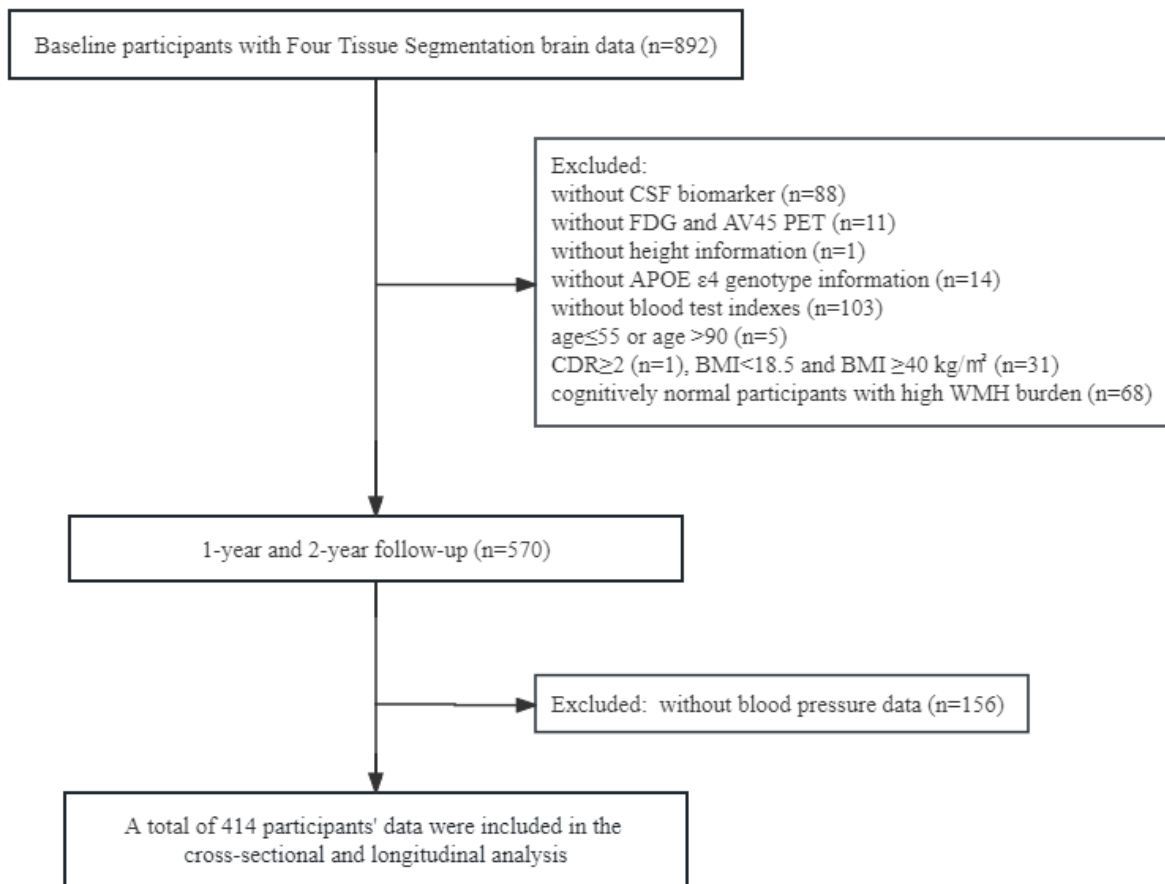


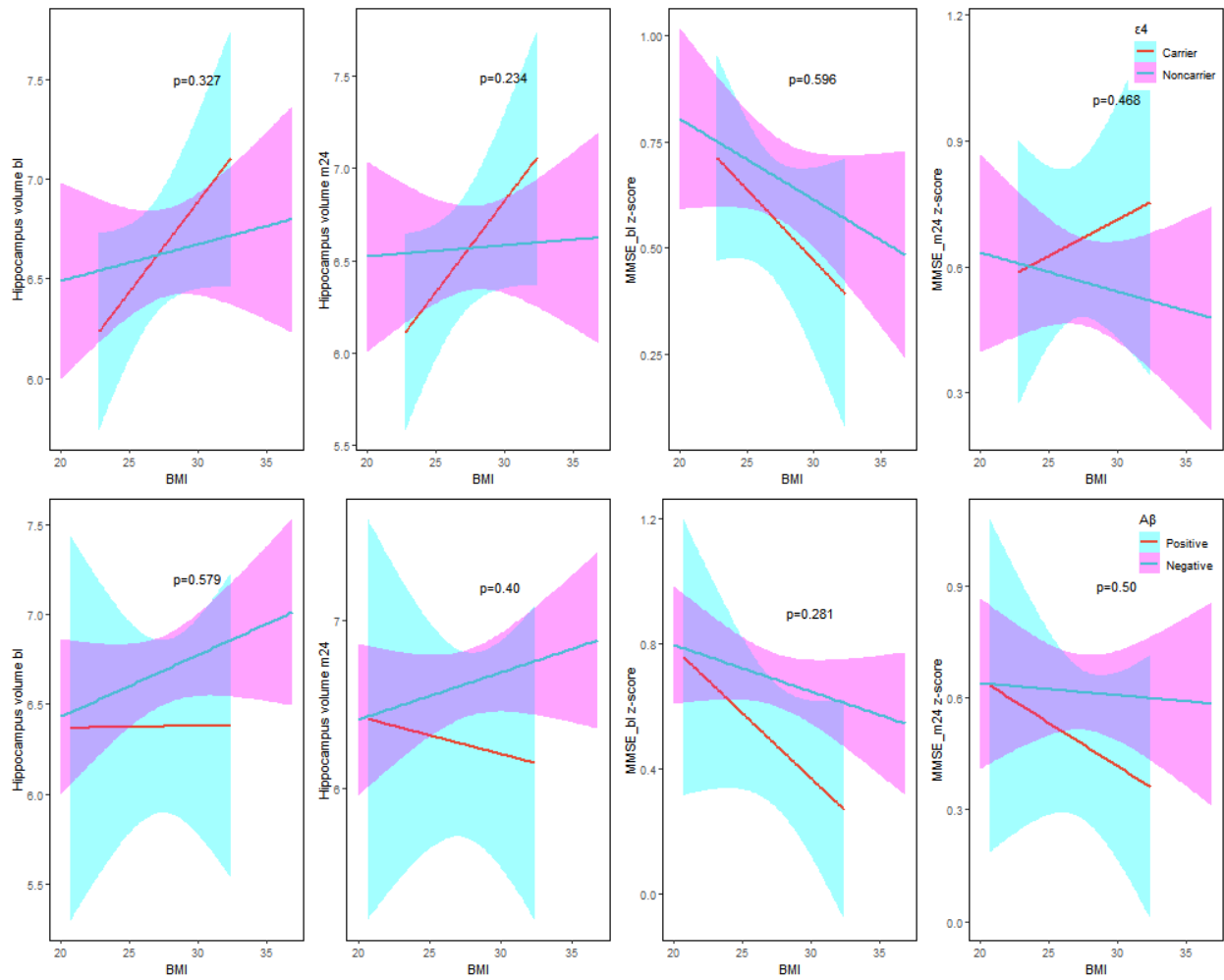
# Supplementary Material

## The Association of Body Mass Index with Cognition and Alzheimer's Disease Biomarkers in the Elderly with Different Cognitive Status: A Study from the Alzheimer's Disease Neuroimaging Initiative Database

**Supplementary Figure 1.** Flow diagram illustrating screening and enrollment of participants.

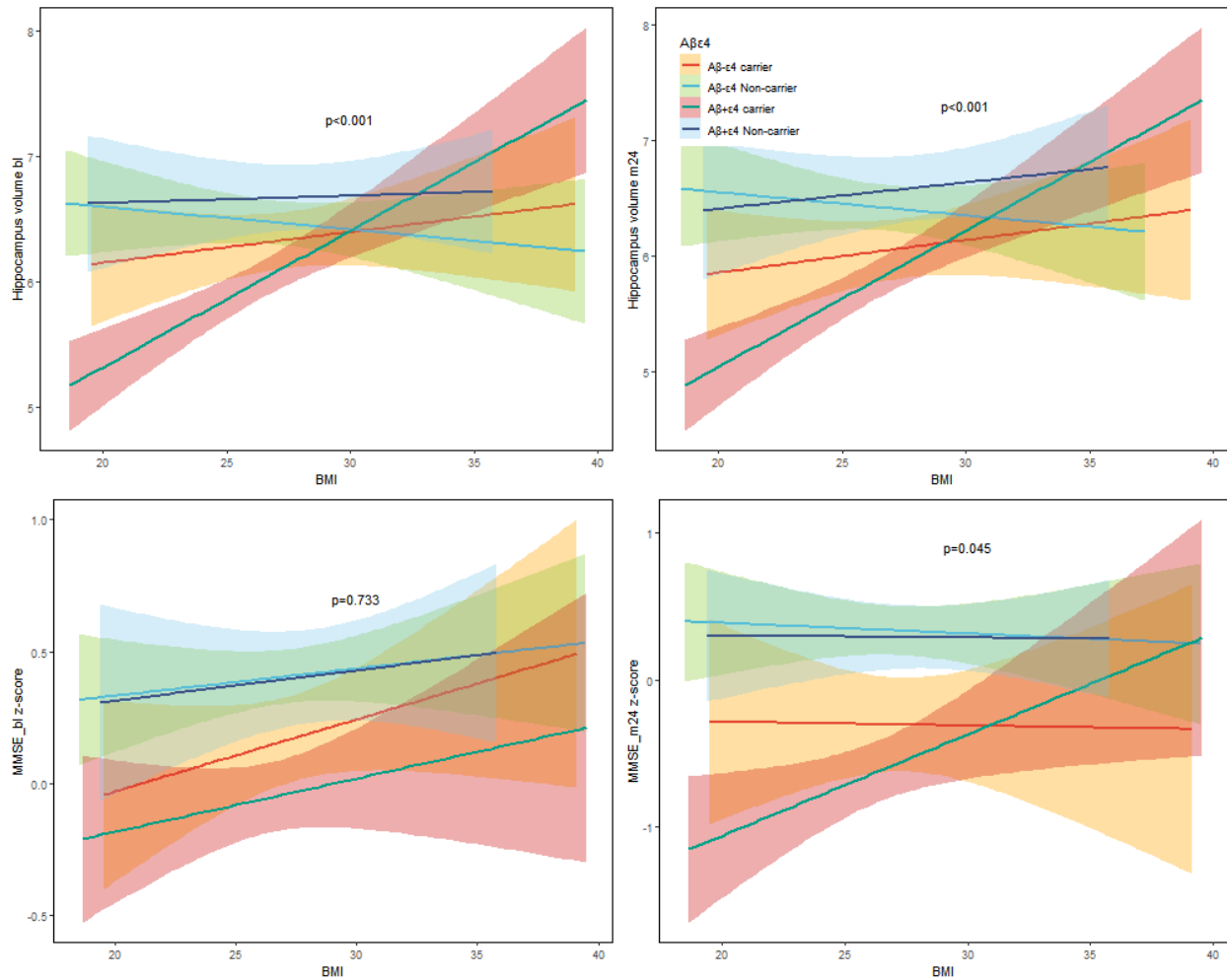


**Supplementary Figure 2.** The effect of BMI on hippocampal volume and MMSE score in the cognitively normal group.



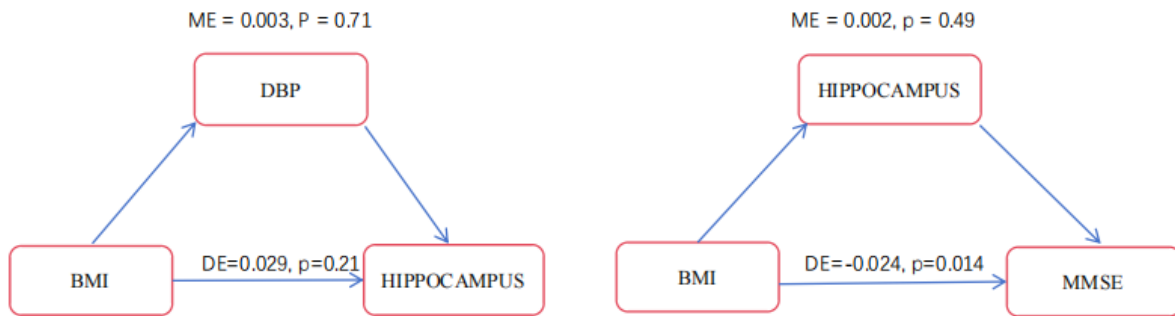
MMSE score has been z-transformed. The definition of Aβ positive was based on the Aβ PET.

**Supplementary Figure 3.** The effect of BMI on hippocampal volume and MMSE score in different *APOE*  $\epsilon 4$  and  $A\beta$  status in the cognitive impairment group.



The MMSE score has been z-transformed. There were significant differences in the slopes of BMI on the baseline and 2-year hippocampus volume between *APOE4*+ $A\beta$ + participants and *APOE4*+ $A\beta$ - (baseline  $p = 0.016$ , 2-year  $p = 0.019$ ) as well as *APOE4*- $A\beta$ + (baseline  $p = 0.008$ , 2-year  $p = 0.02$ ) participants.

**Supplementary Figure 4.** Mediation models of the CN group.



ME, mediation effect; DE, direct effect. The mediation analysis model was adjusted for FHS1 score, *APOE*  $\epsilon 4$  status, and education years.

**Supplementary Table 1.** Baseline characteristics of different body mass index groups.

Indicators	normal (n=126)	overweight (n=205)	obesity (n=83)	<i>p</i>
<b>Population characteristic</b>				
Age	72.4 (7.24)	72.1 (6.85)	70.1 (6.72)	0.045
Gender (Female)	67 (53.2%)	77 (37.6%) *	37 (44.6%)	0.021
SBP (mmHg)	131 (17.2)	131 (15.0)	136 (17.6)	0.055
DBP (mmHg)	71.6 (8.92)	72.7 (8.89)	77.1 (11.0) ***#	<0.001
<b>Vascular risk factors</b>				
Hypertension	42 (33.3%)	86 (42.0%)	42 (50.6%) *	0.043
Diabetes mellitus	8 (6.35%)	25 (12.2%)	17 (20.5%) *	0.009
FHS score	15 [13;18]	17 [15;18] **	17 [15;20] ***#	<0.001
FHS1 score	15.5 [13;18]	16 [14;17]	16 [14;18]	0.437
<b>Accessory examination</b>				
Triglyceride (mg/dl)	116 (64.4)	146 (77.3) **	179 (93.8) ***	<0.001
Total cholesterol (mg/dl)	198 (38.0)	189 (34.9)	189 (42.2)	0.091
NLR	2.18 [1.79;2.95]	2.22 [1.66;2.85]	1.98 [1.58;2.53]	0.082
PLR	143 [117;171]	137 [111;169]	127 [102;152] *	0.020
A $\beta$ <sub>42</sub> (pg/mL)	811 [616;1363]	972 [723;1646] *	1108 [724;1761]*	0.007
p-tau181 (pg/mL)	21.7 [16.5;32.8]	23.4 [17.4;33.0]	21.2 [16.4;30.0]	0.242
Hippocampus (ml)	6.12 (0.92)	6.40 (0.87)	6.55 (0.96) **	0.002
WMH (ml)	2.88 [1.35;8.05]	3.05 [1.78;6.72]	2.13 [1.22;6.31]	0.146
Brain (ml)	1,379 (137)	1,408 (141)	1,410 (130)	0.137
APOE $\epsilon$ 4 carrier	64 (50.8%)	93 (45.4%)	34 (41.0%)	0.36
AV45 SUVR	1.17 [1.03;1.40]	1.13 [1.01;1.38]	1.07 [1.02;1.31]	0.264
FDG-PET SUVR	1.24 [1.14;1.32]	1.26 [1.16;1.35]	1.27 [1.17;1.34]	0.269
<b>Cognitive function</b>				
MMSE	28 [26;30]	29 [27;29]	29 [28;30]	0.372
CDRSB	1 [0.5;2]	1 [0.5;2]	1 [0;1.5]	0.582
ADAS-cog 13	14.0 [9.0;20.0]	14.0 [8.0;18.0]	11.0 [8.0;16.5]	0.148
ADNI-Mem	0.36 (0.88)	0.42 (0.80)	0.53 (0.67)	0.33
ADNI-EF	0.42 (1.04)	0.55 (0.94)	0.46 (0.81)	0.424

Data were presented as mean $\pm$ SD, median (interquartile range), or count (percentage). \*Significant difference between normal and other groups, \**p* < 0.05, \*\**p* < 0.01, \*\*\**p* < 0.001; #significant difference between overweight and obesity, #*p* < 0.05, ##*p* < 0.01, ###*p* < 0.001. SBP, systolic blood pressure; DBP, diastolic blood pressure; FHS score, Framingham Heart Study-cardiovascular risk score; FHS1 score, FHS score did not include body mass index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet to lymphocyte ratio; WMH, white matter hyperintensities; MMSE, Mini-Mental State Examination; CDRSB, Clinical Dementia Rating Scale Sum of Boxes; ADAS13, Alzheimer's Disease Assessment Scale-cognitive subscale 13 item; ADNI-Mem, memory composite score; ADNI-EF, executive function score.

**Supplementary Table 2.** Different BMI categories predict baseline cognition.

Indicators	CI (n=330)		CN (n=84)	
	$\beta$ (95% CI)	<i>p</i>	$\beta$ (95% CI)	<i>p</i>
<b>MMSE</b>				
normal weight (ref)				
overweight	0.21 (0.04, 0.39)	0.017	-0.15 (-0.37, 0.06)	0.148
obesity	0.38 (0.15, 0.61)	0.001	-0.23 (-0.48, 0.01)	0.063
<b>ADNI-MEM</b>				
normal weight (ref)				
overweight	0.05 (-0.10, 0.21)	0.511	-0.09 (-0.40, 0.23)	0.582
obesity	0.21 (0.01, 0.42)	0.037	-0.38 (-0.74, -0.02)	0.041
<b>ADNI-EF</b>				
normal weight (ref)				
overweight	0.11 (-0.09, 0.31)	0.275	0.31 (-0.11, 0.73)	0.142
obesity	0.09 (-0.16, 0.35)	0.472	-0.11 (-0.60, 0.38)	0.658

CN, cognitively normal; CI, cognitive impairment; MMSE, Mini-Mental State Examination; ADNI-MEM, ADNI memory composite score; ADNI-EF, ADNI executive function score. MMSE score has been z-transformed. All models were adjusted for FHS1 (Framingham risk score did not include body mass index) score, *APOE*  $\epsilon$ 4 status, education years, and the use of anti-dementia medications.