


Prediction of Cognitive Functioning and Dementia with Neurodegenerative Markers: LASI-DAD and HRS

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Question

Do blood-based neurodegenerative markers predict cognitive functioning and dementia similarly in India (LASI-DAD) and US (HRS)?



Neurodegenerative Markers in the Two Countries

HRS

LASI-DAD

NfL

NfL

GFAP

GFAP

A β 42/A β 40

A β 42/A β 40

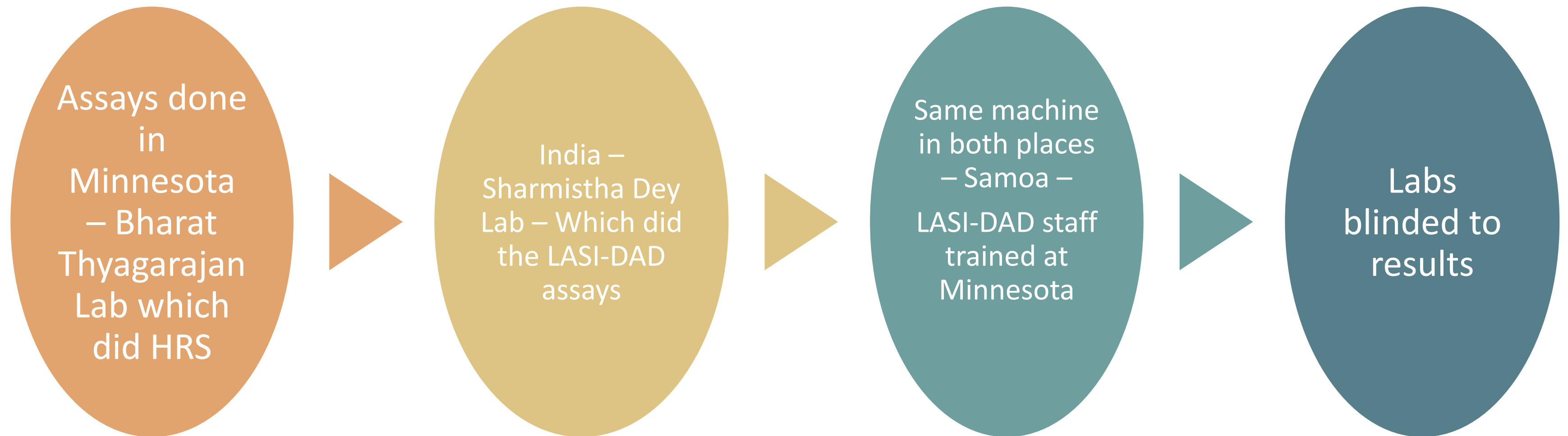
pTau 181*
*serum

pTau181**
***plasma*

Total Tau

Harmonization of Measurement Before we Began Assays in India:

84 cases plated identically on two plates in Minnesota and shipped frozen to India



Correlations of Values Between the Two Labs

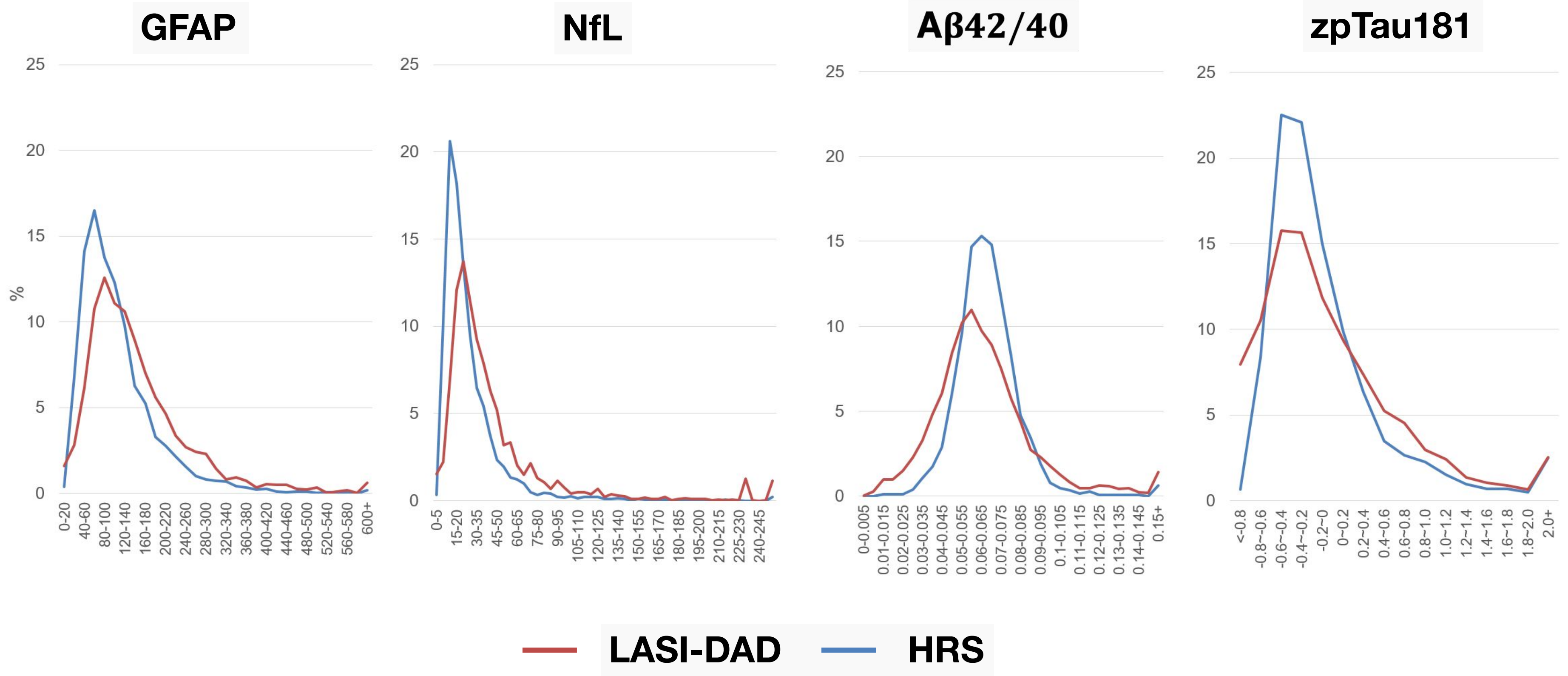
Minnesota–
Bharat
Thyagarajan
Lab

GFAP	.98
NFL	.94
A β 42	.95
A β 40	.98
A β 42/40	.88

India–
Sharmistha
Dey
Lab

We can use equations to make harmonized values for LASI

Distributions of Neurodegenerative Markers in LASI-DAD and HRS



Sample Description

	LASI-DAD N=2151	HRS N=3466
Mean Age (Years)	69.6	70.5
%Female	50.2	54.6
Mean (SD) Neurodegenerative Marker		
GFAP	153.92	109.37
NfL	44.38	26.48
A β 42/40	0.06	0.07
pTau 181	41.21	2.18
Mean Neuro Biomarker Factor Score (from GFAP, NfL, pTau 181)	1.33	-0.02

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Correlations among Markers in Two Countries: Similar Except for A β 42/40

LASIDAD

	NfL	AB42/40	ptau181
GFAP	0.40	-0.11	0.14
NfL		-0.04	0.16
AB42/40			-0.09

HRS

	NfL	AB42/40	ptau181
GFAP	0.47	0.00	0.28
NfL		0.00	0.28
AB42/40			-0.03

Measures of Cognition

Cognitive Functioning

Factor Score for LASIDAD and HRS (HCAP): Z scored for Analysis

General cognitive factor score reflecting the broadest cognitive summary variable including memory, executive functioning, visuospatial, and language domains (Gross et al. 2023)

Dementia

LASIDAD CDR Final - Demented

No dementia includes no or questionable impairment

Dementia includes mild, moderate, and severe impairment

HRS HCAP Demented

Cognitive Decline

Negative change between time 1 and time 2 among those without dementia at time 1

LASIDAD - factor score

HRS - Langa Weir score – 2016- 2020

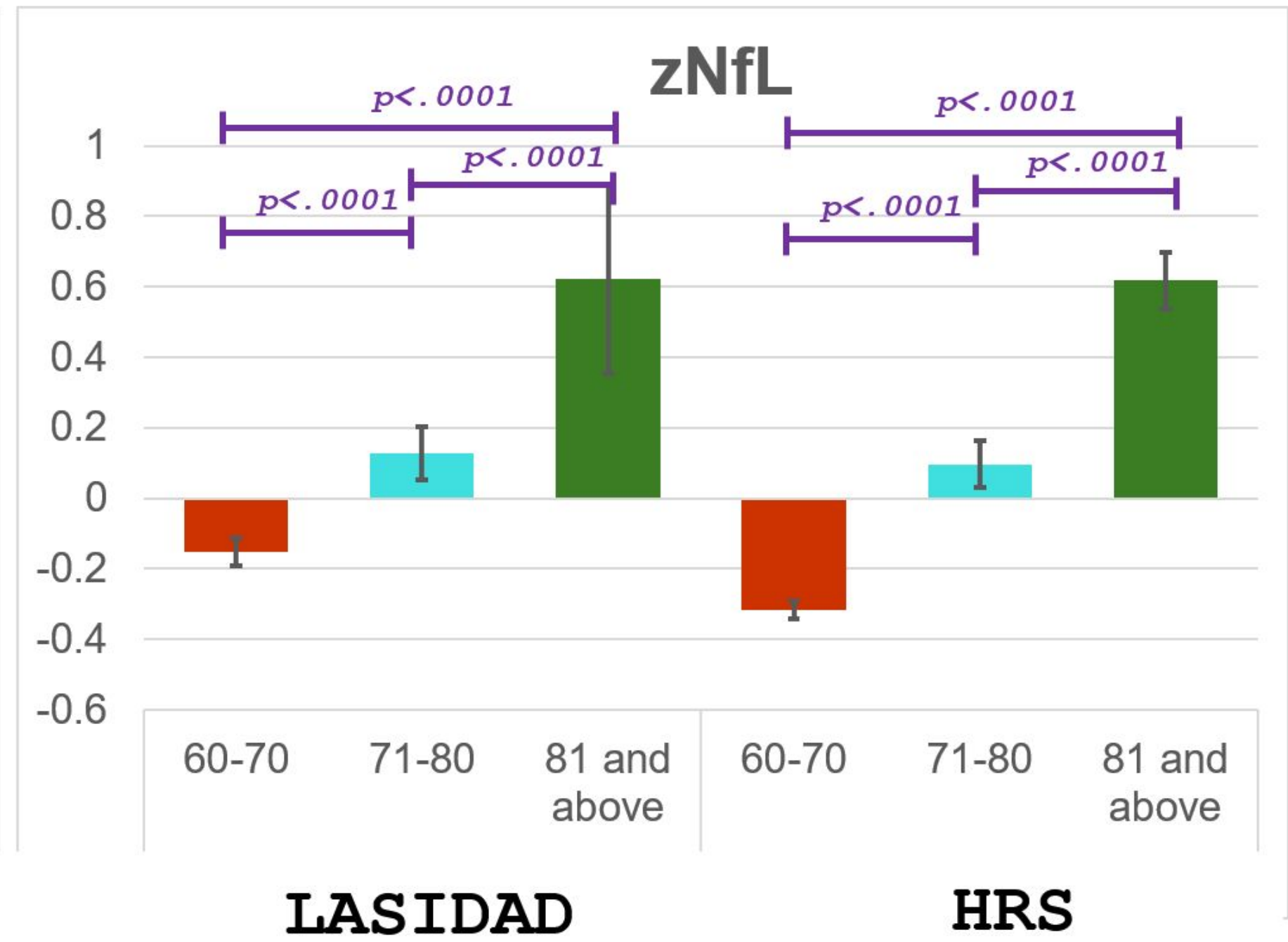
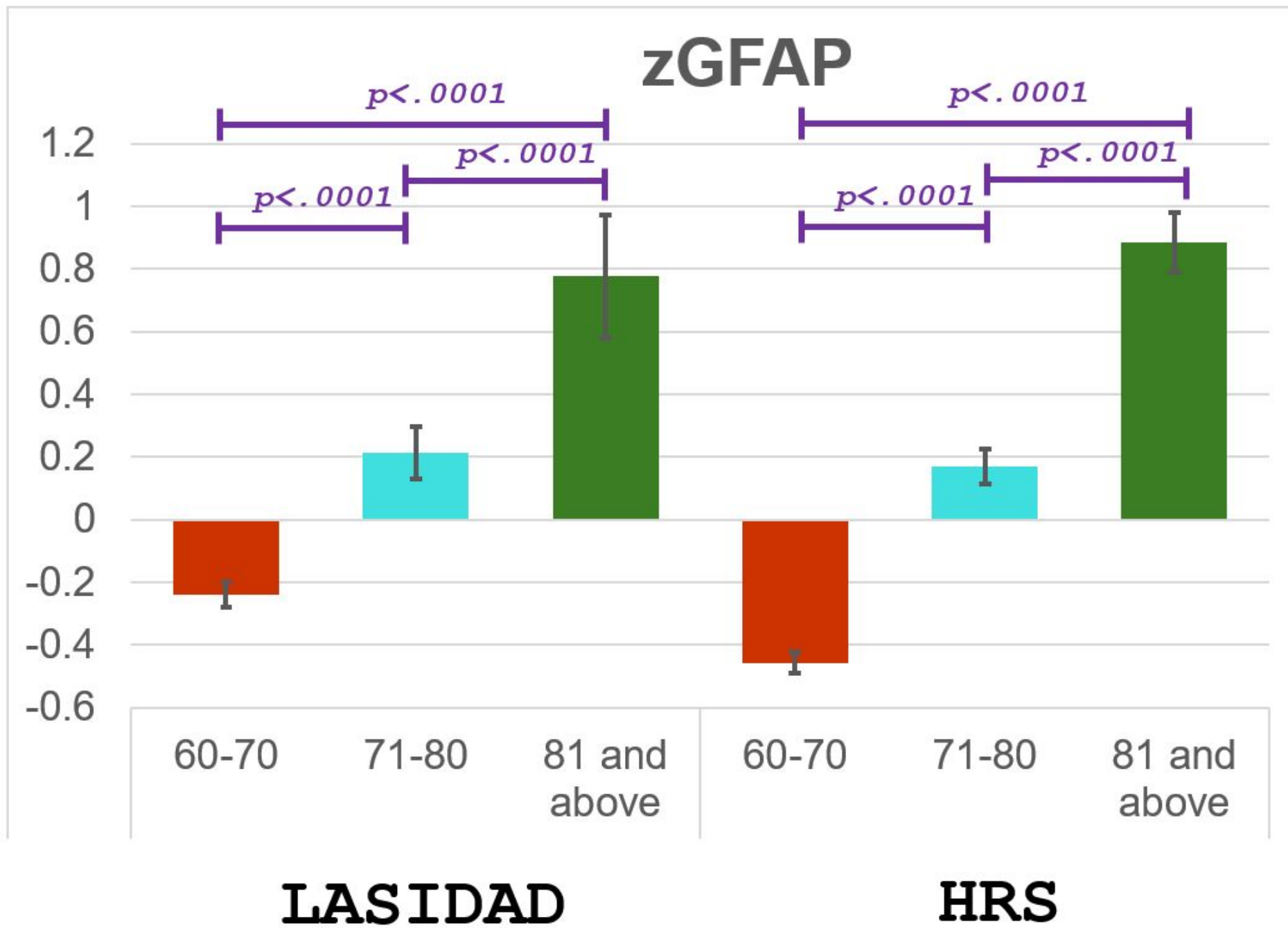
Cognitive Measures

	LASIDAD N=2151	HRS N=3466
Mean (SD) Standardized Cognitive Score		
z Factor Score	-0.07	0.12
Dementia	<i>n=1405</i>	<i>n=2323</i>
%Demented (CDR)	6.7	
%Demented (HCAP)		6.8
Cognitive Change	<i>n=2661</i>	<i>n=3093</i>
%No Cognitive Decline	21.6	33.3
%Cognitive Decline	51.9	54.1
%Death	26.6	12.5

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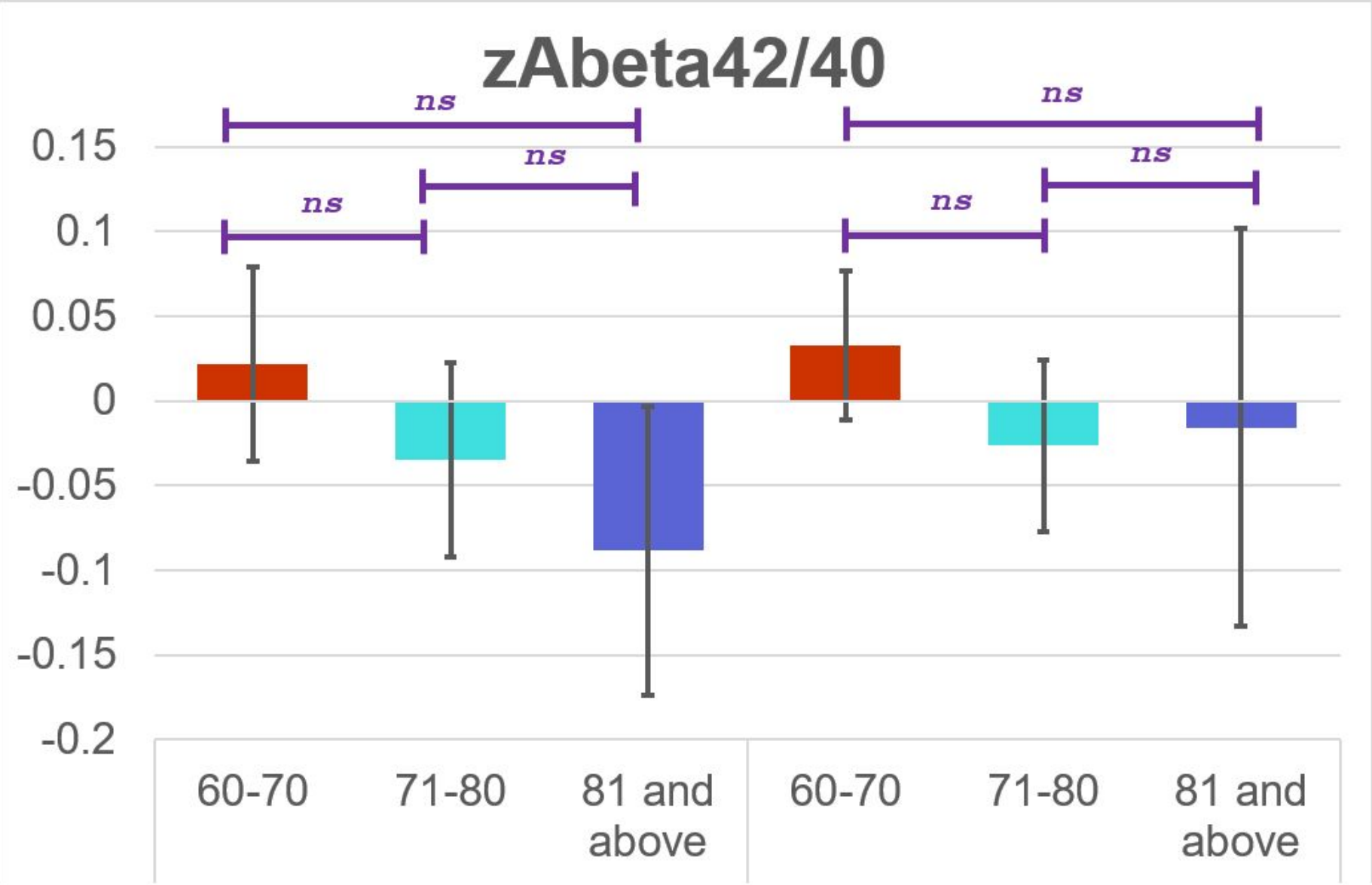
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Increase with age as expected for zGFAP and zNfL Levels



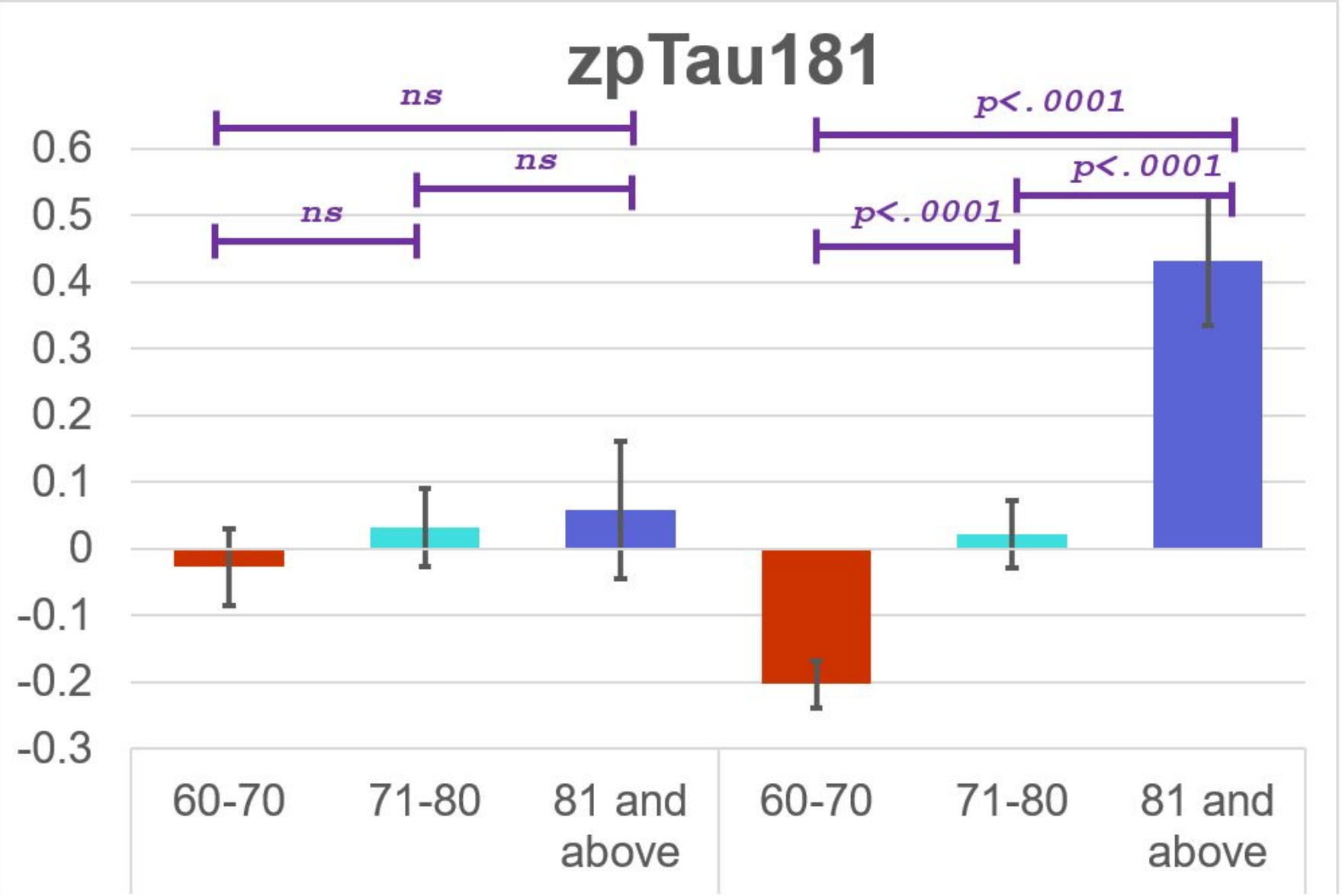
zAβ42/40 Decreases with Age; zpTau181 Levels Increase with Age

LA SIDAD HRS



LASIDAD

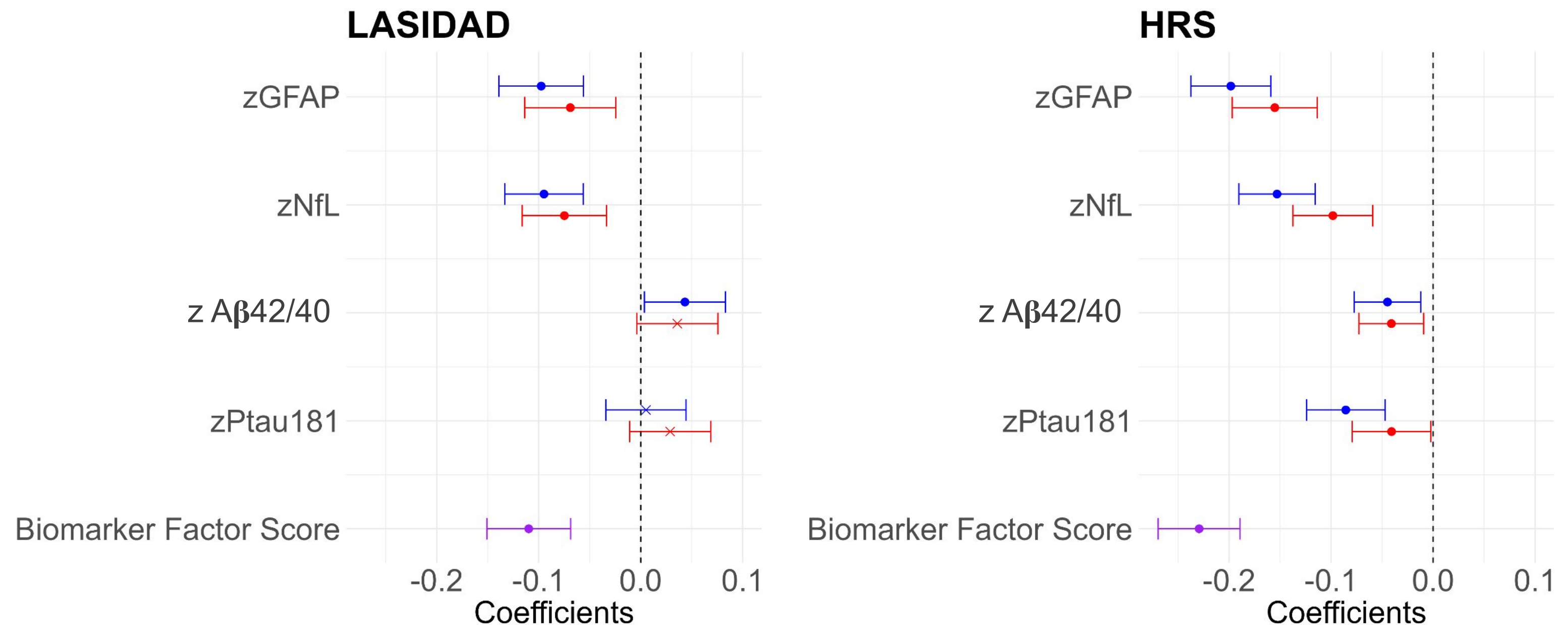
HRS



LASIDAD

HRS

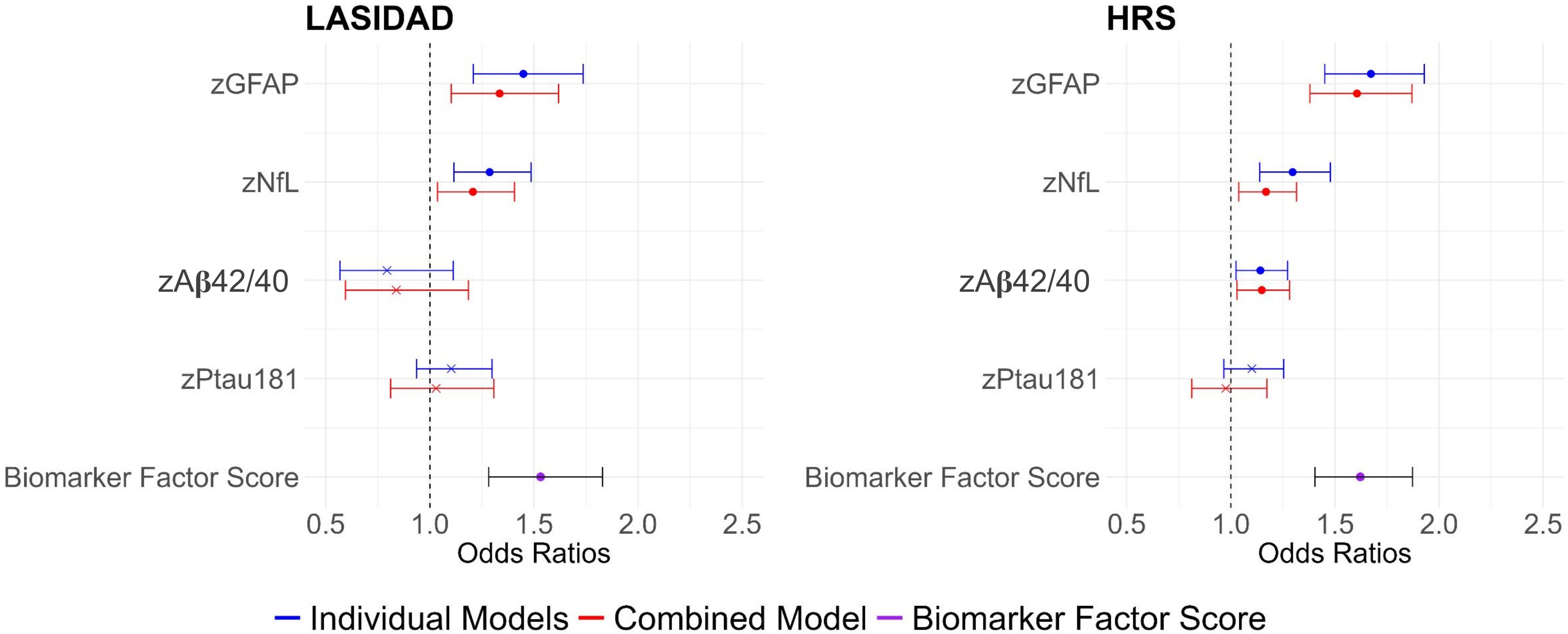
Association from Regression of Standardized Factor Cognitive Score on Neurodegenerative Markers in India and the US



— Individual Models — Combined Model — Biomarker Factor Score

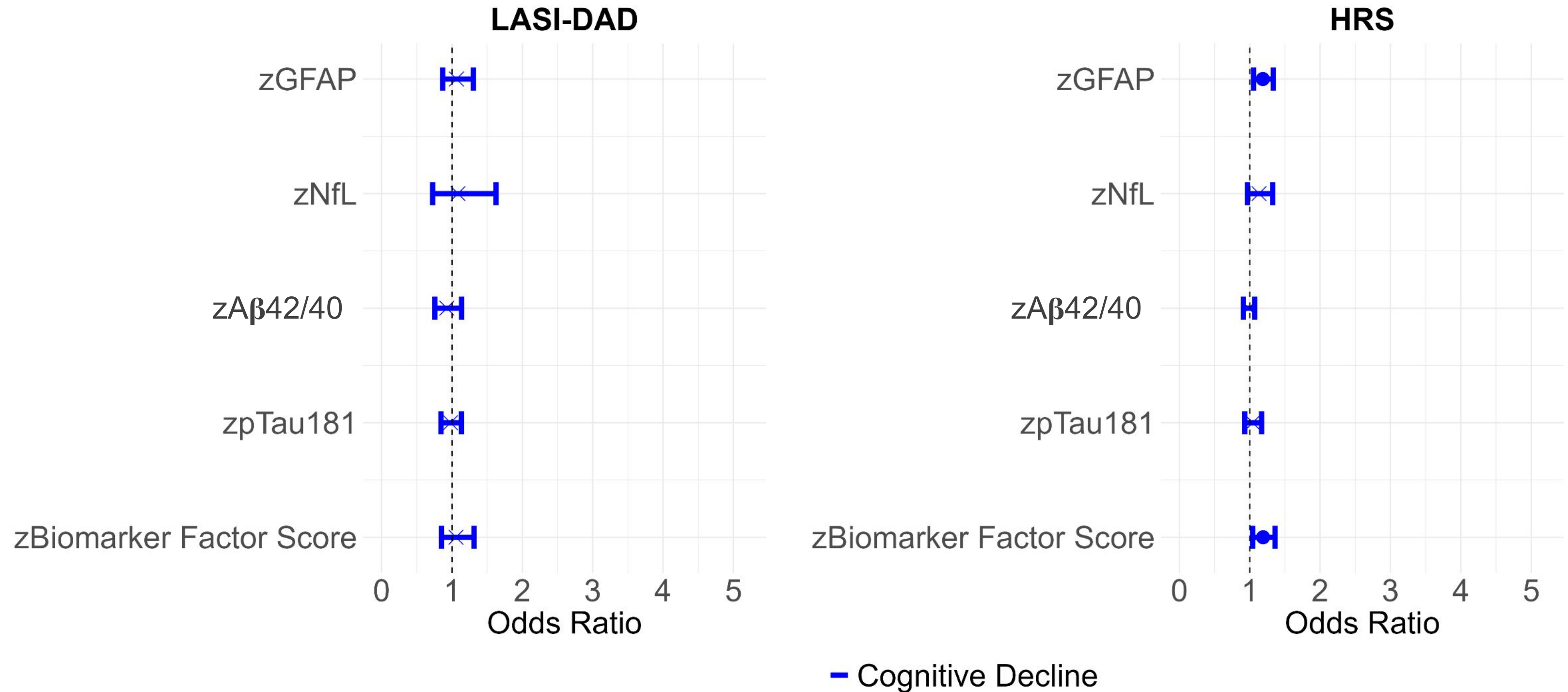
Regression coefficients from OLS regression of standardized cognitive score on standardized GFAP, NfL, AB42/40, and pTau181 or neurodegenerative biomarker factor score (based on GFAP, NfL, pTau181); HRS: age, gender, race/ethnicity controlled; LASIDAD: age, gender controlled

Association of Dementia with Neurodegenerative Markers in India and the US



Odds ratios from Logistic Regression of having “dementia” on standardized GFAP, NfL, AB42/40 and pTau181 or neurodegenerative biomarker factor score; HRS: age, gender, race/ethnicity controlled; LASIDAD: age, gender controlled

Odds Ratios for Cognitive Decline in India and the US



Cognitive decline is defined as having a negative change between time 1 and time 2 cognitive score among those without dementia in time 1

What Have We Learned?



1 NfL and GFAP associated as expected with age and cognitive outcomes at time of measurement

2 The associations are quite similar in LASI-DAD and HRS and significant in the cross section – but do not predict change

3 A β 42/40 looks like we might have more expected associations in LASI-DAD but they are fairly small.

4 pTau181 is related to age as expected but cognitive association limited to HRS



What I Have Not Told You

1

The results are not affected by controls for education and caste in India and education and race in the HRS.

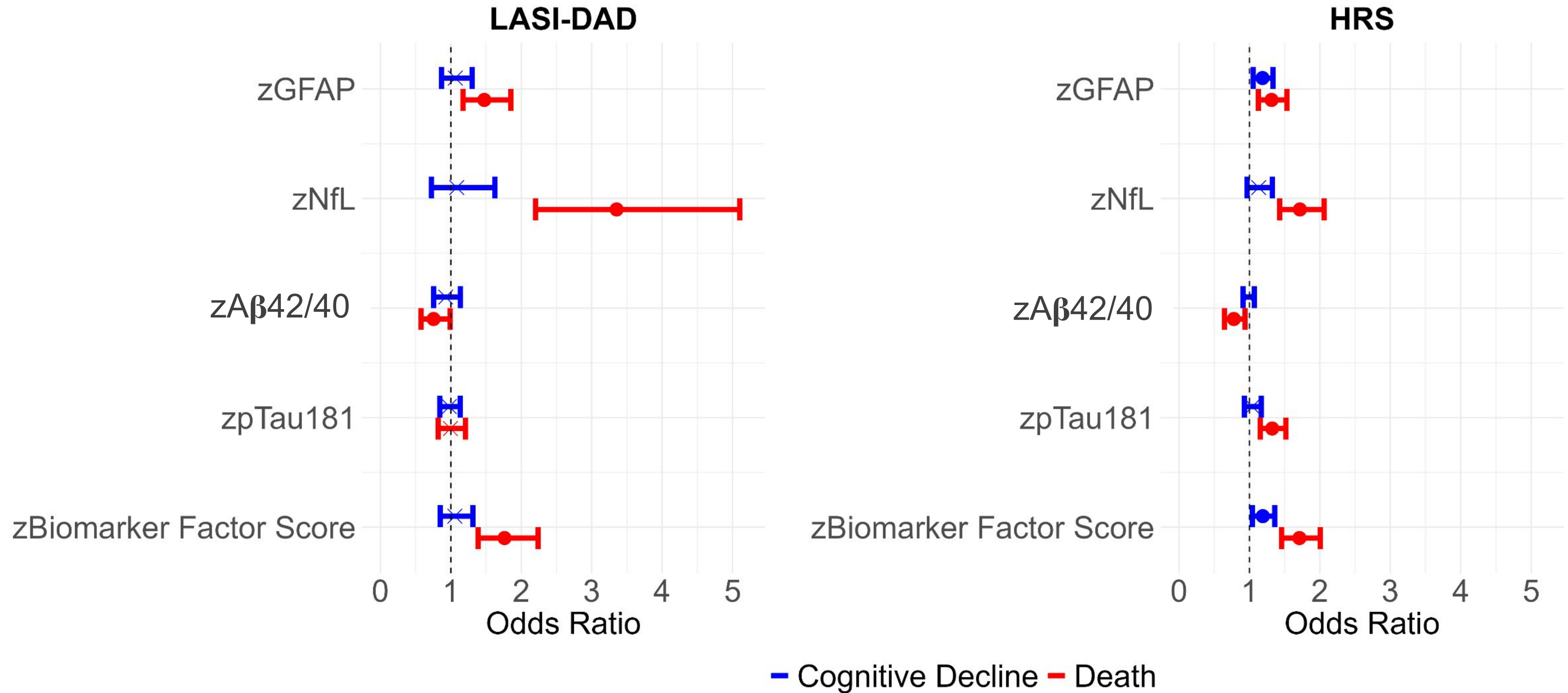
2

In both India and the US, the variance in the cognitive outcomes explained is quite small

3

These appear to be among the most important biomarkers in predicting both cognitive outcomes and other age-related outcomes in HRS

Odds Ratios for Cognitive Decline and Death in India and the US



Cognitive decline is defined as having a negative change between time 1 and time 2 cognitive score among those without dementia at time 1

Where Do We Go from Here?

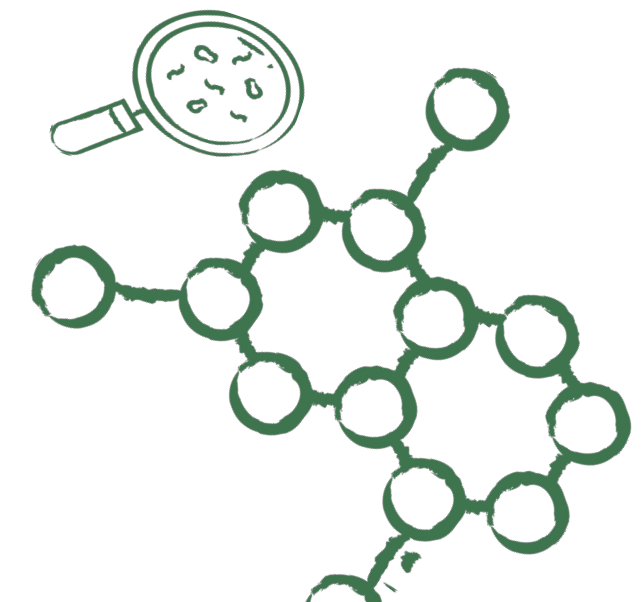


pTau217

We will have better
cognitive change and
onset measures

Have a longer time
period

Determine
mediation patterns
with our social
variables



Acknowledgement

LASI-DAD - U.S. National Institute on Aging R01AG051125, U01AG064948, R01AG080473,
RF1AG055273, R01AG042778, Bright Focus Foundation, Gates Ventures
HRS – U.S. National Institute on Aging (U01AG009740) and the Social Security Administration

LASI-DAD measures are released; HRS are on the cusp of release

