

MINUTES
Observational Study Monitoring Board
Atherosclerosis Risk in Communities
Meeting, 12/03/2008

PARTICIPANTS:

OSMB Members Present: Morton Hawkins (Chair); Karen Kaplan, Jose Ordovas, Veronique Roger, Jerome Rotter

OSMB Members Absent: Robert Goldberg, Jeremiah Stamler, Marvin Ziskin

Investigators: Alvaro Alonso, Christie Ballantyne, Eric Boerwinkle, Diane Catellier, Josef Coresh, Jing-fei Dong, Aaron Folsom, Gerardo Heiss, Ron Hoogeveen, Thomas Mosley, Jennifer Nettleton, Richey Sharrett

Data Coordinating Center Staff: Lloyd Chambless (PI); Wayne Rosamond

NHLBI Staff: Cashell Jaquish, Executive Secretary; Kristi Cooper, Michael Lauer, Hanyu Ni, Jean Olson, Mona Pandey, Phyliss Sholinsky, Paul Sorlie, Elizabeth Zoller

INTRODUCTION (closed session)

Dr. Hawkins called the meeting to order at 8:00 am and introduced the new Board member (Dr. Ordovas). Dr. Jaquish reminded Board members of the importance of completing COI forms in a timely manner and confirmed that the Board members had no new conflict of interest issues to report subsequent to their annual filing. The minutes from the November 28, 2007 meeting were discussed and approved.

Dr. Ni from the Project Office reported that heart failure (HF) surveillance has been streamlined; however it is about 1 year behind schedule due to complicated case reviews. The GWAS genotyping is completed and data will be shared through dbGAP. Investigators are discussing follow up of findings with sequencing. Dr. Ni commented on the study's productivity and the NHLBI sponsored Working Group on Future Research Opportunities in the ARIC study, as well as ancillary studies. The proposed ARIC Neurocognitive ancillary study has been submitted to the NIH and should be reviewed in February 2009. The Project Office is satisfied with the progress of the study and accomplishments of the investigators.

The Board found the responses to recommendations from 2007 to be satisfactory. They also supported future participation of ARIC in the NHLBI Cohort Studies Workshop.

OPEN SESSION

Progress and Overview (Dr. Folsom)

The investigators have been very successful in their annual follow up and surveillance. Approximately 93% of living participants are still in contact with the study. Dr. Folsom summarized events at each field center and overall. Abstraction and classification activities were summarized.

Publication rates remain high with 59 in the last year and 635 total. Dr. Folsom then highlighted many recent, important publications in the areas of surveillance, HF and genomics. ARIC

currently has >80 funded ancillary studies, not all currently active. Rationale for a new exam in the ARIC cohort was presented.

Coordinating Center Report (Drs. Chambless, Heiss and Rosamond)

Dr. Chambless gave an overview of quality control (QC) procedures including abstraction QC and laboratory QC. Dr. Chambless reported on the training and certification for morbidity and mortality classification and site visits. The percent disagreement for HF classification increased in 2006; the Coordinating Center is investigating this further. Out of hospital deaths were summarized by field center.

Dr. Heiss reported on annual follow up, now in year 22-23. The refusal rate is about 1% per year and the mortality rate about 2% per year. An additional 2% are living but direct contact is not possible. Some items have been added to follow-up questionnaires for ancillary studies. Proxies have been identified for older participants. Many of those who refused commented that they would participate when and if a new exam is instituted. HF has been self reported in follow up with a confirmation from the participant's physician. Approximately 70-80% of physicians responded and about 60% of those responses confirmed HF diagnosis.

Dr. Rosamond reported on surveillance efforts. Although the goal is no more than a 2-year lag in surveillance, they are currently a bit behind. An overview of the HF surveillance protocol was presented. Efforts are being made to differentiate between decompensated HF, chronic stable HF and unlikely HF. Agreement between 4 algorithms and reviewers was presented. The fact that reviewers have access to additional information may contribute to increased disagreement with the algorithm results. In an effort to streamline the process: (1) only one review will be performed if all algorithms are positive and reviewer finds decompensated HF, otherwise will adjudicate, (2) one review for all algorithms classified negative or other and (3) double review for all cohort events with differences adjudicated.

ARIC Genetics Research (Dr. Boerwinkle)

There are 3 major genetic activities occurring: 1) Contract genotyping and analysis (focus on G x E), 2) GWAS discovery and consortia, and 3) Medical resequencing. Dr. Boerwinkle emphasized the need for large sample sizes and consortia for GWAS. He highlighted some interesting findings linking the umodulin gene to CKD; this finding was consistent across age, sex, diabetic and hypertensive status. Medical resequencing has been progressing. The investigators have sequenced diabetes candidate genes and are working on HDL (124 genes to be sequenced in 2009). They are finding a tremendous amount of variation. Dr. Boerwinkle predicted genome wide sequencing in 2011-12. The major difficulty is analysis and interpretation of large amounts of data with greater than anticipated genetic variation.

ARIC Laboratory Report (Drs. Ballantyne & Dong)

New blood analytes were reviewed. Several are being measured on 793 PAD samples. Additional measures related to CKD, diabetes, as well as sex hormone markers, oxysterols, troponin, BNP and GDF-15 are underway. Dr. Dong outlined a pathways approach to analyzing these markers. The status of the lipid sample inventory was reviewed. Inventory of Exam 3 samples is underway.

Working Group on Future Research Opportunities in the ARIC study (Dr. Ni)

Dr. Ni gave an overview of the recommendations from the NHLBI Working Group convened in July 2008 on future research opportunities in ARIC. The current contract ends in 2012. The

Working Group recommended consideration of a new exam in the renewal to focus on HF and healthy aging. The meeting report will be sent to the OSMB.

Scientific Presentations

- Dr. Ballantyne: Use of 9p21 in deciding lipid therapy
- Dr. Coresh: Serum 13C to 12C ratio as a biomarker of sweet intake
- Dr. Alonso: Atrial Fibrillation
- Dr. Rosamond: Obesity and HF
- Dr. Hoogeveen: Carotid MRI, MMP, RANTES and 9p21

CLOSED SESSION

The Board members agreed that overall, the study investigators are doing an outstanding job and agreed that the study should continue. They also complimented the study's sustained high productivity in both quality and quantity of publications. The Board also commended NHLBI for considering a new exam in ARIC in response to the Working Group and OSMB recommendations.

Recommendations:

- 1) The Board commended the overall study. The CC is doing a great job with retention and performing complex analyses. ARIC is leading the field in genetic epidemiology. The publication record and productivity of ARIC is outstanding and there has been a concerted effort to incorporate new investigators.
- 2) The Board recommends ARIC participation in future NHLBI sponsored Cohort Studies Workshops.
- 3) The Board requests information regarding processes for prioritization for use of limited samples and resources, particularly with respect to large "-omics" projects.
- 4) The Board recommends considering more in depth "-omic" phenotypes, such as metabolomics and deep phenotyping (transcriptomics, proteomics, high resolution imaging, cell based phenotypes, etc.) in future ARIC research proposals.
- 5) The Board recommends interaction between NHLBI and ARIC investigators in evaluating importance and feasibility of possible exam components in the eventuality of a new clinical exam.
- 6) The Board recommends that the ARIC investigators consider incorporating additional measures, such as BNP and LV ejection fraction, in the criteria for review and adjudication of heart failure. Incorporation of such measures may help to streamline the process and reduce reviewer work load.

NEXT MEETING

The next ARIC OSMB meeting was scheduled for Wednesday, December 2, 2009.

SIGNATURES

_____ APPROVAL _____ DISAPPROVAL

Deputy Director, NHLBI

Date

ARIC OSMB meeting minutes is attached. Here are the recommendations:

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