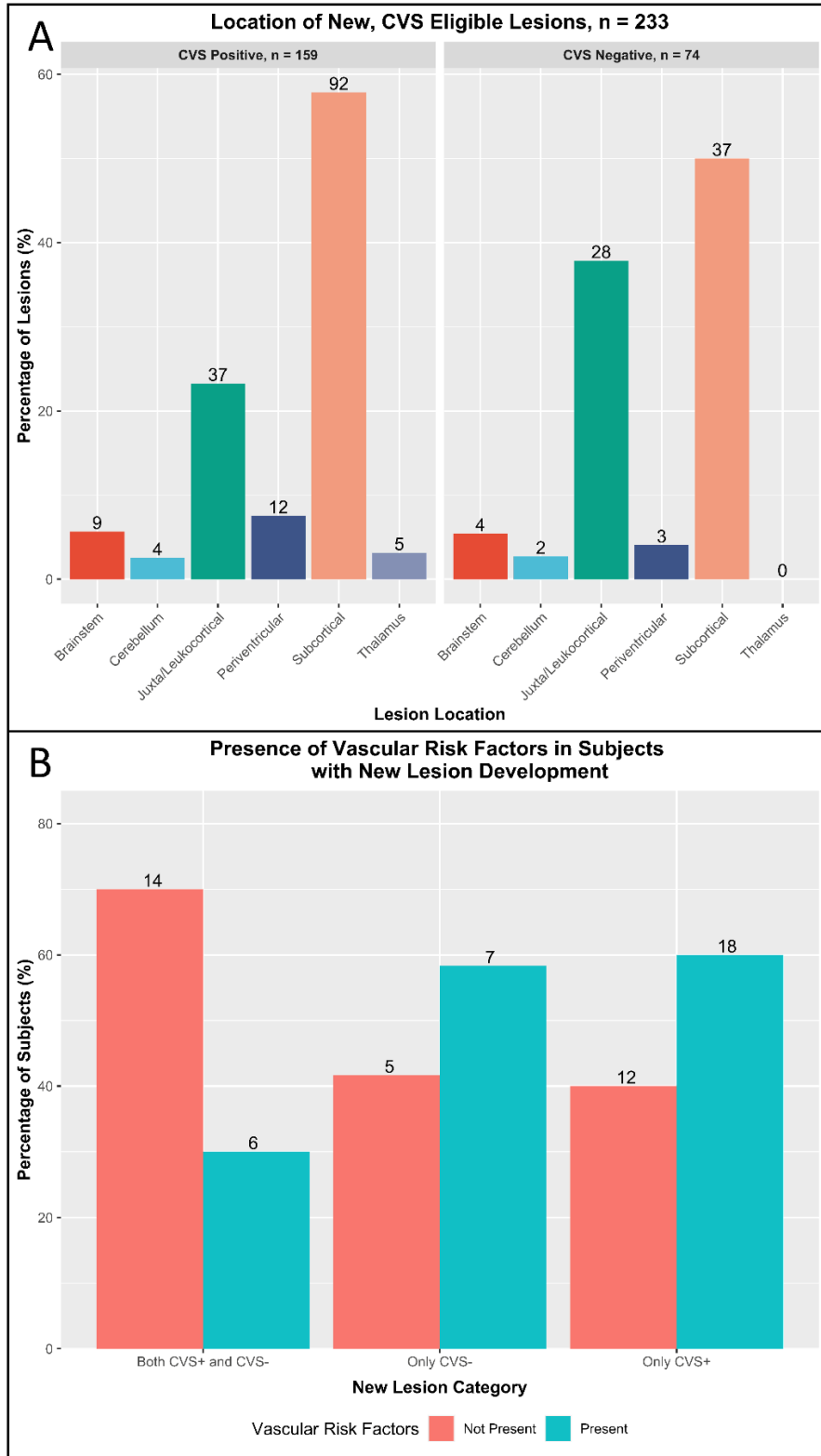## Supplementary Figure Titles/Captions

e Figure 1 title: Lesion location and vascular risk factor characteristics of newly developing lesions stratified by CVS category.

eFigure 1 legend: Panel (A) illustrates lesion distribution stratified by CVS status (n labeled above bars). Of 233 new CVS-eligible lesions, 159 (68%) were CVS+. Within both the CVS+ and CVS-cohorts, most lesions were subcortical. Panel (B) quantifies the presence of vascular risk factors in subjects developing new lesions, stratified by the CVS category of new lesion development. Frequency of each occurrence listed above bars. Vascular risk factors were present in 60% (18/30) of subjects who developed only new CVS+ lesions and in 58% (7/12) of those who developed only new CVS- lesions.

Abbreviations: CVS = central vein sign.

eTable 1. Location distribution of newly developing lesions stratified by CVS status.

Location	CVS+, n (%)	CVS-, n (%)	p-value[a]
Periventricular	12 (8)	3 (4)	
Subcortical/deep WM	92 (58)	37 (50)	
Juxta/leukocortical	37 (23)	28 (38)	
Thalamic	5 (3)	0 (0)	0.19
Brainstem	9 (6)	4 (5)	
Cerebellum	4 (3)	2 (3)	
Total	159 (100)	74 (100)	

[a] Fisher's exact test.

Abbreviations: CVS = central vein sign; WM = white matter.

eTable 2. Subject disability characteristics stratified by new lesion development.

	No new lesions (n = 57)	Only CVS+ (n = 30)	Only CVS- (n = 12)	Both (n = 20)	p-value[a]
Baseline EDSS, mean (SD)[†]	3.2 (2)	3.3 (2)	2.7 (2)	2.0 (2)	0.17
Baseline MSSS, mean (SD)[†]	3.1 (3)	4.1 (3)	2.9 (3)	3.0 (2)	0.32
Baseline timed 25-foot walk, mean (SD)[†]	7.2 (7)	9.4 (10)	4.7 (1)	5.0 (2)	0.12
Baseline 9-hole peg test, dominant hand, mean (SD)[†]	22.1 (8)	25.2 (8)	20.0 (3)	23.7 (16)	0.38
Baseline PASAT, mean (SD)[†]	50.0 (10)	46.2 (10)	47.4 (10)	47.4 (12)	0.48
Baseline SDMT, mean (SD)[†]	49.8 (14)	45.0 (14)	49.8 (12)	51.7 (18)	0.43

[a]One-way ANOVA

[†]Missing results in 12 EDSS, 15 MSSS, 6 timed 25-foot walk, 7 9-hole peg test, 15 PASAT, and 13 SDMT data.

Abbreviations: EDSS = expanded disability status scale; MSSS = multiple sclerosis severity score; PASAT = paced auditory serial addition test; SD = standard deviation; SDMT = symbol digit modalities test.

eTable 3: Multivariate logistic regression analyses evaluating predictors of only new CVS+, only new CVS-, and both types of lesion development.

Risk factors	OR of developing only new CVS+ lesion(s) during follow-up		
	Adjusted OR[†]	p-value	95% CI
Age, per 10-year increase at baseline	0.66	0.13	0.4, 1.1
Sex, female vs. male	1.24	0.73	0.4, 4.1
Race, AA vs. CA	2.05	0.42	0.4, 11.8
MS disease subtype, relapsing vs. progressive	0.28	0.11	0.1, 1.3
Baseline CVS+ percentage, per 10% increase	**1.60***	**0.02**	**1.1, 2.4**
T2* image gadolinium status, with vs. without	**4.44***	**0.05**	**1.0, 20.1**
	OR of developing only new CVS- lesion(s) during follow-up		
Age, per 10-year increase at baseline	0.84	0.63	0.4, 1.7
Sex, female vs. male	6.65	0.20	0.4, 124.2
Race, AA vs. CA	2.77	0.37	0.3, 25.3
MS disease subtype, relapsing vs. progressive	4.54	0.34	0.2, 98.8
Baseline CVS+ percentage, per 10% increase	0.92	0.72	0.6, 1.5
T2* image gadolinium status, with vs. without	0.74	0.74	0.1, 4.1
	OR of developing both new CVS+ and CVS- lesions during follow-up		
Age, per 10-year increase at baseline	**0.35***	**0.01**	**0.2, 0.8**
Sex, female vs. male	1.71	0.56	0.3, 10.4

Race, AA vs. CA	1.62	0.62	0.2, 11.3
MS disease subtype, relapsing vs. progressive	0.87	0.94	0.02, 32.6
Baseline CVS+ percentage, per 10% increase	1.03	0.90	0.6, 1.8
T2* image gadolinium status, with vs. without	3.24	0.23	0.5, 22.3

*p < 0.05.

Abbreviations: AA = African American; CA = Caucasian American; CI = confidence interval; CVS = central vein sign; MS = multiple sclerosis; OR = odds ratio.