

**Supplementary material**

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**Supplementary Table 1. Items included in the frailty index (N = 45)**

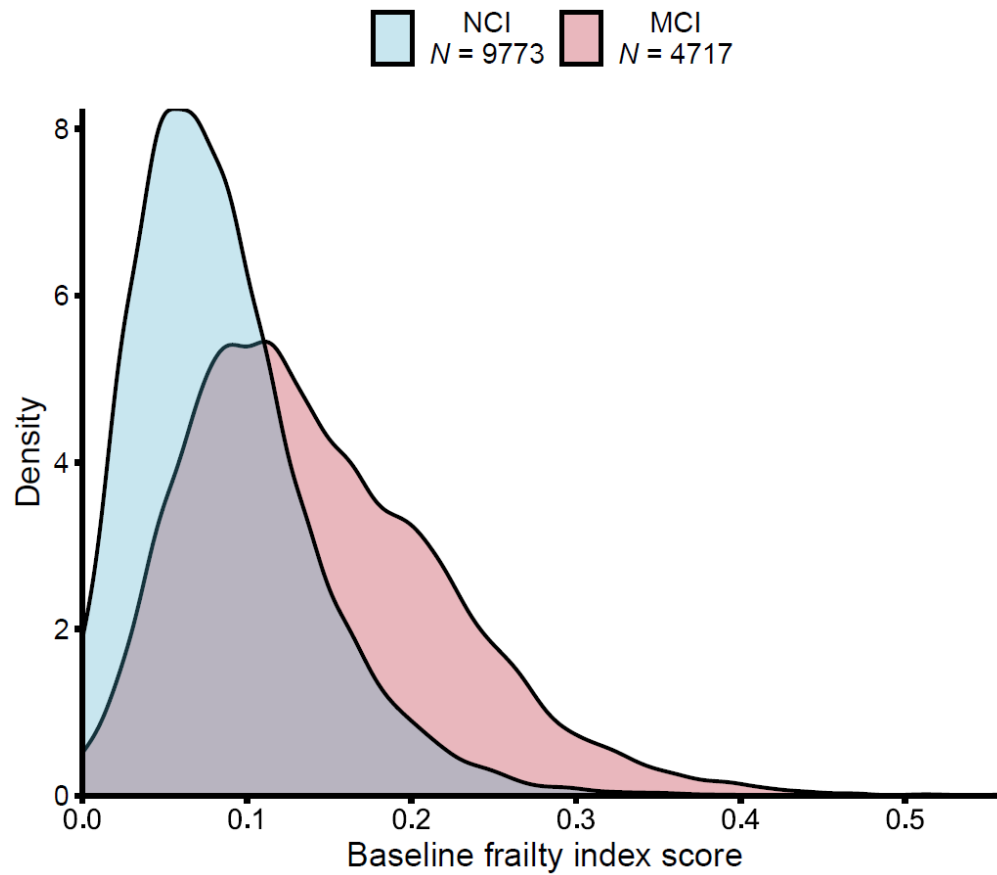
Diagnosis of depression *	Abnormal vision
Delusions in the last month *	Abnormal hearing
Hallucinations in the last month *	Diabetes
Agitation or aggression in the last month *	Hypercholesterolemia
Anxiety in the last month *	Vitamin B12 deficiency
Apathy or indifference in the last month *	Thyroid disease
Disinhibition in the last month *	Incontinence (urinary)
Irritability or lability in the last month *	Incontinence (bowel)
Night-time behaviours in the last month *	Difficulty with paying bills
Psychiatric disorder *	Difficulty with shopping
History of seizures	Difficulty with meal preparation
Not satisfied with life	Difficulty remembering appointments *
Lacking energy	Difficulty with transportation
Appetite and eating problems in the last month	Difficulty with community affairs
Hypertension	History of traumatic brain injury
Heart attack	Motor function (falls)
Atrial fibrillation	Motor function (slowness)
Heart failure	Difficulty arising from a chair
Other cardiovascular disease	Difficulty with postural stability
Diagnosis of stroke	Abnormal posture
Low body massive index	Abnormal gait
Focal neurological symptoms *	Somatic complaints
Focal neurological signs *	

Note: Health deficits marked with an asterisk were excluded from the calculation of the reduced sensitivity frailty index.

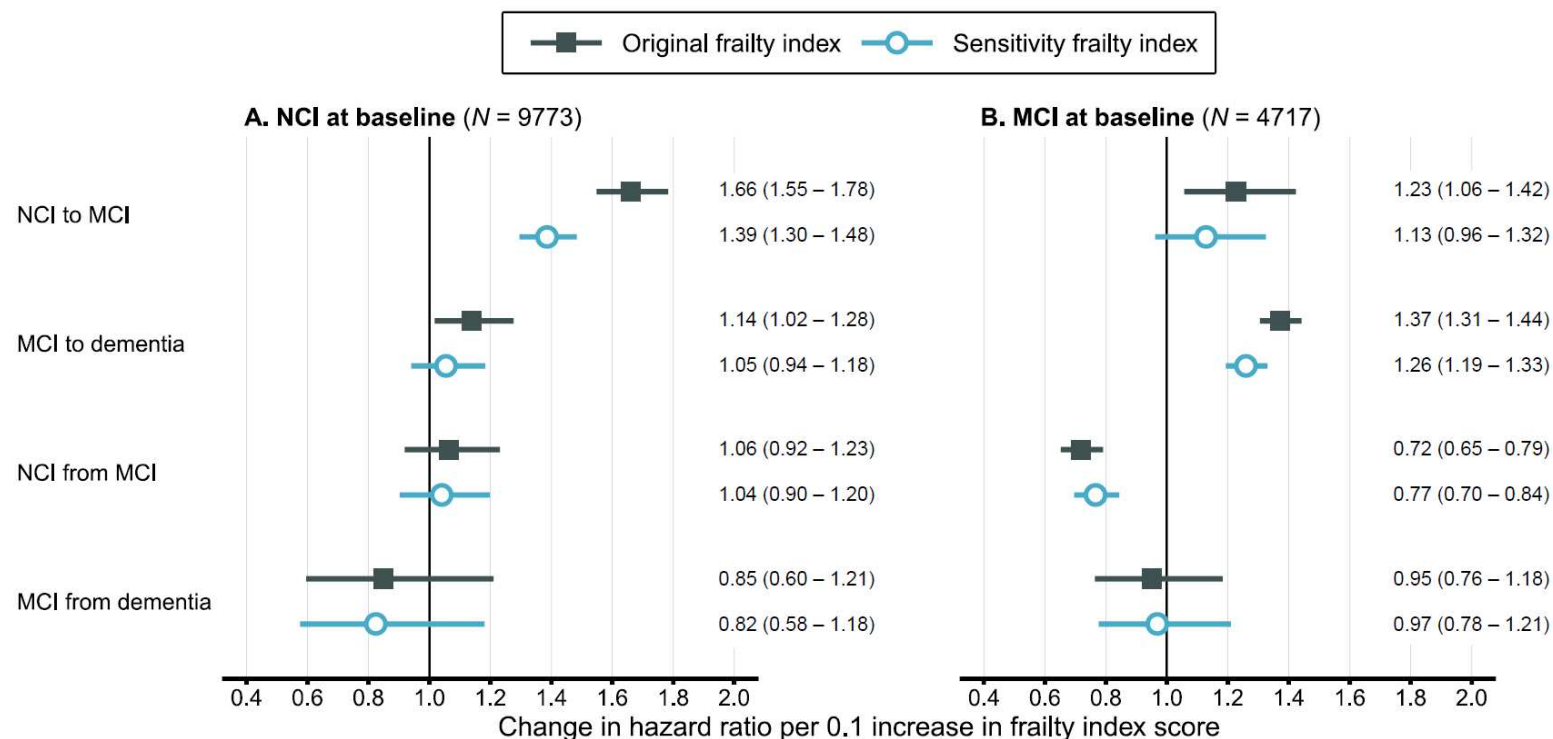
**Supplementary Table 2. Association of study variables with transition probabilities**

Subsample	Transition	Hazard ratio (95% confidence interval)				
		Frailty index score (per 0.1 increase)	Age (per year increase)	Male sex (vs. female sex)	Education (per year increase)	APOE ε4+ (vs. non-carrier)
NCI at baseline	NCI to MCI	<b>1.66 (1.55 - 1.78)</b>	<b>1.06 (1.06 - 1.07)</b>	<b>1.19 (1.12 - 1.26)</b>	<b>0.98 (0.96 - 0.99)</b>	<b>1.41 (1.30 - 1.54)</b>
	MCI to dementia	<b>1.14 (1.02 - 1.28)</b>	<b>1.04 (1.03 - 1.05)</b>	0.99 (0.89 - 1.10)	0.99 (0.97 - 1.02)	<b>1.48 (1.26 - 1.73)</b>
	NCI from MCI	1.06 (0.92 - 1.23)	<b>0.97 (0.96 - 0.98)</b>	<b>1.14 (1.01 - 1.28)</b>	1.01 (0.98 - 1.04)	<b>0.72 (0.60 - 0.87)</b>
	MCI from dementia	0.85 (0.60 - 1.21)	<b>0.95 (0.92 - 0.98)</b>	1.16 (0.84 - 1.61)	1.00 (0.93 - 1.08)	0.65 (0.41 - 1.05)
	NCI to death	<b>1.49 (1.26 - 1.77)</b>	<b>1.10 (1.08 - 1.11)</b>	<b>1.22 (1.06 - 1.42)</b>	0.97 (0.94 - 1.00)	0.84 (0.64 - 1.09)
	MCI to death	1.05 (0.76 - 1.47)	<b>1.11 (1.08 - 1.15)</b>	1.19 (0.86 - 1.66)	1.01 (0.94 - 1.09)	0.78 (0.37 - 1.63)
	Dementia to death	<b>1.20 (1.04 - 1.37)</b>	<b>1.04 (1.03 - 1.06)</b>	<b>1.18 (1.02 - 1.36)</b>	1.01 (0.98 - 1.04)	0.98 (0.79 - 1.22)
MCI at baseline	NCI to MCI	<b>1.23 (1.06 - 1.42)</b>	<b>1.04 (1.03 - 1.05)</b>	1.00 (0.86 - 1.15)	0.99 (0.95 - 1.02)	1.13 (0.92 - 1.40)
	MCI to dementia	<b>1.37 (1.31 - 1.44)</b>	<b>1.03 (1.02 - 1.03)</b>	1.02 (0.96 - 1.08)	1.01 (1.00 - 1.02)	<b>1.55 (1.43 - 1.69)</b>
	NCI from MCI	<b>0.72 (0.65 - 0.79)</b>	<b>0.98 (0.97 - 0.98)</b>	<b>0.89 (0.81 - 0.98)</b>	1.02 (1.00 - 1.04)	<b>0.64 (0.56 - 0.73)</b>
	MCI from dementia	0.95 (0.76 - 1.18)	0.98 (0.96 - 1.00)	0.98 (0.78 - 1.24)	<b>0.95 (0.90 - 1.00)</b>	<b>0.57 (0.41 - 0.80)</b>
	NCI to death	0.99 (0.59 - 1.68)	<b>1.14 (1.10 - 1.19)</b>	<b>1.72 (1.02 - 2.91)</b>	1.05 (0.95 - 1.17)	0.76 (0.34 - 1.67)
	MCI to death	1.46 (0.68 - 3.14)	<b>1.16 (1.03 - 1.31)</b>	1.38 (0.44 - 4.28)	0.92 (0.78 - 1.08)	0.74 (0.13 - 4.28)
	Dementia to death	<b>1.17 (1.09 - 1.27)</b>	<b>1.04 (1.03 - 1.05)</b>	<b>1.28 (1.16 - 1.40)</b>	0.99 (0.97 - 1.01)	<b>0.80 (0.70 - 0.92)</b>

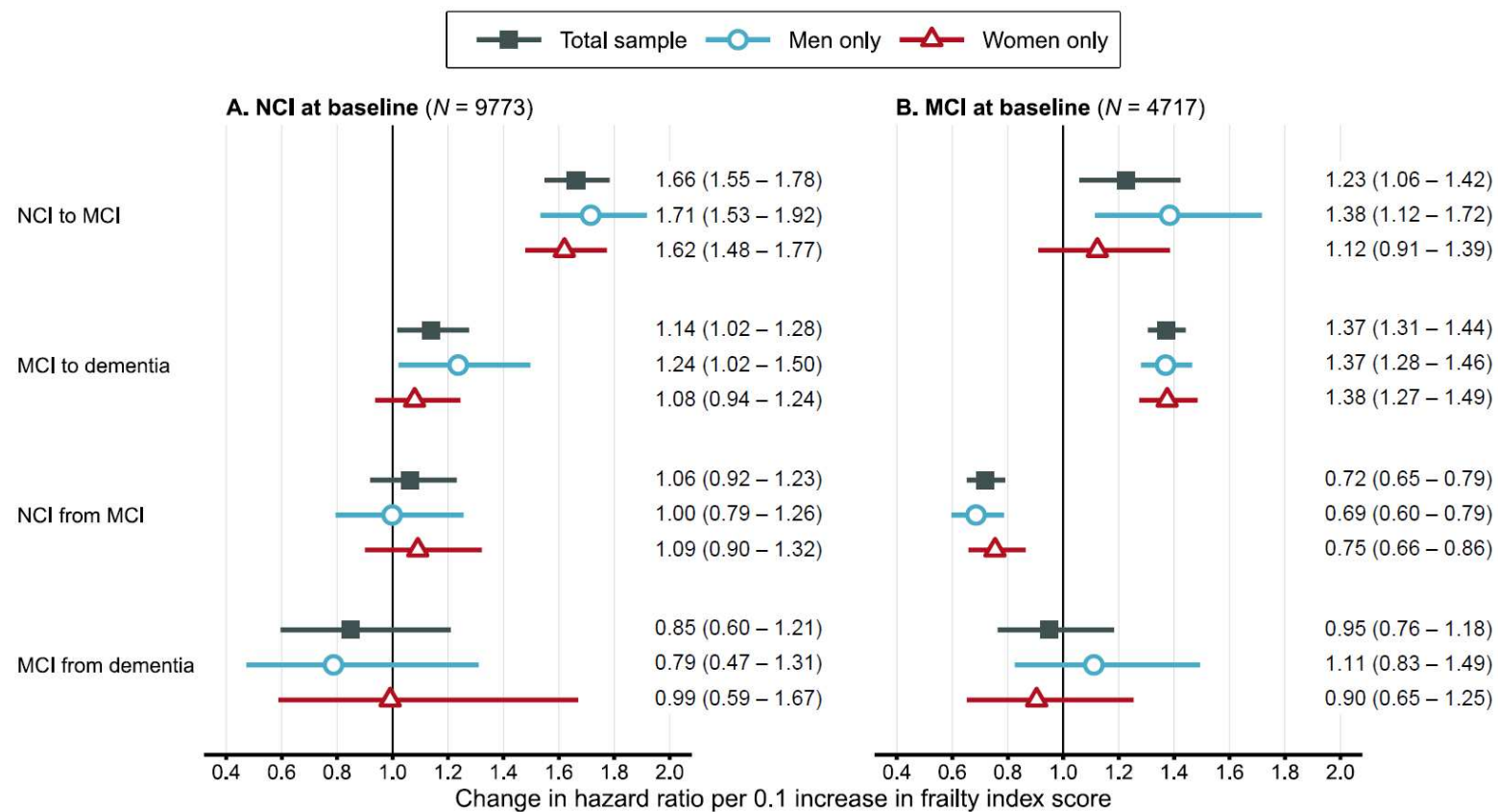
Note: Values were derived from multi-state transition models stratified by baseline cognitive status. NCI, not cognitively impaired; MCI, mild cognitive impairment. Bolded values denote statistically significant values (confidence interval does not include 1.00).



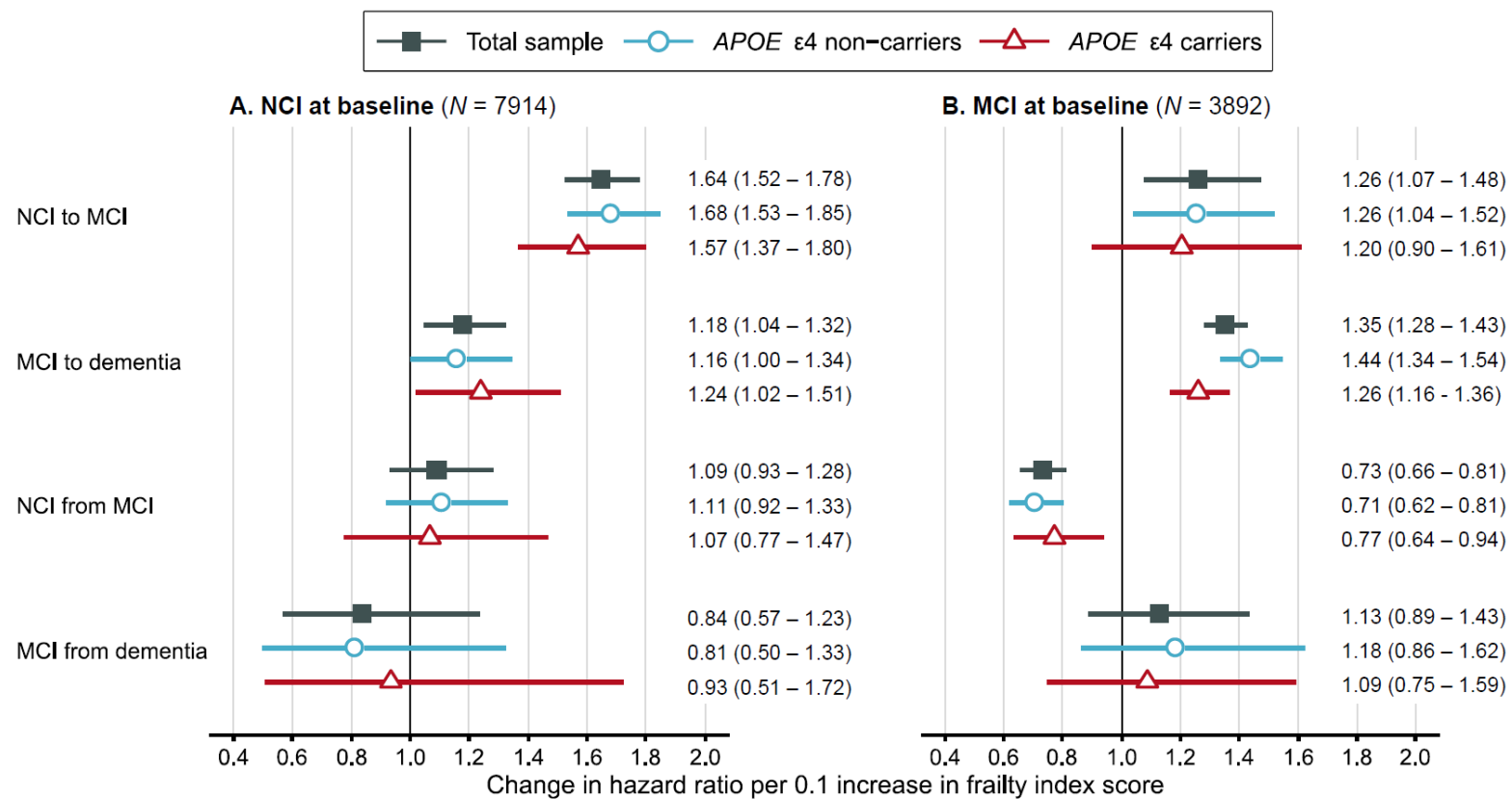
**Supplementary Figure 1. The distribution (density plot) of the frailty index score at baseline.** NCI, not cognitively impaired; MCI, mild cognitive impairment.



**Supplementary Figure 2. Results of the first sensitivity analysis.** Associations were calculated using the original frailty index and using a frailty index with items that might represent early symptoms of dementia removed from its calculation (sensitivity frailty index). Hazard ratios were calculated from multi-state transition models stratified by baseline cognitive status and presented with 95% confidence intervals. Associations were adjusted for age at study entry, sex, education level and *APOE*  $\epsilon$ 4 allelic status. NCI, not cognitively impaired; MCI, mild cognitive impairment; HR, hazard ratio; CI, confidence interval.



**Supplementary Figure 3. Results of the second sensitivity analysis.** Associations for men and women were calculated in separate stratified models. Hazard ratios were calculated from multi-state transition models stratified by baseline cognitive status and presented with 95% confidence intervals. Associations were adjusted for age at study entry, education level and *APOE*  $\epsilon 4$  allelic status. NCI, not cognitively impaired; MCI, mild cognitive impairment; HR, hazard ratio; CI, confidence interval.



**Supplementary Figure 4. Results of the third sensitivity analysis.** Associations for *APOE* ε4 carriers and non-carriers were calculated after the removal of participants whose race was other than White. Hazard ratios were calculated from multi-state transition models stratified by baseline cognitive status and presented with 95% confidence intervals. Associations were adjusted for age at study entry, sex, and education level. NCI, not cognitively impaired; MCI, mild cognitive impairment; HR, hazard ratio; CI, confidence interval.