THE SISTER STUDY BREAST CANCER RESEARCH

WOMAN BY WOMAN, SISTER BY SISTER, WE CAN MAKE A DIFFERENCE!

2011

Sisters –

It has been another busy year for the Sister Studies. It is hard to believe that we have almost completed the first round of biennial follow-up questionnaires. The last group will be receiving their first follow-up questionnaires with this newsletter. Some of you will even be receiving the next round! Your response rates have been terrific. We are grateful to each of you for taking the time to complete these questionnaires and hope you will continue to be active in the Sister Study. The information we get from every single participant really makes a difference.

The Two Sister Study and the Early Life Exposures Study are completing enrollment data collection as we ramp up for several new efforts described in this newsletter. We are excited about a new partnership with the CDC (Centers for Disease Control and Prevention) that will allow us to address new areas of interest including how having a sister with breast cancer affects families, and factors associated with good quality of life among breast cancer survivors.

About 1,300 Sister Study participants have reported breast cancer. Others have reported other cancers or conditions for which we may be asking additional information about the diagnosis or treatment. Sometimes medical records or pathology reports are the best source of information on details needed for researchers to study links between exposures and disease. If you are asked to provide this information we hope you will be willing to make this additional important contribution to our efforts to learn how to prevent breast cancer and other diseases in the future.

We hope you've had a good year and we look forward to hearing from you in the coming months. We also hope you'll like the new look of the Sister Study newsletter and our soon-to-be-updated Web site (www.sisterstudy.org).

Yours,

Dale P. Sandler PhD
Principal Investigator
The Sister Study

Research
Making A Difference

Sister Study Advances EARLY Act Goals

In 2010, Congress passed the Young Women's Breast Health Awareness and Support of Young Women Diagnosed with Breast Cancer bill. This legislation, known as the EARLY Act, directed the CDC to develop evidence-based programs to advance understanding and awareness of breast cancer among young women, especially those at increased risk for developing the disease. The EARLY ACT also required the CDC to carry out public and health care professional education activities, to conduct prevention research, and to provide support for young breast cancer survivors.

With the Two Sister Study's focus on women under 50 and the Sister Study's focus on women with a family history of breast cancer, the Sister Studies can make a valuable contribution toward achieving this mission. Experts from the CDC have joined forces with the Sister Studies to accomplish 3 goals. The first goal has already been accomplished – to have a workshop on the state-of-the-art in research on breast cancer survivors, especially young survivors. (See *Healthy Survival Following Breast Cancer*).

Starting this year, we will be including a set of questions with the Annual Updates that ask about breast cancer screening and about the impact having a sister with breast cancer has had on women and their families. We are also in the planning stages for a special survey of breast cancer survivors that will focus on quality of life and other areas of concern for women who have experienced a breast cancer diagnosis and treatment. By including participants in the Two Sister Study we will be able to address issues that are important to women who develop breast cancer at younger ages. This research provides a unique opportunity to better inform clinicians and researchers about what life is like for women with breast cancer and their families. These efforts may help inform public health initiatives to maximize healthy survivorship after breast cancer.

CDC Collaborators: Top row (from left to right): Nikki Hawkins PhD, Juan Rodriguez MPH, Lucy Peipins PhD. Middle row: Steven Leadbetter MS, Loria Pollack MD, Judith Lee Smith PhD. Front row: Mary White ScD and Katrina Trivers PhD. Frances McCarty PhD (not pictured).

> *This collaboration allows for investigations into important topics such as quality of life, work-life balance, barriers to healthy behaviors, stress and coping, medical decision-making, treatment related side-effects, and other areas…*

This collaboration allows for investigations into important topics such as quality of life, work-life balance, barriers to healthy behaviors, stress and coping, medical decision-making, treatment-related side-effects, and other areas that will enrich our ongoing and future research and will prove useful for cancer survivors and their families.

Healthy Survival Following Breast Cancer

Millions of women have found that life goes on after a breast cancer diagnosis, albeit sometimes with new challenges. We have a large cohort of survivors that may be able to teach us a great deal about living well after breast cancer and about the long-term needs and concerns of breast cancer survivors.

As a first step, we held a workshop in Chapel Hill, North Carolina, at the end of January. We set out to bring together the most knowledgeable people in the area of survivorship research, and we succeeded in assembling a "dream team" of experts. For a day and a half we listened to them describe the state of knowledge, with plenty of time for discussion so they could advise us about where the Sister Studies can contribute the most to this area of research.

Four general topics were considered. The first was behavioral, psychosocial and economic outcomes after cancer. What are consequences of a diagnosis for the quality of work life? What about job mobility? The second topic was health effects after treatment, which dealt with possible long-term problems such as lymphedema and fatigue. The third topic was reproductive health effects after

Participants and sisters with breast cancer are important members of the Sister Study family!

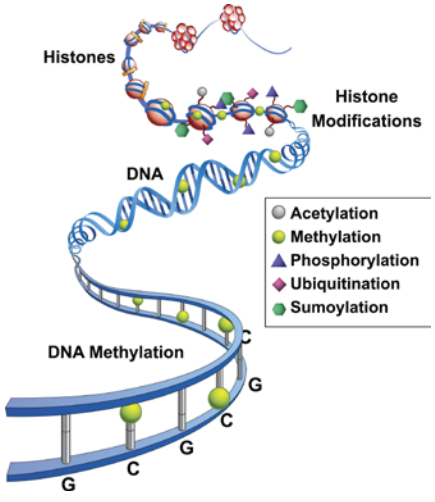
treatment. Here we heard about sexuality, accelerated menopause, and concerns of young survivors related to fertility and child-bearing. Topic four had to do with cancer recurrence and factors related to long-term cancer-free survival.

We are grateful to the experts who contributed their valuable time and energy to this effort. Now the work of deciding which promising avenues to pursue is under way.

We hope you will remember that if you are diagnosed with breast cancer, that should not mark the end of your participation in the Sister Study. Participants and sisters with breast cancer are important members of the Sister Study family!

Environment can modify genes

Inherited differences in DNA sequence – the ordering of the roughly 3 billion As, Cs, Gs, and Ts that make up our genome, begin to make us who we are. Inherited genes also may affect our susceptibility to disease. But there are other changes that normally occur to DNA that are not necessarily inherited. These so called "epigenetic" changes are of growing scientific interest because they can be associated with the way genes are expressed. Research has shown that epigenetic patterns differ between cancer cells and normal cells. DNA ***methylation***, one form of epigenetic change, is especially interesting because these methylation "marks" can be inherited (sometimes from your mother, sometimes from your father), may happen to babies *in utero*, or may occur later in life, in some cases because of environmental exposures. Sister Study investigator Jack Taylor has been studying these epigenetic marks using DNA from a subgroup of 1000 Sister Study participants. Using highly specialized instruments, he is able to look at levels of DNA methylation at as many as 27,000 specific sites within each woman's genome. This work has already shown that some methylation patterns are correlated with a woman's age. His research group is now examining whether other factors, including known breast cancer risk factors, are related to DNA methylation patterns. In addition, by comparing DNA samples from women who developed breast cancer after joining the Sister Study to samples from those who did not, we hope to see whether DNA methylation patterns can be used to identify women who may be at higher risk of developing breast cancer, or can be used for early detection. "It's an exciting opportunity to try to link environmental exposures with these subtle DNA modifications and disease risk," says Dr. Taylor. "And among women who develop cancer, we'd like to eventually examine whether these patterns can be used to better direct therapy or targets for successful treatment."



Arrival of our Komen Fellow, Chunyuan Fei

In August, with support from Susan G Komen for the Cure, Dr. Chunyuan Fei joined the Sister research group. She came to us with a record of achievement that was already impressive, having published, while still a student, ten papers, including several that described effects of perfluorinated environmental chemicals on reproduction. Chunyuan was born in Changzhou, China, and she completed an MD in preventive medicine and earned a Master's degree in biostatistics and epidemiology in China. She came to the US to earn a PhD in epidemiology at the University of California, Los Angeles. In her time at NIEHS, she has been learning about breast cancer and working on the analysis of data from the Two Sister Study. Chunyuan will soon be submitting our first Two Sister Study research paper on possible associations between use of fertility drugs and young-onset breast cancer. We are excited to have Chunyuan on the Sister team!

Research
Making A Difference

2010-11 Research Round Up

The American Cancer Society Nutrition and Physical Activity Guidelines for Cancer Prevention

Created every 5 years by a panel of experts, these guidelines focus on dietary and other factors that may reduce the risk of cancer. Here are the current guidelines for women.

Maintain a healthy weight throughout life.

- Balance calorie intake with physical activity.
- Avoid excessive weight gain throughout life.
- Achieve and maintain a healthy weight if currently overweight or obese.

Adopt a physically active lifestyle.

- Engage in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week; 45 to 60 minutes of intentional physical activity are preferable.

Eat a healthy diet, with an emphasis on plant sources.

- Choose foods and drinks in amounts that help achieve and maintain a healthy weight.
- Eat 5 or more servings of a variety of vegetables and fruits each day.
- Choose whole grains over processed (refined) grains.
- Limit intake of processed and red meats.

If you drink alcoholic beverages, limit your intake.

- Drink no more than 1 drink per day for women.

Association of intrauterine and early life exposures with age at menopause in the Sister Study.

The age a woman undergoes menopause helps determine her lifetime exposure to estrogen and progesterone which are important in the development of breast cancer. This paper reported that events occurring early in life – both before birth and during early childhood – may influence age at menopause. For example, participants whose mothers had used diethylstilbestrol (DES) when pregnant with the participant had an earlier age at menopause. Other factors potentially associated with earlier menopause were low birthweight and mother's history of diabetes.

Steiner A *et al., American Journal of Epidemiology* 2010;**172(2)**:140-148.

Lifestyle behaviors in Black and White women with a family history of breast cancer.

We examined how well participants were meeting the American Cancer Society (ACS) cancer prevention guidelines when they joined the Sister Study (See *sidebar*). On average, Black women consumed a slightly lower percentage of calories from fat and were more likely to meet ACS alcohol recommendations than Whites. White women consumed more fruits and vegetables/day than Black women and were more likely to meet ACS guidelines for physical activity and body size. Like women in the general population, the majority of Black and White women in the Sister Study were not meeting most guidelines for healthy lifestyle behaviors recommended by the ACS.

Spector DJ *et al., Preventive Medicine* 2011;**52**:394-397.

Family based gene-by-environment interaction studies: revelations and remedies.

Studying families is a powerful way to learn how our genetic make-up and life experiences may work together to influence our chances of getting breast cancer or other diseases. Using the Two Sister Study as motivation, we developed a new statistical method that allows us to efficiently analyze data from families with two siblings (one with and one without breast cancer), even when the sibling without the disease is not genotyped but does provide data on environmental exposures. The new approach is less likely to produce misleading results about gene-by-environment interactions than earlier designs that studied only cases with disease and their parents. This insight will allow us to make the best possible use of the data from the Sister Studies.

Shi M *et al., Epidemiology* 2011:**22(3)**:400-407.

Eating patterns and nutritional characteristics associated with sleep duration.

Inadequate sleep duration has been reported to be associated with obesity and risk of some chronic diseases. This paper found that women who slept the least were more likely to eat outside of conventional eating hours and more likely to eat snacks. Women who reported sleeping more than 10 hours a day also reported more snacking and eating at unusual times.

Kim S *et al., Public Health Nutrition* 2011;**14**:889-895.

Employment and work schedule are related to telomere length in women.

Telomeres are genetic sequences that cap and protect the ends of chromosomes. Short telomeres have been associated with chronic stress in some studies, and may be a marker of cellular aging. We examined how employment and work schedule may be related to telomere length measured in blood cells. Compared to non-employed women who may have worked in the past, those currently working fulltime had shorter telomere length. Longer duration of fulltime work also was associated with shorter telomere length. These differences in telomere length were greater in working women reporting higher stress levels.

CG Parks *et al., Occupational and Environmental Medicine* 2011, in press.

Other Papers in Progress:

- Early life exposures and fibroids in Black women
- Accuracy and reliability of self-reported weight and height
- Use of fertility drugs and young-onset breast cancer
- Early life factors and the timing of menarche
- Genetic variants and breast cancer risk

Telomere length in peripheral blood and breast cancer risk in a prospective case-cohort analysis: results from the Sister Study.

Some studies have found that shorter telomere length is associated with obesity and chronic diseases including cancer. Studies of breast cancer have had inconsistent results, possibly because many of these studies used blood samples collected after women had already developed breast cancer. Using blood samples collected at the time women joined the Sister Study, we compared telomere length in 342 women who later developed breast cancer and a random sample of 735 women who did not develop the disease. Telomere length was not associated with an increased risk of breast cancer in our prospectively collected data. Our analysis does not support using telomere length to predict breast cancer risk.

Kim S *et al., Cancer Causes & Control* 2011, in press.

In the last two years, about 90% of Sister Study participants report having a routine physical exam. In the same time period, 92% have had a breast exam and 92% have had a mammogram.

Sisters
Making A Difference

Sister Studies Are A Family Affair

As you probably know, the Sister Study, now 50,000+ strong, began by focusing on individual women whose sister had breast cancer. Although we did not specifically recruit families, about 19% of our participants have at least one other sister who joined the Sister Study, either on their own, unbeknownst to their sisters, or purposefully joining as a group. In the past few years, we have reached out to other family members for related studies such as the Two Sister Study, the Young Women's Breast Cancer Project, and the Early Life Exposures Study. So the Sister Studies are now a family affair, with some families having as many as nine members - sisters, mother, and father - all participating in some aspect of our breast cancer research. We are delighted to share the stories of two of these special families. Our thanks go out to all of the sisters, mothers and fathers who make this research possible.

Bottom row (left to right): John (brother), Sarah, Kathy; Second row: Ursula, Patricia; Third row: Maryann, Tom (brother), Theresa; Top row: Eileen, Sarah (mom)

After their sister Eileen developed breast cancer in 2006, Kathleen, Patricia, Sarah, Theresa, Ursula, and Maryann joined the Sister Study at Eileen's request. "This was a tangible way for us to support our sister through a difficult time," shared Sarah. "I've remained in the Sister Study because I've made a commitment to my sisters, and cherish that bond." Kathleen's reasons include contributing to the science and participating "for my daughter's sake. I'd think any research that could help prevent breast cancer would benefit her, as well as all my nieces." Patricia hopes that this effort "will lead to a decrease in the occurrence of breast cancer and early, successful treatment." Some of the more challenging aspects of the study for the sisters have included the blood draw and finding the time to complete each phase. The most positive aspect, they agree, is the reward of contributing to a national breast cancer study of such magnitude. Even after Eileen's full recovery, all of her sisters continue to show their dedication by their ongoing participation in the Sister Study. "It seemed like a small thing to do to support your sister," said Patricia. Their mother showed her support by completing the Early Life Exposures Study last year.

> ***I've remained in the Sister Study because I've made a commitment to my sisters, and cherish that bond.***

At age 45, Vivian was the first sister to be diagnosed with breast cancer. Two more of the sixteen siblings soon followed: Audrey, diagnosed at age 62, and Debra, at age 46. Seven of the eleven sisters (Mary, Stephanie, Earline, Suzanne, Linda, Patricia, and Jennie) joined the Sister Study in order to answer some of the questions they had about their experience and to help others who were going through similar situations. "One question that was always on our minds was why those three sisters? We all grew up in the same environment as children but in our early adult life we moved to different states." Since the Sister Study is also interested in the role that genes and the environment play in developing breast cancer, "we never hesitated a moment about whether or not we would participate." All 15 sisters and brothers are still with us today in good health, including Vivian, Audrey, and Debra, who are successful breast cancer survivors. "We are truly blessed three times over."

From right to left: Linda, Patricia, Debra, Vivian, Audrey, Mary, Earline, Jennie, Suzanna, Stephanie, Marie

Communication
Making A Difference

How do I report any changes to my health?

Each year, we send you a "Sister Study Health Update" that you can use to record major changes in your health status (for example, a diagnosis of breast cancer, heart attack, etc.). We ask you to return it even if there have not been any changes to your health. If you develop any medical conditions, you may also let us know by calling us toll-free at 1-877-4SISTER or 877-474-7837 and following the directions for enrolled participants.

Are you still enrolling participants for any studies?

We are no longer enrolling new participants in the Sister Study or the Two Sister Study. However, we are still looking for *parents* of women enrolled in the Two Sister Study. If your parents have been invited to participate in that study, please encourage them to complete their saliva collection and mail it in soon. From time to time, some of the 50,000 Sisters or the 1400 Two Sisters may receive invitations from us to participate in related studies on special topics. In addition, we are also happy to pass along information about national organizations that have information about other research studies that are looking for participants. A listing of these organizations is available on the Sister Study Web site (www.sisterstudy.org) and by contacting the Sister Study Helpdesk toll-free at 877-4SISTER or 877-474-7837.

How long will the study last?

Women in the Sister Studies will be followed for at least ten years. The information that we collect becomes more valuable over time as women in the study experience changes in their health, environment and lifestyle.

Can I still participate in the Sister Study if I am diagnosed with breast cancer?

YES. We want to learn how environmental, lifestyle, and genetic factors influence treatment outcomes, survival, and quality of life following breast cancer diagnosis. In fact, it is very important to the success of the study that women diagnosed with breast cancer continue to stay with us.

Did you know?

Sister Study participants have a wide range of hobbies. Gardening is the most popular—31% report spending time on this activity.

About 52% of Sister Study participants report spending some time each week caring for children or grandchildren; while 34% report spending some time each week caring for a disabled or ill family member.

Over 56% of Sister Study participants have a pet in the home.

About 68% of Sister Study participants have worked outside the home in recent years.

Over 60% of Sister Study participants have received the flu shot in the past 12 months; about 3% have had the flu.

We're All
Making A Difference

Congratulations, Dale!

At the recent Annual NIEHS Science Awards Day, scientists and trainees stepped away from their laboratories and devoted the day to recognizing the achievements of their colleagues. The Sister Study's own Principal Investigator Dale Sandler was presented with the prestigious Scientist of the Year award. Dr. Sandler has been with NIEHS since 1979 and has served as chief of the Epidemiology Branch since 2004. One of the letters nominating Sandler for the award read, "Sandler's work has been characterized as a major catalyst in the evolution of epidemiology, [with] seminal contributions across the field of epidemiology through publication of important papers on chronic renal disease, cancer, cardiovascular disease, and breast cancer."

Dr. Sandler presented an overview of the work encompassed in her distinguished career, which has included the establishment of large, scientifically fruitful cohorts such as the Sister Study. Dr. Sandler is the first woman and the first epidemiologist to be recognized as the NIEHS Scientist of the Year.

(Photo courtesy of Steve McCaw, article from the December issue of the NIEHS Environmental Factor)

Did You Know...?

Dr. Sandler and the ship that stopped the oil leak

The Sister Study was the template for the development of a new long-term follow-up study of the possible effects of the recent Deepwater Horizon oil spill in the Gulf.

The GuLF STUDY (www.nihgulfstudy.org), was able to launch in record time by borrowing from the Sister Study design and materials, and taking advantage of what has been learned in the process of building the Sister Study cohort. The study is led by Dr. Dale Sandler and other researchers at the National Institute of Environmental Health Sciences, NIH.

The Sister Study is conducted by the National Institute of Environmental Health Sciences — one of the National Institutes of Health of the US Department of Health and Human Services.

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