CLARiTI

ADRC Consortium for Clarity in ADRD Research Through Imaging

NACC

Impact of CLARiTI National Inclusion & Engagement Plan

October 17, 2024

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Agenda

Scientific Impact of CLARiTI and progress report

Sterling Johnson, PhD
Beth Mormino, PhD

CLARiTI Infrastructure Updates & Impact

Sarah Biber, PhD

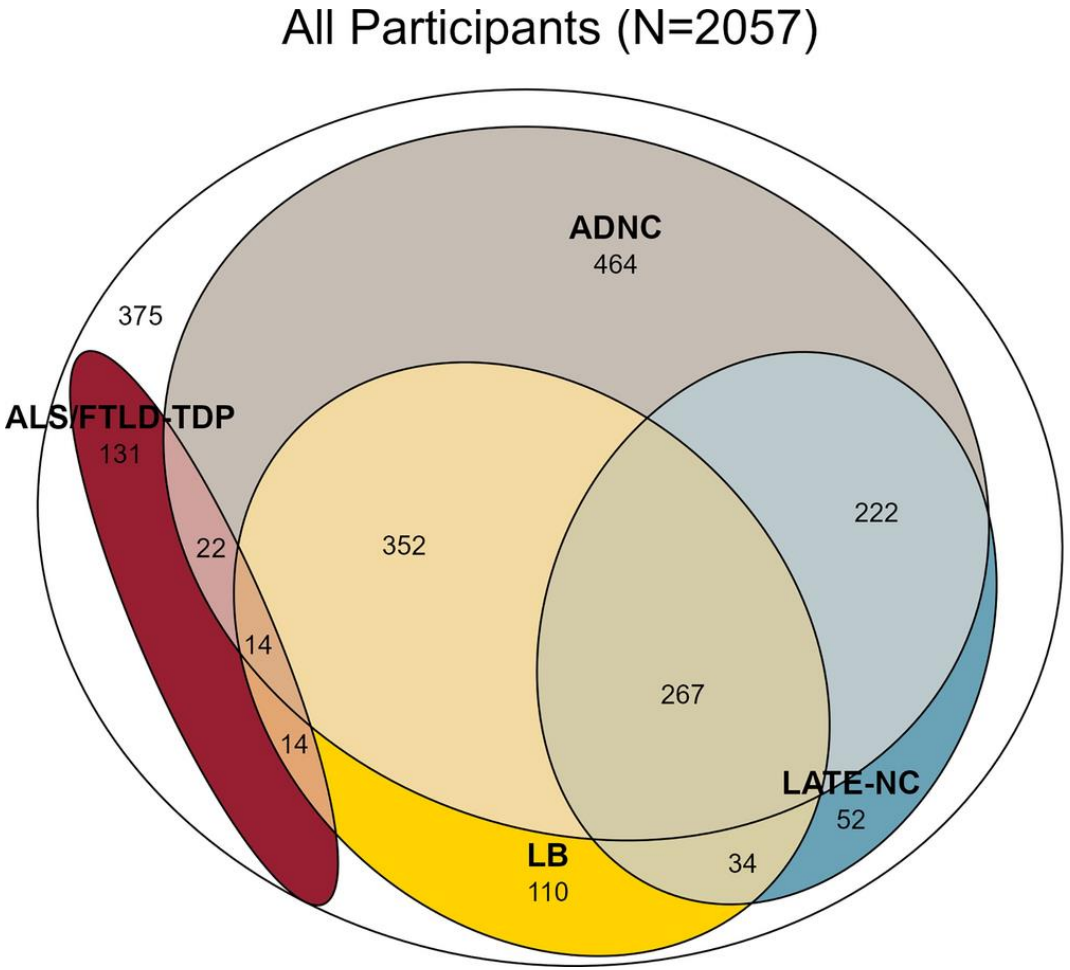
Study Updates

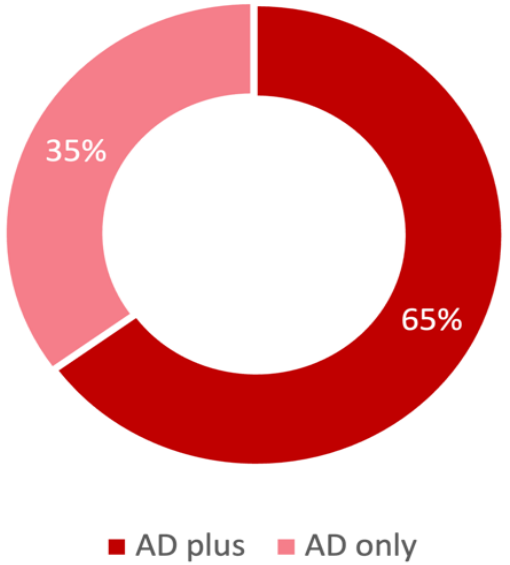
Erin Chin

CLARiTI National Inclusion and Engagement Plan

Ozioma Okonkwo, PhD

Overlap in common proteinopathies from NACC

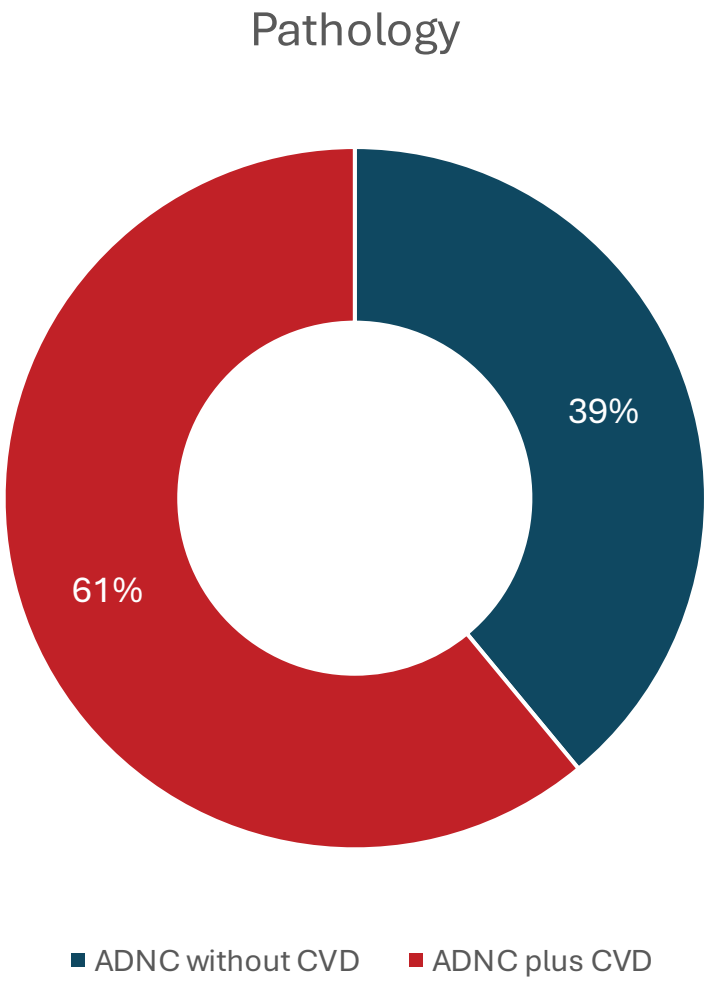




- ADNC only = 35%
- ADNC plus [TDP43, or LB, or both] = 65%
- ADNC plus LB = 46%
- ADNC plus TDP43= 36%
- ADNC plus TDP43 and LB = 20%

Woodworth et al 2024, Acta Neuropathologica

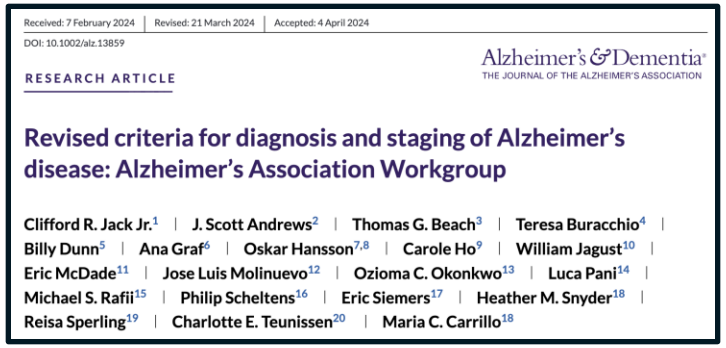
ADNC co-occurs with cerebrovascular disease



- N=2423 NACC brain donors with ADNC and UDS cognitive data
  - ADNC = Braak >=3
- CVD= moderate to severe arteriolosclerosis or atherosclerosis
- People with both diseases declined faster

Frank et al 2022 *Neurology*
From Boston ADRC

ATN profiles fundamental to AD research



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RESEARCH ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup

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2024

ELSEVIER

Alzheimer's & Dementia 14 (2018) 535-562

Alzheimer's & Dementia

2018 National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework

NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

Clifford R. Jack, Jr.[a,*], David A. Bennett[b], Kaj Blennow[c], Maria C. Carrillo[d], Billy Dunn[e], Samantha Budd Haeberlein[f], David M. Holtzman[g], William Jagust[h], Frank Jessen[i], Jason Karlawish[j], Enchi Liu[k], Jose Luis Molinuevo[l], Thomas Montine[m], Creighton Phelps[n], Katherine P. Rankin[o], Christopher C. Rowe[p], Philip Scheltens[q], Eric Siemers[r], Heather M. Snyder[d], Reisa Sperling[s]

Contributors[t]: Cerise Elliott, Eliezer Masliah, Laurie Ryan, and Nina Silverberg

2018

ELSEVIER

Alzheimer's & Dementia 7 (2011) 280–292

Alzheimer's & Dementia

Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Reisa A. Sperling[a,*], Paul S. Aisen[b], Laurel A. Beckett[c], David A. Bennett[d], Suzanne Craft[e], Anne M. Fagan[f], Takeshi Iwatsubo[g], Clifford R. Jack, Jr.[h], Jeffrey Kaye[i], Thomas J. Montine[j], Denise C. Park[k], Eric M. Reiman[l], Christopher C. Rowe[m], Eric Siemers[n], Yaakov Stern[o], Kristine Yaffe[p], Maria C. Carrillo[q], Bill Thies[q], Marcelle Morrison-Bogorad[r], Molly V. Wagster[r], Creighton H. Phelps[r]

ELSEVIER

Alzheimer's & Dementia 7 (2011) 270–279

Alzheimer's & Dementia

The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Marilyn S. Albert[a,*], Steven T. DeKosky[b,c], Dennis Dickson[d], Bruno Dubois[e], Howard H. Feldman[f], Nick C. Fox[g], Anthony Gamst[h], David M. Holtzman[i,l], William J. Jagust[k], Ronald C. Petersen[l], Peter J. Snyder[m,n], Maria C. Carrillo[o], Bill Thies[o], Creighton H. Phelps[p]

ELSEVIER

Alzheimer's & Dementia 7 (2011) 263–269

Alzheimer's & Dementia

The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Guy M. McKhann[a,b,*], David S. Knopman[c], Howard Chertkow[d,e], Bradley T. Hyman[f], Clifford R. Jack, Jr.[g], Claudia H. Kawas[h,i,j], William E. Klunk[k], Walter J. Koroshetz[l], Jennifer J. Manly[m,n,o,e], Richard Mayeux[m,n,o,e], Richard C. Mohs[p], John C. Morris[q], Martin N. Rossor[r], Philip Scheltens[s], Maria C. Carrillo[t], Bill Thies[t], Sandra Weintraub[u,v], Creighton H. Phelps[w]

2011

CONTEMPORARY ISSUES IN PRACTICE, EDUCATION, & RESEARCH OPEN ACCESS

Challenges in a Biological Definition of Alzheimer Disease

Jemma Hazan, MBBS, MRCPsych, iBSc, Kathy Y. Liu, Harry Costello, MBBS, MSc, MRCPsych, BSc, Jeremy D. Isaacs, MA, MBBS, MRCP, PhD, Madhav Thambisetty, MD, PhD, and Robert Howard, MD

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J Prev Alz Dis 2024;4(11):895-896
Published online July 8, 2024, http://dx.doi.org/10.14283/jpad.2024.141

Editorial

On the 2024 Alzheimer's Association Criteria: Still Not Ready for Clinical Use

R.Z. Zhou[1], *A. Wimo*[1], *B. Winblad*[1,2]

Personal View

Clinical diagnosis of Alzheimer's disease: recommendations of the International Working Group

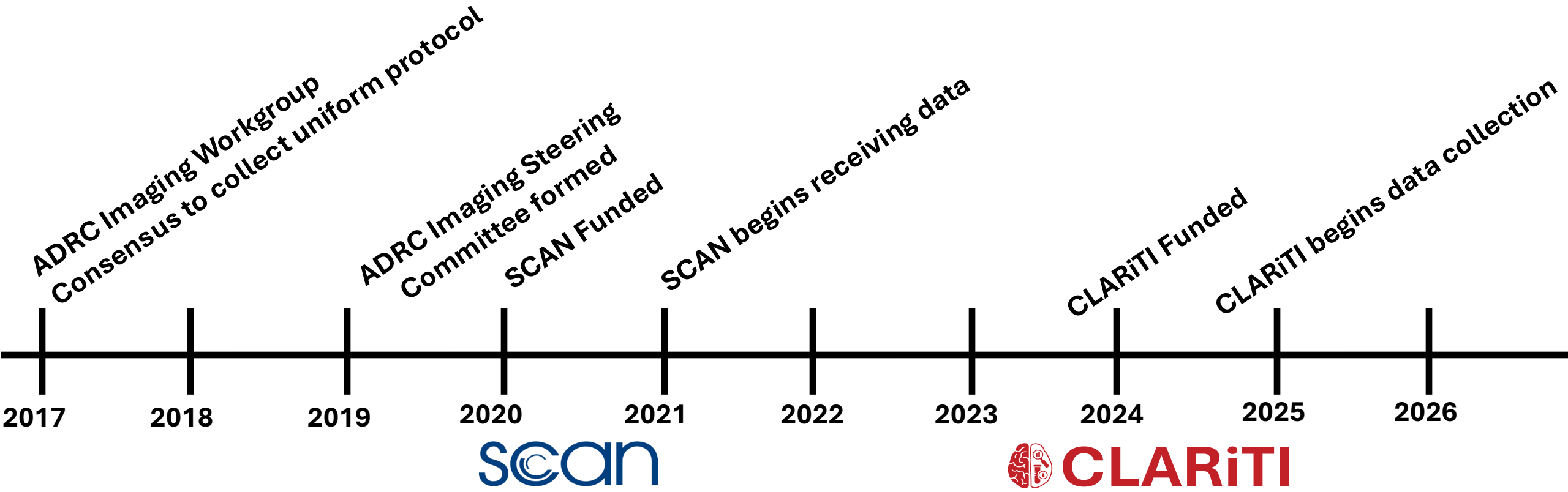
Bruno Dubois, Nicolas Villain*, Giovanni B Frisoni, Gil D Rabinovici, Marwan Sabbagh, Stefano Cappa, Alexandre Bejanin, Stéphanie Bombois, Stéphane Epelbaum, Marc Teichmann, Marie-Odile Habert, Agneta Nordberg, Kaj Blennow, Douglas Galasko, Yaakov Stern, Christopher C Rowe, Stephen Salloway, Lon S Schneider, Jeffrey L Cummings, Howard H Feldman*

GUEST EDITORIAL

Revised NIA-AA criteria for the diagnosis of Alzheimer's disease: a step forward but not yet ready for widespread clinical use

Frisoni, Winblad, O'Brien

Timeline of ADRC Imaging Initiatives

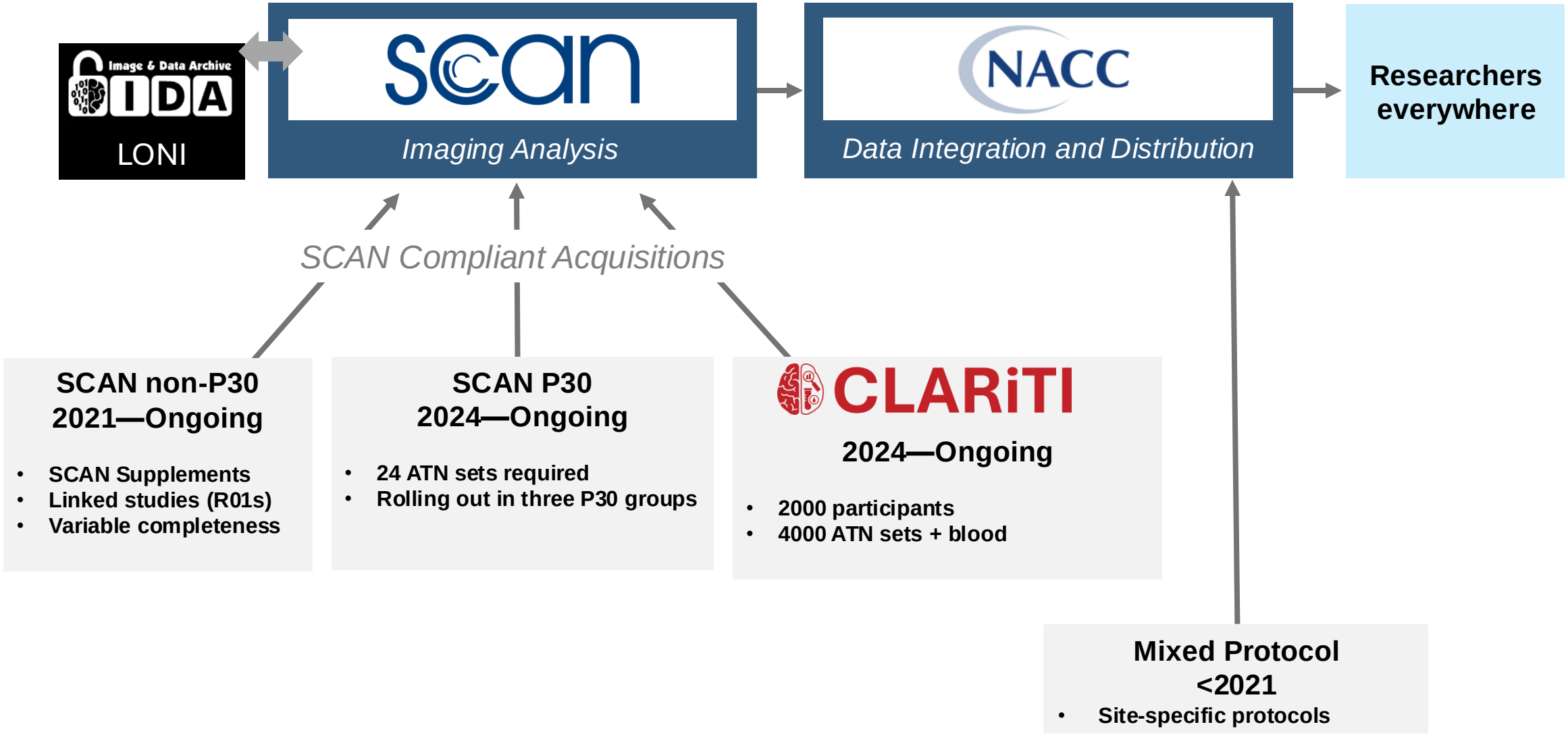


Agree to collect images together

Infrastructure receive and process images

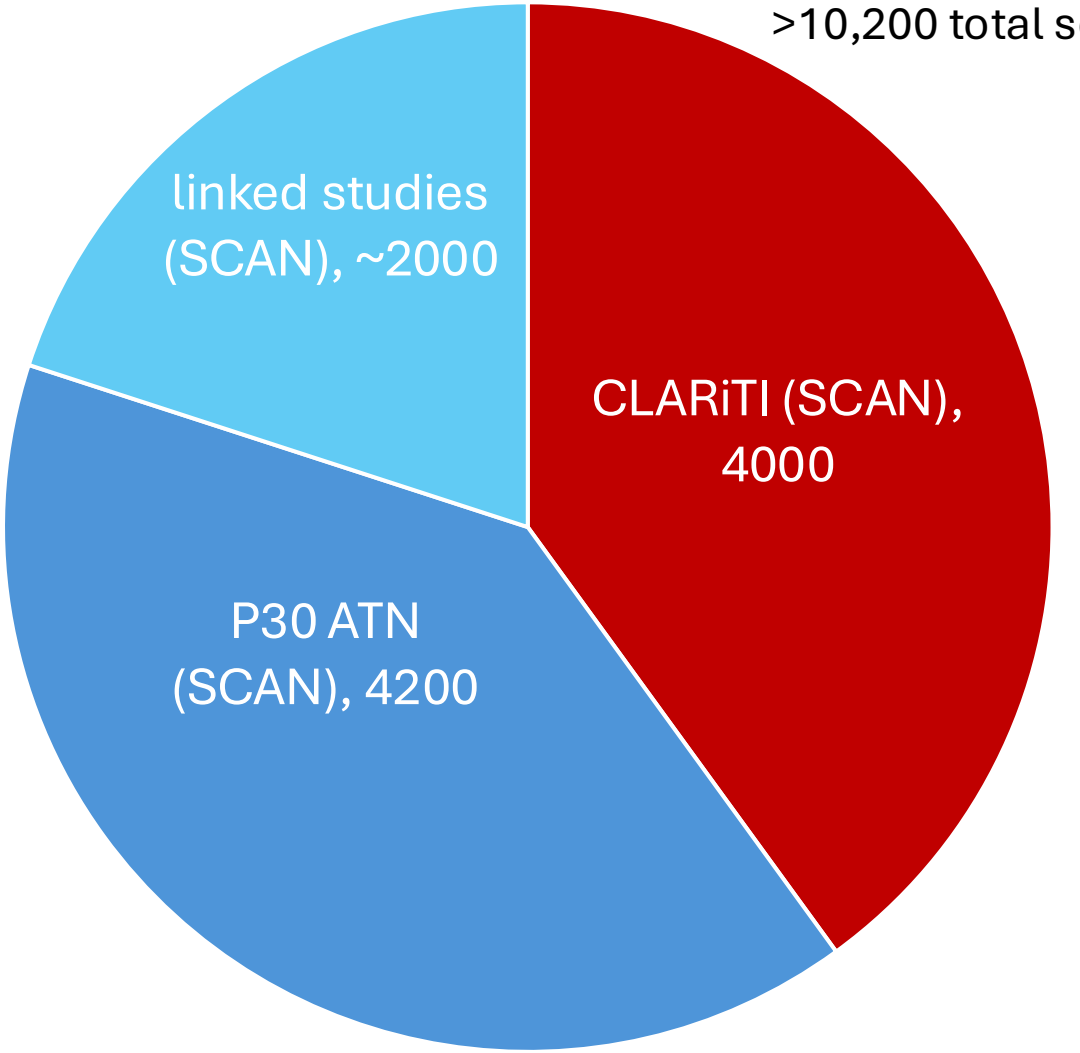
Scientific questions and recruiting plan

The ADRC imaging ecosystem



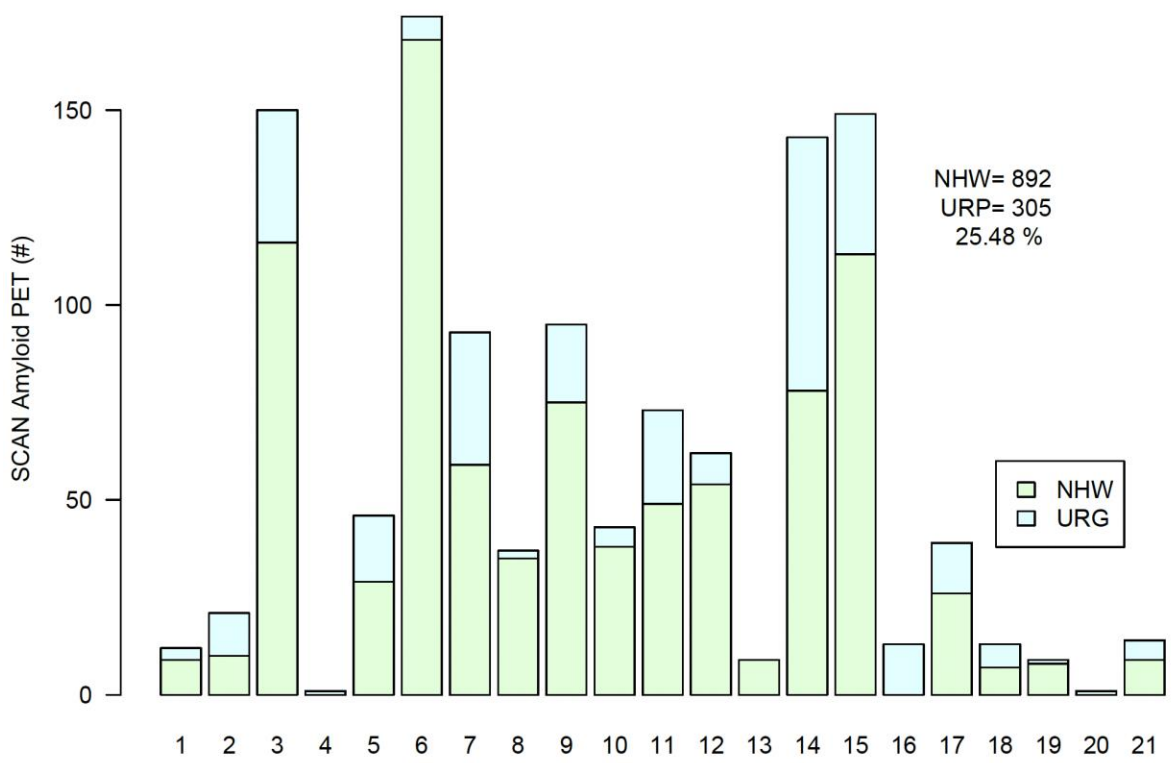
Collective impact: Estimated amyloid PET exams over next 5 years in SCAN

>10,200 total sets from 5-8K people

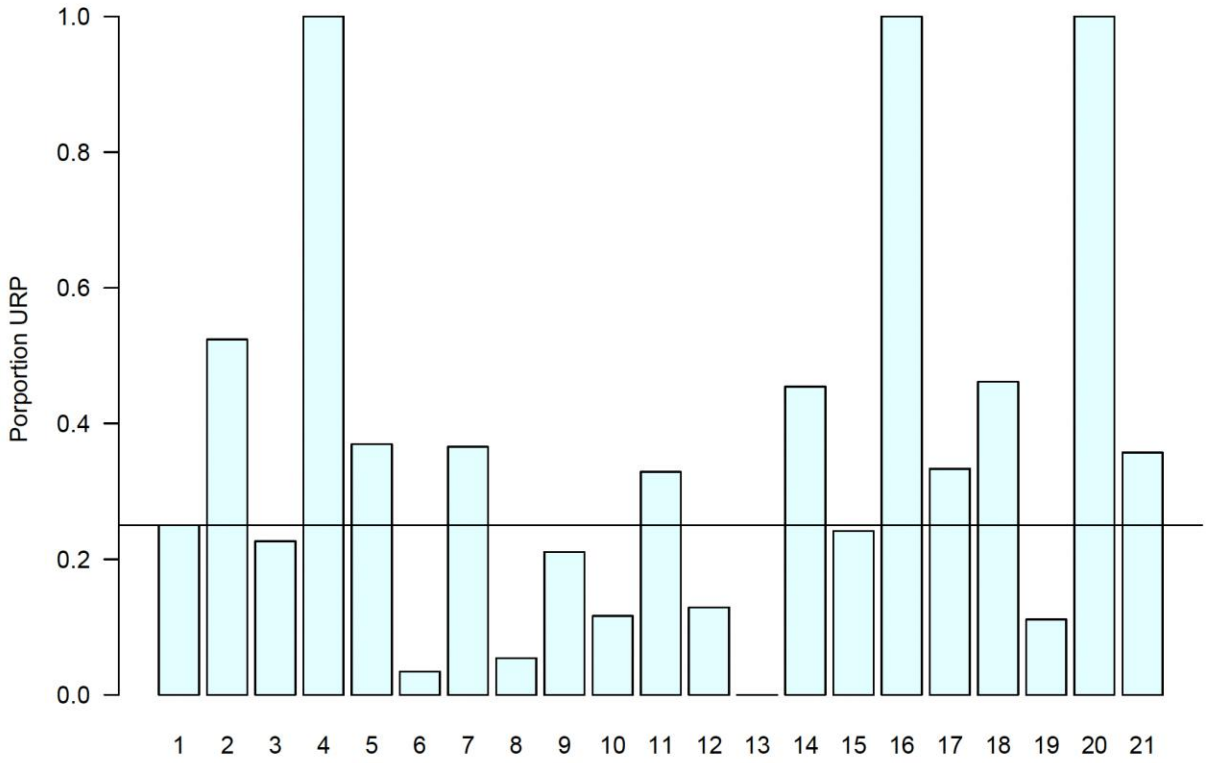


25% SCAN Amyloid data from URPs

Counts by center

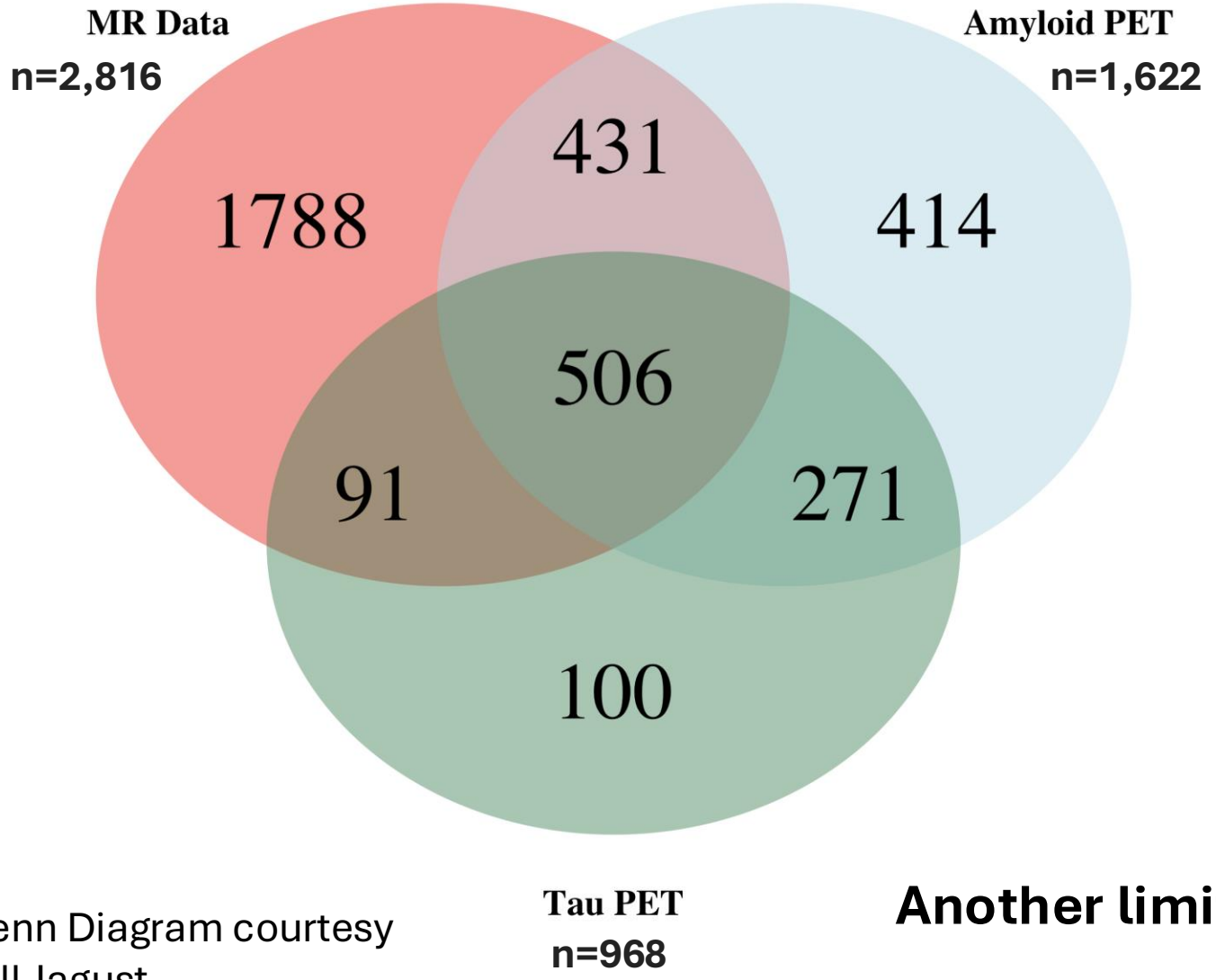


Proportion URG by center



SCAN Limitation: high "missingness"

3601 *participants* with one or more scans



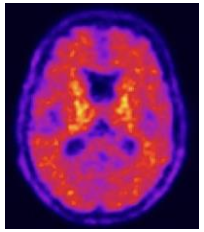
Venn Diagram courtesy
Bill Jagust

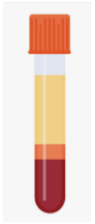
May reflect…
Site level strategies (Tau PET may not be collected in Amyloid-Impaired participants)?

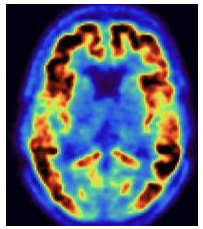
Lack of resources/study protocol for collecting all 3?

Another limitation is high proportion of CU (~60%)

PET, plasma overlap and missingness





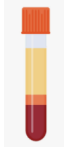


1210 Amyloid (48% with ADCFB plasma)

759 Tau (50% with ADCFB plasma)

638 Both Amyloid+Tau PET

326 also have ADCFB plasma



Flowchart courtesy
Jeff Dage

CLARiTI Aims

Infrastructure Aim: Standardized ATN+Blood acquisition

- The focus of today

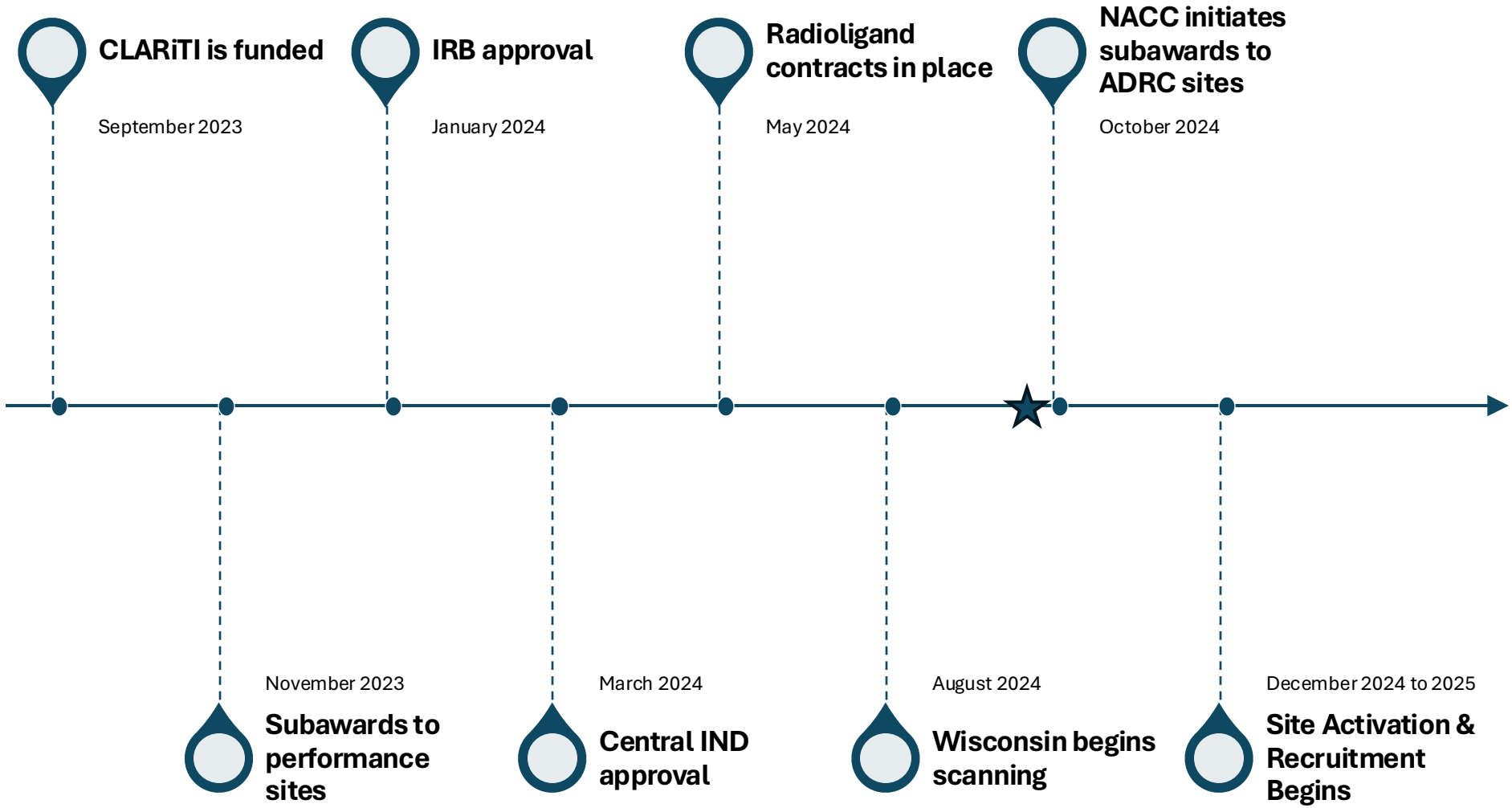
Scientific Aims: Multi-etiologies imaging-based signatures

SYNOPSIS

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
- Diverse representation for generalizable science > 25% URG
- Two time points [**4000** ATN sets] ~2 year interval
- *Embrace Heterogeneity*: syndromes and multi-pathologies

Timeline


CLARiTI is funded
September 2023
IRB approval
January 2024
Radioligand contracts in place
May 2024
NACC initiates subawards to ADRC sites
October 2024
November 2023
Subawards to performance sites
March 2024
Central IND approval
August 2024
Wisconsin begins scanning
December 2024 to 2025
Site Activation & Recruitment Begins

Progress update:
CLARiTI infrastructure now in place

Strategic recruiting plan and resources

Central IRB, IND, regulatory, vendors

Cores are operational

CLARiTI portal at LONI is running

Informatics established

Ready for enrollment when sites are

Next: Scaling up in Q4 and early 2025

Subaward phase Nov 24

Site Activation

Site-level dashboards with diversity monitoring

Core-specific initiatives and rollouts