# The Framingham Heartbeat

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# OBAMA RECOGNIZES FRAMINGHAM HEART STUDY IN SPEECH TO NIH

In a speech delivered at the National Institutes of Health in September of 2009, President Obama announced an additional five billion dollars in research funding. In the same speech, he highlighted the work of the Framingham Heart Study as a prime example of the value of such research dollars. The President said,

"Through these investments in research, we will also have the opportunity to make strides in the treatment and prevention of heart disease, the leading cause of death in the United States. Since 1948, for example, researchers have been following generations of residents in the town of Framingham, Massachusetts, to better understand the cause of cardiovascular illness. Now, we have a chance to study the DNA of these participants and connect what we know after decades of observation to what we'll soon know about their genetic makeup. And perhaps we can identify those who are likely to get high blood pressure or high cholesterol and find ways to intervene before heart disease even develops."

### FRAMINGHAM HEART STUDY AND THE AMERICAN RECOVERY AND REINVESTMENT ACT OF 2009

The Framingham Heart Study is a central participant in high profile genome research projects funded by the American Recovery & Reinvestment Act of 2009. Genome research studies connect the genetic building blocks, DNA, to diseases. President Obama's recent Presidential Proclamation declared February 2010 "American Heart Month". In his comments, President Obama noted that his "administration is investing in cutting-edge research, such as a large DNA sequencing study funded by the NIH which could unlock earlier treatment options". The complete presidential proclamation can be found online at <a href="http://www.whitehouse.gov/the-press-office/presidential-proclamation-american-heart-month">http://www.whitehouse.gov/the-press-office/presidential-proclamation-american-heart-month</a>

The Framingham Heart Study is participating in two large studies:

1) **The NHLBI Large-Scale DNA Sequencing Project** is a two year project with the goal of discovering new genetic connections to heart, lung, and blood diseases. Data from the Framingham Heart Study will be analyzed along with data from multiple other research projects.

Genome research technologies have advanced to the point where scientists can rapidly and efficiently – yet very precisely – analyze the DNA from these population studies that have tracked health outcomes in diverse groups. DNA sequences from more than 8,000 people, who participated in these long-term studies, including the Framingham Heart Study, will be analyzed to find specific genetic causes of heart, lung and blood diseases. This new project builds upon the recent genome research project that began at the Framingham Heart Study in 2006, the SNP Health Association Resource (SHARe), by allowing precise mapping of thousands of DNA sequences in extremely fine detail. Additional information about the National Heart, Lung and Blood Institute (NHLBI) Large-Scale DNA Sequencing Project can be found at the NHLBI Recovery Act web page; <a href="http://www.nhlbi.nih.gov/recovery/media/stimulus.htm">http://www.nhlbi.nih.gov/recovery/media/stimulus.htm</a>

#### 2) Building on Genome Wide Association Studies (GWAS) for NHLBIdiseases: the U.S. Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium

This two year NHLBI project builds on the existing work of a consortium of multiple general population-based cohort studies co-founded by investigators at the Framingham Heart Study, the CHARGE Consortium. Work by the CHARGE Consortium has used genome-wide association approaches to identify strong genetic clues for many diseases such as stroke, lung disease, and high blood pressure. The research team will take the CHARGE research to the next level to sleuth the suspect genes and find the exact inherited risk factors hinted at by the earlier work. The research team will re-read, or re-sequence, large regions of the human genome that look suspicious as disease hotspots from previous data obtained by the CHARGE consortium. This project may lead to new knowledge about the molecular mechanisms of disease. For more information about the "Building on Genome Wide Association Studies for NHLBI-diseases: the U.S. Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium project" visit the NHLIB Recovery Act web page http://www.nhlbi. nih.gov/recovery/researchers/index.php?id=223

All data from both projects will be deposited in an NIH database available to the scientific community, prompting major contributions toward medical discoveries.

# REPORTING FHS RESULTS, VITAMIN D AND WHAT IS CLIA?

Framingham Heart Study (FHS) clinic visits cannot replace regular checkups with your own doctor. Most tests performed by the FHS are designed for research only and for this reason, they are not reported to participants. However, the FHS laboratory is now certified under the rules of the Clinical Laboratory Improvement Amendment (CLIA) to run an increased number of tests that can be reported to individual participants and/or their doctors. There may be small variations in results from different laboratories, but overall the test measures from a CLIA certified lab will be reliable. FHS recently added platelet, red and white blood cell counts, and hemoglobin and hematocrit to the list of measures it reports to your doctor.

Several committees, including the Boston University Medical Center Institutional Review Board, the FHS Ethics Advisory Board and the Observational Studies Monitoring Board, advise FHS on what tests results should be sent to participants and/or their physicians. The decision making is an ongoing process. From time to time, we send updates in newsletters, on the FHS website, or directly to you by mail.

An example of a non-CLIA certified research test performed by a lab working with the FHS is vitamin D; for this reason, individual levels of vitamin D are not being reported to participants. It is well known that getting enough vitamin D is important for strong bones. Some of the vitamin D levels were quite low. As expected, investigators noticed a seasonal variation in FHS vitamin D levels. Participants who gave blood at an FHS exam at the end of the summer tended to have higher vitamin D levels than participants whose exams were at the end of the winter. This effect is due to reduced sunshine we get during New England winters. If you have any questions about vitamin D, please check with your doctor. You may of course also contact FHS through your participant coordinator, 508 935 3417.

# FRAMINGHAM'S NEUROLOGICAL STUDIES: CARING ABOUT YOUR BRAIN AS WELL AS YOUR HEART

Since 1982, neurological studies by the Framingham Heart Study have been contributing to knowledge in the prevention of stroke. One key contribution is the development of the Framingham Stroke Risk Profile score that estimates a person's risk for having a stroke within a 10 year time frame. This composite score of cardiovascular risk factors is used by clinicians worldwide to help patients reduce their risk of a stroke.

In 1989, the neurological studies were expanded to include identifying risk for dementia, particularly Alzheimer's disease. As a result of this research and with the dedicated participation of the Original cohort, Framingham has determined that the lifetime risk for stroke is 1 in 5 for women and 1 in 6 for men; for dementia the risk for women is 1 in 5, and 1 in 10 for men. A middle-aged person has a 1 in 3 chance of developing either a stroke or dementia, odds that Framingham would like to help change.

To this end, beginning in 1999, Framingham further extended its investigations to include cognitive evaluations and brain MRI scans of the Offspring Cohort. The second phase of testing will becompleted this year. Interesting findings are starting to emerge from this Offspring examination that suggest there may be early indicators for risk of stroke and dementia, which would lay the path for potential intervention strategies that could delay onset of clinical disease. We have determined that if the onset of dementia is delayed by just 5 years, it would reduce a person's lifetime risk for this disease by 50%.

Further, it is now believed that these risk markers of potential stroke and dementia may be evident decades before there is any sign of disease, which would create opportunities for prevention of disease altogether. Recognizing the importance of such findings, NIH recently awarded Framingham a grant to administer cognitive tests and brain MRI scans to the Third Generation cohort. This examination has begun and will continue through 2012. With the addition of the Third Generation cohort, we will now have brain imaging and cognitive data spanning three generations; this has led to the start of our genetic studies of stroke and dementia.

Since 1997 Framingham has had a brain donation program that is providing valuable data on where Alzheimer's disease may start in the brain. A study led by Dr. Ann McKee, a neuropathologist, suggests that the very beginning of the disease may start in areas different from what was originally thought. We continue to examine whether these initial findings are true. The brain donation program has also provided comparisons between those who remained cognitively healthy through their entire lives and those who did not. Again, the long-term goal is to figure out strategies for delaying or preventing cognitive decline in the later years of life.

If you would like to learn more about how you can be involved in the neurological studies or the Brain Donation Program at Framingham, please contact Linda Farese at 508-935-3488 or 800-248-0409 (lfarese@bu.edu).

# CARDIOVASCULAR CT SCAN FOR OFFSPRING AND GEN 3 ENDS THIS YEAR

The second Cardiovascular Computed Tomography (CT) scan project, which many Offspring participants, as well as their children enrolled in Third Generation have had or will have, is underway. The CT test requires only about 30 minutes of a participant's time; to date, over 1500 participants have completed it. The CT test is able to detect and measure the amount of calcium deposited in coronary arteries of the heart and the aorta, the main artery of the body. A calcium deposit in the coronary artery is a marker of atherosclerosis. i.e., buildup of fat,

cholesterol and other abnormal substances in the arteries. Heart attacks almost always originate from atherosclerosis in the coronary arteries. The FHS CT scans are measuring calcium in the heart arteries and the aorta for research. FHS investigators are also looking at the images of the lungs, and fat deposits in and around the heart and stomach. Not all of the body is being scanned and not all medically important findings may be identified. **This research-oriented scan does not take the place of regular check-ups with your own physician**. However, sometimes medically important "incidental findings" may be identified while examining CT scans for artery calcium. FHS physicians and our radiologist collaborators at Massachusetts General Hospital want to provide information to our participants that may be important to their health. We review all previous and current CT scans. Should any medically important "incidental" findings appear on the scan, you and your physician will be contacted.

Barbara Inglese, our CT coordinator, is calling eligible participants now for spring and summer CT scan appointments. This scan is done at the Mass General Hospital Chelsea Imaging Center. Transportation will be provided if needed. For information or to schedule an appointment, please call Barbara at (508) 935-3451 or (800) 601-3582.

### OMNI 2, HAVE YOU BEEN IN FOR EXAM 2?

We continue to see our Omni 2 participants for their second clinic exam. Exam 2 is similar to exam 1 but with a few new tests: a bone density scan, a glucose tolerance test and an activity level monitor Exam 2 will continue through March 2011. Please call the Omni Coordinator, Paulina Drummond, at 508-935-3485 or toll free 888-689-1682 to schedule your appointment! If you live out of state, we will try to accommodate you whenever you plan to be in town. Just let us know. If you cannot make it this time, please call Paulina Drummond to update your contact and health records. This is especially important if you have moved or are planning to move. We have also received a grant to see Omni 2 participants for Brain Magnetic Resonance Imaging (MRI) at the Wellness Center in Framingham. Please expect a call from our neurology group to schedule your appointment. Feel free to ask any questions about this test.

We ask our Omni 1 participants to please call us with any health or residence updates if we haven't contacted you in the past two years. As ever, we thank you for your continued enthusiasm and participation!

## PICK YOUR DATE FOR YOUR THIRD GENERATION EXAM NOW

There are just ten months to go until the close of the FHS Third Generation second examination cycle. Response has been excellent since the start in May 2008. Over 2100 Third Generation and New Offspring Spouse participants have already had their second exam. Please plan ahead. Call Maureen at 800-536-4143 to book your appointment while plenty of dates are still available. This exam cycle runs to the end of 2010. Especially if you live outside Massachusetts, let us know when you will be in or near Framingham. The sooner you call FHS, the more choices of clinic appointment dates will be open.

### HEALTH HISTORY UPDATES BRIDGE THE

Individual FHS examinations are scheduled once every few years. We use health history forms every 24 months to keep our records current between examinations. You can complete a health history update either by mail or by telephone. When the form arrives at your home, please fill it out and return it, or call MaryAnn Crossen at 508-935-3430 or 800-854-7582 for a telephone interview. We thank you all for providing this important information for the Framingham Heart Study.



Seated (L to R): Nancy Heard-Costa, Heather Arruda Standing (L to R): Michelle Carey, Jessica Rumpf, Jamila Gales

### **INSIDE THE FRAMINGHAM GENETICS LAB**

The Framingham Heart Study (FHS) Genetics Lab opened in June 2000 at the Boston University Medical Campus. The mission is to receive, catalogue, quality check and appropriately distribute the Heart Study's genetic resources. The Genetics Lab maintains inventories of whole blood, buffy coat, cell lines and DNA. The primary genetic resource distributed to investigators of approved research projects is DNA from cell lines. Utmost care is taken by the staff to protect the security and confidentiality of the samples and related data.

Liquid nitrogen freezers in the genetics lab store over 9000 lymphoblast cell lines, the renewable resource used to provide an ongoing supply of DNA for genetic studies. Cultures from white blood cells of participants who have consented are grown in sterile flasks with barcoded identification labels. After harvesting and extracting DNA from the cells, quality assurance protocols are performed. Each DNA sample is analyzed for concentration and purity and then visually inspected to confirm the primary analysis.

Once DNA quality is established, the samples are grouped by cohort: Generations 1, 2 and 3. To guard against labeling or handling errors, each sample is forensically genotyped. The lab uses 10 markers of human identification. The analysis compares a gender genotype result against the known gender of each participant and additional genotypes across samples. Only after passing rigorous quality checks are DNA samples ready for distribution to the larger scientific community. Each approved DNA distribution released to an investigator is aliquoted by a robotic instrument to ensure accuracy and precision. Statistical analysis of FHS genetic data combined with information participants provide at Framingham examinations and interviews gives researchers a powerful new tool for learning about the development and prevention of disease.

### DAWBER MEMORIAL SCHOLARSHIP

In memory of Dr. Thomas R. Dawber, Director of the Framingham Heart Study from 1949 to 1966, the Friends of the Framingham Heart Study will again award a \$1,000 scholarship to a deserving high school senior upon graduation. The competition for the Dawber Award is open to all children of Framingham Heart Study participants who will be graduating from high school in the spring of 2010 and going on to college. The recipient of the award will be selected by the Board of the Friends upon review of all the essays anonymously. Essays entitled "What It Means to be a Participant in Medical Research" should be sent as a Word document attached to an e-mail to Esta H. Shindler at <a href="mailto:eshindle@bu.edu">eshindle@bu.edu</a> no

later than May 15, 2010. Please include in the e-mail message name, address, and phone number, as well as college and career plans after graduation. If you do not receive an e-mail acknowledging receipt of your essay, please call Esta Shindler at 508-935-3434. The winner will be notified by the end of June of 2010 and will be invited to meet the Friends and receive the award in the Fall of 2010.

# FRAMINGHAM HEART STUDY RESEARCH FELLOWS SPEAK IN THE FRAMINGHAM COMMUNITY

The Heart Study welcomes the opportunity to share its findings in public venues throughout the greater Framingham community. On October 19, 2009, Drs. João Fontes and George Thanassoulis, two post-doctoral research fellows with the Framingham Heart Study, explained to a group of eighth grade students at the McAuliffe Regional Charter school how the heart is structured, how it works and how it can be kept healthy. The multimedia presentation was enthusiastically received. The students' heart projects were displayed in the lobby of the Heart Study.

On February 22, 2010, Dr. João Fontes, spoke to members of a local AARP chapter at the Framingham Callahan Senor Center that included several Heart Study participants, some from the Original Cohort of 1948. Dr. Fontes reviewed the history of the Study and its findings on the risk factors for cardiovascular and cerebrovascular disease and thanked the participants for the tremendous contributions they have made to public health worldwide.



L to R: Evelyn Langley, Nadia Labib, Dr. Fontes



From L to R: Cameron Foley, Dr. Fontes,
Dillon Olmos

## DR. DANIEL LEVY RECIPIENT OF TWO PRESTIGIOUS AWARDS

We congratulate Dr. Daniel Levy, Director of the Framingham Heart Study, on awards he received in 2008 and 2009. On November 15, 2009, the American Heart Association (AHA) presented its Population Research Prize to Dr. Levy "for his leadership of pioneering population-based investigations that profoundly expanded our understanding of how factors including hypertension and genetics influence cardiovascular risk." AHA President Clyde Yancy, MD, said the prize is awarded "in recognition of Dr. Levy's path-finding population-based studies that have shaped much of our thinking about the links between modifiable risk factors ... and genetics."

On March 29, 2008, Dr. Levy was given the Lifetime Achievement Award by the Society for Heart Attack Prevention and Eradication (SHAPE) for his substantial contributions to the field of preventive cardiology. "The pioneering Framingham Heart Study built the foundation of preventive cardiology," said Dr. Morteza Naghavi, Chairman of SHAPE. "We honor all investigators who contributed to the Study. Dr. Levy in particular has contributed the most to raising public awareness and education about the Framingham Heart Study and its discoveries."

### Trustees of Boston University National Heart, Lung and Blood Institute Framingham Heart Study

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### **HAVE YOU CHECKED OUR WEBSITE?**

The Framingham Heart Study website, <a href="www.framinghamheartstudy.org">www.framinghamheartstudy.org</a>, is updated every month. We post contact information, examination content, consent forms, organization of the Study, major findings, back issues of newsletters, our bibliography, lists of investigators and research fellows, and links to other resources. It has proven to be a tremendous tool for investigators throughout the world, as well as the public at large. If you have suggestions for new features, please send them to the editor, Esta Shindler, by phone, (508) 935-3434, by email, <a href="mailto:(eshindle@bu.edu">(eshindle@bu.edu</a>) or by regular mail, (in care of Framingham Heart Study, 73 Mt. Wayte Ave, Framingham, MA 01702.) Our goal is to keep you, the Framingham Heart Study participants, 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. <u>bellwood@bu.edu</u>

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. <u>bji@bu.edu</u>

Paulina Drummond: Omni Coordinator: 508-935-3485 or 888-689-1682. omni@bu.edu

Linda Farese: Brain Donation Program Coordinator: 508-935-3488 or 800-248-0409. <a href="mailto:lfarese@bu.edu">lfarese@bu.edu</a>