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Physical activity , sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province: A cross-sectional study

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Abstract

Aims To investigate the associations between physical activity and sedentary time with clustered metabolic risk in community-managed type 2 diabetes patients in China.

Methods From December 2013 to January 2014, a multi-stage sampling method was used to recruit 20,340 type 2 diabetic patients from the community-based chronic disease management system in Jiangsu province, China. Information on physical activity and sedentary time was collected by interviewer-administered questionnaire, anthropometry and biochemical indices were measured. We constructed clustered metabolic risk by summing standardized values of waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure and the inverse of HDL- cholesterol. Association between physical activity and sedentary time with clustered metabolic risk factors was estimated by multivariate linear regression.

Results A total of 17,750 type 2 diabetic patients (age: 21-94y, 60.3%female) in community were included in this cross-sectional study. A 1-SD (13.8 MET h/d) additional physical activity was inversely associated with clustered metabolic risk (B=-0.097[95%CI -0.131,-0.062]), independently of sedentary time. After accounting for physical activity, each additional 1-SD (2.5 h/d) sedentary time was positively associated with clustered metabolic risk (B=0.119[95%CI 0.085, 0.152]). Both physical activity and sedentary time were associated with waist circumference, triacylglycerol and HDL- cholesterol, but not associated with systolic blood pressure.

Conclusion Physical activity was inversely associated with clustered metabolic risk, whereas sedentary time was positively associated with such risk. Encouraging type 2 diabetic patients to decrease their sedentary time and increase overall physical activity may have protective effects on disease protection and could reduce metabolic risk.

Strengths and limitations of this study

- This study constructed clustered metabolic risk by summing standardized values of waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure and the inverse of HDL- cholesterol.
- A large sample size (20304 patients with type 2 diabetes) in our study was used to explore the association between physical activity and sedentary time with metabolic risk in Asian population.
- We considered physical activity and sedentary time simultaneously in this analysis and further examine the associations of their joint associations with metabolic risk.
- The limitation of this study was that physical activity and sedentary time information were collected through a self-report questionnaire.

Introduction

The clustering of metabolic risk factors for cardiovascular disease and type 2 diabetes mellitus, which occurs together more often than by chance alone, is well known as the metabolic syndrome [1]. Metabolic syndrome is most commonly defined according to the Adult Treatment Panel (ATP) III of the National Cholesterol Education Program (NCEP) criteria as three or more of the following conditions: elevated waist circumference, high triglycerides, reduced HDL cholesterol, elevated fasting glucose and blood pressure [2]. Based on the NCEP definition, a rapidly growing epidemic of metabolic syndrome has taken place in China. A study reported that the pooled estimation of metabolic syndrome prevalence in Mainland China was 24.5 % [3], and was 55.7% in type 2 diabetes patients [4]. Participants with metabolic syndrome have been found suffering from increased risk of diabetes, cardiovascular disease, and all-cause mortality [5-9]. The increasing prevalence and serious health consequences suggested that preventive strategies for improving metabolic health should be required.

Physical activity has been considered to be central to the prevention and management of metabolic risk factors [10-12]. Increasing physical activity has beneficial effects on glycemic control [13], lipid profile [14], and importantly, it reduces risks of several chronic diseases and premature death in both healthy individuals and those with type 2 diabetes [15-17]. Emerging evidence also suggests that excess sedentary activity (.i.e. sleeping, siting, lying down, playing computer, watching television) [18], was positively associated with metabolic risk factors independent of physical activity

levels [19-21]. Interestingly, some studies have reported that the cellular and molecular responses to sedentary time are different from the beneficial responses to physical activity [22], therefore, it is essential to explore the effects of sedentary time at the same time. However, most studies focused on risk associated with lack of physical rather than sedentary time. Furthermore, litter is known about joint associations between physical activity and sedentary time with clustered metabolic risk. When exploring the associations of physical activity and sedentary time with metabolic risk factors, it is crucial to elucidate whether this association is independent of sleep duration, which might confound the association with metabolic risk [23].

In addition, the increasing evidence have suggested that use the continuous summary score of clustered metabolic risk (zMS) in analyses, instead of a binary definition dichotomizing continuous outcome variables, which improve statistical power to detect associations[24, 25]. From a methodological perspective, the use of a clustered risk score is recommended. Moreover, each component of metabolic syndrome is independently associated with cardiovascular diseases and other health problems, but their combined effect is stronger. Thus, it is interest to explore the direction and strength of associations of physical activity and sedentary time with clustered metabolic risk.

While pattern of both physical activity and sedentary activity may generally be quite different in Asian populations than in western population, all of these researches were carried out in Western populations[13-14, 19-21, 25, 37-38], besides only few studies was carried in diabetic populations [13, 21, 25]. However, it is uncertain whether results from

Western diabetic populations can be extrapolated to Asian populations with diabetes. In addition, these findings are limited by small sample size [13, 21, 25]. Thus, the present study aims to examine the associations of physical activity and sedentary time and their joint associations with clustered and individuals metabolic risk among type 2 diabetic patients.

Methods

Participants

Participants were from the project of "Comprehensive Research on the Prevention and Control of the Diabetes (CRPCD)". The method and study design have been previously described [26]. In brief, 29,705 registered diabetic patients were recruited form 44 selected township in two areas of Jiangsu Province, China. After excluding the non-type 2 diabetes patients, and individuals with poor physical or mental status, a total of 20,340 subjects consented to complete the investigation. For the present analyses, we further excluded those who had missing values for physical activity or sedentary time (n=2,038), those who reported spending more than 16 hours on daily physical activity (n=67), and those who with incomplete data for defining metabolic risks (n=198). Finally, 17,750 participants remained in the analyses.

The study protocol was approved by the Ethics Board of Jiangsu Provincial Centers for Disease Control and Prevention (No.2013026). All participants gave written informed consent.

Assessment of physical activity and sedentary time

Information on physical activity and sedentary time during the past years was

collected by using Global Physical Activity Questionnaire (GPAQ). The validity and reliability of GPAQ were undertaken in Western population [27-29] and Asian populations [30, 31]. The duration, frequency, and average intensity of activities related to work, commuting, household chores, and leisure-time exercise were assessed. Participants were asked about their normal time spend on sedentary activities daily—such as reading, using computer outside of work, televising watching, lying on the couch. In addition, duration of sleep per day was also inquired.

Participants were asked to recall the intensity and duration of each activity over the previous weeks. The intensity of activities was defined as moderate or vigorous by the metabolic equivalent (MET). The MET is a ratio of work metabolic rate to a standard resting metabolic rate of 1.0 (4.184 kJ) • kg^{-1} • h^{-1}, 1 MET is equivalent to sitting quietly for 1 hours[32]. The mean MET scores were calculated based on specific activities within corresponding categories for estimating intensity of activities (Table S1). The number of hours spent per day on each kind of activity was multiplied by corresponding mean MET score and days of activity per week, then the weekly amount of physical activity was obtained by summing the MET-hours for activities related to work, commuting, household chores, and non-sedentary leisure-time exercise. Subsequently, the weekly amount of physical activities was divided by 7 to generate the average daily activity. Sedentary time, which was not included in the physical activity calculation, was quantified as hours/day.

Clustered metabolic risk score

Broadly based on the definition proposed by ATP III [2], we constructed a summary

variable (clustered metabolic risk score, zMS) for clustered metabolic risk [24, 25]. This variable was derived by standardizing and then summing the following continuously distributed metabolic syndrome components: waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure and the inverse of HDL- cholesterol, to create a Z score and eliminate dimension of data and to improve statistical power [33]. The zMS is a continuous variable with a mean of zero by definition, with lower score revealing a more favorable profile.

Assessment of anthropometric, metabolic risk factors

In addition to GPAQ, face to face questionnaires were used to collect information on demographic characteristics, medical history and medications, family history of diseases, smoking, alcohol consumption, and adult socioeconomic status. The detail of anthropometric measurement has been previously illustrated [34]. Blood samples were collected in the morning after an overnight fast. Fasting plasma glucose was assessed using the Hexokinase method. HbA_{1c} was measured in venous samples using high efficiency liquid chromatography method. Serum total cholesterol, HDL-cholesterol and triacylglycerol were measured enzymatically, all samples were analyzed in the KingMed Diagnostics (Jiangsu Cultural Industrial Park, Nanjing, China).

Covariate definition

Covariates included age， sex, education (without formal education, primary, middle school, high school and above), smoking status (yes, no), BMI (<18.5, 18.5- 23.9, 24-27.9, ≥28 kg/m^2), annual household income (<30,000yuan, 40,000-100,000yuan,

110,000-150,000yuan, >160,000yuan), drinking (never, former, current) and diabetes duration (1, 1-4, 5-10, >10years). Hypertension was defined as systolic blood pressure (SBP) ⩾140 mmHg or diastolic blood pressure (DBP) ⩾90 mmHg or previously diagnosed with hypertension in a hospital[35]. Any of the following conditions was defined as dyslipidemia: total cholesterol (TC) ⩾ 5.2mmol/L or fasting blood triglyceride (TG) ⩾ 1.7mmol/L, fasting blood low-density lipoprotein cholesterol (LDL-C) ⩾3.4mmol/L, fasting blood high-density lipoprotein cholesterol (HDL-C) <0.9mmol/L for male and <1.0mmol/L for female, respectively, or previously diagnosed with hyperlipidemia in hospital[36].

Statistical analysis

Descriptive statistics were conducted separately for men and women using means ± SD, median [interquartile range(IQR)] or frequencies. The chi-square (χ^2) test, Student's t-test, analysis of variance (ANOVA) and Mann-Whitney U test were used to examine the difference of characteristics between men and women. Welch's ANOVA was used for heterogeneity of variance. Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution. Correlation between physical activity, sedentary time and sleep duration was estimated using Spearman correlation coefficients. Adjusted means and standard errors (SE) of clustered and individual metabolic risk variable were presented to explore the association between physical activity and sedentary time with metabolic risk.

Multivariate linear regression was used to evaluate the association between per

1-SD physical activity and sedentary time with the total clustered metabolic risk score, waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure, and the inverse of HDL- cholesterol. Two models were fitted: model 1 was adjusted for age, sex, occupation，education，annual household income，smoking，drinking and diabetes duration. Model 2 was additionally adjusted for physical activity and sedentary time as appropriate to examine independent associations between physical activity and sedentary time with the clustered metabolic risk and individual metabolic risk factors. All subcomponents except zMS and waist circumference are additionally adjusted for waist circumference. When the dependent variable was Fasting plasma glucose, triacylglycerol, HDL-cholesterol or blood pressure, we additionally adjusted for the use of diabetes medication, the diagnosis of dyslipidemia or hypertension, respectively. For the zMS we adjusted for the use of diabetes medication, the diagnosis of dyslipidemia and hypertension. To investigate the joint associations of physical activity and sedentary time with clustered metabolic risk, participants were classified into 3 groups by sex-specific quartiles of physical activity and 5 groups according to sedentary time. The adjusted mean for zMS was calculated by using general linear regression models with adjustment for age.

In the sensitivity analyses, in the interest of whether the association with physical activity and sedentary time with zMS were independent of sleep duration, we additionally adjusted for sleep duration in model2. Furthermore, in order to verify the stability of the results, we use BMI and DBP to replace WC and SBP to calculate new zMS score, then analyze whether the relationship between physical activity and

sedentary time with the new zMS variable was different from previous results. Finally, in order to explore whether the associations between physical activity and sedentary time with clustered metabolic risk were mediated by adiposity, we also calculated a metabolic syndrome score without the adiposity component (i.e. waist circumference), examine whether the associations between the main exposures (physical activity and sedentary time) and clustered metabolic risk were mediated by adiposity.

All statistical analyses were performed using IBM SPSS Statistics standard 23.0 (SPSS, Inc, Chicago, USA).

3. Results

Table 1 shows the demographic characteristics of study population. Of the 17,750 participants included in the analyses, 39.7% of them were men, and the average age of men and women was 62.61±9.93 and 62.86±9.68 years, respectively. BMI, HDL-cholesterol and fasting plasma glucose did not differ significantly (all P>0.10) between excluded participants (n=2,303) and included participants; however, included participants had slightly higher waist circumference and systolic blood pressure (all P<0.001) (**Table S2**). As shown in Table 1, men had higher education level, household income, overweight rate, and consumed more alcohol and cigarette than women (all P<0.001). Men also had higher waist circumference, HbA1c, DBP and FPG levels than women (all P<0.001), whereas women had higher HDL-cholesterol and triacylglycerol levels (all P<0.001). Proportion of using diabetes medication, prevalence of hypertension and diabetes duration were similar for men and women (all P>0.10). Sex difference was observed in physical activity and sedentary time.

Table 1 Demographic, metabolic characteristics of participants at baseline

characteristic	Men	Women	Total	P value
n	7041	10709	17750	
Age(years)	62.61±9.93	62.86±9.68	62.76±9.78	0.11
High school or above (%)	17.7	4.5	9.8	<0.001
Annual income>40000 Yuan (%)	64.8	57.0	60.1	<0.001
BMI(Kg/m^2)	25.27±3.24	25.35±3.57	25.32±3.44	0.09
Overweight (%)	45.7	42.3	43.7	<0.001
Obesity (%)	18.5	20.4	19.7	0.002
Waist circumference (cm)	87.88±9.41	85.48±9.48	86.43±9.53	<0.001
Systolic blood pressure (mmHg)	147.30±19.82	148.86±21.06	148.01±20.59	0.002
Diastolic blood pressure (mmHg)	83.66±10.65	79.94±10.36	81.41±10.63	<0.001
Triacylglycerol (mmol/L)[a]	1.44(1.02, 2.15)	1.65(1.18, 2.32)	1.57(1.11, 2.26)	<0.001
HDL-cholesterol (mmol/L)	1.42±0.43	1.53±0.43	1.49±0.43	<0.001
Fasting plasma glucose (mmol/L) [a]	8.21(6.37, 10.22)	7.97(6.51, 9.88)	8.07(6.60, 10.01)	<0.001
HbA1c (%) [a]	7.3(6.4, 8.6)	7.2(6.4, 8.4)	7.2(6.4, 8.5)	<0.001
HbA1c(mmol/mol)[a]	56.3(46.5,70.5)	55.2(46.5,68.3)	55.2(46.5,69.4)	<0.001
Diabetes duration (years) [a]	5(2, 9)	5(2, 9)	5(2, 9)	0.26
Smoking (%)	46.0	6.2	22.0	<0.001
Drinking (%)				
never	49.1	96.6	77.7	<0.001
former	10.7	1.1	4.9	<0.001
current	40.1	2.3	17.4	<0.001

On diabetes medication (%)	78.7	78.4	78.5	0.60
Hypertension (%)	77.5	76.6	77.0	0.16
Dyslipidemia (%)	46.1	49.3	48.0	<0.001
Physical activity (MET-h/d) [a]	6.29(2.29, 14.29)	8.00(3.43, 16.00)	8.00(2.85, 15.42)	<0.001
Sedentary time (h/d)	3.51±2.46	3.36±2.59	3.41±2.54	<0.001
Sleep duration (h/d)	7.44±1.56	7.34±1.74	7.37±1.67	<0.001

Data are means±SD unless stated otherwise

[a] Median (interquartile range)

P values are from Student's t-test or Mann-Whitney U test for continuous variables and from chi-squared test for categorical variables.

Table 2 shows the age- and sex- adjusted means of clustered and individual metabolic variables by quartile of physical activity and sedentary time. There was a tendency towards lower zMS, waist circumference, triacylglycerol and higher HDL-cholesterol at higher levels of physical activity (P for trend<0.001) (**Table 2**), by contrast, higher zMS, waist circumference, fasting plasma glucose, triacylglycerol and lower HDL-cholesterol were observed for higher sedentary time (P for trend<0.001) (**Table 2**). Physical activity was weakly inversely related to sedentary time (r=-0.103; P<0.001) and with sleep duration (r=-0.022; P<0.001). In addition, sedentary activity was weakly correlated with sleep duration(r=0.075; P<0.05) (**Table S3**).

Table 2 Adjusted means(SE) of metabolic variables by quartile of physical activity and sedentary time

Metabolic risk	Physical activity (MET h/day)					Sedentary time(h/d)				
	Quartile 1 (<2.9)	Quartile 2 (2.9-8.0)	Quartile 3 (8.1-15.4)	Quartile 4 (>15.4)	P for trend	Quartile 1 (<2)	Quartile 2 (2-3)	Quartile 3 (3.1-4)	Quartile 4 (>4)	P for trend
zMS[a]	0.28(0.40)	0.02(0.04)	-0.12(0.05)	-0.21(0.04)	<0.001	-0.16(0.03)	-0.04(0.04)	0.05(0.06)	0.30(0.05)	<0.001
Waist circumference (cm)	87.19(0.14)	86.56(0.13)	86.13(0.16)	85.76(0.14)	<0.001	85.98(0.11)	86.25(0.16)	86.57(0.20)	87.30(0.14)	<0.001
Fasting plasma glucose (mmol/L)[b]	0.022(0.015)	0.012(0.014)	-0.049(0.017)	0.003(0.015)	0.252	-0.030(0.011)	-0.007(0.017)	-0.004(0.021)	0.055(0.015)	<0.001
Triacylglycerol(mmol/L)[b]	0.066(0.015)	0.004(0.014)	-0.012(0.017)	-0.061(0.015)	<0.001	-0.043(0.011)	0.003(0.017)	0.035(0.021)	0.056(0.015)	<0.001
HDL-cholesterol (mmol/L)	1.45(0.01)	1.49(0.01)	1.50(0.01)	1.52(0.01)	<0.001	1.51(0.01)	1.48(0.01)	1.48(0.01)	1.46(0.01)	<0.001
Systolic blood pressure (mmHg)	148.26(0.30)	147.91(0.28)	147.80(0.34)	148.05(0.30)	0.651	148.08(0.23)	147.56(0.33)	147.87(0.42)	148.35(0.30)	0.326

Date are mean (SE) values for each quartile of physical activity and sedentary time, adjusted for age and sex by using general linear regression models. Test for trend based on variable containing median value for each quartiles.

[a] zMS is a continuously distribute variable for clustered metabolic risk calculated by summing standardized values for Waist circumference， Fasting plasma glucose， Triacylglycerol，Systolic blood pressure and the inverse of HDL-cholesterol.

[b] Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution

Table 3 shows the crude and adjusted associations between physical activity and sedentary time with clustered metabolic risk represented by zMS score and individual risk factors of metabolic syndrome. In crude analyses, physical activity was inversely associated with clustered metabolic risk (B=-0.145; 95%CI -0.184,-0.106) **(Table 3**). After adjusting for sedentary time and measured confounders, the result was still significant (B=-0.097; 95%CI -0.131, -0.062). For individual risk factors, physical activity was strongly inversely associated with waist circumference (B=-0.43; 95%CI -0.57,-0.29), and slight inversely associated with triacylglycerol (B=-0.014; 95%CI -0.021, -0.007). In contrast, per SD physical activity was marginally positively associated with HDL-cholesterol (B=0.012; 95%CI 0.006, 0.018) after accounting for sedentary time and other confounders. However, the association between physical activity and systolic blood pressure (B=-0.907; 95%CI -1.209, -0.604) in crude analysis disappeared after covariates adjusted in the models. No significant association was found between physical activity and fasting plasma glucose (B=0.002; 95%CI -0.003, 0.006).

Contrary to physical activity, sedentary time was strongly positively associated with clustered metabolic risk (B=0.119; 95%CI 0.085, 0.152) and waist circumference (B=0.48; 95%CI 0.34, 0.62) **(Table 3)**, even after adjusting for physical activity and other confounders. Furthermore, in adjusted analyses, sedentary time was found to be weakly associated with fasting plasma glucose (B=0.009; 95%CI 0.004, 0.013), triacylglycerol levels (B=0.015; 95%CI 0.009, 0.022) and HDL-cholesterol (B=-0.007; 95%CI -0.013, -0.001). Similarly, No significant association was found between

physical activity and systolic blood pressure (B=0.202; 95%CI -0.047, 0.448).

Table 3 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables

Metabolic risk	physical activity(per-SD)[c]			Sedentary time(per-SD) [c]		
	B(95%CI)	β	P value	B(95%CI)	β	P value
zMS[a]						
Crude	-0.145(-0.184, -0.106)	-0.054	<0.001	0.195(0.156，0.234)	0.073	<0.001
Model 1	-0.108(-0.142, -0.073)	-0.040	<0.001	0.127(0.094，0.161)	0.048	<0.001
Model 2	-0.097(-0.131, -0.062)	-0.036	<0.001	0.119(0.085，0.152)	0.044	<0.001
Waist circumference (cm)						
Crude	-0.55(-0.69, -0.41)	-0.058	<0.001	0.58(0.44, 0.72)	0.060	<0.001
Model 1	-0.47(-0.62, -0.33)	-0.050	<0.001	0.52(0.38, 0.66)	0.055	<0.001
Model 2	-0.43(-0.57, -0.29)	-0.050	<0.001	0.48(0.34, 0.62)	0.049	<0.001
Fasting plasma glucose (mmol/L)[d]						
Crude	0.005(0.000, 0.010)	0.016	0.038	0.011(0.006, 0.016)	0.034	<0.001
Model 1	0.001(-0.004, 0.005)	0.002	0.749	0.009(0.004, 0.013)	0.027	<0.001
Model 2	0.002(-0.003, 0.006)	0.005	0.506	0.009(0.004, 0.013)	0.027	<0.001
Triacylglycerol(mmol/L)[d]						
Crude	-0.022(-0.030, -0.013)	-0.038	<0.001	0.031(0.023, 0.039)	0.055	<0.001
Model 1	-0.015(-0.022, -0.008)	-0.027	<0.001	0.017(0.010, 0.023)	0.029	<0.001
Model 2	-0.014(-0.021, -0.007)	-0.025	<0.001	0.015(0.009, 0.022)	0.027	<0.001
HDL-cholesterol (mmol/L)						
Crude	0.015(0.009, 0.022)	0.035	<0.001	-0.019(-0.025, -0.012)	-0.043	<0.001
Model 1	0.013(0.007, 0.019)	0.030	<0.001	-0.008(-0.014, -0.002)	-0.018	0.009
Model 2	0.012(0.006, 0.018)	0.029	<0.001	-0.007(-0.013, -0.001)	-0.016	0.023
Systolic blood pressure (mmHg)						

Crude	-0.907(-1.209, -0.604)	0.000	<0.001	0.340(0.037, 0.643)	0.017	0.028
Model 1	0.007((-0.243, 0.257)	0.001	0.955	0.200(-0.045, 0.445)	0.010	0.110
Model 2	0.026(-0.225, 0.277)	0.001	0.841	0.202(-0.047, 0.448)	0.010	0.107

[a]zMS is a continuously distribute variable for clustered metabolic risk calculated by summing standardized values for Waist circumference，Fasting plasma glucose，Triacylglycerol，Systolic blood pressure and the inverse of HDL-cholesterol.

[b] values to calculate new clustered metabolic risk score

[c] Per-SD of physical activity =13.8 MET-h/d，per-SD sedentary time = 2.5 h/d.

Regression results are presented as unstandardized coefficients (B) (95%CI) with standardized coefficients (β) shown for comparison.

All models are adjusted for age，sex，occupation，education，annual household income，smoking，drinking and diabetes duration. All outcomes except zMS and waist Circumference are additionally adjusted for waist circumference. Fasting plasma glucose are additional adjusted for the use of diabetes medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no); Systolic and diastolic blood pressure are additionally adjusted for the diagnosis of hypertension(yes/no); and zMS is additional adjusted for the use of diabetes medication (yes/no)，the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

Model 2 is adjusted for physical activity and sedentary time as appropriate.

[d] Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution.

Figure 1 highlights the joint association of physical activity and sedentary time with zMS after adjusting for age. For both sexes, participants who had the lowest level of physical activity (<5 MET h/d) and the highest sedentary time (>5 h/d) had the highest zMS (**Figure 1**).

Additional adjustments for sleep duration did not change the direction or magnitude of associations of physical activity and sedentary time with clustered and individual metabolic risk (**Table S4**). Furthermore, when substituting waist circumference with BMI and systolic blood pressure with diastolic blood pressure, the associations were unchanged. When excluding waist circumference from the clustered metabolic risk score and additionally adjusting for waist circumference as a confounding factor, the magnitude of association between sedentary time and clustered risk was attenuated and weaker (**Table S4**).

4. Discussion

In this large cross-sectional study of individuals with type 2 diabetes, we confirmed that physical activity and sedentary time were strongly associated with clustered metabolic risk. For individual metabolic risk factor, both physical activity and sedentary time were associated waist circumference, triacylglycerol levels, and HDL-cholesterol. Our findings suggested that increasing overall physical activity and decreasing amount of sedentary time may have protective effects on disease protection and reduction of metabolic risk.

Previous cross-sectional researches, mainly in Western countries, have shown beneficial associations between increasing physical activity with clustered metabolic

risk and triacylglycerol levels and HDL-cholesterol, insulin and waist circumference in general population [10-12]. Furthermore, measures of clustered metabolic risk have also been shown to be detrimentally associated with physical activity among type 2 diabetic patients or participants at a high risk of developing diabetes [25, 37, 38]. An objective study has reported that among type 2 diabetic patients, physical activity energy expenditure significantly and independently associated with reduced clustered metabolic risk [25]. In addition, another objectively study also suggested that total body movement (counts • day $^{-1}$) and moderate-to-vigorous physical activity were inversely associated with clustered metabolic risk score after adjusting for confounding factors[38]. These cross-sectional researches were also consistent with the findings in longitudinal studies [21, 37]. A longitudinal study showed that greater increase in sedentary time and decrease in moderate-to-vigorous physical activity were associated with clear increase in clustered metabolic risk score, however, when additional adjusted for six-year change in sedentary time, no association between moderate-to-vigorous physical activity and clustered metabolic risk was observed [37]. This result may be explained by the fact that the increasing sedentary time attenuated the positively association of physical activity with clustered metabolic risk, and indicated that solely focusing on physical activity, may not be the most effective strategy for future interventions. Our findings also suggested individuals who have the lowest level of physical activity and the highest sedentary time had the highest zMS, meanwhile, both physical activity and sedentary time have the potential to influence clustered and individual metabolic risk independent of each other, which highlighted

the importance not only of increasing physical activity but also reducing sedentary time among patients with type 2 diabetes.

As reported previously, waist circumference was a body fat parameter most closely associated with metabolic syndrome [39]. A study has reported that 1 cm increase in waist circumference, the relative risk (RR) of a cardiovascular disease event increased by 2% [40].Our findings indicated that 13.8 MET h/d increase in physical activity and 2.5 h/d decrease in sedentary time were associated with 0.43 cm and 0.48cm lower waist circumference, respectively. If type 2 diabetic patients spend extra 2.5h to do moderate physical activity, the risk of cardiovascular disease event might consequently be reduced by ~1% [47]. Considering almost 840,000 diabetic patients die in China every year, and more than half of diabetic patients die from cardiovascular complications[41], this small reduction also have significant public health implication in a country with large population. The biological mechanisms for relationships between physical activity, sedentary time and waist circumference with metabolic syndrome are only partially understood [42, 43], however, data from weight loss and exercise training trials have shown that reductions in waist circumference occur concomitantly with reductions in obesity-related metabolic risk factors and disease [44]. In our study, when excluding waist circumference from the clustered metabolic risk score and adjusting for it as a confounding factor, the magnitude of association between physical activity and sedentary time with clustered risk was attenuated. An alternative explanation may be that waist circumference is an important part of the causal pathway between physical activity and sedentary time

with clustered metabolic risk. If this is the case, more attention should be paid on waist circumference of type 2 diabetic patients in health policy planning.

Our results extend previous cross-sectional and longitudinal results in other populations of the independent associations between physical activity and sedentary time with triacylglycerol and HDL-cholesterol levels [21, 37]. The association between physical activity and fasting plasma glucose did not reach statistical significance in our study, which is consistent with result from the ProActive Study[38]. In contrast, significant association was found between sedentary time and fasting plasma glucose in our study. It is, however, in disagreement with the result from Katrien et al, in which no significant association was found with fasting plasma glucose in adult with a family history of type 2 diabetes [37]. Some of the inconsistent results may be partly explained by differences in the study population (e.g. age, health conditions, and ethnicity) as well as differences in potential confounding factors. Furthermore, our non-significant results between physical activity and sedentary time with systolic blood pressure are consistent with the results from most previous studies [21, 25, 37, 38]. A cross-sectional data from 45000 individuals also found that physical activity was not associated with systolic blood pressure [45], this results perhaps because the real effects were attenuated in a cross-sectional study, randomized trial need to apply in further study. Further, we also obtained consistent results after adjusting for sleep duration and demonstrated that the relationship between physical activity and sedentary time are independent of sleep duration.

American Diabetes Association(ADA) recommended that type 2 diabetic patients should call for accumulation of ⩾150 minutes of moderate-to-vigorous intensity aerobic activity per week[46]. However, patients with type 2 diabetes enrolled in exercise intervention projects demonstrate limited success in increasing their physical activity, especially for some high-intensity exercises [47]. Our study found a linear dose –response association between physical activity and sedentary time with clustered metabolic risk, which also suggested patients with type 2 diabetes may obtain health benefit from increasing physical activity and reducing sedentary time, even it is less than the recommendation of guidelines [46]. A prospective cohort study in Taiwan, China reported that individuals who did average 15 min of moderate-intensity physical activity daily had significant health benefits when compared with individuals who were inactive [48]. In further studies, more detailed relationship between different pattern of physical activity and sedentary time with metabolic risks need to be explored and find the most suitable prevention and management strategy for type 2 diabetes patients.

Our study has several strengths. A large sample size (20304 patients with type 2 diabetes) in our study was used to explore the association between physical activity and sedentary time with metabolic risk in Asian population. In addition, physical activity and sedentary time were considered simultaneously in this analysis. There are several potential limitation of our study. First, this is a cross-sectional study, the direction and causality of the association were restricted to infer. Second, we collect physical activity information through a self-report questionnaire, subjective reporting

error may occur because of recall bias. Finally, we cannot exclude the potential confounding including uncontrollable confounding factors and unmeasured factors.

5. Conclusion

Our results suggest that lack of physical activity and excess sedentary time are both independently associated with clustered and individual metabolic risk in community type 2 diabetic patients. Encouraging type 2 diabetic patients to decrease their sedentary time and increase overall physical activity may have protective effects on disease protection and reduction of metabolic risks.

Contributions: Ming Wu and Chong Shen designed this investigation. Jian Su, Yu Qin, Chong Shen, Ying Li, Enchun Pan, Yan Gao, Dandan Miao, Ning Zhang, Jingyi Zhou and Ming Wu were responsible for data collection. Yijia Chen analyzed data and drafted the manuscript. Ming Wu, Yu Qin, Chong Shen, and Enchun Pan revised the manuscript. All authors approved the version published.

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Competing interests: None declared.

Ethical approval: The study protocol was approved by the Ethics Board of Jiangsu Provincial Centers for Disease Control and Prevention (No.2013026).

Data sharing statement： The materials and datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Abbreviations used: MET: Metabolic equivalent; zMS: Standardized clustered metabolic risk score; GAPD: Global Physical Activity Questionnaire; IQA: Interquartile range

References

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *The Lancet* 2005;365:1428. doi：10.1016/S0140-6736(05)66378-7.
2. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome : An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement.

Circulation 2005;112:2735–2752. doi:10.1161/CIRCULATIONAHA.105.169404.

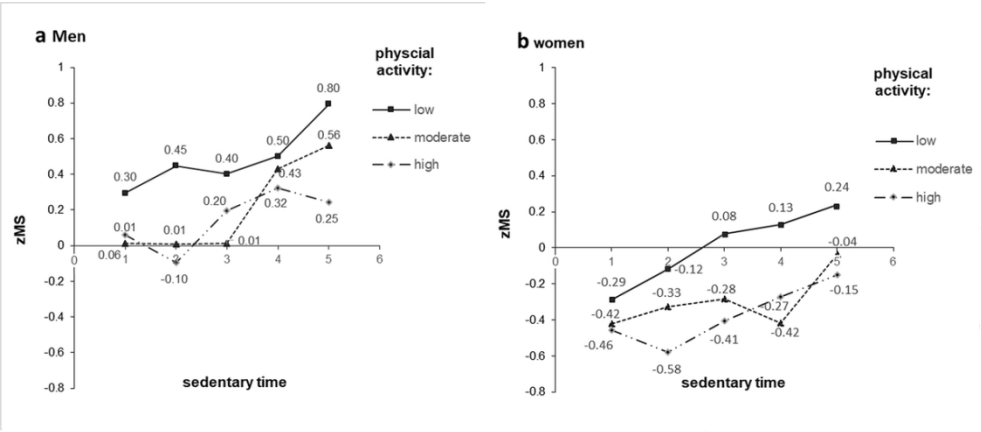
3. Li R, Li WC, Lun ZJ, et al. Prevalence of metabolic syndrome in mainland china: a meta-analysis of published studies. *BMC Public Health* 2016;16:296. doi:10.1186/s12889-016-2870-y.
4. Lu B, Yang HC ,Song XY, et al. An evaluation of the International Diabetes Federation definition of metabolic syndrome in Chinese patients older than 30 years and diagnosed with type 2 diabetes mellitus. *Metabolism* 2006;55: 1088-1096. doi:10.1016/j.metabol.2006.04.003.
5. Laaksonen DE. Metabolic Syndrome and Development of Diabetes Mellitus: Application and Validation of Recently Suggested Definitions of the Metabolic Syndrome in a Prospective Cohort Study. *Am J Epidemiol* 2002;156:1070-1077. doi:10.1093/aje/kwf145.
6. Lakka HM, Laaksonen DE, Lakka TA, et al. The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-aged Men. *JAMA* 2002;288: 2709-2716. doi:10.1001/jama.288.21.2709
7. Girman CJ, Rhodes T, Mercuri M, et al. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). *Am J Cardiol* 2004;93:136-141. doi:10.1016/j.amjcard.2003.09.028.
8. Malik S, Wong ND, Franklin SS, et al. Impact of the Metabolic Syndrome on Mortality From Coronary Heart Disease, Cardiovascular Disease, and All Causes in United States Adults. *Circulation* 2004;110:1245-1250. doi:10.1016/j.amjcard.2003.09.028.
9. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular Morbidity and Mortality Associated With the Metabolic Syndrome. *Diabetes Care* 2001;24:683-689. doi:10.2337/diacare.24.4.683.
10. Lakka TA, Laaksonen DE. Physical activity in prevention and treatment of the metabolic syndrome. *Appl Physiol Nutr Metab* 2007;32:76-88. doi:10.1139/h06-113.
11. Laaksonen DE, Lakka HM, Salonen JT, et al. Low Levels of Leisure-Time Physical Activity and Cardiorespiratory Fitness Predict Development of the Metabolic Syndrome. *Diabetes care* 2002;25:1612-1618. doi:10.2337/diacare.25.9.1612.
12. Rennie KL, McCarthy N, Yazdgerdi S, et al. Association of the metabolic syndrome with both vigorous and moderate physical activity International journal of epidemiology. *Int J Epidemiol* 2003; 32: 600–606. doi:10.1093/ije/dyg179.
13. Boulé NG, Haddad E, Kenny GP , et al. Effects of Exercise on Glycemic Control and Body Mass in Type 2 Diabetes Mellitus A Meta-analysis of Controlled Clinical Trials. *JAMA* 2001;286: 1218 - 1227. doi:10.1001/jama.286.10.1218
14. Gordon LA, Morrison EY, McGrowder DA, et al. Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes. *BMC Complement Altern Med* 2008;8:21. doi:10.1186/1472-6882-8-21.
15. Blair SN ,Kohl III HW , Paffenbarger Jr RS, et al. Physical Fitness and All-Cause Mortality： A Prospective Study of Healthy Men and Women. *JAMA* 1989; 262: 2395 - 2401. doi:10.1001/jama.1989.03430170057028.
16. Thompson PD, Buchner D, Piña IL, et al. Exercise and Physical Activity in the Prevention and Treatment of Atherosclerotic Cardiovascular Disease. *Circulation* 2003;107:3109-3116. doi:10.1161/01.ATV.0000087143.33998/F2.
17. Shiroma EJ, Cook NR, Manson JE, et al. Strength Training and the Risk of Type 2 Diabetes and Cardiovascular Disease. *Med Sci Sports Exerc* 2017;49:40-46. doi:10.1249/MSS.0000000000001063.

18. Pate RR, O'Neill JR, Lobelo F. The Evolving Definition of "Sedentary". *Exerc Sport Sci Rev* 2008; 36: 173-178. doi:10.1097/JES.0b013e3181877d1a.
19. Hamilton MT, Hamilton DG, Zderic TW. Role of Low Energy Expenditure and Sitting in Obesity, Metabolic Syndrome, Type 2 Diabetes, and Cardiovascular Disease. *Diabetes* 2008;56(11):2655-2667.
20. Bankoski A, Harris TB, McClain JJ, et al. Sedentary Activity Associated With Metabolic Syndrome Independent of Physical Activity. *Diabetes care* 2011;34:497-503. doi:10.2337/dc10-0987.
21. Cooper AR, Sebire S, Montgomery AA, et al. Sedentary time, breaks in sedentary time and metabolic variables in people with newly diagnosed type 2 diabetes. *Diabetologia* 2012;55:589-599. doi:10.1007/s00125-011-2408-x.
22. Katzmarzyk PT. Physical Activity, Sedentary Behavior, and Health: Paradigm Paralysis or Paradigm Shift? *Diabetes* 2010;59:2717-2725. doi: 10.2337/db10-0822.
23. Troxel WM, Buysse DJ, Matthews KA, et al. Sleep Symptoms Predict the Development of the Metabolic Syndrome. *Sleep* 2010;33:1633-1640. doi:10.1093/sleep/33.12.1633.
24. Ekelund U, Brage S, Franks PW, et al. Physical Activity Energy Expenditure Predicts Progression Toward the Metabolic Syndrome Independently of Aerobic Fitness in Middle-Aged Healthy Caucasians. *Diabetes care* 2005;28:1195-1200. doi:10.2337/diacare.28.5.1195.
25. Cooper AJM, Brage S, Ekelund U, et al. Association between objectively assessed sedentary time and physical activity with metabolic risk factors among people with recently diagnosed type 2 diabetes. *Diabetologia* 2014;57:73-82. doi:10.1007/s00125-013-3069-8.
26. Miao DD, Pan EC, Zhang Q , et al. Development and Validation of a Model for Predicting Diabetic Nephropathy in Chinese People. *Biomed Environ Sci* 2017;30:106-112. doi:10.3967/bes2017.014.
27. Hoos T, Espinoza N, Marshall S, Arredondo EM. Validity of the Global Physical Activity Questionnaire (GPAQ) in Adult Latinas. *Journal of Physical Activity and Health* 2012;9:698-705. doi:10.1123/jpah.9.5.698.
28. Cleland CL, Hunter RF, Kee F, et al. Validity of the Global Physical Activity Questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. *BMC Public Health* 2014;14:1471-2458. doi: 10.1186/1471-2458-14-1255.
29. Fiona C. Bull TSM, Armstrong T. Global Physical Activity Questionnaire (GPAQ): Nine Country Reliability and Validity Study. *Journal of Physical Activity and Health* 2009;6:790-804. doi:10.1123/jpah.6.6.790.
30. Chu AHY , Ng SHX, Koh D, et al. Domain-Specific Adult Sedentary Behaviour Questionnaire (ASBQ) and the GPAQ Single-Item Question: A Reliability and Validity Study in an Asian Population. Int J Environ Res Public Health 2018;15:739. doi:10.3390/ijerph15040739.
31. Chu AHY, Moy FM. Reliability and Validity of the Malay International Physical Activity Questionnaire (IPAQ-M)Among a Malay Population in Malaysia. *Asia Pacific Journal of Public Health* 2015;27: NP2381-NP2389. doi: 10.1177/1010539512444120.
32. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of Physical Activities: an update of activity codes and MET intensities. *Med Sci Sport Exer* 2000;32 suppl 9:S498-S516. doi:0195-913 l/00/3209-0498/0.
33. Armstrong BK WE, Saracci R. Principles of Exposure Measurement in Epidemiology. Oxford, UK, Oxford University Press 1994.
34. Wu M, Wen JB, Qin Y, et al. Familial History of Diabetes is Associated with Poor Glycaemic Control in Type 2 Diabetics: A Cross-sectional Study. *Sci Rep* 2017;7 : 1432.

doi:10.1038/s41598-017-01527-4.

35. Chobanian AV, Bakris GL, Black HR, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206-1252. doi:10.1161/01.HYP.0000107251.49515.c2.
36. Huang YX, Gao L, Xie XP , et al.Epidemiology of dyslipidemia in Chinese adults: meta-analysis of prevalence, awareness, treatment, and control. *Population Health Metrics* 2014;12:2-9. doi:10.1186/s12963-014-0028-7.
37. Wijndaele K, Orrow G, Ekelund U, et al. Increasing objectively measured sedentary time increases clustered cardiometabolic risk: a 6 year analysis of the ProActive study. *Diabetologia* 2014;57:305-312. doi:10.1007/s00125-013-3102-y.
38. Ekelund U, Griffin SJ, Wareham NJ. Physical Activity and Metabolic Risk in Individuals With a Family History of Type 2 Diabetes. *Diabetes Care 2*007;30:337-342. doi:10.2337/dc06-1883.
39. Carr DB, Utzschneider KM, Hull RL, et al. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome. *Diabetes* 2004;53:2087–2094. doi:10.2337/diabetes.53.8.2087.
40. Koning LD, Merchant AT, Pogue J, et al. Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *Eur Heart J* 2007;28: 850–856. doi:10.1093/eurheartj/ehm026.
41. Federation ID. IDF Diabetes Atlas. 8th edition. Available at: http://wwwdiabetesatlasorg/. Brussels, Belgium. 2017:Last accessed: September 2018.
42. Hu G, Tuomilehto J, Silventoinen K, et al. Joint effects of physical activity, body mass index, waist circumference and waist-to-hip ratio with the risk of cardiovascular disease among middle-aged Finnish men and women. *Eur Heart J* 2004;25:2212-2219. doi:10.1016/j.ehj.2004.10.020.
43. Ekelund U, Brage S, Besson H, et al. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality? *Am J Clin Nutr* 2008; 88: 612–617. doi:10.1093/ajcn/88.3.612.
44. Goodpaster BH,DeLany JP,Otto AD, et al. Effects of Diet and Physical Activity Interventions on Weight Loss and Cardiometabolic Risk Factors in Severely Obese Adults: A Randomized Trial. *JAMA* 2010;304:1795-1802. doi:10.1001/jama.2010.1505.
45. Beijer K, Lampa E, Sundström J, et al. Interaction between physical activity and television time on blood pressure level: : cross-sectional data from 45 000 individuals. *J Hypertens* 2018;36:1041-1050. doi:10.1097/HJH.0000000000001675.
46. ADA. 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018. Diabetes care 2018;41 Supplement 1:S38-S50. doi:10.1097/HJH.0000000000001675.
47. MNSc KEE, MNSc MAA, MSocSc PMH, et al. Motivators and barriers to exercise among adults with a high risk of type 2 diabetes – a qualitative study. *Scand J Caring Sci* 2011;25: 62-69. doi:10.1111/j.1471-6712.2010.00791.x.
48. Wen CP, Wai JPM, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *The Lancet* 2011;378: 1244- 1253. doi:10.1016/S0140-6736(11)60749-6.

Fig 1. Mean of clustered metabolic risk score by sedentary and physical activity among 17750 diabetic patients. The adjusted mean was calculated by using general linear regression models with adjustment for age. The cut off values for defining low, moderate, and high levels of physical activity and sedentary time were 5 and 15 MET-h/d. MET, metabolic equivalent task



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52x23mm (600 x 600 DPI)

Table 1. Classification table of physical activity

Physical activity in Farm work, occupation and household chores		**Physical activity in leisure-time**		**Static behavior**
Moderate-intensity physical activity (4 MET h/d) Make breathing and heart beat slightly faster	**Vigorous-intensity physical activity (8 MET h/d)** Make breathing and heart rate significantly faster	**Moderate-intensity physical activity (4 MET h/d)** Make breathing and heart beat slightly faster	**Vigorous-intensity physical activity (8 MET h/d)** Make breathing and heart rate significantly faster	Lying, sitting and leaning besides sleep time (h/d)
·**Cleaning**(e.g. vacuuming, mopping the floor, polishing floor, wiping the desk, sweeping the floor, ironing clothes) ·**Washing** (e.g. scrubbing the carpet, washing clothes) ·**Gardening** (e.g. watering, turning soil, fertilizing) ·**Hand milking** ·**Hand knitting** ·**carpenter work** (e.g. sawing cork，Chiseling cork) ·**With a shovel and other tools to mix the sand and cement** ·**Walking with a general weight**	·**Forestry workers** (felling and handling timber) ·**Sawing ironwood** ·**tilling land** ·**transplant rice seedlings** ·**harvesting crops** (e.g. wheat, rice, sugarcane) ·**Gardening** (e.g. digging, carrying heavy things) ·**hand milling** (with wooden club or stone mill) ·**architectural work** (e.g. building a wall, handing building materials) ·**Fitness Trainer** (e.g. spinning, aerobics, yoga and some other aerobic exercise) ·**A courier on foot or bike**	·**biking** ·**jogging** ·**dancing** ·**reading a horse** ·**practicing Tai chi** ·**Practicing Yoga and pilates** ·**doing the yangko dance**	·**Long-distance running** ·**playing football** ·**playing rugby** ·**playing tennis** ·**spinning in gym** ·**Lifting barbell** ·**doing ballet** ·**swimming**	·**working** ·**studying** ·**reading** ·**watching TV** ·**using computer** ·**riding** ·**taking a rest**

·Carrying water **·Grazing**	**·Pulling a rickshaw**			

Table 2. Baseline characteristics of those included and excluded participants.

characteristics	Included participants	excluded participants	P
n	17750	2303	
Sex, n(%)			
Male	7041(39.7)	821(35.6)	<0.001
Age(years)	62.76±9.78	63.76±10.27	<0.001
BMI(Kg/m^2)	25.32±3.44	25.45±3.67	0.101
Waist circumference (cm)	86.43±9.53	84.97±13.80	<0.001
Systolic blood pressure (mmHg)	148.01±20.59	142.62±35.61	<0.001
Diastolic blood pressure (mmHg)	81.41±10.63	82.11±10.76	0.004
Triacylglycerol (mmol/L)[a]	1.57(1.11, 2.26)	1.61(1.16, 2.36)	0.004
HDL-cholesterol (mmol/L)	1.49±0.43	1.49±0.48	0.576
Fasting plasma glucose (mmol/L) [a]	8.07(6.60, 10.01)	8.00(6.34, 10.56)	0.576
HbA1c (%) [a]	7.20(6.4, 8.5)	7.4(6.4, 9.0)	<0.001
Diabetes duration (years) [a]	5(2, 9)	4(1, 8)	<0.001

Data are means±SD unless stated otherwise ; [a]Median (interquartile range)

P values are from one-way analysis or Mann-Whitney U test for continuous variables and from chi-squared test for categorical variables.

Table 3. Correlation analysis between physical activity ， sedentary time and sleep duration

	physical activity (MET-h/d),r	Sedentary time (h/d),r	Sleep duration (h/d),r
Physical activity (MET-h/d),r	1	-0.103[a]	-0.022[b]
Sedentary time (h/d),r	-0.103	1	0.075[c]
Sleep duration (h/d),r	-0.	0.075	1

[a] p<0.001; [b] p=0.004; [c] p<0.001

Table 4. Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables in 17750 participant.

Metabolic risk	Physical activity(per-SD)[a]			Sedentary time(per-SD) [a]		
	B(95%CI)	β	P value	B(95%CI)	β	P value
zMS						
Crude	-0.145(-0.184, -0.106)	-0.054	<0.001	0.195(0.156, 0.234)	0.073	<0.001
Model 1	-0.108(-0.142, -0.073)	-0.040	<0.001	0.127(0.094, 0.161)	0.048	<0.001
Model 2	-0.097(-0.131, -0.062)	-0.036	<0.001	0.119(0.085, 0.152)	0.044	<0.001
Model2+sleep duration(h/d)	-0.096(-0.130, -0.062)	-0.036	<0.001	0.115(0.081, 0.149)	0.043	<0.001
zMS[b]						
Crude	-0.023(-0.064, 0.017)	-0.008	0.260	0.169(0.129, 0.210)	0.062	<0.001
Model 1	-0.093(-0.128, -0.057)	-0.034	<0.001	0.103(0.069, 0.138)	0.038	<0.001
Model 2	-0.084(-0.119, -0.048)	-0.030	<0.001	0.096(0.061, 0.130)	0.035	<0.001
Model2+sleep duration(h/d)	-0.083(-0.118, -0.048)	-0.030	<0.001	0.094(0.059, 0.129)	0.034	<0.001
zMS[c]						
Crude	-0.057(-0.085,-0.300)	-0.030	<0.001	0.096(0.068,0.124)	0.051	<0.001
Model 1	-0.026(-0.051,-0.001)	-0.014	0.039	0.059(0.034,0.083)	0.031	<0.001
Model 2	-0.021(-0.045,0.004)	-0.011	0.102	0.057(0.033,0.081)	0.030	<0.001
Model2+sleep duration(h/d)	-0.020(-0.045,0.004)	-0.011	0.106	0.054(0.030,0.079)	0.029	<0.001
Waist circumference (cm)						
Crude	-0.55(-0.69, -0.41)	-0.058	<0.001	0.58(0.44, 0.72)	0.060	<0.001
Model 1	-0.47(-0.62, -0.33)	-0.050	<0.001	0.52(0.38, 0.66)	0.055	<0.001
Model2	-0.43(-0.57, -0.29)	-0.050	<0.001	0.48(0.34, 0.62)	0.049	<0.001
Model2+sleep duration(h/d)	-0.43(-0.57, -0.29)	-0.050	<0.001	0.47(0.33, 0.61)	0.049	<0.001
Log_e Fasting plasma glucose (mmol/L)						
Crude	0.005(0.000, 0.010)	0.016	0.038	0.011(0.006, 0.016)	0.034	<0.001
Model 1	0.001(-0.004, 0.005)	0.002	0.749	0.009(0.004, 0.013)	0.027	<0.001

Model 2	0.002(-0.003, 0.006)	0.005	0.506	0.009(0.004, 0.013)	0.027	<0.001
Model2+sleep duration(h/d)	0.002(-0.003, 0.006)	0.006	0.444	0.008(0.004, 0.013)	0.025	<0.001
Log_e Triacylglycerol(mmol/L)						
Crude	-0.022(-0.030, -0.013)	-0.038	<0.001	0.031(0.023, 0.039)	0.055	<0.001
Model 1	-0.015(-0.022, -0.008)	-0.027	<0.001	0.017(0.010, 0.023)	0.029	<0.001
Model 2	-0.014(-0.021, -0.007)	-0.025	<0.001	0.015(0.009, 0.022)	0.027	<0.001
Model2+sleep duration(h/d)	-0.014(-0.021, -0.007)	-0.025	<0.001	0.014(0.008, 0.021)	0.020	0.001
HDL-cholesterol (mmol/L)						
Crude	0.015(0.009, 0.022)	0.035	<0.001	-0.019(-0.025, -0.012)	-0.043	<0.001
Model 1	0.013(0.007, 0.019)	0.030	<0.001	-0.008(-0.014, -0.002)	-0.018	0.009
Model 2	0.012(0.006, 0.018)	0.029	<0.001	-0.007(-0.013, -0.001)	-0.016	0.023
Model2+sleep duration(h/d)	0.012(0.006, 0.018)	0.028	<0.001	-0.007(-0.013, -0.001)	-0.016	0.027
Systolic blood pressure (mmHg)						
Crude	-0.907(-1.209, -0.604)	0.000	<0.001	0.340(0.037, 0.643)	0.017	0.028
Model 1	0.007((-0.243, 0.257)	0.001	0.955	0.200(-0.045, 0.445)	0.010	0.110
Model 2	0.026(-0.225, 0.277)	0.001	0.841	0.202(-0.047, 0.448)	0.010	0.107
Model2+sleep duration(h/d)	0.021(-0.231, 0.272)	0.001	0.872	0.200(-0.047, 0.447)	0.010	0.113

Regression results are presented as unstandardized coefficients (B) (95%CI) with standardized coefficients (β) shown for comparison.

All models are adjusted for age，sex，occupation，education，annual household income，smoking，drinking and diabetes duration. All outcomes except zMS and waist Circumference are additionally adjusted for waist circumference. Fasting plasma glucose are additional adjusted for the use of diabetes medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no); Systolic and diastolic blood pressure are additionally adjusted for the diagnosis of hypertension(yes/no); and zMS is additional adjusted for the use of diabetes medication (yes/no)，the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).zMS is a continuously distribute variable for clustered metabolic risk calculated by summing standardized values for waist circumference，fasting plasma glucose，triacylglycerol，systolic blood pressure and the inverse of HDL-cholesterol.

Model 2 is adjusted for physical activity and sedentary time as appropriate and additionally adjusted for sleep duration.

[b] Replace WC and SBP with BMI values and DBP values to calculate new clustered metabolic risk score.

[c] Delete the waist circumference to calculate new clustered metabolic score

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract **page 1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Page 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Page 2-4**
Objectives	3	State specific objectives, including any prespecified hypotheses **Page 4**
Methods		
Study design	4	Present key elements of study design early in the paper **Page 5**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Page 5**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **Page 5**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Page 5-8**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Page 5-8**
Bias	9	Describe any efforts to address potential sources of bias **Page 7-8**
Study size	10	Explain how the study size was arrived at **Page 5**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Page 6-7**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses **Page 8-9**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **Page 10**

		(b) Give reasons for non-participation at each stage **Page 10**
		(c) Consider use of a flow diagram **N/A**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Page 11-12**
		(b) Indicate number of participants with missing data for each variable of interest **N/A**
Outcome data	15*	Report numbers of outcome events or summary measures **N/A**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Page 13-17**
		(*b*) Report category boundaries when continuous variables were categorized **Page 13-14**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Page 18**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Page 18**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 22-23**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Page 19-22**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Page 23**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Page 23**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Physical activity, sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province : A cross-sectional study

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Physical activity, sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province: A cross-sectional study

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ABSTRACT

Objective To investigate the associations between total physical activity, physical activity in different domains and sedentary time with clustered metabolic risk among patients with type 2 diabetes in Jiangsu Province of China.

Design Interview-based cross-sectional study conducted between December 2013 and January 2014.

Setting 44 selected township in two cities of Changshu and Huai'an in Jiangsu Province.

Participants 20 340 subjects selected through stratified cluster-randomized sampling method using an interviewer-managed questionnaire.

Methods We constructed clustered metabolic risk by summing gender-specific standardized values of waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure and the inverse of blood high-density lipoprotein cholesterol (HDL-cholesterol). Self-reported total physical activity includes three domains of occupation, commuting and leisure-time exercise. Multivariate linear regression analyses were applied to calculate unstandardized regression coefficient [B]and their 95% confidence interval (CI).

Results A total of 17 750 patients with type 2 diabetes (aged 21-94 years old, 60.3% of female) were included in this study. Results showed that the total (B= -0.080; 95% CI: -0.114, -0.046), occupational (B= -0.066; 95% CI: -0.101, -0.031) and leisure-time physical activity (B= -0.041; 95% CI: -0.075, -0.007) and sedentary time (B= 0.117; 95% CI: 0.083, 0.151) were associated with clustered metabolic risk. Total physical activity, occupational physical activity and sedentary time were associated with waist circumference, triacylglycerol and HDL-cholesterol, but not with systolic blood pressure. Commuting physical activity and sedentary time were significantly associated with triacylglycerol (B= -0.012; 95% CI: -0.019, -0.005) and fasting plasma glucose (B= 0.008; 95% CI: 0.003, 0.01), respectively. Leisure-time physical activity was not found to significantly associate with any individual metabolic risk factors except systolic blood pressure (B= -0.239; 95% CI: -0.542, -0.045).

Conclusions Total, occupational and leisure-time physical activity were inversely associated with clustered metabolic risk, whereas sedentary time was found to increase such risk.

Strengths and limitations of this study

- ▸This study constructed clustered metabolic risk by summing gender-specific standardized values for waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure and the inverse of HDL- cholesterol.
- ▸The study has a relatively large sample size which included 17 750 participants from community-managed type 2 diabetic patients in China.
- ▸The study investigated physical activity in different domains and sedentary time and their associations with metabolic risk factors.
- ▸The limitation of this study was that physical activity and sedentary time information were collected through a self-report questionnaire.

INTRODUCTION

The clustering of metabolic risk factors for cardiovascular disease and type 2 diabetes mellitus is well known as the metabolic syndrome.[1] Based on the National Cholesterol Education Program (NCEP) definition,[2] a rapidly growing epidemic of metabolic syndrome has taken place in China. A meta-analysis estimated that the pooled prevalence of metabolic syndrome in Mainland China was 24.5 %, [3] and was 55.7% among patients with type 2 diabetes.[4] Individuals with metabolic syndrome were found to be with increased risk of diabetes, cardiovascular disease and all-cause mortality.[5-7] The increasing prevalence observed among Chinese population and its sever health consequences call for strategies for prevention, maintenance and improvement of metabolic health among the largest populations in the world.

Physical activity has long been considered as one of the key factors to the prevention and management of metabolic risk factors.[8] A certain number of studies have investigated the association between physical activity and glycemic control,[9] lipid profile,[10] and clustered metabolic risk.[11 12] Most of them emphasized the value of assessing overall physical activity or leisure-time physical activity,[9-12] but few have focused on other domains of physical activity (e.g. occupational, household or commuting).[13] Evidence showed that information on different domains of physical activity may be crucial for Chinese people because they were found with quite different patterns of physical activity compared with their Western counterparts. For example, it was reported that occupational and household activities contributed substantially more to total physical activity than leisure time or transportation activity

did.[14] Therefore, it is important to examine whether other types of physical activities such as occupational and commuting physical activity are associated with metabolic risk among patients with diabetic problems.

Emerging evidence also suggests that excess sedentary time was positively associated with metabolic risk, effect of which was independent of physical activity levels.[15-17] The formal definition of sedentary time is: any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalent (MET) and a sitting or reclining posture.[18] Some studies found that the cellular and molecular responses to sedentary time are different from the beneficial responses to physical activity,[19] therefore, it is essential to explore the effects of physical activity and sedentary time simultaneously, when exploring the associations of physical activity and sedentary time with metabolic risk factors, it is crucial to elucidate whether this association is independent of sleep duration, which might confound the associations.[20]

While most attention has been focused on metabolic syndrome risk in Western populations,[9-13 15 16] but the relationship between physical activity and sedentary time with risk of metabolic syndrome was not well understood among Chinese population, though there were a few studies carried in diabetic populations, their findings were inconsistent and were limited by small sample size.[10 11 17] Furthermore, it has been suggested that using the continuous summary score of clustered metabolic risk (zMS)[11] for analyses may improve the statistical power to detect possible associations, as compared to a binary definition by dichotomizing continuous outcome variables.[21] Therefore, it is interesting to explore the direction and strength of associations for

physical activity and sedentary time with clustered metabolic risk among Chinese population.

The objective of this study was to examine the associations between total physical activity, physical activity in different domains (i.e. occupation, commuting and leisure-time exercise) and sedentary time with clustered and individual metabolic risk factors among patients with type 2 diabetes in a Chinese population. We hypothesized that both physical activity and sedentary time are associated with clustered and individual metabolic risk factors.

METHORDS

Participants

Participants were from the project of "Comprehensive Research on the Prevention and Control of the Diabetes (CRPCD)". The method and study design have been previously described.[22] Briefly, 29 705 registered patients with diabetes receiving the management of National Basic Public Health Service were recruited form 44 selected township in two cities of Jiangsu Province of China. After excluding non-type 2 diabetic patients, and individuals with poor physical or mental status, a total number of 20 340 participants consented to participate. In this analyses, we further excluded those who had missing values for physical activity or sedentary time (n = 2 038), who reported spending more than 16 hours on daily physical activity (n = 67),[23] and who were with incomplete data of metabolic risks (n = 198). Finally, there were 17 750 participants included in the analyses.

Assessment of physical activity and sedentary time

Information on physical activity and sedentary time was collected by using the Global Physical Activity Questionnaire (GPAQ). The validity and reliability of GPAQ were undertaken in Western populations[24] and Asian populations.[25] Participants were asked to recall the intensity and duration of occupational, commuting and leisure-time physical activities over the previous weeks.

The intensity of activities was defined as moderate or vigorous by MET. The MET is a ratio of work metabolic rate to a standard resting metabolic rate of 1.0 (4.184 kJ) • kg^{-1} • h^{-1}, 1 MET is equivalent to sitting quietly for 1 hour.[26] The average MET scores were calculated based on specific activities within corresponding categories for estimating intensity of activities (Table S1). The number of hours spent per day on each kind of measured activity was multiplied by corresponding average of MET score and frequency of measured activity (days per week). The total physical activity was obtained by summing up the MET-hours for activities related to occupational, commuting, and leisure-time domains. Subsequently, the weekly amount of physical activities was divided by 7 to generate the average daily activity. Participants were also asked about their normal time spent on sedentary activities and sleep (hours/day).

Clustered metabolic risk score

Broadly based on the definition proposed by Adult Treatment Panel III (ATP III),[2] we constructed a summary variable (clustered metabolic risk score, zMS) for clustered metabolic risk.[11] This variable was calculated by summing the standardized values for waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood

pressure and the inverse of HDL-cholesterol. Each of these variables was standardized by subtracting the gender-specific sample means from the individual mean and dividing by the standard deviations (SD). The zMS is a continuous variable with a mean of zero by definition, with lower score revealing a more favorable profile.

Assessment of anthropometric, metabolic risk factors

In addition to the GPAQ, face-to-face questionnaire interview was used to collect information on demographic characteristics, medical history and medications, smoking, alcohol consumption, and adult socioeconomic status. The detail of anthropometric measurement has been previously illustrated.[27] Blood samples were collected in the morning after an overnight fasting. Fasting plasma glucose was assessed using the Hexokinase method. Glycated hemoglobin (HbA_{1c}) was measured in venous samples using high efficiency liquid chromatography method. Serum total cholesterol, HDL-cholesterol and triacylglycerol were measured enzymatically. All samples were analyzed in the KingMed Diagnostics (Jiangsu Cultural Industrial Park, Nanjing, China).

Covariate definitions

Covariates included age, sex, education (no formal education, primary, middle school, high school and above), smoking status (yes, no), annual household income (<30 000 RMB, 40 000-100 000 RMB, 110 000-150 000 RMB, >160 000 RMB), alcohol drinking (never, former, current), diabetes duration, taking medications to lower glucose, lipid or blood pressure (yes, no, unclear). Hypertension was defined as being with a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90

mmHg, or previously being diagnosed with hypertension in a hospital.[28] Being with at least one of the following conditions was defined as dyslipidemia: total cholesterol ≥ 5.2mmol/L, fasting blood triglyceride ≥ 1.7mmol/L, fasting blood low-density lipoprotein cholesterol ≥ 3.4mmol/L, HDL- cholesterol < 0.9mmol/L for male or <1.0 mmol/L for female, or previously being diagnosed with hyperlipidemia in a hospital.[29] Sleep duration was assessed by the question "How many cumulative hours do you have for sleep on an average day?"

Statistical analyses

Descriptive statistics were conducted separately for men and women using means ± SD, median [interquartile range(IQR)] or frequencies. The chi-square (χ^2) test, Student's t-test, one-way analysis of variance (ANOVA) and Mann-Whitney U test were used to examine the difference of characteristics between men and women. Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution. Adjusted means and standard errors (SE) of clustered and individual metabolic risk variables were presented to explore the association between physical activity and sedentary time with metabolic risk. Test for trend was based on variables containing median value for each quartiles. Multiple comparison among groups was performed using Bonferroni method.

Multivariate linear regression was used to evaluate the association between per 1-SD of total physical activity, different domains of physical activity (occupational, commuting and leisure-time) and sedentary time with the total clustered metabolic risk score and individual metabolic risk factors. Preliminary checks were conducted to

ensure no violation of assumptions of normality, homogeneity of variance and absence of multicollinearity. Four models were fitted: Model 1 was the crude model (unadjusted); Model 2 was adjusted for age, sex, education, annual household income, smoking status, drinking and diabetes duration; Model 3 was additionally adjusted for remaining physical activity and sedentary time as appropriate; Model 4 was further adjusted for sleep duration. For Models 2 to 4, all subcomponents except zMS and waist circumference were additionally adjusted for waist circumference. When the dependent variable was fasting plasma glucose, we additionally adjusted for the use of glucose-lowering medication. For triacylglycerol and HDL-cholesterol we adjusted for the diagnosis of dyslipidemia and use of lipid-lowering medication. When the outcome of interest was systolic blood pressure, we additionally adjusted for the diagnosis of hypertension and use of antihypertensive medication. For zMS we adjusted for the use of medications on glucose-lowering, lipid-lowering, or antihypertensive and the diagnosis of dyslipidemia and hypertension.

To investigate the joint associations of total physical activity and sedentary time with clustered metabolic risk, participants were classified into 3 groups and 4 groups by sex-specific tertiles of physical activity and quartiles of sedentary time. The adjusted mean for zMS was calculated by using general linear regression models after adjusting for age. Interactions between the main predictive variables with sex and age (continuous) were examined by entering the centered interaction terms in multivariate linear regression models in order to examined whether the association between physical activity and sedentary time with metabolic risks were modified by sex and

age.[30] In further sensitivity analyses, we also calculated a metabolic syndrome score without the waist circumference in order to examine whether the associations between the main exposures (physical activity and sedentary time) and clustered metabolic risk were mediated by waist circumference.

All statistical analyses were performed using IBM SPSS Statistics standard 23.0 (SPSS, Inc, Chicago, USA). Statistical significance was set at $P < 0.05$ for main effects, and $P < 0.10$ for interactions; tests were two-sided.

Patient and public involvement statement

Development of the research questions was informed by qualitative interviews, physical examination and laboratory test with a purposively selected sample of residents who were included in the National Basic Public Health Services in Jiangsu province. Summary reports about the study results will be disseminated to each participants, policy-makers and healthcare workers in the community (village doctors in rural areas or general practitioners in urban areas of China) through mass media, such as local newspapers, the Internet, radios or workshops.

RESULTS

Demographic and basic characteristics of participants

Of the 17,750 participants included in the analyses, 39.7% of them were men, and the average age of men and women was 62.6 ± 9.9 and 62.8 ± 9.7 years, respectively (Table 1). Indices of body mass index, HDL-cholesterol and fasting plasma glucose did not differ significantly (all P>0.10) between excluded (n = 2 303) and included participants, but included participants had a slightly higher waist circumference and

systolic blood pressure (all P<0.001) (Table S2) than excluded ones. Compared with women, men were higher in education level, household income and consumption of alcohol and cigarettes (all P < 0.001). Men were also higher in waist circumference, HbA1c, diastolic blood pressure and fasting plasma glucose levels than women (all P<0.001). By contrary, women were higher in HDL-cholesterol, systolic blood pressure and triacylglycerol levels than their male counterparts (all P<0.001).

Differences between genders were also observed in physical activity, sedentary time and sleep duration. Women had higher total and occupational physical activity than man (all P<0.001), whereas man had higher sedentary time, sleep duration, commuting and leisure time physical activity than women (all P<0.001). The proportion of subjects participating in leisure-time physical activity was 21.6% (Table 1).

Adjusted means of clustered and individual metabolic variables by physical activity and sedentary time

There was a tendency towards lower zMS, waist circumference, triacylglycerol and higher HDL-cholesterol at higher levels of total physical activity (P for trend<0.001) (Table 2), while individuals with higher zMS, waist circumference, fasting plasma glucose, triacylglycerol and lower HDL-cholesterol were apt to have a higher sedentary time (P for trend<0.001) (Table 2).

Associations between physical activity and sedentary time with metabolic risk

Overall, total physical activity was inversely associated with zMS (B=-0.080; 95% CI: -0.114, -0.046), waist circumference (B=-0.449; 95% CI: -0.591, -0.308) and

triacylglycerol (B=-0.012; 95% CI: -0.019, -0.006) in analyses after adjusting for sedentary time and sleep duration. In contrast, per SD physical activity was marginally positively associated with HDL-cholesterol (B=0.009; 95% CI: 0.003, 0.015). No significant associations were found between total physical activity with fasting plasma glucose (B=0.004; 95% CI: -0.001, 0.008) and systolic blood pressure (B=-0.096; 95% CI: -0.346, 0.155) (Table 3).

In adjusted analyses, occupational physical activity was found to be associated with zMS (B=-0.066; 95% CI: -0.101, -0.031), waist circumference (B=-0.475; 95% CI: -0.620, -0.334), triacylglycerol (B=-0.007; 95% CI: -0.014, -0.001) and HDL-cholesterol (B=0.006; 95% CI: 0.001, 0.013), but not with fasting plasma glucose (B=0.005; 95% CI: -0.001, 0.009) and systolic blood pressure (B=0.081; 95% CI: -0.173, 0.334). Commuting physical activity was only inversely associated with triacylglycerol (B=-0.012; 95% CI: -0.019, -0.005). Furthermore, leisure-time physical activity was found to be inversely associated with zMS (B=-0.041; 95% CI: -0.075, -0.007) and systolic blood pressure (B=-0.293; 95% CI: -0.542, -0.045), but not with waist circumference, fasting plasma glucose or triacylglycerol (all $P > 0.05$) (Table 3).

Different from that of physical activity, sedentary time was strongly positively associated with zMS (B=0.117; 95% CI: 0.083, 0.151) and waist circumference (B=0.474; 95% CI: 0.334, 0.613), after adjustment for physical activity and sleep duration. Furthermore, sedentary time was found to be weakly associated with fasting plasma glucose (B=0.008; 95% CI: 0.003, 0.013), triacylglycerol levels (B=0.015;

95% CI: 0.008, 0.022) and HDL-cholesterol (B=-0.007; 95%CI: -0.013, -0.001). Similarly, no significant association was observed between sedentary time and systolic blood pressure (B=0.215; 95% CI: -0.033, 0.462) (Table 3).

Joint association of total physical activity and sedentary time with metabolic risk

Figure 1 illustrates the joint association of total physical activity and sedentary time with zMS after adjustment of age. Participants with the lowest level of physical activity or with the highest sedentary time were consistently found to have the highest zMS among both genders. Interaction analyses indicated significant effects among different age groups, greater associations of sedentary time, total and occupational physical activity with zMS (P for interaction <0.10) and waist circumference (P for interaction <0.05) were observed among older age groups. In addition, there was no significant interaction for sex in the results of total physical activity, different domains of physical activity or sedentary time (Table S3). When excluding waist circumference from the clustered metabolic risk score and additionally adjusted for waist circumference, the magnitude of association between sedentary time and clustered risk was attenuated and weaker but remaining statistically significant (Table S4).

DISCUSSION

In this cross-sectional study with a large sample-size of individuals with type 2 diabetes in China, we found that total physical activity, occupational physical activity and sedentary time were independently associated with clustered metabolic risk, waist circumference, triacylglycerol levels, and HDL-cholesterol. Moreover, leisure-time

physical activity was found to associate with systolic blood pressure and commuting physical activity was inversely associated with triacylglycerol, while higher level of sedentary time was positively associated with higher levels of fasting plasma glucose. Our findings suggested that increasing physical activity across all domains and decreasing amount of sedentary time may have protective effects on reducing metabolic risks.

Findings on the association between total physical activity and clustered metabolic risk in this study were consistent with previous researches with objective data.[11 12] Importantly, we observed that occupational physical activity reduces the clustered metabolic risk in patients with type 2 diabetes. Occupational physical activity is a major source of total physical activity for Chinese people and other Asian populations (In this study, 75.8% of patients with diabetes reported engaging in occupational physical activity.).[14] This finding suggested a special importance of occupational physical activity as a single domain for the management of metabolic risk among Chinese people or even broadly among Asian populations. Though there was a trend for lower levels of commuting physical activity to be associated with higher metabolic risk in recent study,[31] there was no statistically significant association observed between commuting physical activity and clustered metabolic risk in this study, which is similar to the finding of the J-ECOH Study.[32] This may partly be explained that the level of commuting physical activity is low in our study.

previous studies also suggested that the associations between physical activity and clustered metabolic risk may be weaken by increasing sedentary time.[11 33] For

example, a longitudinal study reported that the association between moderate-to-vigorous physical activity and clustered metabolic risk was attenuated when additional adjusted for six-year change in sedentary time, which indicated that solely focusing on physical activity may not be the most effective strategy for interventions.[33] In this study, we also found that sedentary time was associated with clustered and individual metabolic risk, which is independent of the effect of physical activity. This highlights the importance of not only increasing physical activity levels among patients with type 2 diabetes, but also reducing their sedentary time besides.

As reported previously, waist circumference was a body fat parameter most closely associated with metabolic syndrome.[34] Our findings indicated that total and occupational physical activity were strongly associated with waist circumference. There is a growing body of evidence that exercise may lose weight by regulating adipokines (adiponectin, leptin, resistin, interleukin-6), which are known to contribute to cardiometabolic health.[35] However, the biological mechanisms for associations between sedentary time and waist circumference with metabolic risk are not fully understood yet. Results of a study reported that the association could be attenuated once adiposity component was included in the regression model.[36] Our findings suggested that more sedentary time was associated with higher waist circumference, however, whether central obesity is a cause or a consequence of a sedentary behavior has not yet been fully elucidated.[37] Sedentary time may displace physical activity time, leading to a decrease in energy expenditure and unfavorable weight changes.[38] Additional pathways linking sedentary time, waist circumference and metabolic risk

include the established associations between major sedentary behavior (TV viewing) and unhealthy diet.[39] In addition, when excluding waist circumference from the clustered metabolic risk score and adjusting for it as a confounding factor, the magnitude of association between physical activity and sedentary time with clustered metabolic risk was attenuated. An alternative explanation is that waist circumference might be an important part of the causal pathway between sedentary time and clustered metabolic risk, but further researches are needed. We also found that relationship between sedentary time with zMS and waist circumference was modified by age. This may partly due to time spent in sedentary behavior increased with age.[40] Older patients may at a higher risk of clustered metabolic risk than younger people based on this age-related increase of sedentary time.

The association between total and individual domains of physical activity with fasting plasma glucose did not reach statistical significance in this study, which is consistent with result from the ProActive Study.[12] In contrast, significant association was found between sedentary time and fasting plasma glucose in our study. The potential mechanism between sedentary time and fasting plasma glucose includes involvement of markers of inflammation, insulin resistance, and adiposity.[41] Obesity has been proved associated with increased risk of developing insulin resistance, and may result in disordered regulation of glucose levels by reducing insulin release.[42] Further, some studied have suggested that sleep loss can lead to disordered glucose metabolism.[43] In our study, we obtained consistent results even after adjusting for

sleep duration, which suggested that the relationship between sedentary time and metabolic risk are independent of sleep duration.

In the present analysis, non-significant results between total physical activity, occupational physical activity and sedentary time with systolic blood pressure are consistent with the results from most previous studies,[11 12 17 31 33] Moreover, a significant inverse association between leisure-time physical activity and systolic blood pressure was found in our study. Clays et al. also observed that objectively measured moderate and vigorous leisure time physical activity, but not occupational physical activity, were inversely associated with systolic blood pressure.[44] Further study showed bouts of high-intensity exercise elicited greater systolic blood pressure reductions than lower intensity bouts.[45] However, practice recommendations of advocating high-intensity exercise as antihypertensive therapy is challenging because adverse cardiovascular effects are more likely to occur with vigorous than moderate to low levels of physical exertion,[46] especially in patients with type 2 diabetes which who had significantly greater systolic blood pressure response to a given exercise intensity than the healthy population.[47] The American Diabetes Association (ADA) recommended that type 2 diabetic patients should be assessed for conditions that might be associated with risk of cardiovascular disease before undertaking vigorous intensity exercise.[48] Our findings also suggested that patients with type 2 diabetes should complying with the ADA recommendations to increase overall physical activity through working, active transport and participation in exercise and reduce sedentary behavior to reduce metabolic risks.

This study has several strengths. A relative large sample size (n= 17 750) was used to explore the association between physical activity, sedentary time and metabolic risk in a Chinese population. In addition, to the best of our knowledge, this is the first study in China evaluated physical activity at different domains and sedentary time with metabolic risk factors in patients with type 2 diabetes. Several limitations also should be mentioned here. First, as a cross-sectional study, the direction and causality of the association obtained from this study were restricted to infer. Second, waist circumference and systolic blood pressure of included participants were observed to be slightly higher than excluded cases, which may cause less accurate estimation of our results. Third, all participants were recruited from two areas in Jiangsu province, China, whether the findings can be generalized to the population at large need to be discussed. Finally, we used physical activity information through a self-report questionnaire, so that reporting error may occur due to recall bias. The self-reported measures of physical activity is easier to use but may have limited validity when compared to objective measures.[49] Moreover, the patterns of physical activity and sedentary behaviors may vary between weekdays and weekends, but such variation is hard to be obtain by self-report measures used in the study. Further researches are needed to explore more detailed relationship between different pattern of physical activity and sedentary behavior (specifically comparing weekdays and weekends) with metabolic risks in type 2 diabetic patients.

CONCLUSIONS

Findings of this study suggest that total physical activity, physical activity in different domains and sedentary time are associated with clustered and individual metabolic risk in community patients with type 2 diabetes. Encouraging patients with type 2 diabetes to increase physical activity at different domains and decrease sedentary time may have protective effects against metabolic risks. Findings from this study extend previous cross-sectional and longitudinal evidence in associations of physical activity, sedentary time and metabolic risk in the Chinese population.

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Contributions Ming Wu and Chong Shen designed this study. Jie Yang, Jian Su, Yu Qin, Chong Shen, Ying Li, Shurong Lv, Enchun Pan, Yan Gao, Dandan Miao, Ning Zhang, Jinyi Zhou and Ming Wu were responsible for data collection. Yijia Chen analyzed the data and drafted the manuscript. Ming Wu, Yu Qin, Chong Shen, and Enchun Pan revised the manuscript.

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REFERENCES

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome.*The Lancet* 2005;365:1428. https://doi.org/10.1016/S0140-6736(05)66378-7.
2. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome : An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement.*Circulation* 2005;112:2735–2752. https://doi.org/10.1161/CIRCULATIONAHA.105.169404.
3. Li R, Li WC, Lun ZJ, et al. Prevalence of metabolic syndrome in mainland china: a meta-analysis of published studies.*BMC Public Health* 2016;16:296. https://doi.org/10.1186/s12889-016-2870-y.
4. Lu B, Yang HC, Song XY, et al. An evaluation of the International Diabetes Federation definition of metabolic syndrome in Chinese patients older than 30 years and diagnosed with type 2 diabetes mellitus.*Metabolism* 2006;55: 1088-1096. https://doi.org/10.1016/j.metabol.2006.04.003.
5. Laaksonen DE. Metabolic Syndrome and Development of Diabetes Mellitus: Application and Validation of Recently Suggested Definitions of the Metabolic Syndrome in a Prospective Cohort Study.*Am J Epidemiol* 2002;156:1070-1077. https://doi.org/10.1093/aje/kwf145.
6. Lakka HM, Laaksonen DE, Lakka TA, et al. The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-aged Men.*JAMA* 2002;288:2709-2716. https://doi.org/10.1001/jama.288.21.2709.
7. Girman CJ, Rhodes T, Mercuri M, et al. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS).*Am J Cardiol* 2004;93:136-141. https://doi.org/10.1016/j.amjcard.2003.09.028.
8. Lakka TA, Laaksonen DE. Physical activity in prevention and treatment of the metabolic syndrome.*Appl Physiol Nutr Metab* 2007;32:76-88. https://doi.org/10.1139/h06-113.
9. Boulé NG, Haddad E, Kenny GP, et al. Effects of Exercise on Glycemic Control and Body Mass in Type 2 Diabetes Mellitus: A Meta-analysis of Controlled Clinical Trials.*JAMA* 2001;286: 1218 - 1227. https://doi.org/10.1001/jama.286.10.1218.
10. Gordon LA, Morrison EY, McGrowder DA, et al. Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes.*BMC Complement Altern Med* 2008;8:21. https://doi.org/10.1186/1472-6882-8-21. https://doi.org/10.1139/h06-113.
11. Cooper AJM, Brage S, Ekelund U, et al. Association between objectively assessed sedentary time and physical activity with metabolic risk factors among people with recently diagnosed type 2 diabetes.*Diabetologia* 2014;57:73-82. https://doi.org/10.1007/s00125-013-3069-8.
12. Ekelund U, Griffin SJ, Wareham NJ. Physical Activity and Metabolic Risk in Individuals With a Family History of Type 2 Diabetes.*Diabetes Care* 2007;30:337-342. https://doi.org/10.2337/dc06-1883.
13. Kwaśniewska M, Kaczmarczyk-Chałas K, Pikala M, et al. Commuting physical activity and prevalence of metabolic disorders in Poland. *Prev Med* 2010;51:482-487. https://doi.org/10.1016/j.ypmed.2010.09.003.
14. Ng SW, Popkin BM. Time use and physical activity: a shift away from movement across the globe.*Obesity Reviews.* 2012; 13:659-680. https://doi.org/10.1111/j.1467-789X.2011.00982.x.

15. Healy GN, Wijndaele K, Dunstan DW, et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab).*Diabetes Care* 2008;31:369-371. https://doi.org/10.2337/dc07-1795.
16. Knaeps S, De Baere S, Bourgois J, et al. Substituting Sedentary Time With Light and Moderate to Vigorous Physical Activity is Associated With Better Cardiometabolic Health.*J Phys Act Health* 2018;15:197-203. https://doi.org/10.1123/jpah.2017-0102.
17. Cooper AR, Sebire S, Montgomery AA, et al. Sedentary time, breaks in sedentary time and metabolic variables in people with newly diagnosed type 2 diabetes.*Diabetologia* 2012;55:589-599. https://doi.org/10.1007/s00125-011-2408-x.
18. Sedentary Behaviour Research Network. Letter to the editor: standardized use of the terms "sedentary" and "sedentary behaviours".*Appl Physiol Nutr Metab* 2012; 37:540-542. https://doi.org/ 10.1139/h2012-024.
19. Katzmarzyk PT. Physical Activity, Sedentary Behavior, and Health: Paradigm Paralysis or Paradigm Shift?*Diabetes* 2010;59:2717-2725. https://doi.org/10.2337/db10-0822.
20. Troxel WM, Buysse DJ, Matthews KA, et al. Sleep Symptoms Predict the Development of the Metabolic Syndrome.*Sleep* 2010;33:1633-1640. https://doi.org/10.1093/sleep/33.12.1633.
21. Douglas GA, Patrick R. The cost of dichotomising continuous variables.*BMJ* 2006;323:1080. https://doi.org/10.1136/bmj.332.7549.1080.
22. Miao DD, Pan EC, Zhang Q, et al. Development and Validation of a Model for Predicting Diabetic Nephropathy in Chinese People.*Biomed Environ Sci* 2017;30:106-112. https://doi.org/10.3967/bes2017.014.
23. Fan M, lyu J, He P . Chinese guidelines for data processing and analysis concerning the International Physical Activity Questionnaire.*Chin J Epidemiol* 2014;35:961-964. https://doi.org 3760/cma.j.issn.0254-6450.2014.08.019.
24. Bull FC, Masile TS, Armstrong T. Global Physical Activity Questionnaire (GPAQ): Nine Country Reliability and Validity Study.*J Phys Act Health* 2009;6:790-804. https://doi.org/10.1123/jpah.6.6.790.
25. Chu AHY, Ng SHX, Koh D, et al. Domain-Specific Adult Sedentary Behaviour Questionnaire (ASBQ) and the GPAQ Single-Item Question: A Reliability and Validity Study in an Asian Population.*Int J Environ Res Public Health* 2018;15:739. https://doi.org/10.3390/ijerph15040739.
26. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of Physical Activities: an update of activity codes and MET intensities.*Med Sci Sport Exer* 2000;32 suppl 9:S498-S516. https://doi.org/ 0195-913 l/00/3209-0498/0.
27. Wu M, Wen JB, Qin Y, et al. Familial History of Diabetes is Associated with Poor Glycaemic Control in Type 2 Diabetics: A Cross-sectional Study.*Sci Rep* 2017;7:1432. https://doi.org/10.1038/s41598-017-01527-4.
28. Chobanian AV, Bakris GL, Black HR, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.*Hypertension* 2003;42:1206-1252. https://doi.org/10.1161/01.HYP.0000107251.49515.c2.
29. Huang YX, Gao L, Xie XP, et al. Epidemiology of dyslipidemia in Chinese adults: meta-analysis of prevalence, awareness, treatment, and control.*Popul Health Metr* 2014;12:2-9. https://doi.org/10.1186/s12963-014-0028-7.
30. Aiken LS, West SG. Multiple regression: Testing and interpreting interactions. Newbury Park, California: SAGE Publications 1991: 116-137.

31. Chu AHY, Moy FM. Associations of occupational, transportation, household and leisure-time physical activity patterns with metabolic risk factors among middle-aged adults in a middle-income country.*Pre Med* 2013;57:S14-S17. https://doi.org/10.1016/j.ypmed.2012.12.011.
32. Kuwahara K, Honda T, Nakagawa T, et al. Leisure-time exercise, physical activity during work and commuting, and risk of metabolic syndrome.*Endocrine* 2016;53:710–721. https://doi.org/10.1007/s12020-016-0911-z.
33. Wijndaele K, Orrow G, Ekelund U, et al. Increasing objectively measured sedentary time increases clustered cardiometabolic risk: a 6 year analysis of the ProActive study.*Diabetologia* 2014;57:305-312. https://doi.org/10.1007/s00125-013-3102-y.
34. Carr DB, Utzschneider KM, Hull RL, et al. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome.*Diabetes* 2004;53:2087–2094. https://doi.org/10.2337/diabetes.53.8.2087.
35. Vella CA, Allison MA, Cushman M, et al. Physical Activity and Adiposity-related Inflammation: The MESA.*Med Sci Sports Exerc* 2017;49:915-921. https://doi.org/10.1249/MSS.0000000000001179.
36. Stamatakis E, Pulsford RM, Brunner EJ, et al. Sitting behaviour is not associated with incident diabetes over 13 years: the Whitehall II cohort study.*Br J Sports Med* 2017;51:818-823. https://doi.org/10.1136/bjsports-2016-096723.
37. Ekelund U, Brage S, Besson H, et al. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality?*Am J Clin Nutr* 2008;88:612–617. https://doi.org/10.1093/ajcn/88.3.612.
38. Mekary RA, Willett WC, Hu FB, et al. Isotemporal substitution paradigm for physical activity epidemiology and weight change.*Am J Epidemiol* 2009;170:519–527. https://doi.org/10.1093/aje/kwp163.
39. Pearson N, Biddle SJ. Sedentary behavior and dietary intake in children, adolescents, and adults. A systematic review.*Am J Prev Med* 2011;41:178–188. https://doi.org/10.1016/j.amepre.2011.05.002.
40. Matthews CE, Chen KY, Freedson PS, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004.*Am J Epidemiol* 2008;167:875-881. https://doi.org/10.1093/aje/kwm390.
41. Yates T, Khunti K, Wilmot EG, et al. Self-reported sitting time and markers of inflammation, insulin resistance, and adiposity.*Am J Prev Med* 2012;42:1-7. https://doi.org/10.1016/j.amepre.2011.09.022.
42. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes.*Nature* 2006;444:840-846. https://doi.org/10.1038/nature05482.
43. Rafalson L, Donahue RP, Stranges S, et al. Short sleep duration is associated with the development of impaired fasting glucose: the Western New York Health Study.*Ann Epidemiol* 2010;20:883-889. https://doi.org/10.1016/j.annepidem.2010.05.002.
44. Clays E, De Bacquer D, Van Herck K, et al. Occupational and leisure time physical activity in contrasting relation to ambulatory blood pressure.*BMC Public Health* 2012;12:1002. https://doi.org/10.1186/1471-2458-12-1002.
45. Eicher JD, Maresh CM, Tsongalis GJ, et al. The additive blood pressure lowering effects of exercise intensity on post-exercise hypotension.*Am Heart J* 2010;160:513-520. https://doi.org/10.1016/j.ahj.2010.06.005.
46. Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events placing the

risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology.*Circulation* 2007;115:2358-2368. https://doi.org/10.1161/CIRCULATIONAHA.107.181485.

47. Brett SE, Ritter JM, Chowienczyk PJ. Diastolic blood pressure changes during exercise positively correlate with serum cholesterol and insulin resistance.*Circulation* 2000;101:611-615.
48. American Diabetes Association. 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018.*Diabetes care* 2018;41 Suppl 1:S38-S50. https://doi.org/ 10.2337/dc18-S004。
49. Skender S, Ose J, Chang-Claude J, et al. Accelerometry and physical activity questionnaires-a systematic review.*BMC Public Health* 2016;16:515. https://doi.org/10.1186/s12889-016-3172-0.

Fig 1. Means of clustered metabolic risk score by sedentary time and physical activity among 17 750 diabetic patients. The adjusted mean was calculated by using general linear regression models after adjustment for age. For physical activity, in men, the cut-off values for defining low, moderate, and high tertile groups were 4.00 and 11.14 MET-h/d for men and 4.57 and 12.00 MET-h/d for women. For sedentary time, the 4 groups by quartiles of sedentary time were ＜2.2, 2.3-3.3, 3.4-4.9 and ⩾5.0 h/d for men and ＜ 2.2, 2.3-3.3, 3.4-4.4 and ⩾ 4.5 h/d for women. MET, metabolic equivalent task.

Table 1 Demographic, metabolic characteristics of participants

characteristic	Men	Women	Total	P value
n	7041	10709	17750	
Age(years)	62.6 ± 9.9	62.8 ± 9.7	62.8 ± 9.8	0.11
High school or above (%)	17.7	4.5	9.8	<0.001
Annual income>40000￥(%)	64.8	57.0	60.1	<0.001
Body mass index(Kg/m^2)	25.3 ± 3.2	25.4 ± 3.6	25.3 ± 3.4	0.09
Waist circumference (cm)	87.9 ± 9.4	85.5 ± 9.5	86.4 ± 9.5	<0.001
Systolic blood pressure (mmHg)	147.3 ± 19.8	148.9 ± 21.1	148.0 ± 20.6	0.002
Diastolic blood pressure (mmHg)	83.7 ± 10.7	79.9 ± 10.4	81.4 ± 10.6	<0.001
Triacylglycerol (mmol/L)*	1.4 (1.0, 2.2)	1.7 (1.2, 2.3)	1.6 (1.1, 2.3)	<0.001
HDL-cholesterol (mmol/L)	1.4 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	<0.001
Fasting plasma glucose (mmol/L)*	8.2 (6.4, 10.2)	8.0 (6.5, 9.9)	8.1 (6.6, 10.0)	<0.001
HbA1c(mmol/mol) *	56.3 (46.5, 70.5)	55.2 (46.5, 68.3)	55.2 (46.5, 69.4)	<0.001
Diabetes duration (years) *	5 (2, 9)	5 (2, 9)	5 (2, 9)	0.26
Smoking (%)	46.0	6.2	22.0	<0.001
alcohol drinking (%)				
never	49.1	96.6	77.7	<0.001
former	10.7	1.1	4.9	<0.001
current	40.1	2.3	17.4	<0.001
On glucose-lowering medication (%)	78.7	78.4	78.5	0.60
On lipid-lowering medication (%)	5.8	5.9	6.0	0.005
On antihypertensive medication (%)	52.7	53.9	53.4	0.002
Hypertension (%)	77.5	76.6	77.0	0.16

Dyslipidemia (%)	46.1	49.3	48.0	<0.001
Total physical activity (MET-h/d) *	6.3 (2.3, 14.3)	8.0 (3.4, 16.0)	8.0 (2.9, 15.4)	<0.001
Physical activity domains (MET-h/d) †				
Occupational	68.2 [2.9 (0.0, 8.6)]	81.9 [5.1 (1.7, 12.0)]	76.5 [4.0 (0.6, 12.0)]	<0.001‡
Commuting	59.4 [1.1 (0.0, 1.3)]	62.0 [1.0 (0.0, 2.9)]	60.1 [1.0 (0.0, 2.9)]	<0.001‡
Leisure-time	25.6 [3.1 (1.7, 6.0)]	19.0 [2.9(1.5, 5.1)]	21.6 [3.0 (1.7, 5.7)]	<0.001‡
Sedentary time (h/d)	3.5 ± 2.5	3.4 ± 2.6	3.4 ± 2.5	<0.001
Sleep duration (h/d)	7.4 ±1.6	7.3 ± 1.7	7.4 ± 1.7	<0.001

Data are means±SD unless stated otherwise

* Median (IQR)

† (%) [Median (IQR)]

‡ P values are from chi-square test

P values are from Student's t-test or Mann-Whitney U test for continuous variables and from chi-squared test for categorical variables.

Table 2 Adjusted means(SE) of metabolic variables by quartile of physical activity and sedentary time

Metabolic risk	Total physical activity (MET h/day)					Sedentary time(h/d)				
	Quartile 1 (<2.9)	Quartile 2 (2.9-8.0)	Quartile 3 (8.1-15.4)	Quartile 4 (>15.4)	P for trend	Quartile 1 (<2.2)	Quartile 2 (2.2-3.3)	Quartile 3 (3.4-4.4)	Quartile 4 (>4.5)	P for trend
zMS¶	0.28(0.04) †, ‡, §	0.01(0.04) *, §	-0.11(0.05) *	-0.21(0.04) *, †	<0.001	-0.16(0.03) ‡, §	-0.07(0.10) §	0.004(0.03) *, §	0.29(0.04) *, †, ‡	<0.001
Waist circumference (cm)	87.19(0.14) †, ‡, §	86.56(0.13) *, §	86.13(0.16) *	85.76(0.14) *, †	<0.001	85.98(0.11) §	86.25(0.16)	86.57(0.20) §	87.30(0.14) *, ‡	<0.001
Fasting plasma glucose (mmol/L)**	2.13(0.005) ‡	2.12(0.005) ‡	2.10(0.005) *, ‡	2.12(0.005)	0.427	2.11(0.004) §	2.10(0.012) §	2.12(0.005) §	2.14(0.005) *, †, ‡	<0.001
Triacylglycerol(mmol/L)**	0.54(0.008) †, ‡, §	0.50(0.008) *, §	0.48(0.009) *	0.45(0.008) *, †	<0.001	0.46(0.006) ‡, §	0.47(0.021) §	0.50(0.008) *, §	0.54(0.009) *, †, ‡	<0.001
HDL-cholesterol (mmol/L)	1.45(0.01) †, ‡, §	1.49(0.01) *, §	1.50(0.01) *	1.52(0.01) *, †	<0.001	1.51(0.01) ‡, §	1.48(0.01) §	1.48(0.01) *, §	1.46(0.01) *, †, ‡	<0.001
Systolic blood pressure (mmHg)	148.26(0.30)	147.91(0.28)	147.80(0.34)	148.05(0.30)	0.651	148.08(0.23)	147.56(0.33)	147.87(0.42)	148.35(0.30)	0.326

Date are mean (SE) values for each quartile of physical activity and sedentary time, adjusted for age and sex by using general linear regression models. Test for trend based on variable containing median value for each quartiles. Multiple comparison between the groups was performed using Bonferroni method:

* significantly different compared with Quartile 1 (P< 0.05)

† significantly different compared with Quartile 2 (P< 0.05)

‡ significantly different compared with Quartile 3 (P< 0.05)

§ significantly different compared with Quartile 4 (P< 0.05)

¶ zMS is a continuously distribute variable for clustered metabolic risk calculated by summing gender-specific standardized values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

** Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution

Table 3 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables

	Physical activity (per-SD) ‡				Sedentary time
Metabolic risk	Total	Occupational	Commuting	Leisure-time	(per-SD) ‡
zMS†					
Model 1	-0.147(-0.187, -0.108)***	-0.132(-0.171,-0.093)***	-0.047(-0.086,-0.007)*	-0.068(-0.107,-0.029)**	0.188(0.148, 0.227)***
Model 2	-0.091(-0.126, -0.057)***	-0.077(-0.111,-0.042)***	-0.013(-0.047, 0.021)	-0.044(-0.078,-0.010)*	0.128(0.094, 0.162)***
Model 3	-0.080(-0.115, -0.046)***	-0.066(-0.101,-0.031)***	-0.011(-0.045, 0.022)	-0.042(-0.076,-0.008)*	0.121(0.087, 0.155)***
Model 4	-0.080(-0.114, -0.046)***	-0.066(-0.101,-0.031)***	-0.011(-0.045, 0.023)	-0.041(-0.075,-0.007)*	0.117(0.083, 0.151)***
Waist circumference (cm)					
Model 1	-0.552(-0.692, -0.412)***	-0.625(-0.765,-0.485)***	0.096(-0.044, 0.237)	-0.026(-0.167, 0.114)	0.575(0.435, 0.715)***
Model 2	-0.495(-0.635, -0.355)***	-0.519(-0.661,-0.376)***	0.021(-0.118, 0.161)	-0.051(-0.191, 0.089)	0.525(0.386, 0.663)***
Model 3	-0.450(-0.591, -0.309)***	-0.475(-0.618,-0.332)***	0.028(-0.112, 0.167)	-0.042(-0.182, 0.098)	0.483(0.344, 0.623)***
Model 4	-0.449(-0.591, -0.308)***	-0.475(-0.620,-0.334)***	0.030(-0.109, 0.170)	-0.039(-0.179, 0.102)	0.474(0.334, 0.613)***
Fasting plasma glucose(mmol/L) §					
Model 1	0.005(0.000, 0.010)	0.007(0.002, 0.012)**	-0.005(-0.010, 0.000)	-0.001(-0.006, 0.004)	0.011(0.006, 0.016)***
Model 2	0.003(-0.002, 0.007)	0.005(-0.001, 0.009)	-0.001(-0.005, 0.004)	-0.002(-0.007, 0.002)	0.008(0.004, 0.013)***
Model 3	0.004(-0.001, 0.008)	0.005(-0.001, 0.010)	-0.001(-0.005, 0.004)	-0.002(-0.007, 0.003)	0.009(0.004, 0.013)***
Model 4	0.004(-0.001, 0.008)	0.005(-0.001, 0.009)	-0.001(-0.005, 0.004)	-0.002(-0.006, 0.003)	0.008(0.003, 0.013)***
Triacylglycerol (mmol/L) §					
Model 1	-0.022(-0.030, -0.013)***	-0.017(-0.025,-0.009)**	-0.015(-0.024,-0.007)***	-0.020(-0.019,-0.003)**	0.031(0.023, 0.039)***
Model 2	-0.014(-0.021, -0.007)***	-0.009(-0.015,-0.002)*	-0.012(-0.019,-0.005)***	-0.007(-0.014,-0.001)*	0.017(0.010, 0.024)***
Model 3	-0.012(-0.019, -0.006)***	-0.007(-0.014,-0.001)*	-0.012(-0.019,-0.005)***	-0.006(-0.013, 0.001)	0.016(0.009, 0.023)***
Model 4	-0.012(-0.019, -0.006)***	-0.007(-0.014,-0.001)*	-0.012(-0.019,-0.005)***	-0.006(-0.013, 0.001)	0.015(0.008, 0.022)***
HDL-cholesterol (mmol/L)					
Model 1	0.015(0.009, 0.022)***	0.016(0.009, 0.022)**	0.002(-0.005, 0.008)	0.003(-0.004, 0.009)	-0.019(-0.025, -0.012)***

Model 2	0.010(0.004, 0.016)***	0.007(0.001, 0.013)*	0.003(-0.003, 0.009)	0.007(-0.001, 0.013)	-0.008(-0.014, -0.002)*
Model 3	0.009(0.003, 0.015)***	0.006(0.001, 0.013)*	0.003(-0.003, 0.009)	0.007(-0.001, 0.013)	-0.007(-0.013, -0.001)*
Model 4	0.009(0.003, 0.015)***	0.006(0.001, 0.013)*	0.003(-0.003, 0.009)	0.007(-0.001, 0.013)	-0.007(-0.013, -0.001)*
Systolic blood pressure (mmHg)					
Model 1	-0.907(-1.209, -0.604)***	-0.625(-0.928, -0.322)***	-0.549(-0.852,-0.246)***	-0.871(-1.174,-0.568)***	0.340(0.037, 0.643)*
Model 2	-0.110(-0.359, 0.139)	0.065(-0.187, 0.317)	-0.212(-0.459, 0.034)	-0.300(-0.548,-0.052)*	0.224(-0.022, 0.470)
Model 3	-0.091(-0.341, 0.159)	0.084(-0.169, 0.337)	-0.210(-0.456, 0.037)	-0.296(-0.544,-0.048)*	0.216(-0.031, 0.462)
Model 4	-0.096(-0.346, 0.155)	0.081(-0.173, 0.334)	-0.219(-0.466, 0.028)	-0.293(-0.542,-0.045)*	0.215(-0.033, 0.462)

Regression results are presented as unstandardized coefficients (B) (95%CI)

† zMS is a continuously distribute variable for clustered metabolic risk calculated by summing gender-specific standardized values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

‡ Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.2 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

All models (except model 1) are adjusted for age, sex, education, annual household income, smoking status, drinking and diabetes duration. All outcomes except zMS and waist circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of glucose-lowering medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing drugs (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of glucose-lowering medication (yes/no), lipid-lowing medication (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

Model 3 is adjusted for remaining physical activity and sedentary time as appropriate; Model 4 is additional adjusted for sleep duration

§ Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution.

*P＜0.05; **P＜0.01; **P＜0.001

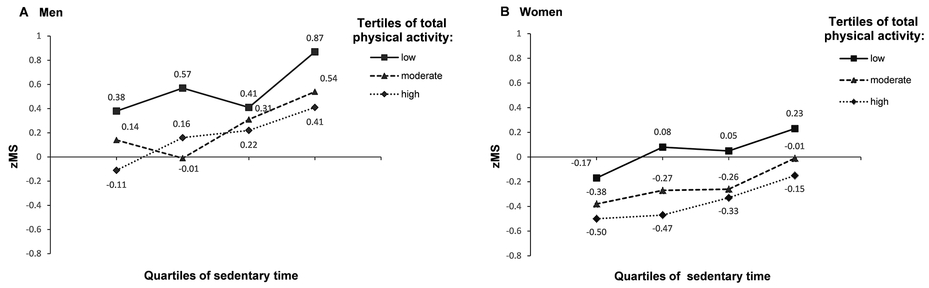

Fig 1. Means of clustered metabolic risk score by sedentary time and physical activity among 17 750 diabetic patients. The adjusted mean was calculated by using general linear regression models after adjustment for age. For physical activity, in men, the cut-off values for defining low, moderate, and high tertile groups were 4.00 and 11.14 MET-h/d for men and 4.57 and 12.00 MET-h/d for women. For sedentary time, the 4 groups by quartiles of sedentary time were $<$2.2, 2.3-3.3, 3.4-4.9 and ≥5.0 h/d for men and $<$2.2, 2.3-3.3, 3.4-4.4 and ≥4.5 h/d for women. MET, metabolic equivalent task.

42x15mm (600 x 600 DPI)

Table S1. Classification table of physical activity and sedentary behaviour

Physical activity in Farm work, occupation and household chores		**Physical activity in leisure-time**		**Static behavior**
Moderate-intensity physical activity (4 MET h/d) Make breathing and heart beat slightly faster	**Vigorous-intensity physical activity (8 MET h/d)** Make breathing and heart rate significantly faster	**Moderate-intensity physical activity (4 MET h/d)** Make breathing and heart beat slightly faster	**Vigorous-intensity physical activity (8 MET h/d)** Make breathing and heart rate significantly faster	Lying, sitting and leaning besides sleep time (h/d)
·**Cleaning**(e.g. vacuuming, mopping the floor, polishing floor, wiping the desk, sweeping the floor, ironing clothes) ·**Washing** (e.g. scrubbing the carpet, washing clothes) ·**Gardening** (e.g. watering, turning soil, fertilizing) ·**Hand milking** ·**Hand knitting** ·**carpenter work** (e.g. sawing cork，Chiseling cork) ·**With a shovel and other tools to mix the sand and cement** ·**Walking with a general weight**	·**Forestry workers** (felling and handling timber) ·**Sawing ironwood** ·**tilling land** ·**transplant rice seedlings** ·**harvesting crops** (e.g. wheat, rice, sugarcane) ·**Gardening** (e.g. digging, carrying heavy things) ·**hand milling** (with wooden club or stone mill) ·**architectural work** (e.g. building a wall, handing building materials) ·**Fitness Trainer** (e.g. spinning, aerobics, yoga and some other aerobic exercise) ·**A courier on foot or bike**	·**biking** ·**jogging** ·**dancing** ·**reading a horse** ·**practicing Tai chi** ·**Practicing Yoga and pilates** ·**doing the yangko dance**	·**Long-distance running** ·**playing football** ·**playing rugby** ·**playing tennis** ·**spinning in gym** ·**Lifting barbell** ·**doing ballet** ·**swimming**	·**working** ·**studying** ·**reading** ·**watching TV** ·**using computer** ·**riding** ·**taking a rest**

·Carrying water **·Grazing**	**·Pulling a rickshaw**			

Table S2. Baseline characteristics of those included and excluded participants.

characteristics	Included participants	excluded participants	P
n	17750	2303	
Sex, n(%)			
Male	7041(39.7)	821(35.6)	<0.001
Age(years)	62.76±9.78	63.76±10.27	<0.001
BMI(Kg/m^2)	25.32±3.44	25.45±3.67	0.101
Waist circumference (cm)	86.43±9.53	84.97±13.80	<0.001
Systolic blood pressure (mmHg)	148.01±20.59	142.62±35.61	<0.001
Diastolic blood pressure (mmHg)	81.41±10.63	82.11±10.76	0.004
Triacylglycerol (mmol/L) *	1.57(1.11, 2.26)	1.61(1.16, 2.36)	0.004
HDL-cholesterol (mmol/L)	1.49±0.43	1.49±0.48	0.576
Fasting plasma glucose (mmol/L) *	8.07(6.60, 10.01)	8.00(6.34, 10.56)	0.576
HbA1c (%)*	7.20(6.4, 8.5)	7.4(6.4, 9.0)	<0.001
Diabetes duration (years) *	5(2, 9)	4(1, 8)	<0.001

Data are means±SD unless stated otherwise ; *Median (IQR)

P values are from one-way analysis or Mann-Whitney U test for continuous variables and from chi-squared test for categorical variables.

Table S3 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables, stratified by sex and age

Variables	zMS†	Waist circumference (cm)	Fasting plasma glucose (mmol/L) §	Triacylglycerol (mmol/L) §	HDL-cholesterol (mmol/L)	Systolic blood pressure (mmHg)
Total physical activity (per-SD) ‡						
Sex						
Men	-0.108***	-0.550***	0.001	-0.019***	0.015**	0.101
Women	-0.046*	-0.312**	0.007*	-0.006	0.003	-0.340
P-interaction	0.335	0.248	0.261	0.222	0.111	0.400
Age(years)						
＜55	-0.112***	-0.513***	0.001	-0.019**	0.011*	1.161
55~	-0.039	-0.204	0.007	-0.008	0.011*	-0.063
65~	-0.120**	-0.852***	-0.002	-0.015*	0.014*	-0.121
≥75	-0.288***	-1.359***	-0.025	-0.019	0.002	-0.027
P-interaction ¶	**0.073**	**0.007**	0.110	0.771	0.511	0.386
Occupational physical activity (per-SD) ‡						
Sex						
Men	-0.089***	-0.565***	0.003	-0.016**	0.013**	0.270
Women	-0.040*	-0.358**	0.008	0.001	-0.001	-0.171
P-interaction	0.452	0.294	0.349	0.165	0.560	0.440
Age(years)						
＜55	-0.098**	-0.463***	0.003	-0.017**	0.004	0.260
55~	-0.030	-0.258*	0.007	-0.003	0.008	0.095
65~	-0.137***	-0.961***	-0.002	-0.010	0.024**	0.353
≥75	-0.199*	-1.264***	-0.036*	0.024	-0.014	0.235
P-interaction ¶	**0.092**	**0.003**	0.132	0.185	0.761	0.129

Commuting physical activity (per-SD) ‡						
Sex						
Men	-0.036	0.032	-0.002	-0.017**	0.002	-0.234
Women	0.016	0.063	0.001	-0.006	0.003	-0.177
P-interaction	0.092	0.669	0.418	0.057	0.892	0.946
Age(years)						
＜55	0.042	0.075	-0.001	0.006	0.008	-0.032
55~	-0.008	0.109	-0.001	-0.015*	0.001	-0.207
65~	0.007	0.027	0.004	-0.009	-0.003	-0.393
≥75	-0.127*	-0.326	0.003	-0.037**	0.024*	0.162
P-interaction ¶	0.306	0.517	0.525	0.301	0.222	0.836
Leisure-time physical activity (per-SD) ‡						
Sex						
Men	-0.043	-0.052	-0.003	-0.003	0.005	-0.349*
Women	-0.039	-0.025	0.001	-0.008	0.008	-0.247
P-interaction	0.699	0.734	0.464	0.368	0.677	0.930
Age(years)						
＜55	-0.085*	-0.152	-0.002	-0.013	0.017**	-0.175
55~	-0.022	0.100	0.001	-0.007	0.008	-0.187
65~	-0.005	-0.071	-0.005	0.002	0.011	-0.610*
≥75	-0.068	-0.326	-0.002	-0.012	-0.010	-0.492
P-interaction ¶	0.964	0.502	0.380	0.886	0.320	0.170
Sedentary time (per-SD) ‡						
Sex						
Men	0.088**	0.327**	0.011**	0.020**	-0.004	0.030

Women	0.130***	0.540***	0.006*	0.010*	-0.008*	0.328*
P-interaction	0.541	0.330	0.237	0.035	0.793	0.268
Age(years)						
＜55	0.059	0.144	0.006	0.017*	-0.018**	-0.261
55~	0.108***	0.428***	0.006	0.015**	-0.005	0.438*
65~	0.172***	0.723***	0.015***	0.014*	-0.001	0.259
≥75	0.101*	0.684**	-0.005	0.006	-0.007	0.276
P-interaction ¶	0.143	**0.001**	0.774	0.190	0.252	0.291

Regression results are presented as unstandardized coefficients (B)

†zMS is a continuously distribute variable for clustered metabolic risk calculated by summing gender-specific standardized values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

‡ Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.3 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

Adjusted for age, sex, education, annual household income, smoking, drinking, diabetes duration, physical activity and sedentary time as appropriate (different domain of physical activity is adjusted for the other two physical activities), sleep duration. All outcomes except zMS and waist circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of glucose-lowering medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing medication (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of glucose-lowering medication (yes/no), lipid-lowing medication (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

§ Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution.

¶ P-interaction calculated using age as a continuous variable.

*P＜0.05; **P＜0.01; ***P＜0.001

Table S4 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables

Metabolic risk	Physical activity (per-SD) †				Sedentary time (per-SD) †
	Total	Occupational	Commuting	Leisure-time	
zMS‡					
Model 1	-0.087(-0.120, -0.054)***	-0.067(-0.100,-0.033)***	-0.054(-0.088,-0.021)**	-0.058(-0.091,-0.025)**	0.131(0.097, 0.164)***
Model 2	-0.050(-0.079, -0.021)***	-0.033(-0.063,-0.004)*	-0.019(-0.048, 0.010)	-0.038(-0.067,-0.010)*	0.085(0.056, 0.113)***
Model 3	-0.050(-0.079, -0.021)***	-0.026(-0.055, 0.003)	-0.018(-0.047, 0.011)	-0.037(-0.066,-0.008)*	0.082(0.053, 0.110)***
Model 4	-0.043(-0.072, -0.014)***	-0.026(-0.056, 0.003)	-0.018(-0.047, 0.011)	-0.036 (-0.065,-0.007)*	0.078(0.049, 0.107)***

Regression results are presented as unstandardized coefficients (B) (95%CI)

† Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.2 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

‡ Delete the waist circumference to calculate new clustered metabolic score.

All models (except model 1) are adjusted for age, sex, education, annual household income, smoking status, drinking and diabetes duration. All outcomes except zMS and waist Circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of diabetes medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing medication (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of diabetes medication (yes/no), lipid-lowing drugs (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

Model 3 is adjusted for remaining physical activity and sedentary time as appropriate; Model 4 is additional adjusted for sleep duration.

*P < 0.05; **P < 0.01; **P < 0.001

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Physical activity, sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province: A cross-sectional study

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Physical activity, sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province: A cross-sectional study

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ABSTRACT

Objective Investigating the association between total physical activity, physical activity in different domains, and sedentary time with clustered metabolic risk in patients with type 2 diabetes from Jiangsu Province, China.

Design Interview-based cross-sectional study conducted between December 2013 and January 2014.

Setting 44 selected townships across two cities, Changshu and Huai'an, in Jiangsu Province.

Participants 20,340 participants selected using stratified cluster-randomised sampling and an interviewer-managed questionnaire.

Methods We constructed clustered metabolic risk by summing sex-specific standardised values of waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure, and the inverse of blood high-density lipoprotein cholesterol (HDL-cholesterol). Self-reported total physical activity included occupation, commuting, and leisure-time physical activity. The un-standardised regression coefficient [B] and its 95% confidence interval (CI) were calculated using multivariate linear regression analyses.

Results This study included 17,750 type 2 diabetes patients (aged 21-94 years, 60.3% female). The total (B=-0.080; 95% CI: -0.114, -0.046), occupational (B=-0.066; 95% CI: -0.101, -0.031) and leisure-time physical activity (B=-0.041; 95% CI: -0.075, -0.007), and sedentary time (B=0.117; 95% CI: 0.083, 0.151) were associated with clustered metabolic risk. Total physical activity, occupational physical activity, and sedentary time were associated with waist circumference, triacylglycerol, and HDL-cholesterol, but not with systolic blood pressure. Commuting physical activity and sedentary time were significantly associated with triacylglycerol (B=-0.012; 95% CI: -0.019, -0.005) and fasting plasma glucose (B=0.008; 95% CI: 0.003, 0.01), respectively. Leisure-time physical activity was only significantly associated with systolic blood pressure (B=-0.239; 95% CI: -0.542, -0.045).

Conclusions Total, occupational and leisure-time physical activity were inversely associated with clustered metabolic risk, whereas sedentary time increased metabolic risk. Commuting physical activity was inversely associated with triacylglycerol. These findings suggest that increased physical activity in different domains and decreased sedentary time may have a protective effect against metabolic risk in type 2 diabetes patients.

Strengths and limitations of this study

- ▸This study constructed clustered metabolic risk by summing sex-specific standardised values for waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure, and the inverse of HDL- cholesterol.
- ▸The study has a relatively large sample size of 17,750 participants, all of whom are community-managed patients with type 2 diabetes in China.
- ▸The study investigated physical activity in different domains and sedentary time and their associations with metabolic risk factors.
- ▸The limitation of this study was that information regarding physical activity and sedentary time was collected through the use of a self-reporting questionnaire.

INTRODUCTION

The clustering of metabolic risk factors for cardiovascular disease and type 2 diabetes mellitus is known as metabolic syndrome.[1] Based on the National Cholesterol Education Program definition,[2] metabolic syndrome is a rapidly growing epidemic in China. A meta-analysis estimated that the pooled prevalence of metabolic syndrome in mainland China was 24.5 %,[3] but was 55.7% among patients with type 2 diabetes.[4] Individuals with metabolic syndrome were found to be at an increased risk of developing diabetes, cardiovascular disease, and all-cause mortality.[5-7] This increasing prevalence among Chinese populations and its severe health consequences has led to a call for prevention and maintenance strategies, and the improvement of metabolic health in one of the largest populations in the world.

Physical activity has long been considered a key factor in the prevention and management of metabolic risk factors.[8] A number of studies have investigated the association between physical activity and glycemic control,[9] lipid profile,[10] and clustered metabolic risk.[11 12] Most emphasised the value of assessing overall physical activity or leisure-time physical activity,[9-12] but few have focused on other domains of physical activity (e.g. occupational, household or commuting).[13] Information on different domains of physical activity may be crucial for Chinese people since they have been found to have quite different patterns of physical activity compared to their Western counterparts. For example, it has been reported that occupational and household activities contribute substantially more to total physical activity than leisure-time or transportation activity.[14] Therefore, it is important to examine whether

other types of physical activities, such as occupational and commuting physical activity, are associated with metabolic risk among diabetic patients.

Emerging evidence also suggests that excess sedentary time is positively associated with metabolic risk factors, an effect that is independent of physical activity levels.[15-17] Sedentary behaviours have been defined as any waking behaviour that is in a sitting, reclining, or lying down posture, expending little energy (i.e. 1.0 to 1.5 metabolic equivalents).[18] Some studies have found that the cellular and molecular responses to sedentary time are different to the beneficial responses to physical activity.[19] Therefore, it is essential to explore the effects of physical activity and sedentary time simultaneously, when exploring the associations between physical activity and sedentary time with metabolic risk factors. It is also crucial to elucidate whether this association is independent of sleep duration, which might confound results.[20]

Furthermore, it has been suggested that using the continuous summary score of clustered metabolic risk (zMS)[11] for analyses may improve the statistical power to detect associations, compared to using a binary definition of dichotomising continuous outcome variables.[21] Many studies have focused on the risk of metabolic syndrome in Western populations,[9-13 15 16] but the relationship between physical activity and sedentary time with the risk of metabolic syndrome is not well understood among Chinese populations. Although there have been a few studies in diabetic populations, their findings were inconsistent and limited by small sample sizes.[10 11 17] Therefore, it is interesting to explore the direction and strength of

associations between physical activity and sedentary time with clustered metabolic risk factors among the Chinese population.

The objective of this study was to examine the association between total physical activity, physical activity in different domains (i.e. occupation, commuting and leisure-time physical activity), and sedentary time with clustered and individual metabolic risk factors among Chinese patients with type 2 diabetes. We hypothesised that physical activity is inversely associated with clustered and individual metabolic risk factors, whereas sedentary time increases such risk.

METHODS

Participants

Participants were from the "Comprehensive Research on the Prevention and Control of the Diabetes" project. The method and study design have been previously described.[22] Briefly, 29,705 registered diabetic patients, receiving management from National Basic Public Health Service, were recruited from 44 selected townships across two cities in Jiangsu Province, China. After excluding non-type 2 diabetic patients, and individuals with poor physical or mental status, a total of 20,340 individuals consented to participate. In our analyses, we further excluded those with missing physical activity or sedentary time values (n = 2,038), those who reported spending ≥16 hours on daily physical activity (n = 67),[23] and those with incomplete metabolic risk data (n = 198). Finally, there were 17,750 participants included in the analyses.

Assessment of physical activity and sedentary time

Information on physical activity and sedentary time was collected using the Global Physical Activity Questionnaire (GPAQ). The validity and reliability of GPAQ has been assessed in Western[24] and Asian populations.[25] Participants were asked to recall the intensity and duration of occupational, commuting, and leisure-time physical activities over the previous weeks.

The intensity of activities was defined as moderate or vigorous by metabolic equivalent (MET).[26] Average MET scores were calculated based on specific activities within corresponding categories to estimate activity intensity (Table S1). The number of hours spent per day on each measured activity was multiplied by the corresponding average MET score and the measured activity frequency (days per week). Total physical activity was calculated by adding together the MET-hours for activities related to occupational, commuting, and leisure-time domains. The average daily activity was calculated by dividing the weekly amount of physical activities by seven. Participants were also asked about their normal time spent on sedentary activities and sleep (hours/day).

Clustered metabolic risk score

We constructed a summary variable (clustered metabolic risk score, zMS) for clustered metabolic risk[11] that was broadly based on the definition proposed by Adult Treatment Panel III (ATP III).[2] This variable was calculated by adding the standardised values for waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure, and the inverse of HDL-cholesterol. Each of these variables was standardised by subtracting the sex-specific sample means from the

individual mean and dividing by the standard deviations (SD). The zMS is a continuous variable with a mean of zero, by definition, with lower scores revealing a more favourable profile.

Assessment of anthropometric, metabolic risk factors

Face-to-face questionnaire interviews were also used to collect information on demographic characteristics, medical history, medications, smoking status, alcohol consumption, and adult socioeconomic status. The detail of anthropometric measurements have been previously illustrated.[27] Blood samples were collected in the morning following overnight fasting. Fasting plasma glucose was assessed using the Hexokinase method. Glycated haemoglobin (HbA_{1c}) was measured in venous samples using high efficiency liquid chromatography. Serum cholesterol, HDL-cholesterol, and triacylglycerol were measured enzymatically. All samples were analysed by KingMed Diagnostics (Jiangsu Cultural Industrial Park, Nanjing, China).

Covariate definitions

Covariates included age, sex, education (no formal education, primary-, middle-, high school or above), smoking status (yes, no), annual household income (<30 000 RMB, 40 000-100 000 RMB, 110 000-150 000 RMB, >160 000 RMB), alcohol consumption (never, former, current), diabetes duration, taking medications to lower glucose, and lipid or blood pressure (yes, no, unclear). Hypertension was defined as a systolic blood pressure ≥ 140 mm Hg and/or a diastolic blood pressure ≥ 90 mm Hg, or a previous hypertension diagnosis in a hospital.[28] Dyslipidemia was defined as having at least one of the following conditions: total cholesterol ≥5.2 mmol/L, fasting blood

triglyceride ≥1.7 mmol/L, fasting blood low-density lipoprotein cholesterol ≥3.4 mmol/L, HDL-cholesterol <0.9 mmol/L for males or < 1.0 mmol/L for females, or previously being diagnosed with hyperlipidemia in a hospital.[29] Sleep duration was assessed by the question "How many cumulative hours do you have for sleep on an average day?"

Statistical analyses

Descriptive statistics were conducted separately for men and women using the mean ± SD, median (interquartile range [IQR]) or frequencies. The Chi-square (χ^2) test, Student's t-test, one-way analysis of variance (ANOVA), and Mann-Whitney U test were used to examine characteristics differences between men and women. Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution. Adjusted means and standard errors (SE) of clustered and individual metabolic risk variables were presented to explore the association between physical activity and sedentary time with metabolic risk. Test for trend was based on variables containing median value for each quartiles. Multiple comparisons among groups were performed using a Bonferroni method.

Associations between per 1-SD of total physical activity, different domains of physical activity (occupational, commuting and leisure-time), and sedentary time with total clustered metabolic risk score and individual metabolic risk factors were evaluated using multivariate linear regression. Preliminary checks were conducted to ensure no violation of assumptions of normality, homogeneity of variance, and absence of multicollinearity. Four models were fitted: Model 1 was unadjusted; Model

2 was adjusted for age, sex, education, annual household income, smoking status, drinking, and diabetes duration; Model 3 was additionally adjusted for remaining physical activity and sedentary time, for each individual domain of physical activity was adjusted for the other physical activity domains and sedentary time as appropriate; Model 4 was further adjusted for sleep duration. For Models 2 to 4, all subcomponents except zMS and waist circumference were additionally adjusted for waist circumference. When the dependent variable was fasting plasma glucose, we additionally adjusted for the use of glucose-lowering medication. For triacylglycerol and HDL-cholesterol, we adjusted for the diagnosis of dyslipidemia and use of lipid-lowering medication. When the outcome of interest was systolic blood pressure, we additionally adjusted for the diagnosis of hypertension and use of antihypertensive medication. For zMS we adjusted for the use of glucose-lowering, lipid-lowering, or antihypertensive medications, and the diagnosis of dyslipidemia and hypertension.

To investigate the joint associations of total physical activity and sedentary time with clustered metabolic risk, participants were classified into three and four groups of sex-specific tertiles of physical activity and quartiles of sedentary time, respectively. The adjusted zMS mean was calculated using general linear regression models after adjusting for age. Interactions between the main predictive variables, and sex and age (continuous) were examined by entering the centred interaction terms into multivariate linear regression models to determine whether the association between physical activity and sedentary time with metabolic risk was modified by sex and age.[30] In further sensitivity analyses, we also calculated a metabolic syndrome score

without the waist circumference in order to examine whether the associations between the main exposures (physical activity and sedentary time) and clustered metabolic risk were mediated by waist circumference.

All statistical analyses were performed using IBM SPSS Statistics standard 23.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was set at $P < 0.05$ for main effects, and $P < 0.10$ for interactions. Tests were two-sided.

Patient and public involvement statement

Research question development was informed by qualitative interviews, physical examinations, and laboratory tests with a purposively selected sample of residents from the National Basic Public Health Services in Jiangsu province. Summary reports about the study results will be disseminated to participants, policy-makers, and healthcare workers in the community (village doctors in rural areas or general practitioners in urban areas of China) through mass media, such as local newspapers, the internet, radios or workshops.

RESULTS

Demographic and basic characteristics of participants

Of the 17,750 participants included in the analyses, 60.3% were women, and the average age of men and women was 62.6 ± 9.9 and 62.8 ± 9.7 years, respectively (Table 1). Indices of body mass index, HDL-cholesterol and fasting plasma glucose did not differ significantly (all $P>0.10$) between excluded (n = 2,303) and included participants, but included participants had a slightly higher waist circumference and systolic blood pressure (all $P<0.001$) (Table S2) than those who were excluded.

Compared with women, men had a higher education level, household income and consumption of alcohol and cigarettes (all P < 0.001). Men also had higher waist circumference, HbA1c, diastolic blood pressure and fasting plasma glucose levels than women (all P<0.001). In contrast, women had higher HDL-cholesterol, systolic blood pressure and triacylglycerol levels than men (all P<0.001).

Differences between sexes were also observed in physical activity, sedentary time, and sleep duration. Women had higher total and occupational physical activity than men (all P<0.001), whereas men had higher sedentary time, sleep duration, commuting and leisure-time physical activity than women (all P<0.001). The proportion of subjects participating in leisure-time physical activity was 21.6% (Table 1).

Adjusted means of clustered and individual metabolic variables by physical activity and sedentary time

There was a tendency towards lower zMS, waist circumference, triacylglycerol and higher HDL-cholesterol at higher levels of total physical activity (P for trend<0.001) (Table 2), while individuals with higher zMS, waist circumference, fasting plasma glucose, triacylglycerol and lower HDL-cholesterol were apt to have a higher sedentary time (P for trend <0.001) (Table 2).

Associations between physical activity and sedentary time with metabolic risk

Total physical activity was inversely associated with zMS (B=-0.080; 95% CI: -0.114, -0.046), waist circumference (B=-0.449; 95% CI: -0.591, -0.308) and triacylglycerol (B=-0.012; 95% CI: -0.019, -0.006), after adjusting for sedentary time and sleep

duration. In contrast, the SD for physical activity was marginally positively associated with HDL-cholesterol (B=0.009; 95% CI: 0.003, 0.015). No significant associations were found between total physical activity with fasting plasma glucose (B=0.004; 95% CI: -0.001, 0.008) and systolic blood pressure (B=-0.096; 95% CI: -0.346, 0.155) (Table 3).

In adjusted analyses, occupational physical activity was associated with zMS (B=-0.066; 95% CI: -0.101, -0.031), waist circumference (B=-0.475; 95% CI: -0.620, -0.334), triacylglycerol (B=-0.007; 95% CI: -0.014, -0.001) and HDL-cholesterol (B=0.006; 95% CI: 0.001, 0.013), but not with fasting plasma glucose (B=0.005; 95% CI: -0.001, 0.009) and systolic blood pressure (B=0.081; 95% CI: -0.173, 0.334). Commuting physical activity was only inversely associated with triacylglycerol (B=-0.012; 95% CI: -0.019, -0.005). Furthermore, leisure-time physical activity was found to be inversely associated with zMS (B=-0.041; 95% CI: -0.075, -0.007) and systolic blood pressure (B=-0.293; 95% CI: -0.542, -0.045), but not with waist circumference, fasting plasma glucose or triacylglycerol (all $P>0.05$) (Table 3).

Different from that of physical activity, sedentary time was strongly positively associated with zMS (B=0.117; 95% CI: 0.083, 0.151) and waist circumference (B=0.474; 95% CI: 0.334, 0.613), after adjustment for physical activity and sleep duration. Furthermore, sedentary time was found to be weakly associated with fasting plasma glucose (B=0.008; 95% CI: 0.003, 0.013), triacylglycerol levels (B=0.015; 95% CI: 0.008, 0.022) and HDL-cholesterol (B=-0.007; 95% CI: -0.013, -0.001). No significant association was observed between sedentary time and systolic blood

pressure (B=0.215; 95% CI: -0.033, 0.462) (Table 3).

Joint association of total physical activity and sedentary time with metabolic risk

The joint association of total physical activity and sedentary time with zMS after adjustment for age is illustrated in Figure 1. Participants with the lowest level of physical activity or the highest sedentary time were consistently found to have the highest zMS among both sexes. Interaction analyses indicated significant effects among different age groups, where greater associations with sedentary time, total and occupational physical activity for zMS (P for interaction <0.10) and waist circumference (P for interaction <0.05) were observed in older age groups. In addition, there was no significant interaction with sex in the results of total physical activity, different domains of physical activity or sedentary time (Table S3). When excluding waist circumference from the zMS and additionally adjusting for waist circumference, the magnitude of association between sedentary time and clustered risk was weaker but remained statistically significant (Table S4).

DISCUSSION

In this cross-sectional study of a large sample-size of individuals with type 2 diabetes in China, we found that total physical activity, occupational physical activity, and sedentary time were independently associated with clustered metabolic risk, waist circumference, triacylglycerol levels, and HDL-cholesterol. Moreover, leisure-time physical activity was associated with systolic blood pressure and commuting physical activity was inversely associated with triacylglycerol. However, a higher level of sedentary time was positively associated with higher levels of fasting plasma glucose.

Our findings suggest that increasing physical activity across all domains and decreasing amount of time spent sedentarily may have protective effects on reducing metabolic risk.

The finding of an association between total physical activity and clustered metabolic risk in this study is consistent with previous research findings with objective data.[11] [12] Importantly, we observed that occupational physical activity reduced the clustered metabolic risk in patients with type 2 diabetes. Occupational physical activity is a major source of total physical activity among Chinese and other Asian populations,[14] for example, in this study, 75.8% of diabetic patients reported engaging in occupational physical activity. This suggests that occupational physical activity as a single domain may be important in the management of metabolic risk among Chinese or, perhaps more broadly, Asian populations. In a recent study, a trend was observed between lower levels of commuting physical activity and higher metabolic risk.[31] Our findings have also suggested that commuting physical activity is inversely associated with triacylglycerol, but there was no statistically significant association observed between commuting physical activity and clustered metabolic risk in this study, similar to the finding of the J-ECOH study.[32] This may partly be explained by the low level of commuting physical activity in our study, since 40% of patients reported that they did not engage in commuting physical activity.

Previous studies have also suggested that the associations between physical activity and clustered metabolic risk may be weakened by increasing sedentary time.[11] [33] For example, a longitudinal study reported that the association between

moderate-to-vigorous physical activity and clustered metabolic risk was attenuated when additionally adjusted for a six-year change in sedentary time, indicating that focusing solely on physical activity may not be the most effective intervention strategy.[33] In this study, we also found that sedentary time was associated with clustered and individual metabolic risk, which is independent of the effect of physical activity. This highlights the importance of not only increasing physical activity levels of patients with type 2 diabetes, but also reducing their sedentary time.

As reported previously, waist circumference is a body fat parameter most closely associated with metabolic syndrome.[34] Our findings indicate that total and occupational physical activity are strongly associated with waist circumference. There is growing evidence to suggest that physical activity may support weight loss through regulation of adipokines (adiponectin, leptin, resistin, interleukin-6), which are known to contribute to cardiometabolic health.[35] However, the biological mechanisms for associations between sedentary time and waist circumference with metabolic risk are not fully understood. One study has reported that this association can be attenuated once an adiposity component was included in the regression model.[36] Our findings suggested that more sedentary time was associated with a higher waist circumference, however, whether central obesity is a cause or a consequence of a sedentary behaviour has not yet been fully elucidated.[37] Sedentary time may displace physical activity time, leading to a decrease in energy expenditure and unfavorable weight changes.[38] Additional pathways linking sedentary time, waist circumference and metabolic risk include the established associations between major sedentary behaviour (TV viewing)

and an unhealthy diet.[39] In addition, when excluding waist circumference from the clustered metabolic risk score and adjusting for it as a confounding factor, the magnitude of association between physical activity and sedentary time with clustered metabolic risk was attenuated. An alternative explanation is that waist circumference might be an important part of the causal pathway between sedentary time and clustered metabolic risk, but further research is needed. We also found that the relationship between sedentary time with zMS and waist circumference was modified by age. This may be partly due sedentary time increasing with age.[40] Older patients may have a higher chance of clustered metabolic risk than younger people based on this age-related increase of sedentary time.

The association between total and individual domains of physical activity with fasting plasma glucose did not reach statistical significance in this study, which is consistent with result from the ProActive Study.[12] In contrast, a significant association was found between sedentary time and fasting plasma glucose in our study. The potential mechanism between sedentary time and fasting plasma glucose involves markers of inflammation, insulin resistance, and adiposity.[41] Obesity has a proven association with the increased risk of developing insulin resistance, and may result in disordered regulation of glucose levels by reducing insulin release.[42] Furthermore, another study has suggested that sleep loss can lead to disordered glucose metabolism.[43] In our study, we obtained consistent results even after adjusting for sleep duration, suggesting that the relationship between sedentary time and metabolic risk is independent of sleep duration.

In the present analysis, non-significant results between total physical activity, occupational physical activity and sedentary time with systolic blood pressure are consistent with the results from most previous studies,[11 12 17 31 32] Moreover, our study identified a significant inverse association between leisure-time physical activity and systolic blood pressure. Clays et al. also observed that objectively measured moderate and vigorous leisure-time physical activity, but not occupational physical activity, were inversely associated with systolic blood pressure.[44] A further study showed that bouts of high-intensity physical activity elicited greater systolic blood pressure reductions than lower-intensity bouts.[45] However, practice recommendations advocating high-intensity physical activity as an antihypertensive therapy is challenging because adverse cardiovascular effects are more likely to occur with vigorous than moderate to low levels of physical exertion,[46] especially in patients with type 2 diabetes who have a significantly greater systolic blood pressure response to a given physical activity intensity than that of the healthy population.[47] The American Diabetes Association (ADA) recommended that patients with type 2 diabetes should be assessed for conditions that might be associated with risk of cardiovascular disease before undertaking vigorous physical activity.[48] Our findings also suggest that patients with type 2 diabetes should comply with ADA recommendations to increase overall physical activity through work, active transport and participation in physical activity, as well as reducing sedentary behaviour to lower metabolic risk.

This study has several strengths. A relatively large sample size (n= 17,750) was used to explore the association between physical activity, sedentary time and

metabolic risk in a Chinese population. To the best of our knowledge, this is the first study in China that has evaluated physical activity in different domains and sedentary time with metabolic risk factors in patients with type 2 diabetes. Several limitations should also be mentioned. First, as a cross-sectional study, the direction and causality of the associations obtained from this study were restricted to inference. Second, the waist circumference and systolic blood pressure of included participants were slightly higher than those of excluded cases, which may reduce the accuracy of the estimation of our results. Third, all participants were recruited from just two areas in Jiangsu province, China, so whether these findings can be generalised to the population at large still needs to be discussed. Finally, a self-reporting questionnaire was used to acquire information on physical activity, so reporting errors may have occurred due to a recall bias. Self-reported measures of physical activity are easier to use but they may have limited validity when compared to objective measures.[49] Moreover, the patterns of physical activity and sedentary behaviours may vary between weekdays and weekends, but such variation is hard to obtain through the self-reporting measures used in this study. Further research is needed to explore a more detailed relationship between different patterns of physical activity and sedentary behaviour (specifically comparing weekdays and weekends) with metabolic risk in patients with type 2 diabetes.

CONCLUSIONS

The findings of this study suggest that total physical activity, physical activity in different domains, and sedentary time are associated with clustered and individual

metabolic risk factors in community-managed patients with type 2 diabetes. Encouraging patients with type 2 diabetes to increase physical activity in different domains and decrease sedentary time may have a protective effect against metabolic risk. Therefore, the findings from this study extend previous cross-sectional evidence of associations between physical activity, sedentary time, and metabolic risk in the Chinese population.

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Contributions Ming Wu and Chong Shen designed this study. Jie Yang, Jian Su, Yu Qin, Chong Shen, Ying Li, Shurong Lv, Enchun Pan, Yan Gao, Dandan Miao, Ning Zhang, Jinyi Zhou and Ming Wu were responsible for data collection. Yijia Chen analysed the data and drafted the manuscript. Ming Wu, Yu Qin, Chong Shen, and Enchun Pan revised the manuscript.

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Data sharing statement The data sets generated and/or analysed during the current study are available from the corresponding authors on reasonable request.

REFERENCES

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome.*The Lancet* 2005;365:1428. https://doi.org/10.1016/S0140-6736(05)66378-7.
2. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome : An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement.*Circulation* 2005;112:2735–2752. https://doi.org/10.1161/CIRCULATIONAHA.105.169404.
3. Li R, Li WC, Lun ZJ, et al. Prevalence of metabolic syndrome in mainland china: a meta-analysis of published studies.*BMC Public Health* 2016;16:296. https://doi.org/10.1186/s12889-016-2870-y.
4. Lu B, Yang HC, Song XY, et al. An evaluation of the International Diabetes Federation definition of metabolic syndrome in Chinese patients older than 30 years and diagnosed with type 2 diabetes mellitus.*Metabolism* 2006;55: 1088-1096. https://doi.org/10.1016/j.metabol.2006.04.003.
5. Laaksonen DE. Metabolic Syndrome and Development of Diabetes Mellitus: Application and Validation of Recently Suggested Definitions of the Metabolic Syndrome in a Prospective Cohort Study.*Am J Epidemiol* 2002;156:1070-1077. https://doi.org/10.1093/aje/kwf145.
6. Lakka HM, Laaksonen DE, Lakka TA, et al. The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-aged Men.*JAMA* 2002;288:2709-2716. https://doi.org/10.1001/jama.288.21.2709.
7. Girman CJ, Rhodes T, Mercuri M, et al. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS).*Am J Cardiol* 2004;93:136-141. https://doi.org/10.1016/j.amjcard.2003.09.028.
8. Lakka TA, Laaksonen DE. Physical activity in prevention and treatment of the metabolic syndrome.*Appl Physiol Nutr Metab* 2007;32:76-88. https://doi.org/10.1139/h06-113.
9. Boulé NG, Haddad E, Kenny GP, et al. Effects of Physical activity on Glycemic Control and Body Mass in Type 2 Diabetes Mellitus: A Meta-analysis of Controlled Clinical Trials.*JAMA* 2001;286: 1218 - 1227. https://doi.org/10.1001/jama.286.10.1218.
10. Gordon LA, Morrison EY, McGrowder DA, et al. Effect of physical activity therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes.*BMC Complement Altern Med* 2008;8:21. https://doi.org/10.1186/1472-6882-8-21. https://doi.org/10.1139/h06-113.
11. Cooper AJM, Brage S, Ekelund U, et al. Association between objectively assessed sedentary time and physical activity with metabolic risk factors among people with recently diagnosed type 2 diabetes.*Diabetologia* 2014;57:73-82. https://doi.org/10.1007/s00125-013-3069-8.
12. Ekelund U, Griffin SJ, Wareham NJ. Physical Activity and Metabolic Risk in Individuals With a Family History of Type 2 Diabetes.*Diabetes Care* 2007;30:337-342. https://doi.org/10.2337/dc06-1883.
13. Kwaśniewska M, Kaczmarczyk-Chałas K, Pikala M, et al. Commuting physical activity and prevalence of metabolic disorders in Poland. *Prev Med* 2010;51:482-487. https://doi.org/10.1016/j.ypmed.2010.09.003.
14. Ng SW, Popkin BM. Time use and physical activity: a shift away from movement across the globe.*Obesity Reviews.* 2012; 13:659-680. https://doi.org/10.1111/j.1467-789X.2011.00982.x.
15. Healy GN, Wijndaele K, Dunstan DW, et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab).*Diabetes Care*

2008;31:369-371. https://doi.org/10.2337/dc07-1795.

16. Knaeps S, De Baere S, Bourgois J, et al. Substituting Sedentary Time With Light and Moderate to Vigorous Physical Activity is Associated With Better Cardiometabolic Health.*J Phys Act Health* 2018;15:197-203. https://doi.org/10.1123/jpah.2017-0102.
17. Cooper AR, Sebire S, Montgomery AA, et al. Sedentary time, breaks in sedentary time and metabolic variables in people with newly diagnosed type 2 diabetes.*Diabetologia* 2012;55:589-599. https://doi.org/10.1007/s00125-011-2408-x.
18. Sedentary Behaviour Research Network. Letter to the editor: standardized use of the terms "sedentary" and "sedentary behaviours".*Appl Physiol Nutr Metab* 2012; 37:540-542. https://doi.org/ 10.1139/h2012-024.
19. Katzmarzyk PT. Physical Activity, Sedentary Behavior, and Health: Paradigm Paralysis or Paradigm Shift?*Diabetes* 2010;59:2717-2725. https://doi.org/10.2337/db10-0822.
20. Troxel WM, Buysse DJ, Matthews KA, et al. Sleep Symptoms Predict the Development of the Metabolic Syndrome.*Sleep* 2010;33:1633-1640. https://doi.org/10.1093/sleep/33.12.1633.
21. Douglas GA, Patrick R. The cost of dichotomising continuous variables.*BMJ* 2006;323:1080. https://doi.org/10.1136/bmj.332.7549.1080.
22. Miao DD, Pan EC, Zhang Q, et al. Development and Validation of a Model for Predicting Diabetic Nephropathy in Chinese People.*Biomed Environ Sci* 2017;30:106-112. https://doi.org/10.3967/bes2017.014.
23. Fan M, lyu J, He P . Chinese guidelines for data processing and analysis concerning the International Physical Activity Questionnaire.*Chin J Epidemiol* 2014;35:961-964. https://doi.org 3760/cma.j.issn.0254-6450.2014.08.019.
24. Bull FC, Masile TS, Armstrong T. Global Physical Activity Questionnaire (GPAQ): Nine Country Reliability and Validity Study.*J Phys Act Health* 2009;6:790-804. https://doi.org/10.1123/jpah.6.6.790.
25. Chu AHY, Ng SHX, Koh D, et al. Domain-Specific Adult Sedentary Behaviour Questionnaire (ASBQ) and the GPAQ Single-Item Question: A Reliability and Validity Study in an Asian Population.*Int J Environ Res Public Health* 2018;15:739. https://doi.org/10.3390/ijerph15040739.
26. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of Physical Activities: an update of activity codes and MET intensities.*Med Sci Sport Exer* 2000;32 suppl 9:S498-S516. https://doi.org/ 0195-913 l/00/3209-0498/0.
27. Wu M, Wen JB, Qin Y, et al. Familial History of Diabetes is Associated with Poor Glycaemic Control in Type 2 Diabetics: A Cross-sectional Study.*Sci Rep* 2017;7:1432. https://doi.org/10.1038/s41598-017-01527-4.
28. Chobanian AV, Bakris GL, Black HR, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.*Hypertension* 2003;42:1206-1252. https://doi.org/10.1161/01.HYP.0000107251.49515.c2.
29. Huang YX, Gao L, Xie XP, et al. Epidemiology of dyslipidemia in Chinese adults: meta-analysis of prevalence, awareness, treatment, and control.*Popul Health Metr* 2014;12:2-9. https://doi.org/10.1186/s12963-014-0028-7.
30. Aiken LS, West SG. Multiple regression: Testing and interpreting interactions. Newbury Park, California: SAGE Publications 1991: 116-137.
31. Chu AHY, Moy FM. Associations of occupational, transportation, household and leisure-time physical activity patterns with metabolic risk factors among middle-aged adults in a

middle-income country.*Pre Med* 2013;57:S14-S17. https://doi.org/10.1016/j.ypmed.2012.12.011.

32. Kuwahara K, Honda T, Nakagawa T, et al. Leisure-time physical activity, physical activity during work and commuting, and risk of metabolic syndrome.*Endocrine* 2016;53:710–721. https://doi.org/10.1007/s12020-016-0911-z.
33. Wijndaele K, Orrow G, Ekelund U, et al. Increasing objectively measured sedentary time increases clustered cardiometabolic risk: a 6 year analysis of the ProActive study.*Diabetologia* 2014;57:305-312. https://doi.org/10.1007/s00125-013-3102-y.
34. Carr DB, Utzschneider KM, Hull RL, et al. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome.*Diabetes* 2004;53:2087–2094. https://doi.org/10.2337/diabetes.53.8.2087.
35. Vella CA, Allison MA, Cushman M, et al. Physical Activity and Adiposity-related Inflammation: The MESA.*Med Sci Sports Exerc* 2017;49:915-921. https://doi.org/10.1249/MSS.0000000000001179.
36. Stamatakis E, Pulsford RM, Brunner EJ, et al. Sitting behaviour is not associated with incident diabetes over 13 years: the Whitehall II cohort study.*Br J Sports Med* 2017;51:818-823. https://doi.org/10.1136/bjsports-2016-096723.
37. Ekelund U, Brage S, Besson H, et al. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality?*Am J Clin Nutr* 2008;88:612–617. https://doi.org/10.1093/ajcn/88.3.612.
38. Mekary RA, Willett WC, Hu FB, et al. Isotemporal substitution paradigm for physical activity epidemiology and weight change.*Am J Epidemiol* 2009;170:519–527. https://doi.org/10.1093/aje/kwp163.
39. Pearson N, Biddle SJ. Sedentary behavior and dietary intake in children, adolescents, and adults. A systematic review.*Am J Prev Med* 2011;41:178–188. https://doi.org/10.1016/j.amepre.2011.05.002.
40. Matthews CE, Chen KY, Freedson PS, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004.*Am J Epidemiol* 2008;167:875-881. https://doi.org/10.1093/aje/kwm390.
41. Yates T, Khunti K, Wilmot EG, et al. Self-reported sitting time and markers of inflammation, insulin resistance, and adiposity.*Am J Prev Med* 2012;42:1-7. https://doi.org/10.1016/j.amepre.2011.09.022.
42. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes.*Nature* 2006;444:840-846. https://doi.org/10.1038/nature05482.
43. Rafalson L, Donahue RP, Stranges S, et al. Short sleep duration is associated with the development of impaired fasting glucose: the Western New York Health Study.*Ann Epidemiol* 2010;20:883-889. https://doi.org/10.1016/j.annepidem.2010.05.002.
44. Clays E, De Bacquer D, Van Herck K, et al. Occupational and leisure time physical activity in contrasting relation to ambulatory blood pressure.*BMC Public Health* 2012;12:1002. https://doi.org/10.1186/1471-2458-12-1002.
45. Eicher JD, Maresh CM, Tsongalis GJ, et al. The additive blood pressure lowering effects of physical activity intensity on post-physical activity hypotension.*Am Heart J* 2010;160:513-520. https://doi.org/10.1016/j.ahj.2010.06.005.
46. Thompson PD, Franklin BA, Balady GJ, et al. Physical activity and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical

Cardiology.*Circulation* 2007;115:2358-2368. https://doi.org/10.1161/CIRCULATIONAHA.107.181485.

47. Brett SE, Ritter JM, Chowienczyk PJ. Diastolic blood pressure changes during physical activity positively correlate with serum cholesterol and insulin resistance.*Circulation* 2000;101:611-615.
48. American Diabetes Association. 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018.*Diabetes care* 2018;41 Suppl 1:S38-S50. https://doi.org/ 10.2337/dc18-S004。
49. Skender S, Ose J, Chang-Claude J, et al. Accelerometry and physical activity questionnaires-a systematic review.*BMC Public Health* 2016;16:515. https://doi.org/10.1186/s12889-016-3172-0.

Fig 1. Means of clustered metabolic risk scores by sedentary time and physical activity among 17,750 diabetic patients. The adjusted mean was calculated using general linear regression models after adjustment for age. For physical activity, in men, the cut-off values for defining low, moderate, and high tertile groups were 4.00 and 11.14 MET-h/d, while they were 4.57 and 12.00 MET-h/d for women. For sedentary time, the 4 groups by quartiles of sedentary time were ＜2.2, 2.3-3.3, 3.4-4.9, and ⩾5.0 h/d for men and ＜2.2, 2.3-3.3, 3.4-4.4, and ⩾4.5 h/d for women. MET, metabolic equivalent task.

Table 1 Demographic, metabolic characteristics of participants

characteristic	Men	Women	Total	P value
n	7041	10709	17750	
Age(years)	62.6 ± 9.9	62.8 ± 9.7	62.8 ± 9.8	0.11
High school or above (%)	17.7	4.5	9.8	<0.001
Annual income>40000￥(%)	64.8	57.0	60.1	<0.001
Body mass index(Kg/m^2)	25.3 ± 3.2	25.4 ± 3.6	25.3 ± 3.4	0.09
Waist circumference (cm)	87.9 ± 9.4	85.5 ± 9.5	86.4 ± 9.5	<0.001
Systolic blood pressure (mmHg)	147.3 ± 19.8	148.9 ± 21.1	148.0 ± 20.6	0.002
Diastolic blood pressure (mmHg)	83.7 ± 10.7	79.9 ± 10.4	81.4 ± 10.6	<0.001
Triacylglycerol (mmol/L)*	1.4 (1.0, 2.2)	1.7 (1.2, 2.3)	1.6 (1.1, 2.3)	<0.001
HDL-cholesterol (mmol/L)	1.4 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	<0.001
Fasting plasma glucose (mmol/L)*	8.2 (6.4, 10.2)	8.0 (6.5, 9.9)	8.1 (6.6, 10.0)	<0.001
HbA1c(mmol/mol) *	56.3 (46.5, 70.5)	55.2 (46.5, 68.3)	55.2 (46.5, 69.4)	<0.001
Diabetes duration (years) *	5 (2, 9)	5 (2, 9)	5 (2, 9)	0.26
Smoking (%)	46.0	6.2	22.0	<0.001
alcohol consumption (%)				
never	49.1	96.6	77.7	<0.001
former	10.7	1.1	4.9	<0.001
current	40.1	2.3	17.4	<0.001
On glucose-lowering medication (%)	78.7	78.4	78.5	0.60
On lipid-lowering medication (%)	5.8	5.9	6.0	0.005
On antihypertensive medication (%)	52.7	53.9	53.4	0.002
Hypertension (%)	77.5	76.6	77.0	0.16

Dyslipidemia (%)	46.1	49.3	48.0	<0.001
Total physical activity (MET-h/d) *	6.3 (2.3, 14.3)	8.0 (3.4, 16.0)	8.0 (2.9, 15.4)	<0.001
Physical activity domains (MET-h/d) †				
Occupational	68.2 [2.9 (0.0, 8.6)]	81.9 [5.1 (1.7, 12.0)]	76.5 [4.0 (0.6, 12.0)]	<0.001‡
Commuting	59.4 [1.1 (0.0, 1.3)]	62.0 [1.0 (0.0, 2.9)]	60.1 [1.0 (0.0, 2.9)]	<0.001‡
Leisure-time	25.6 [3.1 (1.7, 6.0)]	19.0 [2.9(1.5, 5.1)]	21.6 [3.0 (1.7, 5.7)]	<0.001‡
Sedentary time (h/d)	3.5 ± 2.5	3.4 ± 2.6	3.4 ± 2.5	<0.001
Sleep duration (h/d)	7.4 ±1.6	7.3 ± 1.7	7.4 ± 1.7	<0.001

Data are means±SD unless stated otherwise

* Median (IQR)

† (%) [Median (IQR)]

‡ P values are from chi-square test

P values are from Student's t-test or Mann-Whitney U test for continuous variables and from chi-squared test for categorical variables.

Table 2 Adjusted means(SE) of metabolic variables by quartile of physical activity and sedentary time

Metabolic risk	Total physical activity (MET h/day)					Sedentary time(h/d)				
	Quartile 1 (<2.9)	Quartile 2 (2.9-8.0)	Quartile 3 (8.1-15.4)	Quartile 4 (>15.4)	P for trend	Quartile 1 (<2.2)	Quartile 2 (2.2-3.3)	Quartile 3 (3.4-4.4)	Quartile 4 (>4.5)	P for trend
zMS¶	0.28(0.04) †, ‡, §	0.01(0.04) *, §	-0.11(0.05) *	-0.21(0.04) *, †	<0.001	-0.16(0.03) ‡, §	-0.07(0.10) §	0.004(0.03) *, §	0.29(0.04) *, †, ‡	<0.001
Waist circumference (cm)	87.19(0.14) †, ‡, §	86.56(0.13) *, §	86.13(0.16) *	85.76(0.14) *, †	<0.001	85.98(0.11) §	86.25(0.16)	86.57(0.20) §	87.30(0.14) *, ‡	<0.001
Fasting plasma glucose (mmol/L)**	2.13(0.005) ‡	2.12(0.005) ‡	2.10(0.005) *, ‡	2.12(0.005)	0.427	2.11(0.004) §	2.10(0.012) §	2.12(0.005) §	2.14(0.005) *, †, ‡	<0.001
Triacylglycerol(mmol/L)**	0.54(0.008) †, ‡, §	0.50(0.008) *, §	0.48(0.009) *	0.45(0.008) *, †	<0.001	0.46(0.006) ‡, §	0.47(0.021) §	0.50(0.008) *, §	0.54(0.009) *, †, ‡	<0.001
HDL-cholesterol (mmol/L)	1.45(0.01) †, ‡, §	1.49(0.01) *, §	1.50(0.01) *	1.52(0.01) *, †	<0.001	1.51(0.01) ‡, §	1.48(0.01) §	1.48(0.01) *, §	1.46(0.01) *, †, ‡	<0.001
Systolic blood pressure (mmHg)	148.26(0.30)	147.91(0.28)	147.80(0.34)	148.05(0.30)	0.651	148.08(0.23)	147.56(0.33)	147.87(0.42)	148.35(0.30)	0.326

Date are mean (SE) values for each quartile of physical activity and sedentary time, adjusted for age and sex by using general linear regression models. Test for trend based on variable containing median value for each quartiles. Multiple comparison between the groups was performed using Bonferroni method:

* significantly different compared with Quartile 1 (P< 0.05)

† significantly different compared with Quartile 2 (P< 0.05)

‡ significantly different compared with Quartile 3 (P< 0.05)

§ significantly different compared with Quartile 4 (P< 0.05)

¶ zMS is a continuously distribute variable for clustered metabolic risk calculated by summing sex-specific standardised values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

** Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution

Table 3 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables

	Physical activity (per-SD) ‡				Sedentary time
Metabolic risk	Total	Occupational	Commuting	Leisure-time	(per-SD) ‡
zMS†					
Model 1	-0.147(-0.187, -0.108)***	-0.132(-0.171,-0.093)***	-0.047(-0.086,-0.007)*	-0.068(-0.107,-0.029)**	0.188(0.148, 0.227)***
Model 2	-0.091(-0.126, -0.057)***	-0.077(-0.111,-0.042)***	-0.013(-0.047, 0.021)	-0.044(-0.078,-0.010)*	0.128(0.094, 0.162)***
Model 3	-0.080(-0.115, -0.046)***	-0.066(-0.101,-0.031)***	-0.011(-0.045, 0.022)	-0.042(-0.076,-0.008)*	0.121(0.087, 0.155)***
Model 4	-0.080(-0.114, -0.046)***	-0.066(-0.101,-0.031)***	-0.011(-0.045, 0.023)	-0.041(-0.075,-0.007)*	0.117(0.083, 0.151)***
Waist circumference (cm)					
Model 1	-0.552(-0.692, -0.412)***	-0.625(-0.765,-0.485)***	0.096(-0.044, 0.237)	-0.026(-0.167, 0.114)	0.575(0.435, 0.715)***
Model 2	-0.495(-0.635, -0.355)***	-0.519(-0.661,-0.376)***	0.021(-0.118, 0.161)	-0.051(-0.191, 0.089)	0.525(0.386, 0.663)***
Model 3	-0.450(-0.591, -0.309)***	-0.475(-0.618,-0.332)***	0.028(-0.112, 0.167)	-0.042(-0.182, 0.098)	0.483(0.344, 0.623)***
Model 4	-0.449(-0.591, -0.308)***	-0.475(-0.620,-0.334)***	0.030(-0.109, 0.170)	-0.039(-0.179, 0.102)	0.474(0.334, 0.613)***
Fasting plasma glucose(mmol/L) §					
Model 1	0.005(0.000, 0.010)	0.007(0.002, 0.012)**	-0.005(-0.010, 0.000)	-0.001(-0.006, 0.004)	0.011(0.006, 0.016)***
Model 2	0.003(-0.002, 0.007)	0.005(-0.001, 0.009)	-0.001(-0.005, 0.004)	-0.002(-0.007, 0.002)	0.008(0.004, 0.013)***
Model 3	0.004(-0.001, 0.008)	0.005(-0.001, 0.010)	-0.001(-0.005, 0.004)	-0.002(-0.007, 0.003)	0.009(0.004, 0.013)***
Model 4	0.004(-0.001, 0.008)	0.005(-0.001, 0.009)	-0.001(-0.005, 0.004)	-0.002(-0.006, 0.003)	0.008(0.003, 0.013)***
Triacylglycerol (mmol/L) §					
Model 1	-0.022(-0.030, -0.013)***	-0.017(-0.025,-0.009)**	-0.015(-0.024,-0.007)***	-0.020(-0.019,-0.003)**	0.031(0.023, 0.039)***
Model 2	-0.014(-0.021, -0.007)***	-0.009(-0.015,-0.002)*	-0.012(-0.019,-0.005)***	-0.007(-0.014,-0.001)*	0.017(0.010, 0.024)***
Model 3	-0.012(-0.019, -0.006)***	-0.007(-0.014,-0.001)*	-0.012(-0.019,-0.005)***	-0.006(-0.013, 0.001)	0.016(0.009, 0.023)***
Model 4	-0.012(-0.019, -0.006)***	-0.007(-0.014,-0.001)*	-0.012(-0.019,-0.005)***	-0.006(-0.013, 0.001)	0.015(0.008, 0.022)***
HDL-cholesterol (mmol/L)					
Model 1	0.015(0.009, 0.022)***	0.016(0.009, 0.022)**	0.002(-0.005, 0.008)	0.003(-0.004, 0.009)	-0.019(-0.025, -0.012)***

Model 2	0.010(0.004, 0.016)***	0.007(0.001, 0.013)*	0.003(-0.003, 0.009)	0.007(-0.001, 0.013)	-0.008(-0.014, -0.002)*
Model 3	0.009(0.003, 0.015)***	0.006(0.001, 0.013)*	0.003(-0.003, 0.009)	0.007(-0.001, 0.013)	-0.007(-0.013, -0.001)*
Model 4	0.009(0.003, 0.015)***	0.006(0.001, 0.013)*	0.003(-0.003, 0.009)	0.007(-0.001, 0.013)	-0.007(-0.013, -0.001)*
Systolic blood pressure (mmHg)					
Model 1	-0.907(-1.209, -0.604)***	-0.625(-0.928, -0.322)***	-0.549(-0.852,-0.246)***	-0.871(-1.174,-0.568)***	0.340(0.037, 0.643)*
Model 2	-0.110(-0.359, 0.139)	0.065(-0.187, 0.317)	-0.212(-0.459, 0.034)	-0.300(-0.548,-0.052)*	0.224(-0.022, 0.470)
Model 3	-0.091(-0.341, 0.159)	0.084(-0.169, 0.337)	-0.210(-0.456, 0.037)	-0.296(-0.544,-0.048)*	0.216(-0.031, 0.462)
Model 4	-0.096(-0.346, 0.155)	0.081(-0.173, 0.334)	-0.219(-0.466, 0.028)	-0.293(-0.542,-0.045)*	0.215(-0.033, 0.462)

Regression results are presented as unstandardised coefficients (B) (95%CI)

† zMS is a continuously distribute variable for clustered metabolic risk calculated by summing sex-specific standardised values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

‡ Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.2 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

All models (except model 1) are adjusted for age, sex, education, annual household income, smoking status, alcohol consumption and diabetes duration. All outcomes except zMS and waist circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of glucose-lowering medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing drugs (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of glucose-lowering medication (yes/no), lipid-lowing medication (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

Model 3 is adjusted for remaining physical activity and sedentary time as appropriate; Model 4 is additional adjusted for sleep duration

§ Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution.

*P＜0.05; **P＜0.01; **P＜0.001

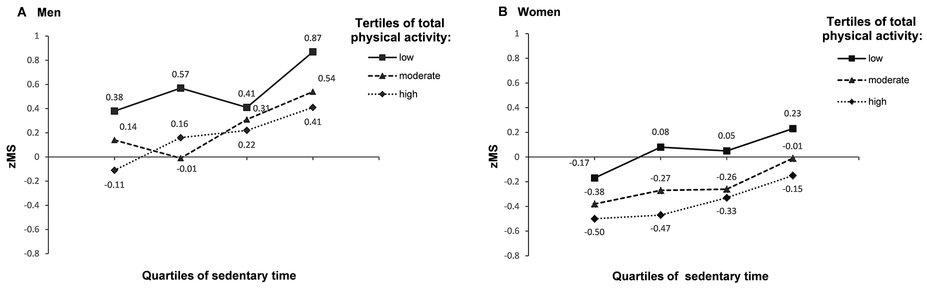

Fig 1. Means of clustered metabolic risk scores by sedentary time and physical activity among 17,750 diabetic patients. The adjusted mean was calculated using general linear regression models after adjustment for age. For physical activity, in men, the cut-off values for defining low, moderate, and high tertile groups were 4.00 and 11.14 MET-h/d, while they were 4.57 and 12.00 MET-h/d for women. For sedentary time, the 4 groups by quartiles of sedentary time were <2.2, 2.3-3.3, 3.4-4.9, and ≥5.0 h/d for men and <2.2, 2.3-3.3, 3.4-4.4, and ≥4.5 h/d for women. MET, metabolic equivalent task.

42x15mm (600 x 600 DPI)

Table S1. Classification table of physical activity and sedentary behaviour

Physical activity in Farm work, occupation and household chores		**Physical activity in leisure-time**		**Static behavior**
Moderate-intensity physical activity (4 MET h/d) Make breathing and heart beat slightly faster	**Vigorous-intensity physical activity (8 MET h/d)** Make breathing and heart rate significantly faster	**Moderate-intensity physical activity (4 MET h/d)** Make breathing and heart beat slightly faster	**Vigorous-intensity physical activity (8 MET h/d)** Make breathing and heart rate significantly faster	Lying, sitting and leaning besides sleep time (h/d)
·**Cleaning**(e.g. vacuuming, mopping the floor, polishing floor, wiping the desk, sweeping the floor, ironing clothes) ·**Washing** (e.g. scrubbing the carpet, washing clothes) ·**Gardening** (e.g. watering, turning soil, fertilizing) ·**Hand milking** ·**Hand knitting** ·**carpenter work** (e.g. sawing cork，Chiseling cork) ·**With a shovel and other tools to mix the sand and cement** ·**Walking with a general weight**	·**Forestry workers** (felling and handling timber) ·**Sawing ironwood** ·**tilling land** ·**transplant rice seedlings** ·**harvesting crops** (e.g. wheat, rice, sugarcane) ·**Gardening** (e.g. digging, carrying heavy things) ·**hand milling** (with wooden club or stone mill) ·**architectural work** (e.g. building a wall, handing building materials) ·**Fitness Trainer** (e.g. spinning, aerobics, yoga and some other aerobic exercise) ·**A courier on foot or bike**	·**biking** ·**jogging** ·**dancing** ·**reading a horse** ·**practicing Tai chi** ·**Practicing Yoga and pilates** ·**doing the yangko dance**	·**Long-distance running** ·**playing football** ·**playing rugby** ·**playing tennis** ·**spinning in gym** ·**Lifting barbell** ·**doing ballet** ·**swimming**	·**working** ·**studying** ·**reading** ·**watching TV** ·**using computer** ·**riding** ·**taking a rest**

·Carrying water **·Grazing**	**·Pulling a rickshaw**			

Table S2. Baseline characteristics of those included and excluded participants.

characteristics	Included participants	excluded participants	P
n	17750	2303	
Sex, n(%)			
Male	7041(39.7)	821(35.6)	<0.001
Age(years)	62.76±9.78	63.76±10.27	<0.001
BMI(Kg/m^2)	25.32±3.44	25.45±3.67	0.101
Waist circumference (cm)	86.43±9.53	84.97±13.80	<0.001
Systolic blood pressure (mmHg)	148.01±20.59	142.62±35.61	<0.001
Diastolic blood pressure (mmHg)	81.41±10.63	82.11±10.76	0.004
Triacylglycerol (mmol/L) *	1.57(1.11, 2.26)	1.61(1.16, 2.36)	0.004
HDL-cholesterol (mmol/L)	1.49±0.43	1.49±0.48	0.576
Fasting plasma glucose (mmol/L) *	8.07(6.60, 10.01)	8.00(6.34, 10.56)	0.576
HbA1c (%)*	7.20(6.4, 8.5)	7.4(6.4, 9.0)	<0.001
Diabetes duration (years) *	5(2, 9)	4(1, 8)	<0.001

Data are means±SD unless stated otherwise ; *Median (IQR)

P values are from one-way analysis or Mann-Whitney U test for continuous variables and from chi-squared test for categorical variables.

Table S3 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables, stratified by sex and age

Variables	zMS†	Waist circumference (cm)	Fasting plasma glucose (mmol/L) §	Triacylglycerol (mmol/L) §	HDL-cholesterol (mmol/L)	Systolic blood pressure (mmHg)
Total physical activity (per-SD) ‡						
Sex						
Men	-0.108***	-0.550***	0.001	-0.019***	0.015**	0.101
Women	-0.046*	-0.312**	0.007*	-0.006	0.003	-0.340
P-interaction	0.335	0.248	0.261	0.222	0.111	0.400
Age(years)						
＜55	-0.112***	-0.513***	0.001	-0.019**	0.011*	1.161
55~	-0.039	-0.204	0.007	-0.008	0.011*	-0.063
65~	-0.120**	-0.852***	-0.002	-0.015*	0.014*	-0.121
≥75	-0.288***	-1.359***	-0.025	-0.019	0.002	-0.027
P-interaction ¶	**0.073**	**0.007**	0.110	0.771	0.511	0.386
Occupational physical activity (per-SD) ‡						
Sex						
Men	-0.089***	-0.565***	0.003	-0.016**	0.013**	0.270
Women	-0.040*	-0.358**	0.008	0.001	-0.001	-0.171
P-interaction	0.452	0.294	0.349	0.165	0.560	0.440
Age(years)						
＜55	-0.098**	-0.463***	0.003	-0.017**	0.004	0.260
55~	-0.030	-0.258*	0.007	-0.003	0.008	0.095
65~	-0.137***	-0.961***	-0.002	-0.010	0.024**	0.353
≥75	-0.199*	-1.264***	-0.036*	0.024	-0.014	0.235
P-interaction ¶	**0.092**	**0.003**	0.132	0.185	0.761	0.129

Commuting physical activity (per-SD) ‡						
Sex						
Men	-0.036	0.032	-0.002	-0.017**	0.002	-0.234
Women	0.016	0.063	0.001	-0.006	0.003	-0.177
P-interaction	0.092	0.669	0.418	0.057	0.892	0.946
Age(years)						
＜55	0.042	0.075	-0.001	0.006	0.008	-0.032
55~	-0.008	0.109	-0.001	-0.015*	0.001	-0.207
65~	0.007	0.027	0.004	-0.009	-0.003	-0.393
≥75	-0.127*	-0.326	0.003	-0.037**	0.024*	0.162
P-interaction ¶	0.306	0.517	0.525	0.301	0.222	0.836
Leisure-time physical activity (per-SD) ‡						
Sex						
Men	-0.043	-0.052	-0.003	-0.003	0.005	-0.349*
Women	-0.039	-0.025	0.001	-0.008	0.008	-0.247
P-interaction	0.699	0.734	0.464	0.368	0.677	0.930
Age(years)						
＜55	-0.085*	-0.152	-0.002	-0.013	0.017**	-0.175
55~	-0.022	0.100	0.001	-0.007	0.008	-0.187
65~	-0.005	-0.071	-0.005	0.002	0.011	-0.610*
≥75	-0.068	-0.326	-0.002	-0.012	-0.010	-0.492
P-interaction ¶	0.964	0.502	0.380	0.886	0.320	0.170
Sedentary time (per-SD) ‡						
Sex						
Men	0.088**	0.327**	0.011**	0.020**	-0.004	0.030

Women	0.130***	0.540***	0.006*	0.010*	-0.008*	0.328*
P-interaction	0.541	0.330	0.237	0.035	0.793	0.268
Age(years)						
＜55	0.059	0.144	0.006	0.017*	-0.018**	-0.261
55~	0.108***	0.428***	0.006	0.015**	-0.005	0.438*
65~	0.172***	0.723***	0.015***	0.014*	-0.001	0.259
≥75	0.101*	0.684**	-0.005	0.006	-0.007	0.276
P-interaction ¶	0.143	**0.001**	0.774	0.190	0.252	0.291

Regression results are presented as unstandardized coefficients (B)

†zMS is a continuously distribute variable for clustered metabolic risk calculated by summing sex-specific standardized values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

‡ Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.3 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

Adjusted for age, sex, education, annual household income, smoking, alcohol consumption, diabetes duration, physical activity and sedentary time as appropriate (different domain of physical activity is adjusted for the other two physical activities), sleep duration. All outcomes except zMS and waist circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of glucose-lowering medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing medication (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of glucose-lowering medication (yes/no), lipid-lowing medication (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

§ Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution.

¶ P-interaction calculated using age as a continuous variable.

*P＜0.05; **P＜0.01; ***P＜0.001

Table S4 Cross-sectional linear regression analysis of association of physical activity and sedentary time with clustered metabolic risk

Metabolic risk	Physical activity (per-SD) †				Sedentary time (per-SD) †
	Total	Occupational	Commuting	Leisure-time	
zMS‡					
Model 1	-0.087(-0.120, -0.054)***	-0.067(-0.100,-0.033)***	-0.054(-0.088,-0.021)**	-0.058(-0.091,-0.025)**	0.131(0.097, 0.164)***
Model 2	-0.050(-0.079, -0.021)***	-0.033(-0.063,-0.004)*	-0.019(-0.048, 0.010)	-0.038(-0.067,-0.010)*	0.085(0.056, 0.113)***
Model 3	-0.050(-0.079, -0.021)***	-0.026(-0.055, 0.003)	-0.018(-0.047, 0.011)	-0.037(-0.066,-0.008)*	0.082(0.053, 0.110)***
Model 4	-0.043(-0.072, -0.014)***	-0.026(-0.056, 0.003)	-0.018(-0.047, 0.011)	-0.036 (-0.065,-0.007)*	0.078(0.049, 0.107)***

Regression results are presented as unstandardized coefficients (B) (95%CI)

† Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.2 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

‡ Delete the waist circumference to calculate new clustered metabolic score.

All models (except model 1) are adjusted for age, sex, education, annual household income, smoking status, alcohol consumption and diabetes duration. All outcomes except zMS and waist Circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of diabetes medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing medication (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of diabetes medication (yes/no), lipid-lowing drugs (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no). Model 3 is adjusted for remaining physical activity and sedentary time as appropriate; Model 4 is additional adjusted for sleep duration.

*P < 0.05; **P < 0.01; **P < 0.001