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Lao, Xiang Qian; Deng, Han-Bing; Liu, Xudong; Chan, Ta-Chien; Zhang, Zilong; Chang, Ly-Yun; Yeoh, Eng-Kiong; Tam, Tony; Wong, Martin Chi Sang; Thomas, G Neil

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Increased leisure-time physical activity associated with lower onset of diabetes in 44,828 adults with impaired fasting glucose: A population based prospective cohort study

Xiang Qian Lao[1], Han-Bing Deng[1], Xudong Liu[1], Tai-Chien Chan[2], Zilong Zhang[1], Ly-yun Chang[3, 4], Eng-Kiong Yeoh[1], Tony Tam[5], Martin Chi Sang Wong[1], G. Neil Thomas[6].

[1]Jockey Club School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China;
[2]Research Center for Humanities and Social Sciences, Academia Sinica, Taiwan;
[3]Institute of Sociology, Academia Sinica, Taiwan;
[4]MJ Health Research Foundation, MJ Group, Taiwan;
[5]Department of Sociology, The Chinese University of Hong Kong, Hong Kong SAR, China;
[6]Institute for Applied Health Research, College of Medical and Dental Sciences, the University of Birmingham, UK.

Correspondence to:
Prof Xiang Qian Lao, Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Shatin, NT, Hong Kong. Fax: +852 26063500; Tel: +852 22528763; Email: xqlao@cuhk.edu.hk

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Abstract

Aims: To evaluate the effects of habitual leisure-time physical activity (LTPA) on incident type 2 diabetes in a prospective cohort of Chinese adults with impaired fasting glucose (IFG).

Methods: 44,828 Chinese adults aged 20-80 with newly detected IFG but free from cardiovascular and cerebrovascular disease were recruited and followed up from 1996 to 2014. Incident type 2 diabetes was identified by fasting plasma glucose ≥ 7 mmol/L. The participants were classified into four categories based on their self-reported weekly LTPA: inactive, low, moderate or high. Hazard ratios (HRs) and population attributable fractions (PAFs) were estimated with adjustment for established diabetic risk factor.

Results: After 214,148 person-years of follow-up, we observed an inverse dose-response relationship between LTPA and diabetes risk. Compared to inactive participants, diabetes risk in individuals reporting low, moderate and high volume LTPA were reduced by 12% (HR 0.88 [0.80-0.99], $P = 0.015$), 20% (HR 0.80 [0.71-0.90], $P < 0.001$), and 25% (HR 0.75 [0.67-0.83], $P < 0.001$), respectively. At least 19.2% (PAF 19.2% [5.9%-30.6%]) of incident diabetes cases could be avoided if the inactive participants had engaged in WHO recommendation levels of LTPA. This would correspond to a potential reduction of at least 7 million diabetic patients in Greater China area.

Conclusions: Our results show higher levels of LTPA are associated with lower risk of diabetes in IFG subjects. These data emphasise the urgent need for promoting physical activity as preventive strategy against diabetes to offset the impact of population aging and the growing obesity epidemic.

What are the new findings?

1) Leisure-time physical activity (LTPA) is negatively associated with the risk of diabetes in Chinese adults with impaired fasting glucose. The risk reduction associated with low to high volume of LTPA (≥ 3.75 MET-hours/week) ranged from 12% to 25% after adjusting for physical labour at work and other confounding factors.
2) About one fifth of the observed incident diabetes cases could have been avoided if the inactive individuals had engaged in WHO recommended levels of LTPA. In the approximately 370 million Chinese adults with IFG, increasing LTPA by one category this would correspond to a potential reduction of at least 7 million cases of diabetes.
3) The risk reduction associated with physical activity can largely (60%-67%) be explained by adiposity and associated factors.

How might it impact on clinical practice in the near future?

Our findings emphasise the urgent need to promote physical activity as a strategy for diabetes prevention.

Abbreviations:

ADA: American Diabetes Association

BMI: body mass index

DBP: diastolic blood pressures

FPG: fasting plasma glucose

HDL-C: high density lipoprotein-cholesterol

HR: hazard ratio

IFG: impaired fasting glucose

IGT: impaired glucose tolerance

LDL-C: low density lipoprotein-cholesterol

LTPA: leisure-time physical activity

MET: metabolic equivalent value

PAF: Population attributable fraction

SBP: systolic blood pressure

TC: total cholesterol

Introduction

Estimations suggest there are about 112 million diabetic patients across Greater China area (Mainland China, Hong Kong and Taiwan) accounting for 40-60% of premature deaths before the age of 60 and at least 51 billion US dollars of economic burden [1]. Progressive deterioration in glucose metabolism occurs many years before the clinical diagnosis of type 2 diabetes, for which impaired fasting glucose (IFG) is an early detectable pathological change. Individuals with IFG constitute a significant proportion of the Chinese population, with one in four Chinese adults meeting the American Diabetes Association (ADA) definition of IFG [2]. Every year 6–9% of individuals with IFG progress to diabetes [3]. More importantly, persistent dysglycaemia driven by insulin resistance leads to endothelial dysfunction and vascular complications. Compared to normoglycaemic individuals, people with IFG have a higher risk of vascular and chronic kidney disease and all-cause mortality [4]. It is therefore clinically important to promote preventive strategies targeting individuals with IFG to delay the progression to type 2 diabetes, vascular complications and premature death.

Physical activity is an effective strategy to maintain cardiometabolic health [5, 6]. In individuals with impaired glucose tolerance (IGT), a diet and physical activity intervention programme has been shown to reduce the risk of diabetes and cardiovascular mortality by 45% and 41%, respectively [7]. IFG represents hepatic insulin resistance, while IGT occurs when insulin production is impaired. IGT is therefore considered as an advanced stage of prediabetes, and the majority of previous prevention trials focus on individuals with IGT. Although it is believed that prevention programmes against type 2 diabetes should start as early as possible, studies demonstrating the protective effects of physical activity in IFG populations are scarce. Therefore, we assessed the association between habitual leisure-time physical activity (LTPA) and incident type 2 diabetes in a prospective cohort of Chinese adults with IFG as defined by

the ADA criteria. Population attributable fractions (PAFs) were computed to estimate the proportion of preventable diabetic cases in this IFG population.

Methods

Study population

The present study was based on an on-going population-based cohort of 570,414 Chinese adults aged 20-80 (up to December 2014) who participated in a standard medical screening programme run by the MJ Health Management Institution in Taiwan. Details of the cohort has been published in elsewhere [8]. Briefly, this is an open cohort starting in 1996. All the participants were of Chinese descent residing in Taiwan. They joined the MJ Health Screening Programme through a paid membership and were encouraged to visit the Institution periodically for receiving a comprehensive medical assessment, including a fasting blood test of glucose and lipids, physical and biomedical examinations, and a self-administered questionnaire of sociodemographic parameters, lifestyle information (physical activity, diet, smoking, drinking and sleep) and detailed history of physician-diagnosed disease and treatments. From 1996 to 2014, a total of 248,481 participants visited the Institution at least twice. Among them 56,451 non-diabetic participants whose fasting plasma glucose (FPG) levels ranged from 5.6 to 6.9 mmol/L in their first visit were identified as IFG. Their glycaemic status was monitored in subsequent visits. The subsequent development of type 2 diabetes in these individuals was used to determine incidence. Yearly visits were made by 98.7% of the participants, and the total number of visits ranged from 2 to 19. To reduce the risk of reverse causality, we further excluded 6,905 participants who reported pre-existing physician-diagnosed cardiovascular and cerebrovascular disease, such as hypertension, coronary heart disease and stroke, from analyses; and 4,718 participants missing physical activity information were also excluded. The final study population comprised 44,828 participants with newly detected IFG. Selection of the participants

was presented in the Supplementary Figure 1. Compared with those IFG participants with only one visit, the 44,828 participants in the present study had similar baseline distribution of age (mean: 43.7 vs. 42.6 years), sex (male: 59.6% vs. 63.6%), LTPA (mean: 5.3 vs. 5.9 MET-hours/week), FPG (mean: 5.9 vs. 5.9 mmol/L), and body mass index (BMI) (mean: 24.4 vs. 24.2 kg/m^2).

All participants gave informed consent to authorise the MJ Health Management Institution to analyse data generated from the MJ Programme. Personal identification were removed and remained anonymous when data were released for the purpose of research. The ethics approval of the present study was obtained from the Joint Chinese University of Hong Kong and New Territories East Cluster Clinical Research Ethics Committee in Hong Kong (No. 2015.672).

Assessment of physical activity

The physical activity was assessed by three questions in a self-administered questionnaire at every visit. Firstly, participants were asked to report the intensity of weekly LTPA performed in the past month with examples of activities under four intensity categories, i.e. light (e.g. walking), moderate (e.g. brisk walking), medium vigorous (e.g. jogging) and high vigorous (e.g. running). According to the Ainsworth's compendium of physical activities [9], a metabolic equivalent value (MET; 1 MET = 1 kcal/h/kg) was assigned to each intensity categories as follows: 2.5 METs for light, 4.5 METs for moderate, 6.5 METs for medium vigorous, and 8.5 METs for high vigorous [8]. Secondly, they were asked to estimate the duration usually spent on LTPA every week in the past month. The participants who did not do any leisure-time exercise or exercised less than 1 hour a week were classified as inactive [8, 9]. The volume of LTPA (MET-hours/week) was calculated by multiplying the intensity (METs) by duration (hours/week). It requires 7.5 MET-hours/week to achieve the minimum level of the WHO

recommended LTPA [10]. The participants were therefore classified into one of the following categories using cutpoints of 3.75 MET-hours/week (half of the recommended level), 7.5 MET-hours/week (recommended level), and 15.0 MET-hours/week (double the recommended level). This resulted in the designation of the following categories: inactive (no LTPA or LTPA < 3.75 MET-hours/week), low (LTPA 3.75 to < 7.5 MET-hours/week), moderate (LTPA 7.5 to < 15.0 MET-hours/week) and high (LTPA ≥ 15.0 MET-hours/week). Thirdly, the participants were asked to categorise their physical labour intensity at work with various examples: "Mostly sedentary (e.g. clerk)", "Sedentary with occasional walking (e.g. seamstress)", "Mostly standing or walking (e.g. retail salesperson)", "Hard labour (porter)". The details of conversion, content validity and reliability of the physical activity questions have been published previously [8].

Outcome and covariates measurements

The incident type 2 diabetes was defined as FPG ≥ 7 mmol/L measured after an overnight fasting for 12 hours and/or self-reported physician-diagnosed type 2 diabetes. Body height and weight were measured in participants with light clothing and barefoot using an auto-anthropometer (Nakamura KN-5000A, Tokyo, Japan). Waist circumference was measured at the midway between the top of hip bone and the bottom of ribs. Systolic (SBP) and diastolic blood pressures (DBP) and heart rate were measured on the right arm by an auto-sphygmomanometer (Citizen CH-5000, Tokyo, Japan). FPG, total (TC), high- (HDL-C) and low- (LDL-C) density lipoprotein-cholesterol, and triglycerides were measured in plasma enzymatically with a validated auto-analyser (Hitachi 7150, Tokyo, Japan). Complete blood count was measured by a hematology analyser (Abbott Cell-Dyn 3500/3700, USA).

Statistical analysis

We examined the association of LTPA and incident type 2 diabetes using Cox proportional hazards method. Model 1 was adjusted for sex and age (continuous). Model 2 was further adjusted for marital status (single, married or cohabiting, divorced or widowed), education (primary school or less, secondary school, tertiary level or higher), physical labour at work (mostly sedentary, sedentary with occasional walking, mostly standing or walking, hard labour), smoking (never, ever), alcohol drinking (frequency: < 1/week, ≥ 1/week), sleep duration (< 6 hours/day, 6-8 hours/day, > 8 hours/day), vegetable intake (< 1 bowl/day, ≥ 1 bowl/day), SBP (continuous), heart rate (continuous) and TC (continuous). Model 3 attempted to identify possible factors mediating the association by further adjusting for BMI, waist circumference, FPG, triglycerides, white blood cell count to determine whether physical activity exert the anti-diabetic effect through its impact on these factors..

The population attributable fraction (PAF) [11, 12] associated with LTPA (i.e. how many incident type 2 diabetes can be prevented if the participants in inactive group engaged in more physical activity) was estimated by the punafcc module in STATA [13] using the adjusted hazard ratios from Model 2. As the prevalence of physical activity and its hazard ratios for type 2 diabetes in the general population were similar between Mainland China, Hong Kong and Taiwan [8, 14, 15], we assumed the prevalence of LTPA and risk for diabetes found in the current population to be similar to those found in those settings. The PAFs calculated from this study (a Taiwanese IFG population) were used to estimate the number of preventable diabetic cases in the total IFG population for the Greater China area.

The proportional hazard assumption was examined by plotting the Kaplan-Meier survival curves and by Schoenfeld residuals. There was no evidence against the proportionality assumption. Because no interaction with sex was found in any models of analyses (all *P* for interaction terms

> 0.05), combined results for both sexes were reported. Sensitivity analysis was conducted by excluding incident type 2 diabetes identified in the first two years of follow-up to address potential reverse causality. All statistical analyses were performed using STATA version 14.0 (Stata Corporation, College Station, TX). A two-tailed *P* value < 0.05 was considered statistically significant.

Results

Table 1 shows the baseline characteristics of the study population across the four categories of LTPA. More than half (54.6%) of the participants were inactive. Participants engaging in low and moderate volumes of physical activity constituted 18.9% (n = 8,450) and 11.9% (n = 5,328) of the study population with 14.7% (n = 8,450) performing a high volume of LTPA. There was no significant difference in baseline characteristics across four groups. After 214,148 person-years of follow-up, we identified 2,535, 731, 542 and 612 new cases of type 2 diabetes in the groups with inactive, low, moderate and high physical activity volume, respectively. The incidence rate of type 2 diabetes was 2.15 per 100 person-years in inactive individuals and 1.95 per 100 person-years in individuals doing low to high volume LTPA.

A dose-response relationship was observed between LTPA and the risk of type 2 diabetes (Table 2 and Supplementary Table 1). The coefficient between volume of LTPA and incident diabetes was -0.66 (-1.04 to -0.28) (*P* = 0.001) (Supplementary Table 1). Higher volume of LTPA was associated with lower hazard ratios of type 2 diabetes (Table 2). Compared to inactive participants, diabetes risk in individuals reporting low, moderate and high volume LTPA were reduced by 12% (HR 0.88 [0.80-0.99]), 20% (HR 0.80 [0.71-0.90]), and 25% (HR 0.75 [0.67-0.83]), respectively (Model 2, *P* for trend < 0.001). Repeated analyses excluding SBP, heart rate

and TC from Model 2 showed similar results (Supplementary Table 2). Further adjustment for BMI, waist circumference, FPG, triglycerides and WBC (Model 3) attenuated the estimates in low, moderate and high LTPA groups by 67%, 65% and 60%, respectively, suggesting physical activity may reduce the risk of diabetes via reducing central obesity, improving glucose and lipid metabolism and decreasing systemic inflammation.

The PAFs were calculated to evaluate the incidence reduction can be achieved in the study participants if the inactive IFG subjects were to engage in higher volume of LTPA (Table 3). In general, the onset of type 2 diabetes in the study population could have been reduced by 9.09% (95% CI: 2.15-15.54%) if the inactive subjects had taken part in low volume of LTPA (3.75 to < 7.5 MET-hours/week), by 15.83% (95% CI: 7.47-23.43%) if the inactive subjects had performed moderate volume of LTPA (7.5 to < 15.0 MET-hours/week), and by 18.75% (95% CI: 11.80-25.15%) if the inactive subjects had engaged in high volume of LTPA (≥ 15 MET-hours/week). The reduction of type 2 diabetes incidence by LTPA was also estimated for different combinations of intensity and duration of physical activity (Table 4). The incident diabetic cases would have been reduced by 19.2% if the inactive subjects had performed at least 150 minutes of moderate-intensity physical activity as recommended by the WHO.

These findings remained unchanged when incident type 2 diabetes diagnosed within the first 2 years were excluded in sensitivity analyses (Supplementary Table 3-5).

Discussion

The incidence rate of type 2 diabetes in adults with IFG is approximately 10 times that in the normoglycaemic adults according to our observation from 570,414 participants of the MJ Programme (2.06 vs. 0.24 per 100 person-years, unpublished data). However, compared with

those with IGT, individuals with IFG have been largely overlooked in prevention programme trials for type 2 diabetes. To our knowledge, this is the largest prospective cohort to investigate the protective effects of physical activity against type 2 diabetes among the IFG subjects. We observed an inverse dose-response relationship between LTPA and the risk of diabetes in the IFG subjects. The risk reduction associated with low to high volume of LTPA (≥ 3.75 MET-hours/week) ranged from 12% to 25% after adjusting for physical labour at work and other confounding factors. Our findings were consistent with a small prospective study of 1,318 Chinese adults with IFG in which the risk of type 2 diabetes was found to be 35% lower in physically active subjects [15]. Additionally, we estimated the PAF of LTPA which takes into account both the relative risk and prevalence of an exposure (i.e. physical activity) in the study population. The advantage of PAF is to reveal the total effect size of an exposure (i.e. physical activity) for the whole study population, for instant, an exposure may have a weak relative risk but large total effect size if it is widely prevalent and affects a large proportion of the population. In this study, about one fifth of the observed incident diabetes cases could have been avoided if the inactive individuals had engaged in WHO recommended levels of LTPA. In the approximately 370 million Chinese adults with IFG in the Greater China area [2, 16], increasing LTPA by one category would correspond to a potential reduction of at least 7 million cases of diabetes under the assumption that the prevalence of LTPA in the whole IFG population is similar to that observed in the Taiwanese IFG population.

Potential mechanisms underlying the protective effects of physical activity against type 2 diabetes include favourable changes in body weight, adiposity, insulin sensitivity, lipids profile and systemic inflammation [17-20]. In this study, further adjustments for the potential mediating factors BMI, waist circumference, FPG, triglycerides and WBC attenuated the

effects of LTPA, which suggested the risk reduction associated with physical activity was largely (60-67%) explained by adiposity and associated factors. This is consistent with previous studies in other populations [20-22].Experimental studies have demonstrated that physical activity helps to build muscle mass and stimulates glucose uptake in skeletal muscle by activating AMP-activated protein kinase (AMPK) pathway and deactivating the Rab-GTPase-activating protein TBC1D1 [23, 24]. Physical activity also improve insulin sensitivity by reducing intramuscular triglycerides and ceramides [25].

It should be noted that LTPA was assessed via self-administered questionnaire rather than direct objective measures. Currently no direct, objective method can capture both energy expenditure and information documenting physical activity. Motion sensors may record the intensity and duration of physical activity but the estimation of energy expenditure varies by algorithms used. Current sensor technology is expensive and logistically inconvenient to use in large population-based studies. Therefore, we estimated LTPA using a questionnaire whose content validity and reliability had been examined previously [8]. In the present study, participants who exercised not more than 1 hour/week were classified as inactive; however, some individuals may have exercised less than 60 minutes a week but satisfied the minimum requirement of the WHO recommendations might have been misclassified. Since these 'inactive' individuals carry less disease risk than those with no exercise at all, the risk for diabetes in the inactive group of our study might be underestimated.

The annual rate of progression from IFG to diabetes in this study is lower than data from previous studies (6-9%) [3]. This is probably because our study used a higher cutoff of IFG (FPG $\geq$ 5.6 mmol/L) than those previous studies (FPG $\geq$ 6.1 mmol/L), and thus included a larger denominator. We did not measure OGTT and HbA_1c that could not be used in identifying all

those with diabetes as outcome measures, which might underestimate the incidence of diabetes and potentially provides a conservative estimate of the true risk. Another issue is that we only included the IFG participants with 2 or more visits in this study. There might be a concern on risk of selection bias because we excluded those IFG participants with only one visit. However, these two populations had similar distributions in the important characteristics including age, sex, and the levels of LTPA and glucose. There is no other evidence showing that the exclusion may affect the associations observed in the present study. As vegetables are considered as a key indicator of healthy diet [26, 27], we asked the participants to report their intake of vegetables in the past week and adjusted our estimates for this factor. However, our estimates did not include information describing the effects of other dietary components than vegetable intake, family history of diabetes, or time-varying covariates. Further studies investigating the interactions between genetic makeup and physical activity and diet and longitudinal changes of these factors may provide more insights into the pathophysiological pathways of physical activity and help to tailor physical activity and diet intervention programmes to the needs of individuals.

Conclusions

In summary, we found that higher levels of LTPA are associated with a lower risk of diabetes in a large population of Chinese adults with IFG. The beneficial associations of physical activity can be observed even at low intensity/volume of LTPA which are attainable by an aging population. If the prevalence of LTPA in the whole IFG population of Greater China area is similar to that in our study (a Taiwanese IFG population), the risk reduced by LTPA corresponds to a potential decrease of at least 7 million cases of Chinese diabetic patients and may offset the rapid increases resulting from population aging and the ongoing obesity epidemic. However, physical inactivity is still highly prevalent in Greater China area. More than

three quarters of Chinese adults are not able to perform sufficient physical activity to reap such health benefits [8, 14]. Our findings emphasise the urgent need to promote physical activity as a strategy for diabetes prevention.

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Contributors

XQL designed the study, reviewed and revised the manuscript. HBD analysed and interpreted the data and drafted the manuscript. GNT interpreted the data, reviewed the manuscript and contributed to critical revision of the manuscript for important intellectual content. XL, TCC, ZZ, LC, EKY, TT and MCSW interpreted the data, reviewed and revised the manuscript. All authors can take responsibility for the integrity of the data and the accuracy of the data analysis and have read and approved the final manuscript.

Competing Interests

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisation that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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Ethics approval

This study was approved by the Joint Chinese University of Hong Kong and New Territories East Cluster Clinical Research Ethics Committee in Hong Kong (No. 2015.672).

Transparency

The lead author (XQL) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies are disclosed.

Data sharing

The access policy and procedures are available at

http://www.mjhrf.org/main/page/resource/en/%23resource08

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Table 1. Baseline characteristics of the participants by volume of leisure-time physical activity

Characteristic	Volume of leisure-time physical activity			
	Inactive	Low	Moderate	High
All participants	24,469 (54.6%)	8,450 (18.9%)	5,328 (11.9%)	6,581 (14.7%)
Women	9,694 (39.6%)	2,758 (32.6%)	2,000 (37.5%)	1,652 (25.1%)
Men	14,775 (60.4%)	5,692 (67.3%)	3,328 (62.5%)	4,929 (74.9%)
Age				
20-49 years	18,634 (76.2%)	6,624 (78.4%)	3,160 (59.3%)	4,108 (62.4%)
≥ 50 years	5,835 (23.9%)	1,826 (21.6%)	2,168 (40.7%)	2,473 (37.6%)
Education				
Primary school or less	4,006 (16.5%)	802 (9.5%)	972 (18.3%)	901 (13.7%)
Secondary school	6,989 (28.8%)	1,799 (21.3%)	1,449 (27.2%)	1,636 (24.9%)
Tertiary level or higher	13,258 (54.7%)	5,846 (69.2%)	2,900 (54.5%)	4,040 (61.4%)
Marital status				
Single	4,562 (20.4%)	1,979 (24.2%)	711 (13.8%)	1,344 (21.0%)
Married or cohabiting	16,515 (73.8%)	5,773 (70.5%)	4,031 (78.1%)	4,625 (72.3%)
Divorced or widowed	1,305 (5.8%)	440 (5.4%)	417 (8.1%)	428 (6.7%)
Physical labour at work				
Mostly sedentary	12,027 (53.9%)	5,306 (63.9%)	3,138 (61.0%)	3,690 (58.2%)
Sedentary with occasional walking	6,595 (29.6%)	2,249 (27.1%)	1,461 (28.4%)	1,776 (28.0%)
Mostly standing or walking	2,800 (12.6%)	610 (7.3%)	438 (8.5%)	683 (10.8%)
Hard labour	892 (4.0%)	143 (1.7%)	109 (2.1%)	194 (3.1%)
Ever smokers	7,327 (32.9%)	2,495 (30.2%)	1,535 (29.6%)	2,059 (31.9%)
Regular drinkers	4,991 (22.9%)	1,717 (21.1%)	1,263 (24.9%)	1,758 (27.7%)
Vegetable intake ≥ 1 bowl/day	19,110 (83.6%)	7,488 (89.5%)	4,734 (89.7%)	5,872 (90.0%)
Sleep duration				
< 6 hours/day	4,867 (21.7%)	1,626 (19.4%)	1,093 (20.7%)	1,347 (20.7%)
6-8 hours/day	15,644 (69.9%)	6,220 (74.3%)	3,809 (72.3%)	4,687 (72.1%)
> 8 hours/day	1,878 (8.4%)	521 (6.2%)	368 (7.0%)	468 (7.2%)
Body mass index (kg/m^2)	24.2±3.6	24.3±3.5	24.2±3.2	24.2±3.1
Waist circumference (cm)				
Women	74.5±8.8	74.1±8.5	75.7±8.3	74.5±7.8
Men	84.6±8.7	84.1±8.6	84.1±8.0	83.4±8.0
Systolic blood pressure (mmHg)	122±17	123±16	125±17	125±16
Diastolic blood pressure (mmHg)	74.1±11.0	74.3±10.9	75.3±10.9	75.4±10.7
Fasting plasma glucose (mmol/L)	5.9±0.3	5.9±0.3	5.9±0.3	5.9±0.3
Total cholesterol (mmol/L)	5.2±1.0	5.2±0.9	5.3±0.9	5.2±1.0
HDL-C (mmol/L)				

Women	1.4±0.4	1.5±0.4	1.5±0.4	1.6±0.4
Men	1.2±0.3	1.2±0.3	1.2±0.3	1.3±0.3
LDL-C (mmol/L)	3.2±0.8	3.2±0.8	3.3±0.9	3.2±0.8
Triglycerides (mmol/L)	1.6±1.2	1.5±1.1	1.5±1.1	1.5±1.1
White blood cell count (10^9/L)	6.4±1.5	6.2±1.4	6.1±1.4	6.1±1.4

Inactive (no LTPA or LTPA < 3.75 MET-hours/week; reference category), low (LTPA 3.75 to < 7.5 MET-hours/week), moderate (LTPA 7.5 to < 15.0 MET-hours/week) and high (LTPA ⩾ 15.0 MET-hours/week). Baseline characteristics of participants are presented as number (%) for categorical variables or mean ± standard deviation for continuous variables.

Table 2. Hazard ratios (95% CI) for incident diabetes by volume of leisure-time physical activity

	Volume of leisure-time physical activity				Trend *P*
	Inactive	Low	Moderate	High	
Model 1	1.00	0.90 (0.83-0.98) †	0.82 (0.74-0.90) §	0.74 (0.67-0.80) §	< 0.001
Model 2	1.00	0.88 (0.80-0.98) †	0.80 (0.71-0.90) §	0.75 (0.67-0.83) §	< 0.001
Model 3	1.00	0.96 (0.87-1.06)	0.93 (0.82-1.05)	0.90 (0.80-1.00)	0.038

Inactive (no LTPA or LTPA < 3.75 MET-hours/week; reference category), low (LTPA 3.75 to < 7.5 MET-hours/week), moderate (LTPA 7.5 to < 15.0 MET-hours/week) and high (LTPA ⩾ 15.0 MET-hours/week).

Model 1: adjusted for age, sex;

Model 2: Model 1 + marital status, education, physical labour at work, smoking, alcohol drinking, sleep duration, vegetable intake, systolic blood pressure, heart rate and total cholesterol;

Model 3: Model 2 + body mass index, waist circumference, fasting plasma glucose, triglycerides and white blood cell count.

†$P < 0.05$; ‡$P < 0.01$; §$P < 0.001$.

Table 3. Population attributable fraction (%) (95% CI) for incident diabetes by volume of leisure-time physical activity

	Volume of leisure-time physical activity			
	Inactive	Inactive → Low	Inactive → Moderate	Inactive → High
No. participants	24,469	8,450	5,328	6,581
Case/Person-years	2535/117641	731/39257	542/25004	612/32247
Population attributable fraction (%)	----	9.09 (2.15-15.54)	15.83 (7.47-23.43)	18.75 (11.80-25.15)

Inactive (no LTPA or LTPA < 3.75 MET-hours/week; reference category), low (LTPA 3.75 to < 7.5 MET-hours/week), moderate (LTPA 7.5 to < 15.0 MET-hours/week) and high (LTPA ⩾ 15.0 MET-hours/week). Population attributable fractions (PAFs) were calculated from hazard ratios that were adjusted for age, sex, marital status, education, physical labour at work, smoking, alcohol drinking, sleep duration, vegetable intake, systolic blood pressure, heart rate and total cholesterol.

Table 4. Adjusted population attributable fractions (95% CI) for incident diabetes by combinations of intensity and duration of leisure-time physical activity

	Duration		
	Inactive → 0.5-2.4 hours/week	Inactive → 2.5 to 6.9 hours/week	Inactive → ≥ 7 hours/week
Intensity			
Inactive → Light (2.5 METs)	7.73 (-0.88-15.60)	12.54 (2.28-21.71)	12.86 (-6.38-28.61)
Inactive → Moderate (4.5 METs)	16.29 (1.89-28.58)	19.20 (5.92-30.60)	33.60 (9.62-51.22)
Inactive → Vigorous (≥ 6.5 METs)	29.90 (12.60-43.78)	27.80 (13.81-39.52)	27.52 (3.29-45.78)

Inactive (no LTPA or LTPA < 3.75 MET-hours/week). Population attributable fractions (PAFs) were calculated from hazard ratios that were adjusted for age, sex, marital status, education, physical labour at work, smoking, alcohol drinking, sleep duration, vegetable intake, systolic blood pressure, heart rate and total cholesterol. The MET values for each intensity category were assigned by investigators according to the Ainsworth's compendium of physical activities [9].