

# National Institutes of Health Cohorts on Vascular Contributions to Cognitive Impairment and Dementia

A COLLABORATIVE ANALYSIS BY NINDS, NHLBI, NIA, AND NIDDK  
NIH VCID COHORTS WORKING GROUP

## Background

In 2017, NIH released a new Funding Opportunity Announcements (FOA) to stimulate research that leverages existing cohort studies to identify or clarify risk and protective factors for Alzheimer's disease and related dementias (AD/ADRD) ([PAR-17-054](#)). The development of this FOA is a direct result of a multi-Institute working group analysis of major NIH-funded epidemiology cohort studies that incorporate measures of relevance to vascular contributions to cognitive impairment and dementia (VCID). With unprecedented opportunities to stimulate research in AD/ADRD due to recent attention and funding from Congress, this NIH working group comprised of policy and program experts from NINDS, NIA, NHLBI, and NIDDK was formed to identify relevant cohort studies that could be leveraged or expanded for targeted emphasis on VCID.

VCID research investigates a range of processes and disorders involving the vasculature in the brain and their relationship with cognitive impairment and dementia, including Alzheimer's disease<sup>1</sup>. These include, for example, overt stroke, silent cerebral infarction, small vessel disease, and white matter abnormalities. The relationship between cardiovascular risk factors and onset of cognitive impairment or dementia is poorly understood and represents an area of current focus within the research community. The NIH VCID Cohorts Workgroup set out to identify new collaborative opportunities to simulate science in this area in a way that leverages ongoing NIH investments in cohort studies. This effort was also in alignment with recommendations from the Alzheimer's Disease-Related Dementias Summit<sup>2</sup>, an activity that informs the National Plan to Address Alzheimer's Disease that is mandated by the [National Alzheimer's Project Act](#). This summary of the workgroup's activities was developed to share results, processes, and lessons learned with others across NIH and the extramural research community who may find the information useful for similar inquiries.

## Analysis approach and methods

*Identification of VCID-relevant cohorts:* The ability to identify opportunities for leveraging current or recent investments requires a comprehensive listing of NIH-funded cohort studies that are relevant to VCID. To achieve this, the group queried the NIH's IMPAC II grants database to identify RCDC<sup>3</sup>-coded "Epidemiology and Longitudinal Studies" funded by any of the participating Institutes, which resulted in 501 projects. These were then screened for parent cohorts that included measures of cardiovascular risk factors and/or cognitive outcomes. Additional cohorts were added manually based on workgroup participants' knowledge of the scientific landscape, and [130 cohorts](#) were ultimately deemed relevant for this analysis.

*Collection of data on key cohort characteristics:* In parallel, the group developed a list of key characteristics that would be important to know for each study, such as descriptive information, risk factors and outcomes assessed, metrics and measures used for the assessments, availability and storage of data, among others. The group agreed upon [a list of data elements](#) that would enable careful comparison and assessment across cohorts, and an Excel template was created to facilitate data collection. This list may be helpful to consider by others who are interested

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<sup>1</sup> Corriveau RA, Bosetti F, Emr M, Gladman JT, Koenig, JI, Moy CS, Pahigiannis K, Waddy SP, Koroshetz W. Cell Mol Neurobiol. 2016 Mar;36(2):281-8 [PMID 27095366](#)

<sup>2</sup> [Alzheimer's Disease-Related Dementias Prioritized Research Milestones](#) (see [Topic 6, Focus Area 2](#))

<sup>3</sup> The Research, Condition, and Disease Categorization (RCDC) system is the official coding system for NIH grants and spending.

in assessing or compiling data on cohort studies addressing a defined scientific topic. Each primary or co-funding Institute provided data on their cohorts using internal (e.g., grant databases, internal records and program director knowledge) and external (e.g., published studies, websites, study investigators) information sources.

*Identifying scientific opportunities:* Based on these data, the group identified opportunities to leverage the cohorts for targeted investigation of VCID questions and discussed their potential scientific impact and feasibility for short-term action. Scientific opportunities were identified among a subset of studies and these fell into five themes<sup>4</sup>: Prevention, Diagnostics, Intervention, Health Disparities, and Genetics. Most cohorts assessed had opportunities in multiple scientific categories, and most involved opportunities for new data collection as well as secondary data analysis. This information was organized in a table format to enable assessment of overlapping opportunities and the potential to facilitate cross-cohort collaborations. The group also discussed potential strategies for harmonizing data across cohorts more broadly.

## **Results and recommendations**

*Supporting ancillary studies to gain insight into VCID:* In parallel with this assessment activity, there has been mounting interest among investigators and epidemiologists in collecting data on cognitive outcomes and brain imaging through ancillary projects to major cardiovascular cohorts. This growing momentum in the research community will continue to increase our ability to address important research questions related to VCID. Examples of projects recently funded include a pooled assessment of dementia risk using data from four cardiovascular cohorts ([1RF1AG054443-01](#)) and several projects that add novel imaging and enhanced risk and outcomes assessments to ongoing major cardiovascular cohort studies (e.g. Atherosclerosis Risk in Communities, Framingham Heart Study, and others).

*Facilitating cross-cohort collaborations:* Based on the workgroup's assessments, the group discussed strategies for stimulating work to address the identified opportunities. Recognizing the complementary nature and overlapping scientific goals of many of the cohorts, the workgroup members and Institute leadership realized the need to incentivize cohorts to work collaboratively on scientific questions relevant to VCID. The following funding opportunity announcement is a direct result of the group's analysis and discussions: [PAR-17-054 Leveraging Existing Cohort Studies to Clarify Risk and Protective Factors for Alzheimer's Disease and Related Dementias](#). As of April 2018, three projects ([1UF1AG057707-01](#), [1RF1AG057531-01](#), [1R56AG057548-01](#)) have been funded through this initiative. This funding opportunity encourages combining longitudinal data from existing cohort studies to increase statistical power and improve understanding of the AD/ADRD etiology and cognitive resilience and remains active until November 6, 2019.

*Harmonizing data across cohort studies:* Throughout this analysis, the need for compatible data across cohorts, and processes that would enable investigators to combine data to answer scientific questions unlikely to be

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<sup>4</sup> Scientific Opportunity Categories included: Prevention Research and Burden Estimates (risk factor identification, prevalence studies), Diagnostics and Disease Monitoring (biomarker discovery, test validation, methods development), Intervention Research (drug discovery, drug effects, lifestyle interventions, clinical testing), Health Disparities Research (racial/ethnic comparisons, urban vs. rural, SES, international), and Genetics (family or twin studies, whole genome sequencing, genetic database, etc.)

addressed by single studies, were recurring themes in the discussions. Harmonization and standardization of data collection and outcome measurement would also facilitate meta-analyses and validation of scientific findings in different study populations and across age ranges. The group recognized several ongoing projects that include data alignment efforts, such as: the [Cohorts for Heart and Aging Research in Genomic Epidemiology \(CHARGE\) Consortium](#), [MarkVCID](#), [Chronic Kidney Disease Epidemiology \(CKD-EPI\) Collaboration](#), Health and Retirement Study [Harmonized Cognitive Assessment Protocol](#), the [Alzheimer's Disease Sequencing Project](#), [NHLBI Trans-Omics for Precision Medicine \(TOPMed\)](#), and the [NINDS Common Data Elements Project](#). The Institutes are currently exploring additional strategies for encouraging further efforts that would support data harmonization across cohorts particularly with regard to critical outcomes data.

*Systematic tracking of cohort studies:* The group considered the potential value in establishing a database tool or process to enable systematic identification of cohorts relevant to a particular scientific topic and to facilitate future collaborative prioritization. Many NIH Institutes currently support repositories that store data and biospecimens from some of these cohort studies that the group identified, however there is currently no centralized point through which to identify and access these repositories. There are also external resources that serve to facilitate cross-cohort comparisons, data sharing and collaboration, and secondary analyses. These include, for example, the [Global Alzheimer's Association Interactive Network \(GAAIN\)](#), the [Integrative Analysis of Longitudinal Studies of Aging & Dementia](#) (partially funded by NIA), and the [Maelstrom Research](#) resource. However, systematic collection and maintenance of detailed information about ongoing cohort studies, which is complex and requires significant manual data entry and curation, remains challenging. The group's work highlighted the potential utility of a comprehensive database that is easy to navigate and would promote collaborative research and future portfolio analyses.

*Visual representation of VCID-relevant cohorts:* The workgroup developed visual representations of a subset of the identified cohorts to display overlapping or complementary features in terms of population, follow-up period, and measurements from a life span perspective. It is important to note that the selection of these cohorts in no way reflects a higher value or priority as compared to the other cohorts funded by the NIH, rather it reflects the cohorts deemed most relevant to the workgroup's focused objective at one point in time. This type of visualization provides another example of unique ways in which gaps and synergies can be revealed across cohorts, and where opportunities to probe data across studies may allow us to ask bigger picture questions about the relationship of vascular risk factors to cognitive outcomes over the life course. The [VCID Cohorts Lifespan Figure](#) displays 29 of the cohorts by age range and provides descriptive information such as cohort size and type of data collected. The accompanying [VCID Cohorts Summary Tables](#) provide descriptive information for these cohorts in a table format. Finally, [the VCID Cohorts Interactive Data Visualization Tool](#) allows the user to view information on a smaller subset of the cohorts in a more dynamic fashion.

In sum, this collaborative analysis of NIH-funded cohorts with relevance to VCID led to short-term opportunities to facilitate collaboration across major cohorts. The work also led to identification of potential longer-term opportunities to advance VCID research by enabling data harmonization across studies and developing systematic tools for assessing potential areas of synergy. The goal of this summary is to share the process in a way that may be informative for future similar cohort portfolio assessments. For further information on the process or results of this project, please feel free to contact Dr. Katie Pahigiannis ([katie.pahigiannis@nih.gov](mailto:katie.pahigiannis@nih.gov)) or Dr. Sophia Jeon ([sophia.jeon@nih.gov](mailto:sophia.jeon@nih.gov)).

## NIH VCID Cohorts Working Group participants

### NINDS

Rod Corriveau, PhD

Sophia Jeon, PhD

Claudia Moy, PhD

Katie Pahigiannis, PhD, MPH

### NIA

Dallas Anderson, PhD

Jonathan King, PhD

Lenore Launer, PhD

Susan Ziemann, MD

Chhanda Dutta, PhD

### NIDDK

Luke Stoeckel, PhD

Christine Lee, MD

### NHLBI

Jacqueline Corrigan-Curay, JD, MD\*

Zorina Galis, PhD

Peter Kaufmann, PhD\*

Jean Olson, MD, MPH

Jared Reis, PhD

Jacqueline Wright, DrPH

\*Drs. Corrigan-Curay and Kaufmann left their positions with NHLBI prior to the publication of this report.

NIH VCID Cohorts Workgroup Summary  
**List of Cohorts Initially Considered in Analysis**

1. Action for Health in Diabetes (Look AHEAD)
2. Action to Control Cardiovascular Risk in Diabetes (ACCORD): Memory in Diabetes (ACCORD MIND)
3. Adult Changes in Thought (ACT) Study
4. Adult Children Study
5. Age, Gene/Environment Susceptibility—Reykjavik Study (AGES)
6. Aging, Demographics and Memory Study (ADAMS)
7. Alzheimer's Disease Neuroimaging Initiative (ADNI, ADNI GO, ADNI 2)
8. Amish Complex Disease Research Program (ACDRP)
9. Amish Family Calcification Study (AFCS)
10. Atherosclerosis Risk in Communities (ARIC) Neurocognitive Study (NCS)
11. Atherosclerosis Risk in Communities (ARIC) Study
12. Baltimore Longitudinal Study of Aging (BLSA)
13. Bogalusa Heart Study (BHS)
14. Boston Puerto Rican Health Study and San Juan Obese Adult Longitudinal Study in Puerto Rico
15. Brain Attack Surveillance in Corpus Christi (BASIC)
16. Cache County Memory Study
17. Cardiovascular Health Study (CHS); CHS Cognition Study
18. Cardiovascular Inflammation Reduction Trial (CIRT)
19. Cardiovascular Risk Factors, Aging and Dementia (CAIDE)
20. Cebu Longitudinal Health and Nutrition Survey (CLHNS)
21. Chicago Health and Aging Project (CHAP)
22. Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life (CASCADE)
23. Chronic Kidney Disease in Children Study (CkiD)
24. Chronic Renal Insufficiency Cohort Study (CRIC)
25. Cognitive Function and Aging Study (CFAS)
26. Colorado Adoption/Twin Study of Lifespan (CATSLife)
27. COPDGene Study
28. Coronary Artery Risk in Young Adults (CARDIA)
29. Diabetes Control and Complications Trial/Epi of Diabetes Interventions and Complications (DCCT/EDIC)
30. Diabetes Heart Study (DHS), DHS-MIND
31. Diabetes Prevention Program (DPP) Outcomes Study (DPPOS)
32. Einstein Aging Study (EAS)
33. English Longitudinal Study of Aging (ELSA)
34. Established Populations for Epidemiologic Studies of the Elderly (EPESE)/Hispanic Epidemiologic Study of the Elderly (Hispanic EPESE)
35. Estudio Familiar de Influencia Genetica de Alzheimer (EFIGA; Family Study of the Genetic Influence of Alzheimer's Disease)
36. Family Heart Study (FamHS)

37. Family Study of Carotid Atherosclerosis and Stroke Risk
38. Framingham Heart Study (Original, Offspring, Offspring Spouse, Minority Omni-II, 3rd Gen)
39. Genetic Epidemiology Network of Atherosclerosis (GENOA)
40. Ginkgo Evaluation of Memory (GEMS)
41. Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS)
42. Growing Up Today Study (GUTS)
43. Guam Dementia Project
44. Harmonized Cognitive Assessment Protocol (HCAP)
45. Health Aging and Body Composition (Health ABC) Study
46. Health and Retirement Study (HRS)
47. Health Professionals Follow-Up Study (HPFS)
48. Healthy Start Study
49. HEALTHY Study (HEALTHY)
50. Heart Score Study
51. Hispanic Community Health Study / Study of Latinos (HCHS-SOL) / ECHO-SOL (Echocardiographic Study of Latinos/Hispanics)
52. Honolulu Asia Aging Study (HAAS) (Kuakini Hawaii Lifespan Study)
53. Hyperglycemia and Pregnancy Outcomes Follow-Up Study Consortium (HAPO-FUS)
54. Hypertension Genetic Epidemiology Network (HyperGEN) Study of the Family Blood Pressure Program (FBPP)
55. Indianapolis-Ibadan Dementia Study
56. Indonesia Family Life Survey of Aging (IFLS)
57. Indo-US Cross National Dementia Epidemiology Study
58. Interdisciplinary Longitudinal Study of Adult Development (ILSE)
59. International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) (trial)
60. Invecchiare in Chianti, aging in the Chianti area (InCHIANTI)
61. Irritable Bowel Syndrome Outcome Study (IBSOS)
62. Israel Diabetes and Cognitive Decline Study
63. Jackson Heart Study (JHS)
64. Jerusalem Perinatal Study and the Omega Study
65. Kerala-Einstein Study: Healthy Lifestyle, Vascular Disease, and Cognitive Decline [in India]
66. Leukoaraiosis and Disability Study (LADIS)
67. Lifestyle Interventions for Expectant Moms (LIFE-Moms)
68. Long Life Family Study (LLFS)
69. Longitudinal Study of American Youth (LASA) / LASL
70. Maastricht Aging Study (MAAS)
71. Mayo Clinic Study of Aging (MCSA)
72. Mediators of Atherosclerosis in South Asians Living in America (MASALA) study
73. Mexican Health and Aging Study (MHAS)
74. Midlife in the United States (MIDUS)
75. Minority Aging Research Study (MARS)

76. Monongahela Valley Independent Elders Survey (MoVIES)
77. Mon-Yough Healthy Aging Team (MYHAT)
78. Multi Ethnic Study of Atherosclerosis (MESA)
79. Multi Site Study of AD in African Americans
80. Multicenter AIDS Cohort Study (MACS)
81. Multicenter Osteoarthritis Study (MOS)
82. National Health Aging Trends Study (NHATS)
83. National Long Term Care Survey
84. National Longitudinal Study of Adolescent Health (Add Health)
85. National Social Life, Health and Aging Project (NSHAP)
86. New York University Women's Health Study (NYUWHS)
87. NHLBI Twin Study
88. North Karelia Project
89. Northern Manhattan Study (NOMAS)
90. Nurses' Health Study (NHS)
91. Nutrition, Aging, and Memory in Elders Study (NAME)
92. Osteoporotic Fractures in Men (MrOS)
93. Physician's Health Study
94. Pregnancy Outcomes and Community Health (POUCHMoms) study
95. Prospective Cohort of Older Puerto Ricans
96. PROspective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) (trial)
97. Queensland Twins
98. Reasons for Geographic and Racial Differences in Stroke (REGARDS)
99. Religious Orders Study (ROS)
100. Rochester Epidemiology Project (REP)
101. Rotterdam study
102. Rush Memory and Aging Project (MAP)
103. Sacramento Area Latino Study of Aging (SALSA)
104. SEARCH for Diabetes in Youth (SEARCH)
105. Selenium and Cognitive Decline Project
106. Shanghai Women's Health Study (SWHS)
107. Strong Heart Study (SHS) / Strong Heart Family Study (SHFS)
108. Study of Dementia in Swedish Twins
109. Study of Osteoporotic Fractures (SOF)
110. Study of Women's Health Across the Nation (SWAN)
111. Study on Global Ageing and Adult Health (SAGE)
112. Swedish Kungsholmen Project
113. Systolic Blood Pressure Intervention Trial (SPRINT): Memory and Cognition in Decreased Hypertension (trial)
114. The 90+ Study
115. The Losartan Intervention For Endpoint reduction (LIFE) (trial)
116. The Nun Study

117. The Ohasama Study
118. The Scottish Longitudinal Study of Ageing (THSLs)
119. Three City Study
120. Treatment Options for type 2 Diabetes in Adolescents and Youth Trial (TODAY)
121. UAB Study of Aging
122. Veterans Aging Cohort Study Virtual Cohort (VACS-VS)
123. Victoria Longitudinal Study
124. Vietnam Era Twin Registry (VET)/Vietnam Era Twin Study of Aging (VETSA)/The VETSA Longitudinal Twin Study of Cognition and Aging (VETSA 3)
125. Washington Heights-Inwood Community Aging Project (WHICAP)
126. Whitehall Study
127. Wisconsin Longitudinal Study (WLS)
128. Wisconsin Sleep Cohort Study
129. Women's Health Study / Women Genome Health Study (WGHS)
130. Women's Health Initiative (WHI) Memory Study/WHI Observational Study (WHI-OS)

## NIH VCID Cohorts Workgroup Summary

### List of Key Cohort Characteristics (Data Elements)

These characteristics were considered for each cohort to inform discussions of potential scientific opportunities.

- A. Cohort name (hyperlinked to webpage)
- B. PI(s) and Lead Institution
- C. Current funding mechanism:
  - Ongoing data collection (grant/contract #)
  - Ongoing data analysis or processing (Y/N or grant #)
- D. Project period (from cohort initiation through last funded year)
- E. Funding ICOs (primary NIH IC in bold)
- F. Cohort size and geographic location
  - n=
  - Location(s):
- G. Cohort demographics
  - Age range at baseline:
  - Current age range:
  - Sex (M for men only, W for women only, B for both sexes):
  - Race/ethnicity:
  - Clinical disease status and/or source population:
- H. Diagnostic phenotype(s) (cognitive) [select all that apply from drop down menu, or enter N/A]
  - Dementia
  - Alzheimer Dementia
  - Vascular Dementia
  - Mixed Dementia
  - Other Dementia
  - Mild Cognitive Impairment (MCI)
  - Vascular Cognitive Impairment
  - Cognitive Impairment, Not Dementia (CIND)
  - Lewy Body Dementia
  - Frontotemporal Dementia
- I. Waves
  - Total number
  - Examination settings (i.e. phone, in-person, clinical)
- J. Timing / follow-up
  - Average length of follow-up:
  - Most recent examination:
  - Planned examinations:
- K. Cardiovascular risk assessments
  - Factors assessed

- Self-report or clinical or both
- Other methodological or technical aspects
- Waves/ yrs conducted

[If none, enter N/A]

L. Cognitive testing

- Tests used
- Other methodological or technical aspects
- Waves/ yrs conducted

[If none, enter N/A]

M. Brain imaging

- Type
- Other methodological or technical aspects
- Waves/ yrs conducted

[If none, enter N/A]

N. Biosamples

- Type
- Waves/ yrs conducted

[If none, enter N/A]

O. Genetics

- Data type/methodology (SNP, whole genome, etc.)
- GWAS (y/n)

[If none, enter N/A]

P. Autopsy (Y/N)

Q. Data available in a bank or registry? [enter resource name or N if no]

R. Other noteworthy factors? [select one or more from the drop-down menu]

- SES
- Neighborhood characteristics
- Educational attainment
- Language
- Psychosocial stress
- Sleep apnea
- Other medical or health-related factors

S. Re-consent needed (Y/N)?