Building a National Cohort



Eric Boerwinkle; February, 2015 Precision Medicine Workshop



The University of Texas Health Science Center at Houston





What is a Cohort?

- Sample of people
- Who share some characteristic (e.g. a place) and time frame
- Cohort study
 - Longitudinal
 - Measure/monitor/estimate some things
 - Assess outcomes (usually in the future)
- Does not have to be a representative sample, but clear eligibility criteria allow making generalizable inferences.

CHARGE (Cohorts for Heart & Aging Research in Genome Epidemiology) Consortium, N>>100,000





*Psaty BM, O'Donnell CJ, et al. Circulation CV Genetics 2009.

COHORTS FOR HEART AND AGING RESEARCH

>600 Investigators, >80 Cohorts
>60 Phenotype Working Groups
Published Collaboration Principles
>370 Publications since 2008

CHARGE (Cohorts for Heart & Aging Research in Genome Epidemiology) Consortium, N>>100,000





Sequencing in Cohorts



- Update
 - WES (N=11,500)(F4)
 - WGS (N=5,700)
 - Collaborations (ESP) (N=23,000)
 - Strong analytic infrastructure



Morrison A. Nat Genet 2013; 45: 899-901.



FHS: phs000651.v4.p9; CHS: phs000667.v1.p1; ARIC phs000668.v1.p1

Building a National Cohort



Consortium Of Cohorts

Artist: Chuck Close



A National Cohort

Building A National Cohort

Enhanced Opportunities

- Participatory
- Enhanced phenotyping
- Platform for clinical trials
- Pilot for national health/EMRs
- Enhanced community resources

• Virtuous cycle of health care and research



Technical Challenges

- Harmonization
- Big Data Challenges
 - Storage
 - Analytics
 - Connectivity



The CHARGE Data Commons

Clinical and Biologic Continuum of Simple/Complex and Rare/Common







The NEW ENGLAND JOURNAL of MEDICINE

PCSK9, Cohen, 2006; PMID: 16554528 APOC3, Crosby, 2013; PMID: 24941081 NPC1L1, Stitziel, 2014; PMID: 25390462 PLA2G7, Polfus, 2015;





Clinical and Biologic Continuum of Simple/Complex and Rare/Common

Rare Mendelian...... 'Oligogenic' Common Complex

Low frequency/High impact Not related to sporadic cases in a simple way





Jim Lupski Richard Gibbs Eric Boerwinkle

Few Actionable Alleles Missing 'Heritability'













Building a National Cohort





A National Cohort

Virtuous Cycle of Health Care and Research