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Article

Sedentary behavior and risk of incident cardiovascular disease among Chinese adults

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ABSTRACT

Although emerging studies from high-income countries investigated the relationship between sedentary behavior (SB) and cardiovascular risk, little evidence came from developing countries. Moreover, the benefits of reallocating time from SB to physical activity (PA) on incident cardiovascular disease (CVD) are unknown. Using three cohorts from the Prediction for Atherosclerotic Cardiovascular Disease Risk in China project, we included 93 110 adults who were free from CVD at baseline. Cox proportional hazards models were used to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) for CVD, including stroke, coronary heart disease, and CVD death. Isotemporal substitution models were applied to estimate the per-hour effects of replacing SB with PA. After 5.8 years follow-up, 3799 CVD cases were identified. A gradient positive association between sedentary time and incident CVD was observed. Relative to those with < 5 h/d sedentary time, the multivariable-adjusted HRs (95% CIs) of CVD incidence were 1.07(0.96–1.20), 1.27(1.13–1.43) and 1.51(1.34–1.70) for those having 5–<8, 8–<10, and ≥ 10 h/d sedentary time, respectively. When participants were cross-classified by SB and moderate to vigorous physical activity (MVPA) level, the CVD risk was highest in those with ≥ 10 h/d SB and < 150 min/week MVPA. Among those who reported ≥ 5 h/d sedentary time, per-hour substitution of SB with light, moderate, and vigorous PA reduced incident CVD risk by 5%, 6%, and 8%, respectively. The study first found that sedentary time was associated with increased incident CVD risk among Chinese adults and that substitution of SB with PA of any intensity could convey cardiovascular benefits among those with ≥ 5 h/d SB.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in China and worldwide [1,2]. Moderate to vigorous physical activity (MVPA) conveys various health benefits [3] and has been established as an attractive strategy for CVD prevention and management [4,5]. However, in China and globally, nearly one third of adults are physically inactive [6,7], and sedentary time is ubiquitous and increasing [8,9], thus MVPA alone may not be enough to reduce the risk for CVD.

Up to now, several meta-analyses have found that sedentary behavior (SB) was associated with increased risk of CVD incidence or mortality in a nonlinear manner [10–12]. However, most of the studies were from high-income countries, and the findings could not be generalized to China and other developing countries, considering differences in epidemic characteristics of CVD [2,6,13,14]. For example, the CVD mortality has been increasing

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in China, while the declined trend occurred in high-income countries [2]; the prevalence of unhealthy lifestyle factors such as cigarette smoking rate is much higher while hypertension control rate is much lower in China, compared with developed western countries [13,14]. China has faced such a great challenge in prevention and control for CVD burden that, as one of the major modifiable factors, the sedentary behavior is important to be concerned [6]. However, among Chinese population, only the associations of SB with detrimental cardiometabolic health have been reported, such as diabetes and obesity [15,16]. The evidence about effects of sedentary time on CVD incidence and mortality is still limited, which remains an essential gap for evidence-based guideline recommendations regarding SB for Chinese adults and other populations with similar characteristics.

Several guidelines recommended that reducing sedentary time and increasing physical activity had great health benefits [4,17,18]. Previous cohort studies from Western countries identified that substitution of SB with light physical activity (LPA) or MVPA was related to risk reduction of type 2 diabetes, cardiovascular mortality and all-cause mortality [19,20]. However, no prospective studies have investigated the substitution effects on incident CVD risk worldwide [20].

Thus, this study was aimed to determine the association between SB and CVD incidence, and then to explore the theoretical effects of replacing SB with PA of any intensity on CVD risk, using large-scale prospective cohorts of Chinese adults.

2. Methods

2.1. Study population

Subjects were from 3 cohorts in the Prediction for Atherosclerotic Cardiovascular Disease Risk in China (China-PAR) project, including the China Multi-Center Collaborative Study of Cardiovascular Epidemiology-1998 (China MUCA-1998), the International Collaborative Study of Cardiovascular Disease in Asia (InterASIA), and the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study (CIMIC). China MUCA-1998 and InterASIA were established in 1998 and 2000–2001, respectively. Both studies had their first follow-up survey performed during 2007–2008, and the second conducted from 2012 to 2015. The CIMIC study, established during 2007–2008, was only followed up once from 2012 to 2015. Detailed information for the cohorts has been published elsewhere [21]. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review Board at Fuwai Hospital in Beijing, China and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consents were obtained from all study participants before data collection.

SB was first assessed during 2007–2008 examination using the same questionnaire for all the three cohorts, thus 2007–2008 survey served as the baseline for this study. Eligible participants for this study were those who responded to the 2007–2008 survey (n = 104 957), and then we excluded participants in 3 sites of InterASIA which were followed up until 2008 (n = 1255), lost to follow-up (n = 7654), reporting a prior diagnosis of CVD (n = 2652), or with missing or invalid information on daily activities (n = 286), leaving 93 110 participants for the final analysis (Fig. S1 online).

2.2. Assessment of sedentary behavior and physical activity

Average time (h/d) spent on different activities was assessed via the question "During the previous year, how many hours in each 24-h day did you usually spend on the following activities on weekdays/weekends". Daily activities included vigorous (activities $\geq$ 6.0 metabolic equivalents (METs), e.g. running, heavy farming work), moderate (activities between 3.0 and 5.9 METs, e.g. brisk walking, yard work), light (activities between 1.5 and 2.9 METs, e.g. walking slowly, standing work) intensity PA, SB (activities $\leq$ 1.5 METs, e.g. watching television, reading, reclining), and sleeping activity. For this study, sedentary time was divided into four categories < 5, 5–<8, 8–<10, and $\geq$ 10 h/d according to the quartiles, with the lowest quartile as the reference category. In addition, MVPA was calculated as the sum of time spent on vigorous physical activity (VPA) weighted by 2 and moderate physical activity (MPA), and categorized by the guideline recommended level (150 min/week) [4].

2.3. Assessment of other variables

Information on demographics, lifestyle information, and medical history were collected by standardized questionnaires. Family history of CVD was defined as at least a parent with CHD or stroke. Body weight and height were measured with the subject wearing light indoor clothes without shoes, and body mass index (BMI) was calculated as kilograms per meters squared. The predicted 10-year atherosclerotic cardiovascular disease (ASCVD) risk was obtained using the China-PAR equations for adults aged $\geq$ 20 years, and those with predicted risk of < 5%, 5%–<10%, and $\geq$ 10% were classified into low-, moderate-, and high-risk categories, respectively [21,22].

2.4. Outcome ascertainment

CVD was defined as the first diagnosis of stroke, unstable angina, non-fatal acute myocardial infarction, heart failure, or death with a cardiovascular event. We further analyzed 3 components of CVD events, including stroke (fatal or non-fatal stroke events, ICD-10 I60 to I69), coronary heart disease (CHD, fatal or non-fatal CHD events, ICD-10 I20 to I25), and CVD death (ICD-10 I00 to I99). Information regarding CVD outcomes was collected through interviewing study participants or their proxies and then checking hospital records and/or death certificates to validate the diagnosis. An expert committee at Fuwai Hospital reviewed and adjudicated the final end-point events by reviewing all incidence and death records.

2.5. Statistical analyses

We performed Cox proportional hazards models stratified by cohort to generate hazard ratios (HRs) and 95% confidence intervals (CIs) for incident CVD risk associated with sedentary time. The proportional hazards assumption was examined by evaluating weighted Schoenfeld residuals and no violations were observed (P > 0.05). Person-years of follow-up for all participants were calculated from the baseline to the date of events, death, or the follow-up interview, whichever occurred first. Results were presented from 3 models: Model 1 was adjusted for age and sex; Model 2 was additionally adjusted for geographic region (north, east, north eastern, south, central, south western, and north western), education level (below high school, high school or above), family history of CVD (yes or no), urbanization (urban or rural), alcohol consumption (yes or no), current smoking status (yes or no); Model 3 was further adjusted for the volume of MVPA based on Model 2, and was used as the main analysis. Since BMI, diabetes, dyslipidemia, and hypertension were more likely to be mediators on the causal pathway [23], we additionally adjusted for potential mediators in sensitivity analysis to avoid over-adjustment. Tests of trend were conducted by modeling the median of sedentary time of each category as a continuous variable. Dose-response relationships were assessed by restricted cubic spline analyses with five knots placed at the 5th, 25th, 50th, 75th and 95th percentiles of the sedentary time, with 5 h/d serving as the reference level [24,25]. The nonlinear associations were checked first with the likelihood ratio test. If tests for nonlinearity were significant, the spline model was used to describe the overall association for each outcome; otherwise, the linear model was used.

As a 24-h day is finite, the increase of one type of activity will be accompanied by the decrease of another activity. Isotemporal substitution models (ISM) were used to estimate the theoretical effects of replacing SB with physical activity of equal duration while keeping total time constant [26]. In this model, LPA, MPA, VPA and total time (the sum of the time spent on SB, LPA, MPA, and VPA) were included, and sedentary time was dropped based on Model 3. To satisfy the ISM assumption of linearity between independent and dependent variables [27], SB was treated as a piecewise variable, with a breakpoint at 5 h/d.

To assess the joint association of sedentary behavior and MVPA with the risk of incident CVD, subjects were cross-classified into 8 groups according to the levels of sedentary time (<5, 5–<8, 8–<10, and ≥ 10 h/d) and MVPA (<150 and ≥ 150 min/week). Subgroup analysis was performed to evaluate the effect modification by selected characteristics, and test for interaction was conducted by adding a cross-product term between sedentary behavior and variables of interest. Sensitivity analyses were conducted after excluding all participants suffering CVD within the first year of follow-up, and considering non-CVD deaths as competing events using the Fine and Gray competing-risk regression methodology [28]. SAS 9.4 (SAS Institute Inc., Cary, North Carolina) was used, and statistical tests were two-sided, with a P value < 0.05 considered statistically significant.

3. Results

Of the 93 110 participants, the mean age was 52.8 ± 12.3 years, 39.4% were males, and the mean sedentary time was 7.8 ± 3.4 h/d. The characteristics of participants by categories of sedentary time are presented in Table 1. Subjects with increasing sedentary time were older, more likely to live in urban area, to have higher education level and higher BMI, and to have higher prevalence of hypertension, diabetes mellitus, and dyslipidemia.

During a median follow-up of 5.8 years, 3799 incident CVD cases were recorded, including 2352 stroke events, 914 CHD events, and 1525 CVD deaths. A graded positive association between sedentary time and elevated CVD risk was observed for all the models conducted (P for trend < 0.001, Table 2). Compared with those who reported sedentary time < 5 h/d, the HRs (95% CIs) for CVD risk were 1.07(0.96–1.20), 1.27(1.13–1.43), and 1.51(1.34–1.70) for those with sedentary time of 5–<8, 8–<10, ≥10 h/d, respectively (Model 3). Results for stroke, CHD, and CVD death were similar to that of CVD incidence. The associations were slightly attenuated after further adjustment for potential mediators, including BMI, hypertension, diabetes mellitus, and dyslipidemia, but remained significant for all the outcomes analyzed (Table S1 online). The results did not appreciably change after excluding CVD events within the first year of follow-up (Table S2 online), and considering competing risk (Table S3 online).

When cross-classified by sedentary time and MVPA, participants who reported ≥ 10 h/d SB and < 150 min/week MVPA level had the highest CVD risk with the HR (95% CI) of 1.98 (1.76–2.23), compared with those who reported the least sedentary time and ≥ 150 min/week MVPA level. However, the interaction between sedentary time and MVPA was not significant (P for interaction = 0.079, Fig. 1). In subgroup analyses, the associations between categories of sedentary time and CVD incidence were consistent across several subgroups (Table 3). However, the association was stronger in women than that in men (P for interaction = 0.008).

The results of the dose-response analyses were in accordance with the categorical analyses. There was a nonlinear "J" shape association between sedentary time and CVD incidence (P for nonlinear relationship: 0.008, Fig. 2). Incident CVD risk showed a non-significant decreasing trend from the lowest sedentary time to approximately 5 h/d and then continually increased. The shapes of dose–response relationship for CHD and CVD death were similar to that of CVD incidence, whereas the risk for stroke reached a plateau after approximately 11 h/d of SB.

Table 4 presents the estimates of per-hour substitution effects stratified by low (<5 h/d) and high (≥5 h/d) SB level. Substituting SB with PA was associated with CVD risk reduction among those who reported high sedentary time only. The HR (95% CI) of incident CVD risk related to per-hour substitution of SB with LPA was 0.95 (0.93–0.96). Replacing SB with higher intensity physical activities tended to produce even greater benefits. The corresponding HRs (95% CIs) for replacing SB by MPA and VPA were 0.94(0.92–0.96), and 0.92(0.90–0.93), respectively.

4. Discussion and conclusion

In this large prospective cohort study, we identified a nonlinear deleterious relationship between total sedentary time and incident CVD among Chinese adults for the first time. The harmful cardiovascular effect was most pronounced in those with ≥ 10 h/d SB and < 150 min/week MVPA. In addition, this study was the first

Table 1
Baseline characteristics of participants according to categories of sedentary time.

Characteristics	Total	Sedentary time (h/d)			
		<5	5–<8	8–<10	≥10
No. of participants	93 110	16 607	29 128	21 461	25 914
Age, y	52.8 ± 12.3	51.3 ± 11.8	50.8 ± 11.9	52.1 ± 12.1	56.7 ± 12.4
Male, No. (%)	36 654(39.4)	6016(36.2)	11 743(40.3)	8806(41.0)	10 089(38.9)
Urban, No. (%)	5170 (5.6)	133(0.8)	820(2.8)	991(4.6)	3226(12.4)
Education level ≥ high school, No. (%)	11 680(12.6)	1362(8.2)	3477(11.9)	2952(13.8)	3889(15.0)
Hypertension, No. (%)	34 060(36.6)	4570(27.5)	9226(31.7)	8177(38.1)	12 087(46.6)
Diabetes mellitus, No. (%)	5704(6.5)	708(4.3)	1465(5.0)	1231(5.7)	2300(8.9)
Dyslipidemia, No. (%)	26 090(30.7)	4470(26.9)	8242(28.3)	6048(28.2)	8330(32.1)
Predicted 10-year ASCVD risk, %	5.9 ± 6.2	4.2 ± 4.7	4.8 ± 5.3	5.8 ± 5.9	8.3 ± 7.4
Current smoker, No. (%)	19 433(21.0)	3303(19.9)	6386(21.9)	4709(21.9)	5035(19.4)
Alcohol drinker, No. (%)	19 482(21.0)	3501(21.1)	6436(22.1)	4723(22.0)	4822(18.6)
Body mass index, kg/m^2	23.8 ± 3.6	23.4 ± 3.5	23.7 ± 3.5	23.9 ± 3.6	24.2 ± 3.7
Family history of CVD, No. (%)	10 327(11.1)	1525(9.2)	3129(10.7)	2270(10.6)	3403(13.1)

Values were presented as frequency with percentage for categorical variables, or mean with standard deviation (SD) for continuous variables.

Table 2
HRs and 95% CIs for risk of CVD associated with categories of sedentary time.

	Sedentary time (h/d)				*P* for trend
	<5	5–<8	8–<10	≥10	
CVD incidence					
Cases	481	871	810	1637	
Person-years	100 308	171 114	123 301	144 105	
Model 1	1.00	1.16(1.04–1.30)	1.42(1.27–1.59)	1.87(1.68–2.07)	<0.001
Model 2	1.00	1.12(1.01–1.26)	1.40(1.25–1.56)	1.77(1.59–1.96)	<0.001
Model 3	1.00	1.07(0.96–1.20)	1.27(1.13–1.43)	1.51(1.34–1.70)	<0.001
Stroke					
Cases	351	598	502	901	
Person-years	100 391	171 338	123 585	144 800	
Model 1	1.00	1.10(0.96–1.25)	1.22(1.06–1.39)	1.45(1.28–1.64)	<0.001
Model 2	1.00	1.04(0.91–1.18)	1.18(1.03–1.36)	1.33(1.17–1.51)	<0.001
Model 3	1.00	1.00(0.87–1.14)	1.11(0.96–1.28)	1.19(1.03–1.38)	0.003
CHD					
Cases	89	170	191	464	
Person-years	100 714	171 910	123 959	145 346	
Model 1	1.00	1.18(0.92–1.53)	1.74(1.35–2.24)	2.69(2.13–3.40)	<0.001
Model 2	1.00	1.15(0.89–1.49)	1.70(1.32–2.19)	2.56(2.03–3.24)	<0.001
Model 3	1.00	1.08(0.84–1.41)	1.52(1.17–1.98)	2.12(1.63–2.75)	<0.001
CVD mortality					
Cases	191	323	286	725	
Person-years	100 793	172 086	124 193	145 912	
Model 1	1.00	1.07(0.89–1.28)	1.21(1.00–1.45)	1.76(1.50–2.08)	<0.001
Model 2	1.00	1.03(0.86–1.23)	1.19(0.99–1.43)	1.70(1.44–2.00)	<0.001
Model 3	1.00	0.94(0.79–1.13)	1.00(0.82–1.21)	1.27(1.05–1.52)	<0.001

Model 1: Stratified by cohort and adjusted for sex and age; Model 2: Model 1 + adjusted for geographic region, urbanization, education, family history of CVD, current smoking status, and alcohol consumption; Model 3: Model 2 + adjusted for the volume of MVPA.

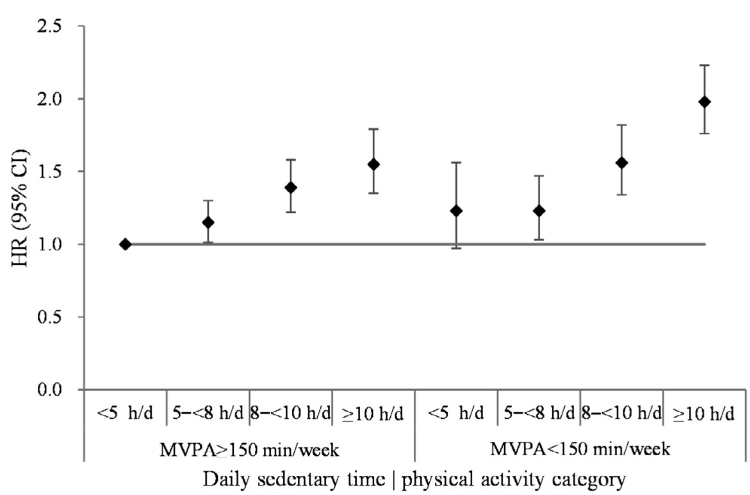

Fig. 1. HRs for incident CVD for joint association between sedentary time and MVPA. The model was stratified by cohort and adjusted for age, sex, geographic region, urbanization, education, family history of CVD, current smoking status, alcohol consumption. The *P* for interaction is 0.079.

to report that replacing SB with LPA conveyed risk reduction of incident CVD, and substitution SB with MPA or VPA might obtain greater benefits. Our findings have great public health implications on reducing sedentary time to prevent CVD.

We found a nonlinear dose–response association between sedentary time and CVD events, and suggested a potential threshold of 5 h/d, which was lower than that from other populations. A recent cohort study from U.S. including 5638 women reported a linear relationship between objectively measured SB and CVD incidence [29]. However, when taking into account the relatively high level of sedentary time, the CVD risk began to increase at 5.5 h/d. Several meta-analyses of studies from Western populations also showed nonlinear relationships of sedentary time with several health outcomes [10,12,30], with the risk beginning to increase at 6.8 h/d and 6 h/d for CVD incidence [10] and CVD mortality [12], respectively. The mean of sedentary time was 7.8 h/d in our cohort, and that was about 9 h/d for Hong Kong, China [31], both of which were beyond the potential cut-offs mentioned above (5 to 6.8 h/d). This indicated that most adults in China were at elevated CVD risk due to excessive sedentary time. Thus, immediate action was needed to address the rise of sedentary lifestyle as a national trend, and successful experiences from western countries could be taken into consideration [32].

In addition, our subgroup analyses provided timely evidence on how sex, age, and weight status modified the association between sedentary behavior and CVD risk, which was raised as a major

Table 3
HRs and 95% CIs for incident CVD associated with sedentary time in different subgroups.

Subgroups	Sedentary time (h/d)				*P* for interaction
	< 5	5–<8	8–<10	≥10	
Age, y					0.153
16–45	1.00	0.88(0.56–1.38)	1.10(0.67–1.81)	1.89(1.14–3.13)	
45–60	1.00	1.07(0.88–1.30)	1.27(1.04–1.56)	1.65(1.33–2.04)	
≥60	1.00	1.07(0.92–1.24)	1.24(1.07–1.45)	1.40(1.21–1.63)	
Gender					0.008
Male	1.00	0.98(0.84–1.14)	1.18(1.00–1.39)	1.35(1.14–1.59)	
Female	1.00	1.16(0.98–1.37)	1.36(1.15–1.61)	1.69(1.43–2.00)	
BMI, kg/m^2					0.052
<24	1.00	1.15(0.99–1.35)	1.41(1.20–1.66)	1.65(1.40–1.94)	
24–28	1.00	1.02(0.83–1.24)	1.04(0.84–1.29)	1.40(1.14–1.73)	
≥28	1.00	0.84(0.62–1.15)	1.15(0.85–1.56)	1.09(0.80–1.49)	
Predicted 10-year ASCVD risk					0.103
Low	1.00	1.06(0.84–1.33)	1.06(0.82–1.38)	1.37(1.04–1.81)	
Medium	1.00	1.04(0.84–1.28)	1.27(1.02–1.58)	1.52(1.21–1.89)	
High	1.00	0.91(0.76–1.09)	0.96(0.80–1.15)	1.05(0.87–1.25)	

HRs were derived from the Cox proportional hazards model stratified by cohort and adjusted for age, sex, geographic region, urbanization, education, family history of CVD, current smoking status, alcohol consumption, and the volume of MVPA; gender and BMI were not adjusted for in corresponding subgroup analyses.

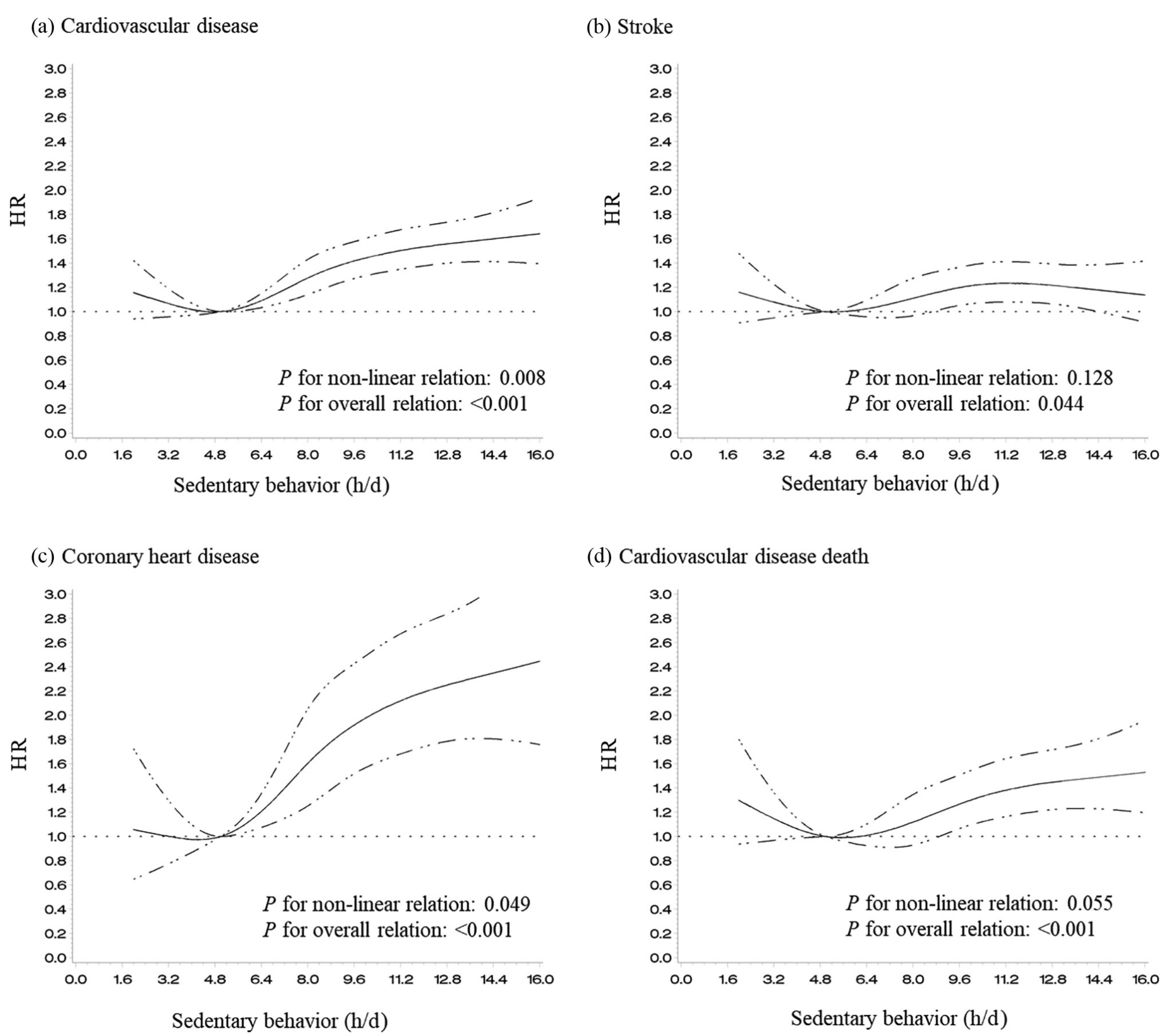

Fig. 2. Restricted cubic spline analyses of sedentary behavior and CVD outcomes. Spline analyses were performed using restricted cubic splines with five knots placed at the 5th, 25th, 50th, 75th, and 95th percentiles of sedentary time. Models were stratified by cohort and adjusted for sex, age, geographic region, urbanization, education, family history of CVD, current smoking status, alcohol consumption, and MVPA. Results were reported as HRs (solid line) and 95% CIs (dashed line).

Table 4
Substitution effects* of replacing 1 h of sedentary time with physical activity on the risk of CVD.

Replace 1 h of	With 1 h of		
	LPA	MPA	VPA
Sedentary time (<5 h/d)			
CVD	1.07(0.97–1.17)	1.04(0.95–1.14)	1.04(0.95–1.14)
Stroke	1.05(0.94–1.17)	1.06(0.95–1.17)	1.04(0.94–1.15)
CHD	0.85(0.66–1.09)	0.78(0.61–1.00)	0.83(0.64–1.06)
CVD mortality	1.08(0.94–1.24)	1.04(0.91–1.20)	1.01(0.87–1.16)
Sedentary time (≥5 h/d)			
CVD	0.95(0.93–0.96)	0.94(0.92–0.96)	0.92(0.90–0.93)
Stroke	0.98(0.96–0.99)	0.97(0.94–0.99)	0.95(0.93–0.97)
CHD	0.92(0.89–0.94)	0.89(0.86–0.93)	0.88(0.86–0.91)
CVD mortality	0.94(0.92–0.96)	0.92(0.89–0.95)	0.89(0.87–0.91)

Values were HRs (95% CIs). *Stratified by cohort and adjusted for age, sex, geographic region, urbanization, education, family history of CVD, current smoking status, alcohol consumption, LPA, MPA, VPA, and total time in all activity classes.

evidence gap by the 2018 U.S. Physical Activity Guidelines Advisory Committee due to the paucity of studies [19,33]. We found consistent associations among adults with different age, weight status. However, the adverse cardiovascular effects of SB were more pronounced in women than those in men, corroborating previous cohort studies reporting stronger associations on SB and mortality among women [34,35]. The specific mechanism of the sex disparity remains unknown, and further research is needed to confirm this finding. It should be noted that although individuals with high ASCVD risk had similar relative CVD risk of prolonged sedentary time to low-risk group, they would suffer more absolute risk elevation. Similar to previous studies [36,37], we found that both low MVPA level and excessive SB added to the cardiovascular risk, with the incident CVD risk being highest for those who did not meet recommended MVPA level and reported highest sedentary time. Thus, these findings supported that in addition to MVPA level, reducing sedentary time might be necessary for optimal cardiovascular health benefits.

Consistent with previous studies, the current study identified significant associations of sedentary time with CVD risk, even adjusting for the volume of MVPA. This suggested that the physiologic mechanisms for prolonged sedentary time might be distinct from the physiologic benefits of physical activity. Potential physiologic mechanisms associated with sedentary behaviors have been raised by some studies. First, sedentary behaviors have been proved to have negative effect on traditional cardiovascular risk factors (e.g., blood pressure, body weight and blood lipids) or other cardiometabolic biomarkers [23,38,39]. Second, sedentary behaviors may induce vascular dysfunction through downregulating shear rate and blood flow, as well as altering glucose metabolism, inflammatory pathway and oxidative stress pathway [17,40–42]. However, further studies to ascertain the physiologic mechanisms associated with sedentary behaviors are still warranted.

In our study, reallocating time from SB to any intensity of PA could reduce incident CVD risk among those who spent at least 5 h/d sedentary time. Previous studies also reported that substitution of SB with LPA or MVPA had beneficial effects for various outcomes rather than incident CVD, including cardiometabolic health [43], CVD mortality [44], and all-cause mortality [27,44,45]. The evidence mentioned above emphasized that any movement, irrespective of intensity, was significantly related to reduced risk of CVD. This was particularly pertinent for individuals with prolonged sedentary time or older adults, among whom LPA was much more practical and achievable than MVPA. The 2018 US physical activity guideline [4] and The American Diabetes Association [18] have recommended replacing SB with LPA, and our results supported such recommendations for Chinese adults. Nonetheless, it should be acknowledged that reductions in CVD risk were further improved when sedentary time was replaced with higher intensities of physical activity. Thus, MPA or VPA should be the ultimate target for adults to prompt cardiovascular health.

Using a large sample size cohort under stringent quality control procedures, the current study added to the literature by providing the association between daily total sedentary time and cardiovascular incidence among Chinese adults. Furthermore, this was the first study to analyze the effect of replacing sedentary time with physical activity on CVD incidence. Nevertheless, the present study also had several limitations. First, sedentary time was assessed via questionnaire other than objectively measured, which tended to bias the findings toward the null and more studies using objective measures were needed. Second, our ISM results were based on statistical model and not on actual replacements. However, since it is unrealistic to conduct randomized controlled trials with hard endpoints (CVD incidence or mortality) by changing physical activity behaviors, this well-designed observational study has provided the best available evidence.

In conclusion, daily sedentary time was associated with raised incident CVD risk, and substitution of SB with even LPA was beneficial to cardiovascular health among those having SB of at least 5 h/d. Individuals should be encouraged to sit less and move more, which is an important lifestyle intervention in CVD prevention and control.

Conflict of interest

The authors declare that they have no conflict of interest.

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Author contributions

Qiong Liu participated in the discussion of study design, performed statistical analysis, and drafted the manuscript; Fangchao Liu interpreted data and revised the manuscript; Jianxi Li and Keyong Huang verified data and checked statistical analysis; Xueli Yang, Jichun Chen, Xiaoqing Liu, Jie Cao, Chong Shen, Ling Yu, Yingxin Zhao, Xianping Wu, Liancheng Zhao, Ying Li, Dongsheng Hu, Xiangfeng Lu, and Jianfeng Huang collected data, and revised the manuscript; Dongfeng Gu designed and implemented the study, and revised the manuscript critically.

Appendix A. Supplementary materials

Supplementary materials to this article can be found online at https://doi.org/10.1016/j.scib.2020.05.029.

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