Hartford HealthCare and OHRP Symposium
FOUNDATIONS OF TRUST:
CONNECTING COMMUNITY TO RESEARCH

FRAMINGHAM HEART STUDY:
HISTORY, DESIGN AND OUTREACH IN
Three Generations and Two Omni Cohorts

October 25, 2016, 2:00 PM
Greta Lee Splansky, MS
Framingham Heart Study
Boston University and NHLBI
Absence of conflict of interest

Hartford HealthCare Symposium
Foundations of Trust:
Connecting Community To Research
October 25, 2016

The presenter of this session on the Framingham Heart Study, Greta Lee Splansky, MS, is an employee of Boston University, School of Medicine, and has no relevant financial relationship with Hartford HealthCare.
FRAMINGHAM HEART STUDY

Downtown Framingham, MA (circa 1950-60)
WHAT CAN WE LEARN FROM THE FRAMINGHAM EXPERIENCE?

- EVOLUTION OVER 68 YEAR HISTORY OF EPIDEMIOLOGICAL RESEARCH IN A COMMUNITY
- DESIGN AND OVERSIGHT OF A MULT-FACETED STUDY
- INFORMED CONSENT AND COMMUNICATION
- ACCOMODATING NEEDS OF NON-PATIENT PARTICIPANTS
- RETURNING RESEARCH RESULTS TO INDIVIDUALS
- THE CURRENT EXAM OF 3RD GENERATION AND OMNI GROUP
WHY THE TOWN OF FRAMINGHAM?

- Success of Framingham community health & Tuberculosis demonstration study sponsored by Metropolitan life Insurance company (1917-23)
- Proximity to Boston research centers
- Community: mixed retail and industrial employment; disease rates resembled that for rest of US
Plan: 20 year community study to identify factors predisposing to the development of CHD & Hypertension

Initial document did not define how variables would be measured or analyzed
LOCATION, LOCATION, LOCATION!
2/3 of all adults ages 30-59 years, by random selection of households from town census
The Kingman House
Framingham
THE FRAMINGHAM HEART STUDY DESIGN OVERVIEW

- Population-based observational study
- Prospective longitudinal design - 20 year
- Clinic and off-site exams
- 2 to 6 year exam cycles plus surveillance
- Repeated and novel measures
- Six cohorts enrolled to date
- Dense phenotyping and genotyping
Six Framingham Cohorts

Original Cohort (n=5,209)
Began in 1948

Offspring Study (n=5,124)
Began in 1971

Third Generation (n=4,095)
Began in 2002

New Offspring Spouses (n=103)
Began in 2002

Omni I
Began in 1994 (n=506)

Omni II
Began in 2002 (n=410)

N=15,447
F.H.S. ENDPOINT REVIEW PROCESS

F.H.S. EXAMS → SURVEILLANCE Hospital, Obituaries → Medical History Updates → DEATH NOTIFICATIONS

MEDICAL RECORDS OBTAINED → RECORDS PREPARED FOR REVIEW → END-POINT REVIEW → REVIEW RESULTS CODED AND ENTERED INTO DATABASE
DATA MANAGEMENT, PROGRAMMING, QUALITY CONTROL, AND STATISTICAL ANALYSIS

Consult on New Projects: Hypothesis, Design, Feasibility, Projections, Power Calculations

Planning: Test Methods, Document Procedures, Assign Staff, Prepare Forms, Pilot

Data Collection: Obtain measures, Images and Scores, Key Data, File Records


Data sets: Prepare, name, catalogue, organize, document, post and distribute.

Statistical analyses of data

Manuscript drafting and review
FHS DATA REPOSITORY

FHS INSTITUTIONAL AFFILIATIONS

US National Institutes of Health
  • NHLBI CONTRACT
  • GRANTS FROM NIH INSTITUTES
  • GRANTS FROM OTHER SPONSORS

Ancillary Studies
  Conducted At or by other Universities and Institutions

Boston University Medical Center
  Contract and Grants

Third Party Consultants, Collaborators, Laboratories and Imagining Center Sub-contracts
FHS OVERSIGHT AND MONITORING

- FHS NHLBI Project Office and Contract Office
- Executive Committee – BU and NHLBI membership
- FHS DNA and Laboratory Reviews – with external members
- BUMC Institutional Review Board and other IRB’s – Human Subject Protection
- FHS NHLBI Observational Studies Monitoring Board - Human Subject Protection
- US OMB – Burden on US public
- FHS Ethics Advisory Board – Previews major initiatives (Focus Group of Experts and Study Participants)
**FHS CORE MANAGEMENT OVERVIEW**

**Principal Investigator- BU**
Ramachandran Vasan, MD

**Director – NHLBI**
Daniel Levy, MD

**FHS Executive Committee**
Senior BU and NHLBI Investigators

**Directors of FHS Clinics, Labs, And Administration, Statisticians, And PI’s of Ancillary Studies**

**FHS Team Managers, Administrators and Supervisors**

**FHS WORK TEAMS**

- Administration
- Recruitment
- Clinic
- Laboratories
- Medical Records
- Tracking and Review
- Data Management
- Quality Control
- IT
1. New Research Questions And Hypotheses
2. Designing Proposal to Answer Questions
3. Submitting Proposal For Review And Funding
4. Refining Protocol details And Preparing for Data Collection
5. Data Collection, Cleaning, and Analyses
6. Publication of Results, Conclusions, And Limitations
CONDUCTING ANCILLARY STUDIES AT FHS
OPEN TO QUALIFIED INVESTIGATORS

- PI proposes ancillary study via FHS web application*
- Application reviewed by FHS committees
- Project approved by FHS, IRB, OSMB
- Project submitted and approved by sponsor
- Plans for integration of project with FHS teams detailed
- Project conducted
- Project reporting and QC carried out
  - *or apply to NHLBI dbGaP or NHLBI BioLINCC for data only
CONSENT FOR INTERVIEW AND EXAMINATION

I have been fully informed of the nature of this study which includes a medical history, physical examination, blood tests and electrocardiogram and give my consent to be examined. I also authorize the Framingham Study staff to secure pertinent medical information from my family, physicians, and/or hospital records for the purposes of this study.

Name________________ Date____________

NIH – 1635-3 9-71 OMB 66-R1236 Expires Dec. 31, 1974
FHS WEB LINKS FOR EXAM 3

Consent Form for Exam 3


Newsletter 2016 Describing Exam 3 Components

### Consent Check Boxes (2005-2008)

<table>
<thead>
<tr>
<th>Option</th>
<th>Frequency (Percent)</th>
</tr>
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<tbody>
<tr>
<td>I agree to provide a blood sample from which DNA and other components can be extracted. The DNA will be made available to researchers studying the diseases listed above.</td>
<td>Yes 2891 (99.9)</td>
</tr>
<tr>
<td></td>
<td>No 3 (0.1)</td>
</tr>
<tr>
<td>If a cell line has not already been collected, I agree to allow a cell line to be made from a sample of my blood to provide a renewable supply of DNA. (A cell line is a frozen sample of specially processed white cells from your blood that allows us to grow more white cells and get more DNA from them in the future as needed for research projects).</td>
<td>Yes 2969 (99.7)</td>
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<tr>
<td></td>
<td>No 10 (0.3)</td>
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<tr>
<td>I agree to participate in the genetic studies of factors contributing to heart and blood vessel diseases, lung and blood diseases, stroke, and memory loss.</td>
<td>Yes 2978 (99.9)</td>
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<tr>
<td></td>
<td>No 2 (0.1)</td>
</tr>
<tr>
<td>I agree to participate in genetic studies of other diseases and health conditions including but not limited to joint disease, bone loss, and cancer.</td>
<td>Yes 2974 (99.8)</td>
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<tr>
<td></td>
<td>No 5 (0.2)</td>
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<tr>
<td>I agree to participate in genetic studies of reproductive conditions and mental health conditions such as alcohol use and depressive symptoms.</td>
<td>Yes 2970 (99.7)</td>
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<td>No 10 (0.3)</td>
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<tr>
<td>Consent Check Boxes (2005-2008)</td>
<td>Option</td>
</tr>
<tr>
<td>---------------------------------</td>
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</tr>
<tr>
<td>I agree to allow researchers from private companies to have access to my DNA and genetic data which may be used to develop diagnostic lab tests or pharmaceutical therapies that could benefit many people. (Note: You or your heirs will not benefit financially from this, nor will your DNA be sold to anyone.)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>If a genetic condition is identified that may have potentially important health and treatment implications for me, I agree to allow the Framingham Heart Study to notify me and with my permission to notify my physician.</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
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### Draft Classification of FHS Result Reporting – revised 5/12/08

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<th>Pt/MD* For All</th>
<th>Prior By Protocol</th>
<th>Applied</th>
<th>BP, ECG, Cholesterol</th>
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<td>B</td>
<td>Special Report</td>
<td>Pt/MD* If over Threshold</td>
<td>MD* If over Threshold</td>
<td>Prior By Protocol And MD Investigator</td>
<td>Applied</td>
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<td>Consider*</td>
<td>Expert Committee, Exec, IRB, National Panel, Etc</td>
<td>Consider</td>
<td>Genetic Finding, Biomarkers, Etc</td>
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<td>No</td>
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</table>

*Results that are sent to participants and MDs may become part of medical record

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**Genetic findings.** Participant notification of genetic findings is a rapidly moving, relatively uncharted area for observational cohort studies. The elements of such a program must incorporate the flexibility to adapt to rapidly changing conditions, participant autonomy, participant education, and responsible follow-up. It is not the intent of the Framingham Heart Study research program to advise or provide medical treatment in general or in areas of genetic testing, but rather to provide result reporting to participants in an appropriate and responsible manner.
FHS WEB SITE HOME PAGE WITH LINKS TO NEW CONSENT AND TO NEWSLETTER INFORMATION ABOUT EXAM 3 LAUNCH IN APRIL 2016

http://www.framinghamheartstudy.org/
ACCOMODATING PARTICIPANTS’ SCHEDULES

EVERY EXAM SLOT IS PRECIOUS
EVERYONE’S PARTICIPATION IS PRECIOUS

- 30 MONTH WINDOW OF DATES AT START OF EXAM
- SOME SATURDAY DATES
- WAITING LISTS FOR SPECIAL DATES
- SPLIT EXAMS
- ABBREVIATED EXAMS
- FORGIVENESS FOR CANCELLATIONS AND NO-SHOWS
- REMINDER CALLS AND POST CARDS
- SPECIAL BOOKINGS FOR OUT OF STATE RESIDENTS
- TAXI AND LIMO SERVICE AS NEEDED
- HOME VISITS AND NURSING HOME VISITS
Generation 3, New Offspring Spouse and Omni 2
Exam 3 Attendance

Exam Timeline

Number of Participants per Month

Cumulative Number
### CURRENT EXAM 2016 - 2019

**Exam 3 Components Gen 3/Omni Group 2**

- Informed consent
- Change into gown
- Blood draw/urine
- ECG
- Anthropometry
- Physician-administered medical hx
- Resting BP x 2
- Lifestyle questionnaires
- Exit interview

**Total: ≈85 to 95 minutes**
Fasting and post-exercise blood draw to measure metabolites
- Platelet reactivity
- Induced pluripotent stem cells derived from white blood cells
  (act like cells from other organs, such as liver cells, fat cells, heart cells, lung cells, vascular cells, and nerve cells to learn more about health and disease)
- Cell-based phenotyping of white blood cells to examine immune response
- Serum/plasma sample & urine for bio-repository for future studies
Administer “brief” (30 minutes) set of testing
- CERAD (done at exam 2)
- STROOP (done at exam 2)
- Montreal cognitive test (new)
- AD8 (new)

Identify pre-clinical determinants of brain aging, dementia

Identify changes in cognitive testing over time

200 participants will undergo functional MRI brain and PET scan
State-of-the-art High resolution CT of forearm and lower leg to examine the microarchitecture of the bone

- DEXA scan to measure bone density and body composition (body fat)

- Desktop AGE reader that measures the amount of a special type of collagen in the skin of the forearm that can be affected by levels of blood sugar.
CARDIOPULMONARY FITNESS EVALUATION

- Designed to find out the efficiency of the heart, lungs and circulation of blood
- To determine how standard risk factors, genetic variation & familial traits relate to metabolic responses to exercise
Arterial tonometry- a measurement of the blood vessel waveform at the carotid, aorta, brachial and femoral artery sites

Done at exam 2

Allows investigation of change in blood vessel stiffness with age and identification of the associated risk factors and disease outcomes (heart, brain, kidneys)
The fibroscan is a test to measure the presence of fat or scarring in the liver.

A painless pulse is generated on the skin that travels to the liver and measures how stiff the liver is.

Determine prevalence of liver fibrosis in the community and its risk factors.
ELECTRONIC FHS (eFHS)

- App to ask questions about risk factors, lifestyle and health events & invite participants to use devices to track BP, weight
- Validate the app against in-person exam
- Can the app/devices augment or replace in-person data?

President Obama is launching
Precision Medicine initiative and we may be able to provide important Information on digital data collection
NEW: DATA COLLECTION USING DIRECT ELECTRONIC DATA CAPTURE
Thank You

Some slides used in this presentation were provided by

Dr. Ramachandran Vasan,
Principal Investigator of the Framingham Heart Study
Boston University School of Medicine

Dr. Joanne Murabito
Director of Examinations of the Framingham Heart Study
Boston University School of Medicine

Lois Abel
Review and End Point Manager
Framingham Heart Study, Boston University
Thank You


To 15,447 generous and dedicated individuals who are the participants in the Framingham Heart Study.