



Jeanne Petrek, M.D.

Breast surgeon

Researcher

Teacher

Patient advocate

Wife

Mother

Colleague

Friend

Halsted, Fisher, Peto and the Re-Emergence of Reason

The rumors of the death of breast surgery have been greatly exaggerated.





Background

- Halsted hypothesized that the extent of surgery impacted eventual outcome in (stage III) breast cancer. Lowered local regional recurrence rates from 60% to 15% establishing the radical mastectomy as the gold standard for nearly 100 years.
- Urban's attempts to expand the radical mastectomy did not impact survival.
- Fisher declared that breast cancer was a systemic disease from its inception.
- Trials of BCT failed to show a survival disadvantage in those groups with a higher local recurrence rate.

Randomized Trials of Mastectomy vs. CS + RT

<u>Trial</u>	<u>Follow-up (yrs.)</u>	<u>Overall Survival</u>	
		<u>Lumpectomy</u>	<u>Mastectomy</u>
Gustave-Roussy	15	73	65
Milan	20	42	41
NSABP B06	20	46	47
NCI	18	59	58
EORTC	10	65	66
Danish	6	79	82

Fall out.....

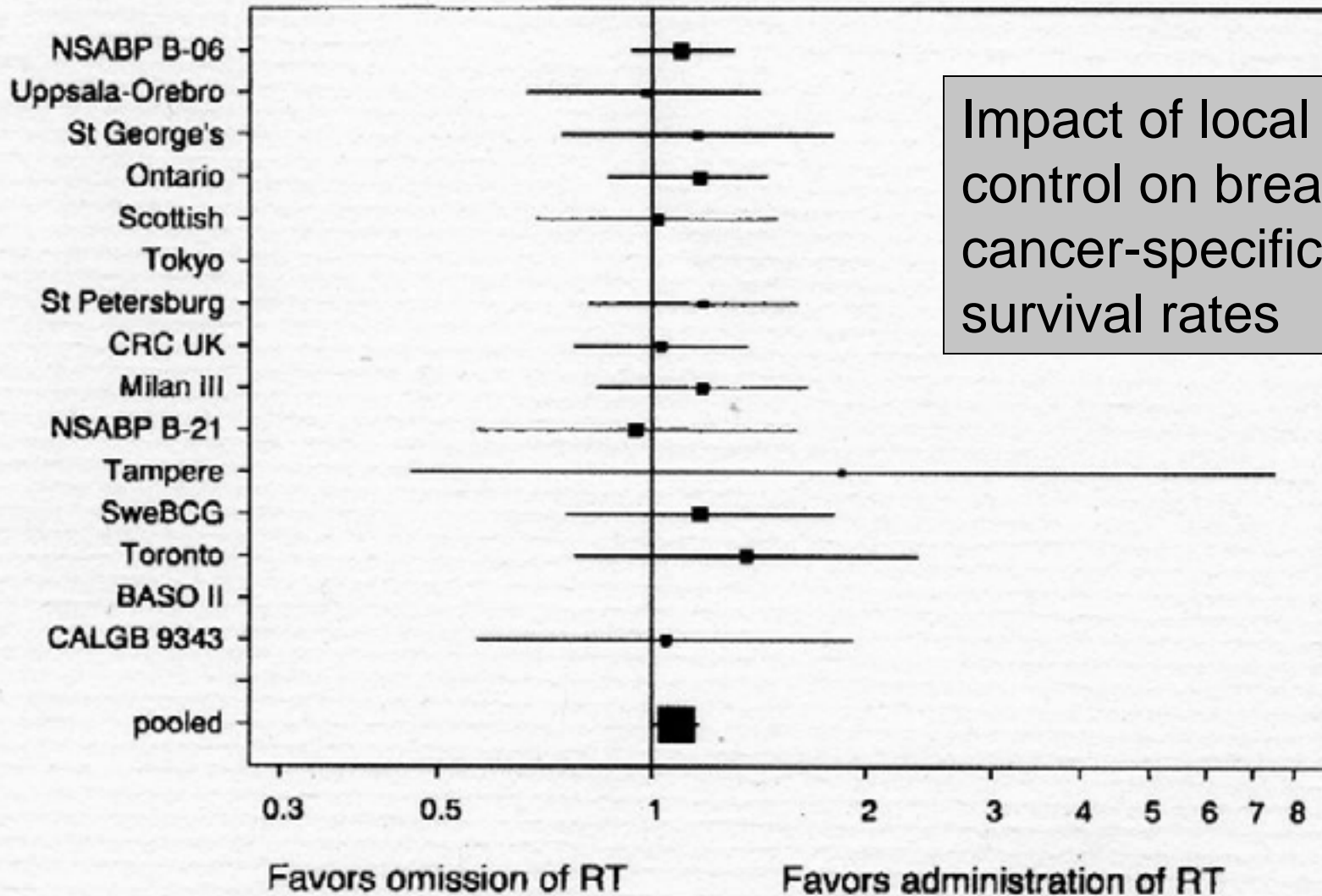
- Value of local regional control fell while value of systemic therapy rose.
 - Decade of the 1990s was the 'chemo decade';
- Fundamental trials, such as a margin width trial never carried out.
- Breast surgery 'dying specialty'; SSO Breast Surgery Fellowship Program rejected in the 1990s;
- Reimbursement for breast surgery fell precipitously between 1990 and 2000; emerging techniques such as SNB introduced at a very low rate of reimbursement.
- Suggestion for extreme surgical minimalism; the demise of the mastectomy.

Bernard Fisher, M.D.

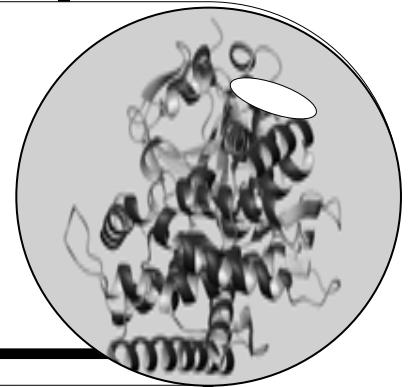
- “It has been one of my secret goals to eliminate mastectomy....and, we have done it. There is no reason to mention mastectomy to the overwhelming majority of our patients today. This is one of my proudest accomplishments.”
 - Miami International Breast Conference 2003; Neal Love Productions (Research to Practice: Breast Cancer Update audio series)

Local Control Impacts Breast Cancer Specific Survival

Vinn et al, JCO, February 2004



Early Breast Cancer Trialists' Collaborative Group (EBCTCG)

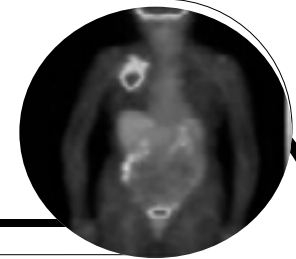


Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival:
an overview of the randomised trials

(The Lancet 2005; 366: 2087-2106)

EBCTCG Lancet 2005; 366: 2087-2106

Hypothesis



In early breast cancer, variations in local treatment that substantially affect the risk of locoregional recurrence could also affect long-term breast cancer mortality.

The individual trials of BCT with and without radiation vs. mastectomy were under-powered to detect a survival difference attributed to local recurrence.

To examine this relationship, collaborative meta-analyses were undertaken, based on individual patient data, of the relevant randomised trials that began by 1995.

Data available



Information was available on 42 000 women in 78 randomised treatment comparisons:

- radiotherapy vs no radiotherapy, 23 500
- more vs less surgery, 9300
- more surgery vs radiotherapy, 9300

Breast-conserving surgery (BCS)

There were 7300 women with BCS in trials of \pm RT
RT was generally just to the conserved breast

5-year local recurrence risks (mainly in the conserved breast):

- 7% vs 26% (reduction 19%)

15-year breast cancer mortality risks:

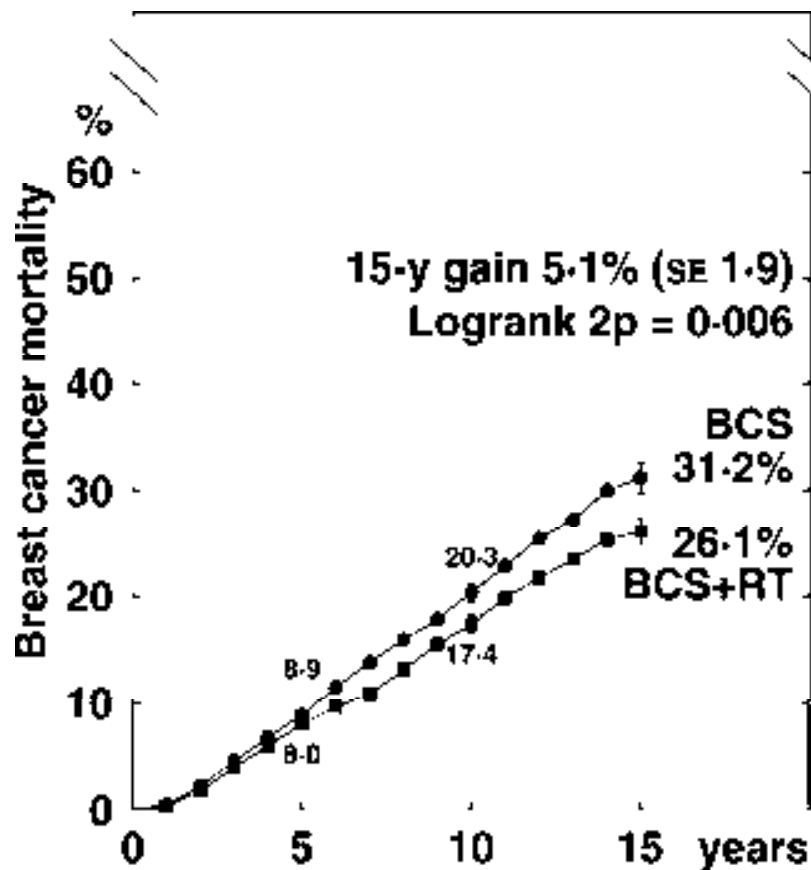
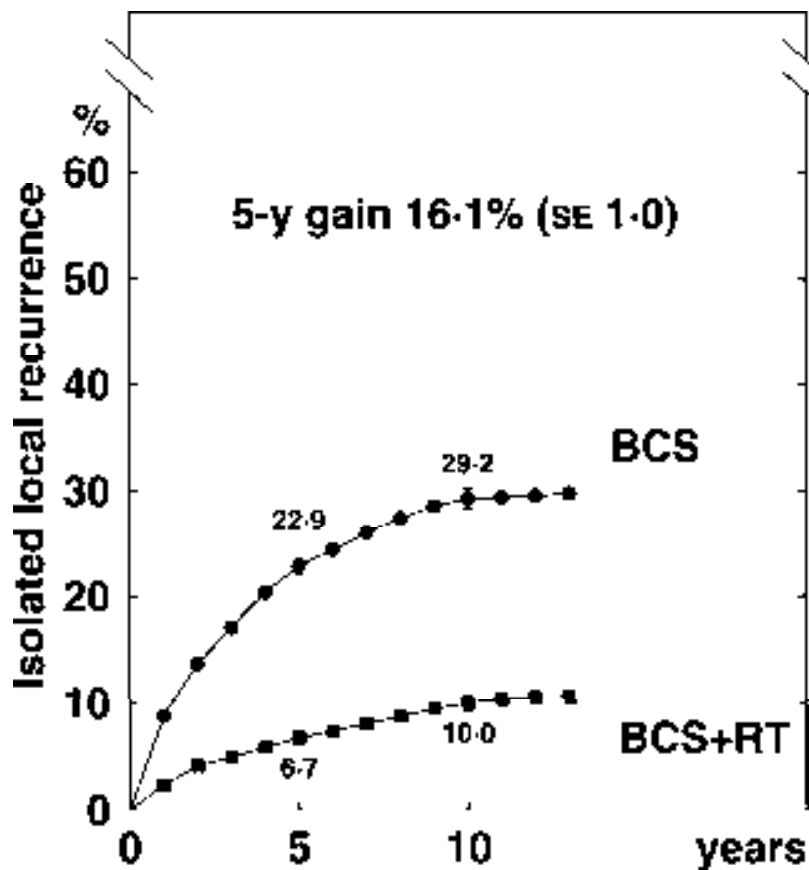
- 30.5% vs 35.9% (**reduction 5.4%, SE 1.7, 2p=0.002**)

15-year overall mortality risks:

- 35.2% vs 40.5% (reduction 5.3%, SE 1.8, 2p=0.005)

Effect of radiotherapy after breast-conserving surgery (10 trials of BCS ± RT) on local recurrence and on breast cancer mortality

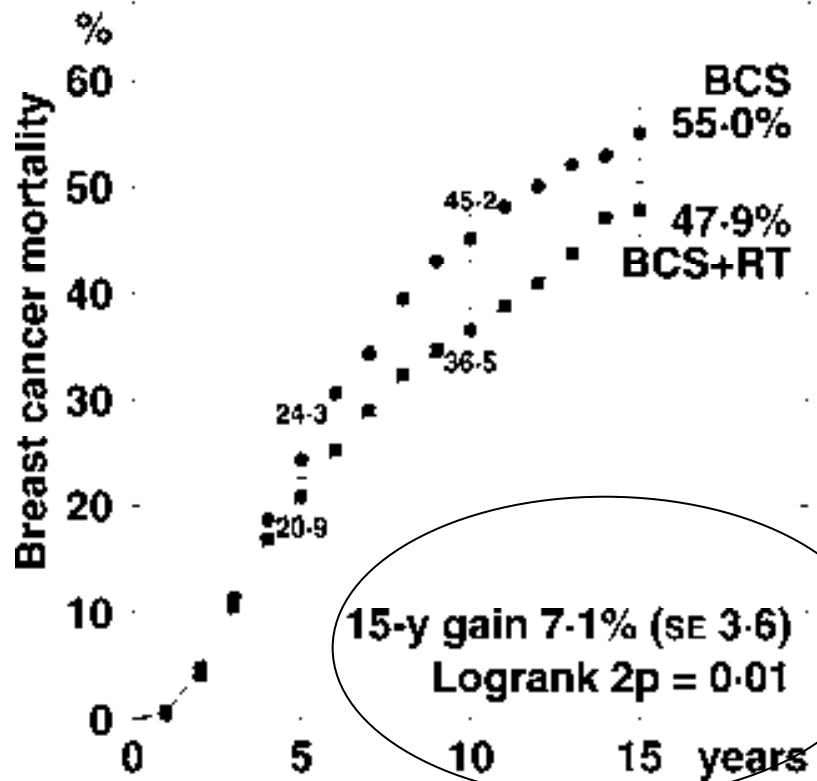
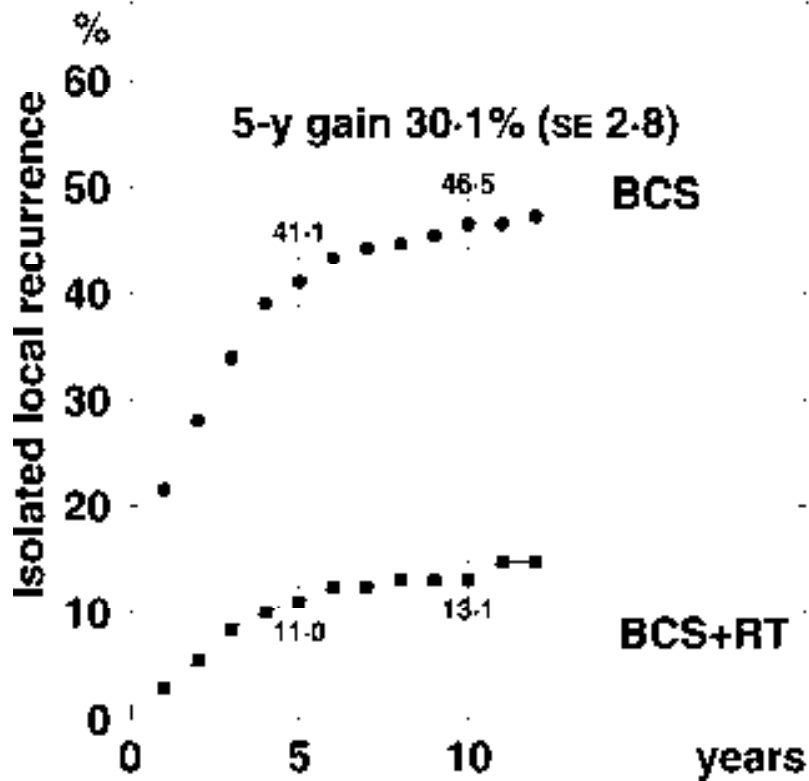
6097 women with node-negative disease





**Effect of radiotherapy after breast-conserving surgery
(10 trials of BCS ± RT) on local recurrence and on breast cancer mortality**

1214 women with node-positive disease



Impact of RT in Mastectomy and axillary clearance: Node Negative

There were 1400 women with mastectomy, axillary clearance, and N-ve disease in trials of \pm RT

RT was generally to the chest wall and regional lymph nodes

5-year local recurrence risks:

- 2% vs 6% (reduction 4%)

15-year breast cancer mortality risks:

- 31.3% vs 27.7% (increase 3.6%, SE 3.6, 2p=0.01)

15-year overall mortality risks:

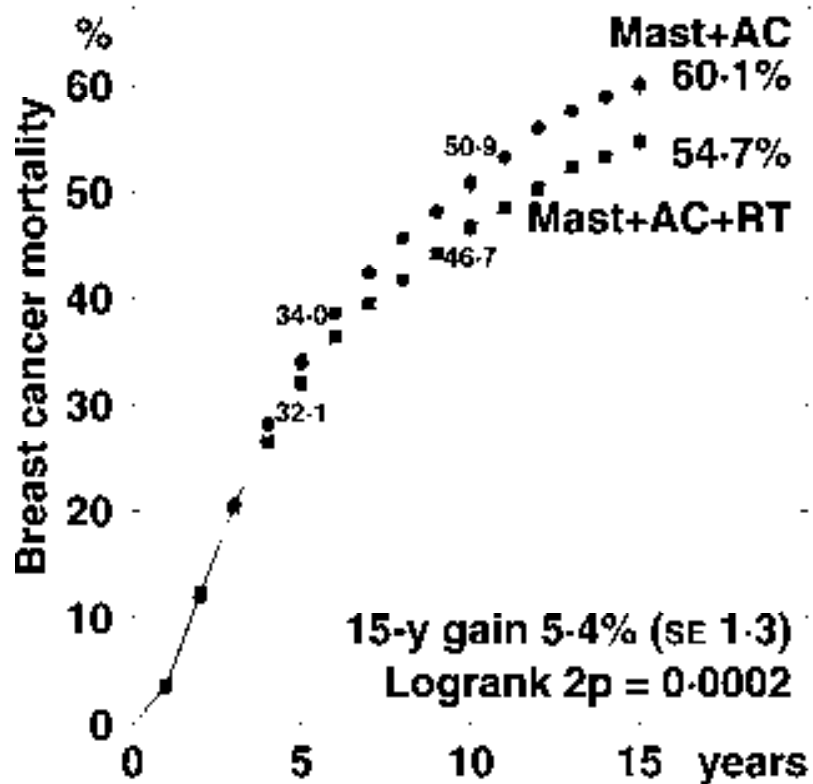
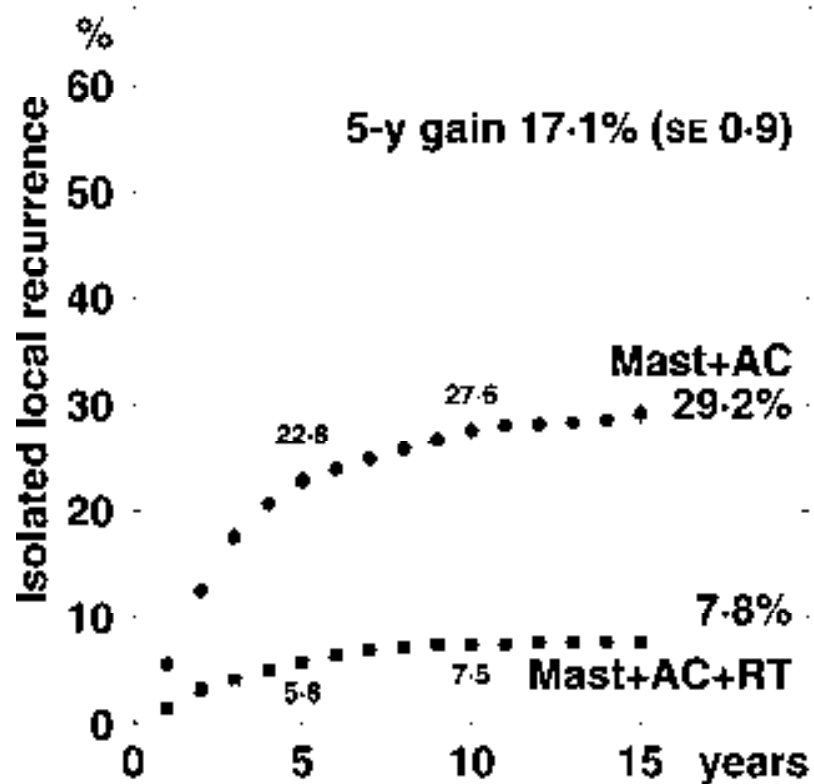
- 42.4% vs 38.2% (increase 4.2%, SE 2.7, 2p=0.0002)

Radiotherapy side-effects

- Trials of \pm RT were combined with those of RT vs more surgery.
- There was an excess incidence of contralateral breast cancer (rate ratio 1.18, SE 0.06, 2p=0.002).
- There was also an excess of non-breast-cancer mortality (rate ratio 1.12, SE 0.04, 2p=0.001), heart disease (rate ratio 1.27, SE 0.07, 2p=0.0001) and lung cancer (rate ratio 1.78, SE 0.22, 2p=0.0004).
- Both excesses were slight during the first 5 years, but continued after year 15.

**Effect of radiotherapy after mastectomy and axillary clearance
(25 trials of Mast+AC ± RT) on local recurrence and on breast cancer mortality**

8505 women with node-positive disease



Conclusions

These trials of radiotherapy and of the extent of surgery show that, in the hypothetical absence of other causes of death, about **one breast cancer death over the next 15 years would be avoided for every four local recurrences avoided.**

Although the management of early breast cancer continues to change, it is reasonable to assume that this approximate four-to-one relationship will continue to apply and will still be of relevance to future treatment choices.

Implications....

- Local control matters
 - It's not when you diagnose a breast cancer, it is when you treat it correctly
- Nihilism about local control unjustified
 - Radiation therapy to the breast critically important
 - Margins/volume of resection matter

Implications...Should more mastectomies be performed?

- What about groups at increased risk for local regional relapse?
 - Patients who cannot receive radiation therapy?
 - Scleroderma/Lupus; prior radiation therapy;
 - Multicentric/multifocal breast cancer?
 - EIC with clear but close margins?
 - Young patients with breast cancer?
 - Affected BRCA heterozygotes?

Study	N	N BRCA	FU (yr)	Local Recur (%)		Contralateral Cancer (%)	
				Genetic	Sporadic	Genetic	Sporadic
Seynaeve	261	87	6.1	30	16	13.8	6.3
Pierce	469	170	10	12.5	8.6	25	4
Haffty	127	22	12.7	49	21	42	9
Bremer	110	9	5	29	6	NR	NR
Delaloge	96	37 B1	10	9	12	NR	NR
				37	12		
Robson	514	61	10	12.5	8	27	8

Multi-Institutional 10-Year Results of Breast-Conserving Surgery and Radiotherapy in *BRCA1/2*-Associated Stage I/II Breast Cancer

Published Ahead of Print on April 24, 2006 as 10.1200/JCO.2005.02.7888
The latest version is at <http://www.jco.org/cgi/doi/10.1200/JCO.2005.02.7888>

VOLUME 24 · NUMBER 18 · JUNE 1 2006

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

- **Methods**

- A total of 160 *BRCA1/2* mutation carriers with breast cancer were matched with 445 controls with sporadic breast cancer. Primary end points were rates of in-breast tumor recurrence (IBTR) and contralateral breast cancers (CBCs). Median follow-up was 7.9 years for mutation carriers and 6.7 years for controls.

- **Results**

- There was no significant difference in IBTR overall between carriers and controls; 10- and 15-year estimates were 12% and 24% for carriers and 9% and 17% for controls, respectively (hazard ratio [HR], 1.37; *P* .19). **Multivariate analyses for IBTR found *BRCA1/2* mutation status to be an independent predictor of IBTR when carriers who had undergone oophorectomy were removed from analysis (HR, 1.99; *P* .04);** the incidence of IBTR in carriers who had undergone oophorectomy was not significantly different from that in sporadic controls (*P* .37). CBCs were significantly greater in carriers versus controls, with 10- and 15-year estimates of 26% and 39% for carriers and 3% and 7% for controls, respectively (HR, 10.43; *P* .0001). Tamoxifen use significantly reduced risk of CBCs in mutation carriers (HR, 0.31; *P* .05).

Multi-Institutional 10-Year Results of Breast-Conserving Surgery and Radiotherapy in *BRCA1/2*-Associated Stage I/II Breast Cancer

- *Lori J. Pierce, Albert M. Levin, Timothy R. Rebbeck, Merav A. Ben-David, Eitan Friedman, Lawrence J. Solin, Eleanor E. Harris, David K. Gaffney, Bruce G. Haffty, Laura A. Dawson,*

Conclusion

- IBTR risk at 10 years is similar in *BRCA1/2* carriers treated with breast conservation surgery who undergo oophorectomy versus sporadic controls.
- As expected, CBCs are significantly increased in carriers.
- Although the incidence of CBCs was significantly reduced in mutation carriers who received tamoxifen, this rate remained significantly greater than in controls.

Overall IBTR in BRCA Mutation Carriers vs. Controls

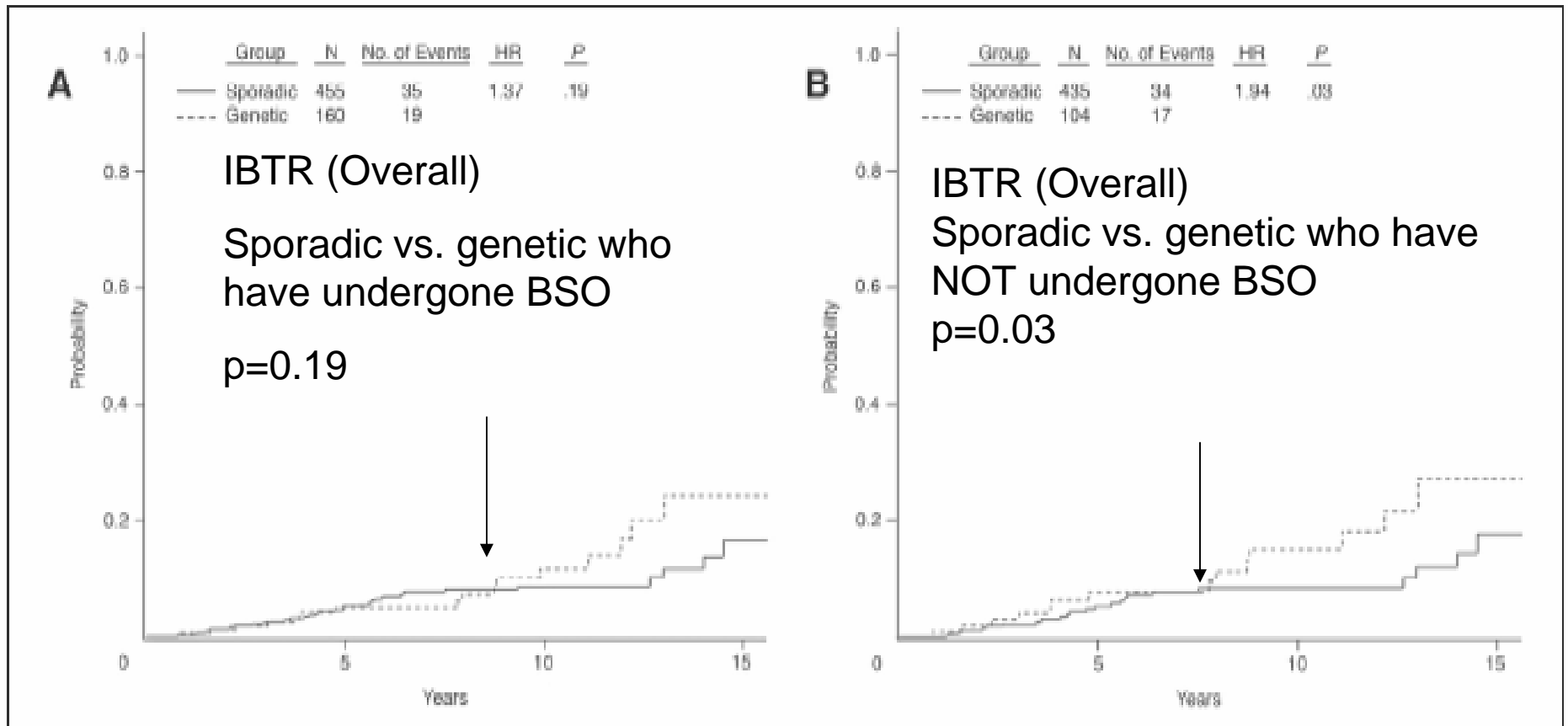


Fig 1. (A) Overall in-breast tumor recurrence in BRCA1/2[+] mutation carriers and sporadic controls. (B) In-breast tumor recurrence in BRCA 1/2 mutation carriers and sporadic controls who have not undergone bilateral prophylactic mastectomy. HR, hazard ratio.

Implications....

- Does this explain the impact of surgeon volume on outcome in breast cancer?

Surgeon workload and survival from breast cancer.

We recommend that patients with breast cancer be dealt with only by clinicians who see more than 30 new cases per year and who have a full range of treatment options available within a multidisciplinary setting.

Implications....

- **Skinner, Helsper, Deapen, Ye, Sposto**

- Department of Surgery, Norris Comprehensive Cancer Center, University of Southern California/Keck School of Medicine, Los Angeles, California, USA. kristin.skinner@med.nyu.edu
- The Cancer Surveillance Program database for Los Angeles County was reviewed. Between 1990 and 1998, **43,411 cases of breast cancer were diagnosed, of which 29,666 had complete data on surgeon, hospital, and staging information.**
- **Treatment at a specialty center did not affect survival. Multivariate analysis indicated that type of surgeon was an independent predictor of survival (relative risk,.77), as were both hospital and surgeon case volume.**
- **CONCLUSIONS:** Treatment by a surgical oncologist resulted in a 33% reduction in the risk of death at 5 years. The effect of surgical specialization cannot be entirely attributed to volume effects.

Implications....

- Roohan, Bickell, Baptiste, Therriault, Ferrara, Siu
New York State Department of Health, Albany, USA.

OBJECTIVES: The purpose of this study was to determine the effect of hospital volume on long-term survival for women with breast cancer.

METHODS: Survival analysis and proportional-hazard modeling were used to assess 5-year survival and risk of death, adjusting for clinical and sociodemographic variables.

- RESULTS: At 5 years, patients from very low-volume hospitals had a 60% greater risk of all-cause mortality than patients from high-volume hospitals.
- CONCLUSIONS: **Hospital volume of breast cancer surgical cases has a strong positive effect on 5-year survival.**

**How do we define
high volume?**

Breast Cancer In-Patient Volume by Surgeon, New York State 2003

Healthcarechoices.com

25% of the inpatient cases were performed by a doctor who did **2 or fewer** inpatient cases per year.

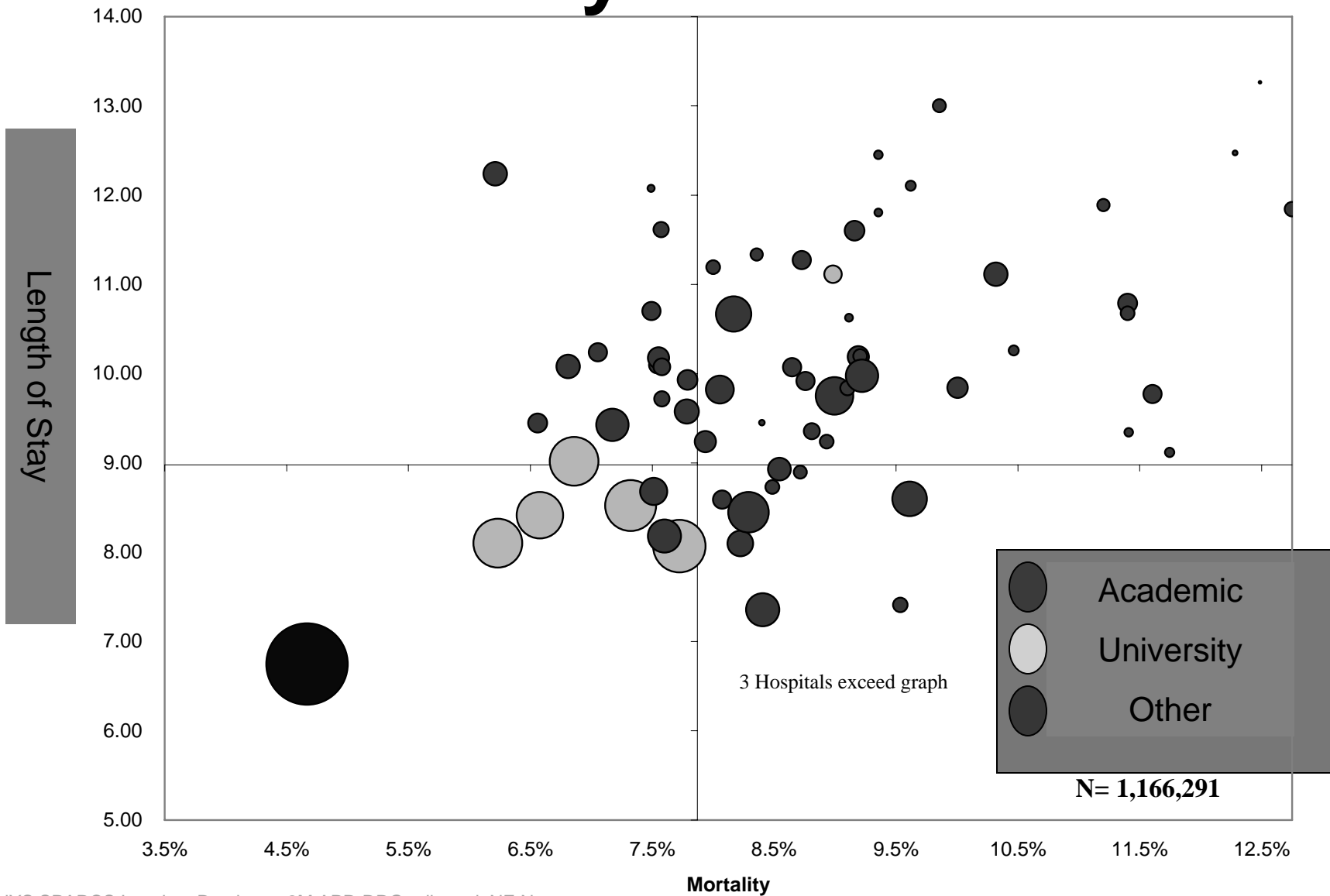
50% of the inpatient cases were performed by a doctor who did **4 or fewer inpatient cases per year.**

75% of the inpatient cases were performed by a doctor who did **9 or fewer inpatient cases per year.**

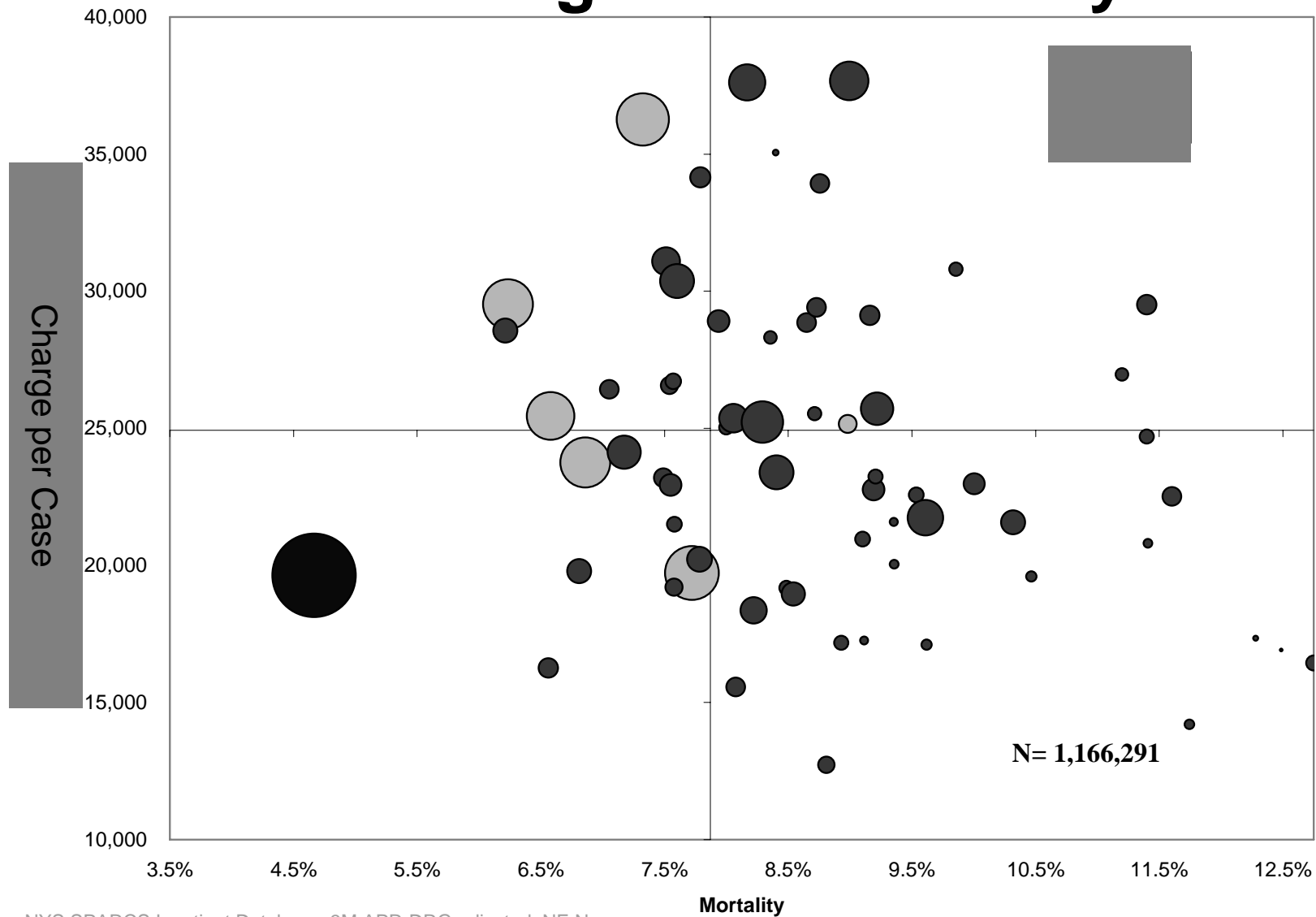
Inpatient Cancer Mortality Analysis

- Data Source:
 - Based on 1994-2003 NYS SPARCS Inpatient Database
 - ~ 11 million total / 1,166,291 cancer discharges in NYC
- Severity adjusted by 3M APR-DRG
 - Wide industry acceptance - Used by ~ 4,000 organizations
 - Highly evolved system based on statistically valid normative data
 - Uses categorical disease modeling
 - Diagnosis and procedure driven
 - Recognizes related complications
 - Hannan E, Radzyner M, Rubin D, Borgen P, Dougherty J, Brennan M. The influence of hospital and surgeon volume on in-hospital mortality for colectomy, gastrectomy, and lung lobectomy in patients with cancer. *Surgery*, Jan 2002

1994-2003 NYC Cancer Outcome Analysis

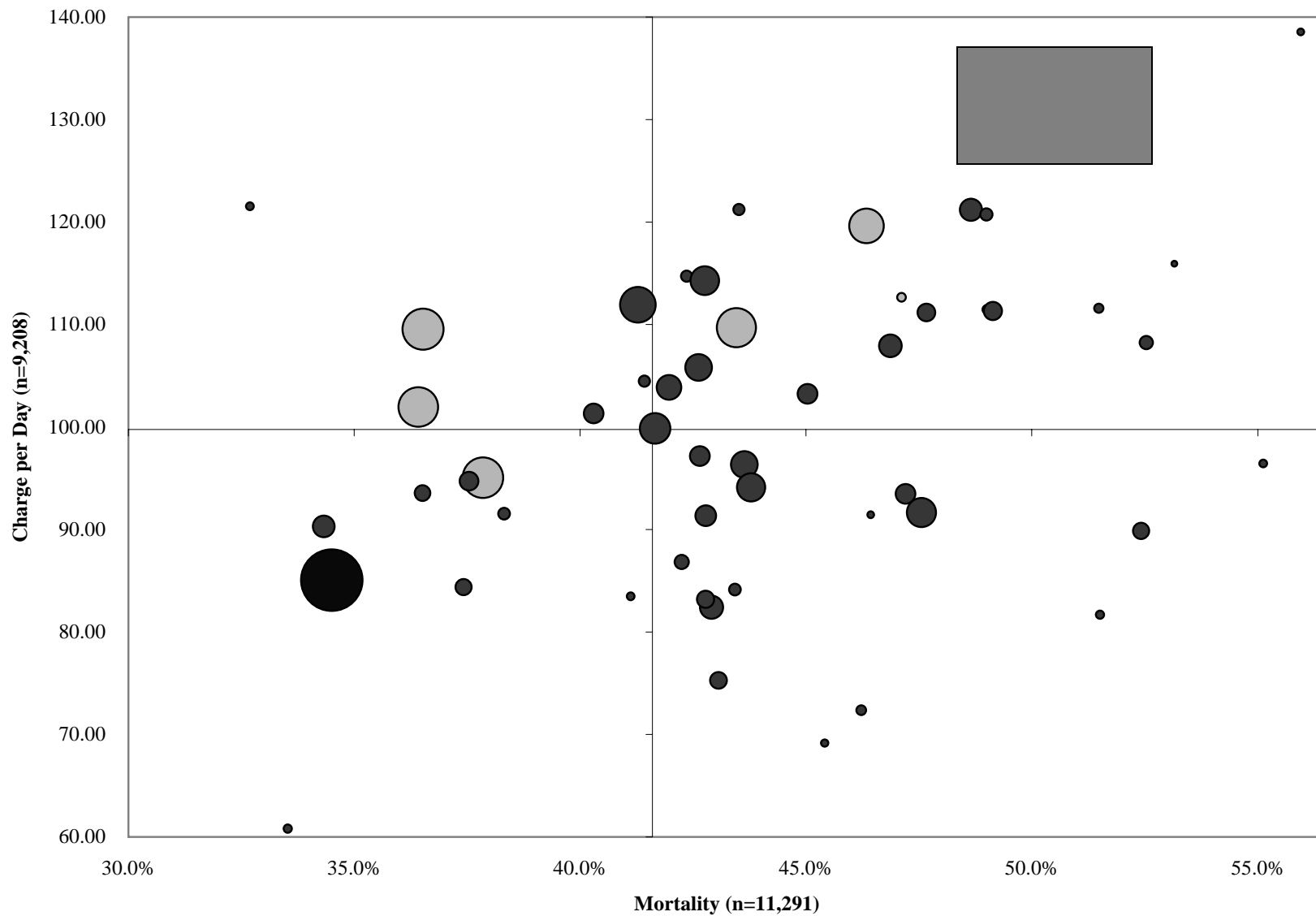


1994-2003 NYC Cancer Outcome Analysis: High Volume associated with lower charges and mortality



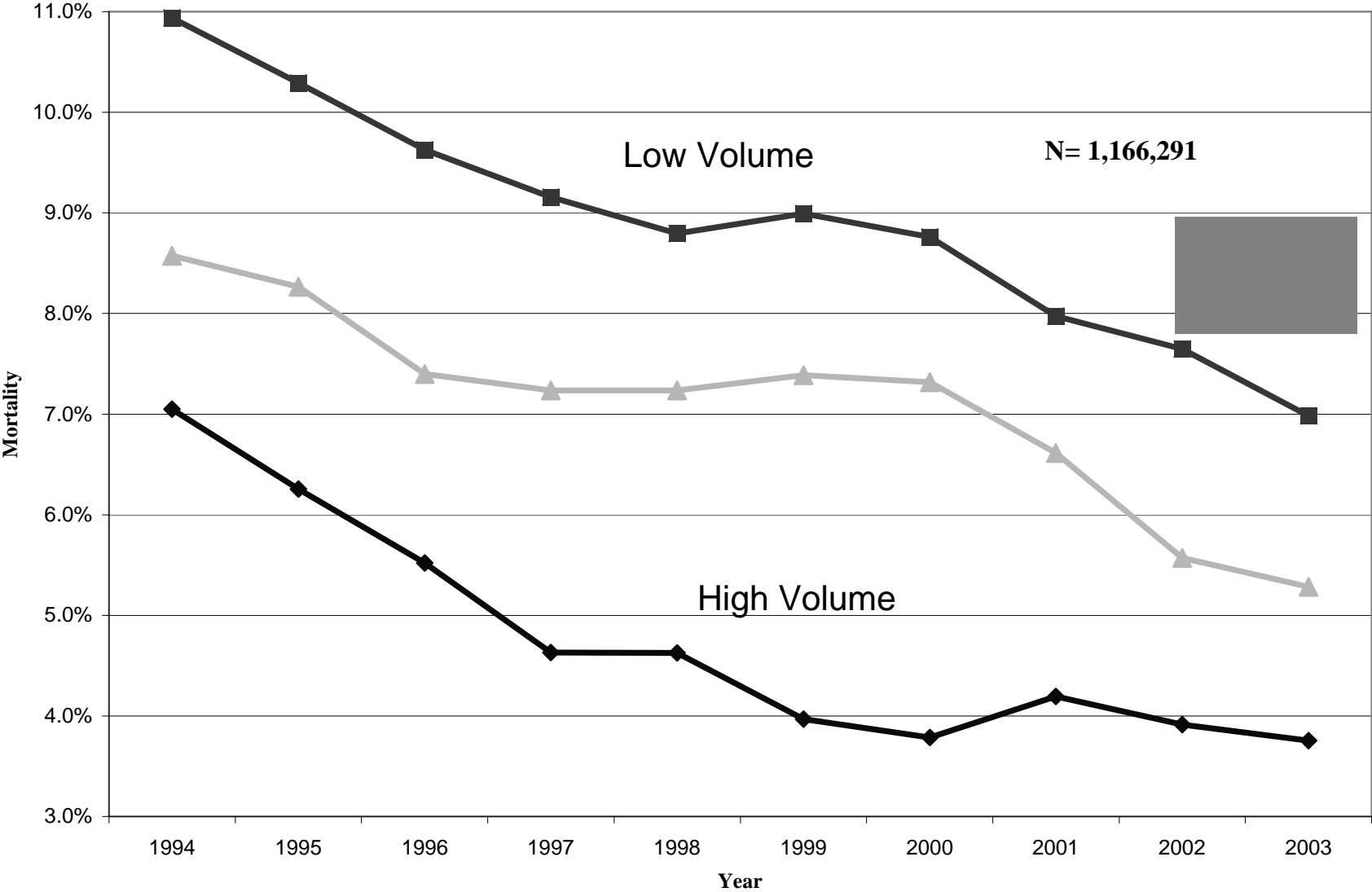
Source: NYS SPARCS Inpatient Database; 3M APR-DRG adjusted, NE Norm

NYC Medicare 5-Year Mortality and Charge per Day



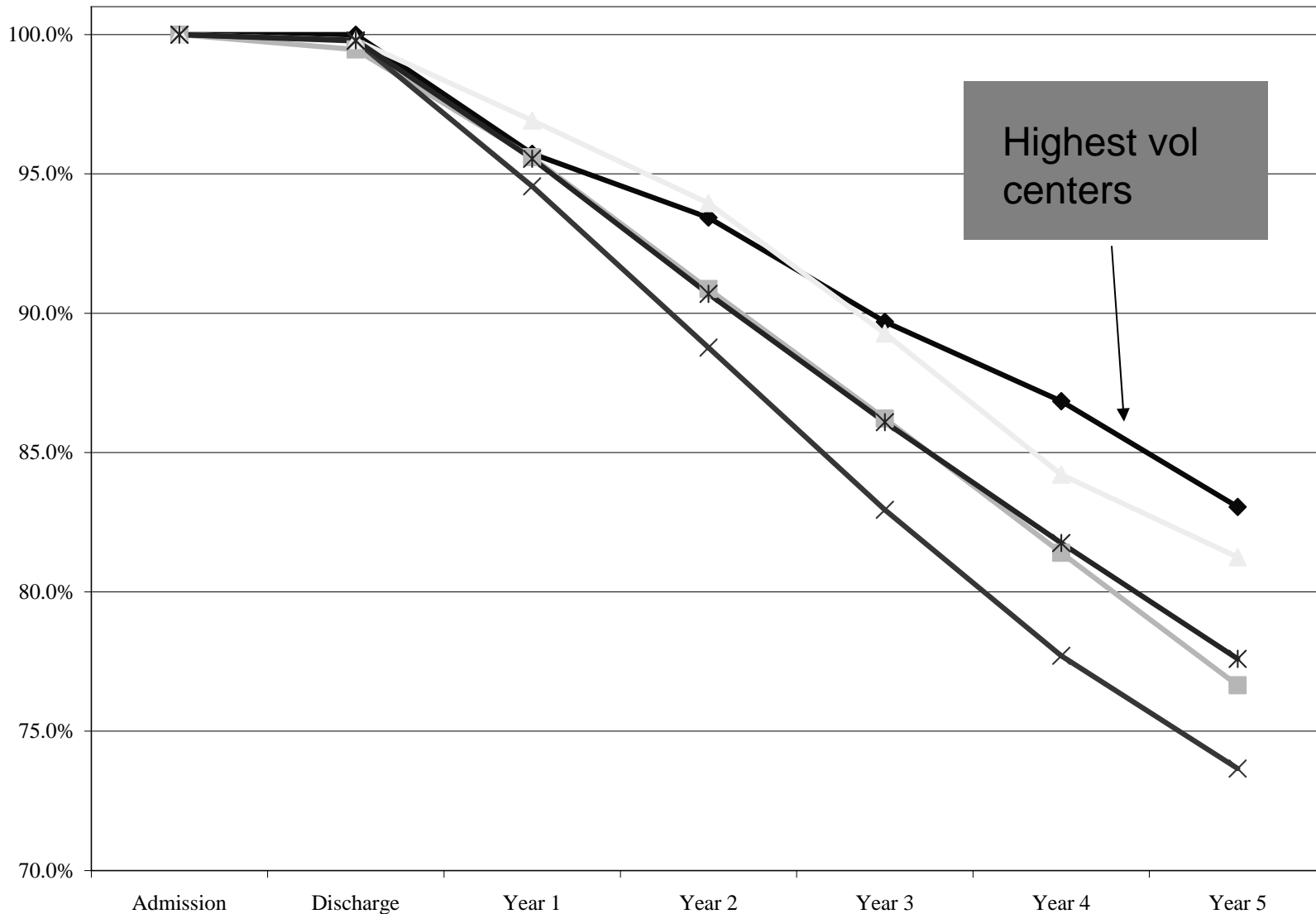
Source: 1995-2001 Medicare Standard Analytical Files (High Volume Procedures); Severity Adjusted

NYC Inpatient Cancer Mortality Analysis 1994 -2003



Source: NYS SPARCS Inpatient Database; 3M APR-DRG adjusted, NE Norm

US Medicare 5-Year Survival Mastectomy



Source: 1995-2001 Medicare Standard Analytical Files (High Volume Procedures); Severity adjusted death by any cause

New York State Breast Cancer Volume/Outcomes Project



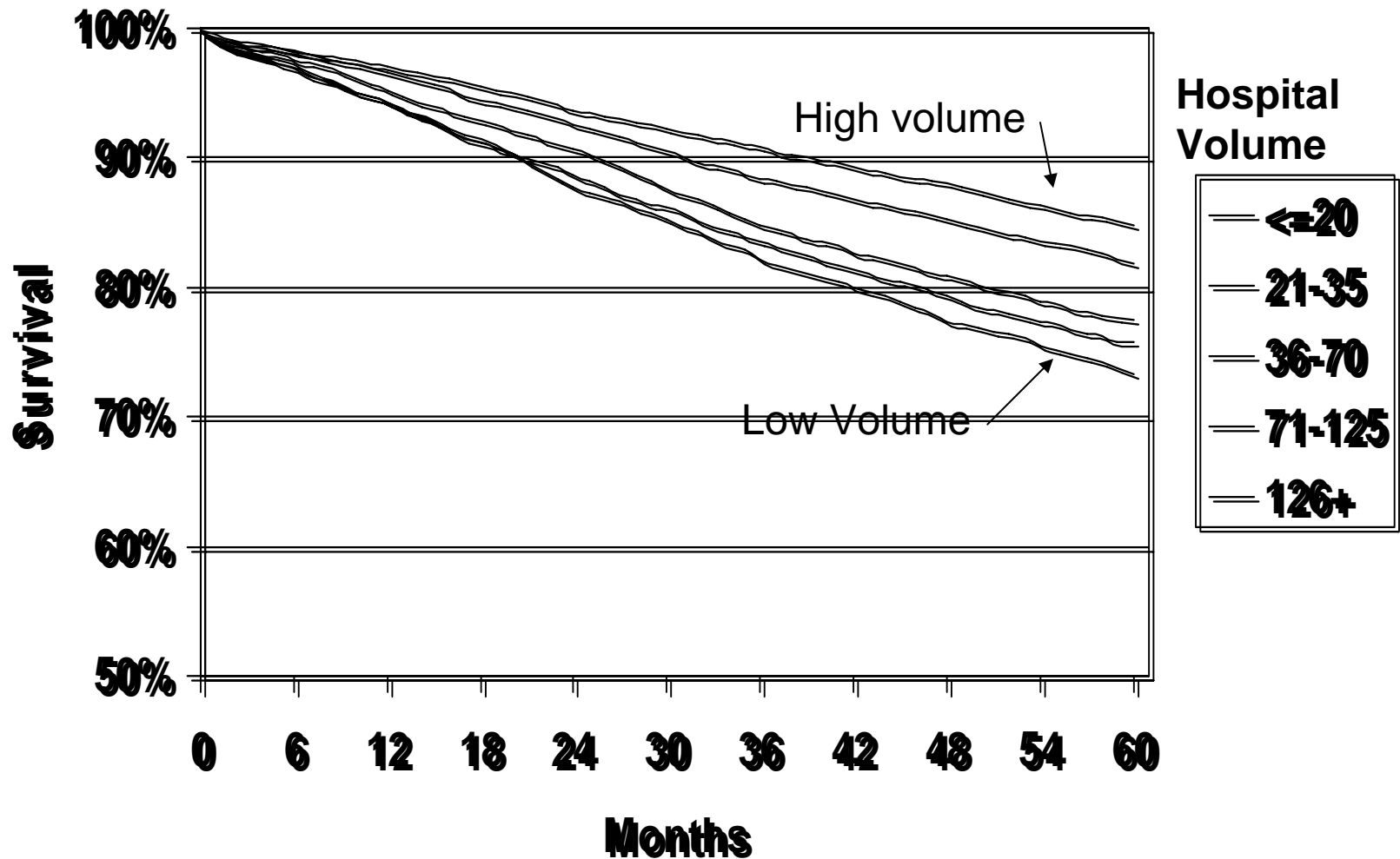
- Grant funded data retrieval and analysis from NYS Health Department's Cancer Registry and the NYS Statewide Planning and Research Cooperative SPARCS Database
- The Project examined survival in 2 ways. It looked at 5 year survival of patients receiving surgery on a hospital inpatient basis (1995-1998).
- It also looked at 3 year survival of patients whose surgery was done either on an inpatient or outpatient basis (1997-1998).
- Death rates were adjusted to take into account differences in the health and treatment of patients in the study. This included adjusting for such factors as age, race/ethnicity, cancer stage, whether or not there was an axillary node dissection, type of surgery (mastectomy or breast conserving surgery) and other medical conditions of the patients.

New York State Breast Cancer Volume/Outcomes Project



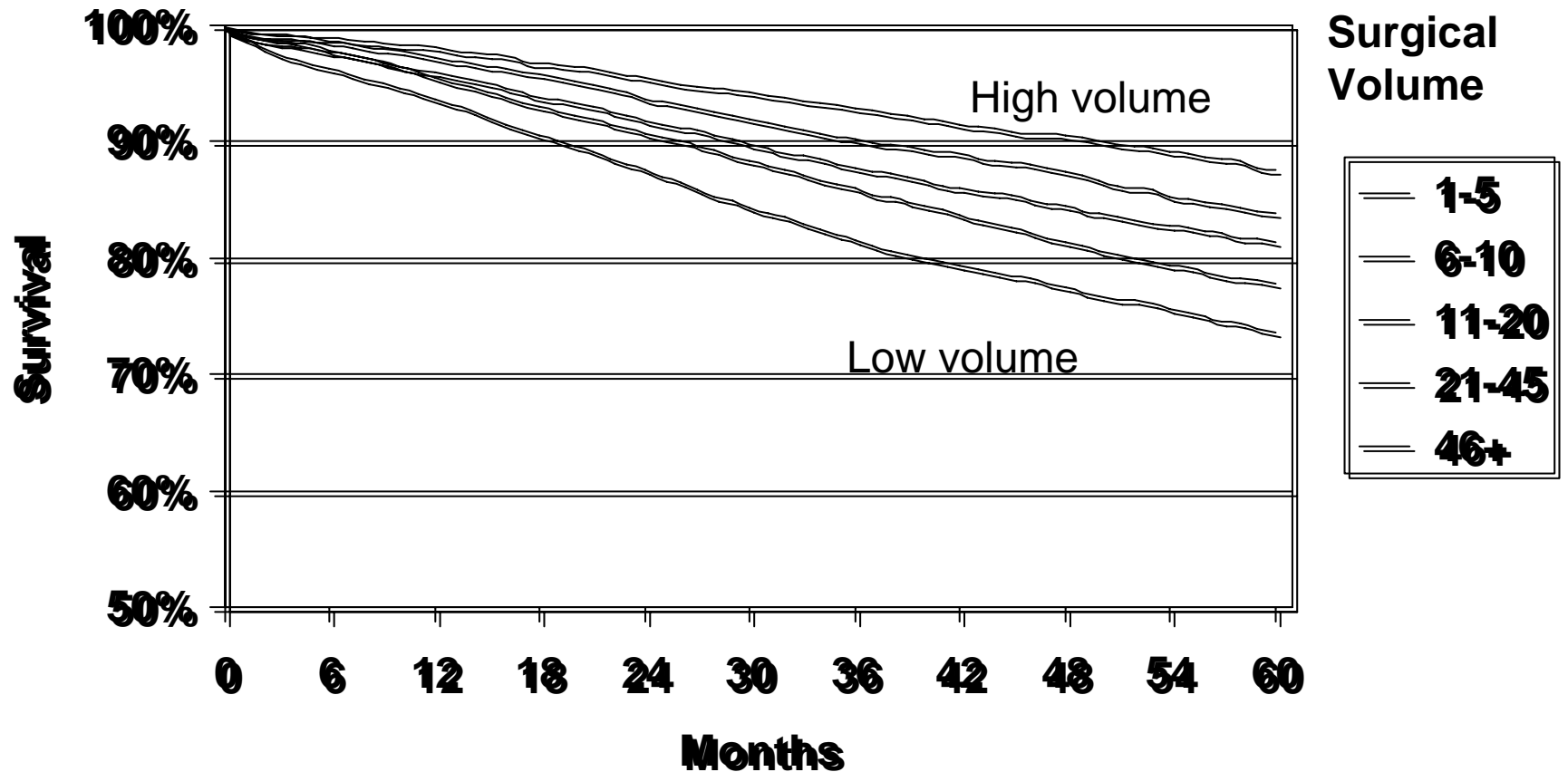
- Data available on 1600 surgeons who perform breast cancer surgery in NYS
- Data available on 68,000 patients
- Excellent follow-up (<3% lost to follow-up)
- Coding challenges along the way
 - P.Borgen, S. Edge, B. Smith, S. Rosenfeld, E. Beatty, F. Gesten, P. Roohan

**Figure 1:
Breast Cancer Survival by Hospital Volume
Inpatient Data 1995-1998 Stage I**



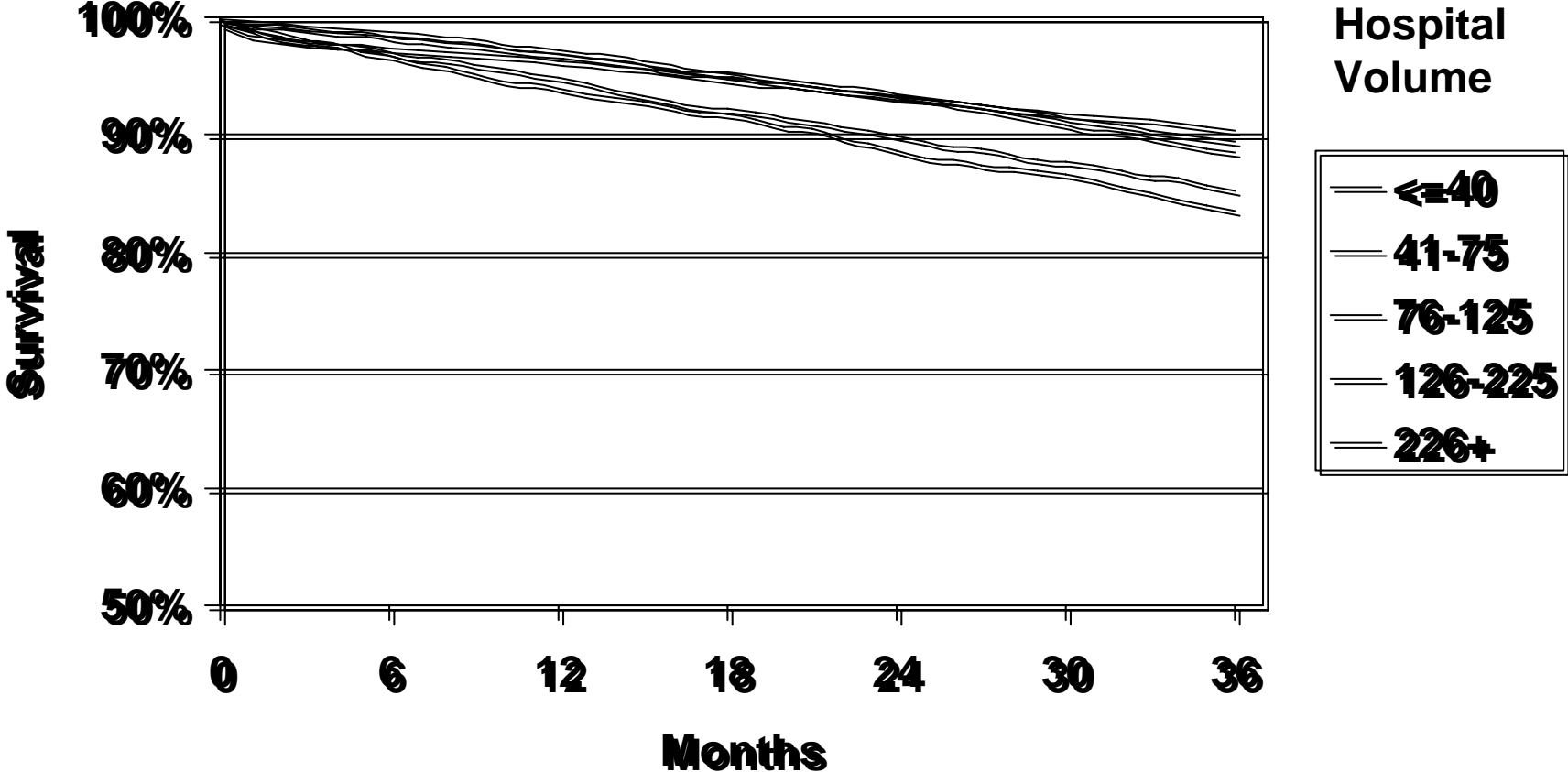
•P.Borgen, S. Edge, B. Smith, S. Rosenfeld, E. Beatty, F. Gesten, P. Roohan

**Figure 2:
Breast Cancer Survival by Surgical Volume
Inpatient Data 1995-1998**

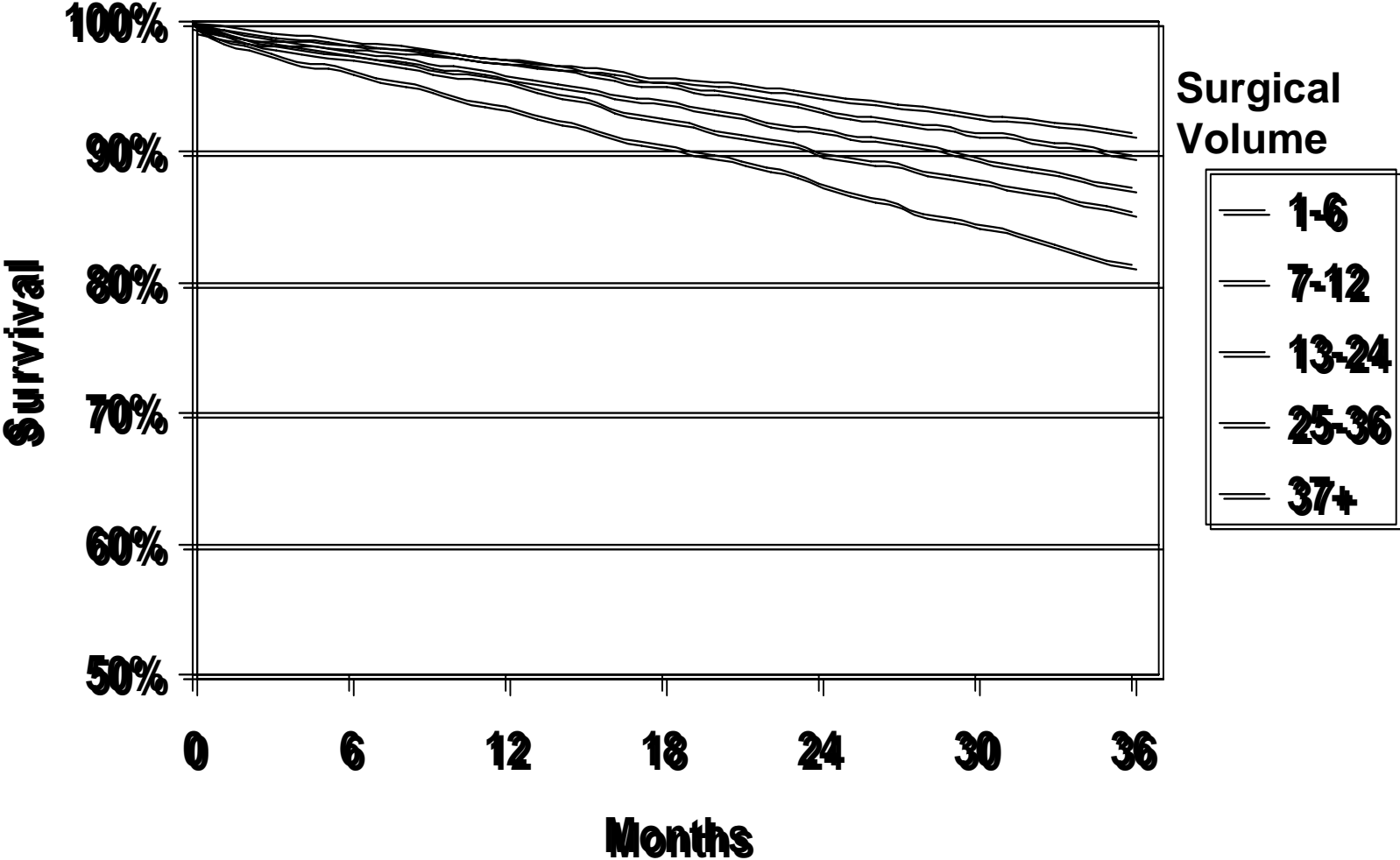


•P.Borgen, S. Edge, B. Smith, S. Rosenfeld, E. Beatty, F. Gesten, P. Rooha

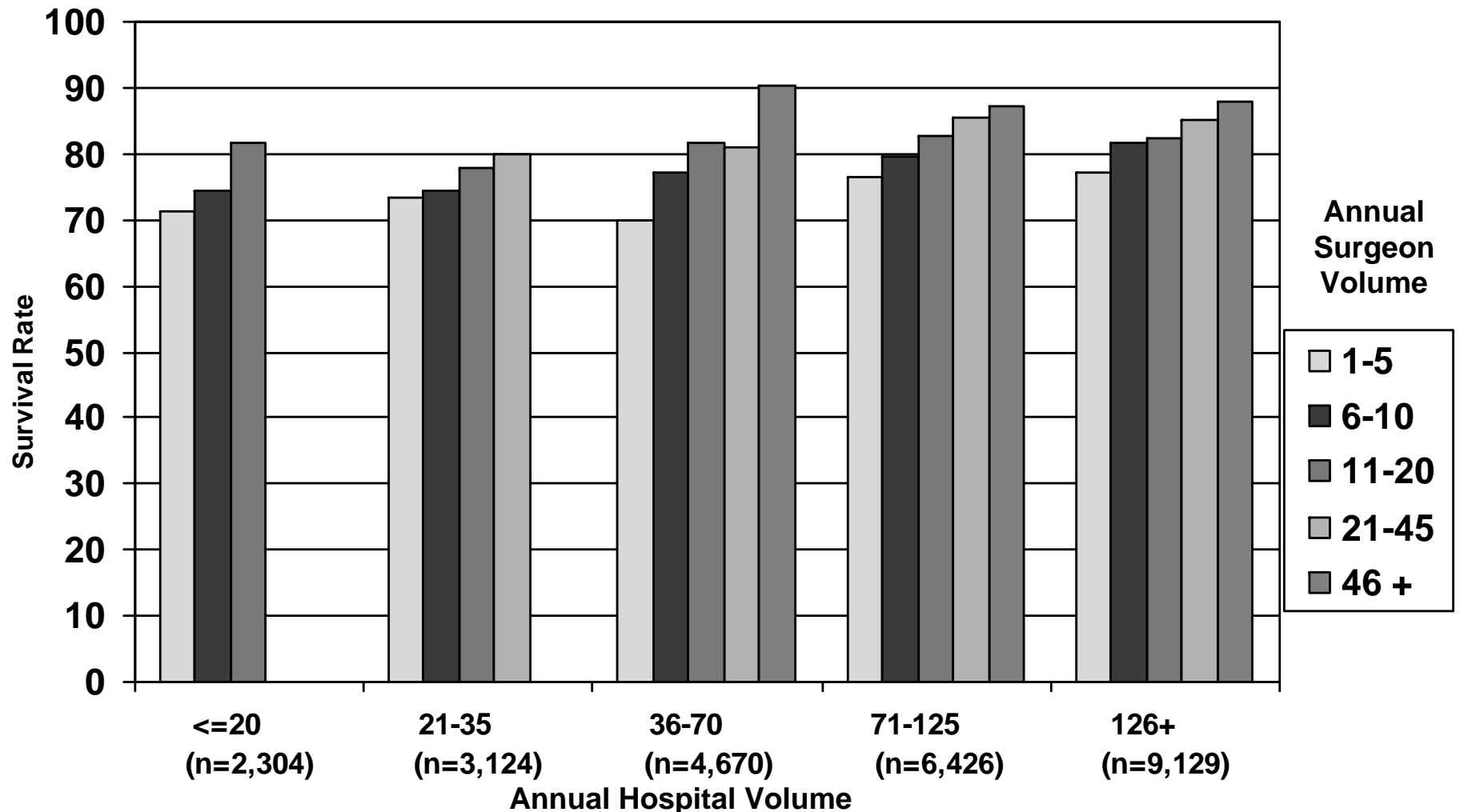
**Figure 4:
Breast Cancer Survival by Hospital Volume
Inpatient/Outpatient Data 1997-1998**



**Figure 5:
Breast Cancer Survival by Surgical Volume
Inpatient/Outpatient Data 1997-1998**

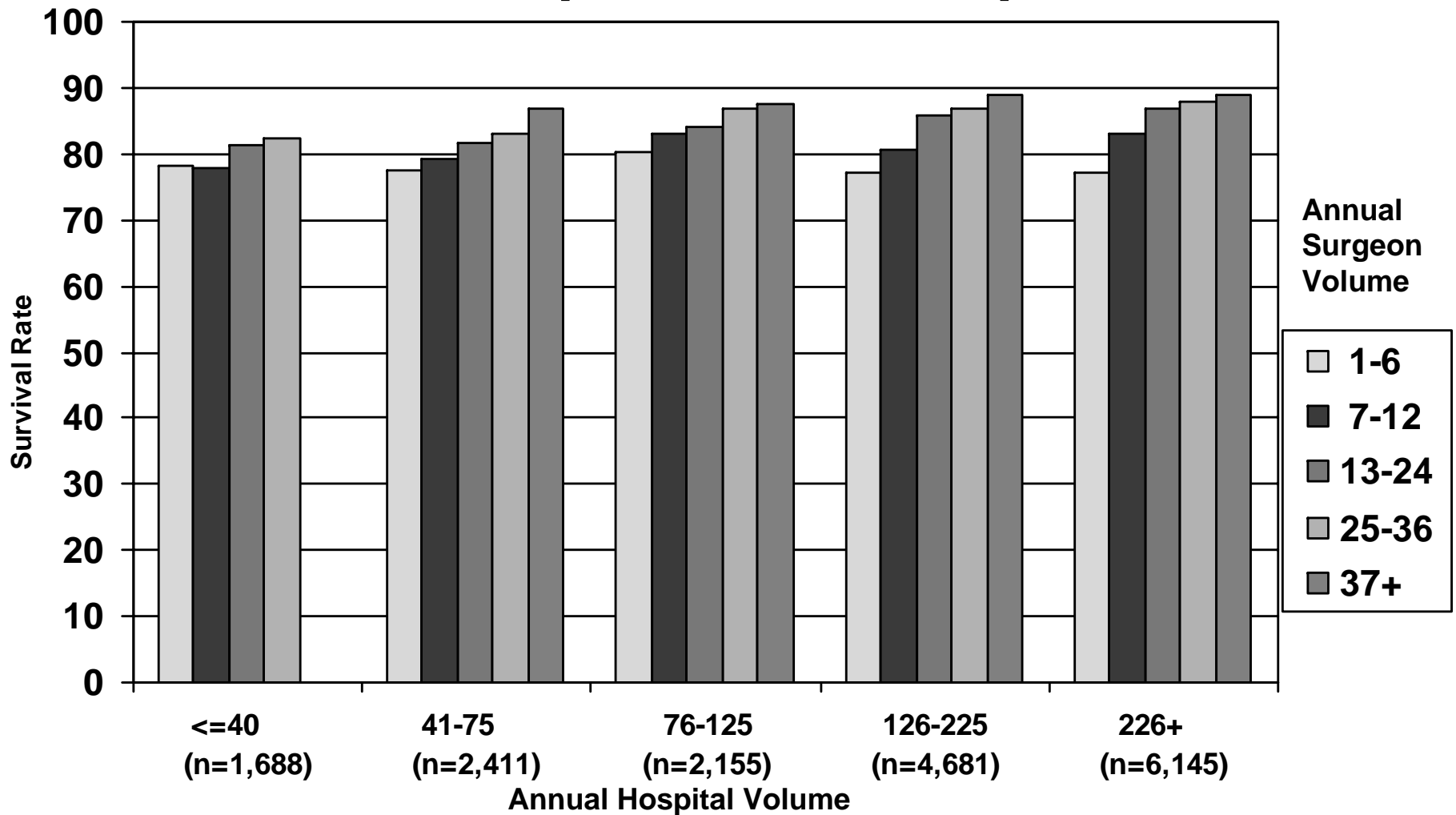


Survival Rate by Annual Hospital Volume and Annual Surgeon Volume 1995-1998 Inpatient



•P.Borgen, S. Edge, B. Smith, S. Rosenfeld, E. Beatty, F. Gesten, P. Roo

Survival Rate by Annual Hospital Volume and Annual Surgeon Volume 1997-1998 Inpatient and Outpatient



Conclusions



- There was a linear relationship between volume and outcome in patients with primary operable breast cancer
- On univariate analysis both hospital volume and surgeon volume impacted outcome
- On multivariate analysis only surgeon volume was independently associated with outcome
- Greatest survival advantage was seen when annual case volume exceeded 35 cancers/year

So What?

- Breast Cancer Surgery is alive and well....
- Patient selection for BCT is increasingly important; mastectomy is not dead....
 - Association between patient understanding of her disease (time spent by surgeon) and the likelihood of patient CHOOSING mastectomy.
 - Monica Morrow, 2005
- Patients do better when they are treated by high volume surgeons compared to outcomes with low volume surgeons.....
- How do we use this information?



What are you **SINKING** about?

- Increased emphasis on collective bargaining for improved reimbursement
- Consider including breast cancer surgery in later phases of U.S. Surgical Residency Programs (years 4 and 5)
- Improve your situation back home through
 - Negotiating with your institution to support sub-specialization (practice emphasis)
 - Encouraging the hospital to consider this as marketable
 - Reduce other responsibilities such as Emergency Room call
 - Join collective bargaining groups who are lobbying for improved reimbursement for breast cancer procedural codes
 - Use information, in collaboration with advocacy groups, in patient education programs

**You won't cure everyone with local
control but you won't cure anyone
without it**



Alfred Fracchia, M.D.

1968