

## **OUTCOME STUDY**

### **PATIENT CARE EVALUATION BILATERAL BREAST CARCINOMA**

Breast cancer is the second most common cancer diagnosis in women in the United States. In 2008 there will be approximately 180,000 cases of breast cancer diagnosed in the United States. While most of these cases will be early in stage, some cases are diagnosed at a later stage, and consequently the survival is inferior. Bilateral breast cancer represents a significant dilemma to clinicians. Fortunately, synchronous bilateral breast cancers are rare. Patients with early stage ipsilateral breast cancer are still at risk for developing a second primary tumor over the course of their lifetime. Prophylactic contralateral mastectomy significantly decreases, but does not eliminate, the risk of developing a contralateral breast cancer. This risk appears to increase as time goes on, but will level off after a period of time has elapsed.

As breast cancer incidence has increased, we've seen improved prognosis and growing life expectancy. This has increased the risk and the number of women at risk for developing bilateral breast cancer. There are an estimated 2.2 million women living in the United States who have been diagnosed at some time with breast cancer. The optimal surveillance and clinical management of women who have had one or two breast cancers represents a challenge. There was only limited data on the incidence of synchronous and metachronous breast cancer and little is known about the prognostic outlook after treatment of the primary cancer or patients with bilateral synchronous primaries.

The South Jersey Healthcare Frank and Edith Scarpa Regional Cancer Pavilion is accredited by the American College of Surgeons as a Community Hospital Comprehensive Program. SJH's Tumor Registry has been abstracting all cancer cases since January 1, 1982 and we have reviewed all cases of bilateral breast carcinoma present in the tumor registry through December 31, 2007. The following represents the narrative from that review.

There were a total of 123 patients representing 246 breasts of which 122 were female and only one was a male. When examining the stage of tumor in the metachronous patients (n=164 tumors, 82 patients), there appears to be a slight shift to early stage cancers when the second primary tumor was diagnosed. On review of the synchronous patients (n=82 tumors, 41 patients) there appears to be a slightly higher distribution toward higher stage breast cancer being initially diagnosed. These 123 patients had a total of 17 primary tumors other than breast cancer. There were 15 patients with a third primary tumor and two patients with a fourth primary tumor. This represents an overall crude rate of 17 divided by 123 which equals 13.8%. The site distribution for these third and fourth primary tumors is displayed in graph #1.

The age range of the 82 metachronous patients went from 29 to 86 with a median of 68. Synchronous patients had a median age of 68 years also. The metachronous patients had a median age of 64 years when they were diagnosed with their first cancer and 71 when they were diagnosed with their second cancer. There were 110 Caucasian patients and

thirteen African-Americans representing 220 and 26 cases, respectively. No other races were identified.

The distribution by zip code is depicted in pie chart #2. The majority of Cumberland County patients were referred from three major urban centers of Vineland, Millville and Bridgeton. Age by diagnosis is seen in graph #3. There is a peak diagnosis of bilateral breast cancer in the 60-79 age group although there appears to be almost bell-shaped curve distribution regardless.

In reviewing patterns of initial treatment, the metachronous patient population had three patients who had no primary therapy other than a biopsy. There were 4 simple mastectomies, 71 modified radical mastectomies and a total of 86 partial mastectomies (as designated by partial mastectomy, lumpectomy or re-excision). In cases of synchronous presentations, there were nine simple mastectomies, 37 modified radical mastectomies, 30 partial mastectomies (labeled as lumpectomy, partial mastectomy or re-excision) and six receiving no treatment due to patient refusal. There did not appear to be more modified radical mastectomies in the patients presenting with synchronous tumors. In summary, the 246 breasts that were in the study, nine refused treatment (two-thirds of these were synchronous patients), 116 had less than mastectomy treatments (which include lumpectomy, partial mastectomy or re-excision), 108 modified radical mastectomies, and 13 simple mastectomies.

In terms of chemotherapy, there appears to be an almost even distribution of chemotherapy administered to the metachronous patients either with their first or second primary tumor. Of the 41 patients that presented with synchronous bilateral primaries, there was an approximate 50% chance that they would have received chemotherapy although the stage spread appears to be similar to metachronous patients.

Of the 82 tumors diagnosed synchronously, 23 were ER/PR status unknown. One of these was treated with tamoxifen or an aromatase inhibitor. Of the 49 ER positive synchronous primary tumors, 32 were documented to have received tamoxifen or aromatase inhibitors. None of the ER negative tumors (N=10) received tamoxifen or aromatase inhibitor. In looking at the first primary of the 82 metachronous tumors, in 35 cases the ER status was unknown. In 40 cases the tumor was ER positive, 23 of these were treated with hormone manipulation and 17 tumors were not.

Looking at the second primary tumor, 44 of these were ER positive tumors of which 27 were treated with an aromatase inhibitor or tamoxifen. Twelve tumors were ER negative and one of these tumor was treated with tamoxifen or an aromatase inhibitor. In 26 tumors the receptor status was unknown. Half of these, 13, received tamoxifen or an aromatase inhibitor. We are unable to draw any conclusions concerning whether or not the administration of tamoxifen or an aromatase inhibitor in any way influenced ER receptor status of the second primary tumor although it would appear as if more of the secondary primary tumors were ER positive than the first primary tumors.

The crude rate of bilateral breast cancer is 4.5% of all the patients in the South Jersey Healthcare tumor database. This represents 123 patients out of 2,714 breast cancer cases. Of the 82 patients who presented with metachronous primary tumors, the range of time from the first primary tumor to the second diagnosis ranged from 3.1 to 8.5 years with a median of 6.5 years.

There were a total of 53 recurrences reported in the 246 breasts which were studied. This represents an overall crude rate of 21%. In five cases the recurrence was unknown and in four cases the recurrence was local, nine had regional recurrences, but the vast majority of the patients, 36, developed distant metastatic disease. The median time to a recurrence was 35 months. In terms of family history, we were limited with the ability to determine what the family history of cancer was as some of the metachronous patients did not have a family history when the first breast cancer was diagnosed, but subsequently picked up a family history. We were able to make an overall crude determination that 61 of the patients out of 123 reported a family history of cancer which is approximately 49%. There were a total of 55 (roughly representing 26 patients) in whom the family history of cancer diagnosis was unknown.

The relative survival of the cohort of 110 patients is represented in graph #4. As expected, the five year relative survival goes from 33% (Stage IV) to 94.3% (stage I tumors). Stage 0 cases appear to have a slightly inferior relative survival compared to stage I patients. Relative survival of all combined stages as seen in graph #5 is 80% in five years. Relative survival by race is depicted in graph #6. African-Americans appeared to have an inferior overall survival rate. graph #7 shows relative survival by age at diagnosis. Extremes of age (0-29 and 90 and over) appeared to have inferior survival compared with the cohorts between the ages of 30 and 89. graph #8 is relative survival by initial therapy. It demonstrates that those treated with surgery, radiation, and hormones (N=39) had a superior survival when compared to the other cohorts. This is not controlled for age and would not reflect degrees of therapy at more advanced stage of cancer.

Relative survival by pathological morphology is depicted in graph #9. Two hundred and thirteen cases were reported. There appears to be 100% survival for those designated with cystic or mucinous carcinoma (N=5). Those with ductal carcinomas were noted to have an inferior survival (79%). There were three patients with epithelial carcinoma that had a 51% five year relative disease survival.

Graph #10 demonstrates the five year survival of metachronous (N=145) versus synchronous (N=66) breast cancer diagnosis for South Jersey Healthcare. It is clear that metachronous patients appear to have a superior five year survival. Graph #11 shows the five year survival of unilateral (n=2,287) versus bilateral (n=211) breast cancer. Comparing internally it would appear that patients with unilateral breast cancer appear to have a higher five year survival except for stage IV, although this may not be statistically significant.

Graph #12 shows South Jersey Healthcare versus The National Cancer Data Base (NCDB) five year survival for bilateral and unilateral breast carcinoma. The SJH cohort represents 2,357 patients and NCDB supplied 443,377 patients. This demonstrates that the survival of bilateral and unilateral carcinoma as a group appears to be comparable to NCDB data applied for the same time period. Patients with metachronous breast carcinoma appear to have a slightly better prognosis than those with synchronous carcinoma when studying five year survival. When comparing the treatment outcomes for patients treated at SJH as a group, the group shows a comparable five year survival when looking at NCDB data.

Bilateral breast cancer represents a diagnostic and therapeutic dilemma for most clinicians. There are very few long term studies done in patients with either synchronous or metachronous breast carcinomas. Also, comparative data is at best, limited. It is felt perhaps that a smaller institution is able to review its caseload more completely, therefore, eliminating duplication of abstracting and more accurate results.

The Tumor Registry Database of the Frank and Edith Scarpa Regional Cancer Pavilion at South Jersey Healthcare is a useful tool for analyzing prognostic factors related to bilateral breast carcinoma.

Joseph Fanelle, MD

# **SOUTH JERSEY HEALTHCARE BILATERAL BREAST CANCER**

**METACHRONOUS      SYNCHRONOUS**

**82 Patients**

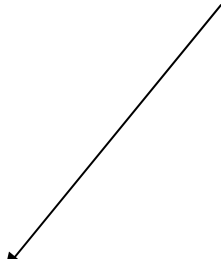
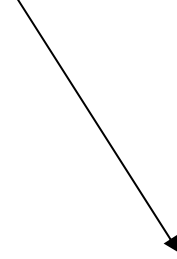


**164 Breasts**

**41 Patients**



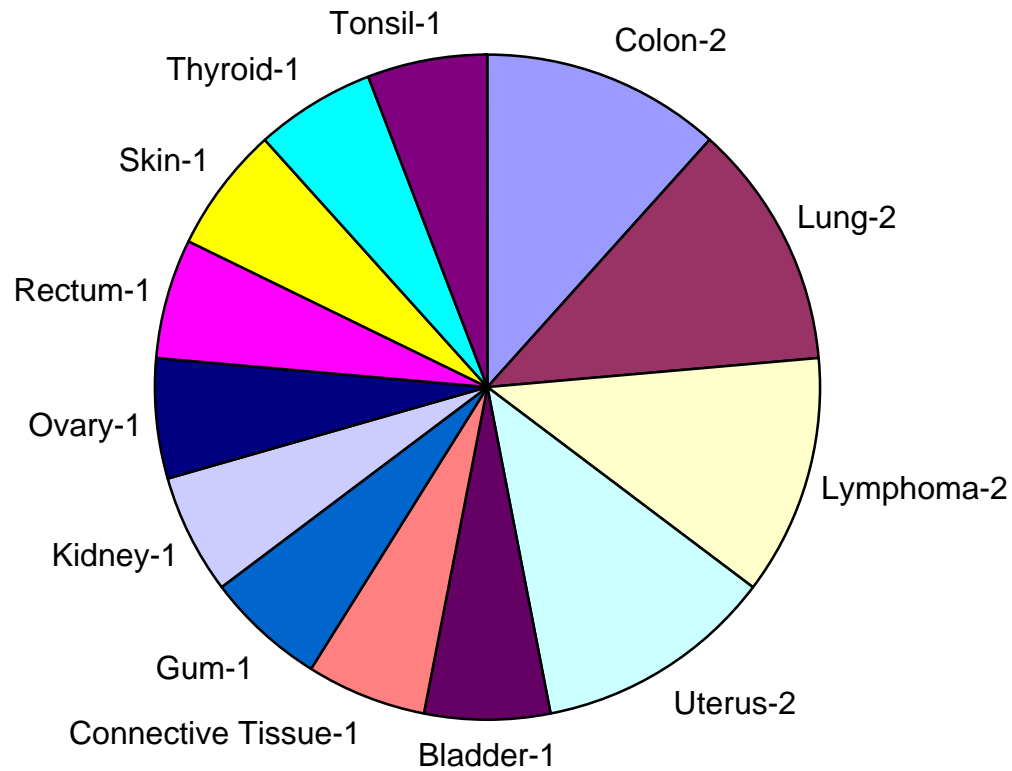
**82 Breasts**



**246 Breasts**

Graph 1

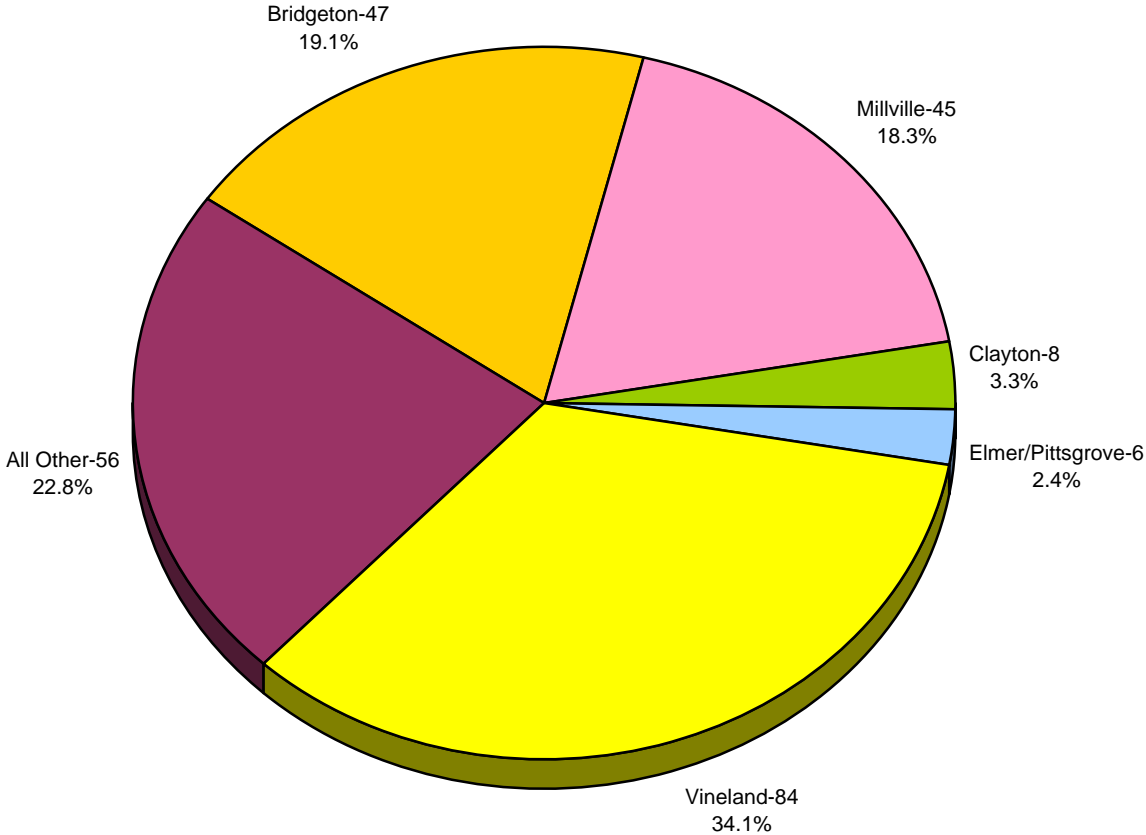
# SOUTH JERSEY HEALTHCARE - BILATERAL BREAST CANCER 1982-2007 SUBSEQUENT PRIMARY CANCERS



N=15 third primary tumors  
2 fourth primary tumors

Graph 2

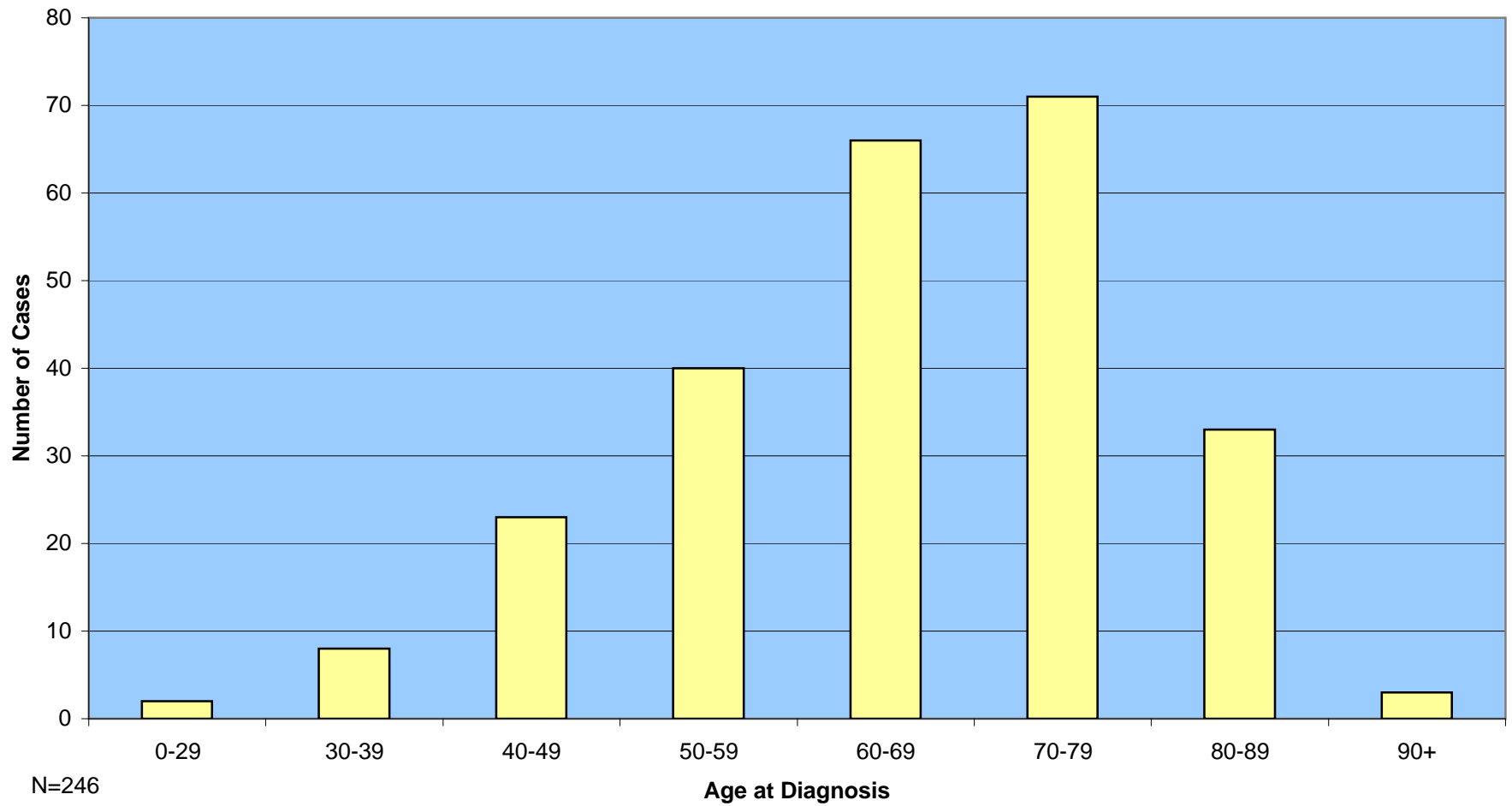
# SJH BILATERAL BREAST CANCER DISTRIBUTION BY MUNICIPALITY 1982-2007



N=246

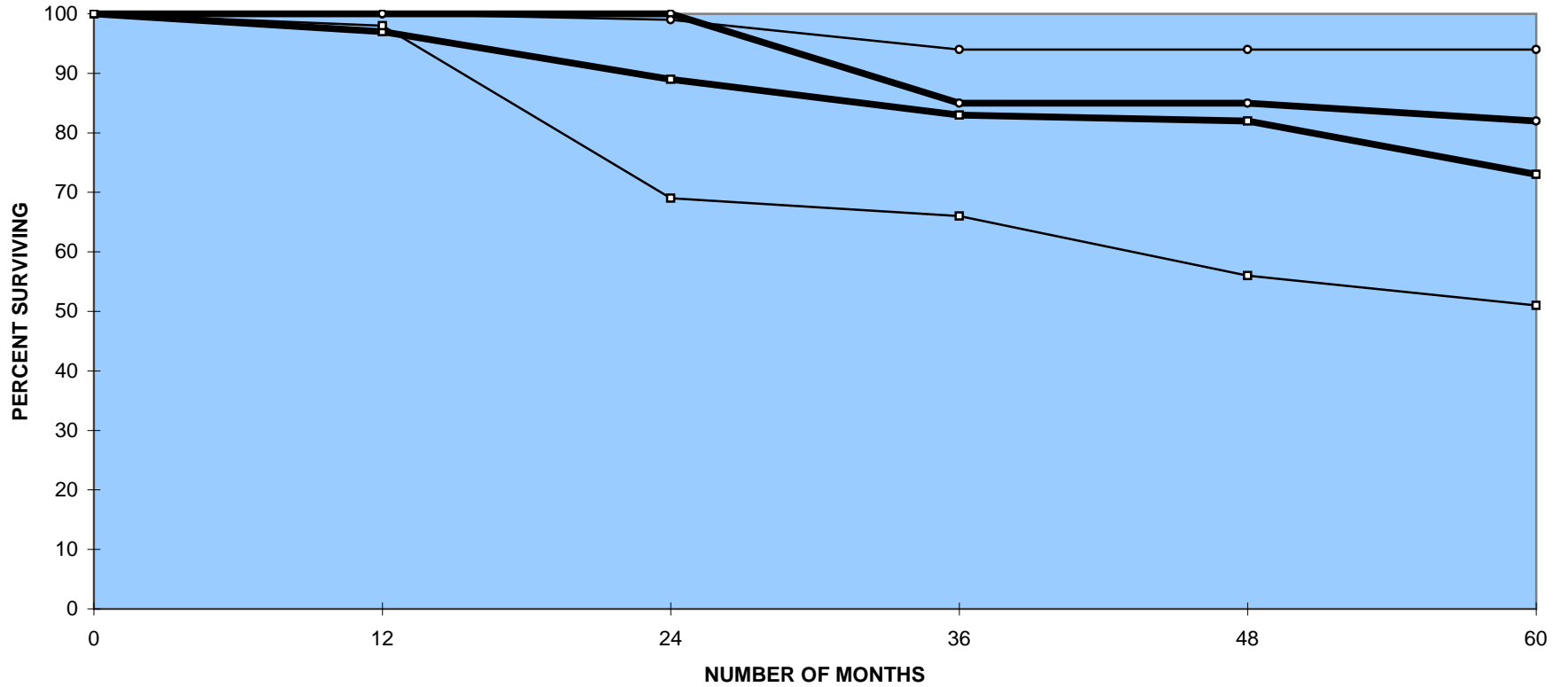
Graph 3

### SJH BILATERAL BREAST CANCER AGE AT DIAGNOSIS 1982-2007



Graph 4

### SJHS BILATERAL BREAST CANCER RELATIVE SURVIVAL BY AJCC STAGE 1982-2005



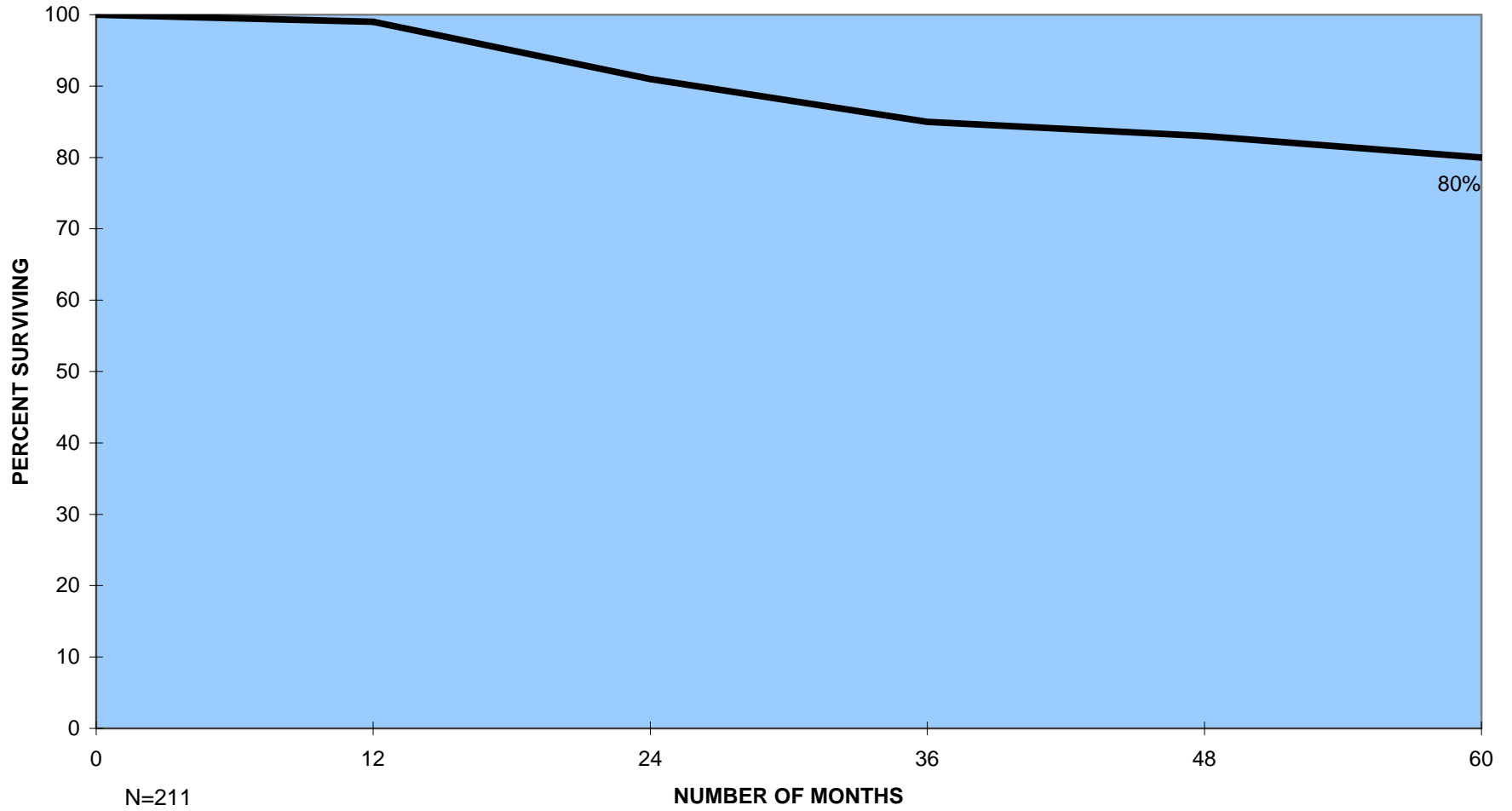
N= Stage 0 - 16      Stage III - 20  
Stage I - 93      Stage IV - 7  
Stage II - 75

N=211

—○— Stage 0    —○— Stage I    —■— Stage II    —□— Stage III

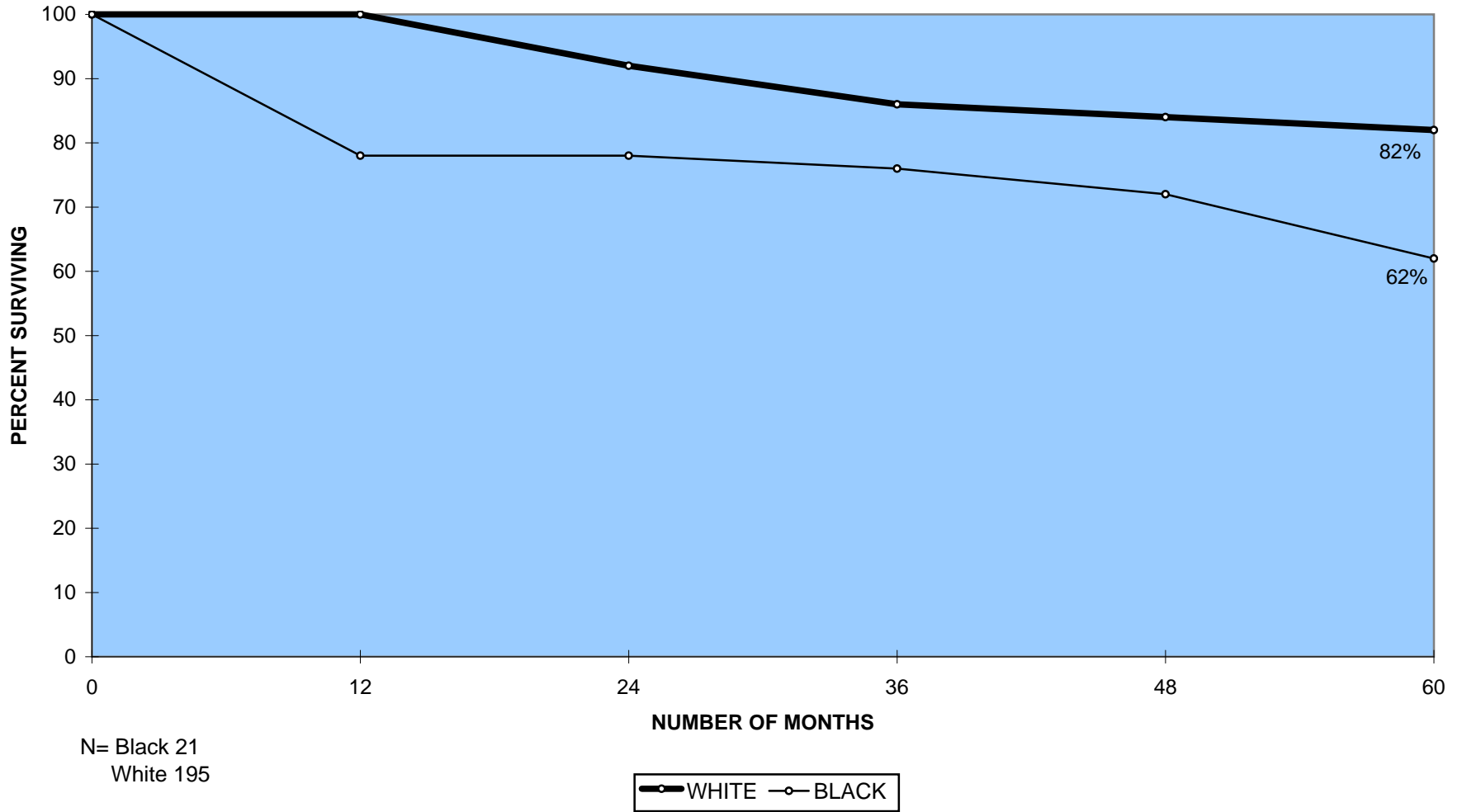
Graph 5

### SJH BILATERAL BREAST CANCER RELATIVE SURVIVAL BY COMBINED STAGE 1982-2005



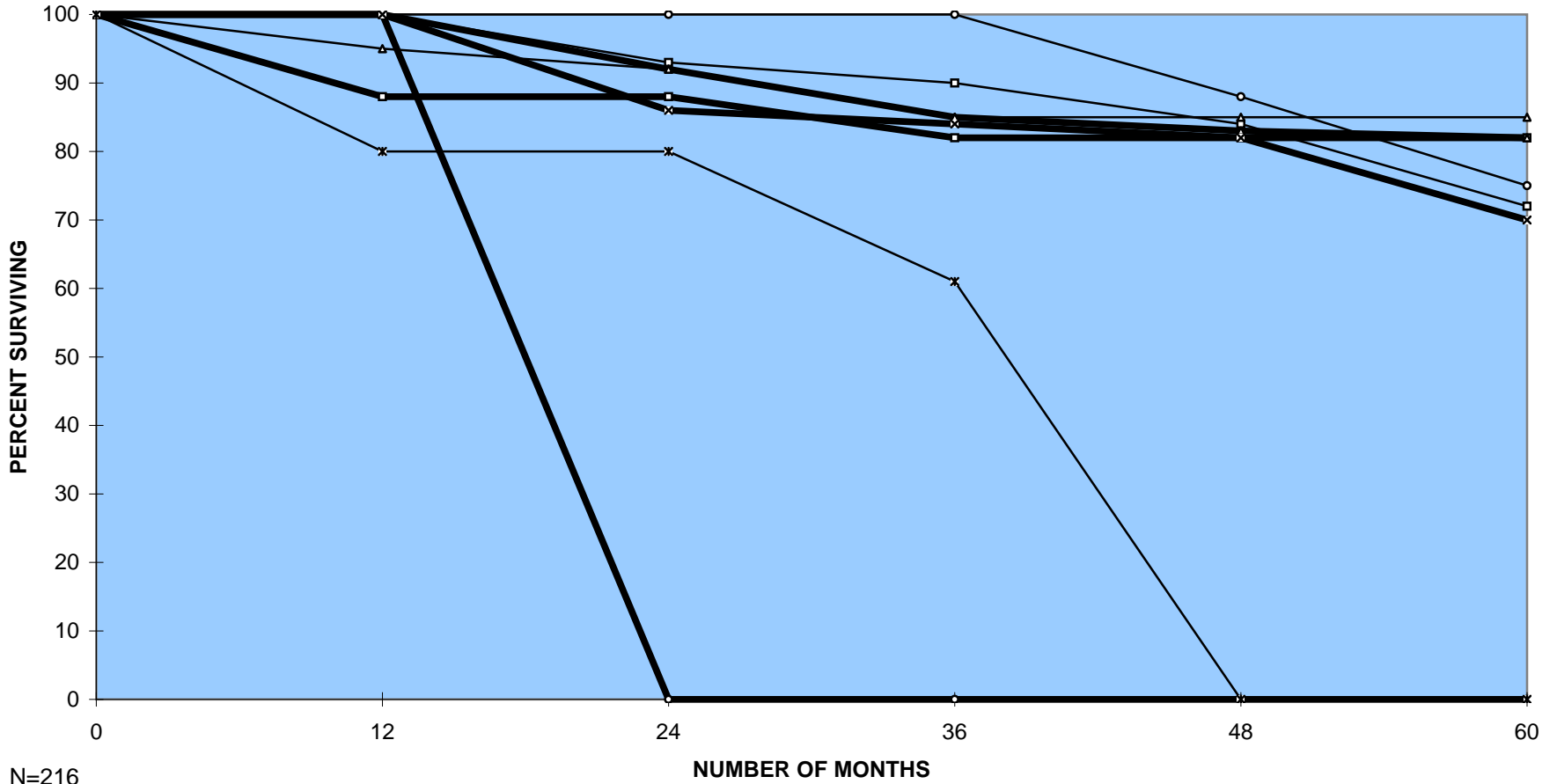
Graph 6

### SJH BILATERAL BREAST CANCER RELATIVE SURVIVAL BY RACE 1982-2005



Graph 7

### SJH BILATERAL BREAST CANCER RELATIVE SURVIVAL BY AGE AT DIAGNOSIS 1982-2005

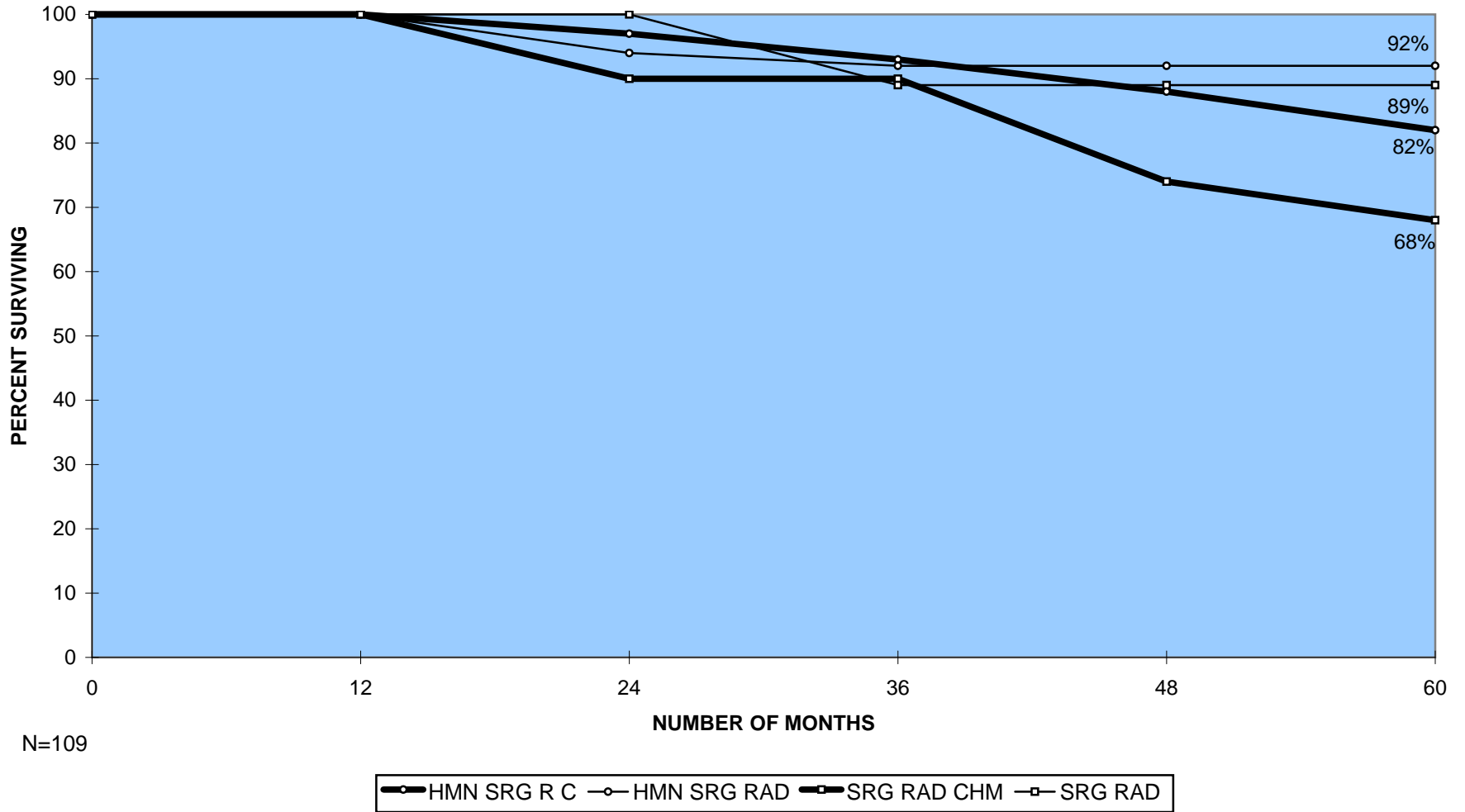


N=216

0 - 29   30 - 39   40 - 49   50 - 59   60 - 69   70 - 79   80 - 89   90 & OVER

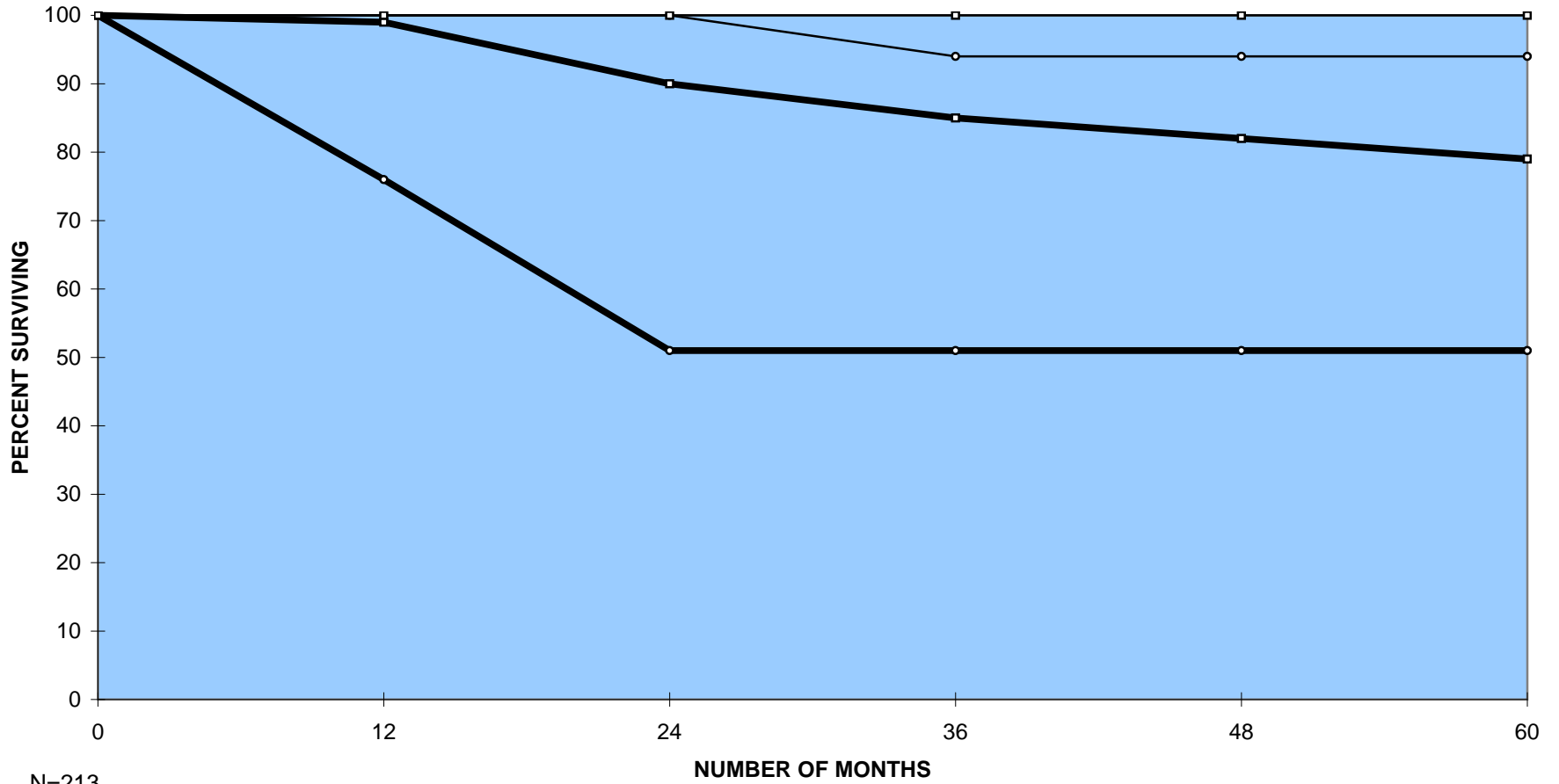
Graph 8

### SJH BILATERAL BREAST CANCER RELATIVE SURVIVAL BY INITIAL THERAPY 1982-2005



Graph 9

### SJH BILATERAL BREAST CANCER RELATIVE SURVIVAL BY MORPHOLOGY 1982-2005

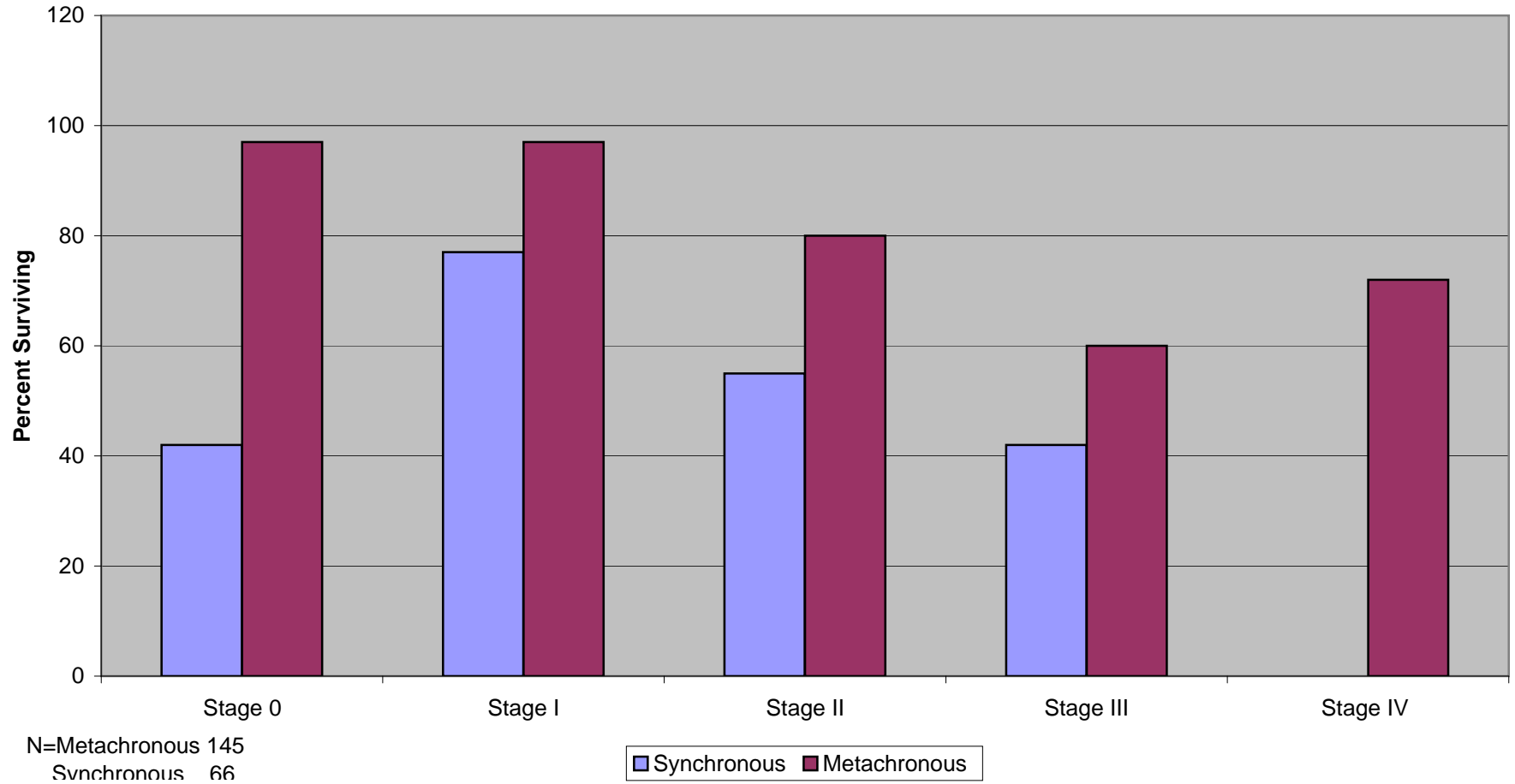


N=213

—●— Epithelial Neo=4 —○— Adenocarcinoma=7 —■— Ductal/Lobul/Med=197 —□— Cystic/Mucid/Ser=5

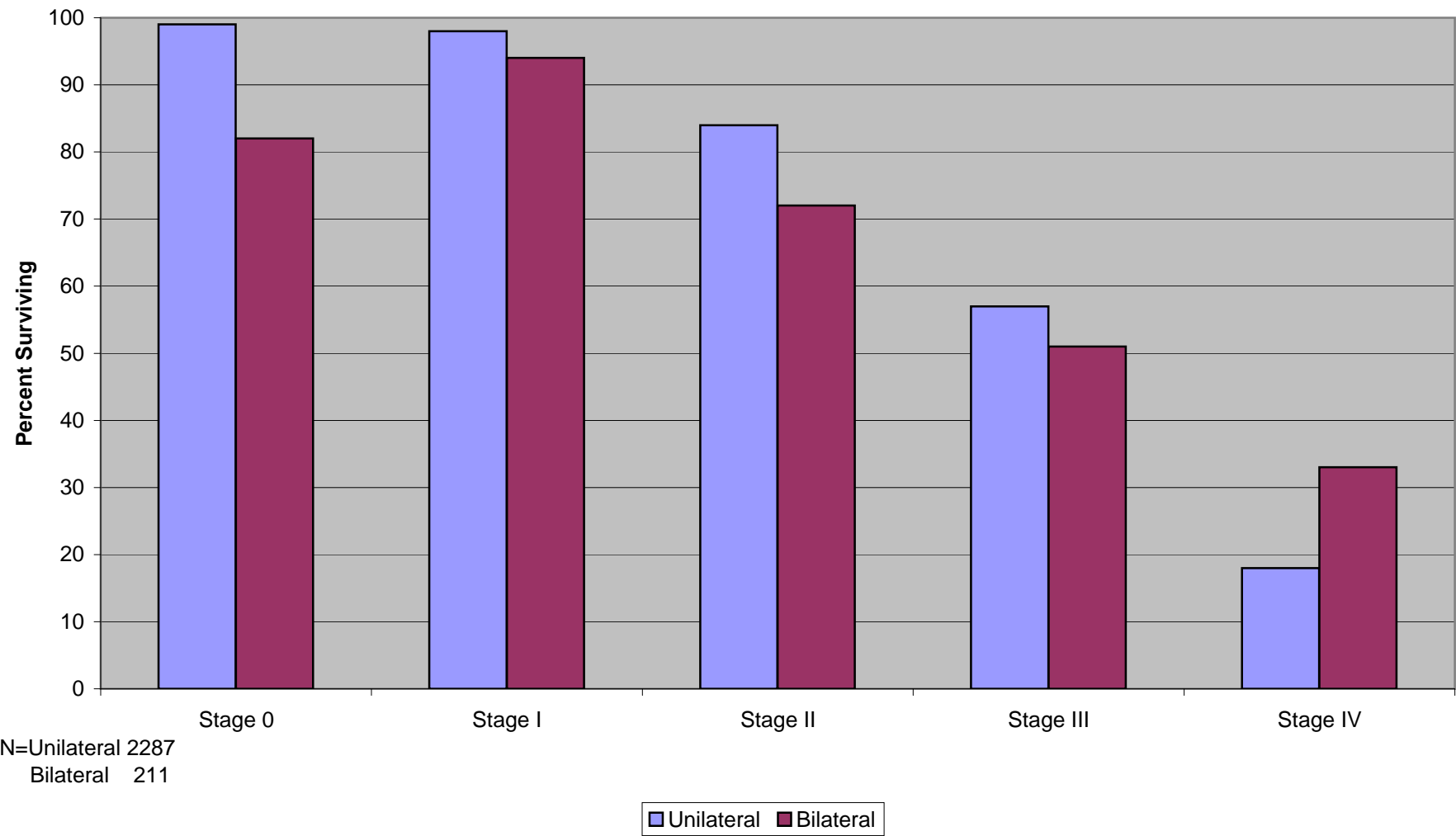
Graph 10

# SJH BILATERAL BREAST CANCER FIVE YEAR SURVIVAL METACHRONOUS DIAGNOSIS vs SYNCHRONOUS DIAGNOSIS 1982-2005



Graph 11

### SJH FIVE YEAR SURVIVAL UNILATERAL VS BILATERAL BREAST CANCER 1982-2005



Graph 12

### SJH vs NCDB FIVE YEAR SURVIVAL BILATERAL AND UNILATERAL BREAST CANCER

