



## RESEARCH ARTICLE

AMERICAN JOURNAL  
OF  
INDUSTRIAL MEDICINE

WILEY

# Current work hours and coronary artery calcification (CAC): The Multi-Ethnic Study of Atherosclerosis (MESA)

Penelope J. Allison PhD<sup>1</sup> | Neal W. Jorgensen MS<sup>2</sup> | Desta Fekedulegn PhD<sup>1</sup> |  
Paul Landsbergis PhD<sup>3</sup> | Michael E. Andrew PhD<sup>1</sup> | Capri Foy PhD<sup>4</sup> |  
Karen Hinckley Stukovsky MS<sup>2</sup> | Luenda E. Charles PhD, MPH<sup>1</sup>

<sup>1</sup>Bioanalytics Branch, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, West Virginia

<sup>2</sup>Department of Biostatistics, University of Washington, Seattle, Washington

<sup>3</sup>Department of Environmental and Occupational Health Sciences, Downstate Medical Center, School of Public Health, State University of New York, New York, New York

<sup>4</sup>Public Health Sciences Division, Department of Social Sciences & Health Policy, School of Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina

**Correspondence**

Penelope J. Allison, PhD, CDC-NIOSH, HELD/BB, 1095 Willowdale Rd, MS 4050, Morgantown, WV 26505.

Email: goz2@cdc.gov

**Funding information**

National Heart, Lung, and Blood Institute, Grant/Award Numbers: HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, N01-HC-95169; National Center for Advancing Translational Sciences, Grant/Award Numbers: UL1-TR-000040, UL1-TR-001079, UL1-TR-001420; National Institute for Occupational Safety and Health, Grant/Award Number: NORA FY08 CRN SLB8

**Abstract**

**Background:** Long work hours may be associated with adverse outcomes, including cardiovascular disease. We investigated cross-sectional associations of current work hours with coronary artery calcification (CAC).

**Methods:** Participants (n = 3046; 54.6% men) were from the Multi-Ethnic Study of Atherosclerosis. The number of hours worked in all jobs was obtained by questionnaire and CAC from computed tomography. The probability of a positive CAC score was modeled using log-binomial regression. Positive scores were modeled using analysis of covariance and linear regression.

**Results:** Sixteen percent of the sample worked over 50 hours per week. The overall geometric mean CAC score was  $5.2 \pm 10.0$ ; 40% had positive scores. In fully-adjusted models, prevalence ratios were less than 40 hours: 1.00 (confidence interval [CI]: 0.88-1.12), 40:(ref), 41 to 49:1.13 (CI: 0.99-1.30), and  $\geq 50$ :1.07 (CI: 0.94-1.23) and longer current work hours were not associated with higher mean CAC scores ( $<40$ :56.0 [CI: 47.3-66.3], 40:57.8 [CI: 45.6-73.3], 41 to 49:59.2 [CI: 45.2-77.6],  $\geq 50$ :51.2 [CI: 40.5-64.8];  $P = .686$ ).

**Conclusions:** Current work hours were not independently associated with CAC scores.

**KEYWORDS**

atherosclerosis, coronary artery calcification, coronary artery calcium score, work hours, work schedule

## 1 | INTRODUCTION

Long working hours (>40 hours per week) have become more commonplace in the United States and many other countries in recent years.<sup>1-3</sup> This increasing trend represents a public health

problem because of the number and variety of related adverse health consequences. Abundant scientific evidence indicates that long work hours may lead to or are associated with physical and psychological health problems including cardiovascular disease (CVD).<sup>4-20</sup> Long work hours may also lead to poor lifestyle behaviors such as insufficient leisure-time physical activity, less healthy dietary intake, and inadequate sleep duration<sup>14,21-24</sup> that not only affects quality of life, but are also associated with adverse health conditions.<sup>23,25</sup> Systematic reviews and

**Institutions at which the work was performed:** Bioanalytics Branch, National Institute for Occupational Safety and Health, Morgantown, West Virginia; Department of Biostatistics, University of Washington, Seattle, Washington

meta-analyses of studies on long work hours have identified an increased risk of CVD, particularly at 60 or more work hours, and an increased risk of stroke.<sup>26-28</sup> A retrospective cohort study of the relationship between work hours and CVD found that working more than 45 hours per week for at least 10 years was associated with increased risk of CVD.<sup>29</sup> From the Whitehall II study, Kivimäki et al<sup>30</sup> demonstrated that data on working hours may improve risk prediction of coronary heart disease (CHD) using the Framingham risk score in low-risk, working populations. According to a recent meta-analysis, the evidence that long working hours are a risk factor for CVD suggests a small increased risk associated with CHD (relative risk: 1.12 [95% confidence interval: 1.03-1.21]).<sup>20</sup>

Virtanen and Kivimäki<sup>20</sup> suggested the basis of the mechanism is that long working hours may increase the number of time workers are exposed to workplace hazards, including psychosocial hazards such as high demands. The mechanism linking long working hours and CVD is hypothesized as possible effects associated with psychological over-activation, feelings of stress, and their influence on cardiovascular health such as elevated blood pressure, a risk factor for coronary artery calcification (CAC).<sup>20,31</sup> Long work hours may also be related to subclinical CVD through unhealthy lifestyle behaviors or other stress-related mechanisms, one of which could involve increased systemic inflammation (IL-17, C-reactive protein) related to sleep deprivation.<sup>32,33</sup> In a case-control study, long working hours and short sleep duration were independently associated with CHD in men.<sup>34</sup> Another study showed a significant inverse association between sleep duration and CAC.<sup>31</sup> As a component of atherosclerosis, calcified coronary artery plaques can be quantified by using cardiac computed tomography (CT) to create the CAC score that is a measure of subclinical CVD.<sup>35</sup> CAC is a more sensitive marker of atherosclerosis and a stronger predictor of incident CHD than carotid intima-media thickness and high-sensitivity C-reactive protein.<sup>36-40</sup>

The primary objective of this study was to evaluate whether current work hours are independently associated with CAC. To our knowledge, this is the first study to investigate the association between current work hours and CAC in a well-described epidemiologic study. Previous research indicates that CAC increases with age has a higher prevalence in men than women, and varies among races and ethnicities.<sup>38,41</sup> Longer work hours are more common for certain groups of workers such as salaried and highly-paid workers, nurses, physicians in postgraduate training (for licensure or specialization), and long-haul truck drivers.<sup>42-44</sup> From the Atherosclerosis Risk in Communities Study, the complexity of work and skill discretion were inversely associated with subclinical CVD (carotid intima-media thickness) and positive associations were identified with physical demands and with job insecurity.<sup>45</sup> Therefore, additional objectives were to determine whether gender, race/ethnicity, occupational group, job strain, or physical activity modified the association between current work hours and CAC.

## 2 | METHODS

### 2.1 | Study population

The Multi-Ethnic Study of Atherosclerosis (MESA) began in July 2000. Participants were recruited at six US field centers (Forsyth County, North Carolina; Northern Manhattan and the Bronx, New York; Baltimore City and Baltimore County, Maryland; St Paul, Minnesota; Chicago, Illinois; and Los Angeles, California). Investigators attempted to balance recruitment by gender, race/ethnicity (White, African American, Hispanic, and Chinese American), and age group. Before recruitment, the purpose, rationale, and design of the study were publicized. Households received letters and brochures, and telephone or in-person contact. Eligibility was determined using a screening questionnaire that provided information about the study (eg, MESA is a study about heart disease and atherosclerosis or "hardening of the arteries"), determined age eligibility and history of heart disease, as well as willingness to participate. All eligible participants in the household were recruited for the study. Detailed information on the study design and protocol have been published previously.<sup>46,47</sup> A total of 6814 men and women aged 45 to 84 years were in the original cohort. Individuals were excluded from participation for any physician-diagnosed CVD or cerebrovascular disease, cancer or any serious medical condition, pregnancy or nursing, poor cognitive function, weight more than 300 lbs (>136 kg), language barrier (not proficient in English, Spanish, Cantonese, or Mandarin), living in a nursing home, or planning to relocate within 5 years. Written informed consent was obtained from participants upon arrival at the study clinic. Participants received a free evaluation of health aspects related to subclinical atherosclerosis and results were made available to participants and their doctor if desired. Participants did not receive remuneration for participation but were reimbursed for parking or public transportation costs associated with the clinic visits. All participants were informed of serious or abnormal clinical results with the suggestion that they should follow-up with their personal physician. Institutional review boards at the six field centers and the National Heart, Lung, and Blood Institute approved the study protocol.

Our study involved participants from the first examination (July 2000-August 2002). For the current analyses, we included only those participants who answered "yes" to the question "Do you work to earn money?" ( $n = 3700$ ). The study sample included 3046 (54.6% men) currently employed persons with nonmissing values for current work hours and coronary artery calcium.

## 3 | STUDY MEASURES

### 3.1 | Current work hours

Participants who were currently employed were asked about the amount of time spent in all jobs. The number of days per week and

hours worked per day were determined from the question "How many days per week and hours per day do you work in all jobs?" The total number of hours of work per week was calculated by multiplying the two responses. Questionnaires (including current work hours questions) were completed before CT.

### 3.2 | Coronary artery calcification

CAC was measured with electron-beam or four-detector row CT at the six field centers.<sup>35</sup> Experienced technologists were provided a 2-day training and were certified upon successful completion. For the study, the hearts of consenting participants were scanned twice to obtain an accurate and reproducible assessment of coronary calcium deposits. At consent, participants were told not to participate if they have had more than one chest CT scan or radiation therapy within the past year. A large proportion of the cohort was expected to have some coronary calcium, based upon earlier data collected.<sup>48</sup>

The testing required approximately 20 minutes. The participant was asked to remain still and hold his/her breath during scanning to obtain images of good quality. All scanning was done with a single breath-hold requiring 15 to 40 seconds depending upon the scanner model used. Imaging required approximately 30 to 40 seconds, but double scanning required about 5 to 7 minutes in total. After the first scan, the technologist assessed its quality before conducting the second scan. The CAC measurements resulted in a phantom-adjusted Agatston score among other measurements. A standardized calibration phantom was used to prevent artifacts and to standardize CT attenuation between sites and across participants.

With regard to data quality, there was good compliance with the standardized protocol. Scan quality was excellent with regard to key characteristics, including phantom placement, arterial coverage, lack of misregistration, noise, and motion artifacts. Recommended quality assurance of the scanners involved calibrating the unit at least weekly. Every 2 weeks, scans of a torso phantom verified the accuracy and precision of scanners at different sites. Scans were highly reproducible as assessed by reviews for inter-scan variability (<3%) among the scanning sites and/or technicians and for inter-reader and intra-reader variability (intraclass correlation coefficients >0.99). Agreement with regard to the presence or absence of calcified plaque was high between ( $\kappa$  statistic = 0.90) and within ( $\kappa$  statistic = 0.93) image analysts.

### 3.3 | Covariates

Demographic and lifestyle characteristics were collected by self-administered questionnaires that included age, race/ethnicity, and educational attainment. Height and weight were measured while participants wore light clothing and no shoes. Body mass index (BMI) was calculated as kilograms divided by height in meters squared. Waist circumference was measured at the level of the umbilicus keeping the tape horizontal while the participant was breathing normally. The resulting measurement was rounded to the nearest

centimeter. Smoking status and alcohol status were defined as current, former, or never. Pack-years of smoking were calculated. Resting blood pressure was measured three times in a seated position using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon; Wipro GE Healthcare, Waukesha, WI). The average value for the last two measurements was used in our study. Hypertension was defined as systolic pressure  $\geq 140$  mm Hg, diastolic pressure  $\geq 90$  mm Hg or current use of antihypertensive medication. Blood samples were collected after fasting for at least 12 hours. Aliquots were prepared and stored at  $-70^{\circ}\text{F}$  at the University of Vermont and the University of Minnesota. Laboratory analysis was performed for lipids, lipoproteins, and markers of inflammation such as high-sensitivity plasma C-reactive protein, and other factors. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation<sup>49</sup> and the use of lipid-lowering medication identified participants having problems with abnormal cholesterol levels. Diabetes was defined as fasting glucose  $\geq 126$  mg/dL or the use of hypoglycaemic medication. A family history of heart attack, family history of stroke, and aspirin use was recorded in a medical history questionnaire.

The MESA Typical Week Physical Activity Survey (adapted from the Cross-Cultural Activity Participation Study) collected the time and frequency associated with various physical activities in a typical week during the previous month. The survey has 28 items across categories of activity: household chores, yard/lawn/garden work, care of others (children or adults), transportation, nonoccupational walking, team sports, and dancing, leisure activities (eg, reading, watching TV), work (occupational or volunteer), and intentional exercise.<sup>50</sup> The average number of days per week, time spent per day, and intensity level (light, moderate, or heavy) were reported. A composite physical activity level was derived by summing the minutes of activity for each activity type and then multiplying by the metabolic equivalent level.

Occupational information was collected by questionnaire.<sup>51</sup> Four open-ended questions identified the respondent's current occupation (For whom do/did you work? What type of business or industry is/was this? What kind of work do/did you do? What is/was your job title?). These were adapted from the US Census occupation questions. Responses were coded and grouped using the Census 2000 Occupational Codes: (a) management/professional, (b) service, (c) sales/office, (d) farming, fishing, and forestry, (e) construction, extraction, and maintenance, and (f) production, transportation, and material moving.<sup>51</sup> The last three categories contained few participants and were combined into a "blue-collar jobs" category.

Data were also obtained for job decision latitude (control) and job demands from a subsample of participants ( $n = 6233$ ) who were working at the second examination (September 2002-February 2004), using the Job Content Questionnaire.<sup>51,52</sup> Job control scores ranged from 24 to 96. Job demands scores ranged from 12 to 48. Internal consistency within the study sample was acceptable (Cronbach  $\alpha = .70$  for job demands and 0.84 for job control).<sup>51</sup> The continuous values for job control and job demands were dichotomized at their median values to create low and high groups. Analyses were also conducted using the continuous form of these data.

## 4 | STATISTICAL ANALYSIS

The analysis of the CAC scores was conducted using a two-part model. First, the probability of a positive CAC score was predicted using a log-binomial regression model with a binary outcome (CAC = 0 vs CAC > 0) ( $n = 3046$ ). Second, a linear regression model was used to predict the CAC score given that it is positive ( $n = 1229$ ). The CAC scores were log-transformed for analysis because the data were skewed. Following the analysis, the results were back-transformed for ease of interpretation. Additionally, mean values for the CAC scores were compared across categories of current work hours using analysis of covariance (ANCOVA), including stratified analyses (gender, race/ethnicity, occupational group, and job strain). The variable, current work hours per week, was categorized by placing participants who worked 40 hours per week in a group and then placing the remaining participants into groups of reasonable and fairly equal sample sizes (<40, 41–50, >50). Analyses were also conducted by work days per week (<5, 5, >5), current work hours per day ( $\leq 8$ , 9–11, >11), and the combination of these categories. Potential covariates chosen for adjustment included demographics (age, gender, race/ethnicity, and education), health risk behaviors (smoking status, pack-years, and alcohol status), CVD risk factors (diabetes, hypertension, lipid-lowering medication, aspirin use, family history of heart attack, family history of stroke, BMI, and waist circumference), and job strain (a binary variable created using the median [–9] as the cut point in a continuous job strain variable). The continuous form was calculated as (job demands score) minus (job decision latitude score multiplied by 0.5), to equivalently scale the two constructs.<sup>53</sup> The confounders were selected based on relevant literature or their association with both current work hours and CAC in our sample. We assessed for effect modification between current work hours and CAC for five variables (gender, race/ethnicity, occupational group, job strain, and physical activity) using the full sample ( $n = 3046$ ) and in the sample with only positive CAC scores ( $n = 1229$ ). SAS V.9.4 was used to analyze these data.<sup>54</sup>

## 5 | RESULTS

Descriptive statistics for demographic, lifestyle, cardiovascular, and occupational characteristics of the 3046 participants in the study sample are shown in Table 1. The average age was 56.7 years and 54.6% of participants were men. The race/ethnicity of participants was White (39.8%), African American (27.7%), Hispanic (20.8%), and Chinese American (11.7%). The majority of participants were married or living as married (65.3%) and over 40% had either some college or technical school education or had attained a college degree. Regarding potential risk factors for CVD, 49.9% of participants were current or former smokers, 62.3% reported current alcohol use, but the majority of participants did not have hypertension (65.7%) or diabetes (83.7%), take lipid-lowering medication (88.0%) or aspirin (79.9%), or have a family history of heart attack (59.5%) or stroke (69.6%). The average number of hours worked per week was 39.1, 33.7% worked more than 40 hours per week, and 48.0% were

employed in a management/professional occupation. More than half (59.7%) of the sample had a CAC score of 0 and the average CAC phantom-adjusted score was  $5.2 \pm 10.0$  (range: 0–6315.9).

Age-adjusted associations of selected characteristics with CAC scores and with current work hours are presented in Table 2. There were statistically significant associations with gender and race/ethnicity for both CAC scores and current work hours. Men had higher mean CAC scores and current work hours. White participants had the highest mean CAC scores, while African American participants had the lowest mean CAC scores and the highest mean current work hours. Educational status was positively associated with mean CAC scores. Higher mean CAC scores were observed among participants who were married or living as married, blue-collar workers, current or former smokers, current or former alcohol users, had untreated or treated diabetes, had hypertension, taking lipid-lowering medication, taking aspirin, and those who had a family history of a heart attack. Current work hours were positively associated with a family history of stroke and job control and job demands as were CAC scores with job control. Current work hours were inversely associated with aspirin use. As for the correlations, there were significant positive correlations of both CAC scores and current work hours with BMI, waist circumference, pack-years of smoking, systolic and diastolic blood pressure, fasting glucose, and job control, along with a negative correlation with high-density lipoprotein cholesterol (Table S1). There was a positive correlation between CAC scores and LDL cholesterol and triglycerides. Current work hours were positively correlated with job demands.

The age-adjusted prevalence ratio (CAC > 0) for 41 to 49 hours per week was significant as compared with 40 hours per week (<40 hours: 1.01 [0.90–1.13], 40: (ref), 41 to 49: 1.18 [1.03–1.36],  $\geq 50$ : 1.11 [0.98–1.27]), but not after further adjustment (Table 3a). In models using only the positive CAC scores, longer current work hours were not associated with higher mean CAC scores in results from ANCOVA (<40: 58.8 [51.2–67.6], 40: 55.2 [44.9–67.9], 41–49: 76.9 [59.7–98.9],  $\geq 50$ : 59.6 [48.1–73.9];  $P = .602$  from multivariate linear regression) (Table 3b). None of the selected potential effect modifiers (gender, race/ethnicity, occupational group, job strain, and physical activity) significantly modified the association between current work hours and CAC. Hence, results from stratified analyses (gender, race/ethnicity, occupational group, and job strain) were not statistically significant.

The age-adjusted prevalence ratios (CAC > 0) were not significant for work days per week (<5: 0.91 [0.83–1.00], 5: (ref), >5: 1.09 [0.99–1.19]) (Table 4). For current work hours per day, only 9 to 11 hours were significant as compared with  $\leq 8$  hours ( $\leq 8$ : (ref), 9–11: 1.12 [1.02–1.23], >11: 0.79 [0.67–1.07]) (Table 5). In models combining the categories of days per week and hours per day, the age-adjusted prevalence ratios (CAC > 0) for less than 5 days and more than 11 hours (1.42 [1.07–1.88]) and for more than 5 days and  $\leq 8$  hours (1.14 [1.02–1.27]) were significant as compared with 5 days and  $\leq 8$  hours, but not after further adjustment (Table 6). In models using only the positive CAC scores, increasing work days per week were not associated with higher mean CAC scores (<5: 51.1 [41.6–62.6], 5: 61.7 [54.6–69.9], >5: 67.4 [55.4–82.1];  $P = .050$ ) and increasing

**TABLE 1** Demographic, lifestyle, cardiovascular, and occupational characteristics of MESA study participants, (2000-2002)

Characteristics	All (n = 3046) N (%)	<40 (n = 1288) N (%)	40 (n = 732) N (%)	41-49 (n = 432) N (%)	≥50 (n = 594) N (%)	P value*
Age (y)						
45-54	1419 (46.6)	441 (34.2)	395 (54.0)	246 (56.9)	337 (56.7)	<.001
55-64	1045 (34.3)	430 (33.4)	264 (36.1)	153 (35.4)	198 (33.3)	
65-74	475 (15.6)	324 (25.2)	70 (9.6)	31 (7.2)	50 (8.4)	
75-84	107 (3.5)	93 (7.2)	3 (0.4)	2 (0.5)	9 (1.5)	
Gender						
Women	1382 (45.4)	670 (52.0)	326 (44.5)	170 (39.4)	216 (36.4)	<.001
Men	1664 (54.6)	618 (48.0)	406 (55.5)	262 (60.6)	378 (63.6)	
Family history of heart attack						
No	1723 (59.5)	679 (56.1)	457 (65.5)	251 (59.8)	336 (59.5)	.001
Yes	1171 (40.5)	532 (43.9)	241 (34.5)	169 (40.2)	229 (40.5)	
Family history of stroke						
No	2120 (69.6)	899 (69.8)	504 (68.9)	298 (69.0)	419 (70.5)	.909
Yes	926 (30.4)	389 (30.2)	228 (31.1)	134 (31.0)	175 (29.5)	
Race/ethnicity						
White	1213 (39.8)	533 (41.4)	256 (35.0)	188 (43.5)	236 (39.7)	<.001
Chinese American	355 (11.7)	140 (10.9)	82 (11.2)	62 (14.4)	71 (12.0)	
African American	843 (27.7)	352 (27.3)	191 (26.1)	113 (26.2)	187 (31.5)	
Hispanic	635 (20.8)	263 (20.4)	203 (27.7)	69 (16.0)	100 (16.8)	
Educational status						
≤High school grad/GED	365 (12.0)	164 (12.7)	111 (15.2)	37 (8.6)	53 (8.9)	<.001
Some college/tech school	1389 (45.6)	611 (47.5)	352 (48.1)	170 (39.4)	256 (43.2)	
Bachelor's degree	588 (19.3)	230 (17.9)	144 (19.7)	91 (21.1)	123 (20.7)	
Graduate/professional	702 (23.1)	282 (21.9)	125 (17.1)	134 (31.0)	161 (27.2)	
Marital status						
Married/living as married	1969 (65.3)	792 (62.0)	476 (65.7)	298 (69.5)	403 (68.7)	.022
Widowed/divorced/separated	786 (26.1)	374 (29.3)	180 (24.9)	95 (22.1)	137 (23.3)	
Never married	262 (8.7)	111 (8.7)	68 (9.4)	36 (8.4)	47 (8.0)	
Smoking status						
Never	1527 (50.2)	654 (50.8)	362 (49.5)	219 (50.7)	292 (49.2)	.407
Former	1068 (35.1)	460 (35.7)	247 (33.7)	156 (36.1)	205 (34.6)	
Current	449 (14.8)	173 (13.4)	123 (16.8)	57 (13.2)	96 (16.2)	
Occupation						
Management/professional	1443 (48.0)	592 (46.6)	284 (39.0)	248 (58.5)	319 (54.5)	<.001
Sales/office	600 (20.0)	285 (22.4)	154 (21.2)	67 (15.8)	94 (16.1)	
Service	478 (15.9)	244 (19.2)	107 (14.7)	42 (9.9)	85 (14.5)	
Blue-collar	486 (16.2)	149 (11.7)	183 (25.1)	67 (15.8)	87 (14.9)	
Job decision latitude (control) (n = 2427)						
Low	1290 (53.2)	550 (57.9)	358 (61.0)	162 (43.0)	220 (42.9)	<.001
High	1137 (46.8)	400 (42.1)	229 (39.0)	215 (57.0)	293 (57.1)	
Job psychological demands (n = 2427)						
Low	1230 (50.7)	568 (59.9)	312 (53.0)	158 (42.0)	192 (37.4)	<.001
High	1197 (49.3)	381 (40.1)	277 (47.0)	218 (58.0)	321 (62.6)	
Alcohol use (n = 3034)						
Never	488 (16.1)	222 (17.3)	115 (15.7)	60 (14.0)	91 (15.5)	.35
Former	656 (21.6)	284 (22.1)	160 (21.9)	81 (18.8)	131 (22.3)	
Current	1890 (62.3)	778 (60.6)	457 (62.4)	289 (67.2)	366 (62.2)	
Coronary artery calcium						
0	1817 (59.7)	707 (54.9)	483 (66.0)	266 (61.6)	361 (60.8)	<.001
>0	1229 (40.3)	581 (45.1)	249 (34.0)	166 (38.4)	233 (39.2)	
Diabetes mellitus <sup>a</sup>						
Normal	1151 (83.7)	997 (77.8)	584 (80.2)	352 (81.7)	456 (77.0)	.162
Impaired fasting glucose	124 (9.0)	157 (12.2)	80 (11.0)	43 (10.0)	79 (13.3)	
Untreated diabetes	21 (1.5)	22 (1.7)	17 (2.3)	9 (2.1)	20 (3.4)	
Treated diabetes	79 (5.7)	106 (8.3)	47 (6.5)	27 (6.3)	37 (6.3)	

(Continues)



**TABLE 1** (Continued)

Characteristics	All (n = 3046) N (%)	<40 (n = 1288) N (%)	40 (n = 732) N (%)	41-49 (n = 432) N (%)	≥50 (n = 594) N (%)	P value*
Hypertension <sup>b</sup>						
No	2001 (65.7)	797 (61.9)	504 (68.9)	294 (68.1)	406 (68.4)	.002
Yes	1045 (34.3)	491 (38.1)	228 (31.1)	138 (31.9)	188 (31.6)	
Lipid-lowering medication						
No	2673 (88.0)	1107 (86.1)	656 (90.2)	381 (88.2)	529 (89.4)	.034
Yes	363 (12.0)	178 (13.9)	71 (9.8)	51 (11.8)	63 (10.6)	
Aspirin use						
No	2435 (79.9)	971 (75.4)	618 (84.4)	349 (80.8)	497 (83.7)	<.001
Yes	611 (20.1)	317 (24.6)	114 (15.6)	83 (19.2)	97 (16.3)	
Characteristics	All (n = 3046) Mean ± SD	<40 (n = 1288) Mean ± SD	40 (n = 732) Mean ± SD	41-49 (n = 432) Mean ± SD	≥50 (n = 594) Mean ± SD	P value*
Age (y)	56.7 ± 8.3	59.7 ± 9.1	54.8 ± 6.7	54.2 ± 6.5	54.5 ± 7.2	<.001
Body mass index, Kg/m <sup>2</sup>	28.4 ± 5.4	28.1 ± 5.4	28.4 ± 5.4	28.4 ± 5.3	28.8 ± 5.4	.111
Waist circumference, cm	97.4 ± 14.3	97.0 ± 14.2	97.1 ± 14.0	97.6 ± 14.7	98.6 ± 14.4	.148
Physical activity (MET), min/wk	1627 ± 2539	1740 ± 2,588	1457 ± 2307	1540 ± 2208	1653 ± 2895	.093
Pack-years of smoking (ever-smokers)	10.4 ± 19.9	10.7 ± 20.4	9.7 ± 19.2	9.4 ± 17.0	11.5 ± 21.5	.256
Systolic blood pressure, mm Hg	121.9 ± 19.4	122.9 ± 20.2	121.2 ± 19.1	120.6 ± 17.3	121.4 ± 19.1	.084
Diastolic blood pressure, mm Hg	72.7 ± 10.2	71.8 ± 10.3	72.9 ± 10.0	74.1 ± 9.8	73.4 ± 10.5	<.001
LDL cholesterol, mg/dL	118.6 ± 31.5	118.2 ± 32.2	120.1 ± 30.7	118.2 ± 32.4	117.7 ± 30.1	.501
HDL cholesterol, mg/dL	50.0 ± 14.6	51.4 ± 15.2	50.2 ± 14.9	47.9 ± 13.8	48.3 ± 13.3	<.001
Triglycerides, mg/dL	131.3 ± 90.2	129.8 ± 99.1	131.5 ± 79.1	131.8 ± 76.8	134.0 ± 92.1	.818
Fasting glucose (calibrated, mg/dL)	94.5 ± 27.0	93.7 ± 24.1	93.7 ± 26.0	95.9 ± 33.0	96.2 ± 29.4	.151
C-reactive protein, mg/L	3.3 ± 4.8	3.3 ± 4.5	3.2 ± 5.0	3.3 ± 4.4	3.3 ± 5.5	.922
Job decision latitude (control)	74.5 ± 15.2	73.1 ± 15.4	72.1 ± 15.3	77.6 ± 14.1	77.2 ± 14.7	<.001
Job psychological demands	28.6 ± 7.5	26.9 ± 7.7	28.5 ± 7.1	30.0 ± 7.2	30.8 ± 7.3	<.001
Job strain	-8.6 ± 10.5	-9.7 ± 10.8	-7.6 ± 10.6	-8.8 ± 9.5	-7.8 ± 10.2	<.001
Coronary artery calcium score, phantom-adj. <sup>c</sup>	5.2 ± 10.0	7.0 ± 11.4	3.7 ± 8.0	4.9 ± 9.8	4.5 ± 8.6	.053

Abbreviations: ANOVA, analysis of variance; MET, metabolic equivalent level; SD, standard deviation.

<sup>a</sup>Diabetes mellitus: fasting glucose ≥100 mg/dL (2003 ADA fasting criteria).

<sup>b</sup>Hypertension: systolic pressure ≥140 mm Hg, diastolic pressure ≥90 mm Hg, or current use of antihypertensive medication (JNC VI 1997 criteria).

<sup>c</sup>Geometric means and standard deviations are used for coronary artery calcium scores.

\*P values are for differences between current work hours and were obtained from chi-square and ANOVA tests.

current work hours per week were not either (≤8:59.0 (52.9-65.7), 9-11:63.3 (52.0-77.1), >11:68.8 (43.7-108.2);  $P = .129$ ) (Tables SII-SIII). There were also no significant differences in mean CAC scores across the combinations of the days per week and hours per day categories ( $P = .519$ ) (Table SIV).

## 6 | DISCUSSION

Long work hours (>40 hours per week) are commonplace and associated with adverse health outcomes including CVD.<sup>1,2</sup> We evaluated the independent association of current work hours with CAC, a marker of subclinical CVD. Higher levels of mean CAC scores were not associated with longer current work hours. In addition, gender, race/ethnicity, occupational group, job strain, and physical

activity did not significantly modify the association between current work hours and CAC.

There is much research on associations between long work hours and CVD. Studies involving clinical disease have identified associations of long work hours with acute myocardial infarction, hypertension, CHD, stroke, biological functioning related to the development of CVD, disease pathways, and hematologic markers indicating an increased risk of CVD.<sup>4-16,26-28,34</sup> Specific work hour thresholds have been associated with increased risk of CVD.<sup>28,29</sup> In a low-risk, employed population (Whitehall II Study), the addition of data on work hours to the Framingham risk score improved risk prediction of CHD by 4.7%.<sup>30</sup> In the Atherosclerosis Risk in Communities study, work organization was associated with carotid intima-media thickness.<sup>45</sup> The results from these studies provided a strong rationale for our study on subclinical CVD using CAC.

**TABLE 2** Age-adjusted mean coronary artery calcium (CAC) scores and current hours of work per week by characteristics of participants

Characteristics	CAC scores Mean (95% CI)	Current hours per week Mean (SE)
Gender		
Women	2.86 (2.58-3.18)	37.1 (0.5)
Men	8.62 (7.83-9.50)	40.7 (0.4)
P value*	<.001	<.001
Race/ethnicity		
White (reference for P value)	7.32 (6.52-8.23)	38.5 (0.5)
Chinese American	5.52 (4.45-6.84)	38.9 (0.9)
African American	3.53 (3.08-4.06)	40.9 (0.6)
Hispanic	4.49 (3.82-5.27)	37.9 (0.7)
P value*	<.001	.003
Educational status		
≤High school grad/GED	4.14 (3.35-5.13)	37.3 (0.9)
Some college/tech school	5.04 (4.52-5.62)	39.1 (0.5)
Bachelor's degree	5.58 (4.72-6.61)	38.9 (0.7)
Graduate/professional	5.99 (5.13-6.99)	40.1 (0.7)
P value**	.036	.097
Marital status		
Married/living as married	5.94 (5.42-6.51)	39.0 (0.4)
Widowed/divorced/separated	3.82 (3.30-4.42)	39.4 (0.6)
Never married	5.20 (4.04-6.69)	38.5 (1.1)
P value*	.002	.739
Occupation		
Management/professional	5.49 (4.94-6.12)	39.6 (0.5)
Sales/office	4.48 (3.79-5.28)	38.1 (0.7)
Service	4.07 (3.38-4.90)	38.1 (0.8)
Blue-collar	6.99 (5.81-8.41)	39.7 (0.8)
P value*	<.001	.143
Smoking status		
Never	4.10 (3.70-4.55)	38.7 (0.4)
Former	6.59 (5.82-7.47)	39.3 (0.5)
Current	6.86 (5.66-8.32)	39.9 (0.8)
P value*	.006	.374
Alcohol use		
Never	3.78 (3.14-4.54)	39.0 (0.8)
Former	5.78 (4.93-6.78)	39.0 (0.7)
Current	5.46 (4.97-5.99)	39.1 (0.4)
P value*	.001	.982
Diabetes mellitus <sup>a</sup>		
Normal	4.70 (4.33-5.11)	38.9 (0.4)
Impaired fasting glucose	6.05 (4.88-7.50)	40.1 (0.9)
Untreated diabetes	8.47 (5.18-13.85)	43.0 (2.1)
Treated diabetes	11.48 (8.71-15.13)	38.6 (1.2)
P value**	<.001	.153
Hypertension <sup>b</sup>		
No	4.45 (4.06-4.88)	38.6 (0.4)
Yes	7.12 (6.26-8.09)	39.9 (0.6)
P value*	<.001	.056
Lipid-lowering medication		
No	4.69 (4.34-5.07)	39.0 (0.3)
Yes	11.91 (9.62-14.75)	39.3 (0.9)
P value*	<.001	.804
Aspirin use		
No	4.60 (4.24-5.00)	39.4 (0.4)
Yes	8.69 (7.35-10.26)	37.9 (0.7)
P value*	<.001	<.001

(Continues)

**TABLE 2** (Continued)

Characteristics	CAC scores Mean (95% CI)	Current hours per week Mean (SE)
Family history of heart attack		
No	4.09 (3.71-4.51)	39.3 (0.4)
Yes	7.13 (6.34-8.03)	39.1 (0.5)
P value*	<.001	.777
Family history of stroke		
No	5.17 (4.73-5.65)	38.9 (0.3)
Yes	5.37 (4.70-6.14)	42.2 (1.4)
P value*	.638	<.001
Job decision latitude (control)		
Low	4.35 (3.89-4.86)	39.0 (0.5)
High	5.12 (4.54-5.76)	42.1 (0.5)
P value*	.050	<.001
Job psychological demands		
Low	4.77 (4.25-5.35)	37.8 (0.5)
High	4.60 (4.10-5.18)	43.2 (0.5)
P value*	.680	<.001

Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; SE, standard error.

<sup>a</sup>Diabetes mellitus: fasting glucose  $\geq 100$  mg/dL (2003 ADA fasting criteria).

<sup>b</sup>Hypertension: systolic pressure  $\geq 140$  mm Hg, diastolic pressure  $\geq 90$  mm Hg, or current use of antihypertensive medication (JNC VI 1997 criteria).

\*P value obtained from ANCOVA, tests of differences between mean values.

\*\*P value obtained from ANCOVA, linear contrasts.

To our knowledge, there are no studies on the association between long current work hours and CAC, but there are few related studies involving occupational factors and CAC. Kang et. al.<sup>55</sup> studied the association of shift work with CAC and coronary artery stenosis in male chemical plant workers. In contrast to our results with current work hours, rotating shift work employment, and duration were associated with an increased risk of CAC. In the Coronary Artery Risk Development in Young Adults (CARDIA) study, job strain was not associated with nonzero CAC at 5 or 18 years of follow-up. Participants in managerial or professional occupations were less likely to have a nonzero CAC than those in laborer occupations.<sup>56</sup> Also from the CARDIA study, lower socioeconomic status (SES) defined by education, occupation, and household income with repeated measurements over 15 years was associated with increased risk of CAC at year 20.<sup>57</sup> Similar to these studies, job strain was not positively associated with CAC in our study. The occupation was associated with CAC in a U-shaped manner, where both the lowest status (blue-collar workers) and highest status (management/professional) had the highest mean CAC values. Educational status was positively associated with current work hours and CAC. CVD is associated with non-White race/ethnicity, and with lower levels of education, occupational status, and job decision latitude. However, in the current sample, CAC was associated with White race/ethnicity, higher education, and higher job decision latitude, raising questions about associations between SES and risk in the MESA study.

**TABLE 3a** Prevalence ratio of coronary artery calcium (CAC) score more than 0 by current work hours per week

	<40 (n = 1288) PR (95% CI)	40 (n = 732) PR (95% CI)	41-49 (n = 432) PR (95% CI)	≥50 (n = 594) PR (95% CI)
Model 1	1.01 (0.90-1.13)	Referent	1.18 (1.03-1.36)	1.11 (0.98-1.27)
Model 2	1.05 (0.95-1.18)	Referent	1.15 (1.01-1.32)	1.08 (0.95-1.23)
Model 3	1.00 (0.88-1.12)	Referent	1.13 (0.99-1.30)	1.07 (0.94-1.23)

Note: Model 1: Adjusted for age; Model 2: Adjusted for age and gender; Model 3: Adjusted for age, gender, race/ethnicity, education, smoking status, pack-years of smoking, alcohol status, diabetes, hypertension, lipid-lowering medication, family history of heart attack, family history of stroke, aspirin use, BMI, waist circumference, and job strain.

Abbreviations: BMI, body mass index; CI, confidence interval.

**TABLE 3b** Adjusted mean coronary artery calcium (CAC) scores by current work hours per week for subjects with a CAC score more than 0

	<40 (n = 581) Mean (95% CI)	40 (n = 249) Mean (95% CI)	41-49 (n = 166) Mean (95% CI)	≥50 (n = 233) Mean (95% CI)	P value
Model 1	58.8 (51.2-67.6)	55.2 (44.9-67.9)	76.9 (59.7-98.9)	59.6 (48.1-73.9)	.602
Model 2	61.3 (53.4-70.2)	54.5 (44.6-66.7)	73.4 (57.3-93.9)	56.5 (45.8-69.7)	.980
Model 3	56.0 (47.3-66.3)	57.8 (45.6-73.3)	59.2 (45.2-77.6)	51.2 (40.5-64.8)	.686

Note: Model 1: Adjusted for age; Model 2: Adjusted for age and gender; Model 3: Adjusted for age, gender, race/ethnicity, education, smoking status, pack-years of smoking, alcohol status, diabetes, hypertension, lipid-lowering medication, family history of heart attack, family history of stroke, aspirin use, BMI, waist circumference, and job strain. Interaction by gender (Model 3):  $P = .867$ ; Interaction by race/ethnicity (Model 3):  $P = .862$ ; Interaction by occupational group (Model 3):  $P = .110$ ; Interaction by job strain (Model 3):  $P = .429$ ; Interaction by physical activity (Model 3):  $P = .619$ .

Abbreviations: BMI, body mass index; CI, confidence interval.

\*P values are obtained from multivariate linear regression models.

Although we did not find an independent association between current work hours and CAC, studies have shown that long work hours are associated with lifestyle risk factors, including suboptimal dietary intake, inadequate levels of exercise, and insufficient sleep, that may promote CAC through disease processes such as dyslipidemia, hypertension, or inflammation.<sup>14,21-24,58,59</sup> A recent review emphasizes that the interplay between demographic and occupational factors may shape the effects of long work hours for different working populations in different ways based on gender, age, working conditions, and other factors.<sup>60</sup>

One limitation of the study is that we cannot infer causality due to the cross-sectional study design. Other limitations of this study design include the possibility of selection and temporal biases. The presence of symptoms not collected, such as fatigue, dyspnea, and chest pain on exertion, may have resulted in a selection bias to shorter work hours.

This bias may be limited because individuals who reported doctor-diagnosed angina were ineligible. There is possible selection bias regarding increased participation of the medically uninsured to receive medical services, but there was probably little effect on the results because only 10% of the participants were uninsured. The use of self-reported current work hours, as opposed to information from administrative records, could likely bring about misclassification that could bias the results. Bias in self-reported current work hours may reduce the accuracy and/or precision of the data, obscuring the effect of the exposure. For example, it is unclear whether participants reported unpaid hours worked at home for the job, work-related mobile communications outside work hours, or overtime work hours. If work hours do influence the development of atherosclerosis, this is likely to occur over a long time period. The reported work hours in our study were based on all currently held jobs at the time of the interview, which

**TABLE 4** Prevalence ratio of coronary artery calcium (CAC) score more than 0 by current work days per week

	<5 d (n = 568) PR (95% CI)	5 d (n = 1827) PR (95% CI)	>5 d (n = 651) PR (95% CI)
Model 1	0.91 (0.83-1.00)	Referent	1.09 (0.99-1.19)
Model 2	0.98 (0.88-1.10)	Referent	1.06 (0.96-1.16)

Note: Model 1: Adjusted for age; Model 2: Adjusted for age, gender, race/ethnicity, education, smoking status, pack-years of smoking, alcohol status, diabetes, hypertension, lipid-lowering medication, family history of heart attack, family history of stroke, aspirin use, BMI, waist circumference, and job strain.

Abbreviations: BMI, body mass index; CI, confidence interval.

**TABLE 5** Prevalence ratio of coronary artery calcium (CAC) score more than 0 by current work hours per day

	≤8 h (n = 2169) PR (95% CI)	9-11 h (n = 713) PR (95% CI)	>11 h (n = 162) PR (95% CI)
Model 1	Referent	1.12 (1.02-1.23)	0.85 (0.67-1.07)
Model 2	Referent	1.11 (1.01-1.23)	0.79 (0.62-1.02)

Note: Model 1: Adjusted for age; Model 2: Adjusted for age, gender, race/ethnicity, education, smoking status, pack-years of smoking, alcohol status, diabetes, hypertension, lipid-lowering medication, family history of heart attack, family history of stroke, aspirin use, BMI, waist circumference, and job strain.

Abbreviations: BMI, body mass index; CI, confidence interval.



**TABLE 6** Prevalence ratio of coronary artery calcium (CAC) score more than 0 by current work days per week and current work hours per day

	<5 d			5 d			>5 d		
	≤ 8 h (n = 451) PR (95% CI)	9-011 h (n = 84) PR (95% CI)	>11 h (n = 33) PR (95% CI)	≤ 8 h (n = 1389) PR (95% CI)	9-11 h (n = 389) PR (95% CI)	>11 h (n = 47) PR (95% CI)	≤ 8 h (n = 329) PR (95% CI)	9-11 h (n = 240) PR (95% CI)	>11 h (n = 82) PR (95% CI)
Model 1	0.89 (0.81-0.99)	1.05 (0.84-1.30)	1.42 (1.07-1.88)	Referent	1.12 (0.98-1.29)	0.77 (0.48-1.24)	1.14 (1.02-1.27)	1.13 (0.97-1.31)	0.82 (0.57-1.19)
Model 2	0.96 (0.85-1.08)	1.20 (0.94-1.53)	1.16 (0.79-1.72)	Referent	1.09 (0.94-1.26)	0.71 (0.40-1.26)	1.08 (0.95-1.22)	1.13 (0.98-1.31)	0.84 (0.59-1.19)

Note: Model 1: Adjusted for age; Model 2: Adjusted for age, gender, race/ethnicity, education, smoking status, pack-years of smoking, alcohol status, diabetes, hypertension, lipid-lowering medication, family history of heart attack, family history of stroke, aspirin use, BMI, waist circumference, and job strain.

Abbreviations: BMI, body mass index; CI, confidence interval.

may not accurately reflect hours worked in a participant's entire work history and limits our ability to estimate the association under study. For example, participants age 65 and above represent 19% of the study sample and 32% of those working less than 40 hours per week. Although the measurement of CAC was state of the art, CT has limitations with regard to detecting microcalcifications.<sup>58</sup> CAC has different presentations and its formation is complex, that is, densely and minimally-calcified plaque, microcalcification, and so on.<sup>58,61</sup> Information on shift work, work organization (eg, work and employment conditions), sleep duration, or sleep quality was not available for our study. These data would have been highly relevant in our investigation of the association of current work hours and CAC. Data were not available to assess differences between characteristics of currently employed participants and nonparticipants or to calculate a specific participation rate among those currently employed.

The strengths of the study include a standardized protocol and a large sample size, with sizeable numbers of participants by gender and race/ethnicity. The study also offered CAC scores, an uncommon and useful indicator of subclinical CVD. Central training and certification were required of study staff before conducting the clinical examinations of MESA study participants. Study measurements were subject to internal and external quality control programs. The MESA study offered a rich data set to examine these associations with subclinical CVD, with information on multiple factors that could potentially modify or confound the associations of interest.

To our knowledge, this is the first study to investigate the association between current work hours and CAC in a well-described epidemiologic study. In this sample of MESA participants, we did not observe an association between works hours and CAC that was independent of demographic characteristics, and lifestyle and cardiovascular risk factors. This lack of an independent association suggests that, in our study, current work hours may have been a surrogate for the risk factors that are typically associated with them. A longitudinal study, including an objective measure of work hours collected over time, may be needed to investigate this association. Further characterization of the work organization, such as work and employment conditions, may also be warranted.

## ACKNOWLEDGMENTS

We thank the other MESA investigators, staff, and the MESA study participants for their contribution. A full list of participating MESA investigators and institutions can be found at <http://www.mesa-nhlbi.org>. This manuscript has been reviewed by the MESA investigators for scientific content and consistency of data interpretation with previous MESA publications and significant comments have been incorporated before submission for publication. The MESA is conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with MESA investigators. MESA is supported by contracts HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, and N01-HC-95169 from the National Heart, Lung, and Blood Institute, and by grants UL1-TR-000040, UL1-TR-001079, and UL1-TR-001420 from NCATS. Occupational coding was supported by the National Institute for Occupational Safety and Health (NORA FY08 CRN SLB8).

## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

## DISCLOSURE BY AJIM EDITOR OF RECORD

John D. Meyer declares that he has no conflict of interest in the review and publication decision regarding this article.

## AUTHOR'S CONTRIBUTIONS

PA, DF, and LC participated in the conception and design of the study. PA and LC drafted the manuscript. NJ performed all statistical analyses. All authors (a) revised the paper for important intellectual content, (b) provided the final approval of the version to be published, (c) and participated in the agreement to be accountable for all aspects of the work.



## ETHICS APPROVAL AND INFORMED CONSENT

The work was performed at the National Institute for Occupational Safety and Health and the University of Washington. In MESA, institutional review boards at the six field centers (Forsyth County, North Carolina; Northern Manhattan and the Bronx, New York; Baltimore City and Baltimore County, Maryland; St Paul, Minnesota; Chicago, Illinois; and Los Angeles, California) and the National Heart, Lung, and Blood Institute approved the study protocol. Written informed consent was obtained from participants upon arrival at the study clinic.

## DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

## ORCID

Penelope J. Allison  <http://orcid.org/0000-0002-5384-3621>  
 Neal W. Jorgensen  <http://orcid.org/0000-0003-2311-0424>  
 Desta Fekedulegn  <http://orcid.org/0000-0002-1820-4373>  
 Paul Landsbergis  <http://orcid.org/0000-0002-4066-566X>  
 Michael E. Andrew  <http://orcid.org/0000-0001-8191-3642>  
 Capri Foy  <http://orcid.org/0000-0001-7838-3820>  
 Karen Hinckley Stukovsky  <http://orcid.org/0000-0003-4781-2471>  
 Luenda E. Charles  <http://orcid.org/0000-0002-8683-1539>

## REFERENCES

- Rones PL, Ilg RE, Gardner JM. Trends in hours of work since the mid-1970s. *Mon Labor Rev*. April 1997;120:3-14.
- Landsbergis P. Long work hours, hypertension, and cardiovascular disease. *Cad Saude Publica*. 2004;20(6):1746-1748.
- Lee S, McCann D, Messenger JC. *Working time around the world*. Geneva, Switzerland: International Labour Organization; 2007.
- Sokejima S, Kagamimori S. Working hours as a risk factor for acute myocardial infarction in Japan: case-control study. *BMJ*. 1998;317(7161):775-780.
- Iwasaki K, Sasaki T, Oka T, Hisanaga N. Effect of working hours on biological functions related to cardiovascular system among salesmen in a machinery manufacturing company. *Ind Health*. 1998;36(4):361-367.
- Park J, Kim Y, Cho Y, et al. Regular overtime and cardiovascular functions. *Ind Health*. 2001;39(3):244-249.
- Liu Y, Tanaka H, Fukuoka Heart Study G. Overtime work, insufficient sleep, and risk of nonfatal acute myocardial infarction in Japanese men. *Occup Environ Med*. 2002;59(7):447-451.
- Chen JC, Chen YJ, Chang WP, Christiani DC. Long driving time is associated with haematological markers of increased cardiovascular risk in taxi drivers. *Occup Environ Med*. 2005;62(12):890-894.
- Fukuoka Y, Dracup K, Sivarajan Froelicher E, et al. Do Japanese workers who experience an acute myocardial infarction believe their prolonged working hours are a cause? *Int J Cardiol*. 2005;100(1):29-35.
- Harma M. Workhours in relation to work stress, recovery and health. *Scand J Work Environ Health*. 2006;32(6):502-514.
- Yang H, Schnall PL, Jauregui M, Su TC, Baker D. Work hours and self-reported hypertension among working people in California. *Hypertension*. 2006;48(4):744-750.
- Virtanen M, Singh-Manoux A, Ferrie JE, et al. Long working hours and cognitive function: the Whitehall II Study. *Am J Epidemiol*. 2009;169(5):596-605.
- Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Long work hours and physical fitness: 30-year risk of ischaemic heart disease and all-cause mortality among middle-aged Caucasian men. *Heart*. 2010;96(20):1638-1644.
- Caruso CC. Negative impacts of shiftwork and long work hours. *Rehabil Nurs*. 2014;39(1):16-25.
- Kawada T. Long working hours and the risk of coronary heart disease. *Am J Ind Med*. 2016;59(4):336-337.
- Charles LE, Fekedulegn D, Burchfiel CM, et al. Associations of work hours with carotid intima-media thickness and ankle-brachial index: the Multi-Ethnic Study of Atherosclerosis (MESA). *Occup Environ Med*. 2012;69(10):713-720.
- Charles LE, Fekedulegn D, Landsbergis P, et al. Associations of work hours, job strain, and occupation with endothelial function: the Multi-Ethnic Study of Atherosclerosis (MESA). *J Occup Environ Med*. 2014;56(11):1153-1160.
- Bannai A, Tamakoshi A. The association between long working hours and health: a systematic review of epidemiological evidence. *Scand J Work Environ Health*. 2014;40(1):5-18.
- Lee DW, Kim HR, Myong JP, Choi J, Hong YC, Kang MY. Does working long hours increase the risk of cardiovascular disease for everyone? *J Occup Health*. 2019;00:1-11.
- Virtanen M, Kivimäki M. Long working hours and risk of cardiovascular disease. *Curr Cardiol Rep*. 2018;20(11):123.
- Sasaki T, Iwasaki K, Oka T, et al. Effect of working hours on cardiovascular-autonomic nervous functions in engineers in an electronics manufacturing company. *Ind Health*. 1999;37(1):55-61.
- Dahlgren A, Kecklund G, Akerstedt T. Overtime work and its effects on sleep, sleepiness, cortisol, and blood pressure in an experimental field study. *Scand J Work Environ Health*. 2006;32(4):318-327.
- Mullington JM, Haack M, Toth M, Serrador JM, Meier-Ewert HK. Cardiovascular, inflammatory, and metabolic consequences of sleep deprivation. *Prog Cardiovasc Dis*. 2009;51(4):294-302.
- Virtanen M, Ferrie JE, Gimeno D, et al. Long working hours and sleep disturbances: the Whitehall II prospective cohort study. *Sleep*. 2009;32(6):737-745.
- van der Hulst M. Long workhours and health. *Scand J Work Environ Health*. 2003;29(3):171-188.
- Virtanen M, Heikkilä K, Jokela M, et al. Long working hours and coronary heart disease: A systematic review and meta-analysis. *Am J Epidemiol*. 2012;176(7):586-596.
- Kivimäki M, Jokela M, Nyberg ST, et al. Long working hours and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603 838 individuals. *Lancet*. 2015;386(10005):1739-1746.
- Kang MY, Park H, Seo JC, et al. Long working hours and cardiovascular disease: a meta-analysis of epidemiologic studies. *J Occup Environ Med*. 2012;54(5):532-537.
- Conway SH, Pompeii LA, Roberts RE, Follis JL, Gimeno D. Dose-response relation between work hours and cardiovascular disease risk: findings from the panel study of income dynamics. *J Occup Environ Med*. 2016;58(3):221-226.

30. Kivimäki M, Batty GD, Hamer M, et al. Using additional information on working hours to predict coronary heart disease. *Ann Intern Med*. 2011;154(7):457-463.
31. King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident coronary artery calcification. *JAMA*. 2008;300(24):2859-2866.
32. Meier-Ewert HK, Ridker PM, Rifai N, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *J Am Coll Cardiol*. 2004;43(4):678-683.
33. van Leeuwen WMA, Lehto M, Karisola P, et al. Sleep restriction increases the risk of developing cardiovascular diseases by augmenting proinflammatory responses through IL-17 and CRP. *PLoS One*. 2009;4(2):e4589.
34. Cheng Y, Du CL, Hwang JJ, Chen IS, Chen MF, Su TC. Working hours, sleep duration and the risk of acute coronary heart disease: a case-control study of middle-aged men in Taiwan. *Int J Cardiol*. 2014;171(3):419-422.
35. Carr JJ, Nelson JC, Wong ND, et al. Calcified coronary artery plaque measurement with cardiac CT in population-based studies: standardized protocol of Multi-Ethnic Study of Atherosclerosis (MESA) and Coronary Artery Risk Development in Young Adults (CARDIA) study. *Radiology*. 2005;234(1):35-43.
36. Folsom AR, Kronmal RA, Detrano RC, et al. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA). *Arch Intern Med*. 2008;168(12):1333-1339.
37. Budoff MJ, Gul KM. Expert review on coronary calcium. *Vasc Health Risk Manag*. 2008;4(2):315-324.
38. Taylor AJ, Bindeman J, Feuerstein I, Cao F, Brazaitis M, O'Malley PG. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. *J Am Coll Cardiol*. 2005;46(5):807-814.
39. Qureshi WT, Rana JS, Yeboah J, bin Nasir U, Al-Mallah MH. Risk stratification for primary prevention of coronary artery disease: roles of C-reactive protein and coronary artery calcium. *Curr Cardiol Rep*. 2015;17(12):110.
40. Gepner AD, Young R, Delaney JA, et al. Comparison of carotid plaque score and coronary artery calcium score for predicting cardiovascular disease events: The Multi-Ethnic Study of Atherosclerosis. *J Am Heart Assoc*. 2017;6(2):e005179.
41. Nasir K, Shaw LJ, Liu ST, et al. Ethnic differences in the prognostic value of coronary artery calcification for all-cause mortality. *J Am Coll Cardiol*. 2007;50(10):953-960.
42. Kuhn P, Lozano F. The expanding workweek? Understanding trends in long work hours among US men, 1979-2006. *J Labor Econ*. 2008;26(2):311-343.
43. Trinkoff A, Geiger-Brown J, Brady B, Lipscomb J, Muntaner C. How long and how much are nurses now working? *Am J Nurs*. 2006;106(4):60-71.
44. Arnold PK, Hartley LR, Corry A, Hochstadt D, Penna F, Feyer AM. Hours of work, and perceptions of fatigue among truck drivers. *Accid Anal Prev*. 1997;29(4):471-477.
45. Muntaner C, Nieto FJ, Cooper L, Meyer J, Szklo M, Tyroler HA. Work organization and atherosclerosis: findings from the ARIC study. Atherosclerosis risk in communities. *Am J Prev Med*. 1998;14(1):9-18.
46. Bild DE. Multi-Ethnic Study of Atherosclerosis: objectives and design. *Am J Epidemiol*. 2002;156(9):871-881.
47. Multi-Ethnic Study of Atherosclerosis (MESA) protocol 2002; <https://www.mesa-nhlbi.org/aboutMESAOverviewProtocol.aspx>. Accessed May 19, 2019.
48. Janowitz WR, Agatston AS, Kaplan G, Viamonte M Jr. Differences in prevalence and extent of coronary artery calcium detected by ultrafast computed tomography in asymptomatic men and women. *Am J Cardiol*. 1993;72(3):247-254.
49. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18(6):499-502.
50. Bertoni AG, Whitt-Glover MC, Chung H, et al. The association between physical activity and subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol*. 2009;169(4):444-454.
51. Fujishiro K, Diez Roux AV, Landsbergis P, et al. Associations of occupation, job control and job demands with intima-media thickness: the Multi-Ethnic Study of Atherosclerosis (MESA). *Occup Environ Med*. 2011;68(5):319-326.
52. Karasek R, Brisson C, Kawakami N, Houtman I, Bongers P, Amick B. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. *J Occup Health Psychol*. 1998;3(4):322-355.
53. Landsbergis PA, Diez-Roux AV, Fujishiro K, et al. Job strain, occupational category, systolic blood pressure, and hypertension prevalence: the Multi-Ethnic Study of Atherosclerosis. *J Occup Environ Med*. 2015;57(11):1178-1184.
54. SAS/STAT® 9.2 User's Guide [computer program]. Cary, NC: SAS Institute Inc.; 2008.
55. Kang W, Park WJ, Jang KH, et al. Coronary artery atherosclerosis associated with shift work in chemical plant workers by using coronary CT angiography. *Occup Environ Med*. 2016;73(8):501-505.
56. Greenlund KJ, Kiefe CI, Giles WH, Liu K. Associations of job strain and occupation with subclinical atherosclerosis: the CARDIA Study. *Ann Epidemiol*. 2010;20(5):323-331.
57. Matthews KA, Schwartz JE, Cohen S. Indices of socioeconomic position across the life course as predictors of coronary calcification in black and white men and women: coronary artery risk development in young adults study. *Soc Sci Med*. 2011;73(5):768-774.
58. Nakahara T, Dweck MR, Narula N, Pisapia D, Narula J, Strauss HW. Coronary artery calcification: from mechanism to molecular imaging. *JACC Cardiovasc Imaging*. 2017;10(5):582-593.
59. Mallikethi-Reddy S, Rubenfire M, Jackson LA, Brook RD. Coronary artery calcium in hypertension: a review. *J Am Soc Hypertens*. 2015;9(12):993-1000.
60. Ganster DC, Rosen CC, Fisher GG. Long working hours and well-being: what we know, what we do not know, and what we need to know. *J Bus Psychol*. 2016;33:1-15.
61. Zaid M, Fujiyoshi A, Kadota A, Abbott RD, Miura K. Coronary artery calcium and carotid artery intima media thickness and plaque: clinical use in need of clarification. *J Atheroscler Thromb*. 2017;24(3):227-239.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

**How to cite this article:** Allison PJ, Jorgensen NW, Fekedulegn D, et al. Current work hours and coronary artery calcification (CAC): The Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Ind Med*. 2020;63:348–358. <https://doi.org/10.1002/ajim.23084>