Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium

Principles and procedures for consortium of population-based cohort studies

(Formally approved by all participating cohort studies; Feb 1, 2008)

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1. **Purpose:** collaboration to improve reliability and validity of genome-wide association findings.

2. **Organization and Responsibilities:** Research Collaboration Committee (RCC), 2 members per cohort, to coordinate activities.

RCC shares among members: phenotype lists, sample size, genotyping platforms, data cleaning methods, analysis methods, imputation methods, and lists of high priority phenotypes.

RCC establishes guidelines for timely participation, the overall analytic approach, the joint selection of phenotypes, the publication strategies, and the approaches to authorship.

RCC forms Analysis Subcommittee to recommend a optimal analysis strategies for in silico replication and other analyses involving two or more cohorts.

RCC establishes working groups (WGs) for each phenotype of joint interest, and appoints Coordinator to take lead responsibility for for practical management. Coordinator role across phenotype WGs is shared among cohorts, according to expertise and interests.

RCC aims for transparency, timely communication, effective coordination, and a sharing of responsibilities, challenges, and opportunities among cohort members.

RCC encourages collaboration among members of the consortium and valuable non-consortium partners.

RCC may recruit other population-based cohort studies to join the consortium.

RCC may encourage joint ancillary-study grant applications to accomplish new scientific aims.

RCC may form additional committees as needed, for instance, to formulate plans for resequencing and genotyping in new populations

RCC agrees to seek opportunities to promote careers of junior investigators and fellows.

Working Groups (WG): Primary work takes place in the Analytic Committee and in Phenotype WGs.

WG Coordinator, appointed by the Research Collaboration Committee (RCC), convenes the WG (unless a WG for that phenotype already exists at the time that the RCC is established).

At the outset, cohort member participation in WG may depend on timing, size of the study, and availability of genome-wide data. Each cohort may join each WG or may opt out of one or more WGs for any reason.

The decision of each member study to join or opt out of a working group must take place before WGA genotype-

phenotype data are shared.

Each Working Group Steering Committee (WGSC) consists of cohorts participating in the consortium of population-based cohorts (one or two members per study). It is the responsibility of the WGSC to initiate or prepare proposals and submit them to all WG members for discussion and revision.

Each WGSC selects a Coordinator, who may or may not be the WG Coordinator originally identified by the RCC, to run meetings and calls for practical management.

Each WG may add non-member studies, such as case-control studies or other consortia, to WG.

Whether other studies may join the WG will be decided by the WGSC based on consensus, and will depend on the availability of GWA data, size of the study, quality of the phenotype data and timing.

The WGSC for each phenotype may decide whether and when a new study may become a member of the WGSC.

WGs standardize phenotypes across cohorts, evaluate results, write papers, decide on publications, on authorship, and on the need for additional follow-up studies in confirmation samples.

The WGSC decides on a date for data freeze after which studies can no longer contribute their data to the active wave of papers.

WGs need to be flexible to accommodate pre-existing agreements about collaboration,

For any phenotype, each cohort may work with other studies or consortia rather than the consortium and not join the WG for that phenotype.

WG members may agree to work with other studies and serve as a replication study for top hits for other GWA studies or candidate gene studies. This plan should be disclosed to other WG members and should be considered acceptable as long as the number of replicated SNPs is not so large that much of the data of the participating study is made public outside of the consortium. If studies wish to share their data in other ways, these plans too should be disclosed to other WG members.

Collaborating groups with confirmation samples for new genotyping are eligible to become members of the WG.

WG members agree not to share whole-genome genotype-phenotype findings from other studies in the WG with any outside groups without permission of the WG members who generated the data.

If WG members have access to other unshared data, the results that emerge from a combined analysis of shared and unshared data will be treated as if they arose from the WG shared data.

WGs may encourage joint ancillary-study application to accomplish new scientific aims.

3. Phenotype-specific working-group efforts

Data sharing: results for all successfully genotyped markers in the primary GWA scan; these shared data may not be used for other purposes than the WG aims without permission from other cohort members.

Data to be shared: rs#, allele designation, genotype counts, model type (additive), estimated effect sizes, 95% CIs, p-values for association tests, data summaries, quality control information (duplicates, HW); plus the same sort of data for imputed SNPs to facilitate sharing across platforms.

Publication plans: Initial publication plan will be developed at the time of WG formation.

Plans may be modified by WG agreement based on the shape of the results.

For parallel publications, one month is a tolerable wait time; three months may not be tolerable.

WG needs to balance rapid publication, strength of findings from replication, and equal partnership.

WG members assure that parent-study disclaimers, reviews, and approvals take place as required. These approvals should occur within one month of the completion of the final draft.

Abstracts should follows the same rules as publications. Authorship for abstracts may be less due to space constraints, but the name of the consortium must be included.

Authorship: The goal is fair scientific representation from cohort members participating in the WG.

Multiple first and multiple senior authors may be designated as such.

First and senior authors, including the overall first and the overall last author, should generally come from different cohorts.

Long lists of authors are permitted if all authors meet standards for authorship (such as those required by major journals, for instance the criteria used by JAMA). Contributing scientists from outside the working group may be coauthors.

Authorship position in first papers will be determined in advance by a group consensus by the researchers actively participating in the proposed pooled study. Some of the factors that may be considered include effort in WG, contributions, by size of the GWA, phenotype data quality, and the contribution of the cohort's data to the results of the pooled study. In later papers, successful efforts to obtain additional funding for new scientific work is another criterion.

Rapid publication from a WG should generally include authors from all member cohorts contributing data.

The number of authors per study should generally reflect the contribution of the study to the paper.

Consortium authorship for the writing group is another possible model that may be considered as an alternative model if there is no group consensus on named authorship.

Involvement of Other Collaborating Studies: Other collaborating studies may be proposed for inclusion in individual working group analyses. If the working group is part of this proposed consortium, then the other collaborating studies will be asked to abide by all of the principles set forth by this consortium for the purpose of the proposed working group project. These are summarized in a separate document for WG members. The document for WG members also applies to individual studies asked to join the WG.

Communication: WG members agree to communicate when an action is taken (ordering primers for genotyping) on the basis of shared data; when an analysis is completed for follow-up genotyping or when there is a proposal to modify publication plans

Data posting: Upon publication in a scientific journal, shared results including results from joint analyses will be posted on a public website. The RCC may wish to develop policies and procedures about other uses of data.

Intellectual property: According to the NIH GWAS policy (Federal Register; 72 (166) 28 Aug 2007: 49290-7), "it is the hope of the NIH that genotype-phenotype associations identified through NIH-supported and NIH-maintained GWAS datasets and their obvious implications will remain available to all investigators, unencumbered by intellectual property claims." If in case intellectual property related to the GWAS's covered under these principles is pursued by a participating investigator, their institution, or the study itself, then the consortium needs to be made aware of the pursuit of such claims. An abstract of the claim(s) needs to be made available to the consortium at the time of submission to the relevant governing body (e.g. US patent office).

In developing these guidelines, the cohorts benefited from guidelines developed by other genetics working groups, including the "International Lung Cancer Consortium Data Sharing and Access Policy" and the "Draft guidelines for sharing genome-wide association results for quantitative traits" (drafted by Gonçalo Abecasis, Michael Boehnke, Joel Hirschhorn, Karen Mohlke, David Schlessinger).

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