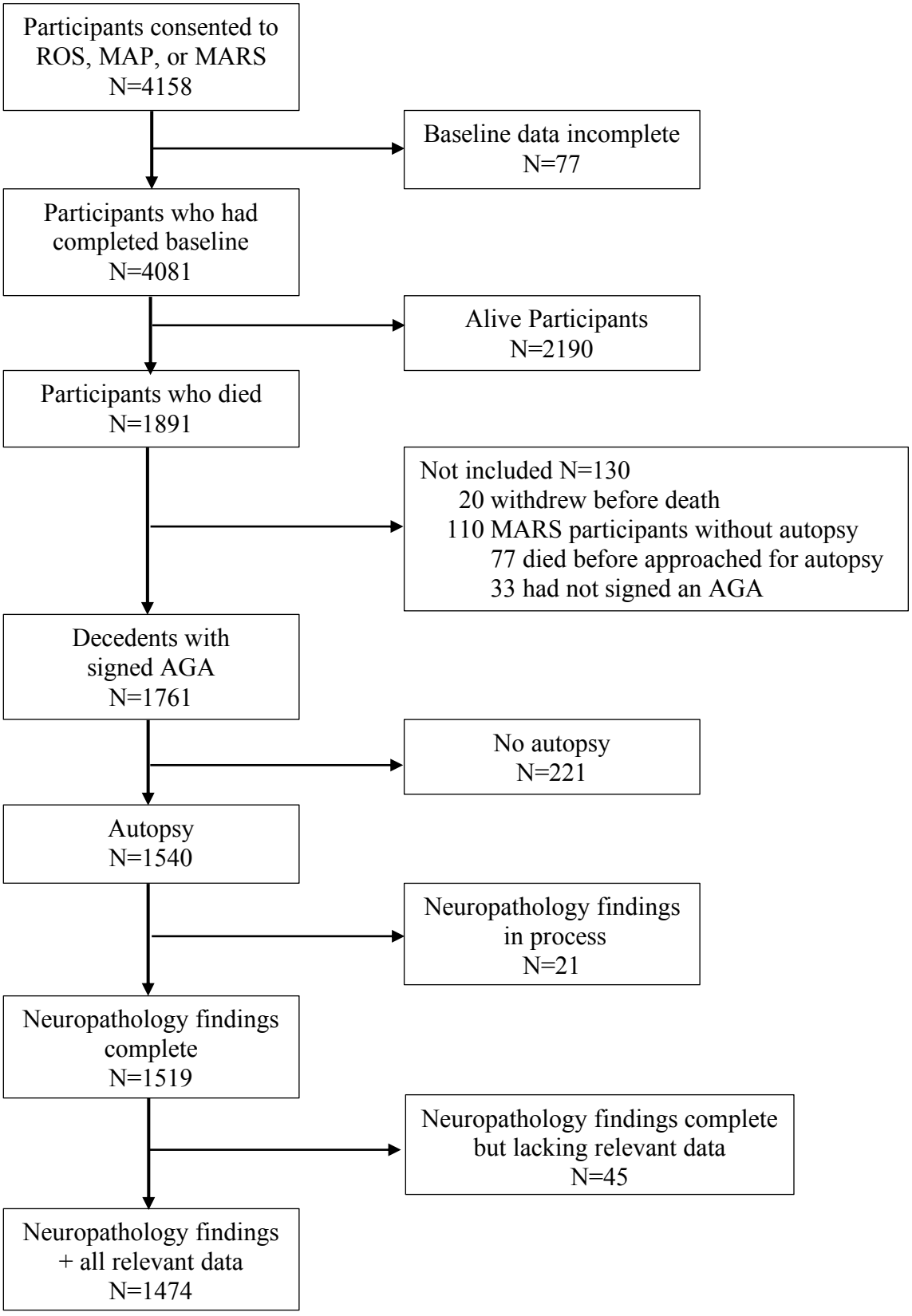
SUPPLEMENTAL MATERIAL

Supplemental Table I. Flow chart for analytic sample.



Supplemental Table II. Characteristics of single versus mixed CVD neuropathology groups

	Single CVD Pathology (n=442)	**Mixed CVD Pathology** (N=742)	**Reference Group** (n=290)
Demographics			
Age at death (years)^^^	88.2±6.9**	90.2±6.3***	86.9±6.9
Sex (% female)	65.3%	67.6%	69.3%
Education (years)	16.3±3.7	16.0±3.5*	16.5±3.5
Race (% white)	95.7%	95.9%**	92.7%
CVD-Related Neuropathology			
Arteriolosclerosis (mod to severe, %)	15.6%	50.3%	0%
Atherosclerosis (mod to severe, %)	16.9%	55.8%	0%
CAA (mod to severe, %)	33.4%	50.5%	0%
Macroinfarcts (one or more, %)	18.7%	60.1%	0%
Microinfarcts (one or more, %)	15.1%	49.4%	0%
AD-Related and Other Neuropathology			
NIA-Reagan Diagnosis of AD (high or intermediate, %)^^	59.7%	70.7%**	57.2%
Hippocampal Sclerosis (present with CA1 region affected, %)	8.1%	9.2%	5.2%
TDP-43 (neocortical, %)	13.9%	15.1%	8.8%
Lewy Bodies (neocortical, %)	13.1%	10.5%*	15.8%
Cognitive Scores			
Global Cognition^^^	-0.05±0.6	-0.23±0.7***	0.04±0.6
Episodic Memory^^^	-0.08±0.8	-0.29±0.8***	0.02±0.7
Semantic Memory^^^	-0.06±0.8	-0.25±0.9***	-0.01±0.9
Working Memory^^	-0.04±0.8	0.11±0.8**	0.08±0.8
Visuospatial Ability	-0.02±0.8	0.02±0.8*	0.10±0.7
Perceptual speed^^^	-0.09±0.8	-0.31±0.9***	0.007±0.9

all values equal mean±standard deviation unless otherwise noted; CVD=cerebrovascular disease; %=percent; CAA=cerebral amyloid angiopathy. ^$p<0.05$, ^^$p\leq0.01$, ^^^$p<0.0001$ for comparisons between single and mixed CVD pathology groups; *$p<0.05$, **$p\leq0.01$, ***$p<0.0001$ for comparisons between either the single or the mixed CVD pathology group (separately) and the reference group; comparisons involving AD-Related and Other Neuropathology were adjusted for age at death.

Supplemental Table III. Associations between single and mixed CVD neuropathology groups (in the same model) and decline in domain-specific cognitive functioning

	Cognitive Composite Score Outcomes unstandardized beta coefficient of interaction of stated group/pathology with time (95% confidence intervals)				
	Episodic Memory	Semantic Memory	Working Memory	Visuospatial Ability	Perceptual speed
all SINGLE CVD profiles	0.003 (0.003, 0.002)	-0.01 (-0.010, -0.009)	-0.01 (-0.010, -0.009)	-0.01 (-0.010, -0.009)	-0.01 (-0.010, -0.009)
all MIXED CVD profiles	**-0.03 (-0.030, -0.029)**	**-0.04 (-0.040, -0.039)**	**-0.02 (-0.020, -0.019)**	**-0.02 (-0.020, -0.019)**	**-0.03 (-0.030, -0.029)**
AD-Related and Other Neuropathology covariates:					
NIA-Reagan Diagnosis of AD	**-0.07 (-0.015, -0.004)**	**-0.07 (-0.087, -0.059)**	**-0.03 (-0.047, -0.024)**	**-0.03 (-0.042, -0.019)**	**-0.05 (-0.065, -0.037)**
Hippocampal Sclerosis	**-0.04 (--0.063, -0.015)**	**-0.06 (-0.093, -0.038)**	-0.01 (-0.033, 0.005)	-0.02 (-0.038, -.0006)	-0.01 (-0.043, 0.003)
TDP-43	**-0.02 (-0.029, -0.010)**	**-0.01 (-0.025, -0.010)**	**-0.008 (-0.013, -0.003)**	-0.004 (-0.009, 0.001)	**-0.01 (-0.016, -0.003)**
Neocortical Lewy Bodies	**-0.05 (-0.074, -0.036)**	**-0.07 (-0.098, -0.053)**	**-0.04 (-0.064, -0.033)**	**-0.03 (-0.050, -0.018)**	**-0.05 (-0.077, -0.040)**

NOTE: CVD=Cerebrovascular disease. Linear mixed effect regression model included terms for each of the 21 profiles listed in the table and their interactions with time (years before death), adjusting for age, sex, education, NIA-Reagan AD diagnosis, hippocampal sclerosis, TDP-43, neocortical Lewy bodies and their interactions with time. Bolded entries signify significance based on 95% confidence intervals and a corrected p-value$\leq$0.01.

STROBE statement: Reporting guidelines checklist for cohort, case-control and cross-sectional studies

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
TITLE AND ABSTRACT			
	1a	Indicate the study's design with a commonly used term in the title or the abstract	Page 1
	1b	Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2 to 3
INTRODUCTION			
Background and objectives	2	Explain the scientific background and rationale for the investigation being reported	Page 3 to 4
	3	State specific objectives, including any pre-specified hypotheses	Page 3 to 4
METHODS			
Study design	4	Present key elements of study design early in the paper	Page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4
Participants	6a	Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	Page 4
	6b	Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case Variables	n/a not a matched study; case and control details on page 10

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 4 to 8
Data sources/measurements	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.	Page 4 to 8
Bias	9	Describe any efforts to address potential sources of bias.	Page 8
Study size	10	Explain how the study size was arrived at	Pages 5 to 6 and page 10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why .	Page 6 to 9
Statistical methods	12a	Describe all statistical methods, including those used to control for confounding	Page 9
	12b	Describe any methods used to examine subgroups and interactions	Page 9
	12c	Explain how missing data were addressed	Page 5 to 6
	12d	Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	n/a cohort study
	12e	Describe any sensitivity analyses	n/a
RESULTS			
Participants	13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 5 to 6, page 10 to 12
	13b	Give reasons for non-participation at each stage	Page 5 to 6

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
	13c	Consider use of a flow diagram	n/a
Descriptive Data	14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	page 10 to 12
	14b	Indicate number of participants with missing data for each variable of interest	Page 5 to 6
	14c	Cohort study—Summarise follow-up time (eg, average and total amount)	Page 5
Outcome Data	15*	Cohort study—Report numbers of outcome events or summary measures over time Case-control study—Report numbers in each exposure category, or summary measures of exposure Cross-sectional study—Report numbers of outcome events or summary measures	Page 23 and Supplemental table
Main Results	16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 24 to 26, page 29
	16b	Report category boundaries when continuous variables were categorized	n/a
	16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
	16d	Report results of any adjustments for multiple comparisons	Page 9 to 13, page 24 to 26
Other Analyses	17a	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	n/a
	17b	If numerous genetic exposures (genetic variants) were examined, summarize results from all analyses undertaken	n/a
	17c	If detailed results are available elsewhere, state how they can be accessed	n/a

SECTION	ITEM NUMBER	CHECKLIST ITEM	REPORTED ON PAGE NUMBER:
DISCUSSION			
Key Results	18	Summarise key results with reference to study objectives	Page 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 14 to 18
Generalisability	21	Discuss the generalisability (external validity) of the study results Other information	Page 15
FUNDING			
	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.