

Implementing CLARiTI: A Scalable Approach to Multi-Site Observational Study Start-up Under IND Requirements

Kelsey Shuda^{1,2}, Erin Chin^{1,2}, Heather O'Connell^{3,4}, Hanzhe Gao^{1,2}, Hannah Koenig^{3,4}, Terry Ward^{1,2}, Sandra Mabel Duran Rojas^{1,2}, Joel Hetelle^{1,2}, Laurie Lewis Robertson^{1,2}, Phoebe Frenette^{1,2}, Nathaniel A. Chin^{1,2}, Sarah Biber^{5,6}, Elizabeth C. Mormino^{7,8}, Sterling C. Johnson^{1,2}.

¹Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, ²Wisconsin Alzheimer's Disease Research Center, Madison, WI, USA, ³University of Washington School of Public Health, Seattle, WA, USA, ⁴National Alzheimer's Coordinating Center, Seattle, WA, USA, ⁵Department of Neurology, Washington University, St. Louis, MO, USA, ⁶Washington University Medicine Knight Alzheimer Disease Research Center, St. Louis, MO, USA, ⁷Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, CA, USA, ⁸Stanford Alzheimer's Disease Research Center, Stanford, CA, USA

BACKGROUND

- **CLARiTI's Vision: Accurate individualized biologic diagnosis and staging of the multiple intersecting neurodegenerative causes of cognitive impairment.**
- CLARiTI aims to harmonize data collection and imaging protocols and address the scientific and clinical challenges associated with mixed pathology causes of cognitive impairment.
- A scalable operational framework was developed to meet regulatory, operational, and contractual requirements across diverse sites.
- Collaboration among the following entities established best practices to streamline CLARiTI site activations and ensure compliance under the Investigational New Drug (IND) requirements:
 - ADRC Consortium
 - National Alzheimer's Coordinating Center (NACC)
 - Standardized Centralized Alzheimer's & Related Dementias Neuroimaging (SCAN)
 - National Centralized Repository for Alzheimer's Disease & Related Dementias (NCRAD)

OBJECTIVES

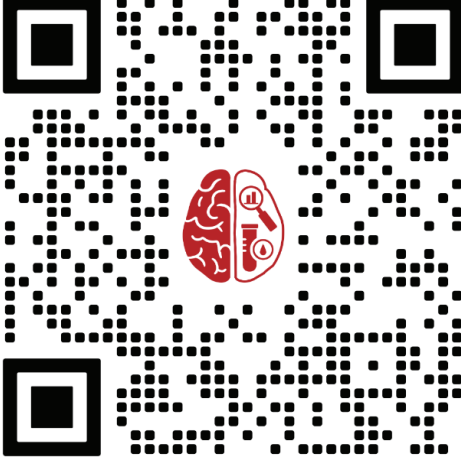
- **Develop a harmonized, scalable infrastructure** to support multi-site ATN imaging and biofluid collection across the national ADRC network.
- **Standardize regulatory and operational processes** to reduce site-level variability and accelerate study activation.
- **Evaluate site readiness, activation timelines,** and operational barriers to inform future multi-site biomarker studies.
- **Establish a platform capable of integrating emerging biomarkers** and supporting future ADRC research initiatives.

METHODS

Site Needs Assessment:

- Detailed surveys evaluated each site's needs to adapt start-up procedures to local infrastructures.

Site Engagement & Communication:

- Regular electronic newsletters (CLARiTI Connect)
- Webinars
- Ongoing communications with an assigned project coordinator for each site
- Centralized study website, scan here: 

Standardized Tools & Resources:

- Site readiness checklist
- Progress dashboard (**Figure 2**)
- Custom CLARiTI contact directory
- Comprehensive study handbook

These tools enhanced transparency and alignment across participating sites. They also streamlined expectations, timelines, and progress tracking to capitalize on efforts to reduce ambiguity and strengthen accountability.

Start-Up Process:

- Each site completed a kickoff meeting with the Sponsor team and the study's Principal Investigator prior to initiating start-up activities.
- Sites completed a remote site initiation visit to confirm regulatory compliance prior to activation.
- Completion of multiple operational and regulatory dependencies were required prior to issuance of the CLARiTI Site Activation Notice by the CLARiTI Admin Team (**Figure 3**).

FIGURES & TABLES

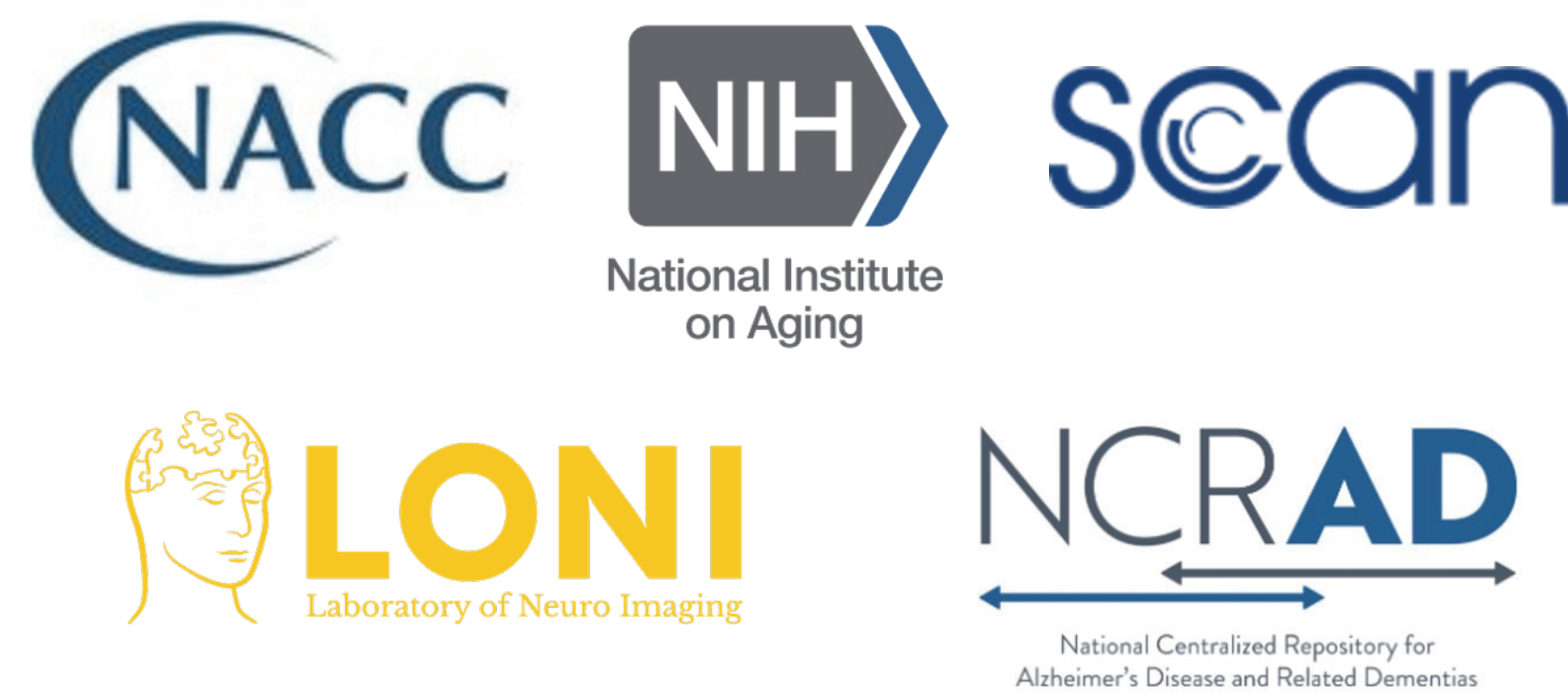


Figure 1: The ADRC Consortium for Clarity in ADRC Research Through Imaging (CLARiTI) is a nationwide initiative, involving 35 NIA-funded Alzheimer's Disease Research Centers (ADRCs).

Figure 1. States With NIA-Funded ADRCs

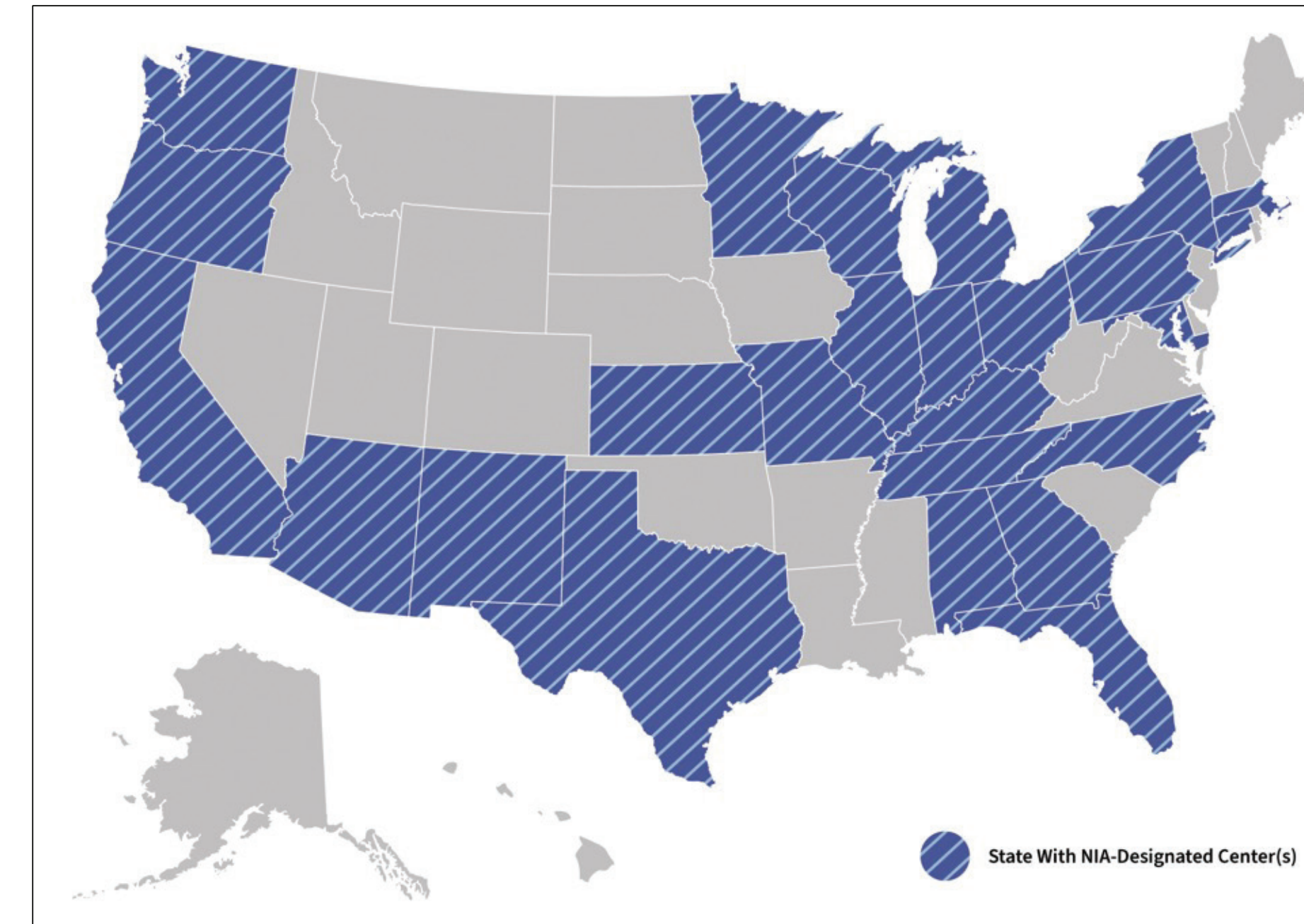


Figure 2. CLARiTI Study Start-Up Progress Dashboard

ADRC Affiliation	Site Kickoff Meeting with CLARiTI	CLARiTI Study Coordinator Designated at Local Site	CLARiTI Outreach Specialist Designated at Local Site	WCG Approval	Site SCAN Recertification for CLARiTI	Radiotracers Selected and Onboarding	Regulatory Documents Completed	Site Initiation Visit (SIV) by ULVSC Central Monitoring Service (CMS)	Required CLARiTI Trainings	NCRAD ADRFB Protocol Training	Access Core Recruitment Strategy Meeting	NACC Subaward Executed	Site Activation Notice Sent
Wisconsin ADRC	Complete	Complete	Complete	Complete	Complete	Complete	Complete	Complete	Complete	Complete	Complete	Complete	Complete

Figure 3. CLARiTI Site Activation Dependencies

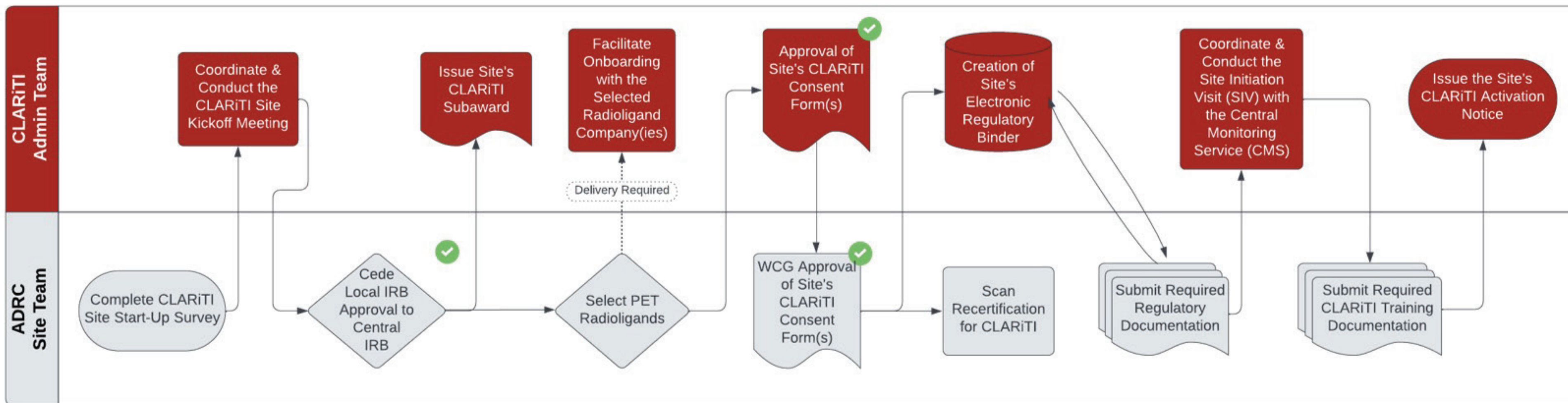


Figure 4. CLARiTI Site Start-Up Duration

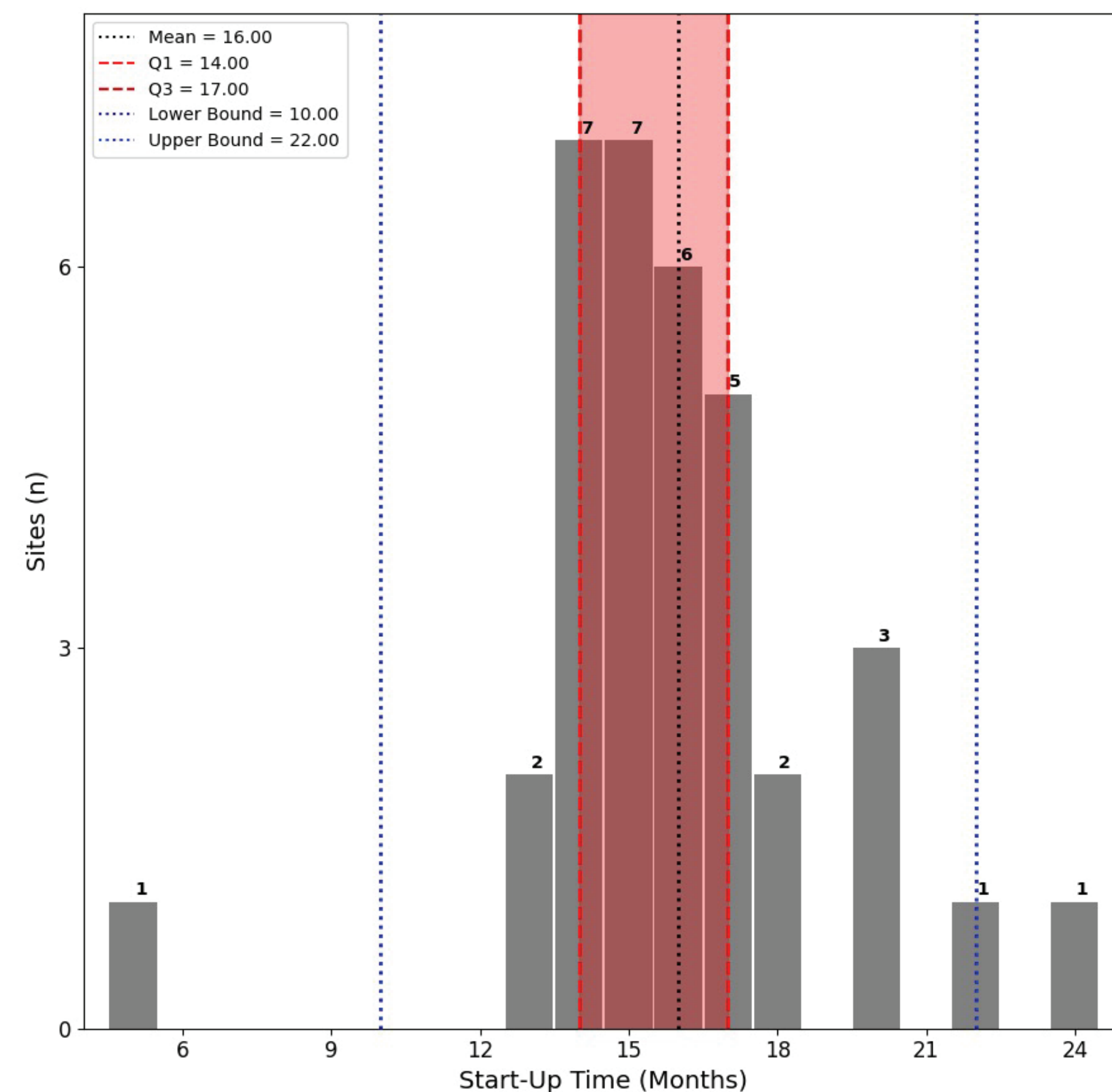


Figure 4: Start-up duration was defined as time from Site Kickoff Meeting (formal engagement with CLARiTI Admin Team) to receipt of Site Activation Notice.

Figure 5. CLARiTI Radioligand Selection Frequency

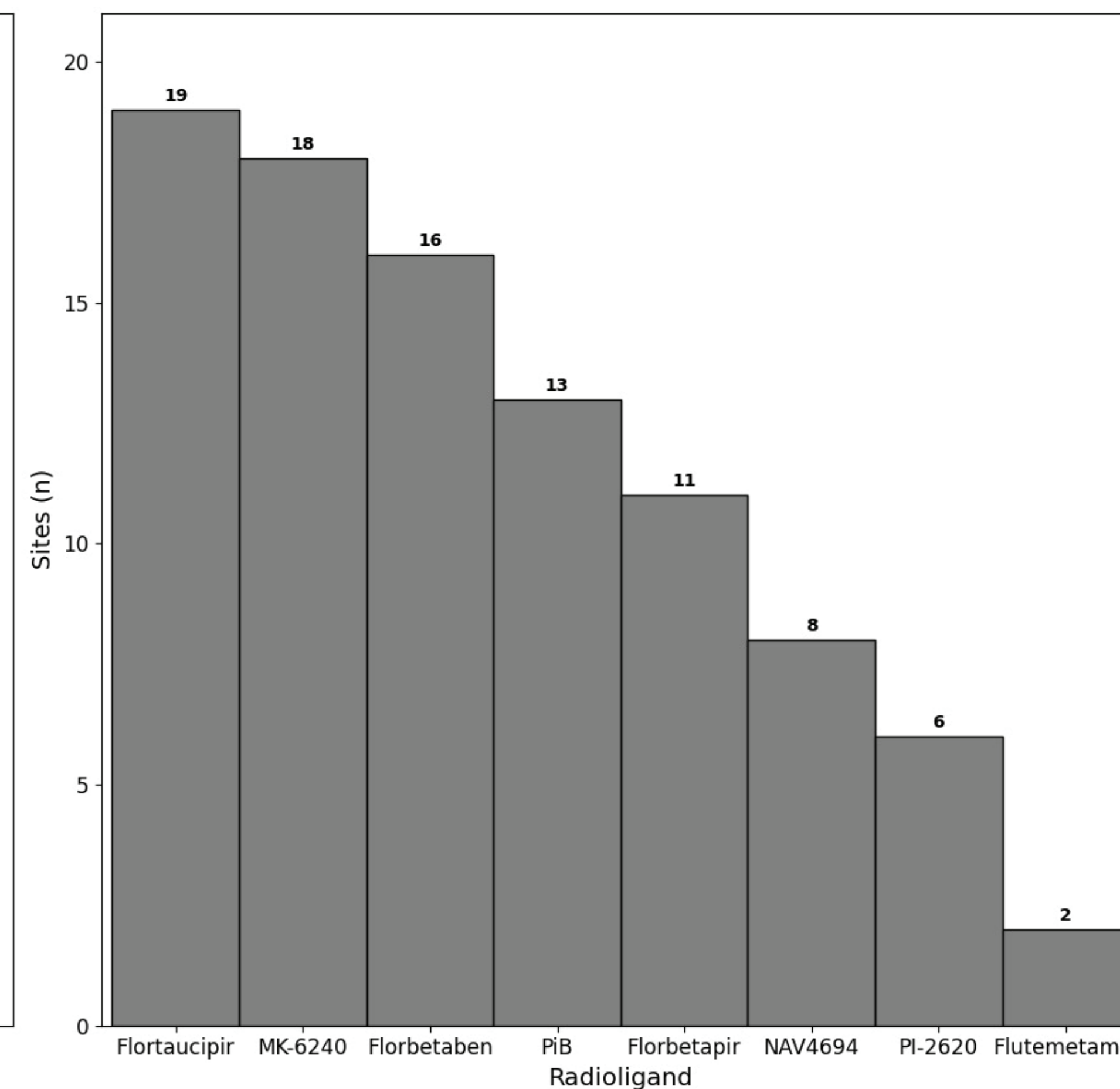


Figure 5: The 35 participating ADRCs were able to select multiple amyloid and tau PET radioligands, with individual centers choosing between two and six radioligands for use throughout the study.

RESULTS

Activation & Enrollment:

- Following funding in September 2023, each of the 35 participating ADRC sites were activated.
- **700 participants** have been enrolled as of April 2026.

Start-Up Timelines (**Figure 4**):

- Average start-up duration from kickoff to activation: **16 months**
- Range: **5-24 months**

Radioligand Selection Varied Across Sites:

- Site-specific radioligand selections for CLARiTI amyloid and tau PET imaging were collected prior to issuance of the CLARiTI Site Activation Notice (**Figure 5**).
- Variability in radioligand selection across centers was influenced by several factors, including continued use of tracers employed in other studies at the site, the site's ability to self-manufacture doses, proximity of a radioligand pharmacy within feasible ground transportation distance, and delivery day and time availability.

Operational Insights:

- Comprehensive training and standardized documentation were prioritized to harmonize site-specific practices and ensure alignment with study standards.
- Barriers included sequencing dependencies, extensive monitoring requirements, and staffing constraints.
- Centralized oversight and collaborative problem-solving supported timely activations.

CONCLUSIONS

- The CLARiTI start-up phase illustrates the ability to both leverage pre-existing infrastructure across individual ADRCs and create new infrastructure to support FDA-regulated, protocol-driven, multi-site imaging and biofluid collection to address scientific questions related to Alzheimer's disease and related disorders.
- This scalable operational platform provides a foundation for the **rapid integration of novel biomarkers** and future multi-site studies within the national ADRC program.

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 - National Institute on Aging (NIA)
 - National Alzheimer's Coordinating Center (NACC)
 - Standardized Centralized Alzheimer's & Related Dementias Neuroimaging (SCAN)
 - Laboratory of Neuro Imaging (LONI)
 - National Centralized Repository for Alzheimer's Disease & Related Dementias (NCRAD)