

SUPPLEMENTARY DATA

**Supplementary Table S1.** Characteristics of the study population by standard deviations of sleep onset timing across 7 days

	SD of 7-day actigraphy-based sleep duration			
	≤30 min	31-60 min	61-90 min	>90 min
N	399	710	459	435
<b>Sociodemographic factors</b>				
Age, years	71.6 (8.9)	69.0 (8.9)	68.8 (9.3)	69.2 (9.5)
Male, %	47	45	46	49
Race/ethnicity				
White, %	51	40	34	28
African-American, %	16	24	31	38
Hispanic, %	25	24	23	22
Chinese, %	8	12	13	12
Work schedule				
Day shift, %	28	33	33	28
Other shift, %	9	11	13	16
Do not work, %	64	57	54	56
Education				
High school or less, %	31	32	30	29
Some college, %	28	28	31	35
College graduate, %	20	21	20	16
Graduate school, %	21	19	19	20
<b>Lifestyle factors</b>				
Current smokers, %	4	6	7	12
Physical activity, MET-hrs/week	78.9 (70.0)	91.9 (97.6)	99.1 (142.7)	84.8 (90.0)
CES-D	6.9 (6.3)	7.8 (7.4)	8.1 (7.4)	9.7 (8.1)
Number of meals/snacks per day	3.8 (1.1)	3.7 (1.1)	3.6 (1.1)	3.5 (1.2)
Total caloric intake, kcal	1666 (709)	1630 (770)	1718 (812)	1753 (852)
<b>Sleep-related factors</b>				
Sleep duration, h	7.7 (1.1)	7.5 (1.2)	7.0 (1.4)	6.3 (1.6)
Apnea-Hypopnea Index	18.3 (15.8)	19.3 (16.5)	20.7 (18.4)	22.9 (20.1)
Insomnia <sup>1</sup> , %	18	24	26	26
Excessive daytime sleepiness <sup>2</sup> , %	11	13	14	17

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<b>Chronotype<sup>3</sup></b>				
Evening type, %	3	6	10	10
Intermediate type, %	38	40	37	50
Morning type, %	59	53	53	41
<b>Metabolic factors</b>				
Body mass index, kg/m <sup>2</sup>	28.1 (5.2)	28.7 (5.5)	28.8 (5.6)	29.6 (6.0)
Waist circumference, cm	98.8 (14.9)	99.0 (13.7)	99.4 (14.6)	101.7 (15.4)
Diastolic blood pressure, mmHg	67.0 (9.7)	67.2 (9.5)	69.6 (9.5)	69.7 (10.5)
Systolic blood pressure, mmHg	123.8 (20.2)	120.4 (18.5)	124.2 (19.1)	124.8 (22.9)
Total triglycerides, mg/dL	110.8 (70.1)	110.4 (56.0)	107.7 (62.5)	114.0 (73.6)
HDL cholesterol, mg/dL	55.0 (15.0)	56.3 (16.4)	56.0 (17.2)	54.5 (17.1)
Fasting glucose, mg/dL	98.8 (22.6)	100.2 (24.1)	102.6 (29.6)	106.1 (32.7)

Abbreviations: MET, Metabolic Equivalent; CES-D, Center for Epidemiologic Studies Depression Scale

<sup>1</sup> Defined as the Women's Health Initiative Insomnia Rating Scale >10

<sup>2</sup> Defined as the Epworth Sleepiness Scale >10

<sup>3</sup> Defined as the modified Horne-Ostberg Morningness-Eveningness Questionnaire score 4-11 for evening type, 12-17 for intermediate type and 18-25 for morning type

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**Supplementary Table S2.** Cross-sectional associations of number of altered metabolic factors with every 1-hour increase of variability in sleep duration and sleep onset timing at MESA exam 5 (n=2,003)

	Sleep duration variability		Sleep timing variability	
	Model 1	Model 2	Model 1	Model 2
	Odds ratio (95% CI)			
Number of altered metabolic factors				
0	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
1	1.10 (0.85, 1.42)	1.04 (0.80, 1.36)	1.12 (0.85, 1.48)	1.11 (0.82, 1.49)
2	1.10 (0.85, 1.42)	1.03 (0.79, 1.35)	1.25 (0.95, 1.64)	1.23 (0.91, 1.65)
3	1.26 (0.97, 1.64)	1.12 (0.85, 1.48)	1.33 (1.01, 1.77)	1.25 (0.92, 1.70)
4	1.50 (1.10, 2.04)	1.25 (0.91, 1.73)	1.81 (1.32, 2.48)	1.61 (1.14, 2.28)
5	2.11 (1.47, 3.05)	1.93 (1.31, 2.84)	1.67 (1.12, 2.48)	1.57 (1.01, 2.43)
P-trend	<0.0001	0.005	<0.0001	0.006

Model 1: Adjusted for age, sex, study site, race/ethnicity, education and work schedules

Model 2: Model 1 + adjusted for smoking status, physical activity, total caloric intake, number of meals/snacks per day, depressive symptoms, average sleep duration, insomnia symptom scores, chronotype, Epworth Sleepiness Scale score and AHI

Odds ratios were estimated from multinomial logistic regression, and P-trend was calculated using ordinal logistic regression

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**Supplementary Table S3.** Cross-sectional associations of individual components of metabolic syndrome with 1-hour increase of variability in sleep duration and timing

	Case/N	Prevalence	Sleep duration variability		Sleep onset timing variability	
			Model 1	Model 2	Model 1	Model 2
			Odds ratio (95% CI)			
High blood pressure	1318/2003	65.8%	1.11 (0.96, 1.29)	1.10 (0.94, 1.29)	1.08 (0.92, 1.26)	1.08 (0.91, 1.28)
Central obesity	1181/2003	59.0%	1.21 (1.05, 1.40)	1.12 (0.96, 1.31)	1.30 (1.12, 1.52)	1.25 (1.06, 1.48)
High triglycerides	357/2003	17.8%	1.22 (1.03, 1.45)	1.16 (0.97, 1.39)	1.14 (0.96, 1.36)	1.07 (0.88, 1.30)
Low HDL cholesterol	481/2003	24.0%	1.31 (1.12, 1.52)	1.24 (1.06, 1.45)	1.17 (1.00, 1.36)	1.08 (0.91, 1.29)
High fasting glucose	791/2003	39.5%	1.20 (1.04, 1.37)	1.12 (0.97, 1.29)	1.30 (1.13, 1.50)	1.26 (1.08, 1.47)

Model 1: Adjusted for age, sex, study site, race/ethnicity, education and work schedules

Model 2: Model 1 + adjusted for smoking status, physical activity, total caloric intake, number of meals/snacks per day, depressive symptoms, average sleep duration, insomnia symptom scores, chronotype, Epworth Sleepiness Scale and AHI

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**Supplementary Table S4.** Subgroup analysis of the cross-sectional and prospective associations between 7-day variability in sleep duration and timing (per 1 hour) and metabolic syndrome

	Sleep duration variability		Sleep onset timing	
	OR (95% CI)	P-interaction	OR (95% CI)	P-interaction
Cross-sectional sample				
Age		0.96		0.54
<70 years	1.30 (1.07, 1.57)		1.31 (1.07, 1.60)	
≥70 years	1.32 (1.07, 1.62)		1.22 (0.99, 1.49)	
Sex		0.34		0.42
Male	1.38 (1.13, 1.69)		1.30 (1.05, 1.59)	
Female	1.25 (1.02, 1.52)		1.26 (1.03, 1.54)	
Race/ethnicity		0.76		0.11
White	1.44 (1.13, 1.83)		1.23 (0.95, 1.60)	
African American	1.31 (1.00, 1.73)		1.49 (1.15, 1.92)	
Hispanic	1.28 (0.98, 1.67)		1.14 (0.88, 1.48)	
Chinese	1.24 (0.90, 1.71)		1.34 (0.97, 1.85)	
Longitudinal sample				
Age		0.32		0.17
<70 years	1.12 (0.81, 1.56)		1.05 (0.74, 1.49)	
≥70 years	1.54 (1.03, 2.31)		1.71 (1.17, 2.51)	
Sex		0.87		0.74
Male	1.27 (0.89, 1.84)		1.23 (0.87, 1.74)	
Female	1.25 (0.89, 1.78)		1.30 (0.90, 1.87)	
Race/ethnicity		0.29		0.11
White	1.63 (1.05, 2.52)		1.64 (1.03, 2.63)	
African American	0.82 (0.47, 1.43)		0.72 (0.41, 1.26)	
Hispanic	1.45 (0.88, 2.40)		1.63 (1.05, 2.54)	
Chinese	1.51 (0.81, 2.81)		1.51 (0.75, 3.05)	

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Adjusted for age, sex, study site, race/ethnicity, education, current employment status, smoking status, physical activity, total caloric intake, number of meals/snacks per day, and depressive symptoms

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**Supplementary Table S5.** Cross-sectional and prospective associations of weekday variability in sleep duration and timing with metabolic syndrome

	Cases/N	Model 1	Model 2	Model 3
		Odds ratio (95% CI)		
<b>Cross-sectional sample</b>				
<b>SD of sleep duration</b>				
≤60 min	278/851	1.00 (ref)	1.00 (ref)	1.00 (ref)
61-90 min	171/499	1.03 (0.81, 1.31)	0.99 (0.78, 1.27)	0.95 (0.74, 1.21)
91-120 min	115/325	1.13 (0.86, 1.50)	1.13 (0.85, 1.50)	1.01 (0.75, 1.36)
>120 min	143/328	1.58 (1.20, 2.08)	1.53 (1.16, 2.01)	1.36 (1.02, 1.81)
Per 1 hour		1.26 (1.11, 1.43)	1.25 (1.10, 1.42)	1.19 (1.04, 1.36)
P-trend		0.0003	0.0008	0.01
<b>SD of sleep onset timing</b>				
≤30 min	188/575	1.00 (ref)	1.00 (ref)	1.00 (ref)
31-60 min	236/686	1.09 (0.86, 1.40)	1.09 (0.86, 1.40)	1.05 (0.81, 1.34)
61-90 min	131/375	1.15 (0.87, 1.53)	1.13 (0.85, 1.51)	1.11 (0.83, 1.50)
>90 min	152/367	1.54 (1.15, 2.05)	1.48 (1.11, 1.98)	1.36 (1.00, 1.86)
Per 1 hour		1.24 (1.08, 1.41)	1.21 (1.06, 1.39)	1.19 (1.03, 1.37)
P-trend		0.002	0.005	0.02
<b>Longitudinal sample</b>				
<b>SD of sleep duration</b>				
≤60 min	64/442	1.00 (ref)	1.00 (ref)	1.00 (ref)
61-90 min	57/240	1.83 (1.22, 2.76)	1.84 (1.22, 2.77)	1.82 (1.20, 2.78)
91-120 min	26/155	1.17 (0.70, 1.96)	1.21 (0.72, 2.03)	1.24 (0.72, 2.12)
>120 min	34/133	1.97 (1.20, 3.21)	2.03 (1.23, 3.33)	2.04 (1.21, 3.44)
Per 1 hour		1.32 (1.06, 1.64)	1.35 (1.08, 1.69)	1.38 (1.09, 1.74)
P-trend		0.01	0.008	0.008
<b>SD of sleep onset timing</b>				
≤30 min	48/288	1.00 (ref)	1.00 (ref)	1.00 (ref)
31-60 min	59/336	1.00 (0.65, 1.54)	1.02 (0.66, 1.58)	0.98 (0.63, 1.54)

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61-90 min	37/181	1.30 (0.79, 2.13)	1.33 (0.81, 2.20)	1.44 (0.87, 2.40)
>90 min	37/165	1.42 (0.85, 2.35)	1.49 (0.89, 2.50)	1.58 (0.91, 2.77)
Per 1 hour		1.20 (0.96, 1.49)	1.22 (0.98, 1.52)	1.28 (1.01, 1.62)
P-trend		0.10	0.08	0.04

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Model 1: Adjusted for age, sex, study site, race/ethnicity, education and work schedules

Model 2: Model 1 + adjusted for smoking status, physical activity, total caloric intake, number of meals/snacks per day, and depressive symptoms

Model 3: Model 2 + adjusted for average sleep duration, insomnia symptom scores, chronotype, Epworth Sleepiness Scale and AHI



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**Supplementary Table S6.** Comparison of metabolic factors between Exams 5 and 6 among individuals without metabolic syndrome at exam 5 (n=970)

	Exam 5	Exam 6
Age, years	66.7 (8.5)	73.0 (8.4)
Body mass index, kg/m <sup>2</sup>	27.0 (4.6)	27.0 (4.9)
Waist circumference, cm*	94.4 (12.2)	95.6 (12.5)
Diastolic blood pressure, mmHg	68.4 (9.6)	68.9 (9.9)
Systolic blood pressure, mmHg*	119.1 (19.2)	124.9 (19.8)
Total triglycerides, mg/dL*	92.7 (46.6)	89.3 (53.9)
HDL cholesterol, mg/dL*	59.8 (16.9)	64.5 (19.2)
Fasting glucose, mg/dL*	94.1 (13.4)	98.9 (21.1)
Antidiabetic medications, %*	6	9
Antihypertensive medications, %*	39	51
Lipid-lowering medications, %*	32	39

\*P<0.05 based on the paired t-test for continuous variables and the McNemar test for proportions

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**Supplementary Table S7.** Incidence of individual metabolic syndrome components with every 1-hour increase of variability in sleep duration and timing

	Case/N	Incidence	Sleep duration variability		Sleep onset timing variability	
			Model 1	Model 2	Model 1	Model 2
			Odds ratio (95% CI)			
High blood pressure	180/489	36.8%	0.95 (0.70, 1.30)	0.84 (0.60, 1.19)	1.07 (0.78, 1.48)	0.99 (0.70, 1.42)
Central obesity	117/563	20.8%	1.17 (0.85, 1.60)	1.22 (0.87, 1.72)	0.88 (0.62, 1.25)	0.92 (0.62, 1.36)
High triglycerides	63/918	6.9%	1.41 (0.97, 2.05)	1.47 (0.98, 2.20)	1.77 (1.24, 2.53)	2.07 (1.38, 3.11)
Low HDL cholesterol	47/883	5.3%	1.19 (0.76, 1.84)	1.27 (0.78, 2.08)	1.12 (0.66, 1.90)	1.16 (0.69, 1.97)
High fasting glucose	168/769	21.8%	0.93 (0.70, 1.24)	0.84 (0.62, 1.15)	0.89 (0.65, 1.20)	0.78 (0.56, 1.10)

Model 1: Adjusted for age, sex, study site, race/ethnicity, education and work schedules

Model 2: Model 1 + adjusted for smoking status, physical activity, total caloric intake, number of meals/snacks per day, depressive symptoms, average sleep duration, insomnia symptom scores, chronotype, Epworth Sleepiness Scale and AHI

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**Supplementary Table S8.** Prevalence of individual metabolic factors by clusters of metabolic syndrome at MESA Exam 5

	Cluster 1 (Few metabolic abnormalities)	Cluster 2 (Hypertension without dyslipidemia)	Cluster 3 (Multiple metabolic abnormalities)	Cluster 4 (Metabolically abnormal obese diabetes)
N (%)	509 (25)	889 (44)	394 (20)	211 (11)
High blood pressure, %	0	100	61	90
Central obesity, %	41	57	65	100
High triglycerides, %	0	0	56	65
Low HDL cholesterol, %	6	0	71	82
High fasting glucose, %	23	42	24	100

Metabolic clusters were determined by the Latent Class Analysis (LCA) based on AIC

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**Supplementary Table S9.** Incidence of individual metabolic factors by clusters of metabolic syndrome at MESA Exam 6

	Cluster 1 (Few metabolic changes)	Cluster 2 (Incident high blood pressure)	Cluster 3 (Incident high fasting glucose)	Cluster 4 (Significant overall metabolic changes)
N (%)	320 (33)	417 (43)	190 (20)	43 (4)
Incident high blood pressure, %	1	37	0	51
Incident central obesity, %	24	7	0	23
Incident high triglycerides, %	7	0	5	91
Incident low HDL cholesterol, %	4	3	4	37
Incident high fasting glucose, %	10	17	28	30

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Metabolic clusters were determined by the Latent Class Analysis (LCA) based on AIC