

**Supplementary Table 1.** Demographic information of the total sample at 3 and 4-year follow-up.

<b>Study</b>	<b>Diagnostic Group</b>	<b>Number</b>	<b>Gender (M/F)</b>	<b>Age (years)</b>	<b>MMSE Score</b>	<b>APOE <math>\epsilon</math>4 (Heterozygote / Homozygote)</b>
ADNI1	sMCI-3y	100	68/32	74.4 [55-88]	28 [24-30]	37/4
	pMCI-3y	108	59/49	75.0 [56-88]	27 [23-30]	59/20
	sMCI-4y	56	41/15	74.9 [60-86]	28 [24-30]	22/2
	pMCI-4y	122	69/53	74.6 [55-88]	27 [23-30]	64/21
ADNIGO/2	sMCI-3y	52	27/25	70.6 [55-85]	28.5 [25-30]	15/5
	pMCI-3y	48	27/21	73.0 [57-85]	26 [24-30]	24/10
	sMCI-4y	39	20/19	71.0 [55-85]	29 [25-30]	13/3
	pMCI-4y	51	28/23	72.7 [57-85]	27 [24-30]	25/10

**Model Equations.** Model equations for ADNI1 (1.5T) and ADNIGO/2 (3T) of hippocampus, entorhinal cortex and MRI combined models. The derived index has the following structure

$$\mu = a_0 + a_1 \cdot Age + a_2 \cdot TIV + a_3 \cdot HC + a_4 \cdot Ento$$

where Age stands for patient age in years, TIV as total intracranial volume in liters, HC is the hippocampal volume in  $mm^3$  and Ento is the entorhinal cortex volume in  $mm^3$ .  $a_i$  are the coefficients for each model. A patient is classified as non-AD if  $\mu \leq t$ , being  $t$  the threshold derived by requiring 85% sensitivity in mild AD detection. All these parameters are presented in the following table:

Model	$a_0$	$a_1$	$a_2$	$a_3$	$a_4$	$t$
Hippocampus (1.5T)	16,5540200293699	-0,125098962265963	4,90075950015938	-0,00218579393149564		-0,189493300236705
Hippocampus (3T)	15,0083668957070	-0,109003838384900	5,94285958979306	-0,00228561258743557		-0,1288841986170784
Entorhinal C. (1.5T)	9,78924572370382	-0,0733882412558537	4,06286198139163		-0,00306863312750679	-0,206346173072900
Entorhinal C. (3T)	3,79931957433598	-0,0297481699372104	6,99499129948445		-0,00340811929972149	-0,390072193310068
MRI model (1.5T)	17,6867818108503	-0,128584764860547	6,23975126435520	-0,00156931758995348	-0,00202264730414833	0,0820047210224786
MRI model (3T)	15,8173032270286	-0,122034153919801	9,30690418085413	-0,00180448281018123	-0,00228877290486069	-0,167674233421213

## MCI classification with sMRI

### ADNI 1

**Supplementary Table 2.** AUC, Sensitivity and Specificity for ADNI1 MCI participants at 2-5-year follow-up.

Biomarker	AUC (% [95%CI])		Sensitivity (% [95%CI])		Specificity (% [95%CI])	
	2y	3y	2y	3y	2y	3y
Hippocampus	72 [65-78]	73 [66-79]	86 [78-93]	81 [73-88]	49 [40-58]	52 [42-62]
Entorhinal C.	70 [63-76]	74 [67-80]	76 [66-85]	77 [68-84]	52 [43-61]	59 [49-69]
MRI Model	73 [66-78]	76 [70-82]	81 [71-88]	79 [70-86]	57 [48-65]	64 [54-73]

Biomarker	AUC (% [95%CI])		Sensitivity (% [95%CI])		Specificity (% [95%CI])	
	4y	5y	4y	5y	4y	5y
Hippocampus	78 [71-83]	80 [74-86]	80 [72-87]	80 [72-87]	61 [47-74]	64 [48-77]
Entorhinal C.	79 [72-85]	81 [75-87]	75 [67-83]	76 [67-83]	66 [52-78]	72 [57-84]
MRI Model	81 [75-87]	84 [78-90]	77 [66-84]	77 [69-84]	71 [58-83]	74 [60-86]

**Supplementary Table 3. (Subanalysis 1)** Proportions of correctly classified [95%CI] short and mid-term ADNI1 MCI converters for each sMRI model.

Converter type \ Model	Hippocampus (% [95%CI])	Entorhinal Cortex (% [95%CI])	MRI model (% [95%CI])
Short-term	86 [78-93]	76 [66-85]	81 [71-88]
Mid-term	65 [48-80]	76 [59-88]	68 [50-82]

**Supplementary Table 4. (Subanalysis 2)** Proportions of correctly classified [95%CI] stable ADNI1 MCI with follow-up times shorter than 5 years for each sMRI model versus stable over 5 years.

sMCI type \ Model	Hippocampus (% [95%CI])	Entorhinal Cortex (% [95%CI])	MRI model (% [95%CI])
< 5 years	41 [31-52]	41 [31-52]	47 [36-58]
5 years	64 [48-77]	72 [57-84]	74 [60-86]

**Supplementary Table 5. (Subanalysis 3)** AUCs for the comparison between ADNI1 sMCI during at least 5 years (excluding those sMCI stable during at least 5 years) and short-term MCI converters and the comparison between sMCI during at least 5 years (excluding those sMCI stable during at least 5 years) and mid-term MCI.

Comparison \ Model	Hippocampus (% [95%CI])	Entorhinal Cortex (% [95%CI])	MRI model (% [95%CI])
Short-term	83 [76-89]	82 [74-88]	85 [79-92]
Mid-term	74 [64-83]	81 [72-91]	82 [74-91]

## ADNI2

**Supplementary Table 6.** AUC, Sensitivity and Specificity for ADNI2 MCI participants at 2-5-year follow-up.

Biomarker	AUC (% [95%CI])		Sensitivity (% [95%CI])		Specificity (% [95%CI])	
	2y	3y	2y	3y	2y	3y
Hippocampus	74 [64-82]	74 [64-82]	77 [62-88]	77 [63-88]	51 [39-64]	56 [41-70]
Entorhinal C.	68 [58-76]	70 [60-79]	80 [65-90]	81 [67-91]	44 [31-57]	46 [32-60]
MRI Model	74 [64-82]	76 [66-84]	82 [67-92]	81 [67-91]	55 [42-67]	58 [43-71]

Biomarker	AUC (% [95%CI])		Sensitivity (% [95%CI])		Specificity (% [95%CI])	
	4y	5y	4y	5y	4y	5y
Hippocampus	78 [68-86]	79 [68-88]	76 [62-87]	76 [62-87]	62 [45-77]	62 [41-81]
Entorhinal C.	70 [60-80]	73 [62-83]	82 [69-92]	82 [69-92]	49 [32-65]	54 [33-74]
MRI Model	78 [68-86]	80 [69-88]	80 [67-90]	80 [67-90]	62 [45-77]	67 [45-84]

**Supplementary Table 7. (Subanalysis 1)** Proportions of correctly classified [95%CI] short and mid-term ADNI2 MCI converters for each sMRI model.

Converter type \ Model	Hippocampus (% [95%CI])	Entorhinal Cortex (% [95%CI])	MRI model (% [95%CI])
Short-term	77 [62-88]	80 [65-90]	82 [67-92]
Mid-term	71 [29-96]	100 [59-100]	71 [29-96]

**Supplementary Table 8. (Subanalysis 2 )** Proportions of correctly classified [95%CI] stable ADNI2 MCI with follow-up times shorter than 5 years for each sMRI model versus stable over 5 years.

<b>sMCI type \ Model</b>	<b>Hippocampus (% [95%CI])</b>	<b>Entorhinal Cortex (% [95%CI])</b>	<b>MRI model (% [95%CI])</b>
< 5 years	45 [29-62]	38 [23-54]	48 [38-56]
5 years	62 [41-81]	54 [33-74]	67 [45-84]

**Supplementary Table 9. (Subanalysis 3)** AUCs for the comparison between ADNI2 sMCI during at least 5 years (excluding those sMCI stable during at least 5 years) and short-term MCI converters and the comparison between sMCI during at least 5 years (excluding those sMCI stable during at least 5 years) and mid-term MCI.

<b>Comparison \ Model</b>	<b>Hippocampus (% [95%CI])</b>	<b>Entorhinal Cortex (% [95%CI])</b>	<b>MRI model (% [95%CI])</b>
Short-term	81 [69-89]	73 [60-83]	80 [69-92]
Mid-term	71 [52-85]	76 [59-94]	79 [62-96]

### *Pooled ADNI1 and ADNI2*

**Supplementary Table 10.** Pooled results of Supplementary Tables 8 and 12, along with chi-square p-values of the comparison.

<b>Converter type \ Model</b>	<b>Hippocampus (% [95%CI]) (p = 0.013)</b>	<b>Entorhinal Cortex (% [95%CI]) (p = 0.77)</b>	<b>MRI model (% [95%CI]) (p=0.072)</b>
Short-term	83 [76-89]	77 [69-84]	81 [73-87]
Mid-term	65 [50-79]	80 [66-90]	67 [52-80]

**Supplementary Table 11.** Pooled results of Supplementary Tables 9 and 13, along with chi-square p-values of the comparison.

<b>sMCI type \ Model</b>	<b>Hippocampus (% [95%CI]) (p = 0.005)</b>	<b>Entorhinal Cortex (% [95%CI]) (p &lt; 0.001)</b>	<b>MRI model (% [95%CI]) (p &lt; 0.001)</b>
< 5 years	43 [34-52]	40 [32-49]	47 [38-56]
5 years	63 [51-74]	66 [54-77]	71 [60-81]

**Supplementary Table 12.** Pooled results of Supplementary Tables 10 and 14.

<b>Model</b> <b>Comparison</b>	<b>Hippocampus</b> <b>(% [95%CI])</b>	<b>Entorhinal Cortex</b> <b>(% [95%CI])</b>	<b>MRI model</b> <b>(% [95%CI])</b>
Short-term	82 [76-88]	79 [73-86]	84 [78-90]
Mid-term	74 [64-83]	80 [72-88]	82 [74-89]