Supplemental Data

METHODS:

Table e-3: White matter hyperintensities (WMH) were calculated using an automated algorithm designed to segment WMH volume, with manual editing to exclude infarcts and other lesions and standardized to an intracranial volume of 1500 cm^3. Lacunes were defined by size 3-15mm according to STRIVE reporting standards.[1] For the sensitivity analysis, a higher burden of arteriolosclerosis/small vessel disease was defined by having at least one lacune or a WMH volume of >9400 cm^3, which represents the cutpoint between the 2nd and 3rd quintile in the population. Those with no lacunes or a WMH volume ≤ 9400 cm^3 where classified as having a low burden of arteriolosclerosis/small vessel disease.

1. Wardlaw JM, Smith EE, Biessels GJ, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. *The Lancet Neurology*. 2013;12(8):822-838.

Table e-1: Neuropsychological Test Battery at Visit 5

Test	**Cognitive Domain**
Mini Mental Status Exam	Nonspecific
CES Depression	Depression screen
Delayed Word Recall*	Memory
Logical Memory 1	Memory
Incidental Learning	Memory
Animal naming	Language
Boston naming	Language
Word Fluency*	Language
Trails A	Sustained attention and processing speed (SAPS)
Trails B	SAPS
Digit Symbol Substitution*	SAPS
Digit Span Backwards	SAPS
* Also at visit 2 and visit 4	

Table e-2. Intracranial atherosclerotic disease (ICAD) and Risk of Cognitive Impairment, prevalent stroke excluded (n=60)

	MCI		Dementia	
RPR (95% CI)	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Any Plaque	1·12 (0·88, 1·42)	1·06 (0·83, 1·35)	1·07 (0·64, 1·77)	1·01 (0·61, 1·69)
MCA plaque	0·86 (0·55, 1·34)	0·80 (0·51, 1·26)	1·44 (0·69, 3·04)	1·41 (0·66, 3·03)
ACA plaque	1·79 (0·96, 3·31)	1·82 (0·98, 3·39)	3·79 (1·53, 9·42)	4·45 (1·74, 11·43)
PCA plaque	1·40 (1·05, 1·94)	1·39 (0·99, 1·94)	1·29 (0·66, 2·51)	1·44 (0·74, 2·79)
Basilar plaque	1·25 (0·83, 1·89)	1·21 (0·78, 1·86)	1·31 (0·59, 2·89)	1·24 (0·55, 2·80)
Vertebral plaque	1·09 (0·74, 1·59)	1·05 (0·72, 1·54)	1·79 (0·92, 3·49)	1·78 (0·92, 3·45)
ICA plaque	0·88 (0·65, 1·18)	0·83 (0·62, 1·12)	1·26 (0·71, 2·21)	1·22 (0·68, 2·19)
Any Stenosis >50%	1·39 (0·94, 2·03)	1·31 (0·89, 1·90)	1·81 (0·95, 3·43)	1·85 (0·95, 3·58)
Number of Plaques				
0	(ref)	(ref)	(ref)	(ref)
1-2	1·15 (0·88, 1·50)	1·07 (0·81, 1·40)	0·78 (0·41, 1·52)	0·69 (0·35, 1·35)
>2	1·07 (0·73, 1·56)	1·04 (0·71, 1·54)	1·58 (0·82, 3·03)	1·68 (0·87, 3·21)
Number of territories with plaque*				
0	(ref)	(ref)	(ref)	(ref)
1-2	1·08 (0·84, 1·39)	1·02 (0·79, 1·32)	0·81 (0·44, 1·48)	0·74 (0·40, 1·36)
>2	1·33 (0·81, 2·17)	1·26 (0·76, 2·08)	2·16 (1·01, 4·61)	2·23 (1·04, 4·80)

RPR= relative prevalence ratio, normal cognition reference group; CI = confidence interval
ACA = anterior cerebral artery; MCA = middle cerebral artery; ICAD = intracranial atherosclerotic disease
Model 1 is adjusted for socio-demographic factors: age, race-center, sex, education, history of alcohol use and smoking
Model 2 is adjusted for model 1 and vascular risk factors: body mass index, systolic blood pressure (per 10mmHg increase), diabetes, low density lipoprotein (per 10 mg/dl increase), APOε4 allele
* Territories include: ACA, MCA, PCA, vertebral, basilar, ICA

Table e-3. Intracranial Atherosclerotic Disease (ICAD) Characteristics in Participants by Cognitive Status in those with low and higher burden of small vessel disease (SVD)

	Low Burden SVD (n=640)				**SVD** (n=1,104)			
	Normal	**MCI**	**Dementia**	**p-value**	**Normal**	**MCI**	**Dementia**	**p-value**
Any Plaque	129 (29·5)	58 (30·9)	5 (35·7)	0·841	242 (38·9)	170 (41·2)	31 (44·9)	0·540
MCA plaque	24 (5·5)	8 (4·3)	2 (14·3)	0·261	63 (10·1)	39 (9·4)	10 (14·5)	0·437
ACA plaque	5 (1·1)	3 (1·6)	2 (14·3)	<0·001	27 (4·3)	25 (6·1)	7 (10·1)	0·091
Vertebral plaque	36 (8·2)	14 (17·5)	2 (14·3)	0·659	77 (12·4)	63 (15·3)	13 (18·8)	0·197
ICA plaque	78 (17·8)	32 (17·0)	2 (14·3)	0·924	128 (20·6)	76 (18·4)	20 (29·0)	0·124
Any Stenosis >50%	32 (7·3)	12 (6·4)	3 (21·4)	0·114	68 (10·9)	62 (15·0)	12 (17·4)	0·081
Any Stenosis >70%	14 (3·2)	4 (2·1)	3 (21·4)	<0·001	36 (5·8)	31 (7·5)	8 (11·6)	0·147

Values are N (%) unless otherwise stated. Small vessel disease was defined by having at least 1 lacune or a white matter hyperintensity volume of >9400 cm^3, which represents the cutpoint between the 2nd and 3rd quintile for the population. Posterior cerebral and basilar artery not shown above as there was ≤1 participant with plaque, WMH <9400 and dementia. ACA = anterior cerebral artery; MCA = middle cerebral artery; ICA = internal carotid artery

Table e-4: Distribution of Plaques by Territory

Plaque territory	**Participants with plaque in territory** (n, %)	**Participants with plaque in territory and at least one other territory** (n, %)*	**Number of other territories with at least one plaque** (mean, SD)	**Number of plaques per territory** (mean, SD)	**Number of plaques in other territories** (mean, SD)
MCA	146 (8·4)	121 (82·9)	2·0 (1·5)	1·8 (1·3)	4·3 (3·4)
ACA	69 (4·0)	57 (82·6)	2·5 (1·7)	1·3 (0·88)	6·2 (4·5)
PCA	239 (13·7)	170 (71·1)	1·6 (1·5)	1·7 (1·0)	3·7 (3·4)
Basilar	167 (9·6)	135 (80·8)	1·8 (1·5)	1·4 (0·74)	4·0 (3·8)
Vertebral	205 (11·8)	148 (72·2)	1·5 (1·5)	1·2 (0·54)	3·8 (3·9)
ICA	336 (19·3)	187 (55·7)	1·1 (1·4)	1·4 (0·85)	3·3 (3·3)

ACA = anterior cerebral artery; MCA = middle cerebral artery; PCA = posterior cerebral artery; ICA = internal carotid artery; SD = standard deviation

*Percentage is of participants with plaque in territory in left column