Reallocating time to sleep, sedentary behaviors, or active behaviors: associations with cardiovascular disease risk biomarkers, NHANES 2005-2006

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Abstract

Purpose: Sleep, sedentary, and active behaviors are all independently linked with cardiovascular disease and diabetes outcomes and associated biomarkers. Across a 24h day, time is disproportionately distributed between these behaviors and increasing time in one behavior inevitably requires decreasing time in another. This study explored the impact of alternating the allocation of time spent in sleep, sedentary, and active behaviors on cardiometabolic biomarkers.

Methods: Data from the cross-sectional, 2005-2006 US National Health and Nutritional Examination Survey (NHANES) were analyzed, adjusting for the complex sampling design. Adults aged ≥20 years with 4+ days of accelerometer data and self-reported sleep duration were included in the full analyses (N=2637), with those with fasting serum measures included in subanalyses (N=1173). Adults with sleep disorders and pregnant/lactating women were excluded. An Actigraph accelerometer was used to derive sedentary and active behaviors and respondents self-reported their sleep duration.

Results: After adjustment for study covariates (age, gender, ethnicity, income, smoking, depression, and energy intake) and time spent in other activities, replacing …

Discussion: Replacing sedentary time with moderate-vigorous physical activity or extending sleep duration, even after controlling for other activities, was associated with improvements in a range of important biomarkers associated with cardiovascular disease and diabetes. The effect of sedentary and active behaviors on biomarkers appears relatively homogenous among adults with varying levels of sleep duration. Future research should explore these replacement associations longitudinally using objective methods (i.e., wrist actigraphy) to assess sleep parameters.

KEYWORDS: Exercise, diabetes, cardiovascular disease, isotemporal substitution, metabolic syndrome

Introduction

Paragraph Number 1 Increased physical activity and reduced sedentary behavior can reduce the risk of chronic illness, including physiological biomarkers linked to cardiovascular disease and diabetes (1, 10, 17). Optimal sleep duration is independently associated with many of the same biomarkers (6-9). The relationship between physical activity and sleep may also be important, with evidence suggesting that regular physical activity is associated with improved subjective (19) and objective sleep quality (11) and lower incidence and severity of sleep-disordered breathing (2, 18).

Paragraph Number 2 Across a 24h day, time is disproportionately distributed between sleep, sedentary activities (sitting or lying with low energy expenditure), and more active behaviors. Increasing time in active behaviors or extending sleep duration inevitably requires decreasing time in another behavior (14). To date neither the physical activity/sedentary behavior or sleep literatures have adequately accounted for the fixed time nature in which these behaviors occur, or how varying distributions of sleep, sedentary, and activity behaivors may impact various health parameters.

Paragraph Number 3 The isotemporal substitution paradigm explores the effect of alternating time in one behavior with another while holding total time constant (14). While historically rooted in nutritional epidemiology (23-24), isotemporal substitution modeling has recently been applied in physical activity epidemiology to study the effects on physical activity (of varying types and intensities) on weight change (14) and rated physical and psychosocial health (3). The present study, using data from the National Health and Nutrition Examination Survey (NHANES) in 2005-2006, examined the impact of alternating the allocations of time spent in sleep, sedentary activity, and active behaviors (both light- and moderate-intensity activity) on

cardiometabolic and inflammatory risk biomarkers. An additional aim of the study was to examine whether the strength of the relationship between active and sedentary behaviors with biomarkers differed among adults with varying levels of sleep duration.

Methods

Study Sample

Paragraph 4 Data on the study participants were drawn from NHANES survey, which uses a complex sampling design to produce a representative sample of the U.S. civilian (both children and adults) non-institutionalized population, and over-samples low-income respondents, adolescents, persons 60+ years old, African-Americans and Mexican Americans. The methods are described in detail on the CDC website (4). NHANES includes an in-person home interview and a visit to a Mobile Examination Center (MEC) where laboratory and examination data are collected. The interview data include demographic, socioeconomic, and health-related questions. The examination component includes medical and physiological measurements, as well as laboratory tests. The CDC Ethics Review Board approved the survey protocols and informed consent was obtained for all subjects. This analysis included NHANES data during the 2005-06 dataset where both accelerometry and sleep questionnaires were collected. A total of 4979 respondents ages 20 years and older were interviewed and examined. Respondents were excluded progressively due to none or invalid accelerometer data (N=1907), missing self-reported sleep duration data (N=5), currently taking insulin (N=96), women who were pregnant or lactating (N=142), and a diagnosed sleep disorder (N=192). Data from 2637 adults were available for the full analyses, with a subsample of 1173 available for fasting analyses.

Sociodemographic and Health Behavior/Status Variables

Paragraph 5 A set of sociodemographic variables was used as the covariates in the analyses. These variables include age (as a continuous variable), gender, race/ethnicity recoded into five categories (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other/Multi-Racial), and ratio of family income to poverty (as a continuous variable, range: 0 to 5). Health behavior/status variables including smoking status as measured by serum cotinine levels (range: 0.011 to 1156), depressive symptoms as measured by the 9-item Patient Health questionnaire (12) (range: 0 to 27), total energy intake estimated by two 24-h dietary recall interviews (4), and a general health rating (*excellent* to *poor*) (21).

Physical Activity and Sedentary Variables

Paragraph Number 6 Subjects were asked to wear an Actigraph (Actigraph, LLC; Ft. Walton Beach, FL) model 7164 accelerometer over the right hip on an elasticized belt during the waking day for 7 days following their MEC examination. Details of the accelerometer protocol are described elsewhere (13, 20)and the SAS code used to determine wear/non-wear time is publically available on the National Cancer Institute website (15). Days with ≥10h of wear time were considered valid and ≥4 valid days were needed to be included in the analyses. Standard accelerometer counts·min^{-1} (cpm) thresholds were used to classify all wear time as sedentary (SED; <100 cpm) (13), low-light activity (LOLITE; 101-759 cpm) (cit), high-light activity (HILITE; 760-1951cpm) (cit), or moderate-intensity and greater activity (MVPA, ≥1952 cpm) (5).

Sleep Duration

Paragraph Number 7 Sleep questions were introduced to NHANES in the 2005-2006 cycle and include 24 items related to sleeping patterns, outcomes, and general productivity. Sleep duration, or total sleep time (TST), was assessed with a single-item worded as “How much sleep do you

usually get at night on weekdays or workdays?" Acceptable values range from 1 to 24 hours, with values ≥12 set at 12.

Cardiometabolic Outcomes

Paragraph Number 8 Clinically measured biomarkers included waist circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP). Laboratory-based non-fasting biomarkers included high-density lipoprotein (HDL), low-density lipoprotein (LDL), and C-reactive protein (CRP). A subsample of subjects (N=1173) provided fasting measures of triglycerides, plasma glucose, and insulin. Additional measures of insulin sensitivity (HOMA-%S) and β-cell function (HOMA-%B) were derived using standard procedures (10). Finally, a continuous metabolic syndrome risk score was calculated as a summary measure using principal components analysis (22).

Data Analysis

Paragraph Number 9 All statistical analyses were performed with procedures to account for the complex survey design of NHANES using SAS Enterprise Guide 4.2 software (SAS Institute, Inc., Cary, North Carolina). All analyses included the use of appropriate sample weights, clustering variables, and primary sampling units to assure population-representative estimates. Biomarker variables were log-transformed to account for non-normal distributions. Statistical significance was established at $p < 0.05$ for main effects and $p < 0.10$ for interaction effects.

Paragraph Number 10 Three sets of regression models were fitted to assess associations of the accelerometer-derived (SED, LOLITE, HILITE, MVPA) and TST variables with the outcomes. All models were adjusted for study covariates (described earlier). First, single variable models were used to estimate the "total effect" for each variable. These models depict the raw associations between each variable and the outcome. Second, partition models were used to

estimate the “unique effect” of each variable by holding time in all other variables constant. These models depict the unique association of each variable with the outcome. Finally, isotemporal substitution models were used to estimate the “substitution effect” of replacing time from one variable for an equal amount of time in a different variable (e.g., replacing 30 $min \cdot d^{-1}$ of SED with 30 $min \cdot d^{-1}$ of MVPA). This was accomplished by entering a total time variable (i.e., SED + LOLITE + HILITE + MVPA + TST) and each unique variable into the models simultaneously. The variable of interest was then dropped from the model (similar practice to dropping reference group within dummy-coded analyses). These models depict the effect of replacing time from the dropped variable with all other variables entered in the model. By including a total time variable in the model, the overall assessment time is constrained and allows direct comparisons to be made between variables and their impact on the outcome of interest. Greater detail on isotemporal substitution models is presented elsewhere (14).

Paragraph Number 11 To examine whether the strength of the relationship between SED, LOLITE, HILITE, and MVPA with biomarkers differed by TST, interaction analyses were performed. The TST variable was recoded into 5 levels: ≤5 hours, 6 hours, 7 hours, 8 hours, and ≥9 hours. TST ≥9 hours was collapsed with 8 hours in the fasting variables due to the small sample size (N=185). In light of previous literature suggesting a U-shaped relationship between TST and health outcomes around median TST (7, 16), seven hours of TST was used as the reference category for all comparisons. Only HILITE was examined given high collinearity between SED and LOLITE. Accelerometer-derived variables were entered into the models continuously (adjusting for main effects of the other accelerometer variables); however, results are presented graphically in quartiles to aid interpretation of results.

Results

Paragraph Number 12 The population-weighted sociodemographic, health behavior/status, accelerometry, and cardiometabolic biomarker characteristics are displayed by total sleep time in Table 1. Median accelerometer mins·d^{-1} were as follows: 499.0 (interquartile range [IQR] 418.1, 589.0), 257.4 (IQR 212.4, 302.4), 76.8 (IQR 48.3, 114.1), 16.3 (IQR 5.8, 32.9) for SED, LOLITE, HILITE, and MVPA, respectively.

Isotemporal substitution: Impacts of Alternating Allocations between Active, Sedentary, and Sleep Time

Paragraph Number 13 Isotemporal substitution results are presented in Table 2. Replacing 30 min/day of sedentary time with 30 min/day of MVPA was associated with improved levels waist circumference, HDL cholesterol, CRP, triglycerides, HOMA-B, and HOMA-S. Replacing 30 min/day of TST with 30 min/day of MVPA was associated with improved levels waist circumference, HDL cholesterol, CRP, triglycerides, and HOMA-S. Replacing 30 min/day of sedentary time with 30 min/day of light activity was associated with improved levels of insulin, HOMA-B, and HOMA-S. Replacing 30 min/day of sedentary time with 30 min/day of TST was associated with improved HOMA-S. Replacing 30 min/day of light intensity activity with 30 min/day of extended sleep duration was associated with improved waist circumference. Replacing 30 min/day of light intensity activity with 30 min/day of MVPA was associated with …..>>>>

Behavior-Biomarker Relationships across Total Sleep Time Categories

Paragraph Number 14 The majority of interaction outcomes were not significant, suggesting that the relationship between active and sedentary behaviors with the selected biomarkers was similar across TST categories. Significant interactions are displayed in Figure 1. For waist circumference, there was a small but significant difference between 6 vs. 7h of TST, with 7h

sleepers receiving greater benefit from additional HILITE activity. For systolic blood pressure, there was a small but significant difference between ≤5h vs. 7h of TST, with 7h sleepers receiving greater benefit from MVPA. Also, while only significant for ≤5h and 6h vs. 7h sleepers, 7h sleepers appeared to benefit more from less sedentary time than all other TST groups. For diastolic blood pressure, there was a small but significant difference between ≥9 vs. 7h of TST, with 7h sleepers receiving greater benefit from HILITE, and 7h sleepers receiving greater benefit from less sedentary time than 6h sleepers. For fasting triglycerides, 7h sleepers benefited more from both MVPA and HILITE than ≥8h sleepers. For HOMA-IR and HOMA-S, 7h sleepers benefited more from MVPA than did 6h sleepers.

Discussion

<please include any points of discussion, limitation, strengths, etc… that you think should be addressed in the discussion>

Atienza A, Moser RP, Perna F, Dodd KW, Ballard-Barbash R, Troiano RP, and Berrigan D. Objective and self-reported physical activity and biomarkers of chronic disease in NHANES. *Medicine & Science in Sports & Exercise*. 2010.

Awad KM, Drescher AA, Malhotra A, and Quan SF. Effects of exercise and nutritional intake on sleep architecture in adolescents. *Sleep Breath*. 2012.

Buman MP, Hekler EB, Haskell WL, Pruitt LC, T. L., Cain KL, Sallis JF, Saelens BE, Frank LD, and King AC. Objective light intensity physical activity associations with rated health in older adults. *Am J Epidemiol*. 2010;172(10):1155-65.

Centers for Disease Control and Prevention. NHANES: National Health and Nutrition Examination Survey Hompage. In: 2012.

Freedson PS, Melanson E, and Sirard J. Calibration of the Computer Science and Applications, Inc. Accelerometer. *Med Sci Sports Exerc*. 1998;30(5):777-81.

Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, and Malaspina D. Short Sleep Duration as a Risk Factor for Hypertension. *Hypertension*. 2006;47(5):833-9.
Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, and Malaspina D. Sleep duration as a risk factor for diabetes incidence in a large U.S. sample. *Sleep*. 2007;30(12):1667-73.
Gottlieb DJ, Punjabi NM, Newman AB, Resnick HE, Redline S, Baldwin CM, and Nieto FJ. ASsociation of sleep time with diabetes mellitus and impaired glucose tolerance. *Archives of Internal Medicine*. 2005;165(8):863-7.
Gottlieb DJ, Redline S, Nieto FJ, Baldwin CM, Newman AB, Resnick HE, and Punjabi NM. Association of usual sleep duration with hypertension: the Sleep Heart Health Study. *Sleep*. 2006;29(8):1009-14.
Healy GN, Matthews CE, Dunstan DW, Winkler EAH, and Owen N. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003–06. *European Heart Journal*. 2011;32(5):590-7.
King AC, Pruitt LA, Woo S, Castro CM, Ahn DK, Vitiello MV, Woodward SH, and Bliwise DL. Effects of Moderate-Intensity Exercise on Polysomnographic and Subjective Sleep Quality in Older Adults With Mild to Moderate Sleep Complaints. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences*. 2008;63(9):997-1004.
Kroenke K, Spitzer RL, and Williams JBW. The PHQ-9:Validity of a brief depression severity measure. *Journal of General Internal Medicine*. 2001;16(9):606-13.
Matthews CE, Chen KY, Freedson PS, Buchowski MS, Beech BM, Pate RR, and Troiano RP. Amount of time spent in sedentary behaviors in the united states, 2003-2004. *Am J Epidemiol*. 2008;167(7):875-81.
Mekary RA, Willett WC, Hu FB, and Ding EL. Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol*. 2009;170(4):519-27.
National Cancer Institute. SAS Programs for Analyzing NHANES 2003-2004 Accelerometer Data. In: 2007.
Patel SR, Malhotra A, White DP, Gottlieb DJ, and Hu FB. Association between reduced sleep and weight gain in women. *American Journal of Epidemiology*. 2006;164(10):947-54.
Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Committee Report*. Washington, DC: U.S. Department of Health and Human Services2008. Available from: U.S. Department of Health and Human Services.
Quan SF, O'Connor GT, Quan JS, Redline S, Resnick HE, Shahar E, Siscovick D, and Sherrill DL. Association of physical activity with sleep-disordered breathing. *Sleep and Breathing*. 2007;11(3):149-57.
Sherrill DL, Kotchou K, and Quan SF. Association of physical activity and human sleep disorders. *Archives of Internal Medicine*. 1998;158(17):1894-8.
Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, and McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc*. 2008;40(1):181-8.
Ware JE, Kosinski M, and Keller SD. A 12-item short-form health survey - Construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220-33.
Wijndaele K, Beunen G, Duvigneaud N, Matton L, Duquet W, Thomis M, Lefevre J, and Philippaerts RM. A Continuous Metabolic Syndrome Risk Score. *Diabetes Care*. 2006;29(10):2329.
Willett W, and Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *American Journal of Epidemiology*. 1986;124(1):17-27.
Willett WC, Howe GR, and Kushi LH. Adjustment for total energy intake in epidemiologic studies. *The American Journal of Clinical Nutrition*. 1997;65(4):1220S-8S.

Table 1. Characteristics of the eligible, full, and fasting samples, weighted to the population of US adults ≥20 years by total sleep time (NHANES 2005-06).

Characteristic	Eligible sample[a] n=4130	Full Sample[b] n=2185	Fasting subsample[c] n=923
Sociodemographic			
Age, yrs	46.6 (0.3)	46.6 (0.4)	46.6 (0.6)
Female gender	2050 (49.4)	1028 (47.0)	492 (47.6)
Race/Ethnicity			
Mexican American	772 (7.9)	430 (19.7)	183 (8.0)
Other Hispanic	123 (3.4)	67 (3.1)	34 (4.1)
Non-Hispanic White	1987 (72.1)	1159 (53.0)	474 (71.1)
Non-Hispanic Black	906 (11.2)	449 (20.5)	189 (11.1)
Other/Multi-Racial	154 (5.3)	80 (3.7)	43 (5.7)
Marital status			
Married/living together	2402 (65.4)	1418 (64.9)	614 (67.4)
Widowed	385 (6.7)	188 (8.6)	69 (5.3)
Divorced/separated	503 (12.2)	288 (13.2)	116 (11.8)
Never married/single	647 (15.7)	291 (13.3)	124 (15.4)
Education			
< Year 12	1095 (17.7)	552 (25.3)	220 (15.0)
Year 12 or equivalent	943 (25.2)	520 (23.8)	236 (25.7)
Some college of above	1898 (57.2)	1113 (50.9)	467 (59.3)
Work Status			
Not working	1549 (31.0)	800 (36.6)	340 (28.9)
Part-time (<35 $h \cdot wk^{-1}$)	314 (8.8)	182 (8.3)	84 (10.7)
Full-time (≥35 $h \cdot wk^{-1}$)	2075 (60.2)	1203 (55.1)	499 (60.4)
Poverty Income Ratio†	3.1 (0.0)	3.2 (0.0)	3.2 (0.1)
Health behavior/status			
Smoking (serum cotinine)			
non, <10 ng/dL	2953 (72.9)	1674 (76.6)	715 (75.2)
light, 10-99 ng/dL	216 (5.6)	108 (4.9)	42 (5.4)
moderate, 100-299 ng/dL	479 (13.3)	245 (11.2)	98 (11.7)
heavy, ≥300 ng/dL	294 (8.2)	158 (7.2)	68 (7.7)
Depressive symptoms	2.4 (0.1)	2.2 (0.1)	2.4 (0.1)
Total energy intake, MJ	9.3 (0.1)	9.2 (0.1)	9.1 (0.2)
Saturated fat, % total energy	11.0 (0.1)	11.1 (0.1)	11.1 (0.1)
Caffeine, g	190.4 (4.5)	196.3 (6.1)	190.1 (9.2)
Alcohol intake, g			
none	1191 (26.9)	730 (33.4)	327 (29.9)
light (M<28; F<14)	1489 (43.7)	930 (42.6)	388 (44.2)
moderate (M 28-55; F 14-27)	403 (13.7)	250 (11.4)	90 (12.0)
heavy (M≥56; F≥28)	506 (15.7)	275 (12.6)	118 (13.9)
General health rating‡	2.6 (0.0)	2.5 (0.0)	2.6 (0.0)
Previous diagnoses			
Cancer or malignancy	331 (7.8)	190 (8.7)	83 (8.0)
Cardiovascular disease	372 (7.2)	185 (8.5)	79 (7.0)
Diabetes	362 (6.7)	204 (9.3)	84 (6.2)
Current medication use			
Diabetic	241 (4.2)	143 (6.5)	58 (4.1)
Antihypertensive	214 (4.9)	125 (5.7)	44 (3.8)
Lipidemic	889 (18.8)	362 (16.6)	145 (12.7)
Other cardiovascular	930 (18.6)	518 (23.7)	229 (19.1)

Data are n (%) or mean (SEM). Weights used: [a]examination (2005-06) sample weight; [b]reweighted examination weight for missing data; [c]reweighted fasting subsample weight.

Actual n varies due to missing data.

†Range: 0 to 5, higher numbers reflects increased income;

‡Range: 1(excellent) to 5(poor).

SUPPLEMENTAL MATERIAL

Supplementary Table 1. Covariates retained through backward elimination.

Outcome	Covariates retained through backward elimination†
Non-fasting biomarkers	
Waist circumference	Marital status, education, alcohol intake, smoking, saturated fat, general health rating, diabetes history, antihypertensive medication, lipidemic medication, other CVD medication
Systolic blood pressure	Alcohol intake, poverty-income ratio, energy intake, caffeine, general health rating, cancer history, CVD history, diabetes history, antihypertensive medication, other CVD medication
Diastolic blood pressure	Alcohol intake, poverty-income ratio, CVD history, antihypertensive medication
HDL-cholesterol	Marital status, education, alcohol intake, poverty-income ratio, energy intake, saturated fat, caffeine, general health rating, other CVD medication
C-reactive protein	Marital status, education, poverty-income ratio, energy intake, saturated fat, caffeine, general health rating, lipidemic medication
Fasting biomarkers	
LDL-cholesterol	Marital status, education, work status, smoking, depression, energy intake, saturated fat, caffeine, general health rating, lipidemic medication
Triglycerides	Marital status, education, caffeine, general health rating, CVD history, lipidemic medication, other CVD medication
Plasma glucose	Education, energy intake, saturated fat, general health rating, CVD history, lipidemic medication, other CVD medication
Insulin	Marital status, work status, alcohol intake, smoking, saturated fat, caffeine, general health rating, antihypertensive medication, lipidemic medication, other CVD medication
HOMA-%B	work status, alcohol intake, smoking, energy intake, saturated fat, caffeine, general health rating, diabetes history, diabetes medication, antihypertensive medication, lipidemic medication, other CVD medication
HOMA-%S	Marital status, education, alcohol intake, smoking, saturated fat, caffeine, general health rating, diabetes history, antihypertensive medication, lipidemic medication, other CVD medication

†Covariate was retained where $p<0.2$; all models were adjusted for age (linear and curvilinear), gender, and race/ethnicity.

Supplemental Table 2. Characteristics of the full sample, weighted to the population of US adults ≥20 years by categories of total sleep time (NHANES 2005-06, n=2185).

Characteristic	Total Sleep Time				
	≤5 hrs	6 hrs	7 hrs	8 hrs	≥9 hrs
Sociodemographic					
Age, yrs	46.9 (0.8)	46.9 (0.7)	44.7 (0.6)	47.6 (0.8)	49.9 (2.1)
Female gender	122 (11.9)	245 (23.8)	313 (30.4)	271 (26.4)	77 (7.5)
Race/Ethnicity					
Mexican American	58 (13.5)	98 (22.8)	126 (29.3)	129 (30.0)	19 (4.4)
Other Hispanic	9 (13.4)	16 (23.9)	22 (32.8)	17 (25.4)	3 (4.5)
Non-Hispanic White	104 (9.0)	236 (20.4)	375 (32.4)	354 (30.5)	90 (7.8)
Non-Hispanic Black	99 (22.0)	137 (30.5)	89 (19.8)	98 (21.8)	26 (5.8)
Other/Multi-Racial	11 (13.8)	20 (25.0)	25 (31.3)	17 (21.3)	7 (8.8)
Marital status					
Married/living together	165 (11.6)	319 (22.5)	456 (32.2)	397 (28.0)	81 (5.7)
Widowed	25 (13.3)	41 (21.8)	41 (21.8)	55 (29.3)	26 (13.8)
Divorced/separated	47 (16.3)	81 (28.1)	66 (22.9)	79 (27.4)	15 (5.2)
Never married/single	44 (15.1)	66 (22.7)	74 (25.4)	84 (28.9)	23 (7.9)
Education					
< Year 12	82 (14.9)	124 (22.5)	139 (25.2)	154 (27.9)	53 (9.6)
Year 12 or equivalent	75 (14.4)	119 (22.9)	147 (28.3)	146 (28.1)	33 (6.3)
Some college of above	124 (11.1)	264 (23.7)	351 (31.5)	315 (28.3)	59 (5.3)
Work Status					
Not working	100 (12.5)	173 (21.6)	180 (22.5)	261 (32.6)	86 (10.8)
Part-time (<35 $h \cdot wk^{-1}$)	22 (12.1)	22 (12.1)	65 (35.7)	62 (34.1)	11 (6.0)
Full-time (≥35 $h \cdot wk^{-1}$)	159 (13.2)	312 (25.9)	392 (32.6)	292 (24.3)	48 (4.0)
Poverty Income Ratio†	2.9 (0.1)	3.3 (0.1)	3.4 (0.1)	3.1 (0.1)	2.8 (0.2)
Health behavior/status					
Smoking (serum cotinine)					
non, <10 ng/dL	198 (11.8)	373 (22.3)	500 (29.9)	489 (29.2)	114 (6.8)
light, 10-99 ng/dL	20 (18.5)	18 (16.7)	32 (29.6)	33 (30.6)	5 (4.6)
moderate, 100-299 ng/dL	37 (15.1)	64 (26.1)	71 (29.0)	61 (24.9)	12 (4.9)
heavy, ≥300 ng/dL	26 (16.5)	52 (32.9)	34 (21.5)	32 (20.3)	14 (8.9)
Depressive symptoms	3.6 (0.3)	2.5 (0.2)	1.8 (0.1)	2.0 (0.1)	2.2 (0.3)
Total energy intake, MJ	9.5 (0.3)	9.4 (0.3)	9.2 (0.2)	9.2 (0.2)	8.5 (0.4)
Saturated fat, % total energy	11.6 (0.3)	11.1 (0.2)	11.0 (0.2)	11.0 (0.2)	11.5 (0.3)

Caffeine, g	261.7 (23.7)	200.5 (11.9)	198.2 (10.1)	176.2 (11.6)	149.0 (17.6)
Alcohol intake, g					
none	127 (17.4)	154 (21.1)	187 (25.6)	205 (28.1)	57 (7.8)
light (M<28; F<14)	95 (10.2)	242 (26.0)	282 (30.3)	252 (27.1)	59 (6.3)
moderate (M 28-55; F 14-27)	26 (10.4)	55 (22.0)	87 (34.8)	68 (27.2)	14 (5.6)
heavy (M≥56; F≥28)	33 (12.0)	56 (20.4)	81 (29.5)	90 (32.7)	15 (5.5)
General health rating‡	2.8 (0.1)	2.6 (0.0)	2.4 (0.0)	2.5 (0.0)	2.7 (0.1)
Previous diagnoses					
Cancer or malignancy	18 (9.5)	36 (18.9)	56 (29.5)	60 (31.6)	20 (10.5)
Cardiovascular disease	32 (17.3)	43 (23.2)	34 (18.4)	56 (30.3)	20 (10.8)
Diabetes	41 (20.1)	40 (19.6)	45 (22.1)	56 (27.5)	22 (10.8)
Current medication use					
Diabetic	29 (20.3)	27 (18.9)	27 (18.9)	43 (30.1)	17 (11.9)
Antihypertensive	18 (14.4)	32 (25.6)	29 (23.2)	37 (29.6)	9 (7.2)
Lipidemic	43 (11.9)	77 (21.3)	84 (23.2)	115 (31.8)	43 (11.9)
Other cardiovascular	71 (13.7)	109 (21.0)	119 (23.0)	169 (32.6)	50 (9.7)

Data are n (%) or mean (SEM). †Range: 0 to 5, higher numbers reflects increased income; ‡Range: 1(excellent) to 5(poor).

Supplemental Table 3. Spearman (ρ) correlation coefficients for total sleep time, sedentary behavior, light intensity activity, and moderate-vigorous physical activity (NHANES 2005-06; n=2185).

	1	2	3	4
(1) TST	1.000	-0.550 ***	-0.109 ***	-0.029
(2) SED		1.000	-0.295 ***	-0.015
(3) LITE			1.000 ***	0.321 ***
(4) MVPA				1.000

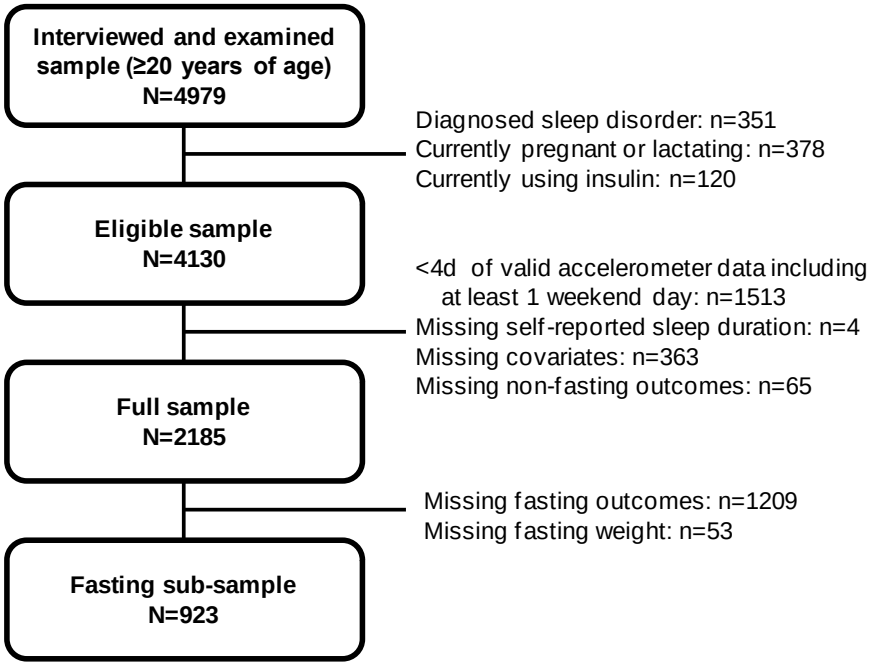
***p<.001; TST, total sleep time; SED, sedentary (<100 counts·min^{-1} [cpm]); LITE, light intensity (100-1951 cpm); MVPA, moderate-vigorous intensity (≥1952 cpm); .

Supplementary Table 4. Population-weighted single and partition regression models† of non-fasting and fasting cardiovascular risk biomarkers on total sleep time, sedentary behavior, light intensity activity, and moderate-vigorous physical activity (NHANES 2005-06)‡.

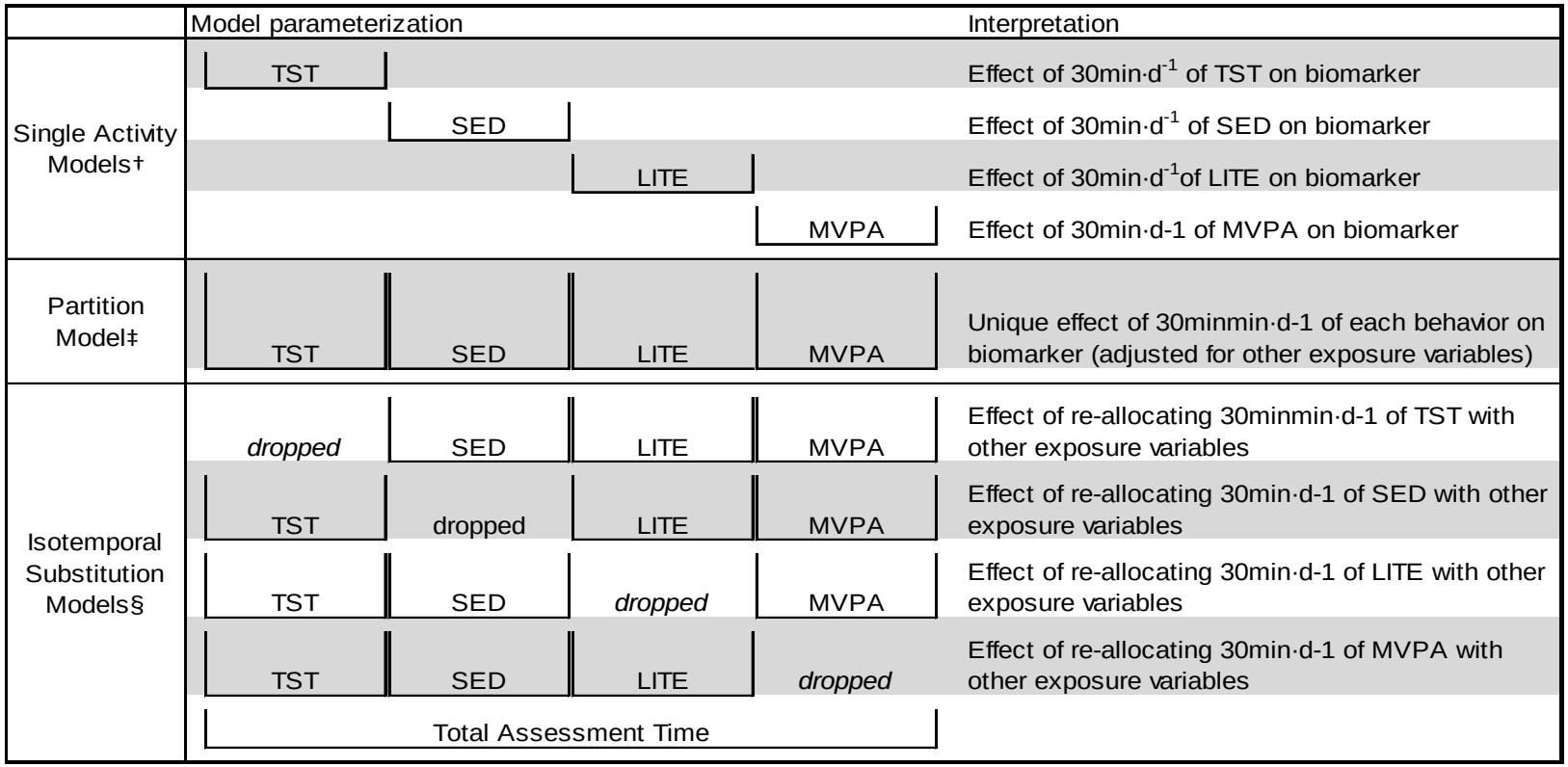
	TST (linear)	TST (curvilinear)	SED	LITE	MVPA
Non-fasting biomarkers (n=2187)					
Waist circumference					
Single	0.997 (0.994 ,1.000) *	1.000 (0.999 ,1.000)	1.001 (0.999 ,1.003)	0.997 (0.995 ,0.999) **	0.971 (0.964 ,0.979) ***
Partition	0.996 (0.992 ,0.999) *	1.000 (0.999 ,1.000)	0.999 (0.997 ,1.001)	0.998 (0.996 ,1.000)	0.972 (0.963 ,0.981) ***
Systolic BP					
Single	0.999 (0.996 ,1.002)	1.000 (1.000 ,1.001)	0.999 (0.997 ,1.000) *	1.002 (1.000 ,1.004) *	1.000 (0.992 ,1.007)
Partition	1.000 (0.997 ,1.003)	1.000 (1.000 ,1.001)	0.999 (0.997 ,1.000)	1.001 (0.999 ,1.003)	0.996 (0.989 ,1.004)
Diastolic BP					
Single	1.001 (0.998 ,1.004)	1.001 (1.000 ,1.001)	0.998 (0.996 ,1.001)	1.002 (0.999 ,1.005)	1.007 (0.991 ,1.023)
Partition	1.003 (1.000 ,1.007)	1.001 (1.000 ,1.001) *	0.999 (0.997 ,1.002)	1.002 (0.999 ,1.005)	1.004 (0.985 ,1.023)
HDL-cholesterol					
Single	1.002 (0.994 ,1.010)	1.000 (0.999 ,1.001)	0.997 (0.994 ,1.000)	1.005 (1.001 ,1.010) *	1.050 (1.032 ,1.068) ***
Partition	1.003 (0.994 ,1.012)	1.000 (0.999 ,1.002)	1.000 (0.996 ,1.004)	1.003 (0.997 ,1.009)	1.046 (1.027 ,1.066) ***
C-reactive protein					
Single	0.989 (0.963 ,1.014)	1.006 (1.002 ,1.009) **	1.002 (0.985 ,1.019)	0.983 (0.953 ,1.014)	0.801 (0.714 ,0.898) ***
Partition	1.001 (0.978 ,1.025)	1.005 (1.002 ,1.009) ***	0.987 (0.973 ,1.002)	0.988 (0.958 ,1.019)	0.797 (0.719 ,0.883) ***
Fasting biomarkers (n=923)					
LDL-cholesterol					
Single	0.997 (0.989 ,1.005)	1.002 (1.001 ,1.004) *	0.999 (0.993 ,1.005)	1.001 (0.994 ,1.008)	1.001 (0.971 ,1.033)
Partition	1.005 (0.994 ,1.016)	1.002 (1.001 ,1.004) *	0.999 (0.993 ,1.005)	1.000 (0.993 ,1.007)	0.999 (0.962 ,1.036)
Triglycerides					
Single	0.998 (0.979 ,1.017)	1.002 (0.998 ,1.006)	1.010 (1.001 ,1.020) *	0.975 (0.967 ,0.984) ***	0.892 (0.837 ,0.951) **
Partition	1.004 (0.987 ,1.022)	1.002 (0.998 ,1.006)	0.998 (0.989 ,1.008)	0.980 (0.968 ,0.992) **	0.911 (0.857 ,0.969) **
Plasma glucose					
Single	1.003 (0.998 ,1.008)	1.000 (0.999 ,1.001)	0.999 (0.997 ,1.001)	1.000 (0.997 ,1.003)	0.989 (0.980 ,0.997) *
Partition	1.003 (0.996 ,1.009)	1.000 (0.999 ,1.001)	0.999 (0.996 ,1.001)	1.000 (0.997 ,1.004)	0.986 (0.975 ,0.997) *
Insulin					
Single	0.981 (0.962 ,1.001)	0.998 (0.993 ,1.002)	1.019 (1.008 ,1.029) **	0.970 (0.957 ,0.984) ***	0.848 (0.772 ,0.932) **
Partition	0.973 (0.948 ,0.999)	0.998 (0.994 ,1.002)	1.004 (0.993 ,1.016)	0.980 (0.964 ,0.997) *	0.878 (0.791 ,0.975) *
HOMA-%B					
Single	0.985 (0.970 ,0.999) *	0.999 (0.996 ,1.002)	1.014 (1.009 ,1.019) ***	0.977 (0.969 ,0.985) ***	0.926 (0.879 ,0.975) **
Partition	0.982 (0.967 ,0.997) *	0.999 (0.996 ,1.003)	1.004 (0.998 ,1.011)	0.982 (0.971 ,0.993) **	0.956 (0.900 ,1.015)

Homa-%S					
Single	1.014 (0.997 ,1.032)	1.002 (0.998 ,1.005)	0.985 (0.975 ,0.994) **	1.028 (1.017 ,1.039) ***	1.146 (1.058 ,1.240) **
Partition	1.020 (1.000 ,1.040)	1.001 (0.998 ,1.005)	0.997 (0.986 ,1.008)	1.020 (1.006 ,1.034) **	1.111 (1.019 ,1.212) *

Data are relative rates (95% confidence interval); ***p<.001; **p<.01; *p<.05; †All models were adjusted for age (linear and curvilinear), gender, and race/ethnicity. Marital status, education, work status, poverty, smoking, depressive symptoms, energy intake, saturated fat, caffeine, alcohol use, general health rating, previous diagnosis of cancer or malignancy, cardiovascular disease, or diabetes, and current diabetic, antihypertensive, lipidemic, or other CVD medication were included as covariates through backward elimination (p<0.2). ‡TST, SED, LITE, and MVPA are in 30min·d^{-1} units to aid interpretation. TST, total sleep time; SED, sedentary (<100 cpm); LITE, light intensity (100-1951 cpm); MVPA, moderate-vigorous intensity (≥1952 cpm); HDL, high-density lipoprotein; LDL, low-density lipoprotein.



Supplementary Figure 1. Study inclusion flow chart.



Supplementary Figure 2. Three types of regression models of cardiovascular risk biomarkers fitted to assess assocations with total sleep time, sedentary time, light intensity activity, and moderate-vigorous physical activity. †Single activity models tested the "total effect" of each exposure variable, unadjusted for activity in other thresholds; ‡Partition models tested the "unique effect" of each exposure variable adjusted for time in other exposure variables; §Isotemporal substitution models tested the "substitution effect" of each exposure variable holding time constant in other exposures. TST, total sleep time; SED, sedentary behavior; LITE, light intensity activity; MVPA, moderate-vigorous physical activity.