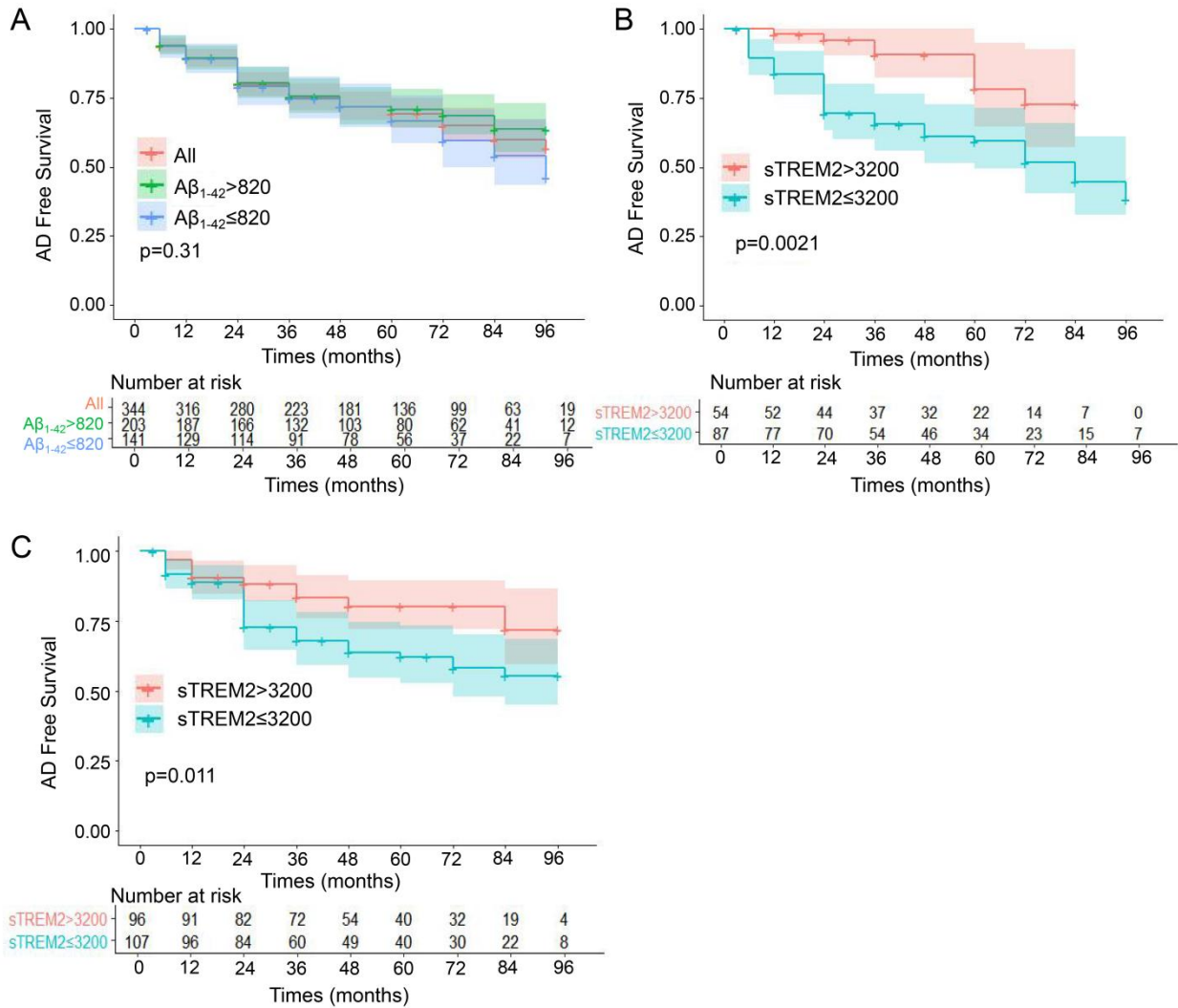


Supplementary Figure 1



Supplementary Figure 1. Kaplan-Meier plot of AD-free survival in MCI patients with different CSF

$A\beta_{1-42}$ levels from ADNI database.

A. No significant difference in mean progression-free survival time in MCI subjects between different

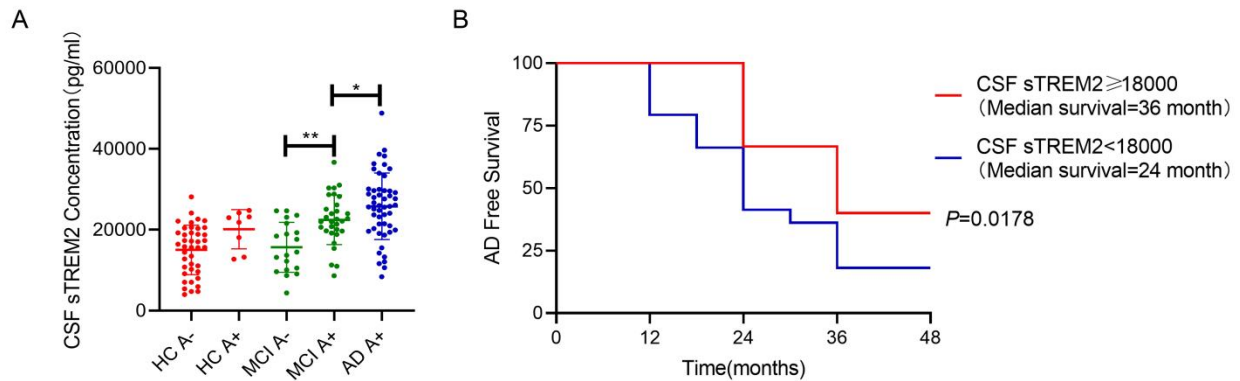
CSF $A\beta_{1-42}$ levels lower than 820 and higher than 820.

B. CSF sTREM2 levels predicted AD-free survival of MCI patients with CSF $A\beta_{1-42} < 820$.

C. CSF sTREM2 levels predicted AD-free survival of MCI patients with CSF $A\beta_{1-42} \geq 820$.

A total of 146, 344 and 111 HCs and MCI and AD patients, respectively, were included for analysis. Data were analyzed by using the Kaplan-Meier method.

Supplementary Figure 2



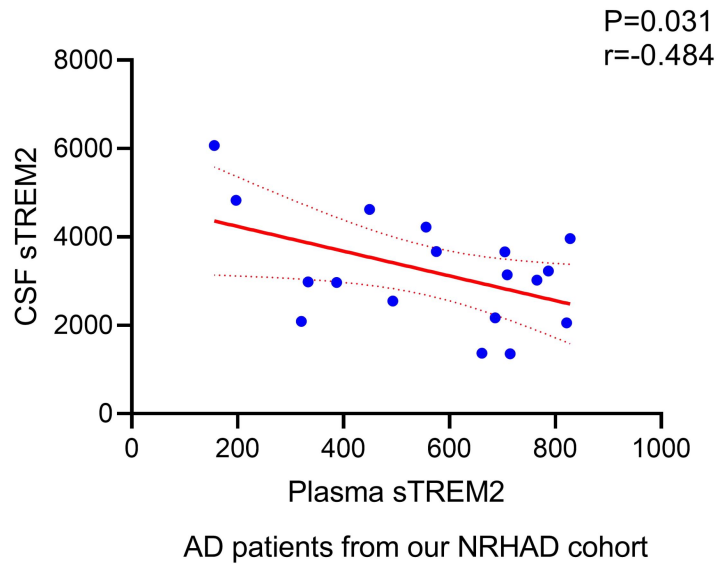
Supplementary Figure 2. CSF sTREM2 levels predicted AD-free survival of MCI patients from CABLE cohort.

A. CSF sTREM2 levels were significant increasing in MCI groups with amyloid deposition (A+) and further significant increasing in AD groups with amyloid deposition (A+).

B. CSF sTREM2 levels predicted AD-free survival of MCI (A+) patients, and CSF sTREM2 levels lower 18000 pg/ml were more liable to develop AD.

Data represent mean \pm SEM. *: $p < 0.05$; **: $p < 0.01$. A total of 50, 50 and 50 HCs and MCI and AD patients, respectively, were included for analysis. One-way ANOVA with the least significant difference post-hoc test, and Kaplan-Meier method were used.

Supplementary Figure 3



Supplementary Figure 3. CSF sTREM2 levels were negative correlation with plasma sTREM2 levels in AD patients in our NRHAD cohort. A total of 18 AD patients were included for analysis. Pearson's correlation test were used.

Supplementary Table S1. Evaluations of MCI non-convertors and convertors from ADNI

database in the follow-up

	MCI-nc (n=241)	MCI-c (n=103)	<i>p</i> value	HR (95% CI)
Follow-up time (month)	54.1(25.8)	53.9(23.3)	0.971	/
Age (y)	70.9(7.6)	71.7(6.8)	0.363	/
Gender				
Female	95(39%)	54(52%)	0.027	/
Male	148(61%)	50(48%)		/
Education (y)	16.8(3.1)	16.3(2.6)	0.592	/
Predictive biomarker				
CSF sTREM2 (pg/ml)				
<3200	122(51%)	71(69%)	0.011^a	1.72
≥3200	119(49%)	32(31%)		(1.13-2.61) ^a
CSF Aβ ₁₋₄₂ (pg/ml)				
<820.0	69(29%)	72(70%)	0.000^a	4.35

≥ 820.0	172(71%)	31(30%)		(2.86-6.67) ^a
AV45				
<1.11	104(43%)	49(48%)		0.94
			0.775 ^a	
≥ 1.11	137(57%)	54(52%)		(0.59-1.49) ^a
ApoE $\epsilon 4$ carrier				
(+)	123(51%)	48(47%)		1.05
			0.834 ^a	
(-)	118(49%)	55(53%)		(0.66-1.67) ^a

a: Student's t test, chi-squared, and Cox proportional hazards model were used, and all results were adjusted for P-Tau/T-Tau, age and gender. The expressed outside the parenthesis of the different values was the mean value, and the inside means the SD value. Actual *p* value: 1: 0.00079.

Supplementary Table 2. Evaluations of MCI non-convertors and convertors in the follow-up from our own NRHAD database

	MCI-nc (n=67)	MCI-c (n=23)	<i>p</i> value	HR (95% CI)
Age (y)	70.0(4.3)	68.6(4.2)	0.157	/
Gender				
Female	37(55%)	12(52%)	0.064	/
Male	30(45%)	11(48%)		/
Education (y)	10.3(3.2)	11.4(3.3)	0.161	/
Predictive biomarker				
Plasma sTREM2 (pg/ml)				
<460	42(63%)	7(30%)	0.008^a	3.45
≥460	25(34%)	16(70%)		(1.39-8.55) ^a
Plasma Aβ ₁₋₄₂ (pg/ml)				
<25	47(70%)	19(83%)	0.039^a	8.34
≥25	20(30%)	4(17%)		(1.11-62.52) ^a
ApoE ε4 carrier				
(+)	21(31%)	12(52%)	0.405 ^a	1.44
(-)	46(69%)	11(48%)		(0.61-3.36) ^a

a: Student's t test, chi-squared, and Cox proportional hazards model were used, and all results were adjusted for P-Tau/T-Tau, age and gender. The expressed outside the parenthesis of the different values was the mean value, and the inside means the SD value.

Supplementary Table 3. Demographic and clinical features of the participants from CABLE cohort in baseline

Demographics	HC (n=50)	MCI (n=50)	AD (n=50)	<i>p</i> value
Age (y)	61.3(8.6)	62.5(7.5)	64.4(8.3)	0.513
Gender				
Female	24(48%)	25(50%)	27(54%)	0.829
Male	26(52%)	25(50%)	23(46%)	
Education (y)	12.5(3.4)	12.3(2.8)	9.9(3.6)	0.025 ^{b,c}
MMSE	29.1(1.3)	27.3(2.7)	21.5(3.9)	0.002 ^{a,b,c}
MoCA	27.9(2.3)	24.2(3.5)	16.5(4.9)	0.001 ^{a,b,c}
ApoE ε4 carrier				
(+)	8(16%)	12(24%)	24(48%)	0.001 ^{b,c}
(-)	42(84%)	38(76%)	26(52%)	

Abbreviations: MMSE: Mini Mental State Examination; MoCA: Montreal Cognitive

Assessment; HC: healthy control; MCI: mild cognitive impairment; AD: Alzheimer’s disease.

The expressed outside the parenthesis of the different values was the mean value, and the inside means the SD value. $p < 0.05$: “a”: HC vs MCI; “b”: HC vs AD ; “c” : MCI vs AD. One-way ANOVA with the least significant difference post-hoc test, chi-squared and split chi-squared tests, and Cox proportional hazards model were used.

Supplementary Table 4. Evaluations of MCI non-convertors and convertors in the follow-up from CABLE cohort

	MCI-nc (n=24)	MCI-c (n=26)	<i>p</i> value	HR (95% CI)
Age (y)	60.5(5.6)	63.1(6.8)	0.227	/
Gender				
Female	10(42%)	15(58%)	0.257	/
Male	14(58%)	11(42%)		/
Education (y)	14.2(3.1)	12.5(2.8)	0.402	/
Predictive biomarker				
CSFsTREM2 (pg/ml)				
≥18000	11(46%)	5(20%)	0.034^a	3.65
< 18000	13(54%)	21(80%)		(1.65-7.64) ^a
CSF Aβ ₁₋₄₂ (pg/ml)				
<215	11(46%)	20(77%)	0.027^a	3.84
≥215	13(54%)	6(23%)		(1.73-9.28) ^a
ApoE ε4 carrier				
(+)	5(21%)	7(27%)	0.615 ^a	1.35
(-)	19(79%)	19(73%)		(0.41-5.68) ^a

a: Student's t test, chi-squared, and Cox proportional hazards model were used, and all results were adjusted for P-Tau/T-Tau, age and gender. The expressed outside the parenthesis of the different values was the mean value, and the inside means the SD value.

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II. DOD ADNI

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