



# THE FRAMINGHAM HEARTBEAT



The Framingham Heart Study is a project of the National Heart, Lung, & Blood Institute & Boston University. Winter 2017

## ALL PARTICIPANTS

	Page
State of the Study	4
The Science Desk	6-7
Medical History Update	8
Risk of Dementia May Be Decreasing	1
Dawber Memorial Scholarship	5
Traumatic Brain Injury Survey	3

## OFFSPRING (Second Generation) and OMNI 1

Bone	7
Consent Choices About Stem Cells	6

## THIRD GENERATION, OMNI 2, and NEW OFFSPRING SPOUSE (NOS)

Exam 3 Recap	2 & 3
Microbiome	1 & 6
Fibroscan	2
Bone	7
eFHS Use of Watch and Phone	3
Cardiopulmonary Fitness	2
Did You Do Your Homework?	8

## Risk of Dementia May Be Decreasing, and Clinical Symptoms Occurring Later in Life

Thanks to the longstanding dedication of Framingham participants, researchers from the Neurology group were able to study the occurrence of dementia over the past 40 years. The findings, published in the prestigious *New England Journal of Medicine*, suggest that new cases of dementia at any given age have declined over time. They also showed that the disease tends to manifest at a more advanced age today than four decades ago. These encouraging observations in Framingham participants have inspired further research worldwide. We are also working hard to discover ways we can accelerate this encouraging trend. Your participation in ongoing research is very important to us. **To be part of this research, please contact Linda Farese at (508) 935-3488.**

## Third Generation, Omni 2, & New Offspring Spouse Exams

Out of state participants: Are you going to be visiting the Framingham area? Come on in and see us for your next exam! Exam 3 includes tests that will be familiar to you, as well as some new and exciting research. Please call to schedule today!

### SCHEDULING YOUR APPOINTMENT:

The exam will be performed Monday-Friday, starting between 7:00 am – 9:00 am. You will be with us for 4.5 hours. Call Maureen Valentino 800-536-4143 or Paulina Drummond 888-689-1682. Please see pages 2-3 for further details about the exam.

## Omni 2 and Omni 1 Are Making Strides!

Over 75 Omni 2 participants have had their Exam 3. We are getting ready to see our Spanish speaking Omni 2 cohort as well. Omni 2 participants also will be invited to a second round of MRI/Neuro testing and a TBI study.

Omni 1 participants continue to contribute with important and much needed **Medical History Updates**. Along with the Offspring cohort, Omni 1 participants will be called for a third round of MRI/Neuro testing.

## We Need (a tiny bit of) Your POOP for Science!

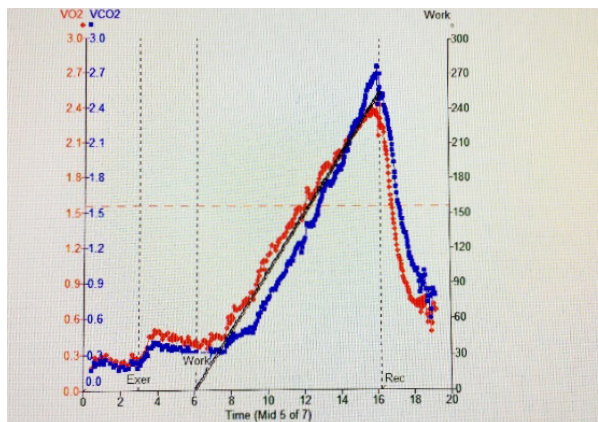
The Framingham Heart Study is conducting research to learn more about your microbiome, which is the community of bacteria that live in our bodies (mostly in our gut, or digestive tract). Many aspects of our lives affect our microbiome: whether or not we were breast fed, our diet, our environment, and what medicines we take. In turn, our microbiome affects our body's metabolism, immune system, inflammation, and even our behavior. Changes in our bacterial community can lead to diseases including heart disease and stroke, diabetes, cancer, and autoimmune diseases like asthma and celiac disease. *(article continues on page 6)*

# EXAM 3

## FHS Cardiopulmonary Fitness Evaluation Update

New to Exam 3 is the Cardiopulmonary Fitness Evaluation (CPFE). As we near almost 1000 exercise evaluations conducted thus far, we are very happy that Framingham Heart Study participants have been so receptive to this addition to the study. During the CPFE, we use specialized equipment to study your body's responses to exercise. This equipment is similar to what one would find in an Olympic training center!

A key measurement is breath-by-breath data, captured both at rest and during exercise. We analyze the oxygen and carbon dioxide content of each breath taken in and out, and graph those variables over time. We can use this information to look at your fitness level and when you begin to perform anaerobic metabolism. These fitness measures may be related to other variables like activity level, body composition, circulating metabolite levels, risk factors, and future cardiovascular health.



*During CPFE you may notice a variety of graphs on our screen. One displays oxygen consumed (in red) and the other, carbon dioxide produced (in blue). These graphs tell us how these variables change as you progress through rest and exercise.*

## Fibroscan

Liver fat is now the most common cause of chronic liver disease, surpassing viruses such as hepatitis B or C and alcohol related liver disease. Liver fat also increases your risk for developing diabetes and heart disease. At the FHS, we are utilizing a new technology called Fibroscan to simultaneously measure liver fat and the stiffness of the liver. Increased liver fat can cause liver scarring in some individuals, which will increase the liver stiffness. So far, we have completed over 900 assessments as a part of the FHS Exam 3. Thank you to all who have participated! Data collection is ongoing and we plan to offer the Fibroscan to all FHS participants at the Exam 3 visit. Our future research plans will be to understand why some people develop liver fat and high liver stiffness and what this means for future cardiovascular health.

## Remember:

*You are a volunteer. If you have any questions about FHS, please ask a staff member.*



## HERE'S WHAT IT LOOKS LIKE:

**Before you come in,** you will receive an appointment package. Please complete the Nutrition form, bring in your medication bottles, and update your Medical History. The Consent Form is available online, and can be read before you come in. Don't forget to bring your cell phone!

**When you come in,** our Exam team will get you started with Admitting and Phlebotomy. Next comes the ECG, Questionnaires, and the MD Interview. Tonometry and the Cardiopulmonary Fitness Evaluation test follow. Then you can relax at the Bone Density and Fibroscan stations. If you have an iPhone, the introduction to eFHS study will be next.

## On the Go with Your Physical Activity Monitor

Did you know that the time you spend being active today can influence your risk for developing dementia? You can help us understand this relationship a little better!

Once again Third Generation, New Offspring Spouse, and Omni 2 participants are being asked to wear an "Actical" physical activity monitor after their FHS exam. The monitor is as small as a wrist watch and is worn on a belt. As you move, it records your activity. After 8 days, you mail it back to the FHS in a pre-paid envelope.

(If the week following your clinic exam is not the best time for you to wear the monitor, simply ask for it to be sent to you at a date that is more convenient.)



## Generation 3 - Omni 2 - New Offspring Spouse Exam 3

At the Exit Interview, you receive your “homework”. We will offer you a Physical Activity Monitor to wear for 8 days, and a chance to participate in the Microbiome Study. Six months after your visit, you may be contacted to participate in the Traumatic Brain Injury Survey. **And you’re done!** Thank you so much for coming to this fast-paced, action-packed exam.

### Remember:

*Framingham Heart Study evaluations are designed for research. They do not replace your regular check-ups with your own doctor(s)!*

## Traumatic Brain Injury

The Traumatic Brain Injury study for all participants in all FHS cohorts will begin in 2017. The study will take place through a computer or mail-based survey, depending on your preference. The self-administered exam will take approximately 20-40 minutes and includes a set of questionnaires that are designed to capture the nature and extent of any head injuries you may have experienced in your lifetime, as well as relevant occupational, military, and athletic exposures. The exam also includes a brief psychosocial assessment of day-to-day mood, behavior, and function.

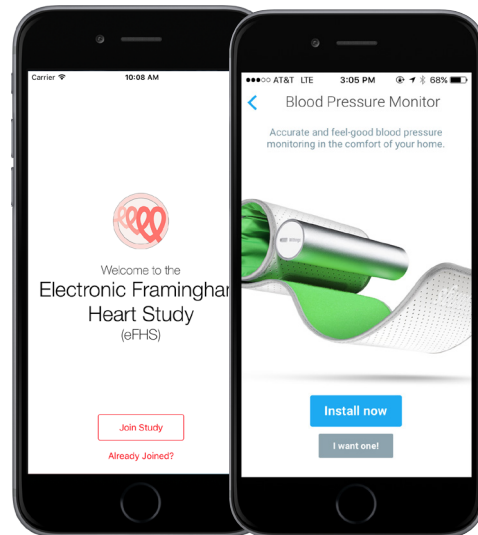


## Watch Out! Heart Study Goes High Tech with eFHS!

We are introducing an eFHS app to find new ways to efficiently and conveniently take measurements from FHS participants as they go about their daily lives. Since June, nearly 400 Third Generation and Omni 2 participants have downloaded the eFHS app onto their iPhone. The eFHS app

pairs with an electronic blood pressure cuff and now with an Apple Watch to track activity level, steps, heart rate, and blood pressure. The app includes short surveys to update medical history and physical activity.

Third Generation and Omni 2 participants with an iPhone are eligible. If you have already come in for your exam and were not asked to participate in eFHS or do not have all the devices, please contact Emily Manders at 508-935-3443. We will be happy to get you set up with the eFHS app and provide you with a wireless blood pressure cuff and Apple Watch if you are able to come back to the Research Center.



## FHS Laboratory and Biorepository

Thank you to all our participants for donating blood samples over the years. The Framingham Heart Study technicians really enjoy interacting with study participants. Our goal is to collect blood with as little discomfort as possible. We’re happy to hear feedback from you, so please feel free to share your thoughts during the exit interview on the day of your exam.

Some of the blood collected during your exam will be used for testing immediately and some will be stored in small volumes for future research projects. Our repository of blood samples is stored in special freezers, at very low temperatures. Some cells are separated immediately after the blood draw. For new studies, white cells and platelets are kept alive by special technologies. In the future, we will report on the results of these projects.

This valuable resource is available to well qualified researchers across the US and all over the world. It is a gift to medical research from the Framingham Heart Study participants.



# STATE *of the* STUDY

## PROGRESS REPORT FROM DR. VASAN RAMACHANDRAN

Dear FHS Research Participants,

I am pleased to share with you that the year 2016 was a very exciting year for the Framingham Heart Study (FHS) with new developments, growth, and productivity. The third examination of the Third Generation (Gen 3) and Omni 2 cohorts began, in parallel with the continued surveillance of all three generations and the Omni cohorts of FHS. We have examined successfully over 1,000 participants as of January 30, 2017. The FHS data management group continues to contribute new FHS data sets to NHLBI and NCBI for web posting, providing an extremely valuable resource for outside researchers. About 228 scientific papers were published in this 12-month period, most in high impact journals.

### Specific Highlights of 2016:

**Integration of grant funded ancillary studies** with the core contract-supported Exam 3 has been accomplished smoothly, and with paperless electronic data capture! **FHS participation in the whole genome sequence (WGS) TOPMED project** continues. Genotyping of ~4100 FHS participants has been completed. **A second workshop to promote the use of Framingham data by young investigators**, held at Boston University's Medical Campus in September, was a major success with 32 attendees. **The reporting of genetic results** for select participants with pathological variants was accomplished. **A scientific retreat was held in October** to plan future FHS research projects. We are very excited about ideas to initiate a series of innovative grant proposals for new research projects.

Stay tuned for information on a possible offspring exam in 2019.

Sincerely yours,



Vasan S. Ramachandran, M.D., DM, FACC  
*The Framingham Heart Study, Boston University School of Medicine*  
*Principal Investigator, The Framingham Heart Study*  
*Professor of Medicine & Epidemiology, Boston University School of Medicine*



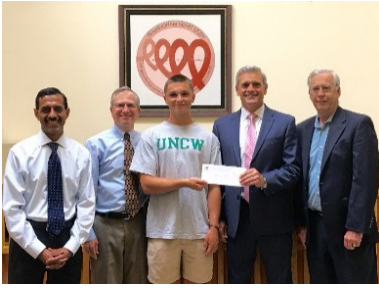
## Joanne Murabito, MD, Now co-PI of the Framingham Heart Study for Boston University



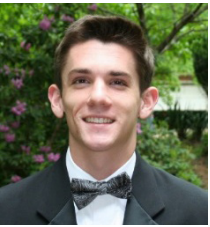
As of January 1, 2017, Joanne takes over this role from Emelia Benjamin, who will continue as a senior FHS investigator. Dr. Murabito conducts both traditional epidemiologic research and genetic epidemiologic research in the areas of longevity, healthy aging, and reproductive aging. She is an active member of the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium and the Long Life Family Study. More recently she is working on efforts to engage participants in the use of mobile technologies to track health. She will continue to lead integration of examinations of FHS participants in the Research Center.

Joanne has a long history with the Heart Study as a senior investigator and FHS Research Center Director. Since 2015, she chaired the Exam 3 committee, bringing together a group of investigators and managers to build a new research program for collecting measurements and specimen from Generation 3 and Omni 2. The exam was launched in April of 2016. (See exam description on pages 2 and 3.) Already over a thousand FHS participants have attended the FHS Research Center Exam. The study includes many new kinds of measurements. Under Joanne's leadership and with the ongoing dedication of FHS participants, the FHS looks forward to innovative research in a wide range of areas.

# Instructions for Applying for the 2017 Scholarship Essay Contest



*Winner – Nolan Dolaher.  
Also pictured from left is Dr. Vasan  
Ramachandran, Dr. Daniel Levy, John  
Galvani, and Peter Allen*



*Runner-Up – Quinn Garrett*

Last year, the Friends of the Framingham Heart Study awarded scholarships to two high school seniors planning to attend college. Friends President John Galvani and the board members announced two scholarships for 2017 based on an essay contest: a \$1,000 scholarship and a \$500 scholarship.

**Eligibility:** Open to children, step-children, and grandchildren of FHS participants. Applicants must be graduating from high school this year and planning to attend college in the fall 2017.

To apply, only two items are needed: an email with the applicant's name, address, telephone number, and college and career plans (roughly a two-sentence description); and a 1,000-word essay titled *"How does FHS help improve public health?"* Applicants are welcome to tell a story, conduct an interview, or pursue any angle of interest. Please fact-check and proofread before submitting. **Please email the essay as an attachment to Emily Manders (emanders@bu.edu) by Monday, April 10, 2017.** We will confirm receipt of all essays within one business day. If you don't receive a confirmation, please call (508) 935-3443. The Friends will review the essays and notify recipients by May 12, 2017. Recipients will be invited to accept their awards at the FHS Research Center.



## A Message from the Friends of the Framingham Heart Study

Greetings, fellow participants. We are participant volunteers from the Offspring (Second Generation), Third Generation, and Omni cohorts who meet periodically throughout the year as members of the Board of Trustees for the Friends of the Framingham Heart Study. With funds donated to the Friends, we provide support for items and activities at FHS, such as occasional travel grants to FHS investigators attending scientific conferences, audio-visual equipment for long-distance conferencing with collaborators, annual scholarships to high-school graduates going to college, and the ECG cards sent to participants after clinic visits. With your help, we'll be able to do more to support FHS in its ground-breaking research for improving public health related to heart disease, diabetes, cancer, sleep disorders, aging, and Alzheimer's disease.

### To make a donation:

please mail a check made out to:  
"Friends of the FHS." Address it to:

Lynda Norton  
ATTN: Friends of the FHS  
73 Mt. Wayte Ave., Suite 2  
Framingham, MA 01702

*The Friends of the FHS is a 501(c) (3) nonprofit organization supported solely by donations.* We invite you to contribute a personal donation or one in the memory of, or in honor of a family member or friend. No donation is too small or too large and all are tax deductible.

## FHS has an ongoing Brain Donation Program

Although we have learned much through our investigations of diseases affecting the brain, we still have many remaining questions. The best way to learn about diseases affecting the brain is to study the brain itself. Our brain donation program is enabling cutting edge research aimed at earlier and more accurate diagnoses of neurological illnesses, providing hope to future gener-

ations. It also helps us understand other diseases in which the brain plays an important role such as obesity and depression. It can provide families with a definitive diagnosis if their loved one had suffered from a neurological illness. **To register to be part of this research, please contact Linda Farese at (508) 935-3488.**



## Updating Consent Choices About Induced Pluripotent Stem Cells (iPSC)

Previously, many FHS participants gave blood samples and permission for the FHS to freeze white cells and convert them into stem cells for future research. Much of that initial lab work has been completed. Now we need to be sure you are also giving consent for specific uses of the stem cells. **A new version of the iPSC consent is given to the Third Generation, New Offspring Spouses, and Omni 2 participants when they attend Exam 3.** Offspring and Omni 1 participants can update their stem cell consent by mail. You may receive a phone call from the FHS to explain the details of the new version of the stem cell consent. After the call, the new form will be mailed to you so you can read it and authorize new uses of the stem cells. Be sure to ask questions if you would like more information.

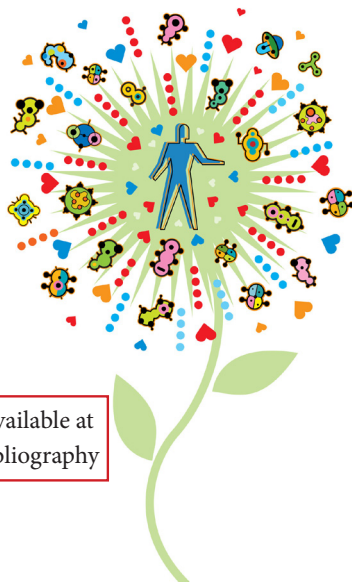
## We Need (a tiny bit of) Your POOP for Science!

(continued from page 1)

This project is a unique opportunity to understand the complex relationships between our microbiome, diet and other environmental factors, and the development of cardiovascular disease. The results of this study may suggest new ways to modulate our bacterial ecosystem to prevent or treat cardiovascular and other diseases.

If you would like to participate, we can give you a kit to take home when you come in for your Gen 3 exam. The kit contains simple step-by-step instructions on how to collect a tiny stool sample and return it by mail. Participants who had their exam in early 2016 will be contacted by FHS staff about how to get a kit and instructions.

We hope you will agree to participate in the Microbiome Study. You will be adding valuable new information to all that you have generously contributed to the Framingham Heart Study over the years.



The complete FHS bibliography is available at [www.framinghamheartstudy.org/bibliography](http://www.framinghamheartstudy.org/bibliography)

## Changes in Our Genes May Provide New Insights Into How Diet, Lifestyle Factors, and Environment Influence Disease



Why do some people seem to be more prone to gain weight despite the same diet and lifestyle as others? New research from the Framingham Heart Study is beginning to shed light on how lifestyle (diet, smoking, alcohol consumption) and environmental factors influence how our genes can be modified to promote disease.

Obesity has been linked to a variety of changes in the sequence or “letters” of our genetic code, yet these differences don’t fully explain the variation in people’s weight. Nor do prior studies fully explain why some overweight people develop health complications from obesity, like elevated cholesterol levels, diabetes, hypertension, and heart disease, while others don’t. The Framingham Heart Study has been examining how genes are turned “off” or “on” as a result of chemical changes in our DNA, known as DNA methylation, whereby a chemical group is added to the DNA backbone. This work is part of a larger effort to understand how our diets, lifestyles, and environment affect the way our genes function and contribute to disease over the course of a lifetime.

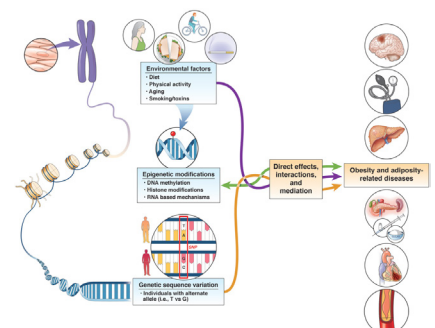
Framingham researchers led by Dr. Dr. Michael Mendelson published a study in *PLOS Medicine* in January 2017 in which they related DNA methylation data from our participants to levels of obesity. We found that DNA methylation changes in 62 different genes were linked to obesity. Knowledge from such new gene-based research in Framingham may pave the way for future approaches to treat or prevent cardiovascular disease.

These scientific advances are possible thanks to your participation in the Framingham Heart Study!

Daniel Levy, MD

Director, Framingham Heart Study

National Heart, Lung, and Blood Institute



## Grist for the Mill – How Your Data Becomes Science



Meet Marty Larson, Co-PI of the FHS and Research Professor, Dept. of Biostatistics, Boston University School of Public Health. He is a leader of the FHS Research Committee, making sure projects are designed properly to yield meaningful conclusions. He also serves on the FHS quality control committee, making sure that measurements are well standardized and accurate.

Read more about Marty on our web at <http://www.framingham-heartstudy.org/investigators/martin-larson.php>.

After all the new measurements from your exams, imaging results, lab values and genetic sequencing are checked and put into neat data sets, the statisticians set to work with other investigators. They have a big library of computer programs that help them find and analyze patterns in the data such as clusters, classifications, similarities, and differences. These patterns are clues to how FHS measurements from so many participants are related to conditions of health and disease. When new patterns are seen that are strong and clear, they are published as FHS scientific findings.

Bravo to FHS statisticians!

Bravo to FHS participants, the people at the source!

## Have You Had a Recent Stroke? Please Let Us Know



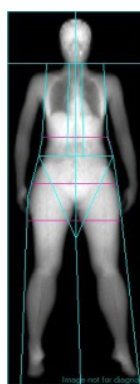
Over the years, your participation has helped FHS researchers study the factors that lead to stroke, how they occur, and what can be done to prevent them over a lifetime. Stroke is an emergency and symptoms can include facial weakness, sudden difficulty speaking, weakness on one side of the body, or sudden vision loss.

***Anyone with symptoms of stroke should call 911 and get immediate help.***

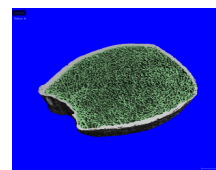
If you or anyone you know had a stroke or received medical care for stroke symptoms, FHS would like to know as soon as you or a family member can contact us. We would like to talk to you and set up an appointment when it is safe and convenient for you.

**Participants are asked to call the FHS Stroke Hotline at 617-630-3627.**

If you live out of state or are unable to be seen in person, we may also schedule an evaluation over the internet by video teleconference. This is a research evaluation only and is not meant to provide any medical care or advice. We greatly appreciate your efforts to help us monitor and research this disabling disease.



**Fat**



## Bone

The Osteoporosis Study team has been scanning the arms and legs of participants during their Exam 3 visit. To prepare for the visit, we completed the upgrade of our scanning equipment to be the highest quality in the world. In fact there are only about 5 such pieces of equipment in the whole United States. Shown here are the types of scans we are doing. You can see that there is a layer of cortical bone (the part that wraps around the outside); some people have thicker layers of cortical bone than others do. Some people have cortical bone that is thick on one side and thin on the other. The inner “trabecular” bone also differs between individuals. We have also been doing the whole body scan to quantify the amount of bone, muscle, and fat. The scan of the whole body provides information on bone, muscle, and fat. The bone study is looking at how the amount of an individual’s fat might affect the bone structure and the risk for fractures. We recently published a paper looking at this in the Framingham Offspring cohort who completed the same scans over the past four years. In that study we found that fat deposits in the abdomen generally resulted in better bone structure except for the finding of more “holes” in the cortical bone in the arm. In the coming years we will do similar analyses with your Exam 3 data, as well as looking at whether abdominal fat tissue has effects on adjacent muscles.

## Study of Preclinical Alzheimer Disease is Ongoing

Thank you to the over 70 participants who have already joined our study to understand the earliest stages of Alzheimer disease before any symptoms develop. Alzheimer and Parkinson’s disease are now known to start as subtle brain changes 20-30 years before the first symptom, and intervention at this preclinical stage may be our best bet for preventing disease. We are now offering all normal participants, and those who have had a stroke recently, an opportunity to join this study. You will be asked to complete a small number of cognitive tests. All interested participants will be invited to undergo a special type of brain MRI and perform additional cognitive tasks at a conveniently scheduled call back exam. You will also be invited for a new type of brain imaging scan (PET scans for amyloid and tau). If you would like to learn more, please call Linda Farese at 508-935-3488

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

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[www.framinghamheartstudy.org](http://www.framinghamheartstudy.org)

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## Did you finish your FHS Homework?

Please check this list and see if you did.

- ✓ Send back your Physical Activity Monitor
- ✓ Answer your eFHS surveys and take your blood pressure weekly (iPhone users only)
- ✓ Collect and FedEx your Microbiome sample
- ✓ Send back your Food Form (if you didn't bring it in at your exam)
- ✓ Complete the Traumatic Brain Injury survey

Then you've earned a Gold Star!



**Need help?** Call **Maureen** at 800-536-4143! THANK YOU!

## Medical History Update It's Important!

One of your most important contributions to the Framingham Heart Study is your medical history information. The facts you provide help us find patterns in the population that show how disease develops over time. Your regular visits and medical history updates make our understanding of disease more accurate and focused. Even if you feel well or your health has not changed in several years, please complete and return these updates to help us document your health status. If you receive a Medical History Update form in the mail, a password is enclosed allowing you to complete the form online. You also have the option of returning the form by mail or completing it on the telephone with one of our staff. Please call Caroline Flessa (508) 935-3437 if you have any questions about the form or would like to complete it on the phone. We greatly appreciate your efforts to keep our records current.

## CONTACT US

### Receptionist

(508) 872-6562 or (800) 854-7582

### Brain Donation, Brain MRI, Cognitive Testing, Stroke Coordinator

Linda Farese

(508) 935-3488, (800) 248-0409

or [lfarese@bu.edu](mailto:lfarese@bu.edu)

### Original, Second Generation (Offspring), Third Generation, New Offspring Spouse Coordinator

Maureen Valentino

(508) 935-3417, (800) 536-4143

or [maureenv@bu.edu](mailto:maureenv@bu.edu)

### Omni Coordinator

Paulina Drummond

(508) 935-3485, (888) 689-1682

or [pautras@bu.edu](mailto:pautras@bu.edu)