Habitual sleep as a contributor to racial differences in cardiometabolic risk

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Insufficient and disrupted sleep is linked with cardiovascular and metabolic dysregulation and morbidity. The current study examines the degree to which differences in sleep between black/African American (AA) and white/European American (EA) adults explain racial differences in cardiometabolic (CMB) disease risk. Total sleep time and sleep efficiency (percent of time in bed asleep) were assessed via seven nights of wrist actigraphy among 426 participants in the Midlife in the United States Study (31% AA; 69% EA; 61% female; mean age = 56.8 y). CMB risk was indexed as a composite of seven biomarkers [blood pressure, waist circumference, hemoglobin A1c (HbA_{1c}), insulin resistance, triglycerides, HDL cholesterol (HDL-C), and C-reactive protein]. Covariates included sociodemographic characteristics and relevant health behaviors. Results indicated that AAs relative to EAs obtained less sleep (341 vs. 381 min) and had lower sleep efficiency (72.3 vs. 82.2%) (P values < 0.001). Further, 41% and 58% of the racial difference in CMB risk was explained by sleep time and sleep efficiency, respectively. In models stratified by sex, race was indirectly associated with CMB risk via sleep time and efficiency only among females (explaining 33% and 65% of the race difference, respectively). Indirect effects were robust to alternative model specifications that excluded participants with diabetes or heart disease. Consideration of sleep determinants and sleep health is therefore needed in efforts to reduce racial differences in CMB disease.

health disparities | race | sleep | cardiometabolic disease | health behaviors

Black/African American adults (AAs) have disproportionately high rates of cardiovascular and metabolic diseases compared with white/European American (EAs), including elevated hypertension, diabetes, and stroke prevalence (1, 2). The reduction of these racial health disparities has become a pillar of the United States' national health strategy (3, 4). However, given the complexity of risk exposures at multiple levels and numerous potential mechanisms (5, 6), the underlying reasons for AA–EA health differences are not well understood. For example, differences in health behaviors related to cardiometabolic (CMB) disease risk—namely, diet, physical activity, and smoking—have been considered as behavioral pathways through which AAs experience greater health risk, but adjusting for these behaviors leaves a substantial racial gap in CMB conditions unexplained (6–8).

Three recent review papers have proposed that differences in sleep patterns are one further behavioral mediator of the unequal cardiovascular disease and diabetes burden between AA and EA adults (9–11). Race differences are apparent across several sleep parameters even after adjusting for socioeconomic characteristics, so that AAs are more likely to sleep for an insufficient duration and to experience fragmented sleep relative to EAs (12, 13). In turn, sleep problems are risk factors for coronary heart disease, stroke, hypertension, and diabetes and predispose to more abdominal adiposity and low-grade systemic inflammation (14–19). Despite the expanding literature, few studies have examined sleep as a mediator of AA–EA differences in CMB diseases. Specifically, to our knowledge, sleep has been considered as a mediator of racial differences only in blood pressure (16, 20, 21), and therefore additional research is needed to examine CMB dysregulation more widely.

Therefore the primary aim of the current study was to test the degree to which differences in habitual sleep explain racial differences in CMB disease risk. Data were derived from 426 AA and EA adults from the Midlife in the United States (MIDUS) study who participated in a sleep substudy. Total sleep time and sleep efficiency (i.e., the percentage of the time in bed spent sleeping) were measured over seven nights using actigraphy—a watch-like activity monitor that has good correspondence with polysomnography (22). CMB risk was measured as a composite of ideal, borderline high, and high (coded as 0, 1, and 2, respectively) levels of waist circumference, hemoglobin A1c (HbA_{1c}), insulin resistance [homeostatic model assessment of insulin resistance (HOMA-IR)], blood pressure, triglycerides, HDL cholesterol (HDL-C), and C-reactive protein (CRP) (Table 1) (23–25). CMB risk scores were averaged across the biomarkers so that total scores ranged from 0 to 2. Additional models were fit to examine whether associations between sleep and CMB risk varied by demographic factors (race, sex, and age) and, given that AA–EA differences in obesity and diabetes are larger for females than for males (26, 27), whether mediation of racial differences in CMB risk varied by sex. To reduce the likelihood of reverse causality, we also tested study hypotheses among participants without heart disease or diabetes.

Results

Sample descriptive statistics are listed by race in Table 2. Race differences were identified in several of the sociodemographics, health behaviors, and CMB markers. Notably, AAs obtained nearly 40 fewer minutes of sleep and had 10% lower sleep efficiency than

Significance

Large differences in cardiovascular disease and diabetes prevalence exist between African American and European American adults. The US federal government has committed to reducing racial disparities in health; however, the precise mechanisms are not well understood. Sleep is one potential behavioral explanation for current racial differences in cardiometabolic conditions. We show that more than one-half of racial differences in cardiometabolic risk can be explained by sleep patterns—namely, less total sleep and lower sleep efficiency among African American than European American adults. Sleep is a malleable health behavior that is linked with characteristics of the social and physical environment and could be an effective target in national efforts to reduce racial health disparities.

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Table 1. Biomarker cut points for CMB risk index

Biomarkers	Ideal, coded 0	Borderline, coded 1	High, coded 2
Waist circumference, cm	Male: <94 Female: <80	≥94 to <102 ≥80 to <88	≥102 ≥88
Blood pressure, mmHG*	<120/80	120/80 to <140/90	≥140/90
HbA_{1c},%	<5.7	5.7 to <6.5	6.5
HOMA-IR	Lowest tertile	Middle tertile	Highest tertile
Triglycerides, mg/dL	<150	150–199	≥200
HDL, mg/dL	≥60	Male: 40–59 Female: 50–59	<40 <50
C-reactive protein, mg/L	<1	1–3	>3

When possible, borderline-high and high cut points are based on recommendations from the NCEP ATP III and the AHA (1–3). HOMA-IR, homeostatic model assessment of insulin resistance.
*Blood pressure cut points were coded as a single biomarker using systolic and diastolic values.

EAs. Further, AAs relative to EAs had significantly larger waist circumference, higher diastolic blood pressure, $HbA1_c$, HOMA-IR, and CRP levels but had a more favorable lipid profile (lower triglycerides and higher HDL-C). In total, AAs had a higher unadjusted CMB risk than EAs including higher risk scores for four of the individual CMB risk scores.

Racial Differences in Sleep and CMB Risk. After adjusting for sociodemographic characteristics, AAs obtained less sleep per night [regression coefficient (B) = −0.72 h, SE = 0.13, $P < 0.001$] and had lower sleep efficiency (B = −10.14 percentage points, SE = 1.12, $P < 0.001$) relative to EAs. Race differences were equivalent to an effect size of 0.63 and 0.95 SD units, respectively.

See Table 3 for parameter estimates for Models 1–4. In Model 1, AAs had elevated CMB risk relative to EAs (B = 0.15, 95% CI: 0.05, 0.26) after adjusting for sociodemographics, a difference equivalent to 0.32 SD units. When CMB risk was further adjusted for diet, exercise, cigarette smoker status, and depressive symptoms (Model 2), the racial gap in CMB risk was attenuated by 27% but remained significant (B = 0.11, 95% CI: 0.01, 0.22).

Sleep Indicators Explain Differences in CMB Risk. Total sleep time and sleep efficiency were added separately as predictors of CMB risk in Models 3 and 4, respectively. We found that shorter sleep time was significantly associated with greater CMB risk (B = −0.07, 95% CI: −0.10, −0.03). Furthermore, a significant indirect effect of race on CMB risk via sleep time was detected (B = 0.05, 95% CI: 0.02, 0.08), explaining 41% of the estimated racial gap, which was no longer significant. Nonlinear associations between sleep time and CMB risk were also tested using sleep time squared, but results indicated no significant association ($P = 0.60$).

In Model 4, lower sleep efficiency was associated with greater CMB risk (B = −0.007, 95% CI: −0.012, −0.002). Notably, racial differences in CMB risk were found to operate partly through sleep efficiency (indirect effect: B = 0.07, 95% CI: 0.02, 0.13), so that the racial gap in CMB risk was reduced by 58% and was nonsignificant. When sleep variables were simultaneously tested as mediators, the race estimate in CMB risk was similar to Model 4 (B = 0.04, 95% CI: −0.07, 0.15; attenuated by 64% from Model 2), but neither of the indirect effects (sleep time: B = 0.03, 95% CI: −0.01, 0.07; sleep efficiency: B = 0.04, 95% CI: −0.02, 0.11) was significant, likely because of multicollinearity.

We also examined race, age, and sex as moderators of the link between sleep and CMB risk (see Table S1 for full results). No evidence of moderation by racial group or age was found for either of the sleep indicators. In contrast, sex moderated associations between both sleep indicators and CMB risk (sleep time: $P = 0.005$; efficiency: $P = <0.001$), indicating that the link between sleep and CMB risk was stronger for females than for males.

Sex-Stratified Models. Models 1–4 were also fit in sex-stratified subsamples. Because the sample of AA males was small, analyses in the male subsample were exploratory and are described in *Supporting Information*. AA females obtained 0.75 h less sleep and had 9.1% lower sleep efficiency than EA females (Ps < 0.001). Differences in CMB risk were also substantial, so that, after adjusting for demographics, AA females had 0.52 SD units higher risk than EAs (B = 0.25, 95% CI: 0.12, 0.38).

As depicted in Models 2–4 of Table S2, health behaviors, sleep time, and sleep efficiency were tested as explanations for differential CMB risk between AA and EA females. Adjusting for sleep time explained 33% of the racial gap in CMB risk, and the test of mediation was significant (indirect effect: B = 0.07, 95% CI: 0.02, 0.12). Sleep efficiency was also associated with CMB risk and explained 65% of the race difference in females (indirect effect: B = 0.14, 95% CI: 0.07, 0.22). When sleep time and sleep efficiency were considered simultaneously, the indirect effect via sleep efficiency was significant (B = 0.13, 95% CI: 0.03, 0.22), but the indirect effect via sleep time was not, and the sleep indicators together explained 73% of the race estimate (B = 0.07, 95% CI: −0.07, 0.20).

Supplemental Analyses. To decrease the possibility of reverse causality (i.e., CMB disease disrupting sleep), we tested mediation hypotheses after excluding participants with heart disease or diabetes (manifest by HbA_{1c} ≥6.5%). In this restricted sample (n = 303), race was still indirectly related to CMB risk via sleep time (B = 0.05, 95% CI: 0.02, 0.11). The indirect effect estimate of race on CMB risk via sleep efficiency was similar in magnitude but was not significant (B = 0.05, 95% CI: −0.02, 0.12). In the female subsample without heart disease or diabetes (n = 190), significant indirect effects of race on CMB risk via sleep time (B = 0.09, 95% CI: 0.03, 0.18) and sleep efficiency (B = 0.12, 95% CI: 0.03, 0.24) were also detected. In addition, to separate poor

Table 2. Descriptives of AAs (n = 133) and EAs (n = 293) in the MIDUS study

Variables	AA, mean ± SD or %	EA, mean ± SD or %	Difference, P value
Age, y	54.9 ± 10.2	57.6 ± 11.8	0.016
Female, %	72.9	54.9	<0.001
Partnered, %	43.2	75.8	<0.001
Educational attainment, %			
≤High school degree	44.4	26.0	<0.001
Some college	32.3	27.7	0.34
≥B.S. or equivalent	23.3	46.2	<0.001
Income, $10^3	39.4 ± 33.3	74.1 ± 56.1	<0.001
Exercise, min/d	35.5 ± 65.2	39.6 ± 46.0	0.47
Fast food consumption, %			
None	13.6	18.1	0.26
Less than once a week	35.6	32.8	0.57
Once a week or more	50.8	49.2	0.76
Depressive symptoms	11.8 ± 9.6	6.34 ± 6.26	<0.001
Cigarette smoker, %	24.8	10.9	0.001
Total sleep time, min	340.6 ± 73.9	381.3 ± 62.9	<0.001
Sleep efficiency	72.3 ± 11.5	82.2 ± 8.7	<0.001
Waist circumference, cm	102.7 ± 19.4	97.1 ± 16.4	0.005
Systolic BP, mmHg	135.0 ± 21.1	131.7 ± 17.1	0.12
Diastolic BP, mmHg	78.8 ± 11.9	76.6 ± 10.2	0.046
HbA_{1c}	6.72 ± 1.79	5.95 ± 0.76	<0.001
HOMA-IR	4.85 ± 4.47	3.49 ± 4.31	0.004
Triglycerides, mg/dL	114.7 ± 66.3	134.2 ± 81.1	0.009
HDL-C, mg/dL	59.1 ± 19.2	52.1 ± 16.2	<0.001
CRP, μg/mL	4.85 ± 5.87	2.79 ± 4.98	0.001
CBM risk	1.17 ± 0.46	1.04 ± 0.50	0.013

Data not designated as percentages are expressed as mean ± SD. Race differences were tested using independent samples t tests and χ^2 tests. BP, blood pressure.

Table 3. Series of regression models demonstrating racial disparities in CMB risk in the full sample (n = 426) after adjusting for sociodemographic covariates (Model 1), health behaviors (Model 2), total sleep time (Model 3), and sleep efficiency (Model 4)

	Model 1		Model 2		Model 3		Model 4	
Variables	B	95% CI	B	95% CI	B	95% CI	B	95% CI
Race (African American = 1)	0.15**	[0.05, 0.26]	0.11*	[0.01, 0.22]	0.07	[−0.04, 0.18]	0.05	[−0.06, 0.16]
Age	0.01***	[0.01, 0.01]	0.01***	[0.01, 0.02]	0.01***	[0.01, 0.02]	0.01***	[0.01, 0.02]
Male	0.02	[−0.07, 0.11]	0.01	[−0.08, 0.10]	−0.03	[−0.12, 0.06]	−0.03	[−0.13, 0.06]
Partnered	0.09	[−0.01, 0.19]	0.09	[−0.01, 0.18]	0.11*	[0.01, 0.20]	0.10	[0.00, 0.19]
Education (referent is ≤high school degree)								
Some college attendance	0.03	[−0.09, 0.15]	0.01	[−0.11, 0.13]	0.01	[−0.11, 0.13]	0.01	[−0.11, 0.13]
≥4 y college degree	0.03	[−0.09, 0.15]	0.03	[−0.08, 0.15]	0.03	[−0.08, 0.14]	0.03	[−0.08, 0.14]
Income	−0.01*	[−0.02, 0.00]	−0.01*	[−0.02, 0.00]	−0.01	[−0.02, 0.00]	−0.01**	[−0.02, 0.00]
Physical activity			−0.07*	[−0.14, 0.00]	−0.08*	[−0.15, −0.01]	−0.07*	[−0.14, 0.00]
Fast food consumption (referent is none)								
Less than once a week			0.08	[−0.05, 0.21]	0.08	[−0.05, 0.21]	0.08	[−0.05, 0.21]
Once a week or more			0.19**	[0.06, 0.31]	0.19**	[0.06, 0.32]	0.18**	[0.05, 0.30]
Current cigarette smoker			0.09	[−0.05, 0.23]	0.07	[−0.06, 0.20]	0.07	[−0.07, 0.20]
Depressive symptoms			0.00	[0.00, 0.01]	0.00	[0.00, 0.01]	0.00	[0.00, 0.01]
Total sleep time, in hours					−0.07***	[−0.10, −0.03]		
Sleep efficiency, %							−0.01**	[−0.01, 0.00]

Significance: *P < 0.05. **P < 0.01. ***P < 0.001.

sleep patterns resulting from sleep disorders, models were also fit excluding participants with chronic sleep problems; the results are described in *Supporting Information*.

Models 2–4 were also fit treating the individual CMB markers as continuously coded outcomes using multivariate regression. Systolic and diastolic blood pressure were modeled separately, constituting two of the eight outcomes. Antihypertensives were included as a predictor of systolic and diastolic blood pressure, and lipid-lowering medications were included as a predictor of triglycerides and HDL-C levels. Results are shown in Table S3. In summary, relative to EAs, AAs had larger waist circumference, greater HbA_{1c}, HOMA-IR, and CRP (and higher HDL-C and lower triglycerides, which are not discussed further). The race estimate for each of respective biomarkers was attenuated by 24, 14, 23, and 13%, respectively, when adjusting for sleep time, and by 26, 24, 23, and 19%, respectively, when adjusting for sleep efficiency. Sex-stratified models also showed that racial health differences and the explanatory role of sleep were driven by the female subsample (see Table S4). In particular, relative to EA women, AA women had larger waist circumference and greater systolic and diastolic blood pressure, HbA_{1c}, HOMA-IR, and CRP. These differences were attenuated by 20, 13, 13, 8, 19, and 16%, respectively, when adjusting for sleep time and by 27, 22, 19, 19, 30, and 22%, respectively, when adjusting for sleep efficiency.

Discussion

Reducing racial/ethnic health disparities is highlighted as one of the four overarching goals in *Healthy People 2020* (3). Given that ∼40% of the gap in premature mortality between AAs and EAs (and more than 50% of the gap between AA and EA females) stems from cardiovascular and metabolic conditions, improving the CMB health of AAs is an important step toward greater health equity (28). Sleep represents one potential intervention point (9, 10), but the relative influence of sleep on racial differences in CMB conditions is largely unknown. In a sample of middle-aged and older adults, we find support for the notion that differences in habitual sleep contribute to the unequal burden of CMB disease risk. In particular, after adjusting for sociodemographics and health behaviors, sleep time and sleep efficiency accounted for 41% and 58% of the AA–EA gap in CMB risk scores, respectively. Path analysis allowed for the simultaneous consideration of the sleep mediator and CMB outcome—each of which was adjusted for sociodemographics—and a formal test of mediation.

These findings are consistent with previous investigations of sleep as a mediator of race differences in blood pressure (16, 21, 29). Specifically, using data from the Coronary Artery Risk Development in Young Adults Study, actigraph-assessed sleep time mediated AA–EA differences in diastolic blood pressure change over a 5-y period (16). In a population-based cohort in Chicago, actigraph-assessed sleep maintenance, but not sleep duration, was associated with hypertension and explained ∼11% of the AA–EA difference in prevalence (29). Another study of middle-aged adults in the Southeast reported that lower sleep quality explained, in part, differences between AAs and EAs in nocturnal blood pressure dipping (21). In contrast, a study using data from the male subsample of the Boston Area Community Health Survey did not find evidence of short sleep duration (≤5 h) to be a mediator of racial disparities in 5-y self-reported hypertension incidence (20), but analyses were tested only for males and were limited by a dichotomous self-report sleep-duration variable. Thus, extant evidence suggests that sleep problems contribute to racial differences in hypertension; this study adds evidence regarding their influence on racial differences in the risk for CMB disease more broadly.

When examining findings by biological sex, sleep indicators were associated with CMB risk among females but not males (see Table S5 for results among male sample), and sleep also explained a substantial portion of the race differences in CMB risk among females. The sex moderation of the sleep–health association is consistent with prior research documenting insufficient sleep as a risk factor for larger waist circumference, hypertension, and elevated inflammatory markers among females but not among males (30–32). However, given the small sample of AA males, the current dataset was able to offer only preliminary support for sex differences in the extent to which sleep explained racial differences in CMB risk. Additional research is needed to determine whether differences in sleep lead to elevated CMB morbidity among AA males relative to EA males, and, if so, to elucidate the mechanisms underlying sex differences in associations between sleep and physical health.

Examining individual biomarkers, we also found broad support for the role of sleep as an explanation of CMB risk. Specifically, relative to EAs, AA females had greater dysregulation in each of the six expected CMB markers, and these differences were attenuated by 8–29% when adjusting for sleep time and by 19–30% when adjusting for sleep efficiency. These findings are consistent with one study that tested associations between sleep and allostatic load (indexed by seven physiologic systems). When

individual systems were examined in this study, inadequate sleep duration was particularly related to cardiovascular, inflammatory, and glucose metabolic systems, all of which constitute our CMB risk index, suggesting that sleep may be especially important for CMB health (33).

In addition to differences in sleep being an issue of public health, the presence of these sleep differences appears to be, in part, a result of social factors. Specifically, sleep has been robustly associated with exposure to social stress (34). Moreover, household and area-level socioeconomic conditions and experiences of discrimination help explain a portion of racial sleep differences (35, 36). Insufficient sleep therefore represents a plausible biobehavioral pathway through which disproportionate exposure to social and economic adversity leads to diverging health trajectories between AAs and EAs. Future studies will need to integrate research on stress exposure and sleep as they relate to a broad variety of racial and socioeconomic inequities in health and well-being. Furthermore, initiatives to reduce racial health disparities will need to consider the costs and benefits of varying points of intervention (e.g., upstream social determinants vs. sleep). Evidence-based sleep interventions could target AA communities and, if successful, could serve to reduce disparities in physical health, socioeconomic factors, and well-being (37, 38).

The use of sleep actigraphy is one strength of the present study. One recent review found that AA–EA differences in sleep time were larger when assessed objectively relative to self-reports (13), so that objective assessments may be key in research on racial sleep differences. Racial differences in the bias of sleep self-reports has also been documented, leading to an underestimation of differences (39). Further, findings considering racial differences in the association between sleep and CMB outcomes vary by the sleep assessment methodology. Namely, some research has shown that self-reported short duration is associated with blood pressure and diabetes to a larger degree among AAs than among EAs (19, 40), whereas one study and the present research found no racial differences in the link between actigraph-assessed sleep duration and cardiovascular markers (16). Polysomnography is also vital because it measures sleep architecture and has an advantage over actigraphy in detecting wakefulness (41). However, actigraphy is a more feasible means of measuring multiple nights of sleep and has significant cost advantages that are important in epidemiologic studies.

An additional strength of this study relates to our conceptualization of CMB risk and the utilization of several key biomarkers that predict subsequent cardiovascular and metabolic disease. One advantage of multisystem indexes of dysregulation is that the biological pathways from risk factors to disease may vary across individuals (42). Although other multisystem indexes have included a broader range of biomarkers relevant to aging, our focus was on the biomarkers of CMB risk because of their relevance to racial disparities in premature mortality and the established associations between sleep and many of the individual biomarkers. Further description of the strengths of our CMB risk index is found in *Supporting Information*.

Several study limitations are also important to note. Analyses used cross-sectional data, and therefore no conclusions could be drawn about temporal ordering. In particular, low sleep efficiency and insufficient sleep may result from health conditions, particularly among older adults (43). However, when participants with heart disease or diabetes were excluded, racial differences in CMB risk continued to be explained by sleep time and sleep efficiency. Moving forward, longitudinal data will be critical to demonstrate the long-term effects of habitual sleep problems.

The possibility of residual confounding, resulting from imprecise controls and lack of consideration of all third-variable explanations, also needs to be acknowledged. Specifically, although we adjusted for coarse indicators of diet and physical activity, detailed measures are needed to remove their influence on sleep fully. Similarly, in addition to controlling for education and income, subsequent research must elucidate the interdependence of a broad variety of socioeconomic factors and sleep as they relate to racial differences in health. Two additional analyses also were conducted to reduce the possibility of age and sleep disorders as confounding variables; these analyses are described in *Supporting Information* and are discussed here only briefly. First, given that normative changes in sleep and CMB functioning occur with aging, we tested and found no evidence of age as a moderator of the link between sleep and CMB risk. Second, we excluded participants with chronic sleep problems and found an identical pattern of results.

Generalizability is limited because the EA subsample was primarily from the Midwest and the AA subsample was from Milwaukee. Milwaukee suffers from hypersegregation (extreme segregation across several indicators) and adverse economic conditions (44), so that racial differences in heath could be larger than would be found in other contexts. Nonetheless, the majority of AAs in the Midwest reside in industrial cities that are segregated and have been adversely affected by changes in the economy resulting in the loss of manufacturing jobs (45). Thus, the sample offers an important context to consider sleep as a behavioral pathway through which an historically disadvantaged racial group may develop elevated CMB disease risk.

Conclusions

The results from the present study highlight the importance of eliminating racial differences in sleep as part of efforts to reduce racial health disparities. Importantly, sleep is a malleable behavior that can be improved through behavioral and educational interventions to influence physical health (38). Further, despite limited information regarding nonclinical samples, sleep interventions have been shown to be cost-effective (37, 46). Thus, recent public health initiatives that include monitoring sleep behaviors and society-wide messaging about adequate sleep duration and sleep hygiene represent important progress (47, 48).

Methods

Participants. Data for the analyses were derived from a sleep substudy that was part of the second wave of the Midlife in the United States (MIDUS II) Study (49). MIDUS began in 1995 as a nationally representative survey of more than 7,000 noninstitutionalized adults. Approximately 75% of surviving respondents of the first wave participated in MIDUS II, ~9–10 y later. As part of this new data collection, a subsample of respondents participated in clinic-based (overnight) biomarker data collection at one of three sites (Los Angeles; Madison, WI; and Washington, DC). Details of the biomarker sample and measures are provided elsewhere (49). Data are publicly available at https://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/29282. To increase the participation of AAs in biomarker data collection, a new oversample from Milwaukee (n = 592) was also recruited. MIDUS staff made travel arrangements and covered travel-related costs to ensure maximum participation in this portion of the study.

We included only participants from the Madison, WI site, which drew primarily on respondents from the Midwest region and Milwaukee, because they were invited to participate in a home-based week-long sleep substudy. A total of 441 adults (83% of the Madison biomarker sample) participated. Because of our focus on AA and EA adults, 15 individuals categorized as other racial/ethnic groups were excluded. Data collection was approved by the University of Wisconsin-Madison Institutional Review Board, and all participants provided written, informed consent.

Measures.

CMB risk. Cardiovascular and diabetes risk can be quantified from markers of abdominal adiposity, dyslipidemia, glucose metabolism, blood pressure, and systemic inflammation (50–52). These risk markers also cluster together to indicate a general state of CMB dysregulation. For the present study, CMB disease risk was indexed using clinical or recommended risk cut points for seven biomarkers: waist circumference, HOMA-IR, HbA_{1c}, blood pressure, CRP, triglycerides, and low HDL levels. This measure of CMB risk includes indicators of metabolic syndrome and two additional biomarkers (HOMA-IR and CRP) that add incremental validity in the prediction of cardiovascular disease (50, 53). Ideal (coded 0), borderline high (coded 1), and high (coded 2) levels for each marker were selected primarily based on recommendations from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the American Heart Association (AHA) (23–25). Scores

(0–2) for each of the seven biomarkers were averaged to create an overall index of CMB risk. Detailed descriptions of blood collection and processing procedures and information about biomarker assays and other assessments have been reported previously (54) and are reviewed briefly below. A further description of the advantages of our CMB risk index is given in *Supporting Information*.

Waist circumference. Waist circumference at the minimal girth was measured by trained nurses according to a standardized protocol (32). Waist circumference risk categories were chosen according to AHA guidelines (25).

Blood pressure. Blood pressure was measured in triplicate according to standardized procedures, and the second and third measurements were averaged (54). Prehypertension and hypertension were coded if either systolic or diastolic blood pressure levels met Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VII) criteria (23). The use of antihypertensives was also coded as hypertension (i.e., given a value of 2).

Glucose metabolism. Fasting blood samples were collected in the morning of the second day of the laboratory visit. Glucose was assessed using an enzymatic assay, performed on an automated analyzer (Roche Modular Analytics P), and insulin was measured using a two-site sandwich immunoassay using direct chemiluminescent technology on a Siemens ADVIA Centaur analyzer (54). Insulin resistance was computed using the original homeostasis model assessment of insulin resistance (HOMA1-IR) equation: HOMA1-IR = fasting glucose (mmol/L) × fasting insulin (mU/L)/22.5 (55). The HOMA1-IR is an acceptable method for considering between-group differences and relative change in insulin resistance but not absolute levels of insulin resistance, because the original HOMA model was calibrated on assays that were no longer in use at the time of the study (56). Recommendations for clinical cut points for HOMA-IR are also varied (57), and therefore insulin resistance tertiles were used to indicate risk levels. Prediabetes/diabetes was indexed using HbA_{1c}, a measure of blood glucose over the past few months, according to recommended cutoffs (58). HbA_{1c} was measured from whole-blood samples using a Cobas Integra analyzer (Roche Diagnostics) (54).

Triglycerides and HDL-C. Concentrations of triglycerides and HDL-C were measured using a Cobas Integra analyzer (Roche Diagnostics) (54). The use of lipid-modifying medications was coded as high levels of triglycerides (high-risk category).

CRP. CRP levels were measured using a high-sensitivity assay performed on a BN II nephelometer (Dade Behring) (54). Borderline and high CRP levels were coded according to previous recommendations (59).

Sleep minutes and sleep efficiency. Sleep characteristics were measured using wrist actigraphy and sleep logs. Detailed procedures relating to the collection and processing of actigraphy data are available at www.midus.wisc.edu/midus2/project4/ and are summarized herein. At the biomarker visit participants received a Mini-Mitter Actiwatch-64 activity monitor (Respironics, Inc.) that was to be worn continuously for 7 d and nights. Physical activity counts were collected in 30-s epochs during the week-long period, and periods of intended sleep were then demarcated in the actigraphy data using bedtimes and rise times reported on sleep logs. Epochs were scored as wake or sleep using Actiware Software (version 5.0) (Respironics, Inc.) based on a medium threshold of 40 activity counts (32).

Total sleep time was measured as the number of minutes coded as asleep between sleep onset and rise time, and sleep efficiency was measured as the percentage of epochs coded as asleep from bedtime to rise time. All participants had at least three nights of actigraphy data, with nearly all (96%) having at least six nights. In the present analyses, daily sleep parameters were averaged across all nights of available data to compute sleep-related outcomes; total sleep time and sleep efficiency showed high internal consistency ($\alpha = 0.85$ and $\alpha = 0.91$, respectively). Sleep time and sleep efficiency were strongly correlated ($r = 0.62$) and therefore were initially considered separately in mediation analyses. Actigraph-assessed sleep time and sleep efficiency show good correspondence with polysomnography in community samples and with the device used in the present study (22, 60).

Sociodemographic covariates. Biological sex, age (in years), and relationship status (married or cohabiting = 1, otherwise = 0) were included as demographic covariates. Total household income was measured using several items assessing wages, pension, social security, and government assistance for all household members. The participant's educational attainment was coded into dummy variables representing high school degree or less (reference category), some college attendance, and a 4-y college degree or greater. All models were adjusted for sociodemographic characteristics.

Mental health and health behaviors. Depressive symptoms were assessed using the Center for Epidemiological Studies Depression Scale, a widely used and well-validated measure (61). One item measuring restless sleep was removed from the computation of the total score to reduce conflation between sleep and depression, and the revised scale had high reliability ($\alpha = 0.89$). Habits relating to physical activity, diet, and cigarette smoking were also assessed (36, 62). Physical activity was reported on nightly sleep logs by the answer to the question "How many minutes of moderate or vigorous exercise did you get today?" The average of all available reports across the 7 d was used. Despite this single item being a coarse indicator of physical activity, the short recall and repeated measurements are considerable strengths that improve the validity of the item (63). Fast-food consumption was selected as an index of a putative unhealthy dietary habit (64) and was coded in three dummy variables: no consumption (referent), less than once per week, and once a week or more. The frequency of fast-food consumption is positively associated with high-fat, high-sugar diets and is inversely associated with the intake of whole grains, fruits and vegetables, and fiber (64). Single-item reports of the frequency of fast-food consumption also correspond closely with typical fast-food items measured using detailed month-long diet histories (64). Smoker status was coded as a dummy variable representing current smoking activity.

Previous heart disease. Participants reported if a doctor had previously suspected or confirmed a "heart trouble" and recalled the diagnosis, broadly categorized as myocardial infarction, angina, valve disease, hole in heart, blocked artery, arrhythmia, heart murmur, or heart failure.

Analysis Plan. Descriptive statistics were examined by race, and unadjusted differences between AAs and EAs were tested using independent-samples *t* tests and χ^2 tests. Linear regression and path models were used to test study hypotheses. An initial regression model estimated racial differences in total sleep time and sleep efficiency, adjusting for sex, age, relationship status, education, and household income. A series of regression models then was estimated to examine racial differences in CMB risk and the role of sleep indicators as mediating variables. In Model 1, differences in CMB disease risk between AAs and EAs were estimated after adjusting for sociodemographics. Model 2 then added health behaviors and mental health—specifically, diet, physical activity, cigarette smoking, and depression—as additional covariates. Two additional models were fit in which total sleep time (Model 3) and sleep efficiency (Model 4) were added, in turn, as predictors of CMB risk. Mediation was tested in path models in which each sleep indicator was simultaneously modeled as a mediator predicted by race (and sociodemographics) and as a predictor of CMB risk. The indirect effect of race on CMB risk via each sleep indicator was estimated using the product of coefficients method with bias-corrected confidence intervals (65), and the proportion of the race difference in CMB risk explained was calculated to indicate the effect size. Modeling indirect effects using path models is a widely used test of mediation that allows simultaneous controls on both the mediator and outcome variable. Further, indirect effects are easily interpreted—the estimate is in the units of the direct effect (in our case, the indirect effect indicates the absolute value of the racial gap in CMB risk explained by the sleep mediator). Study hypotheses were tested using Mplus 7.11 (66). Missing data were handled using full information maximum likelihood, a common estimation technique that uses all available data and allows a consistent sample size across models. Only 2.6% of participants had missing data for physical activity, and all other covariates had less than 1% missing data.

A few sensitivity analyses were also conducted. Given that some studies have shown associations between short sleep duration and CMB risk to vary by demographic factors (19, 40), race, age, and sex were tested as moderators of the link between sleep and CMB risk. The series of models described above was also fit among samples that were stratified by sex to determine if mediation findings were present for both male and female subsamples. In addition, because both short and long sleep duration are correlates of negative health outcomes, each of which is more common among AAs (12), linear and nonlinear associations between sleep minutes and CMB risk were estimated (i.e., sleep minutes squared was included as predictor). Furthermore, to reduce the likelihood of reverse causality, we fit models in which we excluded participants with heart disease or diabetes. Last, mediation models were fit among participants who reported no experience of chronic sleeping problems.

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1. Mozaffarian D, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee (2015) Heart disease and stroke statistics–2015 update: A report from the American Heart Association. *Circulation* 131:e29–e322, and correction (2016) 133:e417.
2. Mensah GA, Mokdad AH, Ford ES, Greenlund KJ, Croft JB (2005) State of disparities in cardiovascular health in the United States. *Circulation* 111:1233–1241.
3. US Department of Health and Human Services (2008) The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020. Phase I Report: Recommendations for the Framework and Format of Healthy People 2020. Section IV (US Department of Health and Human Services, Washington, DC).
4. Frieden TR; Centers for Disease Control and Prevention (CDC) (2013) CDC health disparities and inequalities report - United States, 2013. Foreword. *MMWR Suppl* 62:1–2.
5. Williams DR, Sternthal M (2010) Understanding racial-ethnic disparities in health: Sociological contributions. *J Health Soc Behav* 51(1 Suppl):S15–S27.
6. Dressler WW, Oths KS, Gravlee CC (2005) Race and ethnicity in public health research: Models to explain health disparities. *Annu Rev Anthropol* 34:231–252.
7. Redmond N, Baer HJ, Hicks LS (2011) Health behaviors and racial disparity in blood pressure control in the national health and nutrition examination survey. *Hypertension* 57:383–389.
8. Howard G, et al.; REasons for Geographic And Racial Differences in Stroke (REGARDS) Investigators (2011) Traditional risk factors as the underlying cause of racial disparities in stroke: Lessons from the half-full (empty?) glass. *Stroke* 42:3369–3375.
9. Jackson CL, Redline S, Emmons KM (2015) Sleep as a potential fundamental contributor to disparities in cardiovascular health. *Annu Rev Public Health* 36:417–440.
10. Knutson KL (2013) Sociodemographic and cultural determinants of sleep deficiency: Implications for cardiometabolic disease risk. *Soc Sci Med* 79:7–15.
11. Kingsbury JH, Buxton OM, Emmons KM, Redline S (2013) Sleep and its relationship to racial and ethnic disparities in cardiovascular disease. *Curr Cardiovasc Risk Rep* 7:387–394.
12. Adenekan B, et al. (2013) Sleep in America: Role of racial/ethnic differences. *Sleep Med Rev* 17:255–262.
13. Petrov ME, Lichstein KL (2016) Differences in sleep between black and white adults: An update and future directions. *Sleep Med* 18:74–81.
14. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA (2011) Sleep duration predicts cardiovascular outcomes: A systematic review and meta-analysis of prospective studies. *Eur Heart J* 32:1484–1492.
15. Knutson KL, Spiegel K, Penev P, Van Cauter E (2007) The metabolic consequences of sleep deprivation. *Sleep Med Rev* 11:163–178.
16. Knutson KL, et al. (2009) Association between sleep and blood pressure in midlife: The CARDIA sleep study. *Arch Intern Med* 169:1055–1061.
17. Irwin MR, Olmstead R, Carroll JE (2016) Sleep disturbance, sleep duration, and inflammation: A systematic review and meta-analysis of cohort studies and experimental sleep deprivation. *Biol Psychiatry* 80:40–52.
18. Hairston KG, et al. (2010) Sleep duration and five-year abdominal fat accumulation in a minority cohort: The IRAS family study. *Sleep* 33:289–295.
19. Zizi F, et al. (2012) Race/ethnicity, sleep duration, and diabetes mellitus: Analysis of the National Health Interview Survey. *Am J Med* 125:162–167.
20. Piccolo RS, Yang M, Bliwise DL, Yaggi HK, Araujo AB (2013) Racial and socioeconomic disparities in sleep and chronic disease: Results of a longitudinal investigation. *Ethn Dis* 23: 499–507.
21. Sherwood A, et al. (2011) Blood pressure dipping: Ethnicity, sleep quality, and sympathetic nervous system activity. *Am J Hypertens* 24:982–988.
22. Tryon WW (2004) Issues of validity in actigraphic sleep assessment. *Sleep* 27:158–165.
23. Lloyd-Jones DM, et al.; American Heart Association Strategic Planning Task Force and Statistics Committee (2010) Defining and setting national goals for cardiovascular health promotion and disease reduction: The American Heart Association's strategic impact goal through 2020 and beyond. *Circulation* 121:586–613.
24. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2002) Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation* 106:3143–3421.
25. Alberti KG, et al.; International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity (2009) Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 120:1640–1645.
26. Brancati FL, Kao WHL, Folsom AR, Watson RL, Szklo M (2000) Incident type 2 diabetes mellitus in African American and white adults: The atherosclerosis risk in communities study. *JAMA* 283:2253–2259.
27. Ogden CL, Carroll MD, Kit BK, Flegal KM (2014) Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA* 311:806–814.
28. Kochanek KD, Arias E, Anderson RN (2013) How did cause of death contribute to racial differences in life expectancy in the United States in 2010? *NCHS Data Brief* 1–8.
29. Rasmussen-Torvik LJ, et al. (2016) The mediation of racial differences in hypertension by sleep characteristics: Chicago area sleep study. *Am J Hypertens* 29:1353–1357.
30. Miller MA, et al. (2009) Gender differences in the cross-sectional relationships between sleep duration and markers of inflammation: Whitehall II study. *Sleep* 32:857–864.
31. Cappuccio FP, et al. (2007) Gender-specific associations of short sleep duration with prevalent and incident hypertension: The Whitehall II study. *Hypertension* 50:693–700, and erratum (2007) 50:e170.
32. Mezick EJ, Wing RR, McCaffery JM (2014) Associations of self-reported and actigraphy-assessed sleep characteristics with body mass index and waist circumference in adults: Moderation by gender. *Sleep Med* 15:64–70.
33. Carroll JE, Irwin MR, Stein Merkin S, Seeman TE (2015) Sleep and multisystem biological risk: A population-based study. *PLoS One* 10:e0118467.
34. Hall MH, et al. (2015) Chronic stress is prospectively associated with sleep in midlife women: The SWAN sleep study. *Sleep* 38:1645–1654.
35. Fuller-Rowell TE, et al. (2017) Racial discrimination mediates race differences in sleep problems: A longitudinal analysis. *Cultur Divers Ethnic Minor Psychol* 23:165–173.
36. Fuller-Rowell TE, et al. (2016) Racial disparities in sleep: The role of neighborhood disadvantage. *Sleep Med* 27-28:1–8.
37. Wickwire EM, Shaya FT, Scharf SM (2016) Health economics of insomnia treatments: The return on investment for a good night's sleep. *Sleep Med Rev* 30:72–82.
38. Irwin MR, et al. (2015) Cognitive behavioral therapy and tai chi reverse cellular and genomic markers of inflammation in late-life insomnia: A randomized controlled trial. *Biol Psychiatry* 78:721–729.
39. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ (2008) Self-reported and measured sleep duration: How similar are they? *Epidemiology* 19:838–845.
40. Pandey A, et al. (2013) Linking sleep to hypertension: Greater risk for blacks. *Int J Hypertens* 2013:436502.
41. Sadeh A (2011) The role and validity of actigraphy in sleep medicine: An update. *Sleep Med Rev* 15:259–267.
42. Gruenewald TL, Seeman TE, Ryff CD, Karlamangla AS, Singer BH (2006) Combinations of biomarkers predictive of later life mortality. *Proc Natl Acad Sci USA* 103:14158–14163.
43. Foley D, Ancoli-Israel S, Britz P, Walsh J (2004) Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation sleep in America survey. *J Psychosom Res* 56:497–502.
44. Massey DS, Denton NA (1989) Hypersegregation in U.S. metropolitan areas: Black and Hispanic segregation along five dimensions. *Demography* 26:373–391.
45. US Census Bureau (2000) Majority of African Americans live in 10 states; New York City and Chicago are cities with largest black populations. Newsroom. Available at https://www.census.gov/newsroom/releases/archives/census_2000/cb01cn176.html. Accessed August 26, 2016.
46. Irish LA, Kline CE, Gunn HE, Buysse DJ, Hall MH (2015) The role of sleep hygiene in promoting public health: A review of empirical evidence. *Sleep Med Rev* 22:23–36.
47. Watson NF, et al.; Consensus Conference Panel (2015) Joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society on the recommended amount of sleep for a healthy adult: Methodology and discussion. *J Clin Sleep Med* 11:931–952.
48. Sleep Health | Healthy People 2020. Available at https://www.healthypeople.gov/2020/topics-objectives/topic/sleep-health/objectives. Accessed August 24, 2016.
49. Dienberg Love G, Seeman TE, Weinstein M, Ryff CD (2010) Bioindicators in the MIDUS national study: Protocol, measures, sample, and comparative context. *J Aging Health* 22:1059–1080.
50. Ridker PM, Wilson PWF, Grundy SM (2004) Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk? *Circulation* 109:2818–2825.
51. Rapsomaniki E, et al. (2014) Blood pressure and incidence of twelve cardiovascular diseases: Lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *Lancet* 383:1899–1911.
52. Rader DJ (2007) Effect of insulin resistance, dyslipidemia, and intra-abdominal adiposity on the development of cardiovascular disease and diabetes mellitus. *Am J Med* 120(3 Suppl 1):S12–S18.
53. Reilly MP, et al. (2004) Measures of insulin resistance add incremental value to the clinical diagnosis of metabolic syndrome in association with coronary atherosclerosis. *Circulation* 110:803–809.
54. Gruenewald TL, et al. (2012) History of socioeconomic disadvantage and allostatic load in later life. *Soc Sci Med* 74:75–83.
55. Matthews DR, et al. (1985) Homeostasis model assessment: Insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28:412–419.
56. Wallace TM, Levy JC, Matthews DR (2004) Use and abuse of HOMA modeling. *Diabetes Care* 27:1487–1495.
57. Gayoso-Diz P, et al. (2013) Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: Effect of gender and age: EPIRCE cross-sectional study. *BMC Endocr Disord* 13:47.
58. American Diabetes Association (2014) Standards of medical care in diabetes—2014. *Diabetes Care* 37(Suppl 1):S14–S80.
59. Ridker PM (2003) Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation* 107:363–369.
60. Lichstein KL, et al. (2006) Actigraphy validation with insomnia. *Sleep* 29:232–239.
61. Radloff LS (1977) The CES-D scale a self-report depression scale for research in the general population. *Appl Psychol Meas* 1:385–401.
62. Robinette JW, Charles ST, Almeida DM, Gruenewald TL (2016) Neighborhood features and physiological risk: An examination of allostatic load. *Health Place* 41:110–118.
63. Sallis JF, Saelens BE (2000) Assessment of physical activity by self-report: Status, limitations, and future directions. *Res Q Exerc Sport* 71(Suppl 2):1–14.
64. Pereira MA, et al. (2005) Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. *Lancet* 365:36–42, and erratum (2005) 365:1030.
65. Hayes AF, Scharkow M (2013) The relative trustworthiness of inferential tests of the indirect effect in statistical mediation analysis: Does method really matter? *Psychol Sci* 24:1918–1927.
66. Muthén LK, Muthén BO (2013) *Mplus: Statistical Analysis with Latent Variables. User's Guide* (Muthen and Muthen, Los Angeles), Version 7.11.
67. Seeman TE, et al. (2004) Cumulative biological risk and socio-economic differences in mortality: MacArthur studies of successful aging. *Soc Sci Med* 58:1985–1997.
68. Seeman T, et al. (2010) Modeling multisystem biological risk in young adults: The coronary artery risk development in young adults study. *Am J Hum Biol* 22:463–472.
69. Pawasarat J, Quinn LM (2013) Wisconsin's mass incarceration of African American males: Workforce challenges for 2013. Available at dc.uwm.edu/eti_pubs/9/. Accessed May, 2017.