

UC San Diego

UC San Diego Previously Published Works

Title

Total Sitting Time and Sitting Pattern in Postmenopausal Women Differ by Hispanic Ethnicity and are Associated With Cardiometabolic Risk Biomarkers

Permalink

<https://escholarship.org/uc/item/50f1q3db>

Journal

Journal of the American Heart Association, 9(4)

ISSN

2047-9980

Authors

Chang, Ya-Ju
Bellettiere, John
Godbole, Suneeta
[et al.](#)

Publication Date

2020-02-18

DOI

10.1161/jaha.119.013403

Copyright Information

This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

Total Sitting Time and Sitting Pattern in Postmenopausal Women Differ by Hispanic Ethnicity and are Associated With Cardiometabolic Risk Biomarkers

Ya-Ju Chang, PhD; John Bellettiere, MA, MPH, PhD; Suneeta Godbole, MPH; Samaneh Keshavarz, BS; Joseph P. Maestas; Jonathan T. Unkart, MD, MPH, MS; Daniel Ervin, PhD; Matthew A. Allison, MD, MPH; Cheryl L. Rock, PhD, RD; Ruth E. Patterson, PhD; Marta M. Jankowska, PhD; Jacqueline Kerr, PhD; Loki Natarajan, PhD; Dorothy D. Sears, PhD

Background—Sedentary behavior is pervasive, especially in older adults, and is associated with cardiometabolic disease and mortality. Relationships between cardiometabolic biomarkers and sitting time are unexplored in older women, as are possible ethnic differences.

Methods and Results—Ethnic differences in sitting behavior and associations with cardiometabolic risk were explored in overweight/obese postmenopausal women ($n=518$; mean \pm SD age 63 ± 6 years; mean body mass index 31.4 ± 4.8 kg/m²). Accelerometer data were processed using validated machine-learned algorithms to measure total daily sitting time and mean sitting bout duration (an indicator of sitting behavior pattern). Multivariable linear regression was used to compare sitting among Hispanic women ($n=102$) and non-Hispanic women ($n=416$) and tested associations with cardiometabolic risk biomarkers. Hispanic women sat, on average, 50.3 minutes less/day than non-Hispanic women ($P<0.001$) and had shorter (3.6 minutes less, $P=0.02$) mean sitting bout duration. Among all women, longer total sitting time was deleteriously associated with fasting insulin and triglyceride concentrations, insulin resistance, body mass index and waist circumference; longer mean sitting bout duration was deleteriously associated with fasting glucose and insulin concentrations, insulin resistance, body mass index and waist circumference. Exploratory interaction analysis showed that the association between mean sitting bout duration and fasting glucose concentration was significantly stronger among Hispanic women than non-Hispanic women (P -interaction=0.03).

Conclusions—Ethnic differences in 2 objectively measured parameters of sitting behavior, as well as detrimental associations between parameters and cardiometabolic biomarkers were observed in overweight/obese older women. The detrimental association between mean sitting bout duration and fasting glucose may be greater in Hispanic women than in non-Hispanic women. Corroboration in larger studies is warranted. (*J Am Heart Assoc.* 2020;9:e013403. DOI: 10.1161/JAHA.119.013403.)

Key Words: ActiGraph • cardiovascular risk • glucoregulatory • Latina • machine learning • type 2 diabetes • women's health

Sedentary behavior, characterized by sitting with energy expenditure <1.5 metabolic equivalents, has a strong association with weight gain, metabolic syndrome, type 2 diabetes mellitus, and cardiovascular disease.^{1–4} Excessive sedentary behavior has become a common feature of life for many adults who live in developed nations with advanced technologies.^{5,6} Objective measurement of amount and patterns of sitting can be

used to describe individuals' sitting habits; 2 common measures include total sitting time and mean sitting bout duration. The former reflects the volume of sitting time accrued per day while the latter accounts for how that sitting time is accumulated, be it in short, frequently interrupted sitting bouts or in long, unbroken bouts of sitting.⁷ Detrimental associations of excessive sitting time and of uninterrupted, prolonged sitting patterns with

From the Departments of Family Medicine and Public Health (Y.-J.C., J.B., S.G., J.P.M., J.T.U., M.A.A., C.L.R., R.E.P., J.K., L.N., D.D.S.), and Medicine (Y.-J.C., D.D.S.), Moores Cancer Center (C.L.R., R.E.P., J.K., L.N., D.D.S.), and Calit2/Qualcomm Institute (M.M.J.), UC San Diego, La Jolla, CA; Center for Behavioral Epidemiology and Community Health, San Diego State University, San Diego, CA (J.B.); School of Medicine and Health Sciences, The George Washington University, Washington, DC (S.K.); Department of Research, The East-West Center, Honolulu, HI (D.E.); College of Health Solutions, Arizona State University, Phoenix, AZ (D.D.S.).

An accompanying Table S1 is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013403>

Correspondence to: Dorothy D. Sears, PhD, College of Health Solutions, Arizona State University, 550 N 3rd Street, MC9020, Phoenix, AZ 85004. E-mail: dorothy.sears@asu.edu

Received June 11, 2019; accepted January 6, 2020.

© 2020 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Clinical Perspective

What Is New?

- Significant differences in total sitting time and mean sitting bout duration (an indicator of sitting behavior pattern) were observed between overweight/obese postmenopausal Hispanic and non-Hispanic women wherein Hispanic women, on average, spent 9% fewer minutes sitting per day and had 9% shorter sitting bout durations.
- Among overweight/obese postmenopausal Hispanic and non-Hispanic women, we observed that sitting behavior (total sitting time and mean sitting bout duration) was deleteriously associated with higher levels of cardiometabolic risk biomarkers (body mass index, waist circumference, fasting glucose, insulin, and triglycerides, and insulin resistance).

What Are the Clinical Implications?

- Clinicians and other healthcare providers should encourage patients to reduce their sitting time intervals, in addition to encouraging physical activity.
- Targeting sitting behaviors may benefit cardiometabolic health in overweight/obese postmenopausal women.

cardiometabolic factors have been demonstrated in multiple cross-sectional, longitudinal, and experimental studies, often independent of physical activity.^{4,8–13} These findings indicate that sedentary behavior, including total sitting time and mean sitting bout duration, are relevant to personal and public health.

In the United States, adults aged >60 years comprise the population with the highest rates of sedentary behavior.⁶ Across the lifespan and between sexes, women appear to accumulate more sedentary time than men before the age of 30 years, a trend which appears to reverse for those aged ≥60 years.⁶ Although less sedentary than men of matched age, older women have increased risk for cardiovascular disease (CVD) following menopause as levels of cardioprotective estrogen decline. The identification of mutable lifestyle factors that can prevent or delay CVD onset is especially important among postmenopausal women. Early studies that relied on self-report of sitting time showed a dose-dependent relationship between total sitting time and cardiovascular disease mortality in older women.¹⁴ A follow-up study using data from accelerometers found that both total sedentary time and sedentary time accumulated in prolonged patterns were associated with increased risk for CVD.¹¹ This highlights the importance of characterizing total sitting time and patterns of sitting with respect to cardiovascular risk among postmenopausal women.

While CVD mortality is the leading cause of death in the United States, large racial/ethnic disparities in cardiovascular health exist between Hispanic and non-Hispanic populations.

Compared with non-Hispanic whites, Hispanics have worse measures of overall cardiovascular health, but surprisingly experience lower CVD mortality rates.¹⁵ With the growing Hispanic population in the United States, it is important to study potential behavioral factors related to disparities in CVD risk biomarkers. To accomplish this, we examined total sitting time and patterns of sitting time, determined using accelerometer measures and validated machine-learned algorithms, and their relationship to cardiometabolic risk biomarkers in overweight/obese Hispanic and non-Hispanic postmenopausal women.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Sample and Design

This cross-sectional study was designed to assess associations of total sitting time and patterns of sitting time with cardiometabolic biomarkers in overweight/obese postmenopausal women. Archival data used in the current analysis were combined from 3 separate studies that used identical accelerometers, accelerometer wear protocols, and accelerometer data processing protocols. Signed informed consent was obtained from all participants enrolled in each of the 3 studies. Data from women enrolled in the following 3 clinical studies who were aged ≥55 years and had a body mass index (BMI) at least 25 kg/m² were included (n from each parent study included in our analysis is noted): Community of Mine (a cross-sectional study of community-living people residing in San Diego County)¹⁶ (n=128) and 2 randomized control trials, The MENU (Metabolic, Exercise and Nutrition at University of California, San Diego [UCSD]) study^{17,18} (n=95) and The Reach for Health study¹⁹ (n=295). Women with diabetes were ineligible for the MENU and Reach for Health studies. Women with type 2 diabetes (but not type 1 diabetes) were eligible for the Community of Mine study, but none included in the current analysis who were insulin users (n=6) had taken insulin the morning of their fasting blood draw. Data used in the current analysis were collected at baseline timepoints for the 2 randomized control trials and, from all 3 studies, were critical for enrollment of participants, which resulted in low missingness (see footnote in Table 2). All studies have undergone review and approval through UCSD Institutional Review Board.

Cardiometabolic Biomarkers

BMI, waist circumference, fasting glucose, fasting insulin, homeostatic model assessment of insulin resistance index (HOMA-IR), and HOMA2-IR were primary outcomes of this

study as they were measured in all 3 parent studies. Total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were analyzed as secondary outcome measures, as lipid panel blood tests were conducted only in the MENU and Community of Mine studies, not in the Reach for Health study. Collection of anthropometric data and fasting blood from participants in the 3 parent studies has been described previously, as have the methods for fasting glucose and insulin measurements for Reach for Health and measurement of all MENU biomarkers.^{16,18–20} Body mass index (BMI; computed as kg/m²) was determined measuring weight and height with a calibrated scale and stadiometer, respectively. Waist circumference was measured using a fabric, non-stretchable measuring tape. Glucose and insulin were measured in EDTA plasma using identical assay methods for Reach for Health and Community of Mine. Specifically, the glucose oxidase method using a YSI 2900 Bioanalyzer (Xylem, Inc.) in the Sears laboratory and using a Meso Scale Discovery electrochemiluminescent immunoassay kit and SECTOR Imager 2400 (Meso Scale Discovery, Inc.) at the UCSD ACTRI Biomarker Laboratory, respectively. Insulin was measured in serum in the MENU study using the ADVIA Centaur double antibody immunoassay with chemiluminescent detection at Arup Laboratories (Salt Lake City, UT). Glucose, total cholesterol, HDL-cholesterol, and triglycerides were measured in serum in the MENU study using the Kodak Ektachem Analyzer system (Johnson & Johnson Clinical Diagnostics). In the Community of Mine study, total cholesterol, HDL-cholesterol, and triglycerides were measured in plasma at the UCSD Center for Advanced Laboratory Methods, a CLIA-certified diagnostic laboratory for the UCSD Health System. LDL cholesterol values for both MENU and Community of Mine studies were calculated using the Friedewald equation.²¹ Fasting glucose and insulin concentrations were used to calculate the homeostatic model assessment of insulin resistance index (HOMA-IR; [fasting glucose, mmol/L]×[insulin, mIU/L]/22.5) and HOMA2-IR, which is a model-derived estimate of insulin resistance calculated using the HOMA2 calculator.^{22,23}

Sitting and Activity Measures

Participants wore ActiGraph GT3X+ accelerometers on their right hip for up to 14 days, removing devices only to sleep and when showering or swimming. Participants who did not meet the recommended wear protocol of at least 4 days (Reach for Health and MENU) or 7 days (Community of Mine) with ≥10 hours of accelerometer wear were asked to re-wear the devices. Of the total sample, 99% (n=516) had the recommended²⁴ 4 days with ≥10 hours of accelerometer wear and the remaining participants had at least 2 days with >13.5

hours of wear. Acceleration was measured 30 times per second and the 30 Hz accelerometer data were processed with a machine-learned random forest classifier that was specifically designed and validated for assessing sitting and moving behaviors in older women.^{25,26} The random forest classifier was originally trained and validated using coded images from cameras worn around the neck of 39 community-living women, then validated in 2 separate samples.²⁷ The algorithms were trained to measure free-living behaviors using data collected during free-living conditions. The R software package of these algorithms developed by Katherine Ellis PhD is freely available (<https://cran.r-project.org/web/packages/s/TLBC/TLBC.pdf>). Sitting (not in a vehicle) had sensitivity of 89% and specificity of 91% compared with annotated images; sitting in a vehicle had 84% sensitivity and 99% specificity.²⁵ Accelerometer non-wear was identified using the Choi algorithm using a 90-minute frame, 30-minute stream frame, and 2-minute tolerance.²⁸ All sitting was combined then averaged across adherent days (at least 10-h/day of accelerometer wear, recommended protocol for older adults²⁴) to measure total sitting time. Consecutive minutes spent sitting were classified as sitting bouts (with no minimum and no tolerance) and the mean sitting bout duration was computed across all adherent days to measure sitting patterns, with higher values indicating prolonged patterns and lower values indicating interrupted patterns. To measure moderate-to-vigorous physical activity (MVPA), 30 Hz data were integrated to counts per minute (cpm) using the low frequency extension filter in ActiLife v6.0. The average minutes per day with ≥1952 cpm was used to measure time in MVPA. For sensitivity analyses, we also averaged time spent walking (from the machine learning classifier) as a proxy for MVPA and time spent sedentary (by the commonly used 100 cpm cut point applied to the vertical axis²⁴) over all adherent days.

Covariates

Covariates included education (high school graduate or less; some college/vocational training; and college graduate), marital status (married/living together and not married), race/ethnicity (Hispanic and non-Hispanic), and physical functioning. Physical functioning was measured in Reach for Health and MENU studies using the 10-item subscale from the Short Form-36 (SF-36). The SF-36 was not administered in the Community of Mine study, so we used the 14-items from the Late Life Functioning and Disability Index,²⁹ which was administered in Community of Mine. Results from both measures (SF-36 and Late Life Functioning and Disability Index), which have similar items and have been shown to be highly correlated,³⁰ were harmonized for this combined cohort analysis by placing each item on a measurement scale from 0

to 100 with higher numbers indicating better functioning. The scores were averaged across all items in the measures (SF-36 or Late Life Functioning and Disability Index) for each participant to give a single physical functioning score.

Statistical Analysis

An objective of this study was to examine sedentary behavior and cardiometabolic health in Hispanic women versus non-Hispanic women. Accordingly, we summarized data for the full sample and separately for Hispanic women and non-Hispanic women. Each cardiometabolic outcome was log transformed then modeled using successively adjusted linear regression analyses with total sitting time and mean sitting bout duration evaluated in separate models. Complete case analysis was used. Model 1 was adjusted for age and accelerometer wear time; Model 2 (our main model) was additionally adjusted for Hispanic ethnicity (yes/no), education, marital status, physical functioning, and a variable for the original study from which women were recruited (ie, the parent study). Then, to assess whether associations were present after adjustment for MVPA—which has been conceptualized as a confounder, a mediator, an effect modifier, and a competing behavior (eg, using a compositional or isotemporal framework) in previous studies^{31–33}—Model 3a additionally adjusted for MVPA. Model 3b further adjusted for BMI, which could be in the causal pathway between sedentary behavior and cardiometabolic biomarkers. We tested the assumptions of homoscedasticity by reviewing plots of residuals and no violations were observed.

We were also interested in evaluating whether associations of sedentary behavior and cardiometabolic biomarkers differed among Hispanic women and non-Hispanic women. To accomplish this, our main model (model 2) was repeated separately among Hispanic women and non-Hispanic women to show trends. Formal tests for effect modification were conducted by including a multiplicative interaction term (exposure*Hispanic) in model 2 within the full sample and because of the exploratory nature of this investigation, statistical significance set to $P<0.10$. In a post-hoc analysis, we also examined effect modification of associations between sitting time measures and glycemic control biomarkers by BMI status, the statistical significance threshold was set to $P<0.10$.

Sensitivity Analyses

To test whether associations differed by parent study, we evaluated effect measure modification by including the multiplicative interaction term in model 2 and by comparing beta coefficients that were separately estimated for each

study. We also repeated model 2 with both sedentary behavior variables (total sedentary time and mean bout duration) measured using the 100 cpm threshold. Finally, we repeated Model 3a by replacing MVPA with the machine-learned measure of daily walking time.

Results

Table 1 shows the participant characteristics of the overall sample and separately for Hispanic and non-Hispanic women. The mean±SD age of the sample was 63.4±5.9 years, 62% were married, and just over half (51%) had completed a college education. On average, Hispanic women had lower education, physical functioning, waist circumference, and HDL cholesterol and higher fasting plasma glucose and LDL cholesterol than did non-Hispanic women. Hispanic women sat for an average of 507±95 minutes per day (≈8.5 hours) in bouts of 36.4±13.9 minutes while non-Hispanic women sat for an average of 557±91 minutes per day (≈9.3 hours) in bouts of 40.0±15.8 minutes. Using a multivariable-adjusted model (adjusting for age, physical functioning, education, and Hispanic ethnicity), there were differences in total sitting and sitting patterns between non-Hispanic and Hispanic women; Hispanic women spent 50.3 fewer minutes sitting per day ($P<0.001$) and had shorter sitting bout durations by 3.6 minutes ($P=0.02$).

Table 2 shows associations of total sitting time and mean sitting bout duration with BMI, waist circumference, fasting glucose, fasting insulin, and HOMA-IR. In models adjusted for age, accelerometer wear time, Hispanic ethnicity, education, marital status, physical functioning, and parent study, each additional hour of sitting time was associated with a 1.56% higher BMI (95% CI, 0.80–2.33), 1.71% higher waist circumference (95% CI, 0.62–2.81), 6.38% higher fasting insulin (95% CI, 2.86–10.02), and 7.27% higher HOMA-IR (95% CI, 3.35–11.35) (P -trend<0.01 for all associations). Associations were slightly attenuated after adjustment for MVPA, but the significance of all associations persisted. For fasting insulin and HOMA-IR, attenuation was also observed after adjustment for BMI, but again, the overall patterns and statistical significance of both associations persisted.

After multivariable adjustment, sitting bout duration was significantly associated with BMI (1.64% [95% CI, 0.50%–2.79%]; P -trend=0.005), waist circumference (1.93% [95% CI, 0.31%–3.57%]; P -trend=0.020), fasting glucose (1.36% [95% CI, 0.06%–2.68%]; P -trend=0.041), fasting insulin (7.43% [95% CI, 2.19%–12.95%]; P -trend=0.005), and HOMA-IR (8.92% [95% CI, 3.05%–15.13%]; P -trend<0.01). The associations, except with fasting glucose, were statistically significant after MVPA adjustment. Only HOMA-IR (6.02% [95% CI, 0.56%–11.77%]; P -trend=0.031) was significant with sitting bout

Table 1. Demographics, Activity-Related Measures, and Cardiometabolic-Risk Biomarkers

	Total (n=518)	Hispanic (n=102)	Non-Hispanic (n=416)	P Value*
Age (y), mean (SD)	63.4 (5.9)	63.0 (5.4)	63.5 (6.1)	0.37
Race/ethnicity, n (%)				
White	428 (89)	53 (73)	375 (92)	<0.001 [†]
Black	14 (3)	0 (0)	14 (3)	
Native American	3 (1)	1 (1)	2 (0)	
Asian	3 (1)	2 (3)	1 (0)	
Pacific Islander	9 (2)	1 (1)	8 (2)	
Other/Unknown	13 (3)	12 (16)	1 (0)	
Mixed	9 (2)	4 (5)	5 (1)	
Marital status, n (%)				
Married/Living together	319 (62)	55 (54)	264 (63)	0.10
Single/Divorced/Widowed/Separated	199 (38)	47 (46)	152 (37)	
Highest education level, n (%)				
Up to high school completion	66 (13)	35 (34)	31 (7)	<0.001 [†]
Some college or vocation training	190 (37)	32 (31)	158 (38)	
College graduate	262 (51)	35 (34)	227 (55)	
Physical functioning, mean (SD) [‡]	73.2 (23.5)	66.0 (27.7)	74.9 (22.0)	0.003 [†]
Activity-related measures, mean (SD) [§]				
Total sitting time; min/d	547.4 (93.6)	507.1 (94.6)	557.4 (90.7)	<0.001 [†]
Mean sitting bout duration; min/d	39.2 (15.5)	36.4 (13.9)	40.0 (15.8)	0.02 [†]
Moderate-to-vigorous activity; min/d	21.2 (19.2)	22.2 (19.2)	20.9 (19.2)	0.55
Walking time; min/d	61.1 (40.0)	59.2 (47.6)	61.5 (37.9)	0.65
Cardiometabolic biomarkers, mean (SD)				
Body mass index; kg/m ²	31.4 (4.8)	31.4 (4.8)	31.5 (4.8)	0.96
Waist circumference; cm	98.5 (15.3)	94.8 (20.1)	99.4 (13.8)	0.03 [†]
Fasting glucose; mg/dL [¶]	104.0 (21.2)	109.0 (29.1)	102.7 (18.6)	0.04 [†]
Fasting insulin; pg/mL [¶]	529.3 (329.5)	577.6 (381.0)	517.6 (315.2)	0.15
HOMA-IR [¶]	3.9 (3.1)	4.6 (3.7)	3.8 (2.9)	0.06
HOMA2-IR [¶]	2.0 (1.3)	2.2 (1.5)	2.0 (1.2)	0.11
Fasting LDL cholesterol; mg/dL [#]	119.6 (33.6)	113.1 (30.3)	122.5 (34.7)	0.05
Fasting HDL cholesterol; mg/dL [#]	61.6 (15.3)	56.4 (12.0)	63.9 (16.0)	<0.001 [†]
Fasting triglycerides; mg/dL [#]	125.6 (71.7)	133.1 (78.0)	122.2 (68.7)	0.32

HDL indicates high-density lipoproteins; HOMA-IR, homeostatic model assessment of insulin resistance; LDL, low-density lipoproteins.

*P values computed using Chi-square tests for categorical variables and t tests for continuous.

[†]P<0.05.

[‡]Missing physical functioning data from 1 participant.

[§]Missing machine-learned data from 4 participants.

^{||}Variables adjusted for accelerometer wear time.

[¶]Missing glycemic regulation biomarker data from 3 participants.

[#]Data available from Community of Mine and MENU participants only (n=220, 68 Hispanic).

duration after further adjusting for BMI. Table S1 shows regression modeling results for fasting lipid panel components (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), which were only measured in 2 of the 3 parent studies, and HOMA2-IR (calculated for the full cohort).

The association between sitting bout duration and fasting glucose was significantly stronger for Hispanic women than for non-Hispanic women (*P*-interaction=0.03). An additional 15-minute longer mean sitting bout duration was associated with a 4.8% higher fasting glucose level (95% CI, 0.50%–

Table 2. Associations of Total Sitting Time and Sitting Pattern With Cardiometabolic Risk Biomarkers

	Total Sitting Time*		Mean Sitting Bout Duration	
	% Difference [†] (95% CI)	P Value	% Difference [†] (95% CI)	P Value
Body mass index				
Model 1	2.08 (1.30 to 2.86)	<0.001 [‡]	2.37 (1.18 to 3.58)	<0.001 [‡]
Model 2	1.56 (0.80 to 2.33)	<0.001 [‡]	1.64 (0.50 to 2.79)	0.005 [‡]
Model 3a	1.24 (0.45 to 2.04)	0.002 [‡]	1.26 (0.12 to 2.42)	0.031 [‡]
Model 3b				
Waist circumference				
Model 1	2.82 (1.73 to 3.93)	<0.001 [‡]	2.44 (0.77 to 4.13)	0.004 [‡]
Model 2	1.71 (0.62 to 2.81)	0.002 [‡]	1.93 (0.31 to 3.57)	0.020 [‡]
Model 3a	1.67 (0.51 to 2.83)	0.005 [‡]	1.80 (0.14 to 3.48)	0.034 [‡]
Model 3b				
Fasting glucose				
Model 1	0.68 (−0.17 to 1.54)	0.117	1.66 (0.36 to 2.97)	0.012 [‡]
Model 2	0.83 (−0.04 to 1.72)	0.063	1.36 (0.06 to 2.68)	0.041 [‡]
Model 3a	0.69 (−0.24 to 1.62)	0.145	1.21 (−0.12 to 2.55)	0.076
Model 3b	0.70 (−0.19 to 1.59)	0.126	1.21 (−0.09 to 2.54)	0.070
Fasting insulin				
Model 1	6.39 (2.95 to 9.95)	<0.001 [‡]	6.51 (1.31 to 11.98)	0.014 [‡]
Model 2	6.38 (2.86 to 10.02)	<0.001 [‡]	7.43 (2.19 to 12.95)	0.005 [‡]
Model 3a	5.12 (1.46 to 8.91)	0.006 [‡]	5.94 (0.68 to 11.48)	0.027 [‡]
Model 3b	3.87 (0.57 to 7.27)	0.022 [‡]	4.72 (−0.13 to 9.81)	0.057
HOMA-IR				
Model 1	7.14 (3.30 to 11.13)	<0.001 [‡]	8.29 (2.44 to 14.48)	0.005 [‡]
Model 2	7.27 (3.35 to 11.35)	<0.001 [‡]	8.92 (3.05 to 15.13)	0.003 [‡]
Model 3a	5.85 (1.78 to 10.09)	0.005 [‡]	7.24 (1.36 to 13.46)	0.016 [‡]
Model 3b	4.60 (0.91 to 8.43)	0.015 [‡]	6.02 (0.56 to 11.77)	0.031 [‡]

Model 1 [n=511] is adjusted for age and accelerometer wear time. Model 2 [n=510] is adjusted for Model 1+education, marital status, physical functioning, ethnicity, and parent study. Model 3a [n=510] is adjusted for Model 2+MVPA. Model 3b [n=510] is adjusted for Model 2+ body mass index. HOMA-IR indicates homeostatic model assessment of insulin resistance.

*Adjusted for accelerometer wear time using the residuals method.

[†]Estimates reflect the percentage difference in the geometric mean of each biomarker associated with a 60-minute increase in total sitting time or a 15-minute increase in mean sitting bout duration.

[‡]P<0.05.

9.37%) in Hispanic women compared with a 0.9% higher level (95% CI, −0.40%–2.22%) in non-Hispanic women (Figure). Similar patterns of Hispanic/non-Hispanic differential associations were observed for insulin ($P=0.42$), HOMA-IR ($P=0.22$), and waist circumference ($P=0.46$), but none met levels for statistical significance. Interestingly, the association between total sitting time and BMI was stronger for non-Hispanic women (1.85% increase in BMI associated with 1 hour of sitting time; 95% CI, 0.64%–3.07%) than for Hispanic women (1.00%; 95% CI, −2.42%–3.95%; P -interaction=0.08). There were no other ethnicity-related interactions with sitting time or sitting bout duration and any other biomarker. Nearly all

associations of total sitting time and mean sitting bout duration tested with glycemic regulation biomarkers were stronger, P -interaction<0.1, among obese women (BMI ≥ 30 kg/m²) than for overweight women (BMI 25–29.9 kg/m²) (Table 3).

We tested whether associations of total sitting time and mean sitting bout duration with cardiometabolic biomarkers differed across the parent studies to evaluate whether our results were an artifact of combining data from 3 cohorts. No significant differences were observed in the interaction P values and the beta coefficients were not materially different (data not shown). We repeated Model 2 using the most

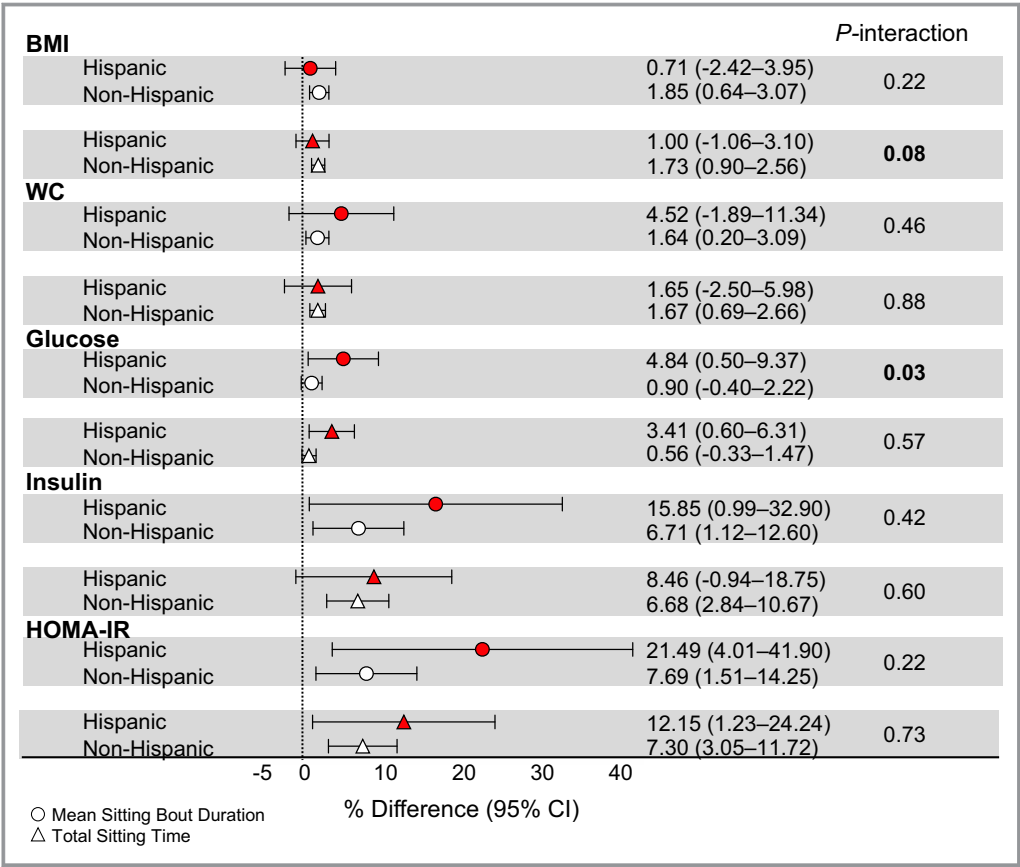


Figure. Associations of total sitting time and sitting pattern with cardiometabolic biomarkers among postmenopausal Hispanic and non-Hispanic women. Model adjusted for age, accelerometer wear time, education, marital status, physical function, and parent study. Red and white fill of symbols indicates Hispanic and non-Hispanic populations, respectively. x-axis indicates the percentage difference in the geometric mean of each biomarker associated with a 60-minute increase in total sitting time (triangle symbols) or a 15-minute increase in mean sitting bout duration. $P<0.10$ are bold to highlight interactions that are below a conservative threshold for statistical significance. BMI indicates body mass index; HOMA-IR, homeostatic model assessment of insulin resistance; WC, waist circumference

common accelerometer data processing protocol to measure sedentary time (vertical axis counts/minute <100) and separately by replacing MVPA by a machine-learned variant of the construct (walking time). Again, there were no significant differences observed (data not shown).

Discussion

In this multi-cohort study of Hispanic and non-Hispanic overweight/obese postmenopausal women, we observed that sitting behavior (total sitting time and mean sitting bout duration) was deleteriously associated with higher levels of cardiometabolic risk biomarkers (BMI, waist circumference, fasting glucose, insulin, insulin resistance, and triglycerides). The persistence of associations between sitting behavior and cardiometabolic risk factors after adjustment for MVPA or BMI highlight the importance of sitting time and patterns on

cardiovascular health among overweight/obese postmenopausal women. Although total daily sitting time and mean sitting bout duration was shorter in Hispanic women compared with non-Hispanic women in our population sample, we observed a significant interaction between mean sitting bout duration and fasting glucose among Hispanic women. Sitting patterns may be an easy-to-target, modifiable lifestyle factor for overweight/obese older women.

Prolonged sitting time is a common feature of modern society at home and work involving television and hand-held electronic device viewing, studying, desk work, computer engagement, and leisure time activities.³⁴ Numerous cross-sectional studies demonstrate detrimental associations of these behaviors with cardiometabolic outcomes and mortality.⁷ A 10-year longitudinal study showed that increases in self-reported sitting time were detrimentally associated with cardiometabolic risk biomarkers.³⁵ Other dimensions of

Table 3. Associations of Total Sitting Time and Sitting Pattern With Glycemic Regulation Biomarkers: Tests of Effect Modification by BMI Status

	BMI 25 to 29.9	BMI ≥30	P-Interaction
	% Difference (95% CI)*	% Difference (95% CI)*	
Total sitting time [†]			
Fasting glucose	−0.24 (−1.43, 0.97)	1.17 (−0.07, 2.43)	0.16
Fasting insulin	2.08 (−3.18, 7.63)	5.06 (0.99, 9.29)	0.08 [‡]
HOMA-IR	1.83 (−3.87, 7.87)	6.32 (1.64, 11.22)	0.05 [‡]
Mean sitting bout duration			
Fasting glucose	−0.71 (−2.56, 1.17)	1.99 (0.18, 3.83)	0.03 [‡]
Fasting insulin	−1.36 (−9.19, 7.14)	7.38 (1.41, 13.70)	0.03 [‡]
HOMA-IR	−2.06 (−10.48, 7.15)	9.57 (2.65, 16.94)	0.02 [‡]

Models [n=220 for body mass index 25–29.9; n=290 for body mass index ≥ 30] are adjusted for age, education, marital status, physical functioning, Hispanic ethnicity, and parent study. Of the body mass index ≥ 30 group, 24 (4.6%) had body mass index ≥ 40 . BMI indicates body mass index; HOMA-IR indicates homeostatic model assessment of insulin resistance.

*Estimates reflect the percentage difference in the geometric mean of each biomarker associated with a 60-minute increase in total sitting time or a 15-minute increase in mean sitting bout duration.

[†]Adjusted for accelerometer wear time using the residuals method.

[‡]P-interaction<0.1.

sitting pattern that are determined objectively by accelerometer, including frequency of sit-to-stand transitions (breaks in sedentary time) and prolonged bouts spent sitting (mean sitting bout duration), are important features of sedentary behavior to consider for cardiometabolic health. Three population-based studies in adults from Australia, the United States, and the United Kingdom demonstrated that a greater number of breaks in sedentary time was beneficially associated with waist circumference, BMI, triglycerides, 2-hour plasma glucose, and C-reactive protein.^{4,36,37} Other studies in adults show that frequent interruption of sitting is associated with better cardiometabolic health and lower fasting insulin and HOMA-IR.^{9,13} Prolonged mean sedentary bout duration was detrimentally associated with insulin, diastolic blood pressure, waist circumference, triglycerides, and HDL cholesterol measures among Canadian adults in the Health Measures Survey and in US adults in the NHANES (National Health and Nutrition Examination Survey) 2003/6.^{4,38,39} Interestingly, total sitting time and sitting patterns are not always correlated within a population group and the various dimensions of sitting behaviors may modify risk outcomes differently. For example, in the NHANES 2003/6 study, women accumulated more total sedentary time but also more breaks in sitting than did men; yet, the women had better

cardiometabolic biomarker measures than did the men ($P<0.05$; age and ethnicity/race adjusted).⁴ Overall, population study-based findings are supported by experimental laboratory studies demonstrating that frequent interruptions of prolonged sitting time lead to improvements in metrics of glycemic control and lipid metabolism.^{8,40–42}

Objective measurement of sedentary time (accelerometer) in US adults indicates that Mexican American adults have sitting behaviors that are less detrimental for cardiometabolic health (less sitting time per day, shorter mean sitting bouts, more breaks in sitting per day) compared with non-Hispanic white adults and tend to accumulate, on average, the lowest overall sitting time among those from Hispanic/Latino backgrounds.^{4,6,43} A cross-sectional study of Hispanic/Latinos showed that higher levels of sedentary time and sedentary patterns were deleteriously associated with HDL-cholesterol, triglycerides, 2-hour glucose, fasting insulin, and HOMA-IR and the relationships consistently appeared across sex and age groups, highlighting the generalizability of cardiometabolic risk associated with sedentary time.^{43,44}

In comparing sedentary time effects on cardiometabolic risk by race/ethnicity, there have been some differences reported. Sedentary time has been reported to be significantly related to higher waist circumference among non-Hispanic whites but not Mexican Americans.⁴ In the present study, although there was a similar magnitude of association in both groups for total sitting time and BMI, we found a significant interaction for non-Hispanic ethnicity. We did not find any differential association of sitting time and waist circumference by ethnicity but point estimates indicated stronger associations with prolonged sitting time among Hispanic women than non-Hispanic women, which is the first time we are aware that such a finding was reported. We detected a significant interaction for Hispanic ethnicity with respect to mean sitting bout duration association with fasting glucose. A large longitudinal study (MESA [Multi-Ethnic Study of Atherosclerosis]) showed that increasing self-report sedentary behavior is associated with incident type 2 diabetes, with variation across race/ethnic groups.⁴⁵ This study also showed less self-reported sedentary behavior in Hispanics. We observed stronger detrimental associations of sitting time patterns with glucose, insulin, and HOMA-IR among obese women (BMI ≥ 30 kg/m²) compared with overweight women (BMI 25.0–29.9 kg/m²). These findings are commensurate with previous epidemiologic and experimental studies showing stronger detrimental effects of sedentary behavior on metabolic health among those who have worse cardiometabolic disease risk factors.^{4,46–48}

There are several strengths in our study. First, it focuses on a homogeneous population of a certain age (≥ 55 years), sex (all women), BMI (≥ 25 kg/m²), and race/ethnicity background that has high cardiometabolic risk. Second, it uses a more

accurate classification of sitting posture than self-report or simple accelerometry alone, based on objectively measured physical activity refined by validated machine-learned algorithms that determine sitting posture in the population we are evaluating. Machine-learned algorithms trained using ground truth data from the target population measured during free-living conditions are thought to be more generalizable and possibly more accurate for measuring actual behavior than previously used data processing protocols that rely on cut points, often developed in a laboratory setting. These study findings can be uniquely leveraged to specifically target sedentary lifestyle in high-risk subpopulations of minority, sex, and age who have high potential for metabolic disorders and poor cardiovascular health. Several limitations of this study need to be noted. First, although we could control for education level, dietary intake data were not available for all 3 parent studies so, we were unable to control for dietary habits. Second, this is a cross-sectional analysis integrating archival data from 3 separate clinical studies and as such can only examine the association among elements but not causality. Therefore, a more comprehensive interventional study for cause-effect is needed to confirm the associations of total sitting time and mean sitting bout duration with cardiometabolic outcomes among older Hispanic and non-Hispanic women. We are currently conducting 2 randomized controlled sitting time intervention trials, Rise for Health (P01 AG052352, NCT #03473145) and Arriba por la Vida Estudio (NCT #02905929) that will address these important questions.⁴⁹ Third, in our modeling, we assumed additivity and linearity of the specified confounding effects, thus residual confounding attributable to non-linear associations may persist. Finally, many tests were done for effect measure modification and as a result the 1 significant finding related to sitting bout duration and fasting glucose by Hispanic ethnicity could be attributed to chance alone. Corroboration in other studies is needed.

The findings in this study add to the body of evidence showing detrimental cardiometabolic effects of sitting patterns and extends the literature by showing associations in Hispanic and non-Hispanic postmenopausal women. The clinical implications that stem from this line of research highlight an importance of expanding activity-related counseling by physician and other public health practitioners from a focus on exercise and MVPA to include improving sitting habits with respect to both the total amount of time and the patterns in which that time is accumulated. Traditionally, clinicians focus on encouraging their patients to exercise more and increase physical activity with little focus specifically on sitting time. We are entering a new phase of public health focus that could change the physician-patient counseling encounter. The recent 2018 Physical Activity Guidelines, an update from 2008, have included some preliminary

recommendations on the reduction of sedentary time. Our data, in addition to the previous literature, demonstrate the importance of total sitting time and sitting patterns on important cardiometabolic risk factors that can be directly addressed in the clinical setting.

Conclusions

Using validated machine-learned algorithms to measure “sitting,” our results highlight ethnic differences in sitting behaviors and suggest that associations of sitting patterns and fasting glucose vary by ethnicity, with more deleterious associations observed for Hispanic women. Intervention and longitudinal cohort studies with repeated measurements are needed to determine if changes in sitting behavior affect cardiometabolic biomarkers and are modified by ethnicity.

Acknowledgments

The authors thank the investigators, staff members, and volunteers involved in Community of Mine, Reach for Health, and Metabolism, Exercise and Nutrition studies. We also appreciate the valuable contributions from participants in these 3 clinical studies. A special thank you goes out to Paul Chavez for help editing the manuscript and for help identifying relevant literature.

Sources of Funding

This research was supported by the Go Red For Women Strategically Focused Research Network Award from the American Heart Association (16SFRN28420000) and the National Institutes of Health: Community of Mine (R01 CA179977), Reach for Health (U54 CA155435) and Metabolism, Exercise and Nutrition at UCSD (MENU; U54 CA155435 and also the California Walnut Commission), and training grant from NHLBI (T32 HL079891 to Bellettiere and Unkart). The funders had no role in the design of the study; the collection, analysis, or interpretation of the data; the writing of the manuscript; or the decision to submit the manuscript for publication. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Disclosures

None.

References

1. Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, Latimer-Cheung AE, Chastin SFM, Altenburg TM, Chinapaw MJM, Aminian S, Arundell L, Hinkley T, Hnatiuk J, Atkin AJ, Belanger K, Chaput JP, Gunnell K, Larouche R, Manyanga T, Gibbs BB, Bassett-Gunter R, Biddle S, Biswas A, Chau J, Colley R, Copping T,

- Craven C, Cristi-Montero C, de Assis Teles Santos D, del Pozo Cruz B, del Pozo Cruz J, Dempsey P, do Carmo Santos Gonçalves RF, Ekelund U, Ellingson L, Ezeugwu V, Fitzsimons C, Florez-Pregonero A, Friel CP, Fröberg A, Giangregorio L, Godin L, Halloway S, Husu P, Kadir M, Karagounis LG, Koster A, Lakerveld J, Lamb M, LeBlanc AG, Lee EY, Lee P, Lopes L, Manns T, Ginis KM, McVeigh J, Meneguci J, Moreira C, Murtagh E, Patterson F, da Silva DRP, Pesola AJ, Peterson N, Pettitt C, Pilutti L, Pereira SP, Poitras V, Prince S, Rathod A, Rivière F, Rosenkranz S, Routhier F, Santos R, Smith B, Theou O, Tomasone J, Tucker P, Meyer RU, van der Ploeg H, Villalobos T, Viren T, Wallmann-Sperlich B, Wijndaele K, Wondergem R. Sedentary Behavior Research Network (SBRN)—terminology consensus project process and outcome. *Int J Behav Nutr Phys Act*. 2017;14:75.
2. Hu FB, Li TY, Colditz GA, Willett WC, Manson JAE. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA*. 2003;14:1785–1791.
 3. Ford ES, Kohl HW, Mokdad AH, Ajani UA. Sedentary behavior, physical activity, and the metabolic syndrome among U.S. adults. *Obes Res*. 2005;13:608–614.
 4. Healy GN, Matthews CE, Dunstan DW, Winkler EAH, Owen N. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 200306. *Eur Heart J*. 2011;32:590–597.
 5. Dunstan DW, Howard B, Healy GN, Owen N. Too much sitting—a health hazard. *Diabetes Res Clin Pract*. 2012;97:368–376.
 6. Matthews CE, Chen KY, Freedson PS, Buchowski MS, Beech BM, Pate RR, Troiano RP. Amount of time spent in sedentary behaviors in the United States, 2003–2004. *Am J Epidemiol*. 2008;167:875–881.
 7. Brocklebank LA, Falconer CL, Page AS, Perry R, Cooper AR. Accelerometer-measured sedentary time and cardiometabolic biomarkers: a systematic review. *Prev Med*. 2015;76:92–102.
 8. Dunstan DW, Kingwell BA, Larsen R, Healy GN, Cerin E, Hamilton MT, Shaw JE, Bertovic DA, Zimmet PZ, Salmon J, Owen N. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. *Diabetes Care*. 2012;35:976–983.
 9. Hartman SJ, Marinac CR, Cadmus-Bertram L, Kerr J, Natarajan L, Godbole S, Patterson RE, Morey B, Sears DD. Sedentary behaviors and biomarkers among breast cancer survivors. *J Phys Act Health*. 2018;15:1–6.
 10. Kerr J, Crist K, Vital DG, Dillon L, Aden SA, Trivedi M, Castellanos LR, Godbole S, Li H, Allison MA, Khemlani GL, Takemoto ML, Schenk S, Sallis JF, Grace M, Dunstan DW, Natarajan L, LaCroix AZ, Sears DD. Acute glucoregulatory and vascular outcomes of three strategies for interrupting prolonged sitting time in postmenopausal women: a pilot, laboratory-based, randomized, controlled, 4-condition, 4-period crossover trial. *PLoS One*. 2017;12:e0188544.
 11. Bellettiere J, LaMonte MJ, Evenson KR, Rillamas-Sun E, Kerr J, Lee I-M, Di C, Rosenberg DE, Stefanick ML, Buchner DM, Hovell MF, LaCroix AZ. Sedentary behavior and cardiovascular disease in older women: the Objective Physical Activity and Cardiovascular Health (OPACH) study. *Circulation*. 2019;139:1036–1046.
 12. Saunders TJ, Atkinson HF, Burr J, MacEwen B, Skeaff CM, Peddie MC. The acute metabolic and vascular impact of interrupting prolonged sitting: a systematic review and meta-analysis. *Sport Med*. 2018;48:2347–2366.
 13. Bellettiere J, Winkler EAH, Chastin SFM, Kerr J, Owen N, Dunstan DW, Healy GN. Associations of sitting accumulation patterns with cardio-metabolic risk biomarkers in Australian adults. *PLoS One*. 2017;12:e0180119.
 14. Seguin R, Buchner DM, Liu J, Allison M, Manini T, Wang CY, Manson JE, Messina CR, Patel MJ, Moreland L, Stefanick ML, Lacroix AZ. Sedentary behavior and mortality in older women: the Women's Health Initiative. *Am J Prev Med*. 2014;46:122–135.
 15. Pool LR, Ning H, Lloyd-Jones DM, Allen NB. Trends in racial/ethnic disparities in cardiovascular health among US adults from 1999–2012. *J Am Heart Assoc*. 2017;6:e006027. DOI: 10.1161/JAHA.117.006027.
 16. Jankowska MM, Sears DD, Natarajan L, Martinez E, Anderson C, Sallis JF, Matthews SA, Crist K, Dillon L, Johnson E, Barrera-Ng A, Full K, Godbole S, Kerr J. Protocol for a cross sectional study of cancer risk, environmental exposures and lifestyle behaviors in a diverse community sample: the Community of Mine study. *BMC Public Health*. 2019;19:186.
 17. Le T, Flatt SW, Natarajan L, Pakiz B, Quintana EL, Heath DD, Rana BK, Rock CL. Effects of diet composition and insulin resistance status on plasma lipid levels in a weight loss intervention in women. *J Am Heart Assoc*. 2016;5:e002771. DOI: 10.1161/JAHA.115.002771.
 18. Rock CL, Flatt SW, Pakiz B, Quintana EL, Heath DD, Rana BK, Natarajan L. Effects of diet composition on weight loss, metabolic factors and biomarkers in a 1-year weight loss intervention in obese women examined by baseline insulin resistance status. *Metabolism*. 2016;65:1605–1613.
 19. Patterson RE, Marinac CR, Natarajan L, Hartman SJ, Cadmus-Bertram L, Flatt SW, Li H, Parker B, Oratowski-Coleman J, Villaseñor A, Godbole S, Kerr J. Recruitment strategies, design, and participant characteristics in a trial of weight-loss and metformin in breast cancer survivors. *Contemp Clin Trials*. 2016;47:64–71.
 20. Patterson RE, Marinac CR, Sears DD, Kerr J, Hartman SJ, Cadmus-Bertram L, Villaseñor A, Flatt SW, Godbole S, Li H, Laughlin GA, Oratowski-Coleman J, Parker BA, Natarajan L. The effects of metformin and weight loss on biomarkers associated with breast cancer outcomes. *J Natl Cancer Inst*. 2018;110:1239–1247.
 21. 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;18:499–502.
 22. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β -cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28:412–419.
 23. Levy JC, Matthews DR, Hermans MP. Correct homeostasis model assessment (HOMA) evaluation uses the computer program. *Diabetes Care*. 1998;21:2191–2192.
 24. Migueles JH, Cadenas-Sanchez C, Ekelund U, Delisle Nystrom C, Mora-Gonzalez J, Löf M, Labayen I, Ruiz JR, Ortega FB. Accelerometer data collection and processing criteria to assess physical activity and other outcomes: a systematic review and practical considerations. *Sports Med*. 2017;47:1821–1845.
 25. Rosenberg D, Godbole S, Ellis K, Di C, Lacroix A, Natarajan L, Kerr J. Classifiers for accelerometer-measured behaviors in older women. *Med Sci Sports Exerc*. 2017;49:610–616.
 26. Kerr J, Carlson J, Godbole S, Cadmus-Bertram L, Bellettiere J, Hartman S. Improving Hip-worn accelerometer estimates of sitting using machine learning methods. *Med Sci Sports Exerc*. 2018;50:1518–1524.
 27. Ellis K, Kerr J, Godbole S, Staudenmayer J, Lanckriet G. Hip and wrist accelerometer algorithms for free-living behavior classification. *Med Sci Sports Exerc*. 2016;48:933–940.
 28. Choi L, Ward SC, Schnelle JF, Buchowski MS. Assessment of wear/nonwear time classification algorithms for triaxial accelerometer. *Med Sci Sports Exerc*. 2012;44:2009–2016.
 29. Haley SM, Jette AM, Coster WJ, Kooyoomjian JT, Levenson S, Heeren T, Ashba J. Late life function and disability instrument: II. Development and evaluation of the function component. *J Gerontol A Biol Sci Med Sci*. 2002;57:M217–M222.
 30. Dubuc N, Haley SM, Ni P, Kooyoomjian JT, Jette AM. Function and disability in late life: comparison of the late-life function and disability instrument to the short-form-36 and the London handicap scale. *Disabil Rehabil*. 2004;26:362–370.
 31. Chastin SFM, Palarea-Albaladejo J, Dontje ML, Skelton DA. Combined effects of time spent in physical activity, sedentary behaviors and sleep on obesity and cardio-metabolic health markers: a novel compositional data analysis approach. *PLoS One*. 2015;10:e0139984.
 32. Mekary RA, Willett WC, Hu FB, Ding EL. Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol*. 2009;170:519–527.
 33. Page A, Peeters G, Merom D. Adjustment for physical activity in studies of sedentary behaviour. *Emerg Themes Epidemiol*. 2015;12:10.
 34. Young DR, Hivert MF, Alhassan S, Camhi SM, Ferguson JF, Katzmarzyk PT, Lewis CE, Owen N, Perry CK, Siddique J, Yong CM. Sedentary behavior and cardiovascular morbidity and mortality: a science advisory from the American Heart Association. *Circulation*. 2016;134:e262–e279.
 35. Knaeps S, Bourgois JG, Charlier R, Mertens E, Lefevre J, Wijndaele K. Ten-year change in sedentary behaviour, moderate-to-vigorous physical activity, cardiorespiratory fitness and cardiometabolic risk: independent associations and mediation analysis. *Br J Sports Med*. 2018;52:1063–1068.
 36. Healy GN, Dunstan DW, Salmon J, Cerin E, Shaw JE, Zimmet PZ, Owen N. Breaks in sedentary time: beneficial associations with metabolic risk. *Diabetes Care*. 2008;31:661–666.
 37. Henson J, Yates T, Biddle SJH, Edwardson CL, Khunti K, Wilmot EG, Gray LJ, Gorely T, Nimmo MA, Davies MJ. Associations of objectively measured sedentary behaviour and physical activity with markers of cardiometabolic health. *Diabetologia*. 2013;56:1012–1020.
 38. Carson V, Wong SL, Winkler E, Healy GN, Colley RC, Tremblay MS. Patterns of sedentary time and cardiometabolic risk among Canadian adults. *Prev Med*. 2014;65:23–27.
 39. Kim Y, Welk GJ, Braun SI, Kang M. Extracting objective estimates of sedentary behavior from accelerometer data: measurement considerations for surveillance and research applications. *PLoS One*. 2015;10:e0118078.

40. Chastin SF, Egerton T, Leask C, Stamatakis E. Meta-analysis of the relationship between breaks in sedentary behavior and cardiometabolic health. *Obesity*. 2015;23:1800–1810.
41. Dempsey PC, Larsen RN, Sethi P, Sacre JW, Straznicki NE, Cohen ND, Cerin E, Lambert GW, Owen N, Kingwell BA, Dunstan DW. Benefits for type 2 diabetes of interrupting prolonged sitting with brief bouts of light walking or simple resistance activities. *Diabetes Care*. 2016;39:964–972.
42. Larsen RN, Kingwell BA, Sethi P, Cerin E, Owen N, Dunstan DW. Breaking up prolonged sitting reduces resting blood pressure in overweight/obese adults. *Nutr Metab Cardiovasc Dis*. 2014;24:976–982.
43. Qi Q, Strizich G, Merchant G, Sotres-Alvarez D, Buelna C, Castañeda SF, Gallo LC, Cai J, Gellman MD, Isasi CR, Moncrieff AE, Sanchez-Johnsen L, Schneiderman N, Kaplan RC. Objectively measured sedentary time and cardiometabolic biomarkers in US Hispanic/Latino adults: the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *Circulation*. 2015;132:1560–1569.
44. Diaz KM, Goldsmith J, Greenlee H, Strizich G, Qi Q, Mossavar-Rahmani Y, Vidot DC, Buelna C, Brintz CE, Elfassy T, Gallo LC, Daviglus ML, Sotres-Alvarez D, Kaplan RC. Prolonged, uninterrupted sedentary behavior and glycemic biomarkers among US Hispanic/Latino Adults. *Circulation*. 2017;136:1362–1373.
45. Joseph JJ, Echouffo-Tcheugui JB, Golden SH, Chen H, Jenny NS, Carnethon MR, Jacobs D, Burke GL, Vaidya D, Ouyang P, Bertoni AG. Physical activity, sedentary behaviors and the incidence of type 2 diabetes mellitus: the multi-ethnic study of atherosclerosis (MESA). *BMJ Open Diabetes Res Care*. 2016;4:e000185.
46. Dempsey PC, Owen N, Yates TE, Kingwell BA, Dunstan DW. Sitting less and moving more: improved glycaemic control for type 2 diabetes prevention and management. *Curr Diab Rep*. 2016;16:114.
47. Dempsey PC, Larsen RN, Winkler EAH, Owen N, Kingwell BA, Dunstan DW. Prolonged uninterrupted sitting elevates postprandial hyperglycaemia proportional to degree of insulin resistance. *Diabetes Obes Metab*. 2018;20:1526–1530.
48. Bellettiere J, Healy GN, LaMonte MJ, Kerr J, Evenson KR, Rillamas-Sun E, Di C, Buchner DM, Hovell MF, LaCroix AZ. Sedentary behavior and prevalent diabetes in 6,166 older women: the objective physical activity and cardiovascular health study. *J Gerontol A Biol Sci Med Sci*. 2019;74:387–395.
49. Takemoto M, Schechtman M, Villa N, Talavera G, Sears DD, Owen N, Rosenberg DE, Dunstan D, Allison M, Kerr J. Arriba por la vida Estudio (AVE): study protocol for a standing intervention targeting postmenopausal Latinas. *Contemp Clin Trials*. 2019;79:66–72.

SUPPLEMENTAL MATERIAL

Table S1. Associations of total sitting time and sitting pattern with additional cardiometabolic risk biomarkers.

	Total sitting time*		Mean sitting bout duration	
	% difference [†] (95% CI)	P-value	% difference [†] (95% CI)	P-value
HOMA2-IR				
Model 1	6.62 (3.21-10.14)	<0.001	7.05 (1.89-12.49)	0.007
Model 2	6.63 (3.15-10.22)	<0.001	7.73 (2.54-13.18)	0.003
Model 3a	5.36 (1.74-9.1)	0.004	6.21 (1.00-11.68)	0.019
Model 3b	4.14 (0.88-7.5)	0.013	5.03 (0.23-10.05)	0.040
Total Cholesterol				
Model 1	0.93 (-0.59-2.46)	0.233	1.31 (-1.00-3.68)	0.269
Model 2	0.31 (-1.33-1.98)	0.714	1.40 (-1.05-3.90)	0.266
Model 3a	0.35 (-1.41-2.13)	0.701	1.44 (-1.05-4.00)	0.260
Model 3b	0.33 (-1.33-2.01)	0.702	1.41 (-1.04-3.93)	0.263
LDL Cholesterol				
Model 1	1.17 (-1.21-3.59)	0.340	1.94 (-1.66-5.69)	0.296
Model 2	0.62 (-1.96-3.27)	0.643	2.41 (-1.45-6.42)	0.226
Model 3a	0.74 (-2.02-3.59)	0.602	2.52 (-1.41-6.62)	0.214
Model 3b	0.46 (-2.13-3.12)	0.730	2.29 (-1.56-6.31)	0.249
HDL Cholesterol				
Model 1	-0.98 (-2.96-1.04)	0.342	-2.16 (-5.12-0.90)	0.166
Model 2	-1.84 (-3.92-0.28)	0.090	-2.68 (-5.73-0.45)	0.094
Model 3a	-1.85 (-4.08-0.42)	0.111	-2.61 (-5.71-0.60)	0.111
Model 3b	-1.63 (-3.71-0.50)	0.134	-2.51 (-5.54-0.62)	0.116
Triglycerides				
Model 1	4.05 (0.22-8.03)	0.039	5.38 (-0.50-11.6)	0.075
Model 2	4.86 (0.68-9.21)	0.023	6.12 (-0.11-12.74)	0.056
Model 3a	4.12 (-0.3-8.75)	0.070	5.31 (-0.97-11.99)	0.101
Model 3b	4.88 (0.67-9.27)	0.024	6.11 (-0.15-12.76)	0.057

HOMA2-IR=Algorithm-based calculation of homeostatic model assessment of insulin resistance;
LDL=low-density lipoprotein; HDL=high-density lipoprotein

* Adjusted for accelerometer wear time using the residuals method

† Estimates reflect the percentage difference in the geometric mean of each biomarker associated with a 60-minute increase in total sitting time or a 15-minute increase in mean sitting bout duration

Model 1 [n=511] is adjusted for age and device wear time

Model 2 [n=510] is adjusted for Model 1+education, marital status, physical functioning, ethnicity, and parent study

Model 3a [n=510] is adjusted for Model 2+MVPA

Model 3b [n=510] is adjusted for Model 2+BMI