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## Evening Chronotype is Associated with Poor Cardiovascular Health and Adverse Health Behaviors in a Diverse Population of Women

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## Abstract

Chronotype reflects time of day preferences for performing daily activities. Previous research within Asian and European cohorts indicates evening chronotype is associated with elevated cardiometabolic risk. However, evidence is limited from population-based US cohorts, particularly among women in whom evening chronotype prevalence may become higher after middle-age, coinciding with life stages associated with higher cardiovascular disease (CVD) risk. This crosssectional study evaluated associations of chronotype with overall cardiovascular health (CVH), health behaviors, and cardiometabolic risk factors among 506 women (mean age=37±16y, 62% racial/ethnic minority) in the American Heart Association (AHA)'s Go Red for Women Strategically-Focused Research Network cohort at Columbia University (New York City, NY, USA). Chronotype was assessed using the validated Morningness-Eveningness Questionnaire (MEQ) and categorized as "evening", "intermediate", and "morning" chronotypes. Health behaviors (diet, physical activity, and sleep) were assessed using validated questionnaires. Anthropometrics, clinical blood pressure, and blood biomarkers were assessed at the clinic visit. CVH was evaluated using the AHA Life's Simple 7 (LS7) metrics; LS7 scores of 0-8 and 9-14 were considered indicative of poor and moderate-to-high CVH, respectively. Linear and logistic regression models adjusted for age, race/ethnicity, education, health insurance, and menopausal status were used to examine associations of MEQ scores and chronotype categories with overall CVH, clinical cardiometabolic risk factors, and health behaviors. Overall, 13% of women identified as evening chronotypes, while 55% and 32% reported being intermediate and morning types. In linear models, higher MEQ scores were associated with higher AHA LS7 scores  $(\beta(SE)=0.02(0.01); p=0.014)$ , indicative of more favorable CVH, and with health behaviors not included in the LS7. Higher MEQ scores were also associated with lower Pittsburgh Sleep Quality Index, i.e. better sleep quality,  $(\beta(SE)=-0.07(0.02), p<0.0001)$ , lower insomnia severity  $(\beta(SE)=-0.07(0.02), p<0.0001)$ -0.14(0.01), p<0.0001), shorter time to fall asleep ( $\beta$ (SE)=-0.28(0.14), p=0.044), and less sedentary time ( $\beta$ (SE)=-0.11(0.03), p=0.001). In logistic regression models, evening chronotype,

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Disclosure of Interest:

The authors report no conflict of interest.

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compared to intermediate/morning type, was associated with higher odds of having poor CVH (OR(95%CI):2.41(1.20–4.85)), not meeting AHA diet (OR(95%CI):2.89(1.59–5.23)) and physical activity guidelines (OR(95%CI):1.78(1.03–3.07)), and having short sleep (OR(95%CI):2.15(1.24–3.73)) or insomnia (OR(95%CI):2.69(1.53–4.75)). The evening type compared to morning type was also associated with being a current smoker (OR(95%CI):2.14(1.02–4.52)) and having poor sleep quality (OR(95%CI:2.35(1.27–4.37)) and long sleep onset latency (OR(95%CI:1.89(1.00–3.56))). In our cohort of women, evening chronotype was related to poor CVH, likely driven by its influence on health behaviors. These findings, although warranting confirmation prospectively in other populations, suggest chronotype is an important factor to consider and possibly target when designing lifestyle interventions for CVD prevention.

#### Keywords

chronotype; cardiovascular health; heath behaviors; sleep; women

## INTRODUCTION

Chronotype represents the phenotypic expression of an individual's innate circadian rhythm, i.e. times of day (ranging between morning and evening) a person prefers for performing daily activities (Levandovski et al., 2013). There is significant inter-individual variation in chronotype evident from differences in preferred bedtimes and subjective times of peak alertness. Later chronotypes, individuals with an evening preference, tend to have more health problems, including psychological, neurological, and gastrointestinal morbidities and greater mortality rates compared to morning chronotypes (Culnan et al., 2013, Yu et al., 2015, Anothaisintawee et al., 2017, Knutson and von Schantz, 2018, Nimitphong et al., 2018). Emerging epidemiological evidence has also linked evening chronotypes with cardiovascular disease (CVD) (Merikanto et al., 2013) and cardiometabolic risk factors, including higher risk for overweight and obesity and for type 2 diabetes (Merikanto et al., 2013, Yu et al., 2015, Patterson et al., 2017). Furthermore, evening chronotypes are more likely to report poor health behaviors, such as higher rates of smoking, unhealthy diets, and later timing of sleep (Merikanto et al., 2013, Patterson et al., 2017). It is hypothesized that evening chronotypes may develop these behavioral and physiological risk factors due to chronic misalignment between internal physiological timing and externally imposed timing of work and social activities, making them particularly vulnerable to CVD (Roenneberg and Merrow, 2016).

In 2010, the American Heart Association (AHA) published "Life's Simple 7" (LS7) to measure cardiovascular health (CVH) and predict subsequent risk for CVD (Lloyd-Jones et al., 2010). The CVH metrics encompass seven health factors and health behaviors linked to CVD risk, including smoking, diet, physical activity, body mass index (BMI), daytime clinic blood pressure (BP), and fasting total cholesterol and blood glucose. While chronotype has been previously examined in relation to some of these health factors and behaviors, its association with overall CVH has not been previously investigated. Furthermore, most studies on chronotype and CVD risk have been conducted on European populations, such as

the United Kingdom Biobank project (Patterson et al., 2016, Patterson et al., 2017, Knutson and von Schantz, 2018), highlighting the need for additional studies among US populations.

Evaluating the relationship between chronotype and CVD risk is of particular significance in women, given that previous data from a nationally representative sample of US women indicate that women are more likely than men to be evening types from middle age onward (Fischer et al., 2017), coinciding with the life stages during which CVD risk is most pronounced. We conducted a cross-sectional study within a racially/ethnically diverse cohort of women to examine the association of chronotype with overall and individual metrics of CVH. We also examined the association of chronotype with other clinical risk factors and health behaviors that are linked to CVD risk in the literature, but are not currently included in the AHA LS7. These other risk factors and health behaviors are sleep habits, sedentary behaviors, waist circumference (WC), and blood lipids (HDL-C, LDL-C, and triglycerides). We hypothesized that women with an evening chronotype, assessed by the Morningness-Eveningness Questionnaire (MEQ) (Horne & Ostberg, 1976) would have poorer CVH, assessed using the AHA LS7 score (Makarem et al. 2019). We also hypothesized that an evening preference would be associated with elevated individual clinical CVD risk factors (BMI, WC, BP, fasting glucose, and dyslipidemia) and with adverse health behaviors (unhealthy diet, lower moderate-to-vigorous physical activity, greater sedentary time, and poorer sleep habits). The purpose of this investigation is to illuminate and inform novel approaches and targets for interventions addressing lifestyle change to combat the burgeoning CVD epidemic among US women.

## METHODS

### **Study Design and Participants**

This study was a cross-sectional analysis of baseline data derived from a prospective cohort study of United States-residing English- and Spanish-speaking women aged 20-79 y. Participants were women enrolled in the AHA Go Red for Women Strategically Focused Research Network cohort that seeks to evaluate the role of sleep patterns in CVD risk. Participants were recruited at Columbia University Irving Medical Center (CUIMC) in the State of New York through a variety of methods, including: online advertisement, recruitment flyers at the CUIMC campus, physician referral, and in person as family members and friends of patients hospitalized at CUIMC. Women who were pregnant at the time of recruitment or who became pregnant during the study were excluded. The final analytical data set was comprised of 506 women. Participants completed a set of standardized questionnaires to provide information on demographics (age, race/ethnicity, employment, insurance status, and income), medical history (history of chronic disease, medication use, and menopausal status), and lifestyle behaviors and additionally underwent clinical assessments to evaluate CVD risk as described in the sections below. All participants provided written informed consent, and the CUIMC institutional review board approved the study. All research activities were consistent with the ethical standards and methods for the conduct of high-quality human biological rhythm research (Portaluppi et al. 2010).

## Assessment of Chronotype and Sleep Habits

Chronotype was evaluated using the Morningness-Eveningness Questionnaire (MEQ) created by Horne & Ostberg in 1976, which represents the first validated questionnaire to assess chronotype (Horne and Ostberg, 1976; Levandovski et al., 2013). The MEQ consists of 19 questions about preferred activity times. The questions relate sleep and activity times to a personal "feeling optimal" rhythm. Scores range from 16–86, with a higher score indicating a stronger morningness preference. Categorization of participants' chronotype was based on the following MEQ scores: 1) 16–30: definite evening, 2) 31–41: moderate evening, 3) 42–58: moderate, 4) 59–69: moderate morning, and 5) 70–86: definite morning (Archer et al. 2003; Levandovski et al. 2013).

Participants also completed validated questionnaires to assess additional aspects of sleep health, including the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989), Berlin Questionnaire 2000 (Netzer et al., 1999), and Insomnia Severity Index (ISI) (Bastien et al., 2001, Morin et al., 2011). The PSQI evaluates seven domains of sleep health, including subjective sleep quality, sleep onset latency (time to fall asleep), duration, efficiency and disturbance of sleep, use of sleep medication, and daytime dysfunction over the last month. Poor overall sleep quality was defined as having a global PSQI score >5 (Buysse et al., 1989). Sleep duration was self-reported on the PSQI, and short sleep duration was defined as <7 h/night (St-Onge et al., 2016). Long sleep onset latency was defined as 30 min. The Berlin questionnaire was used to determine whether participants were high vs. low risk for obstructive sleep apnea (OSA) based on the response to questions regarding snoring, daytime somnolence, hypertension, and body mass index (BMI) (Senaratna et al., 2017). Finally, insomnia severity was evaluated using the ISI, which ranges between 0–28 (Bastien et al., 2001, Morin et al., 2011). The ISI is interpreted as follows: 1) 0-7: no clinically significant insomnia, 2) 8-14: sub-threshold insomnia, 3) 15-21: clinical insomnia with moderate severity, or 4) 22–28: severe clinical insomnia. In these analyses, clinically relevant insomnia was defined as an ISI score 8.

## **Assessment of Health Behaviors**

Physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ). The IPAQ is a tool designed specifically for surveillance of physical activity studies and has been developed and tested for use among adults in diverse settings (Craig et al., 2003). Participants were classified as meeting the physical activity recommendations supported by the AHA if they engaged in 150 min/wk of moderate aerobic activity or 75 min/wk of vigorous activity or 150 min/wk of a combination moderate and vigorous activity (Lloyd-Jones et al., 2010, Piercy et al., 2018). Time spent engaging in sedentary behaviors on a typical weekday (h/day) was assessed using a sedentary activities questionnaire (Rosenberg et al., 2010) that queried participants about the amount of time they spent engaging in activities that are usually done while sitting or lying down both at work and during leisure time (range: none to >6 h/day).

Diet was assessed using the validated Block Brief Food Frequency Questionnaire (Block et al., 1990), which queried participants about frequency and portion size of commonly consumed foods. Derived food and nutrient data was used to examine adherence to AHA

diet guidelines: 4.5 cups/day of fruits and vegetables, 2 servings/wk of fish, 3 servings/d of whole grains, 36 oz/wk of sugar-sweetened beverages, and 1,500 mg/d of sodium (Lloyd-Jones et al., 2010). Smoking history was assessed by answering the following questions: "What is your smoking status?" and "When was your last cigarette?" Smoking was categorized as yes (smoked in the past 12 months) versus no (never smoked or has not smoked in the past 12 months) (Lloyd-Jones et al., 2010).

#### Assessment of Health Factors

Height was measured using a standardized height rod. Weight was measured using a research grade scale. BMI was calculated using the standard equation (weight(kg)/ height<sup>2</sup>(m<sup>2</sup>)). Those with a BMI of 25–29.9 kg/m<sup>2</sup> and >30 kg/m<sup>2</sup> were considered to be overweight and obese, respectively (NHLBI 2000). WC was measured using a standard tape positioned just above the iliac crest, and a WC>35 inches was considered to be "at-risk" in accordance with the AHA's guidelines (Goff et al., 2014). BP was recorded in a clinical setting following a 5-minute rest from the participant's non-dominant arm using a hospital-grade automatic sphygmomanometer and an appropriately sized cuff. Individuals with systolic BP (SBP) 130 mmHg or diastolic BP (DBP) 80 mmHg were classified as having hypertension (Whelton et al., 2018). Participants provided fasting blood samples to assess blood glucose, triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) (Lloyd-Jones et al., 2010, Goff et al., 2014). Blood samples were analyzed in the Core Biomarker Laboratory at CUIMC.

#### Assessment of Overall Cardiovascular Health (CVH) using the AHA Life Simple 7 Score

Overall CVH was assessed by deriving the AHA LS7 score (Lloyd-Jones et al., 2010). The AHA LS7 guidelines are comprised of seven health behaviors and factors: BMI, BP, total cholesterol, fasting blood glucose, physical activity, diet, and smoking status. Participants received a score based on the level of meeting recommendations for AHA LS7 metrics as follows:

- Low score (0) if: BMI 30 kg/m<sup>2</sup>, SBP/DBP 130/80 mmHg, total cholesterol 240 mg/dL, fasting blood glucose 126 mg/dL, no moderate or vigorous activity, met only 0–1 components of healthy diet pattern, and current smokers (Lloyd-Jones et al., 2010).
- Intermediate score (1) if: BMI was 25–29.9 kg/m<sup>2</sup>, SBP: 120–129 or DBP: <80 mmHg or treated to ideal level, total cholesterol 200–239 mg/dL, fasting blood glucose 100–125 mg/dL, reported 1 to 149 min/wk moderate intensity or 1 to 74 min/wk vigorous intensity or 1 to 149 min/wk moderate + vigorous intensity physical activity, met 2–3 components of healthy diet pattern, and former smokers who quit <2 y ago (Lloyd-Jones et al., 2010).</li>
- High score (2) if: BMI <25 kg/m<sup>2</sup>, SBP/DBP <120/80 mmHg, untreated cholesterol 200 mg/dL, fasting blood glucose <100 mg/dL, 150 min/wk of moderate/vigorous activity, met 4–5 components of the healthy diet pattern, and non-smokers or former smokers who quit for >2 y (Lloyd-Jones et al., 2010).

A composite AHA LS7 score was calculated as the sum of the seven individual scores. Composite scores ranged from 0–14 points; higher scores indicated more favorable CVH. Those with AHA LS7 scores of 0–8, 9–10, and 11–14 were considered to have poor, intermediate, and high CVH levels, respectively (Lloyd-Jones et al., 2010).

#### **Statistical Analysis**

All data were entered into a secure Redcap database and analyzed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Participant characteristics were described using mean  $\pm$  standard deviation (SD) for continuous variables and frequencies for categorical variables. T-tests and Fisher's exact tests were used to examine differences in demographic, lifestyle, and medical characteristics by chronotype (morning/intermediate vs. evening). Linear regression models were used to evaluate associations of MEQ score with AHA LS7 score, as a measure of overall CVH, as well as with individual health behaviors and health factors included in the AHA LS7 (diet, smoking, PA, BMI, total cholesterol, fasting glucose, and BP) or strongly linked in the literature to CVD risk (WC, lipid profile, sedentary behaviors, and sleep habits). Logistic regression models were used to evaluate associations of chronotype with odds of having poor CVH (AHA LS7 score=0–8) and odds of meeting individual AHA LS7 guidelines (diet, smoking, physical activity, BMI, glucose, BP, cholesterol). Logistic regression models were also used to examine associations of chronotype with odds of meeting recommendations for sleep behaviors, given the reported strong link between sleep and CVH (Makarem et al., 2019).

In logistic regression models, we evaluated two categorical chronotype variables: 1) a three category chronotype variable comparing "evening-types" (MEQ score of 16–41, which includes definite eveningness and moderate eveningness) and "intermediate-types" (MEQ score of 42–58) to "morning-types" (MEQ score of 59–86, which includes definite morningness and moderate morningness and constitutes the referent group) and 2) a dichotomous chronotype variable comparing "evening-types" to "intermediate- and morning-types". Both linear and logistic regression models were adjusted a priori for socio-demographic and clinical characteristics that are known risk factors for CVD and that were significantly related to CVH in this cohort, including age, race/ethnicity, having health insurance, education, and menopausal status. For all analyses, a p-value <0.05 was considered evidence for statistical significant.

## RESULTS

# Characteristics of the Overall Sample and Women with Evening vs. Morning/Intermediate Chronotypes

The mean age was  $37 \pm 16$  y, and more than two thirds of participants were premenopausal (71%) (Table 1). The racial distribution was as follows: 57% white, 20% black, 19% Asian, and 4% other and 28% reported Hispanic ethnicity; therefore, 62% of the women were a racial or ethnic minority. Half of the study sample had a BMI in the overweight and obese category (50%). A histogram and boxplot of MEQ scores revealed a normal distribution. The mean MEQ score was  $53 \pm 10$ , and scores ranged from 23 to 82. Overall, 13% of women reported being an evening type, while 55% and 32% reported being intermediate and

morning types, respectively. Furthermore, compared to morning/intermediate types combined, evening chronotypes had a significantly lower AHA total LS7 score ( $9.1\pm2.4$  vs.  $9.8\pm2.2$ , p=0.016). However, there were no significant differences between these two chronotype categories in traditional cardiometabolic risk factors (BMI, WC, SBP, DBP, total cholesterol, HDL-C, LDL-C, TG, or fasting blood glucose).

In terms of health behaviors, there were no differences in smoking status by chronotype. However, evening chronotypes had greater sedentary time ( $16.0\pm9.8$  h/d vs.  $13.4\pm6.7$  h/d; p=<0.0001) and were less likely to meet physical activity guidelines (35.9% vs. 48.2%; p=0.081) and 2–5 of AHA LS7 diet guidelines (27.4% vs. 53.1% vs.; p<0.001). Regarding sleep habits, although there were no significant differences in mean sleep duration by chronotype, evening chronotypes were more likely to be short sleepers (<7 h) (56.3% vs. 41.2%; p=0.030). They also had a higher mean PSQI indicative of poorer overall sleep quality ( $6.8\pm3.8$  vs.  $5.4\pm3.7$ ; p=–0.010) and a higher ISI indicative of greater insomnia severity ( $9.1\pm6.1$  vs.  $6.8\pm6.0$ ; p=0.005).

## Associations of MEQ scores with Cardiovascular Health, Clinical Risk Factors, and Health Behaviors

In multivariable-adjusted linear regression models (Table 2), a higher MEQ score, representing greater "morningness", was associated with a higher AHA LS7 score ( $\beta(SE)=0.02(0.01)$ , p=0.014), indicative of a more favorable CVH profile. We observed that associations between chronotype and CVH varied by race/ethnicity, as greater morningness, was significantly associated with a higher AHA LS7 score in racial/ethnic minority women ( $\beta(SE)=0.02(0.01)$ , p=0.039), but not non-Hispanic white women ( $\beta(SE)=0.01(0.01)$ , p=0.285). No significant associations between MEQ scores and individual clinical cardiometabolic risk factors were observed; however, significant associations were substantiated with health behaviors, namely sleep and sedentary behavior. A higher MEQ score was associated with a lower PSQI score, indicative of better sleep quality ( $\beta(SE)=-0.07(0.02)$ , p<0.0001), and a lower ISI, indicative of lower insomnia severity ( $\beta(SE)=-0.14(0.01)$ , p=0.028(0.14), p=0.044) and less sedentary time ( $\beta(SE)=-0.11(0.03)$ , p=0.001).

## Associations of Chronotype with Cardiovascular Health, Clinical Risk Factors, and Health Behaviors

In multivariable-adjusted logistic regression models (Table 3), being an evening vs. morning/ intermediate chronotype was associated with >2-fold higher odds of having a low AHA LS7 score, indicative of poor CVH (OR(95%CI):2.41(1.20–4.85)). Similarly to what was observed in the linear models, there were no significant associations between chronotype and odds of meeting guidelines for health factors in the AHA LS7 (BMI, BP, cholesterol, and glucose). However, significant associations were verified between chronotype and odds of meeting guidelines for health behaviors. In particular, being an evening chronotype was associated with almost 3-fold higher odds of having a low diet score (i.e. meeting 0–1 of AHA diet guidelines) (OR(95%CI):2.89(1.59–5.23)) and with 78% higher odds of not meeting physical activity guidelines (OR(95%CI):1.78(1.03–3.07)). When chronotype was

assessed as a three-category variable (evening vs. intermediate vs. morning), evening types compared to morning types had >2-fold higher odds of having poor CVH (OR(95%CI):2.53(1.27–5.01)), not meeting physical activity guidelines (OR(95%CI):2.03(1.10–3.75)), and being a current smoker (OR(95%CI):2.14(1.02–4.52)). Evening versus morning types also had >3-fold greater odds of not meeting AHA diet guidelines (OR(95%CI):3.61(1.88–6.94)).

When chronotype was evaluated in relation to health behaviors not included in the AHA LS7, being an evening versus intermediate/morning chronotype was associated with >2-fold greater odds of having a short sleep duration (<7h)(OR(95%CI):2.15(1.24–3.73)) or any form of insomnia (OR(95%CI):2.69(1.53–4.75)). Similarly, when chronotype was assessed as a three-category variable, being an evening vs. morning chronotype was also associated >2-fold greater odds of being a short sleeper (OR(95%CI):2.14(1.15–3.99)), having poor sleep quality (OR(95%CI):2.35(1.27–4.37)), and having insomnia (OR(95%CI):2.85(1.53–5.33)). A borderline significant association was observed between evening vs. morning chronotype and odds of having long sleep onset latency (OR(95%CI):1.89(1.00–3.56)). Both intermediate and evening types had >2-fold greater odds of having high OSA risk compared to morning types, but the association was only significant when comparing intermediate vs. morning types ((OR(95%CI):2.22(1.22–4.07)).

## DISCUSSION

In this study of diverse US women encompassing different life stages, an evening chronotype was associated with poorer CVH, and these associations were stronger among racial/ethnic minority women. Although there was no relation between chronotype and individual clinical CVD risk factors, we observed significant associations between chronotype and health behaviors. Higher MEQ scores were associated with better sleep quality, lower insomnia severity, shorter sleep onset latency, and less sedentary time. Furthermore, being an evening chronotype was associated with greater odds of having short sleep, poor sleep quality, and insomnia symptoms and of not meeting AHA LS7 guidelines for diet and physical activity.

To date, there are limited studies among US adults that examine chronotype in relation to CVD and its risk factors. Although reports based on study of European populations have shown that chronotype is associated with higher risk for CVD (Merikanto et al., 2013, Knutson and von Schantz, 2018), no previous studies examined chronotype in relation to overall CVH in US populations. The observed association between greater eveningness and poorer CVH in this cohort of US women is likely the result of several factors, including circadian misalignment. Evening chronotypes are more prone to circadian misalignment due to a desynchrony between their endogenous biological clocks and the timing of social activities (e.g. food intake, physical activity, work, and sleep) making them vulnerable to cardiometabolic dysfunction (Baron and Reid, 2014). Furthermore, evening chronotypes are more prone to "social jetlag" i.e. a variation in their behavioral patterns between weekends and weekdays, particularly going to bed and waking up later on non-work days compared to work days (Wittmann et al., 2006, Roenneberg and Merrow, 2016). In turn, social jetlag is

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increasingly linked in the literature to elevated CVD risk, thus representing another possible underlying mechanism for the association of chronotype with CVH (Rutters et al., 2014).

The associations we observed between chronotype and CVD risk behaviors are consistent with recent evidence from European and Asian studies. In one analysis using data from the UK Biobank (Patterson et al. 2016), early chronotypes reported fewer hours of computer use (likely sedentary time) per day, while late chronotypes were more likely to be smokers. Similarly, in a Brazilian study of 72 medical residents and a Finish study of ~4400 adults, a lower MEQ score (i.e. eveningness) was associated with physical inactivity (Maukonen et al. 2016; Mota et al. 2016). These reports are consistent with our finding that higher MEQ scores are associated with less sedentary time, and that evening chronotypes are less likely to meet physical activity guidelines and more likely to be smokers.

Much of the emerging literature on chronotype and health behaviors has focused on diet. In the UK Biobank study and other studies in Japanese and Finish cohorts (Sato-Mito et al., 2011, Kanerva et al., 2012, Patterson et al., 2016), evening chronotypes had less healthful diets, characterized by lower consumption of fruits and vegetables, whole grains, and fish and higher intakes of fat and sugary beverages. This is consistent with our finding that evening types were less likely to meet AHA diet guidelines. Intuitively, chronotype has also been studied in relation to sleep behaviors with studies thus far demonstrating that evening chronotypes are more likely to have poor sleep habits including short sleep duration and sleep complaints such as insomnia (Roenneberg et al., 2007, Merikanto et al., 2012). This is consistent with our finding of links between eveningness and shorter sleep and insomnia. We also uniquely document that greater eveningness is associated with a higher risk for OSA and with longer sleep onset latency, both of which have been associated with increased CVD risk (St-Onge et al., 2016). However, a recent study in an elderly Italian population showed that morning types had the worst sleep habits, suggesting that the association of chronotype with sleep may vary by life stage (Castelli et al., 2019). On the other hand, research in adolescents demonstrates that evening chronotypes are more likely than morning and intermediate types to engage in unhealthful behaviors; hence, it may be beneficial to commence prevention efforts targeting chronotype to improve CVD-related health behaviors at an early age (Arora et al., 2015; Urban et al., 2011).

In contrast, we did not observe any significant associations between chronotype and clinical CVD risk factors, although previous reports suggest that such associations exist. In the UK Biobank and in Korean and Finish populations, evening chronotype was associated with up to nearly 3-fold higher odds of metabolic syndrome, type 2 diabetes, and hypertension (Merikanto et al., 2013, Yu et al., 2015, Knutson and von Schantz, 2018). Type 2 diabetes prevalence in the present cohort was only 4%, so it was not possible to examine these relations, though we did not observe an association between chronotype and fasting glucose. Similarly, only a third of our population had hypertension and few of those with hypertension were also evening chronotypes. Hence, we did not have sufficient power to assess these relationships. It is possible that the null results observed for chronotype in relation to fasting glucose and BP in this study are due to the moderate sample size and lower prevalence of cardiometabolic abnormalities, resulting in insufficient power to detect these associations.

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The unique strengths of this study include the use of MEQ, the most widely used validated tool by circadian biologists to ascertain chronotype, and the rigorous data collection procedures to assess cardiometabolic risk factors, including anthropometrics, daytime clinical blood pressure, and biomarkers. No previous study in the US has evaluated chronotype in relation to overall and individual metrics of CVH included in the AHA LS7 as well as other cardiovascular risk behaviors and factors. We also used validated, widely used questionnaires and screeners to measure habitual diet, physical activity, sleep, and sedentary time, but self-reported measures are always prone to some degree of measurement error. Furthermore, while we recruited a racially/ethnically diverse cohort that mirrors national estimates for several health factors, our sample was somewhat healthier than the general US population, so the degree to which these results are generalizable is not known, and we may have underestimated the relation between chronotype and cardiometabolic risk.

Another limitation of this work is the cross-sectional nature of the study, so the link between chronotype and prevalent CVH does not indicate causality. Given the moderate sample size and low prevalence of evening chronotypes, the observed effect size should be interpreted with caution, and it was not possible to stratify by factors such as life stage and menopausal status that may modify the association of chronotype with CVD risk in women. Finally, blood pressure was assessed during a daytime clinic visit resulting in possible misclassification of hypertension status; we also did not have blood pressure assessments from 24-h ambulatory blood pressure (Hermida et al., 2017, Hermida et al., 2018). Moreover, some data suggest that blood pressure cut-offs used to diagnose hypertension in women may be too high (Hermida et al., 2013). This may have diluted possible associations between chronotype and blood pressure in our study.

In conclusion, to our knowledge, this study represents the first report on chronotype in relation to overall CVH and cardiometabolic risk factors and behaviors among racially/ ethnically diverse women. Our study uniquely demonstrates that greater eveningness is associated with poorer CVH and with adverse health behaviors, including unhealthy diet, lower levels of physical activity, longer sedentary time, and poor sleep habits. This is an important finding, because unhealthy risk behaviors can lead to adverse CVD outcomes over the lifespan. Therefore, our results suggest that chronotype may be an important factor to consider and possibly target when designing lifestyle interventions for CVD risk reduction. Given that the heritability of chronotype is estimated to range between 21%-52%, environmental determinants of chronotype could be targeted by interventions aimed at advancing circadian phase (e.g. light therapy in the morning or melatonin administration at night). Alternatively, the behavioral and work schedules of evening types could be tailored to suit their chronotypes. Importantly, our findings highlight the need for more research, particularly within US populations, addressing the cardiovascular consequences of being an evening type. Given that chronotype may change across the life course (Fischer et al., 2017, Montaruli et al., 2017), additional larger prospective studies are warranted to decipher these relationships over time and to better understand the complex role of life stage, menopausal status, and race/ethnicity in these associations.

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## Table 1.

Characteristics of Participants in the Overall Sample and by Chronotype (Morning/Intermediate vs. Evening) $\overset{\downarrow}{\downarrow}$ 

			hotype $^{\dot{t}}$	
Characteristics	Total (N=506)	Morning/ Intermediate Type (n=442)	Evening Type (n=64)	p-value
Demographic				
Mean Age (years)	36.9 (15.7)	37.4 (16.0)	34.4 (12.9)	0.010
Race/Ethnicity				
Non-Hispanic White	38.5% (195)	60.7% (268)	67.2% (43)	0.340
Racial or Ethnic Minority	61.5% (311)	39.4% (174)	32.8% (21)	
Marital Status				
Married/Living with partner	28.8% (146)	29.6% (131)	23.4% (15)	0.380
Single/Widowed/ Divorced/Separated	71.2% (360)	70.4% (311)	76.6% (49)	
Health Insurance				
Have	75.7% (383)	76.0% (336)	73.4% (47)	0.640
Not Have	24.3% (123)	24.0% (106)	26.6% (17)	
Employment Status				
Not Employed	13.4% (67)	12.7% (56)	18.6% (11)	0.220
Employed/Student	86.6% (433)	87.3% (385)	81.4% (48)	
Education				
Some college and above	33.4% (169)	32.1% (142)	42.2% (27)	0.120
High school and less	66.6% (337)	67.9% (300)	57.8% (37)	
Menopause Status				
Postmenopausal	28.9% (146)	30.5% (135)	17.2% (11)	0.027
Premenopausal	71.2% (360)	69.5% (307)	82.8% (53)	
Cardiovascular Health and Cardiometabolic Risk Factors				
AHA LS7 score <sup>*,//</sup>	9.7 (2.2)	9.8 (2.2)	9.1 (2.4)	0.016
BMI (kg/m <sup>2</sup> )*	26.0 (5.7)	25.9 (5.8)	26.9 (5.1)	0.533
Waist Circumference (inches)	35.4 (5.5)	35.5 (5.59)	33.4 (4.76)	0.920
Systolic BP (mmHg)*	117.4 (14.3)	117.3 (14.1)	117.6 (15.5)	0.890
Diastolic BP (mmHg)*	73.0 (10.8)	72.9 (10.9)	73.7 (10.5)	0.570
Total Cholesterol (mg/dL)	182.2 (36.4)	182.8 (36.7)	177.6 (34.2)	0.280
HDL-C (mg/dL)*	61.2 (15.6)	61.7 (15.8)	57.9 (13.5)	0.069
LDL-C (mg/dL)*	104.6 (32.1)	104.9 (32.3)	102.7 (30.6)	0.610
Triglycerides (mg/dL)	81.7 (41.5)	81.2 (43.8)	85.1 (43.8)	0.480
Fasting Blood Glucose (mg/dL)	88.9 (17.7)	88.8 (17.5)	90.2 (19.0)	0.530
Health Behaviors				
Never smokers	77.2% (391)	77.6% (343)	75.0% (48)	0.630

		Chronotype <sup>†</sup>		
Characteristics	Total (N=506)	Morning/ Intermediate Type (n=442)	Evening Type (n=64)	p-value
Meets Physical Activity Guidelines $^{\$}$	46.7% (236)	48.2% ( 213)	35.9% (23)	0.081
Sedentary Time (h/day)	13.7 (7.2)	13.4 (6.7)	16.0 (9.8)	<0.0001
Meets 2–5 of AHA LS7 Diet Guidelines (high/ moderate vs. low diet score)*	50% (249)	53.1% (232)	27.4% (17)	<0.001
Sleep Habits				
Sleep duration (h/night)	6.8 (1.2)	6.8 (1.3)	6.6 (1.1)	0.250
Sleep duration <7 h	43.1% (218)	41.2% (182)	56.3% (36)	0.030
Sleep Quality (PSQI Score)*	5.6 (3.8)	5.4 (3.7)	6.8 (3.8)	0.010
Poor sleep quality (PSQI >5) *	38.3% (194)	37.3% (165)	45.3% (29)	0.220
Insomnia Severity Index	7.1 (6.0)	6.8 (6.0)	9.1 (6.1)	0.005
OSA Risk (high vs. low)	17% (86)	17.0% (75)	17.2% (11)	1.00
Insomnia: somewhat, moderate, or severe (ISI 8) $*$	37.9% (190)	35.5% (157)	55.9% (33)	0.004

\* AHA LS7: American Heart Association Life's Simple 7; BMI: Body Mass Index; BP: Blood Pressure; HDL-C: High Density Lipoprotein Cholesterol; ISI: Insomnia Severity Index; LDL-C: Low Density Lipoprotein Cholesterol; PSQI: Pittsburg Sleep Quality Index

 $^{\dagger}$ Evening-type defined as MEQ score <42 and intermediate or morning-type defined as MEQ score 42

 $\frac{1}{2}$  Data presented as mean(SD) for continuous variables and as or %(N) for categorical variables. T-tests were used to examine differences in participant characteristics measured on the continuous scale. Fisher's Exact test was used to examine differences in participant characteristics measured on the categorical scale.

 ${}^{\$}$ Met physical activity guidelines of 150 min/wk or 75 min/wk of vigorous intensity

//Composite score poor (0–8), moderate (9–10), high (11–14)

### Table 2.

Multivariable-Adjusted Linear Regression Models for Associations of the MEQ score with CVH and CVD Risk Factors  $(N=506)^{*},^{\dagger}$ 

	MEQ Score (continuous scale)			
Overall Cardiovascular Health and Clinical CVD Risk Factors	Beta	p-value		
AHA LS7 Total Score	0.02 (0.01)	0.014		
Clinical CVD Risk Factors in AHA LS7				
BMI (kg/m <sup>2</sup> )	-0.02 (0.02)	0.453		
Fasting Blood Glucose (mg/dL)	-0.01 (0.08)	0.893		
Systolic BP (mm Hg)	-0.04 (0.06)	0.453		
Diastolic BP (mmHg)	-0.02 (0.05)	0.636		
Total Cholesterol (mg/dL)	0.09 (0.16)	0.564		
Clinical CVD Risk Factors Not Included in AHA LS7				
Waist Circumference (inches)	-0.03 (0.02)	0.145		
LDL-C (mg/dL)	0.08 (0.14)	0.569		
HDL-C (mg/dl)	0.04 (0.07)	0.600		
Triglycerides (mg/dl)	-0.16 (0.18)	0.372		
Health Behaviors Not Included in AHA LS7				
Sleep Duration (h/night)	0.01 (0.01)	0.148		
PSQI	-0.07 (0.02)	<0.0001		
ISI	-0.14 (0.03)	<0.0001		
Sleep Onset Latency (min)	-0.28 (0.14)	0.044		
Sedentary Time (h/day)	-0.11 (0.03)	0.001		

\* AHA LS7: American Heart Association Life's Simple 7; BMI: Body Mass Index; BP: Blood Pressure; HDL-C: High Density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; MEQ: Morningness-Eveningness score

 $^{\dagger}$ All models were adjusted for age, race/ethnicity, education, health insurance, and menopausal status

#### Table 3.

Multivariable-Adjusted Logistic Regression Models for Associations between Chronotype and Cardiovascular Health Metrics (N=506)<sup>\*</sup>,  $^{\dagger, \ddagger}$ 

Overall and Individual CVH Metrics	Chronotype <sup>†</sup> Morning (ref) Intermediate Evening		Chronotype <sup>†</sup> : Evening vs. Morning/Intermediate	
	OR (95% CI) p-value		OR (95% CI)	p-value
Total AHA LS7 score $^{\delta}$ (low vs. intermediate/ high)	<b>1.00</b> 1.01 (0.61–1.67) <b>2.53 (1.27–</b> <b>5.01</b> )	0.969 <b>0.008</b>	2.41 (1.20-4.85)	0.013
BMI Score <sup>//</sup> (low/intermediate vs. high)	1.00 1.01 (0.65–1.56) 1.32 (0.71– 2.46)	0.984 0.386	1.32 (0.76–2.29)	0.332
Blood Pressure Score <sup><math>//</math></sup> (low/intermediate vs. high)	1.00 0.85 (0.54–1.34) 1.01 (0.53– 1.93)	0.477 0.976	1.13 (0.63–2.01)	0.689
Cholesterol Score <sup>//</sup> (low/intermediate vs. high)	1.00 1.04 (0.65–1.66) 1.23 (0.62– 2.42)	0.882 0.557	1.20 (0.65–2.20)	0.560
Glucose Score <sup>//</sup> (low/intermediate vs. high)	1.00 0.85 (0.42–1.70) 1.76 (0.61– 5.01)	0.642 0.294	1.93 (0.73–5.12)	0.187
Diet Score <sup>  </sup> (low vs. intermediate/high)	<b>1.00</b> 1.41 (0.93–2.13) <b>3.61 (1.88–</b> <b>6.94</b> )	0.105 < <b>0.001</b>	2.89 (1.59–5.23)	0.001
Physical Activity Score <sup>//</sup> (low/intermediate vs. high)	<b>1.00</b> 1.22 (0.81–1.86) <b>2.03 (1.10–</b> <b>3.75</b> )	0.345 0.024	1.78 (1.03–3.07)	0.039
Smoking Score <sup>//</sup> (low/intermediate vs. high)	<b>1.00</b> 1.60 (0.95–2.68) <b>2.14 (1.02</b> – <b>4.52</b> )	0.078 <b>0.045</b>	1.57 (0.82–3.00)	0.175

\*AHA LS7: American Heart Association Life's Simple 7; BMI: Body Mass Index; CVH: cardiovascular health

 $^{\dagger}$  Evening-type defined as MEQ score of 16–41, intermediate-type defined as MEQ score of 42–58, and morning-type defined as MEQ scores of 59–86

<sup>‡</sup>All models were adjusted for age, race/ethnicity, education, health insurance, and menopausal status

<sup>§</sup>For total AHA LS7 score, models examined associations with chronotype with odds of having a low AHA LS7 score i.e. poor cardiovascular health

<sup>#</sup>For individual AHA LS7 criteria, models examined chronotype in relation to odds of not meeting the ideal guideline for each criterion (low/ intermediate vs. high), with the exception of diet, where models examined chronotype in relation to odds of having a low vs. intermediate/high diet score, given the very low prevalence of an ideal diet in this study.

#### Table 4.

Multivariable-Adjusted Logistic Regression Models for Associations of Chronotype with Sleep Characteristics  $(N=506)^*, \stackrel{\dot{\tau}, \, \dot{z}}{}$ 

Health Behaviors	Chronotype <sup>†</sup> : Morning (ref) Intermediate Evening		Chronotype (Evening vs. Morning/ Intermediate) <sup>†</sup>	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Sleep duration (<7 h vs. 7 h)	1.000.99 (0.64–1.54) <b>2.14 (1.15–3.99)</b>	0.974 <b>0.017</b>	2.15 (1.24–3.73)	0.007
Poor Sleep Quality (PSQI >5 vs. 5)	1.001.26 (0.82–1.95) 1.35 (1.27–4.37)	0.299 <b>0.007</b>	1.57 (0.91–2.71)	0.104
Some, Moderate, or Severe Insomnia vs. None (ISI 8 vs. <8)	1.00 1.52 (0.98–2.38) <b>2.85 (1.53–</b> <b>5.33)</b>	0.064 <b>0.001</b>	2.69 (1.53-4.75)	0.001
Sleep Onset Latency ( 30 min vs. <30 min)	1.00 1.12 (0.72–1.74) <b>1.89 (1.00–</b> <b>3.56</b> )	0.610 <b>0.051</b>	1.51 (0.88–2.62)	0.138
OSA Risk (high vs. low)	1.00 <b>1.22 (1.22–4.09)</b> 2.20 (0.93– 5.23)	<b>0.010</b> 0.074	1.29 (0.61–2.73)	0.503

\* AHA LS7: American Heart Association Life's Simple 7; ISI: Insomnia Severity Index; PSQI: Pittsburg Sleep Quality Index; OSA: Obstructive Sleep Apnea

 $^{\dagger}$ Evening-type defined as MEQ score of 16–41, intermediate-type defined as MEQ score of 42–58, and morning-type defined as MEQ scores of 59–86

<sup>‡</sup>All models were adjusted for age, race/ethnicity, education, health insurance, and menopausal status