SUPPLEMENTARY MATERIAL

Supplementary Table 1. Participant characteristics at last visit by Hippocampal Sclerosis of aging and Alzheimer's disease neuropathology (N=1,422), which is operationalized using a relative sensitive method AD-NP(I) which includes Braak stages III and IV.

Characteristic	No HS-Aging Pathology		HS-Aging Pathology Present	
	No AD-NP(I) (n=425)	Yes AD-NP(I) (n=879)	No AD-NP(I) (n=30)	Yes AD-NP(I) (n=88)
	N (%)		N(%)	
Age at death (years)				
70-79	78 (18.4)	267 (30.4)	4 (13.3)	14 (15.9)
80-89	165 (38.8)	418 (47.6)	9 (30.0)	49 (55.7)
90+	182 (42.8)	194 (22.1)	17 (56.7)	25 (28.4)
Sex				
Female	204 (48.0)	398 (45.3)	14 (46.7)	42 (47.7)
Race†				
White	409 (96.5)	837 (95.2)	28 (93.3)	79 (89.8)
Black	7 (1.7)	30 (3.4)	1 (3.3)	7 (8.0)
Other	8 (1.9)	12 (1.4)	1 (3.3)	2 (2.3)
Hispanic ethnicity*	17 (4.0)	31 (3.5)	2 (6.7)	2 (2.3)
Education*				
College graduate	238 (56.0)	476 (54.8)	19 (67.9)	49 (56.3)
Family History of Dementia*				
Yes	123 (36.0)	345 (53.6)	7 (29.2)	31 (53.5)
APOE ε4 alleles*				
0	236 (77.1)	271 (41.6)	16 (76.2)	22 (38.0)
1	63 (20.6)	297 (45.6	5 (23.8)	28 (47.5)
2	7 (2.3)	83 (12.8)	0 (0.0)	9 (15.3)
Cognitive status				
Demented	189 (44.5)	772 (87.8)	21 (70.0)	86 (97.7)
Primary clinical diagnosis				
Probable AD	95 (22.4)	585 (66.6)	18 (60.0)	80 (90.9)
Possible AD	40 (9.4)	94 (10.7)	6 (20.0)	3 (3.4)
Normal	167 (39.3)	45 (5.1)	2 (6.7)	1 (1.1)
Other	123 (28.9)	155 (17.6)	4 (13.3)	4 (4.6)
	Mean (SD)		Mean (SD)	
Number of visits to ADC	2.6 (1.4)	2.2 (1.3)	2.9 (1.9)	2.5 (1.4)
Age of onset † (years)*	80.3 (11.2)	74.3 (8.6)	82.0 (10.3)	74.3 (7.9)
Duration of cognitive symptoms† (years)*	6.0 (4.1)	8.9 (4.2)	6.9 (3.6)	10.9 (4.2)
CDR-SB at last visit	4.5 (5.5)	11.6 (6.0)	6.8 (5.8)	14.3 (4.9)

Abbreviations: AD-NP (I), "intermediate to moderate" Alzheimer's disease neuropathology (Braak Stages III- VI and "moderate" or "frequent" CERAD neuritic plaque frequency); CDR-SB, Clinical Dementia Rating "sum of boxes"; HS-Aging, Hippocampal Sclerosis of Aging. *Missing data: race (n=1, <1%), ethnicity (n=4, <1%), education (n=14, <1%), family history (n=354, 25.2%), APOE ε4 (385, 27.1%), and symptom duration (n=46, 3.7%). † Among participants with MCI or dementia (n=1,227)

Supplementary Table 2. Comparison of Test Scores between Participants with or without HS-Aging and AD-NP (no HS-Aging pathology, no AD-NP chosen as the reference group).*

Neuropsychological or Clinical Test	β†	95% CI	*p*
CDR-SB‡ (N= 689)			
No HS-Aging, no AD-NP	---	---	**---**
No HS-Aging, yes AD-NP	-2.5	-3.1, -1.9	**<0.001**
Yes HS-Aging, no AD-NP	-.42	-1.88, 1.04	**0.57**
Yes HS-Aging, yes AD-NP	-3.85	-5.17, -2.54	**<0.001**
Animal Generation Test (N=609)			
No HS-Aging, no AD-NP	---	---	**---**
No HS-Aging, yes AD-NP	-2.52	-3.40, -1.64	**<0.001**
Yes HS-Aging, no AD-NP	-0.04	-2.12, 2.04	**0.97**
Yes HS-Aging, yes AD-NP	-3.23	-5.22, -1.23	**0.002**
Delayed Logical Memory (N=582)			
No HS-Aging, no AD-NP	---	---	**---**
No HS-Aging, yes AD-NP	-3.86	-4.60, -3.12	**<0.001**
Yes HS-Aging, no AD-NP	-3.32	-5.05, -1.60	**<0.001**
Yes HS-Aging, yes AD-NP	-3.99	-5.67, -2.30	**<0.001**

Abbreviations: CDR-SB, Clinical Dementia Rating "sum of boxes"; HS-Aging, Hippocampal Sclerosis of Aging; AD-NP, Alzheimer's disease neuropathology (Braak Stages V or VI and "moderate" or "frequent" CERAD neuritic plaque frequency).

*Based on linear regression of each test score from a visit 2-5 years prior to death among participants with mild to moderate cognitive impairment, and adjusted for age at death, education and years between visit and death.

†A positive β represents a higher functioning compared to participants with no HS-Aging pathology, no AD-NP (reference)

‡CDR-SB scores were inverted so that an increase in score =higher functioning

Supplementary Table 3. Comparison of Test Scores between Participants with or without HS-Aging and AD-NP(I).

Neuropsychological or Clinical Test	β†	95% CI	*p*
CDR-SB‡ (N= 689)			
Yes HS-Aging Pathology, No AD-NP(I)	---	---	**---**
No HS-Aging Pathology, No AD-NP(I)	0.0	-1.98, 1.99	**1.00**
No HS-Aging Pathology, Yes AD-NP(I)	-2.56	-4.50, -0.61	**0.01**
Yes HS-Aging Pathology, Yes AD-NP(I)	-3.73	-5.91, -1.56	**0.001**
Animals Generation Test (N=609)			
Yes HS-Aging Pathology, No AD-NP(I)	---	---	**---**
No HS-Aging Pathology, No AD-NP(I)	-0.86	-3.62, 1.90	**0.54**
No HS-Aging Pathology, Yes AD-NP(I)	-3.38	-6.08, -0.69	**0.01**
Yes HS-Aging Pathology, Yes AD-NP(I)	-4.16	-7.23, -1.09	**0.01**
Delayed Logical Memory (N=582)			
Yes HS-Aging Pathology, No AD-NP(I)	---	---	**---**
No HS-Aging Pathology, No AD-NP(I)	4.48	2.19, 6.78	**<0.001**
No HS-Aging Pathology, Yes AD-NP(I)	0.36	-1.88, 2.60	**0.75**
Yes HS-Aging Pathology, Yes AD-NP(I)	0.0	-2.57, 2.57	**1.00**

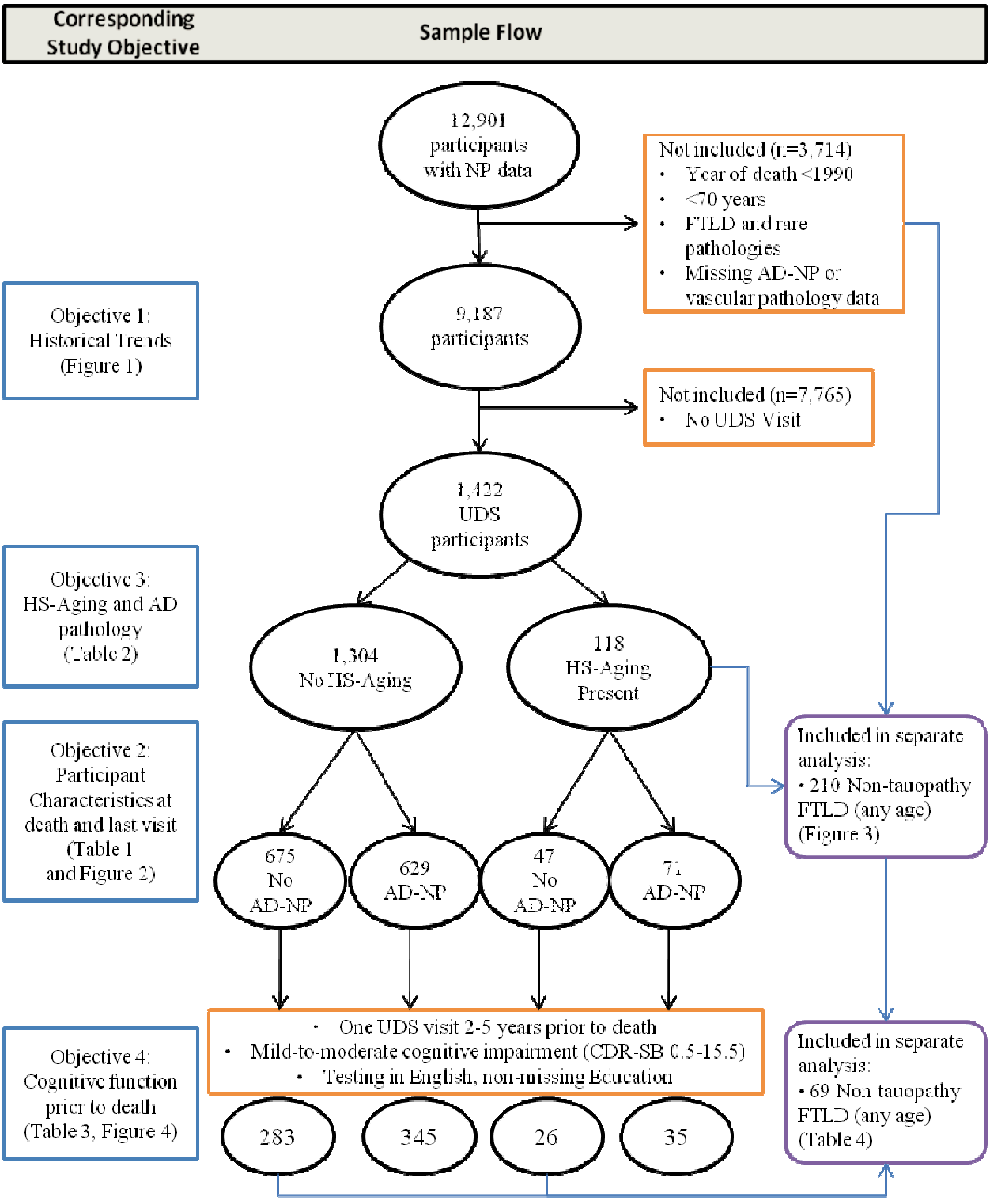
Abbreviations: CDR-SB, Clinical Dementia Rating "sum of boxes"; HS-Aging, Hippocampal Sclerosis of Aging; AD-NP (I), "intermediate to moderate" Alzheimer's disease neuropathology (Braak Stages III- VI and "moderate" or "frequent" CERAD neuritic plaque frequency).

*Based on linear regression of each test score from a visit 2-5 years prior to death among participants with mild to moderate cognitive impairment, and adjusted for age at death, education and years between visit and death.

†A positive β represents a higher functioning compared to participants with HS-Aging pathology, no AD-NP

‡CDR-SB scores were inverted so that an increase in score =higher functioning

Supplementary Figure 1. Study sample flow chart. *Abbreviations:* AD-NP, Alzheimer's disease neuropathology (Braak Stages V or VI and "moderate" or "frequent" CERAD neuritic plaque frequency); CDR-SB, Clinical Dementia Rating "sum of boxes"; FTLD, Frontoemporal lobar degeneration; HS-Aging, Hippocampal Sclerosis of Aging; NP; neuropathology; UDS, Uniform Data Set.



Supplementary Figure 2. Trends by age at death for pathological diagnoses in individuals with dementia. Shown are the primary or contributing pathological diagnosis of Hippocampal Sclerosis of Aging (HS-Aging), "intermediate/moderate" Alzheimer's disease neuropathology (AD-NP(I)), vascular disease, and Lewy bodies charted as a proportion of all pathological diagnoses among participants (70-103 years old at death) with dementia at last visit using fitted curves. (N=1,061).