A Study of the Environmental and Genetic Risk Factors for Breast Cancer

The Sister Study 2008

National Institute of Environmental Health Sciences • National Institutes of Health • Department of Health and Human Services

The Two Sister Study

Women with breast cancer often tell us they feel frustrated because they cannot join the Sister Study. As you know, the Sister Study is enrolling 50,000 women whose sister had breast cancer, but does not involve those sisters with breast cancer directly. Now some of those sisters can join an exciting new study, funded by Susan G. Komen For The Cure®, and directed by Drs. Clarice Weinberg, Dale Sandler, and Lisa DeRoo. The "Two Sister Study," an offshoot of the Sister Study, will focus on young-onset breast cancer. Although breast cancer is uncommon below age 50, women who develop the disease at a young age can tell us a lot about genetic and environmental causes. With support from the Komen Grants Program, and help from Sister Study participants, we plan to enroll about 1600 recently-diagnosed sisters who were under age 50 when diagnosed. Their parents will also be invited to participate, for a powerful approach based on families.

Here is how the study will work. Many Sister Study participants who have an eligible sister with young-onset breast cancer will be asked to mail that sister an invitation to join the Two Sister Study. If the sister who had cancer agrees to join, she will complete telephone interviews like the ones her sister already did for the Sister Study that also ask about her cancer diagnosis and treatment. She will send in a saliva (spit) sample for DNA and will invite her parents to send saliva as well. She will still be able to participate even if her parents do not. We will look for possible environmental effects by comparing histories of sisters with and without breast cancer, and for possible genetic effects by tracking unusual variations in genes that may have been passed from parents to daughters. Sisters who join the Two Sister Study will be part of our long-term effort to study breast cancer survivors, so we can learn about factors related to long-term health following treatment for breast cancer. There is power in sisterhood!

A Message from the Principal Investigator

Greetings to new and continuing Sisters. We are reaching an important milestone in 2008! We will complete enrollment of 50,000 Sisters and begin the next important phase of the study. While this is an exciting milestone, it is also bittersweet as we will need to turn away some women who want to participate in the study. As I write this, more than 45,000 women have signed up for the study, with 37,000 having completed all enrollment activities. Our immediate challenges for 2008 are to get all remaining participants through their enrollment activities, and to recruit the additional women needed to reach our goal of 50,000 diverse Sisters from all walks of life. To make sure that all women are well represented, we continue our special outreach to African American, Latina, Asian, Pacific Islander, American Indian and Alaska Native women, and to women with blue collar or non-traditional jobs. Caucasian women with a high school degree or less, or ages 65-74 are also still needed. Other groups are very well represented in the study group.

We are now turning our attention to regularly updating information on the health of Sisters in the study to learn why some women get breast cancer, or other health conditions, while others do not. We cannot do this without your ongoing commitment to the study. We will be working hard to keep you involved and we want to hear your ideas about what we can do to make your long-term participation rewarding. Some of you will be receiving an Annual Update form for the first time. Others will be receiving the longer questionnaires that should come about every two years. As always, we hope you will complete and return these forms promptly.

This edition of our newsletter contains a lot of new information for you. The articles tell you about new research studies, introduce you to some new staff, and also describe what happens when Sisters in the study are diagnosed with breast cancer.

Remember, woman by woman, sister by sister, we can make a difference!

Developing a Specimen Collection for Quality Control of the Sister Study Samples

The biological and environmental samples you provided are key components to understanding the genetic and environmental factors related to breast cancer. Your samples are stored in different ways at different locations. There are now over 2 million straws, tubes, vials or envelopes safely stored, including—

- 1.2 million blood samples
- 950,000 urine samples
- 72,000 toenail packets
- 37,000 dust samples

We want to preserve your samples to study key hypotheses related to breast cancer and other diseases. Therefore, we also collect samples from other women who are a lot like the Sisters in the Sister Study, to use for quality control tests. These samples are used to—

- Assess how our sample collection, handling, and storage procedures affect your Sister Study samples.
- Evaluate tests that may be done on your specimens.
- Include as control samples along with study samples for research testing.

All of the quality control samples are collected and stored just like the Sister Study samples are. That means that control samples are processed by the same laboratory staff members that handle your Sister Study samples and that samples are stored together, regardless of whether they are "controls" or study samples. This ensures standardized conditions. What we learn from these quality control tests will help the Sister Study and other studies that use stored samples.

When Sisters Report Breast Cancer

Like women everywhere, some women in the Sister Study develop breast cancer. Dealing with breast cancer is challenging and women need to concentrate on getting medical treatment and feeling better after their diagnosis. Nonetheless, we hope that Sisters diagnosed with breast cancer will continue with the study and agree to provide information about their diagnosis and treatment. This additional information, together with the information provided when they joined the study and during updates, will be valuable in helping us identify the causes of breast cancer and factors related to survival and healthy living following diagnosis. The on-going participation of every woman in the Sister Study is important.

We will contact a participant with breast cancer about 12 to 18 months after diagnosis to allow some time for her treatment and recovery. She will be invited to take part, at her convenience, in a 20-minute telephone interview about her diagnosis and treatment. We will also ask permission to contact her medical providers so we may ask for some medical details about her cancer and treatment, and for a sample of the tissue that was collected during diagnosis. The tissue samples will allow us to study changes that may hold clues to the causes of the disease or why it sometimes recurs. As always, participation is voluntary and the information shared with the Sister Study will be kept safe, private and confidential.

If you have been diagnosed with breast cancer or have experienced other major changes in your health, please remember to let us know by returning the Annual Updates or calling us at our toll free number, 1-877-4SISTER. We appreciate your efforts to stay in touch and contribute to this research effort.

Genetic Markers and Breast Cancer Risk

In the past few years, at least three large studies of the roles of specific gene variants in breast cancer risk have been reported. These "Genome Wide Association Studies" used DNA from thousands of breast cancer patients and comparison subjects without breast cancer to look for associations between breast cancer risk and more than 200,000 gene variants. About 5 to 10 gene variants were consistently associated with a small (about 10%) increase in the chance of developing breast cancer. We plan to study these gene variants using information from the Sisters who have already reported a breast cancer diagnosis. Confirming this association in the Sister Study would provide important clues to breast cancer causes in women with a family history of breast cancer. The study will also be an important test of the Sister Study sample storage procedures and will be an example of how we can move quickly to address new theories about breast cancer.

New Researchers Join Sister Study Staff

The Sister Study welcomes Drs. Sangmi Kim and Aimee D'Aloisio, graduates of the University of North Carolina at Chapel Hill, who recently began postdoctoral fellowships with us. Sangmi previously studied biomarkers of inflammation, obesity, use of non-steroidal anti-inflammatory pain medications and colon cancer. She will be using Sister Study data to continue her research on obesity, first focusing on the role of sleep patterns in relation to obesity, as well as studying the influence of obesity on a potential biomarker of cancer risk, telomere shortening. Telomeres are sequences of DNA at the ends of chromosomes. Telomeres get shorter with age, and short telomeres may increase risk for some cancers. Sangmi will study the potential link between telomere length and breast cancer risk. Aimee previously studied risk factors for uterine fibroids, including the role of a biomarker called insulin-like growth factor, that may play a role in breast cancer. Aimee is using questionnaire data to study the possible link between early childhood factors and risk for uterine fibroids. She will also study the roles of gene variants in breast cancer risk.

The Sister Study also welcomes Christine Parks. Now a Research Fellow at NIEHS, Christine joins us from the National Institute of Occupational Safety and Health. She received funding from the Department of Defense to study self-reported stress, biomarkers of stress and telomeres, and will also study the relationship between stress and health in the Sister Study. Christine is an expert on workplace exposures and autoimmune diseases and we look forward to her playing an important role in both these areas in the Sister Study.

Summer Intern

This past summer, the Sister Study hosted Fay Cobb Payton, PhD through NIEHS' Summers of Discovery Program. Fay, who received a PhD from Case Western Reserve University, is an Associate Professor in the College of Management at North Carolina State University, and was recently named to its newly created Diversity Advisory Board. At NC State, Fay studies diversity, health care, data management, outsourcing, and systems implementation. She used her summer at NIEHS to explore the use of the Internet in health research and helped the Sister Study team better understand how the Internet influenced study enrollment.

Sister Study Hosts Scientific Advisors

In September the Sister Study research team hosted our Scientific Advisory Board at NIEHS in Research Triangle Park, NC. The advisors discussed progress reports, reviewed plans for the Two Sister Study (see front page), and discussed ways to optimize diversity. Long-range planning included discussions on biennial questionnaires, possibilities for new sample collections such as saliva or water, studies of genes and gene-environment interactions, and following up with participants who develop breast cancer.

The Sister Study Scientific Advisory Board is composed of research scientists and clinicians from the National Institutes of Health (NIH), the US Environmental Protection Agency, and universities and organizations across the country. The Board also includes two community liaisons, and representatives from the American Cancer Society, NIH National Center on Minority Health and Health Disparities (NCMHD), Susan G Komen for the Cure, Intercultural Cancer Council, Y-ME National Breast Cancer Organization, and Sisters Network, Inc. This year the Board welcomed new members Cindy Geoghegan (Komen), Joyce A Hunter PhD (NCMHD), Montserrat Garcia-Closas MD DrPH and Sholom Wacholder PhD (NIH National Cancer Institute), Kirsten Moysich PhD (Roswell Park Cancer Institute), Anna M Nápoles-Springer PhD (University of California, San Francisco), and Sandra Millon Underwood PhD RN FAAN (University of Wisconsin Milwaukee College of Nursing, and Sister Study Recruitment & Retention Advisory Board Chair).

Sister Recruitment Update

In 2007, the Sister Study was very successful in increasing the enrollment of minority Sisters. For example, we more than tripled the number of African American women and doubled the number of Latinas who enrolled each month. This brings the total percentage of minorities enrolled to 16%. We also increased the participation of older women. As we near the end of the enrollment phase, we will be working to make sure that these percentages are even higher so the results of the study will apply to and benefit all women.

Some highlights from last year's recruitment activities include—

- Partnership with REACH Media featuring the Sister Study on The Tom Joyner Morning Show and BlackAmericaWeb.com.
- Announcements on Univision television, and in *Vanidades, People en Español, Cosmo en Español, and* AARP's *Segunda Juventud.*
- Partnership with AARP.

As we approach our goal of enrolling 50,000 Sisters, we want to make sure that certain groups, that are not yet as well represented among participants as we would like, have an opportunity to join the Sister Study. Unfortunately, this will mean turning away some women as we focus on enrolling Latina, African American, Asian, Pacific Islander, American Indian and Alaska Native women, as well as Caucasian women who are age 65-74 or who have a high school education or less.

There continues to be media interest in the Sister Study. Many are especially interested in the stories of women who decided to join the study. Please contact the Sister Study if you are willing to share your story with others.

Hundreds of participants have identified themselves as willing ambassadors for the Sister Study. Occasionally, one of those "SpokesSisters" goes above and beyond in their efforts to encourage women to join the Sister Study. One of those special volunteers is Edith Joyner of Nashville, Tennessee, who recently sent one of our recruitment team members a specially made Sister Study tee shirt with a beautiful thank you note that moved our entire staff. We believe the note captures how many Sisters feel about their participation in the study. With Ms. Joyner's permission, we are sharing a few lines with you:

"…thank you and the Sister Study for giving Pearl and me the vehicle to grieve and serve at the same time. Hope is what you and the Sister Study give to all of us whose lives have been touched by breast cancer and other diseases."

We thank each and every Sister Study participant and volunteer. Together we can make a difference!

Sister Study on NBC Television!

Dr. Sandler was thrilled to share the stage with study participant and SpokesSister, Barbara Moore (both seen at left after "hair and makeup") for a television interview at the NBC New York studio during National Breast Cancer Awareness Month 2007. Over 60 women cited the interview as the reason they joined the study. Our SpokesSisters have a powerful voice!

Thank you to Steve McCaw for providing photos.

NIEHS
National Institute of Environmental Health Sciences

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

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