SUPPLEMENTAL MATERIAL
Supplemental Tables, Obesity insulin resistance and small vessel disease on MRI: the Atherosclerosis Risk in Communities Study

Supplemental Table I. Factor loadings for Obesity and insulin resistance (IR) score *

	Obesity and insulin resistance score
Waist circumference	**0.42**
Log HOMA-IR	**0.42**
Log insulin	**0.40**
BMI	**0.37**
Waist-to-hip ratio	**0.34**
Systolic blood pressure	0.21
Glucose	0.21
Diastolic blood pressure	0.20
Log Triglycerides	0.20
LDL	0.11
HDL	-0.23
% Total Variance	36.3
% Cumulative Variance	36.3

*Factor loadings represent the correlation between the individual variable and the factor; HOMA-IR= Homeostatic model of insulin resistance; BMI= body mass index; HDL = high density lipoprotein; LDL = low density lipoprotein
Values are shown after orthogonal rotation

Supplemental Table II: Unadjusted association of obesity and insulin resistance and incident lacunes

	WMH Progression (Q5 v. Q1-4)		Incident lacunes 3-20mm	
	OR	95% CI	OR	95% CI
Insulin*	1.0	0.92, 1.24	1.31	0.95, 1.35
HOMA-IR*	1.10	0.95, 1.27	1.17	0.99, 1.38
Body mass index (BMI)*	1.20	1.02, 1.40	1.09	0.89, 1.33
Waist circumference*	1.18	1.0, 1.39	1.18	0.96, 1.45
Waist-to-hip ratio (WTHR)*	1.17	0.99, 1.37	1.34	1.08, 1.67
Triglycerides*	0.89	0.74, 1.08	1.23	1.05, 1.46
High density lipoprotein (HDL)*	1.03	0.88, 1.21	0.78	0.62, 0.98
Systolic blood pressure (SBP)*	1.54	1.32, 1.82	1.25	1.02, 1.52
MetS[ŧ] (yes/no)	1.20	0.86, 1.67	1.86	1.22, 2.82
IR score*[ŧ]	1.27	1.08, 1.50	1.36	1.10, 1.68

Q= quintile; OR = odds ratio; CI = confidence interval; HOMA-IR = Homeostatic model assessment, insulin resistance; *Odds ratios are for each 1-standard deviation (SD) increase

Supplemental Table III. Unadjusted association of obesity and insulin resistance and incident lacunes, by size

	Incident lacunes 3-7mm		Incident lacunes >7-20mm	
	OR	95% CI	OR	95% CI
Insulin*	1.10	0.88, 1.37	1.19	0.96, 1.48
HOMA-IR*,	1.15	0.95, 1.41	1.24	1.02, 1.52
Body mass index (BMI)*	0.95	0.73, 1.23	1.30	1.00, 1.69
Waist circumference*	1.05	0.81, 1.36	1.43	1.08, 1.89
Waist-to-hip ratio (WTHR)*	1.32	1.01, 1.73	1.50	1.10, 2.05
Triglycerides*	1.36	1.14, 1.63	1.20	0.98, 1.47
High density lipoprotein (HDL)*	0.77	0.58, 1.03	0.68	0.48, 0.95
Systolic blood pressure (SBP)*	1.16	0.90, 1.48	1.42	1.09, 1.85
MetS (yes/no)	1.77	1.05, 2.98	3.10	1.68, 5.69
IR score*	1.23	0.94, 1.61	1.72	1.27, 2.33

OR = odds ratio; CI = confidence interval; HOMA-IR = Homeostatic model assessment, insulin resistance;
*Odds ratios are for each 1 standard deviation (SD) increase

Supplemental Table IV. Association of obesity and insulin resistance and increase in white matter hyperintensity (WMH) grade

	WMH grade increase ≥1 point v. none			
	Model 1		Model 2	
	OR	95% CI	OR	95% CI
Insulin *	1.12	0.98, 1.30	1.02	0.88, 1.18
HOMA-IR*	1.11	0.97, 1.29	1.02	0.88, 1.18
Body mass index (BMI)*	1.31	1.14, 1.50	1.14	0.97, 1.34
Waist circumference*	1.24	1.08, 1.42	1.18	1.02, 1.37
Waist-to-hip ratio*	1.07	0.94, 1.22	1.08	0.93, 1.26
Triglycerides*	0.96	0.84, 1.09	1.00	0.87, 1.15
High density lipoprotein (HDL)*	1.12	0.98, 1.29	1.13	0.97, 1.32
Systolic blood pressure (SBP)*	1.42	1.24, 1.65	1.26	1.09, 1.48
MetS[ŧ] (yes/no)	1.19	0.90, 1.57	1.13	0.84, 1.51
IR score*[ŧ]	1.25	1.09, 1.43	1.16	1.00, 1.35

OR = odds ratio; CI = confidence interval; HOMA-IR = Homeostatic model assessment, insulin resistance; *Odds ratios are for each 1-standard deviation increase; Model 1 = unadjusted; Model 2 = adjusted for age, sex, education, race, history of coronary artery disease, history of alcohol use, tobacco use and hypertension; ŧ Model 2 not adjusted for hypertension;

Supplemental Table V. Association of obesity and insulin resistance with (WMH) progression and incident lacunes, excluding diabetics (n=861)

	WMH progression (Q5 v Q1-4, n=152)				Incident lacunes 3-20 mm (n=74)			
	Model 1		Model 2		Model 1		Model 2	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Insulin *	1.10	0.93, 1.30	0.97	0.79, 1.20	1.12	0.91, 1.38	1.13	0.89, 1.43
HOMA-IR*	1.14	0.94, 1.38	0.99	0.78, 1.26	1.15	0.90, 1.45	1.16	0.89, 1.51
Body mass index (BMI)*	1.16	0.98, 1.38	0.95	0.78 1.15	1.12	0.92, 1.37	1.00	0.78, 1.29
Waist circumference*	1.11	0.94, 1.32	0.96	0.80, 1.16	1.15	0.92, 1.43	1.08	0.85, 1.37
Waist-to-hip ratio (WTHR)*	1.09	0.92, 1.30	0.99	0.81, 1.21	1.32	1.05, 1.58	1.25	0.97, 1.62
Triglycerides	0.89	0.72, 1.09	0.91	0.73, 1.14	1.20	1.00, 1.43	1.19	0.99, 1.44
High density lipoprotein (HDL)*	1.02	0.86, 1.20	1.11	0.91, 1.37	0.78	0.61, 1.00	0.79	0.60, 1.05
Systolic blood pressure (SBP) [ţ]	1.53	1.30, 1.81	1.33	1.11, 1.60	1.19	0.96, 1.47	1.13	0.90, 1.44
MetS[ţ] (yes/no)	1.11	0.77, 1.59	1.04	0.71, 1.53	1.73	1.09, 2.74	1.77	1.11, 2.84
IR score*[ţ]	1.23	1.03, 1.48	1.04	0.84, 1.27	1.24	0.97, 1.58	1.23	0.94, 1.59

OR = odds ratio; CI = confidence interval; HOMA-IR = Homeostatic model assessment, insulin resistance; BMI = body mass index. *Odds ratios are for each 1 standard deviation increase; Model 1 = unadjusted; Model 2 = adjusted for age, sex, education, race, center, history of coronary artery disease, history of alcohol use, tobacco use and hypertension
ţ Model 2 not adjusted for hypertension, as is part of MetS definition

Supplemental Table VI. Association of obesity and insulin resistance and incident lacunes, by size, excluding diabetics (n=861)

	Incident lacunes 3-7mm (n=75)				Incident lacunes >7-20mm (n=43)			
	Model 1		Model 2		Model 1		Model 2	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Insulin*	1.11	0.86, 1.43	1.15	0.88, 1.51	1.17	0.89, 1.53	1.18	0.85, 1.65
HOMA-IR*,	1.13	0.85, 1.50	1.18	0.87, 1.59	1.20	0.90, 1.62	1.23	0.86, 1.80
BMI*	0.94	0.71, 1.25	0.98	0.71, 1.34	1.15	0.84, 1.59	1.11	0.77, 1.60
Waist circumference*	1.04	0.79, 1.37	1.03	0.77, 1.38	1.34	0.98, 1.84	1.26	0,89, 1.77
Waist-to-hip ratio (WTHR)*	1.27	0.96, 1.69	1.26	0.93, 1.72	1.48	1.05, 2.09	1.35	0.92, 1.98
Triglycerides*	1.31	1.08, 1.58	1.28	1.04, 1.56	1.21	0.97, 1.51	1.20	0.94, 1.52
High density lipoprotein (HDL)*	0.78	0.58, 1.06	0.74	0.53, 1.06	0.64	0.43, 0.94	0.68	0.43, 1.07
Systolic blood pressure (SBP)[ꝉ]	1.14	0.88, 1.49	1.19	0.90, 1.58	1.32	0.98, 1.78	1.19	0.85, 1.57
MetS[ꝉ] (yes/no)	1.71	0.98, 2.98	1.74	0.99, 3.04	2.48	1.27, 4.86	2.69	1.34, 5.39
IR score*[ꝉ]	1.21	0.90, 1.62	1.28	0.93, 1.76	1.43	1.00, 2.06	1.38	0.93, 2.04

OR = odds ratio; CI = confidence interval; HOMA-IR = Homeostatic model assessment, insulin resistance; *Odds ratios are for each 1 standard deviation increase; Model 1 = unadjusted; Model 2 = adjusted for age, sex, education, race, center, history of coronary artery disease, history of alcohol use, tobacco use and hypertension ꞇ Model 2 not adjusted for hypertension

Supplemental Table VII. Standard deviation of obesity and insulin resistance components

	Standard Deviation
Insulin	9.65 uU/mL
HOMA-IR	3.09
Body Mass Index	4.59 kg/m^2
Waist circumference	11.7cm
Waist-to-hip ratio	0.07
Triglycerides	0.90 mmol/l
High density lipoprotein	17.9 mg/dl
Systolic blood pressure	17.5 mmHg
IR-score	2.0