

Secretary's Advisory Panel on Human Research Protections

March 8, 2011

Returning Individual Research Results: The Framingham Heart Study Experience

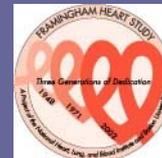
Presenter: Greta Lee Splansky

NHLBI's Framingham Heart Study, Boston University

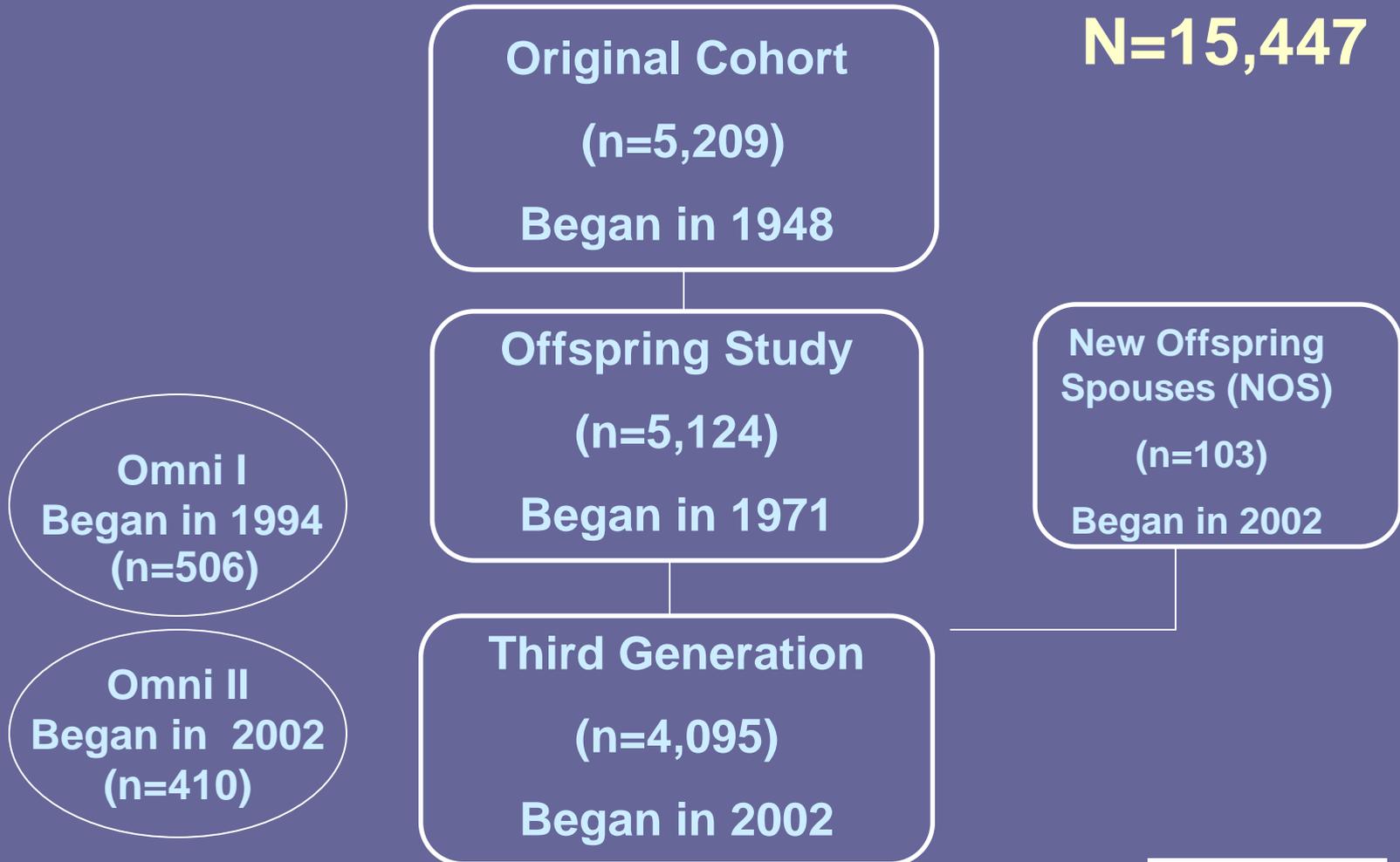


THE FRAMINGHAM HEART STUDY OVERVIEW

- Population-Based Observational Study
- **Prospective Longitudinal Design**
- Clinic and Off-site Exams
- 2 to 6 Year Exam Cycles plus Surveillance
- Repeated and Novel Measures
- Six Cohorts



SIX FRAMINGHAM COHORTS



FIRST FHS CONSENT FORM - 1971

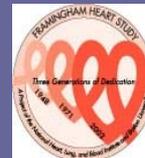
DECK C3 FRAMINGHAM OFFSPRING STUDY EXAM1 RECORD NUMBER _____

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 CONSENT FORMS CODED

DOCUMENTED CONSENTS FROM 1971 THROUGH 2009

COHORT	FREQUENCY
Original Cohort	30,209
Offspring	32,877
New Offspring Spouse	124
Generation 3	6,240
Omni Group 1	1,224
Omni Group 2	415
Total	71,089



HOW DID FHS OFFSPRING RESPOND?

CONSENT CHECK BOXES (2005-2008)	Option	Frequency (Percent)
I agree to participate in the Framingham Heart Study examinations described above to study the frequency of and factors contributing to heart and blood vessel diseases, lung and blood diseases, stroke, memory loss, and other diseases and health conditions.	Yes	2980 (100)
	No	0 (0)
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.	Yes	2891 (99.9)
	No	3 (0.1)
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).	Yes	2969 (99.7)
	No	10 (0.3)
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.	Yes	2978 (99.9)
	No	2 (0.1)
I agree to participate in genetic studies of other diseases and health conditions including but not limited to joint disease, bone loss, and cancer.	Yes	2974 (99.8)
	No	5 (0.2)
I agree to participate in genetic studies of reproductive conditions and mental health conditions such as alcohol use and depressive symptoms.	Yes	2970 (99.7)
	No	10 (0.3)
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.)	Yes	2739 (91.9)
	No	240 (8.1)
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.	Yes	2964 (99.5)
	No	16 (0.5)

WHAT CHANGES AFFECT REPORTING RESEARCH RESULTS ?

- High “throughput” technology
- Non-hypothesis driven analyses
- Repositories - sharing data and biosamples
- Genetic as well as phenotypic results
- Public awareness of genetics in medicine
- Educational programs for staff in protection

WHAT RESULTS DOES FHS REPORT?

Routinely reported measures: BP, ECG, Coronary Calcification Hi/Lo, Cholesterol, HDL, Triglycerides, Glucose, Creatinine, HbA1c, Albumin, Calcium, Bilirubin, AST, ALT, WBC, RBC, Hemoglobin, Hematocrit, Platelet Count, Pulmonary Function Tests, Physical Activity, Bone Density*

Notification of Alert Values Only: Incidental findings (IF) on CT scans, IF vertebral fractures*, IF on Brain MRI*, Vitamin B12*

Additional Individual Results Proposed by FHS for Reporting

Phenotypic - **Vitamin D***

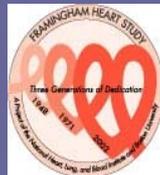
Genetic - **Hemochromatosis, Familial Mediterranean Fever**

*Measurements from Ancillary Studies



HOW MAY FHS ADD A REPORT?

- Principle Investigator (PI) identifies new result that may benefit some or all participants.
- PI presents new result description, justification for reporting, and draft of report letter to the **FHS Executive Committee**.
- The FHS Executive Committee presents the proposal to:
 - **FHS Ethics Advisory Committee**
 - **FHS Genetics Reporting Advisory Committee**
 - **Special Experts in the Field**
 - **OSMB (Review and Approval Required)**
 - **IRB (Review and Approval Required)**
- When approved, FHS Executive Committee adds new report.



WHAT ARE THE BOOKMAN* CRITERIA?

- GENETIC RESULT HAS ESTABLISHED VALIDITY
- GENETIC VARIANT POSES SIGNIFICANT HEALTH RISK
- THERAPEUTIC OR PREVENTIVE INTERVENTIONS EXIST

*Bookman, EB, Langehorne, AA, Eckfeldt, JH, Glass, KC, Jarvik, GP, Klag, M, Koski, G, Motulsky, A, Wilfond, B, Manolio, TA, Fabsitz RR,, and Luepker¹, RV (2006) Reporting Genetic Results in Research Studies: Summary and Recommendations of an NHLBI Working Group. Am J Med Genet A. 2006 May 15; 140(10): 1033–1040.

WHAT ARE TODAY'S QUESTIONS?

Why refrain ever from reporting individual research results?

If analytic validity for the genetic result has not been established, if the genetic variant poses no significant and replicable risk for an important health condition, or if there is no proven therapeutic or preventive interventions the condition, reporting is not useful and not recommended. If consent is limited, reporting may be limited.

Are existing policies adequate for observational studies?

Yes, in the FHS experience, application of current policies and guidelines provided by Bookman and HRPP UCSF, when used with sufficient specific expertise leads to sound decisions on results notification to individual participants in research.

Are there sufficient resources of expertise and education for ongoing evaluation of newly proposed result reporting?

Investigators and review boards could benefit from formalized access to expertise and education in the area of evaluating new research findings for reporting individual results in observational studies.



FHS CONTRIBUTORS TO THIS PRESENTATION:

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