Online Data Supplement

Association between Obstructive Sleep Apnea and Cardiovascular Risk Factors-Variation by Age, Sex and Race: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Table E1. Descriptive Analysis Showing Characteristics of Participants who Underwent Sleep Studies and the Analytical Sample

	Total Sleep study (n=2,057)	Analytical sample (n=1,344)
Age (y)	68 ±9	68±9
Male sex (%)	46	47
BMI (kg/m^2)	29 ±5	29 ±5
Waist circumference (cm)	100 ±14	101 ±14
Education level, (%)		
<High school	15	17
High school	16	18
College or technical	49	49
Graduate School	20	16
Race/ethnicity (%)		
White	36	38
Chinese	12	1
African American	28	29
Hispanic	24	32
Smoking (%)		
Never	47	41
Former	46	51
Current	7	8
Alcohol use (any), (%)	43	46
Statin use, (%)	36	37
Any antihypertensive medication, (%)	53	55
Oral hypoglycemic use, (%)	15	16
eGFR, (ml/min/1.73m^2)	82 ±21	81 ±20

Diabetes Mellitus (%)	20	22
Fasting glucose (mg/dL)	102 ±28	103 ±31
Hypertension (%)	57	59
Systolic BP (mmHg)	123 ±20	123 ±20
Diastolic BP (mmHg)	68 ±10	68 ±10
Total Cholesterol (mg/dL)	184 ±37	182 ±35
HDL-cholesterol (mg/dL)	55 ±16	55 ±15
LDL-cholesterol (mg/dL)	107 ±32	105 ±30
Triglycerides (mg/dL)	110 ±66	110 ±65
Non-HDL cholesterol (mg/dL)	128 ±36	127 ±35
Total sleep time, (min)	360 ±83	359 ±81
Time in Slow-wave sleep, (min)	37 ±34	36 ±34
Time in REM sleep, (min)	66 ±30	67 ±30
WASO, (min)	94 ±65	91 ±64
Time SpO_2 < 92%, (%)	11	12
AHI, events/h	14 ±16	14 ±16
AHI categories, (%)		
0-4	36	35
5-14	32	33
15-29	18	17
≥30	14	14
Arousal index, events/h	22 ±12	22 ±12
Epworth Sleepiness Scale score, mean	6 ±4	6 ±4
Epworth Sleepiness Scale score >10, (%)	14	14

Data are shown as mean ±SD for continuous variables and percentages for categorical variables. BMI= body mass index;eGFR= estimated glomerular filtration rate (measurement of kidney function); BP= blood pressure; HDL= high-density lipoprotein; LDL= low-density lipoprotein;Non-HDL cholesterol is calculated by subtracting the HDL cholesterol value from a total cholesterol reading; REM= rapid eye movement sleep stage; WASO= wake after sleep onset; SpO_2= oxygen saturation; OSA= obstructive sleep apnea; AHI= apnea-hypopnea index; AHI <5= no OSA; AHI 5-14= mild OSA; AHI 15-29= moderate OSA; AHI ≥30= severe OSA; Epworth= daytime excessive sleepiness scale; Epworth >10= daytime excessive sleepiness.

Table E2. Variation of Values for Leukocyte Counts and Cystatin-C with Apnea Hypopnea Index Category, Unadjusted Analyses

	Overall (n= 1,344)	AHI < 5 (n= 470)	AHI 5-14 (n= 449)	AHI 15-29 (n= 234)	AHI ≥ 30 (n= 191)	*P*-value
WBC total counts, x10³/µL	5.80 (4.80, 6.90)	5.50 (4.60,7.60)	5.80 (4.80, 7.00)	6.00 (4.75, 7.20)	6.00 (5.00, 7.40)	**<0.001**
Neutrophils, x10³/µL	3.40 (2.60, 4.20)	3.20 (2.50, 4.00)	3.40 (2.70, 4.25)	3.40 (2.70, 4.20)	3.60 (2.80, 4.75)	**0.001**
Monocytes, x10³/µL	0.40 (0.30, 0.50)	0.40 (0.30, 0.50)	0.40 (0.30, 0.50)	0.41 (0.35, 0.60)	0.45 (0.38, 0.60)	**<0.001**
Lymphocytes, x10³/µL	1.70 (1.40, 2.10)	1.70 (1.35, 2.10)	1.70 (1.30, 1.15)	1.70 (1.40, 2.20)	1.80 (1.50, 2.60)	0.163
Eosinophils, x10³/µL	0.10 (0.10, 0.20)	0.10 (0.10, 0.20)	0.10 (0.10, 0.20)	0.10 (0.10, 0.20)	0.20 (0.10, 0.25)	**0.018**
Cystatin C, mg/L	0.88 (0.78, 1.05)	0.84 (0.74,1.00)	0.90 (0.80, 1.05)	0.91 (0.80, 1.05)	0.90 (0.80, 1.02)	**<0.001**

Data are show as median and IQR (25th, 75th). *P*-value: Kruskal-Wallis a non-parametric test. OSA= obstructive sleep apnea; AHI= apnea-hypopnea index; AHI <5= no OSA; AHI 5-14= mild OSA; AHI 15-29= moderate OSA; AHI ≥30= severe OSA; WBC= White blood cells.

Table E3. Variation of Adjusted Associations between Cardiovascular Risk Factors by Race for Apnea Hypopnea Index (ln transformed) (excluding Chinese; n=13)

	White (n=507)		African American (n=382)		Hispanic (n=434)		*P* for interaction
	Beta	95% CI lower, upper	Beta	95% CI lower, upper	Beta	95% CI lower, upper	
WBC total counts, x10^3/μL	0.020	-0.017, 0.055	0.085	0.022, 0.150	0.004	-0.023, 0.032	**0.04**
Monocyte counts, x10^3/μL	0.230	-0.260, 0.723	1.033	0.360, 1.705	0.030	-0.245, 0.302	**0.02**

Each row represents a unique regression model adjusted for: age, sex, smoking, BMI, waist circumference, statin use, anti-hypertensive medication, and anti-diabetes use in stratified analysis. The *P* interaction terms included an interaction term for race/ethnicity category and exposure. The *P*-value is for interaction testing any significant difference across 3 groups (by Wald Chi-square test). Similar results were shown with Likelihood ratio Chi-square statistics. White is the reference group. The interaction was tested among three race groups. Missing data were excluded for analysis (final sample with all complete n=1323).

Table E4: Descriptive Analysis Showing the CV Risk Factors According to the 3-Race-Groups

	White (n=507)	African American (n=382)	Hispanic (n=434)	P-value
Age (y)	68 ±9	69 ±9	68 ±9	0.725
Age groups, (%)				0.870
< 65y	40	38	39	
≥ 65y	60	62	61	
Male, (%)	48	45	47	0.807
BMI, kg/m^2	28 ±5	31 ±6	30 ±5	**<0.001**
Waist circumf, cm	99 ±15	103 ±14	102 ±13	**<0.001**
Education level, (%)				**<0.001**
< High school	5	7	39	
High school	15	17	22	
College or technical	53	63	33	
Graduate school	27	13	6	
Smoking, (%)				**0.001**
Never	38	43	45	
Former	56	46	49	
Current	6	11	6	
Statin use, (%)	39	35	38	0.368
Any hypertension medication, (%)	47	69	53	**<0.001**
Oral hypoglycemic use, (%)	9	22	20	**<0.001**
Alcohol use (any), (%)	60	42	33	**<0.001**
eGFR,	77 ±19	85 ±23	84 ±21	**<0.001**

(ml/min/1.73m^2)				
	White **(n=507)**	**African American** **(n=382)**	**Hispanic** **(n=434)**	***P*-value**
Diabetes Mellitus (%)	12	29	27	**<0.001**
Fasting glucose (mg/dL)	98 ±25	104 ±36	108 ±33	**<0.001**
Hypertension (%)	50	75	56	**<0.001**
Systolic BP (mmHg)	121 ±20	127 ±21	123 ±21	**<0.001**
Diastolic BP (mmHg)	67 ±10	70 ±10	68 ±10	**<0.001**
Total Cholesterol (mg/dL)	183 ±38	181 ±35	183 ±37	0.806
HDL-cholesterol (mg/dL)	56 ±16	58 ±18	52 ±14	**<0.001**
LDL-cholesterol (mg/dL)	105 ±33	105 ±31	106 ±31	0.972
Triglycerides (mg/dL)	108 ±60	91 ±45	130 ±75	**<0.001**
Non-HDL cholesterol (mg/dL)	127 ±36	123 ±33	131 ±36	**0.005**
Asthma (self-report), (%)	2	4	5	**0.043**
Seasonal allergy past 2-weeks (self-report), (%)	23	23	18	0.102
	White **(n=507)**	**African American** **(n=382)**	**Hispanic** **(n=434)**	***P*-value**
WBC total counts,	5.9 (5.0, 7.0)	5.3 (4.4, 6.6)	6.0 (5.0, 7.0)	**<0.001**

x10³/µL			
Neutrophils, x10³/µL	3.6 (2.8, 4.4)	2.9 (2.0, 3.9)	3.5 (2.8, 4.3)	**<0.001**
Monocytes, x10³/µL	0.4 (0.4, 0.6)	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	**<0.001**
Lymphocytes, x10³/µL	1.6 (1.3, 2.0)	1.8 (1.5, 2.3)	1.8 (1.4, 2.2)	**<0.001**
Eosinophils, x10³/µL	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)	**0.044**
Cystatin C, mg/L	0.9 (0.8, 1.0)	0.9 (0.7, 1.0)	0.9 (0.7, 1.0)	0.426

	White (n=507)	African American (n=382)	Hispanic (n=434)	*P*-value
Total sleep time, (min)	370 ±73	350 ±88	355 ±81	**0.001**
Time in Slow-wave sleep, (min)	41 ±35	30 ±32	34 ±35	**<0.001**
Time in REM sleep, (min)	70 ±30	65 ±29	66 ±28	**0.012**
WASO, (min)	84 ±54	99 ±69	93 ±67	**0.015**
Time SpO_2 <92%, (%)	14	10	10	**0.040**
Time SpO_2<90%, (%)	5	4	4	0.264
Time SpO_2< 85%, (%)	0.8	0.9	1.1	0.590
Min SpO_2 (%) in REM sleep, mean	85 ±7	84 ±8	82 ±10	**<0.001**
Min SpO_2 (%) in NREM sleep, mean(%)	86 ±6	86 ±6	85 ±7	**0.030**
AHI, events/h	13 ±15	14 ±17	16 ±17	**<0.001**

AHI categories, (%)				
0-4	38	38	30	
5-14	36	30	33	**0.002**
15-29	14	18	19	
≥30	12	14	18	
Arousal index, events/h	22 ±12	20 ±11	23 ±12	**<0.001**
Epworth Sleepiness Scale score, mean	6 ±4	7 ±4	6 ±4	**<0.001**
Epworth Sleepiness Score >10, (%)	12	19	13	**0.007**

Data are shown in mean ±SD for continuous and percentage for categorical variables. For non-normal distributed variables, data are shown as median and (25th, 75th). P-value by ANOVA for continuous variables and normal distributed. P-value by chi-square for categorical variables. P-value by Kruskal-Wallis (a non-parametric test) by continuous variables and non-normal distributed. CV= cardiovascular; OSA= obstructive sleep apnea; AHI= apnea-hypopnea index; AHI <5= no OSA; AHI 5-14= mild OSA; AHI 15-29= moderate OSA; AHI ≥30= severe OSA; BMI= body mass index; eGFR= estimated glomerular filtration rate (measurement of kidney function); BP= blood pressure; HDL= high-density lipoprotein; LDL= low-density lipoprotein. Non-HDL cholesterol is calculated by subtracting the HDL cholesterol value from a total cholesterol reading; WBC= white blood cells; REM= rapid eye movement sleep stage; NREM= non-REM sleep stage; WASO= wake after sleep onset; SpO_2= oxygen saturation; Min= minimum; Chinese race-group was excluded (n=13 subjects). Data analysis is all complete. Missing values were excluded.

Table E5. Main Analysis Associating CV Risk Factors and AHI, Excluding those Using Oral Steroids use (n=17). Outcome: AHI log transformed

	Beta	se	*P*-value
Diastolic BP, mmHg	0.007	0.003	**0.009**
HDL-cholesterol, mg/dL	-0.004	0.0018	**0.025**
Neutrophils, x10³µL	0.048	0.018	**0.007**
WBC total, x10³µL	0.016	0.010	0.115
Monocytes, x10³µL	0.224	0.112	**0.047**
Lymphocytes, x10³µL	-0.006	0.017	0.736
Eosinophils, x10³µL	0.060	0.200	0.770
Cystatin C, mg/L	-0.021	0.093	0.820

CV= cardiovascular; AHI= apnea hypopnea index; outcome variable was natural log transformed after added unit; se= standard error; BP= blood pressure; HDL= high-density lipoprotein; WBC= white blood cells; Adjustments for age, sex, race/ethnicity, smoking status, statin use, any anti-hypertension medication, anti-diabetes medication (insulin use and/or oral hypoglycemic use), BMI, and waist circumference. All complete for analysis (n=1,316). Missing data were excluded