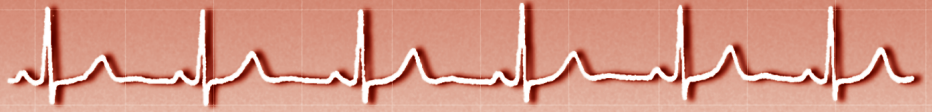


The Framingham Heartbeat



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Esta H. Shindler, Editor

Winter/Spring 2009

THE SABRe IN CVD INITIATIVE (SYSTEMS APPROACH TO BIOMARKER RESEARCH IN CARDIOVASCULAR DISEASE)

For decades, Framingham Heart Study (FHS) participants have generously donated blood samples for research. Hundreds of articles have been published based on analyses of these samples. We store remaining specimens in freezers for future projects. Meanwhile, laboratory techniques have improved, so very small amounts of specimen are enough for a large variety of measurements. In his letter to you, FHS Director, Dr. Daniel Levy, describes the SABRe CVD Initiative. Projects in this program will support highly worthwhile research using FHS specimens and data to discover factors affecting health and disease. We are taking care to protect the confidentiality of participants' information. At least one of the projects will include a partnership called a CRADA (Cooperative Research And Development Agreement) between the National Institutes of Health (NIH), Boston University, and BG Medicine, a private company that has expertise in cutting-edge laboratory measurements. For this project, we will use stored samples according to the preferences of each participant as recorded on consent forms. CRADAs provide opportunities for government biomedical investigators to join with colleagues from industry and academia in the pursuit of common research goals and, relevant to the mission of the NIH, to facilitate the development and commercialization of healthcare-related products and services. CRADAs are authorized by NIH only with collaborators who will make significant intellectual contributions to specific research projects or will contribute essential research materials or technical resources not otherwise readily available to NIH. In some cases, successful commercialization of the fruits of the collaboration may lead to a financial return to one or more of the CRADA partners. We want to ensure that you are informed about FHS research activities. Some questions about the SABRe CVD Initiative are answered below. If you have additional questions, please contact your FHS Coordinator. Phone numbers are provided in this newsletter. We thank you again for your ongoing support of FHS research. ♥

FAQs ABOUT THE SABRe CVD INITIATIVE

1. *What is a biomarker?* It is any characteristic of living things that can be measured and studied, including blood tests. The SABRe CVD Initiative is especially interested in studying FHS biomarkers from blood related to CVD and its risk factors.
2. *Where are specimens from? Where do they go?* Blood samples from past and present FHS exams are processed and stored in various ways. Some tests are performed in the FHS laboratory; other procedures are conducted in off-site labs that have special equipment and expertise. For SABRe CVD, most of the lab tests will be performed at specialized labs.
3. *What is the outcome of the lab measurements?* The results of lab measurements are biomarker levels, scores, percentages, or classifications. These numbers (data) are compared to other FHS information to find new patterns that suggest how disease and health occur in populations.
4. *Who has access to the specimens and data?* Investigators wishing to use specimens or resulting data for analysis must get approval from a review committee that judges the merits of the research. ♥

ARE FHS RESULTS REPORTED?

The Framingham Heart Study collects thousands of physical and genetic research measurements from participants. Overall patterns of biomarkers in FHS cohorts are analyzed, and findings are reported in scientific publications. Most research results obtained at the FHS are preliminary and not directly useful for individual health care. Therefore, they are not reported to Study participants. However, some measurements, such as blood pressure, electrocardiograms and cholesterol levels are standardized and well understood, and reported to you and your physician.

The FHS executive committee, with approval from oversight committees, decides which research measurements should be reported to you and your doctor. The Boston University Medical Center Institutional Review Board (BUMC IRB) and the FHS Ethics Advisory Board review plans for notification based on current medical practice. The National Heart, Lung and Blood Institute conducted a workshop in January 2009 to plan guidelines for reporting genetic research results to individual participants in large observational studies like the FHS. When tests are performed for research rather than for health care, they may be done by non-standard procedures that are different from diagnostic tests obtained through your doctor's office. If you receive a letter from FHS about a research test result, it is up to you and your doctor to decide if there is need for further testing or follow-up. You are also welcome to contact Maureen Valentino, FHS Participant Coordinator, at 800-536-4143 with any questions. **Please remember that participation in FHS research examinations does not take the place of routine physical examinations with your own physician for your health care.** ♥

THIRD GENERATION EXAM 2 UNDERWAY

The FHS Third Generation's second exam cycle began in May 2008, and continues through December 2010. Morning exams are scheduled Monday through Friday at the Perini building, 73 Mt. Wayte Avenue, Framingham. Parking spaces are reserved for participants. Coordinators Maureen Valentino, Marian Bellwood or Sandy Bittenbender will contact you to schedule Exam 2. We look forward to seeing you in clinic! If you live out of town and are planning to visit the Framingham area, please call Maureen at 800-536-4143 to arrange a clinic appointment. ♥

KEEP IN TOUCH AND UPDATE YOUR MEDICAL HISTORY

Once every two years, between clinic visits, FHS participants are asked to complete medical history updates by mail or phone. We ask about your health status since your previous exam or update. Lois Abel oversees the update process. The new health information is reviewed by a panel of physicians and becomes a key part of the FHS research database. Please complete the form when it arrives in the mail and return it to FHS. If you have questions about FHS medical history updating, please call Mary Ann Crossen at 508-935-3430 or 800-854-7582, extension 430. Thank you! ♥



left to right: Dr. Aleksandra Pikula; Yulin Liu; Betty Liu; Jose Romero, MD; Stéphanie Debette, MD; Carlos Kase, MD; Larry Atwood, PhD; Rhoda Au, PhD; Lauren Porretta; Philip Wolf, MD; Linda Farese; Sudha Seshadri, MD; Jacquelyn Harvey; Margaret Kelly-Hayes, Ed.D; Sanford Auerbach, PhD; Justin Nyborn; Deborah Foulkes; Alexa Beiser, PhD; Jayandra Himali

FHS NEUROLOGY TEAM STUDIES RISK OF STROKE AND DEMENTIA

The average lifespan in the U.S. has increased by over 30 years in little over a generation's time. But this increase in life expectancy has led to the emergence of startling health statistics. In Framingham, we have been able to determine the lifetime risk of developing either a stroke or dementia. Based on data collected in the Framingham Heart Study by the Neurology Team, at age 65 one person in three will either sustain a stroke or become demented! We have been working to try to reduce these alarming odds.

Since the 1970s we have been searching for risk factors for neurological disorders, particularly stroke and dementia. The Stroke Study has met with considerable success. It led to the creation of the Framingham Stroke Risk Profile (FSRP) score, a composite score of risk factors which allows prediction of a person's probability of having a stroke within a 10-year period (<http://www.framinghamheartstudy.org/risk/stroke.html>). Physicians around the world use the FSRP score to help patients reduce their risk of stroke. Since the FSRP was published, deaths from stroke in the United States have declined more than 60%, due to better management of stroke risk factors. The Stroke Research Team led by Dr. Philip A. Wolf, is currently updating the computation of the FSRP to reflect these changes.

Similar efforts are underway to help prevent dementia and Alzheimer's disease (AD). Finding strategies to delay disease onset by as little as five years would reduce the number of affected persons by nearly 50%. The National Institute of Neurological Diseases and Stroke (NINDS) and the National Institute on Aging (NIA) of the National Institutes of Health (NIH) recognized the efforts of Dr. Wolf's team, and have provided financial support for this research since 1981. Three separate FHS projects are currently underway. In the **FHS Dementia Study**, participants who have become demented are tested and re-tested to follow disease progression and to determine how cardiovascular health, diet, physical activity and genetics affect the onset and progression of AD.

In 1997 we launched a program requesting permission for **Brain Tissue Donation** to allow detailed neuropathological study of participants' brains and relate these findings to other FHS data. Findings on neuropathology examination is being correlated with decades of life-style and medical data collected by the Heart Study.

Beginning in 1999, all participants from the Original, Offspring and Omni cohorts were invited to have brain MRI scans and cognitive testing. This project provided critical information on changes in the brain as people age. We are now asking for your cooperation in a repeat

Brain MRI Scan and Cognitive Testing to allow us to distinguish the decline attributable to normal aging from that due to AD. Success in identifying early indicators of AD risk may lead to treatments to slow progression of the disorder, and eventually to prevent it. We have just received a new research award from the NIA expanding the MRI study to include Third Generation and Omni Second Generation participants. Subtle changes of AD may be apparent on MRI scan decades before the onset of symptoms. We are searching for the earliest signs of this disease. Few studies other than FHS have the opportunity to conduct such a study over many decades. Through the generous and dedicated participation of Framingham Study subjects over three generations, we can relate how well-known and novel biomarkers, lifelong habits, medical characteristics and genes contribute to risk for stroke and AD. We hope our success will translate into public policy and health practices that will help eradicate these dreaded neurological disorders. ♥

BRAIN TISSUE DONATION PROGRAM

The FHS Brain Tissue Donation Program began in 1997. Over 650 Heart Study members from 35 states have enrolled in the Program. Due to the unique nature of this Study, it is open only to FHS participants. There have been 126 donations from 19 states from which neurological conditions have been documented. We also have a wealth of data on life styles, measures from MRIs, CT scans, and cognitive testing. By relating our clinical information to neuropathological findings, we can identify risk factors for disease.

Analyzing postmortem brain tissue may confirm stroke, Alzheimer's disease, Parkinson's and other neurological illnesses. It also can document the extent of disease or uncover unsuspected conditions. We see that plaques and tangles, signs of Alzheimer's disease, are found to a limited extent in the brains of people who have never shown any significant symptoms of cognitive impairment. We are particularly interested in exploring environmental and genetic links to neurological diseases through postmortem analysis. The donor's family receives a detailed report documenting our findings. Brains of mentally healthy individuals are very useful to compare with those individuals known to have neurological disorders. We continue to learn why some people remain mentally competent and physically healthy throughout their lives, while others develop strokes or become demented.

A brain donation raises the chance of a healthy old age for generations to come. We greatly appreciate our participants' dedication and hope Study members from all generations will contribute to this important research. **If you would like to learn more about the Brain Tissue Donation Program, please contact Linda Farese, Research Coordinator, at 1-800-248-0409 or 508-935-3488, or email her at lfarese@bu.edu.** ♥

OMNI COHORT EXAM UPDATES

Omni Brain MRI: We are continuing to schedule appointments for Omni First Generation at the MetroWest Wellness Center in Framingham. Omni Second Generation will be contacted to schedule brain MRIs in the near future. We greatly appreciate Omni participants, many of whom come from great distances for this examination. Please call the Omni Coordinator, Paulina Drummond, to schedule an appointment if you have not participated in the FHS Brain MRI study in the last four years.

Omni Second Generation Exam 2: We will contact you this fall to schedule your appointment. If you live out of state, please contact **Paulina Drummond, at 508-935-3485 or 800 854 7582 x 485** for a convenient appointment time. ♥

ORIGINAL COHORT'S 30TH EXAM

We are proud to report that the 30th exam cycle for the FHS Original Cohort is underway. These very special and loyal original members had their first exams beginning in 1948 and have participated approximately every two years, making this their 60th year in the Study! We see participants here in the clinic and also visit many at their homes or in nursing homes in New England. With participants who live too far away to visit, we keep in touch by telephone to document changes in health status. Our Original Cohort's long commitment to the Framingham Heart Study is extremely gratifying. Their enthusiasm and dedication have influenced their children and grandchildren to participate as well. We cannot thank them enough. ♥

SECOND CT SCAN FOR OFFSPRING AND THIRD GENERATION

Participants who were in the **Cardiovascular Computer Tomography (CT)** Study during 2002–2005 are invited for another scan. It will measure the amount of calcium deposited in coronary arteries of the heart and in the aorta, the main artery of the body, as well as fat deposits and lung function, for research purposes. FHS physicians and our radiology collaborators at Massachusetts General Hospital will report medically important incidental findings to your designated physician(s). We are calling eligible Offspring participants now to schedule appointments. Eligible Third Generation participants will be informed about the CT program at their Exam 2 clinic visit. **Participants may contact Barbara Inglese, CT Study Coordinator, with questions or to schedule appointments, at 508-935-3451 or 800-601-3582.** ♥

RESEARCH ON HEALTH AND SOCIAL NETWORKS

Researchers led by Dr. Nicholas Christakis of Harvard Medical School used Framingham Heart Study data to examine how our well-being might be influenced by our social ties. Dr. Christakis's team examined family and friendship ties between individuals within the Offspring, Original, and Omni cohorts. The ties within the Study made it possible to get a rich picture of FHS social networks and their relation to health. In fact, there is no other data set in the world that has these kinds of features. As always, names of participants and other identifiers are not included in the data that researchers use for their analysis of relationships.

In one study, the researchers used information about the FHS social networks to look at the "obesity epidemic" and whether our social ties influence weight gain. They found that one person's weight status was related not only to that of close friends and relatives, but to the weight status of individuals up to three degrees removed. See Figure 1. [**New England Journal of Medicine, 357:370-379, July 26, 2007.**] Obesity is

extremely important in the context of cardiovascular disease. This study helps us understand how such a problem spreads across individuals.

Fortunately, the FHS social networks show us that social relations can also have positive effects on health. For example, patterns of quitting smoking look like the obesity findings in reverse. When people quit smoking, there is a ripple effect: it leads to friends, their friends' friends, and their friends' friends' friends also quitting. And the most recent research reveals that even happiness can spread through social networks.

Using a mood scale completed at different exam points (as part of the FHS efforts to understand the relationship between depression and heart attacks), the researchers found a clear indication of happy and unhappy niches in the FHS social network. Like obesity and quitting smoking, the spread of happiness among people was found to extend up to three degrees of separation. People who are surrounded by many happy people report being happier as time goes on. This finding supports the idea that happiness spreads via social contagion with effects lasting up to a year. The FHS data helped researchers to understand the obesity epidemic in the U.S., how smoking has decreased from 45% to 21% of the population over the last 40 years, and how psychological well-being depends on our social ties. Thanks to FHS participants, we better understand how social relations can help us to form better habits and lead healthier lives. ♥

Figure 1: Obesity in the Largest Connected Component of the Framingham Social Network in 2000



DAWBER MEMORIAL SCHOLARSHIP AWARDED TO JULIANNE FERRARO IN 2008.

In her essay Julianne wrote about her pride in the legacy of participation originated by her great-grandparents and continued by her grandparents and her parents.

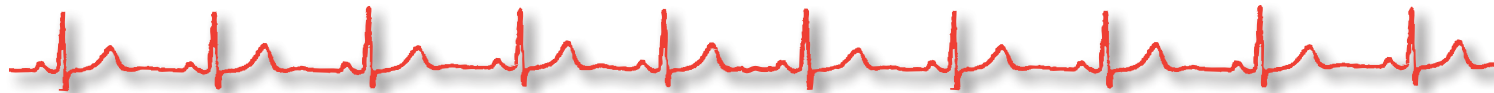
Again in 2009, in memory of Dr. Thomas R. Dawber, Director of the Heart Study from 1949 to 1966, the Friends of the Framingham Heart Study will award a \$1,000 scholarship to the winner of the 2009 essay contest. Eligible contestants are children of Framingham Heart Study participants, graduating from high school in the spring of 2009 and going on to college. The topic of the 1000 word essay is "What It Means to be a Participant in Medical Research". Essays should be sent as a Word document attached to an e-mail to Esta H. Shindler at eshindler@bu.edu by May 1, 2009. Include in the e-mail message plans for college and career after graduation, as well as name, address, and phone number. An e-mail acknowledgment will be sent upon receipt of each essay. (If you do not receive acknowledgement for your entry, please call Esta Shindler at 508-935-3434.) The winner will be notified in June of 2009. ♥

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Find more information about the FHS by browsing at www.framinghamheartstudy.org. See new postings of contact information, examination content, consent forms, organization of the Study, FHS newsletters, bibliography, lists of investigators and research fellows, and links to other resources. Send suggestions for new features to the editor, Esta Shindler, at (508) 935-3434, or to eshindle@bu.edu or by regular mail, (in care of Framingham Heart Study, 73 Mt. Wayte Ave, Framingham, MA 01702.) Our goal is to keep the FHS participants and the public well-informed about our research activities. ♥

TO CONTACT FHS, USE THESE LOCAL OR TOLL-FREE PHONE NUMBERS OR EMAIL

Receptionist: 508-872-6562 or 800-854-7582

Marian Bellwood: Original Cohort Coordinator and Recruitment Supervisor
508-935-3429 or 800-451-0260. bellwood@bu.edu

Maureen Valentino: Offspring, New Offspring Spouse and Third Generation Coordinator:
508-935-3417 or 800-536-4143. maureenv@bu.edu

Barbara Inglese: CT Project Coordinator
508-935-3451 or 800-601-3582 [bjj@bu.edu](mailto:bji@bu.edu)

Paulina Drummond: Omni Coordinator:
508-935-3485 or 800-854-7582 ext 485. omni@bu.edu

Linda Farese: Brain Donation Program Coordinator:
508-935-3488 or 800-248-0409, lfarese@bu.edu

Please call or write us if you have a new address, telephone number (home, work, or cell) or email address. Include in your message a good time for us to return your call. Thank you!