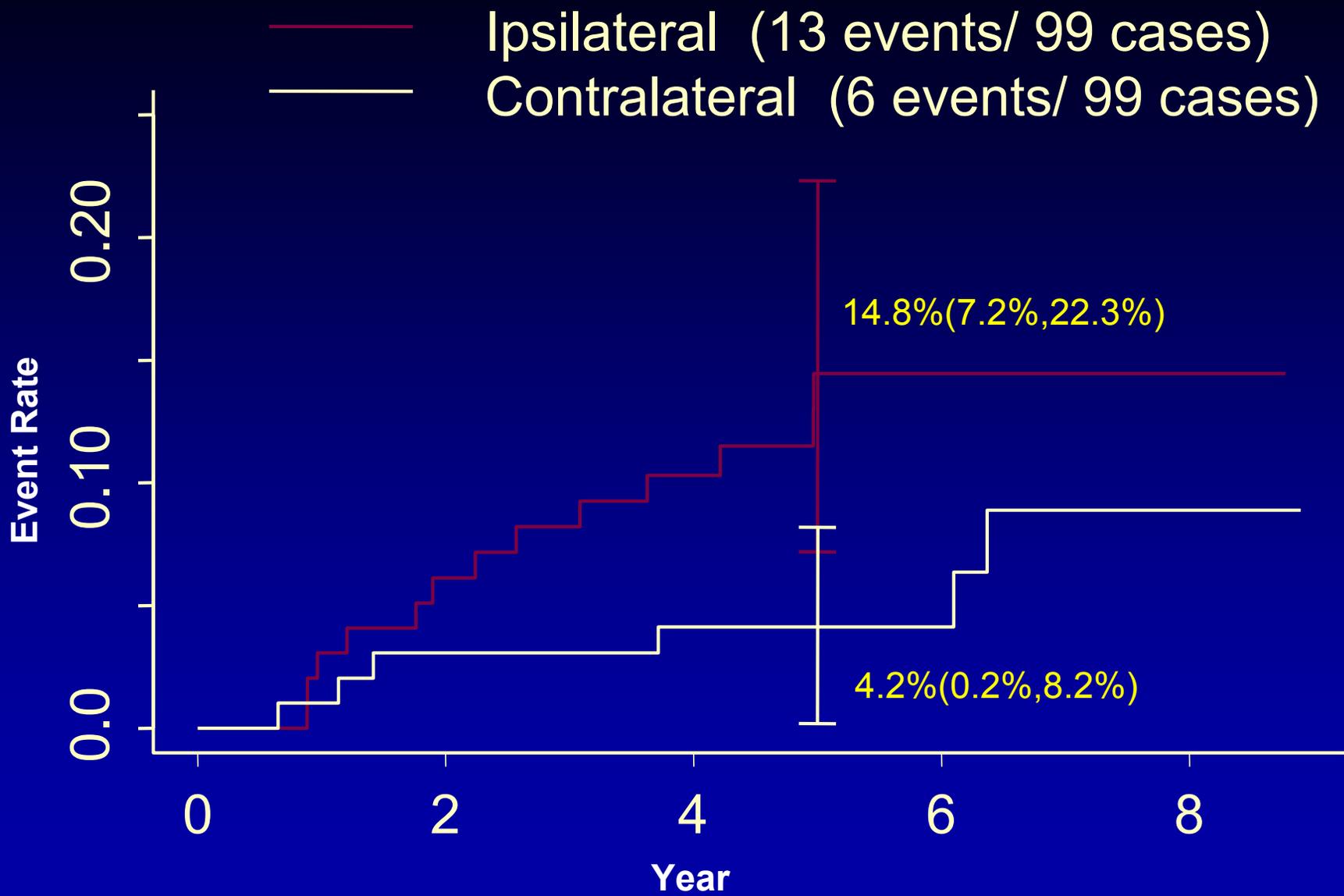
- 579 eligible patients
- Median microscopic size 6 mm, with 82% less than 1cm in size
- 67% with margin width ≥ 5 mm
- 46% with margin width ≥ 10 mm or negative re-excision
- 31% with TAM



Low/intermediate grade stratum

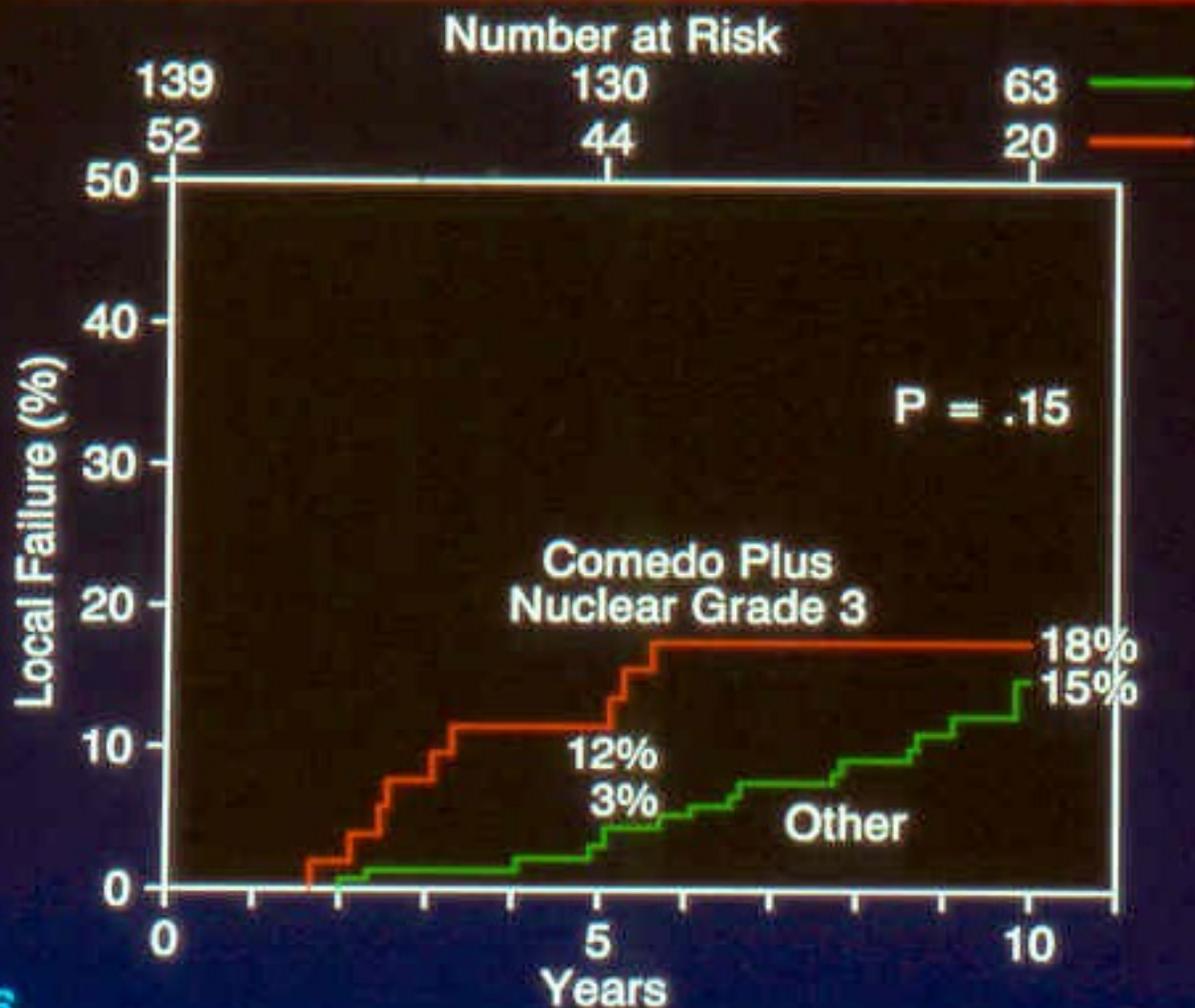
High Grade Stratum

- 101 eligible patients
- Median tumor size 7 mm
- 75% with margin width ≥ 5 mm
- 48% with margin width ≥ 10 mm or negative re-excision
- 31% with TAM

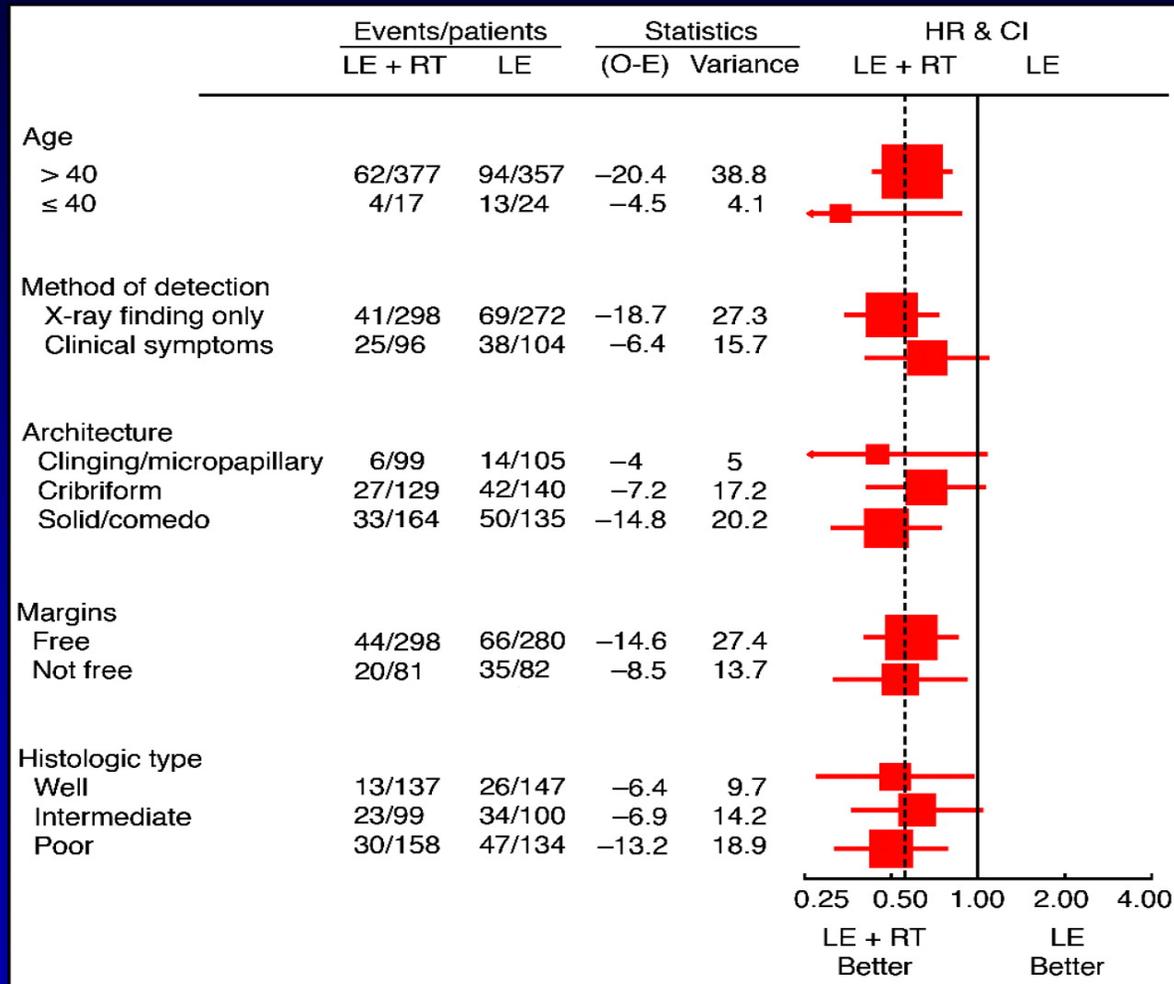


High Grade Stratum

Predictors of Recurrence in DCIS After Excision + RT



Effect of RT by Subgroup EORTC 10853



When is Mastectomy Indicated in DCIS?

- Disease too extensive to resect with a good cosmetic outcome
- Inability to achieve negative margins
 - Micropapillary DCIS
 - DCIS with nipple discharge
- Contraindication to RT in high-risk patient
 - Premenopausal > 1cm in size
 - High grade ER negative

Key Management Concepts in DCIS

DCIS lacks the ability to metastasize

Axillary surgery is indicated because of the risk of unsampled invasive carcinoma

- Mastectomy
- ? Microinvasion
- Gross DCIS

Risk of Axillary Recurrence in DCIS

<u>Treatment</u>	<u>Rate/1000 pt years</u>
Lumpectomy Only	0.76
L+XRT B17	0.86
L+XRT B24	0.49
L+XRT+TAM	0.46

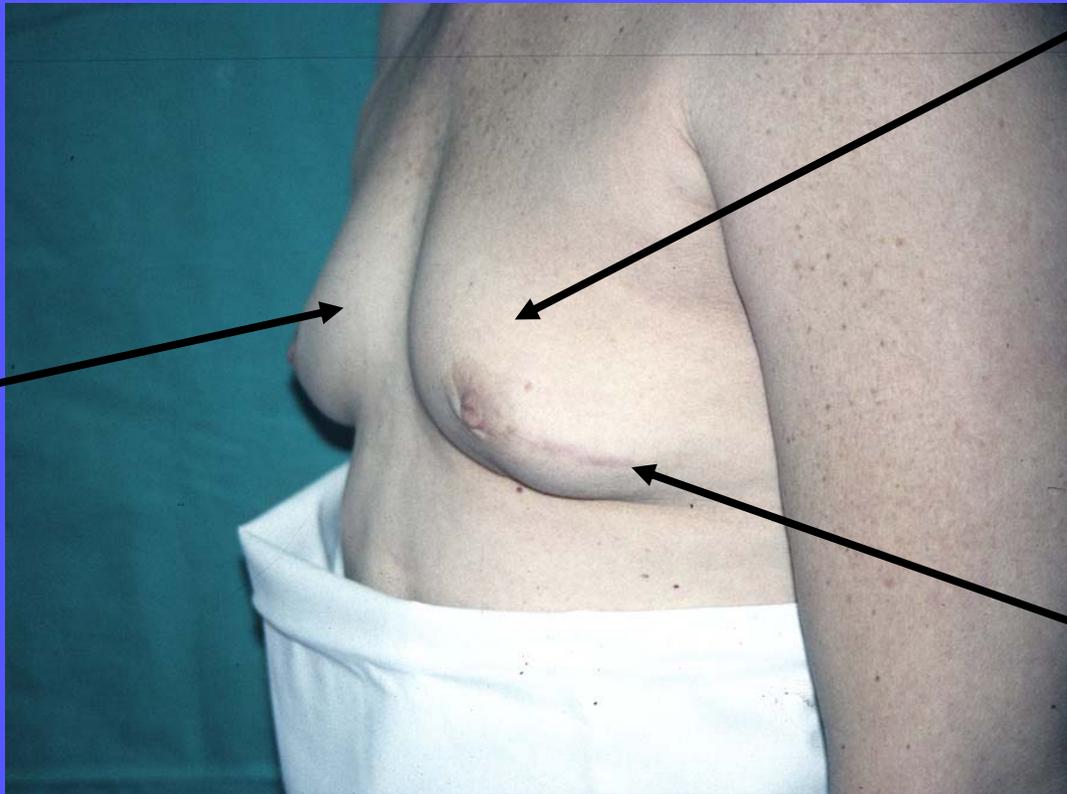
Julian, Ann Surg Oncol 2006

Key Management Concepts in DCIS

DCIS is a marker for an increased risk of
invasive carcinoma in BOTH breasts

Long Term Outcomes of DCIS Treatment

- 5 yr
- 10 yr
- 15 yr



<1%

2%

5%

4%

4%

9%

7%

13%

12%

Tamoxifen in DCIS

NSABP B24
n=1798
med f/u 74 mo

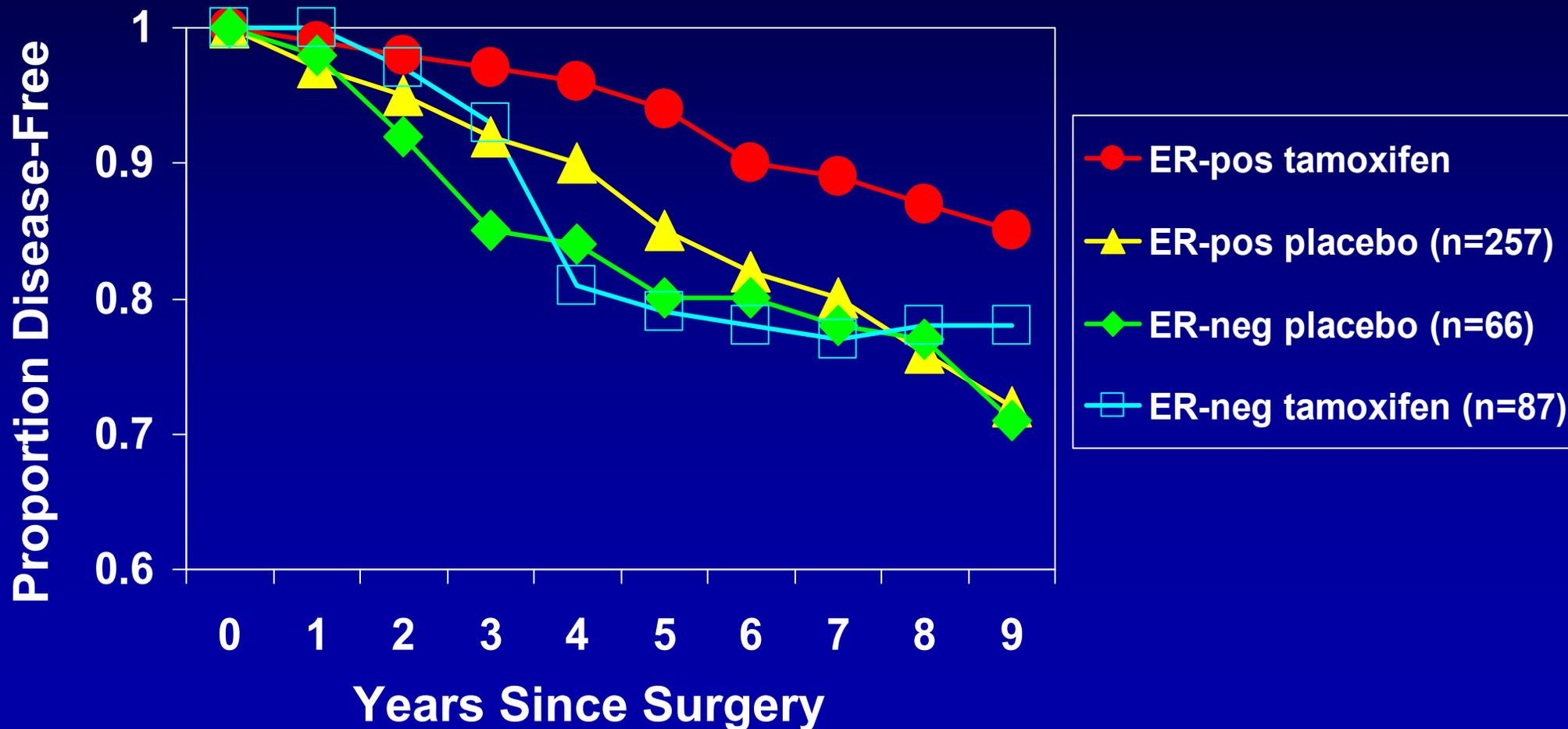
UK/ANZ
n=1576
med f/u 52.6 mo

% Br Ca Events

No Tam Tam

	<u>No Tam</u>	<u>Tam</u>	<u>p value</u>	<u>Hazard Ratio</u>
B24	13.2	8.2	<.0009	0.63
UK/ANZ	14	18	.13	0.83

NSABP B-24 Trial Based on ER Status

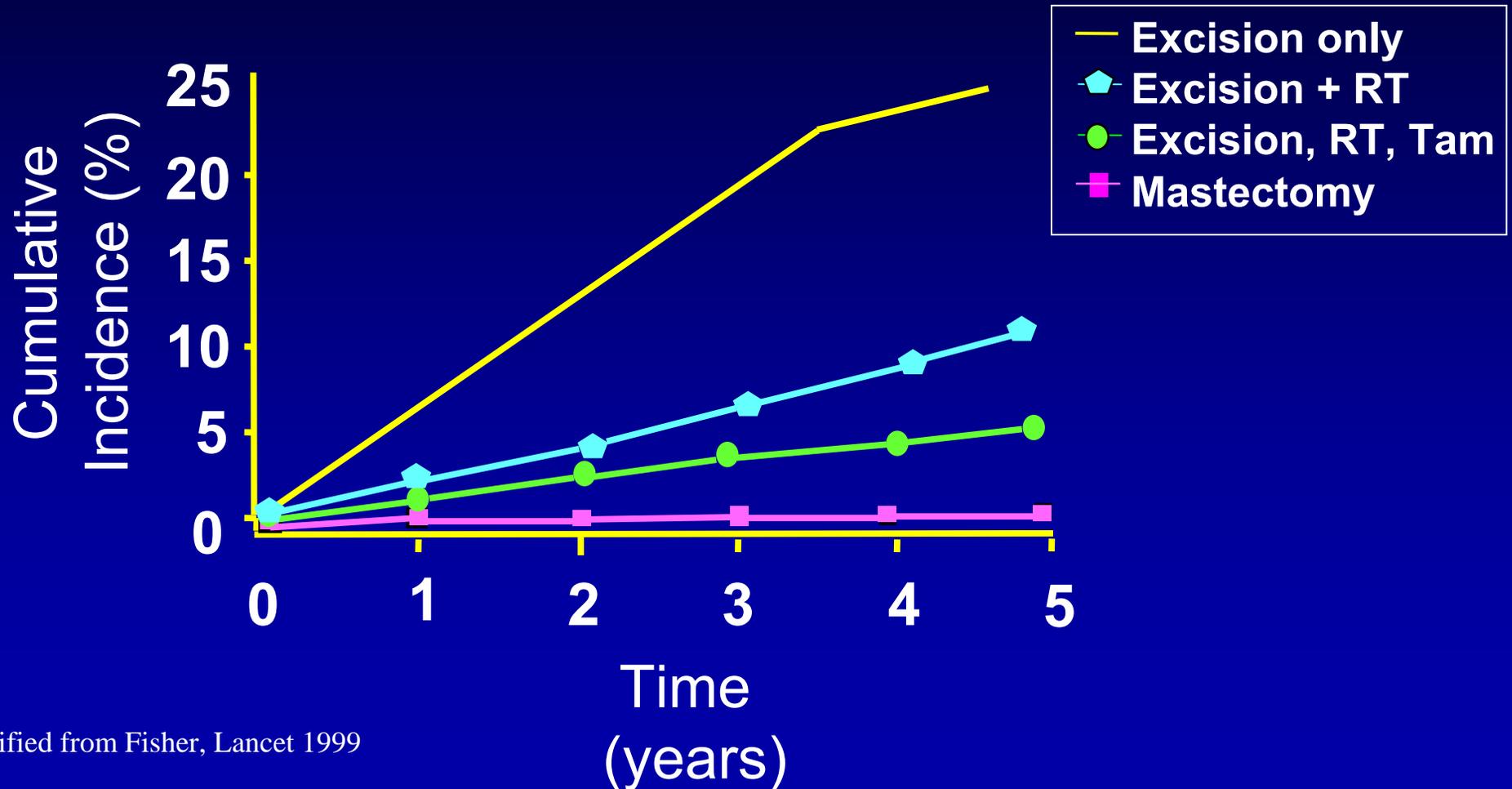


Can Tamoxifen Substitute for RT?

UK Trial: Median follow up 53 months

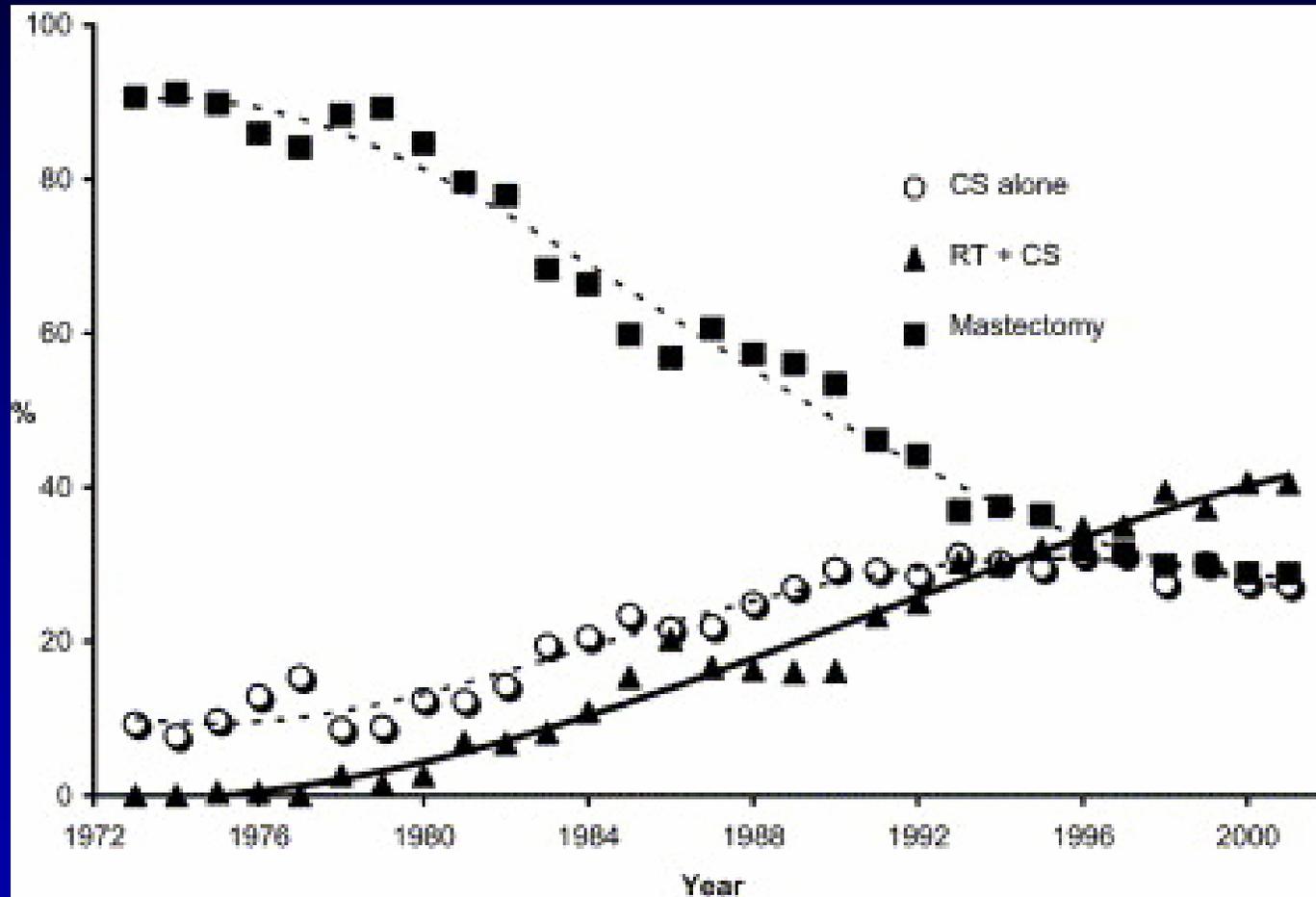
	<u>Excision</u>	<u>Excision+ Tam</u>
<u>Number</u>	782	794
IBTR	14.6%	12.8%
Invasive	4.5%	5.7%
Contralateral	2.7%	1.4%
All events	17.5%	14.4%

Risk of Breast Cancer Events After DCIS



Modified from Fisher, Lancet 1999

Treatment Trends in DCIS SEER



Key Management Concepts in DCIS

Patients are confused about the fundamental nature of DCIS

Risk Perception in Women with DCIS

n=228

<u>Risk</u>	<u>DCIS</u>	<u>T1/T2, N0</u>
Local Recurrence	53%	45%
Distant Recurrence	36%	39%
Death	27%	27%

Correlates of Local Therapy for Women with DCIS

- Population based study from Detroit and LA SEER registries
- Diagnosed with DCIS 2002
Age \leq 79 yrs
- Survey completed by 79.7% of eligible patients.
659 met entry criteria.

Therapy Received

n=659

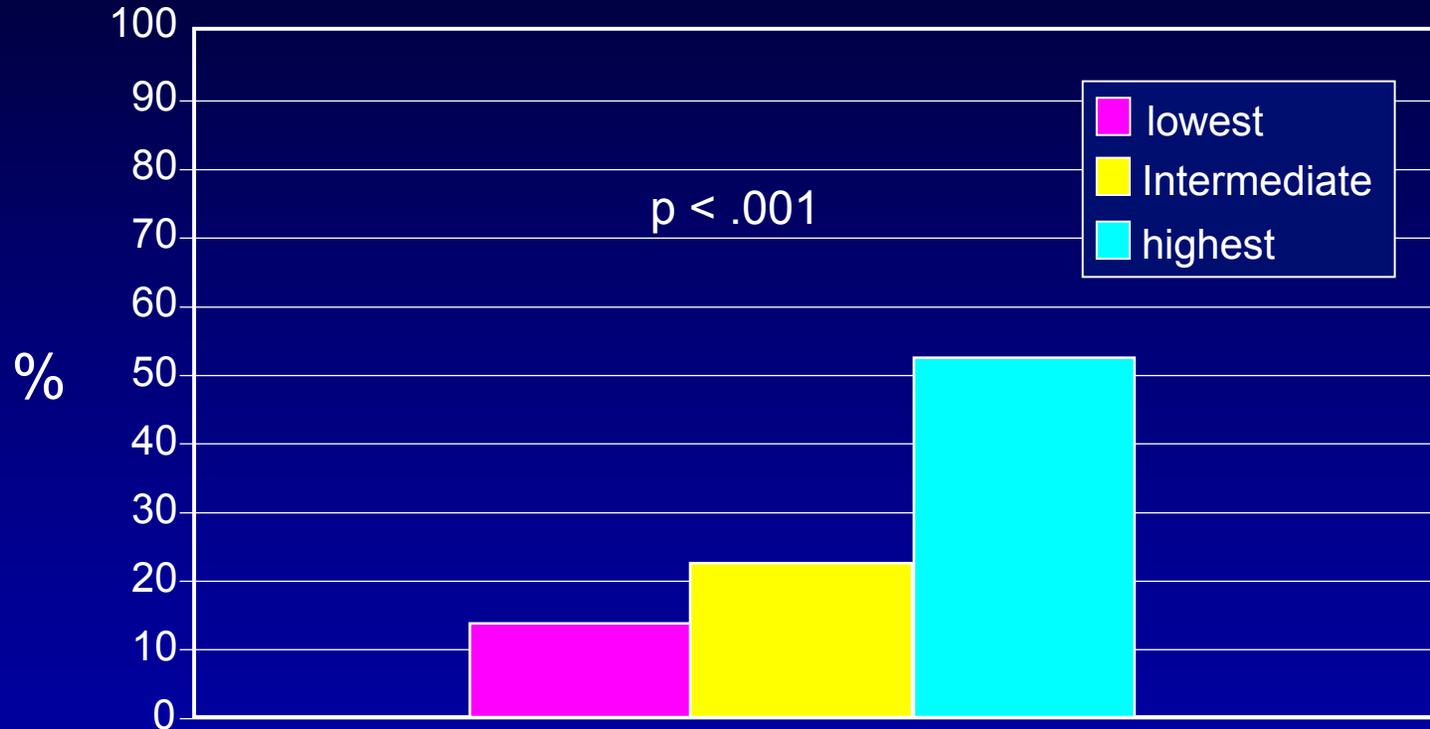
BCS: 69.5%

Mastectomy: 30.5%



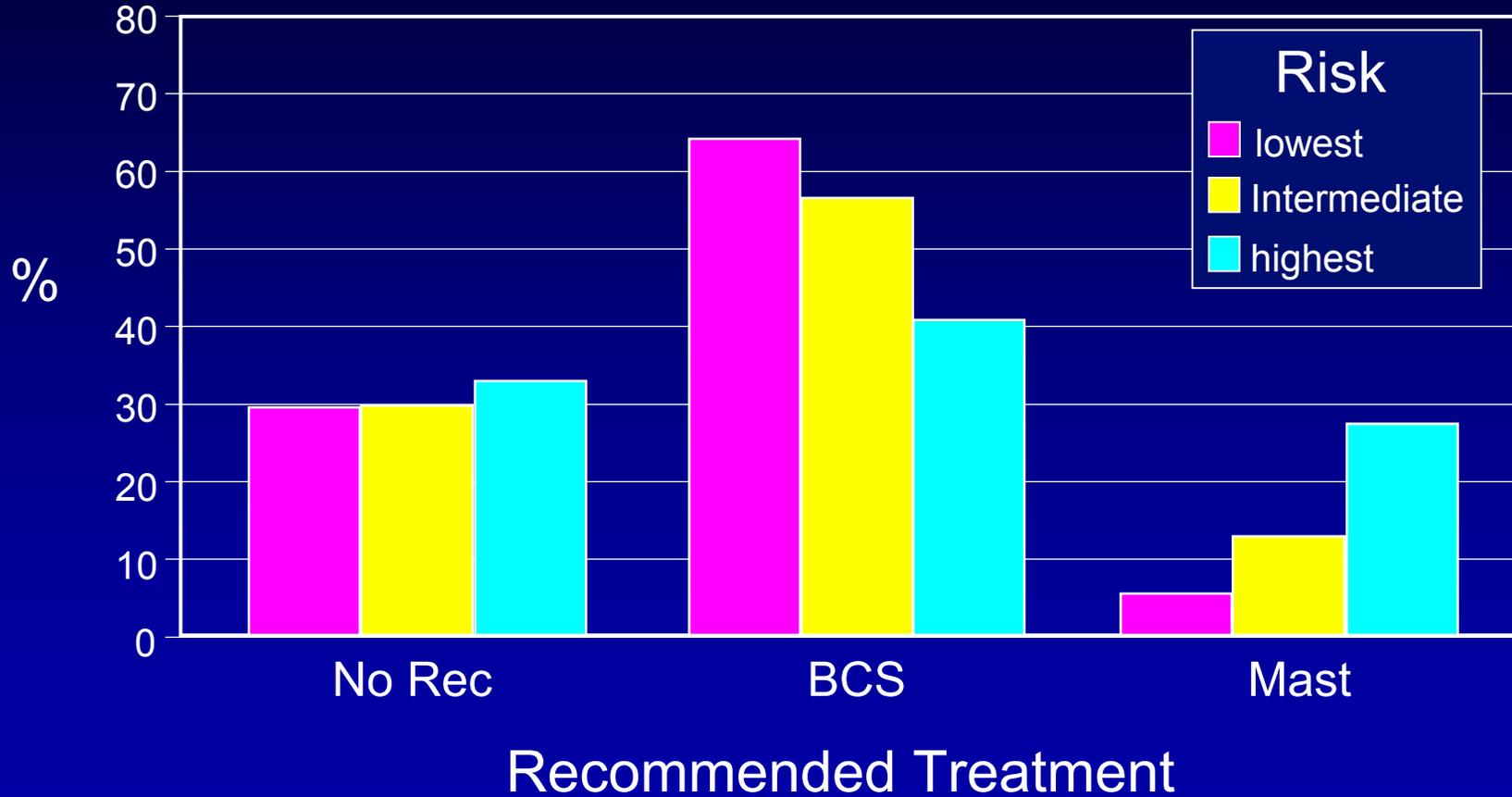
RT: 71%

Receipt of Mastectomy By Risk of Recurrence

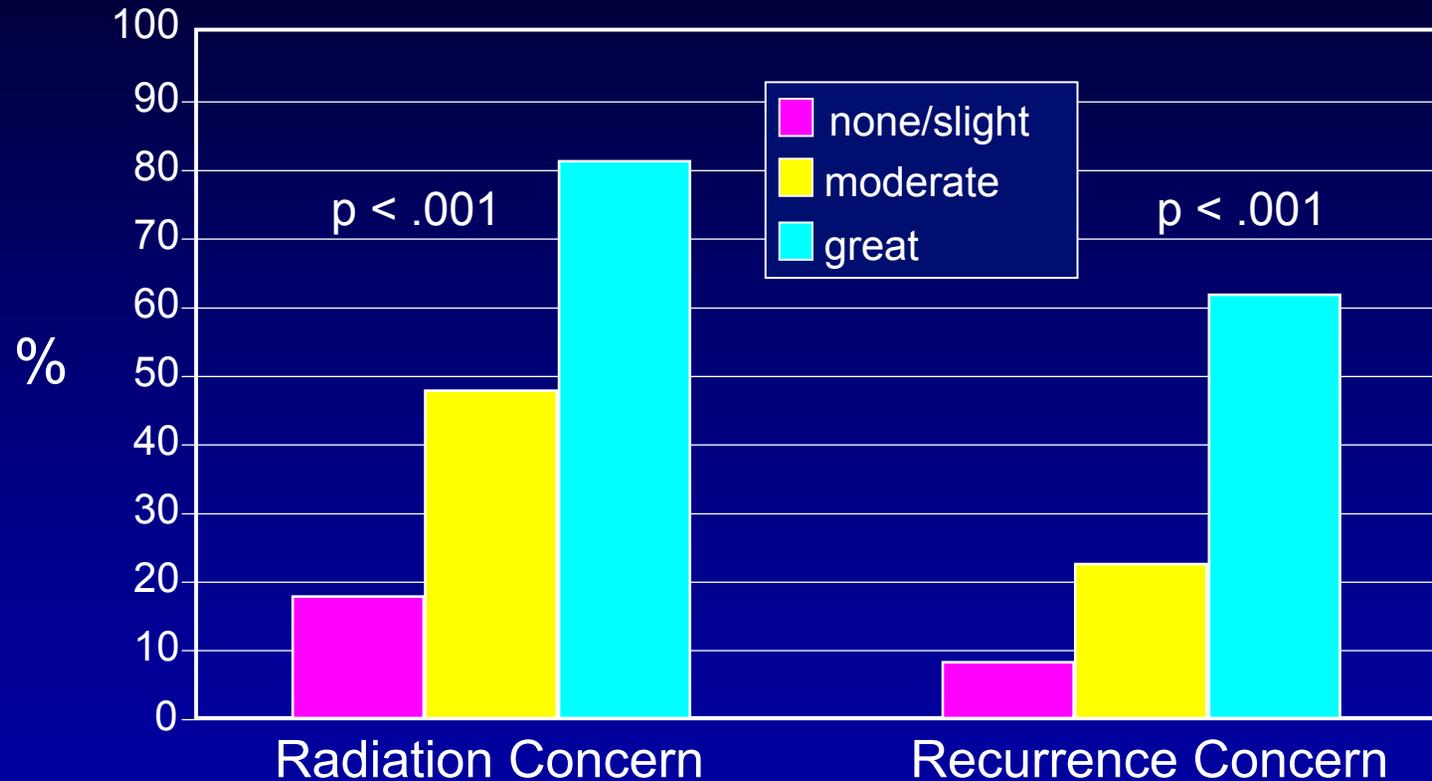


Adjusted for age, marital status, medical comorbidity, and SEER site

Surgeon Recommendation By Risk of Recurrence



Receipt of Mastectomy By Level of Patient Concern



Adjusted for age, marital status, education, ethnicity, medical comorbidity, recurrence risk and SEER site

Conclusions

- There are no histologic or molecular features of DCIS which identify a subgroup at high risk of mortality after any form of local therapy.
- Risk of LR varies among treatments.
- Contralateral breast cancers are a significant risk.

What is Needed to Resolve the Dilemma of DCIS?

- Predictors of biologic behavior
 - Progression to invasive cancer
 - Local recurrence
- Better ways to communicate risks and benefits of treatment choices
 - Frame discussions in terms of complete diagnosis, prevention of invasive cancer