SUPPLEMENTAL METHODS

PET Acquisition and Processing

1Florida ADRC PET scanners (Philip Gemini or Siemens Biograph) and imaging protocols have been approved by ANDI or SCAN. All subjects underwent a 20-min PET scan starting at least 50-90 min after intravenous injection of radiotracers. Florebetaben (F-18 Neuraceq; 90% of scans) or Florebetapir (F-18 Amyvid; 10%) was used. PET scans were reconstructed using Ordered Subsets Expectation Maximization (OSEM) algorithm using 4 iterations and 16 subsets or comparable reconstruction. Acquired PET scan were reconstructed into a 128×128×90 (axial) matrix with voxel dimensions of 2×2×2 mm. Reconstruction was performed using manufacturer-supplied software and included corrections for attenuation, scatter, random coincidences and dead time. Images were smoothed with a 5 mm Gaussian filter. Following reconstruction, image sets were visually inspected. The amyloid PET scans were coregistered linearly with 12 degrees of freedom, onto subject's T1 weighted MPRAGE scan using FSL toolbox (fsl.fmrib.ox.ac.uk) (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). This registration process ensured that the PET image had the same accurate segmentation and parcellation as in the MRI. The segmented MRIs from the FreeSurfer pipeline and the co-registered PET images were used to extract the average intensity of individual ROIs, yielding the regional standardized uptake values (SUVs). Regional SUV ratios (SUVRs) were computed by dividing the regional SUVs by the SUV obtained from the cerebellar grey matter. A composite SUVR was calculated by the mean SUVR of the 5 cortical regions (frontal, temporal, parietal, anterior and posterior cingulate cortex regions, each region averaged from left and right hemispheres). SUVRs were converted to a Centiloids (CL) scale where "0" represents mean uptake in healthy young controls devoid of amyloid pathology and "100" represents the typical degree of cortical amyloid deposition observed in PET imaging in patients diagnosed with mild-moderate dementia due to Alzheimer's disease (Klunk et al., 2015). Aβ-PET scans were classified as either positive or negative by a trained reader following manufacturer interpretation protocols and blinded to clinical and demographic information. Based on internal development and data published across other studies, binary quantification based on CL was defined as CL<25 for negative Aβ-PET and CL >25 for positive Aβ-PET. We additionally classified each participant as Low Aβ-PET (CL<10), Intermediate Aβ-PET (CL 10-49), or High Aβ-PET (CL>49). Cutoffs were based on PET-to-autopsy data showing CL<10 reflected absence of any neuritic plaques at autopsy and CL>49 best confirmed both neuropathological AD and clinicopathological diagnosis of AD-related dementia [Amadoru et al. 2020]. In this cohort, there is >99% agreement between negative visual read and CL<10 and between positive visual read and CL>49, with greater ambiguity occurring in the CL 10-49 range (67% visual read negative). All Aβ-PET scans corresponded to the same study visit as the blood draw.

SUPPLEMENTAL RESULTS

	Overall	Hispanic/Latino White	Non-Hispanic/Latino White	Sig.
Medical History				
Heart Attack/Cardiac Arrest	3.8	5.3	2.7	.50
Atrial Fibrillation	3.0	0.9	5.5	.06
Angio/Endarterectomy/Stent	7.6	5.3	10.9	.14
Cardiac Bypass	3.0	3.5	2.7	>.99
Pacemaker/Defibrillator	0.4	0.0	0.9	.49
Congestive Heart Failure	4.3	4.4	3.6	>.99
Angina	11.1	11.4	10.9	>.99
Stroke	3.4	1.8	3.6	.44
Transient Ischemic Attack	5.2	5.3	5.6	>.99
Diabetes (T1 or T2)	23.4	27.4	17.3	.08
Hypertension	56.8	63.2	50.9	.08
Hypercholesterolemia	62.0	70.8	52.7	.006
Body Mass Index	27.6±5.3	28.0±4.8	27.4±5.8	.13
Vascular Burden Score	1 (1-3), 1.7±1.3	2 (1-3), 1.9 ±.03	1 (1-2), 1.6±1.3	.09

eTable 1: Descriptive characterization of cardiovascular medical history factors for the overall study cohort and stratified by ethnicity. A modified vascular burden score was calculated based on prior publications (DeCarli et al., 2019)**)** as the sum of 7 possible vascular risk factors or diagnoses: cardiac-arrhythmias (atrial fibrillation OR defibrillator), coronary artery disease (angina OR angioplasty/endarterectomy/stent OR cardiac bypass OR heart attack), congestive heart failure, cerebrovascular disease (stroke OR transient ischemic attack), hypertension, hypercholesterolemia, diabetes. All values are shown as percentages within the respective group except for body mass (mean±SD) and the vascular burden score (median and interquartile range and mean±SD). Statistically significant group differences were assessed using chi-square (Mann-Whitney U for body mass index and vascular burden score).

Cognitively Impaired Only			
	Plasma p-tau217 (ALZPath)		
Aβ-PET Result	**All**	**Non-Hispanic/Latino White**	**Hispanic/Latino White**
Visual Read (positive vs. negative)	0.91 (0.87-0.96)	0.93 (0.88-0.98)	0.93 (0.87-0.99)
CL Quantification (CL<25 vs. CL≥25)	0.91 (0.87-0.95)	0.94 (0.89-0.98)	0.90 (0.83-0.97)
High PET (CL>49) vs. Low PET (CL<10)	0.94 (0.91-0.98)	0.96 (0.93-1.0)	0.93 (0.86-0.99)
Intermediate PET (CL 10-49) vs. Low PET (CL<10)	0.73 (0.63-0.82)	0.71 (0.57-0.84)	0.76 (0.61-0.90)

eTable 2. Among cognitively impaired participants only (CDR>0), area under the curve (AUC) and 95% confidence intervals for plasma p-tau217 predicting Aβ-PET results in the combined sample ("All") and stratified by the two largest ethnicity-specific subgroups (non-Hispanic/Latino white, Hispanic/Latino white). Table 2 shows corresponding data for combined cognitively unimpaired and impaired participants.

Cognitively Impaired Only				
		Plasma p-tau217 (ALZPath)		
Aβ-PET Result		**All**	**Non-Hispanic/Latino White**	**Hispanic/Latino White**
Visual Read (positive vs. negative)	***Single cutoff , pg/mL***	***0.60***	***0.61***	***0.60***
	Sens/Spec (Group-Specific)*	88.1/85.3	83.8/90.2	93.2/84.2
	PPV/NPV (Group-Specific)	78.4/90.1	82.5/86.1	82.4/93.8
	Sens/Spec (Universal)**	88.1/85.3	83.8/88.2	93.2/84.2
	PPV/NPV (Universal)	78.4/90.1	80.5/85.9	82.4/93.8
CL Quantification (CL<25 vs. CL≥25)	***Single cutoff , pg/mL***	***0.60***	***0.55***	***0.60***
	Sens/Spec (Group-Specific)	85.7/88.6	87.5/87.5	91.3/86.1
	PPV/NPV (Group-Specific)	83.5/85.9	83.0/90.8	88.2/89.1
	Sens/Spec (Universal)	85.7/88.6	80.0/89.6	91.3/86.1
	PPV/NPV (Universal)	83.5/85.9	82.9/84.5	88.2/89.1
High PET (CL>49) vs. Low PET (CL<10)	***Single cutoff, pg/mL***	***0.61***	***0.55***	***0.61***
	Sens/Spec (Group-Specific)	94.0/88.7	93.5/89.5	97.1/86.2
	PPV/NPV (Group-Specific)	83.3/94.2	84.2/96.0	87.2/95.7
	Sens/Spec (Universal)	94.0/88.7	90.3/92.1	97.1/86.2
	PPV/NPV (Universal)	83.3/94.2	85.7/92.5	87.2/95.7
Intermediate PET (CL 10-49) vs. Low PET (CL<10)	***Single cutoff , pg/mL***	***0.40***	***0.34***	***0.42***
	Sens/Spec (Group-Specific)	75.6/62.0	84.2/50.0	78.9/72.4
	PPV/NPV (Group-Specific)	49.3/77.3	41.9/82.9	61.3/77.1
	Sens/Spec (Universal)	75.6/62.0	68.4/57.9	78.9/69.0
	PPV/NPV (Universal)	49.3/77.3	45.5/80.0	59.4/76.6

*Sensitivity (Sens) and Specificity (Spec) / positive predictive value (PPV) and negative predictive value (NPV) when applying the single cut-off (Youden's Index) derived from group-specific AUC curve

**Sensitivity (Sens) and Specificity (Spec) / positive predictive value (PPV) and negative predictive value (NPV) when universally applying the single cut-off (Youden's Index) derived from overall ("All") sample AUC curve to each subgroup

eTable 3. Among cognitively impaired participants only (CDR>0), single cutoff values for p-tau217 (ALZPath) along with corresponding sensitivity/specificity and positive/negative predictive value to Aβ-PET results for the overall combined sample ("All") and stratified by ethnicity-specific subgroups (non-Hispanic/Latino white, Hispanic/Latino white). Table 3 shows corresponding data for combined cognitively unimpaired and impaired participants.

Cognitively Impaired Only				
		Plasma p-tau217 (ALZPath)		
		All	**Non-Hispanic/Latino White**	**Hispanic/Latino White**
Visual Read (positive vs. negative)	Two-cutoff range, pg/mL	0.42-1.03	0.48-0.89	0.55-0.82
	% Within Group-Specific Range*	33.5	22.3	15.7
	%Agreement (Negative)	*94.2*	*93.0*	*95.1*
	%Agreement (Positive)	*90.2*	*90.0*	*91.7*
	% Within Universal Range**	33.5	33.0	34.8
	%Agreement (Negative)	*94.2*	*93.8*	*94.0*
	%Agreement (Positive)	*90.2*	*92.6*	*96.0*
CL Quantification (CL<25 vs. CL>25)	Two-cutoff range, pg/mL	0.40-0.92	0.42-0.89	0.44-0.82
	% Within Group-Specific Range	31.8	30.4	22.6
	%Agreement (Negative)	*91.9*	*93.8*	*92.5*
	%Agreement (Positive)	*90.6*	*93.3*	*91.7*
	% Within Universal Range	31.8	33.9	29.6
	%Agreement (Negative)	*91.9*	*95.6*	*91.8*
	%Agreement (Positive)	*90.6*	*93.1*	*90.6*

*Percent of participants within the intermediate range when using group (ethnicity) specific reference ranges

**Percent of participants within the intermediate range when applying the reference range derived from the overall combined sample ("universal")

eTable 4. Among cognitively impaired participants only (CDR>0), reference range for plasma p-tau217 using two-cutoff approach where the lower limit represents sensitivity fixed at 95% with maximized specificity and the upper limit represents specificity fixed at 95% with maximized sensitivity. The percentage of participants falling within the intermediate two-cutoff reference range is shown for when the range was based on group-specific reference samples (i.e., within non-Hispanic/White or within Hispanic/White) and for when the range derived from the overall sample was applied universally across the ethnicity subgroups. The percent agreement between "negative" tests (p-tau217 below range plus negative Aβ-PET) and between "positive" tests (P-tau217 above range plus positive Aβ-PET) is reported again using the group-specific reference

ranges and when applying the overall sample reference range universally across ethnicity subgroups). Table 4 shows corresponding data for combined cognitively unimpaired and impaired participants.

		Plasma p-tau217 (ALZPath)		
Aβ-PET Result		**All**	**Hispanic/Latino White**	**Non-Hispanic/Latino White**
Visual Read (negative vs. positive)	p-tau217	0.91 [0.87-0.95]	0.92 [0.86-0.98]	0.92 [0.87-0.97]
	p-tau217+Demographics+*APOE*	0.93 [0.90-0.96]	0.94 [0.90-0.98]	0.94 [0.89-0.98]
CL Quantification (CL<25 vs. CL≥25)	p-tau217	0.90 [0.86-0.94]	0.91 [0.85-0.97]	0.93 [0.88-0.97]
	p-tau217+Demographics+*APOE*	0.91 [0.86-0.95]	0.91 [0.86-0.97]	0.93 [0.88-0.98]
Low PET (CL<10) vs. Intermediate PET (CL 10-49)	p-tau217	0.70 [0.62-0.79]	0.75 [0.63-0.86]	0.69 [0.57-0.81]
	p-tau217+Demographics+*APOE*	0.71 [0.63-0.79]	0.74 [0.63-0.86]	0.74 [0.63-0.86]

eTable 5. Comparison of AUCs for predicting Aβ-PET results based on plasma p-tau217 alone versus a combination of plasma p-tau217 plus demographics (age, sex) and *APOE e4* carrier status. Data shown for the overall combined sample and separately within ethnicity-specific subgroups (Hispanic/Latino white, non-Hispanic/Latino white).