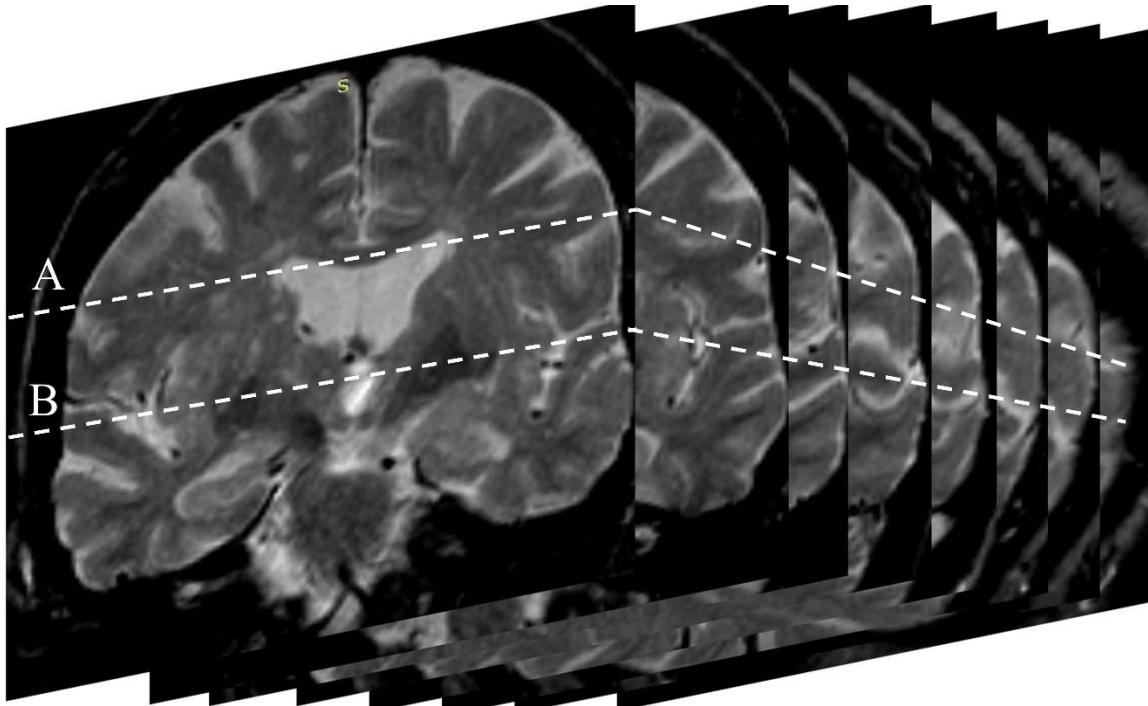


Supplementary eFigure 1



eFigure 1. Perivascular space ratings using T2-weighted coronal views.

Ratings using coronal views were performed separately in the centrum semiovale and basal ganglia regions. To approximate the region evaluated based on the method using axial views (i.e. a single axial slice evaluating the antero-posterior plane), we rated the entire region in the anterior-posterior plane and not a single coronal slice. The basal ganglia region was evaluated above the level of the anterior commissure and below the roof of the lateral ventricles. The centrum semiovale region was rated above the roof of the lateral ventricles up to the subcortical white matter in the corona radiata. We selected the side with highest burden of perivascular spaces, or in the event of incidental covert lesions (such as occasional covert infarcts without clinical events), the contralateral side.

Supplementary eTable 1: Excluded vs Included Participants

Clinical Characteristics*	N**	Excluded (N=364)	Included N=1449
Age (years) at exam closest to MRI		69.5 (9.5)	67.5 (9.8)
Age (years) at MRI date		71.4 (9.4)	68.9 (9.7)
Time Interval		1.4 (1.1)	0.9 (1.0)
Men		148 (41)	664 (46)
Cohort			
Original		41 (11)	138 (10)
Offspring		323 (89)	1311 (90)
Education	357		
Less than High School		16 (4)	70 (5)
High School		84 (24)	458 (32)
Some College		95 (27)	382 (26)
College		162 (45)	539 (37)
Vascular risk factors			
Systolic blood pressure, mm Hg		128.3 (18.0)	128.5 (18.2)
Diastolic Blood pressure, mm Hg		72.3 (9.4)	72.4 (9.7)
Hypertension ^a	362	205 (57)	777 (54)
Hypertension treatment	362	169 (47)	630 (44)
Current smokers	361	26 (7)	117 (8)
Diabetes	281	45 (16)	203 (14)
Diabetes treatment	362	31 (9)	120 (8)
Anti-lipid treatment	363	141 (39)	479 (33)
Prevalent cardiovascular disease		43 (12)	243 (17)
APOE Status			
Any ε4 allele	342	84 (25)	329 (23)
White Matter Hyperintensities			
WMH Percentage		0.4 (0.6)	0.2 (0.4)
Log WMH Percentage		-1.7 (1.3)	-2.3 (1.3)
Log WMH Volume (Z-transformed)		-0.2 (1.1)	-0.3 (1.0)

*Values are mean (SD) for continuous variables and n (%) for categorical variables.

**N excluded based on variable availability when different from 364 participants.

^a Hypertension is defined as SBP \geq 140 mmHg or DBP \geq 90 mmHg and/or use of antihypertensive medication

Supplementary eTable 2

eTable 2. Hazard Ratios relating PVS to all cause dementia adjusted for other CSVD and neurodegeneration markers.

		Model 3	Model 4	Model 5	Model 6	Model 7
PVS location		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
CSO	I	Ref	Ref	Ref	Ref	Ref
	II	2.44 (1.51, 3.93) p<.001	2.22 (1.37, 3.59) p=0.001	2.44 (1.51, 3.94) p<.001	2.05 (1.27, 3.33) P=0.003	2.05 (0.45, 9.31) P=0.353
	III	3.41 (2.03, 5.72) p<.0001	2.60 (1.50, 4.48) p <.001	3.42 (2.03, 5.74) p<.0001	3.01 (1.79, 5.06) p<.0001	1.76 (0.34, 9.16) P=0.501
	IV	5.05 (2.75, 9.26) p<.0001	3.79 (2.01, 7.15) p <.001	5.07 (2.75, 9.34) p<.0001	4.38 (2.38, 8.06) p<.0001	2.38 (0.43, 13.21) P=0.322
BG	I	Ref	Ref	Ref	Ref	Ref
	II	1.62 (1.15, 2.27) p=0.006	1.38 (0.97, 1.95) p=0.069	1.61 (1.15, 2.26) P=0.006	1.35 (0.96, 1.91) P=0.083	0.73 (0.34, 1.58) P=0.425
	III	1.41 (0.90, 2.21) p=0.129	0.90 (0.55, 1.48) p=0.688	1.40 (0.89, 2.19) P=0.147	1.22 (0.78, 1.92) P=0.388	0.90 (0.31, 2.62) P=0.849
	IV	2.67 (1.04, 6.88) p=0.042	1.31 (0.48, 3.54) p=0.599	2.64 (1.02, 6.81) P=0.045	2.14 (0.82, 5.55) P=0.118	9.50 (0.95, 94.68) P=0.055

PVS = perivascular spaces; HR = hazard ratio; CI = confidence interval; CSO = centrum semiovale; BG = basal ganglia

Model 3 adjusts for age, sex, Framingham cohort, interval between MRI and exam cycle, education, smoking, diabetes, hypertension, prevalent cardiovascular disease.

Model 4: model 3 additionally adjusted for white matter hyperintensities (WMHV).

Model 5: model 3 additionally adjusted for covert brain infarcts (CBI).

Model 6: model 3 additionally adjusted for total cranial to brain volume ratio (TCBVR).

Model 7: model 3 additionally adjusted for cerebral microbleeds (CMB).