

Physical activity, sitting, and risk factors of cardiovascular disease: a cross-sectional analysis of the CARRS study

Jingkai Wei¹ · Ranjit Mohan Anjana² · Shifalika Goenka³ · Felipe Lobelo⁴ · Roopa Shivashankar⁵ · Muhammad Masood Kadir⁶ · Nikhil Tandon⁷ · Viswanathan Mohan² · K. M. Venkat Narayan⁴ · Dorairaj Prabhakaran^{3,5} · Mohammed K. Ali⁴

Received: March 18, 2018 / Accepted: November 8, 2018 / Published online: November 16, 2018
© Springer Science+Business Media, LLC, part of Springer Nature 2018

Abstract We aimed to estimate the associations between substituting 30-min/day of walking or moderate-to-vigorous physical activity (MVPA) for 30 min/day of sitting and cardiovascular risk factors in a South Asian population free of cardiovascular disease. We collected information regarding sitting and physical activity from a representative sample of 6991 participants aged 20 years and above from New Delhi, India and Karachi, Pakistan enrolled in 2010–2011 in the Center for cArдио-metabolic Risk Reduction in South Asia study using the International Physical Activity Questionnaire (short form). We conducted isotemporal substitution analyses using multivariable linear regression models to examine the cross-sectional associations between substituting MVPA and walking for sitting with cardiovascular risk factors. Substituting 30 min/day of MVPA for 30 min/day of sitting was associated with 0.08 mmHg lower diastolic blood

pressure ($\beta = -0.08$ [– 0.15, – 0.0003]) and 0.13 mg/dl higher high-density lipoprotein cholesterol ($\beta = 0.13$ [0.04, 0.22]). Substituting 30 min/day of walking for 30 min/day of sitting was associated with 0.08 kg/m² lower body mass index ($\beta = -0.08$ [– 0.15, – 0.02]), and 0.25 cm lower waist circumference ($\beta = -0.25$ [– 0.39, – 0.11]). In conclusion, substituting time engaged in more-active pursuits for time engaged in less-active pursuits was associated with modest but favorable cardiovascular risk factor improvements among South Asians.

Keywords Physical activity · Sitting · Cardiovascular risk factor · Isotemporal substitution models · South Asia

Introduction

Low physical activity has been ranked as one of the leading risk factors for death and disability-adjusted life-years (DALYs) worldwide (Forouzanfar et al., 2015). Lifestyle transitions have been occurring in most countries of South Asia, with decreases in physical activity over time (Misra et al., 2012). It is estimated that 36.9% of India's total population physically inactive (Nethan et al., 2017), and studies have shown that South Asians are more sedentary than American counterparts (Kamath et al., 1999). Sedentary time was found to be associated with double the risk of diabetes, 2.5 times the risk cardiovascular events, and 1.9 times the risk of cardiovascular mortality (Wilmot et al., 2012).

The prevalence of cardiovascular disease (CVD) in South Asia appears to be increasing (Moran & Vedanthan, 2013; Prabhakaran et al., 2016), which is likely due to mechanized lifestyles (Nag & Ghosh, 2013). Physical activity has been associated with reduced cardiovascular

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s10865-018-9989-5>) contains supplementary material, which is available to authorized users.

✉ Jingkai Wei
jingkai@live.unc.edu

¹ Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, 135 Dauer Dr, Chapel Hill, NC 27599, USA

² Madras Diabetes Research Foundation, Chennai, India

³ Public Health Foundation of India, New Delhi, India

⁴ Emory Global Diabetes Research Center, Hubert Department of Global Health, Emory University, Atlanta, GA, USA

⁵ Centre for Chronic Disease Control, New Delhi, India

⁶ Aga Khan University, Karachi, Pakistan

⁷ All India Institute of Medical Sciences, New Delhi, India

risk factors and overall CVD risk in studies from South Asia (Aravindalochanan et al., 2014; Millett et al., 2013; Rastogi et al., 2004). Promoting physical activity is therefore paramount in populations in South Asia for prevention of CVDs (Zachariah & Alex, 2017).

Previous studies have shown that physical activities of various intensities are differentially associated with CVD and its risk factors (Koolhaas et al., 2016; Tanasescu et al., 2002). Using time for physical activity alone may not reflect the true associations between different physical activities and health outcomes. The Consensus Physical Activity Guidelines for Asian Indians proposed that more epidemiological studies examining different types and durations of physical activity and their associations with cardiovascular risk are needed (Misra et al., 2012). Furthermore, evidence assessing physical activities of different intensities and their impacts on health outcomes at the population level are lacking among South Asians.

Willett and Stampfer (1986) have published studies used isocaloric substitution modeling methods in nutritional epidemiology. This approach assumes daily total energy intake is fixed, and it helps to estimate associations between modifying energy sources (e.g., consuming one type of food in place of another) with health outcomes. Similarly, since there are a finite and generally fixed number of hours in the day available for an individual to engage in physical activity, time spent on physical activity of various intensities will be at expense of sedentary time, sleep, or physical activity of other intensities, which may have differential effects on health outcomes. Isotemporal substitution modeling involves statistically modifying the duration and intensity of physical activity. Then, one can estimate associations between theoretically substituting one type of physical activity for others and CVD risk factors. In this study, we used representative data from two large cities in South Asia to estimate associations between different physical activity intensities and CVD risk factor biomarkers using isotemporal substitution modeling. These data will provide valuable estimates of achievable reductions in disease burdens for practitioners and policy makers.

Methods

Design and participants

The Center for Cardio-metabolic Risk Reduction in South Asia (CARRS) Study is a multi-center survey which recruited participants in 2010–2011 from three mega-cities in South Asia: Delhi and Chennai, India, and Karachi in Pakistan. Detailed study methods are published separately (Nair et al., 2012). Respondents aged 20 years or above

that resided in households in these three cities were included. The analysis on physical activity for this study was based on the baseline cross-sectional survey data from two cities (New Delhi, India and Karachi, Pakistan) due to the unavailability of information on physical activity in Chennai. In addition, we further excluded participants with incomplete information of physical activities and participants with prevalent CVD (including heart disease and stroke). Data on biological information was collected in person. Questionnaires were administered by trained interviewers.

The study was approved by the Institutional Review Boards of the Public Health Foundation of India, All India Institute of Medical Sciences, Madras Diabetes Research Foundation, Aga Khan University, and Emory University. In addition, the study received regulatory approvals from the National Heart, Lung, and Blood Institute of the National Institutes of Health and the Health Ministry Screening Committee of India.

Assessment of physical activity and sedentary behaviors

Physical activity was measured using the International Physical Activity Questionnaire, short form (IPAQ-SF) (IPAQ, 2004a). Participants were asked to report the average time spent sitting (sitting and lying down awake at work, at home, while doing course work, and during leisure time) and time spent per week in each of the following activities: vigorous activities (such as heavy lifting, digging, aerobics, or fast bicycling), moderate physical activities (such as carrying loads, bicycling at a regular pace, tennis, badminton, cricket), and walking (including at work and at home, walking to travel from place to place, and solely for recreation, sport, exercise, or leisure). The total time (sum of time for sitting, walking, moderate physical activity, and vigorous physical activity) was coded in 30-min blocks per day. Previous studies indicate that total physical activity measured with IPAQ-SF correlates with objective standards, with correlation coefficients ranging from 0.09 to 0.39. The correlation between IPAQ-SF for vigorous activity or moderate activity level/walking and an objective standard range from -0.18 to 0.76 (Lee et al., 2011). The IPAQ short form has also been validated in Pakistan; total MET minutes per week from the IPAQ-SF was significantly positively correlated counts/minute from the accelerometer ($\rho = 0.23$, $p < 0.001$) (Shenoy et al., 2014).

According to IPAQ guidelines, the total weekly physical activity can also be estimated by weighting time spent in each activity intensity with its estimated metabolic equivalent (MET) energy expenditure (IPAQ, 2004b). The IPAQ scoring protocol assigns the following MET values to

walking, moderate, and vigorous intensity activity: 3.3 METs, 4.0 METs, and 8.0 METs, respectively (IPAQ, 2004b). Vigorous and moderate physical activities were combined into moderate-to-vigorous physical activity (MVPA). Individuals who reported spending $\geq 50\%$ of all their reported time (including sitting, walking, moderate and vigorous physical activity) as sitting were defined as sedentary.

Assessment of cardiovascular risk factors

Participants underwent a number of assessments related to CVD risk, including anthropometric and blood pressure (BP) measurements as well as blood draws for metabolic markers.

Anthropometric measurements involved standardized data collection techniques for weight, height, and waist circumference. Body mass index (BMI) was calculated using measured height and weight [BMI = body weight (kg)/height² (m²)]. For analysis, waist circumference (WC) was treated as a continuous variable.

Trained staff took two BP readings after participants sat at rest for 5 min using an electronic sphygmomanometer (Omron Dalian Company, Liaoning, China). A third measurement was taken if the difference between the first two systolic or diastolic measurements was more than 10 mmHg or 5 mmHg, respectively. For the purpose of analysis, we used the mean of the first two measurements, or the second and third measurements if a third measurement was obtained (Ali et al., 2015).

Biological sample collection involved drawing 15 ml of blood (in fasting state) from each participant. The methods of analysis for all cardiovascular biomarkers including HDL-C, low-density lipoprotein cholesterol (LDL-C), triglycerides, FPG, and glycated hemoglobin (HbA1c), and respective external quality standardization for all biological samples across the study sites are described separately (Nair et al., 2012).

Other measurements

Validated questions were derived from English questionnaires in previous regional and national surveys. Culturally-appropriate and methodologically relevant closed-question instruments for South-Asia were developed and pilot tested for face and construct validity prior to use in the study. Several sections of the baseline questionnaire (e.g., quality of life) were based on validated questionnaires that already exist in regional languages (Hindi and Urdu) (Nair et al., 2012). Information regarding demographic (including age, sex, education, employment) and lifestyle (diet, smoking, alcohol use) factors were collected using questionnaires. Dietary intake was assessed using a

food frequency questionnaire used in the INTERHEART study (Yusuf et al., 2004), which has been validated by 24-h dietary recalls in a sub-sample. Sleep was assessed using a questionnaire from the Sleep Heart Health Study (SHHS) (Quan et al., 1997). Psychosocial factors (depression/anxiety) were collected through the 3-level European Quality of Life 5 Dimensions questionnaire (EQ-5D) (Nair et al., 2012). Treatments used for cardiovascular risk factors were obtained through questionnaires and medical records.

Statistical analysis

For this analysis, we classified individuals with greater than or equal to 50% of total time per day (including time for sitting, walking, and moderate and vigorous activity) reported as sitting as being sedentary. For descriptive analyses, we applied *T* tests and Chi square tests for continuous and categorical variables, respectively.

We used Pearson correlations to assess the associations between total time and with its components. We used multivariable linear regression analyses to estimate cross-sectional associations between physical activity of different intensity (sitting, walking, or MVPA) and cardiovascular risk factors (BMI, waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP), HDL-C, LDL-C, triglycerides, FPG and HbA1c). We first placed each intensity of physical activity in isolation into a single model to assess the associations between each activity and CVD risks, adjusted for covariates, e.g., BMI = $\beta_1 \times$ sitting + $\beta_5 \times$ covariates. We further adjusted for physical activities of other intensities to examine the associations between three types of physical activities and CVD risk factors in one model, e.g., BMI = $\beta_1 \times$ sitting + $\beta_2 \times$ walking + $\beta_3 \times$ MVPA + $\beta_5 \times$ covariates.

If any of the associations tested above was statistically significant, then we applied isotemporal substitution models to estimate the associations between substituting physical activity of one intensity for that of others and CVD risk factors. We expressed the coefficients derived from these regression models as β , which indicates the magnitude of the change in risk factors observed with a substituted 30-min difference in specific intensity of physical activity. Two out of the three physical activity variables (sitting, walking, and MVPA) remained in the models and we adjusted for total time and other covariates, e.g., BMI = $\beta_2 \times$ walking + $\beta_3 \times$ MVPA + $\beta_4 \times$ total time + $\beta_5 \times$ covariates [the association of substituting 30-min walking for 30-min sitting and difference of BMI (β_2), and the association of substituting 30-min MVPA for 30-min sitting and difference of BMI (β_3)]. We stratified the isotemporal substitution models by age (≥ 60 years or < 60 years) which is likely to influence intensities of

physical activity. We applied sampling weights to all the models above.

As common CVD risk factors that may also be related to the main exposure of physical activity intensities, we considered age (as a continuous variable), sex, employment status (not working, unskilled laborer, skilled laborer, and professionals), education level (no education, some primary school, high school, and college or above), depression/anxiety status (not anxious or depressed/moderately anxious or depressed/extremely anxious or depressed), intake of fruits and vegetables (as a continuous variable), ever smoking (yes/no), ever use of alcohol (yes/no) and sleep time (as a continuous variable) as covariates and adjusted for these in linear regression models. All statistical analyses were conducted in SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

There were a total of 16,288 participants recruited to the CARRS study. After excluding participants from Chennai ($n = 6906$), participants with prevalent cardiovascular diseases ($n = 360$), participants with missing information regarding gender ($n = 1$), and participants in New Delhi and Karachi with missing information regarding physical activity ($n = 2030$), the total number of participants included in the final analysis was 6991. Compared to those missing information on physical activity, participants included in the study were younger, with a higher proportion of males respondents with a higher education level. The included participants reported lower consumption of fruits and vegetables, longer sleep hours, higher prevalence of smoking and alcohol use, lower waist circumference, blood pressure, HbA1c, LDL-C, and FPG levels (Supplemental Table 1).

Table 1 displays characteristics of the participants included stratified by sedentary status. Among these participants, 76.7% were categorized as sedentary. Compared to participants who were sedentary, those who were not sedentary were on average 3.5 years younger, less educated, and more likely to be employed. Those who were not sedentary had lower intake of fruits and vegetables, lower BMI, waist circumference, SBP, DBP, HbA1c, FPG, and LDL-C.

The correlations between different activity components were weak (Supplemental Table 2). We did note a strong correlation between total activity and MVPA, as well as sitting, which suggests a potential for confounding. Among physical activity variables (including time for sitting, walking, MVPA, total time), our analysis showed that the maximal correlation between these variables was 0.13.

Single models (Model 1) using multivariable linear regression analysis examining different intensities of physical activity with potential CVD risk factors showed that every block of 30 min spent in MVPA was associated with 0.17 mmHg lower SBP ($\beta = -0.17$, 95% CI -0.27 , -0.07), 0.10 mmHg lower DBP ($\beta = -0.10$, 95% CI -0.16 , -0.03), 0.08 mg/dl higher HDL-C ($\beta = 0.08$, 95% CI 0.01, 0.15), and 0.01% lower HbA1c ($\beta = -0.01$, 95% CI -0.02 , -0.0004), adjusted for age, sex, employment status, education level, depression/anxiety status, intake of fruits and vegetables, and sleep time. Every block of 30 min spent on walking was associated with 0.07 kg/m² lower BMI ($\beta = -0.07$, 95% CI -0.13 , -0.004) and 0.24 cm lower waist circumference ($\beta = -0.24$, 95% CI -0.37 , -0.11). Every block of 30 min spent on sitting was associated with 0.07 mg/dL lower HDL-C ($\beta = -0.07$, 95% CI -0.13 , -0.02). After further adjustments for the other two physical activity variables, except for the association between MVPA and HDL-C, all associations remained statistically significant. No association was found between different types of physical activity with LDL-C, triglycerides, or FPG (Table 2).

The isotemporal substitution models were therefore conducted to estimate the associations between substituting time on one type of physical activity for time on another type of physical activity with differences in BMI, waist circumference, SBP, DBP, HDL-C, and HbA1c. Substituting 30 min/day of MVPA for 30 min/day of sitting was associated with 0.08 mmHg lower DBP ($\beta = -0.08$, 95% CI -0.15 , -0.0003) and 0.13 mg/dl higher HDL-C ($\beta = 0.13$, 95% CI 0.04, 0.22). Substituting 30 min/day of walking for 30 min/day of sitting was associated with 0.08 kg/m² lower BMI ($\beta = -0.08$, 95% CI -0.15 , -0.02) and 0.25 cm lower waist circumference ($\beta = -0.25$, 95% CI -0.39 , -0.11). In addition, substituting 30 min/day of walking for 30 min/day of MVPA was associated with 0.08 kg/m² lower BMI ($\beta = -0.08$, 95% CI -0.15 , -0.001) and 0.24 cm lower waist circumference ($\beta = -0.24$, 95% CI -0.40 , -0.08) (Table 3).

The benefits of isotemporal substitution were moderated by age. Substituting 30 min/day of MVPA for 30 min/day of sitting were more beneficial among adults < 60 years in terms of lower DBP, and that for lower BMI and lower WC were more prominent for adults 60 years or older. Substituting 30 min/day walking for 30 min/day of sitting brought benefits in terms of lower BMI and waist circumference to adults < 60 years (Supplemental Table 3).

Table 1 Demographic, lifestyle, and medical characteristics of study participants in New Delhi and Karachi during 2010–2011 by sedentary status (n = 6991)

Characteristics	Sedentary (sitting \geq 50% of total time; n = 5362)	Not sedentary (sitting < 50% of total time; n = 1621)	P value
Age (year)	42.9 \pm 13.9	39.4 \pm 11.4	< 0.0001
Male (%)	2661 (49.6)	828 (51.1)	0.31
Education [n (%)]			< 0.0001
No schooling or primary	1334 (24.9)	512 (31.6)	
Finished high school	2897 (54.0)	911 (56.2)	
College or above	1130 (21.1)	198 (12.2)	
Unemployed [n (%)]	3037 (56.7)	725 (44.7)	< 0.0001
Fruits and vegetables (servings/month)	38.4 \pm 30.4	36.0 \pm 30.7	< 0.005
Sleeping time (h/day)	7.1 \pm 1.3	7.1 \pm 1.3	0.43
Body weight (kg)	64.8 \pm 14.8	62.9 \pm 13.6	0.0002
Body mass index (kg/m ²)	25.5 \pm 5.6	24.9 \pm 5.1	0.005
Waist circumference (cm)	87.6 \pm 13.8	85.8 \pm 13.1	< 0.0001
Ever smoking [n (%)]	1463 (27.3)	517 (31.9)	0.0003
Ever taking alcohol [n (%)]	532 (9.9)	211 (13.0)	0.0004
Systolic blood pressure (mmHg)	123.8 \pm 20.5	120.8 \pm 18.1	< 0.0001
Diastolic blood pressure (mmHg)	81.9 \pm 12.0	80.7 \pm 11.3	0.0004
HDL-C (mg/dl)	44.0 \pm 12.1	44.7 \pm 12.8	0.07
HbA1c (%)	6.2 \pm 1.5	6.0 \pm 1.3	< 0.0001
LDL-C (mg/dl)	107.7 \pm 32.7	104.6 \pm 31.5	0.002
Triglycerides (mg/dl)	144.5 \pm 106.1	139.7 \pm 95.0	0.14
Fasting plasma glucose (mmol/L)	108.9 \pm 43.6	104.1 \pm 36.4	0.0003
Depression/anxiety [n (%)]	307 (5.7)	80 (4.9)	0.22
Sitting (h/day)	5.4 \pm 2.6	2.5 \pm 1.4	< 0.0001
Walking (h/day)	0.5 \pm 0.6	1.3 \pm 1.8	< 0.0001
Moderate physical activity (h/day)	0.9 \pm 1.1	3.0 \pm 2.3	< 0.0001
Vigorous physical activity (h/day)	0.1 \pm 0.4	1.0 \pm 1.9	< 0.0001
Total time (h/day ^a)	6.9 \pm 3.1	7.8 \pm 4.0	< 0.0001
Total physical activity (METs/day)	368.5 \pm 341.8	1461.5 \pm 1049.7	< 0.0001

Bold indicates results that were statistically significantly different between the groups

HDL-C high-density lipoprotein cholesterol, HbA1c glycated hemoglobin, LDL-C low-density lipoprotein cholesterol

^aTotal time is the sum of sitting, walking, moderate physical activity, and vigorous physical activity

Discussion

Our results demonstrated that substituting MVPA or walking for an equal amount of sitting time was associated with small, but favorable improvements in CVD risk factor profiles among South Asian adults. Age modified the associations between physical activity of different intensities and CVD risk factors.

This isotemporal substitution modeling method has been previously applied in prospective studies examining the associations between physical activity and weight change (Mekary et al., 2009), risk of depression (Mekary et al., 2013), mortality (Fishman et al., 2016; Stamatakis et al., 2015), as well as cross-sectional studies examining preva-

lence of cardio-metabolic disease (Ekblom-Bak et al., 2015; Wellburn et al., 2015), and cardio-metabolic disease risk biomarkers (Buman et al., 2014; Falconer et al., 2015; Hamer et al., 2014; Healy et al., 2015). Previous studies, much like ours did, have shown that replacing sedentary time with MVPA was associated with higher HDL-C levels (Buman et al., 2014; Hamer et al., 2014) and lower HbA1c. All studies showed that MVPA is associated with reduced prevalence of risk factors and CVD, which, in general, aligned with our findings.

Our results also showed that walking has potential benefits for CVD prevention. In our isotemporal substitution models, particularly among participants < 60 years, substituting walking for MVPA was associated with lower

Table 2 Associations between 30-min physical activities of different intensity and cardiovascular risk factors among study participants in New Delhi and Karachi during 2010–2011 from multivariable linear regression analysis (n = 6991)

	Models	Sitting β (95% CI)	Walking β (95% CI)	MVPA β (95% CI)
BMI (kg/m ²)	Model 1	0.01 (– 0.02, 0.03)	– 0.07 (– 0.13 , – 0.004)	0.004 (– 0.03, 0.04)
	Model 2	0.02 (– 0.01, 0.04)	– 0.07 (– 0.13 , – 0.002)	0.01 (– 0.02, 0.05)
WC (cm)	Model 1	0.02 (– 0.01, 0.04)	– 0.24 (– 0.37 , – 0.11)	– 0.02 (– 0.09, 0.05)
	Model 2	0.01 (– 0.04, 0.07)	– 0.24 (– 0.37 , – 0.11)	0.001 (– 0.07, 0.07)
SBP (mmHg)	Model 1	– 0.04 (– 0.12, 0.03)	– 0.07 (– 0.26, 0.11)	– 0.17 (– 0.27 , – 0.07)
	Model 2	– 0.06 (– 0.14, 0.02)	– 0.05 (– 0.23, 0.14)	– 0.17 (– 0.27 , – 0.07)
DBP (mmHg)	Model 1	– 0.01 (– 0.06, 0.04)	– 0.05 (– 0.17, 0.07)	– 0.10 (– 0.16 , – 0.03)
	Model 2	– 0.02 (– 0.07, 0.03)	– 0.03 (– 0.15, 0.09)	– 0.10 (– 0.16 , – 0.03)
HDL-C (mg/dl)	Model 1	– 0.07 (– 0.13 , – 0.02)	0.09 (– 0.05, 0.22)	0.08 (0.01 , 0.15)
	Model 2	– 0.06 (– 0.12 , – 0.01)	0.06 (– 0.08, 0.19)	0.07 (– 0.01, 0.14)
LDL-C (mg/dl)	Model 1	0.08 (– 0.07, 0.23)	– 0.20 (– 0.56, 0.17)	0.07 (– 0.12, 0.27)
	Model 2	0.08 (– 0.07, 0.23)	– 0.20 (– 0.57, 0.17)	0.10 (– 0.10, 0.30)
Triglycerides (mg/dl)	Model 1	– 0.20 (– 0.65, 0.25)	0.42 (– 0.69, 1.53)	– 0.42 (– 1.01, 0.16)
	Model 2	– 0.23 (– 0.68, 0.22)	0.48 (– 0.64, 1.60)	– 0.49 (– 1.09, 0.10)
HbA1c (%)	Model 1	– 0.001 (– 0.01, 0.01)	– 0.01 (– 0.02, 0.01)	– 0.01 (– 0.02 , – 0.0004)
	Model 2	– 0.001 (– 0.01, 0.004)	– 0.01 (– 0.02, 0.01)	– 0.01 (– 0.02 , – 0.0002)
FPG (mmol/L)	Model 1	– 0.04 (– 0.20, 0.11)	0.04 (– 0.35, 0.43)	– 0.09 (– 0.30, 0.12)
	Model 2	– 0.05 (– 0.21, 0.11)	0.05 (– 0.35, 0.45)	– 0.10 (– 0.31, 0.11)

Model 1: adjusted for age (as a continuous variable), sex, employment status (currently employed or not), education level (no education or some primary school, high school, college or above), depression/anxiety status (yes/no), intake of fruits and vegetables (as a continuous variable), ever smoking (yes/no), ever use of alcohol (yes/no), sleep time (as a continuous variable), treatment (yes/no, for the outcomes of SBP, DBP, HDL-C, LDL-C, and triglycerides)

Model 2: adjusted for factors in Model 1 and other types of physical activity

Bold indicates results that were statistically significant

MVPA moderate-to-vigorous physical activity, BMI body mass index, WC waist circumference, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, HbA1c glycated hemoglobin, FPG fasting plasma glucose

BMI and waist circumference. This is consistent with previous findings that walking is associated with weight loss, more favorable waist circumference, and body mass index after replacing sedentary time (JD et al., 2017; Mekary et al., 2009). This may give a hint that walking is good for people with poor anthropometric profiles (elevated BMI or WC).

Isotemporal substitution modeling provides a theoretical exchange between different types of physical activity based on empirically-derived data. It is based on the principle that all types of physical activity are competing against each other, and it takes both time and intensity of physical activity into consideration. For the present study, according to the descriptive analysis, individuals who reported more time total engaged in any type of physical activity spent more of that time engaged in lower-intensity activity. Using either length of time or intensity alone may result in exactly the opposite findings, and a combination of both metrics is likely to make the results more accurate.

Our findings have substantial relevance for public health in South Asian countries. Cardiovascular diseases have been a great burden in this region. According to previous studies, the prevalence of CVD (8–10% in urban areas and 3–4% in rural areas) and diabetes (12–20% in urban areas and 5–6% in rural areas) are high, and the costs associated with CVD, both in terms of health expenditures and lost productivity, are tremendous (Siegel et al., 2014). Improving risk factor profiles through modifying lifestyle is essential—and likely cost-effective—for CVD prevention. A previous study shows that a large percentage of people in India are inactive and fewer than 10% engage in recreational physical activity. As such, urgent steps need to be initiated to promote physical activity in the region (Anjana et al., 2014). Also, physical activity may be promoted along with other components of lifestyle modification at the population level. A recent meta-analysis shows that a combination of physical activity and dietary modifications are more effective for weight loss in the long run than physical activity alone (Johns et al., 2014).

Table 3 The association between types of physical activities and risk factors of cardiovascular disease according to isotemporal substitution modeling among study participants in New Delhi and Karachi during 2010–2011 from multivariable linear regression analysis (n = 6991)

	Sitting β (95% CI)	Walking β (95% CI)	MVPA β (95% CI)
BMI (kg/m²)			
Drop sitting	Dropped	– 0.08 (– 0.15 , – 0.02)	– 0.01 (– 0.05, 0.03)
Drop walking	0.08 (0.02 , 0.15)	Dropped	0.08 (0.001 , 0.15)
Drop MVPA	0.01 (– 0.03, 0.05)	– 0.08 (– 0.15 , – 0.001)	Dropped
WC (cm)			
Drop sitting	Dropped	– 0.25 (– 0.39 , – 0.11)	– 0.01 (– 0.10, 0.07)
Drop walking	0.25 (0.11 , 0.39)	Dropped	0.24 (0.08 , 0.40)
Drop MVPA	0.01 (– 0.07, 0.10)	– 0.24 (– 0.40 , – 0.08)	Dropped
SBP (mmHg)			
Drop sitting	Dropped	0.01 (– 0.18, 0.21)	– 0.11 (– 0.23, 0.01)
Drop walking	– 0.01 (– 0.21, 0.18)	Dropped	– 0.13 (– 0.35, 0.10)
Drop MVPA	0.11 (– 0.01, 0.23)	0.13 (– 0.10, 0.35)	Dropped
DBP (mmHg)			
Drop sitting	Dropped	– 0.01 (– 0.13, 0.12)	– 0.08 (– 0.15 , – 0.0003)
Drop walking	0.01 (– 0.12, 0.13)	Dropped	– 0.07 (– 0.21, 0.07)
Drop MVPA	0.08 (0.0003 , 0.15)	0.07 (– 0.07, 0.21)	Dropped
HDL-C (mg/dl)			
Drop sitting	Dropped	0.12 (– 0.02 , 0.27)	0.13 (0.04 , 0.22)
Drop walking	– 0.12 (– 0.27 , 0.02)	Dropped	0.01 (– 0.15, 0.17)
Drop MVPA	– 0.13 (– 0.22 , – 0.04)	– 0.01 (– 0.17, 0.15)	Dropped
HbA1c (%)			
Drop sitting	Dropped	– 0.004 (– 0.02, 0.01)	– 0.01 (– 0.02, 0.003)
Drop walking	0.004 (– 0.01, 0.02)	Dropped	– 0.003 (– 0.02, 0.01)
Drop MVPA	0.01 (– 0.003, 0.02)	0.003 (– 0.01, 0.02)	Dropped

Models were adjusted for age (as a continuous variable), sex, employment status (currently employed or not), education level (no education or some primary school, high school, college or above), depression/anxiety status (yes/no), intake of fruits and vegetables (as a continuous variable), ever smoking (yes/no), ever use of alcohol (yes/no) and sleep time (as a continuous variable), total time for physical activity, the type of activity other than the dropped one and treatment (yes/no, for the outcomes of SBP and HDL-C)

Bold indicates results that were statistically significant

MVPA moderate-to-vigorous physical activity, BMI body mass index, WC waist circumference, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein cholesterol, HbA1c glycated hemoglobin

The main limitation of our study is the cross-sectional design, which limits causal inference. Another limitation involves assessment of physical activity through self-reported questionnaires, and there are concerns that IPAQ-SF may overestimate the amount of physical activity (Lee et al., 2011). In addition, the IPAQ-SF does not capture some other forms of physical activities (e.g., standing, or physical activity of other intensities with METs between 0 and 4 other than walking). Also, the study is subject to selection bias, since the characteristics of participants with complete information regarding their physical activity were different from those without complete information on physical activity.

Despite the limitations, the isotemporal substitution model offers a novel and informative investigation regarding how substitution of fixed time of an activity type

for the same time engaged in less active endeavors; thus, our analyses help answer the most relevant and realistic questions about health promotion. Furthermore, this study has a large sample size and participants were representative of their urban environments in South Asia, which made the results more generalizable to those contexts.

In conclusion, substituting time of MVPA and/or walking for sitting is associated with favorable CVD risk factor differences. Future prospective research is warranted in investigating the potentially beneficial associations between substituting sitting with MVPA and walking for reducing CVD risk and events in South Asia, which will be needed for designing and evaluating policies and programs to achieve wider health promotion.

Acknowledgements The authors thank all CARRS participants and staff for the providing information for this study.

Funding This project was funded in part by the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Department of Health and Human Services, under Contract No. HHSN268200900026C, and the United Health Group, Minneapolis, MN, US.

Compliance with ethical standards

Conflict of interest Jingkai Wei, Ranjit Mohan Anjana, Shifalika Goenka, Felipe Lobelo, Roopa Shivashankar, Muhammad Masood Kadir, Nikhil Tandon, Viswanathan Mohan, K. M. Venkat Narayan, Dorairaj Prabhakaran and Mohammed K. Ali declares that they have no conflict of interest.

Human and animal rights and Informed consent All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all patients for being included in the study.

References

- Ali, M. K., Bhaskarapillai, B., Shivashankar, R., Mohan, D., Fatmi, Z. A., Pradeepa, R., et al. (2015). Socioeconomic status and cardiovascular risk in urban South Asia: The CARRS Study. *European Journal of Preventive Cardiology*. <https://doi.org/10.1177/2047487315580891>
- Anjana, R. M., Pradeepa, R., Das, A. K., Deepa, M., Bhansali, A., Joshi, S. R., et al. (2014). Physical activity and inactivity patterns in India—Results from the ICMR-INDIAB study (Phase-1) [ICMR-INDIAB-5]. *International Journal of Behavioral Nutrition and Physical Activity*, *11*, 26. <https://doi.org/10.1186/1479-5868-11-26>
- Aravindalochanan, V., Kumpatla, S., Rengarajan, M., Rajan, R., & Viswanathan, V. (2014). Risk of diabetes in subjects with sedentary profession and the synergistic effect of positive family history of diabetes. *Diabetes Technology and Therapeutics*, *16*, 26–32. <https://doi.org/10.1089/dia.2013.0140>
- Buman, M. P., Winkler, E. A., Kurka, J. M., Hekler, E. B., Baldwin, C. M., Owen, N., et al. (2014). Reallocating time to sleep, sedentary behaviors, or active behaviors: Associations with cardiovascular disease risk biomarkers, NHANES 2005–2006. *American Journal of Epidemiology*, *179*, 323–334. <https://doi.org/10.1093/aje/kwt292>
- Eklom-Bak, E., Ekblom, O., Bergstrom, G., & Borjesson, M. (2015). Isotemporal substitution of sedentary time by physical activity of different intensities and bout lengths, and its associations with metabolic risk. *European Journal of Preventive Cardiology*. <https://doi.org/10.1177/2047487315619734>
- Falconer, C. L., Page, A. S., Andrews, R. C., & Cooper, A. R. (2015). The potential impact of displacing sedentary time in adults with Type 2 diabetes. *Medicine and Science in Sports and Exercise*, *47*, 2070–2075. <https://doi.org/10.1249/mss.0000000000000651>
- Fishman, E. I., Steeves, J. A., Zipunnikov, V., Koster, A., Berrigan, D., Harris, T. A., et al. (2016). Association between objectively measured physical activity and mortality in NHANES. *Medicine and Science in Sports and Exercise*. <https://doi.org/10.1249/mss.0000000000000885>
- Forouzanfar, M. H., Alexander, L., Anderson, H. R., Bachman, V. F., Biryukov, S., Brauer, M., et al. (2015). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, *386*, 2287–2323. [https://doi.org/10.1016/s0140-6736\(15\)00128-2](https://doi.org/10.1016/s0140-6736(15)00128-2)
- Hamer, M., Stamatakis, E., & Steptoe, A. (2014). Effects of substituting sedentary time with physical activity on metabolic risk. *Medicine and Science in Sports and Exercise*, *46*, 1946–1950. <https://doi.org/10.1249/mss.0000000000000317>
- Healy, G. N., Winkler, E. A., Brakenridge, C. L., Reeves, M. M., & Eakin, E. G. (2015). Accelerometer-derived sedentary and physical activity time in overweight/obese adults with type 2 diabetes: Cross-sectional associations with cardiometabolic biomarkers. *PLoS ONE*, *10*, e0119140. <https://doi.org/10.1371/journal.pone.0119140>
- IPAQ. (2004a). Retrieved 16 July 2018, from <http://youthrex.com/wp-content/uploads/2017/06/IPAQ-TM.pdf>
- IPAQ. (2004b). Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ)—Short Form. Retrieved 16 July 2018, from http://www.institutferran.org/documentos/scoring_short_ipaq_april04.pdf
- Jd, V. D. B., Jhpm, V. D. V., Eac, D. E. W., Bosma, H., Savelberg, H., Schaper, N. C., et al. (2017). Replacement effects of sedentary time on metabolic outcomes: The Maastricht study. *Medicine and Science in Sports and Exercise*, *49*, 1351–1358. <https://doi.org/10.1249/mss.0000000000001248>
- Johns, D. J., Hartmann-Boyce, J., Jebb, S. A., & Aveyard, P. (2014). Diet or exercise interventions vs combined behavioral weight management programs: A systematic review and meta-analysis of direct comparisons. *Journal of the Academy of Nutrition and Dietetics*, *114*, 1557–1568. <https://doi.org/10.1016/j.jand.2014.07.005>
- Kamath, S. K., Hussain, E. A., Amin, D., Mortillaro, E., West, B., Peterson, C. T., et al. (1999). Cardiovascular disease risk factors in 2 distinct ethnic groups: Indian and Pakistani compared with American premenopausal women. *American Journal of Clinical Nutrition*, *69*, 621–631. <https://doi.org/10.1093/ajcn/69.4.621>
- Koolhaas, C. M., Dhana, K., Golubic, R., Schoufour, J. D., Hofman, A., van Rooij, F. J. A., et al. (2016). Physical activity types and coronary heart disease risk in middle-aged and elderly persons: The Rotterdam Study. *American Journal of Epidemiology*, *183*, 729–738. <https://doi.org/10.1093/aje/kwv244>
- Lee, P. H., Macfarlane, D. J., Lam, T. H., & Stewart, S. M. (2011). Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): A systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *8*, 115. <https://doi.org/10.1186/1479-5868-8-115>
- Mekary, R. A., Lucas, M., Pan, A., Okereke, O. I., Willett, W. C., Hu, F. B., et al. (2013). Isotemporal substitution analysis for physical activity, television watching, and risk of depression. *American Journal of Epidemiology*, *178*, 474–483. <https://doi.org/10.1093/aje/kws590>
- Mekary, R. A., Willett, W. C., Hu, F. B., & Ding, E. L. (2009). Isotemporal substitution paradigm for physical activity epidemiology and weight change. *American Journal of Epidemiology*, *170*, 519–527. <https://doi.org/10.1093/aje/kwp163>
- Millett, C., Agrawal, S., Sullivan, R., Vaz, M., Kurpad, A., Bharathi, A. V., et al. (2013). Associations between active travel to work and overweight, hypertension, and diabetes in India: A cross-sectional study. *PLOS Medicine*, *10*, e1001459. <https://doi.org/10.1371/journal.pmed.1001459>
- Misra, A., Nigam, P., Hills, A. P., Chadha, D. S., Sharma, V., Deepak, K. K., et al. (2012). Consensus physical activity guidelines for

- Asian Indians. *Diabetes Technol Ther*, 14, 83–98. <https://doi.org/10.1089/dia.2011.0111>
- Moran, A., & Vedanthan, R. (2013). Cardiovascular disease prevention in South Asia gathering the evidence. *Global heart*, 8, 139–140. <https://doi.org/10.1016/j.gheart.2013.04.001>
- Nag, T., & Ghosh, A. (2013). Cardiovascular disease risk factors in Asian Indian population: A systematic review. *Journal of Cardiovascular Disease Research*, 4, 222–228. <https://doi.org/10.1016/j.jcdr.2014.01.004>
- Nair, M., Ali, M. K., Ajay, V. S., Shivashankar, R., Mohan, V., Pradeepa, R., et al. (2012). CARRS Surveillance study: Design and methods to assess burdens from multiple perspectives. *BMC Public Health*, 12, 701. <https://doi.org/10.1186/1471-2458-12-701>
- Nethan, S., Sinha, D., & Mehrotra, R. (2017). Non communicable disease risk factors and their trends in India. *Asian Pacific Journal of Cancer Prevention: APJCP*, 18, 2005–2010. <https://doi.org/10.22034/APJCP.2017.18.7.2005>
- Prabhakaran, D., Jeemon, P., & Roy, A. (2016). Cardiovascular diseases in India: Current epidemiology and future directions. *Circulation*, 133, 1605–1620. <https://doi.org/10.1161/circulationaha.114.008729>
- Quan, S. F., Howard, B. V., Iber, C., Kiley, J. P., Nieto, F. J., O'Connor, G. T., et al. (1997). The sleep heart health study: Design, rationale, and methods. *Sleep*, 20, 1077–1085.
- Rastogi, T., Vaz, M., Spiegelman, D., Reddy, K. S., Bharathi, A. V., Stampfer, M. J., et al. (2004). Physical activity and risk of coronary heart disease in India. *International Journal of Epidemiology*, 33, 759–767. <https://doi.org/10.1093/ije/dyh042>
- Shenoy, S., Chawla, J. K., & Sandhu, J. S. (2014). Validation of short international physical activity questionnaire Punjabi version in India. *Saudi Journal of Sports Medicine*, 14, 77.
- Siegel, K. R., Patel, S. A., & Ali, M. K. (2014). Non-communicable diseases in South Asia: Contemporary perspectives. *British Medical Bulletin*, 111, 31–44. <https://doi.org/10.1093/bmb/ldu018>
- Stamatakis, E., Rogers, K., Ding, D., Berrigan, D., Chau, J., Hamer, M., et al. (2015). All-cause mortality effects of replacing sedentary time with physical activity and sleeping using an isothermal substitution model: A prospective study of 201,129 mid-aged and older adults. *Int J Behav Nutr Phys Act*, 12, 121. <https://doi.org/10.1186/s12966-015-0280-7>
- Tanasescu, M., Leitzmann, M. F., Rimm, E. B., Willett, W. C., Stampfer, M. J., & Hu, F. B. (2002). Exercise type and intensity in relation to coronary heart disease in men. *JAMA*, 288, 1994–2000. <https://doi.org/10.1001/jama.288.16.1994>
- Wellburn, S., Ryan, C. G., Azevedo, L. B., Ells, L., Martin, D. J., Atkinson, G., et al. (2015). Displacing Sedentary Time: Association with Cardiovascular Disease Prevalence. *Medicine and Science in Sports and Exercise*. <https://doi.org/10.1249/mss.0000000000000816>
- Willett, W., & Stampfer, M. J. (1986). Total energy intake: Implications for epidemiologic analyses. *American Journal of Epidemiology*, 124, 17–27.
- Wilmot, E. G., Edwardson, C. L., Achana, F. A., Davies, M. J., Gorely, T., Gray, L. J., et al. (2012). Sedentary time in adults and the association with diabetes, cardiovascular disease and death: Systematic review and meta-analysis. *Diabetologia*, 55, 2895–2905. <https://doi.org/10.1007/s00125-012-2677-z>
- Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, F., et al. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet*, 364, 937–952. [https://doi.org/10.1016/s0140-6736\(04\)17018-9](https://doi.org/10.1016/s0140-6736(04)17018-9)
- Zachariah, G., & Alex, A. (2017). Exercise for prevention of cardiovascular disease: Evidence-based recommendations. *Journal of Clinical and Preventive Cardiology*, 6, 109–114. https://doi.org/10.4103/jcpc.jcpc_9_17