School of Medicine and Public Health
UNIVERSITY OF WISCONSIN–MADISON

Wisconsin Alzheimer's Disease Research Center

Vascular contributions to cognitive impairment: Are we ready for a "V" in the AT(N) framework?

May 3, 2019

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Jeff Burns, MD
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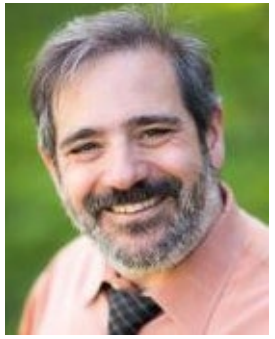


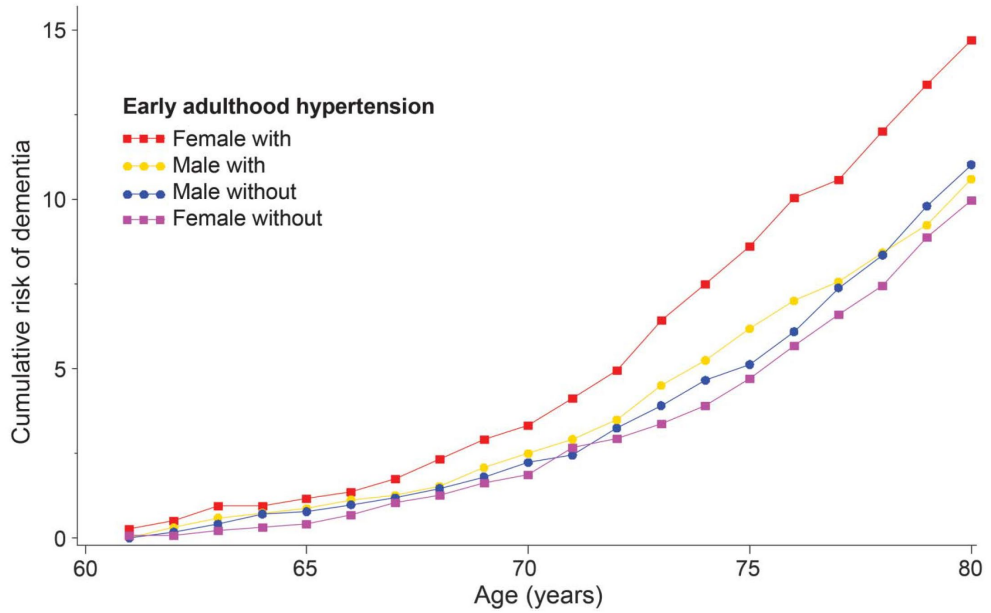
Howie Rosen, MD
(UCSF)

Greg Jicha, MD, PhD
(University of Kentucky)

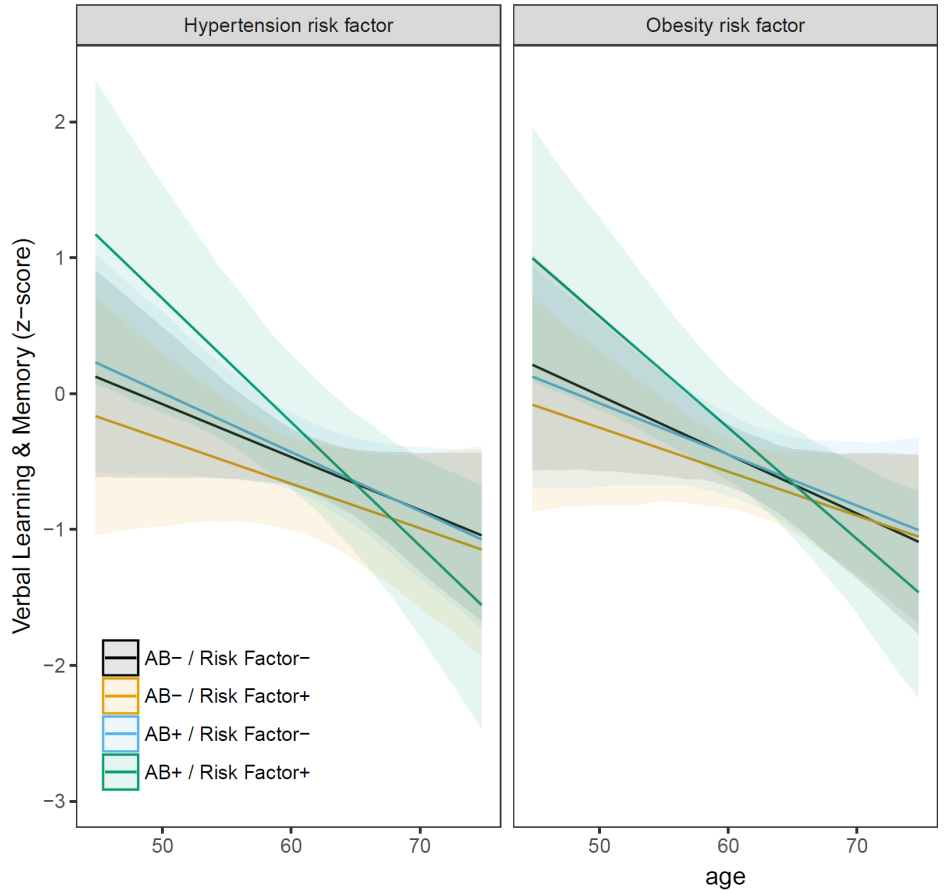
Mary Sano, PhD
(Mt. Sinai)

Vascular risk factors interact with sex and AD pathology to increase risk for dementia

Figure Estimates of the cumulative risk of dementia by sex and early adulthood hypertension status, conditional on survival dementia-free until age 60 and incorporating death rates



Gilsanz P et al. Neurology® 2017;89:1886–1893



L.R. Clark et al. / Alzheimer's & Dementia 15 (2019) 418-428

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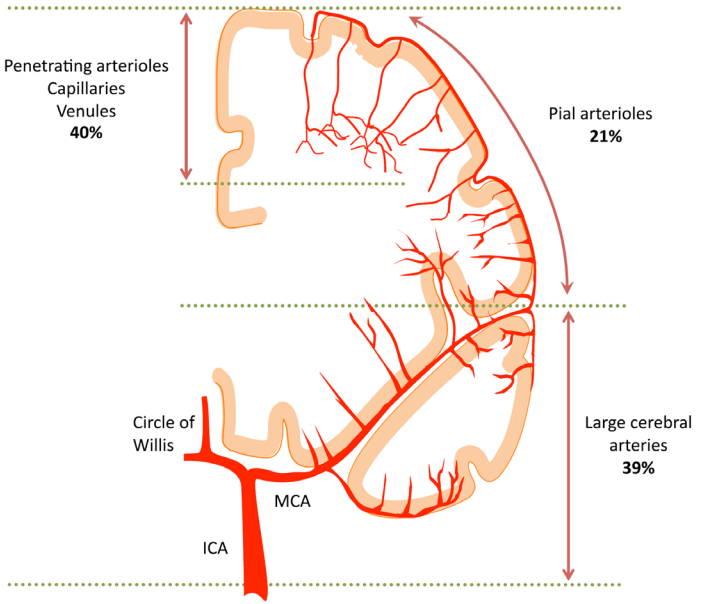
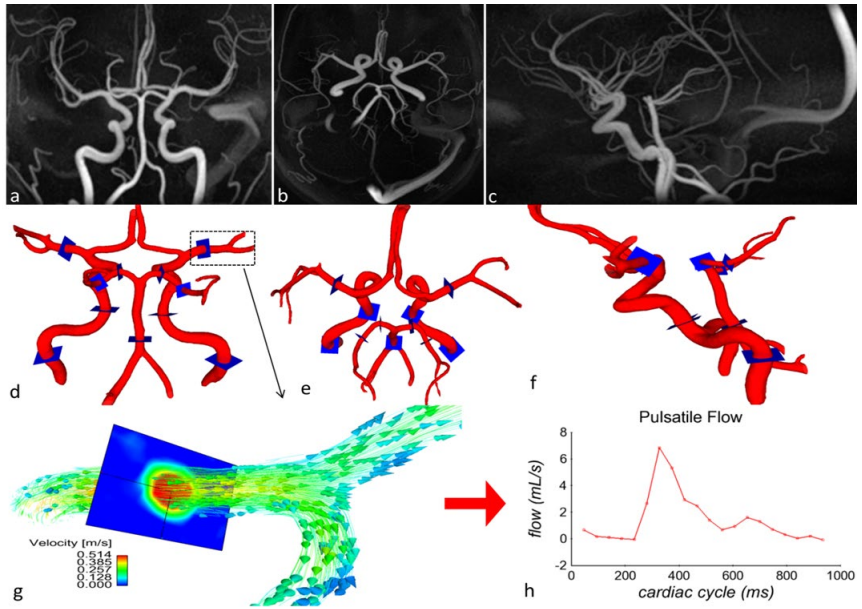
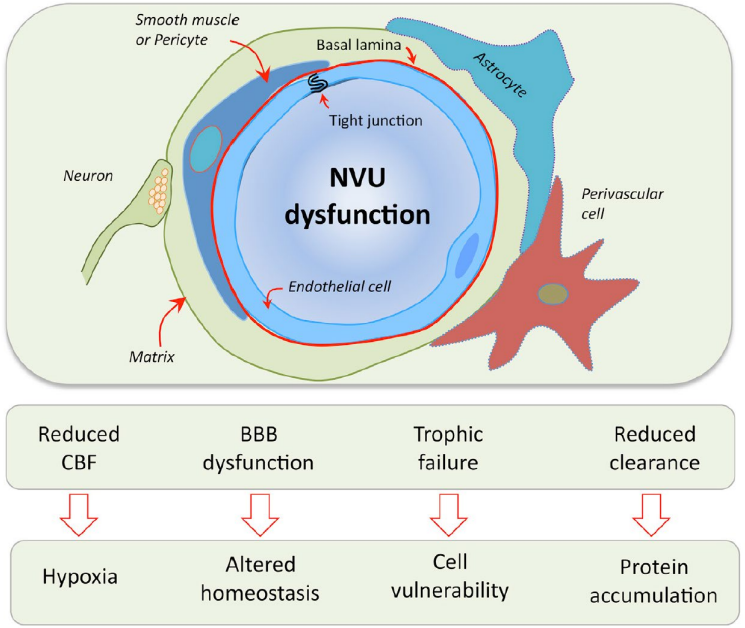
Vascular contributions to cognitive impairment and dementia (VCID)





4-D Flow MRI. Courtesy of Oliver Wieben, PhD, UW-Madison



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Iadecola C. *Neuron.* 2017 Sep 27;96(1):17-42. doi: 10.1016/j.neuron.2017.07.030.

SPRINT-MIND STUDY

Systolic Blood Pressure Intervention Trial – Memory and Cognition in Decreased Hypertension

- **New cases of MCI were reduced by 19%; combined outcome of MCI and dementia was reduced by 15%**

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JAMA. 2019;321(6):553-561. doi:10.1001/jama.2018.21442

Understanding VCID has important therapeutic implications

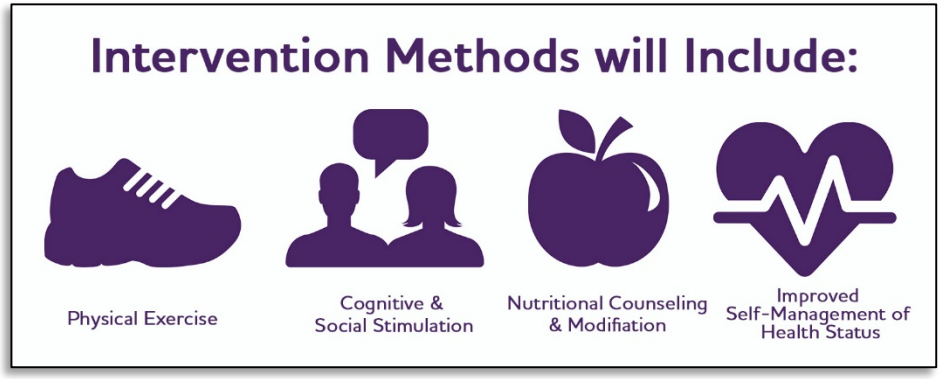
Finnish Geriatric (FINGER) study to Prevent Cognitive Impairment

- 2-year study
- 1260 adults ages 60–77 yrs
- Multi-domain intervention:
  - Diet
  - Exercise
  - Cognitive training
  - Vascular risk monitoring

} Improved cognitive performance

U.S.POINTER

alzheimer's association®



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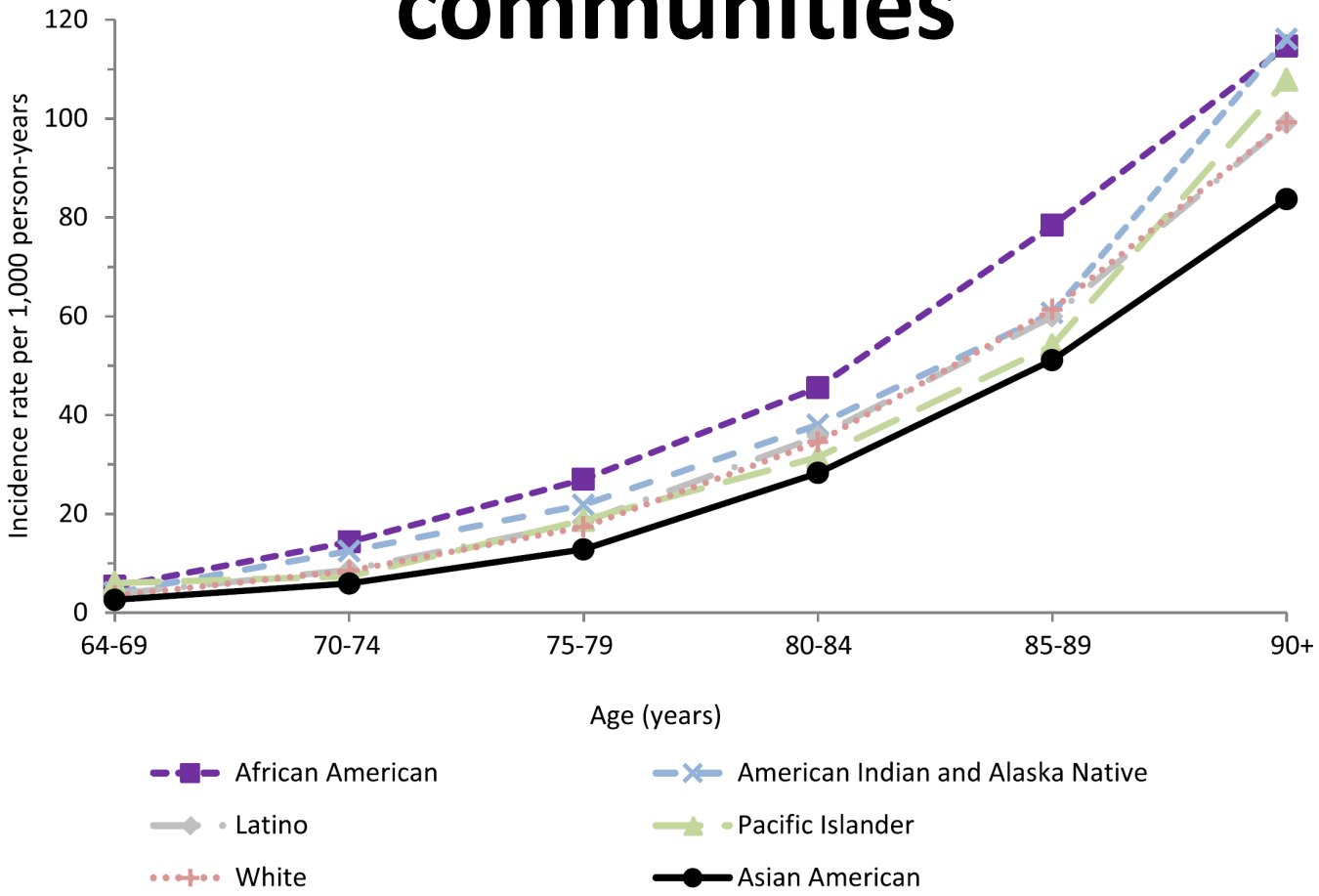
Ngandu et al. *Lancet* 2015; 385: 2255–63

https://alz.org/us-pointer/overview.asp

Understanding VCID may help clarify health disparities in dementia risk in various racial/ethnic communities



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E.R. Mayeda et al. / Alzheimer's & Dementia 12 (2016) 216-224

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		Syndromal Cognitive Stage		
		Cognitively unimpaired	**MCI**	**dementia**
Biomar	$A^- T^- (N)^-$	normal AD biomarkers, cognitively unimpaired	normal AD biomarkers with MCI	normal AD biomarkers with dementia
		concomitant suspected non Alzheimer's pathologic change, cognitively unimpaired	suspected non Alzheimer's pathologic change with MCI	concomitant suspected non Alzheimer's pathologic change with dementia
	$A^+ T^+ (N)^-$	Preclinical Alzheimer's disease	Alzheimer's disease with MCI (Prodromal AD)	Alzheimer's disease with dementia
	$A^+ T^+ (N)^+$			

How can we collectively move the science toward adding a "V" to the AT(N) framework?

C.R. Jack Jr. et al. / Alzheimer's & Dementia 14 (2018) 535-562

National Institute of Neurological Disorders and Stroke

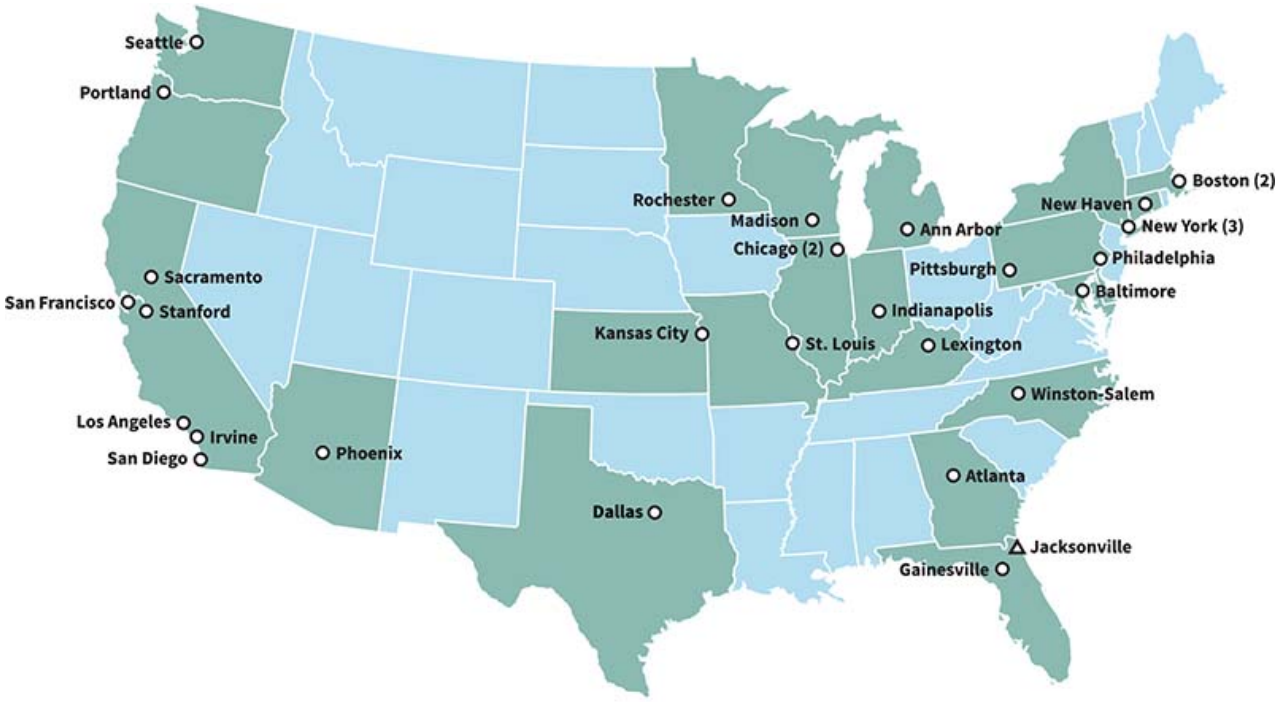
SAVE THE DATE
MARCH 14-15
2019
ALZHEIMER'S DISEASE-RELATED DEMENTIAS SUMMIT 2019:
RESEARCH CHALLENGES AND OPPORTUNITIES

Vascular Contributions to Cognitive Impairment and Dementia

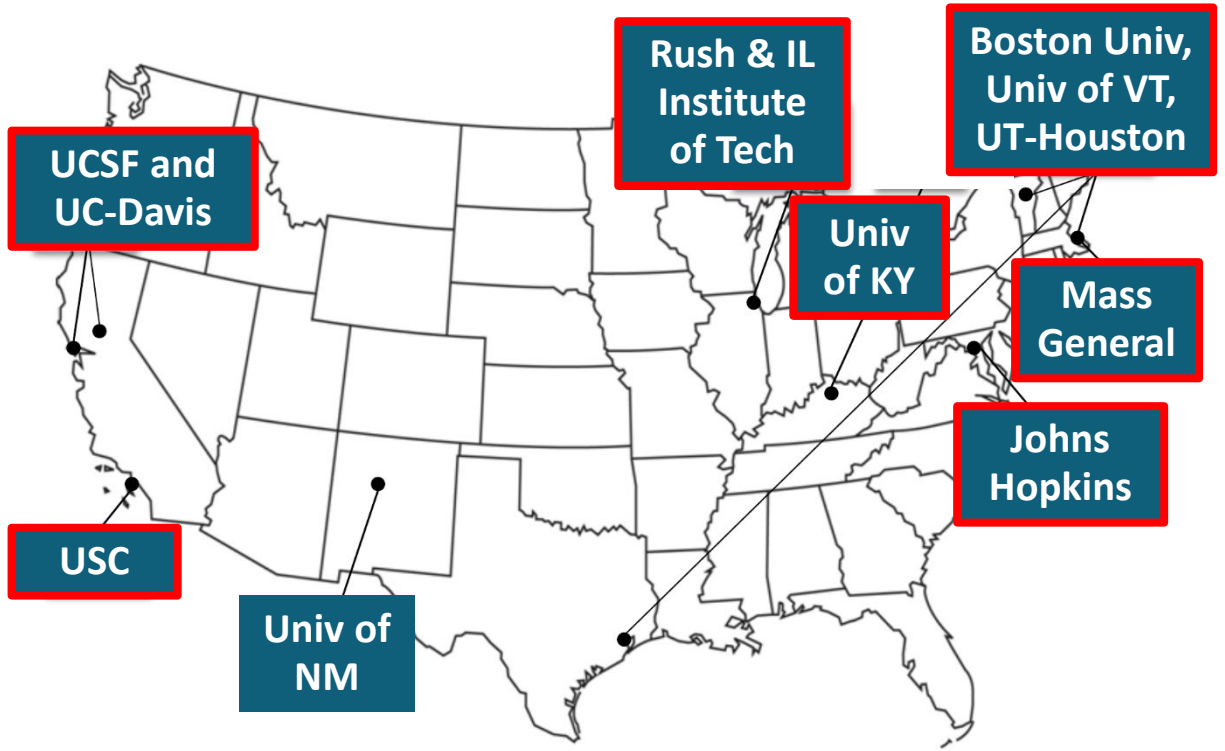
- **Rec. 4 – Priority 1.** Develop, validate & longitudinally track 1) cognitive, physical, functional assessment components that indicate the presence of VCID, & 2) biomarkers of key vascular processes (3-5 y).
- **Rec. 5 – Priority 2.** Identify 1) interventions (medication, lifestyle or a combination) with proven efficacy for reducing cardiovascular and cerebrovascular risk and 2) care models to test their efficacy for prevention and treatment of VCID (3-5 y).
- **Rec. 6 – Priority 4.** Determine interrelationships (cross-sectional & longitudinal) among cerebrovascular disease, cardiovascular disease, and VCID risk factors and aging, resilience, genetics, amyloid, tau, and neurodegeneration along the life-course (3-5 y).
- **Rec. 7 – Priority 2.** Use existing and in-process biospecimens, genomics, and imaging data from large-scale human studies to test hypothesized mechanisms of VCID derived from basic science animal/human studies (3-5 y).
- **Rec. 8 – Priority 3.** Incorporate VCID mechanisms derived from basic science animal/human studies into the design of human trials targeting dementia/MCI as primary outcomes (5-7 y).

https://meetings.ninds.nih.gov/Home/Tab2/21149

NIA Alzheimer's Disease Centers



MarkVCID Consortium Centers



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https://markvcid.partners.org/about/consortium-overview

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- **Clinical phenotyping of cerebrovascular contributions to cognitive impairment** – Jeff Williamson, MD, MHS
- **Neuroimaging of cerebrovascular disease** - Konstantinos Arfanakis, PhD
- **Fluid biomarkers of cerebrovascular disease** - Donna Wilcock, PhD
- **Genetics of cerebrovascular disease** - Christiane Reitz, MD, PhD

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