

SCAN Amyloid Legacy Project

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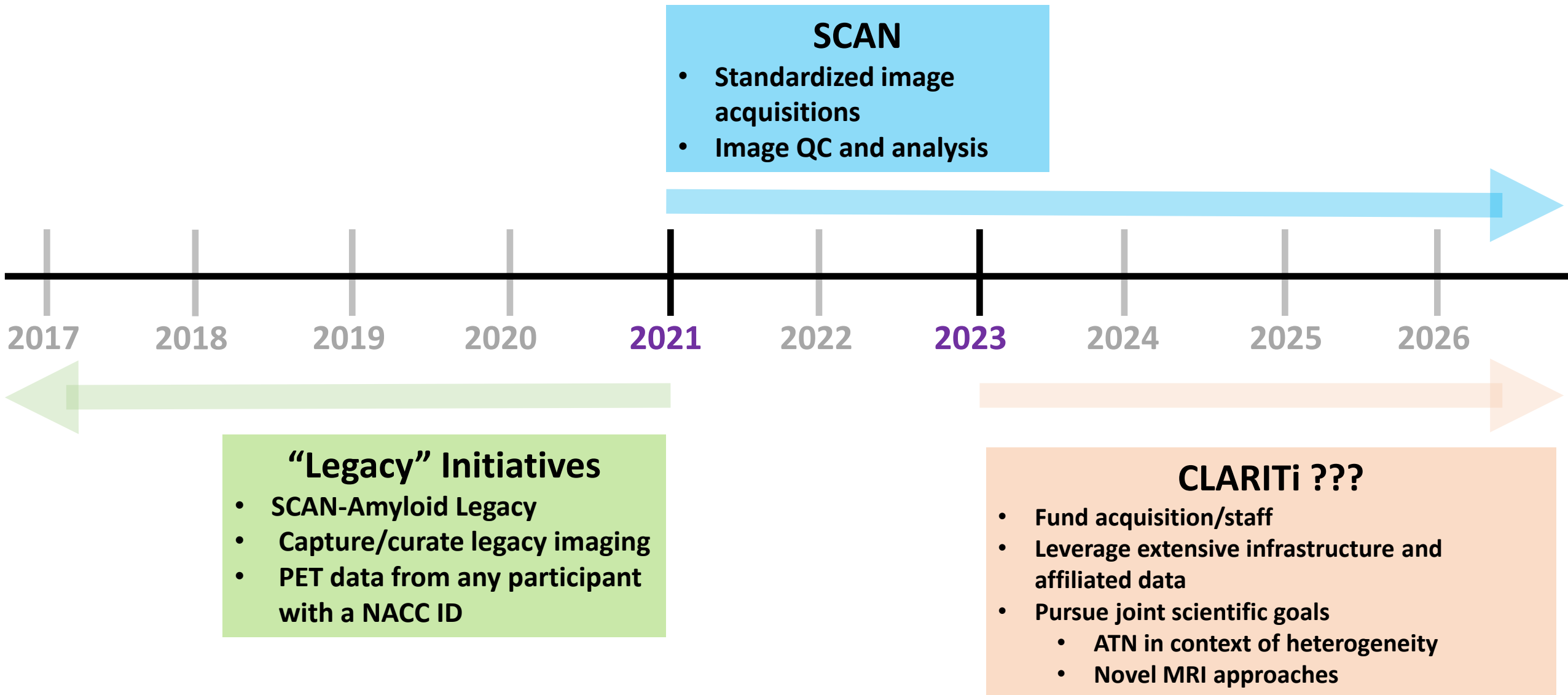
Karen Crawford

ADSP-HC

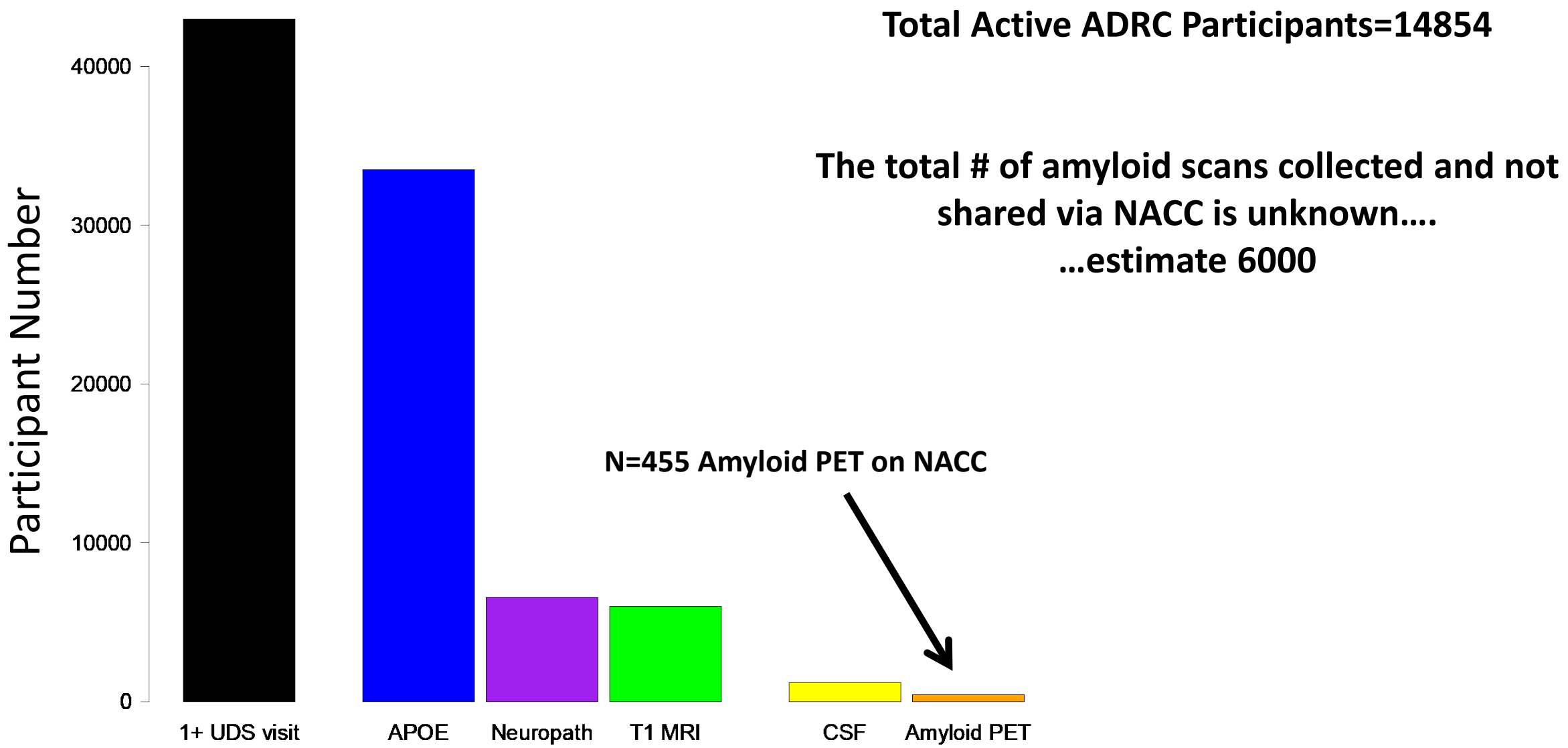
Tim Hohman

Duygu Tosun

Collaborative Program-Wide ADRC ATN Imaging



Amyloid PET data shared via NACC



Site Acknowledgement

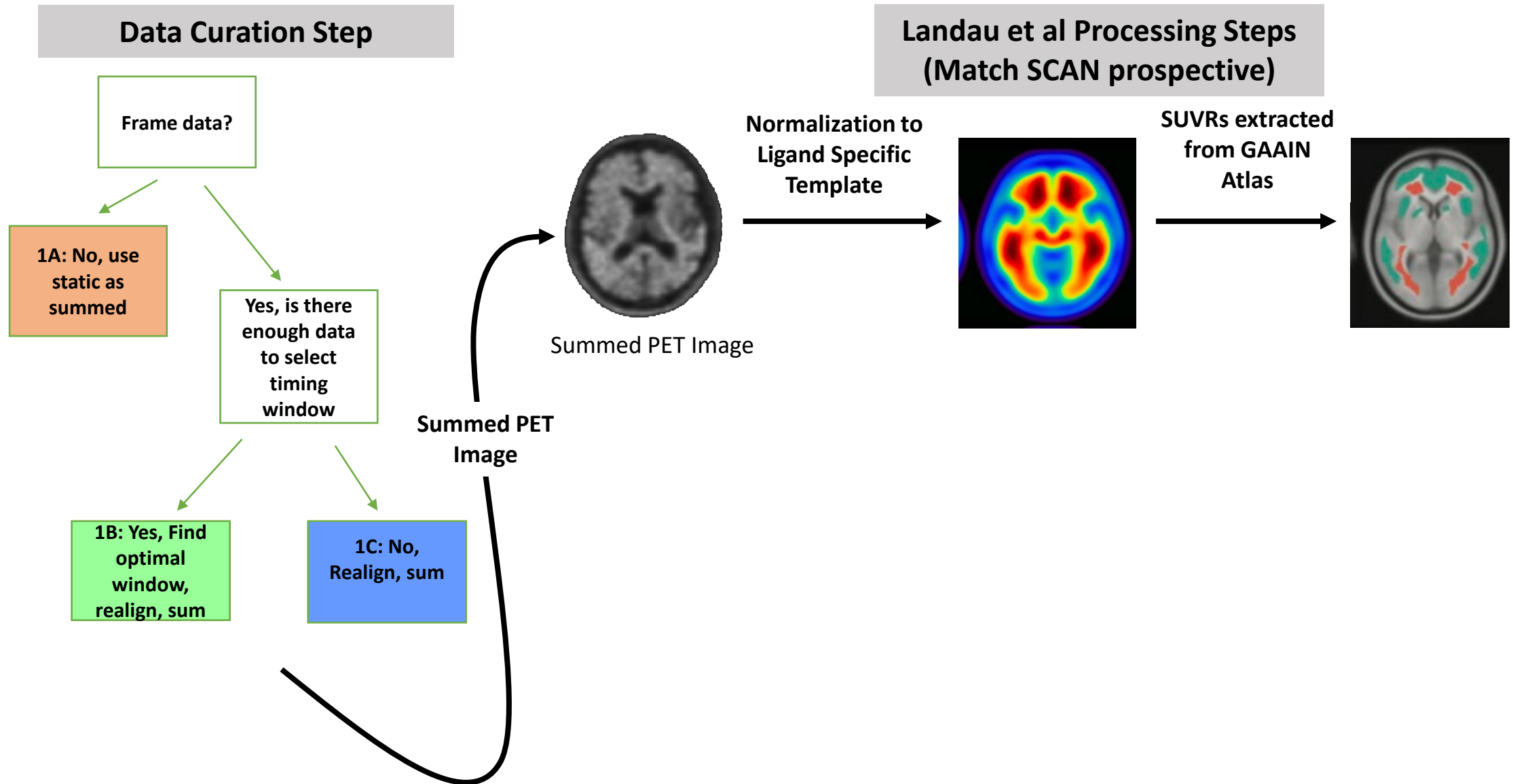
SCAN-AL Upload Completed

ADRC Site	
Cleveland	Frank DiFilippo, Sally Durgerian
Kansas	Rebecca Lepping
University of Florida	David Vaillancourt, Wei-en Wang
UC Davis	Charlie DeCarli, Audrey Fan, Sean McDougall
Stanford	Beth Mormino, Gabriel Kennedy
Wisconsin	Sterling Johnson, Anjali Sridharan, Bill Bevis

SCAN-AL Upload In Progress

ADRC Site	
Arizona	Eric Reiman, Yi Su, Don Saner
NYU	Henry Rusinek, Ricardo Osorio

MRI-Free Pipeline Summary (Landau 2022 Alz & Dementia)



Data Summary

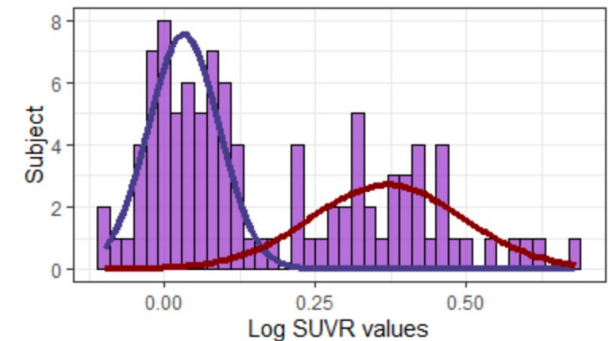
ADRC Processing Complete	
Amyloid Scans	728 (519 FBP, 209 FBB)
Sites	5
Datasets*	6
Pending	
Amyloid Scans	156 (PIB)
Tau Scans	103 (MK6240)
Sites	1
Datasets	2

Demographics (N=728)

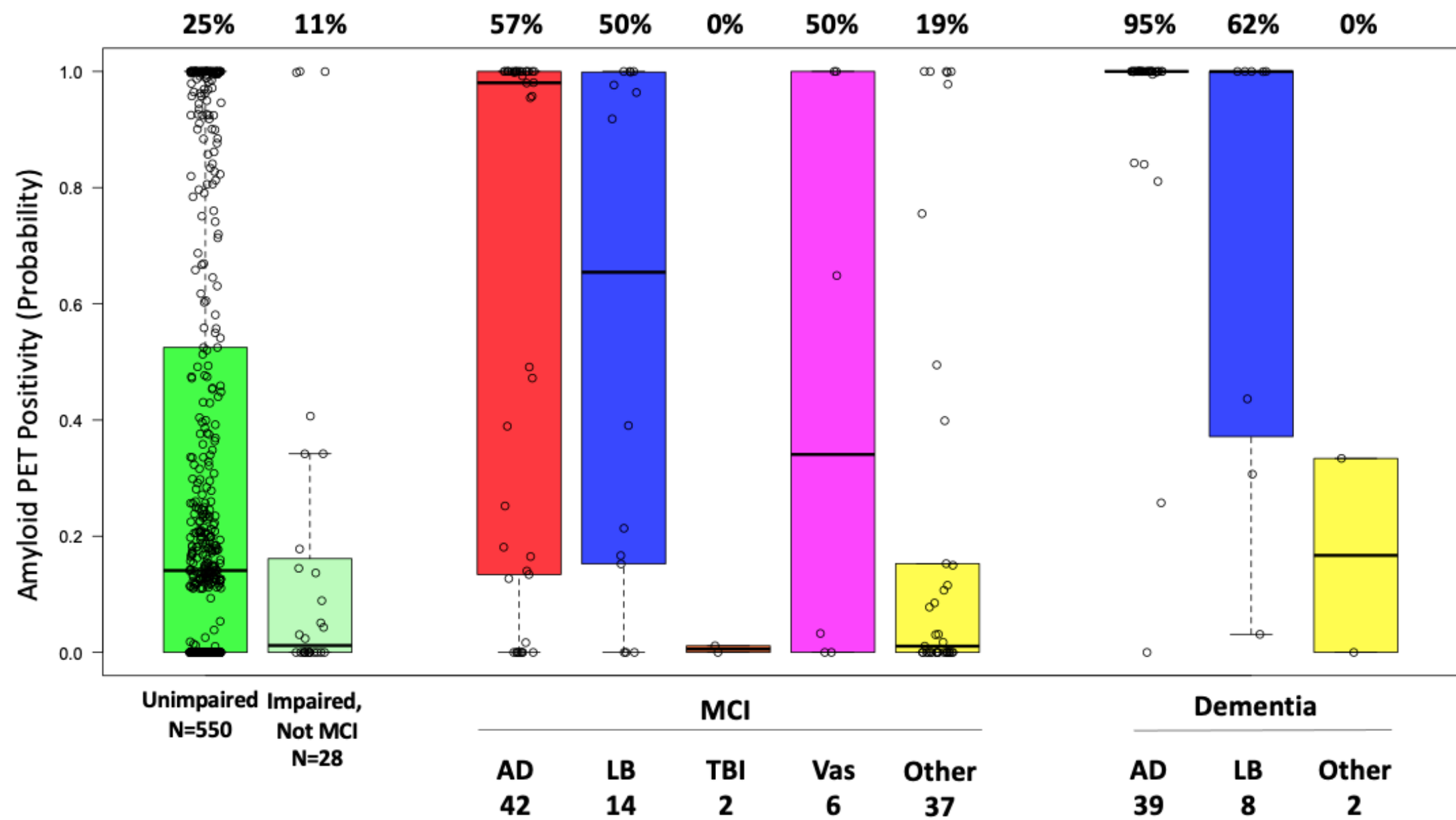
	Unimpaired	Impaired, Not-MCI	MCI	Dementia
N	550	28	101	49
Age	72 (6.5) Range: 36 to 96	72 (9.0) Range: 45 to 85	74 (8.7) Range: 45 to 99	70 (10.0) Range: 44 to 90
Female	66%	82%	43%	47%
Primary Etiology	NA	4 AD 24 Other	42 AD 37 Other 14 LBD 2 TBI 6 VBI	39 AD 8 LBD 2 Other

Challenges and Solutions

- Reconstruction parameters
 - Differ from SCAN prospective
 - However, largely consistent within dataset
 - Define QC/confidence measure based on consistency within site
 - Timing Acquisition
 - Start time varies (some scans start at 50 minutes, some at 70 minutes)
 - Inconsistent with research protocols, but consistent with FDA labels
 - Florbetaben
 - Research protocol: 90-110 minutes post-injection
 - FDA label: start between 45-130 minutes
 - 30 minute shift can translate to a difference 0.10 SUVR for Florbetaben
 - Use dynamic datasets to estimate shift and adjust values
- All recon/acquisition parameters will be shared for future harmonization work
- For data merging and validation, Gaussian Mixture Modeling approach
- Confirmed 2-cluster solution
 - Data driven assignment (probabilities) of being Amyloid+

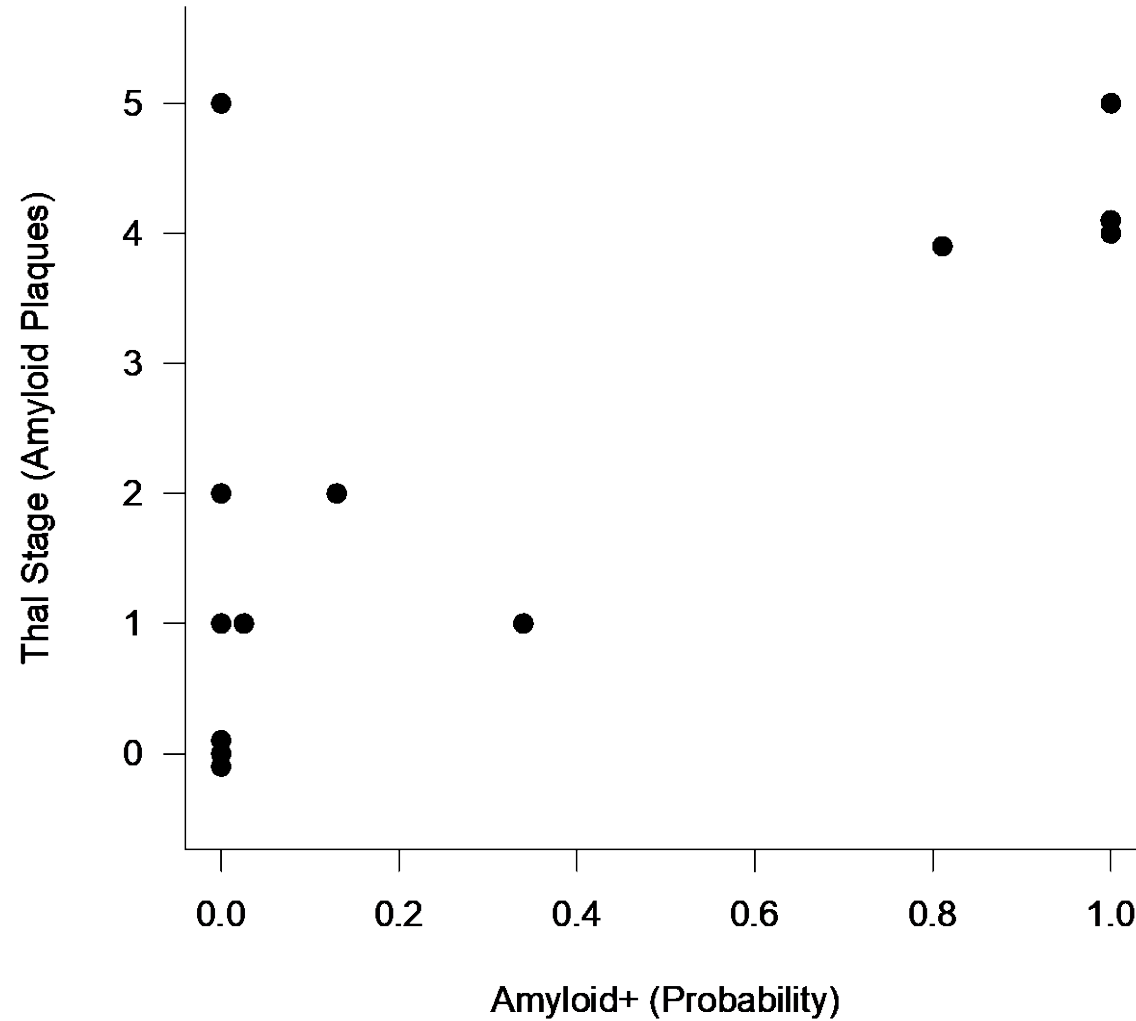


Amyloid PET Positivity by Clinical Diagnosis

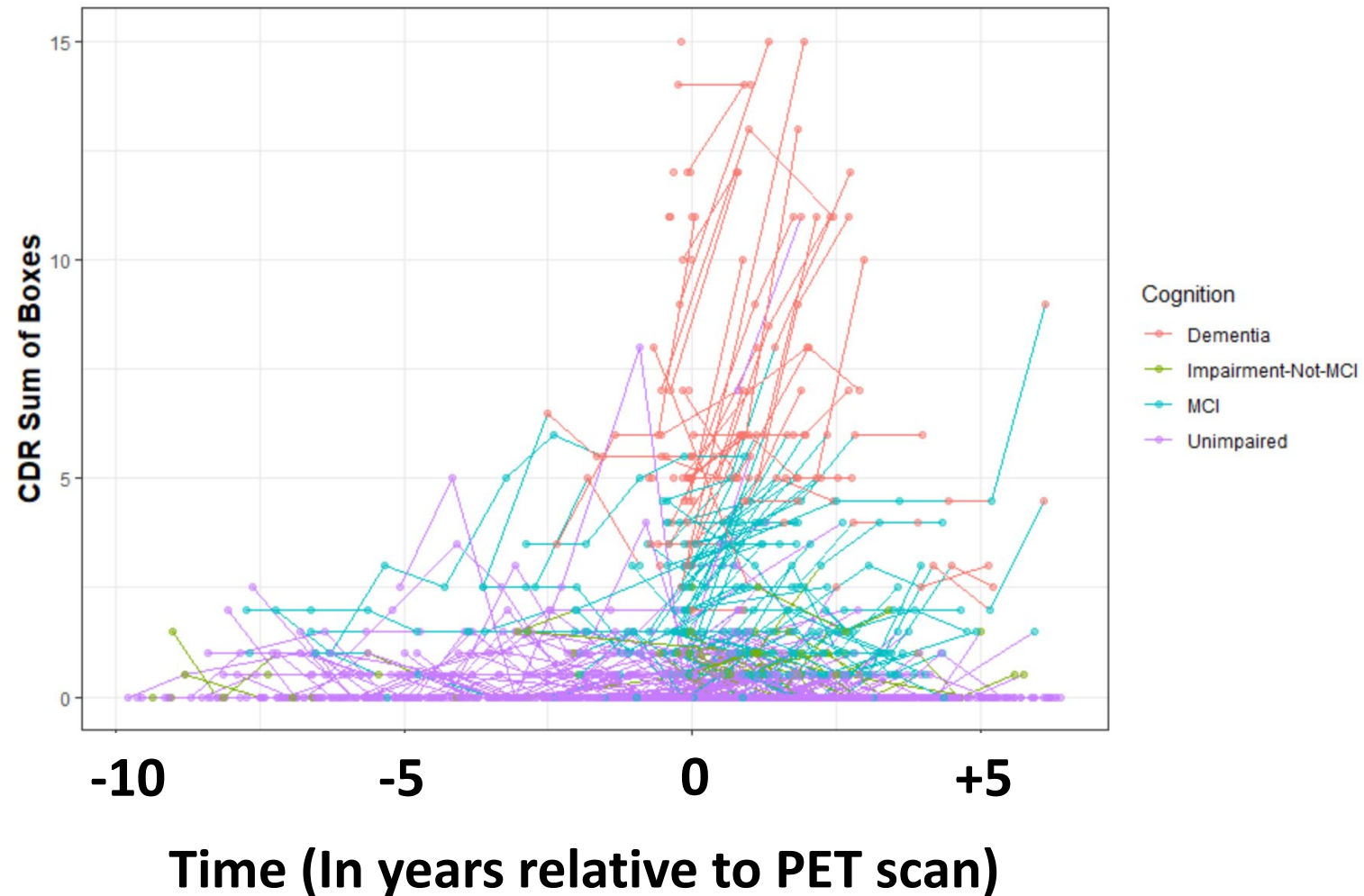


Amyloid Probabilities align with Thal Staging

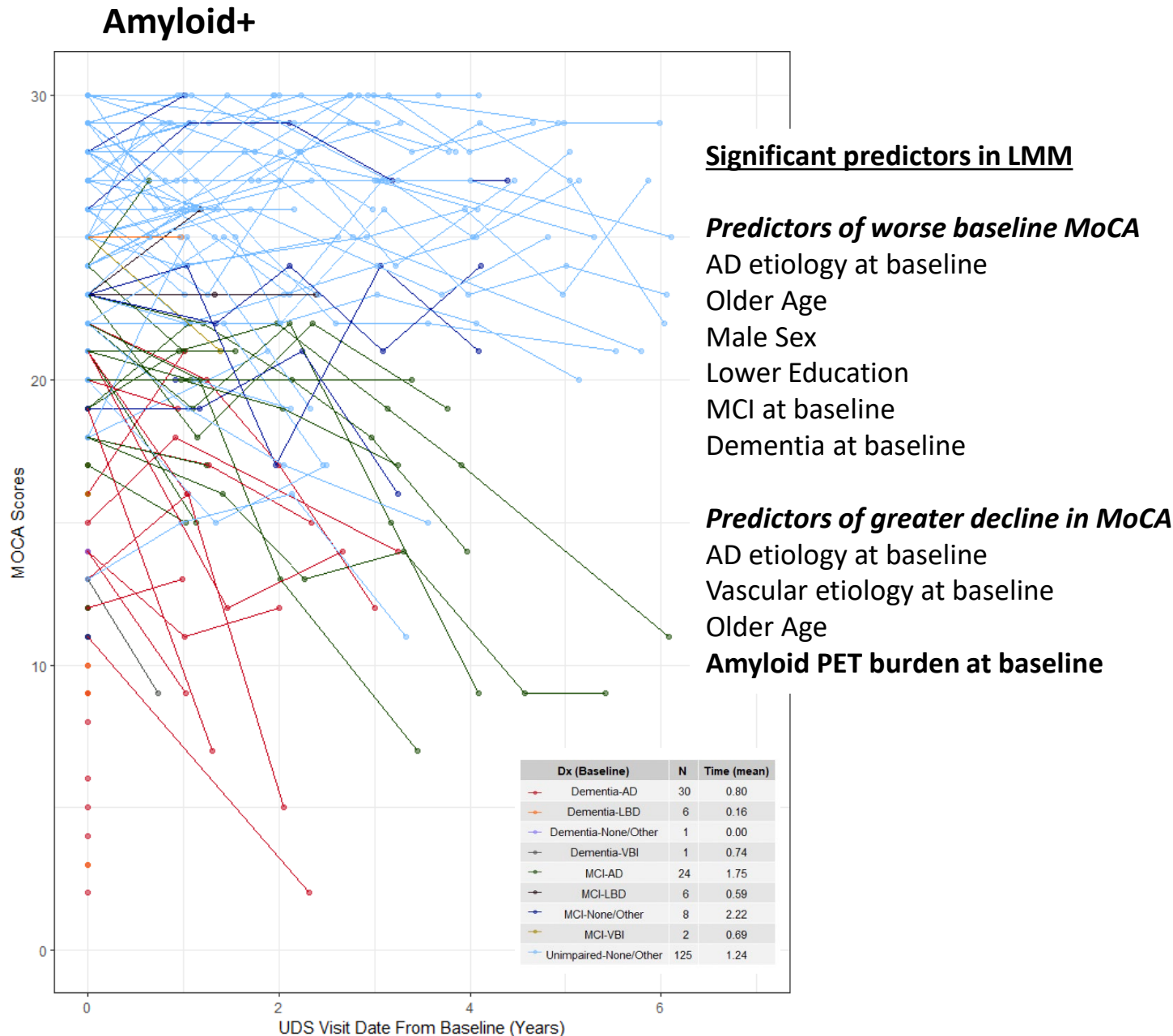
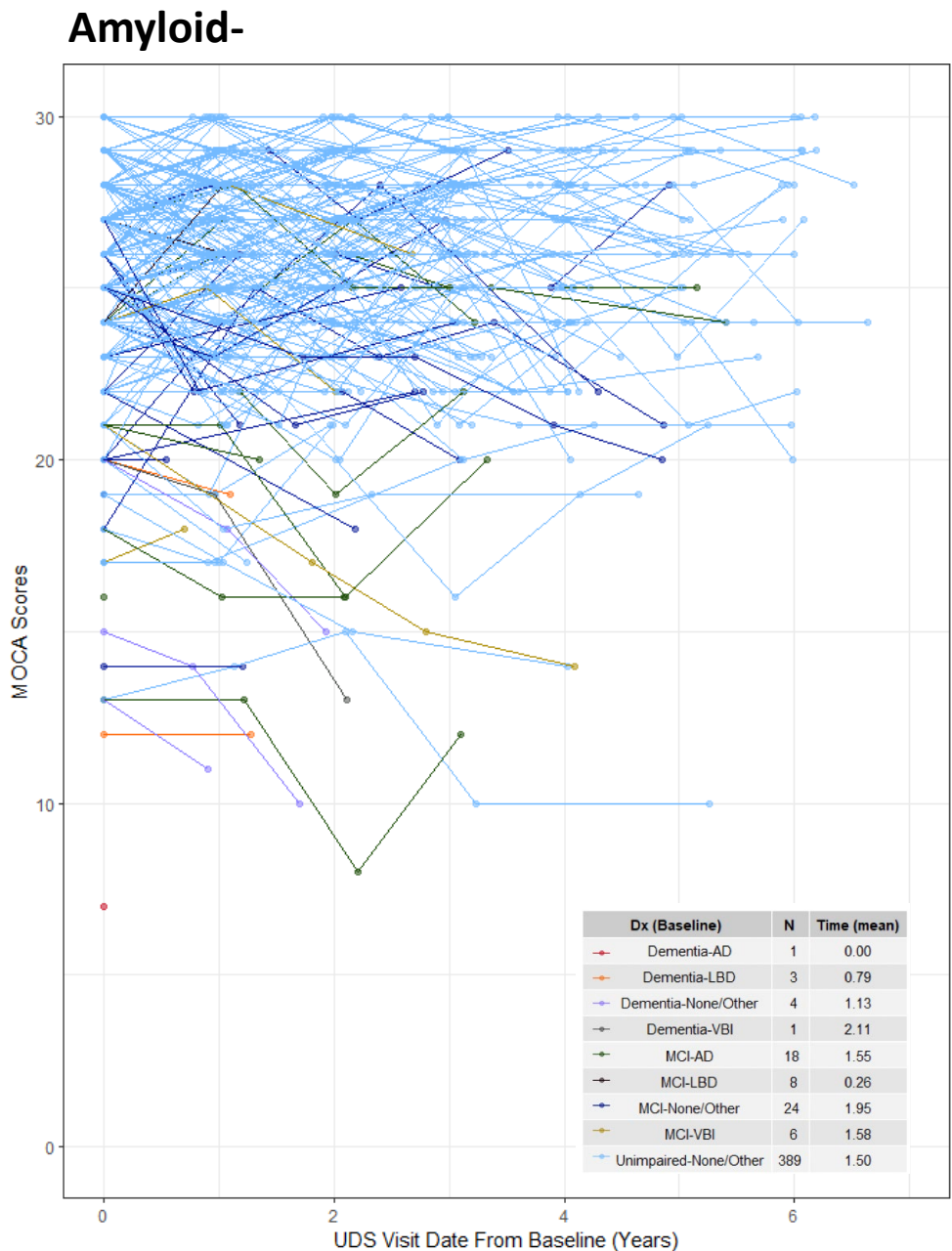
N=13, 4 sites



Retrospective and Prospective Clinical Data (UDS)



Legacy Amyloid PET burden predicts longitudinal decline in MoCA

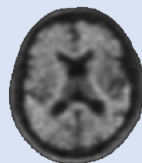


SCAN-Amyloid Legacy Data

Acquisitions & Recons Not Standardized



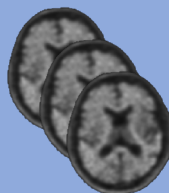
Raw Dicom



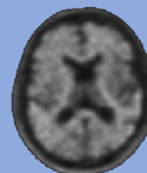
wSummed

SCAN PET Data

Acquisitions & Recons standardized
QCed, Uniform smoothing



Raw Qced Dicom



wSummed



SCAN-Amyloid Legacy Data

Extracted Data

Meta-Data.csv

Dose
Ligand
Recon Parameters
Acquisition Timing
QC metric

Raw SUVRs.csv
Adjusted_SUVRs.csv
GMM.csv

SCAN PET Data

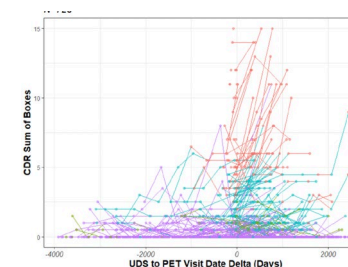
Extracted Data

Meta-Data.csv
Ligand

SUVRs.csv

**Investigators
Download!**

UDS



**Email Blast
Remaining Sites**

**Data
Release 1
N=884**

**Data
Release 2
N=884+???**

**May
'22**

**July
'22**

**Sept
'22**

**Nov
'22**

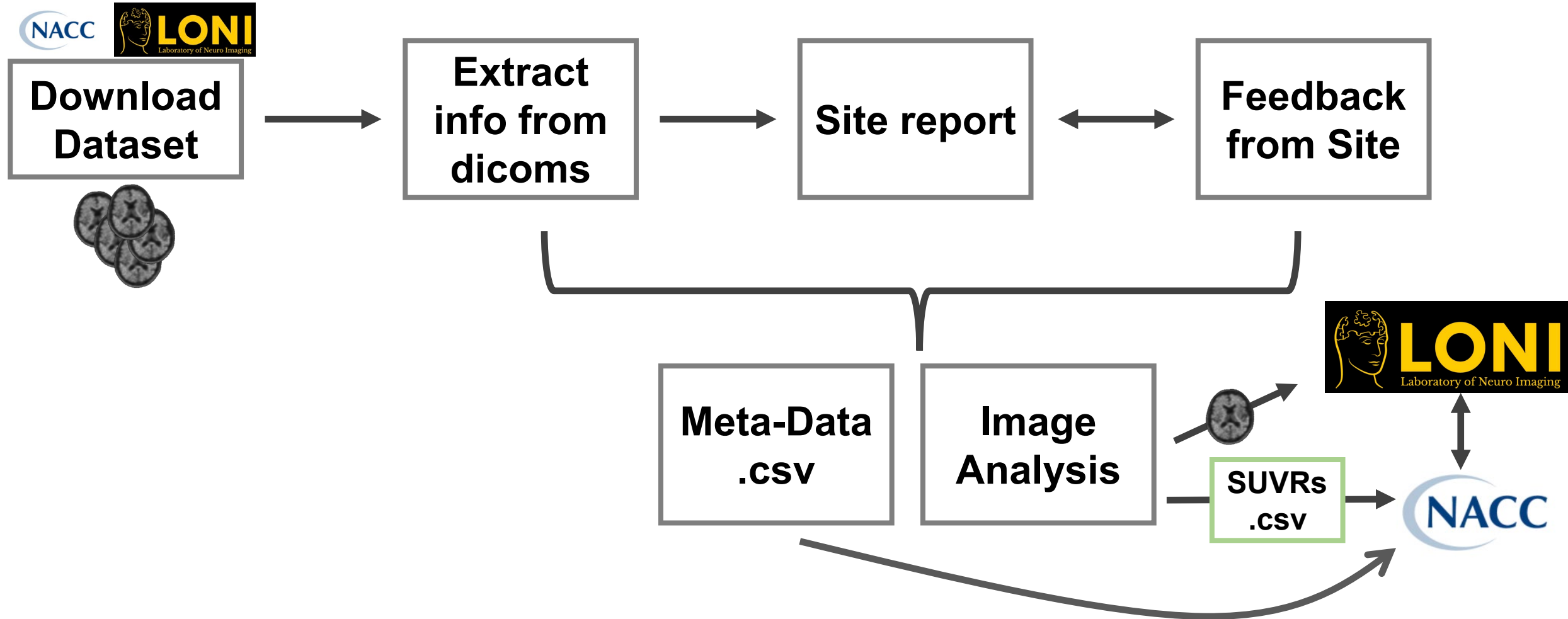
**Jan
'23**

Questions: bmormino@stanford.edu

EXTRA

Stage 1: Connect with Site

- Ability/Willingness
- Identify Barriers
 - Consent/Sharing
 - Resources
- Make site specific plan



Summary of acquisition and re parameters

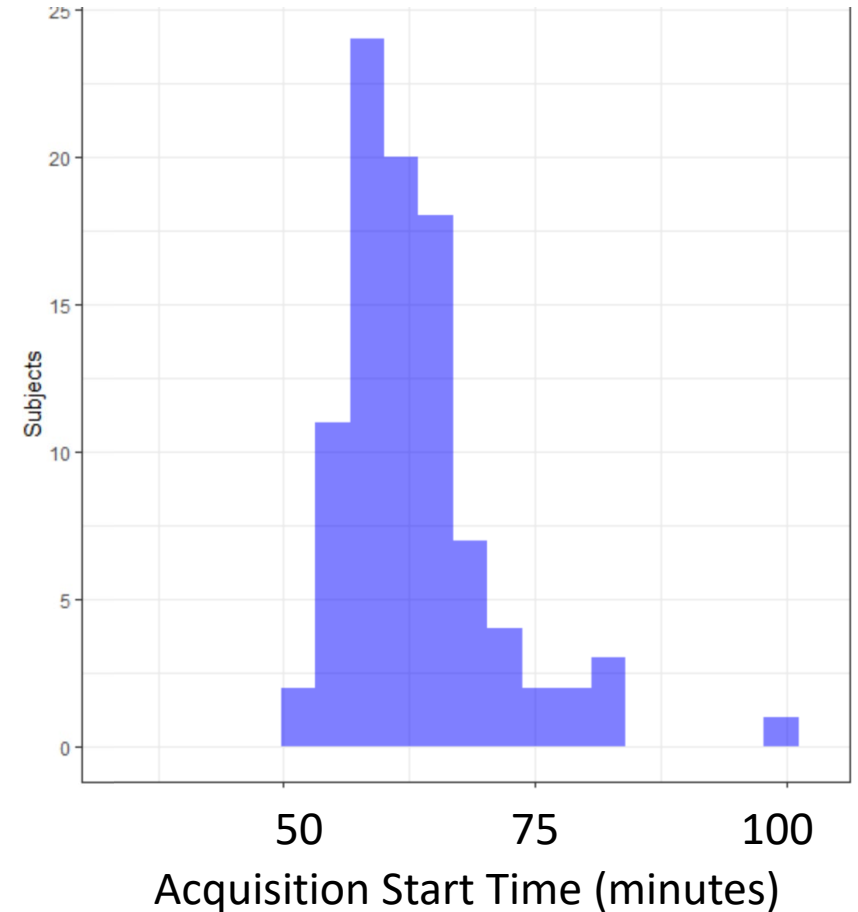
	Suggested Target Dose ± 10%		Minimum injectable dose		Acquisition start- stop time post- injection (min)
Tracer	mCi	MBq	mCi	MBq	
Amyloid Tracers					
PIB	15	555	8	300	40–60 or 50–70, 40–70
Florbetapir	10	370	6	225	50–70
Florbetaben	8	295	5	185	90–110
NAV4694	8.1	300	6.5	240	40–70, 50–70

	Datasets					
	1	2	3a	3b	4	5
Scanner	GE Signa	GE Discovery ST	Siemens 1080	Siemens 1080	Siemens Biograph mCT	GE Discovery 690
Acquisition Timing	90-110 minutes (Dynamic 5 minute frames)	Variable start time 10min	Variable start time 10 minutes	Variable start time 20 minutes	50-70 minutes 20 minutes	10-20 minutes duration
Recon Method	VPFXS	3D FORE IR	OSEM2D	OSEM2D	OSEM3D	VPHD
Iterations	3	4	4	4	4	3
Subsets	28	16	24	24	24	32

Acquisition/Recon parameters
Not SCAN Compliant

....Deeper dive into variable acquisition start times

	FDA Label	SCAN compliance
Florbetapir Amyvid	10-minute PET images starting 30 to 50 minutes	50–70
Florbetaben Neuraceq	15 to 20-minute PET images starting 45 to 130 minutes	90–110



15-20 min FBB
(start 50-80)

Adjust
→

20 min FBB
90-110
Scale

FBB SUVR by Time Analysis

Stanford ADRC FBB Data
N=109 (44 A+)

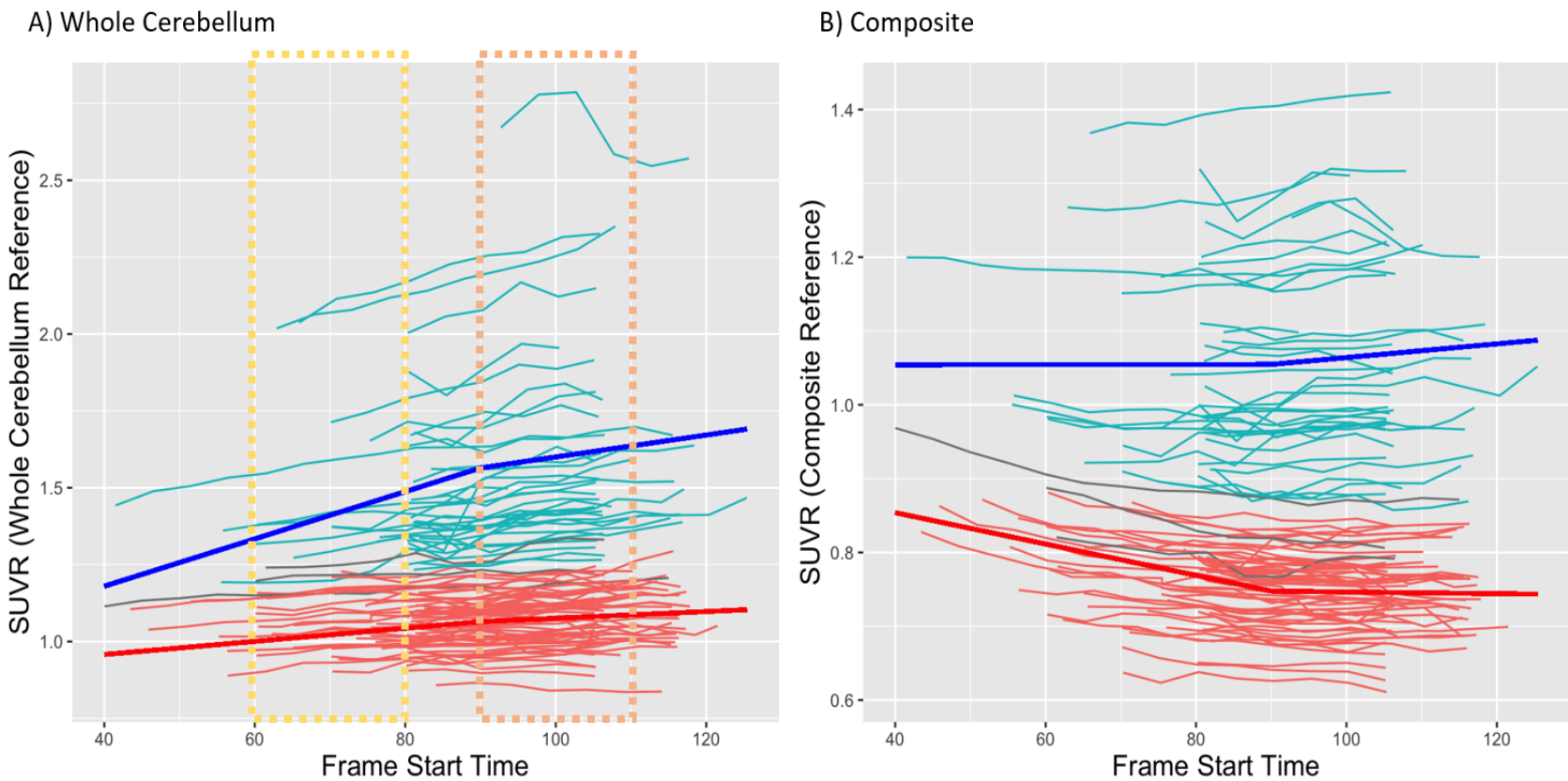
Florbetaben

FDA Label	SCAN
15 to 20-minute PET images starting 45 to 130 minutes	90-110

SUVR of 1.50 at
60-80

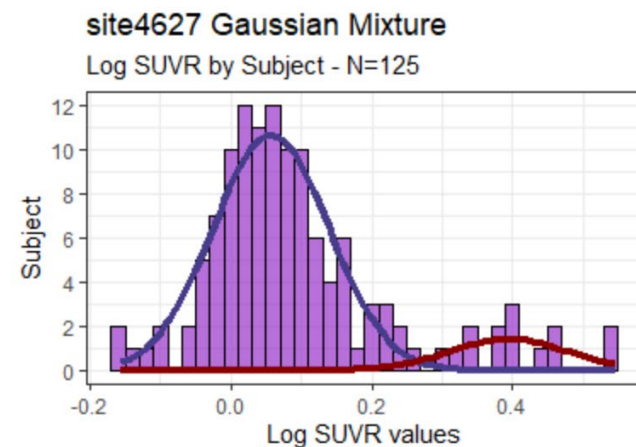
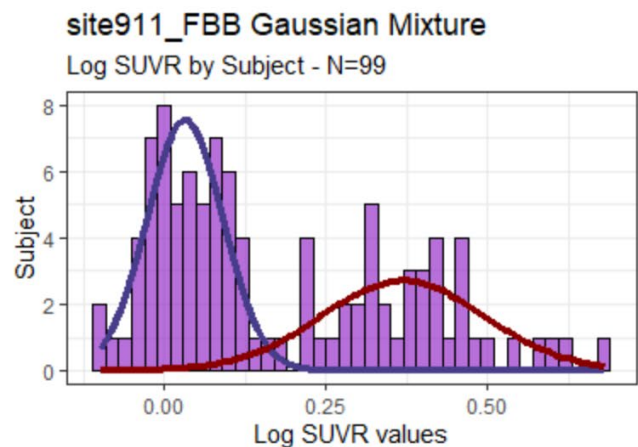
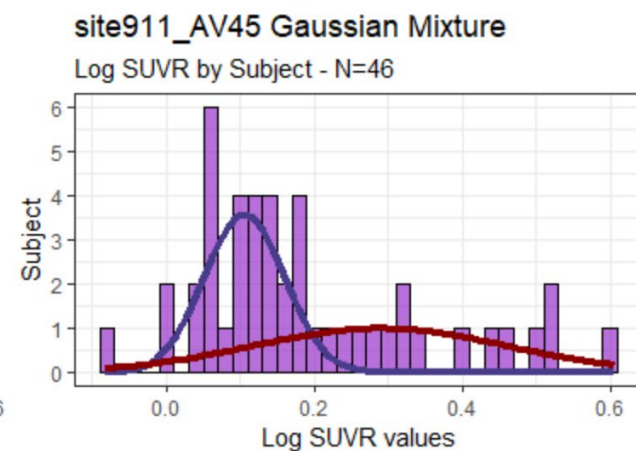
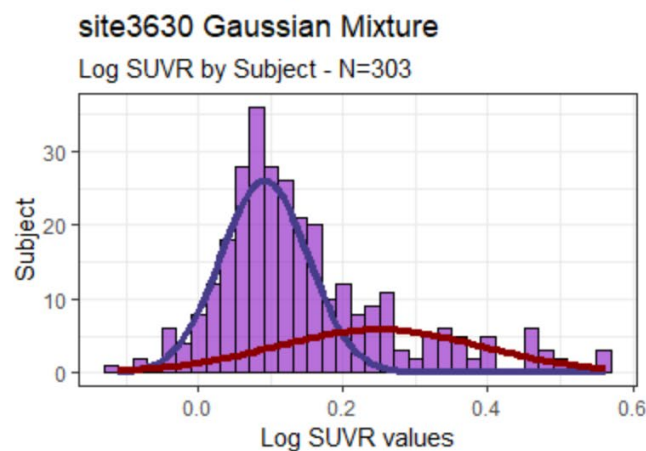
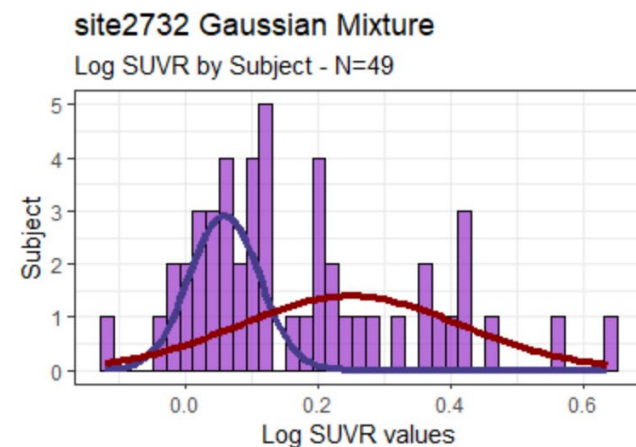
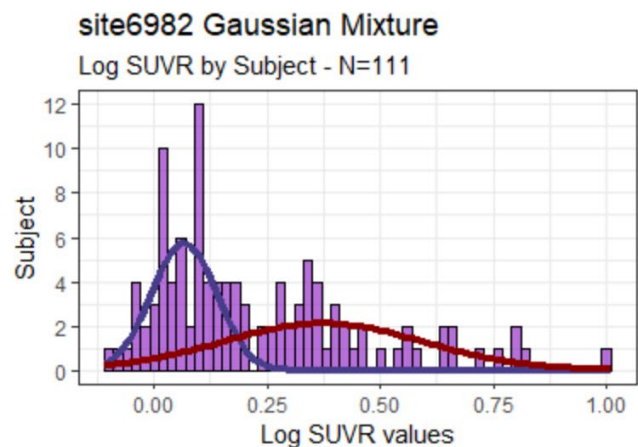


Adjust SUVR to
90-110 Scale
1.6104



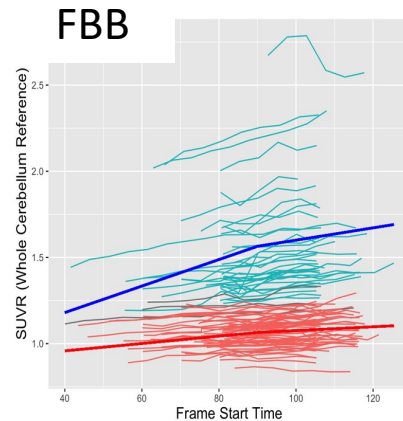
C)	Estimated Slope (SUVR)	
Group by Phase	Whole Cerebellum	Composite
A- < 90	0.001188864 ***	-0.001179469 ***
A+ < 90	0.004271373 ***	0.000005117
A- > 90	0.0007747577 ***	-0.00008287315
A+ >90	0.002524781 ***	0.0006574173 ***
	Estimated Slope (Z-Score)	
Group by Phase	Whole Cerebellum	Composite
A- < 90	0.01499543 ***	-0.02269694 ***
A+ < 90	0.05387586 ***	0.00009847
A- > 90	0.009772206 ***	-0.001594758
A+ >90	0.03184567 ***	0.01265091 ***

Site Specific Gaussian Mixture Models



Next Steps

- Validate FBB adjustment equation (Columbia)
- Timing adjustment equations for FBP



- Test effect of recon parameters (within Stanford)

	Stanford-Legacy	Stanford-SCAN
Scanner	GE Signa	GE Signa
Acquisition Timing	90-110 minutes (Dynamic 5 minute frames)	90-110 minutes (Dynamic 5 minute frames)
Recon Method	VPFXS	VPHD
Iterations	3	4
Subsets	28	16
Slice Thickness	2.78	2.78
Corrections	On	On

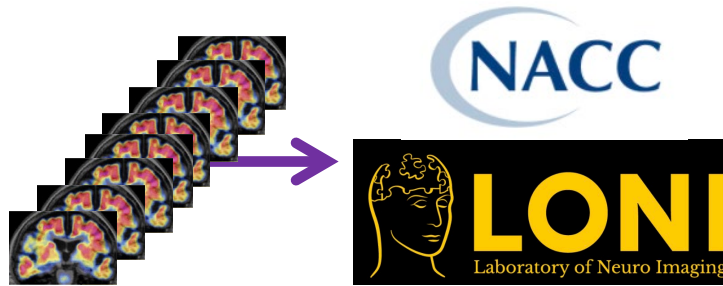
- Request data across all ADRC sites
- MRI-Free pipeline on non-ADRC sites
- Develop “confidence/quality” measure
 - Consistency within site (recon parameters, missing dicom info, etc)
 - Ex: 2/300 scans have inconsistent recon parameters within their site. Provide values in data release but flag those 2 cases?

Overall Flow with ADRC Sites

Stage 1: Site Meeting

- Ability/Willingness
- Identify Barriers
 - Consent/Sharing
 - Resources
- Make site specific plan

Stage 2: Sites Upload



Stage 3: Data Processing & Dissemination

- Pipelines similar to SCAN
- Images at LONI
- Extracted regional values and meta-data at NACC

Model output

MOCA LME

	Estimate	Std. Error	df	t value	P value
(Intercept)	23.011	1.396	741.4	16.485	<0.001
Date_From_Baseline	1.665	0.463	971.9	3.599	<0.001
Closest_etVBI	-0.362	0.967	743.0	-0.374	0.708
Closest_etLBD	0.704	0.789	789.2	0.892	0.373
Closest_etAD	-1.678	0.597	730.3	-2.809	0.005
Age_At_Scan	-0.068	0.016	745.5	-4.322	<0.001
SEX	0.491	0.233	738.6	2.108	0.035
EDUC	0.448	0.037	719.6	12.107	<0.001
Closest_cogMCI	-2.484	0.486	726.2	-5.111	<0.001
Closest_cogDementia	-10.937	0.668	756.9	-16.376	<0.001
GMM_Positivity_Uncertainty	-0.420	0.292	739.4	-1.442	0.15
Date_From_Baseline:Closest_etVBI	-1.253	0.390	957.2	-3.211	0.001
Date_From_Baseline:Closest_etLBD	1.215	0.647	1042.9	1.878	0.061
Date_From_Baseline:Closest_etAD	-1.074	0.190	956.0	-5.665	<0.001
Date_From_Baseline:Age_At_Scan	-0.024	0.006	975.5	-4.338	<0.001
Date_From_Baseline:SEX	0.014	0.071	976.8	0.191	0.849
Date_From_Baseline:EDUC	0.007	0.010	943.3	0.665	0.506
Date_From_Baseline:Closest_cogMCI	0.048	0.146	943.4	0.330	0.742
Date_From_Baseline:Closest_cogDementia	-0.654	0.338	980.8	-1.934	0.053
Date_From_Baseline:GMM_Positivity_Uncertainty	-0.349	0.091	981.7	-3.844	<0.001

	Non-Hispanic	Hispanic
White	544 (75%)	116 (15.9%)
Black or African American	43 (5.9%)	0
Asian	14	0
American Indian or Alaska Native	3	0
Other	2	4
Unknown	2	0