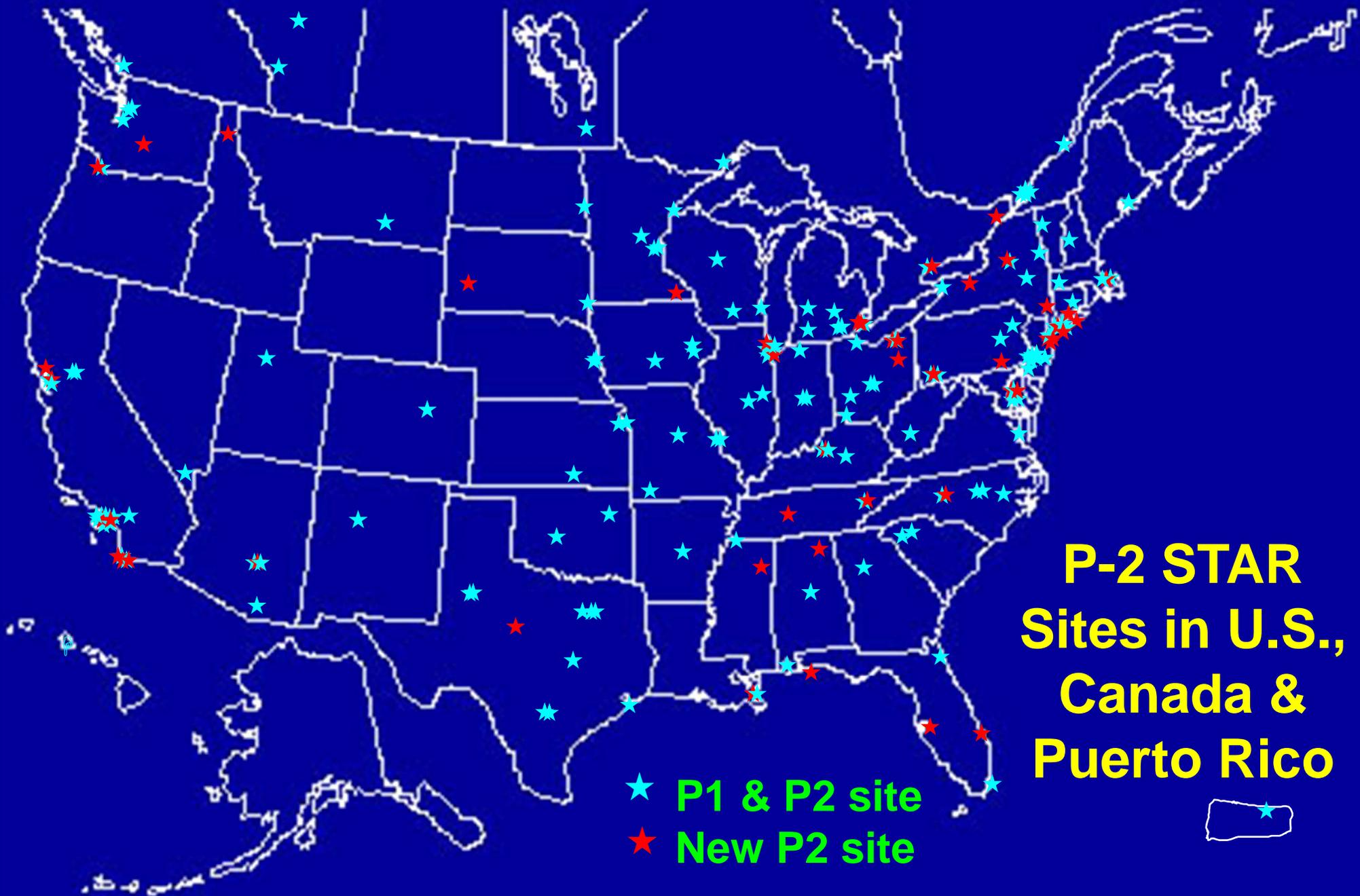


NSABP

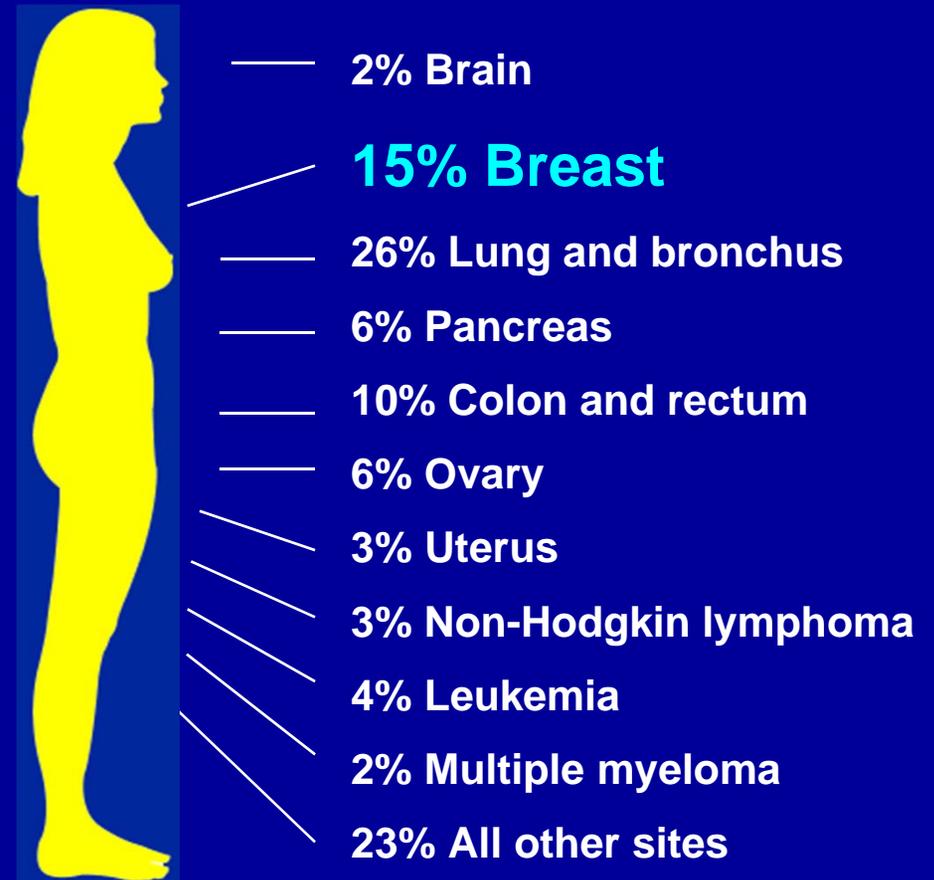
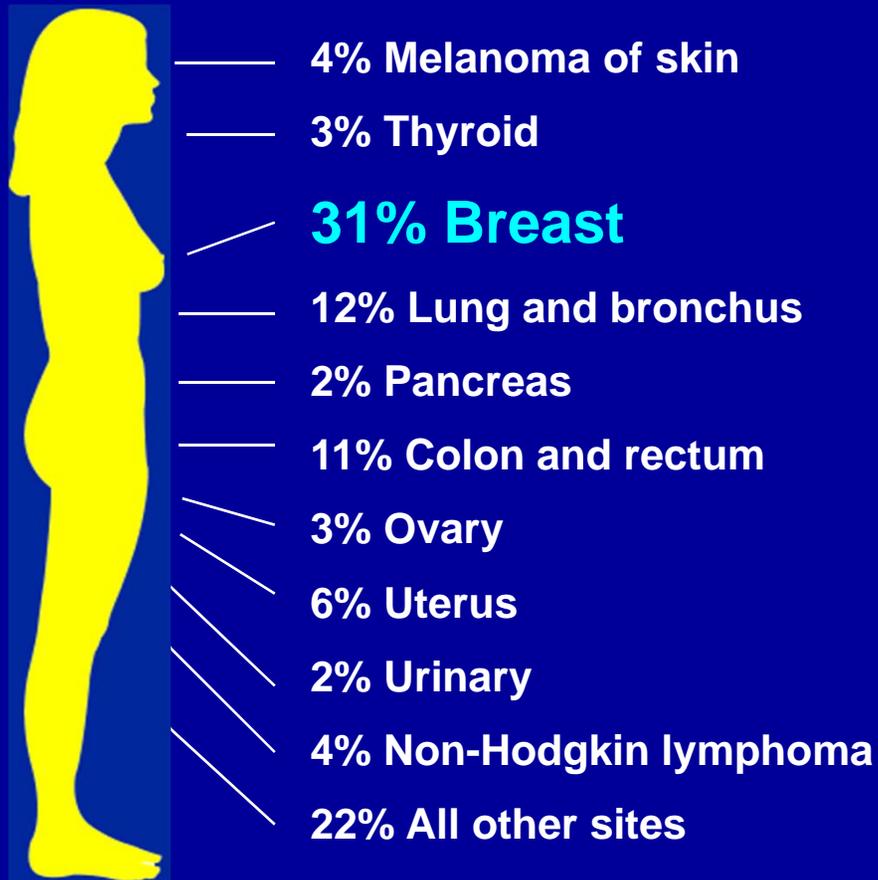
*National Surgical Adjuvant
Breast and Bowel Project*



2006 Breast Cancer Estimates

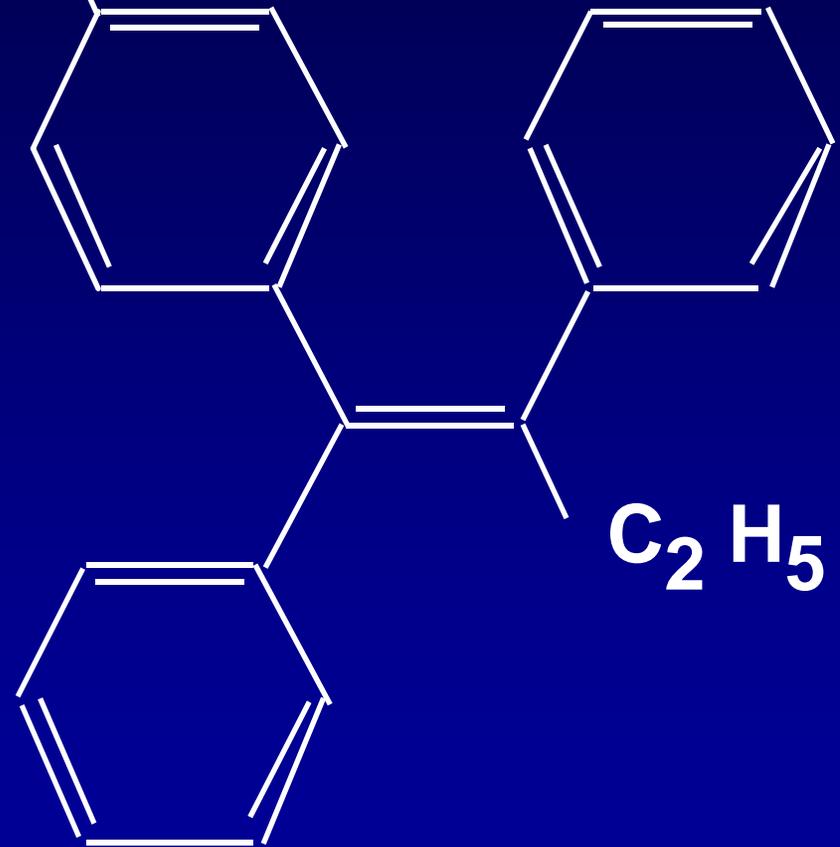
212,290 New Cases

40,970 Deaths



Chemical Structure of Tamoxifen

$(\text{CH}_3)_2\text{N}(\text{CH}_2)_2\text{O}$



NSABP B-14

- Tumors With ER \geq 10 fmol/mg
- Histologically Neg. Axillary Nodes
- TM or Lump. + Ax. Diss. +XRT

Stratification

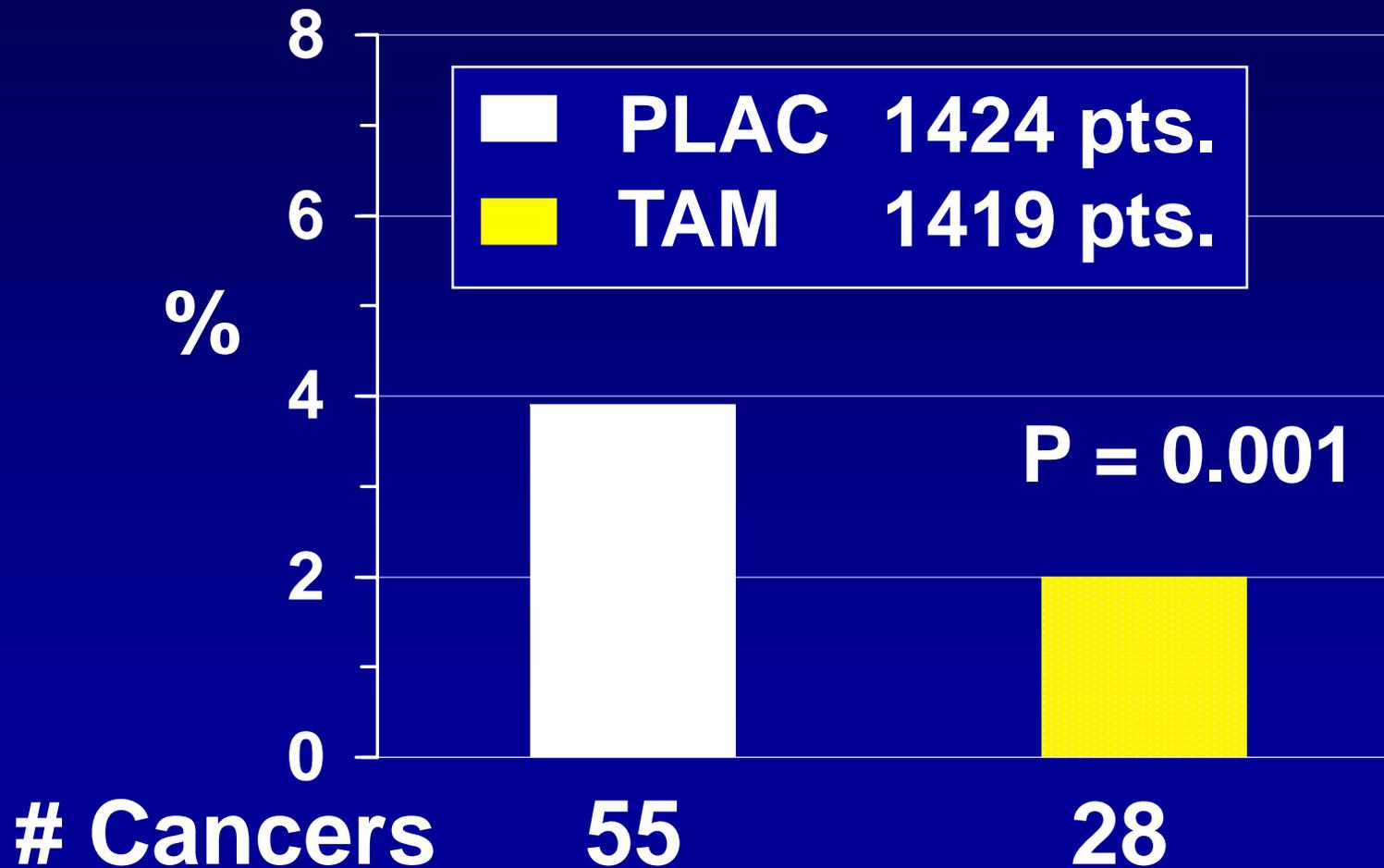
- Age
- Clinical Tumor Size
- Quantitative ER
- Type of Operation

Placebo

TAM

B-14

Second Cancers Opposite Breast



BCPT-P1

Eligible Participants

Stratification

- Age
- Relative Risk
- Race

**TAMOXIFEN
x 5 YRS.**

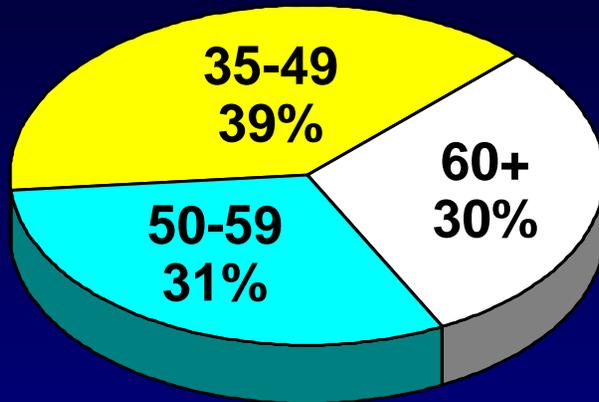
**PLACEBO
x 5 YRS.**

Gail Model Variables Used to Provide Composite Risk Assessment

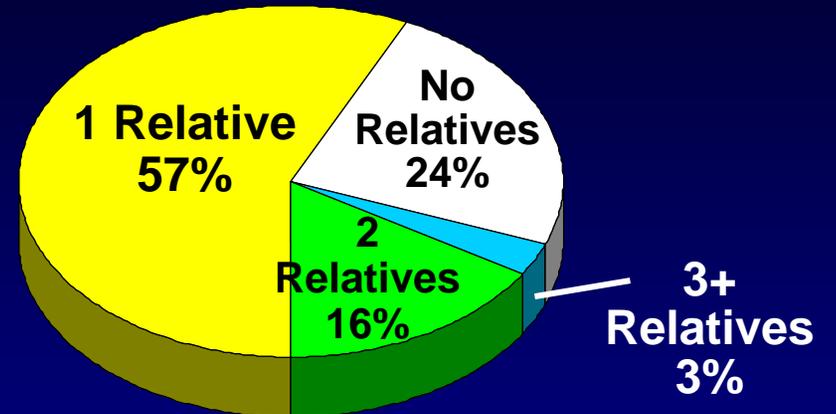
- **No. 1st degree relatives with breast cancer**
- **Nulliparity or age at 1st live birth**
- **No. of benign breast biopsies**
- **Atypical hyperplasia**
- **Age at menarche**
- **Race**

Participant Characteristics

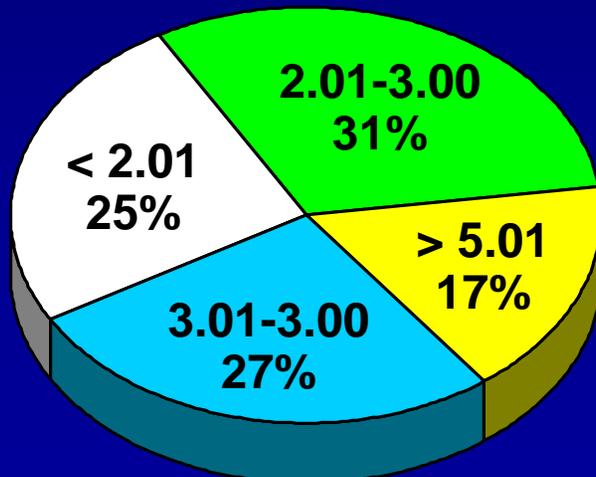
Age (yrs)



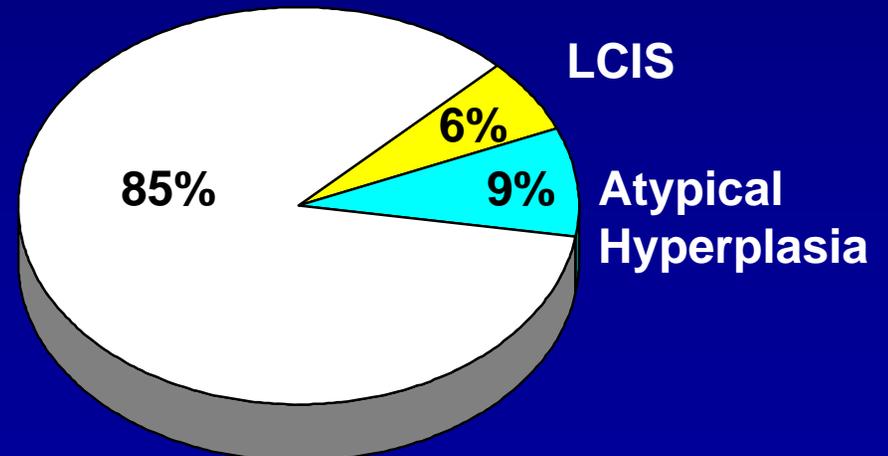
Family History



Gail Risk



Benign Disease



BCPT-P1
Invasive Breast Cancers

Placebo

Tamoxifen

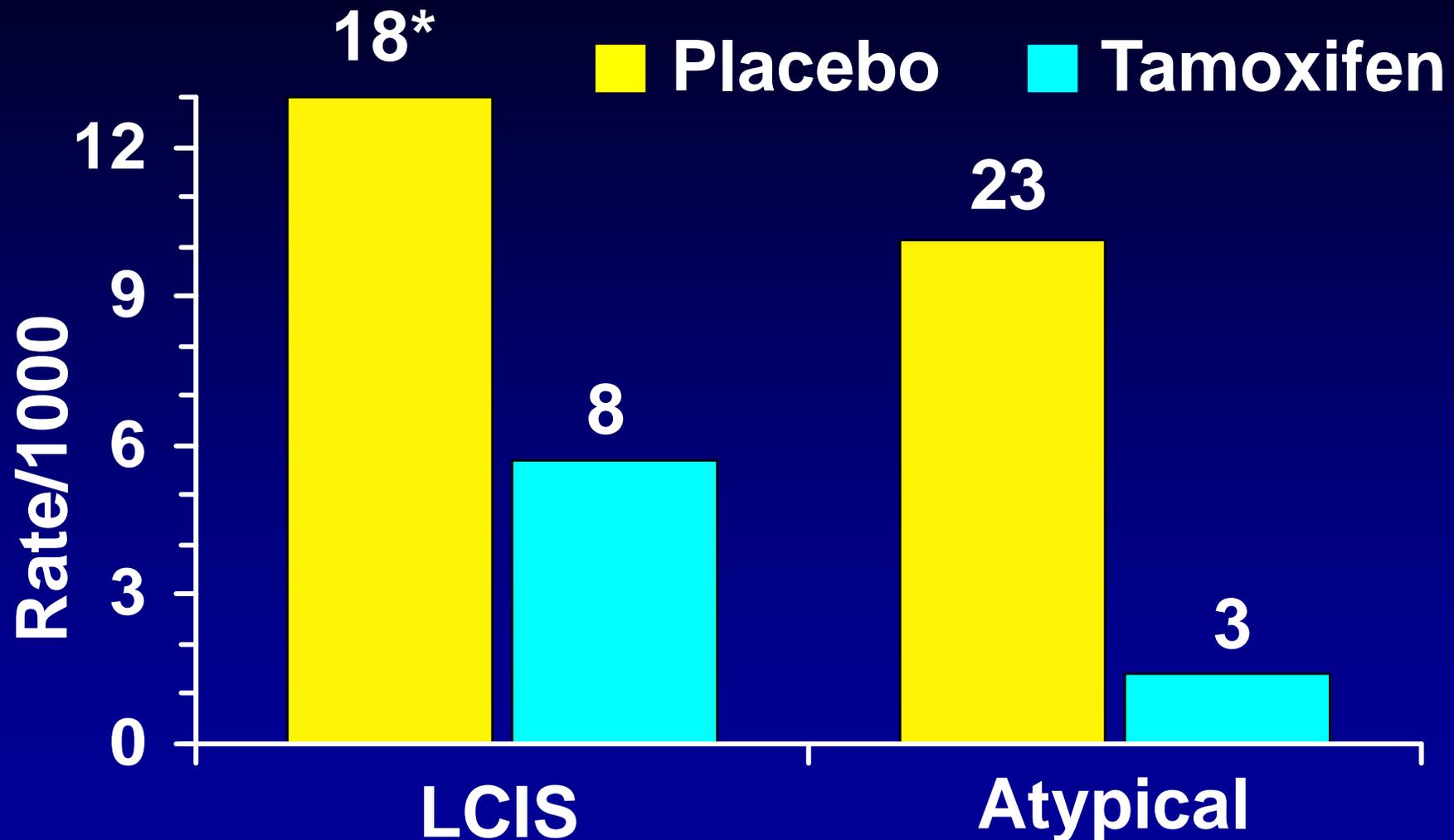
175

89

$P < 0.00001$

49% reduction

P-1 Invasive Breast Cancer



* # of events

NSABP
BCPT

BCPT-P1

Noninvasive Breast Cancers

Placebo	Tamoxifen
---------	-----------

69

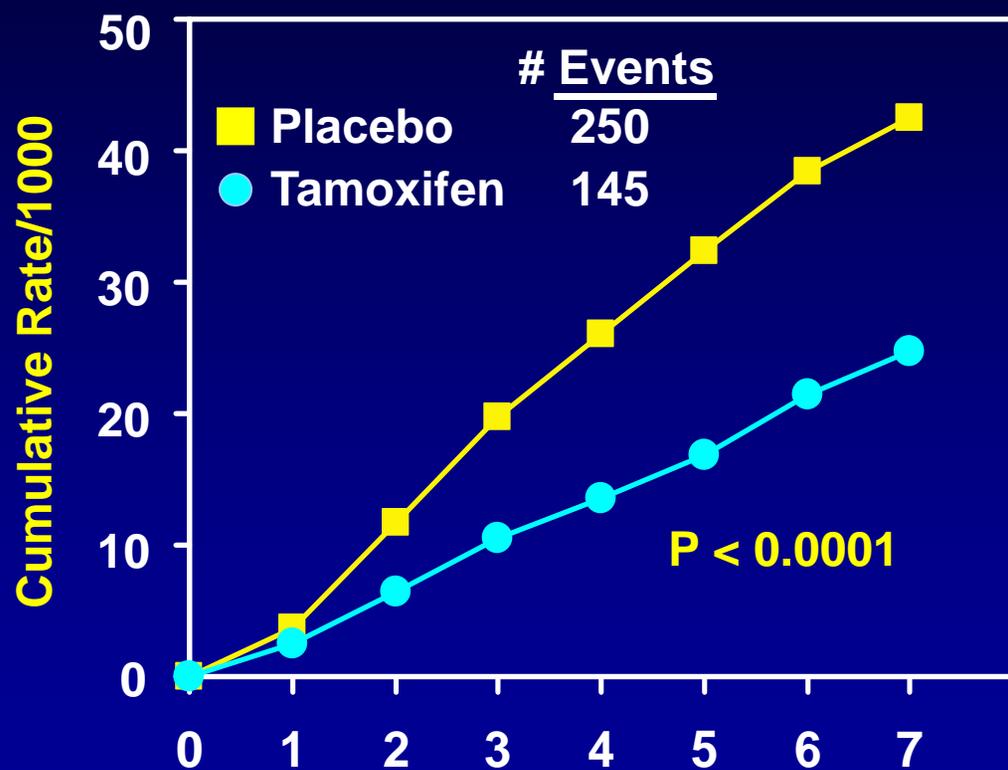
35

$P = 0.002$

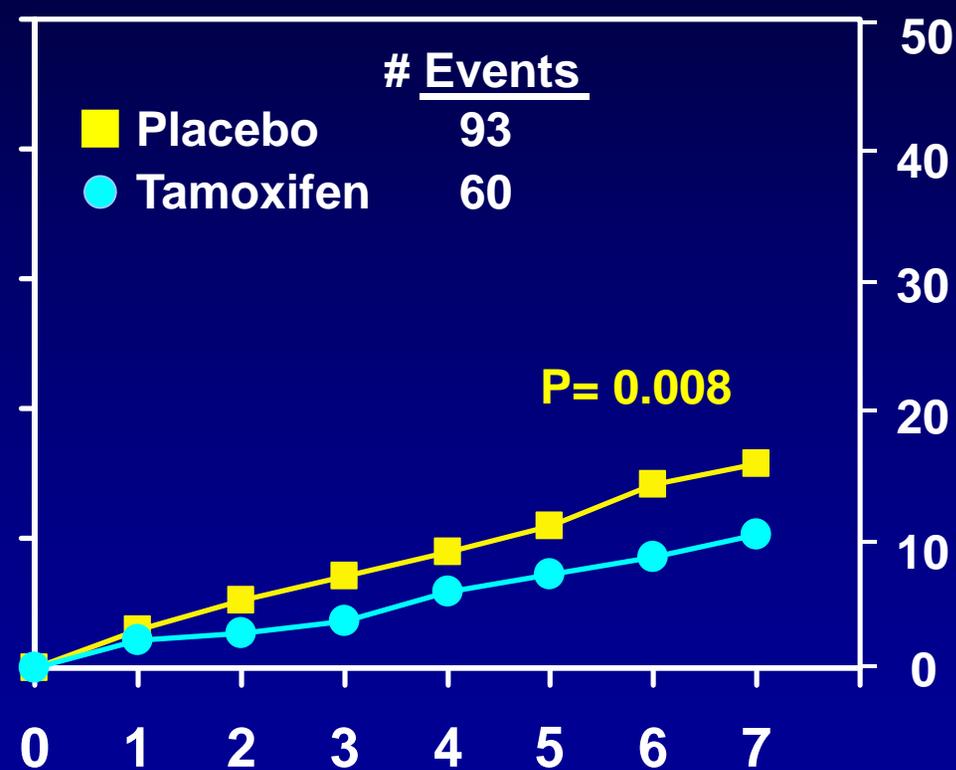
50% reduction

BCPT-P1

Invasive Breast Cancer



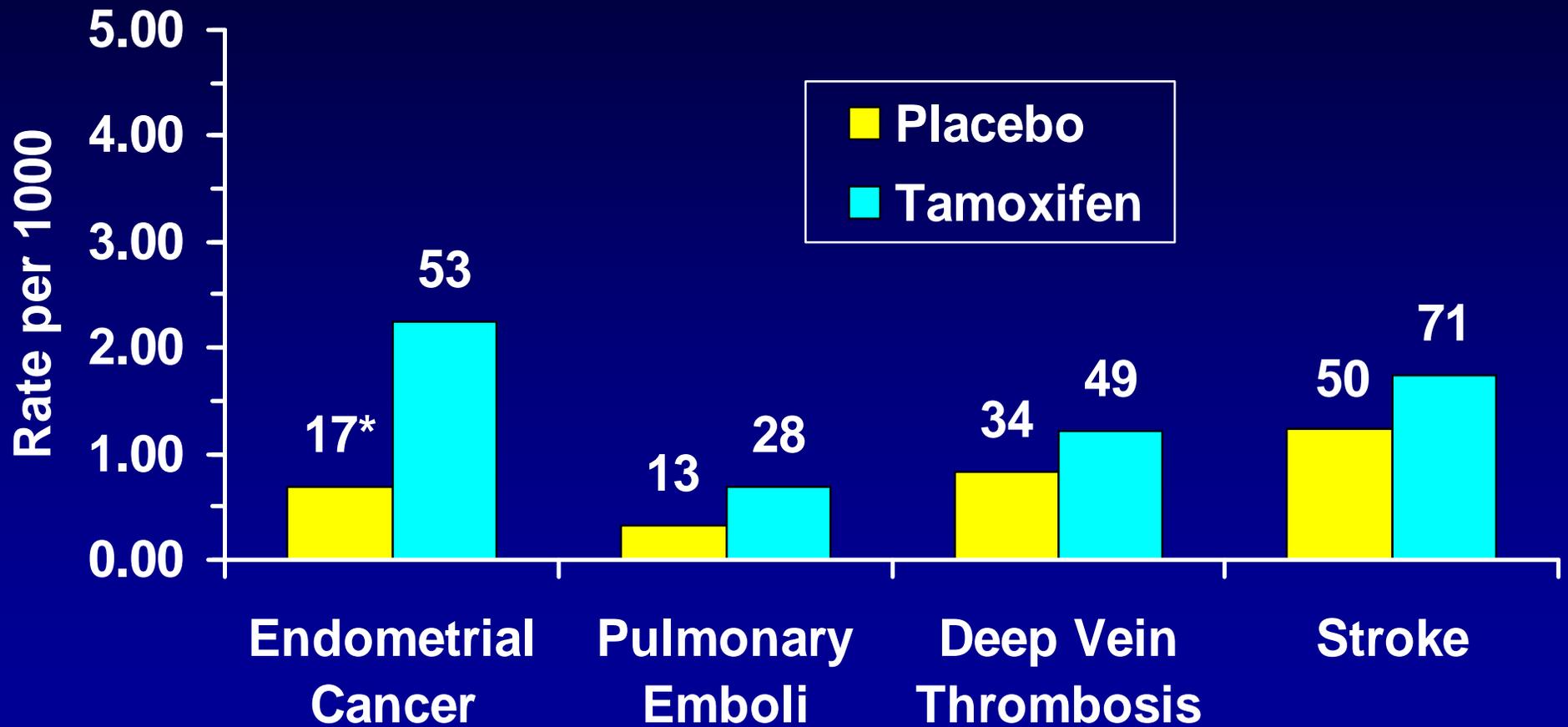
Noninvasive Breast Cancer



Time to Breast Cancer (Years)

BCPT-P1

Detrimental Events

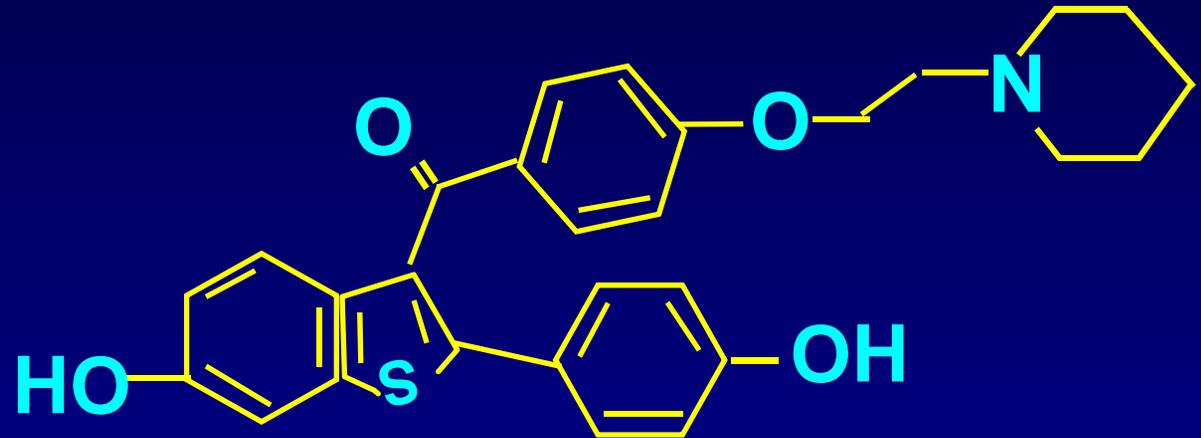


* Number of Events

Chemical Structure



Tamoxifen



Raloxifene

MORE Study

Postmenopausal women
with osteoporosis

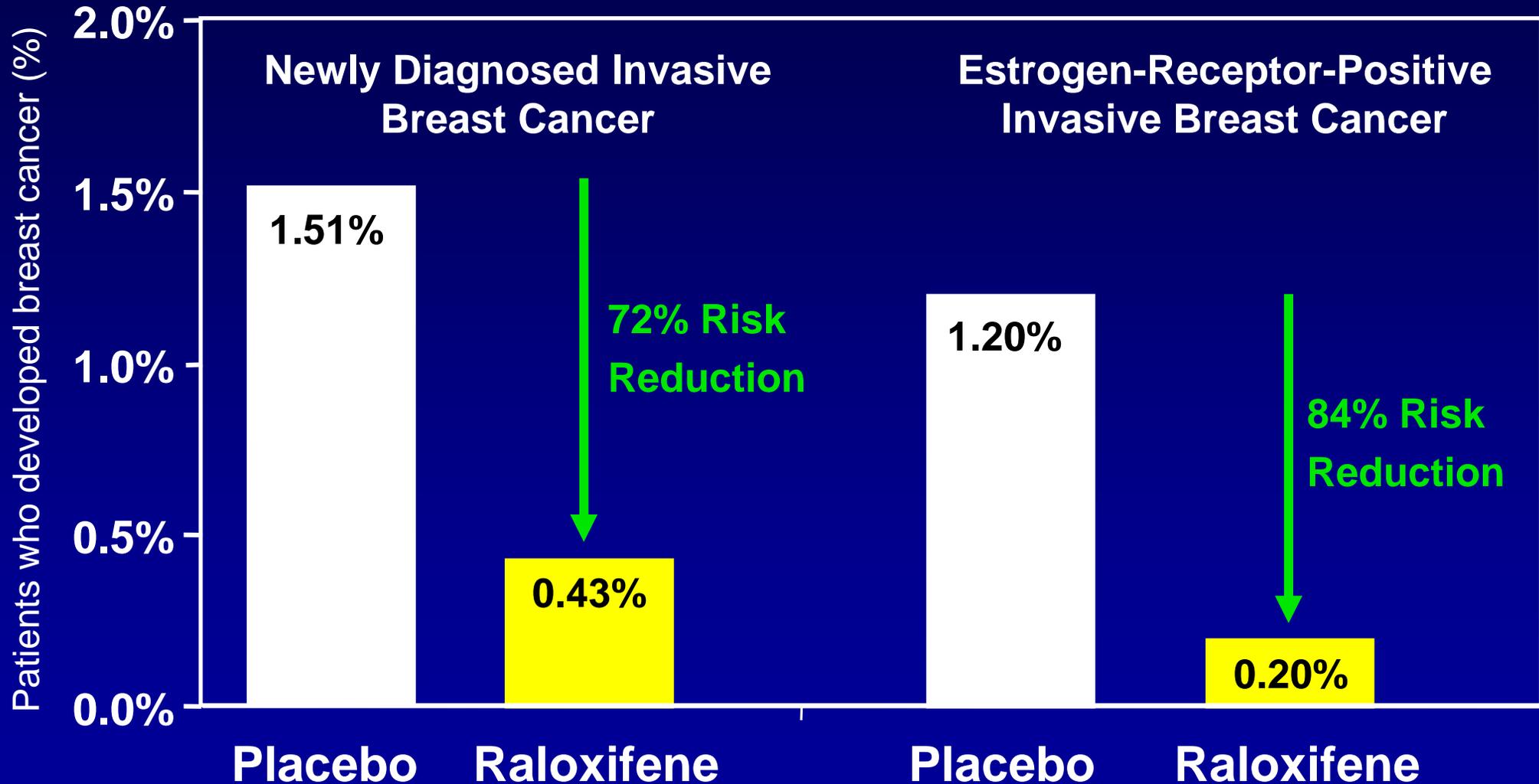
```
graph TD; A[Postmenopausal women with osteoporosis] --> B[Placebo]; A --> C[Raloxifene 60 mg/d]; A --> D[Raloxifene 120 mg/d]
```

Placebo

Raloxifene
60 mg/d

Raloxifene
120 mg/d

Four-Year Incidence Rates of Breast Cancer In the MORE Study



NSABP STAR Schema

**Risk-Eligible
Postmenopausal Women**

STRATIFICATION

- Age
- Relative Risk
- Race
- History of LCIS

TAMOXIFEN
20 mg/day
x 5 years

RALOXIFENE
60 mg/day
x 5 years

STAR Trial Objectives

Primary objective:

Evaluate the effect of raloxifene vs. tamoxifen in reducing the incidence of:

- Invasive breast cancer

STAR Trial Objectives

Secondary objectives:

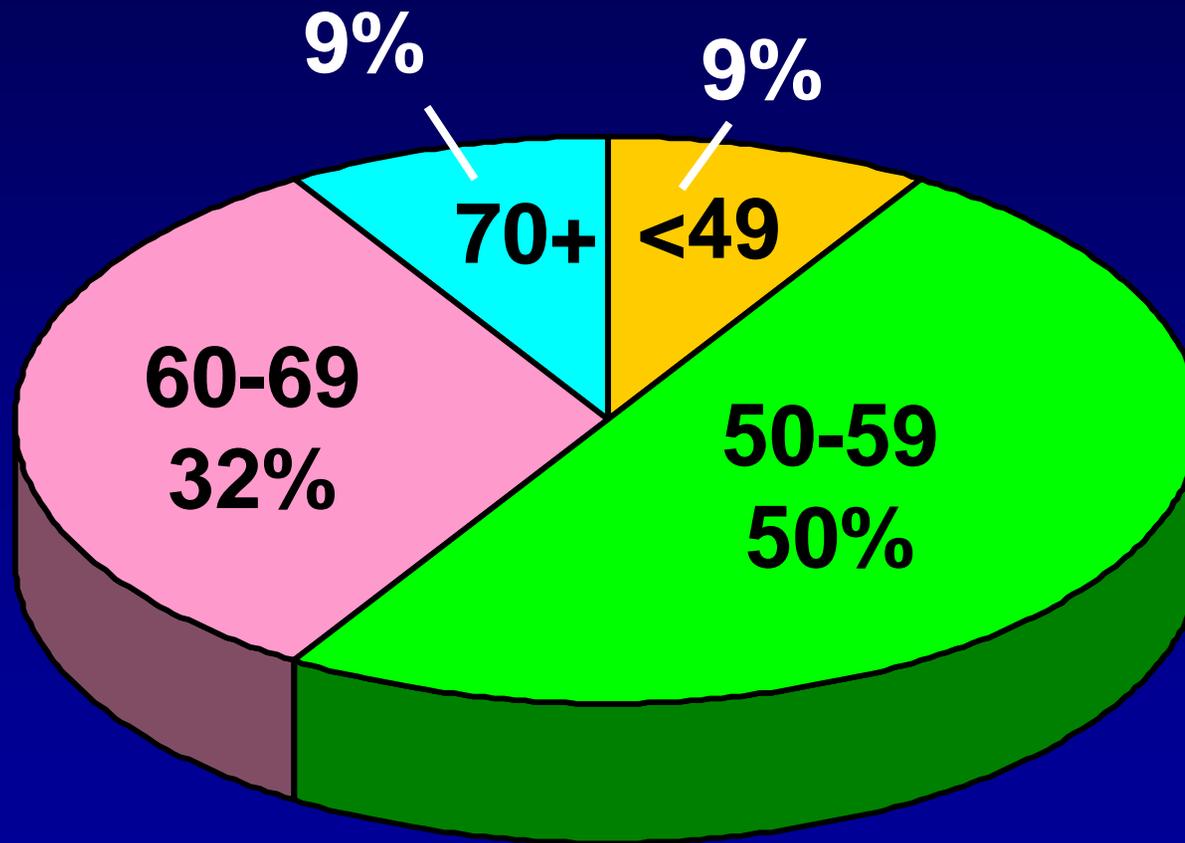
- Noninvasive breast cancer
- Endometrial cancer
- Ischemic Heart Disease
- Fractures of the:
 - Hip
 - Spine
 - Wrist (Colles')

STAR Summary of Screening, Accrual and Follow-Up Information

Women screened for breast cancer risk	184,460
Women who were breast cancer risk eligible	96,368
Women randomly assigned treatment	19,747
Total person-years of follow-up	76,828
Average follow-up (months)	47.3

P-2 STAR

Age Distribution



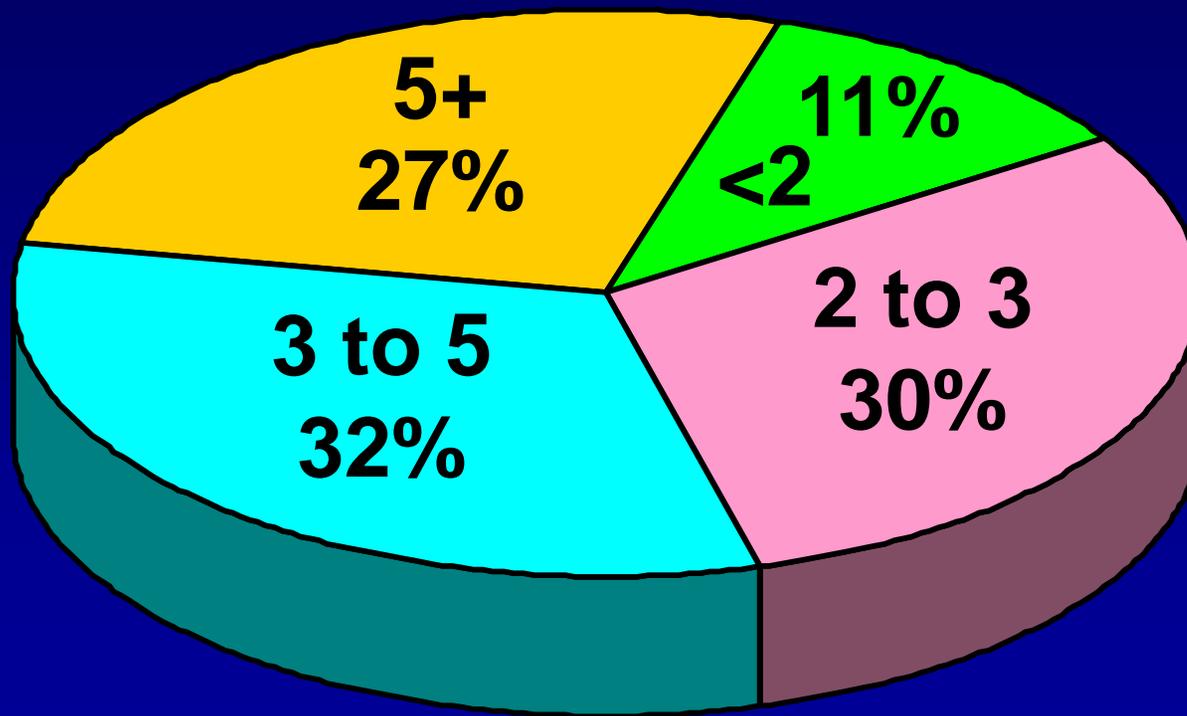
P-2 STAR

Racial/Ethnic Distribution (%)

	TAM	RAL
White	93.5	93.5
African-American	2.4	2.5
Hispanic	2.0	2.0
Other	2.1	2.1

P-2 STAR

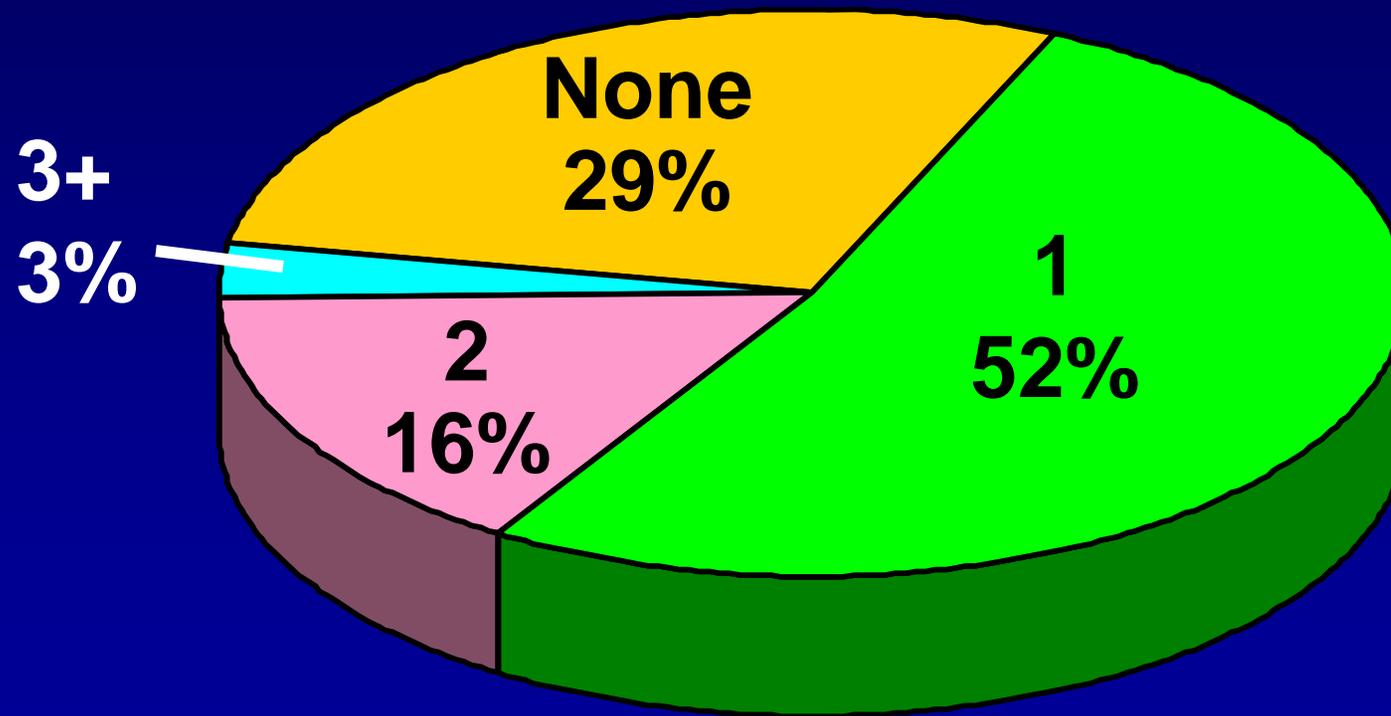
5-year Predicted Risk of Breast Cancer among Participants at Entry



Gail model risk score

P-2 STAR

First-Degree Relatives with Breast Cancer



P-2 STAR

Prior Hysterectomy	51.5% (10,027)
---------------------------	---------------------------------

P-2 STAR

LCIS

**Atypical
Hyperplasia**

Total Number

1,789

4426

**% of
Randomized**

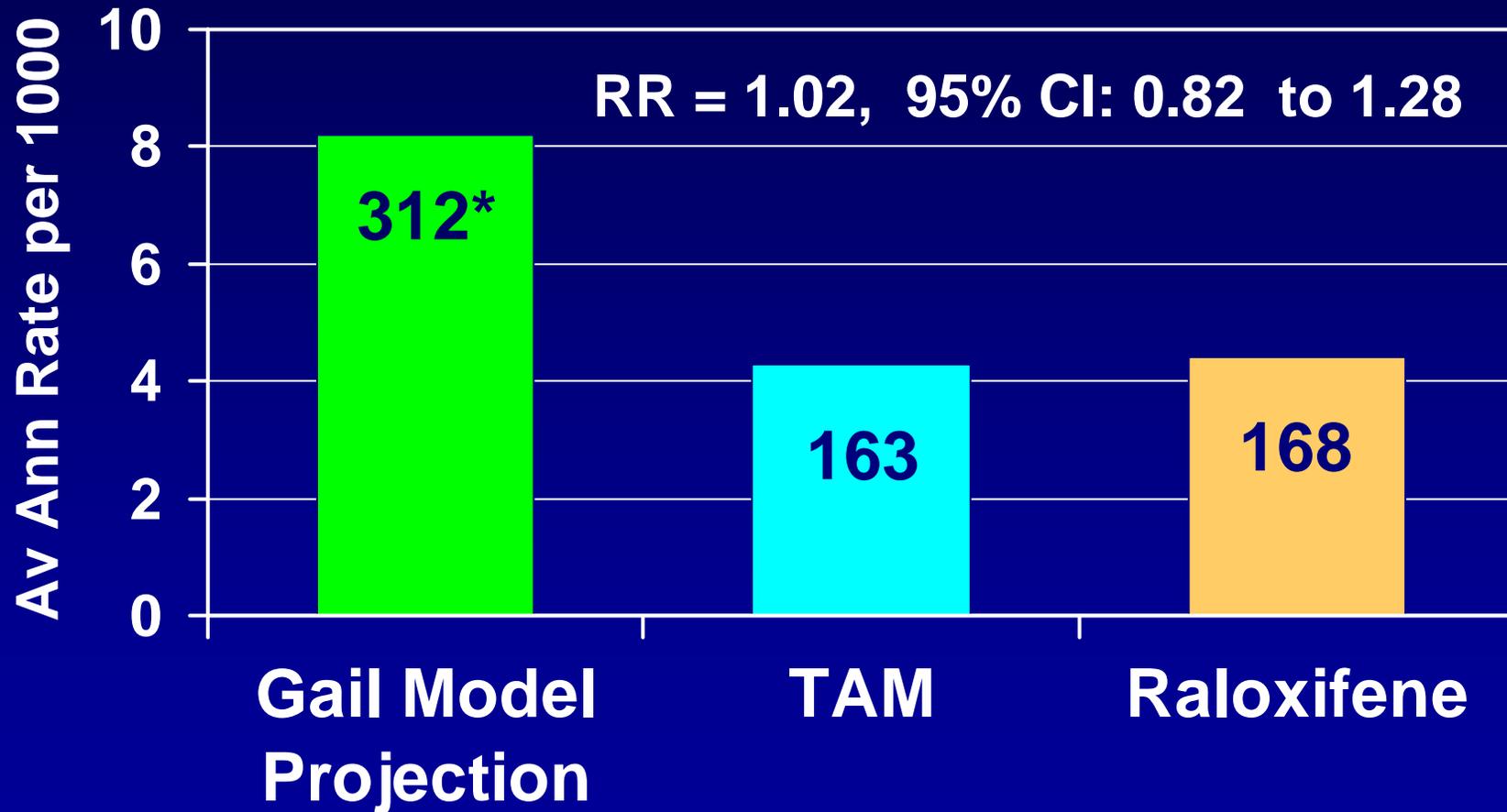
9.2

22.7

RESULTS

P-2 STAR

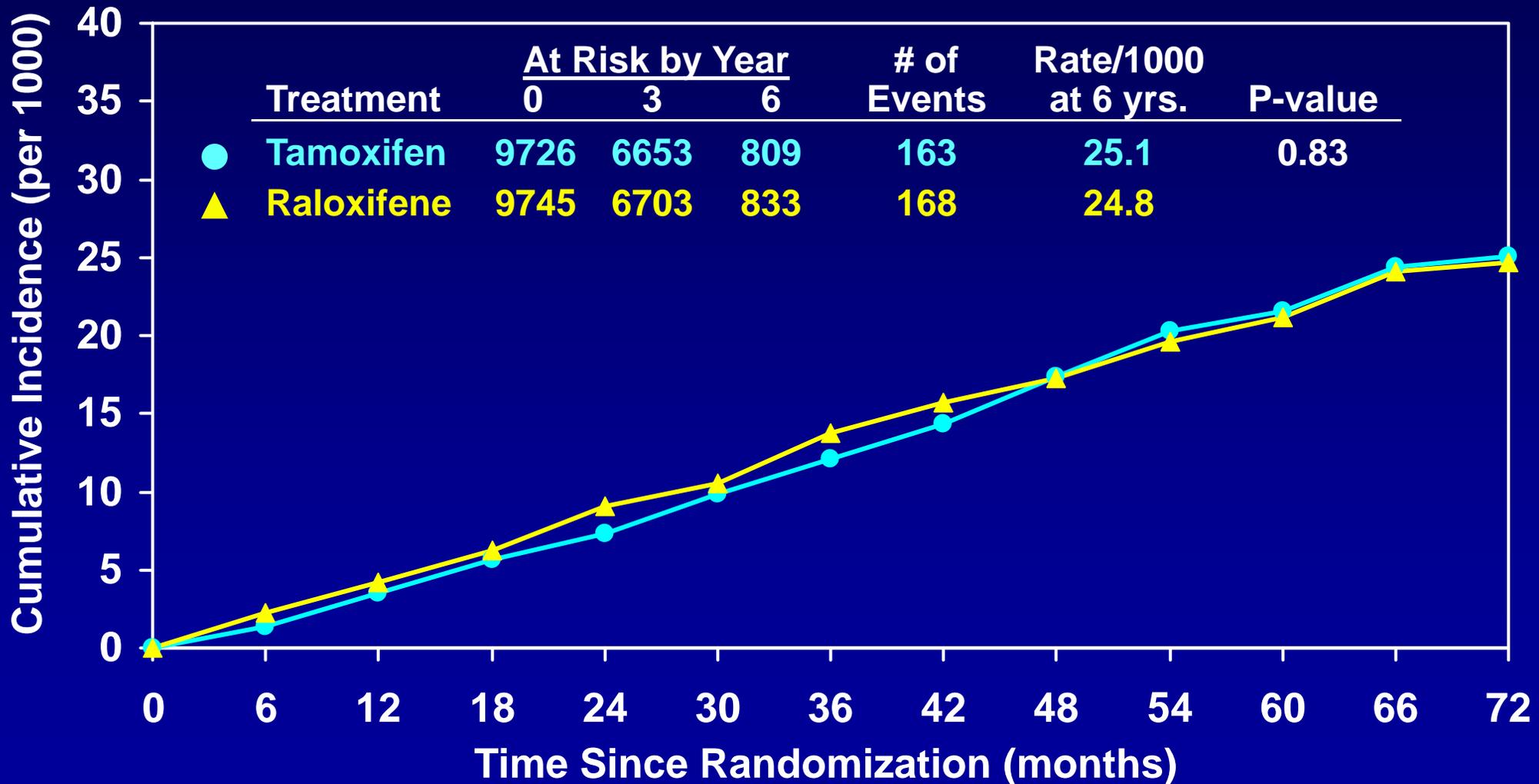
Average Annual Rate and Number of Invasive Breast Cancers



* # of events

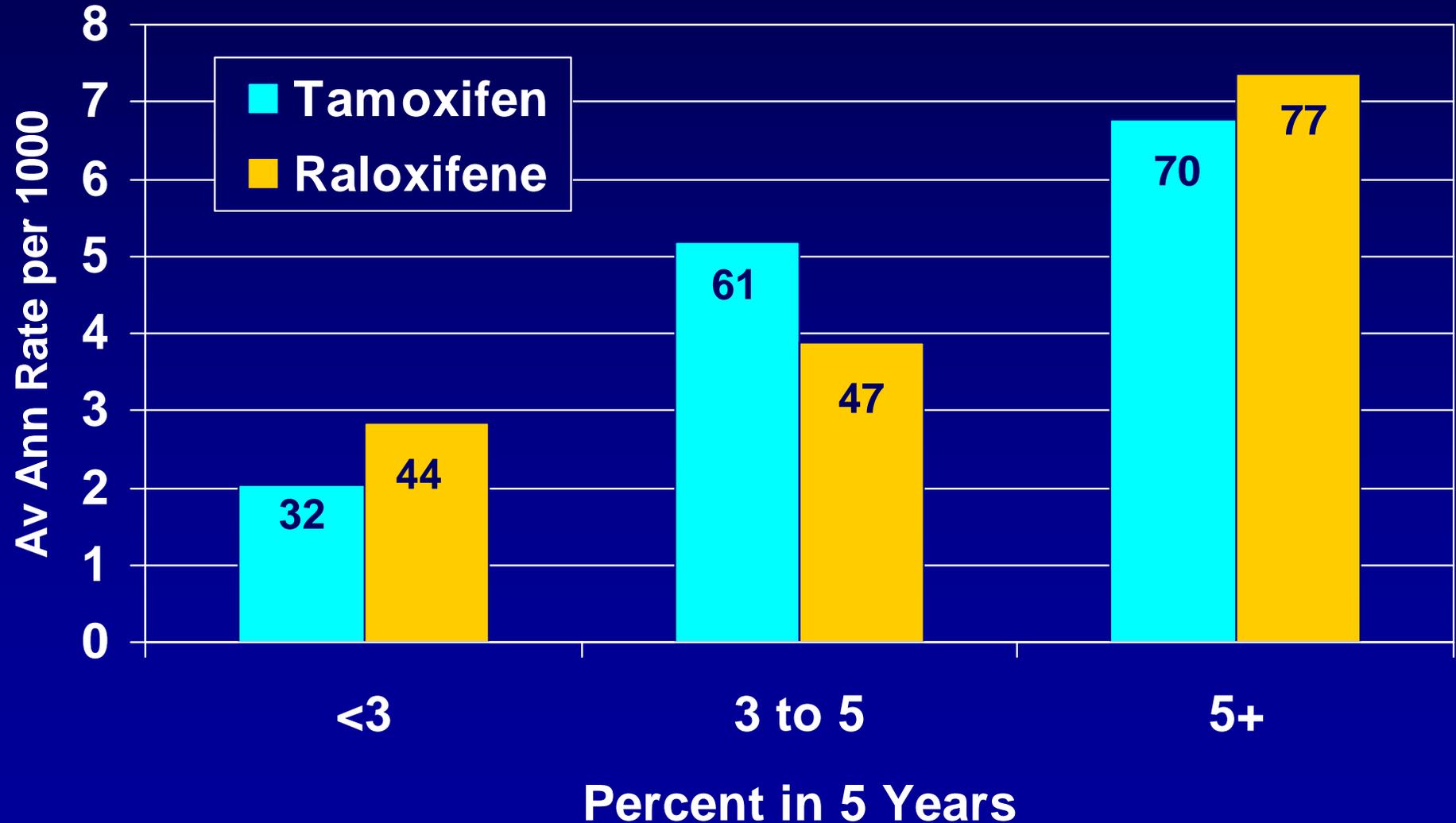
P-2 STAR

Cumulative Incidence of Invasive Breast Cancer



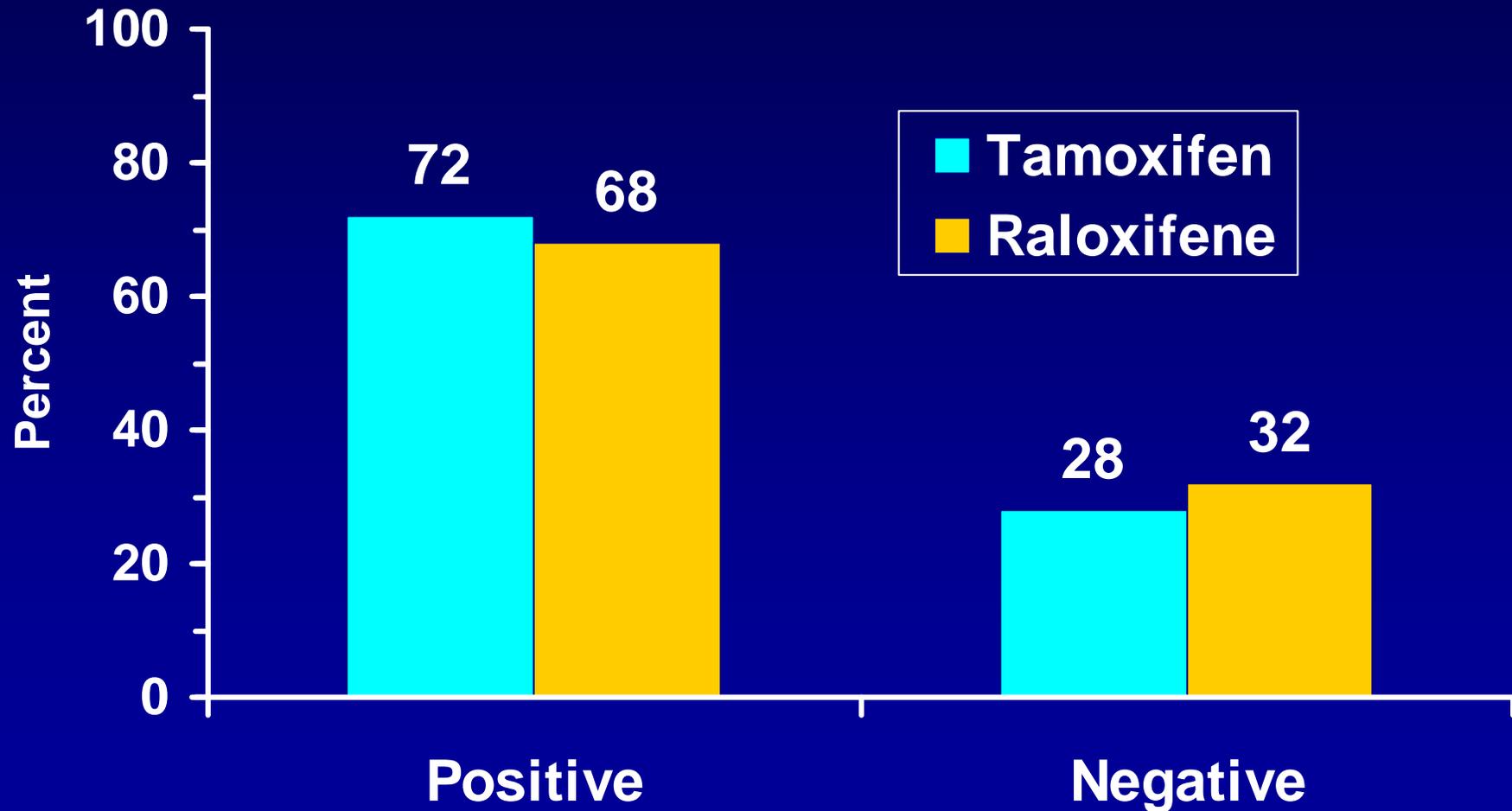
P-2 STAR

Average Annual Rate and Number of Invasive Breast Cancers by 5-year Gail Model Risk



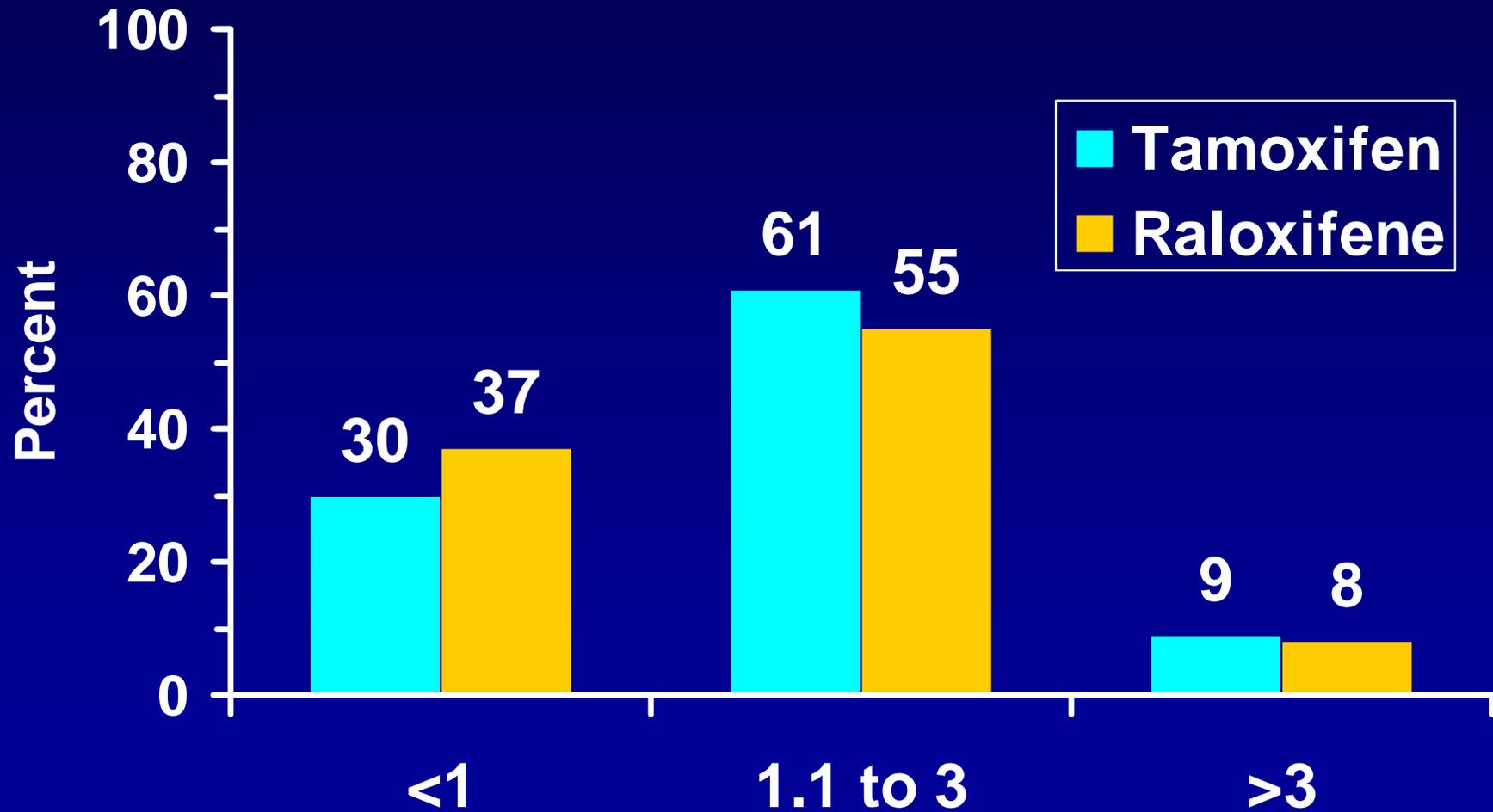
P-2 STAR

Estrogen Receptor of Invasive Cancers



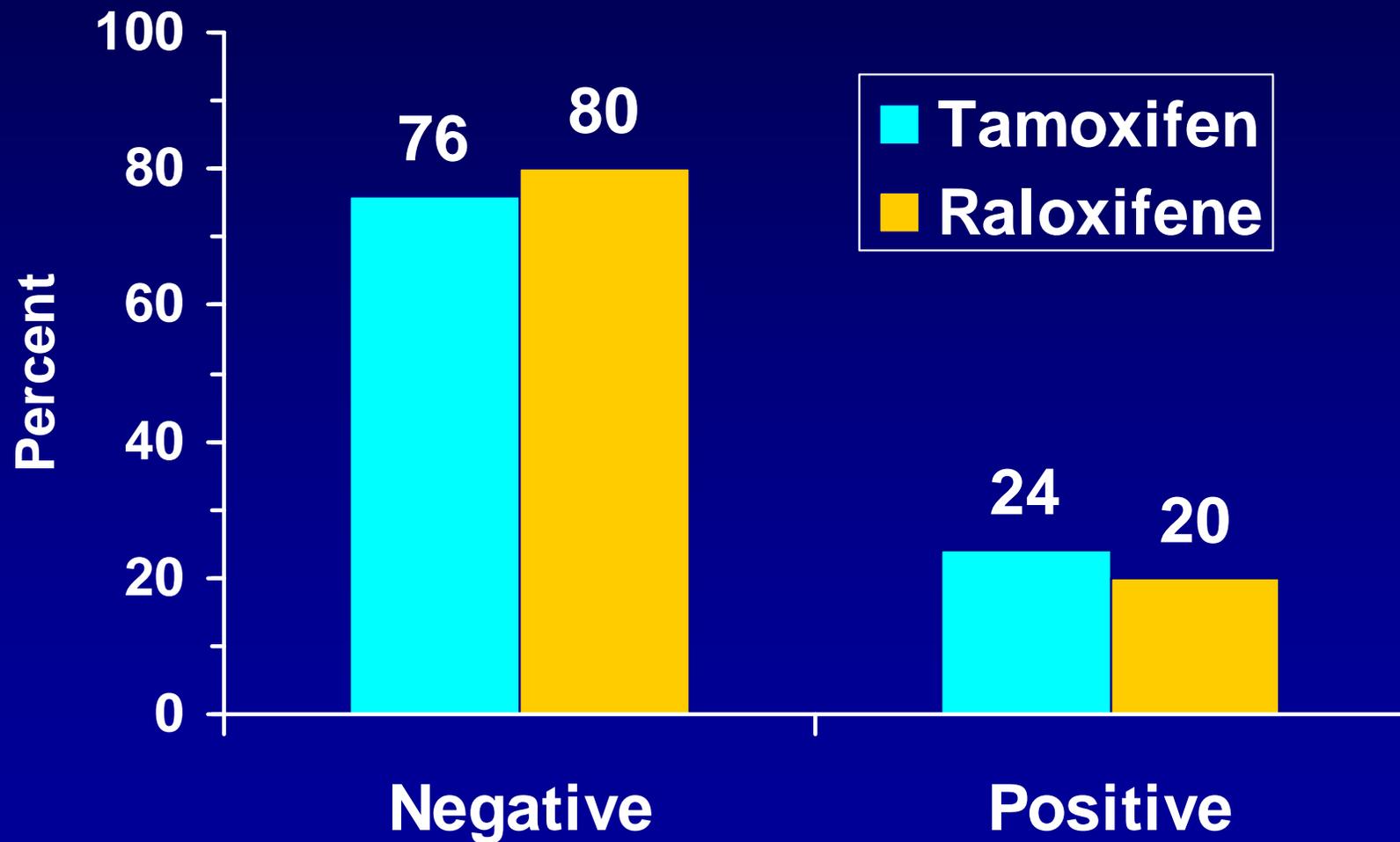
P-2 STAR

Tumor Size (cm) of Invasive Cancers



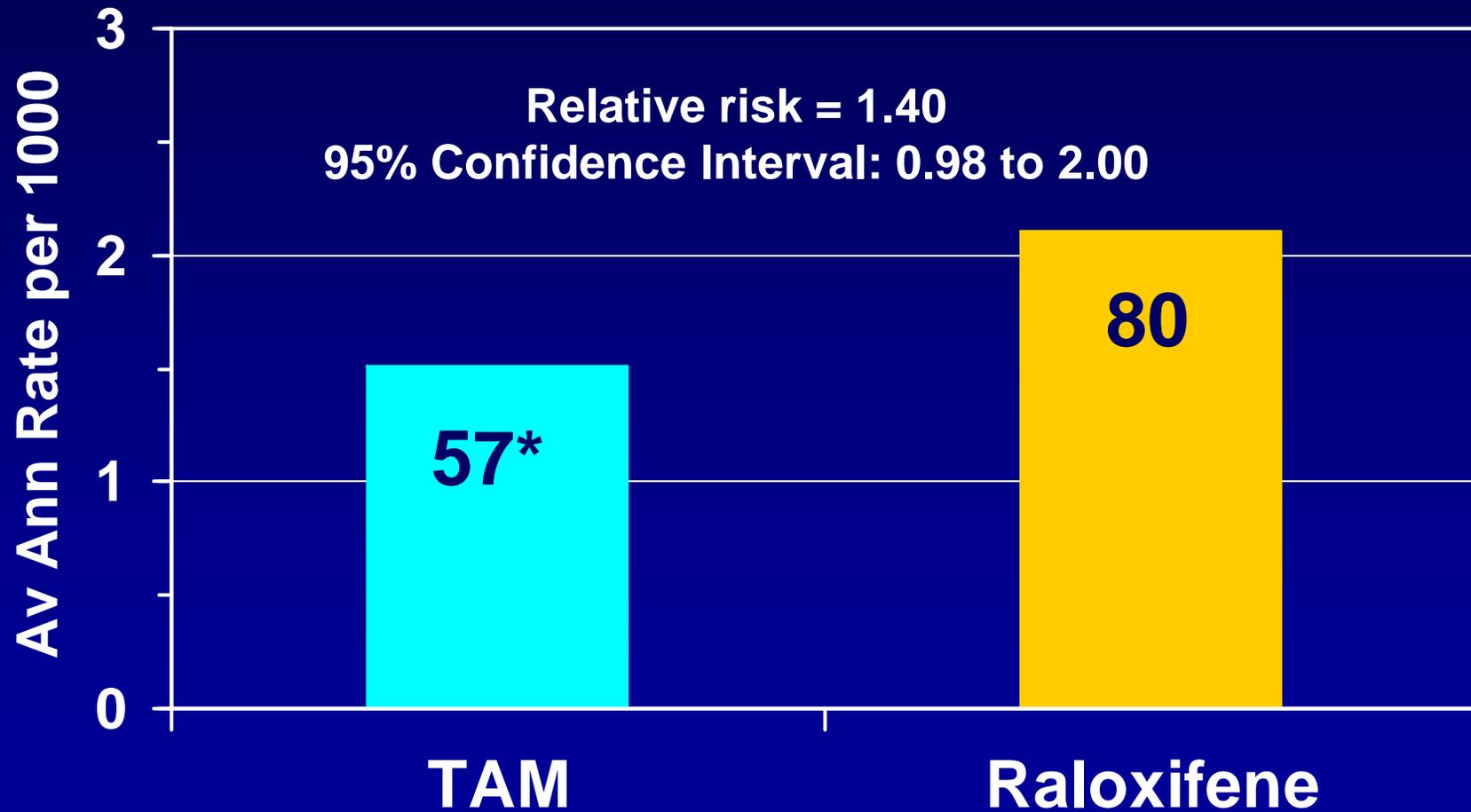
P-2 STAR

Nodal Status of Invasive Cancers



P-2 STAR

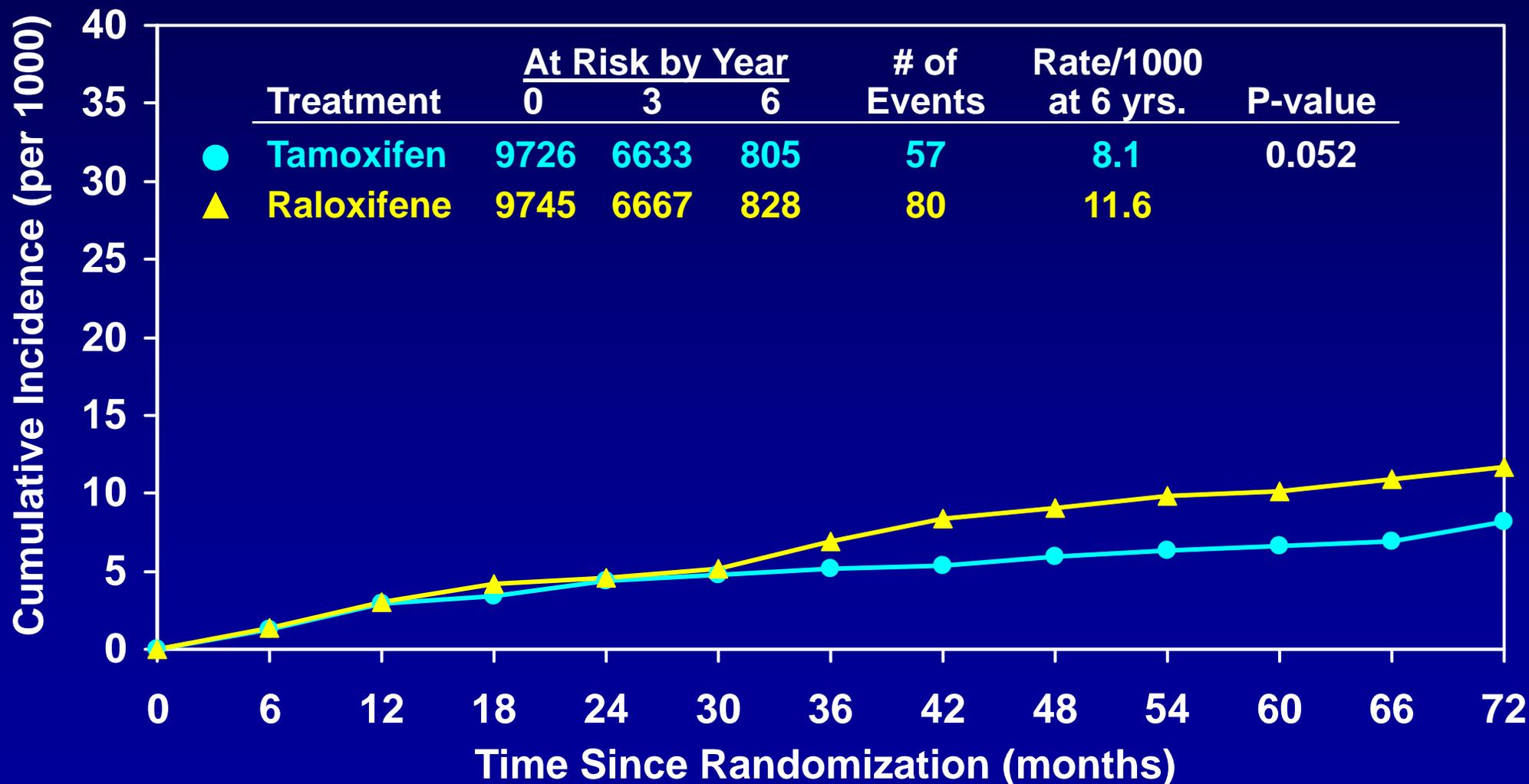
Average Annual Rate And Number Of Non-invasive (*In Situ*) Cancers

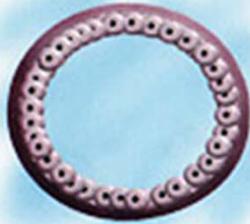


* # of events

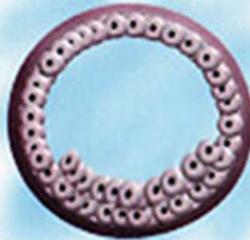
P-2 STAR

Cumulative Incidence of Non-Invasive Breast Cancer

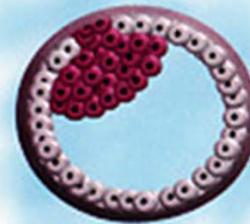




Normal Duct



Atypical Hyperplasia



In Situ Cancer



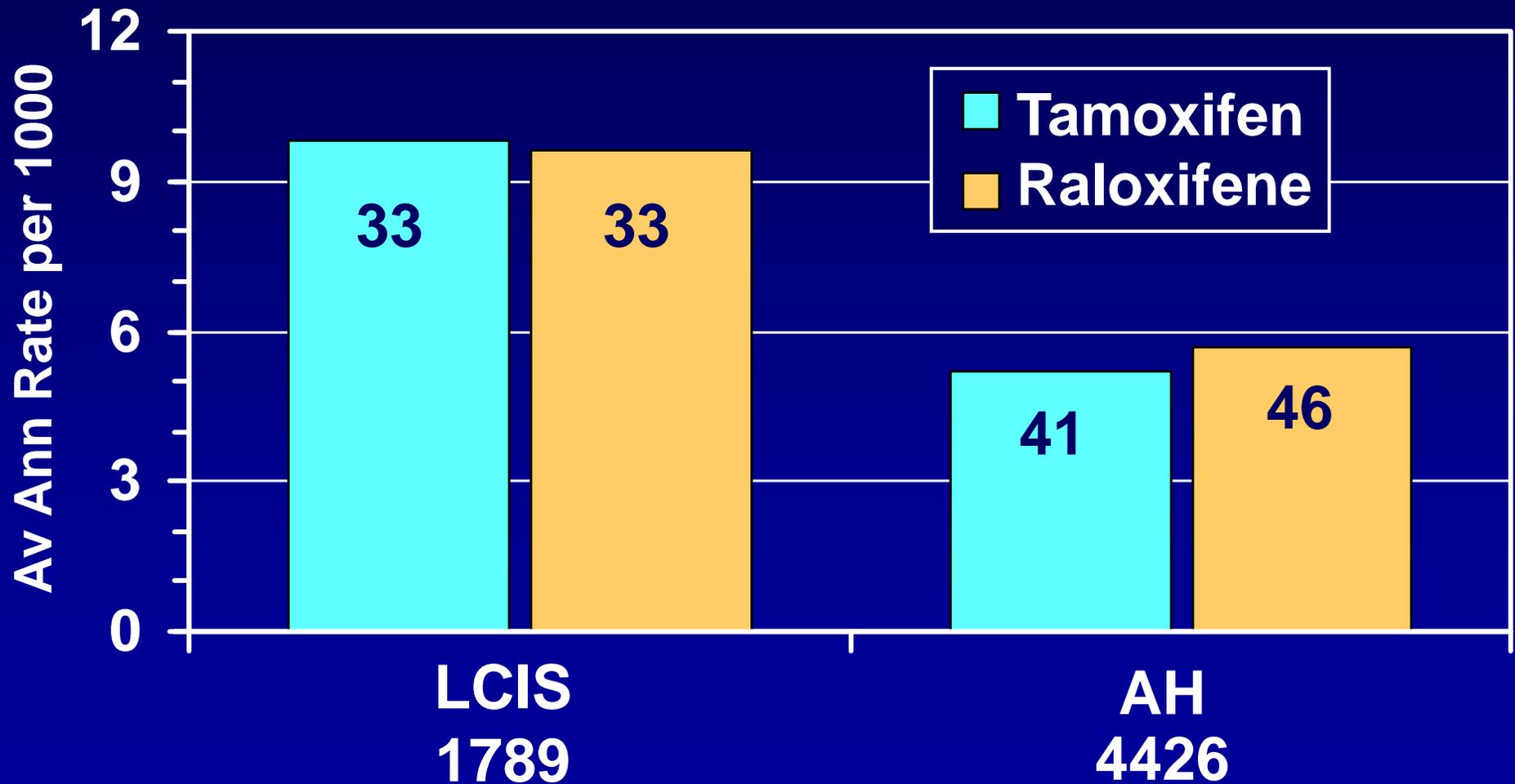
Invasive Cancer

Average Annual Rate of Non-Invasive Breast Cancer by Treatment Group

Tumor Type	# of Events		Rate per 1000		Risk Ratio	RR 95% Confidence Interval
	TAM	RAL	TAM	RAL		
DCIS	30	44	0.79	1.16	1.46	0.90-2.41
LCIS	21	29	0.56	0.76	1.37	0.76-2.54
Mixed	6	7	0.16	0.18	1.16	0.33-4.18
Total	57	80	1.51	2.11	1.40	0.98-2.00

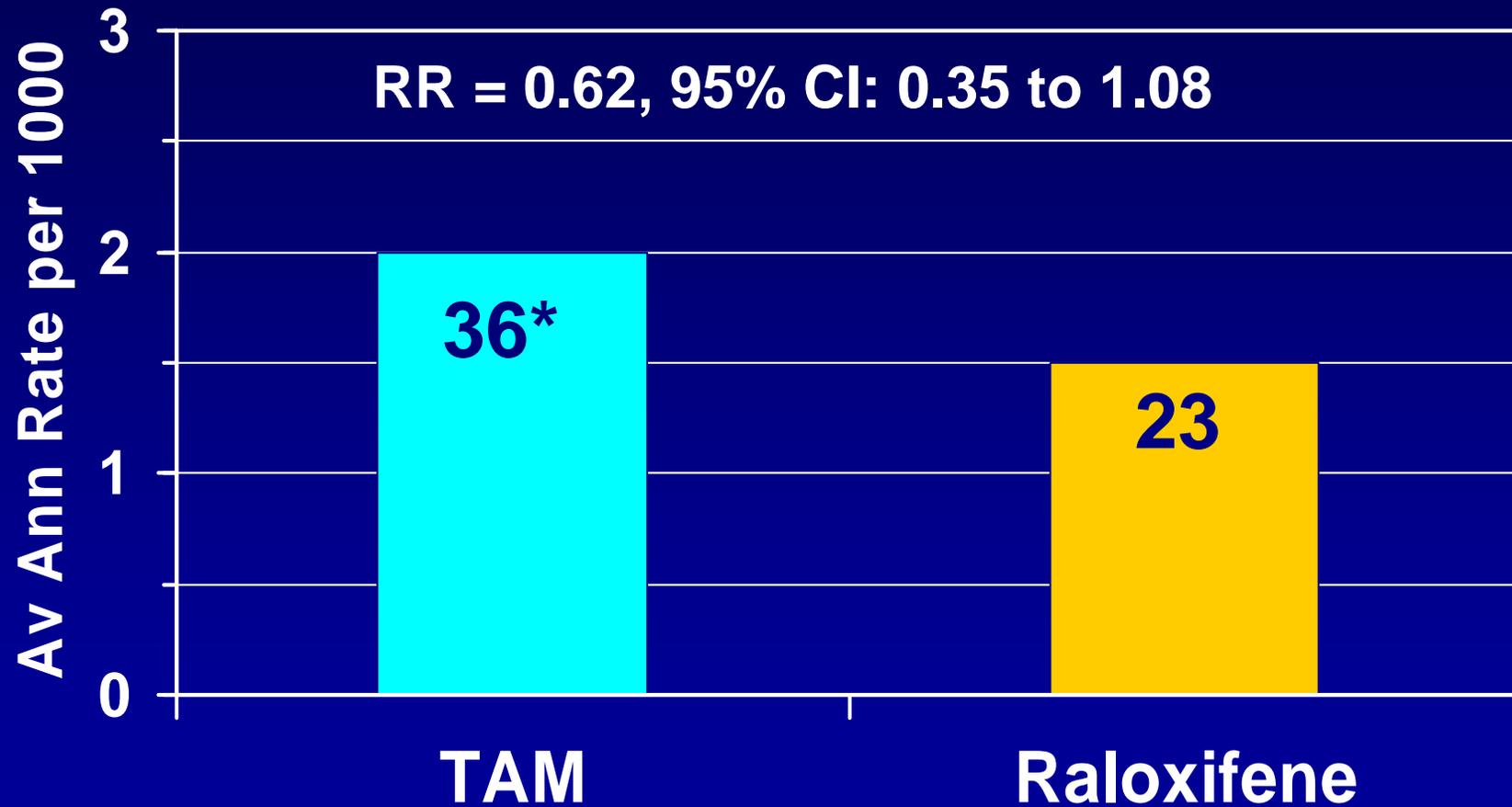
P-2 STAR

Average Annual Rate and Number of Invasive Breast Cancers by History of Atypical Hyperplasia and Lobular Carcinoma *in Situ*



P-2 STAR

Average Annual Rate and Number of Uterine Cancers



* # of events

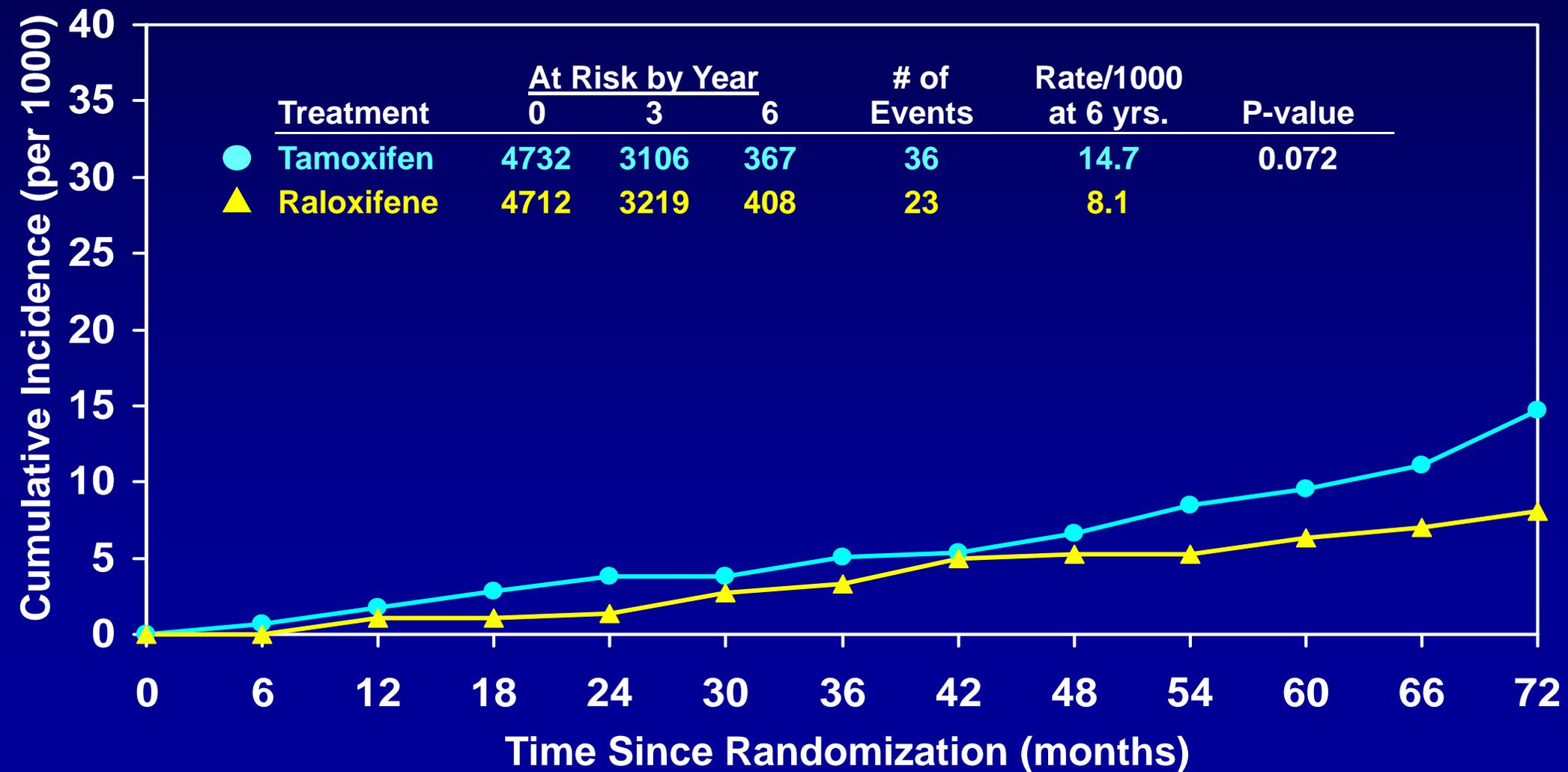
P-2 STAR: Hysterectomy* and Endometrial Hyperplasia

	Tam #	Ral #	Risk Ratio (RR)	RR 95% Confidence Interval
Hysterectomy*	244	111	0.44	0.35-0.56
Hyperplasia	84	14	0.16	0.09-0.29
with atypia	12	1	0.08	0.00-0.55
without atypia	72	13	0.18	0.09-0.32

* Among women not diagnosed with uterine cancer

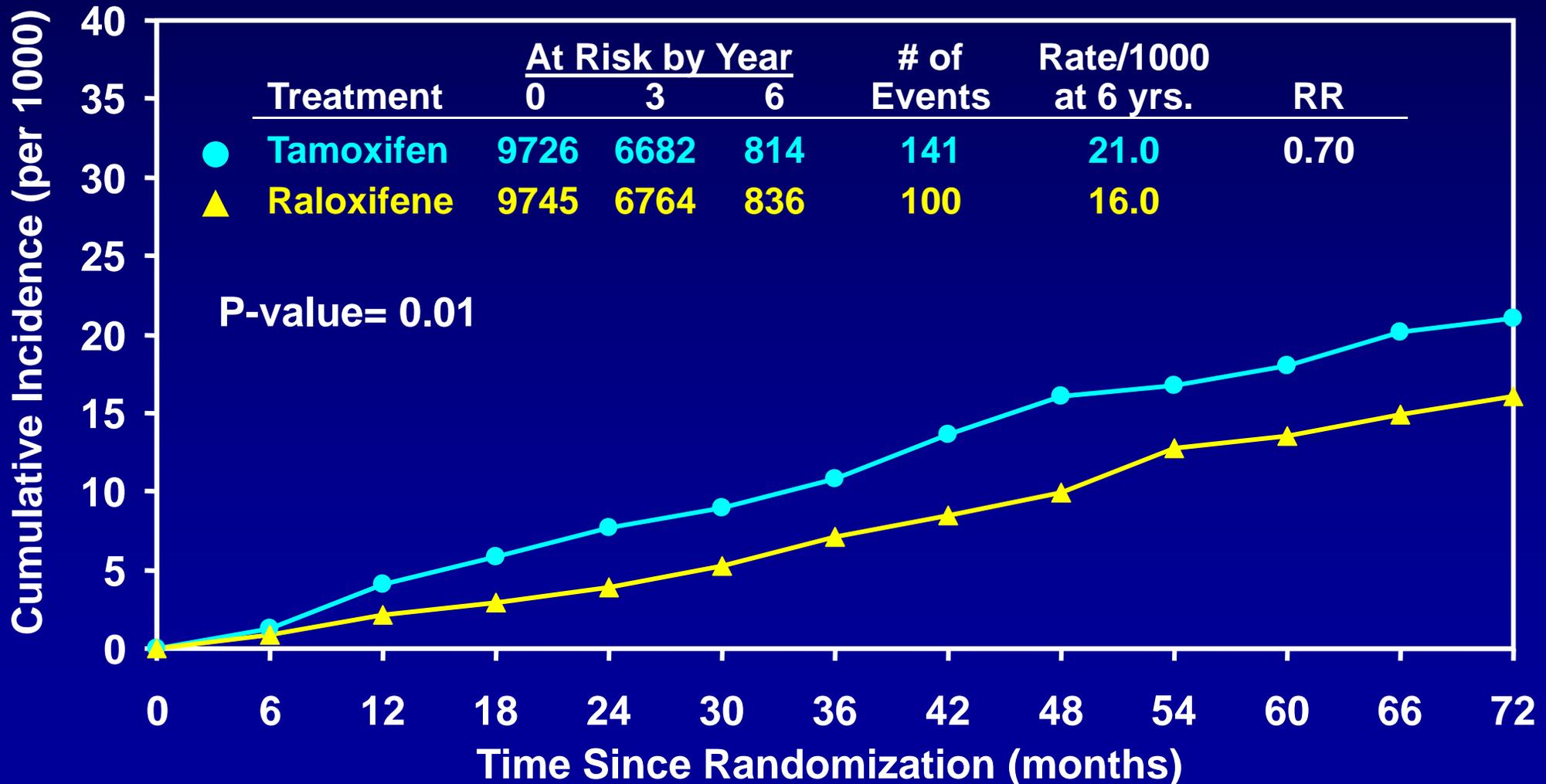
P-2 STAR

Cumulative Incidence of Uterine Cancer



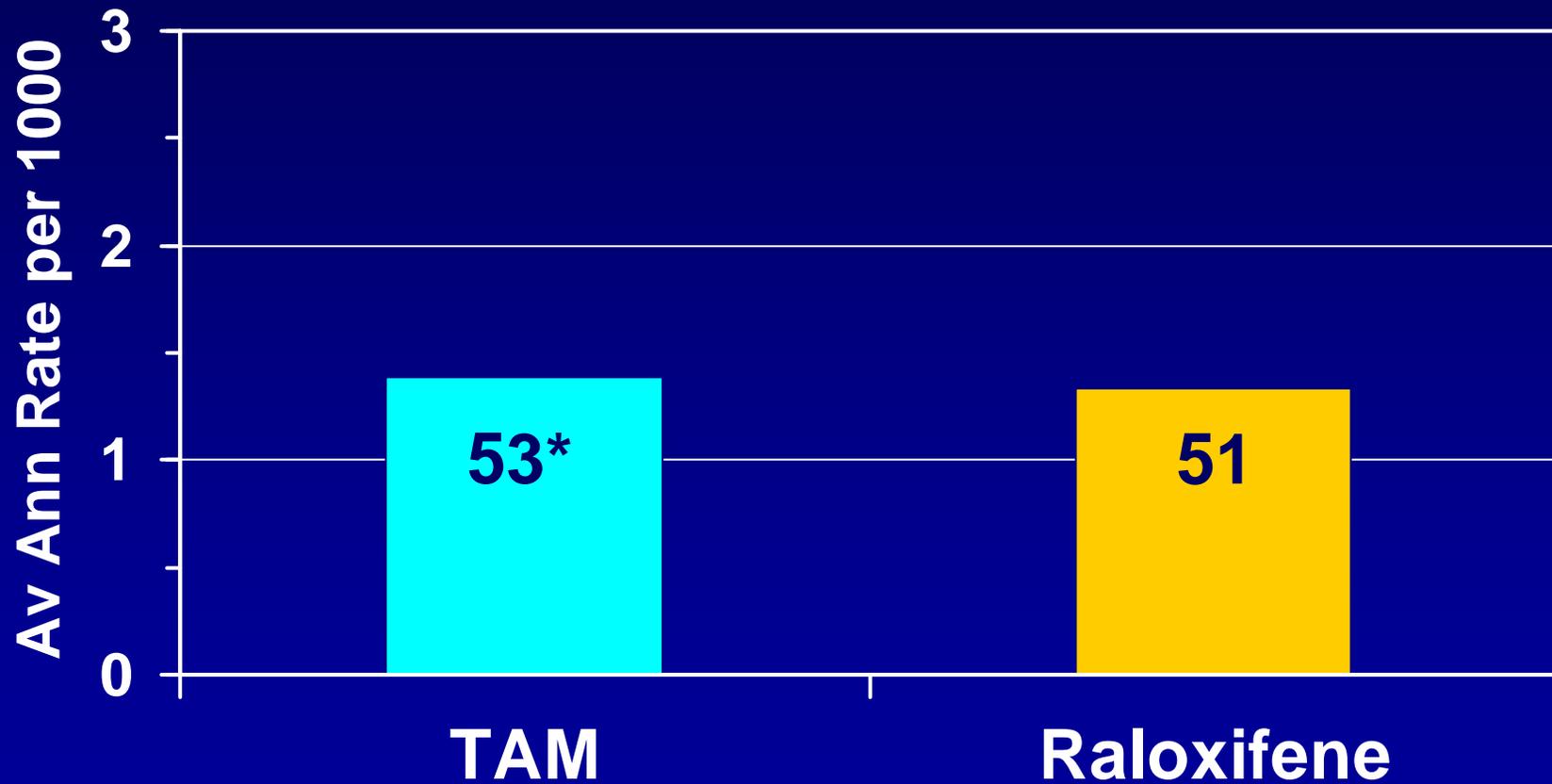
P-2 STAR

Cumulative Incidence of Thromboembolic Events



P-2 STAR

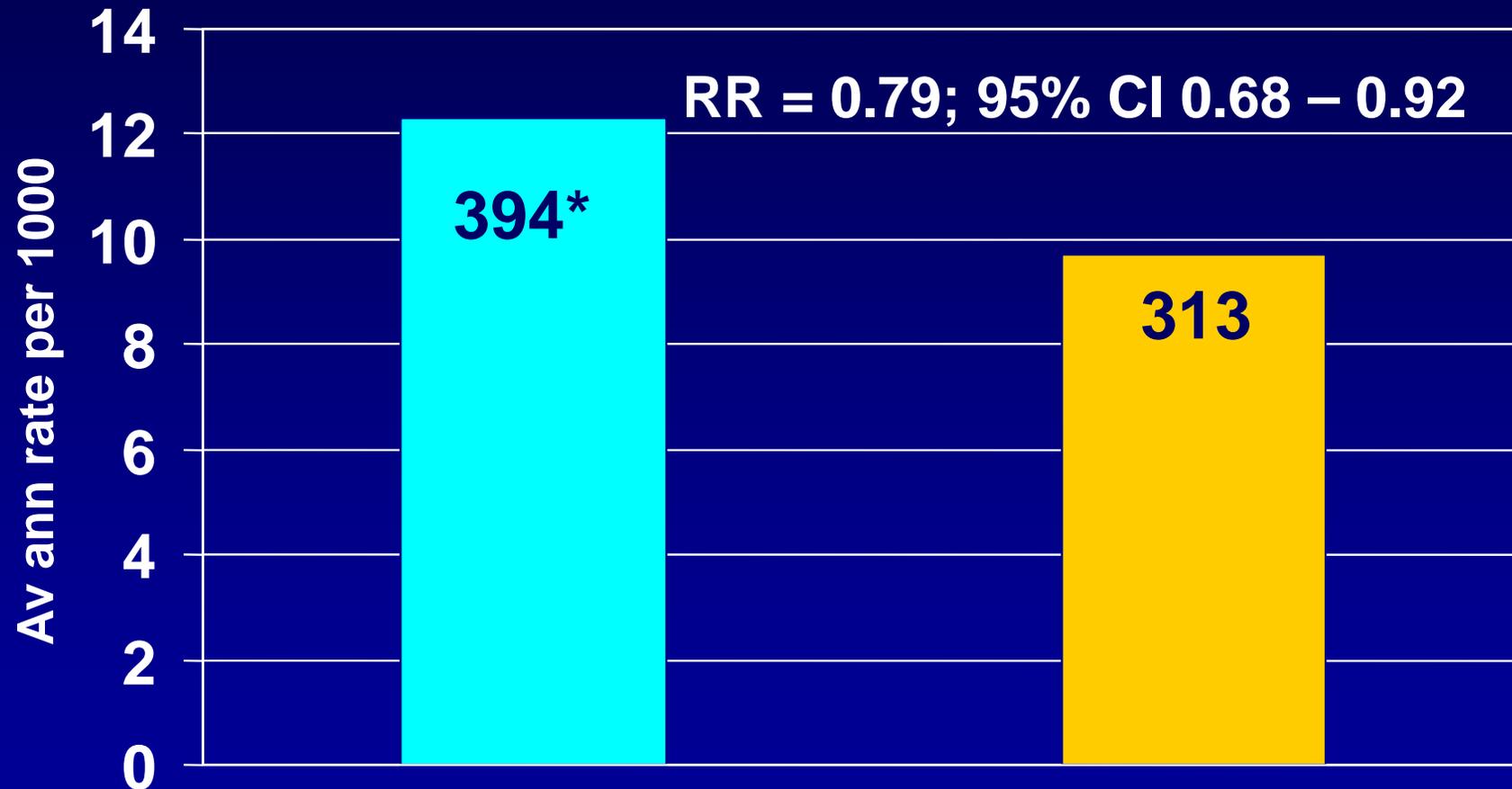
Average Annual Rate and Number of Strokes



* # of events

P-2 STAR

Average Annual Rates of Cataracts



* # of events

TAM

Raloxifene

P-2 STAR

Number of Osteoporotic Fractures by Site and Treatment Group

Type of event	Tamoxifen #	Raloxifene #	Risk Ratio (RR)	RR 95% Confidence Interval
Hip	26	23	0.88	0.48-1.60
Spine	53	52	0.98	0.65-1.46
Radius (Colles')	27	23	0.85	0.46-1.53
Total	106	98	0.92	0.69-1.22

P-2 STAR

QOL Summary

- **No significant difference in primary QOL endpoints; minimal symptom severity**
- **Symptom profile: small differences slightly favoring raloxifene**
- **Sexual function slightly favors tamoxifen**
- **Decision to take one or the other can be assisted by patient-reported outcomes**

P-2 STAR

Summary

- **Raloxifene is as effective as tamoxifen in the prevention of primary invasive breast cancer**
- **Raloxifene is less effective than tamoxifen in the prevention of non-invasive breast cancer (LCIS & DCIS)**
- **Compared to tamoxifen, raloxifene use results in:**
 - **Fewer thromboembolic events**
 - **Fewer endometrial cancers and**
 - **Fewer cataracts**



Study of Tamoxifen
And Raloxifene

NSABP P-4 Schema

**Risk-Eligible
Postmenopausal Women**

STRATIFICATION

- Age
- Relative Risk
- Race
- History of LCIS

**Raloxifene
60 mg / day
x 5 years
+
Letrozole Placebo
x 5 years**

**Letrozole
2.5 mg / day
x 5 years
+
Raloxifene Placebo
x 5 years**

BREAST CANCER



1998

USA

First-Class

NSABP P-4 Schema

**Risk-Eligible
Postmenopausal Women**

STRATIFICATION

- Age
- Relative Risk
- Race
- History of LCIS

**Raloxifene
60 mg / day
x 5 years
+
Letrozole Placebo
x 5 years**

**Letrozole
2.5 mg / day
x 5 years
+
Raloxifene Placebo
x 5 years**

