eAppendix 1

The following acquisition parameters were used to acquire structure MRI 3D T1-weighted images: 1.5T Siemens Avanto (n=5): Magnetization prepared rapid acquisition gradient echo (MPRAGE), coronal plane, repetition time (TR) 2700 ms, echo time (TE) 5.2 ms, inversion time (TI) 950 ms, flip angle (FA) 8°, voxel size 1×1×1.5 mm^3; 3T GE Discovery MR750 (n=9): FSPGR, sagittal plane, TR 7.8 ms, TE 3ms, FA 12°, voxel size 1 mm^3; 1T Siemens Magnetom Impact (n=106): MPRAGE, coronal plane, TR 15 ms, TE 7 ms, TI 300 ms, FA 15°, voxel size 1×1×1.5 mm^3; 3T Philips Ingenuity PET/MR system (n=47): sagittal turbo field echo (TFE), sagittal plane, TR 7 ms, TE 3 ms, FA 12°, voxel size 1×1×1 mm^3; 1.5T GE SignaHDxt (n=8): sagittal fast spoiled gradient echo (FSPGR), sagittal plane, TR 12.4 ms, TE 5.17 ms, TI 450 ms, FA 12°, voxel size 0.98×0.98×1.5 mm^3; 3T GE SignaHDxt (n=119): FSPGR, sagittal plane, TR 708 ms, TE 7 ms, FA 12°, voxel size 0.98×0.98×1 mm^3; 1.5T Siemens Sonata (n=18): MPRAGE, coronal plane, TR 2700 ms, TE 3.97 ms, TI 950 ms, FA 8°, voxel size 1×1×1.5 mm^3; Toshiba Titan 3T (n=53): sagittal fast field echo (FFE) sequence (TR = 9, TE = 3, TI = 800, FA = 7°, 1.00 x 1.00 x 1.00 mm voxels); 1.5T Siemens Vision (n=1): MPRAGE, coronal plane, TR 15 ms, TE 7 ms, FA 8°, voxel size 0.98×0.98×1.5 mm^3.

eTable 1. Risk of MCI or dementia for continuous N biomarkers for complete cases

		Model 1	Model 2	Model 3	Model 4
Biomarker	n	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
T-tau	256	2.26 (1.74 - 2.94)[a,b]	1.98 (1.47 - 2.67)[a,b]	1.57 (1.16 - 2.11)[a,b]	
MTA	256	1.53 (1.16 - 2.02)[a,b]	1.18 (0.86 - 1.62)	1.00 (0.72 - 1.39)	1.01 (0.72 - 1.40)
HV	256	1.65 (1.18 - 2.30)[a,b]	1.52 (1.06 - 2.18)[a,b]	1.47 (1.04 - 2.07)[a,b]	1.52 (1.06 - 2.16)[a,b]
NfL	256	1.83 (1.40 - 2.39)[a,b]	1.49 (1.04 - 2.13)[a,b]	1.30 (0.86 - 1.94)	1.31 (0.87 - 1.98)
GFAP	256	2.47 (1.80 - 3.38)[a,b]	2.08 (1.45 - 2.99)[a,b]	1.49 (1.00 - 2.22)[a]	1.43 (0.96 - 2.12)

Data shown are hazard ratio (95% confidence interval) as estimated by Cox proportional hazards analyses (outcome: clinical progression to mild cognitive impairment or dementia). Predictors included differed per model (model 1: neurodegeneration biomarker; model 2: neurodegeneration biomarker, age and sex; model 3: abeta, neurodegeneration biomarker, age and sex; model 4: abeta, p-tau, neurodegeneration biomarker, age and sex). In models with MTA and HV, scanner type was additionally added as covariate. P-tau, t-tau, NfL and GFAP were log transformed, abeta and hippocampal volume were inverted, all biomarkers were z-transformed. MTA = medial temporal atrophy, HV = hippocampal volume, NfL = neurofilament light, GFAP = glial fibrillary acidic protein. [a] p-value < 0.05. T-tau was not entered in model 4 due to collinearity between t-tau and p-tau. [b] FDR corrected p-value < 0.05.

eTable 2. Risk of cognitive decline for continuous N biomarkers for complete cases

	Model 5	Model 6	Model 7	Model 8
Biomarker	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)
T-tau	-0.22 (0.04)[a,b]	-0.22 (0.05)[a,b]	-0.20 (0.05)[a,b]	
MTA	-0.07 (0.06)	-0.06 (0.06)	-0.04 (0.06)	-0.03 (0.06)
HV	-0.15 (0.05)[a,b]	-0.18 (0.05)[a,b]	-0.17 (0.05)[a,b]	-0.17 (0.05)[a,b]
NfL	-0.09 (0.05)	-0.07 (0.06)	-0.04 (0.07)	-0.03 (0.06)
GFAP	-0.18 (0.05)[a,b]	-0.17 (0.06)[a,b]	-0.13 (0.06)[a]	-0.11 (0.06)

Results shown are beta (SE) as estimated by linear mixed models. Outcome is MMSE score. Predictors: model 5: neurodegeneration, time, neurodegeneration*time; model 6: variables included in model 5, age, sex, age*time and sex*time; model 7: variables included in model 6, CSF abeta and abeta*time; model 8: variables included in model 7, CSF p-tau and p-tau*time). In models with MTA and HV, scanner type was additionally added as covariate. Betas represent the interaction between neurodegeneration biomarker and time, which corresponds to the cognitive slope. P-tau, t-tau, NfL and GFAP were log transformed, abeta and hippocampal volume ere inverted, all biomarkers were z-transformed. MTA = medial temporal atrophy, HV = hippocampal volume, NfL = neurofilament light, GFAP = glial fibrillary acidic protein. T-tau was not entered in model 4 due to collinearity between t-tau and p-tau. [a] p-value < 0.05. [b] FDR corrected p-value < 0.05.