Fast walking is a preventive factor against new-onset diabetes mellitus in a large cohort from a Japanese general population

学位論文

Fast walking is a preventive factor against new-onset diabetes mellitus in a large cohort from a Japanese general population

（速歩きは、日本人一般集団の大規模コホートにおいて
糖尿病新規発症の予防因子である）

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Abstract

Based on questionnaires from 197,825 non-diabetic participants in a large Japanese cohort, we determined impact of 1) habit of exercise, 2) habit of active physical activity (PA) and 3) walking pace on new-onset of type 2 diabetes mellitus. Unadjusted and multivariable-adjusted logistic regression models were used to determine the odds ratio of new-onset diabetes mellitus incidence in a 3-year follow-up. There were two major findings. First, habits of exercise and active PA were positively associated with incidence of diabetes mellitus. Second, fast walking, even after adjusting for multiple covariates, was associated with low incidence of diabetes mellitus. In the subgroup analysis, the association was also observed in participants aged ≥ 65 years, in men, and in those with a body mass index ≥ 25. Results suggest that fast walking is a simple and independent preventive factor for new-onset of diabetes mellitus in the health check-up and guidance system in Japan. Future studies may be warranted to verify whether interventions involving walking pace can reduce the onset of diabetes in a nation-wide scale.

Key words: physical activity, exercise, diabetes mellitus, walking pace

Introduction

Physical inactivity is closely associated with the incidence of new-onset diabetes [1-3]. In meta-analyses of cohort or randomized studies, an inverse association between physical activity (PA) and risk of type 2 diabetes was observed regardless of intensity (low, moderate or vigorous), total time, and type (leisure-time physical activity (LTPA) or walking) of PA [1]. Smith et al. reported that the inverse relationship between the amount of LTPA (metabolic equivalent task score: METs•h/week) and type 2 diabetes was curvilinear [2]. Frequency and intensity of PA and exercise are attributable to physical fitness (PF) [4,5]; therefore, poor physical fitness can also be a risk factor for new-onset diabetes. Walking pace is assumed to be an indicator of PF [6,7]. Mozaffarian et al. reported that a combination score of walking pace and LTPA predicted the 10-year incidence of diabetes mellitus in US participants aged 65 years or older [6]. Joseph et al. reported that diabetes risk was lower in participants with brisk or striding walking pace compared with casual walking pace in a Multi-Ethnic Study of Atherosclerosis participants [7]. Thereby, in official guidelines, promotion of mild and moderate to vigorous PA has been recommended as a prevention and treatment option for diabetes mellitus [8-10].

In Japan, a nationwide health check-up and guidance system called “the Specific Health Check and Guidance System (SHCG)” has been operated since 2008 [11]. The SHCG has been focused on prevention of metabolic syndrome (MetS) and its related disorders such as type 2 diabetes mellitus and health guidance including the promotion of PA/exercise has been provided for individuals who have abdominal obesity and/or additional MetS risk factors. Theoretically, such health guidance can be effective in the nationwide participants with a high MetS risk for preventing new-onset of type 2 diabetes mellitus. In the SHCG, all participants were administered three simple questions regarding PA/exercise: 1) habit of regular exercise

(≥ 2 times/week of exercise ≥ 4 METs•h), 2) habit of active PA (≥ 23 METs•h/week) and 3) walking pace (rapid or not rapid), an indicator of physical fitness. We hypothesized that responses to the questions can be associated with onset of type 2 diabetes mellitus and if so, what characteristics such as sex, age, and leanness/obesity are linked to the association.

We evaluated the associations of the aforementioned three measures of PA and PF with a 3-year incidence of new-onset diabetes mellitus in a nation-wide Japanese general population. Considering the differences in diabetes incidence and mechanisms associating diabetes with PA, we also evaluated whether the association of PA with incident diabetes mellitus varied by sex, age, and leanness/obesity.

Results

General characteristics

Among all participants who did not have diabetes mellitus (n = 577,984) in 2008 (Dataset 1, **Figure 1**, The flow chart of the participants' recruitment. those who visited only in 2008 (n = 162,740) or who had missing data (n = 247,560) were excluded. The main analysis was performed on the complete cases (Dataset 3, n = 167,684, **Table 1**). The mean age was 63.7 years and 38.8% were men. There were 6,229/167,684 (3.7%) patients who had not been diabetic in 2008 and developed diabetes between 2009 and 2011. Frequencies of regular exercise (exercise to sweat lightly) (45.4% vs 41.6%, P < 0.001) and active PA (walking > 1 h/day) (54.1% vs 52.1%, P < 0.001) were significantly higher in patients who developed diabetes compared to non-diabetic patients; however, that of fast walking was lower in the participants who developed diabetes (47.9 vs 50.2%, P < 0.001) (**Table 1**). Frequency of weight change ± 3kg within 1year was higher in the Diabetes onset + group.

Odds ratio (OR) of new-onset diabetes

OR for new-onset diabetes due to differences in exercise, PA and walking pace was examined by logistic regression analysis (**Table 2**). Fast walking was inversely associated with onset of diabetes mellitus (OR 0.91, 95% confidence interval [CI] 0.87–0.96, P < 0.001); however, regular exercise (OR 1.16, 95% CI 1.11–1.23, P < 0.001) and active PA (OR 1.09, 95% CI 1.03–1.14, P =0.002) (Model 1) were positively associated. After adjusting for sex, age and BMI (Model 2), fast walking was negatively associated with onset of diabetes. However, after adjusted with multiple factors including two other PA measures "exercise to sweat lightly" and "walking > 1 h/day", fast walking was negatively associated with onset of diabetes (Model 3). Multivariate analysis was performed also in the subgroups: age < 65 vs ≥ 65 years, men vs women, and BMI < 25 vs ≥ 25. Fast walking was negatively associated with onset of diabetes mellitus in patients aged ≥ 65 years, male sex, and patients with BMI ≥ 25 (**Figure 2 and Table 2**). Exercise to sweat lightly was positively associated with onset of diabetes after multivariate adjustment (Model 2 and 3) in all and in patients aged < 65, male sex and patients with BMI < 25.

Characteristics of participants with or without fast walking (Table 3)

At baseline, BMI and waist circumference were lower, whereas age and the proportion of male participants were higher in fast walking + group compared to those in fast walking – (**Table 3**). HbA1c was slightly lower, and other metabolic parameters in the fast walking + group were: HDL level was higher, and levels of triglycerides, aspartate aminotransferase, and alanine aminotransferase were lower than in the fast walking – group. The frequency of hypertension and current smokers were lower, and frequency of regular drinkers was higher in the fast walking + group. Frequency of weight change ± 3kg within 1year was slightly lower in the fast walking + group**.**

In a subgroup of our participants (n = 183), we investigated whether self-reported walking speed using the questionnaire was related to objectively measured walking speed (10 meters walking speed, sec). Fast walking + group (n = 69) showed a higher speed than fast walking – group (n = 114) [6.20 ± 1.11 sec/10 m (6.0 ± 1.10 kph) vs 7.08 ± 2.11 sec/10 m (5.4 ± 1.19 kph), P = 0.002 (**Table 4**)].

Characteristics of participants with or without exercise to sweat lightly (Additional File 1) and with or without walking>1 hour/day (Additional File 1)

In participants with habits of exercise to sweat lightly (**Additional File 1**) or with walking>1 hour/day (**Additional File 2**), male gender was higher and fasting plasma glucose was slightly higher.

Changes in characteristics in three physical activity measures subgroups (Table 5)

In subgroups with or without three physical activity measures, BMI, waist circumference, fasting plasma glucose, HbA1c and body weight and frequency of weight change ± 3kg within 1 year were higher in Diabetes onset + than in Diabetes onset – group (**Table 5**). In all six subgroups, BMI and waist circumference did not change or changed very slightly at follow-up in Diabetes onset – group, but significantly increased at onset of diabetes in Diabetes onset + group. In all participants, BMI and waist circumference were increased in Diabetes onset +, but not in Diabetes onset – group (**Additional File 3**).

Discussion

Characteristics of participants with or without fast walking

This study revealed two major findings regarding the association between PA measures (habit of exercise, habit of active PA and walking pace) and the incidence of diabetes mellitus in a large Japanese cohort. First, habit of exercise or active PA was positively associated

with incidence of diabetes mellitus. Second, fast walking, even after adjustment with multiple covariates, was associated with low incidence of diabetes mellitus and the association was also observed in participants aged ≥ 65 years, in men, and in those with a body mass index ≥ 25 (**Table 2**, Model 3).

Physical activity, regular exercise and new-onset diabetes

By using the questionnaire integrating PA (habit of exercise and habit of active PA) and physical fitness (walking pace), this study evaluated the association between PA components and the incidence of diabetes mellitus. Helmrich et al. reported that weekly amounts of PA (physical activity index, kcal/week) were associated with a reduced risk for type 2 diabetes in the study assessing PA by questionnaires in 5,990 male alumni of the University of Pennsylvania [12]. Hu et al. examined the risk of developing type 2 diabetes in 70,102 female nurses aged 40 to 65 years and reported that the risk of type 2 diabetes was reduced stepwise by the magnitude of weekly PA (MET) regardless of the type of PA (walking, jogging, running, bicycling, calisthenics, aerobics, aerobic dance, rowing machine, lap swimming, squash or racquetball and tennis) [13].

In this study, habit of regular exercise (defined as ≥ 2 times/week of exercise ≥ 4 METs•h, which indicates moderate to vigorous PA (MVPA)), was not associated with prevention of diabetes mellitus. At least two explanations can be raised for the discrepancy between our study and previous studies [12,13] on the association of MVPA and onset of diabetes. First, the question in our study was too simple and we could not determine the weekly amounts of PA; thus, limiting the power of the study for estimating onset of diabetes mellitus. In the Nurses' Health Study, multivariate relative ratios (RRs) of type 2 diabetes were decreased stepwise from 1.0 to 0.58 across quintiles of total PA/week (P for trend < 0.001) [13], indicating that amount of PA was associated with the risk of diabetes onset. In this study, regular active PA,

equivalent to walking twice per week, did not have the power to estimate onset of diabetes. Collectively, frequency and intensity, not presence or absence, of regular active PA may be required to estimate new-onset of diabetes. Second, the participants with habits of exercise and/or active PA in our study could be a high-risk population (**Additional Files 1 and 2**). In the SHCG, a recommendation has been provided on exercise and PA to prevent or reduce the incidence of metabolic syndrome. Thus, our participants with waist circumference ≥ 85 cm in men or ≥ 90 cm in women[14,15] or with fasting plasma glucose ≥ 100 mg/dL could have been encouraged more for regular exercise or active PA. Actually, the participants with habits of regular exercise and/or active PA showed slightly higher values of fasting plasma glucose (**Additional Files 1 and 2**).

Fast walking and new-onset diabetes

The questions on habits of regular walking had no power to determine low incidence of diabetes mellitus; however, that on fast walking pace had a strong power to do so. There are two possible explanations. First, walking speed may be critical for preventing onset of diabetes. In the Nurses' Health Study, multivariate RRs were 0.86 (95% CI: 0.73–1.01) for "normal or average (3.2–4.8 km/h)" usual walking pace and 0.59 (95% CI: 0.47–0.73) for "brisk (4.8–6.2 km/h) or striding (6.4 km/h or faster)" pace compared to women with "easy or casual (less than 3.2 km/h)" pace [13]. Fast walking is estimated to be 3.8 METs and thus categorized as exercise of moderate intensity (3.0–6.0 MET) [16]. It has been reported that RRs for exercise of moderate intensity was 0.83 (95% CI: 0.75–0.91) [17,18], equivalent to that of normal to brisk walking [16]**.** Combined, walking speed, not presence or absence of regular walking, is efficient to estimate new-onset of diabetes. Second, fast walking can be an indicator of the low-risk group for onset of diabetes discussed below.

Possible explanations why fast walking was negatively associated with new-onset diabetes.

There are three explanations why fast walking is an indicator of the low-risk group for onset of diabetes. First, habit of intentional fast walking may reduce onset of diabetes. Theoretically, METs are higher in fast walking, as compared to non-fasting walking; thus, maintenance of fast walking can be protective for the onset of diabetes by increasing daily METs [17]. Following the guidance in the Specific Health Check and Guidance System, regular exercise and/or active PA had been recommended to our participants who were at or had a risk(s) for metabolic syndrome [14]. However, in the guidance for walking, frequency (3 days/week) and duration (20 minutes plus per day), but not pace of walking, have been recommended; thus, it is not likely that a habit of intentional fast walking was linked to onset of diabetes in our participants.

Second, fast walking may reflect a high level of physical fitness, which could be protective against new-onset of diabetes. Self-reported walking speed was closely related to objectively measured walking speed among community-dwelling older people [19]. In our subgroup, self-reported walking speed using the questionnaire was related to the objectively measured walking speed (10 meters walking speed, sec) [20,21]. Fast walking + vs – showed larger differences in BMI and waist circumference (Table 3) as compared to Exercise to sweat lightly + vs – or Walking>1 hour/day + vs –. A higher METs in subjects with fast walking + might be protective [22,23] against the onset of obesity and/or diabetes as compared to regular exercise or physical activity. BMI and waist circumference were increased only in Diabetes onset +, but not in Diabetes onset – in all three measures subgroups (**Table 5**). In Model 3, fast walking was not significanty associated with onset of diabetes when deleted other two physical activities (data not shown). These three physical activity measures can be linked to onset of

diabetes in a mutually dependent manner.

Third, fast walking may represent a factor in inhibiting onset of diabetes besides physical fitness. In our study, BMI and waist circumference were lower, and age, male sex and frequency of regular drinking were higher in the fast walking + group (**Table 3**). According to a survey on leisure activities targeting adults over the age of 18 years in Michigan, USA, significant characteristics of fast walkers (≥ 5.6 kph) were men, had high educational background and high annual income, and were also associated with being a smoker and had a high frequency of alcohol consumption [24] , exhibiting very similar characteristics to our fast walking + group. Although smoking and alcohol drinking are not factors protecting against diabetes, a low BMI can work as a protective factor. Reportedly, low BMI is a strong predictor of habitual exercise [25,26]; thus, low adiposity can protect ones from diabetes through exercise-induced increase in muscle insulin sensitivity [27]. Actually, walking pace showed correlations with participation in higher intensity PA, high volumes of total non-occupational PA, and higher frequency and total walking volume [24 28]. However, low BMI is thought to be a low risk factor for diabetes due to high insulin sensitivity regardless of exercise habits [29]. In fast walking + group, frequencies of weight gain over 10kg from twenty and weight change ± 3kg within 1year were also lower, suggesting that at least partly fast walking is an indicator for low fluctuation of body weight. Meanwhile, in both subgroups with or without weight gain over 10kg from twenty, and in without weight change ± 3 kg within 1-year, fast walking was negatively associated with onset of diabetes (**Additional File 4**). Considering all of the above, fast walking may be a suppressor of diabetes onset regardless of whether or not there is a history of weight gain.

Intervention in physical activity to prevent new-onset diabetes

There are a number of studies that have investigated the prevention of the onset of type 2 diabetes by intervention in lifestyle habits including exercise therapy. The relative risk reduction (RRR) of diabetes onset in the study intervention groups such as the Finish Diabetes Prevention Study [30,31], Diabetes Prevention Program Research Group [32], Kosaka et al. [33], China Da Qing Diabetes Prevention Study [34], and Indian Diabetes Prevention Programme [35] were 58%, 58%, 67%, 51% and 29%, respectively, compared with the control groups. Results of meta-analysis have also shown a preventive effect on nearly half of the subjects, with a RRR of 49% [36]. However, appropriate assessment scale of current habits for PA/exercise and appropriate personalized goals has not been clarified for preventing type 2 diabetes mellitus in a nation-wide scale. This study suggests that fast walking is a simple and independent preventive factor for new-onset of diabetes mellitus. It may be required to verify that the intervention of walking pace is effective to reduce onset of diabetes in future studies.

Limitations

This study has several limitations. First, in the specific health examination of Japanese citizens aged 40 to 74 years, there were as many as 51.91 million people from March 2008 to April 2009. However, examination is not an obligation; thus, only 20.01 million people (37.4%) were examined. Therefore, this study may have a bias. Second, because of the age range of 40 to 74 years old, the onset of diabetes before 39 years old is unknown. Therefore, it will not be a factor in the analysis of juvenile onset type 2 diabetes. Third, the information recorded on the questionnaires was self-reported and judgment on walking pace was subjective. Fourth, the observation period was short. Fifth, we could determine only “self-reported”, but not real, timing of last meal, suggesting that little non-fasting (<10 hours) glucose may be included in the analysis. Sixth, because comparing group difference for large samples could link to type I error, we should be careful to interpret true differences between

groups.

Conclution

In conclusion, fast walking is a simple and independent preventive factor for new-onset of diabetes mellitus in the health check-up and guidance system in Japan. It is necessary to verify whether intervention of walking pace reduces onset of diabetes in future studies.

Methods

Study population

This study was a cohort study using data of the annual health check program, “The Specific Health Check and Guidance System” (SHCG) in Japan [37-39], launched by the Ministry of Health, Labor and Welfare, Japan in 2008. The target of SHCG was the Japanese general population between the ages of 40 and 74 years, estimated to be 51,919,920 at the beginning of 2008. This study was performed as a part of the ongoing project “Design of the comprehensive healthcare system for chronic kidney disease (CKD) based on the individual risk assessment by specific health checkups.” The completed STROBE checklist was provided as **Additional file 5**.

Twenty-seven of Japan’s 47 prefectural governments (Hokkaido, Miyagi, Yamagata, Fukushima, Ibaraki, Tochigi, Tokyo, Saitama, Chiba, Kanagawa, Niigata, Nagano, Ishikawa, Fukui, Gifu, Osaka, Hyogo, Okayama, Tokushima, Kochi, Fukuoka, Saga, Nagasaki, Oita, Kumamoto, Miyazaki, and Okinawa) had agreed to participate in the study and the residents were included in the analysis. The individual data of the SHCG from 2008 to 2011 had been sent to and verified by an independent data center, the Japan Clinical Research Support Unit (Tokyo, Japan), which is a non-profit organization [38]. The community approval was obtained from prefecture representatives.

Among the participants from the 27 prefectures, we excluded those who visited only once in 2008 and those with incomplete information recorded in the database, such as data on sex, age, body mass index (BMI), systolic (SBP) and diastolic blood pressure (DBP), fasting plasma glucose (FPG) levels, HbA1c, and regular exercise. We finally selected 167,684 without diabetes mellitus from 577,984 participants (see definition below) at baseline 2008.

Measurements

Trained staff measured height, body weight, blood pressure, and waist circumference of each subject. Questionnaires were administered to record data on smoking status (current smoker or not), drinking habits (everyday, sometimes, rarely or never), regular exercise (exercise to sweat lightly for over 30 min on each occasion, two times weekly, walking > 1 h/day, fast walking), anti-hypertensive drug use, anti-hyperglycemic drug use, and lipid-lowering drug use. Fasting blood samples were collected after an overnight fast for ≥ 10 hours (In Japanese; https://www.mhlw.go.jp/file/05-Shingikai-12401000-Hokenkyoku-Soumuka/0000158929.pdf) and were assayed within 24 h with automatic clinical chemical analyzers. We excluded participants who were not available for fasting blood samples. When needed, HbA1c was corrected as a National Glycohemoglobin Standardization Program equivalent value and calculated using the following formula: HbA1c (%) = HbA1c (Japan Diabetes Society) (%) + 0.4% [40].

In a subgroup of participants (n = 183), we evaluated the association between self-reported walking speed on the questionnaire and objectively measured walking speed. The time required for walking 10 meter was measured by modifications [20,21] and the body composition was assessed by a body composition analyzer (InBody 770, InBody, Seoul, Korea)[41] based on the segmental multi-frequency bioelectrical impedance analysis (SMF-BIA)[42].

Definition of diabetes mellitus, dyslipidemia and hypertension

A participant was recognized as diabetes mellitus, when fasting plasma glucose level was ≥ 126 mg/dL, or the HbA1c level was ≥ 6.5% (48 mmol/mol), or the participant had a regular use of anti-hyperglycemic drugs at baseline (2008). Participants without diabetes mellitus at 2008 were followed up for fasting plasma glucose and HbA1c at 2009, 2010 and 2011. If ones met any one of the above diabetes criteria, we defined them as new-onset diabetes mellitus. A participant was recognized hypertension, if SBP was ≥ 140 mmHg, or if DBP was ≥ 90 mmHg, or if she/he had a regular use of antihypertensive drugs. A participant was recognized dyslipidemia if high-density lipoprotein (HDL)-C levels were < 40 mg/dL (1.0 mmol/L), if low-density lipoprotein-cholesterol levels were ≥ 140 mg/dL (3.6 mmol/L), or if triglyceride levels were ≥ 150 mg/dL (1.7 mmol/L), or if they had a regular use of lipid-lowering drugs.

Statistical analyses

Two-tailed paired or unpaired t-test was used for group means comparison. $\chi 2$ test or McNemar test were used for unpaired or paired comparisons of two categorical variables. Unadjusted and multi-variate adjusted logistic regression models were used to evaluate association between three physical activity measures (exercise to sweat lightly, walking>1 hour/day and fast walking) at baseline and new-onset diabetes mellitus. $P<0.05$ was significant. First, we performed unadjusted analyses (**Table 2**, Model 1), adjusted for sex, age, and BMI (Model 2). Finally, we adjusted the model for sex, age, BMI, SBP, current smoking, drink, weight gain over 10 kg from 20-years, weight change of 3 kg within 1 year, exercise to sweat lightly, walking>1 hour/day and fast walking (Model 3). All analyses were performed by SPSS software (version 24.0; SPSS, Chicago, IL, USA).

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Author Contributions Statement

MI and MS developed the concept, analyzed the data and wrote the manuscript, and thus took responsibility for the integrity of the data and the accuracy of the data analysis. AK, KA, NM, KI, HS, TM, KY, KT, SF, IN, TK, MKo, YS, MKa, and TW contributed to the discussion and reviewed the manuscript. KA, KI and TW had full access to all the data in the study.

Competing interests

The authors declare that there is no conflict of interest associated with this manuscript.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The research protocol had been approved by the Ethics Committee of Fukushima Medical University (#1485 and #2771) and all procedures performed in the studies involving human participants were conducted in accordance with its ethical standards and with the 1964 Helsinki declaration and its later amendments or com-parable ethical standards. This study was performed also according to the Ethical Guidelines for Medical and Health Research Involving Human Subjects enacted by the Ministry of Health, Labour and Welfare of Japan (http://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000069410.pdf; http://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000080278.pdf). Informed

Consent was waived by the Ethics Committee of Fukushima Medical University. Instead, we publicized information concerning this study on the web (http://www.fmu.ac.jp/univ/sangaku/data/koukai_2/2771.pdf) and ensured that the subjects could refuse the use of their personal information.

The study protocol to measure objectively measured walking speed was approved by the Fukushima Medical University Ethics Committee (Number 29118). The written informed consent was taken from all patients in the subgroup analysis.

Figure legend

Figure 1. The flow chart of the participant's recruitment.

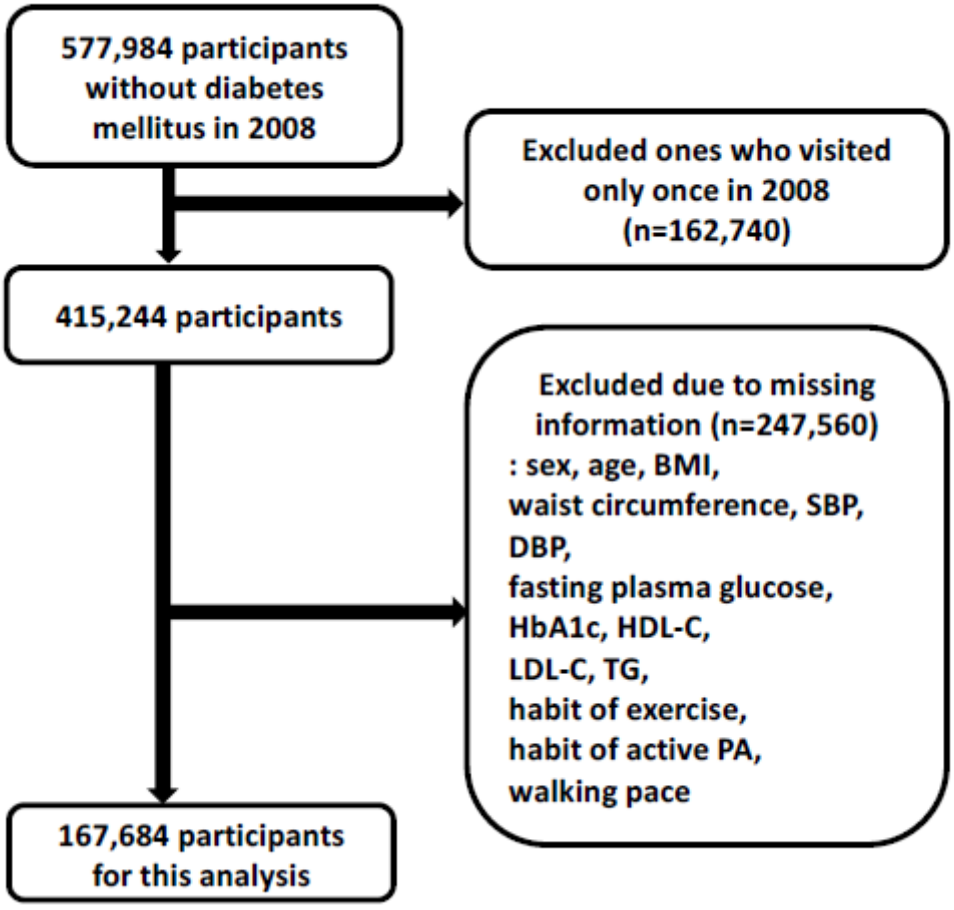

Figure 2. Adjusted odds ratio (OR) for new-onset diabetes mellitus (model 3). Among non-diabetic participants aged 40–74 years (n = 167,684), adjusted ORs (95% confidential intervals) for new-onset diabetes mellitus in the 3-year follow-up were calculated for exercise to sweat lightly (●), walking > 1 h/day (■), and fast walking (▲). Model 3: adjusted for sex, age, body mass index (BMI), systolic blood pressure (SBP), current smoking, drinking, weight gain over 10 kg from 20 years of age, weight change of 3 kg within 1 year, exercise to sweat lightly, walking>1 hour/day and fast walking.

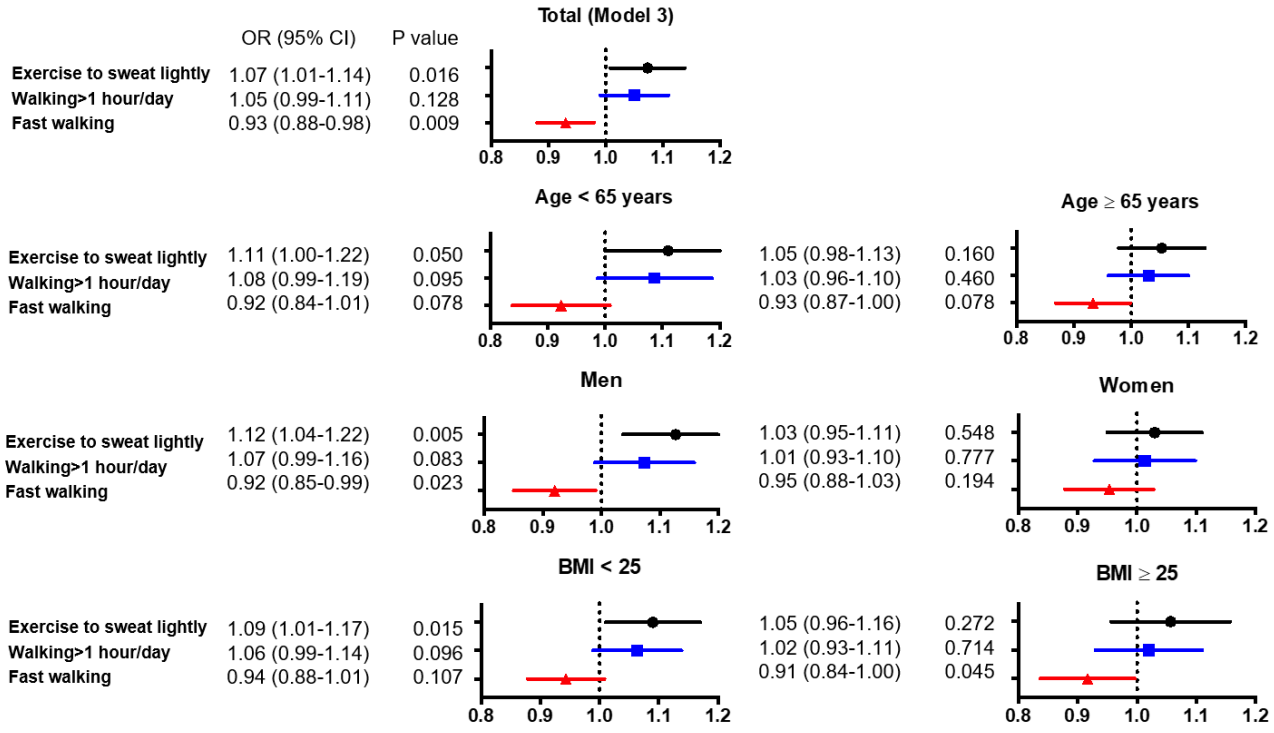

Figure 2

Table 1. Baseline characteristics of participants

	Total	Diabetes onset –	Diabetes onset +	*P*
n	167,684	161,455	6,229	
Age, years	63.7 (7.8)	63.6 (7.8)	65.4 (6.5)	<0.001
% Male	38.8	38.3	51.7	<0.001
BMI, kg/m^2	23.0 (3.1)	22.9 (3.1)	24.3 (3.5)	<0.001
Waist circumference, cm	83.3 (8.8)	83.1 (8.8)	86.8 (9.1)	<0.001
Systolic blood pressure, mmHg	129 (17)	129 (17)	134 (17)	<0.001
Diastolic blood pressure, mmHg	76 (11)	76 (11)	78 (11)	<0.001
Fasting plasma glucose, mg/dl	93.3 (9.7)	92.9 (9.3)	104.8 (11.6)	<0.001
HbA1c, %	5.59 (0.33)	5.57 (0.32)	6.01 (0.34)	<0.001
LDL cholesterol, mg/dL	126.6 (29.7)	126.6 (29.7)	126.5 (31.5)	0.817
HDL cholesterol, mg/dL	62.7 (16.0)	62.9 (16.0)	58.3 (15.2)	<0.001
Triglycerides, mg/dL	112.6 (69.5)	111.8 (68.8)	133.5 (84.5)	<0.001
AST, U/L	24.0 (9.2)	23.9 (9.0)	25.8 (12.4)	<0.001
ALT, U/L	21.2 (12.4)	21.1 (12.2)	25.4 (16.4)	<0.001
γGT, U/L	34.2 (40.5)	33.8 (39.9)	44.4 (53.8)	<0.001
Hypertension, %	44.0	43.4	61.4	<0.001
Dyslipidemia, %	54.5	54.1	64.9	<0.001
Current smoker, %	13.1	12.9	16.9	<0.001
Everyday drinking, %	22.1	22.2	25.6	<0.001
Weight gain over 10kg since 20 years of age, %	31.2	30.6	46.2	<0.001
Weight change ± 3kg within 1year, %	19.9	19.7	26.2	<0.001
Exercise to sweat lightly, %	41.7	41.6	45.4	<0.001
Walking>1 hour/day, %	52.2	52.1	54.1	<0.001
Fast walking, %	50.1	50.2	47.9	<0.001

Values are Mean (SD) or %. *P*: provability by two-tailed unpaired t-test or χ^2 test. BMI: body mass index, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γGT: γ-glutamyl transpeptidase.

Table 2. Unadjusted and multivariable-adjusted odds ratio for the risk of new-onset diabetes mellitus of three physical activity measures

	Model 1 (Unadjusted)		Model 2		Model 3	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
All						
Exercise to sweat lightly	1.16 (1.11-1.23)	<0.001	1.05 (1.00-1.11)	0.052	1.07 (1.01-1.14)	0.016
Walking>1 hour/day	1.09 (1.03-1.14)	0.002	1.04 (0.99-1.10)	0.105	1.05 (0.99-1.11)	0.128
Fast walking	0.91 (0.88-0.98)	<0.001	0.95 (0.90-1.00)	0.044	0.93 (0.88-0.98)	0.009
Age < 65 years						
Exercise to sweat lightly	1.20 (1.09-1.31)	<0.001	1.10 (1.01-1.21)	0.035	1.11 (1.00-1.22)	0.050
Walking>1 hour/day	1.09 (1.00-1.19)	0.055	1.10 (1.01-1.20)	0.039	1.08 (0.99-1.19)	0.095
Fast walking	0.91 (0.83-0.99)	0.032	0.96 (0.88-1.04)	0.315	0.92 (0.84-1.01)	0.078
Age ≥ 65 years						
Exercise to sweat lightly	1.05 (0.99-1.12)	0.108	1.02 (0.96-1.09)	0.479	1.05 (0.98-1.13)	0.160
Walking>1 hour/day	1.02 (0.95-1.08)	0.606	1.02 (0.95-1.08)	0.618	1.03 (0.96-1.10)	0.460
Fast walking	0.89 (0.83-0.95)	<0.001	0.94 (0.88-1.00)	0.046	0.93 (0.87-1.00)	0.036
Men						
Exercise to sweat lightly	1.19 (1.11-1.27)	<0.001	1.11 (1.03-1.19)	0.005	1.12 (1.04-1.22)	0.005
Walking>1 hour/day	1.10 (1.03-1.19)	0.007	1.08 (1.01-1.16)	0.036	1.07 (0.99-1.16)	0.083
Fast walking	0.92 (0.86-0.99)	0.030	0.95 (0.88-1.02)	0.142	0.92 (0.85-0.99)	0.023
Women						
Exercise to sweat lightly	1.06 (0.98-1.14)	0.128	1.00 (0.93-1.08)	0.938	1.03 (0.95-1.11)	0.548
Walking>1 hour/day	1.02 (0.95-1.10)	0.618	1.01 (0.94-1.09)	0.802	1.01 (0.93-1.10)	0.777
Fast walking	0.87 (0.81-0.93)	<0.001	0.95 (0.88-1.02)	0.180	0.95 (0.88-1.03)	0.194
BMI < 25						
Exercise to sweat lightly	1.26 (1.18-1.35)	<0.001	1.07 (1.01-1.15)	0.042	1.09 (1.01-1.17)	0.015
Walking>1 hour/day	1.17 (1.09-1.25)	<0.001	1.06 (1.00-1.14)	0.068	1.06 (0.99-1.14)	0.096
Fast walking	1.01 (0.94-1.07)	0.864	0.96 (0.90-1.03)	0.264	0.94 (0.88-1.01)	0.107
BMI ≥ 25						
Exercise to sweat lightly	1.06 (0.97-1.15)	0.182	1.03 (0.94-1.12)	0.535	1.05 (0.96-1.16)	0.272
Walking>1 hour/day	1.02 (0.94-1.11)	0.571	1.01 (0.93-1.10)	0.738	1.02 (0.93-1.11)	0.714
Fast walking	0.90 (0.83-0.98)	0.011	0.93 (0.85-1.01)	0.079	0.91 (0.84-1.00)	0.045

OR: odds ratio, CI: confidential interval, BMI: body mass index, SBP: systolic blood pressure.

Model 2 (sex, age and BMI, if not applicable to sub-group variables). Model 3 (sex, age, BMI, SBP, current smoking, drink, weight gain over 10 kg from 20-years, weight change of 3 kg within 1 year, exercise to sweat lightly, walking>1 hour/day and fast walking, if not applicable to sub-group variables)

Table 3. Baseline characteristics of participants with or without fast walking

	Fast walking –	Fast walking +	*P*
n	83,705	83,979	
Age, years	63.3 (8.0)	64.1 (7.5)	<0.001
Male, %	37.2	40.3	<0.001
BMI, kg/m^2	23.2（3.3）	22.7（2.9）	<0.001
Waist circumference, cm	83.9（9.2）	82.6（8.4）	<0.001
Systolic blood pressure, mmHg	128.9（17.6）	129.0 (17.3）	0.495
Diastolic blood pressure, mmHg	76.3（10.7）	76.4（10.6）	0.590
Fasting plasma glucose, mg/dl	93.3（9.7）	93.3（9.7）	0.467
HbA1c, %	5.59 (0.33)	5.58 (0.33)	<0.001
LDL cholesterol, mg/dL	126.5（29.8）	126.7（29.7）	0.232
HDL cholesterol, mg/dL	62.0（15.8）	63.4（16.1）	<0.001
Triglycerides, mg/dL	112.6（68.2）	109.8（68.3）	<0.001
AST, U/L	24.0（9.9）	23.9（8.5）	0.016
ALT, U/L	21.5（13.2）	20.9（11.6）	<0.001
γGT, U/L	34.4（41.4）	34.1（39.6）	0.115
Hypertension, %	45.0	43.1	<0.001
Dyslipidemia, %	54.5	54.4	0.492
Current smoker, %	13.8	12.3	<0.001
Everyday drinking, %	20.4	23.7	<0.001
Weight gain over 10kg since 20 years of age, %	32.9	29.6	<0.001
Weight change ± 3kg within 1 year, %	20.3	19.5	<0.001

Values are Mean (SD) or %. *P*: provability by two-tailed unpaired t-test or χ^2 test. BMI: body mass index, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γGT: γ-glutamyl transpeptidase,

Table 4. Baseline characteristics of participants with or without fast walking in a subgroup

	Total	Fast walking –	Fast walking +	P
n	183	114	69	
Age, years	64.6 (12.6)	63.9 (13.2)	65.6 (11.4)	0.341
% Male	51.0	50.9	52.2	0.865
BMI, kg/m^2	26.7 (5.9)	27.6 (6.3)	25.4 (5.1)	0.016
Waist circumference, cm	91.9 (14.2)	94.1 (14.4)	88.5 (13.3)	0.010
Systolc blood pressure, mmHg	132.3 (16.6)	131.6 (16.6)	133.6 (17.5)	0.440
Diastolic blood pressure, mmHg	73.4 (10.6)	73.0 (10.5)	74.0 (10.7)	0.528
Fasting plasma glucose, mg/dl	138.9 (36.6)	136.2 (33.5)	143.3 (41.2)	0.202
HbA1c, %	7.17 (0.98)	7.14 (0.84)	7.22 (1.18)	0.594
LDL cholesterol, mg/dL	98.1 (25.2)	97.2 (24.1)	99.9 (27.0)	0.483
HDL cholesterol, mg/dL	57.9 (15.6)	56.9 (13.2)	59.5 (18.8)	0.287
Triglycerides, mg/dL	125.0 (154.6)	140.8 (190.6)	99.0 (50.3)	0.028
AST,U/L	22.4 (9.1)	24.9 (12.9)	22.4 (9.1)	0.784
ALT, U/L	20.6 (13.7)	23.3 (13.6)	20.6 (13.7)	0.943
Every day drinking, %	25.4	18.4	20.3	0.533
Current smoker, %	19.7	19.3	20.3	0.863
Weight gain over 10kg since 20 years of age, %	61.7	62.3	60.9	0.849
Exercise to sweat lightly, %	26.2	16.7	42.0	<0.001
Walking>1 hour/day, %	38.8	28.9	55.1	0.001
Weight change ± 3kg within 1year, %	47.5	50.9	42.0	0.245
10m walking, sec	6.75 (1.84)	7.08 (2.11)	6.20 (1.11)	0.002

Mean (SD) or %

Table 5. Characteristics of three physical activity measures subgroups at baseline and follow-up or onset of diabetes

Fast walking –	Diabetes onset –			Diabetes onset +			Fast walking +	Diabetes onset –		Diabetes onset +		
	Baseline	Follow-up	*P*	Baseline	At onset	*P*		Baseline	Follow-up	*P*	Baseline	At onset	*P*
n	80,457			3,247				80,995			2,982		
BMI, kg/m^2	23.2 (3.3)	23.2 (3.3)	0.488	24.7 (3.7)*	25.0 (3.9)	<0.001		22.69 (2.89)	22.70 (2.92)	0.035	23.9 (3.1)*	24.2 (3.3)	<0.001
Waist circumference, cm	83.8 (9.1)	83.8 (9.2)	0.345	87.8 (9.5)*	88.4 (9.9)	<0.001		82.5 (8.4)	82.5 (8.4)	0.947	85.6 (8.5)*	86.3 (8.8)	<0.001
Fasting plasma glucose, mg/dl	92.9 (9.3)	92.9 (9.8)	0.528	104.4 (11.7)*	117.3 (24.0)	<0.001		93.0 (9.3)	93.1 (9.8)	<0.001	105.9 (11.4)*	118.7 (22.7)	<0.001
HbA1c, %	5.57 (0.32)	5.59 (0.32)	<0.001	6.00 (0.34)*	6.35 (0.66)	<0.001		5.57 (0.32)	5.59 (0.32)	<0.001	6.02 (0.33)*	6.36 (0.62)	<0.001
Body weight, kg	56.9 (10.2)	56.8 (10.2)	<0.001	61.4 (11.4)*	62.0 (11.8)	<0.001		56.6 (9.8)	56.5 (9.9)	<0.001	60.4 (10.2)*	61.0 (10.6)	<0.001
Exercise to sweat lightly	29.6	–	–	33.9**	–	–		53.4	–	–	57.5**	–	–
Walking>1 hour/day	40.9	–	–	43.7**	–	–		63.3	–	–	65.6*	–	–
Fast walking	0	–	–	0	–	–		100	–	–	100	–	–
Weight change ± 3kg within 1year, %	20.0	–	–	26.8**	–	–		19.3	–	–	25.6**	–	–

Exercise to sweat lightly –	Diabetes onset –			Diabetes onset +			Exercise to sweat lightly +	Diabetes onset –		Diabetes onset +		
	Baseline	Follow-up	*P*	Baseline	At onset	*P*		Baseline	Follow-up	*P*	Baseline	At onset	*P*
n	94,366			3,404				67,086			2,825		
BMI, kg/m^2	22.9 (3.2)	22.9 (3.2)	0.348	24.6 (3.7)*	24.8(3.8)	<0.001		23.0 (2.9)	23.0 (3.0)	0.056	24.1 (3.2)*	24.3 (3.4)	<0.001
Waist circumference, cm	83.14 (9.09)	83.11 (9.09)	0.057	87.4 (9.5)*	88.1 (9.9)	<0.001		83.1 (8.3)	83.1 (8.4)	0.231	86.0 (8.5)*	86.6 (8.8)	<0.001
Fasting plasma glucose, mg/dl	92.7 (9.3)	92.7 (9.7)	0.404	104.7 (11.5)*	118.1 (24.2)	<0.001		93.3 (9.3)	93.4 (9.9)	<0.001	105.5 (11.6)*	117.8 (22.4)	<0.001
HbA1c, %	5.56 (0.32)	5.58 (0.32)	<0.001	6.01 (0.34)*	6.36 (0.66)	<0.001		5.58 (0.31)	5.60 (0.32)	<0.001	6.01 (0.34)*	6.34 (0.61)	<0.001
Body weight, kg	56.6 (10.2)	56.5 (10.3)	<0.001	61.1 (11.3)*	61.7 (11.7)	<0.001		57.0 (9.7)	56.8 (9.7)	<0.001	60.7 (10.3)*	61.2 (10.7)	<0.001
Exercise to sweat lightly	0	–	–	0	–	–		100	–	–	100	–	–
Walking>1 hour/day	36.2	–	–	35.5**	–	–		74.4	–	–	76.6*	–	–
Fast walking	40.0	–	–	37.0**	–	–		64.5	–	–	61.0**	–	–
Weight change ± 3kg within 1year, %	20.3	–	–	26.9**	–	–		18.8	–	–	25.5**	–	–

Walking>1 hour/day –	Diabetes onset –			Diabetes onset +			Walking>1 hour/day +	Diabetes onset –		Diabetes onset +		
	Baseline	Follow-up	*P*	Baseline	At onset	*P*		Baseline	Follow-up	*P*	Baseline	At onset	*P*
n	77,321			2,856				84,131			3,373		
BMI, kg/m^2	23.0 (3.2)	23.0 (3.2)	0.900	24.6 (3.6)*	24.9 (3.8)	<0.001		22.9 (3.0)	22.9 (3.0)	0.005	24.1 (3.3)*	24.4 (3.5)	<0.001
Waist circumference, cm	83.44 (9.05)	83.39 (9.09)	0.007	87.6 (9.3)*	88.3 (9.7)	<0.001		82.8 (8.5)	82.9 (8.6)	0.094	86.1 (8.9)*	86.7 (9.2)	<0.001
Fasting plasma glucose, mg/dl	92.7 (9.3)	92.8 (9.7)	0.048	104.5 (11.7)*	118.2 (24.7)	<0.001		93.1 (9.3)	93.2 (9.8)	0.024	105.6 (11.5)*	117.8 (22.3)	<0.001
HbA1c, %	5.57 (0.32)	5.58 (0.32)	<0.001	6.01 (0.34)*	6.35 (0.61)	<0.001		5.57 (0.31)	5.59 (0.32)	<0.001	6.01 (0.34)*	6.35 (0.66)	<0.001
Body weight, kg	57.0 (10.2)	56.8 (10.3)	<0.001	61.3 (11.2)*	62.0 (11.6)	<0.001		56.6 (9.7)	56.5 (9.9)	<0.001	60.6 (10.5)*	61.1 (10.9)	<0.001
Exercise to sweat lightly	22.2	–	–	23.1**	–	–		59.4	–	–	64.2**	–	–
Walking>1 hour/day	0	–	–	0	–	–		100	–	–	100	–	–
Fast walking	38.5	–	–	36.0**	–	–		60.9	–	–	58.0**	–	–
Weight change ± 3kg within 1year, %	20.4	–	–	27.6**	–	–		19.0	–	–	25.1**	–	–

Values are Mean (SD) or %. *P*: provability by two-tailed unpaired t-test, χ^2 test or McNemar test. BMI: body mass index, *P<0.05, vs Diabetes onset – Baseline

Additional File 1. Baseline characteristics of participants with or without exercise to sweat lightly

	Exercise to sweat lightly –	Exercise to sweat lightly +	*P*
n	97,770	69,914	
Age, years	62.4(8.3)	65.5(6.6)	<0.001
Male, %	35.9	42.8	<0.001
BMI, kg/m^2	23.0(3.2)	23.0(2.9)	0.075
Waist circumference, cm	83.3(9.1)	83.2(8.4)	0.257
Systolc blood pressure, mmHg	128.4(17.6)	129.8(17.2)	<0.001
Diastolic blood pressure, mmHg	76.3(10.8)	76.5(10.4)	<0.001
Fasting plasma glucose, mg/dl	93.1(9.7)	93.7(9.8)	<0.001
HbA1c, %	5.58(0.33)	5.59(0.33)	<0.001
LDL cholesterol, mg/dL	126.8(30.1)	126.2(29.2)	<0.001
HDL cholesterol, mg/dL	62.4(15.9)	63.1(16.1)	<0.001
Triglycerides, mg/dL	114.2(72.3)	110.4(65.5)	<0.001
AST,U/L	23.9(9.4)	24.1(8.8)	<0.001
ALT, U/L	21.5(13.0)	20.9(11.5)	<0.001
ɤGTP, U/L	34.7(41.8)	33.6(38.7)	<0.001
Current smoker, %	14.8	10.6	<0.001
Every day drinking, %	20.8	23.8	<0.001
Weight gain over 10kg from twenty,%	31.7	30.5	<0.001
Weight change ± 3kg within 1year, %	20.5	19.0	<0.001

Mean (SD) or %, N.S. not significant

Additional File 2. Baseline characteristics of participants with or without exercise to sweat lightly

	Walking>1 hour/day –	Walking>1 hour/day +	*P*
n	80,179	87,505	
Age, years	62.8(8.10)	64.5(7.3)	<0.001
Male, %	36.6	40.7	<0.001
BMI, kg/m^2	23.1(3.2)	22.9(3.0)	<0.001
Waist circumference, cm	83.6(9.1)	83.0(8.6)	<0.001
Systolc blood pressure, mmHg	128.6(17.4)	129.3(17.4)	<0.001
Diastolic blood pressure, mmHg	76.4(10.8)	76.3(10.6)	<0.001
Fasting plasma glucose, mg/dl	93.1 (9.7)	93.5(9.7)	<0.001
HbA1c, %	5.58(0.33)	5.59(0.33)	0.095
LDL cholesterol, mg/dL	127.2(29.9)	126.0 (29.5)	<0.001
HDL cholesterol, mg/dL	62.1(15.9)	63.3(16.0)	<0.001
Triglycerides, mg/dL	115.9(71.8)	109.6(67.3)	<0.001
AST,U/L	23.9(9.4)	24.1(9.0)	<0.001
ALT, U/L	21.6(13.1)	20.9(11.7)	<0.001
ɤGTP, U/L	35.1(41.7)	33.5(39.4)	<0.001
Current smoker, %	14.3	11.9	<0.001
Every day drinking, %	21.2	22.9	<0.001
Weight gain over 10kg from twenty,%	32.6	29.9	<0.001
Weight change ± 3kg within 1year, %	20.6	19.2	<0.001

Mean (SD) or %, N.S. not significant

Additional File 3. Characteristics at baseline or at follow-up or onset of diabetes

	Diabetes onset –			Diabetes onset +		
	Baseline	Follow-up	*P*	Baseline	At onset	*P*
n	161,455			6,229		
Age, years	63.6 (7.8)	65.6 (7.7)	0.019	65.2 (6.5)	66.8 (6.4)	<0.001
BMI, kg/m^2	22.9 (3.1)	22.9 (3.1)	0.053	24.3 (3.5)	24.6 (3.6)	<0.001
Waist circumference, cm	83.1 (8.8)	83.1 (8.8)	0.474	86.8 (9.1)	87.4 (9.4)	<0.001
Fasting plasma glucose, mg/dl	92.9 (9.3)	93.0 (9.8)	<0.001	105.1 (11.6)	118.0 (23.4)	<0.001
HbA1c, %	5.57 (0.32)	5.59 (0.32)	<0.001	6.01 (0.34)	6.35 (0.64)	<0.001
Exercise to sweat lightly, %	41.6	43.5	<0.001	45.4	46.4	0.149
Walking>1 hour/day, %	52.1	53.3	<0.001	54.1	55.1	0.190
Fast walking, %	50.2	50.7	<0.001	47.9	48.3	0.298
Weight change ± 3kg within 1year, %	19.7	22.8	<0.001	26.2	25.4	0.263

Mean (SD) or %

Additional File 4. Multivariable-adjusted odds ratio for the risk of new-onset diabetes mellitus of fast walking

	Weight gain over 10kg from twenty				Weight change ± 3kg within 1year			
	–		+		–		+	
	OR* (95% CI)	*P*	OR* (95% CI)	*P*	OR* (95% CI)	*P*	OR* (95% CI)	*P*
Fast walking	0.91 (0.85-0.99)	0.019	0.90 (0.83-0.98)	0.011	0.90 (0.85-0.96)	0.002	0.92 (0.83-1.03)	0.157

*Adjusted for sex, age, BMI, SBP, FPG, exercise to sweat lightly, walking>1 hour/day

Additional file 5: STROBE Statement—Checklist of items that should be included in reports of ***cohort 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 ✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found ✓
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported ✓
Objectives	3	State specific objectives, including any prespecified hypotheses ✓
Methods		
Study design	4	Present key elements of study design early in the paper ✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection✓
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up ✓
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **Not applicable**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable ✓
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 ✓
Bias	9	Describe any efforts to address potential sources of bias ✓
Study size	10	Explain how the study size was arrived at ✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why ✓
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, explain how loss to follow-up was addressed✓
		(*e*) Describe any sensitivity analyses **Not applicable**
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✓
		(b) Give reasons for non-participation at each stage✓
		(c) Consider use of a flow diagram✓
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders✓
		(b) Indicate number of participants with missing data for each variable of interest **Not applicable**
		(c) Summarise follow-up time (eg, average and total amount) ✓
Outcome data	15*	Report numbers of outcome events or summary measures over time✓
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 ✓
		(*b*) Report category boundaries when continuous variables were categorized✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period ✓
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses✓
Discussion		
Key results	18	Summarise key results with reference to study objectives✓
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✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence✓
Generalisability	21	Discuss the generalisability (external validity) of the study results✓
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✓

*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 http://www.strobe-statement.org.