



# Becoming More Multimodal: CLARiTI

**Sterling Johnson, PhD**

---

**NACC Session, October 20, Fall 2023 ADRC Meeting**

# ADRC Consortium for CLARiTi (CLarity in ADRD Research Through Imaging)



Johnson, Mormino, Foroud, Rabinovici, Okonkwo, Rivera-Mindt, Dickerson, Wolk, Kukull

## SYNOPSIS

**Vision:** Empower individuals from all communities to prevent or effectively treat the multiple intersecting causes of cognitive impairment within ADRD

**GOAL: Create individual etiologic profiles from imaging and plasma**

- ATN imaging and plasma study superimposed on existing longitudinal UDS
- 2,000 clinical core participants; 60% impaired, 40% unimpaired with risk factors
- Diverse representation for generalizable science
- Two time points [2-3 years apart]
- *Heterogeneity* is the focus: syndromes and multi-pathologies

## COMPONENT LEAD INVESTIGATORS (partial list of 47 investigators)

- **Johnson/Mormino/NACC:** Admin
- **Rivera-Mindt/Okonkwo:** Inclusion
- **Biber/Kukull/Toga:** Image-Data informatics
- **Keene:** Neuropath
- **Rabinovici:** PET image reads
- **Shibata:** MRI scoring
- **Rahman-Filipiak/Clark/Chin:** Disclosure
- **Rosen:** neuropath MRI templates
- **Jagust/Jack:** SCAN
- **Villemagne:** PET harmonization
- **Detre:** Advanced MRI methods
- **Dage/Foroud:** Biofluid mgmnt, assays

- **Donohue:** Stats
- **Bethausser:** Biomarker time
- **Jones:** FDG analysis
- **Hohman:** Data harmonization integration
- **Kantarci:** LBD image analysis

## Industry collaborators

- LMI
- Lantheus/Cerveau
- Enigma
- Lilly
- Flywheel
- Alzpath
- Amprion
- Merck

# List of Site PIs

| ADRC                                  | Site PI   |
|---------------------------------------|---|
| Alabama                               | Jonathan McConathy                              |
| Arizona                               | Yi Su, Eric Reiman                              |
| BU                                    | Michael Alosco                                  |
| Columbia University                   | Adam Brickman                                   |
| Duke/UNC                              | Weili Lin PI, Co-PI: Allen Song                 |
| Emory U                               | PI: Deqiang Qiu, Co-PI: James Lah               |
| Florida 1                             | David Vaillancourt                              |
| Indiana                               | Shannon Risacher, Andrew Saykin                 |
| Johns Hopkins Univ                    | Marilyn Albert, Arnold Bakker                   |
| Kentucky                              | Greg Jicha                                      |
| Mayo                                  | Kejal Kantarci                                  |
| MGH/Harvard                           | Brad Dickerson                                  |
| Mt Sinai                              | Trey Hedden                                     |
| Nevada Cleveland Clinic               | Justin Miller                                   |
| Northwestern                          | Emily Rogalski                                  |
| NYU                                   | Co-PI: Arjun Masurkar Co-PI: Ricardo Osorio     |
| Ohio Cleveland                        | Co-PI: Frank DiFilippo Co-PI: Mark Lowe         |
| OHSU (Oregon Health Sciences U)       | Lisa Silbert, MRI Site Liasion: Daniel Schwartz |
| Rush                                  | Konstantinos Arfanakis                          |
| UTHSA (U of Texas Health San Antonio) | Mohamad Habes                                   |
| Stanford                              | Beth Mormino                                    |
| U Penn                                | David Wolk CO-PI John Detre                     |
| UC Davis                              | Audrey Fan                                      |
| UC Irvine                             | PI: Craig Stark, David Sultzer                  |
| UCSD                                  | James Brewer                                    |
| UCSF                                  | Gil Rabinovici                                  |
| University of Kansas                  | PI: Rebecca Lepping, Russell Swerdlow           |
| University of Michigan                | PI: Douglas Noll MPI, Benjamin Hampstead        |
| University of New Mexico              | PI: Gary Rosenberg Co-PI: Arvind Caprihan       |
| University of Pittsburgh              | Ann Cohen                                       |
| University of Washington              | Thomas Grabowski MD; Swati Levendovszky         |
| USC                                   | Arthur Toga, Lon Schneider                      |
| Vanderbilt                            | Angela Jefferson, Dr. Mary Ellen Koran          |
| Wake Forest                           | Sam Lockhart, Suzanne Craft                     |
| Wash U                                | Tammie Benzinger                                |
| Wisconsin                             | Sterling Johnson                                |
| Yale                                  | Christopher H. van Dyck, MD                     |

# Rationale: Some Gaps in the ADRD Field

---

- AD doesn't typically occur by itself:
  - Multi-etiology causes of impairment are the norm
- Heterogeneity in mixture of etiologies, and in onset ages
- **Treatment and prevention strategies may not be adequately tailored to the patient**
- **Treatment effects are confounded** by unknown intersecting multi-pathology
- Person level prognosis is not accurate
- Large cohort studies are designed around 1 etiologic pathway
- We need a collaborative platform to rapidly test new markers in the context of MED

# ADRCs are an Untapped Resource

---

- ~37 centers of excellence in ADRD; various specialization
- Amply contain diagnostic heterogeneity
- Donated brains from ADRCs have been key to building the literature on MED
- 27% URP enrollment
- Recrutable pool of > 11,600 (of >14,000 active participants)
- >58% of ADRC participants donate their brains for autopsy
- Well-established site-level infrastructure and expert *workforce*
- National infrastructure: NACC, NCRAD, SCAN/LONI, NIAGADS
- There is strong interest in collaborating as a consortium! (all 37 joined)
- Leverage existing neuropath and imaging!
- Centers are already conducting and uploading PET and MRI via SCAN

# The ADRCs Cover the Etiologic Spectrum

**Table 1. Prominent active cohort studies related to ADRD and their primary enrolling diagnosis**

| Cohort*  | Size or (Goal) | AD | VCID | LBD | Other** | LATE | A,T PET | purpose  |
|----------|----------------|----|------|-----|---------|------|---------|--|
| CLARiTI- | (2,000)        | Y  | Y    | Y   | Y       | nk   | Y       | MED detection in ADRCs                         |
| DVCID*** | (2,250)        | n  | Y    | n   | n       | nk   | N       | vascular risk for cognitive decline            |
| ADNI4    | (1,200)        | Y  | n    | n   | n       | nk   | Y       | Clinical trial planning for AD with biomarkers |
| LEADS    | 700            | Y  | n    | n   | n       | nk   | Y       | Clinical trial planning in early onset AD      |
| ALLFTD   | 1,479          | n  | n    | n   | Y       | nk   | N       | Clinical and biomarker progression             |
| PPMI     | 4500           | n  | n    | Y   | n       | nk   | N       | PD Biomarker progression                       |
| DLBC     | 200            | n  | n    | Y   | n       | nk   | N       | DLB biomarkers                                 |
| DIAN     | 600            | Y  | n    | n   | n       | nk   | Y       | Cohort of autosomal mutation carriers          |

Notes: \*Single-site cohorts not listed. \*\*'Other' includes FTLD and atypical subtypes; \*\*\*Diverse VCID participants may co-enroll because DVCID does not do PET; nk= not known since LATE is a neuropath entity—it is assumed all older cohorts contain some as yet unknown burden of LATE-neuropathologic change; LBD includes Dementia with Lewy Bodies and Parkinson's disease dementia and prodromes. Other abbreviations: VCID Vascular Cognitive Impairment. LEADS Longitudinal Early Onset AD Study; PPMI Parkinson's Progression Marker Initiative; DLBC Lewy Body consortium.

# Guiding Principles: Make it Easy for Sites

---

Funding and support for sites: scans and personnel

Broad consent for sharing with NACC and interlink with other data

Overlay on NACC; no additional cognitive/clinical assessments

Diversity and inclusion

Embrace clinical heterogeneity

Focus on developing and validating tools for MED bioprofiles from biomarkers

Use existing infrastructure (e.g. NACC, NCRAD, SCAN)



# CLARiTI ATN - U01

\$

Data

NACC Data Platform

## Data coordination, collection, integration & sharing

**Data collection coordination:** communication, education, evaluation

**CLARiTI data shared via NACC Data Front Door**

**Multimodal data integration** - Connected via NACCID

**Site subcontracts** to cover staff and image submissions - invoicing tools to track work performed



**Researchers  
Everywhere**

Admin

Diversity Recruitment

Clinical Operations

Image and Data Analysis

Advanced MRI

Plasma Biomarkers

Neuropathology

Results

Advanced MRI

Results

\$ and Results



**NCRAD**

- Store samples, run assays, & results to NACC

**ADRC sites (37)**

- Image acquisition and upload  
- Plasma collection

Image  
Repository

**LONI**

Raw images

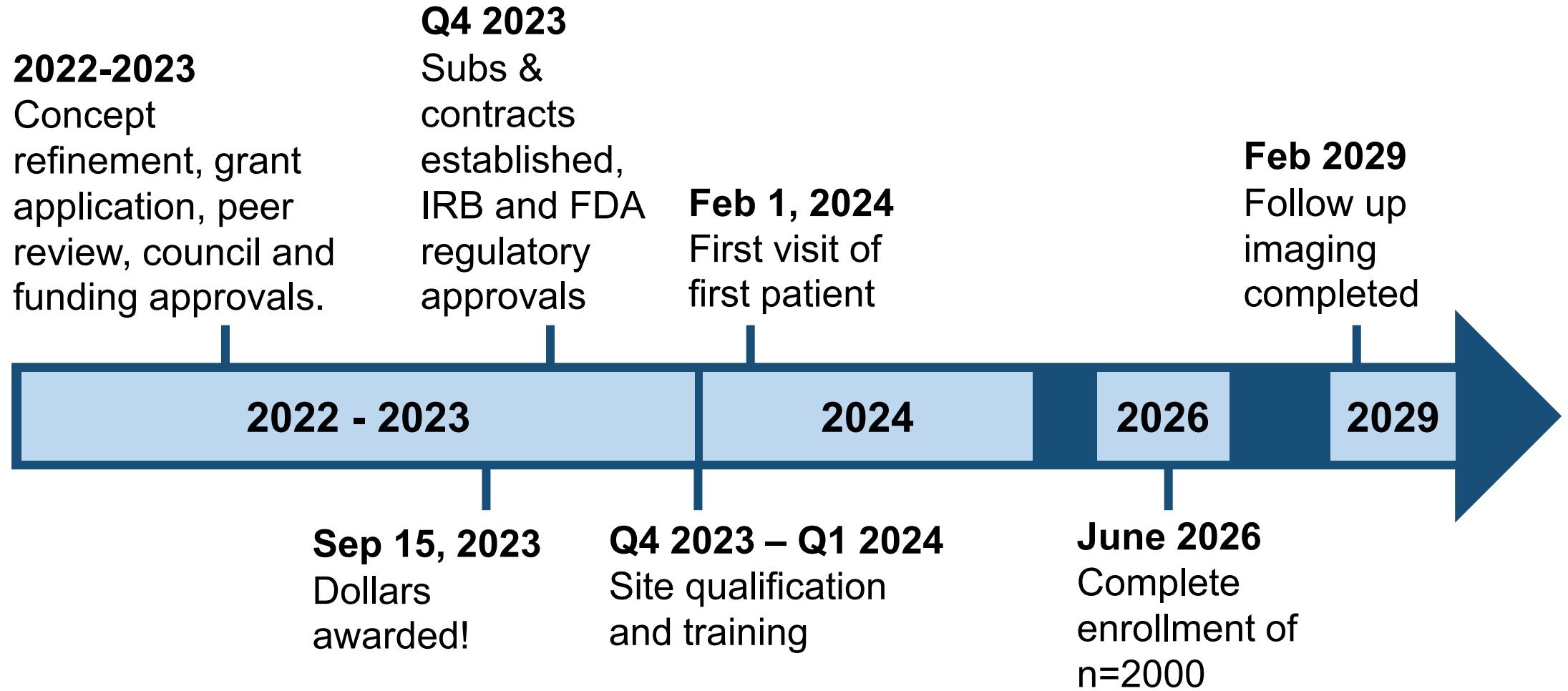
Curated files

**scan**

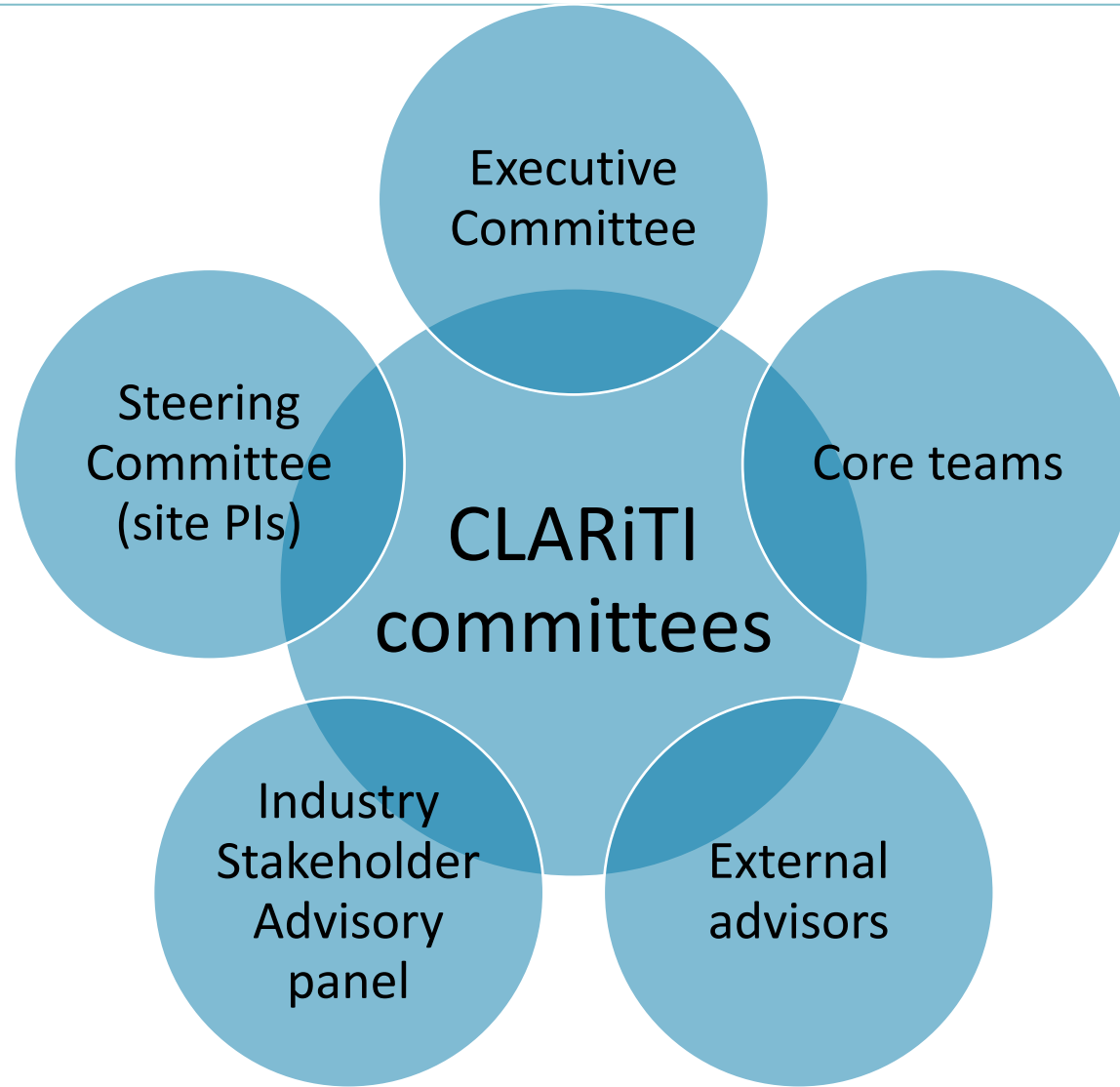
SCAN Data  
Analysis



# Approximate Timeline



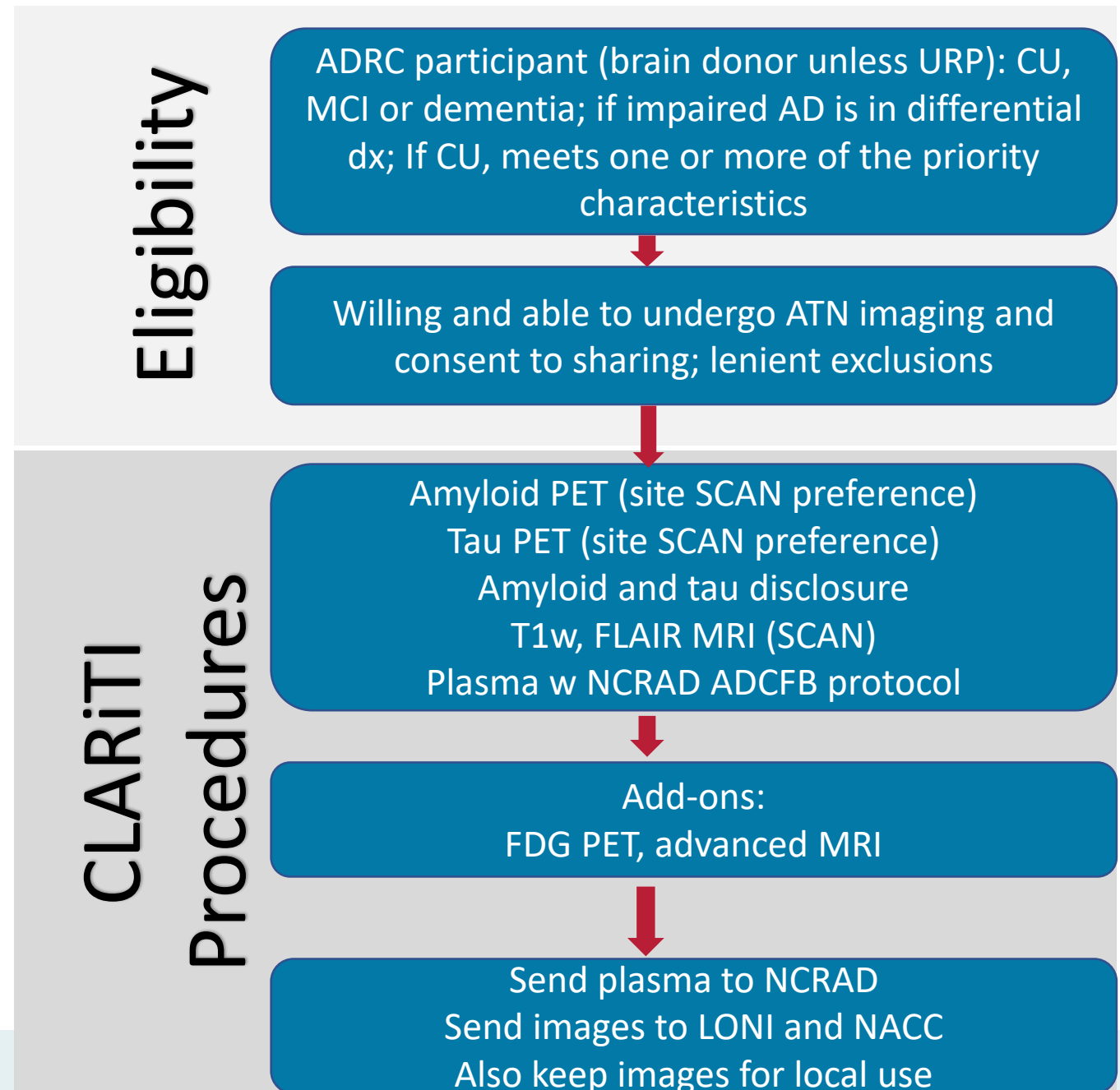
# Committees



- **Admin core**
- **Inclusion core**
- **Visual read**
- **Disclosure**
- **Biofluid core**
- **Advanced MRI**
- **Neuropathology**
- **Informatics**
- **Harmonization**
- **Analysis**

# What Does It Consist Of?

- **Each ADRC gets ~Two 100% staff FTE**
  - Outreach and recruitment (work with ORE cores) to achieve our 25% URG ATN goal! Increase brain donor enrollment
  - FTE for study coordination
- **\$10,000/yr site allowance for local events and to pay community boards etc.**
- **National recruitment support (Rivera-Mindt, Okonkwo, Byrd)**

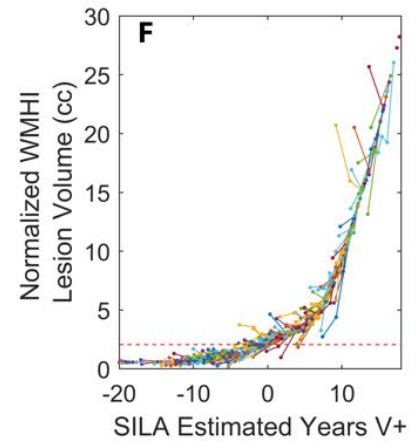
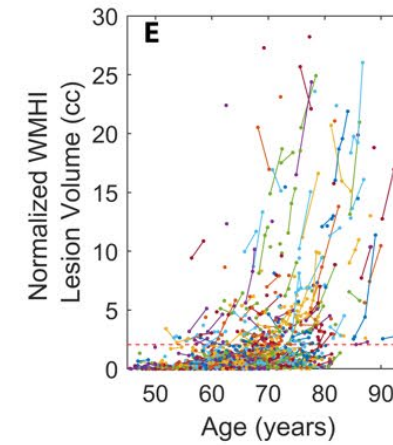
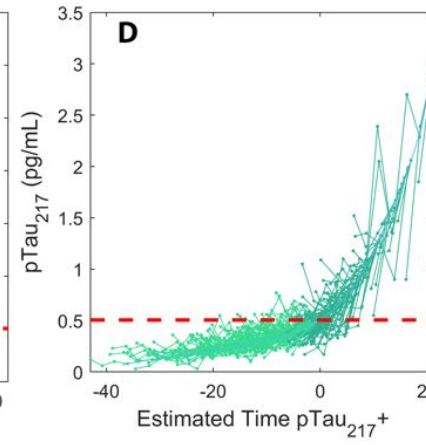
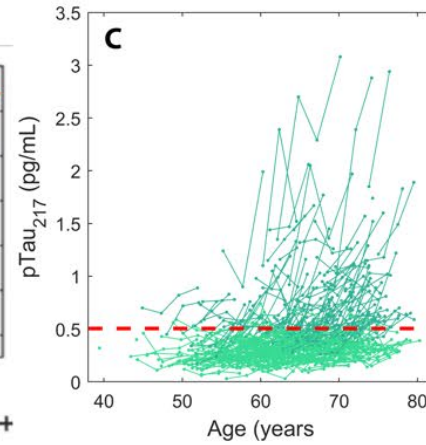
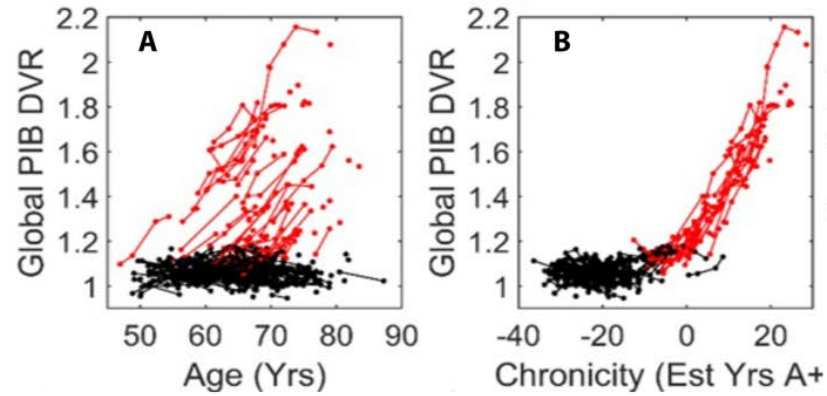


Amyloid PET time

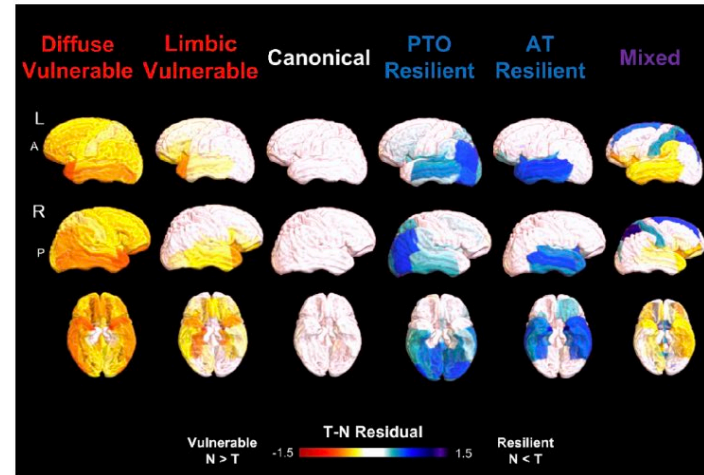
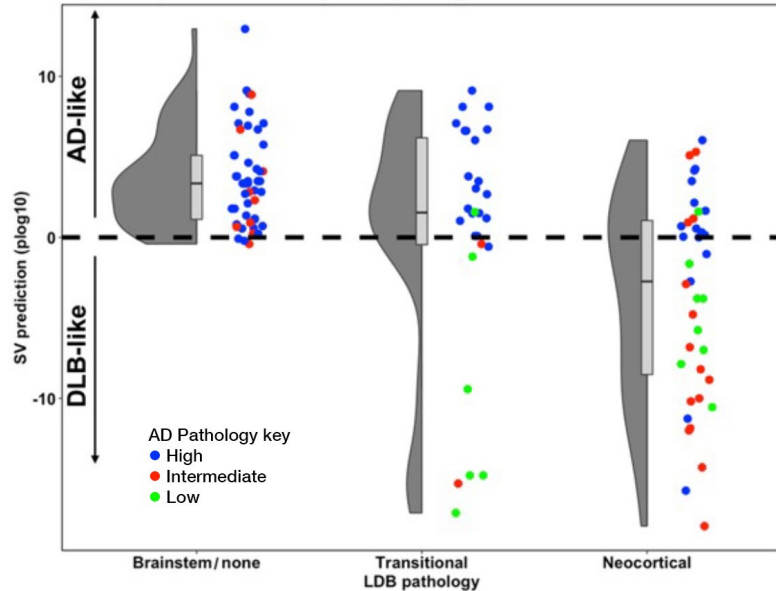
Ptau217 time

WMH (V) time

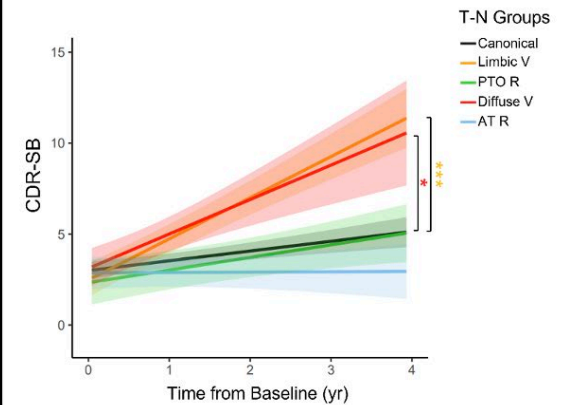
Biological Age  $\rightarrow$  Chronicity



StateViewer predictions according to LBD pathology



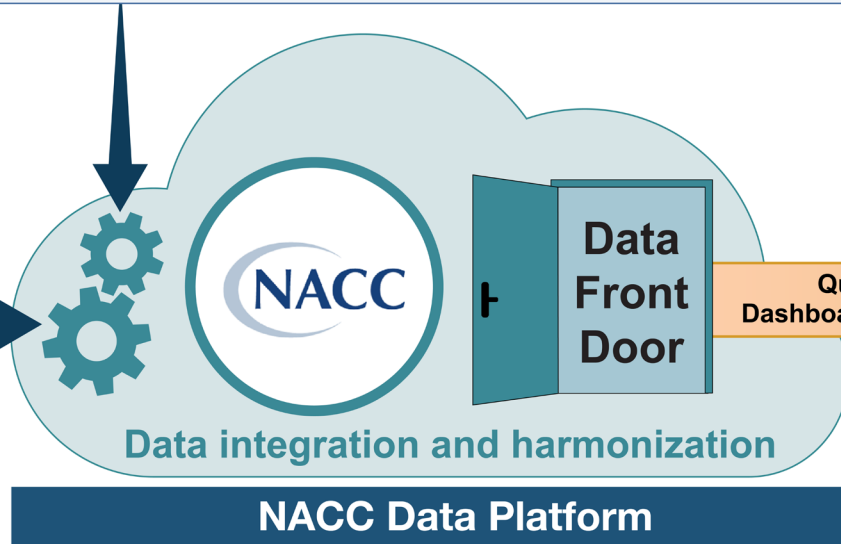
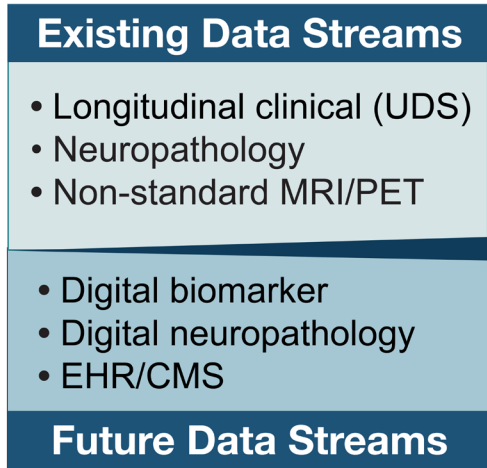
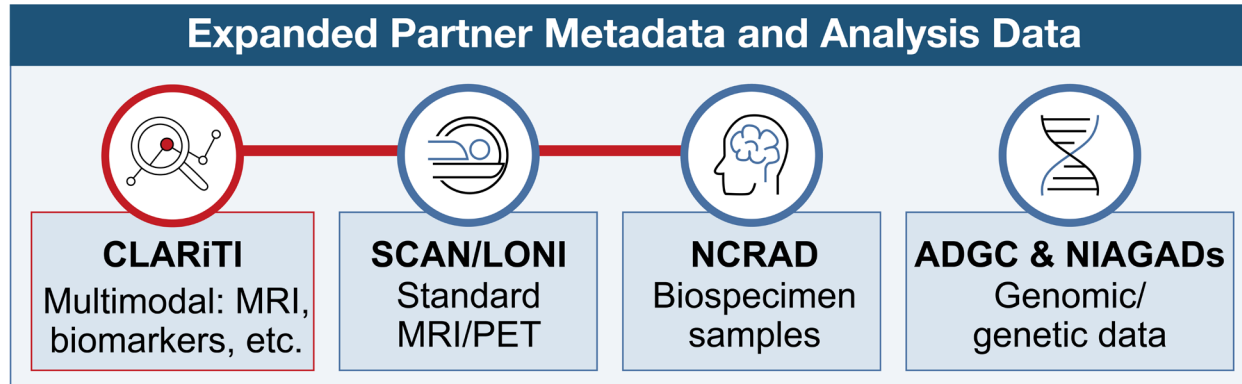
T-N Groups CDR-SB Trajectory



FDG pattern Classification; Jones, Mayo ADRC

Atrophy Disproportionate to T, Penn ADRC

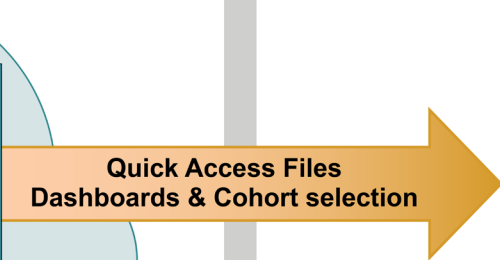
# How Does CLARiTI Fit into the NACC Dataflow?



**Scalable to new data streams**

**Real-time data search, visualization, and access**

**Ready for AI-driven discovery**



**Free for researchers everywhere!**  
[www.naccddata.org](http://www.naccddata.org)

# Next Steps

---

- **Study start up in active phase**
  - First visit first patient by Feb 1, 2024
  - Stay tuned for a site communication/survey regarding ligands and your recruitment goals: this will eventuate into a statement of work/MOU
  - Site startup checklist
  - Stay tuned for a webinar in early December



**Thank you!**







# Connect with Dr. Johnson

**Sterling Johnson, PhD**

---

[scj@medicine.wisc.edu](mailto:scj@medicine.wisc.edu)