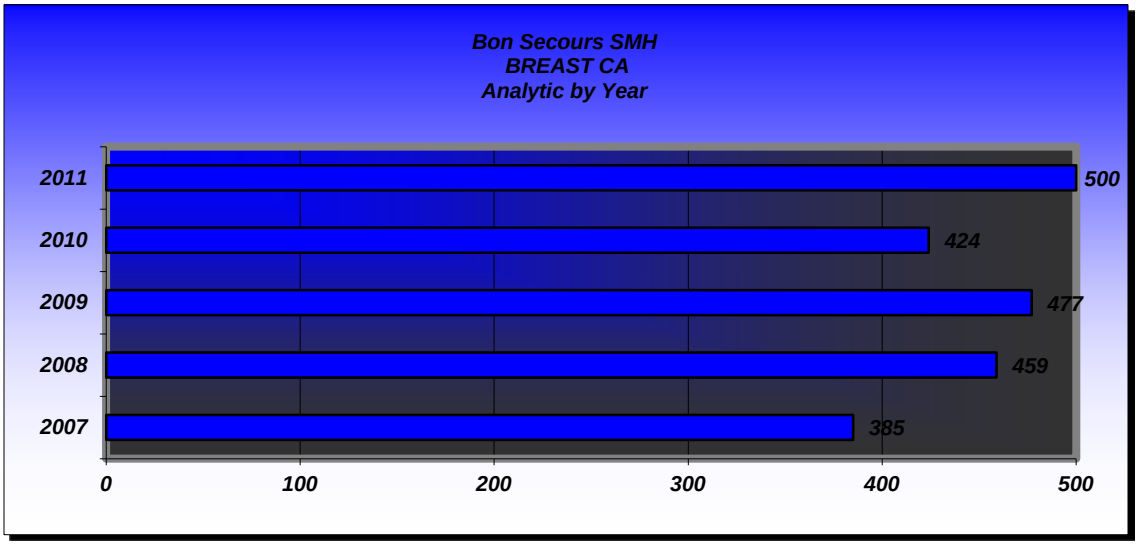
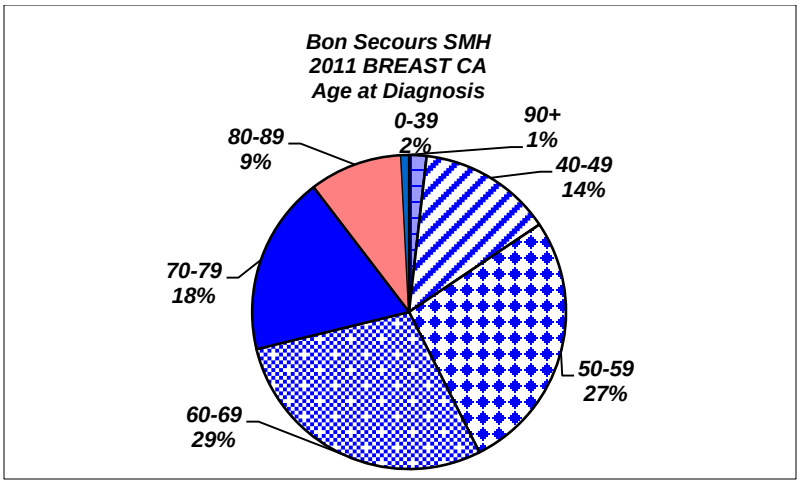
Site Study- Breast Cancer

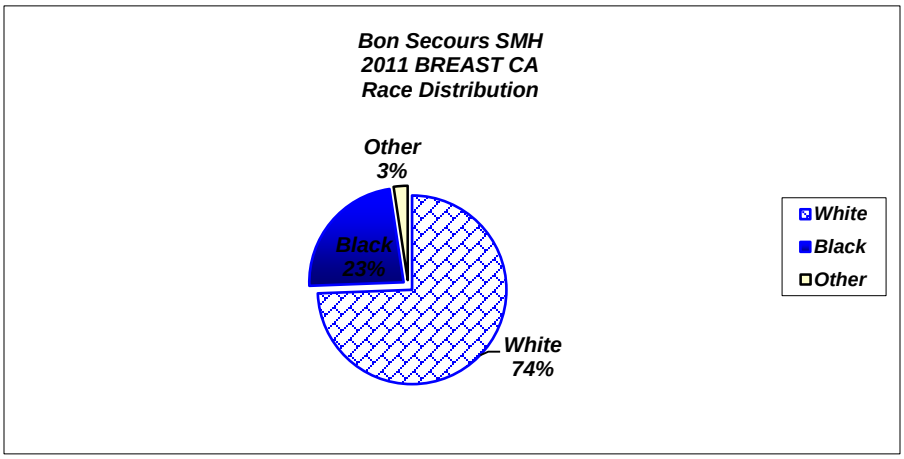
Rashmi Pradhan Vaidya, MBBS, MS,MD,FACS

Aside from non-melanoma skin cancer, breast cancer is the most common cancer among women in the United States. It is also one of the leading causes of cancer death among women of all races and Hispanic origin populations. Breast cancer is the most common cancer and the second leading cause of death in women in the United States. According to the National cancer institute's Surveillance Epidemiology and End results data (SEER) is estimated that there will be 226,870 women diagnosed with breast cancer and 39510 women will die of it , with a death rate of 23.0 per 100,000 women per year and 2190 males diagnosed with breast cancer with 410 men dying of it.9 1.2) From SEER data the mean age at diagnosis for cancer of the breast was 61 years.(2) In 2011 at SMH, 500 patients were treated for breast cancer, an increase of 19% over 424 treated in 2010 and The mean age at diagnosis of breast cancer was 62 years.(figure 1) 2% of patients were <39 years of age at diagnosis, 14% of patients were between 40-49 years, 27% of patients were between 50 and 59 years, 28% of patients were between 60-69 years, 18% of patients were between 70 to 79 years, 10% of patients were between 80-89 years and 1% of patients were over 90 years of age at diagnosis. These are comparable to SEER data.(2)(Figure 2)



The age adjusted incidence rate was 124.3 per 100,000 women per year., according to SEER data from 2005-2009.(2)In 2011 at SMH 75% of breast cancers treated were Caucasian and 23% were African American with 2% being other ethnicities. (Figure 3)

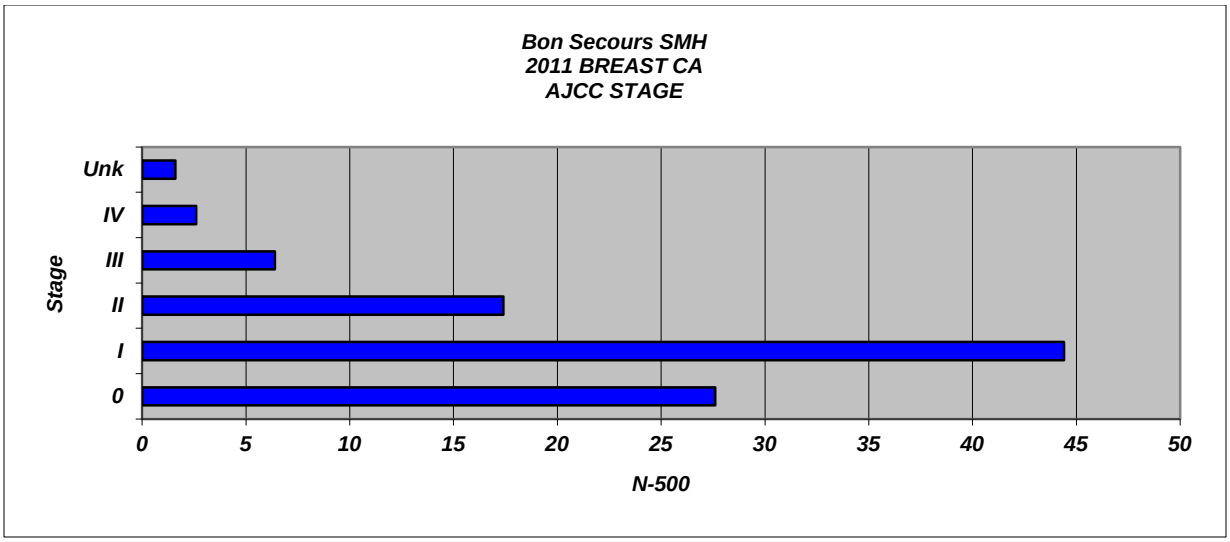


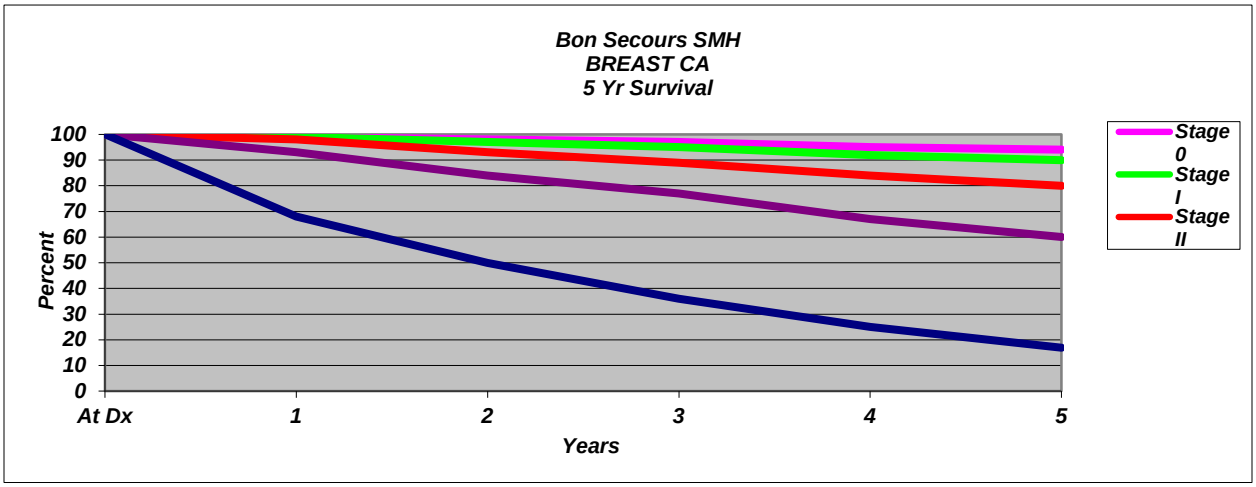


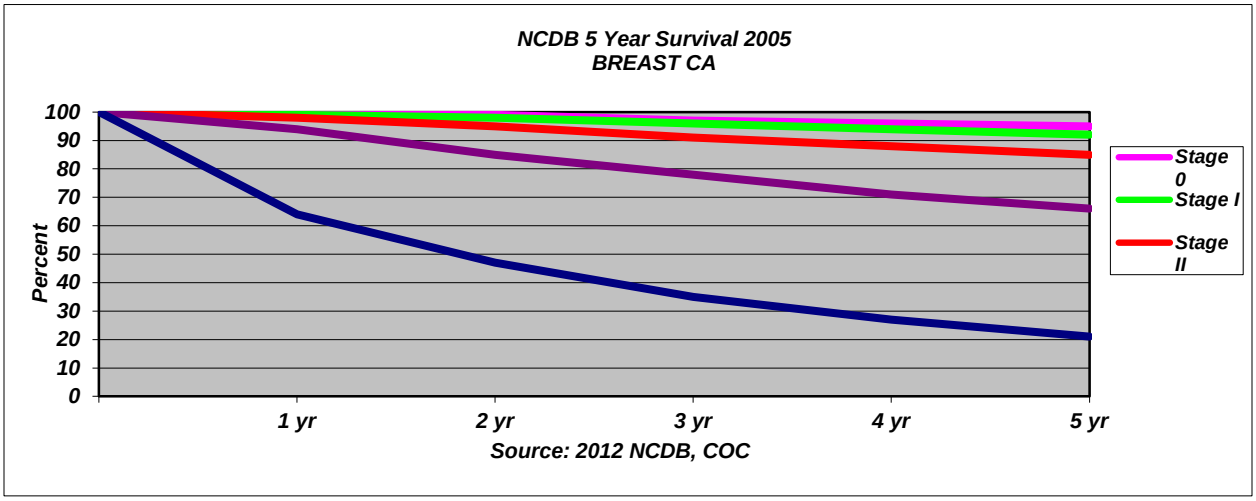
Survival and Stage

Overall 5 year relative survival for 2002-2008 was 89%, with 90.3% for white women and 77.7% for African American women. 5 year survival of patients at different stages treated at SMH mirrored the 5 year survival for stage matched patients in the NCDB database being over 98.4% for localized disease (confined to primary site), 83.9% for regional disease (spread to lymph nodes) and 23.8 % for Stage IV cancer or cancer with systemic metastasis. Stage for stage there is room for improvement in survival at SMH as noted in comparative graphs, esp in patients diagnosed at stages 2,3 and 4 of breast cancer.

At SMH in 2011, 28.04% breast cancers were diagnosed and treated at stage 0) or DCIS, 44.4% patients were treated for Stage 1 disease, 17.4 patients were treated for Stage II disease, 6.4% were treated for Stage II disease and only 2.6% were treated for stage IV disease. Figure 4 and 5





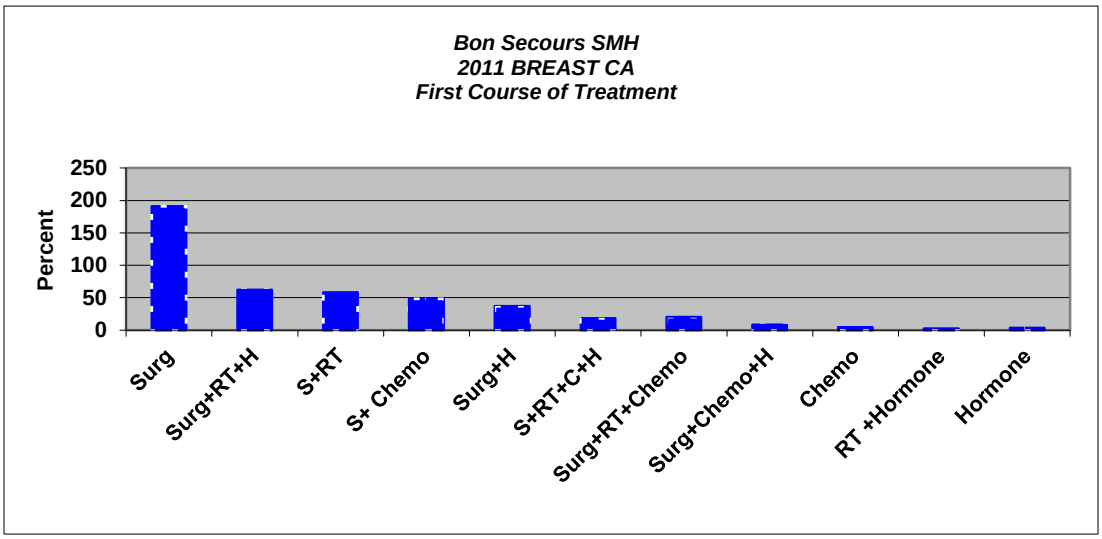


Lifetime risk

12.38% women born today will be diagnosed with breast cancer at some time during their lifetime, i.e. 1 in 8 women.

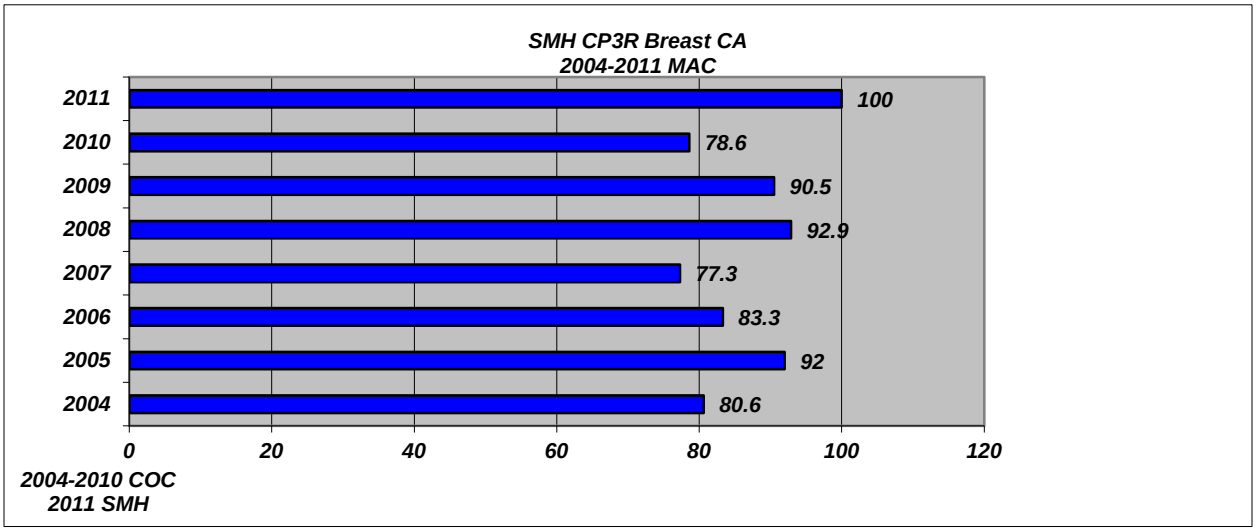
First course of treatment by stage

A majority of patients with disease localized to primary site or regional disease had surgery as the first line of treatment and this was followed by chemotherapy, radiation therapy and hormonal therapy as adequately indicated. Figure 6



SMH CP3R report

100% of indicated patients got treated within 4 months with chemotherapy for breast cancer. Figure 7



Exact etiology of breast cancer is unknown at present but risk factors are known. Combined estrogen and Progesterone hormone replacement therapy causes approximately a 26% increase in incidence of invasive breast cancer, based on a Randomized Controlled trial. There is solid evidence to prove Ionizing

radiation is associated with an increased risk of developing breast cancer starting 10 years after exposure and persisting lifelong. Risk depends on dose and age at exposure, with the highest risk occurring during puberty. Based on solid observational study obesity is associated with an increased breast cancer risk in postmenopausal women who have not used HRT. Based on solid evidence, exposure to alcohol is associated with an increased breast cancer risk in a dose dependant fashion. The relative risk for women consuming approximately 4 alcoholic drinks/day when compared with non drinkers is 1.32. The relative risk increases by 7% for each drink per day. This is based on case control and cohort studies. Based on solid evidence women who inherit gene mutations associated with breast cancer have an increased risk which could vary from 45-85% lifetime risk for developing breast cancer. 5-10% of women diagnosed with breast cancer with have hereditary breast cancer caused by a germline mutation such as BRCA 1 and 2. These mutations also carry a risk for ovarian cancers and other primary cancers. Genetic testing and counseling is available for such individuals.(3,4.5)Based on solid evidence following are the factors that decreased risk for breast cancer: early pregnancy, breast feeding, strenuous exercise for more than four hours per week. Average RR reduction is 30-40%.

Screening mammography and risk reduction from breast cancer mortality: a systematic review that examined ecologic and large cohort studies of women aged 50 to 69 years and found that any relative reduction in breast cancer mortality due to screening in this age group would likely be no greater than 10%.

Breast cancer is classified into a variety of histologic types, some of which have prognostic importance. For example, favorable histologic types include mucinous, medullary, and tubular carcinoma.(6) Invasive ductal carcinoma is the most common histological type found in about 85% cases of breast cancer.

Different types of treatments are used and multimodality therapy is commonly used for treating breast cancer. Surgical options are those of lumpectomy versus a simple mastectomy along with a sentinel node biopsy. Axillary node dissection is now reserved for those patients with biopsy proven axillary nodal disease. Frequently mastectomy is offered with immediate or delayed breast reconstruction with exogenous or autologous tissue used for reconstruction. Chemotherapy uses drugs and targeted therapy uses monoclonal antibodies such as herceptin and tyrosine kinase inhibitors to stop the growth of breast cancer cancer cells or kill them. Radiation therapy uses high energy x-rays or other type of radiation to kill cancer cells in the breast tissue. There are different types of radiation therapy such as external beam radiation therapy, accelerated partial breast radiation therapy using devices such as balloon catheters, interstitial wires or 3 D conformal whole breast radiation therapy.

Anti hormonal therapy in the form of Selective estrogen receptor modulators such as Tamoxifen used in all premenopausal women and some post menopausal women and aromatase inhibitors,in post menopausal women is effective in patients with Estrogen and progesterone receptor positive cancers as is ovarian ablation or oophorectomy in premenopausal women.

Prognosis and selection of therapy may be influenced by the following clinical and pathology features (based on conventional histology and immunohistochemistry):

- The age and menopausal status of the patient.
- The stage of the disease.
- The histologic and nuclear grade of the primary tumor.
- The ER and PR status of the tumor.
- Human epidermal growth factor type 2 receptor (HER2/neu) over expression.
- Proliferative capacity of the tumor (e.g., Ki67).

Molecular profiling has led to classification of breast cancer into the following five distinct subtypes:

- Basal-like.
- *HER2+*.
- Normal.
- Luminal A.
- Luminal B.

The use of molecular profiling in breast cancer includes the following:

- ER and PR status testing.
- HER2/neu receptor status testing.
- Gene profile testing by microarray assay or reverse transcription-polymerase chain reaction (e.g., Mamma Print, *Onco*type DX).(7,8.9)

In SMH in 2011, majority is 243/492 of the patients had ER/PR positive, HER2 negative breast cancer. Triple negative breast cancer was noted in 46/492 patients , ER/PR negative and Her2 positive was noted in 12/492 patients and ER/PR and Her 2 positive disease was noted in 24/492 patients(table)

			SMH	***MRMC***	***SFMC***	***Totals***
Stage 1-3		**ER or PR +, HER2 -**	**237**	**53**	**137**	**427**
		ER/PR -, HER2 +	**12**	**2**	**7**	**21**
		Triple Negative	**44**	**2**	**36**	**82**
		ER or PR + , HER 2 +	**22**	**4**	**19**	**45**

			SMH	***MRMC***	***SFMC***	***Totals***
Stage IV		**ER or PR +, HER2 -**	**6**	**1**	**1**	**8**

		ER/PR -, HER2 +	**0**	**0**		**0**
		Triple Negative	**2**	**2**		**4**
		ER or PR + , HER 2 +	**2**	**3**		**5**

It is heartening though that the age adjusted morality rate from breast cancer currently 23 per 100,000 women per year ,has been trending downward from 1998 to 2009 and given all the state of the art treatment modalities available to patients at SMH we hope to do even better in the future.(2)

References:

1.American Cancer Society.: Cancer Facts and Figures 2012. Atlanta, Ga: American Cancer Society, 2012.

2. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). *SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations)*, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2009_pops09/, based on November 2011 SEER data submission, posted to the SEER web site, 2012.

3. Claus EB, Risch N, Thompson WD: Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. Cancer 73 (3): 643-51, 1994

4. Blackwood MA, Weber BL: BRCA1 and BRCA2: from molecular genetics to clinical medicine. J Clin Oncol 16 (5): 1969-77, 1998

5. Frank TS, Manley SA, Olopade OI, et al.: Sequence analysis of BRCA1 and BRCA2: correlation of mutations with family history and ovarian cancer risk. J Clin Oncol 16 (7): 2417-25, 1998.

6. Nyström L, Andersson I, Bjurstam N, et al.: Long-term effects of mammography screening: updated overview of the Swedish randomised trials. Lancet 359 (9310): 909-19, 2002

7..Diab SG, Clark GM, Osborne CK, et al.: Tumor characteristics and clinical outcome of tubular and mucinous breast carcinomas. J Clin Oncol 17 (5): 1442-8, 1999.

8.Simpson JF, Gray R, Dressler LG, et al.: Prognostic value of histologic grade and proliferative activity in axillary node-positive breast cancer: results from the Eastern Cooperative Oncology Group Companion Study, EST 4189. J Clin Oncol 18 (10): 2059-69, 2000

9.Sørlie T, Perou CM, Tibshirani R, et al.: Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A 98 (19): 10869-74, 2001

10.Perou CM, Sørlie T, Eisen MB, et al.: Molecular portraits of human breast tumours. Nature 406 (6797): 747-52, 2000