SUPPLEMENTAL MATERIAL

Figure I: Probability of Microbleed Presence by Brain Volume (from Poisson Model)

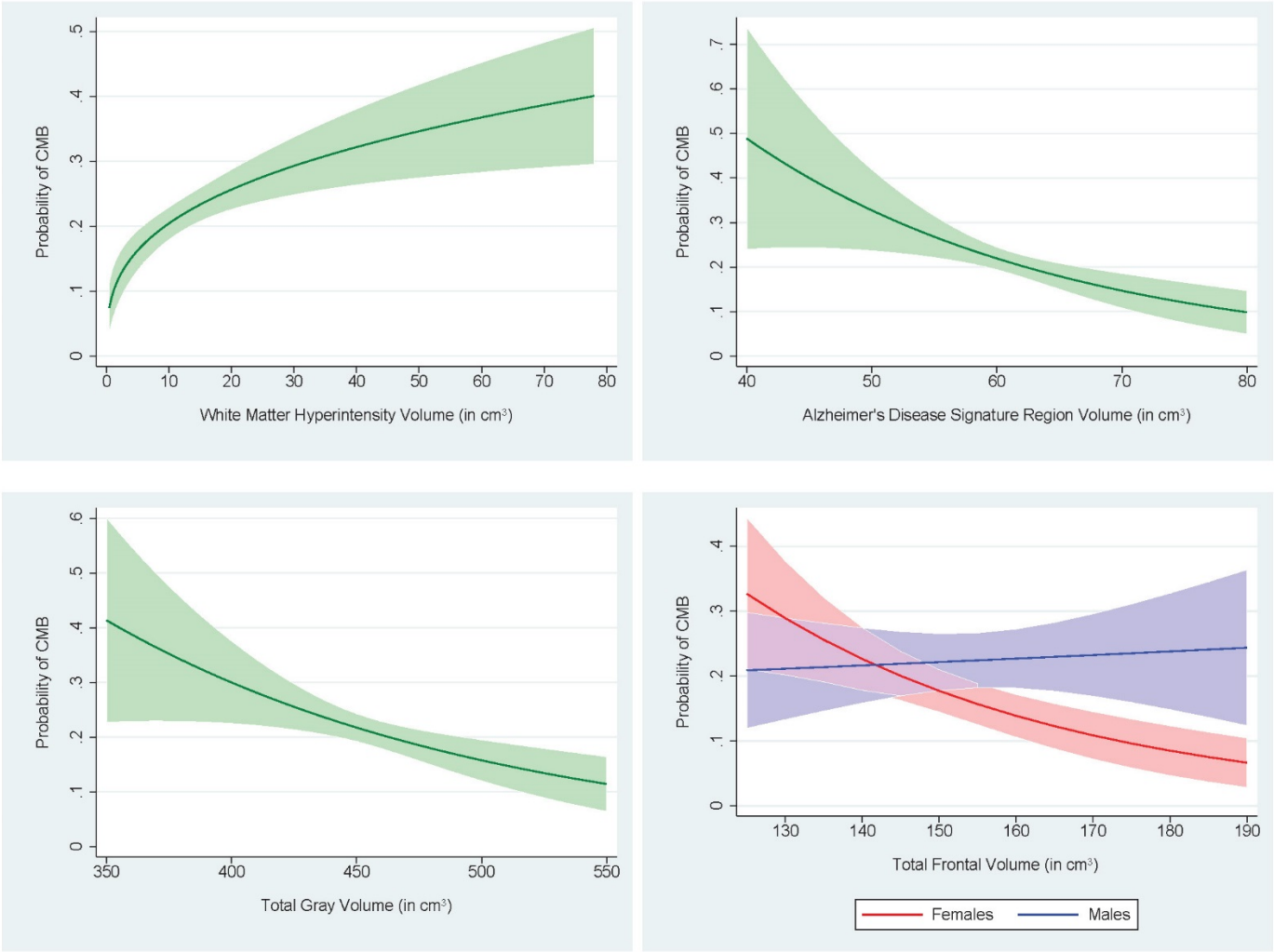


Figure II: Probability of Microbleed Presence by Infarct Count and APOE Genotype (from Poisson Model)

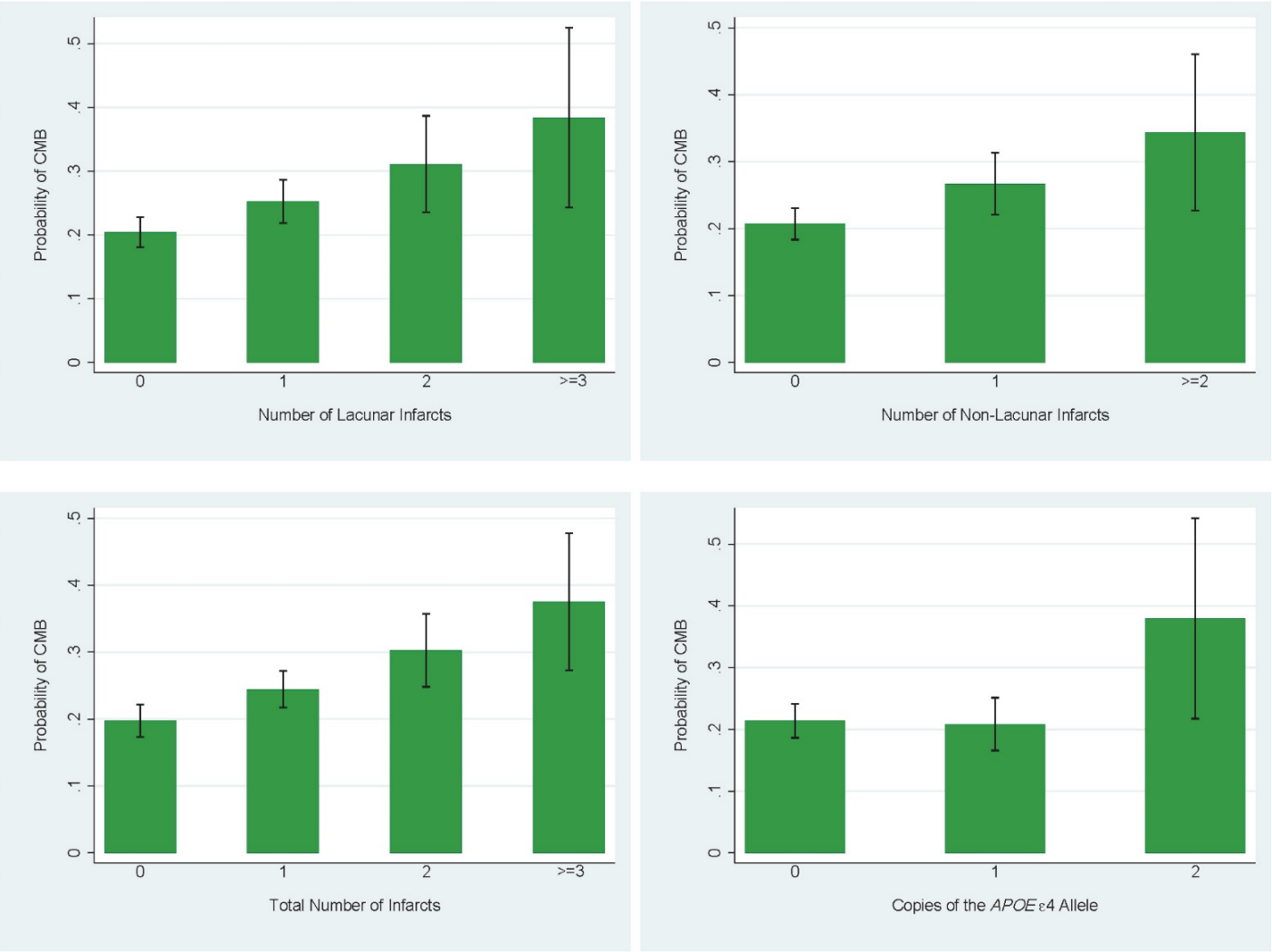
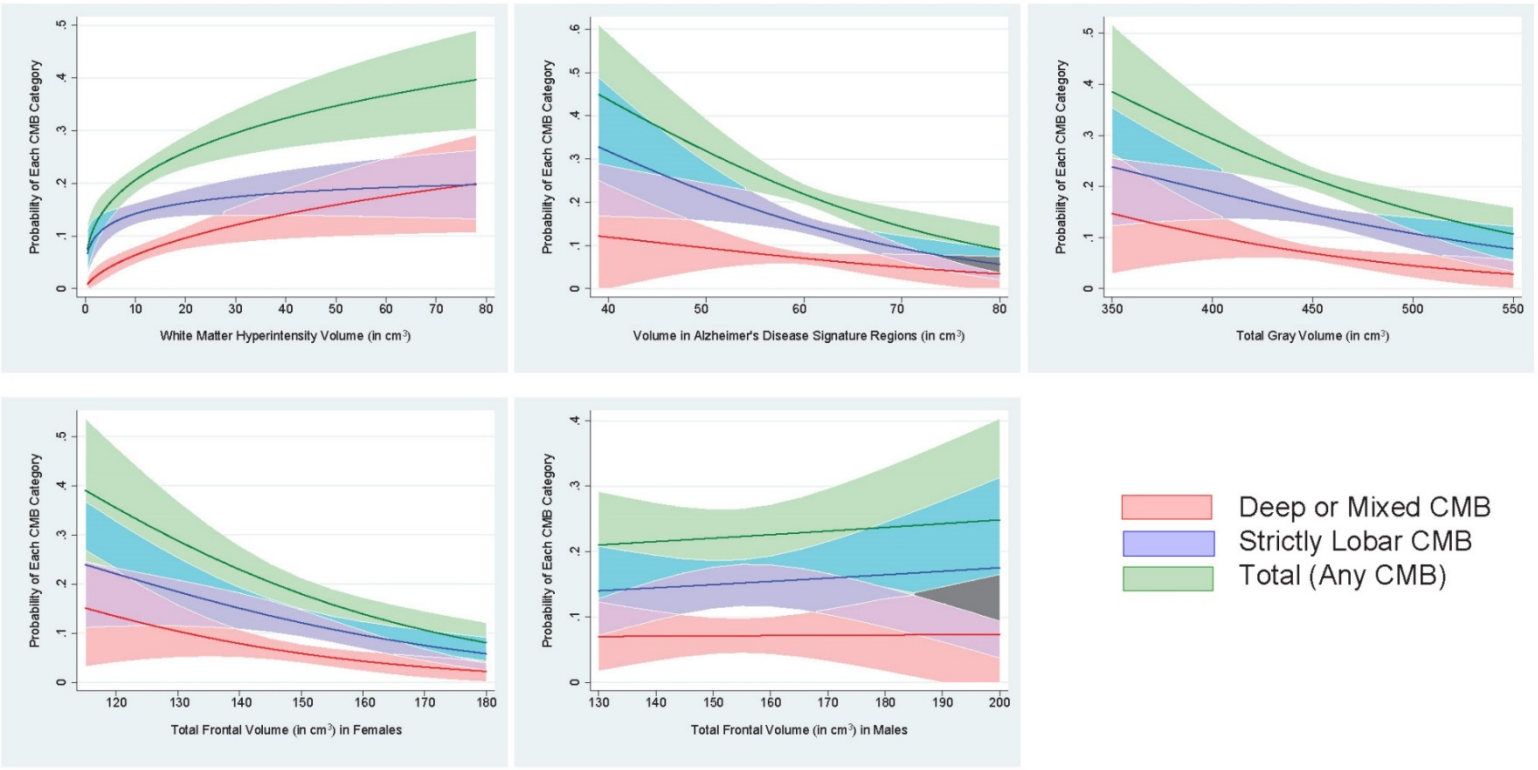


Figure III: Probability of Cerebral Microbleeds by Brain Volumes



NOTE: These plots are the predictive margins from the multinomial logistic regression models adjusted for all covariates. The solid curves are the predicted probabilities while the shaded areas are the 95% confidence bands. Violet shaded areas indicate that the deep/mixed and strictly lobar CMB confidence intervals overlap. Aqua shaded areas indicate that the strictly lobar and total CMB

Table I: Cognitive Outcomes in the Fifth Visit Cohort

Characteristic	All blacks and whites in the full fifth visit cohort (N=6,520)	Excluded from the Analysis (N=4,843)	Included in the Analysis (N=1,677)
Age in years (Mean(SD))	76 (5)	76 (5)	76 (5)
Female (N (%))	3835 (59)	2829 (58)	1006 (60)
Black (N (%))	1544 (24)	1103 (23)	441 (26)
Field Center (N(%))			
Forsyth County, NC	1439 (22)	1049 (22)	390 (23)
Jackson, MS	1417 (22)	976 (20)	441 (26)
Suburban Minneapolis, MN	1903 (29)	1499 (31)	404 (24)
Washington County, MD	1761 (27)	1319 (27)	442 (26)
Prevalent Stroke (N(%))	273 (4)	218 (5)	55 (3)
Cognitive Diagnosis (N(%))			
Normal	4743 (73)	3671 (77)	1072 (64)
Mild Cognitive Impairment	1371 (21)	766 (16)	605 (36)
Dementia	342 (5)	342 (7)	0 (0)
Prorated Mini-mental State Exam (Mean(SD))	27 (3)	27 (3)	27 (2)
Number of failed cognitive domains (out of memory, language, visuospatial, executive function, and attention; N (%))[a]			
0	3959 (65)	3070 (69)	889 (54)
1	1313 (21)	834 (19)	479 (29)
2	515 (8)	307 (7)	208 (13)
3	195 (3)	148 (3)	47 (3)
4	111 (2)	96 (2)	15 (1)
5	29 (0)	26 (1)	3 (0)
Substantial Cognitive Decline Between Visits (N (%)) [b]	4156 (64)	2955 (62)	1201 (72)
Delayed Word Recall Test (age-, sex-, and education-adjusted z-score; Mean (SD))	-0.93 (1.25)	-0.90 (1.27)	-1.00 (1.19)
Digit Symbol Substitution Test (age-, sex-, and education-adjusted z-score; Mean (SD))	-0.47 (0.85)	-0.45 (0.86)	-0.53 (0.79)
Word Fluency Test ((age-, sex-, and education-adjusted z-score; Mean (SD))	-0.03 (0.99)	-0.03 (1.00)	-0.04 (0.96)

Note: [a] Participants missing one or more cognitive domains were excluded from the frequencies. [b] Below the 10^{th} percentile for change in the delayed Word Recall, Digit Symbol Substitution, or Word Fluency Test between visits or below the 20^{th} percentile for change in two or more of these tests)

Table II: Weighted Summary Statistics Stratified By Cerebral Microbleed Location

Characteristic	No CMB	Deep or Mixed CMB	Strictly Lobar CMB
Observed Prevalence (%)	76	8	16
Weighted Prevalence (%)	78	7	14
Mild Cognitive Impairment (%)	21	28	28
Covariates			
Female (%)	63	57	52
Age in years (Mean(SD))	75 (5)	76 (5)	76 (6)
Education (%)			
Less than High School	10	13	14
High School, GED, or Vocational School	40	46	40
Some College	49	40	46
Race-site (%)			
Forsyth whites	20	30	22
Jackson blacks	18	21	24
Minneapolis whites	32	24	33
Washington County whites	29	25	21
Diabetes (%)	25	23	30
Hypertension (%)			
Normal	14	9	8
Prehypertensive	15	8	20
Hypertensive	71	83	72
Current or Former Smoker (%)	56	65	57
Estimated Total Intracranial Volume in cm^3 (Mean(SD))	1381 (150)	1385 (157)	1407 (155)
Predictors of Interest			
White Matter Hyperintensity Volume in cm^3 (Mean(SD))	14 (14)	24 (22)	19 (18)
Total AD Signature Region Volume in cm^3 (Mean(SD))	60 (7)	59 (8)	60 (7)
Total Gray Volume in cm^3 (Mean(SD))	448 (44)	440 (50)	447 (45)
Frontal Volume in cm^3 (Mean(SD))*	152 (15)	150 (17)	152 (17)
Females	147 (13)	141 (12)	142 (11)
Males	161 (14)	162 (16)	163 (15)
Number of Lacunar Infarcts (%)			
0	86	73	81
1	11	19	14
2	2	6	4
≥3	1	2	2
Number of Non-Lacunar Infarcts (%)			
0	91	83	86
1	7	11	11
≥2	2	6	3
Total Number of Infarcts (%)			
0	80	62	72
1	14	22	16
2	4	10	7
≥3	2	6	5
Copies of the *APOE* ε4 Allele (%)			
0	73	71	72
1	25	26	23
2	2	3	5

NOTE: SD=Standard deviation. Statistics were weighted to account to account for sample selection and MRI refusal.* The frontal volume exhibited significant interactions with sex; thus sex-specific summary statistics are presented along with the overall (combined sex) valu

Table III: Modeling the Common Covariates Together Without Neurological Predictors

Predictor	CMB (Presence Versus Absence)		CMB Location					
			Deep/Mixed Versus No CMB		Strictly Lobar Versus No CMB		Strictly Lobar Versus Deep/Mixed CMB	
	RR	95% CI	RRR	95% CI	RRR	95% CI	RRR	95% CI
Male	1.368	(1.104, 1.696)	1.306	(0.814, 2.096)	1.616	(1.168, 2.234)	1.237	(0.724, 2.113)
Age (in 5 year increments)	1.138	(1.027, 1.260)	1.141	(0.926, 1.407)	1.214	(1.031, 1.429)	1.063	(0.827, 1.367)
Education								
Less than High School-Reference								
High School, GED, or Vocational School	0.911	(0.671, 1.237)	1.007	(0.536, 1.895)	0.819	(0.499, 1.347)	0.813	(0.391, 1.692)
Some College	0.742	(0.543, 1.014)	0.665	(0.345, 1.284)	0.673	(0.409, 1.106)	1.011	(0.475, 2.150)
Race-site:								
Forsyth Whites-Reference								
Jackson Blacks	1.023	(0.752, 1.391)	0.745	(0.399, 1.390)	1.235	(0.750, 2.034)	1.659	(0.793, 3.467)
Minneapolis Whites	0.803	(0.590, 1.093)	0.460	(0.242, 0.874)	0.952	(0.588, 1.543)	2.068	(0.977, 4.375)
Washington County Whites	0.665	(0.483, 0.915)	0.514	(0.276, 0.959)	0.638	(0.385, 1.057)	1.240	(0.590, 2.609)
Diabetes	1.004	(0.807, 1.248)	0.732	(0.449, 1.194)	1.169	(0.841, 1.627)	1.598	(0.918, 2.780)
Hypertension Status								
Normal-Reference								
Prehypertension	1.625	(1.027, 2.572)	0.881	(0.334, 2.320)	2.351	(1.242, 4.452)	2.669	(0.891, 7.999)
Hypertension	1.529	(1.029, 2.271)	1.826	(0.822, 4.056)	1.614	(0.932, 2.796)	0.884	(0.351, 2.223)
Current or Former Smoker	1.079	(0.868, 1.340)	1.457	(0.920, 2.308)	0.964	(0.697, 1.335)	0.662	(0.390, 1.123)

NOTE: RR=relative risk; RRR=relative risk ratio. These covariates were included in all Poisson (CMB presence) and multinomial logistic (CMB locations) regression models with the imaging/APOE predictors. The estimated total intracranial volume was included in models assessing brain volumes, thus was not included in this table. Models incorporated weights accounting for the MRI sampling and completion probabilities.

Table IV: Modeling Each Neurological Predictor Separately Without Covariate Adjustments

Predictor	CMB (Presence Versus Absence)		CMB Location					
			Deep/Mixed Versus No CMB		Strictly Lobar Versus No CMB		Strictly Lobar Versus Deep/Mixed CMB	
	RR	95% CI	RRR	95% CI	RRR	95% CI	RRR	95% CI
Log_2(WMH Volume (cm^3))	1.266	(1.161, 1.381)	1.552	(1.251, 1.925)	1.277	(1.127, 1.446)	0.823	(0.652, 1.039)
AD Signature Region Volume (in cm^3)	0.985	(0.969, 1.002)	0.974	(0.935, 1.015)	0.985	(0.963, 1.007)	1.011	(0.966, 1.058)
Total Gray Volume (in cm^3)	0.999	(0.996, 1.001)	0.996	(0.990, 1.002)	1.000	(0.996, 1.003)	1.003	(0.997, 1.010)
Number of Lacunar Infarcts	1.319	(1.153, 1.509)	1.703	(1.270, 2.284)	1.348	(1.055, 1.723)	0.792	(0.564, 1.111)
Number of Non-Lacunar Infarcts	1.380	(1.137, 1.674)	1.781	(1.129, 2.809)	1.446	(1.059, 1.975)	0.812	(0.501, 1.316)
Total Number of Infarcts	1.315	(1.180, 1.465)	1.659	(1.314, 2.094)	1.362	(1.125, 1.650)	0.821	(0.631, 1.068)
Copies of the *APOE* □4 Allele:								
0- Reference								
1	0.999	(0.782, 1.277)	1.097	(0.662, 1.818)	0.951	(0.663, 1.364)	0.867	(0.484, 1.552)
2	1.867	(1.186, 2.941)	1.827	(0.662, 5.039)	2.736	(1.218, 6.143)	1.497	(0.532, 4.217)
Predictor Exhibiting Significant Sex Interactions								
Frontal Volume (in cm^3)								
Female	0.978	(0.968, 0.987)	0.967	(0.947, 0.986)	0.975	(0.962, 0.989)	1.009	(0.987, 1.032)
Male	1.006	(0.995, 1.017)	1.005	(0.978, 1.032)	1.009	(0.993, 1.026)	1.005	(0.975, 1.035)

NOTE: RR=relative risk; RRR=relative risk ratio. The Poisson (CMB presence) and multinomial logistic (CMB location) regression models were not adjusted for any covariates. The number of lacunar infarcts and the total number of infarcts were modeled with a single variable that took values 0, 1, 2, or 3 (for ≥3) infarcts. The number of non-lacunar infarcts was modeled with a single variable that took values 0, 1, or 2 (for ≥2) infarcts. Models incorporated weights accounting for the MRI sampling and completion probabilities.