

## **CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) Consortium Overview and the role of the Research Steering Committee (RSC)**

The CHARGE Consortium was formed in February 2008 from five large prospective population-based cohort studies to facilitate prospectively planned GWAS meta-analyses of a wide range of phenotypes. CHARGE now includes multiple fully participating cohorts including AGES, ARIC, CHS, FHS, RS, HealthABC, MESA, JHS, CARDIA, HCHS/SOL and collaborates with many other cohort studies and biobanks, including the UK Biobank and the Million Veterans Program (MVP). CHARGE represents a unique resource for identifying genetic loci associated with cardiovascular and aging traits. Many of the collaborating studies have substantial ethnic diversity and have obtained whole genome sequence (WGS) data as well as other “omics” data. Research within CHARGE is focused on members of its 40 active Working Groups. The primary organizing structure of each Working Group is the clinical phenotype rather than a specific research study, department, school or academic institution. Most importantly, junior investigators have often taken a leading role in CHARGE analyses and manuscripts. The CHARGE consortium has become a *de facto* international training ground for collaborative epidemiological efforts in the genetics of aging and cardiovascular disease. Support for students and junior investigators and for between-cohort exchanges helps to foster collaboration, enhance the current science, and improve the training of our future scientists.

The primary innovation provided by the CHARGE consortium is the use of the population-based cohort design as the organizing principle. At the same time, the advent of WGS has increased the depth of genomic coverage, greatly expanded the size of datasets, driven the development of analytic methods, and generated new platforms for data sharing and conducting analyses. Advancing our understanding of the genetic bases of health and disease requires novel organizational structures and scientific collaborations. The CHARGE model—central organizational efforts, consortium-wide analysis leadership, and Working Group scientific leadership—represents an efficient and effective method of promoting high-quality science.

The primary goal of CHARGE is to engage in high-quality scientific analyses that produce robust findings across multiple cardiovascular and aging-related phenotypes. The organizational structure consists of a Research Steering Committee (RSC), an Analysis Committee, a Genomics Committee, several cross-cutting ‘omics Working Groups (focused on Exomechip, Metabolomics, Gene Expression and Epigenomics), and many phenotype-specific Working Groups, and a recently established a Mendelian Randomization Working Group. The RSC is responsible for developing guidelines for collaboration and also serves as the advisory body for the CHARGE infrastructure grant that supports the Consortium. The Analysis Committee develops guidelines that the Working Groups are encouraged to adopt or adapt and solves analytic problems that arise as plans are implemented. The Genomics Committee coordinates consortium-wide efforts in ‘omics applications across cohorts.

The RSC recommendations are advisory, and the primary decision-making authority rests within the Working Groups. The RSC, which has representatives from many of the studies and committees, is responsible for coordinating and maintaining communications across population-based cohort studies, the phenotype-specific Working Groups, and committees (*e.g.*, Analysis, Genomics). The RSC has supported the development and implementation of a cloud-based approach to bring harmonized phenotype data and genomic data into a single environment for analysis. Working with NHLBI project officers, the RSC has developed a “consortium” agreement that requires only one agreement, an administrative innovation that is currently used to simplify data sharing and analysis.

CHARGE meetings are modeled on Steering Committee meetings typically held by the NHLBI-funded multi-center studies (*e.g.*, ARIC, CHS, and MESA). These meetings are important for maintaining the collaboration, advancing the science, and informing the investigators. The CHARGE RSC decides on the location of meetings, which are hosted either by a cohort and/or a Working Group. The organizing committee for each meeting consists of the host, selected members of the RSC, and support staff. Responsibility for developing the meeting agenda rests with the CHARGE RSC, which holds twice monthly conference calls. The RSC suggests ideas and themes for the meeting, identifies and recruits invited speakers, decides on Working Group presentations for the main assembly, selects abstracts for the oral or poster presentation, and approves the final agenda. The RSC also approves the applications for CHARGE young-investigator fellowships and travel awards. The CHARGE consortium in general and the CHARGE meetings in particular serve as effective methods of maximizing the shared use of publicly funded research and data collection efforts.