

**Association of novel measures of sleep disturbances with blood pressure: the Multi-Ethnic Study of Atherosclerosis**

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**Supplementary Appendix**

Table S1 Baseline characteristics by Overall Odds Ratio Product Quartiles

	Odds Ratio Product Quartiles			
	1	2	3	4
Participants, n	455	449	454	442
Odds ratio product	0.98 ± 0.12	1.22 ± 0.05	1.41 ± 0.06	1.68 ± 0.13
Age, years	67 ± 9	69 ± 9	69 ± 9	70 ± 9
Female, %	54%	56%	53%	52%
Race/ethnicity, %				
White	40%	38%	37%	32%
Asian	8%	12%	13%	17%
Black	25%	25%	28%	30%
Hispanic	27%	25%	22%	21%
Systolic blood pressure, mmHg <sup>‡</sup>	121.7 ± 19.5	123.1 ± 20.7	122.9 ± 20.6	124.4 ± 20.1
Diastolic blood pressure, mmHg <sup>‡</sup>	68.2 ± 9.7	68.3 ± 10.5	68.1 ± 9.5	68.5 ± 9.8
Hypertension, %	49%	52%	54%	57%
Height, cm	165.6 ± 10.1	165.4 ± 10.0	165.5 ± 9.8	165.3 ± 10.3
Waist, cm	99.6 ± 14.0	98.7 ± 14.0	99.5 ± 14.6	99.1 ± 14.7
Body mass index, kg/m <sup>2</sup>	29.2 ± 5.5	28.3 ± 5.5	28.7 ± 5.7	28.3 ± 5.5
Blood pressure medication use, %	49%	52%	54%	57%
Ever smoker, %	52%	51%	53%	53%
Diabetes, %	20%	17%	19%	21%
Apnea-hypopnea index (AHI), events/hour	13.1 ± 15.2	13.1 ± 14.4	15.1 ± 17.7	17.5 ± 18.0
AHI < 5 events/hour, %	38%	35%	37%	28%
5 ≤ AHI < 15 events/hour, %	33%	34%	31%	29%
AHI ≥ 15 events/hour, %	29%	31%	32%	43%

Data presented as mean ± standard deviation for continuous variables and (%) for categorical variables

<sup>‡</sup>Exam 5 blood pressure measurements unadjusted for medication use

Higher odds ratio product quartiles indicate lower sleep depth

Table S2 Baseline Characteristics by NREM Duty Cycle Quartiles

	NREM Duty Cycle Quartiles			
	1	2	3	4
Participants, n	448	506	481	413
NREM Duty Cycle	0.29 ± 0.03	0.35 ± 0.01	0.38 ± 0.01	0.44 ± 0.03
Age, years	71 ± 9	68 ± 9	69 ± 9	67 ± 9
Female, %	53%	56%	54%	48%
Race/ethnicity, %				
White	36%	36%	39%	34%
Asian	11%	12%	12%	16%
Black	27%	28%	26%	29%
Hispanic	26%	24%	23%	21%
Systolic blood pressure, mmHg <sup>‡</sup>	126.2 ± 21.4	122.9 ± 20.1	122.2 ± 20.5	120.6 ± 18.5
Diastolic blood pressure, mmHg <sup>‡</sup>	68.0 ± 9.7	68.2 ± 9.7	68.3 ± 10.1	68.4 ± 9.9
Hypertension, %	62%	53%	49%	48%
Height, cm	165.1 ± 10.0	164.8 ± 10.0	165.0 ± 9.9	167.0 ± 10.1
Waist, cm	102.7 ± 14.7	98.1 ± 14.9	98.0 ± 13.4	98.0 ± 13.3
Body mass index, kg/m <sup>2</sup>	30.1 ± 6.1	28.2 ± 5.4	28.0 ± 5.1	28.1 ± 5.2
Blood pressure medication use, %	63%	54%	50%	48%
Ever smoker, %	55%	52%	51%	51%
Diabetes, %	23%	17%	15%	23%
Apnea-hypopnea index (AHI), events/hour	18.3 ± 18.9	13.2 ± 15.4	13.9 ± 16.2	13.2 ± 14.2
AHI < 5 events/hour, %	26%	38%	37%	36%
5 ≤ AHI < 15 events/hour, %	31%	34%	31%	32%
AHI ≥ 15 events/hour, %	43%	28%	32%	32%

Data presented as mean ± standard deviation for continuous variables and (%) for categorical variables

<sup>‡</sup>Exam 5 blood pressure measurements unadjusted for medication use

NREM = non-rapid eye movement

Table S3 Baseline Characteristics by Hypoxic Burden Quartiles

	Hypoxic Burden Quartiles			
	1	2	3	4
Participants, n	506	495	499	504
Hypoxic Burden ((%·min)/hr)	14.2 ± 14.0	31.4 ± 21.1	53.5 ± 27.1	126.3 ± 87.3
Age, years	67 ± 9	68 ± 9	69 ± 9	70 ± 9
Female, %	70%	57%	50%	36%
Race/ethnicity, %				
White	34%	41%	37%	33%
Asian	12%	13%	11%	14%
Black	32%	27%	27%	24%
Hispanic	22%	19%	25%	29%
Systolic blood pressure, mmHg <sup>‡</sup>	121.2 ± 21.2	122.2 ± 20.6	123.5 ± 19.3	124.4 ± 19.6
Diastolic blood pressure, mmHg <sup>‡</sup>	67.3 ± 10.1	67.6 ± 9.7	68.6 ± 9.7	69.5 ± 10.0
Hypertension, %	55%	57%	62%	65%
Height, cm	163.4 ± 9.8	165.1 ± 10.0	166.0 ± 10.2	167.1 ± 10.0
Waist, cm	94.6 ± 14.7	97.2 ± 12.6	102.0 ± 13.7	103.8 ± 14.5
Body mass index, kg/m <sup>2</sup>	27.1 ± 5.4	27.9 ± 5.1	29.4 ± 5.3	30.1 ± 5.8
Blood pressure medication use, %	49%	51%	55%	60%
Ever smoker, %	51%	51%	52%	56%
Diabetes, %	16%	17%	21%	25%
Apnea-hypopnea index (AHI), events/hour	3.0 ± 5.2	7.7 ± 7.8	14.3 ± 10.0	34.0 ± 18.6
AHI < 5 events/hour, %	82%	43%	12%	0.4%
5 ≤ AHI < 15 events/hour, %	16%	46%	51%	13.6%
AHI ≥ 15 events/hour, %	2%	11%	37%	86%

Data presented as mean ± standard deviation for continuous variables and (%) for categorical variables

<sup>‡</sup>Exam 5 blood pressure measurements unadjusted for medication use

Table S4 Association of NREM and REM Odds Ratio Product with Systolic and Diastolic Blood Pressure

	<b>% Change in systolic blood pressure (95% CI)*</b>	<b>p-value</b>	<b>% Change in diastolic blood pressure (95% CI)*</b>	<b>p-value</b>
<b>NREM Odds Ratio Product</b>				
Unadjusted Model (n = 1,799)	0.5 (-0.3 to 1.3)	0.21	0.3 (-0.4 to 0.9)	0.38
Model 1 (n = 1,765)	0.3 (-0.4 to 1.0)	0.42	0.3 (-0.3 to 0.9)	0.37
Model 2 (n = 1,754)	0.3 (-0.5 to 1.0)	0.49	0.2 (-0.4 to 0.9)	0.50
Model 3 (n = 1,754)	0.2 (-0.5 to 1.0)	0.51	0.2 (-0.4 to 0.8)	0.52
<b>REM Odds Ratio Product</b>				
Unadjusted Model (n = 1,762)	-0.7 (-1.4 to 0.1)	0.07	-0.6 (-1.2 to 0.1)	0.08
Model 1 (n = 1,728)	-0.5 (-1.2 to 0.2)	0.16	-0.5 (-1.2 to 0.1)	0.11
Model 2 (n = 1,717)	-0.5 (-1.2 to 0.2)	0.18	-0.5 (-1.1 to 0.2)	0.13
Model 3 (n = 1,713)	-0.5 (-1.2 to 0.2)	0.18	-0.5 (-1.1 to 0.1)	0.13

\*All results reported per standard deviation increment of natural log-transformed NREM and REM odds ratio product.

Model 1: Adjusted for age, sex, race/ethnicity, body mass index (kg/m<sup>2</sup>), smoking status, cigarette pack-years, alcohol use, periodic limb movement, education level

Model 2: Model 1 + hypoxic burden ((%·min)/hr)

Model 3: Model 2 + duty cycle

CI = confidence interval; REM = rapid eye movement; NREM = non-rapid eye movement

Table S5 Apnea-Hypopnea Index Stratified Analyses

	Systolic Blood Pressure			Diastolic Blood Pressure		
	Mean % change in SBP (95% CI)*	p-value	p-value for interaction	Mean % change in DBP (95% CI)*	p-value	p-value for interaction
Total Odds Ratio Product			0.10			0.26
5<AHI (n = 611)	0.9 (-0.4 to 2.1)	0.17		0.6 (-0.5 to 1.7)	0.29	
5≤AHI<15 (n = 557)	-0.9 (-2.1 to 0.4)	0.17		-0.5 (-1.6 to 0.6)	0.34	
AHI≥15 (n = 597)	0.7 (-0.6 to 1.9)	0.28		0.6 (-0.5 to 1.7)	0.31	
NREM Odds Ratio Product			0.66			0.53
5<AHI (n = 611)	0.2 (-1.0 to 1.4)	0.75		0.4 (-0.6 to 1.5)	0.44	
5≤AHI<15 (n = 557)	-0.1 (-1.4 to 1.2)	0.86		-0.3 (-1.4 to 0.8)	0.57	
AHI≥15 (n = 597)	0.7 (-0.6 to 2.0)	0.28		0.5 (-0.6 to 1.6)	0.38	
REM Odds Ratio Product			0.03			0.12
5<AHI (n = 601)	-0.1 (-1.3 to 1.1)	0.90		-0.03 (-1.1 to 1.0)	0.96	
5≤AHI<15 (n = 553)	-1.8 (-3.0 to -0.6)	0.003		-1.5 (-2.5 to -0.4)	0.008	
AHI≥15 (n = 574)	0.4 (-0.9 to 1.6)	0.58		-0.1 (-1.2 to 1.0)	0.81	
NREM Inspiratory Flow Limitation			0.57			0.84
5<AHI (n = 626)	-1.2 (-2.3 to -0.2)	0.02		-0.9 (-1.8 to 0.04)	0.06	
5≤AHI<15 (n = 599)	-0.5 (-1.7 to 0.8)	0.45		-0.5 (-1.6 to 0.6)	0.33	
AHI≥15 (n = 574)	-0.5 (-1.9 to 1.0)	0.50		-0.5 (-1.8 to 0.8)	0.42	
REM Inspiratory Flow Limitation			0.33			0.12
5<AHI (n = 619)	-0.5 (-1.5 to 0.5)	0.34		-0.3 (-1.2 to 0.6)	0.52	
5≤AHI<15 (n = 571)	-0.9 (-2.3 to 0.5)	0.20		-1.1 (-2.4 to 0.1)	0.08	
AHI≥15 (n = 588)	0.5 (-0.9 to 1.9)	0.47		0.7 (-0.5 to 1.9)	0.26	
NREM Duty Cycle			0.01			0.03
5<AHI (n = 627)	-1.0 (-2.4 to 0.3)	0.12		-0.9 (-2.0 to 0.3)	0.15	
5≤AHI<15 (n = 577)	-2.1 (-3.3 to -1.0)	<0.001		-1.3 (-2.4 to -0.3)	0.01	
AHI≥15 (n = 609)	0.4 (-0.8 to 1.5)	0.55		0.5 (-0.5 to 1.6)	0.30	
REM Duty Cycle			0.007			0.02
5<AHI (n = 619)	-0.9 (-2.4 to 0.5)	0.20		-0.2 (-1.5 to 1.0)	0.72	
5≤AHI<15 (n = 571)	-2.2 (-3.4 to -1.0)	<0.001		-1.3 (-2.3 to -0.2)	0.02	
AHI≥15 (n = 588)	0.4 (-0.7 to 1.5)	0.50		0.8 (-0.2 to 1.8)	0.14	
Overall Hypoxic Burden			0.43			0.27
5<AHI (n = 694)	0.4 (-1.2 to 1.9)	0.65		1.6 (0.2 to 2.9)	0.02	

5 ≤ AHI < 15 (n = 641)	1.6 (-1.2 to 4.4)	0.27		1.1 (-1.3 to 3.6)	0.37	
AHI ≥ 15 (n = 678)	-0.7 (-2.8 to 1.4)	0.51		-0.3 (-2.2 to 1.6)	0.73	
NREM Hypoxic Burden			0.75			0.57
5 < AHI (n = 685)	0.2 (-1.4 to 1.8)	0.81		1.4 (-0.02 to 2.8)	0.06	
5 ≤ AHI < 15 (n = 640)	-0.3 (-2.5 to 1.9)	0.76		0.1 (-1.9 to 2.1)	0.92	
AHI ≥ 15 (n = 677)	0.9 (-1.3 to 3.1)	0.45		0.7 (-1.2 to 2.7)	0.47	
REM Hypoxic Burden			0.03			0.11
5 < AHI (n = 676)	0.4 (-0.9 to 1.8)	0.56		1.1 (-0.1 to 2.3)	0.08	
5 ≤ AHI < 15 (n = 630)	2.2 (0.6 to 3.9)	0.007		0.8 (-0.6 to 2.2)	0.29	
AHI ≥ 15 (n = 651)	-0.8 (-2.3 to 0.8)	0.31		-0.8 (-2.1 to 0.6)	0.26	

All models adjusted for age, sex, race/ethnicity, smoking status, cigarette pack-years, body mass index (kg/m<sup>2</sup>), alcohol use, periodic limb movement, education level. Inspiratory flow limitation models also adjusted for % of time spent in slow wave sleep.

CI = confidence interval; REM = rapid eye movement; NREM = non-rapid eye movement; SBP = systolic blood pressure (mm Hg); DBP = diastolic blood pressure (mm Hg); AHI = apnea hypopnea index (events/hour)

\*Adjusted mean percent increment in blood pressure per 1-standard deviation increment of natural log-transformed sleep exposure variable.

Table S6 Smoking Stratified Analyses

	Systolic Blood Pressure			Diastolic Blood Pressure		
	Mean % change in SBP (95% CI)*	p-value	p-value for interaction	Mean % change in DBP (95% CI)*	p-value	p-value for interaction
Total Odds Ratio Product			0.81			0.07
Ever smoker (n = 943)	0.4 (-0.6 to 1.3)	0.48		-0.2 (-1.1 to 0.6)	0.48	
Never smoker (n = 854)	0.2 (-0.8 to 1.2)	0.73		0.9 (-0.03 to 1.8)	0.08	
NREM Odds Ratio Product			0.61			0.10
Ever smoker (n = 943)	0.5 (-0.4 to 1.5)	0.30		-0.2 (-1.0 to 0.7)	0.69	
Never smoker (n = 854)	0.2 (-0.6 to 1.2)	0.77		0.9 (-0.1 to 1.8)	0.06	
REM Odds Ratio Product			0.66			0.06
Ever smoker (n = 928)	-0.6 (-1.6 to 0.3)	0.19		-1.1 (-1.9 to -0.2)	0.01	
Never smoker (n = 832)	-0.3 (-1.4 to 0.7)	0.55		0.1 (-0.8 to 1.1)	0.79	
NREM Inspiratory Flow Limitation			0.92			0.47
Ever smoker (n = 965)	-0.8 (-1.7 to 0.2)	0.11		-0.4 (-1.2 to 0.5)	0.40	
Never smoker (n = 866)	-0.7 (-1.7 to 0.3)	0.17		-0.8 (-1.7 to 0.1)	0.08	
REM Inspiratory Flow Limitation			0.73			0.79
Ever smoker (n = 954)	-0.5 (-1.5 to 0.5)	0.31		-0.3 (-1.1 to 0.6)	0.52	
Never smoker (n = 855)	-0.3 (-1.3 to 0.7)	0.61		-0.1 (-1.0 to 0.8)	0.80	
NREM Duty Cycle			0.06			0.007
Ever smoker (n = 973)	-0.2 (-1.2 to 0.7)	0.60		0.3 (-0.5 to 1.1)	0.51	
Never smoker (n = 872)	-1.6 (-2.6 to -0.5)	0.004		-1.4 (-2.3 to -0.5)	0.003	
REM Duty Cycle			0.03			0.01
Ever smoker (n = 954)	-0.1 (-1.1 to 0.8)	0.80		0.5 (-0.3 to 1.4)	0.23	
Never smoker (n = 855)	-1.7 (-2.7 to -0.6)	0.002		-1.2 (-2.1 to -0.3)	0.01	
Overall Hypoxic Burden			0.25			0.13
Ever smoker (n = 1,084)	0.1 (-0.9 to 1.1)	0.89		0.5 (-0.4 to 1.4)	0.24	
Never smoker (n = 961)	0.8 (-0.2 to 1.8)	0.10		1.4 (0.5 to 2.3)	0.001	
NREM Hypoxic Burden			0.49			0.31
Ever smoker (n = 1,081)	0.1 (-0.8 to 1.1)	0.77		0.6 (-0.2 to 1.5)	0.15	
Never smoker (n = 953)	0.6 (-0.4 to 1.6)	0.25		1.2 (0.3 to 2.1)	0.008	
REM Hypoxic Burden			0.11			0.02
Ever smoker (n = 1,055)	0.2 (-0.7 to 1.2)	0.65		0.1 (-0.7 to 0.9)	0.80	
Never smoker (n = 934)	1.3 (0.3 to 2.3)	0.01		1.6 (0.7 to 2.5)	<0.001	



All models adjusted for age, sex, race/ethnicity, body mass index ( $\text{kg}/\text{m}^2$ ), alcohol use, periodic limb movement, education level. Inspiratory flow limitation models also adjusted for % of time spent in slow wave sleep.

CI = confidence interval; REM = rapid eye movement; NREM = non-rapid eye movement; SBP = systolic blood pressure (mm Hg); DBP = diastolic blood pressure (mm Hg)

\*Adjusted mean percent increment in blood pressure per 1-standard deviation increment of natural log-transformed sleep exposure variable.

Table S7 Hypertension Medication Stratified Analyses

	Systolic Blood Pressure			Diastolic Blood Pressure		
	Mean % change in SBP (95% CI)*	p-value	p-value for interaction	Mean % change in DBP (95% CI)*	p-value	p-value for interaction
Total Odds Ratio Product			0.62			0.54
Non-user (n=826)	0.4 (-0.6 to 1.4)	0.44		0.5 (-0.5 to 1.4)	0.33	
Anti-hypertensive user (n=939)	0.1 (-0.9 to 1.0)	0.92		0.1 (-0.8 to 0.9)	0.88	
NREM Odds Ratio Product			0.94			0.54
Non-user (n=826)	0.2 (-0.8 to 1.2)	0.69		0.1 (-0.9 to 1.0)	0.91	
Anti-hypertensive user (n=939)	0.3 (-0.7 to 1.2)	0.58		0.5 (-0.4 to 1.3)	0.30	
REM Odds Ratio Product			0.21			0.15
Non-user (n=811)	-0.7 (-1.8 to 0.3)	0.16		-0.9 (-1.8 to 0.1)	0.07	
Anti-hypertensive user (n=917)	0.1 (-0.8 to 1.1)	0.77		0.1 (-0.8 to 0.9)	0.88	
NREM Inspiratory Flow Limitation			0.24			0.11
Non-user (n=841)	-1.0 (-2.1 to 0.1)	0.07		-1.1 (-2.0 to -0.1)	0.04	
Anti-hypertensive user (n=958)	-0.2 (-1.1 to 0.7)	0.72		-0.01 (-0.8 to 0.8)	0.97	
REM Inspiratory Flow Limitation			0.07			0.18
Non-user (n=831)	-0.9 (-1.9 to 0.2)	0.11		-0.6 (-1.5 to 0.4)	0.25	
Anti-hypertensive user (n=947)	0.4 (-0.5 to 1.4)	0.38		0.3 (-0.5 to 1.1)	0.48	
NREM Duty Cycle			0.44			0.06
Non-user (n=843)	-1.1 (-2.2 to -0.1)	0.04		-1.1 (-2.1 to -0.2)	0.02	
Anti-hypertensive user (n=970)	13.1 (-18.8 to 57.5)	0.48		0.1 (-0.8 to 0.9)	0.87	
REM Duty Cycle			0.23			0.11
Non-user (n=831)	-1.2 (-2.2 to -0.2)	0.02		-0.8 (-1.7 to 0.2)	0.11	
Anti-hypertensive user (n=947)	-0.3 (-1.3 to 0.6)	0.47		0.3 (-0.6 to 1.1)	0.54	
Overall Hypoxic Burden			0.03			<0.001
Non-user (n=932)	1.1 (0.1 to 2.1)	0.03		1.9 (1.0 to 2.8)	<0.001	
Anti-hypertensive user (n=1,081)	-0.4 (-1.3 to 0.6)	0.43		-0.1 (-0.9 to 0.8)	0.88	
NREM Hypoxic Burden			0.03			0.002
Non-user (n=925)	1.1 (0.1 to 2.2)	0.03		1.9 (1.0 to 2.9)	<0.001	
Anti-hypertensive user (n=1,077)	-0.3 (-1.2 to 0.6)	0.53		0.01 (-0.8 to 0.9)	0.98	
REM Hypoxic Burden			0.23			0.04
Non-user (n=910)	1.1 (0.1 to 2.1)	0.03		1.4 (0.5 to 2.3)	0.002	
Anti-hypertensive user (n=1,047)	0.3 (-0.7 to 1.2)	0.58		0.2 (-0.7 to 1.0)	0.71	

All models adjusted for age, race/ethnicity, smoking status, cigarette pack-years, body mass index (kg/m<sup>2</sup>), alcohol use, periodic limb movement, education level. Inspiratory flow limitation models also adjusted for % of time spent in slow wave sleep.

CI = confidence interval; REM = rapid eye movement; NREM = non-rapid eye movement; SBP = systolic blood pressure (mm Hg); DBP = diastolic blood pressure (mm Hg)

\*All results reported % increase in blood pressure per 1-standard deviation increment in natural-log transformed sleep exposure variable.

Figure S1. Directed acyclic graph describing potential association between odds ratio product and blood pressure. (dagitty.net/mMUJ288)

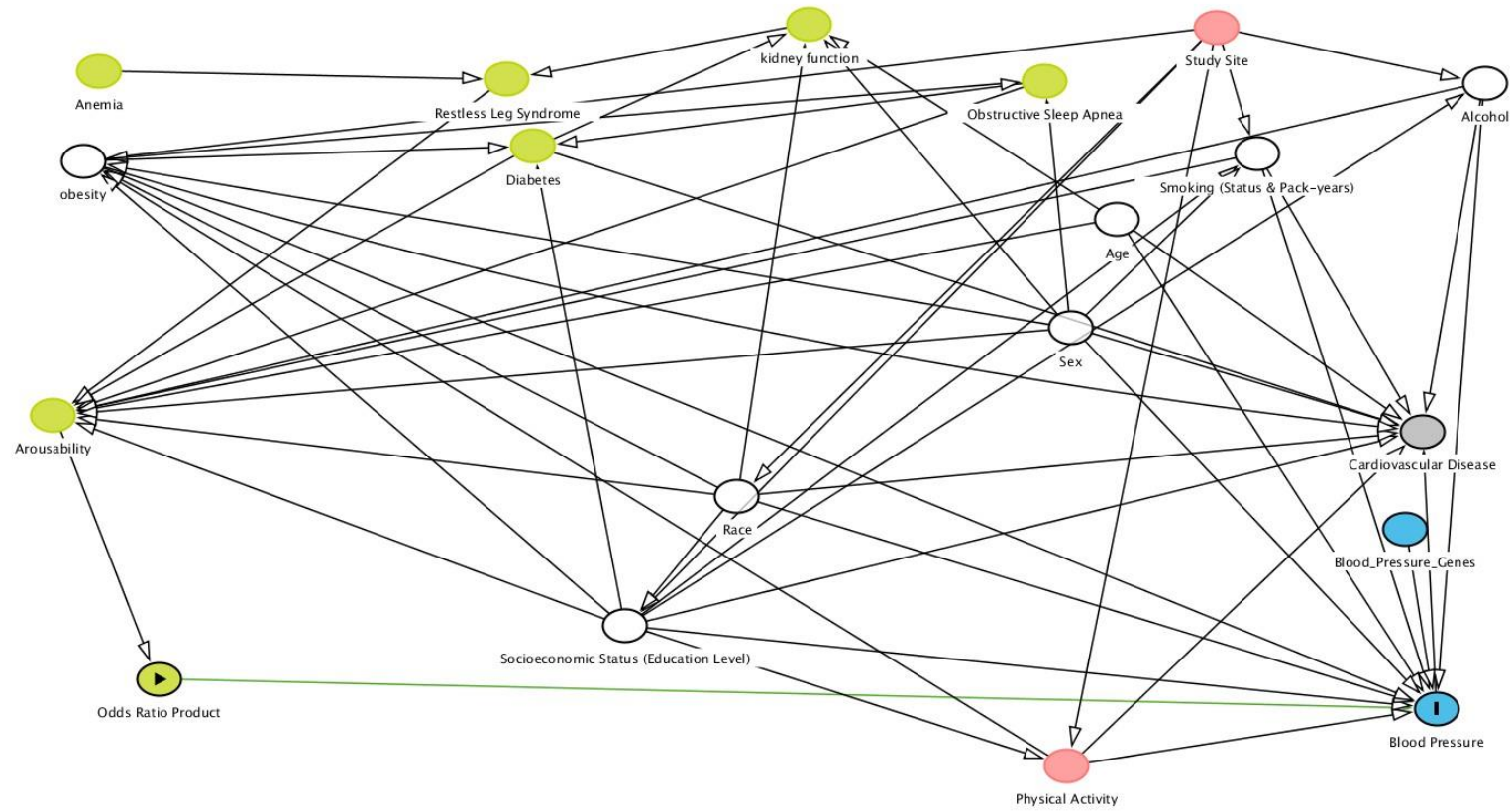


Figure S2. Flow chart of MESA Sleep study population and sleep exposures measured.

